ACTA BIOMEDICA LOVANIENSIA

Cathy LODEWIJCKX

IMPACT OF A CARE PATHWAY FOR
EXACERBATION OF CHRONIC OBSTRUCTIVE
PULMONARY DISEASE (COPD): A CLUSTER
RANDOMISED CONTROLLED TRIAL

LEUVEN UNIVERSITY PRESS

IMPACT OF A CARE PATHWAY FOR COPD EXACERBATION

Cathy LODEWIJCKX

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Katholieke Universiteit Leuven
Faculty of Medicine
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“Quality is never an accident; it is always the result of intelligent effort.”
(John Ruskin)

To my mother and father

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Chapter 1:

General introduction

Chronic obstructive pulmonary disease (COPD)

Definition and burden

COPD is a preventable and treatable disease. COPD is associated with certain significant extrapulmonary problems, which may contribute to disease severity in individual patients. Its pulmonary component is characterised by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases [1-4]. The most common symptoms of COPD are breathlessness on exertion and cough, either with or without sputum production [2;3]. Worldwide, smoking is the most commonly encountered risk factor for COPD. Air pollution resulting from the burning of wood and other biomass fuels, hereditary α 1-antitrypsin (α 1-AT) deficiency, and certain occupational exposures are also established risk factors for COPD [3;5].

Worldwide, COPD affects 9.8% of men and 5.6% of women 40 years and older [6]. Its prevalence is projected to increase in the future due to the long-term impact of an increase in smoking behaviour and population aging [7-10]. COPD continues to be a leading cause of morbidity, mortality, and increased healthcare costs worldwide [5;10-13]. The burden to the patient with COPD is high, both in terms of reduced health-related quality of life and health status. In addition, COPD is one of the major causes of death in adult populations [5;11;12]. The Global Burden of Disease Studies found that COPD was the sixth most common cause of death worldwide in 1990 [10]. These authors made the alarming prediction that COPD would become the third most common cause of death by 2020, irrespective of public health intervention [10]. Finally, COPD also places a high economic burden on healthcare systems and society [14-17]. In 2010, COPD alone was estimated to have cost the global economy USD \$400 billion [18].

COPD exacerbations

COPD patients experience frequent exacerbation of symptoms [19-21]. COPD exacerbations are defined as events in the natural course of the disease—characterised by a change in baseline dyspnoea, cough, and/or sputum—that are beyond normal day-to-day variations, are acute in onset, and may warrant a change in regular management [1;3;22]. The annual rate of COPD exacerbations ranges from 0.5 to 3.5 exacerbations per patient [19;21].

COPD exacerbations contribute tremendously to the disease burden. They are a leading cause of hospital admissions worldwide, with 35% of COPD patients having at least one admission a year and up to 40% of admitted patients having two or more readmissions a year [20;23;24]. These acute hospital admissions account for the majority (43 to 84%) of the overall direct costs related to COPD [16;25-27]. Furthermore, COPD exacerbations have a

serious impact on functional status [19;28] and patients' quality of life [19;21;29], and up to 30% of patients die within one year after hospitalisation [30;31].

Management of exacerbations should focus on prevention and reduction of COPD exacerbations in order to achieve quality of life after exacerbation, and should focus on reduction of healthcare resource utilisation in terms of hospital admissions and length of stay (LOS) [3;32]. The management of a COPD exacerbation can take place on an outpatient basis at home (level I), in the hospital at the emergency department (ED) or in the respiratory ward (RW) (level II), or in the ICU (level III). Research shows that hospital at-home care represents an effective, safe, and cost-reducing alternative, provided that patients do not suffer acidotic respiratory failure [33-35]. The risk of dying from an exacerbation of COPD is closely related to the development of respiratory acidosis, the presence of significant comorbidities, and the need for ventilator support [3;36]. The presence of these features often require hospitalisation [3;22;37], and attempts to manage such patients entirely in a community setting has had only limited success [38].

Several guidelines describe various criteria and indications for hospitalisation of COPD patients, including the presence of high-risk comorbid conditions like pneumonia, cardiac arrhythmia and congestive heart failure, diabetes mellitus, renal or liver failure, inadequate response of symptoms to outpatient management, marked increase in dyspnoea, inability to manage at home, etc. [3;22;37]. ***This PhD dissertation focusses on the in-hospital management of COPD exacerbations in the ED and in the respiratory ward (level II).***

Since 2000, several evidence-based clinical practice guidelines (CPGs) for the management of COPD have been established worldwide [39]. These include, for example, the guidelines of the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) [3]; guidelines of the American Thoracic Society (ATS)-European Respiratory Society Task Force (ERS) [40]; and guidelines of the National Institute for Clinical Excellence [37]. These guidelines have very few areas of clinically relevant variation, are freely available, and provide for regular update [39]. Hence, professionals caring for COPD patients are expected to know these guidelines well, and adherence to these guidelines therefore should be high.

However, according to acknowledged clinical practice guidelines, the care process for patients hospitalised with COPD exacerbations includes a large range of diagnostic, pharmacological, and non-pharmacological interventions, which require a multidisciplinary approach involving physicians, nurses, physiotherapists, social workers, occupational therapists, and dieticians. Furthermore, coordination of the care process among multiple caregivers is complex, an integrated and systematic approach is needed [3;37;40-42]. These considerations led us to pose the following questions: Is the actual care process for patients hospitalised with COPD exacerbations really well organised? Does delivered care fully comply with international guidelines and does this care result in optimal outcomes?

A very popular strategy for reorganising care processes and optimising clinical outcomes is the implementation of care pathways, which are also known as clinical pathways or critical pathways [43-50].

Care pathways

Definition

The care pathway method has been used in industry since the 1950s [48;50]. It was adopted for the first time in healthcare in 1985 at the New England Medical Center (Boston, MA, USA) and was inspired by Karen Zander and Kathleen Bower [48;50]. Today, care pathways are used worldwide in a variety of settings, with the aim of maintaining and improving the quality and efficiency of healthcare process [43-45;48;50-53].

Care pathways are defined as complex interventions for the mutual decision making and organisation of predictable care for a well-defined group of patients during a well-defined period [43-45;48;50]. Their aim is to enhance the quality of care across the continuum by improving risk-adjusted patient outcomes, promoting patient safety, increasing patient satisfaction, and optimising the use of resources [43-45;48;50]. Defining characteristics of care pathways include an explicit statement of the goals and key elements of care based on evidence, best practice and patient expectations; the facilitation of communication and coordination of roles, and sequencing the activities of the multidisciplinary care team, patients, and their relatives; the documentation, monitoring, and evaluation of variances and outcomes; and the identification of relevant resources [43-45;48;50;52]. Different methodologies for development and implementation of care pathways exist [54;55]. These are based on the Plan-Do-Study-Act (PDSA) cycle, as described by Edwards Deming [51;55;56].

A care pathway is explicitly defined as a “complex intervention” [43;45;48;51;52;57;58]. Complex interventions in healthcare comprise a number of interacting components that seem essential to the proper functioning of the intervention, although the effective “active component” of the intervention is difficult to specify [59;60]. Active ingredients of a care pathway might be the level of multidisciplinary teamwork, the integration of a package of evidence-based key interventions, and the active follow-up of the care process [47]. When considering a spectrum of low to high complexity, development of a drug would be at the low end of the complexity spectrum, while evaluation of the effectiveness of a stroke unit would be at the high end of the spectrum. The greater the difficulty in defining precisely what the “active component” of an intervention is and how it relates to other components, the greater the likelihood that one is dealing with a complex intervention [59;60].

Framework for development and evaluation of complex interventions

Evaluating the effectiveness of complex interventions like care pathways is complicated due to a number of special problems, besides dealing with the typical problems related to practical and methodological issues that any successful evaluation must overcome. Many of these special problems are related to the difficulty of standardising the design and delivery of the interventions, their sensitivity to features of the local context, the organisational and logistical difficulty of applying experimental methods to service or policy changes, and the length and complexity of the causal chains linking the intervention with outcome [60].

As a consequence, when evaluating complex interventions like care pathways, several essential questions must be answered. (i) Does the intervention work in everyday practice? (ii) How does the intervention work? What are the active ingredients within the intervention? [59] The second question is crucial in order to identify weak links in the causal chain and consequently remove or strengthen these components, and in order to know how the intervention can be generalised and put into operation in other contexts [60]. (iii) What are the characteristics of the context where the complex intervention is being implemented? Understanding the context and the different organisation levels affected by the intervention is essential for optimisation and generalisation of the intervention [61;62].

To deal with this complexity, the Medical Research Council developed in 2000 the framework for developing and evaluating complex interventions [59;63]. Based on the sequential phases of drug development, this framework presents a step-wise approach composed of five phases (Figure 1): (i) *Preclinical or theoretical phase*, (ii) *Phase 1 or modelling*, (iii) *Phase 2 or exploratory trial*, (iv) *Phase 3 or definitive randomised controlled trial*, and (v) *Phase 4 or long-term implementation* [59;63]. During the Preclinical or theoretical phase, evidence that the intervention might have the desired effect is identified. Phase 1 or modelling involves identification of components of an intervention and their interrelationships. During the Phase 2 or exploratory trial, the intervention is tested for its acceptability and feasibility, the control intervention is defined, sample size is calculated, and outcome measures are piloted. Phase 3 or definitive randomised controlled trial addresses sample size, inclusion exclusion criteria, and methods of randomisation. Finally, Phase 4 or long-term implementation assesses the stability and real-life effectiveness of the intervention, its broader applicability outside of a research context, and possible existence of adverse effects [59;63].

Figure 1. Framework for development and evaluation of complex interventions [59;63].

It is useful for investigators to consider the development and evaluation of complex interventions as several distinct phases. Doing so allows them to separate out the different questions being addressed [63], and it will also help them to determine the state of knowledge and uncertainty regarding the complex intervention at given times [59]. However, in practice these phases may not follow a linear or even a cyclical sequence [59;60;62-64]. In many cases an iterative process occurs: For example, if an exploratory trial finds that a complex intervention is unacceptable to potential recipients, then the theoretical basis and components of the intervention may have to be re-examined [63].

As a consequence, in 2008 the 2000 framework was updated and extended into an iterative, less linear model of the process [60]. Figure 2 presents the main stages and the key functions and activities of each stage. The arrows indicate the main interactions between the phases (Figure 2) [60]. Specific key points in the new model include [60] greater attention to early phase piloting and development work [65], integration of process and outcome evaluation [66], recognition that complex interventions may work best if they are tailored to local context rather than completely standardised [67], and greater use of insights provided by the theory of complex adaptive systems [68].

Figure 2. Updated framework for the development and evaluation of complex interventions [60].

What about existing research on care pathways?

During recent decades, effectiveness of care pathways has been widely studied, and several positive effects on process and clinical outcomes—and to an lesser extent on team, service, and financial outcomes—have been reported [46;69-71]. However, until now, effectiveness of

care pathways remains questionable because methodological quality of available care pathway research is poor with regard to research design and sample size [46;51;52;69].

Firstly, an experimental design is the golden standard of clinical research, although it is not frequently used in the evaluation of care pathways [46;52;69-71]. Care pathways induce change at different levels of the organisation (i.e. patient, team, hospital, etc.). To deal with these multilevel effects, a cluster randomised design (cRCT) should be used when evaluating care pathway effectiveness [60;72-75]. In cRCTs, clusters like organisations or teams, rather than patients, are randomised to an intervention and a control group, but outcomes are measured on the individuals within the clusters [72]. However, it is much more difficult to randomise multidisciplinary teams or organisations into experimental and control groups compared to randomisation of patients, which occurs in conventional RCTs [46]. Consequently, until now, only five cRCTs on pathway effectiveness have been conducted [73;74;76-78]. Furthermore, very often a quasi-experimental design, like a pretest-posttest design, is used to evaluate care pathway effectiveness [46;69-71]. Although this kind of study can produce very useful results, several sources of potential bias are present: (i) *contamination* of the control group with information on the intervention; (ii) *selection bias* – when evaluating a complex intervention in a single organisation with its specific context (e.g. coordination of the care process, the multidisciplinary team, and specific types of patients), it is difficult or even impossible to ascertain whether the results depend on the context under study or whether they are generalisable to a wider context; (iii) *history* – outcomes could have been caused by a historical event and were possibly not related to the intervention (i.e. financial incentives to reduce LOS); (iv) the *Hawthorne effect* or effect of attention due to the project – performance of care processes during the trial could have temporarily improved because of the attention given the project, not because of the implementation of the care pathway itself [62;64;79-83].

Secondly, sample sizes included in existing studies tend to be low [46;69-71], providing for insufficient statistical power and thus inconclusive results.

Thirdly, different interventions are classified under the term ‘care pathway’. Moreover, many published studies fail to clearly report the development, implementation, and characteristics of their intervention. As a consequence, insufficient details are available for identification of possible active components of the studied intervention, and for replication and application of the intervention in other settings [46;52;60;69].

Fourthly, most previous studies fail to describe and explain contextual factors [52]. Care pathway mechanisms involve active ingredients like integration of a set of key interventions, information on the organisation and design of the care process, and the development and follow-up of the care pathway. However, fine-tuning of the intervention is based on bottlenecks and on the context of the organisation and multidisciplinary teams involved [52].

In other words, an effective pathway in one place may be ineffective in another place, and so contextual factors need to be taken into account when evaluating care pathways [52].

In conclusion, we see the need for large multicentre trials that include information on the mechanisms used, and on the context of the involved organisations [84].

European Quality of Care Pathways (EQCP) study

To answer previous questions, the European Pathway Association (www.E-P-A.org) launched in 2009 the EQCP study. This is an international cRCT conducted with two main aims: (i) to study the effect of the implementation of care pathways on care processes and clinical outcomes, and (ii) to study why and under what circumstances pathways work [84]. The study is being performed in four countries: Belgium, Italy, Ireland, and Portugal.

The EQCP study includes three individual trials [84]: a trial including patients hospitalised with COPD exacerbations [85], a trial including proximal femur fracture (PFF) patients [86], and a trial focussing on multidisciplinary teamwork within both populations [87]. In both COPD and PFF patient populations and teams, structure, process, and outcome indicators are studied (Table 1) [84].

Table 1. The European Quality of Care Pathway study approach [84]

EQCP	STRUCTURE	PROCESS	OUTCOMES
COPD exacerbation	<ul style="list-style-type: none"> Team structure indicators COPD organisation factors 	Compliance to COPD evidence-based key interventions	Performance on COPD risk-adjusted outcome indicators
Proximal femur fracture (PFF)	<ul style="list-style-type: none"> Team structure indicators PFF organisation factors 	Compliance to PFF evidence-based key interventions	Performance on PFF risk-adjusted outcome indicators
Teamwork	<ul style="list-style-type: none"> Team structure indicators 	Performance on team process indicators	Performance on team outcome indicators

Three different PhD dissertations have been integrated in the EQCP study according to the three individual trials—(i) COPD exacerbation, (ii) PFF, and (iii) teamwork. ***This PhD dissertation is integrated in the study on COPD exacerbation and focusses on the first study objective: impact of care pathways for in-hospital management of COPD exacerbations on care processes and clinical outcomes.*** Thus, it should be noted that the team component is not addressed in this PhD dissertation but is studied in the other PhD dissertation on teamwork.

As described in Chapter 6, the EQCP study is being conducted in four countries (Belgium, Ireland, Italy, and Portugal). The Belgian EQCP study is one year ahead in

accomplishing study aims compared to the other countries. The results of the three other countries are expected next year in spring 2013, with finalisation of the data analyses taking place in autumn 2013. ***Because of timing and feasibility, we decided not to delay the finalisation of this dissertation until the results from the four countries become available. Instead, we decided to limit the results section (Chapters 7 and 8) to those of the Belgian component of the EQCP study.*** The final results based on data from the four countries and the results answering the second research question ('why and under what circumstances do care pathways work?') will be analysed and reported by the EQCP research group, specifically in future publications and during conference reports in 2013 and 2014.

Objectives and outline of the dissertation

This PhD dissertation focusses on three main objectives: (i) describe the actual quality of care for patients hospitalised with COPD exacerbations; (ii) develop a methodology for international research on the impact of a COPD exacerbation care pathway on care processes and clinical outcomes; (iii) analyse interim data of the EQCP study collected in Belgian hospitals.

This dissertation addresses six research questions (RQ):

RQ1: What is the level of adherence to international guidelines with regard to care processes for in-hospital management of COPD exacerbations according to the literature?

RQ2: What is the impact of existing care pathways for in-hospital management of COPD exacerbations according to the literature?

RQ3: Which indicators should be followed up when evaluating the impact of a care pathway for COPD exacerbations?

RQ4: Which set of key interventions should be included in a care pathway for COPD exacerbations?

RQ5: What is the impact of a care pathway for in-hospital management of COPD exacerbations on performance of care processes and clinical outcomes?

RQ6: What is the level of implementation of the key interventions included as active components in a care pathway for in-hospital management of COPD exacerbations?

This dissertation is a compilation of published research articles and pre-published manuscripts. The following section provides an overview of the dissertation.

In *Chapter 2*, a literature review on the quality of in-hospital management of COPD exacerbations is presented. This chapter is published in the *Journal of Evaluation in Clinical Practice*.

Chapter 3 is a literature review on the characteristics of existing care pathways for in-hospital management of COPD exacerbations and their impact on performance of care processes, clinical outcomes, and team functioning. This chapter is published in the *International Journal of Nursing Studies*.

Chapter 4 presents the methodology and results of a Delphi survey conducted to select process and outcome indicators for follow-up of care for patients hospitalised with COPD exacerbations. This chapter is published in the *Journal of Advanced Nursing*.

Chapter 5 presents the methodology and results on how to build the clinical content of an evidence-based care pathway for COPD exacerbations. This chapter has been submitted for publication.

In *Chapter 6*, the design and rationale of a phase III trial including an international cRCT on the impact of care pathways for in-hospital management of COPD exacerbations is presented. This chapter is published in *Trials*.

Chapter 7 reports the preliminary results of the cRCT on the effectiveness of a care pathway for COPD exacerbations. This chapter includes the results of the Belgian EQCP study.

In *Chapter 8*, an implementation analyses in the Belgian experimental hospitals is presented. This chapter explores the level of implementation of the key interventions included as active components in the care pathway for in-hospital management of COPD exacerbations.

Chapter 9 starts with an overview of the main findings of the dissertation. Next, methodological limitations are addressed. Subsequently, implications for organisation of COPD care and recommendations for research are addressed. Finally, a general conclusion is formulated. Part of this discussion is published in the *International Journal of Integrated Care Pathways*.

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Chapter 2:

In-hospital management of COPD exacerbations: a systematic review of the literature with regard to adherence to international guidelines

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Lodewijckx C, Sermeus W, Vanhaecht K, Deneckere S, Leigheb F, Panella M, Decramer M. In-hospital management of COPD exacerbations: a systematic review of the literature with regard to adherence to international guidelines. J Eval Clin Pract 2009;15:1101-10.

Abstract

Background. Chronic obstructive pulmonary disease (COPD) exacerbations are a leading cause of hospitalisation. Suboptimal in-hospital management is expected to lead to more frequent exacerbations and recurrent hospital admission, and is associated with increased mortality.

Objective. To explore in-hospital management of COPD and to compare the results with recommendations from international guidelines.

Methods. A literature search was carried out for relevant articles published 2000–2009 in the databases Medline, Cochrane Library, Cumulative Index for Nursing and Allied Health Literature and Invert. In addition, the reference lists of the selected articles were examined. Main inclusion criteria were as follows: COPD, exacerbation, hospitalisation, description of inpatient management, and clinical trials. Assessment and treatment strategies in different studies were analysed and compared with American Thoracic Society-European Respiratory Society and Global Initiative for Chronic Obstructive Lung Disease guidelines. Outcomes were analysed.

Results. Seven eligible studies were selected. Non-pharmacological treatment was infrequently explored. When compared with international guidelines, diagnostic assessment and therapy were suboptimal, especially non-pharmacological treatment. Respiratory physicians were more likely to perform recommended interventions than non-respiratory physicians.

Conclusions. Adherence to international guidelines is low for in-hospital management of COPD exacerbations, especially in terms of non-pharmacological treatment. Further investigation is recommended to explore strategies like care pathways that improve performance of recommended interventions.

Introduction

Chronic obstructive pulmonary disease (COPD) is associated with frequent exacerbations [1;2]. A prospective clinical trial demonstrated that some patients with moderate to severe COPD have three or more exacerbations a year [2]. A COPD exacerbation is characterized by a change in baseline dyspnoea, cough, and/or sputum that is beyond normal day-to-day variations, that is acute in onset, and that may warrant additional treatment in a patient with underlying COPD [3].

Worldwide, COPD exacerbations are a leading cause of acute hospital admission [1;4-8]. An audit of hospital readmissions in 1400 patients showed that around 30% of patients presenting with a first exacerbation will be readmitted with another event within 8 weeks [7]. In addition, COPD exacerbations have a serious negative impact on a patient's quality of life [9-11], and causes socioeconomic burden in terms of direct costs (costs related to medical goods and services) and indirect costs (lost work and productivity) [8]. Management of exacerbations should therefore focus on prevention and reduction of COPD exacerbations, with the ultimate aim of achieving quality of life after exacerbation and reducing health care resource utilization.

Suboptimal therapy for COPD is expected to lead to more frequent exacerbations and consequently recurrent hospitalisation. In addition, it is associated with patient errors, sometimes leading to a worsening condition, cardiopulmonary arrest, and death [12]. Several international clinical practice guidelines (CPGs) for the assessment and management of patients with COPD are available. These CPGs propose practices aimed at reducing COPD exacerbations. CPGs most important to clinicians are those from the American Thoracic Society-European Respiratory Society (ATS-ERS), the Global Initiative for Chronic Obstructive Lung Disease (GOLD), and the British National Collaborating Centre for Clinical Excellence. These CPGs are remarkably consistent and have very few areas of clinically relevant variation [13].

The aim of this literature review is to explore in-hospital management of COPD and to compare the findings of our review with international guideline recommendations.

Methods

The methodology used for this review is based on systematic review methods developed by the Cochrane Collaboration and the NHS Centre for Reviews and Dissemination [14].

Search methods

First, to identify relevant articles published between January 2000 and March 2009, we searched electronic databases – Medline, Cochrane Library, Cumulative Index for Nursing

and Allied Health Literature, and Invert – using the Medical subject heading terms COPD, exacerbation, hospitalisation, adherence, management and guideline. Second, we examined the reference lists of selected articles. Finally, we screened the selected articles to determine whether they met the following inclusion criteria: (i) report of original research; (ii) patients hospitalised for a COPD exacerbation; (iii) description of the assessment and treatment of a COPD exacerbation; (iv) clinical trials; and (iv) published in English, Dutch, French or German.

Search outcome

The literature search initially identified 18 eligible studies that fulfilled the search criteria. After reading the full texts with regard to inclusion criteria and quality assessment, we included seven papers for further analysis (Table 1) [15-21].

Quality appraisal

For the quality appraisal of the studies, the list for assessment of observational studies described by the Centre for Reviews and Dissemination was used [22]. The following criteria were assessed: (i) appropriateness of methodology (sampling method, data collection method, and statistics); (ii) description of the groups and distribution of prognostic factors; (iii) description of the content and prevalence of the performed diagnostic and treatment interventions; (iv) generalizability of the results; and (v) limitations of the studies.

Data synthesis

We conducted a descriptive data synthesis and assessed heterogeneity. The data synthesis in this review follows Centre for Reviews and Dissemination procedures [23]. Study characteristics (sample size, setting, aim), assessment, treatment interventions and outcomes were tabulated and compared. The sample sizes of the selected studies varied widely; therefore, we included both percentages and corresponding proportions in presenting the results to assist the reader in making a judgment where studies conflict.

Results

Study characteristics

The selected articles were published between 2001 and 2007, and the studies were conducted between 1997 and 2004. The characteristics of each study are displayed in Table 1. The seven studies employed an observational design. Data were retrospectively collected by reviewing medical records. Only Cydulka et al. (2003) gathered data prospectively [17]. Four studies were multicentre trials, with sample sizes ranging from 397 to 69 820 patients in

29–360 hospitals [15;17;20;21]. In the three remaining monocentre studies, sample sizes ranged from 50 to 94 patients [16;18;19]. Six studies analysed the entire hospitalisation period, while the study of Cydulka et al. (2003) focused on management in the emergency department [17].

Patients were selected by convenience sampling in six studies, in which all patients consecutively admitted with a COPD exacerbation were included. Bratzler et al. (2004) used computerized random sampling for medical record selection [15]. Results were usually reported as percentages. However, two studies presented variations between hospitals by using interquartile range (IQR) and range of hospital percentages. P-values from Chi-square tests and 95% confidence intervals were calculated.

Six of seven studies explicitly stated that patients were hospitalised for a COPD exacerbation by listing the ICD code and by describing symptoms of increased breathlessness, increased sputum volume, increased sputum purulence, and worsening cough [15-17;19;21]. Kelly and Elborn (2002) defined three of these symptoms using the Anthonisen criteria, a classification scheme widely used for diagnosing acute exacerbations of COPD [19;24]. Cydulka et al. (2003) also included patients with mixed asthma/COPD (44%), but all patients were admitted for COPD exacerbation [17].

Table 1. Overview of 7 papers analysed in the present review

Author	Study period	Setting	Patient sample	Design
Roberts et al. (2001) [21]	1997	n=43; UK hospitals with acute respiratory department: 14 university teaching hospitals and 29 district hospitals	n=1400	Multicentre retrospective observational study: medical record audit
Kelly & Elborn (2002) [19]	1998	n=1; Belfast City Hospital	n=50	Retrospective observational study: medical record audit
Cydulka et al. (2003) [17]	1999-2001	n=29; emergency departments in 15 US states and 3 Canadian provinces	n=397	Multicentre prospective observational study: chart review, interview, telephone interview (follow-up)
Bratzler et al. (2004) [15]	2000-2001	n=76; US community hospitals	n=409	Multicentre retrospective observational study: medical record audit
Harvey et al. (2005) [18]	2001	n=1; regional hospital, metropolitan Melbourne	n=49	Retrospective observational study: medical record audit
Lindenauer et al. (2006) [20]	2001	n=360; predominantly small-to-medium-sized non-teaching facilities, representing all regions of the United States	n=69820	Multicentre retrospective observational study: medical record audit
Chang et al. (2007) [16]	2004	n=1; secondary and tertiary referral hospital, Central North Island of New Zealand	n=94	Retrospective observational study: medical record audit

*Before and after study; only results of pre-test are included

Patient characteristics

Patient characteristics are displayed in Table 2. Half of the patients were male. Mean age ranged from 70 to 74 years. The Kelly and Elborn study (2002) was the only study to define disease severity according to British Thoracic Society guidelines [25]: 32% (16/50) of patients had mild COPD (50–80% predicted forced expiratory volume in one second [FEV1]); 54% (27/50) had moderate COPD (30–49% predicted FEV1); and 14% (7/50) had severe COPD (<30% predicted FEV1) [19]. Roberts et al. (2001) and Chang et al. (2007) reported both a median predicted FEV1 of 35% with ranges of 25–53% and 14–83% respectively [16;21]. Arterial blood gases (ABGs) were reported in three studies [15;19;21]: 12% (6/50) to 16% (224/1400) of patients had a pH < 7.35 [19;21]; 32% (16/50 and 456/1400) of patients had PaCO₂ > 6 kPa [19;21]; 18% of patients (246/1400) had PaO₂ < 7.3 kPa [21]; and 5.1% (21/409 and 72/1400) of patients experienced respiratory failure at pH < 7.26 and PaCO₂ > 8 kPa [15;21].

Table 2. Patient characteristics at admission

Author	Patient sample n	Sex		Age mean years (SD)	Smoking status		
		Male %	Female %		Active smoker n (%)	Ex- smoker n (%)	Never smoked n (%)
Roberts et al. (2001) [21]	1400	54.6	45.4	72 (10)	445 (31.8)	64 (4.6)*	
Kelly & Elborn, 2002 [19]	50	48.0	52.0	72 (1)	24 (48.9)	18 (36.7)	7 (14.3)
Cydulka et al. (2003) [17]	397	48.1	51.9	70 (9)			
Bratzler et al. (2004) [15]	409	45.2	54.8	74 (6)	117 (28.6)		
Harvey et al. (2005) [18]	49	53.1	46.9	72 (10)	10 (20.4)	35 (71.4)	4 (8.2)
Lindenauer et al. (2006) [20]	69820	42.5	57.8	70 [†] (IQR: 61-78)			
Chang et al. (2007) [16]	94	57.1	42.9	70 (12)	36 (38.3)	25 (55.3)	6 (6.4)

*Ex-smokers for ≤ 3 months.

[†]Median age.

Regarding previous admissions before the index admission (first admission of the patient during the studied period), Roberts et al. (2001) detailed that 27% (384/1400) of patients had been admitted in the preceding 4 months prior to index admission [16]. Cydulka et al. (2003) mentioned that 42% (176/397) of patients were admitted within the previous year [17]. Six studies examined smoking status, with active smokers ranging from 20% to 49% (Table 2). Co-morbidity was mentioned by Chang et al. (2007) (n = 94), Harvey et al. (2005) (n = 49) and Lindenauer et al. (2006) (n = 69 820), with 70–80% of these patients having at least two co-morbidities [16;18;20]. The most reported co-morbid conditions were ischaemic heart

disease (52%, 49/94); hypertension (18–41%, 17/94 and 28 626/69 820 respectively); diabetes 17–22%, 16/94 and 15360/69820 respectively); malignancies (11–17%, 7682/69 820 and 16/94 respectively); anxiety and depression (10–20%, 6982/69820 and 19/94 respectively); and fluid and electrolyte disorders (18%, 12 568/69 820) [16;20]. Only Chang et al. (2007) reported body mass index (n = 94; mean body mass index: 24; range: 12.6–52.3) [16].

Diagnostic assessment

Table 3. Diagnostic assessments during hospitalisation

Author	Patient sample n	X-ray n (%)	ABGs* n (%)	Sputum sample n (%)	PEF n (%)	Spirometry n (%)
Roberts et al. (2001) [21]	1400	916 (65.4)	1109 (79.2)		648 (46.3)	
Kelly & Elborn (2002) [19]	50	44 (88.0)	38 (76.0)	24 (48.0)	12 (24.0)	9 (18.0)
Cydulka et al. (2003) [17]	397	346 (87.1)	191(48.1)	28 (7.1)	129 (32.5)*	
Bratzler et al. (2004) [15]	409	396 (96.8)	180 (44.0)	31 (7.6)	20 (4.9)	
Harvey et al. (2005) [18]	49		41 (83.7)			
Lindenauer et al. (2006) [20]	69820	66276 (94.9)	44762 (64.1)	10051 (14.4)		8354 (12.0)
Chang et al. (2007) [16]	94	89 (94.7)	66 (70.2)			

*PEF represented 90% of spirometry; only 10% of values were FEV1s.

ABGs, arterial blood gas values; FEV1, forced expiratory volume in one second; PEF, peak expiratory flow.

In the studies analysed, the diagnostic evaluation mainly included chest radiography (X-ray), ABGs, sputum testing, and spirometry (Table 3). The percentage of patients who received X-rays ranged from 87% to 97%. The percentage reported in the Roberts et al. study (2001) (65%) does not indicate the number of patients who received X-rays, but instead the number of patients in which the X-ray was evaluated by a doctor within 24 hours [21]. With the exception of Lindenauer et al. (2006) all studies indicated that ABGs included pH, PaCO₂, PaO₂ analyses; three studies also included SaO₂ in their ABG analyses [15;18;21]. ABGs were performed in 44–84% of patients, with performance rates varying 20% across the hospitals that participated in the Roberts et al. (2001) (IQR: 73–90; n = 43 hospitals) and Lindenauer et al. (2006) (IQR: 52.0–77.0; n=360 hospitals) studies [20;21]. In the Roberts et al. study (2001), 34% of patients (476/1400) who had their ABGs measured at admission also had their ABG measurements repeated within 24 hours of admission [21]. The range of repeat ABG measurements across hospitals was 20% (IQR: 19–44; n=43 hospitals). Moreover, ABGs were more likely to be repeated in acidotic patients [21]. Two studies measured oxygen saturation using oximetry; oxygen saturation ranged from 76% (311/409) to 94% (1316/1400) [15;21]. Sputum testing varied from 7% to 48%, with Lindenauer et al.

(2006) mentioning a variance of 30% across 360 hospitals (IQR: 0.0–29.0; $n = 360$ hospitals). In the five studies that measured performance of peak expiratory flow (PEF) and spirometry, 5 to 46% of the patients underwent one of these or both pulmonary function tests [15;17;19–21] (Table 3).

Pharmacological treatment

Pharmacological treatment included bronchodilators, corticosteroids and antibiotics (Table 4). Bronchodilator use (β -agonists and anticholinergics) ranged from 91% to 100%. Four studies mentioned the route of administration [16;18;20;21]. Nebulizer use ranged from 32% (30/94) [16] to approximately 100% [18;20;21]. Two studies mentioned metered dose inhaler use, which ranged from 44% (10/94) to 60% (41 892/69 280) [16;20]. In most cases, corticosteroids were administered in 80–88% of patients [15;16;18–21][15,16,18–21]; however, in Cydulka et al. (2003) corticosteroid use was 62% (Table 4) [17]. Only the study of Harvey et al. (2005) reported the duration of corticosteroid therapy, stating that 10% (5/49) of patients remained on therapy for 7–14 days [18]. In five studies, 80–90% of patients received antibiotics. However, in Cydulka et al. (2003) only 28% of patients received antibiotics (Table 4) [17].

Non-pharmacological treatment

Non-pharmacological treatment included oxygen therapy, smoking cessation advice, education on inhaler therapy, referral to multidisciplinary disciplines, referral to pulmonary rehabilitation, discharge management, follow-up, assisted ventilation, and screening for vaccination. In four of seven studies, 64–90% of patients received oxygen therapy during admission (Table 4) [15;16;20;21]. Roberts et al. (2001) found that the percentage of patients receiving oxygen therapy varied by more than 20% across 43 hospitals (IQR: 53–77), while Lindenauer et al. (2006) found that this percentage was comparable across 360 hospitals (IQR: 90–97) [20;21]. Roberts et al. (2001) observed that oxygen was more likely to be prescribed if a patient's SaO₂ (measured by pulse oximetry) was less than 92%; they found no obvious trend with PaO₂ levels [21]. Chang et al. (2007) mentioned that the rationale for oxygen administration was poorly documented, and also found no correlation between initial supplemental oxygen administration and SaO₂ ($r = 0.05$) or ABG values ($r = 0.16$) [16].

Two studies reported that home oxygen therapy was prescribed at discharge, ranging from 18% (252/1400) in Roberts et al. (2001) to 43% (21/49) in Harvey et al. (2005) [18;21]. In Roberts et al. (2001) 18% (246/1400) of patients had a PaO₂ < 7.3 kPa at admission, and only few of these (no exact number defined) had a subsequent PaO₂ > 7.3 kPa while breathing room air. However, only 28% (68/246) of these patients were discharged with home oxygen therapy [21].

Table 4. Pharmacological and non-pharmacological treatments

Author	Patient sample n	Broncho- dilators n (%)	Systemic corticosteroids n (%)	Antibiotics n (%)	Oxygen therapy n (%)	Assisted ventilation	
						NIPPV n (%)	IPPV n (%)
Roberts et al. (2001),[21]	1400	1267 (90.5)	1183 (84.5)	1114 (79.6)	896 (64.4)	40 (2.9)	
Kelly & Elborn, 2002 [19]	50	50 (100)	44 (88.0)	45 (90.0)			
Cydulka et al. (2003) [17]	397	361 (90.9)	246 (62.0)	111 (28.0)			
Bratzler et al. (2004) [15]	409	403 (98.5)	348 (85.1)	364 (89.0)	386 (94.4)	40 (9.8)	23 (5.6)
Harvey et al. (2005) [18]	49	47 (95.9)	39 (79.5)				
Lindenauer et al. (2006) [20]	69820	67515 (96.7)	59240 (84.9)	59053 (84.6)	63715 (91.3)	1827 (2.6)	
Chang et al. (2007) [16]	94	91 (96.8)	78 (83.0)	75 (79.8)	74 (78.7)	10 (10.6)	2 (2.1)

Only Roberts et al. (2001) mentioned education on inhaler therapy. Technique was checked in 20% of patients (280/1400) and was more likely to be checked during a patient's first admission rather than readmissions (28 vs. 16%) [21].

Smoking cessation advice for active smokers was explored by three studies; the percentage of patients receiving this advice ranged from 30% (134/445 current smokers) [21], and 34% (40/117) [15], to 42% (10/24) [19]. Moreover, Roberts et al. (2001) found that advice was more likely to be given on a patient's first admission rather than on readmissions (34 vs. 28%) [21]. They also reported that smoking cessation advice was provided to 19% (12/64) of patients who had quit smoking since 3 months or less before being hospitalised [21].

Referral to pulmonary rehabilitation was explored by three studies, with the percentage of patients receiving referrals ranging from 3% (42/1400) [21] and 16% (8/49) [18] to 18% (9/50) [19]. Two other studies mentioned referrals to other disciplines: physiotherapy (65%, 61/94) [16]; a COPD nurse specialist (10–63%, 5/50 and 59/94 respectively) [16;19]; and a dietician (26%, 24/94) [16].

Three studies reported assessment of social situation, including living situation (i.e. living alone) [16;18]; social support system, access to telephone emergency contact, geographic remoteness and access to health care at home [16]; household income and whether or not having an medical assurance [17]. In Bratzler et al. (2004) 57% (n = 409) of patients were discharged home without home care; 17% had home health care services arranged; 9% required skilled nursing or a swing bed; and 5% and 6% were discharged to a rehabilitation facility or a nursing home respectively [15]. Chang et al. (2007) found that 15% (14/94) of patients previously living at home were discharged to residential care facilities [16]. Two studies reported that 38% (19/50) to 63% (882/1400) of patients received outpatient follow-up and review appointments [19;21].

Five studies found that 3–11% of patients received assisted ventilation via non-invasive positive pressure ventilation (NIPPV) (Table 4). Assisted ventilation was more likely to be initiated in patients with acidosis [16;18;21]. Bratzler et al. (2004) reported that 52% (213/409) of patients with pH < 7.26 and PCO₂ > 8 kPa received non-invasive ventilation [16]. On the other hand, Roberts et al. (2001) reported that the following received assisted ventilation: 15.3% of patients (11/77) with pH < 7.26; 7.5% of patients (34/456) with PCO₂ > 6 kPa; and 12.7% of patients (25/179) with pH < 7.35 and PCO₂ > 6.0 [21].

Only two studies examined whether COPD patients were screened for vaccinations. Bratzler et al. (2004) (2004) found that 47% (192/409) of patients were screened for vaccinations, whereas Roberts et al. (2001) noted that only 5% (70/1400) of patients received vaccination advice [15;21].

Respiratory vs. non-respiratory physicians

Three studies compared patient management performed by respiratory physicians and non-respiratory physicians [16;19;21].

Patients receiving care from respiratory physicians varied from 43% (602/1400) [21] and 44% (22/50) [19] to 94% (88/94) [16]. In Roberts et al. (2001) the remaining patients were under care of a geriatrician (20%; 277/1400) or another specialty (32%; 450/1400). Roberts et al. (2001) observed that respiratory physicians, compared with non-respiratory physicians, significantly more performed FEV1 and PEF with a variance of 20% ($P < 0.001$) [21]. They also assessed more often patients' inhaler technique (21% vs. 14%; $P < 0.001$); provided more smoking advice to current smokers (36% vs. 26%; $P < 0.03$); initiated more often home oxygen therapy (24% vs. 14%) ($P < 0.001$); and prescribed significantly more discharge medications (variances ranged between 10% and 20%). Respiratory physicians also arranged significantly more follow-up (73% vs. 46%; $P < 0.001$), and assessed more often the reversibility of bronchodilators (33% vs. 23%; $P < 0.001$) and steroids (10% vs. 4%; $P < 0.001$). Both respiratory and non-respiratory physicians referred patients to pulmonary rehabilitation to similar extents (5% to 1%) [21]. Chang et al. (2007) observed that patients admitted by non-respiratory specialists tended to have longer hospital stays (mean: 4.9 days vs. 3.3 days) [16]. However, Kelly and Elborn (2002) found no difference in length of stay (LOS), spirometry, radiographs performed, or in treatment administered [19].

Outcomes

Six studies computed the median LOS, which varied from 4 days [16;17;20], 5 days [15], and 6 days [19] to 8 days [21]. Lindenauer et al. (2006) and Kelly and Elborn (2002), respectively, reported that 25% (17 455/69 820) and 44% (22/50) of patients remained hospitalised for 7 days or longer [19;20]. Eleven per cent (7750/69 820) to 18% (70/397) of patients were readmitted within 14 days after discharge [17;20]; 17% (12 009/69 820) to 27% (112/409) patients were readmitted within 1 month after discharge [15;20]; and 43% (176/409) of patients were readmitted 6 months after discharge [15]. Two per cent (8/409) to 5% (5/94 and 1793/69 820) of patients died during hospital stay [15;16;20]; 8% (33/409 and 8/94) died within 1 month after discharge [15;16]; and 24% (98/409) to 31% (29/94) of patients died within 6 months to 1 year, respectively, after admission [15;16].

Discussion

Our literature search, which was aimed at exploring in-hospital management of COPD exacerbations, identified seven eligible trials for further in-depth analysis. Both ATS-ERS and GOLD guidelines were used as standards to discuss the in-hospital management of COPD exacerbation in the reviewed studies [26;27]. ATS and ERS separately published position papers on the management of COPD in 1995 [28;29]. A cooperative, the ATS-ERS task force, updated the position papers in 2004, resulting in the Standards for the Diagnosis and Treatments of Patients with COPD [26]. GOLD was set up by the US National Heart, Lung and Blood Institute and the World Health Organisation. This expert panel prepared a consensus report based on their review of existing COPD guidelines and new information on pathogenic mechanisms of COPD: 'The Global Strategy for the Diagnosis, Management and Prevention of COPD' [27]. The first report was published in 2001, and was updated in 2008. Table 5 displays the recommendations of both guidelines. Overall, our review of the seven eligible trials showed poor adherence to the international recommendations.

