Geriatric rehabilitation for older patients with COPD; integration of rehabilitation and palliative care

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Summary and general discussion

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Aim and outline of of this thesis

The central aim of this thesis is to investigate whether developing and implementing a specific geriatric rehabilitation program for older patients with severe COPD that also integrates palliative care aspects, the GR_COPD program, is both feasible and effective.

With this goal in mind, four studies were performed that included two different study populations, as well as a systematic review and meta-analysis of the literature.

First, the feasibility study (that included a retrospective case series of 61 consecutive patients with COPD that followed the GR_COPD program) investigated feasibility in terms of patient characteristics, suitability, safety and preliminary evaluation of patient response to the GR_COPD program. Furthermore, in this specific group and setting, the responsiveness of the clinical COPD questionnaire (CCQ) was examined in order to determine if the CCQ could be used as a primary outcome in the subsequent GR_COPD study.

Second, the GR_COPD study (that included a prospective cohort of 158 patients, hospitalized for an acute exacerbation and indicated for the GR_COPD program), investigated the effect of the GR_COPD program on disease-specific health status (measured with the CCQ), functional status and exacerbation frequency.

Third, a systematic review of the literature was made, including a meta-analysis, that examined the prevalence of pain, factors related to pain and pain management interventions in patients with COPD.

Fourth, cross-sectional data from the GR_COPD study were used to examine the prevalence, characteristics and relationships of pain in patients hospitalized for an acute exacerbation and indicated for the GR_COPD program.

Results

Main findings

Part one: The GR_COPD program

Chapters 3 and 4 present the feasibility study. The results show that patients admitted to the GR_COPD program had complex health issues: i.e. all patients suffered from advanced COPD (GOLD stage 3 or 4), co-morbidities were frequent, health status was severely impaired, and exercise capacity was limited. Furthermore, undernourishment was prevalent and many patients were at risk for an anxiety disorder or depression. These results confirm that patients admitted to the GR_COPD program have specific and complex problems and needs that can be explained by the co-occurrence of disease- and age-related problems. This underpins the need

for a suitable program that addresses these complex health issues. Preliminary evaluation of patient response to the GR_COPD program showed a clinically relevant improvement in both functional status and health status. Moreover, adherence to the program was good, there were no unexpected adverse events and over 90% of these patients were discharged home after a median length of inpatient rehabilitation of 35 days. Thus, we concluded that geriatric rehabilitation for patients with advanced COPD is feasible and is likely to offer substantial benefits.
The study in **Chapter 4** evaluated outcomes of the CCQ in relation to lung function, degree of dyspnoea and (change in) functional status. Results showed that, in this specific group of patients, the CCQ is sensitive to change in response to the GR_COPD program.
Chapter 5 presents the results of the GR_COPD study and shows that, during a three-month follow-up period, the GR_COPD program had a significant and clinically relevant treatment effect on disease-specific health status (measured with the CCQ) and exacerbation rate. This allowed us to conclude that geriatric rehabilitation, for older patients with severe COPD and hospitalized for an acute exacerbation, is effective. However, a longer follow-up period is needed to reveal whether these results can be maintained for a longer period of time. Nevertheless, we also concluded that the GR_COPD program should be implemented in clinical practice, as no alternative rehabilitation programs for this specific group of patients, are available.

Part two: Pain in patients with COPD

Chapters 6 and 7 present two studies that focused on pain in COPD. Overall symptom burden is one of the most important determinants of disease-specific health status and, therefore, adequate symptom control is of major importance, from the perspective of both palliative care and rehabilitation medicine. Patients with COPD suffer from many different symptoms, of which the most commonly known are dyspnea, cough and sputum production. We decided to focus on pain, since pain is also highly relevant but an often unrecognized, underestimated and, therefore, undertreated symptom in patients with COPD; moreover, pain has a negative impact on quality of life and possibly also on functional status.
The results of our systematic review (**Chapter 6**) confirm that pain is prevalent in patients with COPD, with moderate to severe scores on intensity and interference. Furthermore, the results show that pain is related to many other symptoms (e.g. dyspnea, insomnia, fatigue, anxiety and depression) and that pain is negatively associated with health-related quality of life. Nevertheless, much remained unknown due to the relatively few studies on pain in COPD and the considerable amount of heterogeneity in the design of the included studies.