Table 5. Recommendations of ATS-ERS and GOLD guidelines for in-hospital management of an COPD exacerbation [26;27]

ATS-ERS guidelines	GOLD guidelines
Diagnostic assessment	
History before exacerbation	
Chest radiography	
Arterial blood gases	
Sputum testing in all patients	Sputum testing: if an infectious exacerbation does not respond to initial antibiotic treatment
Electrocardiogram (ECG)	
Assessment of nutritional status	
Pharmacological treatment	
Short-acting bronchodilators	
Corticosteroids: 30 – 40 mg for 7 to 10 days (GOLD) or 10 to 14 days (ATS-ERS)	
Antibiotics (based on local bacteria resistance patterns) in the following cases: <ul style="list-style-type: none"> change in sputum characteristics (purulence and/or volume) patients requiring special or care in an intensive care unit 	Antibiotics in the following cases: <ul style="list-style-type: none"> Symptoms: increased sputum purulence, increased dyspnoea and/or increased sputum volume critically ill and needing mechanical support
Non-pharmacological treatment	
Controlled oxygen therapy	
Education on inhaler therapy, coping with dyspnoea, and nature of COPD	
Smoking cessation intervention	
Nutritional support, if necessary	
Physiotherapy	
Referral to pulmonary rehabilitation	
Screening for vaccination status not mentioned	Screening for vaccination status (influenza, pneumococcal vaccines)
Discharge management	
Follow-up appointment	
Non-invasive mechanical ventilation in moderate to severe acidosis (pH<7.35) and/ or hypercapnia (PaCO ₂ > 6.0 kPa, 45 mm Hg)	
Invasive mechanical ventilation	

Methodological quality of the existing research

To limit historical effects, only papers published since 2000 were included for review. Three of the trials reported in these papers used data collected in the late 1990s (Table 1). However, interventions explored in these studies have been internationally recognized as major key interventions since the 1990s, so we believe bias is minimal. Retrospective data collection could bias the accuracy of the results, especially with regard to non-pharmacological management, as those interventions are less likely to be documented and detailed in records. Sample sizes and statistics used in the studies guarantee reliability of the results. Diagnosis of COPD exacerbation was confirmed by explicit definition and ICD code in six of the seven studies.

Demographic characteristics of the studied patients

The studied patients were largely comparable with regard to gender, age and smoking status (Table 2). FEV1 values reported in three studies indicated that patients hospitalised with a COPD exacerbation were classified mainly as having moderate to severe COPD, according to GOLD spirometric classification scheme for COPD [16;19;21;27]. ABGs were largely comparable for the three studies in which ABGs were assessed [15;19;21]. The number of active smokers (20–49%; Table 2) is of concern, as smoking is the main cause of COPD and also an important prognostic factor for the disease [30;31].

Diagnostic assessment

According to ATS-ERS and GOLD guidelines, the major components of the in-hospital assessment of a COPD exacerbation are history before exacerbation, chest X-ray, ABGs, electrocardiogram, sputum testing, and assessment of nutritional status (Table 5) [26;27].

Regarding X-rays, we found that 5–13% of patients presenting with a COPD exacerbation did not receive a chest X-ray (Table 3). X-rays are very useful in identifying alternative diagnoses that can mimic the symptoms of an exacerbation [27].

Our literature review revealed that ABGs are very rarely performed. Two of the reviewed studies reported that ABGs were measured in less than 50% of patients; the other studies reported that ABGs were measured in 64–84% of patients (Table 3). Failing to obtain patients' ABGs may lead to suboptimal management, as ABG values are an important determinant for initiating supplemental oxygen therapy, for prescribing assisted ventilation, and for prescribing home oxygen therapy [32;33].

Sputum stains and cultures are useful in identifying bacterial infections and in directing antibiotic therapy [34]. Performance of sputum tests was very low (7–48% of patients were tested) (Table 3). ATS-ERS guidelines recommend sputum cultures for all patients hospitalised with an exacerbation, while GOLD guidelines only recommend sputum cultures

and antibiograms for patients in which an infectious exacerbation does not respond to the initial antibiotic treatment (Table 5). Although ATS-ERS and GOLD guidelines are incongruent with respect to whether or not all patients need sputum testing, both guidelines do agree that, at a minimum, sputum cultures should be performed in patients with purulent sputum and/or before starting antibiotics therapy [26;27].

Our literature review also revealed that spirometry is seldom performed: 5–46% of patients were reported to undergo spirometry and/or PEF (Table 3). Both ATS-ERS and GOLD guidelines do not routinely recommend spirometric tests, because these tests are inaccurate during acute exacerbations and can even be difficult for a sick patient to perform properly properly [26;27;34]. However, measuring PEFs and especially FEV1s is beneficial in assessing the severity of an exacerbation [35–37].

Other recommended diagnostic interventions (Table 5) that were not or very rarely examined in the included studies will not be discussed.

In conclusion, the studies we analysed revealed that diagnostic assessments according to ATS-ERS and GOLD guidelines are suboptimally performed with regard to X-rays and ABGs.

Pharmacological treatment

Main pharmacological interventions examined by the studies included in the present review were administration of bronchodilators, corticosteroids and antibiotics, all key pharmacological medications according to ATS-ERS and GOLD guidelines (Table 5).

Adherence to bronchodilator therapy was high, ranging from 90% to 100%. Bronchodilators were delivered by nebulizer in 80–98% of cases [18;20;21]. Both ERS and GOLD guidelines advice against the use of nebulizers and recommend use of metereddose inhalers and dry powder inhalers if possible [26;27]. Literature indicates that use of wet nebulizers are more expensive, require appropriate maintenance, and have many adverse effects (i.e. highly variance in performance, less adherence to therapy) [38;39].

Adherence to corticosteroid therapy, however, was less than optimal, as 15–40% of patients did not receive corticosteroid therapy (Table 4). Systemic glucocorticosteroids shorten recovery time, improve lung function (FEV1) and hypoxemia (PaO₂), and may reduce the risk of early relapse, treatment failure, and length of hospital stay [40].

According to evidence and recommendations from ATS-ERS and GOLD guidelines, antibiotics should be given to patients with exacerbations that present with increased sputum purulence, and also show increased dyspnoea and or increased sputum volume (Table 5). Patients who are critically ill and who need mechanical support also should receive antibiotics [26;27;40]. In four studies in which the patients showed the three key symptoms [15;16;19;21], 80–90% of patients were treated with antibiotics; in Cydulka et al. (2003) only

28% of patients received antibiotics, even though 84% of the patients also presented with the three key symptoms [17].

In conclusion, adherence to ATS-ERS and GOLD guidelines for bronchodilator and antibiotic treatment was acceptable, while adherence to guidelines for corticosteroid treatment was suboptimal.

Non-pharmacological treatment

Non-pharmacological treatments comprise an essential part of treatment for exacerbations. However, we discovered that the use of non-pharmacological treatments was poorly studied by the reports we included in our review. In Cydulka et al. (2003) this may have to do with the fact that the study was focused on emergency department management only [17]. Table 5 lists the main nonpharmacological interventions recommended by ATS-ERS and GOLD guidelines [26;27].

Oxygen therapy is the treatment cornerstone for severe COPD exacerbations [41]. Administration of oxygen therapy was mentioned in four studies, and the percentage of patients prescribed oxygen therapy was rather high (Table 4). Appropriateness of oxygen prescriptions cannot be discussed, because the studies rarely reported the ABGs of patients that received oxygen. Only two studies examined the use of home oxygen therapy [18;21]. Furthermore, Roberts et al. (2001) reported that prescribing home oxygen was suboptimal and not adjusted according to low PaO₂ values subsequent to the exacerbation [21].

Only one study, Roberts et al. (2001) examined education provided to patients, and found out that patient education was limited to inhalation therapy and was only given in 20% of patients [21]. This is a very concerning finding as inhaler therapy is a cornerstone in the management of COPD patients [42;43]. Yet adherence to inhaler therapy with regard to dose and inhaler technique in COPD patients has been shown to be very low [44;45], and research has demonstrated that education can have a large impact on patients' understanding of their medication regimen and on inhaler technique [44-46]. Smoking cessation advice was rarely provided, with only about one-third of active smokers receiving advice [15;19;21]. ATS-ERS and GOLD guidelines state that smokers should be offered the most intensive smoking cessation intervention feasible [26;27]. Ceasing to smoke can prevent or delay the development of airflow limitations or can reduce the progression of these limitations, and can have a substantial effect on subsequent mortality [30;31].

The study of Chang et al. (2007) noted a rather high referral rate for physiotherapy, at 65% [16]. Three other studies, stated that only 3–18% of patients were referred to pulmonary rehabilitation [18;19;21]. This finding is of concern, as COPD patients are markedly inactive during and after hospitalisation for an exacerbation, and patients who have low activity levels for 1 month after discharge are more likely to be readmitted within the following year [47].

Early outpatient pulmonary rehabilitation after hospitalisation for a COPD exacerbation is safe and results in clinically significant improvement in exercise capacity, health status, and health-related quality of life, and reduces the risk of hospital admission and mortality [48].

Assessment of patients' social situation and discharge management was not examined extensively; however, two included studies showed that a large number of patients (15–57%) needed referral to home care or institutionalization after hospitalisation for exacerbation [15;16]. Also a study of Gruffydd-Jones et al. (2007) in patients discharged home after an exacerbation found that one-third of these patients were concerned about their social situation, especially with regard to care, housing, social benefits, and the health of their caregiver [49]. Roberts et al. (2001) and Kelly and Elborn (2002) reported that only 38–63% of patients received outpatient follow-up [19;21], which contrasts with literature indicating that intensive outpatient follow-up significantly improves quality of life after hospitalisation for an acute exacerbation [50].

The NIPPV in patients with hypercapnic respiratory failure reduces the need for intubation and reduces mortality [51-55]. However, Bratzler et al. (2004) reported that only half of the patients with hypercapnic failure received NIPPV, and Roberts et al. (2001) reported that 15% or less of patients with acidosis or hypercapnia received assisted ventilation (NIPPV) or invasive positive pressure ventilation [15;21]. In conclusion, these results indicate that assisted ventilation is highly underutilized.

The main limitation of the assessment of non-pharmacological treatment is the limited quantity and quality of the data available. In general, non-pharmacological interventions recommended by international guidelines were rarely performed, according to the studies included in this review.

Respiratory vs. non-respiratory physicians

Roberts et al. (2001) showed that respiratory physicians are significantly more likely to provide optimal management than non-respiratory physicians, especially with regard to non-pharmacological management [21]. These findings are consistent with those of several other clinical trials [56-59], and encourage the involvement of a respiratory physician in the in-hospital management of a COPD exacerbation.

Length of stay, readmission and mortality

In the studies included in the present review, the mean LOS decreased from 8 to 4 days with increasing year of publication, which suggests an overall trend of decreasing LOS for patients hospitalised for COPD exacerbations during the last decades.

Regarding readmission and mortality, the degree to which data could be pooled was restricted by the different reported measures of outcomes, but rates within the same intervals

were similar. Readmission and mortality was high in the studied patients [15-17;20]; however, similar rates were found in other outcome studies on COPD exacerbations [5;59-64].

The need for standardization of the care process

Transparency and standardization of care processes is one of the main challenges for clinicians, managers and policy makers. With respect to the findings in this literature review, we see the need for more standardization in COPD care. One of the possibilities to re-organize the care process around patient needs for COPD is the development of a care pathway, also known as critical pathways or clinical pathways [65-71]. Care pathways are complex interventions for the mutual decision making and organisation of predictable care for a well-defined group of patients during a well defined period (<http://www.E-P-A.org>) [66;68;71;72]. Although they are used worldwide [70], the knowledge on pathways on COPD is not found in literature. International knowledge sharing networks like the European Pathway Association and international respiratory societies should therefore not only focus on the clinical content of the COPD pathways but also on the organisation of the care process. These international societies should develop a list of evidence-based key interventions which should be included in every COPD pathway. Our research team is preparing an international cluster randomized trial to further explore and understand how pathways for COPD should be developed, implemented, evaluated and what their impact is on outcome, efficiency and multidisciplinary teamwork.

Conclusions

Overall adherence is poor with regard to international guidelines in in-hospital management of COPD exacerbations, especially for non-pharmacological therapy. Further investigation is recommended to investigate strategies that might improve adherence to CPGs and enhance the quality of care, e.g. through the implementation of a care pathway.

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Chapter 3:

Impact of care pathways for in-hospital management of COPD exacerbation: A systematic review

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Lodewijckx C, Sermeus W, Vanhaecht K, Panella M, Deneckere S, Leigheb F, Decramer M, for the EQCP study group. Impact of care pathways for in-hospital management of COPD exacerbation: a systematic review. *Int J Nurs Stud*. 2011;48:1445-56.

Abstract:

Background. In-hospital management of COPD exacerbation is suboptimal, and outcomes are poor. Care pathways are a possible strategy for optimizing care processes and outcomes.

Objectives. The aim of the literature review was to explore characteristics of existing care pathways for in-hospital management of COPD exacerbations and to address their impact on performance of care processes, clinical outcomes, and team functioning.

Methods. A literature search was conducted for articles published between 1990 and 2010 in the electronic databases of Medline, CINAHL, EMBASE, and Cochrane Library. Main inclusion criteria were (I) patients hospitalised for a COPD exacerbation; (II) implementation and evaluation of a care pathway; (III) report of original research, including experimental and quasi experimental designs, variance analysis, and interviews of professionals and patients about their perception on pathway effectiveness.

Results. Four studies with a quasi-experimental design were included. Three studies used a pre–posttest design; the fourth study was a non-randomized controlled trial comparing and experimental group where patients were treated according to a care pathway with a control group where usual care was provided. The four studied care pathways were multidisciplinary structured care plans, outlining time-specific clinical interventions and responsibilities by discipline. Statistical analyses were rarely performed, and the trials used very divergent indicators to evaluate the impact of the care pathways. The studies described positive effects on blood sampling, daily weight measurement, arterial blood gas measurement, referral to rehabilitation, feelings of anxiety, length of stay, readmission, and in-hospital mortality.

Conclusions. Research on COPD care pathways is very limited. The studies described few positive effects of the care pathways on diagnostic processes and on clinical outcomes. Though due to limited statistical analysis and weak design of the studies, the internal validity of results is limited. Therefore, based on these studies the impact of care pathways on COPD exacerbation is inconclusive. These findings indicate the need for properly designed research like a cluster randomized controlled trial to evaluate the impact of COPD care pathways on performance of care processes, clinical outcomes, and teamwork.

Introduction

Patients with chronic obstructive pulmonary disease (COPD) experience frequent exacerbations of symptoms [1-3]. COPD exacerbations are characterized by a change in baseline dyspnea, cough, and/or sputum, that is beyond normal day-to-day variations, is acute in onset, and may warrant additional treatment in a patient with underlying COPD [4]. The annual rate of COPD exacerbations varies from 0.5 to 3.5 exacerbations per patient [1;3].

COPD exacerbations contribute tremendously to the disease burden. They are a leading cause of hospital admission worldwide, with 35% of COPD patients having at least one admission a year and up to 40% of admitted patients having two or more readmissions a year [2;5;6]. These acute hospital admissions account for the majority (52–84%) of the overall direct costs related to COPD. In the Confronting COPD Survey conducted in 2003, the annual direct costs per patient were found to be higher in the USA (US\$4119/s3028) and Spain (US\$3196/2349s) and to be lower in the Netherlands (US\$606/s446) and France (US\$522/s384) [7]. COPD exacerbations also have a serious impact on functional status [1;8] and patients' quality of life [1;9;10], and up to 30% of patients die within one year after hospitalisation, [11;12]. Furthermore, we see high variation in outcomes after hospitalisation for COPD exacerbation; for example, for 30-day mortality (range 5.2–17.2%) [13], 1-year mortality (23–37%) [11;12], and 1-year readmission rate (37–67%) [2;5;6;14].

Several worldwide established evidence-based clinical practice guidelines (CPGs) are available for the assessment and management of patients with COPD [15]; for example, the guidelines of the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) [16]; the American Thoracic Society (ATS)-European Respiratory Society Task Force (ERS) [17]; and the National Institute for Clinical Excellence [18]. These guidelines are remarkably consistent, as only two discrepancies with regard to sputum culture and performance of spirometric tests were found. For these two recommendations no research evidence is available, and so both advices are derived from expert committee reports or opinions and/or clinical experience of respected authorities. Sputum culture is useful in identifying bacterial infections and in directing antibiotic therapy. ATS-ERS guidelines recommend sputum cultures for all patients hospitalised with an exacerbation, while GOLD and NICE guidelines only recommend sputum cultures and antibiograms for patients with purulent sputum and in which an infectious exacerbation does not respond to the initial antibiotic treatment [16-18]. With regard to spirometric tests, ATS-ERS and GOLD guidelines do not routinely recommend spirometric tests because these tests are difficult for a sick patient to perform properly and therefore can be inaccurate during acute exacerbations [17]. On the other hand, NICE guidelines recommend measuring spirometry in all patients before discharge [18].

Several studies concerning in-hospital management of COPD exacerbation show that guideline adherence is poor and varies highly across organisations [19-21]. Lodewijckx et al. (2009) reviewed delivered care in more than 70,000 patients hospitalised with COPD exacerbation. Results showed that non-pharmacological management is extremely suboptimally performed, especially with regard to smoking cessation intervention (30–42% of active smokers), education regarding inhaler therapy (20%), and referral to pulmonary rehabilitation (3–18%). Also diagnostic and pharmacological management were found to be suboptimal, especially with regard to arterial blood gas measurement (performed in 44–79% of patients), and administration of corticosteroids (administered in 62–85% of patients) [21]. Decramer et al. (2003), who questioned management of COPD in 86 pulmonologists in Belgian Hospitals, also found several areas of non-adherence to recommendations of international guidelines, especially with regard to pulmonary rehabilitation, smoking cessation, and non-invasive ventilation [19]. Finally, Hosker et al. (2007) explored hospital care for COPD exacerbation in 233 UK units and found large differences in organisation of care. To illustrate, a considerable number of hospitalised COPD patients had no access to a specialist respiratory ward (35% of patients had no access), a pulmonary rehabilitation program (36%), or an early discharge scheme (56%) [20].

One possible strategy to standardize care processes and to optimize outcomes after hospitalisation for COPD exacerbation is the implementation of a care pathway, also known as clinical pathway or critical pathway [22-26]. Care pathways are complex interventions for the mutual decision making and organisation of predictable care for a well-defined group of patients during a well-defined period, with the aim to enhance the quality of care across the continuum by improving risk-adjusted patient outcomes, promoting patient safety, increasing patient satisfaction, and optimizing the use of resources [27]. In several reviews positive effects of care pathways on clinical outcomes, performance of care processes, costs, teamwork, and patient satisfaction are reported Rotter, 2010 1044 /id; Sermeus, 2005 154 /id; Van Herck, 2004 764 /id}. Most of care pathways were developed for surgery (50%) such as hip fracture surgery and knee arthroplasty, and for medical conditions (30%) such as asthma, pneumonia, and stroke. Other domains included were emergency care, psychiatry, palliative care and rehabilitation. However, none of the reviews reported on COPD care pathways. Therefore, two main research questions are explored in this review: (i) What are the characteristics of existing care pathways for in-hospital management of COPD exacerbation with regard to development, implementation, components, and pathway performance; (ii) What is the impact of existing care pathways for in-hospital management of COPD exacerbation on performance of care processes, clinical outcomes, and team functioning?

Methods

The methodology used for this review is based on the PRISMA Statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses of studies that evaluate healthcare interventions) [28;29], and on systematic review methods developed by the NHS Centre for Reviews and Dissemination [30].

Search strategy

A three-step search strategy was used by author CL to identify relevant peer-reviewed articles between January 1990 and May 2010 (Fig. 1). Firstly, an electronic search was carried out by the first author (CL) in the electronic databases Medline, CINAHL (Cumulative Index for Nursing and Allied Health Literature), EMBASE, and Cochrane Library. The search terms included chronic obstructive pulmonary disease, combined with critical pathway, clinical pathway, and critical path. Since the electronic search resulted in limited amount of records, no search limits were included. Secondly, reference lists of the selected papers were screened for additional literature. Thirdly, Rotter, who conducted a Cochrane review on impact of care pathways on professional practice, patient outcomes, length of stay and hospital costs [31], was consulted to compare our search results with his literature findings regarding impact of COPD care pathways.

Since the literature search in electronic databases revealed a limited amount of papers, we conducted an additional search for unpublished information. Firstly, Google was explored. The search terms COPD, exacerbation, and critical pathway were used. The first ten Google pages were assessed. Secondly, members of the European Respiratory Society (www.ersnet.org) and the European Pathway Association (www.E-P-A.org) were contacted with a request for additional information regarding COPD and care pathways. Finally, the international care pathway conference held in London 2010 was visited to look for recent conducted studies on development and evaluation of COPD care pathways.

Figure 1. Search strategy

Appraisal for inclusion

Appraisal of the retrieved records occurred in two phases. Records were primary assessed by the first author (CL) on title and abstract, and a first selection was made based on the description of the studied population, the setting, and the general characteristics of the care pathways. Subsequently, the full text of the selected articles was independently screened by two researchers (CL and KV) to determine whether they met the following inclusion criteria: (I) patients hospitalised with a COPD exacerbation; (II) implementation and evaluation of a care pathway; (III) report of original research, including experimental and quasi experimental designs, variance analysis, and interviews of professionals and patients about their perception of pathway effectiveness. To appraise whether an intervention could be considered a care pathway, we evaluated the intervention on five criteria, based on the care pathway definition of the European Pathway Association (www.E-P-A.be) [27]: (I) aimed for a well-defined group of patients during a well-defined period; (II) an explicit statement of the goals and key elements of care based on evidence, best practice, patients' expectations, and their characteristics; (III) coordination of the roles and sequencing of the activities of the multidisciplinary care team, patients, and their relatives; (VI) documentation, monitoring, and evaluation of variances and outcomes; (V) identification of relevant resources.

Quality appraisal of included studies

The quality appraisal of the included studies was based on five criteria: (I) appropriateness of methodology (sampling method, data collection, method, and statistics); (II) description of the groups and distribution of prognostic factors; (III) description of the intervention; (IV) generalizability of the results; and (V) limitations of the studies. The description of the intervention was assessed on two main subjects: (I) development and implementation of the care pathway, based on the ingredients for successful pathway implementation, as described by Harkleroad et al. (2000) [32]; and (II) pathway components and performance, based on the care pathway definition of E-P-A [27].

Data extraction

For each included study, the following data were extracted and reported in overview tables: publication details (date, title, authors); background; objectives; methodology (design, location, inclusion and exclusion, variables and measurement tools, study procedure, analysis); sample size; relevant results; quality assessment of results; conclusion; and implications. For the three studies, the authors were contacted to provide additional information regarding pathway characteristics and results. However, only McManus et al. (2005) could provide us with additional information, solely on the exact time frame of implementation of the pathway and timing of the measurements [33].

Data synthesis

A descriptive data synthesis was conducted, and heterogeneity was assessed. Due to limited data and use of divergent variables within the studies, a meta-analysis of the results could not be performed. For the corresponding variables, differences in means were reported.

Data of the included studies were summarized according to three main areas: study characteristics (study design, aims of the paper, study location, study population, sample size); pathway characteristics (pathway objectives, development, and implementation; pathway components and performance); pathway indicators; baseline variables; process outcomes; clinical outcomes; and team outcomes. Reported p-values were considered statistically significant if $p < 0.05$.

In this review, the organisation of care before pathway implementation is referred to as “usual care,” and care after the implementation as “pathway care.”

Results

The literature search of the electronic databases revealed a total of 140 publications. After exclusion of the duplicates and quality appraisal, four articles were selected (Fig. 1) [33-36] (Fig. 1). These four articles included three studies on development and impact of COPD exacerbation care pathways [33;34;36] The fourth paper (Marley, 2000) provided additional information on the development and the outcomes of the care pathway investigated in McManus et al. (2005) [33;35]. The screening of the reference lists of the selected articles and the comparison with the search results of Rotter et al. (2010) did not provide additional papers [31].

The additional search for unpublished information revealed one unpublished study on the impact of a care pathway for COPD exacerbation [37]. The study was presented twice on the European Respiratory Congress, firstly in 2006 in Munich by means of a poster presentation, and secondly in 2008 in Berlin during a detailed oral presentation on development, implementation and impact of the COPD care pathway. Since two authors of the study were also involved in this literature review, detailed data on development, implementation, evaluation method, and results were available, and therefore the study of Celis et al. (2006) was also included in this review [37]. Finally, ten interesting blueprints of COPD care pathways were found, however no further information on development, implementation, evaluation and impact of the care pathways was available, and therefore these results were not eligible for inclusion in the literature review.

Study characteristics

The aim of the four studies was to evaluate the impact of a care pathway for COPD exacerbation on performance of care processes [33;34;37] and clinical outcomes (Table 1) [33;34;36;37]. All studies are monocenter trials, conducted in four university hospitals in the United States [34] Australia [36], Northern Ireland [33] and in Belgium [37]. The studies were performed between 1994 and 2005.

Three studies used a pre–post design, comparing a group where a care pathway was implemented with a historical control group [33;34;36]. Celis et al. (2006) conducted a monocenter non-randomized controlled trial, where an experimental group in which patients were cared for according to a care pathway were compared with a control group in which usual care was provided [37]. Assignment of the patients to each group occurred retrospectively and was based on the assignment of the supervising medical doctor. The medical doctor in the experimental group treated his patients according to a recently updated care pathway, while the medical doctor of the control group was rather reluctant to the use of care pathways and provided usual care. So according to each group, patients were supervised by a specific medical doctor, cared for by specific team, and hospitalised on a specific ward. The wards on which the patients of the experimental and control group were hospitalised were located next to each other. Samples in the four studies varied from 20 to 94 patients per sample.

Data collection occurred prospectively for all four pathway care groups and for two usual care groups in the study of Santamaria et al. (2004) and Celis et al. (2006) [36;37]. In the two other studies, data of usual care patients were gathered retrospectively by reviewing the medical records over the past 12 months [33;34]. With regard to length of stay (LOS), McManus et al. (2005) compared data after pathway implementation (2000–2001) with data over a three-year period before implementation (1996–1998) [33]. The time span between start of pathway implementation and data collection for evaluation was mentioned in three studies, varying from measurements immediately after pathway introduction [33], to five months after the start of the implementation [34]. In Celis et al. (2006) the care pathway was implemented in 2000 and updated in 2003 with regard to evidence based content and coordination of the multidisciplinary team, and the updated pathway was evaluated four months after re-implementation [37].

Celis et al. (2006) and Santamaria et al. (2004) reported baseline patient data in both usual care and pathway care groups [36;37]. McManus et al. (2005) only gathered baseline data in the usual care group [33]; and in the study of Farley (1995) no baseline data were reported [34].

Statistical power was calculated only in the study of Santamaria et al. (2004) (power of 80%) [36]. Differences between outcomes in usual care and pathway care groups were statistically analyzed in three studies [34;36;37].

Table 1. Study characteristics

Author and year	Aim	Design	Setting and studied period	Sample
Farley (1995) [34]	To evaluate the impact of a care pathway for COPD exacerbation on <i>performance of care processes and clinical outcomes</i>	Pre-post test design	<i>Setting:</i> University hospital, Vermont, USA; 560 beds <i>Studied period:</i> 1993-1994	<i>Usual care:</i> n=30 <i>Pathway care:</i> n=20
Santamaria et al. (2004) [36]	To evaluate the impact of a care pathway for COPD exacerbation on <i>clinical outcomes</i>	Pre-post test design	<i>Setting:</i> University hospital, Melbourne, Australia; 390 beds <i>Studied period:</i> 2000-2001	<i>Usual care:</i> n=90 <i>Pathway care:</i> n=88
McManus et al. (2005) [33] Marley (2000) [35]	To evaluate the impact of a care pathway for COPD exacerbation on <i>performance of care processes and clinical outcomes</i>	Pre-post test design	<i>Setting:</i> University hospital, Belfast, Northern Ireland; 240 beds <i>Studied period:</i> 2000-2001	<i>Usual care:</i> not specified <i>Pathway care:</i> n=85
Celis et al. (2006) [37]	To evaluate the impact of a care pathway for COPD exacerbation on <i>performance of care processes and clinical outcomes</i>	Non randomized controlled trial	<i>Setting:</i> University hospital, Leuven, Belgium, 1950 beds <i>Studied period:</i> 2004	<i>Usual care:</i> n=94 <i>Pathway care:</i> n=68

Pathway characteristics

The reported objectives of implementing the care pathway were focused on optimizing processes and clinical outcomes, namely: “delivering evidence-based care” [33;35;37], “improving care” [33;34], “reducing variability” [34], “maximizing the effective use of resources” [36;37], “reducing length of stay and readmission” [33;37], “reducing mortality” [33], and “improving patient understanding and degree of self-control” [36].

In all four studies, a multidisciplinary team was involved in the development and implementation process, and included the following disciplines: medical doctors, nurses physiotherapists, dieticians, occupational therapists, and social workers (Table 2). Two studies, Celis et al. (2006) and Marley (2000) reported the involvement of a clinical nurse specialist COPD, responsible for coordination of the multidisciplinary team, follow-up of patient inclusion and performance of processes, measurement of outcomes, and education of the multidisciplinary team regarding the care pathway [37;38].

As main characteristics of the implementation process, three studies [33;35;37] reported an audit of actual performance of care, reviewing of evidence, piloting of the pathway in

subsets of patients, and education of hospital staff. None of this was addressed in the study of [36].

Finally, two studies reported involvement of a hospital leader, namely the nurse manager [34], and the head of the respiratory department [37]. The development of the care pathway of McManus et al. (2005) was described in detail in the paper of Marley (2000) [33;35].

With regard to the pathway components and performance, all four pathways included an explicit statement of goals and key elements, and focused on a well-defined group of patients during a well-defined period (Table 2). The four care pathways included key interventions on diagnosis, pharmacological treatment, and non-pharmacological management, according to evidence-based clinical practice guidelines [16-18;39-41]. Furthermore, the four care pathways were multidisciplinary structured care plans, outlining time-specific clinical interventions and responsibilities by discipline [33;34;36;37]. With regard to monitoring and documentation of variances in care and outcomes, Santamaria et al. (2004) mentioned variance tracking and remedial action if a specific intervention was not completed or a timeframe was exceeded [36]. Farley (1995) reported on a semi-automated system of data collection and reporting, in which both compliance to key interventions and documentation was followed up. Finally, none of the studies reported on the identification of appropriate resources [34].

Table 2. Pathway characteristics

	Farley (1995) [34]	Santamaria et al. (2004) [36]	McManus et al. (2005) [33]	Celis et al. (2006) [37]
<i>Development and implementation of the care pathway:</i>				
• Multidisciplinary team	X	X	X	X
• Evaluation and analysis of the current care process	X		X	X
• Evaluation of medical evidence and external practices	X		X	X
• Establishment of preliminary goals and measurable outcomes	X	X	X	X
• Involvement and strong support from hospital leaders	X			X
• Piloting of the care pathway in subsets of patients	X		X	X
• Education of hospital staff	X		X	X
<i>Care pathway components and performance:</i>				
• Aimed for a well-defined group of patients	X	X	X	X

• Aimed for a well-defined period	X	X	X	X
• Multidisciplinary team	X	X	X	X
• An explicit statement of the goals and key elements of care	X	X	X	X
• The care pathway outlines time specific clinical interventions on day to day basis and nominates responsibilities by discipline	X	X	X	X
• Documentation, monitoring, and evaluation of variances and outcomes	X	X		
• Identification of the appropriate resources				

Pathway indicators

The indicators used to evaluate the care pathways included process, outcome, and team indicators (Table 3). Process indicators were followed up in the studies of Farley (1995) (n = 11 process indicators), McManus et al. (2005) (n = 1 process indicator) and Celis et al. (2006) (n = 4 process indicators) [33;34;37]. Six process indicators focused on diagnostics, three on pharmacological treatment, and five on non-pharmacological interventions.

Most commonly used outcome indicators included LOS, readmission, and in-hospital death [33-37]. Team indicators were only explored in McManus et al. (2005), including effect of the care pathway on multidisciplinary communication, staff satisfaction, and ongoing education [33].

Table 3. Pathway indicators

	Farley, 1995 [34]	Santamaria et al. (2004) [36]	McManus et al. (2005) [33]	Celis et al. (2006) [37]
Process indicators:				
• Arterial blood gas measurement	X			X
• Performance of chest radiography	X			X
• Lung function tests				X
• Daily weight measurement when ordered	X			
• Blood sampling	X			
• Oxygen saturation measurement	X			
• Prescription of steroids	X			
• Prescription of antibiotics	X			
• Use of air driven nebulizer				
• Social work consult	X			
• Physiotherapist consult within 24 hours of admission	X			
• Nutrition consult within 48 hours	X			
• Discharge plan documented within 48 hours of admission	X			

• Referral to rehabilitation				X
Outcome indicators:				
• Length of stay	X	X	X	X
• Readmission	X	X	X	X
• In-hospital mortality		X	X	
• Charges per case	X			
• Oxygen saturation		X		
• Dyspnoea score		X		
• Peak flow		X		
• Anxiety score		X		
• Complications rate		X		
Team indicators:				
• Multidisciplinary communication and care planning			X	
• Staff satisfaction			X	
• Communication with the primary care team			X	
• Facilitation of staff training and education			X	

Baseline variables

Comparison of the baseline data between the usual care and pathway care group was performed in [36;37]. Baseline characteristics in both groups were highly comparable, with the following data being measured: age, gender [36;37], BMI, COPD severity [37], saturation, pulse rate, respiratory rate, peak flow, dyspnea, anxiety, number of comorbidities, and presence of cough [36].

Process indicators

With regard to diagnostic processes, a significant increase of 47% was found for “blood sampling” (23% vs. 70%; $p = 0.01$) [34] (Table 4). Farley (1995) also reported a large improvement of 28% for “daily weight measurement when ordered” (47% vs. 75%; $p = 0.05$) and “performance of arterial blood gases” (63% vs. 90%; $p = 0.05$), but results were not found to be significant [34]. Finally, Celis et al. (2006) assessed the number of diagnostic tests performed per patient [37]. They reported a smaller number of chest X-rays performed per patient (4.6 vs. 3.3; $p = 0.05$) and a significant smaller number of arterial blood gas measurements per patient (9.2 vs. 3.5; $p < 0.05$) in the care pathway patients. On the other hand, a considerable higher number of lung function tests per patient was performed in the pathway group (3.1 vs. 7.4; $p = 0.05$). Also, 22 of 94 patients in the control group (23.4%) did not perform any lung function test, while all patients in the experimental group at least performed two lung function tests during hospitalisation [37].

With regard to pharmacological management, A 17-fold increase in the use of air-driven nebulizers was reported in the study of McManus et al. (2005), yet no detailed data on the shift of oxygen driven to air-driven nebulizers were reported [33].

Finally, one significant improvement for non pharmacological management was found, namely an increase of more than 25% with regard to inclusion of patients in a rehabilitation program (8.8% vs. 25.3%; $p < 0.05$) [37].

McManus et al. (2005) and Marley (2000) also mentioned overall improvements in the performance of care processes in terms of “improved clinical audit reporting and interpretation,” “care exceeding existing quality standards,” “more structured approached to care,” “reduced undesirable practice variation,” “identification of shortfalls in current practice,” and “development of a drugs/oxygen protocol.” However, no numeric data on these findings were reported [33;35].

Clinical outcomes

With regard to clinical outcomes, significant improvements were found for LOS and interval before readmission [37], and for feelings of anxiety (Table 4) [36].

Mean LOS was measured in all four studies (Table 4). In the three pre–post test studies, LOS before implementation differed considerably in the three studies, ranging from 6.5 and 7.6 days [34;36], to 9.4 days [33]. LOS after pathway implementation was highly comparable in the three studies, with a reduction in LOS of less than a day in Santamaria et al. (2004) (7.60 vs. 6.71 days) to 4 days in McManus et al. (2005) (9.4 vs. 5.5 days) [33;36]. In Farley (1995), LOS increased by half a day (6.5–7.1 days) [34]. However, LOS results were not statistically significant [36] or not statistically tested [33;34]. Moreover, in McManus et al. (2005) LOS in usual care was calculated over the three-year period before implementation of the pathway [33]. In comparison with the three pre–posttest studies, Celis et al. (2006) reported a considerable higher mean LOS in both pathway care group and usual care group (10.2 vs. 13.2), however the pathway group had a significant shorter LOS of three days ($p = 0.03$) [37].

Thirty-day readmission was measured in Santamaria et al. (2004) and McManus et al. (2005), and showed a considerable difference between both studies before implementation (19% vs. 12%, respectively) (Table 4) [33;36]. After pathway implementation 30-day readmission decreased by 4% in both studies, varying from 15% [36] to 8% [33], although results were not statistically confirmed. Celis et al. (2006) measured readmission rate within one year and found a considerable higher readmission rate in the care pathway group compared to the control group (45.6% vs. 35.1%; $p > 0.05$), however results were not statistically significant. On the other hand, interval before readmission was significantly larger in the pathway group compared to the control group (160.8 vs. 94.4 days; $p = 0.029$) [37].

Anxiety was scored on a 100 mm Visual Analogue Scale (VAS), with “0” meaning “feeling calm” and “100” meaning “feeling panic.” A significant improvement of 4.5 units was found after pathway implementation [36].

Two studies addressed in-hospital mortality (Table 4) [33;36]. Santamaria et al. (2004) reported a 1% decrease in in-hospital deaths in the care pathway group (10% vs. 9%), however this result was not statistically analyzed [36]. McManus et al. (2005) presented a decrease of 57%, though no data on the number of in-hospital deaths were provided [33].

Finally, the standard care group in Santamaria et al. (2004) had numerically more complications than the pathway group (19 vs. 13), however this difference was not found to be significant (Table 4) [36]. Other outcomes of oxygen saturation and dyspnea-score assessed in Santamaria et al. (2004) showed no relevant differences after pathway implementation [36].

Team outcomes

Team outcomes were only reported by McManus et al. (2005) [33]. Improvement in team functioning was reported in terms of “improved multidisciplinary communication and care planning,” “improved staff satisfaction,” “facilitation of staff training and education,” and “improved communication with the primary care team,” though no details on measurements of these team outcomes were mentioned [33;35].

Table 4. Outcomes in usual care group versus pathway care group

	Usual care	Pathway care	
Farley (1995) [34]:	n=30	n=20	p
• Mean length of stay, days	6.5	7.1	/
• Number of patients in which LOS > 6 days, n (%)	14 (46.6)	7 (35.0)	/
• Number of patients in which:			
○ Daily weight was measured when ordered, n (%)	14 (46.6)	15 (75.0)	0.05
○ Chest radiography was performed, n (%)	24 (80.0)	17 (85.0)	/
○ Arterial blood gases within first 24 hours were measured, n (%)	19 (63.3)	18 (90.0)	0.05
○ Albumin/nutrition profile was obtained, n (%)	7 (23.3)	14 (70.0)	0.01
○ Standing orders were used, n (%)	/	15 (75.0)	/
○ Oxygen saturations were obtained every 4 hours, n (%)	/	12 (60.0)	/
Santamaria et al. (2004) [36]:	n=90	n=88	p
• Mean length of stay, days (SD)	7.6 (7.0)	6.7 (4.3)	0.15
• In-hospital mortality, n (%)	9 (10.0)	8 (9.1)	/
• Readmission within 30 days, n (%)	19 (21.1)	15 (17)	0.24

• Number of patients who developed complications, n (%)	11 (12.2)	4 (4.5)	/
• Mean dyspnoea score on 100 mm Visual Analogue Scale (SD) ^a	2.2 (1.7)	1.8 (1.0)	0.11
• Mean anxiety score, score on 100 mm Visual Analog Scale (SD) ^b	14.2 (1.4)	9.7 (0.8)	0.02
• Mean oxygen saturation, % (SD)	94.2 (22.7)	94.3 (19.8)	0.65
McManus et al. (2005) [33]:	Usual care n=not specified	Pathway care n=85	p
• Mean length of stay, days	9.4 ^c	5.5	/
• In-hospital mortality	/	Reduction of 57%	/
• Readmission within 30 days, n (%)	n (12.0) ^d	7 (8.2)	/
• Use of air driven nebulizers	/	17 fold increase	/
Celis et al. (2006) [37]	Usual care n=94	Pathway care n=68	
• Mean Length of stay, days (SD)	13.2 (12.7)	10.2 (3.9)	0.04
• Readmission rate within one year, n (%)	33 (35.1)	31 (45.6)	>0.05
• Interval before readmission, days (SD)	94.4 (95.2)	160.8 (117.8)	0.03
• Referred to a rehabilitation program, n (%)	8 (8.5)	17 (25.0)	<0.05
• Mean number of times processes were performed per patient:			
○ Chest X-ray was performed, n	4.6	2.3	0.05
○ Arterial blood gases were performed, n	9.2	3.5	<0.05
○ Lung function tests were performed, n	3.1	7.4	0.05

^a Scoring Visual Analogue Scale: 0 = no shortness of breath; 100 = worst shortness of breath ever experienced

^b 0 = feel calm; 100 = feeling panic; ^c Calculated over a three-year period 1996-1998; ^d n = not specified

Discussion

COPD exacerbation is worldwide a leading cause of hospital admission. However, care for patients hospitalised with COPD exacerbation is suboptimal according to recommendations of international guidelines, and outcomes during and after hospitalisation are poor and vary highly. These findings indicate the critical need for standardization and optimisation of the care processes for patients hospitalised with COPD exacerbation. Care pathways are known to improve care processes and to optimize outcomes. A literature search on care pathways for in-hospital management of COPD exacerbation revealed only four studies, of which three studies with a pre–post design, and one randomized controlled trial. The four studied care pathways were multidisciplinary-structured care plans, outlining time-specific clinical

interventions and responsibilities by discipline. The studies showed positive effects on blood sampling, daily weight measurement, arterial blood gas measurement, feelings of anxiety, LOS, readmission, and in-hospital mortality.

Methodological quality of the studies

The methodological quality of the included studies was weak for several reasons. Firstly, the design of the studies needs to be discussed. Three of the four studies used a pre–post design, comparing an experimental group in which a care pathway was implemented with a historical control group. This design leads to limited internal validity of the results due to the following reasons. (I) History: Outcomes could have been caused by an historical event, and were possibly not related to the intervention; for instance, financial incentives to reduce LOS. (II) Maturation or effect of time: Because of organisational and management evolutions, the same outcomes could have been achieved without implementing a pathway. (III) Testing or effect of measuring: Performing the pretest could have made the multidisciplinary COPD care team more aware of bottlenecks in the care for COPD patients, and consequently could have made them change their care irrespective of the implementation of a pathway. (IV) The Hawthorne-effect or effect of attention due to the project: Performance of care processes could have been improved because of the attention of the project, not because of the implementation of the care pathway itself [42-44]. In the fourth study of [Celis et al. \(2006\)](#), patients out of a single organisation were assigned to an experimental group where care was provided according to a care pathway, and a control group where usual care was delivered [37]. Assignment did not occur randomly, but was based on assignment to a specific medical doctor. The lack of randomization could lead to incomparable groups which could compromise internal validity of results, however in this study baseline characteristics of age, gender, COPD severity and BMI were highly comparable. The design of [Celis et al. \(2006\)](#) [37] also carries an important risk for contamination of the control group, because the multidisciplinary team and the patients in the pathway group might affect the team and the patients in the control group by sharing information and experiences about the treatment [45]. Finally, the four included trials, all conducted in a single organisation, include the risk for selection bias. When evaluating a complex intervention in a single organisation, with its specific context like the coordination of the care process, the multidisciplinary team and the specific types of patients, it is difficult or even impossible to ascertain whether the results are dependent of the context under study or whether they are generalizable to a wider context [46;47] To overcome these issues and so to appropriately evaluate complex interventions like care pathways, adequately designed research is needed. As described by the medical research council, the golden standard to evaluate complex interventions is a cluster randomized controlled trial (cRCT) [48]. In cRCTs clusters, instead of patients, are

randomized into an intervention and a control group, and outcomes are measured in the patients within those clusters [45].

A second methodologically issue has to do with power calculation and sample size. Power calculation was only performed in the study of Santamaria et al. (2004) [36], and sample sizes in the four studies were small, especially in Farley (1995) (Table 1) [34]. Also, Farley (1995) and Celis et al. (2006) reported considerably unequal sample sizes in experimental and control groups (Table 1), and therefore power of the statistical t-tests is limited [34;37]. Finally, statistical analyses were limited calculated in three of the four studies [34;36].

Thirdly, comparison of baseline patient characteristics was only performed in the study of Celis et al. (2006) and Santamaria et al. (2004) [36;37]. This implies that improvement in outcomes in the studies of Farley (1995) and McManus et al. (2005) are possibly the result of better patient characteristics in the post-test instead of being related to the pathway implementation [33;34].

Finally time span between start of pathway implementation and evaluation varied from measurements immediately after pathway introduction [33] to five months after the start of the implementation [34]. The first months after implementation certain key elements of care and organisational aspects may need refinement or adjustment. To obtain stable and valid results, it is strongly recommended to start a first thoroughly evaluation no earlier than two or three months after pathway implementation [32].

Pathway characteristics

The care pathways of Celis et al. (2006) [37], Farley (1995) [34] and McManus et al. (2005) [33] were well described with regard to objectives, development, implementation, and characteristics (Table 2), and correspond very well with the care pathway criteria addressed in the definition of E-P-A [27] and in the review of Harkleroad et al. (2000) [32]. In contrast, the pathway of Santamaria et al. (2004) was incompletely described in several aspects (Table 2) [36], which makes it difficult to appraise the quality of the intervention, especially with regard to the evidence-based level of the pathway intervention, focus on bottlenecks in actual care, feasibility of the pathway in clinical practice, and knowledge level of the multidisciplinary care team. Importantly, education of the team needs to include information on the pathway content and process, but also justification on the implementation of the care pathway, in order to encourage team motivation and adherence to the key interventions of the care pathway [32]. Also, only two studies reported involvement of a hospital leader [34;37], and none of the studies addressed identification and utilization of resources like staffing or electronic support, even though both support of hospital leaders and availability of

appropriate resources are important conditions for successful implementation and performance of the pathway [32].

Pathway indicators

The four studies mostly addressed outcome indicators (Table 3). Farley (1995) indeed also reported on ten process indicators, but results for only five indicators were very limitedly displayed and discussed (Table 4) [34]. Finally, McManus et al. (2005) also mentioned improved team outcomes but did not detail any results [33;35].

Care pathways are defined by the European Pathway Association as complex interventions comprising active components, such as evidence-based key interventions, feedback on actual performance, and development and implementation strategies [27;49]. Furthermore, context of the organisation (e.g., type of hospital, availability of resources) and the involved multidisciplinary team will influence the effect of the care pathway [50-53]. Therefore, to fully understand the achieved outcomes after implementation of a care pathway, also knowledge on performance of care processes, organisational context, and team working is essential [50]. Consequently, next to outcome indicators, also process indicators, team indicators and variables on organisational context should be measured in research on the impact of complex interventions like care pathways [50;51].

Pathway outcomes

Although the studies mentioned the follow-up of a considerable number of indicators (Table 3), outcomes of these indicators were scarcely reported (Table 4). Also, because of the use of divergent indicators in the four studies, meta-analysis of the results was not possible.

With regard to process outcomes, a clinically important improvement of 30–47% in the care pathway group was reported for daily weight measurement, arterial blood gas measurement, blood sampling and inclusion in a rehabilitation program, although only the two last results were reported significant (Table 4). However, performance of these care processes was still suboptimal, especially with regard to referral to rehabilitation. Interestingly, Celis et al. (2006) focused on the number of times a particular process was performed per patient [37]. The results showed a lower number of ABG measurements and a lower number of chest X-ray performances per patient in the care pathway group, suggesting a reduction of unnecessary diagnostic tests in patients by implementing a care pathway. On the other hand, in the care pathway group more lung function tests were performed per patient in comparison with the control group (Table 4). Whether this finding indicates a positive or negative result is disputable, since existing guidelines are divergent regarding benefit of performing spirometry tests in acute exacerbated patients [16-18]. However, it is

certainly questionable if it is necessary to perform so many lung function tests per patient (mean number of seven tests per patient) during hospitalisation for exacerbation.

Concerning clinical outcomes, 30-day readmission rate, interval before readmission, in-hospital death, and mean LOS improved after implementation of the pathway (Table 4) [33;36;37], however only one result, interval before readmission, was found significant. In Farley (1995), LOS increased by almost a day after implementation of the care pathway; however, this result was not statistically confirmed [34]. Only feelings of anxiety were found to significantly improve after pathway implementation, but a very little and so not clinically relevant change on the 100 mm VAS was found [36]. Moreover, the study did not mention on what hospitalisation day and at what time anxiety was measured in both groups. Results of anxiety analogue scales fluctuate over time [54], so it is unclear if this is a valid comparison of anxiety scores between the pre- and posttest group.

Finally, team outcomes reported by McManus et al. (2005) [33] seem reasonable, as one of the characteristics of a care pathway is “coordination of the roles and sequencing of the activities of the multidisciplinary care team, patients and their relatives” [27]. However, due to lack of measuring details these outcomes cannot be verified.

Overall, the weak methodology and limited reporting of pathway outcomes put a serious threat on the internal validity of the results. In addition, three of the four studies were performed 10 years ago or even earlier [33;34;36], which makes the results less applicable for current COPD health care.

Additional literature search

The findings of the additional search for unpublished information, including an interesting unpublished study [37] and several blueprints of COPD care pathways, indicate that probably hundreds of care pathways for COPD have been developed, but like many quality projects, they not have been evaluated and published. To further understand why and when pathways work, publications on project reports and evaluations of COPD pathways must be supported.

Conclusions

COPD patients hospitalised with exacerbation are a high volume, a high cost and high risk population, and actual care for these patients has shown to be very suboptimal. Therefore this literature review on the impact of care pathways on COPD processes and outcomes is relevant for all health care professionals caring for COPD patients. Next to that, a comprehensive discussion on evaluation of complex interventions like care pathways is included in this review.

The four studies included in the review described few positive effects of the care pathways on diagnostic processes and on clinical outcomes, though due to limited statistical analysis and weak design of the studies, the internal validity of the results is limited. Furthermore, limited data and use of different indicators in the four studies make meta-analysis of results impossible. Therefore, based on current research, accurate conclusions on the impact of COPD exacerbation care pathways cannot be drawn. These findings indicate the need for appropriately designed research like a cluster randomized controlled trial to study the impact of COPD exacerbation pathways.

In 2009 the European Pathway Association launched the European Quality of Care Pathways study (EQCP study) [55;56]. The EQCP study is an international clustered randomized controlled trial, with the aim to measure the impact of care pathways on compliance to care processes and performance of clinical outcomes in patients hospitalised with a COPD exacerbation. An evidence-based set of process and outcome indicators will be followed up in organisations in which a pathway was implemented compared to organisations in which usual care is provided. Additionally, multidisciplinary teamwork and organisational context will be assessed using a set of evidence based team indicators and organisational variables [27;55;57].

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Chapter 4:

Quality indicators for in-hospital management of exacerbation of chronic obstructive pulmonary disease: results of an international Delphi study

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Abstract

Background. Management of patients hospitalized with exacerbation of chronic obstructive pulmonary disease is suboptimal and outcomes are poor. To evaluate the impact of care pathways properly, relevant indicators need to be selected.

Objective. To report a Delphi study that was conducted to select process and outcome indicators that are relevant to study quality of care and impact of care pathways for patients hospitalized with exacerbation of chronic obstructive pulmonary disease.

Methods. The study was conducted over 4 months in 2008, with 35 experts out of 15 countries, including 19 medical doctors, 8 nurses and 8 physiotherapists. Participants were asked to rate, for 72 process and 21 outcome indicators, the relevance for follow-up in care pathways for in-hospital management of exacerbation of chronic obstructive pulmonary disease. Consensus (agreement by at least 75% of the participants) that an indicator is relevant for follow-up was sought in two rounds.

Results. Consensus was reached for 26 of 72 process indicators (36.1%) and 10 of 21 outcome indicators (47.6%). Highest consensus levels were found for the process indicators regarding oxygen therapy (100%), pulmonary rehabilitation (100%) and patient education (94.5–88.6%) and for the outcome indicators concerning understanding of therapy (91.4–85.7%) and self-management (88.6–88.2%).

Conclusions. The selected indicators appear to be sensitive for improvement. Therefore, researchers and clinicians that want to study and improve the care for patients hospitalized with exacerbation of chronic obstructive pulmonary disease should primarily focus on these indicators.

Introduction

Chronic obstructive pulmonary disease (COPD) is a disease state characterized by airflow limitation that is not fully reversible [1]. Worldwide, the disease affects 9.8% of men and 5.6% of women [2] and is a leading cause of morbidity and mortality [3].

Patients with COPD experience frequent exacerbations of symptoms, varying from 0.5–3.5 a year [4-6]. COPD exacerbations are characterized by a change in baseline dyspnoea, cough and/or sputum that is beyond normal day-to-day variations; is acute in onset; and may warrant additional treatment in a patient with underlying COPD [7]. COPD exacerbations contribute tremendously to the disease burden. They are a leading cause of hospital admission worldwide, with 35% of COPD patients having at least one admission a year and up to 40% of admitted patients having two or more readmissions a year [5;8;9].

Studies about in-hospital management of COPD exacerbations have shown suboptimal performance of care activities recommended by worldwide accepted guidelines, especially for arterial blood gas measurement, administration of corticosteroids, smoking cessation, patient education and referral to pulmonary rehabilitation [10-12]. Similarly, studies about outcomes in patients hospitalized due to a COPD exacerbation have demonstrated poor and varying outcomes, especially for 6-month readmission (30–43%) [13-15]; 30-day mortality (5.2–17.2%) [16]; and 1-year mortality (23–37%) [14;15].

A possible strategy to optimize care processes and to improve outcomes is the implementation of a care pathway, also known as critical pathway or clinical pathway [17-20]. Care pathways are ‘complex interventions for the multidisciplinary decision-making and organization of predictable care for a well-defined group of patients during a well-defined period, with the aim to enhance the quality of care across the continuum by improving risk-adjusted patient outcomes, promoting patient safety, increasing patient satisfaction and optimizing the use of resources’ [21].

Although care pathways are used worldwide [22-25], the effectiveness of care pathways for in-hospital management of COPD exacerbation is not known. A recent literature review on care pathways for COPD exacerbation revealed only four studies [26]. Three studies used a pre-posttest design; the fourth study was a non-randomized controlled trial comparing an experimental group where patients were treated according to a care pathway with a control group where usual care was provided. The studies described few positive effects of the care pathways on diagnostic processes and on clinical outcomes. Although, due to follow-up of very few and diverse indicators, limited statistical analysis and weak design of the studies, the internal validity of results is limited and so reliable conclusions could not be drawn [26]. Therefore, appropriately designed research like a cluster randomized controlled trial is needed to evaluate the impact of COPD care pathways on performance of care processes and clinical outcomes ([27;28]. To study quality of care and impact of care pathways for

patients hospitalized with COPD exacerbation appropriately, a valid and feasible set of process and outcome indicators needs to be defined [29-31].

Methods

Objective

The aim of this Delphi study was to select process and outcome indicators that are relevant to study quality of care and impact of care pathways for patients hospitalized with COPD exacerbation.

Design

To select relevant process and outcome indicators, the Delphi consensus method was used. This method, which rigorously solicits and synthesizes expert opinion, is recommended in areas of knowledge where methodologically rigorous research evidence is limited and experts disagree on its interpretation. The Delphi method is a group facilitation technique designed to transform individual opinions into group consensus and includes two or more postal rounds of questionnaires. With this technique, a large group of experts can be consulted from a geographically dispersed population [29;32;33]. In this Delphi survey, consensus on relevance of indicators for follow-up in care pathways for COPD exacerbation was sought in two rounds of questionnaires (Figure 1)

Participants

The objective was to generate an international and multidisciplinary Delphi panel of medical doctors, nurses and physiotherapists [32;33]. Selection of the participants occurred by purpose sampling and was performed by a medical doctor, a clinical nurse specialist and a physiotherapist with internationally recognized experience and networking in COPD care.

For the selection of the medical doctors, members of the committee of the Global Initiative for Chronic Obstructive Lung Disease and the authors who contributed to the European Respiratory Monograph booklet regarding management of COPD were contacted [1;34]. The nursing group and the physiotherapists were selected by contacting the allied respiratory professionals, assembly representatives of respective nurses and physiotherapists of the European Respiratory Society (<http://www.ersnet.org>). Finally, the first authors of the trials included in the reviews about 'adherence to international guidelines' [12] and about 'Impact of COPD care pathways' [26] were contacted.

To avoid major influence of organizational factors such as professional culture and clinical practice in organizations, we included for each of the three disciplines the criterion

that experts from the same country had to be affiliated with different organizations. Also, the authors of this article were not part of the expert panel.

Figure 1. The Delphi Survey

Delphi questionnaire and rating

To develop a Delphi questionnaire including all possible process and outcome indicators for in-hospital management The objective was to generate an international and multidisciplinary Delphi panel of medical doctors, nurses and of COPD exacerbations, an extensive literature review was conducted by the first author. The following resources were explored: (i) Websites of international respiratory societies: American Thoracic Society (ATS), British Thoracic Society (BTS), European Respiratory Society (ERS), Global Strategy for Diagnosis, Management and Prevention of COPD (GOLD), National Institute for Health and Clinical Excellence (NICE) and (ii) Electronic databases: Medline, EMBASE, Cochrane library, CINAHL. The following search terms were used: COPD, disease exacerbation, management, patient care management, practice guideline and outcomes. Applied limits included: published between 2003–2008; written in English, French, German, Italian or Dutch; and (iii) Map of Medicine (<http://www.mapofmedicine.com>). A two level screening of the publications was applied. Firstly, publications were assessed on relevance based on review of the title

and abstract. Subsequently, the full text of the selected guidelines, reviews or process flows were reviewed. Following inclusion criteria were applied: (i) description of management or outcomes of patients hospitalized with COPD exacerbation; (ii) process indicators: evidence was reported in terms of guidelines, reviews or process flows; (iii) published between 2003–2008; (iv) published in English, French, German; Italian or Dutch; and (v) possible to assess strength of recommendations and the quality of the evidence.

As result five clinical practice guidelines [1;34-37]; two process flows (Map of Medicine, 2009 721 /id; Map of Medicine, 2009 721 /id); and 12 outcome studies were included [8;9;15;38-42]. Based on the selected literature, 72 process and 21 outcome indicators were identified.

The Delphi questionnaire, based on the literature search, included three main parts: 72 process indicators; 21 outcome indicators; and 9 demographic questions (city, country, name and type of organization, number of beds, professional group, years of experience, age and gender) (see appendix 1). The provisional Delphi questionnaire was pretested by a medical doctor, a nurse and a physiotherapist. These experts did not participate in the expert panel. Based on their feedback, the questionnaire was adapted where needed and a final version was constructed for surveying the expert panel.

For the first part with the 72 process indicators, experts were asked to rate, on a 6-point scale, what impact they believe that the listed processes have on clinical outcomes and therefore how relevant they believe that these process indicators are for follow-up in studies investigating quality of in-hospital management of COPD exacerbation. Score '1' meant 'low impact on outcomes and thus not relevant,' and score '6' meant 'high impact on outcomes and thus highly relevant.' For the second part with the 21 outcome indicators, experts were asked to rate, on a 6-point scale, how sensitive to change they believe the listed outcome indicators would be when implementing a COPD care pathway and therefore how relevant they believe that these outcome indicators are for follow-up in studies investigating quality of in-hospital management of COPD exacerbations. Score '1' meant 'low sensitive to change and thus not relevant,' and score '6' meant 'high sensitive to change and so highly relevant.' A 6-point rating scale was used to avoid a tendency to score 'in the middle' [43]. Panellists were also offered the opportunity to suggest additional process and outcome indicators, or other remarks concerning the Delphi questionnaire.

Content validity index and consensus

The content validity index (CVI) refers to the proportion of experts who are in agreement about content validity and thus relevance of a specific item [44]. In this study, CVI for a specific indicator refers to that proportion of experts that scored 5 or 6 for that indicator. A CVI of 75% or higher in round 2 was considered to be consensus by the panel that an

indicator is relevant for follow-up in COPD exacerbation care pathways [32]. This cut-off point was defined at the outset of the study.

Delphi survey

The Delphi survey was conducted by electronic mail between September 2008–December 2008 [32]. At the outset of the study, it was decided that the Delphi survey would include two rounds of responses (Figure 1) [32;33]. Invitation for participation in the Delphi study, together with explanation about the aim of the study and the Delphi procedure was included in the mailing of round 1 [32]. Also, as background information, the GOLD guidelines were included. These are evidence-based guidelines for COPD diagnosis, management and prevention, developed by GOLD (2009). For each mailing round, panellists were asked to return the completed datasheets in 2 weeks. Confidentiality was guaranteed in this way that respondents will be known to the researcher and even to one another, but their judgments and opinions remain strictly confidential [45].

For the first round, according to each discipline, the panelists were contacted by three recognized leaders of the European Respiratory Society (ERS) (<http://www.ersnet.org>), namely the vice president (MD), the secretary of the ERS assembly group ‘Physiotherapists’ and the chair of the ERS assembly group ‘Nurses’. We believed this mailing strategy would increase the response rate [32;33]. The mailing for round 2 was sent by the main researcher (CL). A reminder was sent 1 month after the initial mailing [32].

In the first round, the panellists were asked to rate the relevance of each process and outcome indicator and to provide the demographic information. In round 2, feedback on the round 1 responses was provided to all panellists, presented by following summary statistics: number of respondents who answered the questionnaire; number of respondents who rated 1 or 2, 3 or 4 and 5 or 6 (percentage); central tendencies (median, mode); and the respondent’s own responses [32;33]. Using this information, respondents were asked to re-rate the indicators in case they wanted to change their previous answer. Experts were also asked to rate the process and outcome indicators suggested by the respondents in round 1. The results of round 2 were considered as the final results of the Delphi survey. If participants of round 1 did not respond in round 2, their answers of round 1 were considered as final answers.

In a final and third mailing, feedback on the final group results was provided. This included a final list of all process and outcome indicators for which consensus ($CVI \geq 75\%$) was obtained, or in other words, all the indicators that were rated 5 or 6 by at least 75% of the panellists in round 2. Also an overview of the involved experts was provided. Ethical considerations

The research protocol was approved by the research ethics committee at Leuven University (identifier: ML5617). Consent to participation was considered to be present when the participant returned the questionnaire. To inform potential participants in a proper manner, we provided one sheet with explanation and aim of the study, their involvement in it, how the Delphi works and what was expected of them. Finally, to respect privacy of each participant, it was guaranteed to the panellists that their judgments and opinions would remain strictly confidential [45].

Data analysis

Results were analysed and presented in two ways: results obtained by the overall panel and results obtained per discipline. Descriptive statistics were used to report the expert panel responses. To assess the differences in CVIs between the three disciplines, P values from the Kruskal–Wallis exact test were calculated. Two-tailed tests were used and P values were considered statistically significant if $P < 0.05$. If important differences were found, a post hoc Mann–Whitney U-test was performed to assess which pairs of groups had important differences. Finally, to adjust for multiple testing, the Bonferroni correction was used; consequently P values were considered statistically significant if $P < 0.017$. Data were analysed using the statistical software program SPSS version 16.0 [IBM SPSS Statistics 19 International Business Machines Corporation (IBM)., Armonk, NY, USA].

Results

Participant characteristics

In round 1, 35 of 50 contacted experts returned the questionnaire (response rate: 70.0%). The panel included representatives from three continents (Table 1) and 15 countries: Australia (n = 1), Belgium (n = 4), France (n = 2), Germany (n = 2), Greece (n = 1), Ireland (n = 1), Italy (n = 1), Poland (n = 1), Portugal (n = 1), Spain (n = 2), Sweden (n = 1), the Netherlands (n = 2), Turkey (n = 1), UK (n = 11) and USA (n = 4). The respondents included 19 medical doctors (54.3%), 8 nurses (22.9%) and 8 physiotherapists (22.9%). All respondents had at least 5 years of experience in respiratory care, with 77.1% of the experts reporting 15 years or more of experience. Twenty-five panellists (71.4%) were affiliated with academic hospitals and 4 (11.4%) with community teaching hospitals. Other affiliated organizations were respiratory physiotherapy centres (n = 2), primary care trusts (n = 2) and research centres for medical studies (n = 2). The number of beds in the 29 hospitals varied from less than 200 beds (31.0%) to 800 beds and more (27.6%). In round 2, 31 of 35 panellists who participated in round 1 returned the completed questionnaire (response rate:

88.6%), including 17 of 19 medical doctors (89.5%), 6 of 8 nurses (75.0%) and all 8 physiotherapists (100%).

Table 1. Characteristics of the Delphi panel (n=35)

Characteristics	n (%)
Sex	
Male	22 (62.9)
Female	13 (37.1)
Age*	
30-49	14 (40.0)
50-69	19 (54.3)
≥70	1 (2.9)
Discipline	
Medical doctor	19 (54.3)
Nurse	8 (22.9)
Physiotherapist	8 (22.9)
Years of experience in respiratory care*	
5-14	7 (20.0)
15-24	11 (31.4)
25-34	11 (31.4)
≥40	5 (14.3)
Type of institution	
Academic hospital	25 (71.4)
Community teaching hospital	4 (11.4)
Respiratory physiotherapy center	2 (5.7)
Primary care trust	2 (5.7)
Research center for medical studies	2 (5.7)
Number of beds, n (%)†	
< 200	9 (31.0)
200-399	5 (17.2)
400-599	6 (20.7)
600-799	5 (17.2)
≥ 800	8 (27.6)
Continent, n (%)	
Australia	1 (2.9)
Europe	30 (85.7)
North America	4 (11.4)

*n=34 (missing: n=1; 2.9%).

†n=29 hospitals.

Results of the overall panel: process indicators

Experts reached consensus (CVI $\geq$ 75%) for 26 of 72 process indicators (36.1%). Table 2 lists the indicators in descending order of the CVIs. A CVI of 100% was reached for three process indicators: 'controlled oxygen therapy', 'initiation of long-term oxygen therapy (LTOT)', and 'referral to pulmonary rehabilitation'. Also, a CVI of more than 90% was

reached for five other process indicators: 'education about recognition and treatment of exacerbations' (97.1%), 'identification for pulmonary rehabilitation' (94.3%), 'education about inhaler therapy' (94.3%), 'smoking cessation advice when active smoker' (91.4%) and 'treatment of comorbid conditions' (91.4%).

Table 2 also displays the CVIs obtained after round 1. Ten indicators shifted from CVI <75% in round 1 to consensus (CVI $\geq$ 75%) in round 2 (Table 2, nos. 9, 11, 15, 19, 20, 22, 23, 24, 25, 26). Furthermore, for all other indicators, except for 'arterial blood gas measurement at admission' (Table 2, no. 21), CVIs increased from 5–10% in round 2.

Four other process indicators were suggested by participants in round 1: 'glucose control', 'assessment and management of anxiety and depression', 'patient education about coping strategies for possible depression and self-management' and 'monitoring following discharge for at least 2 weeks'. In the second round no consensus was reached for these additional indicators.

Results of the overall panel: outcome indicators

Consensus (CVI $\geq$ 75%) was reached by the overall panel for 10 of 21 outcome indicators (47.6%). Table 2 also lists the outcome indicators in descending order of the CVIs. A CVI of 91.4% was obtained for the indicator 'correct use of inhaler therapy'. Six indicators reached a CVI between 85–89%: 'successful management at home' (88.6%), 'able to cope in usual environment' (88.2%), 'correct use of oral therapy' (85.7%), 'correct use of oxygen therapy' (85.7%), 'interval before next admission' (85.7%) and 'health-related quality of life' (85.7%).

Outcome indicators for which consensus (CVI $\geq$ 75%) was obtained in round 1 were the same in round 2; however, CVIs of 8 of the 10 outcome indicators (80%) increased in round 2 (Table 2). Six additional indicators were suggested by the panellists: 'fat-free mass index (FMI)', 'fatigue', 'functional status', 'type of social support', 'type of follow-up' and 'unplanned use of healthcare system'. No consensus was reached for these extra indicators in the second round.

*Table 2: Content validity indexes of the process indicators for which consensus was reached by the overall panel**

Indicators	Content validity index* ROUND 1 n/n (%)	Content validity index* ROUND 2 n/n (%)
Process indicators:		
1. Controlled oxygen therapy in hypoxemic patients	31/35 (88.6)	35/35 (100)
2. Initiation of long-term oxygen therapy (LTOT) if the patient remains hypoxemic	30/35 (85.7)	35/35 (100)
3. Referral to pulmonary rehabilitation	34/35 (97.1)	35/35 (100)
4. Patient education: Information about recognition and treatment of exacerbations	32/35 (91.4)	34/35 (97.1)
5. Identification for pulmonary rehabilitation	31/35 (88.6)	33/35 (94.3)
6. Patient education: Instruction on how to use inhalers and other treatments	31/35 (88.6)	33/35 (94.3)
7. Smoking cessation advice when active smoker	30/35 (85.7)	32/35 (91.4)
8. Treatment of comorbid conditions	31/35 (88.6)	32/35 (91.4)
9. Medical history before exacerbation: Number of previous exacerbations in the previous year	25/35 (71.4)	31/35 (88.6)
10. Medical history before exacerbation: Pre-existing comorbidities	27/35 (79.4)	31/35 (88.6)
11. Pulse oximetry: Prior to discharge in patients hypoxemic during a COPD exacerbation	26/35 (74.3)	31/35 (88.6)
12. Appropriate prescription of long-acting bronchodilators (B-agonists and/or anticholinergics)	28/35 (80.0)	31/35 (88.6)
13. Antibiotics in patients if indicated	29/35 (82.9)	31/35 (88.6)
14. Patient education: Information about oxygen treatment	27/35 (77.1)	31/35 (88.6)
15. Medical history before exacerbation: Documentation of possible limitation of daily activities	26/35 (74.3)	30/35 (85.7)
16. Appropriate prescription of glucocorticosteroids: Oral or intravenous	25/35 (75.8)	30/35 (85.7)
17. Physiotherapy: Activities of Daily Life	28/35 (80.0)	30/35 (85.7)
18. Assessment of differential diagnosis	28/35 (80.0)	30/35 (85.7)
19. Medical history before exacerbation: Cardiovascular status	24/35 (68.6)	29/35 (82.9)
20. Pulse oximetry at admission	24/35 (68.6)	29/35 (82.9)
21. Arterial blood gas measurement at admission	29/35 (82.9)	29/35 (82.9)
22. Arterial blood gas measurement: Prior to discharge in patients hypoxemic during a COPD exacerbation	24/35 (70.6)	29/35 (82.9)
23. Fluid administration in dehydrated patients	26/35 (74.3)	29/35 (82.9)
24. Assessment of symptoms	23/35 (65.7)	28/35 (80.0)
25. Assessment and management of social situation	26/35 (74.3)	28/35 (80.0)
26. Patient education: Information about the nature of COPD	22/35 (62.9)	28/35 (80.0)
Outcome indicators:		
1. Patient and/or home caregiver fully understands correct use of inhaler	30/35 (85.7)	32/35 (91.4)
2. Patient, family, and physician are confident that the patient can	28/35 (80.0)	31/35 (88.6)

manage successfully at home		
3. Able to cope in usual environment	26/35 (76.5)	30/35 (88.2)
4. Patient and/or home caregiver fully understand correct use of oral therapy	30/35 (85.7)	30/35 (85.7)
5. Patient and/or home caregiver fully understand correct use of inhaler therapy	28/35 (80.0)	30/35 (85.7)
6. Patient and/or home caregiver fully understand correct use of oxygen therapy (LTOT)	27/35 (77.1)	30/35 (85.7)
7. Interval before next admission	26/35 (76.5)	30/35 (85.7)
8. Health-related Quality of Life	24/35 (70.6)	30/35 (85.7)
9. Patient, if previously ambulatory, is able to cope with basic needs in his/her situation	27/35 (77.1)	28/35 (80.0)
10. Mortality within one year after exacerbation	30/35 (85.7)	28/35 (80.0)

*Content validity index (CVI): Proportion of experts scoring 5 or 6 for a specific indicator (score of 5 or 6 means that the indicator is scored as highly relevant for follow-up); Consensus: CVI $\geq$ 75% obtained in round 2.

Results per discipline: process indicators

Medical doctors reached consensus (CVI $\geq$ 75%) for 22 of 72 process indicators (30.6%) and nurses and physiotherapists each for 40 of 72 indicators (55.6%). Table 3 lists all process and outcome indicators for which consensus was reached in each professional group. The indicators are presented in descending order of the CVIs of the medical doctors, because this discipline was mostly represented in the panel (Table 1) and because 39 of 72 scored indicators (54.2%) included strict medical indicators. The Kruskal–Wallis test, performed for all 72 scored process indicators, revealed 12 important differences in CVIs between disciplines, varying from differences of 5% to 70% (Table 3, nos. 5, 8, 14, 22, 24, 26, 33, 38, 40, 42, 43). One important difference was not displayed in the table, namely ‘medical history: documenting frequency and severity of cough,’ as no consensus was reached for this indicator by any of the three disciplines. CVIs for this indicator of medical doctors, nurses and physiotherapists were, respectively, 5.3%, 25.0% and 0.0% ($P = 0.026$).

After Mann–Whitney U-tests with Bonferroni correction, eight important differences in CVIs between disciplines were found (Table 4). These included differences in CVIs of 30–60% between medical doctors and physiotherapists about hydration, nutrition, education and physiotherapy (Table 4, nos. 2, 3, 4 and 5) and a difference of more than 60% between medical doctors and nurses concerning deep venous prophylactics (Table 4, no. 7).

*Table 3: Content validity indexes of process and outcome indicators for which consensus was reached by medical doctors, nurses, and physiotherapists**

	Content validity index*†‡			
	ROUND 2			
	Medical doctors n/n (%)	Nurses n/n (%)	Physio-therapists n/n (%)	P§
Process indicators[†]				
1. Controlled oxygen therapy in hypoxemic patients [‡]	19/19 (100)	8/8 (100)	8/8 (100)	1.000
2. Initiation of long-term oxygen therapy (LTOT) if the patient remains hypoxemic [‡]	19/19 (100)	8/8 (100)	8/8 (100)	0.336
3. Referral to pulmonary rehabilitation [‡]	19/19 (100)	8/8 (100)	8/8 (100)	0.065
4. Treatment of comorbid conditions [‡]	19/19 (100)	6/8 (75.0)	7/8 (87.5)	0.885
5. Patient education: Information about recognition and treatment of exacerbations [‡]	18/19 (94.7)	8/8 (100)	8/8 (100)	0.048
6. Medical history before exacerbation: Number of previous exacerbations in the previous year [‡]	18/19 (94.7)	7/8 (87.5)	6/8 (75.0)	0.128
7. Medical history before exacerbation: Pre-existing comorbidities [‡]	18/19 (94.7)	7/8 (87.5)	6/8 (75.0)	0.803
8. Identification for pulmonary rehabilitation [‡]	17/19 (89.5)	8/8 (100)	8/8 (100)	0.026
9. Patient education: Instruction on how to use inhalers and other treatments [‡]	17/19 (89.5)	8/8 (100)	8/8 (100)	0.170
10. Smoking cessation advice when active smoker [‡]	17/19 (89.5)	7/8 (87.5)	8/8 (100)	0.575
11. Assessment of differential diagnosis [‡]	17/19 (89.5)	7/8 (87.5)	6/8 (75.0)	0.813
12. Medical history before exacerbation: Cardiovascular status [‡]	17/19 (89.5)	6/8 (75.0)	6/8 (75.0)	0.462
13. Appropriate prescription of long-acting bronchodilators (B-agonists and/or anticholinergics) [‡]	16/19 (84.2)	8/8 (100)	7/8 (87.5)	0.463
14. Antibiotics in patients if indicated [‡]	16/19 (84.2)	8/8 (100)	7/8 (87.5)	0.046
15. Patient education: Information about oxygen treatment [‡]	16/19 (84.2)	8/8 (100)	7/8 (87.5)	0.347
16. Appropriate prescription of glucocorticosteroids: Oral or intravenous [‡]	16/19 (84.2)	8/8 (100)	6/8 (75.0)	0.436
17. Pulse oximetry: Prior to discharge in patients hypoxemic during a COPD exacerbation [‡]	15/19 (78.9)	8/8 (100)	8/8 (100)	0.137
18. Arterial blood gas measurement at admission [‡]	15/19 (78.9)	7/8 (87.5)	7/8 (87.5)	0.842
19. Arterial blood gas measurement: Prior to discharge in patients hypoxemic during a COPD exacerbation [‡]	15/19 (78.9)	6/8 (75.0)	8/8 (100)	0.291
20. Assessment and management of social situation [‡]	15/19 (78.9)	6/8 (75.0)	7/8 (87.5)	0.391
21. Pulmonary testing after discharge: Spirometry [‡]	15/19 (78.9)	4/8 (50.0)	6/8 (75.0)	0.357

22. Deep venous thrombosis prophylaxis	15/19 (78.9)	1/8 (12.5)	5/8 (62.5)	0.041
23. Medical history before exacerbation: Documentation of possible limitation of daily activities [‡]	14/19 (73.7)	8/8 (100)	8/8 (100)	0.070
24. Physiotherapy: Activities of Daily Life [‡]	14/19 (73.7)	8/8 (100)	8/8 (100)	0.016
25. Pulse oximetry at admission [‡]	14/19 (73.7)	8/8 (100)	7/8 (87.5)	0.395
26. Fluid administration in dehydrated patients [‡]	14/19 (73.7)	7/8 (87.5)	8/8 (100)	0.019
27. Patient education: Information about the nature of COPD [‡]	14/19 (73.7)	6/8 (75.0)	8/8 (100)	0.571
28. Assessment and management for anxiety and depression	11/16 68.8	4/5 (80.0)	5/6 (83.3)	0.289
29. Assessment of symptoms [‡]	13/19 (68.4)	7/8 (87.5)	8/8 (100)	0.143
30. Smoking status	13/19 (68.4)	7/8 (87.5)	6/8 (75.0)	0.203
31. Pulse oximetry: In the following three months in patients hypoxemic during a COPD exacerbation	13/19 (68.4)	7/8 (87.5)	6/8 (75.0)	0.836
32. Assessment of comorbidities	12/19 (63.2)	6/8 (75.0)	4/8 (50.0)	0.503
33. Physiotherapy: Endurance exercise training	12/19 (63.2)	6/8 (75.0)	7/8 (87.5)	0.023
34. Patient education: self-management plan	10/16 (62.5)	4/5 (80.0)	5/6 (83.3)	0.530
35. Medical history before exacerbation: Present treatment regimen	11/19 (57.9)	7/8 (87.5)	5/8 (62.5)	0.538
36. Pulse oximetry: After discharge in patients with LTOT	11/19 (57.9)	6/8 (75.0)	6/8 (75.0)	0.388
37. Appropriate prescription of short-acting bronchodilators	10/19 (52.6)	6/8 (75.0)	5/8 (62.5)	0.296
38. Patient education: Strategies for minimizing dyspnea	10/19 (52.6)	6/8 (75.0)	8/8 (100)	0.005
39. Referral to dietician in patient with obesity or cachexy	10/19 (52.6)	6/8 (75.0)	7/8 (87.5)	0.515
40. Physiotherapy: Resistance training to improve skeletal muscle strength	9/19 (47.4)	6/8 (75.0)	8/8 (100)	0.003
41. Monitoring following discharge for at least 2 weeks	3/16 (37.5)	4/5 (80.0)	3/6 (50.0)	0.224
42. Supplementary nutrition in patients with BMI>20	7/19 (36.8)	6/8 (75.0)	8/8 (100)	0.001
43. Physiotherapy: Chest physiotherapy	6/19 (31.6)	5/8 (62.5)	8/8 (100)	0.002
Outcome indicators:				
1. Able to cope in usual environment	17/19 (89.5)	7/8 (87.5)	7/8 (87.5)	0.941
2. Patient and/or home caregiver fully understand correct use of inhaler	16/19 (84.2)	8/8 (100)	8/8 (100)	0.158
3. Patient, family, and physician are confident that the patient can manage successfully at home	16/19 (84.2)	7/8 (87.5)	8/8 (100)	0.819
4. Interval before next admission	16/19 (84.2)	7/8 (87.5)	7/8 (87.5)	0.553
5. Patient and/or home caregiver fully understand correct use of oral therapy	15/19 (78.9)	8/8 (100)	7/8 (87.5)	0.107
6. Patient and/or home caregiver fully understand correct use of inhaler therapy	15/19 (78.9)	8/8 (100)	7/8 (87.5)	0.248

7. Patient and/or home caregiver fully understand correct use of oxygen therapy (LTOT)	15/19 (78.9)	8/8 (100)	7/8 (87.5)	0.095
8. Health-related Quality of Life	15/19 (78.9)	8/8 (100)	7/8 (87.5)	0.683
9. Unplanned use of the healthcare system	11/14 (78.6)	2/6 (33.3)	3/6 (50.0)	0.406
10. Mortality within one year after exacerbation	14/19 (73.7)	7/8 (87.5)	7/8 (87.5)	0.690
11. Patient, if previously ambulatory, is able to cope with basic needs in his/her situation	13/19 (68.4)	7/8 (87.5)	8/8 (100)	0.263
12. Patient has been clinically stable for 12-24 hours	13/19 (68.4)	7/8 (87.5)	5/8 (62.5)	0.941
13. Symptoms at rest and during exercise	11/18 (61.1)	5/8 (62.5)	7/8 (87.5)	0.125
14. Patient satisfaction with therapy and care	10/19 (52.6)	6/8 (75.0)	6/8 (75.0)	0.082
15. Patient is able to eat and sleep without frequent awakening by dyspnea	10/19 (52.6)	7/8 (87.5)	7/8 (87.5)	0.144
16. Patient satisfaction with therapy and care	10/19 (52.6)	6/8 (75.0)	6/8 (75.0)	0.082
17. Patient's perception of coordination between hospital and home health care	9/19 (47.4)	4/7 (57.1)	6/8 (75.0)	0.183
18. Type of social support	6/14 (42.9)	4/5 (80.0)	2/6 (33.3)	0.321
19. Length of stay (LOS)	8/19 (42.1)	5/8 (62.5)	6/8 (75.0)	0.131
20. Six-minute walking distance	7/19 (36.8)	4/8 (50.0)	6/8 (75.0)	0.130

* Content validity index (CVI): Proportion of experts scoring 5 or 6 for a specific indicator (score of 5 or 6 means that the indicator is scored as highly relevant for follow-up); Consensus: CVI $\geq$ 75% obtained in round 2; *Italic* means no consensus (CVI < 75% obtained in round 2)

† Process and outcome indicators are displayed in descending order of CVIs obtained by medical doctors.

‡ Indicators for which overall consensus was obtained in round 2 (nos. 1-20; nos. 23-27; no. 29).

§ p values were considered significant if <0.05.

Results per discipline: outcome indicators

Concerning outcome indicators, medical doctors reached consensus for 4 of 20 outcome indicators (20%), nurses for 13 of 20 indicators (60.0%) and physiotherapists for 11 of 20 indicators (55.0%) (Table 3). The outcome indicators are also presented in descending order of the CVIs of the medical doctors in Table 3. The Kruskal–Wallis test showed no important differences in CVIs between disciplines; however, non-significant differences in consensus of 30% or more were found for six outcome indicators (Table 3, nos. 9, 11, 15, 18, 19 and 20).