The cross-sectional study (**Chapter 7**) on the prevalence and characteristics of pain in patients indicated for the GR_COPD program, shows that pain was also a prevalent and significant symptom in this specific population, as 40% of all patients suffered from pain, with moderate to severe scores on intensity and interference. Furthermore, compared to patients without pain, patients with pain had an overall higher symptom burden and a more impaired disease-specific health status. Although we found no difference in objective measurements of activities of daily living and exercise capacity, patients with pain experienced more limitations in functional status, as measured with the functional domain of the CCQ. Results from this study also indicate that pain treatment was probably suboptimal in terms of pain relief and prescription of analgetics. These results tend to confirm that, in patients with COPD, pain is often unrecognized, underestimated and undertreated. Thus, we concluded that, in this group of patients and setting, pain needs more attention and standard assessment of pain should be implemented into daily practice, together with patient education on this subject.

Reflection

To further discuss the outcomes of the work presented in this thesis, the postacute rehabilitation (PAC) quality framework of Jesus and Hoenig was used as a theoretical context and translated to the GR_COPD program and study.[1]

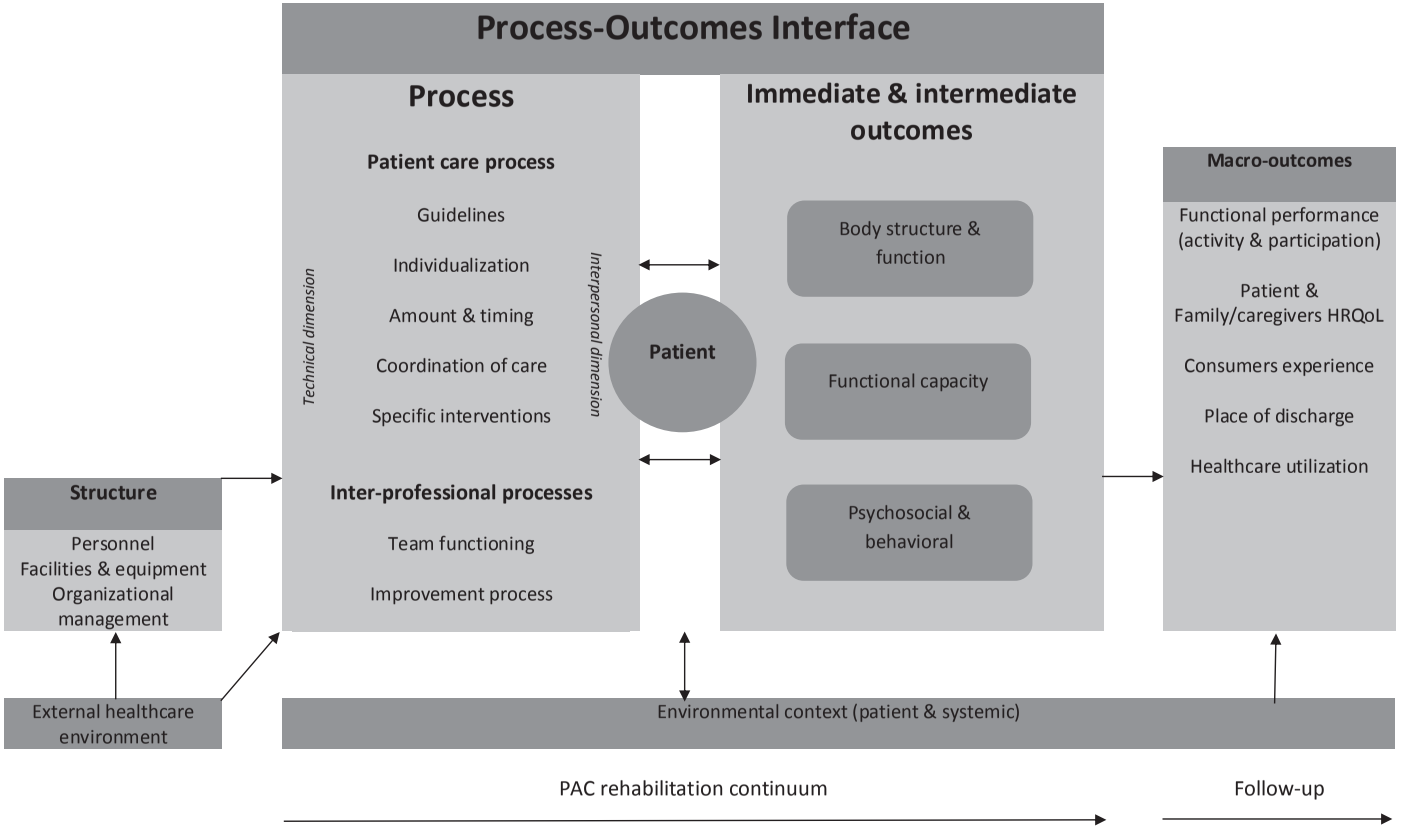
The PAC quality framework was based on the structure, process, outcome (SPO) model of Donabadian and the International Classification of Functioning, Disability and Health (ICF) model of the World Health Organization (WHO). It was developed in order to clarify what constitutes 'quality of care' in postacute rehabilitation, and to provide a sound and evidence-based framework that can be used for quality of care evaluation and improvement (Figure 1). The PAC quality framework was therefore used as a model to evaluate the results of the present work, and to develop a broader and more generic view on geriatric rehabilitation for patients with chronic diseases, in terms of implications for clinical practice and recommendations for research. Below, we discuss the different elements of the framework in a stepwise reverse order, i.e. we start with the outcomes, because these reflect what really matters: namely, benefit for our patients.