Table 4: Significant differences in content validity indexes between disciplines after Mann-Whitney test with Bonferroni correction

Process indicators	Content validity index*			
	ROUND 2			P [†]
	Medical doctors n/n (%)	Nurses n/n (%)	Physio-therapists n/n (%)	
1. Identification for pulmonary rehabilitation	17/19 (89.5)		8/8 (100)	0.016
2. Fluid administration in dehydrated patients	14/19 (73.7)		8/8 (100)	0.011
3. Supplementary nutrition in patients with BMI > 20	7/19 (36.8)		8/8 (100)	0.000
4. Patient education: Strategies for minimizing dyspnea	10/19 (52.6)		8/8 (100)	0.002
5. Physiotherapy: Resistance training to improve skeletal muscle strength	9/19 (47.4)		8/8 (100)	0.002
6. Physiotherapy: Chest physiotherapy	17/19 (89.5)		6/8 (75.0)	0.001
7. Deep venous thrombosis prophylaxis	15/19 (78.9)	1/8 (12.5)		0.010
8. Physiotherapy: Endurance exercise training		6/8 (75.0)	7/8 (87.5)	0.001

* Content validity index (CVI): Proportion of experts scoring 5 or 6 for a specific indicator (score of 5 or 6 means that the indicator is scored as highly relevant for follow-up); Consensus: CVI ≥ 75% obtained in round 2; Italic means no consensus (CVI < 75% obtained in round 2)

† Bonferroni correction: p values are considered significant if <0.017.

Discussion

Consensus that an indicator is relevant for follow-up in studies on quality of in-hospital management of COPD exacerbation was reached by the overall Delphi panel for 26 of 72 process indicators (36.1%) and 10 of 21 outcome indicators (47.6%). Highest consensus levels were reached for the process indicators concerning oxygen therapy (100%), patient education (100%) and pulmonary rehabilitation (100%) and for the outcome indicators regarding understanding of therapy (91.4–85.7%) and self-management (88.6–88.2%) (Table 2).

Strengths and limitations

Some methodological issues need to be addressed. Firstly, we used the Delphi technique, which is a structured facilitation technique that explores consensus among a group of experts by synthesizing opinions [29;32]. Several other consensus techniques exist, including consensus development conferences, the nominal group technique, the RAND appropriateness method and iterated consensus rating procedures [29]. The Delphi method was selected because it does not require face-to-face contact and therefore enables the

anonymous inclusion of a large number of individuals across diverse locations and expertise [29]. Moreover, one of the key advantages of Delphi is that persuasive or prestigious experts cannot have undue influence on the opinions of others, as could happen in a face-to-face meeting of experts [33].

Secondly, selection procedure and composition of the expert panel need to be discussed. Delphi studies use individuals with known or demonstrable expertise in the subject being investigated [32;33]. Based on this principle, participants cannot be selected randomly. Instead, purposive sampling needs to be used, which implies that individuals are selected by an experienced investigator based on particular characteristics required of the sample members [46]. The sampling procedure resulted in 35 international experts from 15 developed countries, with 30 experts from Western Europe, one expert from Australia and finally four experts, respectively, from the United States. While 12 of 15 involved countries had a comparable representation of one participant ($n = 8$ countries) or two participants ($n = 3$ countries) in the panel, two countries (Belgium and the US) had four representatives. Finally, the UK was represented in the panel by a considerably higher number of 11 experts (including seven medical doctors, three nurses and one physiotherapist). The unequal representation of the countries and lack of representatives from other developed countries in the Delphi panel could have biased the results because of influence of cultural and economic features. However, since 2000, several worldwide established, rigorous evidence-based clinical practice guidelines (CPGs) have been developed for the assessment and management of patients with COPD [47]; for example, the guidelines of the GOLD (2009); the American Thoracic Society (ATS)-European Respiratory Society (ERS Task Force Celli & Macnee (2004); and the NICE (2004) [1;35;36]. These CPGs are remarkably consistent and have very few areas of clinically relevant discrepancy [47]. Moreover, these guidelines, intended for worldwide use, are available free via the internet and provide for regular updating. Therefore, it is assumed that COPD experts out of developed countries are more or less familiar with these guidelines and the optimal management strategies addressed in the guidelines. In consequence, it is a reasonable assumption that lack or unequal representation of certain developed countries in the panel, although each with their own socio-demographic influences did not have major impact on Delphi results. Also important, no experts from continents like Africa, Asia and South America were included. However, we believe that non-representation of these continents in the Delphi panel would not have affected our results, as our primary aim was to achieve knowledge for the developed healthcare systems. In conclusion, it is to believe that selected indicators and related management strategies are universal applicable in developed countries [48]. A third issue is the multidisciplinary character of the Delphi panel. This multidisciplinary approach is unique and favourable for validity and credibility of results, since COPD patients require specific

multidisciplinary care, with medical doctors, nurses and physiotherapists being the prime actors in care for patients hospitalized with COPD exacerbation [49]. After Mann–Whitney test with Bonferroni correction, eight important differences between the disciplines were found, including differences between medical doctors, on the one hand and physiotherapists and nurses, on the other hand (Table 4). These eight indicators were ‘non-medical’ interventions like physiotherapy, rehabilitation, hydration and nutrition. These results confirm the need for inclusion of a multidisciplinary panel to rate multidisciplinary indicators. Also, these findings suggest that it is recommendable to also consider those indicators for which no overall consensus but consensus in one or two disciplines was obtained (Table 3).

We note that twice as many doctors were included in the Delphi panel in comparison to the nurses and physiotherapists (Table 1). On the one hand, this is justifiable as 39 of 72 scored process indicators (54.2%) were strictly medical indicators. On the other hand, this unequal representation could have biased the overall results and the results per discipline. Firstly, as also indicated by the findings of our study (Table 3), it is evident that each panellist tends to rate higher for indicators related to their own discipline. In this study, the higher presentation of medical doctors may have biased the overall results in favour of the strictly medical indicators. In our study, 18 of 26 finally selected process indicators (69.2%) were strictly medical indicators (Table 2). Although, this finding could also be explained by the fact that half of 72 process indicators (54.2%) included in the Delphi questionnaire were indeed strictly medical indicators. Secondly, with regard to the results per discipline, medical doctors reached consensus for half as many process and outcome indicators (20–30%) compared with nurses and physiotherapists (55–60%). We believe that this finding can possibly be explained by the higher representation of medical doctors in the panel, since it is evident that the more persons are included, the fewer the likelihood that consensus will be reached [43]. A fourth methodological issue has to do with the identification of the indicators to build the Delphi questionnaire. It would have been interesting if we also considered the document of the ATS/ERS about outcomes for COPD pharmacological trials, as this provides a systematic overview of possible outcome measures [50]. Based on this document, outcomes as functional status, dyspnoea, frequency of exacerbation and topics regarding socioeconomic burden (i.e. use of healthcare resources, productivity losses and economic analysis) could also have been included in the questionnaire. The initial included outcome parameters could have been described in a more standardized way. Finally, response rates could be considered high and so favourable for validity of results, as they varied from 70% in round 1 to 88.6% in round 2.

Relevance of the set of process and outcome indicators

Looking to the 26 process indicators for which consensus was reached by the overall Delphi panel, it turned out that these indicators refer to care activities that are suboptimally performed according to the literature regarding COPD management [10-12]; for example, referral to pulmonary rehabilitation, smoking cessation and patient education. Similarly, the selected outcome indicators refer to clinical outcomes that, according to outcome studies, are poor and show high variability across different hospitals; for example, readmission, mortality and quality of life. The high accordance between Delphi results and the literature suggests that the selected indicators have potential for improvement and therefore are relevant for follow-up when studying the impact of interventions implemented to improve performance on care processes and clinical outcomes concerning in-hospital management of COPD exacerbation [18].

The European Quality of care pathways study on COPD exacerbation

The European Pathway Association has launched the European Quality of Care Pathways (EQCP) study, a cluster randomized controlled trial, with the aim to measure the impact of care pathways on performance of care processes and clinical outcomes in patients hospitalized with an COPD exacerbation [51]. Care pathways aim to standardize care processes and to improve clinical outcomes [20;52]. In the EQCP study, process and outcome indicators will be followed up in organizations where a pathway was implemented compared with organizations where usual care is provided. The selected set of process and outcome indicators will be applied in this study [51].

Conclusions

By conducting the Delphi survey with 35 experts out of 15 countries, 26 process and 10 outcome indicators were selected as being relevant for follow-up of care provided to patients hospitalized with COPD exacerbation. The selected indicators refer to care activities and outcomes that, according to earlier studies, are poor and show high variability across different hospitals, which indicate that these indicators are sensitive for improvement. Therefore, researchers and clinicians who want to appropriately study quality of care and impact of care pathways for patients hospitalized with COPD exacerbation should primarily focus on these indicators. In addition, indicators should be embedded in daily clinical practice to encourage continuous quality assessment and improvement. Moreover, variance analysis Future randomized controlled trials are needed to address whether or not the selected indicators are really sensitive to change and furthermore to evaluate reliability and feasibility of the indicators. Also, when applying these indicators in a clinical practice setting, multidisciplinary decision-making by all stakeholders is recommended to decide which of

these indicators should be followed up with regard to feasibility (data collection, time and man power) and interest of the involved stakeholders.

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Appendix 1: The Delphi questionnaire

EQCP-PROJECT
EUROPEAN QUALITY OF CARE PATHWAYS
INTERNATIONAL EXPERT PANEL QUESTIONNAIRE
ROUND 1

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IMPORTANT TO READ BEFORE FILLING IN THE QUESTIONNAIRE

Care pathways, also known as clinical pathways or critical pathways, are used worldwide for a variety of patient groups to lower unwanted variation and standardize care based on the latest evidence. Nonetheless very few strong prospective studies have been performed and published on the impact of pathways on quality and efficiency of care. The goal of the European Quality of Care Pathways (EQCP) study is to evaluate the effectiveness of a care pathway for patients with an acute exacerbation of Chronic Obstructive Pulmonary Disease (COPD) in acute hospitals and the immediate link with primary care. Inclusion criteria on patient level are: patients admitted with an acute exacerbation of COPD; an ASA-score of 2 or 3 (patient with mild or systemic disease that is not in constant threat of life). Exclusion criteria on patient level are: admission required to intensive care unit; need for Non Invasive Positive Pressure Ventilation (NIPVV) or Invasive Positive Pressure Ventilation (IPVV); cognitive impairment; and expected not to be discharged at home.

To evaluate the impact of the care pathway, the adherence to key interventions and the obtained clinical outcomes will be compared between an experimental and control group through a **cluster randomized controlled trial**. The project will be conducted in several European countries.

As it is not feasible to follow up all possible interventions and outcomes published in literature, we would like **your expert opinion and assistance in selecting these key interventions and outcome indicators to follow up in our study**. Regarding the variance in management of a COPD exacerbation worldwide, we want to consult a multidisciplinary and multinational panel of experts to guarantee that our research results can be generalised to a broad population and are relevant for international clinical practice.

The questionnaire is built up in three parts:

1. Part I: Selection of key interventions for follow-up

Based on the GOLD guideline (Global Strategy for Diagnosis, Management, and Prevention of COPD) (appendix 1), a list of interventions for the management of a COPD exacerbation was defined. **We would like you to indicate, on a 6-point rating scale, which impact you believe that the listed key interventions have on clinical outcomes in patients with a COPD exacerbation.** The interventions with highest impact on outcomes, according to the international expert panel, will be selected for follow-up in our study.

2. Part II: Selection of clinical outcome indicators

Based on literature review a selection of outcome indicators was defined. **We would like you to indicate, on a 6-point rating scale, how sensitive for change you believe the listed outcome indicators would be when implementing an evidence based care pathway for patients with a COPD exacerbation.** The indicators which are most sensitive for change, according to the international expert panel, will be selected for follow-up in our study.

3. Part III: Demographic information

In this part we would like you to fill in some general information to describe our expert panel.

This questionnaire will be answered by a selected group of experts on COPD on an international level. **We would like you to return the answered questionnaire to cathy.lodewijckx@uzleuven.be by October 24th.** Completion of the survey has to be done electronically by marking and filling in the grey boxes below and will take you about twenty minutes. In a second round you will receive feedback on the group results compared with your own results. In addition you will have the possibility to adjust your answers based on the group responses. **Anonymity is guaranteed.**

We would like to thank you in advance for your effort in helping us with our project. Please do not hesitate to contact us if you have questions about the project.

PART I: KEY INTERVENTIONS IN THE HOSPITAL MANAGEMENT OF A COPD EXACERBATION

Please indicate on a 6-point rating scale, which impact you believe that the following key interventions have on clinical outcomes in patients with an exacerbation of COPD.

For example:

	Low impact on outcomes			High impact on outcomes		
	1	2	3	4	5	6
Key intervention X	☐	☐	☐	☐	☐	☒

If you mark 6, this would mean that you believe that key intervention X has a high impact on clinical outcomes and therefore should be followed up in the study.

	Low impact on outcomes			High impact on outcomes		
	1	2	3	4	5	6
1. Medical history before exacerbation:						
a. Spirometric classification of severity	☐	☐	☐	☐	☐	☐
b. Documenting frequency and severity of attacks of breathlessness	☐	☐	☐	☐	☐	☐
c. Documenting frequency and severity of chronic cough	☐	☐	☐	☐	☐	☐
d. History of chronic sputum production	☐	☐	☐	☐	☐	☐
e. Documenting possible limitation of daily activities	☐	☐	☐	☐	☐	☐
f. Prior arterial blood gas measurements in stable condition	☐	☐	☐	☐	☐	☐
g. Number of previous exacerbations in the previous year	☐	☐	☐	☐	☐	☐
h. Pre-existing co-morbidities	☐	☐	☐	☐	☐	☐
i. Cardiovascular status	☐	☐	☐	☐	☐	☐
j. Screening for diabetes	☐	☐	☐	☐	☐	☐
k. Present treatment regimen	☐	☐	☐	☐	☐	☐
l. Smoking status	☐	☐	☐	☐	☐	☐
2. Assessment of symptoms	☐	☐	☐	☐	☐	☐
<u>Definition:</u> changes in baseline dyspnoea, cough and sputum production						
3. Physical examination	☐	☐	☐	☐	☐	☐
<u>Definition:</u> inspection, palpation and percussion, and auscultation						

	Low impact on outcomes			High impact on outcomes		
	1	2	3	4	5	6
4. Assessment of co-morbidities	☐	☐	☐	☐	☐	☐
5. Monitoring of fluid balance	☐	☐	☐	☐	☐	☐
6. Body mass index (BMI)	☐	☐	☐	☐	☐	☐
7. Temperature	☐	☐	☐	☐	☐	☐
8. Pulse rate	☐	☐	☐	☐	☐	☐
9. Blood pressure	☐	☐	☐	☐	☐	☐
10. Pulse oximetry						
a. At admission	☐	☐	☐	☐	☐	☐
b. Prior to discharge in patients hypoxemic during a COPD exacerbation	☐	☐	☐	☐	☐	☐
c. In the following three months in patients hypoxemic during a COPD exacerbation	☐	☐	☐	☐	☐	☐
d. After discharge in patients with Long-Term Oxygen Therapy (LTOT)	☐	☐	☐	☐	☐	☐
11. Arterial blood gas measurement						
a. At admission	☐	☐	☐	☐	☐	☐
b. prior to discharge in patients hypoxemic during a COPD exacerbation	☐	☐	☐	☐	☐	☐
c. In the following three months in patients hypoxemic during a COPD exacerbation	☐	☐	☐	☐	☐	☐
d. After discharge in patients with LTOT	☐	☐	☐	☐	☐	☐
12. Chest X-Ray	☐	☐	☐	☐	☐	☐
13. ECG	☐	☐	☐	☐	☐	☐
14. Blood examination:						
a. Hematology	☐	☐	☐	☐	☐	☐
<u>Definition:</u> Hemoglobin, RBC count, hematocrit, WBC count, Platelet count, WBC differentiation						
b. Biochemical tests	☐	☐	☐	☐	☐	☐
<u>Definition:</u> glucose, Glycohemoglobine (A _{1c}), CRP, total cholesterol, triglyceride, HDL cholesterol, LDL Cholesterol						
15. Sputum culture and antibiogram	☐	☐	☐	☐	☐	☐
16. Pulmonary testing during hospitalization (not earlier then day 3 because of acute condition)						
a. Spirometry	☐	☐	☐	☐	☐	☐
b. Residual volume	☐	☐	☐	☐	☐	☐
c. Lung diffusion testing	☐	☐	☐	☐	☐	☐
d. Bronchodilator reversibility testing	☐	☐	☐	☐	☐	☐
e. Total Lung Capacity (TLC)	☐	☐	☐	☐	☐	☐

	Low impact on outcomes			High impact on outcomes		
	1	2	3	4	5	6
17. Pulmonary testing after discharge						
f. Spirometry	☐	☐	☐	☐	☐	☐
g. Residual volume	☐	☐	☐	☐	☐	☐
h. Lung diffusion testing	☐	☐	☐	☐	☐	☐
i. Bronchodilator reversibility testing	☐	☐	☐	☐	☐	☐
j. Total Lung Capacity (TLC)	☐	☐	☐	☐	☐	☐
18. Identification for pulmonary rehabilitation	☐	☐	☐	☐	☐	☐
19. Identification for lung volume reduction surgery	☐	☐	☐	☐	☐	☐
20. CT THORAX: 1 X year	☐	☐	☐	☐	☐	☐
21. ECHO CARDIO: 1 X year	☐	☐	☐	☐	☐	☐
22. Appropriate prescription of short-acting bronchodilators	☐	☐	☐	☐	☐	☐
23. Appropriate prescription of long-acting bronchodilators (β-agonists and/or anticholinergics)	☐	☐	☐	☐	☐	☐
24. Appropriate prescription of - glucocorticosteroids: oral or intravenous	☐	☐	☐	☐	☐	☐
25. Appropriate prescription of - methylxanthines (theophylline or aminophylline)	☐	☐	☐	☐	☐	☐
Indication: inadequate or insufficient respons to short-acting bronchodilators						
26. Antibiotics in patients <u>if indicated</u>	☐	☐	☐	☐	☐	☐
<u>Indication:</u>						
<ul style="list-style-type: none"> Patients with 1) increased dyspnoe, 2) increased sputum volume and 3) increased sputum purulence OR <ul style="list-style-type: none"> Patients with 1) increased sputum purulence, 2) increased sputum volume or increased dyspnoe, 3) need for mechanical ventilation 						
27. Controlled oxygen therapy in hypoxemic patients	☐	☐	☐	☐	☐	☐
28. Initiation of long-term oxygen therapy (LTOT) if the patient remains hypoxemic	☐	☐	☐	☐	☐	☐
29. Assessment and management of social situation (i.e. living status, visiting nurse, meal provisions, etc.)	☐	☐	☐	☐	☐	☐
30. Fluid administration in dehydrated patients	☐	☐	☐	☐	☐	☐
31. Supplementary nutrition in patients with BMI < 20	☐	☐	☐	☐	☐	☐

	Low impact on outcomes			High impact on outcomes		
	1	2	3	4	5	6
32. Deep venous thrombosis prophylaxis	☐	☐	☐	☐	☐	☐
<u>Definition:</u> mechanical devices, heparins, etc.						
33. Smoking cessation advice when active smoker	☐	☐	☐	☐	☐	☐
34. Patient Education:						
a. Information about the nature of COPD	☐	☐	☐	☐	☐	☐
b. Instruction on how to use inhalers and other treatments	☐	☐	☐	☐	☐	☐
c. Information about oxygen treatment	☐	☐	☐	☐	☐	☐
b. Information about recognition and treatment of exacerbations	☐	☐	☐	☐	☐	☐
c. Strategies for minimizing dyspnoea	☐	☐	☐	☐	☐	☐
35. Physiotherapy:						
a. Chest physiotherapy for breathing and sputum clearance when increased sputum volume and/or impaired mucus transport	☐	☐	☐	☐	☐	☐
b. Endurance exercise training	☐	☐	☐	☐	☐	☐
c. Resistance training to improve skeletal muscle strength	☐	☐	☐	☐	☐	☐
d. Activities of Daily Life	☐	☐	☐	☐	☐	☐
<u>I.e.:</u> walking stairs, cooking dinner, dressing, going outside, cleaning, ...						
36. Referral to dietician in patient with obesity or cachexia	☐	☐	☐	☐	☐	☐
37. Referral to pulmonary rehabilitation	☐	☐	☐	☐	☐	☐
38. Treatment of co-morbid conditions	☐	☐	☐	☐	☐	☐
<u>I.e.:</u> heart failure, arrhythmias, etc.						
39. Assessment of differential diagnosis	☐	☐	☐	☐	☐	☐
<u>Definition:</u> Re-evaluation of other medical conditions that can aggravate symptoms or mimic COPD exacerbations when patients with apparent exacerbation do not respond to treatment (i.e. pneumonia, congestive heart failure, pneumothorax, pleural effusion, pulmonary embolism and cardiac arrhythmia).						

OTHER SUGGESTIONS on KEY INTERVENTIONS:

PART II: OUTCOME INDICATORS

Please indicate on a 6-point rating scale how sensitive for change you believe the listed outcome indicators would be when implementing a care pathway for patient hospitalized with an exacerbation of COPD.

For example:

	Low sensitive for change			High sensitive for change		
	1	2	3	4	5	6
Outcome indicator X	☐	☐	☐	☐	☐	☒

If you mark 6, this would mean that you believe that outcome indicator X will be very sensitive for change when implementing a care pathway for patient hospitalized with an exacerbation of COPD and therefore should be followed up in the study.

Outcome indicators AT discharge

	Low sensitive for change			High sensitive for change		
	1	2	3	4	5	6
1. Inhaled β -agonist therapy is required no more frequently than every 4 hours	☐	☐	☐	☐	☐	☐
2. Patient, if previously ambulatory, is able to cope with basic needs in his/her situation	☐	☐	☐	☐	☐	☐
3. Patient is able to eat and sleep without frequent awakening by dyspnea	☐	☐	☐	☐	☐	☐
4. Patient has been clinically stable for 12-24 hours	☐	☐	☐	☐	☐	☐
5. Last measure of arterial blood gases were acceptable according to condition of the patient	☐	☐	☐	☐	☐	☐
6. Patient and/or home caregiver fully understands correct use of therapy:						
a. Oral medication therapy	☐	☐	☐	☐	☐	☐
b. Inhaler therapy	☐	☐	☐	☐	☐	☐
c. Oxygen therapy if LTOT	☐	☐	☐	☐	☐	☐
7. Patient and/or home caregiver fully understands correct use of inhaler	☐	☐	☐	☐	☐	☐
8. Patient, family and physician are confident that the patient can manage successfully at home	☐	☐	☐	☐	☐	☐

	Low sensitive for change			High sensitive for change		
	1	2	3	4	5	6
9. Ability to cope in usual environment	☐	☐	☐	☐	☐	☐
10. Forced Expiratory Volume in one second (FEV ₁)	☐	☐	☐	☐	☐	☐
11. Forced Vital Capacity (FVC)	☐	☐	☐	☐	☐	☐
12. Inspiratory capacity	☐	☐	☐	☐	☐	☐
13. 6 minute walking distance	☐	☐	☐	☐	☐	☐
14. Symptoms at rest and during exercise	☐	☐	☐	☐	☐	☐
15. Length of stay (LOS)	☐	☐	☐	☐	☐	☐
16. Quality of sleep	☐	☐	☐	☐	☐	☐

Outcome indicators AFTER discharge

	Low sensitive for change			High sensitive for change		
	1	2	3	4	5	6
17. Interval before next admission	☐	☐	☐	☐	☐	☐
18. Health Related Quality of Life (HRQL)	☐	☐	☐	☐	☐	☐
19. Patients' perception of coordination between hospital and home health care	☐	☐	☐	☐	☐	☐
20. Patient satisfaction with therapie and care	☐	☐	☐	☐	☐	☐
21. Mortality within 1 year after exacerbation	☐	☐	☐	☐	☐	☐

OTHER SUGGESTIONS on OUTCOME INDICATORS:

PART III: DEMOGRAPHIC INFORMATION

1. **City and Country in which you are currently working:**
2. **Name of your hospital / organization:**
3. **Type of hospital:**
 - ☐ Academic hospital
 - ☐ Community teaching hospital
 - ☐ Community hospital
 - ☐ Other:
4. **Number of beds in your organization:** **beds**
5. **Professional group:**
 - ☐ Medical doctor
 - ☐ Nurse
 - ☐ Physiotherapist
6. **Years of experience in respiratory care:** **years**
7. **Age:**
 - ☐ 20-29 ☐ 30-39 ☐ 40-49 ☐ 50-59 ☐ 60-69 ☐ > 70
8. **Sex:**
 - ☐ Male ☐ Female
9. **Date you completed the questionnaire:** / /

Chapter 5:

How to build the clinical content of an evidence-based care pathway for COPD exacerbation

This chapter was submitted for publication in 2012 as: How to build the clinical content of an evidence-based care pathway for COPD exacerbation. Lodewijckx C, Decramer M, Sermeus W, Panella S, Deneckere S, Vanhaecht K.

Abstract

Background: Optimisation of the clinical care process by integration of evidence-based knowledge is one of the active components in care pathways. When studying the impact of a care pathway by using a cluster-randomised design, standardisation of the care pathway intervention is crucial.

Objective: To develop the clinical content of an evidence-based care pathway for in-hospital management of COPD exacerbations in the context of a cluster-randomised controlled trial (cRCT) on care pathway effectiveness.

Methods: The clinical content of the COPD care pathway was developed using an eight-step method, following recognized process design and guideline development methods.

Results: The development strategy resulted in a set of 38 key interventions for in-hospital management of COPD exacerbations, and a set of 24 process and 15 outcome indicators. Nine Belgian multidisciplinary teams piloted both the key interventions and indicators. The key intervention set was judged by the teams as being valid and clinically applicable. The pilot study determined that the measurements on the indicators were feasible for the involved clinicians and patients.

Conclusions: The set of 38 key interventions and the set of process and outcome indicators were found to be appropriate for the development and standardisation of the clinical content of the COPD care pathway in the context of a cRCT on pathway effectiveness. The newly developed eight-step method may facilitate multidisciplinary teams who care for other patient populations in designing the clinical content of their own proposed care pathways.

Background

Standardisation of the clinical care process through integration of evidence-based knowledge has proven to be an effective strategy for reducing unwanted variations in treatment and for minimising the probability of medical errors [1]. However, major difficulties arise when introducing evidence and clinical guidelines into routine daily practice, and many patients, as a result, do not receive appropriate care, or receive unnecessary or harmful care [2-5].

A possible tool to facilitate implementation of evidence into practice is a care pathway. Care pathways are complex interventions for mutual decision making, organisation, and standardisation of predictable care for a well-defined group of patients during a well-defined period [6-8]. One of the active ingredients in care pathways is the integration of a set of evidence-based key interventions [8;9].

Care pathways induce change at different levels of the organisation (i.e. patient, team, hospital); consequently, variability at individual level outcomes may reflect the impact of higher-level complexity processes. To deal with these multilevel effects, cluster randomised designs should be used when studying the impact of care pathways [10;11]. Importantly, in cluster randomised controlled trials (cRCTs) the care pathway under evaluation is implemented at different sites. Consequently, a challenge within cRCT designs is to standardise the intervention in order to deliver the 'same' intervention at the different sites under study [10;12-14]. Standardisation in complex interventions refers to adaptation of the care pathway components to the context level, without compromising the integrity of the intervention being evaluated across multiple sites [10;14;15].

In 2009, the European Pathway Association (E-P-A) launched the European Quality of Care Pathways (EQCP) study, an international cRCT addressing the impact of a care pathway for chronic obstructive pulmonary disease (COPD) exacerbations [9]. In the context of the EQCP study, the evidence-based clinical content of a care pathway for COPD exacerbations needed to be developed, including a set of evidence-based key interventions and a set of process and outcome indicators, which could be implemented at the different experimental sites.

This paper describes the development of the clinical content of a care pathway for in-hospital management of COPD exacerbations.

Methods

The method for developing the evidence-based clinical content of the COPD care pathway included eight different steps (Figure 1). The applied method is based on the process design methodology developed by Berry et al. [16], and the guideline development methods of the American College of Chest Physicians (ACCP) [17], the World Health Organization (WHO)

[18], and the Healthcare Infection Control Practices Advisory Committee (HICPAC) [19].

Figure 1. Eight-step method for clinical content development of an evidence-based care pathway for COPD exacerbation

† **Scottish Intercollegiate Guidelines Network (SIGN)** grading system [20]

- 1++ High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
- 1+ Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
- 1- Meta-analyses, systematic reviews, or RCTs with a high risk of bias
- 2++ High-quality systematic reviews of case control or cohort or studies
High-quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
- 2+ Well-conducted case control or cohort studies with a low risk of confounding or bias and a

- moderate probability that the relationship is causal
 - 2- Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
 - 3 Non-analytic studies, e.g. case reports, case series
 - 4 Expert opinion
- A At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a body of evidence consisting principally of studies rated as 1+, and directly applicable to the target population and demonstrating overall consistency of results
 - B A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating overall consistency of results
 - C A body of evidence including studies rated as 2+, and directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++
 - D Evidence level 3 or 4; or extrapolated evidence from studies rated as 2+

Results

A set of 38 evidence-based key interventions (Appendix 1) and a set of 24 process and 15 outcome indicators (Table 3) were developed in eight different steps. In the following section, descriptions and rationale for each development step are presented.

Step 1: Specification of the care population and selection of an expert panel [8;18;19;21;22]

The patient population under study was specified as 'Patients hospitalised with COPD exacerbation'. To ensure clinical validity and feasibility of the end product, an expert panel was involved in each step of the development method. This panel was composed of the following: (i) three clinicians with internationally recognised clinical and scientific expertise in COPD exacerbations: a pulmonologist (MD), who is also president of the European Respiratory Society; a physiotherapist (TT), who specialises in pulmonary rehabilitation, and a clinical nurse specialist in COPD (CL); (ii) an epidemiologist (MP), who specialises in organisation of primary and secondary chronic care; and (iii) two professors (WS, KV) in patient care management, who have extensive clinical and scientific expertise in development and implementation of care pathways. All six experts had extensive research experience.

Step 2: Literature review and extraction of clinical activities and outcomes [23]

An extensive literature review was conducted by the main researchers, CL and KV (Figure 2). Firstly, an initial literature search was carried out in April 2008 in the context of the Delphi study, and an updated search was performed in June 2011. In the following section, the updated search is described. The following resources were explored: (I) websites of

international respiratory societies: American Thoracic Society (ATS) (www.thoracic.org); British Thoracic Society (BTS) (www.brit-thoracic.org.uk); European Respiratory Society (ERS) (www.ersnet.org); Global Strategy for Diagnosis, Management, and Prevention of COPD (GOLD) (www.goldcopd.org); National Institute for Health and Clinical Excellence (NICE) (www.nice.org.uk); Scottish Intercollegiate Guidelines Network (SIGN) (www.sign.ac.uk); (II) Public resources for evidence-based clinical practice guidelines (www.guideline.gov, www.g-i-n.net); (III) electronic databases including Medline and Embase and Cochrane; (IV) available process flow diagrams founded on evidence-based medicine (www.mapofmedicine.com, <http://group.bmj.com/products/evidence-centre.com>).

For guidelines developed by international societies, only those guidelines were considered that were updated within the last five years. For Pubmed and Cochrane, we used the MeSH terms 'COPD' combined with (i) 'practice guideline', (ii) 'disease exacerbation and patient care management', and (iii) 'outcomes'. For Embase, we used the MeSH terms 'chronic obstructive lung disease' combined with (i) 'practice guideline' and (ii) 'disease exacerbation and patient care', and (iii) 'outcomes'. Non-MeSH terms used in Embase were 'COPD' in combination with 'exacerbation and management'. Search limit parameters included: (i) [dp], published between 2005 and 2011, and (ii) [lang], written in English, French, German, Italian, or Dutch.

Secondly, we performed a two-phase screening evaluation of publications selected from websites of the respiratory societies, Map of Medicine, and the electronic databases. In the first phase, publications were scrutinised for relevance based on appropriateness of the title and abstract. If relevance was unclear, or if the abstract was unavailable, the publication was included for further appraisal of the full text for relevance. In the second phase, two independent researchers (CL and KV) reviewed the full text of the selected guidelines, reviews, or process flow diagrams. The following inclusion criteria were used: (i) reportage of clinical processes and outcomes regarding in-hospital management of COPD exacerbation; (ii) evidence was reported in terms of guidelines, process flow diagrams, reviews, or overview papers; (iv) published between 2005 and 2011; (v) published in English, French, German, Italian, or Dutch; and (vi) quality of underlying evidence can be appraised by in-text references. The literature research revealed initially three guidelines, one process-flow diagram, and 2939 digital records from the electronic medical databases (Figure 2). After exclusion of irrelevant publications (n=2851), we included for development of the evidence-based clinical content of the care pathway three guidelines, two process flow diagrams, and 37 reviews [5;5;24-57].

Figure 2. Flow diagram of literature search strategy and numbers of identified candidate articles at each step

Finally, the selected literature was thoroughly screened for identification of all possible clinical activities and outcomes related to in-hospital management of COPD exacerbations. The detected clinical activities were extracted and listed, and the corresponding literature sources were recorded. In total, 58 different clinical activities were extracted from the selected literature (Table 1, no. 1-58). Besides these, 34 outcome categories were identified (Table 2).

Table 1. Identified clinical activities for in-hospital management of COPD exacerbations

1.	Medical history before exacerbation: Prior measures of lung function (B)*
2.	Medical history before exacerbation: Spirometric classification of severity (B)
3.	Medical history before exacerbation: Documenting frequency and severity of attacks of breathlessness (B)
4.	Medical history before exacerbation: Documenting frequency and severity of chronic cough (B)
5.	Medical history before exacerbation: History of chronic sputum production (B)
6.	Medical history before exacerbation: Documenting possible limitation of daily activities (B)
7.	Medical history before exacerbation: Prior arterial blood gas measurements in stable condition (B)
8.	Medical history before exacerbation: Number of previous exacerbations in the previous year (B)
9.	Medical history before exacerbation: Number of previous hospitalisations (B)
10.	Medical history before exacerbation: Pre-existing co-morbidities (A)
11.	Medical history before exacerbation: Present treatment regimen (A)
12.	Medical history before exacerbation: Smoking status (B)
13.	Medical history before exacerbation: Sleeping and eating difficulties (B)
14.	Assessment of symptoms: Physical examination (B)
15.	Assessment of differential diagnosis (B)
16.	Assessment of co-morbidities (B)
17.	Temperature (B)
18.	Pulse rate (B)
19.	Blood pressure (B)
20.	Alertness (B)
21.	Skin color (B)
22.	Pulse oximetry (D)
23.	Arterial blood gas measurement: At admission (B)
24.	Arterial blood gas measurement: Prior to discharge in patients hypoxaemic during a COPD exacerbation (B)
25.	Arterial blood gas measurement: In the following three months in patients hypoxaemic during a COPD exacerbation (D)
26.	Arterial blood gas measurement: After discharge in patients with long term oxygen therapy (LTOT) (B)
27.	Chest X-Ray (B)
28.	ECG (B)
29.	Blood examination: Hemaetology (B)
30.	Blood examination: Biochemical tests (B)
31.	Blood examination: Theophylline level in patients on theophylline therapy at admission (B)
32.	Sputum culture and antibiogram (B)
33.	Spirometry during hospitalisation (not earlier then day 3 because of acute condition) (C)

34. Admission of ICU if exacerbation is life threatening (B)
35. Appropriate prescription of short-acting bronchodilators (A)
36. Appropriate prescription of long-acting bronchodilators (β -agonists and/or anticholinergics) (A)
37. Appropriate prescription of inhaled corticosteroids (A)
38. Appropriate prescription of glucocorticosteroids: oral or intravenous (A)
39. Appropriate prescription of methylxanthines (theophylline or aminophylline) (A)
40. Antibiotics in patients if indicated (A)
41. Controlled oxygen therapy in hypoxemic patients (A)
42. Assisted ventilation if necessary (A)
43. Smoking cessation advice when active smoker (A)
44. Patient Education Information about recognition and treatment of exacerbation (A)
45. Patient Education: Instruction on how to use inhalers (A)
46. Chest physiotherapy: sputum clearance (A)
47. Referral to pulmonary rehabilitation (A)
48. Monitoring of fluid balance (A)
49. Fluid administration in dehydrated patients (A)
50. Supplementary nutrition in patients with BMI < 20 (B)
51. Screening and update of vaccination status (B)
52. Deep venous thrombosis prophylaxis (A)
53. Treatment of co-morbid conditions (A)
54. Initiation of long-term oxygen therapy (LTOT) if the patient remains hypoxemic (A)
55. Assessment of medical discharge criteria (D)
56. Assessment and management of home situation (A)
57. Oral information and discharge letter regarding predyspnscribed home therapy and follow-up appointment (B)
58. Arrangement of follow-up appointment 4-6 weeks after discharge (D)
59. Medical history before exacerbation: Number of previous admissions to ICU (D)
60. Medical history before exacerbation: Cardiovascular status (B)
61. Glucose monitoring (B)
62. CT THORAX: 1 X year (B)
63. ECHO CARDIO: 1 X year (B)
64. Patient Education: nformation about the nature of COPD (A)
65. Patient education: Self-management plan (A)
66. Patient Education Strategies for minimising dyspnoea (A)
67. Patient Education Information about oxygen treatment (A)
68. Physiotherapy: Breathing techniques (A)
69. Physiotherapy: Activities of Daily Life (A)
70. Physiotherapy: Positioning (A)
71. Identification for pulmonary rehabilitation determinant (B)
72. Body mass index (BMI) determinant (A)
73. Screening for weight loss (A)
74. Referral to dietician in patient with obesity or cachexie (B)
75. Assessment and management of anxiety and depression (B)
76. Information letter for general practitioner (B)
77. Discharge checklist (B)

*SIGN grading system (see explanation in Figure 1) [20]

Table 2. Identified outcomes for in-hospital management of COPD exacerbations

<ul style="list-style-type: none"> • Readmission: 30-day, 3-month, 6-month, 1-year • Number of hospital admissions • Interval before next admission • Frequency and severity of exacerbation • Mortality: In-hospital, 30-day, 3-month, 6-month, 1-year • Survival: 1-year • Length of stay (LOS) • Level of understanding of inhaler therapy • Compliance with home oxygen therapy • Performance of physical exercise • Smoking status: 30-day, 3-month, 6 month, 1-year • Symptoms of anxiety and depression • Health-related quality of life (HRQL): symptoms, disability, morbidity and quality of life; psychological well being) • Health status • Quality-adjusted life expectancy measure (QALY) and disability adjusted life years (DALY) • Functional capacity • Exercise capacity • Physical performance: 6-Minute walking distance (6-MWD), 20-MWD, Shuttle walk test, maximum workload, treadmill time, maximum oxygen uptake, quadriceps strength, hand grip force, maximal inspiratory mouth pressure • Severity of breathlessness: dyspnoea, symptoms at rest and during exercise 	<ul style="list-style-type: none"> • Inhaled β-agonist therapy is required no more frequently than every 4 hours • Patient, if previously ambulatory, is able to cope with basic needs in his/her situation, in usual environment • Patient is able to eat and sleep without frequent awakening by dyspnoea • Patient has been clinically stable for 12-24 hours • Last measure of arterial blood gases (ABGs) were acceptable according to condition of the patient • Patient and/or home caregiver fully understands correct use of therapy: oral medication therapy, inhaler therapy, oxygen therapy if home oxygen therapy • Patient, family, and physician are confident that the patient can manage successfully • Lung function parameters: Forced expiratory volume in one second (FEV₁), forced vital capacity (FVC), inspiratory capacity • Quality of sleep • Nutritional status • Patients' perception of coordination between hospital and home healthcare • Patient satisfaction with therapy and care • Adverse event related to regular clinical examination by an investigator • Cost of illness (COI) analysis • Absenteeism
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Step 3: International Delphi study for rating of content validity [58-61]

Content validity was rated for 72 process and 21 outcome indicators by conducting an international Delphi study with a panel composed of 35 medical professionals from 15 countries. This panel consisted of 19 medical doctors, 8 nurses, and 8 physiotherapists. The detailed methodology and the results of this study are published [61] and appears as Chapter 4 in this dissertation.

In summary, panellists were asked to rate the relevance for follow-up of the process and outcome indicators in care pathways for COPD exacerbations. Consensus was defined as agreement by at least 75% of panel members that an indicator is relevant for follow-up. Consensus was reached for 26 of 72 process indicators (36.1%) and 10 of 21 outcome

indicators (47.6%). Highest consensus was reached for the process indicators for oxygen therapy (100%), pulmonary rehabilitation (100%), and patient education (94.5 to 88.6%), and for the outcome indicators for understanding of therapy (91.4 to 85.7%) and self-management (88.6 to 88.2%) [61].

Step 4: Final selection of the clinical activities and grading of evidences

Firstly, the list of 58 extracted clinical activities (step 2), together with the Delphi results (step 3), were sent by mail to the clinical experts of the panel (MD, TT, and CL) with a request to complete two tasks: (i) to review the 58 identified activities for validity and feasibility; and (ii) if indicated, to propose any additional clinical activities they believe are essential for in-hospital management of COPD exacerbations and which were lacking in the current list of clinical activities. Secondly, a consensus meeting was held with the entire expert panel (step 1) in order to make a final selection of the clinical activities. As a result, all 58 clinical activities were appraised to be valid and feasible. In addition, 19 clinical activities beyond the 58 original ones were included (Table 1, nos. 59-77). Interestingly, for almost all these additional clinical activities, a more or less comprehensive description was available in the guidelines for management of stable COPD [28;33;62].

Finally, strength of the evidence for the final 77 clinical activities was graded, so that clinicians know how much confidence they can place on the clinical recommendations included in the clinical care pathway [63]. The grading was performed by the clinical nurse specialist (CL) using the SIGN approach [20]. The systematic grading approach of SIGN was chosen because it is very transparent and workable from the perspective of the user of evidence-based recommendations [20;63;64]. Importantly, if the level of evidence could not be derived based on the selected literature out of the search in step 2, an additional literature search was performed in Medline, Embase, and Cochrane. Search terms included 'COPD' and key words related to the particular key intervention. Primarily, the search for additional evidence was focussed on reviews performed according to standard criteria for reviews [23]. If not available, an additional search for clinical trials was conducted. Subsequently, two other clinical experts of the panel (MD and TT) checked the final grading. As a result, 30 activities were graded as evidence level A (39.0 %), 39 activities as level B (50.6%), 1 activity as level C (1.3%), and 5 as level D (6.5%) (Table 1).

An extensive list of care activities was generated by following the above-mentioned steps. However, providing such an exhaustive list of 77 care activities to the multidisciplinary teams would likely not encourage them to use this evidence in practice. Therefore, the next two steps were specifically undertaken to distil the list of care activities to a set of key interventions that would be usable and manageable in clinical practice.

Step 5: Clustering of clinical activities into key interventions and categorisation into process flow diagram

Firstly, the 77 clinical activities were clustered into key interventions with subcomponents, based on the following criteria: (i) clinical activities are inextricably linked to each other (i.e. measurement of basal metabolic index (BMI), advice on malnutrition, supplementary nutrition, etc. were clustered into 'nutrition'); (ii) clinical activities need to be performed by a specific team member (i.e. breathing exercises, positioning, etc. were categorised under physiotherapy); (iii) clinical activities need to be performed at a specific time point or within a specific time span of the care process (i.e. activities regarding discharge management). As result, the 77 clinical activities were clustered into 38 key interventions, with 9 of them comprising 2-15 subcomponents (Appendix 1).

Secondly, the key interventions were categorised into three core processes (diagnostic, pharmacological, and non-pharmacological management) and subsequently presented by means of a process flow diagram. In addition, within each of three core processes, key interventions were grouped into care blocks based on the overall content of these key interventions (e.g. education, ventilation) (Appendix 1).

Step 6: Detailed description of the key interventions (Figure 3)

For each key intervention, the following components were included in the detailed description: (i) rationale, which addresses why it is of crucial importance that the key intervention is performed, and which describes expected impact on patient outcomes; (ii) description, which defines the exact content of the key intervention; (iii) in-text references and reference list; and (iv) grading of evidence (Figure 3). In order to search for detailed information on the description and the rationale, selected publications and their reference list were explored. Secondly, information from the additional literature search, performed to establish level of evidence (step 5), was included.

Figure 3: Example of detailed description of one key intervention: arterial blood gas measurement

Argumentation

Measurement of arterial blood gases (ABGs) is essential to detect hypercapnia and to assess the severity of an exacerbation. Consequently, ABG values are the key determinant for initiating supplemental oxygen therapy, prescribing assisted ventilation, and prescribing home oxygen therapy. A $\text{PaO}_2 < 8.0$ kPa (60 mm Hg) and/or $\text{SaO}_2 < 90\%$ with or without $\text{PaCO}_2 > 6.7$ kPa (50 mmHg) when breathing room air indicate respiratory failure. In addition, moderate-to-severe acidosis ($\text{pH} < 7.36$) plus hypercapnia ($\text{PaCO}_2 > 6-8$ kPa; 45-60 mmHg) in a patient with respiratory failure is an indication for mechanical ventilation (Barbera *et al.*, 1997; Calverley, 2000; Celli *et al.*, 2004; Gibson *et al.*, 2008; GOLD, 2009; NICE, 2004; Rodriguez-Roisin, 2006; Siafkas & Wedzicha, 2006).

In the Delphi study 82.9% of experts were convinced that the key intervention has a high impact on clinical outcomes and therefore should be included in the pathway.

Description: (Celli et al., 2004; Gibson et al., 2008; GOLD, 2009; NICE, 2004; Rodriguez-Roisin, 2006; Siafkas & Wedzicha, 2006)

Measurement of PaO₂, PaCO₂, H₂CO₃⁻, SaO₂, and pH by arterial puncture (a. radialis, brachialis, or femoralis) while breathing room air at admission. If measurement of ABGs while breathing room air is not feasible (severe cases), oxygen flow (l/min) should be noted. Twenty to 30 minutes should pass before rechecking the gas tensions when the FiO₂ has been changed.

References:

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Step 7: Translation into a set of process and outcome indicators [65-67]

Besides the set of key interventions, a set of process and outcome indicators needed to be developed to verify compliance to key interventions and to follow up the impact on outcomes. Firstly, to select the final set of indicators, the expert panel convened for a consensus meeting. The selection process was based on the (updated) literature search (step 2), the Delphi survey (step 3), and the developed set of 38 evidence-based key interventions (step 5) [61]. As result, a set of 24 process and 15 outcome indicators was developed (Table 3). The 24 process indicators include measurements on performance of diagnostic, pharmacological, and non-pharmacological interventions. The 15 outcome indicators include measurements on readmission, mortality, length of stay (LOS), understanding of inhaler therapy, compliance with home oxygen therapy, performance of physical exercise, smoking status, anxiety and depression, health-related quality of life, management at home, functional status, self-reported health condition, medical consumption, and an economic evaluation (Table 3). On the basis of their expertise, the panel also selected a set of 15 baseline variables, including medical, socioeconomic, demographic, and COPD-specific data (Table 3).

Table 3. Set of selected process and outcome indicators

Process indicators	Typology	Criterion met	Unit
1. Performance of arterial blood gas (ABG) measurement during first 24 hours of admission	Process	Performed in all patients	Percentage
2. Performance of chest X-ray during first 24 hours of admission [†]	Process	Performed in all patients	Percentage
3. Performance of electrocardiogram during first 24 hours of admission [†]	Process	Performed in all patients	Percentage
4. Performance of sputum culture and antibiogram during hospitalisation (additional information)	Process	Differences in rates	Percentage
5. Measurement of FEV1 during hospitalisation	Process	Differences in rates	Percentage
6. Prescription of short acting bronchodilators	Process	Performed in all patients	Percentage
7. Prescription of long-acting bronchodilators	Process	Performed in all patients	Percentage
8. Adequate prescription of systemic glucocorticoids [†]	Process	Performed in all patients	Percentage
9. Prescription of antibiotics (additional information)	Process	Performed in all patients	Percentage
10. Administration of controlled oxygen therapy in patients hypoxaemic during admission [†]	Process	Performed in all patients	Percentage
11. Assessment of smoking status at admission	Process	Performed in all patients	Percentage
12. Smoking cessation intervention in active smokers at admission [†]	Process	Performed in all patients	Percentage
13. Adequate education regarding inhaler therapy	Process	Performed in all patients	Percentage
14. Adequate education regarding home oxygen therapy [†]	Process	Performed in all patients	Percentage
15. Performance of rehabilitation tests during the past year	Process	Performed in all patients	Percentage
16. Referral to pulmonary rehabilitation during the past year [†]	Process	Differences in rates	Percentage
17. Assessment of nutritional status	Process	Performed in all patients	Percentage
18. Adequate management of underweight [†]	Process	Performed in all patients	Percentage
19. Adequate management of overweight [†]	Process	Performed in all patients	Percentage
20. Screening and updating of influenza vaccination	Process	Performed in all patients	Percentage
21. Screening and updating of pneumococcal vaccination	Process	Performed in all patients	Percentage
22. Measurement of ABGs 1 or 2 days before discharge inpatients hypoxemic at admission	Process	Performed in all patients	Percentage
23. Prescription of home oxygen therapy in patients hypoxaemic at discharge [†]	Process	Performed in all patients	Percentage

24. Adequate discharge management [†]	Process	Performed in all patients	Percentage
Outcome indicators	Typology	Criterion met	Unit
1. Readmission: 30-day, 6-month	Outcome	Differences in rates	Percentage
2. Mortality: In-hospital, 30-day, 6-month	Outcome	Differences in rates	Percentage
3. Length of stay (LOS)	Outcome	Differences in values	Days
4. Level of understanding of inhaler therapy	Outcome	Differences in values	Score
5. Compliance with home oxygen therapy 30 days after discharge ^a	Outcome	Differences in values	Score
6. Performance of physical exercise during 30 days after discharge	Outcome	Differences in values	Score
7. Smoking status: 30 days after discharge, 6 months after discharge	Outcome	Differences in rates	Percentage
8. Symptoms of anxiety and depression: at discharge, 30 days after discharge <i>Hospital Anxiety and Depression Scale (HADS) (Zigmond 1983)</i>	Outcome	Differences in rates	Percentage
9. Health-related quality of life (HRQL) 30 days after discharge <i>Saint George Respiratory Questionnaire (SGRQ) [68]</i>	Outcome	Differences in values	Score
10. Able to cope at home/place of residence at 30 days after discharge	Outcome	Differences in values	Score
11. Functional status: at discharge, 30 days and 6 months after discharge <i>Katz Scale [69]</i>	Outcome	Differences in rates	Percentage
12. Self-reported health condition: at discharge, 30 days and 6 months after discharge	Outcome	Differences in values	Score
13. Severity of breathlessness at 30 days after discharge Modified Medical Research Council Dyspnoea scale [70]	Outcome	Differences in values	Score
14. Number of visits by general practitioner at 30 days after discharge	Outcome	Differences in values	Score
15. Health status http://www.euroqol.org/	Outcome	Used for economic analyses	Score
Baseline variables <ul style="list-style-type: none"> • <i>Socioeconomic variables:</i> income, medical insurance, level of education, profession • <i>Demographic variables:</i> age, gender, nationality • <i>COPD-related variables:</i> COPD severity, comorbidities, cognitive status, smoking status at admission, COPD-related hospitalisation in the previous year, medication prescribed before hospitalisation, use of home oxygen therapy before admission, body mass index, lung function parameters before discharge, arterial blood gas values at admission, non-invasive positive pressure ventilation (NIPPV) 			

[†]Multi-component indicators.

Subsequently, the selected indicators and baseline variables were operationalised into objective measurements [66]. Based on the guidance of the Agency for Health Care Research and Quality (www.qualitymeasures.ahrq.gov) and the Joint Commission (www.jointcommission.org), each indicator and baseline variable was defined in an indicator protocol by the main researcher (CL). This process included defining of description, rationale or relation to quality, type of indicator (process, outcome, baseline), nominator and denominator, data collection method, data elements, data reporting (i.e. proportion, relative proportion), criteria to meet, expected outcomes, and references (Figure 4). Subsequently, the indicator protocol was mailed to the entire expert panel with a request to appraise each indicator description thoroughly for accuracy and feasibility. A meeting with the entire expert panel was convened to discuss the feedback and finalise the indicator protocol.

Figure 4. Example description on an indicator

Indicator number	2.1.
Indicator name	Arterial blood gas (ABG) measurement at admission
Description	At admission, measurement of PaO ₂ , PaCO ₂ , H ₂ CO ₃ ⁻ , SaO ₂ , and pH by arterial puncture (radialis, brachialis, or femoralis), while breathing room air in patients admitted with the principal diagnosis ICD-9-CM code 491.21. If measurement of ABGs while breathing room air is not feasible (severe cases), oxygen flow (l/min) should be noted. Twenty to 30 minutes should pass before rechecking the ABG tensions when the FiO ₂ has been changed.
Rationale/Relation to quality	Blood gas monitoring is mandatory for patients that require hospitalisation during acute exacerbations of COPD, as measurement of ABGs is important to assess the severity of an exacerbation. A PaO ₂ <8.0 kPa (60 mm Hg) and/or SaO ₂ <90% with or without PaCO ₂ >6.7 kPa (50 mmHg) when breathing room air indicate respiratory failure. In addition, moderate-to-severe acidosis (pH <7.36) plus hypercapnia (PaCO ₂ >6-8 kPa; 45-60 mmHg) in a patient with respiratory failure is an indication for mechanical ventilation. Since arterial blood pH is usually relatively normal in stable COPD, its value during an hypercapnic exacerbation is a useful index of the acute rise in PaCO ₂ , and in turn, is also related to the prognosis of the exacerbation. In conclusion, failing to obtain patients' ABGs may lead to suboptimal management, as ABG values are an important determinant for initiating supplemental oxygen therapy, for prescribing assisted ventilation, and for prescribing home oxygen therapy. Furthermore, patients presenting with exacerbations often suffer from hypercapnia, which can only be detected through ABG measurement. Studies point out that performance of ABGs range from 44% to 84%, with a variance across hospitals of more than 20%.
Type of indicator	Process
Numerator	Number of patients in which ABG measurement at admission was performed among cases meeting the inclusion and exclusion criteria for the denominator among cases meeting the inclusion and exclusion criteria for the denominator.
Denominator	Total number of patients discharged with a principal diagnosis ICD-9-CM code 491.21 as defined in <i>Preface Table 1</i> . Inclusion criteria: all inclusion criteria defined in <i>Preface Table 2</i> . Exclusion criteria: all exclusion criteria defined in <i>Preface Table 2</i> .

Data collection method	Retrospective: Patient record <u>Who:</u> External researcher <u>Time point:</u> After discharge from the ward <u>Data:</u> <ul style="list-style-type: none"> ABG measurement within first 24 hours of admission? (ABGAD) <u>Data for check:</u> <ul style="list-style-type: none"> Date of admission (PRADDate) Date of first ABG measurements at admission (ABGADDa) ABG values (PaO₂, PaCO₂, pH, SaO₂, H₂CO₃) measured at times 1, 2, and 3
Data elements for indicator	<ul style="list-style-type: none"> ABG measurement at day of admission? (ABGAD)
Data reported as	Aggregate rate (%) generated from count data (n) reported as proportion (n/n)
Expected outcome	44-84%
Criteria to meet	Performed in all patients (100%)
References:	(Barbera et al., 1997; Bratzler et al., 2004; Calverley, 2000; Celli & Macnee, 2004; Chang et al., 2007; Cydulka et al., 2003; Gibson & Macnee, 2008; Global Initiative for Chronic Obstructive Lung Disease, 2008a; Harvey et al., 2005; Kelly & Elborn, 2002; Lindenauer et al., 2006b; Roberts et al., 2001; Rodriguez-Roisin, 2006a; Siafkas & Wedzicha, 2006)

Finally, based on the indicator protocol, the objective measurement forms were developed by the main researcher (CL). In summary, data collection need to be performed at three time points, including: a structured interview performed by a team member at discharge from the ward, patient questionnaires completed at discharge from the ward, patient questionnaires completed 30 days after discharge from the ward, and two structured telephone interviews performed by the study coordinator 30 days and 6 months after discharge from the ward. Additionally, a patient record analysis is performed by the study coordinator after inclusion of the 20 patients. The completed forms were sent to the entire expert panel for feedback, and during a subsequent consensus meeting, the forms were discussed and finalised.

Step 8: Piloting by multidisciplinary teams

The set of 38 key interventions, and the set of 24 process and 15 outcome indicators, were piloted by nine Belgian experimental COPD teams in the context of the EQCP study [9]. The multidisciplinary teams included pulmonologists, nurses, physiotherapists, dieticians, social workers, and ergotherapists. The piloting occurred in four phases. Firstly, feasibility of data collection was evaluated during a clinical audit before pathway implementation. For this phase, 105 patients from nine hospitals were included [9]. Mean age was 67 years (SD: 10.0), and 68.6% of patients were male. Approximately half of the patients had severe COPD, 21% had moderate COPD, and another 21.9% had very severe COPD. Overall, after

data analyses we determined that data collection is feasible, and only minor adaptations in the patient record analysis were made.

Secondly, during a workshop in which team members of all nine multidisciplinary COPD teams attended, the process flow diagram, including the 38 key interventions, was presented. Subsequently, all possible remarks were extensively discussed. Thirdly, the detailed set of key interventions was mailed as pdf to the study coordinator of each hospital. We requested that all members of the multidisciplinary COPD team extensively review the key intervention set and subsequently to provide feedback within two weeks. As a result, the feedback given during the workshop and provided after extensive appraisal by all teams showed that teams were very enthusiastic about the process flow diagram and underlying key interventions. Moreover, they agreed by consensus that the set of key interventions was valid and applicable for use in their practice. Six main remarks regarding spirometry, inhaler medications, content and workload of patient education, and feasibility of pulmonary rehabilitation were provided by the teams. All remarks were thoroughly appraised by the expert panel and discussed with the teams, and after consensus the necessary modifications were made.

Finally, the nine multidisciplinary COPD teams implemented the set of key interventions as an active component of their care pathway for in-hospital management of COPD exacerbation in the context of the EQCP study [9]. Six months after start of development and implementation of the care pathway, the nine teams had the opportunity to report experiences, barriers, and successful actions during a workshop. One major difficulty in implementing the educational package into a team's daily work routine was reported. Overall, the teams confirmed validity and clinical applicability of the set of 38 key interventions.

Discussion

A set of 38 evidence-based key interventions for in-hospital management of COPD exacerbation was developed (Appendix 1) and subsequently piloted and approved for validity and clinical applicability by nine Belgian multidisciplinary COPD teams from nine different hospitals. This unanimous approval indicates that the set of key interventions is appropriate for the development and standardisation of the clinical content of the evidence-based care pathway for COPD exacerbation. Secondly, a set of 24 process and 15 outcome indicators was also developed. The pilot study showed that the measurements on the indicators were feasible for the multidisciplinary teams and the patients; only some minor adaptations were required.

The literature on management of COPD is mostly in agreement, including congruency of guidelines, process flow diagrams, and reviews. Only two important discrepancies

concerning sputum culture and performance of spirometric tests were found [71]. Availability of rigorous evidence was very beneficial for 'easy' selection of the care activities (step 4). For other disease states, such as proximal femur fracture (PFF), conflicting evidence exists, or available evidence is scarce (www.mapofmedicine.com/hipfracture). This situation will considerably complicate the selection and description of the key interventions for PFF.

The applied strategy will likely inspire and guide other teams in the development of evidence-based content of their own future care pathways. It is important to note that designing the care pathway content according to the eight-step strategy is a time-consuming process, especially with regard to the Delphi survey (step 3) and pilot testing (step 8). However, results of the Delphi survey and piloting are essential to ensure that the key intervention set is widely clinically applicable. This is especially important when conducting a cRCT, in which the 'same' care pathway intervention needs to be implemented by different teams at different sites and possibly in different countries [9]. Teams developing care pathways should budget enough time in their project plan for proper development of the clinical content of their care pathway.

An important limitation in the current strategy is the lack of patient involvement [72]. Patients can bring a different perspective to the quality improvement process, as they are likely to prioritise different aspects of care compared to clinicians, including interpersonal and amenity aspects; for example, communication with healthcare staff and quality of the food, rather than the technical and clinical aspects [73]. We believe that patients, for instance by contacting patient societies, should have been involved in three phases of the eight-step method: (i) step 4: final selection of the clinical activities; (ii) step 7: Translation of outcome measures; and (iii) step 8: piloting of the final set of key interventions. Including patients in these phases could have provided extra activities and outcomes, important from the patient perspective. After implementation of the key interventions, it will be interesting to gather information on patient preferences and opinions by performing open interviews with the patient and relatives, or by performing walkthroughs together with the patient [74]. Also, when applying the evidence-based care intervention in daily practice, clinicians should ensure that each of their individual patients are involved in decision making [72]. In this context, it is also recommended to develop a patient version that includes a brief and understandable summary of the set of key interventions.

We believe that developing the clinical care pathway content by using this newly developed and validated eight-step method will facilitate adequate integration of evidence-based knowledge into daily practice. Since the beginning of the 1990s, evidence-based clinical practice guidelines for almost all domains of medicine have been available worldwide, accessible more recently via the Internet [4;71;75]. However, we see high variability in the integration of knowledge from evidence-based guidelines into daily practice [4;76]. Common

barriers for integration of evidence-based knowledge are disagreement with the evidence; lack of outcome expectancy; lack of time; and available evidence, such as guidelines being unnecessarily complex, and thus not so directly applicable for clinical practice [4;76;77]. This eight-step methodology can facilitate translation of evidence-based knowledge into clinically applicable key interventions, which can overcome barriers and assist clinicians both in selecting best treatment options and in delivering safe and effective care [4]. However, besides providing a set of detailed evidence-based key interventions, consideration of factors like culture (safety, commitment to do better in practice, peer norms); teamwork; skills management; communication; leadership alignment; and support will be critical to successfully integrate evidence into practice and improve the care process [78]. In this context, care pathways can be very effective tools, as they bring all these pieces together [8;26;79].

Finally, we want to emphasise the potential role of professional medical associations in clinical content development for evidence-based care pathways. Many national and international societies have extensive clinical and research experience in the patient population of their clinical field, comprise a global network of experts in the field, have funding available, and, last but not least, have comprehensive understanding and experience in synthesising evidence-based knowledge and making this knowledge usable for daily clinical practice. Therefore, we think that professional societies could play a major role in developing the clinical content of future evidence-based care pathways, especially in terms of clinical support, expert networking, and input of resources.

Conclusion

The set of 38 key interventions was determined to be appropriate for the development and standardisation of clinical content of the COPD care pathway. Implementation of the set of key interventions in the three other countries involved in the EQCP study (Italy, Ireland, and Portugal) will provide additional information on transferability of the key intervention set to other countries. The novel eight-step method developed in this PhD work will likely help teams to shape the clinical content of their future evidence-based care pathways; for instance, those developed for pathologies such as hip fracture, heart failure, and diabetes.

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Appendix 1. Set of 38 key interventions for in-hospital management of COPD exacerbations

DIAGNOSTIC ASSESSMENT

NON-PHARMACOLOGICAL MANAGEMENT

Chapter 6:

Impact of a care pathway for COPD exacerbation: rationale and design of a cluster randomised controlled trial

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Vanhaecht K, Sermeus W, Peers J, Lodewijckx C, Deneckere S, Leigheb F, Decramer M, Panella M, for the EQCP study group. The impact of care pathways for exacerbation of chronic obstructive pulmonary disease: Rationale and design of a cluster randomised controlled trial (NCT00962468). *Trials* 2010,11:111 doi:10.1186/1745-6215-11-111.

This chapter is not identical to the original publication in the journal *Trials*. References to newly published papers related to the study protocol were added. Additional new details obtained as the study was being conducted were included in the following sections: Sample size, The complex intervention, Measurements, and Data collection.

Abstract

Background: Hospital treatment of chronic obstructive pulmonary disease (COPD) frequently does not follow published evidence. This lack of adherence can contribute to the high morbidity, mortality, and readmissions rate.

Aim: The European Quality of Care Pathway (EQCP) study on acute exacerbations of COPD (NCT00962468) was undertaken to determine how care pathways as complex interventions for hospital treatment of COPD affect care variability, adherence to evidence-based key interventions, and clinical outcomes. *This chapter presents the rationale and design of the EQCP study.*

Methods: An international cluster randomised controlled trial (cRCT) will be performed in Belgium, Italy, Ireland, and Portugal. Power analysis showed that a sample of 40 hospital teams and 398 patients are required for the study. In the control arm of the study, usual care will be provided. The experimental teams will implement a care pathway as a complex intervention. This intervention will include three active components: a formative evaluation of the quality and organisation of care, a set of evidence-based key interventions, and support for the development and implementation of the care pathway. The main outcome will be 6-month readmission rate. As a secondary endpoint, a set of clinical outcome and performance indicators (including care process evaluation and team functioning indicators) will be measured in both groups.

Discussion: The EQCP study is the first international cRCT on care pathways. The EQCP project is designed as both a research study and a quality improvement project and will include a realistic evaluation framework and process analysis to further understand why and when care pathways can best work.

Trial Registration number: NCT00962468

Background

Healthcare is changing towards more patient-focussed care. The organisation of the care process related to quality, efficiency, and accessibility is one of the main areas of interest in the next years for clinicians, healthcare managers, and policy makers. A main method to (re)organise a care process is the development and implementation of a care pathway. Care pathways, also known as clinical pathways or critical pathways, are used worldwide for a variety of patient groups [1-7]. A care pathway is defined as a complex intervention for the mutual decision making and organisation of predictable care for a well-defined group of patients during a well-defined period. Defining characteristics of pathways includes an explicit statement of the goals and key elements of care based on evidence, best practice, and patient expectations; facilitation of communication and coordination of roles; sequencing activities of the multidisciplinary care team, patients, and their relatives; documentation, monitoring, and evaluation of variances and outcomes; and identification of relevant resources [8-10].

A care pathway is explicitly defined as a 'complex intervention' [8-12]. Complex interventions in healthcare, whether therapeutic or preventive, comprise a number of interacting components that seem essential to the proper functioning of the intervention, although the effective 'active component' of the intervention is difficult to specify. When considering a spectrum of low to high complexity, developing a drug would be at the low end of the complexity spectrum, while the evaluation of the effect of a stroke unit would be at the high end of the spectrum. The greater the difficulty in defining precisely what the 'active component' of an intervention is and how these component(s) relate to each other, the greater the likelihood that one is dealing with a complex intervention. Pathways in the realm of stroke units seem to be at the higher end of the complexity spectrum [13-16]. Active ingredients of a care pathway complex intervention might be the level of multidisciplinary teamwork, the integration of a package of evidence-based key interventions, and the active follow-up of the care process [6].

A recent Cochrane review concludes that clinical pathways reduce in-hospital complications and improve documentation without negatively affecting length of stay (LOS) and hospital costs [17]. The effects, however, are still quite small in comparison to what we might expect theoretically. One possible reason is the high variability in effect from one organisation to another, which seems to stress the idea that context factors might be extremely important [9;18-20]. These context factors are not considered in these meta-analyses. An indicator of context influence is the heterogeneity of meta-analyses, which seem to be quite high in the Rotter meta-analysis paper [17]. Completion of large multicentre trials that include information on the mechanisms used and the context of the involved

organisations will be necessary to fully understand why and when pathways lead to their effect [9;16;21].

To evaluate pathway effectiveness, the European Pathway Association (E-P-A), an international not-for-profit association, launched the European Quality of Care Pathways (EQCP) study on exacerbation of chronic obstructive pulmonary disease (COPD) [21]. COPD exacerbations are a leading cause of acute hospital admissions worldwide [22-24]. Patients with COPD exacerbations need multidisciplinary care. Moreover, the coordination of the care process among multiple caregivers is complex [25;26]. Thirty-five percent of COPD patients are admitted because of acute exacerbations within one year, and up to 40% of admitted patients have two or more readmissions a year [22-24]. A systematic review about in-hospital management of COPD exacerbations showed that implementation of care processes recommended by widely accepted guidelines is very poor and show high variance, especially for performance of non-pharmacological interventions [27]. Also, Decramer et al. observed several important deviations from international guidelines in the management of COPD by pulmonologists and general practitioners [28].

Up to now, four non-randomised trials on the impact of a care pathway for inpatient management of COPD exacerbations have been published [29]. The studies were conducted between 2000 and 2001, and the methodology was rather weak. However, there are some indications in these studies suggesting that a COPD exacerbation care pathway improves performance with regard to diagnostic assessment and use of standing orders, and that it may reduce LOS and the number of hospitalisations [29].

Objectives

The primary goal of the EQCP study on COPD exacerbations is to evaluate care pathway effectiveness in acute hospitals. A secondary goal is to understand how and under which circumstances the implementation of a care pathway for COPD exacerbations is successful.

Methods

The project

The EQCP study is an international multicentre research project launched by the E-P-A (www.E-P-A.org) [21]. The E-P-A has been collaborating with the Centre for Health Services and Nursing Research of the Faculty of Medicine of the Catholic University Leuven (Belgium) and the School of Public Health of the Amedeo Avogadro University of Eastern Piedmont (Italy) for the scientific lead in the this study. The study is conducted in four countries: Belgium, Ireland, Italy, and Portugal. In each country, a research centre coordinates the project in that country based on the agreed international protocol. In Belgium, the lead

coordinating centre is the Centre for Health Services and Nursing Research of the Faculty of Medicine of the Catholic University Leuven. For Ireland, the lead centre is the Health Service Executive in Dublin. In Italy, the School of Public Health of the Amedeo Avogadro University of Eastern Piedmont coordinates the project with support from ARESS Piemonte. In Portugal, the lead coordinating centre is the National School of Public Health in Lisbon. In each of the four countries hospitals will be selected by E-P-A in close cooperation with a national coordinator. In every participating hospital a pathway facilitator is appointed as a local facilitator for implementing the care pathway. In each country except Belgium, the E-P-A team trains the pathway facilitator in implementing care pathways. In Belgium, hospitals were selected from the members of the Belgian-Dutch Clinical Pathway Network (BDCPN), and all pathway facilitators were trained beforehand within the network [21].

Study design

The complex intervention and the trial are designed according to the 'Framework for development and evaluation of complex interventions' [15;16]. This study is a phase 3 study that includes a cluster randomised controlled trial (cRCT) [15;16;30]. In cRCTs, organisations, rather than individuals, are randomised to intervention and control groups, and outcomes are measured on individuals within the clusters [30]. Care pathways induce change at different levels of the organisation (i.e. patient, team, hospital, etc.). To deal with these multilevel effects when evaluating a care pathway, it will be appropriate to use a cRCT, implying randomisation occurs at the highest level of the intervention (i.e. randomise the team rather than the practitioners or patients) [12;16;30-33]. In addition, if the effect of a care pathway would be explored in a single organisation, the intervention given to the individuals in the experimental group may also inadvertently affect individuals of the control group within that organisation (i.e. contamination) [30;33].

In this study, each cluster will consist of a hospital where patients are hospitalized for COPD exacerbation and cared for by a specific multidisciplinary team [21]. Hospitals will be randomised to an experimental group, where a care pathway will be implemented, and to a control group, where usual care will be delivered (no intervention). To ensure that hospitals in both arms are balanced, we will use stratified randomisation based on country level, hospital type (teaching versus non-teaching) and hospital size (<600 and $\geq$ 600 beds) [34;35]. Additionally, several organisational factors will be explored: availability of an early discharge scheme, presence of a formal pulmonary rehabilitation programme, availability of non-invasive ventilation, and volume of patients annually treated for COPD exacerbations [34;35]. These variables will be treated as covariates in the data analysis.

Measurements will include follow-up of care processes and clinical outcomes (Figure 1), and results of the intervention and control groups will be compared to evaluate whether the

implementation of a care pathway leads to better compliance to care processes and improved clinical outcomes.

Figure 1. Study design of the European Quality of Care Pathways (EQCP) study on COPD exacerbation

Inclusion-exclusion criteria

Organisations can be included if (i) they provide written agreement to participate in the study; and (ii) if they agree not to develop and implement a pathway for COPD within the time frame of the study when randomised into the control group.

In every hospital, 20 consecutive patients need to be followed up. Patients can be included in the study if (i) admitted with COPD exacerbation as the primary diagnosis, (ii) hospitalised for at least 48 hours, (iii) admitted in a ward where COPD exacerbations are usually treated, (iv) able to understand and read the native language, and (v) written informed consent is given. A patient can be included in the study only once, specifically at his or her first admission during the study period. Patients are excluded if one of the following criteria is present: (i) already included in another study of which the measurements could influence the measurements or outcomes of the EQCP study; and/or (ii) need for invasive positive pressure ventilation (IPPV) at admission into the hospital.

Patients initially included in the study could drop out for three reasons: (i) if patient voluntarily decides to withdraw from the study, (ii) if patient is incorrectly diagnosed with a COPD exacerbation, and (iii) if diagnosis of COPD exacerbation remains unconfirmed. If the patient dies or is transferred to another hospital, the data collection ceases for that particular patient, but the patient remains included in the study and so is part of the total sample of 20 patients in the particular hospital. Hospitals will be asked to keep a logbook for included

patients, to keep a summary of the included patients, and especially to be able to look for additional information when necessary and to check why patients dropped out or were not followed up during the whole study. Secondly, they will be asked to keep a logbook for excluded patients in order to check for selection bias.

Study sample

An important consequence of a cluster randomised design is that, unlike individually randomised trials, the outcome for each participant cannot be assumed to be independent of any other participant, since those within a cluster are more likely to have similar outcomes. Thus, the statistical power of a cRCT may be substantially less than that of a similar-sized, individually randomised trial [30]. In order to take into account the cluster effect, the variance term in standard statistical formulae for sample size calculation needs to be increased by the 'design effect', also called the 'inflation factor'. In other words, the design effect is a measure for the number of extra patients needed to deal with this cluster effect. The design effect is calculated based on the intra-cluster correlation coefficient (ICC) [36-38], which accounts for the relatedness of clustered data by comparing the variance within clusters with the variance between clusters. The ICC needs to be estimated from previous studies that used similar-sized clusters containing similar types of individuals and used the same outcome [36-38]. The dependency in outcomes also implies that increasing the number of clusters offers more power than does increasing the number of individuals per cluster. However, this adjustment is sometimes very difficult, considering the logistical and economic implications when performing a cRCT. Furthermore, cRCTs with fewer than five clusters per arm are inadvisable, since parametric tests may be unreliable with such small numbers and since nonparametric tests require at least four to six clusters per arm to achieve statistical significance [30].

Sample size calculation in cRCTs is based on the improvement in the main outcome parameters [36;38]. The selection of main outcomes for the EQCP study is based on three parameters: frequency of use in the literature, opinions of experts, and timing of the research with regard to organisational factors (sustainability of the design, time to include patients). Based on these criteria, 6-month readmission rate was identified as the main study outcome for in-hospital management of COPD exacerbations [39;40]. Other important parameters are LOS, 30-day readmission, and 6-month mortality [39;40]. Achieving a power of 80% and a significant α of 0.05, requires 296 patients per arm to observe a 10% reduction in readmission rates of 41% to 30% [39;40]. After adjustment for the cluster design, based on two previous cRCTs by Panella et al. (ICC: 0.018; Design effect: 1.342; $n=20$) [12;31;41], the effective sample size is increased to 398 patients per arm. This means that, with our criterion of 20 consecutive admitted patients in each unit, 20 hospitals are required to be included in

both the intervention and control group. As four countries are involved in the study, each country had to enrol at least 10 hospitals, with randomisation into five intervention cases and five control cases.

Between September 2008 (Belgium) and September 2009 (Ireland, Italy, and Portugal), 117 hospitals out of the four countries were invited to participate in the study (Figure 2). Seventy-one of them consented. After assessment of eligibility, 65 hospitals were included in the study (Belgium: n=15; Ireland: n=14; Italy: N=12; Portugal: N=24) (Figure 2). The participating hospitals in Belgium were all members of the BDCPN, which explains the unusually high number of hospitals in Belgium excluded (i.e. already having a COPD care pathway in operation). Based on stratified randomisation according to country level, hospital type (teaching vs. non-teaching), and of hospital size (<600 and ≥600 beds) [34;35], in total 33 hospitals were enrolled in the intervention group and 32 hospitals in the control group (Figure 2). As a consequence, up to 600 potential patients will be included in each arm.

The complex intervention: care pathway implementation in the experimental arm

The care pathway will include three active components. (i) *A formative evaluation on the quality and organisation of the care process before care pathway implementation.* A clinical audit, including follow-up of 24 process indicators in 20 patients (Chapter 5, Table 2), will be performed 6 months before developing the care pathway and during a 2-3 month period. During a workshop, a formative feedback report, based on the results of the clinical audit, will be provided to the teams describing the relative performance of every team against the evidence-based protocol and against the performance of all other teams in the study. This feedback will help the teams in understanding their bottlenecks and their actual overall organisation of the care process.

(ii) *Integration of a set of evidence-based key interventions on in-hospital management of COPD exacerbations (Chapter 5, Appendix 1).* A set of 38 evidence-based key interventions will be provided to the multidisciplinary team of all participating hospitals, and a workshop on the content of the key interventions will be organised. This set of key interventions was developed based on (i) the literature, (ii) an international Delphi study [42], and (iii) a consensus meeting with a multidisciplinary expert panel, including a medical doctor, a physiotherapist, and a clinical nurse specialist—each with extensive clinical and scientific expertise in COPD—and three experts in patient care management (Chapter 5, Appendix 1).

(iii) *Training on care pathway development and implementation (Plan Do Study Act [PDSA] cycle and teamwork).* The pathway facilitator of each hospital is trained to develop and implement a care pathway, based on the findings of the formative evaluation of the care process and the set of evidence-based key interventions. Pathway facilitators use a care

pathway implementation protocol based on the Deming-PDSA cycle [43]. Meetings with the pathway facilitators are organised to present and discuss the feedback reports and the set of evidence-based key interventions, and to discuss actual bottlenecks in implementing the care pathway. Change is supported by providing the possibility for participants to exchange best practices. During these meetings local clinical champions and team change experts support and stimulate the pathway facilitators to effective knowledge sharing processes.

Figure 2. Flow diagram: hospital recruitment and randomisation

The control group

In the control group, the complex intervention will not be implemented, and so the control hospitals agree not to change their actual organisation of the care process and not to develop a care pathway during the study period. The team members provide care in the same way as they did before the start of the study. This is referred to as usual care. The hospitals included in the control group will be offered the opportunity to develop a care pathway one year later, based on the protocol and experience gained in the experimental group. By this means, the design incorporated some characteristics of a step wedge design in which the implementation of the intervention is spread over time.

Measurements

To measure compliance to care processes and performance of clinical outcomes, a set of 24 process and 15 outcome indicators will be followed up. These indicators were developed on the basis of (i) an extensive literature review, (ii) an international Delphi survey [42], and (iii) consensus meetings with a multidisciplinary expert panel that included a pulmonologist, a physiotherapist, a clinical nurse specialist in COPD, and three experts in patient care management (Chapter 5, Table 2). The primary outcome measure in the EQCP study is 6-month readmission. Main secondary outcome measures included 30-day readmission, 30-day mortality, 6-month mortality, LOS, and quality of life, (Chapter 5, Table 3). Measurements on the quality of the clinical care processes include monitoring the performance of diagnostic, pharmacological, and non-pharmacological processes during hospital stay and at discharge (Chapter 5, Table 3). Finally, 15 baseline variables will be measured, including socioeconomic, demographic, and COPD-specific data (Chapter 5, Table 3). Process and outcome indicators were translated into objective measurements by the multidisciplinary expert panel, according to the guidelines of the Agency for Healthcare Research and Quality (www.qualitymeasures.ahrq.gov) and The Joint Commission (www.jointcommission.org) (Chapter 5, Figures 4 and 5).

To further understand why pathways are effective, information on the context of the organisation is important. Therefore, in a parallel study on teamwork (included in another PhD dissertation), a set of both generic and COPD-specific context indicators and team structure indicators will followed up [21;44;45].

Data collection

Data collection will occur at three time points through (i) structured interviews performed by a team member at discharge, (ii) patient questionnaires to be completed at discharge and 30 days after discharge from the ward, and (iii) two structured telephone interviews performed by the study coordinator 30 days and 6 months after discharge from the ward.

Additionally, the study coordinator together with a clinician will perform a patient record analysis after inclusion of the 20 patients. To carry out these analyses, an external researcher will be involved to ensure that an objective 'snapshot' of the patient record will be obtained. Should a team member carry out the patient record analyses, a high risk for bias would be present, as the member might also report care activities that were not documented in the patient record as 'performed', but of which the caregiver is convinced that they were being performed in that particular patient. In our opinion, if performance of a care activity or the results of performing an activity (for instance, lab results or understanding after education on inhaler therapy) are not documented in the patient record, this performance and these results are not detectable by the other team members caring for this patient. As a consequence, they will not know if the particular care activity was carried out or not, and if the intervention was effective or not. In such circumstances, the results cannot be used to optimise further care for the patient. So in conclusion, non-documentation of performance of a care activity or related results was interpreted as non-optimal performance in our study. In addition, team members could provide a 'better snapshot' of their care in the context of 'social desirability', which is also avoided by assigning an external researcher to the patient record analyses. Also, it was recommended that the external researchers ask a clinician for assistance when analysing the first patient record to ensure that all available data in the patient record will be captured.

Overall, in order to minimise risk for missing data, we limited the amount of data collected by the patient questionnaire at 30 days to those data that could not be collected in another way. Thus, most data collected through the patient record analyses and questionnaires will be completed by the team at discharge. All outcomes will be measured using validated instruments available in literature.

The data collection forms were printed and classified per collection time point for 20 patients, and delivered into two binders to each organisation. All data will be collected centrally in every hospital, and then will be provided to the national coordinators of all participant countries. Data will be entered into a central database at the Catholic University Leuven.

Registration and Ethical approval

The study is registered as a cRCT at clinicaltrials.gov (identifier: NCT00962468). The ethical approval will be country specific, but overall ethical approval will be maintained on three levels: (i) ethical approval by the ethical committee of the coordinating centre at the country level; (ii) ethical approval with regard to participation in the intervention at the cluster level, namely by the ethical committee of each of the participating hospitals; and (iii) individual informed consent will be sought from the patients with regard to the access to the patient record and participation in surveys. As indicated by the Medical Research Council, patients' consent to participate in the study is not possible, because randomisation occurs at the hospital level and not at the patient level [30]. Moreover, the aim of the study is to improve adherence to evidence-based care through clinical pathways in the intervention group. In the control group, no intervention will be implemented and, thus, patients will receive usual care. Therefore, being included in the experimental or control group should not imply any risk for the patients.

Approval from the ethical committee of the coordinating centre at Leuven University was obtained (identifier: ML5617), and the proposal was also approved by the ethical committees of all participating hospitals.

Discussion

The EQCP study is the first international cRCT on the effect of care pathways [21]. Within this study, a cRCT design is combined with a realistic evaluation approach [46]. In this way, any differences between the experimental and control arms can be analysed, but also the process evaluations within the experimental arm itself can be followed up and evaluated [47]. As suggested by Berwick in 2008, it is not only important to understand whether an intervention is effective, but it is also important to understand why and under what circumstances it works [19]. The approach in the EQCP study will allow us to analyse whether pathways work and also will provide information on when and how they work [21]. Within this international trial, three active ingredients define the complex intervention: feedback on the actual situation, information on the evidence-based key interventions, and implementation and design process.