Outcomes of the GR_COPD program

Macro level

The primary outcome measure of the GR_COPD study was change in disease-specific health status, as measured by the clinical COPD questionnaire (CCQ).

Figure 1. The postacute rehabilitation (PAC) quality framework developed by Jesus and Hoenig.[1]



Abbreviations: HRQoL: health related quality of life

Our results show a clinically relevant effect of the GR_COPD program on disease-specific health status. Choosing disease-specific health status as primary outcome is important, as it reflects the patient's personal experience of disease severity and covers other domains beyond the functional domain, such as symptoms and mental status. This is also in line with literature and guidelines on pulmonary rehabilitation and palliative care in COPD, which also state that improvement of (health-related) quality of life should always be the ultimate aim of any intervention or treatment program within these domains.[2-5]

Exacerbation rate was defined as secondary outcome. Results from the GR_COPD study show a relevant effect on exacerbation rate during a three-month follow-up period: i.e. patients in the control group had an exacerbation rate of 2.7 as compared to 1.0 in the GR_COPD group. Exacerbation rate can be related to several macro outcomes. First, in patients with COPD, exacerbations are strongly related to diminished health-related quality of life and have a negative impact on functional performance and prognosis.[6,7] Second, exacerbation rate can be seen as a derivative of healthcare utilization, because exacerbations are the most frequent reason for hospital admission in these patients.[8] However, secondary analysis with a longer follow-up period that also focuses on other outcome measures more strongly related to healthcare utilization (i.e. cost-effectiveness), such as rehospitalizations and preventable follow-up care, is needed.

In the ICF-based construct of functional performance, social participation and the extent to which patients can perform tasks of daily living in their own environment (i.e. activity) are considered the primary outcomes of rehabilitation. Both activity and participation are complex concepts, not only determined by individual factors but also by the dynamics of social roles and the direct environment in which they take place. However, measurement of participation was not part of the primary analysis of the GR_COPD study. Although validated and widely used instruments are available that measure activity [e.g. functional independence measure (FIM)], no internationally used and validated tool that includes the complexity of participation in this domain is available.[1] In the Netherlands, the Utrecht scale for evaluation of rehabilitation-participation (USER-p) was developed and appears to be a valid measure to rate participation in persons with physical disabilities.[9] Integrating personal goals on the level of participation into geriatric rehabilitation programs is important, as was recently stated in the Dutch Position Paper on geriatric rehabilitation, and has already been confirmed in stroke survivors aged 70 years and older.[10,11] Therefore, validating the USER-p as outcome measure on a macro level could prove important for research in geriatric COPD rehabilitation.

It should be mentioned that the patients' and caregivers' actual experience with the program was not measured. This can be seen as an important shortcoming of our

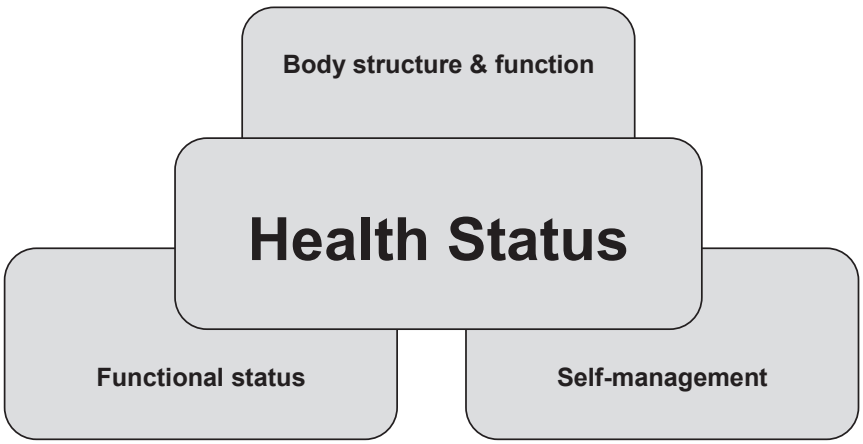
study, as the patient's perspective is an important outcome measure that directly reflects the degree of patient centeredness and, thus, the quality of healthcare.[1] In addition to the relevance of the patient's perspective, it is also important to note that the construct of 'experience' was preferred to 'satisfaction', the latter being more expectancy-dependent and more subjective.[12]

Intermediate/immediate level

Intermediate outcomes of the GR_COPD program can be categorized into three domains: i) body structure and function, ii) functional status and iii) self-management. These three domains encompass several standard treatment modules, all targeted at improving disease-specific health status as the ultimate goal (on a macro level) of the program (Figure 2). These three domains are very similar to the immediate/intermediate outcomes defined in the PAC quality framework (body structure & function; functional capacity; psychosocial & behavioural), although the third domain (i.e. self-management) needs additional clarification and elaboration (further discussed below).

Improvement in body structure and function was achieved through treatment modules that focussed on a) optimizing pharmacological treatment, inhalation techniques and oxygen use, b) prevention and treatment of co-morbidities, c) optimizing nutritional status and/or treatment of undernourishment, and d) improving symptom burden. There is considerable evidence to support the important role of symptoms in COPD driving the burden of the disease.[13] Therefore, optimal symptom control is considered to be a key target in COPD treatment and of major importance for improving health status, also from a palliative care perspective.[14]

Figure 2. Three-domain-model of the GR_COPD program.