Hawe and colleagues argued that the crucial point in the evaluation of complex interventions lies in what is standardised: In complex interventions, the function and process of the intervention should be standardised, not only the components themselves [48]. This argument is important for pathway research and was previously addressed by Panella et al. [11]. In pathway research, the pathway process or quality improvement cycle that is run

through is part of the intervention. In that way the improvement and implementation process is included as one of the basic active ingredients.

One challenge in carrying out multicentre trials on pathways, studying quality improvement methods in general, or in comparing pathways from or between different organisations, is to understand the role of context. Pawson and Tilley defined an action as causal only if its outcome is triggered by a mechanism acting in a context (context + mechanism = outcome) [46]. They argued that programmes work (i.e. have good outcomes) only insofar as they introduce the appropriate ideas and opportunities (the mechanism) to groups in the appropriate social and cultural conditions (the context) [19;46]. This realistic evaluation paradigm has already been used in pathway research [7] and was recently suggested by Berwick in a publication on the science of improvement [19]. For pathways, the mechanism will need to be based on the basic active ingredients described above. However, the fine-tuning of the intervention will be based on the actual bottlenecks and on the context of the organisation and multidisciplinary team involved. Therefore, in the present international cRCT on pathways, also a set of team indicators and organisational factors will be measured [44]. The process and outcome indicators will provide data to help us understand whether pathways work, but the team indicators will help us understand why and how they work [21;44;45].

With this study, E-P-A will be able to influence health professionals and hospital managers in actively improving the quality and efficiency of care [21]. The teams receive support in the reorganisation of the COPD care processes and can later use this implementation knowledge in other care processes. Teams will receive feedback on their own organisation, including benchmark data in comparison with other international teams. In this way the design of the EQCP project is both a research study and a quality improvement project.

The following chapters (Chapters 7 and 8, respectively) describe (i) the preliminary results of the EQCP study, including the results of the Belgian EQCP study, and (ii) an implementation analyses with regard to the second component of the complex intervention, 'integration of a set of evidence-based key interventions'.

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Chapter 7:

Impact of a care pathway for COPD exacerbation: preliminary results of the European Quality of Care Pathways (EQCP) Study

Context

Chapter 6 presented the design and rationale for the European Quality of Care Pathways (EQCP) study on COPD exacerbations. This study is conducted in four countries (Belgium, Ireland, Italy, and Portugal) with two aims: (i) to evaluate whether the implementation of a care pathway, compared with usual care, improves compliance to evidence-based care processes and performance of clinical outcomes for patients hospitalised with COPD exacerbations; and (ii) to study why and under what circumstances care pathways work.

This PhD dissertation research was integrated into the EQCP study and ***focuses on the first study aim: the impact of care pathways for in-hospital management of COPD exacerbations on care processes and clinical outcomes***. The Belgium component of the EQCP study is one year ahead of the other countries and is also considered to be a pilot test. Because of timing and feasibility of the PhD dissertation, ***only the results of the Belgium EQCP study are included in the results section and are described in the present chapter***. Final results based on the data of all four countries are expected to be analysed in autumn 2013. These results will be disseminated by the EQCP study group via publications and conference proceedings in 2013 and 2014.

Belgian sample size and interpretation of results

Belgian sample size

Of the 12 hospitals included in the Belgium component of the EQCP study, 7 hospitals were randomly assigned to the experimental group and 5 to the control group, resulting in a final sample size of 136 patients in the experimental group and 100 patients in the control group (cf. results section). Power analyses show that 400 patients should be included in each arm to have a statistical power of 80% and a significant α of 0.05 (Chapter 6) [1]. As the current sample size of the Belgian study is too small to achieve this level of statistical power, these data were analysed as first phase results. These results will not be published as a separate paper in a peer-reviewed journal. A final analysis will be performed on the combined data of the four participating countries at the end of the EQCP study, as this final sample size will be sufficient to guarantee a statistical power of 80% [1].

Interpretation of results

Because of low statistical power, the chance for detecting statistically significant results is reduced [2-4]. However, with regard to process indicators, even non-significant results provide valid information regarding quality of care and differences in both groups. Indeed, clinical practice guidelines, which are very congruent and continuously updated [5-8], recommend unambiguously that the evaluated indicators should be performed in every

patient that is hospitalised for COPD exacerbations. In other words, the criterion to meet for every process indicator is 100% performance, regardless of patient characteristics. Consequently, results on the process indicators do reflect performance levels of the teams, and so should not be considered to be coincidental results arising from chance variation in small samples.

For outcome indicators, statistical power is essential for detecting true differences between the control and experimental groups. Thus, with low statistical power, only less confident conclusions can be drawn. In addition, risk adjustment is needed to identify and adjust for variation in patient outcomes that stem from differences in patient characteristics (or risk factors) across both groups [9-15]. Furthermore, the main outcome for the EQCP study was assessed at three time points: 6-month readmission, 30-day readmission, and 6-month mortality. However, according to power calculation at least 400 patients are needed to detect an effect size of up to 11% for 6-month readmission.

Since the outcome indicators are very prone to bias related to limited statistical power of the Belgian trial, ***this chapter will mainly focus on the results on the process indicators.***

Methods

Design

To evaluate pathway effectiveness, a cluster randomised controlled trial (cRCT) was conducted, in which the experimental group included patients treated according to a specific care pathway, while the control group included patients receiving usual care. ***The methodology of the study was described in detail in Chapter 6 [1].***

In the next three sections, some specific remarks are included on outcome measures, data input, and interim statistical analyses. In Appendix 1, statistical model details are provided.

Outcome measurements

In the overall EQCP study, the primary outcome measure is 6-month readmission. The secondary outcome measures are 30-day readmission, 30-day and 6-month mortality, quality of life, and finally, performance on 24 process indicators regarding diagnostic, pharmacological, and non-pharmacological management. A complete overview of the outcome measures is provided in Table 3 of Chapter 5. As explained above, this results chapter will mainly focus on the findings on the 24 process indicators (Chapter 5, Table 2).

Data input

Data of 20 patients were collected centrally in every hospital and subsequently provided to Leuven University, where the data were input into a central database. A Microsoft Access® database was developed by a non-profit organisation specialising in healthcare information systems (<http://www.higis.eu.org/>). The database was designed in English to facilitate input of the data sheets from the different languages of the four countries in the EQCP study. Data input was extensively tested for errors and feasibility by the responsible researcher CL and KV.

Four students, enrolled in the Masters in Management and Policy programme, entered data into four central computers. Data input was supervised by the main researcher (CL). The students were blinded with regard to the data and thus did not have information on the study aim and design. Three steps were taken to facilitate proper data input. Firstly, a user manual was produced that included (i) contact details of the responsible researcher (CL), (ii) detailed instructions on how to use the application; and (iii) specific remarks with regard to the patient data itself (i.e. medications, risks of errors, etc.). Secondly, the four students were trained for two days to master the data-input procedure. Thirdly, to minimise the risk of input errors, students were asked to report specific remarks (i.e. missing bundles on a specific time point) and uncertainties in an excel logbook. Finally, quality controls on data input were performed twice weekly by the responsible researchers (CL and KV) in terms of verification of randomly picked samples of five patients. No major errors were found.

Interim statistical analysis

Differences in patient characteristics were analysed by using Chi² and t-tests for categorical and continuous variables, respectively. Statistical significance was defined as a two-sided p value of <0.05. Differences in results on process and outcome indicators between groups were evaluated at an individual level using random effects logistic regression (binary variables) or linear regression (continuous variables), accounting for the clustering effect (Appendix 1) [16]. Results on outcome indicators were adjusted for patient characteristics, including age, gender, comorbidities, previous hospital admissions, COPD severity, and selected clinical parameters (Table 1). All analyses were intention-to-treat and were carried out using SAS statistical software, version 9.2 for Windows.

EQCP Belgium: preliminary results**Hospital inclusion**

For Belgium, 39 hospitals were invited to participate in the study in September 2008. Fifteen were interested, and after assessment of eligibility, 13 hospitals were included. Based on

stratified randomisation [17;18], seven hospitals were assigned to the experimental group and six hospitals to the control group. After the randomisation process, one hospital in the control group withdrew because of changing leadership (Figure 1).

Figure 1. Flow diagram of hospital inclusion and randomisation

Study timing

The clinical audit before implementation was carried out between April and July 2009. Feedback on the results of the clinical audit was provided in March 2010. Consequently, organisations developed a care pathway between May and December 2010. Between March

and November 2011 measurements on process and outcome indicators were performed in both the seven experimental hospitals and the five control hospitals. Data input and analysis occurred between September 2011 and January 2012.

Table 1. Baseline characteristics of the sample

Variable	Care pathway (CP) n=136	Usual care (UC) n=100	P Value*
Male gender, n (%)	90 (66.2)	63 (63.0)	0.679
Mean age, years (SD)	68.4 (10.8)	68.8 (9.5)	0.765
Cardiac failure, n (%)†	43 (31.6)	36 (36.0)	0.486
Diabetes, n (%)‡	17 (12.5)	13 (13.0)	1.000
Smoker at admission, n (%)	(51) 37.5	30 (30.0)	0.300
Number of hospitalisations in the previous year, n (%)§			
None	84 (61.8)	50 (50.0)	0.315
1	23 (16.9)	19 (19.0)	
2	11 (8.1)	11 (11.0)	
3 or more	14 (10.3)	16 (16.0)	
BMI (SD)	24.7 (6.0)	24.7 (5.2)	0.927
FEV1%	45.4 (16.1)	46.8 (20.6)	0.528
Missing data, n (%)	24 (17.6)	22 (22.0)	
COPD severity, n (%)§			
GOLD I: Mild	4 (2.9)	7 (7.0)	0.031
GOLD 2: Moderate	47 (34.6)	21 (21.0)	
GOLD 3: Severe	57 (41.9)	38 (38.0)	
GOLD 4: Very Severe	27 (19.9)	31 (31.0)	
PaO ₂ (kPa)	9.34 (3.43)	9.34 (3.00)	0.998
Missing data, n (%)	23 (16.9)	21 (21.0)	
Treated by a pulmonologist, n (%)	131 (96.3)	97 (97.0)	1.000
Hospitalised in a respiratory ward, n (%)	113 (83.3)	82 (82.2)	0.728

BMI, basal metabolic index ; FEV1, forced expiratory volume ; GOLD, Global Initiative for Obstructive Lung Disease (stages 1-4).

*Chi² and t-tests for categorical and continuous variables, respectively.

†Includes heart failure, arrhythmia, valvular disease, acute myocardial infarction, Ischemic heart disease [19].

‡Includes diabetes, uncomplicated and complicated [19].

§Missing data: (i) Previous readmissions: CP: n=4, UC: n=3; COPD severity: CP: n=1; UC: n=3.

Hospital characteristics

The total number of beds of included hospitals varied from 314 to 749 beds in the experimental group, and from 169 to 714 beds in the control group. Annual volume of hospitalised COPD patients varied from 126 to 405 patients in the experimental group, and from 133 to 377 in the control group. Four of 7 experimental hospitals were teaching hospitals, while only one control hospital had a teaching status. Dedicated pneumology

wards were present in only two control hospitals. A formal rehabilitation programme was available in all seven experimental hospitals, but in only 1 of 5 control hospitals.

Patient characteristics

The final sample consisted of 236 patients, with 136 patients receiving care pathway care, and 100 patients receiving usual care (Table 1). At admission, there were no significant differences with regard to age, gender, selected clinical conditions, or number of previous admissions. However, in the control group, the number of patients with very severe COPD was 11% higher (UC: 31.0% vs. CP: 19%), and the number of patients with moderate COPD was 13% lower (UC: 21.0% vs. CP: 34.6%) ($p=0.031$).

Results on process indicators

Results on process indicators are presented in Table 2, according to each core process: diagnostic management (Table 2, nos. 1-5); pharmacological management (Table 2, nos. 6-9); and non-pharmacological management (Table 2, nos. 10-24). Appendix 2 provides a guided on the results tables (table 2, 3 and 4). Seven of 24 indicators (29.2%) (Table 2, nos. 3, 10, 13, 14, 17, 19, 24) and 25 of 42 subcomponents (59.5%) (Table 2, nos. 3a, 7a, 8c-d, 12a-c, 13a-d, 14a-e, 17a, 18a-c, 19a-b, 24a, 24i-j, 24l) showed better results of 10% and up to 50% in the care pathway group (Table 2). However ***significant improvements*** were found for only three indicators, specifically: education on inhaler therapy (CP: 40.7% vs. UC: 1.0%; OR=2120.27; 95% CI, 3.17-1417636.22); education on oxygen therapy (CP: 40.0% vs. UC: 0.0%; OR=11.77; 95% CI, 1.59-87.25); measurement of basal metabolic index (BMI) (CP: 75.5% vs. UC: 27.0%; OR=78.61; 95% CI, 2.26-2736.73); and for 10 subcomponents. The 10 subcomponents were adequate dose prescription of corticoids (CP: 92.1% vs. UC: 74.4%; OR=2.80; 95% CI, 1.24-6.33); education on inhaler medication (CP: 68.1% vs. UC: 3.1%; OR=64.12; 95% CI, 19.22-213.88); education on inhaler technique (CP: 67.4% vs. UC: 3.1%; OR=62.69; 95% CI, 18.18-208.93); education on inhaler device (CP: 67.4% vs. UC: 4.1%; OR=46.01; 95% CI, 15.89-133.20); providing leaflet on inhaler therapy (CP: 55.7% vs. UC: 39.2%; OR=4.60; 95% CI, 1.69-12.50); education on oxygen source (CP: 56.7% vs. UC: 0.0%; OR=13.60; 95% CI, 1.85-99.53); education on oxygen equipment (CP: 53.3% vs. UC: 0.0%; OR=21.41; 95% CI, 6.99-66.63); education on oxygen precautions (CP: 60.0% vs. UC: 0.0%; OR=14.27; 95% CI, 1.95-104.50); providing patient letter with information on follow-up appointment (CP: 59.1% vs. UC: 43.4%; OR=4.18; 95% CI, 1.64-10.64); and planning of follow-up appointment (CP: 89.0% vs. UC: 67.0%; OR=4.43; 95% CI, 1.05-18.65) (Table 2). In addition, two indicators in the control group—arterial blood gas (ABG) measurement at discharge and assessment of social support within two days—had lower performance at 20%

(UC: 48.6% vs. CP: 27.1%; OR=0.34; 95% CI, 0.09-1.29) and 10%, respectively (UC: 92.5% vs. CP: 82.6% OR=0.27; 95% CI, 0.00-17.89). This difference, however, was not significant.

Overall, **optimal performance**—defined as correct performance of an indicator **in more than 90% of patients**—was found **in both groups** for three indicators: performance of chest X-ray, prescription of short-acting bronchodilators, and prescription of long-acting dilators (Table 2, nos. 2, 6, 7). Optimal performance was also observed for five subcomponents: performance of X-ray during hospitalisation, performance of X-ray within 24 hours, systemic glucocorticosteroids prescribed during hospitalisation, assessment of residential status within 3 days of admission, and availability of letter for general practitioner in medical record (Table 2, nos. 2a-b, 8a, 24b, 24k). Additionally, **in the care pathway group** optimal performance was found for two indicators: assessment of smoking status and administration of controlled oxygen therapy (Table 2, nos. 10, 11). Optimal performance was also found for two subcomponents: performance of electrocardiogram during hospitalisation and assessment of residence during hospitalisation (Table 2, nos. 3a, 24a). **In the control group**, optimal performance for two subcomponents was found: assessment of living status within 3 days and assessment of social support within 3 days (Table 2, nos. 24d, 24f).

Aside from these results, performance showed a downward trend. Very suboptimal performance, defined as correct performance of an indicator in **less than 50% of patients**, was found **in both groups** for 12 of 24 indicators (50.0%), including adequate prescription of corticoids, smoking cessation intervention education for inhaler and oxygen therapy, performance of rehabilitation tests and referral to rehabilitation, management of nutritional overweight and underweight, pneumococcal vaccination, adequate discharge management, ABG measurement before discharge (Table 2, nos. 8, 12-16, 18, 19, 21-24); and for 8 of 42 subcomponents (19.0%) for nutritional management, adequate prescription of corticoids, smoking cessation, and prescription of home oxygen therapy (Table 2, nos. 8b, 12b, 12e, 18a-c, 23a-). Additionally **in the control group**, very suboptimal management was found for 16 additional subcomponents. Except for oral administration of corticoids, these subcomponents dealt with non-pharmacological management (Table 2, nos. 8d, 12a, 12c, 12d, 13a-d, 14a-e, 19a-b, 24g, 24i). However, it is notable that 5 of 24 indicators (20.8%) (Table 2, nos. 12, 13, 14, 23, 24), and 12 of 42 subcomponents (28.6%) (Table 2, nos. 12a-c, 12e, 13d, 14d-e, 23b, 24g-i, 24l) had missing data of up to 60%; both groups had about the same amount of missing data. All of these missing data were related to patient questionnaires. The biggest reason for this high rate of missing data was that 40 patient questionnaires were lost due to internal organisation mail errors.

Results on outcome indicators

Risk adjustment was used to account for the impact of individual risk factors as reported in Table 1. No significant differences were found between care pathway and control groups (Table 3 and 4), although potentially interesting non-significant improvements in the care pathway group were found for 30-day readmission (CP: 13.6 % vs. UC: 22.2%) (Table 3) and length of stay (LOS) (CP: 11.65 days vs. UC: 13.36 days) (Table 4).

Table 2. Results on process indicators for Belgium European Quality of Care (EQCP) study

Indicator	Subcomponent	bold	Significant differences	<i>italic</i>	30-50% missing data
Process Indicator			Care pathway (Experiment) Optimal performance n/N (%)	Usual care (Control) Optimal performance n/N (%)	Odds Ratio (95% CI) [†]
1. Performance of ABG measurement during the first 24 hours of admission			103/136 (75.7)	75/100 (75.0)	1.07 (0.39-2.91)
2. Performance of chest X-ray performance during the first 24 hours of admission			129/136 (94.9)	91/100 (91.0)	1.72 (0.31-9.56)
a) Performance of chest X-ray during hospitalisation			135/136 (99.3)	98/100 (98.0)	1.34 (0.09-22.13)
b) Performance occurred within first 24 hours of admission			129/135 (95.6)	91/98 (92.9)	1.71 (0.43-6.80)
3. Performance of electrocardiogram (ECG) during the first 24 hours of admission			108/136 (79.4)	68/100 (68.0)	1.99 (0.48-8.24)
a) Performance of ECG during hospitalisation			128/136 (94.1)	83/100 (83.0)	2.78 (0.90-8.55)
b) Performance occurred within first 24 hours of admission			108/128 (84.4)	68/83 (81.9)	1.05 (0.78-14.36)
4. Sputum culture and antibiogram in patients with purulent sputum and/or before starting antibiotics therapy			91/122 (74.6)	71/88 (80.7)	0.87 (0.23-3.34)
5. Measurement of FEV1 during current hospitalisation (beneficial)			112/136 (82.4)	78/100 (78.0)	1.26 (0.32-4.99)
6. Prescription of short-acting bronchodilators during hospitalisation			131/136 (96.3)	97/100 (97.0)	0.82 (0.17-3.80)
7. Prescription of long-acting bronchodilators during hospitalisation			125/136 (91.9)	92/100 (92.0)	1.49 (0.21,10.49)
a). Additional: Prescription of nebuliser at the day of discharge (less = better!)			45/136 (33.1)	55/100 (55.0)	0.08 (0.00-3.04)
8. Prescription of 30 to 40 mg of oral prednisolone daily for 7-10 days (maximum 14 days)			23/136 (16.9)	10/100 (10.0)	1.95 (0.32-11.97)
a) Systemic glucocorticosteroids prescribed during hospitalisation			126/136 (92.6)	90/100 (90.0)	0.84 (0.24-2.92)
b) Prescription of systemic glucocorticosteroids for minimum 7 days to maximum 14 days starting at admission in patients in which glucocorticoids were prescribed			41/126 (32.5)	33/90 (36.7)	0.83 (0.29-2.37)

c) Dose of systemic glucocorticosteroids prescribed during first 7 days of hospitalisation was 30-40 mg in patients in which glucocorticoids were prescribed	116/126 (92.1)	67/90 (74.4)	2.80 (1.24-6.33)
d) Oral administration since hospitalisation day 2 or earlier in patients in which glucocorticoids were prescribed	70/126 (55.6)	30/90/ (33.3)	3.14 (0.37-26.89)
9. Prescription of antibiotics (additional information)	107/136 (78.7)	81/100 (81.0)	0.72 (0.22-2.31)
10. Administration of controlled oxygen therapy in patients hypoxaemic during admission	28/31 (90.3)	17/22 (77.3)	1.10 (0.51-2.35)
11. Assessment of smoking status	127/136 (93.4)	88/100 (88.0)	2.23 (0.28-18.01)
12. Smoking cessation intervention in active smokers at admission§	3/37 (8.1)	0/20 (0.0)	/ /
a) Providing of spoken information about quitting strategies by physician or nurse in active smokers at admission	20/37 (54.1)	7/20 (35.0)	2.06 (0.69-6.20)
b) Providing of smoking cessation leaflet in active smokers at admission	15/37 (40.5)	1/20 (5.0)	3.49 (0.49-26.49)
c) Providing of quitting aids before discharge in active smokers at admission who want to quit smoking by using quitting aids (patches, gum, medication)	8/14 (57.1)	3/8 (37.5)	2.29 (0.21-24.96)
d) Referral to counselling in active smokers at admission who want to quit smoking by counselling (individual/group)	2/3 (66.7)	1/4 (25.0)	2.12 (0.13-35.93)
e) Contacting of patient in the following month after discharge by the general practitioner, primary nurse, or somebody of the hospital about his/her smoking or attempt to quit in active smokers at admission	6/37 (16.2)	3/20 (15.0)	0.48 (0.15-1.53)
13. Adequate education regarding inhaler therapy in patients in which inhaler therapy is prescribed	55/135 (40.7)	1/98 (1.0)	2120.57 (3.17-1417636.22)
a) Providing of education regarding inhaler MEDICATION in patients in which inhaler therapy is prescribed	92/135 (68.1)	3/98 (3.1)	64.12 (19.22-213.88)
b) Providing of education regarding inhaler TECHNIQUE in patients in which inhaler therapy is prescribed	91/135 (67.4)	3/98 (3.1)	62.69 (18.81-208.93)
c) Providing of education regarding inhaler DEVICE in patients in which inhaler therapy is prescribed	91/135 (67.4)	4/98 (4.1)	46.01 (15.89-133.20)
d) Providing of a LEAFLET with explanation regarding inhaler therapy in patients in which inhaler therapy is prescribed	73/131 (55.7)	38/97 (39.2)	4.60 (1.69-12.50)

14. Education regarding home oxygen therapy in patients in which home oxygen is prescribed	12/30 (40.0)	0/35 (0.0)	11.77 (1.59-87.25)
a) Providing education regarding oxygen SOURCE in patients in which home oxygen is prescribed ‡	17/30 (56.7)	0/35 (0.0)	13.60 (1.85-99.53)
b) Providing education regarding equipment (cannulae/mask) in patients in which home oxygen is prescribed ‡	16/30 (53.3)	0/35 (0.0)	21.41 (6.99-66.63)
c) Providing education regarding SAFETY PRECAUTIONS in patients in which home oxygen is prescribed ‡	18/30 (60.0)	0/35 (0.0)	14.27 (1.95-104.50)
d) Providing SPOKEN INFORMATION regarding oxygen therapy in patients in which home oxygen is prescribed at	15/27 (55.6)	10/34 (29.4)	2.33 (0.54-10.00)
e) Providing a LEAFLET with explanation regarding oxygen therapy in patients in which home oxygen is prescribed	16/27 (59.3)	9/34 (26.5)	2.62 (0.80-8.52)
15. Performance of rehabilitation tests during the past year (inclusive current hospitalisation)	16/136 (11.8)	13/100 (13.0)	0.57 (0.06-5.37)
16. Referral to pulmonary rehabilitation during the past year (inclusive current hospitalisation)	57/136 (41.9)	40/40 (40.0)	1.26 (0.30-5.30)
17. Nutritional assessment (BMI measured)	103/136 (75.7)	27/100 (27.0)	78.61 (2.26-2736.73)
• Additionally: measurement of weight during current hospitalisation	116/136 (85.3)	63/100 (63.0)	5.20 (0.72-37.74)
18. Nutritional management of UNDERWEIGHT in underweight patients	8/47 (17.0)	4/27 (14.8)	2.13 (0.13-36.21)
a) Referral to dietician in underweight patients	23/47 (48.9)	4/27 (14.8)	8.27 (0.75-91.75)
b) Providing of nutritional ADVICE in underweight patients	17/47 (36.2)	2/27 (7.4)	10.61 (1.66-67.71)
c) Providing of nutritional SUPPLEMENT in underweight patients	19/47 (40.4)	7/27 (25.9)	2.24 (0.45-11.16)
19. Nutritional management of OVERWEIGHT in overweight patients	10/25 (40.0)	1/14 (7.1)	17.75 (0.33-944.46)
a) Referral to dietician in overweight patients	15/25 (60.0)	2/14 (14.3)	8.27 (0.75-91.75)
b) Providing of advice regarding weight loss in overweight patients	13/25 (52.0)	1/14 (7.1)	17.04 (1.08,160.36)
20. Patient received an influenza vaccination within the past year (inclusive current hospitalisation)	100/136 (73.5)	73/100 (73.0)	1.14 (0.62-2.10)
21. Patient received an pneumococcal vaccination within the past five years (inclusive current hospitalisation)	57/136 (41.9)	49/100 (49.0).	0.78 (0.41-1.49)
22. Arterial blood gas (ABG) measurement 1 or 2 days prior to discharge in patients hypoxaemic during a COPD exacerbation	13/48 (27.1)	17/35 (48.6)	0.34 (0.09-1.29)

23. Prescription of home oxygen therapy in patients who remain hypoxaemic at discharge§	0/1 (0.0)	1/6 (16.7)	/ /
a) Proportion of patients in which home oxygen is prescribed in patients who remain hypoxaemic at discharge	0/1 (0.0)	2/6 (33.3)	0.47 (0.24-0.93)
b) Proportion of patients with indication for home oxygen therapy, in which home oxygen therapy was prescribed for at least 16 hours a day in patients who remain hypoxaemic at discharge §	0/1 (0.0)	1/6 (16.7)	/ /
24. Adequate discharge management	50/136 (36.8)	22/100 (22.0)	2.47 (0.71-8.60)
a) Assessment of residence during current hospitalisation	134/136 (98.5)	86/100 (86.0)	3.07 (0.02-402.85)
b) Assessment of residential status within 3 days at admission	131/134 (97.8)	79/86 (91.9)	27.74 (0.04-22706.83)
c) Assessment of living status during current hospitalisation	119/136 (87.5)	84/100 (84.0)	0.57 (0.02-19.01)
d) Assessment of living status within 3 days of admission	106/119 (89.1)	78/84 (92.9)	1.21 (0.03-54.21)
e) Assessment of social status during current hospitalisation	121/136 (89.0)	80/100 (80.0)	1.57 (0.12-20.11)
f) Assessment of social support within 3 days	100/121 (82.6)	74/80 (92.5)	0.27 (0.00,17.89)
g) Providing spoken explanation about home medication	71/132 (53.8)	49/99 (49.5)	1.29 (0.55-3.05)
h) Providing discharge letter with explanation about further medication after discharge	82/132 (62.1)	61/99 (61.6)	0.46 (0.09-2.37)
i) Providing patient with letter with information about follow-up appointment	78/132 (59.1)	43/99 (43.4)	4.18 (1.64-10.64)
j) Planning of follow-up appointment at 4 to 6 weeks after discharge	121/136 (89.0)	67/100 (67.0)	4.43 (1.05-18.65)
k) Availability of letter for general practitioner in medical record	135/136 (99.3)	96/100 (96.0)	4.22 (0.43-41.17)
l) If need for more support at discharge: support arranged at discharge? (by the hospital, the patient him/herself, or the family)	17/22 (77.3)	7/15 (46.7)	1.44 (0.24-8.75)

† Chi square

‡ Odds not calculable: No data in 2X2 table for Resgroup = 0 and outcome (IndEduOx = 1; PREduSource = 1; PREduEqui = 0; INDLTOT = 0)

§ Odds not calculable: Too much missings to analyse Odds ratios

Table 3. Results on outcome indicators: binary variables

Outcome Indicator	Care pathway Optimal performance n/N (%)	Control (Usual care) Optimal performance n/N (%)	Odds Ratio (95% CI) [†]
1. 30-day readmission	18/132 (13.6)	22/99 (22.2)	1.48 (0.50-4.66)
2. 6-month readmission	54/119 (45.4)	40/90 (44.4)	1.59 (0.44-5.82)
3. In-hospital mortality	0/136 (0.0)	0/136 (0.0)	/ /
4. 30-day mortality	4/136 (2.9)	1/100 (1.0)	1.98 (0.17-22.64)
5. 6-month mortality	17/136 (12.5)	10/100 (10.0)	2.06 (0.36-11.91)
6. Compliance with home oxygen therapy 30 days after discharge	6/10 (60.0)	4/12 (33.3)	Too much missing data
7. Patient does at least once a week 20-30 minutes vigorous physical activity that makes him/her sweat or puff and pant	33/132 (25.0)	25/99 (25.3)	0.60 (0.13-2.78)
8. Smoking status 30 days after discharge in active smokers at admission in active smokers at admission motivated to quit	15/35 (42.9)	7/20 (35.0)	2.02 (0.45-9.01)
9. Smoking status 6 months after discharge in active smokers at admission motivated to quit	14/32 (43.8)	8/18 (44.4)	1.00 (0.17-5.69)
10. Symptoms of depression at discharge	72/136 (52.9)	55/100 (55.0)	1.36 (0.61,3.02)
11. Symptoms of anxiety at discharge	31/136 (22.8)	22/100 (22.0)	0.97 (0.52-1.82)
12. Symptoms of anxiety 30 days after discharge	30/132 (22.7)	22/99 (22.2)	2.45 (0.79-7.63)
13. Able to cope at home or place of residence at 30 days	114/132 (86.4)	78/99 (78.8)	5.76 (0.46-71.46)
14. Functional status: independent at discharge	78/136 (57.4)	53/100 (53.0)	0.92 (0.25-3.30)
15. Functional status: dependent on 1-3 items at discharge	42/136 30.9	32/100 32.0	0.91 (0.36-2.28)
16. Functional status: dependent on 4-6 items at discharge	11/136 8.1	12/100 12.0	0.65 (0.27-1.53)
17. Functional status: independent 30 days after discharge	63/132 (47.7)	46/99 (46.5)	1.36 (0.54-3.39)
18. Functional status: dependent on 1-3 items 30 days after discharge	42/132 31.8	25/99 25.3	1.27 (0.50-3.24)
19. Functional status: dependent on 4-6 items 30 days after discharge	16/132 12.1	16/99 16.2	0.70 (0.31-1.55)
20. Functional status: independent at 6 months after discharge	48/119 (40.3)	30/90 (33.3)	0.92 (0.29-2.95)

21. Functional status: dependent on 1-3 items 6 months after discharge	38/119	31.9	25/90	27.8	1.13 (0.50-2.55)
22. Functional status: dependent on 4-6 items 6 months after discharge	13/119	10.9	14/90	15.6	0.63 (0.25,1.61)
23. Severity of breathlessness Score 0	20/132	(15.2)	10/99	(10.1)	1.52 (0.65-3.52)
Score 1	9/132	(6.8)	5/99	(5.1)	1.29 (0.41-4.05)
Score 2	19/132	(14.4)	17/99	(17.2)	0.72 (0.34-1.53)
Score 3	13/132	(9.8)	12/99	(12.1)	0.71 (0.30-1.69)
Score 4	25/132	(18.9)	16/99	(16.2)	1.13 (0.54-2.36)
24. Visits by general practitioner at 30 days after discharge	67/132	(50.8)	55/99	(55.6)	0.057 (0.53-6.12)

† Risk adjusted.

Table 4. Results on outcome indicators: continuous variables

Indicator	Care pathway		Control (Usual care)		β, Resgroup (95% CI) †
	Optimal performance Mean	(SD)	Optimal performance Mean	(SD)	
1. Length of stay	11.65	(10.36)	13.36	(14.49)	-2.12 (-6.10-1.89)
2. Score on the HADS Depression scale at discharge	9.06	(4.67)	9.52	(4.24)	0.53 (-1.29-2.35)
3. Score on the HADS Depression scale 30 days after discharge	9.91	(4.69)	10.79	(4.89)	0.89 (-2.09,3.87)
4. Score on the HADS Anxiety scale at discharge	5.12	(3.84)	5.34	(3.35)	0.40 (-1.15-1.95)
5. Score on the HADS Anxiety scale 30 days after discharge	6.01	(4.35)	6.32	(4.07)	1.24 (-0.89,3.37)
6. Health-related quality of life (HRQL) 30 days after discharge: total score	57.84	(22.89)	61.60	(23.03)	-4.01 (12.94-4.92)
7. HRQL 30 days after discharge: symptom score	74.02	(18.96)	75.11	(20.99)	-1.83 (-15.39-11.72)
8. HRQL 30 days after discharge: activity score	51.80	(23.79)	55.44	(23.61)	-6.64 (-2.76-16.02)
9. HRQL 30 days after discharge: impact score	58.34	(21.07)	62.35	(20.73)	2.68 (-14.92-20.28)
10. Self-reported health condition at discharge from the ward	6.17	(1.57)	6.26	(1.78)	-0.19 (-0.91-0.54)
11. Self-reported health condition 30 days after discharge from the ward	6.10	(1.66)	5.81	(1.98)	-0.00 (-0.88-0.87)
12. Self-reported health condition 6 months after discharge from the ward	6.34	(1.67)	5.98	(1.95)	-0.21 (-1.55-1.12)
13. Number of visits to the general practitioner within 30 days after discharge	2.39	(3.80)	2.04	(1.64)	0.20 (-3.24-3.64)

† Risk adjusted.

‡ Resgroup = covariate (see Appendix 1)

Discussion

Findings of the Belgium component of the EQCP study show that in the experimental group (i.e. care pathway was implemented), 7 of 24 process indicators (29.2%) and 25 of 42 process subcomponents (59.5%) improved from 10% up to 50% (Table 2). In addition, better results were found for outcome indicators regarding 30-day readmission and LOS (Table 2-3). Statistical significance was rarely found, but this was expected because of the low statistical power resulting from analysing only the Belgian part of the larger EQCP study. According to sample size calculations, at least 400 patients in each arm were required to attain a statistical power of 80% ($\alpha=0.05$). The Belgian sample size included 100 and 136 patients in the experimental and control group, respectively, implying that statistical power was very low. Therefore, the chance of detecting a statistically significant difference was small. However, as discussed earlier, our criterion was all process indicators had to meet 100% performance, regardless of patient characteristics. Consequently, for the process indicators, improvement of up to 50% in the care pathway group reflect better performance levels, and so should not be considered to be coincidental results arising from chance variation in small samples.

Despite large improvements in the care pathway group, there still exists room for much improvement, as 11 of 24 indicators (45.8%) and 8 of 42 subcomponents (20%) had a performance of less than 50%. We need to bear in mind that in the case of multicomponent indicators, low performance of just one or two subcomponents will result in suboptimal performance of the main indicator (Table 2, i.e. nos. 15, 18, 32). For several indicators, organisations performed quite well for most subcomponents. Thus, to improve the main indicator, they need to focus on improving only one or two subcomponents.

The normalisation theory of May et al. [20] states that the normalisation process consists of the collective action—the work—involved in enacting a complex intervention. When that work leads to the routine embedding of an intervention in everyday practice, it may be said to have become normalised. Normalisation is only one possible outcome of collective action. Others include adoption, where a complex intervention is adopted but does not become routinely embedded in everyday work, and rejection, where users disregard, subvert, or otherwise refuse to use a complex intervention [20]. In our study, a considerable amount of indicators are still suboptimal performed, which indicates that by implementing the care pathway, the set of key interventions was adopted but not yet routinely embedded in daily practice. Therefore, we believe that continuous quality improvement will be needed to obtain optimal performance on the different indicators, and furthermore to enhance sustainability of the improved results.

Results on outcome indicators show a non-significant improvement in 30-day readmission and LOS. Compared to the literature, we found that the 30-day readmission rate

in the care pathway group (13.6%) was more or less within the range of rates reported in the literature (range: 8.9-16%) [9;11;21]. Moreover, rather low rates were found in both groups for in-hospital mortality (both groups: 0.0%), 30-day mortality (CP: 2.9%; UC: 1.0), and 6-month mortality (CP: 12.5%; UC 10.0%) (Table 4), in comparison with earlier studies, which found much higher rates for In-hospital mortality (4.7-8.3%) [13;22-27], 30-day mortality (4.5-8.4%) [24;25], and 6-month mortality (18-24%) [21;26]. However, the present results need to be interpreted with caution due to limited statistical power.

Methodological strengths and limitations

Firstly, an important strength of our research is its cluster randomised design. When evaluating a complex intervention that affects different levels of the organisation, this kind of design provides the most valid results. In contrast, with a quasi-experimental design (see review on care pathways and COPD, Chapter 3 [28]), there is a strong possibility that better results arise not because of care pathway implementation, but because of other reasons like history effect, Hawthorn effect, selection bias, or contamination of the control group.

Secondly, close examination of the randomisation strategy using stratification [1], reveals that hospitals were comparable with regard to size and annual volume of hospitalised patients. Also type of hospital (teaching vs. non-teaching) was balanced in the initial sample. However, because of dropout of two hospitals in the control group, 4 of 7 hospitals (57.1%) in the experimental group, as opposed to 1 of 5 hospitals (20%) in the control group that had a teaching status, which might have influenced the results. On the other hand, all participating hospitals in the Belgian EQCP study were members of the Belgian Dutch Clinical Pathway Network (BDCPN; www.nkp.be) [29], implying that the study coordinators of both experimental and control groups were already experienced in the development, implementation, and evaluation of care pathways.

Thirdly, we want to highlight the three components included in the complex intervention. The first component included feedback on actual performance. Participants of the experimental hospitals clearly stated that the feedback on the actual care process (before care pathway implementation) showed them exactly where the bottlenecks were in their actual care process. This helped them to focus on those key interventions that really needed improvement. The results on process indicators seem to confirm these statements. Indeed, the most important improvements were found for process indicators that were suboptimally performed in the clinical audit before implementation, including prescription of corticoids, education, smoking cessation, and referral to rehabilitation (Table 2). Overall, understanding their bottlenecks—through the comparison of results on actual care processes and evidence-based key interventions—appears to motivate teams to improve their actual care process and is therefore believed to be a strong determinant for adoption of new knowledge [30-33].

The second component included the integration of the set of 38 evidence-based key interventions. As described in Chapter 5, the set of key interventions produced by the eight-step method, was well accepted by the seven experimental teams. This was because of validity and clinical applicability of the interventions, indicating that the eight-step strategy (Chapter 5) was an important approach to increase adoption of these key interventions by the different teams. However, to know to what extent the key interventions were effectively implemented and which actions were undertaken to improve performance on process indicators, implementation analyses needed be performed (Chapter 8).

Finally, the third component—including (i) a structured protocol for development and implementation of the care pathway, and (ii) strategies for effective knowledge sharing—turned out to be very useful for distilling knowledge out of the feedback and bringing evidence into practice. This especially occurred during the meetings with the team and team change experts, where experiences, successes and bottlenecks (i.e. difficulties regarding implementation of educational strategies) were discussed.

Fourthly, another strength of this study concerns the validity of quality measures: The process and outcome indicators were developed based on the literature, Delphi survey, and face-to-face consensus meetings, and were piloted during the clinical audit before pathway implementation [34].

Fifthly, we highlight the importance of using a logbook listing excluded patients. These patients were admitted with COPD exacerbations but were not included in the study due to a specific reason. Seven of 12 participating Belgian hospitals provided a logbook containing blinded data on excluded patients. Two other hospitals (one experimental and one control), coordinated by one study coordinator, estimated that each hospital had around five excluded patients. However, the coordinator stated that the logbooks of both hospitals were lost by mail.

Of the 7 hospitals that provided a logbook, 6 hospitals reported a range of 6 to 12 excluded patients, while one hospital reported three excluded patients. For the seven hospitals, a total of 67 patients admitted with COPD exacerbations were not included in the study; 34 of the patients were admitted in the experimental hospitals, and 33 in the control hospitals. The mean age of the excluded patients was comparable to that of patients included in the study, for both experimental (care pathway or CP) and control (usual care or UC) groups (CP: 70.4, SD 2.0; UC: 73.3 years, SD 2.1). With regard to gender, in the experimental group 17 of 34 excluded patients were male (50%), while in the control group only 9 of 33 excluded patients were male (27.3%). Although this difference was not significant (Fisher exact, $p=0.08$), we need to interpret these findings with caution because of the small sample size. The most frequently reported reason for exclusion was 'not interested in participating' (CP: $n=17/34$, 50%; UC: $n=18/33$; 54.5%). Most of the remaining patients

were excluded because of the preset exclusion criteria: (i) having mental disorders and thus unable to provide informed consent and/or to understand and read the native language (CP: 9/34, 25.5%; 7/33, 21.1%); admitted to another ward (CP: 1/34, 2.9%; UC: 4/33, 12.1%); in bad condition (CP: 2/34, 5.9%; UC: 2/33, 6.1%); and already included in another study (CP: n=2/34, 5.9%; UC: n=0/34, 0.0%). Of the 3 remaining patients, 1 'needed a pacemaker' (CP), 1 was discharged without notifying the researchers (CP), and 1 was admitted for less than 3 days (UC). Overall, these findings indicate that one in every two or three admitted patients were not included in the study, leading to possible selection bias. Although excluded patients were comparable to included patients in age, they differed with regard to gender distribution (50% males vs. 27.3%, respectively). For future studies, we recommend that more detailed information should be collected on the patient characteristics of excluded patients, specifically with regard to their comorbidities and COPD severity.