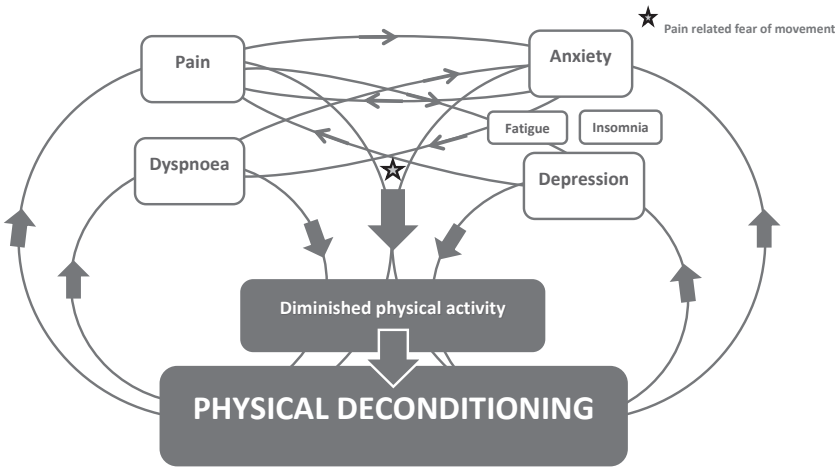


Symptom burden in patients with advanced COPD is known to be high: this is also confirmed by our data (**Chapters 3, 4 and 7**). Participants of the GR_COPD study suffered from many symptoms, the most prevalent being dyspnoea, fatigue, muscle weakness and pain (**Chapter 7**). Furthermore, in patients with COPD, symptoms (including pain) seem to cluster, thereby aggravating each other, causing several 'vicious circles in COPD' (Figure 3). In this concept, originally based on the study of Lohne et al, and further developed based on the results from our systematic review (**Chapter 6**), cross-sectional data from the GR_COPD study (**Chapter 7**) and (more recently) studies on pain in COPD, physical deconditioning is seen as the underlying process that could explain the observed co-occurrence of pain and many other symptoms. This process is mediated by diminished physical activity and pain-related fear of movement, and is often aggravated by co-morbidities and poor nutritional status.[15-18]

The central role of symptoms in the burden of COPD emphasizes that standard systematic assessment and follow-up of symptom burden should be part of clinical care for patients with COPD during the stable phase of the disease, and also during exacerbations and rehabilitation (**Chapter 7**). This requires a valid multidimensional symptom assessment instrument and specific interventions aimed at optimal control of several symptoms, such as pain, fatigue, dyspnoea, insomnia, anxiety and depression.

The GR_COPD study could not establish any treatment effect on functional status (**Chapter 5**). Considering the fact that postacute rehabilitation in general primarily focusses on functional recovery and functional performance, this result is some-

Figure 3. The vicious circles in COPD.



what surprising and might even be concerning. Functional status as intermediate outcome refers to the ability of the patients to function (i.e. perform. activities of daily living such as washing, getting dressed, going to the bathroom, walking and eating) regardless of social roles or environmental variables.[1] We defined functional recovery as improvement in two functional domains: 1) change in the level of care dependency concerning activities of daily living, as measured with the Barthel Index (BI), and 2) change in exercise capacity, as measured with the six-minute walking test (6MWT). When analysing the results of the BI and 6MWT we concluded that, although both outcome measures had improved to a clinically-relevant extent, the BI is probably less suitable as an outcome measurement in this specific group of patients because of (amongst other reasons) its ceiling effect. Results of the 6MWT showed a high amount of missing data and a wide range, leading to limited statistical power. Based on these results, the relevance of the BI and the 6MWT as outcomes in geriatric COPD rehabilitation can be questioned, also because of the possible limited correlation of these instruments to activity and participation. When the GR_COPD study was designed, choosing these instruments to measure (improvement in) functional status was based on international literature and guidelines on pulmonary rehabilitation (6MWT) and generic geriatric rehabilitation (BI). Thus, we conclude that, based on our results, together with the construct of activity and participation from the PAC framework, additional instruments are needed.

For this, the Utrecht scale for evaluation of rehabilitation (USER) and the USER-participation (USER-p), might be a more suitable choice for measuring functional status and participation, and improvement of these outcomes in response to geriatric COPD rehabilitation. The USER was developed in the Netherlands, and is a valid and reliable instrument to measure immediate/intermediate outcomes of rehabilitation on an individual level, and can also be used to measure the effectiveness of specific rehabilitation programs.[10] The USER consists of several domains including activities of daily living, mobility, cognition, psychosocial functioning and several symptoms (including fatigue and pain). The USER is also part of the Standard Measurement Plan for Geriatric rehabilitation, developed at the University Network for the Care Sector South Holland (UNC-ZH) that is currently being implemented and tested in several geriatric rehabilitation units.

Improvement of self-management, as the third intermediate outcome of the GR_COPD program, was pursued by the following treatment modules: education, peer-group support, smoking cessation support, training of energy saving techniques, general advice concerning healthy aging (e.g. nutrition, exercise), and assessment of compliance and coping responses (e.g. patients compliance with care recommendations, adaptive coping responses). Motivation for the program and psychological status, expressed by symptoms of anxiety and depression and