Finally, one of the challenges of cRCTs is that data collection occurs at different sites. Hence, it is difficult and time-consuming to follow up the data collection across the different organisations. In our study, only 20 patients per hospital needed to be followed up, and the data collection duties were distributed among three parties: teams, patients, and external researcher. We realise that many indicators were followed up, though, with regard to all process indicators and 8 of 15 outcome indicators, all indicators were binary, implying that they were measured by using one variable. In case of the 10 multicomponent process indicators, we measured two to maximum five variables to compose the indicators. Overall, data collection was very complete with regard to these binary indicators, especially when performed by the team members and the external researcher. This indicated that the workload burden for data collection for these parties was feasible. We think that the low number of patients that needed to be included per organisation, as well as providing the data collection forms classified per collection time point and delivered in two binders for each organisation, played an important role in making data collection successful. With regard to data collected via self-reported patient questionnaires, we observed a high rate of missing data for questionnaires that needed to be returned by mail 30 days after discharge. Indeed, up to 40% of missing data were noted for 5 of 24 indicators (20.8%) and 12 of 42 of their underlying subcomponents (28.6%), and for 3 of 15 outcome indicators (20%). In total 84 of 236 patients did not return their questionnaire (35.6%). However, 40 of these 84 patient questionnaires (47.6%) from two hospitals were lost due to mailbox problems associated with the study coordinator responsible for these two hospitals.

In conclusion, although logistic and economic issues can make conducting cRCTs challenging, we believe that opportunities to collect data through multicentre studies should be fully utilised. However, self-reported patient questionnaires, especially during the follow-up period, should be limited. Consequently, collecting data on patient opinions and experiences

during the follow-up period should be integrated into other opportunities like follow-up consultations.

Conclusion

The results of the Belgium component of the larger EQCP study suggest that implementation of a care pathway has potential to improve care processes and clinical outcomes. However, due to the necessarily small sample size, and hence limited statistical power, strong conclusions on effectiveness can only be confidently drawn when the final results of the other three involved countries become available in 2013.

Continuous quality improvement will be needed to obtain optimal performance on the different indicators, and to enhance sustainability of the improved results.

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Appendix 1: Statistical model details

It is reasonable to assume that observations or data from the same group or cluster would be correlated. Hence, naïve approaches for analysing data cannot be used since they assume that data are independent (i.e. no clustering). Ignoring the clustering of data may lead to incorrect conclusions, since variability would be over- or underestimated, resulting in biased p-values. When data are independent, regression models can be used. However, in the presence of correlations, regression models are extended to multilevel models.

Figure 2. Two-level model **Statistical multilevel model:**

$$Y_{ij} = \beta_0 + \beta_1 x_{ij} + b_i + \varepsilon_{ij}$$

- where Y_{ij} is the dependent variable or outcome from patient j belonging to hospital i ,
- and x_{ij} is the covariate from patient j belonging to hospital i

In this model, x_{ij} includes the covariate 'Resgroup' (1 = Experimental group; 2 = control group),

- β_0 is the intercept
- β_1 is the regression coefficients explaining the effect of the covariate x_{ij} "Resgroup" (Experimental / control)
- b_i is the random effects at hospital level (clustering effect)

With $b_i \sim N(0, \sigma^2)$ (N: b has a normal distribution; $\sigma^2 = \tau =$ variance at cluster level (very high = very high clustering effect))

Continuous outcomes:

UN (1,1) = σ_1^2 = variance on hospital level (clustering effect)

Residual = σ_2^2 = variance at patient level

$$ICC = \frac{U[1,1]}{U[1,1] - Residual}$$

- ε_{ij} is the residuals/errors at the patient level (deviation for the overall mean only for continuous variables).

With $\varepsilon_{ij} = N(0, \sigma^2) \Rightarrow \sigma^2 = \text{variance at the patient level}$

Statistical models for specific outcomes:

- 1) Binary outcomes: multilevel

$$\text{Logit} \frac{PR(Y=1)}{1-PR(Y=1)} = \beta_0 + \beta_1 \text{Resgroup} + \beta_i$$

With $b_i \sim N(0, \sigma^2)$

- 2) Continuous outcomes: multilevel

$$Y_{ij} = \beta_0 + \beta_1 \text{Resgroup} + b_i + \varepsilon_{ij}$$

With $b_i \sim N(0, \sigma_1^2)$

And $\varepsilon_{ij} \sim N(0, \sigma_2^2)$

Appendix 2: Guided by the results

1. *Presentation of the indicators*

There will be single component and multicomponent indicators.

- Single component indicators are composed of one component. A particular case is scored as '1' if the single component is well performed, and thus satisfies the conditions of the indicator.
- Multicomponent indicators are composed of two or more components. A particular case is scored as '1' if all underlying components are scored as '1' (and thus are well performed).

Indicators are indicated *by a number and displayed without shading*.

Components are indicated *by a letter and displayed with blue shading*.

2. *Presentation of results*

- Odds ratios and 95% confidence interval (CI)

Odds ratio:

- The odds ratio is one of a range of statistics used to assess the risk/chance of a particular outcome (or disease) if a certain factor (or exposure) is present. The odds ratio is a relative measure of risk that reveals the likelihood that a subject who is exposed to the factor under study will develop the outcome as compared to another subject who is not exposed.
- If the odds are greater than one then the event is more likely to happen than not. If the odds are less than one, then the outcome is less likely to occur.

http://www.blackwellpublishing.com/specialarticles/jcn_10_268.pdf

Example: The odds ratio for performance of chest X-ray in care pathway group/usual care is 1.72. Thus, patients in the care pathway group are 1.72 times more likely for to receive a chest X-ray.

95% CI:

- When the 95% CI for the differences in two proportions includes the value 1, the accompanying significance test does not provide a significant result.
- When the 95% CI for the differences in two proportions does not include the value 1, the accompanying significance test provides a significant result.

- β_1 Resgroup and 95% CI

β_1 Resgroup:

- β_1 : β is the regression coefficient that explains the slope of the difference between the scores of the intervention and the control group
- If the coefficient is greater than 0, the difference is positive (outcome in intervention group > control group); if coefficient is less than zero, difference is negative (outcome in experimental group < outcome in control group).

Example: Odds for LOS is -1.76, so LOS in intervention group will be lower than in control group (under condition being significant!)

95% CI:

- When the 95% CI for the differences in two proportions includes the value 0, the accompanying significance test does not provide a significant result.
- When the 95% CI for the differences in two proportions does not include the value 0, the accompanying significance test provides a significant result.

3. Specific meaning of scores on HADS Scale and SGRQ

- HADS: Hospital Anxiety and Depression Scale:

- Depression/anxiety was measured with the Hospital Anxiety and Depression Scale (score: 0-21).
- Score of ≥ 8 means caseness (possible or probable presence of depression/anxiety)
- Caseness can be specified in two categories:
 - score of 8-10 means possible case (possible presence for depression/anxiety)
 - score of ≥ 11 means probable case (probable presence for depression/anxiety)

- SGRQ: St. George Respiratory Questionnaire

- Quality of life was measured with the St. George Respiratory Questionnaire. The scoring includes four separate scores:
- Total score (0-100)
- 3 subscores: symptoms, activity, and impact (0-100)
- **NOTE: the lower the score, the better the HRQL**

Chapter 8:

Process analyses in seven Belgian hospitals: level of implementation of a set of evidence-based key interventions for in-hospital management of COPD exacerbation

Context

Chapter 6 presented the rationale and design of the European Quality of Care Pathways (EQCP) study on the impact of care pathways for COPD exacerbations. Chapter 7 presented the preliminary results of the Belgian EQCP study. The present chapter presents results of a process evaluation of the Belgian EQCP study.

Process evaluations within trials explore the implementation, receipt, and setting of an intervention. These evaluations assist researchers in several ways. Firstly, they promote understanding on how outcomes are achieved and what factors promote or hinder them [1-4]. Secondly, they help determine why a programme was or was not successful, and they are essential in order to distinguish between interventions that are inherently faulty (failure of intervention concept or theory) and those that are just poorly delivered (implementation failure) [1;2;5;6]. Finally, process evaluations are particularly useful in multisite trials, where the 'same' intervention may be implemented and received in different ways [2].

Elements of process evaluations include assessment of fidelity (quality), dose delivered (completeness), dose received (exposure and satisfaction), reach (participation rate), recruitment, and context [7].

In the Belgian EQCP study, all seven participating experimental hospitals implemented a care pathway that included three active components: (i) feedback on actual performance, (ii) integration of a set of evidence-based key interventions for in-hospital management of COPD exacerbations (Chapter 5), and (iii) training on development and implementation of the care pathway [8]. The process evaluation described in this chapter addresses the implementation of the second component of the care pathway: integration of a set of 38 evidence-based key interventions. This implementation analyses focusses on four implementation aspects (fidelity, dose delivered, recruitment, and context) and has three main aims: (i) to explore the level of complete inclusion of the different key interventions, (ii) to study the actions undertaken to improve performance of the implemented key interventions, and (iii) to explore barriers for implementation of the key interventions.

Methodology

Questionnaire for implementation analyses

To explore the level of implementation, undertaken improvement actions, and barriers for implementation, we developed a self-reporting questionnaire.

The questionnaire included all care activities that were followed up in the EQCP study by the 24 process indicators (Chapter 5, Table 3). Essentially, these 24 process indicators refer to care activities that (i) have high impact on patient outcomes according to the literature and

expert opinion [9-12], and (ii) are suboptimally performed according to both earlier studies [13] and results of the seven Belgian hospitals (Chapter 7, Table 2). In other words, we are particularly interested in the results of the implementation analysis on these care activities, because strong implementation of these key interventions has high potential for improving the performance of care processes and for optimising results on clinical outcomes [9-12]. In addition, including these care activities allowed us to correlate results on the implementation analyses with the results on the performance indicators.

It was explicitly decided to not study all 38 key interventions and underlying components (which refer to a total of 77 care activities; Chapter 5, Table 1). Indeed, this would have been excessively time-consuming for the respondents and consequently might compromise the accuracy and completeness of reporting overall.

In total, based on the 24 process indicators and subcomponents, 48 activities were included for implementation analysis in the questionnaire. This questionnaire included three main parts based on the three core processes for in-hospital management of COPD exacerbations: diagnostic tests, pharmacological management, and non-pharmacological management. For each of the 48 care activities, respondents were asked to fill out whether the particular key intervention was entirely included in their developed care pathway (Yes/No). Consequently, if the answer was 'yes', the respondent was asked to indicate whether specific actions were undertaken to improve the performance of this key intervention (Yes/No). If the answer was again 'yes', the respondent was asked to describe the undertaken answers. If the answer on the initial question regarding complete inclusion of the key intervention was 'no', respondents were asked to report their reason for failing to include or only partially including the key intervention. Possible answer categories for the latter question were (i) 'not organisable' (respondents were asked to report why it was not organisable); (ii) 'no consensus within the team'; and (iii) 'other' (respondents were asked to describe what was meant by 'other'). Multiple answers were possible.

The questionnaire was piloted by a care pathway coordinator of one of the seven included Belgian experimental hospitals. We asked him to appraise the questionnaire for clarity, feasibility, completeness, and time needed to complete it. Additionally, we requested this feedback within one week. Some minor suggestions were made on formulation of a few key interventions, but overall, the questionnaire was approved for all these criteria.

Survey and participants

The process evaluation was conducted in the seven experimental hospitals included in the Belgian EQCP study. The implementation analysis was conducted by e-mail. The questionnaire was sent to the study coordinators on Monday, 12 January 2012, by the first author (CL). Invitation for participation in the implementation analysis, together with

explanation about the aim of the evaluation and the procedure was included. The study coordinators were asked to complete the questionnaire together with one or more team members, and to return the completed questionnaires by e-mail no later than Friday, 27 January 2012. In addition, respondents were requested to include in their reply developed care pathway documents, like time tasks and checklists, to give the research team an idea about the composition and structure of the care pathway. Confidentiality was guaranteed in this way that the results of the respondents remained strictly confidential to the researchers [14]. A reminder e-mail was sent to coordinators on Monday, 30 January 2012. For missing values or unclear answers, the study coordinators were queried by mail or phone.

Data analyses

We analysed the reported levels of implementation of care activities using the following summary statistics: (i) number of hospitals where the care activity was completely implemented in the care pathway, and (ii) number of hospitals where a specific action was undertaken. In addition, reported actions undertaken to improve performance of the included care activities and reported reasons for failing to include or partial inclusion were listed and categorised into general concepts based on content and format. Data were analysed using the statistical software program SPSS version 19 (International Business Machines Corporation, Armonk, New York, 2011).

Results

Response rate

Study coordinators of all seven hospitals returned the completed questionnaire within the provided time span. An additional e-mail with the request to complete missing values resulted in 100% completion.

Hospital characteristics

Four of the 7 hospitals were teaching hospitals (57.1%) (Table 1). Hospital size ranged between 300 and 400 beds in four hospitals (57.1%), while in the other three hospitals size varied from 589 to 749 beds. None of the hospitals had dedicated respiratory wards; however, in each hospital, 26 to 34 beds were dedicated to hospitalised COPD patients. Finally, all included hospitals had a rehabilitation programme for COPD patients.

Table 1. Hospitals characteristics

Hospital	Teaching status	Total number of beds	Annual patient volume (2007)	Number of beds dedicated for COPD patients
H1	Teaching	314	126	30
H2	Non-teaching	334	169	32
H3	Non-teaching	369	155	33
H4	Non-teaching	382	233	34
H5	Teaching	589	170	26
H6	Teaching	598	405	33
H7	Teaching	749	208	32

Overall implementation level and undertaken actions

According to respondents, 24 of 48 evaluated care activities (50.0%) were completely included in all seven hospitals (100%), and 18 of 48 care activities (37.5%) were fully implemented in 6 of 7 hospitals (85.7%) (Table 2). Only 4 care activities (8.2%) were reported as partially implemented, ranging from inclusion in 2 hospitals (28.6%) to 4 hospitals (57.1%). These four activities were “measurement of ABGs between 30 and 60 minutes after start of oxygen therapy”, “follow-up contact with regard to smoking cessation”, “performance of revalidation tests”, and “arterial blood gas (ABG) measurement prior to discharge in hypoxemic patients”.

Furthermore, the reported implementation level of the care activities according to the three core processes (diagnostic, pharmacological, and non-pharmacological management) indicated that diagnostic care activities were best implemented, and pharmacological interventions were least included (Table 2).

Table 2. Level of implementation of care activities based on the number of hospitals in which each care activity was reported as completely included in the care pathway.

	Reported implementation level				
	Completely implemented in all 7 hospitals (100.0%)*	Completely implemented in 6 of 7 hospitals (85.7%)	Completely implemented in 5 of 7 hospitals (71.4%)	Completely implemented in 4 of 7 hospital (57.1%)	Completely implemented in 2 of 7 hospitals (28.6%)
All care activities, n/N (%)	24/48 (50.0)	18/48 (37.5)	2/48 (4.2)	1/48 (2.1)	3/48 (6.3)
Diagnostic care activities, n/N (%)	4/5 (80.0)	1/5 (20.0)			
Pharmacological care activities, n/N (%)	3/8 (37.5)	3/8 (37.5)	2/8 (25.0)		
Non-pharmacological care activities, n/N (%)	17/35 (48.6)	14/35 (40.0)		1/35 (2.9)	3/35 (8.6)

*Relative number of hospitals where the care activity is reported as implemented.

Examining the reported implementation level per hospital, we found a range of 80% to 100% (Figure 1). Only one hospital (H2) reported a lower implementation level of 66.7%, with less pharmacological and non-pharmacological interventions being reported as completely included.

Figure 1. Reported percentage of completely included care activities at the hospital level

The percentage of completely included key interventions for which improvement actions were reported ranged from 28.6% to 97.7% over the seven hospitals (Figure 2). Looking at the overall included care activities, two hospitals (H2 and H6) reported considerably fewer improvement actions. Furthermore, H2 was the only hospital that reported no improvement actions for pharmacological care activities. Most frequently reported actions were (i) inclusion in checklist of the care pathway, standing order, standard performed action; recruitment or specific assignment of multidisciplinary staff (tabaccologist, occupational therapist, physiotherapist, dietician, and social worker); staff education, information technology (IT) applications (reminders, automatic generation of e-mails); and generation of materials and time slots for patient education.

Most frequently reported reasons for non-inclusion or partial inclusion of the key interventions were associated with organisational factors. Detailed descriptions of these organisational factors were rarely provided. These include “tabaccologist not recruited yet” and ‘devices for rehabilitation tests very recently purchased’. Other commonly reported reasons for non-implementation were ‘no consensus within the team’, ‘depending on the prescription of the physician’, and ‘depending on the condition of the patient’.

Figure 2. Percentage of included care activities for which an action was reported at the hospital level

Reported implementation level and undertaken actions according to diagnostic, pharmacological, and non-pharmacological management

Table 3 shows for each evaluated care activity (i) the number of hospitals that reported complete inclusion of the care activity into the care pathway, (ii) the number of hospitals that reported an improvement action for the included care activity, (iii) the reported action, (iv) the reported reason for failing to include or for only partial inclusion of the care activity in the care pathway.

With regard to diagnostic management (Table 3, Part I), according to respondents, 4 of 5 care activities (80.0%) were completely implemented in all hospitals, whereas the remaining activity, performance of sputum culture, was completely implemented in six hospitals (Table 2; Table 3, Part I). With regard to actions for improving the performance of diagnostic care activities, the greatest number of actions were reported for inclusion of arterial blood gas (ABG) measurement at admission, in example “inclusion into pathway checklist”, “reminder in patient record”, and “education of staff” (Table 3 Part I, no. 1).

For the second core process of pharmacological management (Table 3, Part II), 6 of 8 evaluated interventions (75.0%) were reported as completely implemented in six to seven hospitals, (Table 2; Table 3, Part II). Reported as less optimally implemented were specific interventions regarding systemic corticoid therapy (dose, time span, and administration route) and prescription of long-acting bronchodilators and inhaled corticoids (Table 3, Part II,

no. 5). The most frequently reported reasons for non-implementation were 'therapy depends on condition of the patient' and 'therapy depends on prescription of the patient' (Table 3, Part II). In addition, remarkable reasons for non-implementation were found for the subcomponent 'switch of intravenous to oral corticoid therapy' (Table 3, Part II, no. 5c); 'no consensus within the team', and 'what would patient think of care if no intravenous therapy was started'. Finally, most improvement actions were taken for prescription of corticoids, including checklists, standard orders, and use of standard medication schemes (Table 3, Part II, no. 5a-5c).

Finally, with regard to non-pharmacological interventions, 17 of 34 evaluated activities (48%) were fully implemented in all seven hospitals, and 14 of 35 activities (40%) were completely included in six of seven hospitals (Table 2; Table 3, Part III). Only four non-pharmacological care activities (11.4%) were reported as not or partially implemented in two to four hospitals (Table 2; Table 3, Part III), mostly because of organisational reasons and no consensus within the team: (i) ABG measurement after starting oxygen, (ii) follow-up contact regarding smoking cessation one month after discharge, (iii) performance of rehabilitation tests, and (iv) ABG measurement in hypoxaemic patients before discharge (Table 3, Part III, nos.1, 4e, 7, 15). Furthermore, the number of reported actions undertaken to improve performance of non-pharmacological interventions was considerably higher than those for diagnostic and pharmacological management. These included specific interventions like alignment of specialised caregivers like tabaccologist, dieticians, occupational therapists, and physiotherapists; development and use of education tools like leaflets and placebo inhalers; planning of education session for patients; and generation of automatic e-mails to a dietician and social worker when a COPD patient is admitted.

Care pathway documents

All seven hospitals provided their care pathway documents, which all included a Gantt Chart or time-task matrix listing the different interventions in one column according to the responsible team members and cross-aligning these entries with columns pertaining to time [15;16]. In all hospitals the time task was integrated into the patient record and included a clear starting and end point. The most important differences in time tasks were alignment of the tasks to the different professional disciplines, integration of the key interventions at different points in the time process, and the overall time span of the care pathway, which varied from 4 to 10 days.

Table 3. Reported implementation level of the key interventions according to each core process

Part I: Diagnostic tests during hospitalisation for COPD exacerbations

Key intervention	Number of hospitals who reported the care activity as completely implemented n/N (%)	Number of hospitals who reported specific improvement action (s) n/N (%)	Reported action(s)	Reported reasons why not completely included
1. Arterial blood gas (ABG) measurement during first 24 hours of admission	7/7 (100.0)	5/7 (71.4)	<ul style="list-style-type: none"> • Checklist (H7, H5) • Systematically on emergency room (H1) • Reminder IT (H6) • Education staff (H2) • New device (H2) 	
2. Performance of chest X-ray during the first 24 hours of admission	7/7 (100.0)	2/7 (28.6)	<ul style="list-style-type: none"> • Checklist (H7, H5) 	
3. Performance of electrocardiogram (ECG) during the first 24 hours of admission	7/7 (100.0)	2/7 (28.6)	<ul style="list-style-type: none"> • Checklist (H7, H5) 	
4. Performance of sputum culture and antibiogram in patients with purulent sputum and/or before starting antibiotic therapy	6/7 (87.5)	2/6 (33.3)	<ul style="list-style-type: none"> • Consult physician (H1) • Standing order on antibiotic therapy (H4) 	<ul style="list-style-type: none"> • Organisational factors (H5)
5. Performance of spirometric tests during hospitalisation	7/7 (100.0)	1/7 (14.3)	<ul style="list-style-type: none"> • Checklist (H5) 	

Part II: Pharmacological management during hospitalisation for COPD exacerbations

Key intervention	Number of hospitals who reported the care activity as completely implemented n/N (%)	Number of hospitals who reported specific improvement action (s) n/N (%)	Reported action(s)	Reported reasons why not completely included
1. Prescription of SHORT-ACTING bronchodilators	7/7 (100.0)	1/7 (14.3)	<ul style="list-style-type: none"> Checklist (H5) 	
2. Prescription of LONG-ACTING bronchodilators	6/7 (85.7)	1/6 (16.7)	<ul style="list-style-type: none"> Checklist (H5) 	<ul style="list-style-type: none"> Therapy depends on condition of patient (H2) Therapy depends on physician's prescription (H2)
3. Prescription of inhaled corticoids	6/7 (85.7)	1/6 (16.7)	<ul style="list-style-type: none"> Checklist (H5) 	<ul style="list-style-type: none"> Therapy depends on condition of patient (H2) Therapy depends on physician's prescription (H2)
4. Prescription of metered dose inhalers (MDIs) and dry powder inhalers instead of nebulisers	7/7 (100.0)	2/7 (28.6)	<ul style="list-style-type: none"> Standing order (H4) Checklist (H5) 	
5. Prescription of systemic corticoids	7/7 (100.0)	3/7 (42.9)	<ul style="list-style-type: none"> Standing order (H7) Standard scheme (H5) Checklist (H5) 	
a) Standard prescription: dose of 30 to 40 mg	6/7 (85.7)	3/6 (50.0)	<ul style="list-style-type: none"> Standing order (H7, H4) Medication profile (H5) 	<ul style="list-style-type: none"> Therapy depends on condition of patient (H2)
b) Standard prescription: time span of 7 to 14 days	5/7 (71.4)	3/5 (60.0)	<ul style="list-style-type: none"> Standard scheme 8 days: (H1) Standing order (H4) Medication profile (H5) 	<ul style="list-style-type: none"> No formal agreements in care pathway included (H7) Therapy depends on condition of patient (H2)
c) Standard prescription: oral administration instead of intravenous administration if possible	5/7 (71.4)	4/5 (80.0)	<ul style="list-style-type: none"> Supervision by physician (H7) Standard scheme (H1) Standing order (H4) Medication profile (H5) 	<ul style="list-style-type: none"> No consensus within team (H6) Perception of patient if no intravenous medication (H3)

Part III: Non-pharmacological management during hospitalisation for COPD exacerbations

Key intervention	Number of hospitals who reported the care activity as completely implemented n/N (%)	Number of hospitals who reported specific improvement action (s) n/N (%)	Reported action(s)	Reported reasons why not completely included
1. Prescription of supplementary oxygen in hypoxaemic patients	7/7 (100.0)	3/7 (42.9)	<ul style="list-style-type: none"> • Standing order (H7) • Checklist (H5) • Standard daily oxymetry and evaluation/adaptation oxygen therapy based on results (H4) • New portable device (H4) 	
2. Measurement of ABGs between 30 and 60 minutes after start of oxygen therapy	2/7 (28.6)	1/2 (50.0)	<ul style="list-style-type: none"> • Standing order (H4) 	<ul style="list-style-type: none"> • Organisational factors (H6, H3, H4) • No consensus within team (H6) • Therapy depends on condition of patient (H2) • Physician specific (H5)
3. Assessment of smoking status	7/7 (100.0)	4/7 (57.1)	<ul style="list-style-type: none"> • Checklist (H7, H5) • Standard anamnesis (H3, H4) 	
4a. Providing spoken information about quitting strategies	6/7 (85.7)	5/6 (83.3)	<ul style="list-style-type: none"> • Recruitment of tabaccologist (H7, H6, H3, H4) • Checklist (H7) • Leaflet (H7, H3, H4, H5) • Education of nursing team (H7) • Update information (content, format, timing, checklist, uniformity, completeness, clarity) (H5) 	<ul style="list-style-type: none"> • Tabaccologist recruited but not yet included in the care pathway (H2)
4b. Providing smoking cessation leaflet	6/7 (85.7)	4/6 (66.7)		

4c. Providing quitting aids if preferred by patient	6/7 (85.7)	3/6 (50.0)	• Idem 4a-b	• Idem 4a-b
4d. Referral to counselling if preferred by patient	6/7 (85.7)	3/6 (50.0)		
4e. Contacted in the following month after discharge by the general practitioner, primary nurse, other hospital staff about his/her attempt to quit smoking	2/7 (28.6)	1/2 (50.0)	• Follow-up consult (H6)	<ul style="list-style-type: none"> • Included in pulmonological follow-up (H7) • Organisational factors (H2, H3, H4, H5); tabaccologist included yet (H2)
5a. Providing oral information regarding inhaler medication	7/7 (100.0)	7/7 (100.0)	<ul style="list-style-type: none"> • Leaflet (H7, H2, H3, H4) • evaluation checklist (H7) • Education staff (H1, H6, H2, H4); collaboration with companies and pharmacists (H1) • Patient education sessions by occupational therapist (H3), physiotherapists (H4), and nurses (H4) • Update information (content, format, timing, checklist, uniformity, completeness, clarity) (H5) • Placebo (H7) 	<ul style="list-style-type: none"> • Leaflet not possible because of organisational factors (H2)
5b. Providing oral information regarding inhaler device	7/7 (100.0)	3/6 (50.0)		
5c. Providing oral information/demonstration regarding inhaler technique	7/7 (100.0)	3/6 (50.0)		
5d. Providing patient leaflet regarding inhaler therapy	7/7 (100.0)	3/6 (50.0)		
6a. Providing oral information regarding oxygen source	7/7 (100.0)	5/7 (71.4)	<ul style="list-style-type: none"> • Leaflet (H2, H6, H3, H4) • Education staff by medical company: home oxygen sources, (home) ventilation • Education by nurse (H3, H4) • Education package and strategy (H5) 	<ul style="list-style-type: none"> • Education reserved for oxygen supplier (H7)
6b. Providing oral information regarding oxygen equipment	7/7 (100.0)	5/7 (71.4)		
6c. Providing oral information regarding safety precautions	7/7 (100.0)	4/7 (57.1)		
6d. Providing a patient leaflet regarding home oxygen therapy	6/7 (85.7)	4/6 (66.7)		

6. Performance of rehabilitation tests	2/7 (28.6)	1/2 (50.0)	<ul style="list-style-type: none"> • Standing order: physiotherapist performs tests (H4) 	<ul style="list-style-type: none"> • No consensus within the team (H7, H6, H5) • Organisational factors (H2, H3); devices for specific revalidation tests available since January 2012 (H2)
7. Referral to pulmonary rehabilitation if patient is eligible	7/7 (100.0)	4/7 (57.1)	<ul style="list-style-type: none"> • Patient visit rehabilitation room (H2) • Physiotherapist of rehabilitation assigned to CP (H2) • Physiotherapist: patient education (H3) • Referral if eligible (H4) • Systematic screening (H5) 	
8. Screening and updating of current vaccination status with regard to influenza vaccination	6/7 (85.7)	4/6 (66.7)	<ul style="list-style-type: none"> • Checklist (H7, H5) • Documentation in patient record by physician (H3) • Questioning patient (H4) • Advice in letter for general practitioner (H4) 	<ul style="list-style-type: none"> • Follow-up during consultation (H2)
9. Screening and updating of current vaccination status with regard to pneumococcal vaccination	6/7 (85.7)	5/6 (83.3)		
10. Measurement of weight	7/7 (100.0)	6/7 (85.7)	<ul style="list-style-type: none"> • Checklist (H7, H5) • Systematic weight measurement (H1, H3, H4) • Dietician (H2) • IT: auto-mail to dietician at admission (H2) 	
11. Calculation of BMI	7/7 (100.0)	6/7 (85.7)	<ul style="list-style-type: none"> • Checklist (H5) • Dietician (H7, H1, H2) • Systematic measurement (H3, H4) • IT: auto-mail to dietician at admission (H2) 	
12a. In <u>underweight</u> patients: referral to dietician.	6/7 (85.7)	6/6 (100.0)	<ul style="list-style-type: none"> • Checklist (H5) • Systematic contact (H7, H1, H2) • Malnutrition screening (H6) • Standing order (H4) • IT: auto-mail to dietician at admission (H2) 	<ul style="list-style-type: none"> • Organisational factors (H3)
12b. Nutritional advice regarding supplementation	6/7 (85.7)	6/6 (100.0)		

12c. Prescription of nutritional supplementation	6/7 (85.7)	6/6 (100.0)	admission (H2) • Standing order (H4) • Written advice to general practitioner (H4)	
13a. In overweight patients: referral to dietician	6/7 (85.7)	5/6 (83.3)	• Checklist (H5) • Systematic contact (H7, H1, H2) • Standing order (H4) • IT: auto-mail to dietician at admission (H2) • Standing order (H4) • Written advice to general practitioner (H4)	• Organisational factors (H3)
13b. Advice regarding weight loss	6/7 (85.7)	5/6 (83.3)		
14. ABG measurement 1 or 2 days prior to discharge in patients hypoxaemic during a COPD exacerbation	4/7 (57.1)	1/4 (25.0)	• Checklist (H5)	• No consensus within the team (H7, H6) • Follow up of hypoxaemia by other parameters (H2)
15. Prescription of home oxygen therapy in patients who remain hypoxaemic at discharge	7/7 (100.0)	2/7 (28.6)	• Social worker arranges discharge with oxygen: equipment, prescription (H3) • Checklist (H5)	
16a. Assessment of place of residence during current hospitalisation	6/7 (85.7)	3/6 (50.0)	• Systematic inclusion, social worker (H7, H1) • Checklist (H5)	• Standard anamneses (H2)
16b. <u>Assessment of living status</u> during current hospitalisation	6/7 (85.7)	2/6 (33.3)	• Social worker (H7) • Checklist (H5)	• Standard anamneses (H3)
16c. <u>Assessment of social support</u> during current hospitalisation	7/7 (100.0)	3/7 (42.9)	• Systematic inclusion, social worker (H7) • IT: auto-mail to social worker at admission (H2) • Checklist (H5)	
16d. At discharge provide <u>spoken explanation about home medication</u>	7/7 (100.0)	2/7 (28.6)	• Spoken information by nurse (H3) • Checklist (H3)	
16e. At discharge provide <u>letter with explanation about home medication</u>	7/7 (100.0)	2/7 (28.6)	• Checklist (H3) • Spoken information by nurse (H3)	

16f. At discharge provide <u>letter with information about follow-up appointment</u>	7/7 (100.0)	1/7 (14.3)	<ul style="list-style-type: none"> Letter with follow-up information (H3) 	
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ABGs, arterial blood gases; BMI, basal metabolic rate.

*Based on the results presented in Chapter 7.

Discussion

Overall results

Implementation level of 48 care activities for in-hospital management was evaluated in seven hospitals by means of self-reporting questionnaires. Overall, teams evaluated the care activities as highly implemented, with 87.5% of care activities reported as fully implemented in six to all seven hospitals (Table 2).

Methodological strengths and limitations

This high reported implementation level of the key interventions may reflect the effectiveness of the 'feedback strategy' described in Chapter 6 [8]. When looking at the applied improvement actions, it turns out that teams applied most actions for the care activities showing the most room for improvement according to the clinical audit before care pathway implementation. These included smoking cessation, education, nutrition, and referral to rehabilitation (Table 3). These findings strongly suggest that understanding bottlenecks appears to motivate teams to improve their actual care process. Thus, feedback on actual performance seems to be a strong and active component in care pathway implementation [15-18].

Another determining factor for the high reported implementation level in this study may be that, since 2000, several rigorous, evidence-based clinical practice guidelines (CPGs) on optimal assessment and management of patients with COPD have been established worldwide [19]. As a consequence, it is assumed that COPD teams are familiar with this rigorous evidence on COPD management, and therefore provide best practice for at least a number of these 38 key interventions. This assumption implies that not all 38 interventions need to be newly implemented or optimised. However, as shown by the clinical audit (feedback on actual care process) and the results of the Belgian EQCP study (Chapter 7), there is a considerable number of these evidence based interventions that are suboptimally performed. Each team should focus their improvement efforts on the key interventions that were suboptimally performed in their organisation.

An important challenge in conducting a cRCT is delivering a standardised intervention in the different sites under study [2;6;20;21]. The high implementation level reported is favourable with regard to standardisation of the intervention. Interestingly, as reflected in the different care pathway documents from each organisation, the care pathways developed in the different sites were not identical because of organisational adaptations at the sites. However, this finding is considered to be beneficial, as complex interventions may work best if they are tailored to local context rather than being completely standardised, provided that the core elements of the interventions (i.e. set of key interventions) are maintained [6;22].

For non-pharmacological interventions, several improvement actions referred to the care activity itself (i.e. dietician [Table 3, Part 3, no. 12] and patient leaflet [Table 3, Part 3, no. 6a] and did not describe so-called improvement actions. However, an interview with the study coordinator responsible for two included hospitals indicated that the reported actions referred to newly implemented measures. In addition, we expected to find improvement actions like multidisciplinary team meetings; meetings with other services such as emergency room, lung function services, and radiology (e.g. reserving time slots for diagnostic assessments like chest X-rays or ECGs); and time allocation for specific time-consuming tasks like education of patients [23;24]. It is highly plausible that such actions were undertaken, but were not specifically reported by the study coordinators or team members who were involved in completing the questionnaires.

The most reported reason for non-inclusion or partial inclusion of the key interventions was “organisational factors”, which were reported 21 times for 15 different care activities (Table 3). Unfortunately, detailed descriptions of the nature of the organisational issues were provided in only two cases, including ‘no tabaccologist recruited yet’ and ‘devices for rehabilitation tests purchased recently’ (Table 3, Part III). In addition, the reason “no consensus within the team” was reported seven times for four different interventions: oral administration of corticoids, ABG measurement after start of supplemental oxygen, ABG measurement before discharge in hypoxaemic patients, and performance of rehabilitation tests (Table 3, Part III). Also here, no further details on the nature of disagreement within the team were reported.

Although this process analyses revealed lots of interesting information, we acknowledge that in future process analyses, it is recommendable to include answer categories like ‘multidisciplinary meetings’ and ‘communication with other disciplines’, and to ask team members to explicitly describe the nature of reported action and barriers. Moreover, we believe that conducting structured interviews instead of using mailed questionnaires could have provided more in-depth information on improvement actions and implementation barriers. On the other hand, mailed questionnaires provide the opportunity for the study coordinator to present the questionnaire to different team members for feedback or to organise a team meeting to discuss the different items. In conclusion, we believe that the mailed questionnaires should be combined with an additional interview of the different study coordinators and teams. Alternatively, we recommend organisation of a workshop where all teams are invited to exchange more in-depth information on applied improvement actions.

Implementation level versus study results: first interpretation

In this section, preliminary results on the process indicators of the Belgium component of the EQCP study (Chapter 7) will be linked to the results of the implementation analysis. According to the principles of randomisation, experimental group results during formative evaluation and control group results during summative evaluation should be identical. Indeed, in the present study, both groups were highly comparable for almost all indicators, except for adequate prescription of bronchodilators (Formative: 55.9%; summative: 97.0%). As a consequence, results of the summative evaluation will be correlated with the implementation analyses.

Overall, the findings indicate that organisations improved most with regard to process indicators with the highest reported implementation level and most reported improvement actions. Highest improvement levels were found for smoking cessation, education on inhaler and home oxygen therapy, and nutritional management (Table 3, Part III, nos. 4a-4d, 5a-6d, 10-13b; Chapter 7, Table 2, nos. 12,13, 14, 17-19). Also to be expected, all care activities with lower reported implementation levels, like ABG measurement before discharge and performance of rehabilitation tests, showed no improvement (Table 3, Part I, no. 1; Part II, no. 5b; Part III nos. 2, 4e, 6, 14; Chapter 7, Table 2, nos. 8b, 15, 22).

Overall, the high implementation levels reported do not correspond with the post-implementation process indicator results (Chapter 7, Table 2), where suboptimal performance was still found for a considerable number of indicators. These findings suggest that the teams may have overestimated their own implementation level. Therefore, it will be interesting to perform additional interviews with team members to gain more in-depth information on the improvement actions they applied and any barriers against implementation they experienced. In this context it would also be useful to obtain more objective information on the implementation level of key interventions through direct observations of independent observers [1].

Regardless of the risk for overestimation of implementation level, this kind of implementation analysis is considered to be very useful for two main reasons. Firstly, this analysis allows us show teams existing discrepancies between high reported implementation levels and suboptimal performance of the particular key interventions. Consequently, this discrepancy might sensitize the teams that further improvements and actions are necessary. Secondly, these analysis will provide other COPD teams, intended to implement the care pathway intervention, with valuable information about potential improvement actions and possible barriers for implementation.

Conclusions

The set of 38 evidence-based key interventions was reported as highly implemented in the seven experimental hospitals, which is favourable for the standardisation of the care pathway intervention in different sites. However, despite high reported implementation levels, performance levels of key interventions were not optimal for over half of the indicators. This discrepancy between perceived implementation level and performance results may indicate that the teams may have overestimated their own implementation level, and that the intervention is not yet routinely deployed in daily practice. Additional interviews and direct observations are recommended to obtain more in-depth information on implementation level, improvement actions and implementation barriers.

This process evaluation may also contribute to the second phase of the EQCP study, in which an attempt will be made to describe the relationships between care process structure, multidisciplinary team processes, and outcomes.

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Chapter 9:

General discussion and recommendations

Introduction

The care process for patients hospitalised with chronic obstructive pulmonary disease (COPD) exacerbations is complex [1-5]. Care pathways have become a very popular strategy for improving care processes and optimising outcomes [6;7]. However, until now it is unclear whether care pathways actually work and what active components are responsible for their effect [6;8-11].

The research comprising this PhD dissertation examined the impact of a care pathway for COPD exacerbations on care processes and clinical outcomes. This was achieved by developing new methodology and by analysing and presenting interim results from an international cluster randomised controlled trial (cRCT).

For this chapter, the main results of this dissertation are presented first, organised according to the six research questions formulated in Chapter 1. Secondly, methodological limitations are discussed. Thirdly, implications for the organisation of COPD care are formulated, and recommendations for future research are addressed. Finally, overall conclusions of the PhD dissertation are presented.

Contributions to the field of COPD care and healthcare organisation

RQ1: What is the level of adherence to international guidelines with regard to care processes for in-hospital management of COPD exacerbation according to the literature?

A systematic literature review conducted to explore in-hospital management of COPD (Chapter 2) showed that adherence to guidelines is low, with non-performance ranging from 15% up to 80% [12]. Non-pharmacological interventions were especially poorly performed, such as those involving smoking cessation, rehabilitation, education, nutrition, and discharge management. Clearly from this review, further research on process adherence is needed, as measured indicators from different published studies varied widely and compliance to non-pharmacological processes was scarcely assessed.

RQ2: What is the impact of existing care pathways for in-hospital management according to the literature?

A systematic literature review identified only four pertinent studies. This handful of studies suggested that care pathways might have positive effects on diagnostic and non-pharmacological processes. However, due to limited statistics, divergent measures, and evaluation of a care pathway by means of a historical control group, it must be concluded that the internal validity of results from these studies is limited. Hence, strong conclusions

about the impact of COPD care pathways could not be confidently drawn on the basis of these four published studies.

RQ3: Which indicators should be followed up when evaluating the impact of a care pathway for COPD exacerbations?

A set of 24 process and 15 outcome indicators was developed [13] based on literature, an international Delphi survey, and face-to-face discussions with experts in the field. These indicators refer to care activities and clinical outcomes that, according to the literature, are suboptimally performed and show high variability across different hospitals [12;14;15]. These findings suggest that the selected indicators have potential for improvement when being used to study the impact of interventions aimed at improving performance of COPD care processes and clinical outcomes [16]. Furthermore, indicators were piloted in nine Belgian hospitals, and measurements were determined as feasible by different involved parties.

RQ4: Which set of key interventions should be included in a care pathway for COPD exacerbations?

Within this dissertation work, we developed an eight-step method for designing the clinical content of a care pathway based on acknowledged design and guideline development methods (Chapter 5, Figure 1). By using this eight-step method, a set of 38 evidence-based key interventions was developed (Chapter 5, Appendix 1). The key interventions were categorised into three main processes (diagnostic, pharmacological, and non-pharmacological management), and then formulated into a process flow diagram. Every key intervention was described in detail, including the rationale, description, references, and grading of evidence. The set of key interventions were studied and approved by nine multidisciplinary COPD teams. The new eight-step method will likely help teams in shaping the clinical content of their future evidence-based care pathways aimed at other diseases and conditions, such as hip fracture, heart failure, and diabetes.

RQ5: What is the impact of a care pathway for in-hospital management of COPD exacerbations on performance of care processes and clinical outcomes?

In 2009, the European Quality of Care Pathways (EQCP) study, an international cRCT, was launched in four countries (Belgium, Ireland, Italy, and Portugal), with two aims: (i) to study the impact of a care pathway for in-hospital management of COPD exacerbations on care processes, clinical outcomes, and teamwork; and (ii) to investigate why and under what circumstances care pathways are effective [17;18]. In total 65 hospitals were included. Thirty-three hospitals were randomised to the experimental group, which implemented a care pathway, while the remaining 32 hospitals were randomised to the control group, which

provided usual care. The care pathway included three active components: (i) feedback on actual performance, (ii) integration of evidence-based key interventions in daily care, (iii) training on care pathway development and implementation.

This work conducted for the author's PhD was included as part of the larger EQCP study and *focussed on the first study objective: impact of care pathways for in-hospital management of COPD exacerbations on care processes and clinical outcomes*. The EQCP study in Belgium is one year ahead of the other countries (Ireland, Italy, and Portugal) and is also considered to be a pilot test. Because of timing and feasibility of carrying out the PhD work, *only the results of the Belgian EQCP study are included in the results section of this dissertation*. Final results comprising data of all four countries are expected to be analysed in autumn 2013 and will be disseminated by the EQCP study group via publications and conference proceedings in 2013 and 2014.

Seven experimental and five control hospitals were included in the Belgian EQCP study. Analyses showed that performance of process indicators improved 10-50% in the care pathway group for 7 of 24 indicators (29.2%) and 25 of 42 subcomponents (59.5%), most improvements coming from activities associated with education, nutrition, administration of corticoids, and discharge management. Statistical significance was found for only three indicators and ten subcomponents. This was to be expected because data from only the Belgian hospitals were used, which led to a small sample size and hence low statistical power. However, criteria to meet for every process indicator is 100% performance, regardless of patient characteristics. Consequently, results on the process indicators, in this case better performance up to 50% in the care pathway group, do reflect the performance level of the teams, and so should not be considered to be coincidental results arising from chance variation in small samples.

Interesting but also expected, for the outcome indicators we found no significant results, though considerable non-significant improvements were found for 30-day readmission (care pathway: 13.6% vs. usual care: 22.2%) and length of stay (LOS) (care pathway: 11.65 days vs. usual care: 14.49 days).

Results of the EQCP study in Belgium suggest that implementation of a COPD care pathway can improve performance of care processes and has the potential to positively affect clinical outcomes. However, because of limited statistical power, especially for outcome indicators, conclusions on effectiveness can only be confidently drawn when results of the total sample of the four countries become available. It is promising, however, that the hospitals who implemented a care pathway showed higher performance levels with a 10-50% increase. In the care pathway group, however, suboptimal performance of less than 50% was found for 12 of 24 indicators (50.0%) and for 8 of 42 evaluated subcomponents

(19.0%). In conclusion, we see the need for a continuous quality improvement approach to achieve normalisation and thus optimal performance of the processes.

One strength of the EQCP study is that it is designed as both a research study and a quality improvement project. The involved teams receive support in the reorganisation of care for COPD patients, and they can later use the knowledge they gained in other care processes. To illustrate, experimental teams stated in interviews conducted for the parallel EQCP trial on teamwork [19], that they considered this project to be one of the best improvement projects they had ever participated in, especially because of the combination of the three components of care process auditing, integration of evidence-based knowledge, and structured support in care pathway development and implementation. As a result of this study, the involved organisations were chosen to become centres of excellence in the organisation of care processes and will function as examples of good practice on the national and international level for professionals and hospital managers aiming to improve the quality of their care [17]. This network will support other organisations currently not involved in the EQCP study in the optimisation and evaluation of their own care processes [18].

The EQCP methodology, which was designed according to the framework for complex interventions by a team of experts with widely recognised experience in care pathways, may guide other researchers when implementing and evaluating a care pathway or other complex intervention using a cluster randomised design. Before the launch of the EQCP study, only five cRCTs on care pathways had been conducted, all performed on national level [20-24]. The EQCP study is the first international cRCT to study care pathway effectiveness [17], and therefore it will provide new knowledge on design and performance of a cross-border cRCT, which can pose a major challenge due to logistic, economic, and cultural issues. Finally, previous studies on care pathways focussed on the integration of a set of key interventions as a main active component. This is the first study on care pathway effectiveness that includes the additional components of feedback on actual performance and the training of teams on development and implementation of care pathways.

RQ6: What is the level of implementation of the key interventions included as active components in the care pathway for in-hospital management of COPD exacerbations?

We used self-reported questionnaires to evaluate 48 care activities for their level of implementation in the seven experimental hospitals (Chapter 8). These activities are related to the set of 24 process indicators and their 42 subcomponents (which are part of the multicomponent indicators). According to the study coordinators and the team members, care activities were highly implemented: 42 of 48 evaluated care activities (87.5%) were fully implemented in six to all seven hospitals. The number of included care activities for which a

specific action was reported ranged from 28.6% to 97.7% over the seven hospitals, with most actions undertaken for non-pharmacological interventions.

However, the high implementation levels do not correspond with the results on process indicators after implementation, as a considerable number of indicators were still suboptimally performed (Chapter 7, Table 2). These findings suggest that the teams may have overestimated their own implementation level, and consequently additional measures like interviews and direct observation may be needed to provide more objective information on the implementation process. However, this implementation analyses give teams insight into discrepancies between highly reported implementation levels and suboptimal performance of the implemented care activities. Consequently, these analyses may sensitise the teams that further improvements and actions are necessary. Furthermore, these analyses will provide important insights to other teams planning to implement the care pathway intervention, especially which regard to potential improvement actions and barriers for implementation.

Overall methodological limitations

An important limitation with regard to reporting of data in this dissertation is that, because of timing and feasibility, interim analyses were performed on the Belgian data only. Thus, the necessarily small sample size resulted in less-than-desired statistical power, and consequently the chance of finding statistically reliable results was poorer at this interim stage. Nevertheless, as comprehensive addressed in chapter 7, criterion to meet for every process indicator is 100%. Consequently, results on the process indicators do reflect performance levels of the teams, and so should not be considered to be coincidental results arising from chance variation in small samples.

An important point of discussion is patient involvement. In the care pathway intervention in our study, no components for facilitating patient-focused care were included. The Institute of Medicine emphasised the importance of patient centredness, stating that high-quality care should be *safe* (avoiding patient injuries due to care intended to help them); *effective* (evidence-based, avoiding underuse and overuse); *patient centred* (*respectful of and responsive to individual patient preferences, needs, and values*); *timely* (no needless delay); *efficient* (avoiding waste); and *equitable* (no variation in quality because of person's class) [25]. Moreover, research on patient involvement showed that patients who are actively involved in their care tend to make healthier lifestyle choices, were more likely to adhere to treatment recommendations, showed improved clinical outcomes, and often used fewer healthcare resources [26-29].

When examining the literature on patient involvement in COPD patients, we found a very limited number of interesting publications, all addressing COPD-specific preferences and concerns such as ‘experiencing breathlessness’, ‘being housebound’, and ‘need for medical care’. [30-32]. However, this literature research revealed two interesting frameworks that focussed on identifying and understanding individual needs of patients and establishing patient-centred therapeutic care in COPD patients [33;34]. Furthermore, a brief literature search on patient focused care identified following possible active ingredients for improving patient involvement: (i) decision aids and training of healthcare professionals in communication skills and shared decision making [26;27;35]; (ii) tools and strategies to measure and explore context-related preferences (i.e. waiting, unreliable administrative processes, rude and difficult staff, misunderstandings in communication, handovers) [29]; and (iii) instruments for assessing patient satisfaction during their care process (i.e. conducting surveys, open interviews with patient or relatives, performing walkthroughs with a patient) [36-38]. Furthermore, Jaques et al. indicated that patients should have a broader role in improving care by contributing to policy and major systems design. Involving patients in audit will help in measuring processes and outcomes of real value for patients, not just those that clinicians think are important [29;39]. Finally, we believe that patient societies could play an important role in making our care more patient-focused.

Finally, we need to address that, within the timeframe of this PhD dissertation, no economic evaluation was included. However, health status was followed up by using the Euroqol 5D (<http://www.euroqol.org>). When all data of the four countries are collected, economic analyses will be performed [40].

Implications for the organisation of COPD care

Firstly, findings with regard to low adherence to evidence-based guidelines should encourage all multidisciplinary teams and hospital managers to audit and optimise their care process for patients hospitalised with COPD exacerbation.

When optimizing their care process, teams should look into the care pathway strategy as presented and studied in this dissertation. Moreover, teams should pay additional attention to non-pharmacological interventions, as they are very suboptimally performed. Integration of these interventions into daily care may be more difficult for several reasons. (i) Most of these interventions are multicomponent interventions, which are very time-consuming and are difficult to integrate into the wide range of daily clinical tasks (i.e. education on inhaler therapy). (ii) The non-pharmacological interventions are all focussed on long-term outcomes of prognoses, quality of life, coping and self-management, and hence do not provide early and ongoing results of delivered care. (iii) Adequate performance of these interventions

requires qualified staff with specific competencies—like a tabaccologist, a dietician, and a physiotherapist—and use of specific protocols (in example how to adequately educate a patient regarding inhaler therapy).

One outcome of this dissertation work is a newly developed set of 38 evidence-based key interventions for in-hospital management of COPD exacerbations (Chapter 5), piloted and approved by nine multidisciplinary teams. COPD teams that aim to optimise their care should carefully examine this set of key interventions. The rationale included for each intervention will help leaders motivate their teams to improve performance of the different key interventions. Moreover, the descriptions for each intervention will facilitate their practical integration into daily care, especially for complicated or time-consuming interventions like patient education and discharge management.

Another outcome of this dissertation is a set of 39 quality indicators for in-hospital management of COPD exacerbations, operationalised into objective measurements. COPD teams should audit their care processes for in-hospital management of COPD exacerbations based on this validated and ready-to-use set of indicators. However, follow-up of 39 indicators in daily practice would be impractical. Therefore, we need to make a distinction between research and clinical practice. When conducting research on care pathway effectiveness, in this case a cRCT, the aim is to collect as much evidence and knowledge as possible in order to fill the “blind spots” about care pathway effectiveness. Furthermore, considering that it is challenging to conduct cRCTs due to logistic and economic issues, we believe that the opportunity to collect data in a multicentre study should be fully utilised. In daily practice, however, we recommend that a subset of indicators should be identified for follow-up. Selection should be performed by primary stakeholders (team, managers, etc.), and should be based on following criteria: (i) knowledge of daily practice, referring to processes known or presumed to be suboptimally performed in the organisation and so being targets for improvement; and (ii) the SMART principles [41], referring to the idea that indicators should be **S**pecific (the goal is clear and unambiguous, what knowledge do you want to get out of it); **M**easurable (are the measurements feasible); **A**ttainable (are the indicators realistic); **R**elevant (sensitivity to change, interest of stakeholders like team and management), and **T**imely (timeframe of measurements, when should feedback be available). Furthermore, according to achieved improvements on indicators and input of new evidence based knowledge on the care process, these set of indicators for daily monitoring should be systematically updated according to the criteria mentioned above.

A validated set of indicators also provides important opportunities for benchmarking between organisations, although some barriers need to be considered. As indicated by the literature [12;42] and as highlighted in the report of the Belgian Healthcare Knowledge Centre (KCE) [43], hospitals invest significant time and manpower collecting data for internal

audits or for delivery to different healthcare institutions, though the use of divergent measure formats does not provide for benchmarking. The KCE report also identified different excellent initiatives on quality indicator development and measurement, though some initiatives tended to overlap, implying unnecessary duplication [43]. We see a leading role for governments to centralise all initiatives and to provide for a global system incorporating standardised indicator sets with standardised measure and feedback formats; these should be usable for internal and external audit and allow for proper benchmarking.

Implications for future research

Continuation of the EQCP study

The EQCP study is also being conducted in three other countries: Ireland, Italy, and Portugal. The same study protocol is being used, including implementation of the complex intervention (feedback, evidence-based key interventions, training on care pathway implementation) and follow-up of the same set of quality indicators. However, in the context of differences in professional culture and clinical practice, some minor adjustments needed to be made to the set of key interventions and the quality indicators. Furthermore, the level of expertise in care pathway development and implementation varies considerably in the different countries. In the Belgium study, all participating hospitals were members of the Belgian Dutch Clinical Pathway Network (www.nkp.be) [44]. This means that the study coordinators in the Belgian hospitals were already experienced in pathway development, implementation, and evaluation, which proved to be an enormous advantage, enabling us to easily conduct the study. At the same time, lack of care pathway experience of researchers from the other involved countries needs to be acknowledged. Careful attention with regard to training on care pathway development and implementation will be required in order to ensure that the 'same' experiment is performed across all the participating countries. However, the Italian hospitals, recruited out of the Piedmont region, are more or less familiar with care pathways due to earlier research and initiatives of the Amedeo Avogadro University of Eastern Piedmont. Also, national coordinators and several quality managers of the involved hospitals of Ireland, Italy and Portugal received comprehensive education on care pathway development, implementation, and evaluation during an international summer school (www.E-P-A.org) organised by the European Pathway Association (E-P-A). Moreover, as members of E-P-A, they have access to worldwide networking and regular newsletters, conferences, and additional training on care pathways and organisation of care [7].

The first results of the clinical audit conducted before care pathway implementation are now available for the three other countries involved. Initial observations show that adherence

to guidelines is comparable to that of the Belgium component of the study. This implies that there is also considerable room for improvement in Ireland, Italy, and Portugal.

It is important to note that Ireland, Italy, and Portugal are currently under great economic pressure. However, this study can be an opportunity for healthcare leaders to leverage the results in economic terms. During economic crises, governments are stressed more than ever to rapidly but effectively reform their healthcare system. Because care pathways are used to standardise care, improve coordination, and optimise outcomes with optimal allocation of resources, policy makers might see this study as a first step in the right direction for healthcare reform. In addition, the research in these three countries may provide more insight into how governments and healthcare systems manage (or tend to manage) an acceptable level of safety and quality in healthcare delivery under economic depression.

In the second phase of the EQCP study, when all data on process, outcome, and team indicators from all four countries are collected [18] and when the results on the parallel trial on teamwork are available [19], we will investigate why and under what circumstances care pathways work [17]. More specifically, we will explore (i) which mechanisms (active ingredients) in care pathways underlie their effect ('what are active components?'), and (ii) the role of contextual factors and multidisciplinary team work when implementing and evaluating care pathways [10;17]. Therefore, we will use the approach described in the Care Process Organisation Triangle, developed by Vanhaecht et al. [45] This approach is based on the Donabedians' structure-process-outcome framework [46], the realistic approach of Pawson and Tilly [10;47], and the terminology used by Heskett et al. [48], Teboul [49], Batalden and Davidoff [50], and Mitchell et al. [51]. This triangular framework describes the relationships between the structure of the care pathway care process, multidisciplinary team processes, and outcomes.

Need for continuous quality improvement

Implementation of the complex intervention in the seven Belgian hospitals improved performance rates by 10 to 50%. However, in the experimental group assigned to the care pathway, suboptimal performance of less than 50% was found for 11 of 24 indicators (45.8%) and for 8 of 42 (19%) evaluated subcomponents. By contrast, the study coordinators and team members reported that almost all interventions were highly implemented. These findings indicate that the experimental teams already adopted the intervention, but that the intervention was not routinely imbedded in everyday practice [52].

There are several possible reasons why routine integration of the intervention (normalisation) was not achieved. Firstly, developing and implementing the intervention according to the Plan Do Study Act (PDSA) cycle was apparently insufficient for reaching

normalisation within the studied time span. This finding indicates that more PDSA cycles are necessary in order to reach optimal performance. Moreover, a fundamental principle of the PDSA cycle is iteration: Once an hypothesis is supported, executing the cycle again will extend the knowledge further and bring the outcomes closer to the goal, including an improved operation and output [53]. Secondly, the change capacity of the involved teams may also play an important role. More specifically, team competencies, including the knowledge, skills, and attitudes of staff members related to change processes, will be crucial determinants of success [45;54;55]. Team effectiveness is strongly driven by local organisational culture. Consequently, change behaviour in clinical practice is not a 'one-shot deal' but is progressive and requires long-term cultural change initiatives [55].

Strongly related to the normalisation process is sustainability, which is defined by the four characteristics of Wiltsey et al. (2012): (i) the extent the core elements are maintained (core elements are the most closely related elements associated with desired health benefits); (ii) the extent desired health benefits are maintained or improved over time after initial funding or supports have been withdrawn; (iii) how strong impact modifications have on the core ingredients of the intervention; and (iv) continued capacity to function at the required level in order to maintain the desired benefits [56]. Long-term effectiveness of care pathways had not yet been evaluated [6;57-61]. Also in the EQCP study, the impact of the care pathways was assessed at a maximum of 6 months after implementation [18]. Interesting, Savits et al. (2000), who described the life cycle of clinical care processes, indicated that clinical processes will reach a critical point in which they could further improve, maintain, or decline [62]. In the 2009 study of Vanhaecht et al., data collected using the Care Process Self Evaluation Tool [63] indicated that the critical point at which improvement slowed down for care pathways was about one year [62;63]. A possible explanation for this slowing was (i) the lack of continuous follow-up of the pathways, and (ii) deterioration of pathway standardisation and coordination [63]. As noted by Goldmann, it is relatively easy to engage a multidisciplinary team in creating a pathway, but it is much harder to motivate members to update it regularly [64]. Many models of sustainability exist but have not been evaluated yet [56]. In conclusion, it will be interesting to explore (i) the critical point for alternative crossroads of improving, maintaining, or declining care pathways, and (ii) possible active ingredients for enhancing sustainability of care pathways.

Based on previous findings, we conclude that a continuous quality improvement (CQI) approach will be necessary to achieve normalisation and subsequent optimal performance, and to maintain sustainability. CQI is operationally defined as a philosophy of continual improvement of a processes associated with providing a good or service that meets or exceeds customer expectations [65]. The emphasis lies on understanding and improving the

underlying work processes and systems in order to add value rather than on correction of individuals' mistakes after the fact [65].

Using an expert panel that reviewed 161 articles on CQI projects, O'Neill et al. (2009) identified six key features of CQI: (i) iterative development process, (ii) feedback at meetings involving participant leaders, (iii) feedback of systematically collected data, (iv) recognised change method (i.e. Deming approaches), (v) driven by data collected systemically during implementation, and (vi) local conditions considered. However, these authors indicated that only a few articles included all these features. Therefore, future research will be necessary to theorise active ingredients for successful implementation of a CQI intervention [66]. In addition, use of information technologies (ITs) may facilitate embedding of care pathway content and continuous follow-up of care pathways [67;68]. An interesting example of the impact of IT is the clinical management information system used by Intermountain Healthcare in Salt Lake City [67]. Their enhanced IT system provides for a centralized patient database that is accessible for clinicians over the whole geographically dispersed health network, and also includes a data measurement system that captures data on guideline adherence as well as on clinical cost, and service outcomes built around specific clinical care processes [67].

In 1998, Shortell et al. identified the strengths and limitations of the clinical application of CQI. According to their review, successful factors in CQI might be participation of physicians, feedback to individual practitioners, and a supportive culture to maintain the gains that are achieved. Failures were reported because of non-acceptance by local physicians, poor dissemination of knowledge, and vague feedback to practitioners [65]. With regard to existing research on the impact of CQI, Shortell et al. found that relatively few appropriate RCTs are available. Most of the studies are single-centre studies, with a before-and-after design. Hence, it is difficult to determine whether the reported improvements are due to the CQI interventions or to competing explanations [65].

On the basis of previous findings, we decided to start a Belgian clinical working group on in-hospital management of COPD exacerbations, with the aim of (i) assessing sustainability of results, and (ii) improving in-hospital care for COPD patients with exacerbations by using the CQI approach. Follow-up measures will be conducted in the 12 hospitals already included in the EQCP study and in newly recruited organisations of the Belgian-Dutch Clinical Pathway Network (BDCPN). Of the set of 39 process and outcome indicators we developed, a select subset will be followed up and chosen based on the SMART principles [41;52]. Based on initial conclusions of the Belgium EQCP study, important additional emphasis will focus on patient involvement [26;27;35], team training [52;55;69-71], and organisational context [8;15;54;67;68;72-77].

A new model for care pathways for reorganisation of chronic care [78]¹

Future care pathway research should focus on chronic transmural care for several reasons. Firstly, the increasing prevalence of chronic disease represents major challenges for healthcare systems [28;79-81]. It is estimated that 70% of healthcare expenses are related to chronic diseases [82]. In addition, the current fragile economic climate may progressively limit resources available to healthcare systems [28;79]. Secondly, another challenge lies in the actual organisation of healthcare delivery systems. Current healthcare delivery systems are often unable to meet the complex needs of chronically ill patients because healthcare is traditionally focussed on acute care management and short term goals [83]. Also, fragmented delivery of health and social services, including disconnection of primary and secondary care, is an acknowledged problem in many healthcare systems [28;80;83-85]. Thirdly, too often, chronic care approaches feature an uninformed, passive patient interacting with a poorly coordinated team of health professionals, resulting in frustrating and inadequate encounters [86-88]. Finally, despite the availability of worldwide evidence-based practice guidelines for a wide range of chronic diseases, the use of evidence-based standards remains limited [79;80;89].

A well-established model designed to guide the reorganisation of healthcare delivery systems from acute and reactive care to chronic, proactive, and community-based care is the Chronic Care Model (CCM) developed in 1996 by Wagner et al. [88]. In this systemic model, improved functional and clinical outcomes of disease management are the results of productive interactions between informed, activated patients and prepared, proactive practice teams of healthcare professionals. These productive interactions are supported by six components: healthcare organisation, community resources, self-management support, delivery system design, decision support, and clinical information systems [83]. To better integrate aspects of prevention and health promotion into the CCM, an enhanced version called the Expanded Chronic Care Model was developed in 2003 by Barr et al. [90] (Figure 1).

¹ An editorial on this subject is published in the *International Journal of Care Pathways*, April 2012; 13:1-2.

Figure 2. The Expanded Chronic Care Model [90]

Several attempts have aimed to adequately measure the effectiveness of care reorganisation in the context of the CCM [91;92]. However, because of defragmented implementation, different change strategies, and use of different outcome indicators, effectiveness of reorganising health care delivery systems according to the CCM on patient outcomes and on healthcare costs remains unclear [91-93].

A possible strategy for facilitating integration of the CCM framework is implementation of a care pathway [45;79]. An integrated care pathway that bridges primary care and hospitals, and allows multidisciplinary teams to interact with active patients and communities, facilitated by ITs, can encounter defragmented implementation of the CCM and has an enormous potential for optimising patient care and outcomes like hospital admissions and quality of life [45;79;94]. This hypothesis is supported by the fact that the CCM framework and the care pathway tool include comparable concepts like mutual decision making, coordination and supportive environment and resources [45;88;90].

However, as addressed earlier, because of defragmented and diverse CCM implementation strategies and the use of diverse outcome measures, one does not know the active essential components and best practices necessary to build these integrated chronic care pathways [8;9;45]. For this reason, we think that research on the implementation and effectiveness of integrated chronic care pathways should be included on the agenda of next

challenges in care pathways. Furthermore, when developing this care pathway, the CCM components should be integrated.

Overall conclusions

Care for patients hospitalised with COPD exacerbations is suboptimal according to widely acknowledged international guidelines, and outcomes are poor and vary greatly among organisations. Care pathways are a possible strategy to optimize care processes and outcomes, though until now the effectiveness of COPD care pathways remained unclear.

An eight-step method was designed to develop the clinical content of an evidence-based COPD care pathway. By applying this eight-step method, a valid and feasible set of 38 key interventions and 39 quality indicators was developed.

An international cluster randomized trial was launched in four countries (Belgium, Ireland, Italy and Portugal), with the aim to evaluate the impact of a care pathway for in-hospital management of COPD exacerbation. The care pathway included three active components: feedback on actual performance, integration of the set of 38 evidence based key interventions, and training on care pathway implementation. Evaluation of care pathway effectiveness was based on the set of 39 indicators. Preliminary results of the Belgian cRCT strongly suggest that implementation of this care pathway improved the care process, as an increase in performance levels of 10 to 50% was found. Moreover, the care pathway has potential for improving clinical outcomes. However, because of limited statistical power, strong conclusions on effectiveness can be drawn only when results of the total sample of the four involved countries become available in 2013-2014.

Despite the improved performance levels demonstrated to date, a considerable number of process indicators remained suboptimal performed. Continuous quality improvement will be needed to further optimise the care process for in-hospital management of COPD exacerbation, and to enhance sustainability of the improved results.

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Summary

Management of patients hospitalised with COPD exacerbations involves a wide range of diagnostic, pharmacological, and non-pharmacological processes. In addition, coordination of the multidisciplinary care process is complex. Implementation of care pathways has become very popular for improving care processes and optimising outcomes. However, until now it remains unclear whether care pathways actually work and which active components are responsible for their effect.

In this PhD research, we examined the impact of a care pathway for COPD exacerbation on care processes and clinical outcomes, by developing new methodology and analysing interim data of an international cluster Randomized Controlled Trial (cRCT).

Firstly, a systematic review was conducted to explore the level of adherence of actual care to internationally acknowledged COPD guidelines. The findings showed that quality of care for these patients was very suboptimal, especially for non-pharmacological management. However, measured indicators were very discordant among previously published studies, and compliance to non-pharmacological processes was scarcely assessed, implying that further research on process adherence is needed.

Secondly, a systematic literature review sought to identify all studies that had examined the development, implementation, and characteristics of existing COPD care pathways, and that had evaluated their impact on care processes, clinical outcomes, and team functioning. Only four studies with a quasi-experimental design were found. The studies described positive effects on diagnostic and non-pharmacological processes; though because of limited reporting of statistics, divergent measurements, and evaluation of a care pathway by means of a historical control group, the internal validity of the results was questionable. Therefore, confident conclusions on the impact of COPD care pathways based on these studies could not be drawn.

Thirdly, in order to rate content validity of process and outcome indicators, an international Delphi study was conducted with a Delphi panel composed of 35 panelists from 15 countries. Among the panellists were 19 medical doctors, 8 nurses, and 8 physiotherapists. Consensus by at least 75% of panelists that an indicator is relevant for follow-up was reached for 26 of 72 evaluated process indicators (36.1%) and for 10 of 21 outcome indicators (47.6%).

Fourthly, an eight-step method was developed for designing the clinical content of an evidence-based care pathway. Applying this method resulted in a set of 38 evidence-based key interventions and a set of 24 process and 15 outcome indicators, which were piloted and approved by nine multidisciplinary teams. These findings indicate that the sets of key interventions and indicators are appropriate for the standardisation and follow-up of in-

hospital management of COPD exacerbations. Furthermore, the eight-step method can also help teams in shaping the clinical content of their future care pathways for other patient populations.

Fifthly, the European Quality of Care Pathways study was launched in four countries (Belgium, Ireland, Italy, and Portugal). This is a cRCT aiming to study the impact of care pathways for COPD exacerbations on care processes and clinical outcomes. A second aim was to study why and under what circumstances care pathways work, but this research question was not included in this PhD dissertation. In total, 65 hospitals were randomised, with 33 hospitals assigned to the experimental group in which a care pathway is implemented, and 32 hospitals assigned to a control group in which usual care is provided. The experiment is a complex intervention comprising three active components: (i) feedback on actual performance based on a clinical audit before care pathway implementation, (ii) integration of a set of evidence-based key interventions, and (iii) training on care pathway development and implementation based on the PDSA cycle. The measurements, including follow-up of 24 process and 15 outcome indicators, were conducted in both groups and results were compared to see if care pathway implementation leads to better results.

The EQCP study in Belgium is one year ahead of the other countries (Ireland, Italy, and Portugal), and was conducted between July 2009 and November 2011. Because of timing and feasibility of the PhD, only the results of the Belgian EQCP study are included in the results section of this dissertation. Final results based on the data of all four countries are expected to be analysed in autumn 2013, and will be disseminated by the EQCP study group via publications and conference proceedings in 2013 and 2014. The preliminary results of the Belgian EQCP study strongly suggest that care pathways lead to improved care processes, as an increase in performance levels of 10 to 50% were found. These results also show that care pathways have the potential to improve clinical outcomes. However, the Belgian sample size is small, and consequently statistical power is limited. Not surprisingly, then, only scarce significant results were found, leading to provisional conclusions at this time. Significant conclusions on the effectiveness of care pathways can only be drawn based on the results of the total sample of the four involved countries. However, according to clinical practice guidelines, the criterion is that all process indicators must meet 100% performance, regardless of patient characteristics. Consequently, the results on the process indicators, in this case better performance levels of up to 50% in the care pathway group, may not be considered to be coincidental results arising from chance variation in small samples.

Finally, a process evaluation on the implementation level of the set of evidence-based key interventions was conducted in the seven experimental hospitals in the Belgium EQCP study. Although study coordinators and team members reported that the care activities were highly implemented, these implementation levels did not correspond with the results on

process indicators after implementation, as a considerable number of indicators were still suboptimally performed. These findings suggest that the teams may have overestimated their own implementation level, and consequently additional measures like interviews and direct observation may be needed to provide more objective information on the implementation process. However, this implementation analysis give teams insight into discrepancies between highly reported implementation levels and suboptimal performance of the implemented processes. Consequently, this analysis may sensitise the teams that further improvement of the care process is necessary. Secondly, this analysis will provide important insights for other teams planning to implement the care pathway intervention, especially with regard to possible improvement actions and potential barriers for implementation.

The EQCP study will be continued in Ireland, Italy, and Portugal, and the same protocol will be used, including the same intervention and the same measurements. Preliminary results from these countries show that adherence to guidelines is comparable with the Belgian data, implying that considerable room for improvement exists also in these countries.

Although performance levels improved in the care pathway group, half of the indicators remained suboptimally performed, indicating that the complex intervention was adopted but not integrated into daily practice. As a consequence, a Belgian clinical working group on in-hospital management of COPD exacerbations will be initiated. The aims of this group will be (i) to further improve in-hospital care for COPD patients experiencing exacerbations, and (ii) to assess and enhance sustainability of results. Therefore, a continuous quality improvement (CQI) approach will be used. Important additional focus will be put on team training, patient involvement, and organisational context.

Future research on care pathways should focus on reorganisation of chronic care in order to deal with the current challenges of rising chronic disease, ageing population, and the inevitable shift from hospital-centred medicine to home care and self-management. An integrated care pathway that bridges primary care and hospitals, and allows multidisciplinary teams to interact with active patients and communities, facilitated by information technology (IT), can encounter the current defragmented implementation of the Chronic Care Model (CCM) and has enormous potential for optimising chronic patient care.

In conclusion, the results of this PhD dissertation strongly suggest that care pathways lead to improved care processes and have potential to optimise clinical outcomes. Nevertheless, to further improve the care process and to enhance sustainability, continuous quality improvement will be needed.

Samenvatting

De zorg voor patiënten gehospitaliseerd met een opstoot van Chronisch Obstructief Longlijden (COPD) omvat een heel aantal diagnostische, farmacologische en non-farmacologische processen, en coördinatie van het multidisciplinaire zorgproces is complex. Een courant gebruikte strategie voor reorganisatie van zorgprocessen en optimalisatie van outcomes is de ontwikkeling en implementatie van een klinisch zorgpad. Echter, omwille van talrijke methodologische redenen blijft het tot vandaag onduidelijk of zorgpaden effectief werken, en welke actieve componenten in zorgpaden juist verantwoordelijk zijn voor een bepaald effect.

In dit proefschrift werd de impact van een zorgpad voor COPD exacerbatie met betrekking tot performantie van zorgprocessen en klinische outcomes bestudeerd. Hiertoe werd een methodologie voor adequaat zorgpadonderzoek ontwikkeld, en vervolgens werd een interim analyse uitgevoerd op de data van een internationale cluster randomized controlled trial (cRCT).

Ten eerste werd een systematisch literatuuronderzoek uitgevoerd om na te gaan in welke mate huidige zorg voor patiënten gehospitaliseerd met COPD exacerbatie voldoet aan internationaal erkende evidence-based standaarden. De bevindingen toonden aan dat zorg voor deze patiënten erg suboptimaal is, zeker met betrekking tot non-farmacologisch management.

Ten tweede werd een literatuuronderzoek uitgevoerd naar studies betreffende ontwikkeling, implementatie, en karakteristieken van COPD zorgpaden, en vervolgens werd hun impact op zorgprocessen, klinische outcomes en teamwerking nagegaan. Slechts vier studies werden gevonden, allen gebruik makend van een quasi-experimenteel design. De studies beschreven positieve effecten met betrekking tot diagnostische en non-farmacologische processen. Echter de interne validiteit van de studies is beperkt omwille van methodologische tekortkomingen. Bijgevolg was accurate besluitvorming omtrent impact van zorgpaden niet mogelijk op basis van de huidige beschikbare evidentie.

Ten derde werd een internationale Delphi survey uitgevoerd om de inhoudsvaliditeit van een set van proces- en outcome-indicatoren te beoordelen. Het Delphi panel bestond uit 35 panelleden uit 15 verschillende landen, waaronder 19 medische dokters, 8 verpleegkundigen en 8 fysiotherapeuten. Consensus tussen tenminste 75% van de panelleden dat een indicator relevant is voor follow-up werd bekomen voor 26 van de 72 geëvalueerde procesindicatoren (36.1%) en voor 10 van de 21 geëvalueerde outcome-indicatoren (47.6%).

Ten vierde werd een acht-stappenplan opgezet om de inhoud van een evidence-based zorgpad voor COPD-exacerbatie te ontwikkelen. Toepassing van deze methode resulteerde in een set van 38 sleutelinterventies en een set van 24 proces- en 15 outcome-indicatoren,

welke werden uitgetest en goedgekeurd door negen Belgische multidisciplinaire teams. Dit geeft aan dat de sets van sleutelinterventies en indicatoren geschikt zijn voor standaardisatie en follow-up van zorg voor patiënten gehospitaliseerd met COPD-exacerbatie. Daarnaast heeft het acht-stappenplan ook potentieel om teams te faciliteren in ontwikkeling en standaardisatie van de klinische inhoud van toekomstige klinisch zorgpaden voor andere patiëntengroepen.

Ten vijfde werd de European Quality of Care Pathways (EQCP) Study gelanceerd in vier landen (België, Ierland, Italië, en Portugal). Dit is een cRCT, uitgevoerd met als doel de impact van zorgpaden voor COPD exacerbatie met betrekking tot performantie van zorgprocessen en klinische outcomes na te gaan. Een tweede doel is na te gaan hoe en onder welke omstandigheden zorgpaden werken, maar deze onderzoeksvraag was niet inbegrepen in dit proefschrift. In totaal werden 65 ziekenhuizen gerandomiseerd, waarvan 33 ziekenhuizen werden toegewezen aan de experimentele groep waar een klinisch zorgpad wordt geïmplementeerd, en 32 ziekenhuizen werden gerandomiseerd naar de controlegroep waar zorg wordt verleend zoals vóór aanvang van de studie. Het experiment is een complexe interventie, bestaande uit drie actieve componenten: (i) feedback betreffende de kwaliteit van het huidige zorgproces gebaseerd op een klinische audit vooraleer zorgpadimplementatie, (ii) Integratie van een set van evidence based sleutelinterventies, en (iii) training en begeleiding in ontwikkeling en implementatie van een klinisch zorgpad op basis van de Plan Do Act Study cirkel. De metingen, bestaande uit follow-up van 24 proces en 15 outcomen indicatoren, werden uitgevoerd in beide groepen en dan vergeleken om te kijken of zorgpadimplementatie leidt tot betere resultaten.

De Belgische studie is een jaar vooruit op de andere landen en werd uitgevoerd tussen april 2009 en november 2011. Vanwege timing en haalbaarheid werden enkel de resultaten van de Belgische EQCP studie geïncludeerd in deze thesis. Finale resultaten gebaseerd op data van de vier landen worden verwacht in het voorjaar van 2013, en de resultaten zullen bekendgemaakt worden via publicaties en conferenties. De voorlopige resultaten suggereren dat de implementatie van een klinisch zorgpad leidt tot verbeterde uitvoering van zorgprocessen, aangezien een verbetering van 10 tot 15% werd gevonden. De resultaten geven ook aan dat zorgpaden potentieel hebben om klinische outcomes te verbeteren. Echter de Belgische steekproefgrootte is klein, en bijgevolg is de statistische power laag. Zoals verwacht werden dan ook slechts enkele significante resultaten gevonden. Significante conclusies omtrent zorgpadeffectiviteit zijn pas mogelijk op basis van alle data uit de vier landen. Echter, in overeenstemming met de klinische praktijkrichtlijnen dient elke procesindicator uitgevoerd te worden voor elke patiënt (performantieniveau van 100%), ongeacht patiëntenkarakteristieken. Bijgevolg mogen de resultaten van 50% verbeterde

performantie in de zorgpadgroep niet bestempeld worden als toevallige resultaten die voortvloeien uit de toevallige variatie in kleine steekproeven.

Tot slot werd een procesevaluatie met betrekking tot implementatie van de set van 38 sleutelinterventies uitgevoerd in de zeven experimentele ziekenhuizen uit de Belgische EQCP study. Hoewel de studievoördinatoren en teamleden rapporteerden dat de sleutelinterventies in sterke mate geïmplementeerd werden, komen deze resultaten niet overeen met de performantieresultaten na implementatie, aangezien een belangrijk aantal indicatoren suboptimaal werd uitgevoerd. Deze bevindingen geven aan dat de teams hun implementatieproces mogelijk overgeschat hebben. Bijkomende interviews en directe observatietechnieken zijn dan ook aangewezen om meer objectieve informatie omtrent het implementatieproces te verzamelen. Echter, deze implementatie-analyse kantgenstrijdigheden tussen de hoog gerapporteerd implementatieniveaus en suboptimale uitvoering van de geïmplementeerde processen belichten, en bijgevolg teams sensibiliseren met betrekking tot nood aan verdere optimalisatie van het zorgproces. Ten tweede kan deze procesanalyse ook belangrijke inzichten leveren omtrent verdere verbeteracties en implementatiebarrières voor andere COPD teams die de zorgpadinterventie willen implementeren.

De EQCP studie zal verder gevoerd worden in de andere drie landen: Ierland, Italië en Portugal, en hierbij zal gebruik gemaakt worden van hetzelfde protocol, inclusief dezelfde interventie en dezelfde metingen. De eerste resultaten geven aan dat ook in deze landen compliance met betrekking tot internationale standaarden laag is, en dat ook hier belangrijke ruimte voor verbetering aanwezig is.

Ondanks een verbetering van de performantie in de zorgpadgroep, werd de helft van de indicatoren nog steeds suboptimaal uitgevoerd. Dit wijst er op dat de interventie nog niet volledig is ingebed in de dagelijkse klinische praktijk. Daarom zal in België een klinische werkgroep betreffende zorg voor patiënten gehospitaliseerd met COPD exacerbatie opgestart worden. Het doel is tweeledig: (i) zorg voor patiënten gehospitaliseerd met COPD verder optimaliseren, en (ii) duurzaamheid van de verbeterde resultaten nagaan en bewerkstelligen. Hiertoe zal gebruikt gemaakt worden van een Continuous Quality Improvement (CQI)-benadering. Bijzondere focus zal liggen op teamtraining, patiëntgerichtheid, en de organisationele context.

Tenslotte, in de context van het stijgend aantal chronisch zieken, de vergrijzing van de bevolking, en de onvermijdbare shift van ziekenhuiszorg naar thuiszorg en zelfzorg, zien wij de nood voor onderzoek naar een nieuw model van zorgpaden, gericht op organisatie van chronische zorg. Geïntegreerde zorgpaden die een brug vormen tussen de eerstelijns gezondheidszorg en ziekenhuizen, en die multidisciplinaire teams toelaten om samen te werken met actieve patiënten en gemeenschappen, gefaciliteerd door informatiesystemen,

kunnen tegemoetkomen aan de huidige gedefragmenteerd implementatie van het Chronic Care Model en hebben enorm potentieel voor het optimaliseren van de chronische patiëntenzorg.

In conclusie, de resultaten van dit proefschrift suggereren in sterke mate dat implementatie van zorgpaden leidt tot optimalisatie van zorgprocessen, en dat er potentieel is voor een verbetering in klinische outcomes. Echter, continue kwaliteitsverbetering is aangewezen, enerzijds om het zorgproces verder te optimaliseren, en anderzijds om het effect op lange termijn te bewerkstelligen.

Curriculum Vitae Cathy Lodewijckx

Cathy Lodewijckx was born on November 17, 1976, in Diest, Belgium. She obtained her bachelor degree in nursing in 1997, and in the same year she started working as a registered nurse in an inpatient respiratory ward at the University Hospitals Leuven. In 1998 she fulfilled a postgraduate course in pulmonary nursing at the University Hospitals Leuven.

In 2001 she started her studies for a Master of Nursing Science degree at KU Leuven, Belgium, while she worked part-time as a bachelor nurse. She obtained her master's degree in nursing science in 2004. In the same year she incorporated a part-time mandate as clinical nurse specialist in COPD, while being employed part-time in the respiratory ward at the University Hospitals Leuven. From 2007 to 2008 she participated in the Clinical Leadership Project at the University Hospitals Leuven. She has been an active member of the Belgian Society for Respiratory Nurses (BVPV) since October 2004. In September 2006 she was elected vice-president of this society, and in 2011 she became president of the BVPV. In addition, she has been a member of the European Respiratory Society (ERS) since 2005. In 2012 she was elected chair of the ERS Group 09.03 Nurses.

In October 2008 she started a research fellowship at the Centre for Health Services and Nursing Research, KU Leuven, while working part-time as a clinical nurse specialist in COPD at the University Hospitals Leuven. At the same time, she started her PhD study on the impact of care pathways for COPD exacerbation. This study was integrated into the European Quality of Care Pathways (EQCP) study, an international cluster randomised controlled trial on care pathway effectiveness. Subsequently, she became a member of the European Pathway Association (E-P-A), who managed the EQCP study. From 2010 to 2012 she has participated in a 3-year doctoral summer school on Complex Interventions at the European Academy of Nursing Science (EANS).

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