cognitive impairment, are also known to affect macro outcomes of postacute rehabilitation.[1] Furthermore, the interaction between motivation and psychological status is of interest and importance. For instance, symptoms of depression can predict uptake and non-completion of rehabilitation, and cognitive impairment increases the risk for dropout during pulmonary rehabilitation.[19,20] From a broader perspective, research questions should move from focussing on effectiveness of postacute rehabilitation for patients with COPD to how referral, uptake and adherence can be improved, also in relation to patients' motivation and preferences in terms of setting and timing.[6,21] In the GR_COPD study, indication for the program was based on a set of standard criteria, probably resulting in a relatively high referral rate (although evaluation of the referral rate was not part of the study). Also, the feasibility study showed good adherence, as only one patient dropped out due to lack of motivation. However, uptake of the program can be interpreted as being relatively low: of the 158 included patients only 78 were motivated for the GR_COPD program. This finding again raises the important discussion concerning which variables influence and constitute patients' motivation for rehabilitation, and how to improve uptake.
The GR_COPD study was not aimed at measuring the direct effects of the program on self-management, or one or more of its individual components. Also, we did not investigate the relationship between (components of) self-management and psychological status as independent variables and health status as a dependent primary outcome measure, nor did we investigate the effect of specific self-management and psychological treatment modules on an intermediate or macro outcome level. However, more knowledge on the effectiveness of these specific elements of the GR_COPD program (also in relation to motivation and uptake) is important since improvement of self-management is a key component of treatment in general for chronic conditions, such as COPD.[1,5] The PAC quality framework does not present an evidence-based conceptual understanding and approach for definitions and quality evaluation of self-management; this emphasizes the need for the development of concepts that describe and explain the complex interactions between motivation, psychological status and self-management in this specific group of patients and setting.

Patient care process: evaluation of the GR_COPD program

The GR_COPD program was developed as a structured care pathway, in close collaboration with the pulmonary department of the adjacent hospital. Coordination of care across settings enables smooth transitions and helps to synchronize the care provided by different healthcare providers interfacing with the patients. The resultant synergies are known to have a positive effect on patients' outcomes.[1]

The GR_COPD program was based on (inter)national guidelines on comprehensive evidence-based pulmonary rehabilitation.[5,22] Implementation and dissemination of these guidelines into clinical practice was assured by repeated knowledge transition from the pulmonary department to the multidisciplinary rehabilitation team, and vice versa. Furthermore, the feasibility study (**Chapters 3 and 4**) was developed to evaluate the program and the results were also used for quality improvement.

Although guidelines should direct practice, rehabilitation should always be tailored to patients' needs and possibilities and, therefore, programs need to be individualized. This also applies to the treatment plan of the GR_COPD program, which is based on an individual comprehensive assessment. Outcomes from this assessment, combined with the experience of the rehabilitation team, are used as input for the complex process of individualized clinical reasoning about the wide variety of variables that constitute a patient's disabilities and limitations. At the next level, individualization should be part of the process of defining specific rehabilitation goals, i.e. use patient-centred goal setting and shared decision-making. Structured goal setting in rehabilitation has the potential to improve macro outcomes via higher levels of motivation and self-efficacy.[23] Although patient-centred goal setting does take place within the GR_COPD program, this is not done in a formalized way [e.g. by using an instrument that facilitates the goal-setting process, such as the Canadian Occupational Performance Measure (COPM) or Goal Attainment Scale (GAS)] and, therefore, implementation cannot be guaranteed. In the Standardized Measurement Plan for Geriatric Rehabilitation, the COPM is one of the core instruments. Preliminary results of pilot studies show that the COPM is feasible in this population.[24]

The GR_COPD program was developed as a modular program that combines specific interventions of rehabilitation medicine and palliative care. The program is aimed at restoring patients' health status to the level before hospital admission or, in other patients, to counteract or stabilize the gradual decline in health status that preceded hospital admission and prevent hospital readmissions (**Chapter 2**). The GR_COPD program consists of several standard treatment modules within the three domains (Figure 2). Using standardized treatment modules that specify exactly what kind of treatment is provided, facilitates quality monitoring and presumably improves outcomes.[1] However, the complexity of most disabilities, and the rehabilitation process itself, challenge the use of standardized treatment modules. Nevertheless, using a modular program (categorized into the three domains) seems to be a suitable and workable structure for this specific group of patients. Moreover, it can be argued that geriatric rehabilitation after an acute exacerbation of a chronic ('acute-on-chronic') disease (e.g. heart failure, renal failure, Parkinson's disease, oncological diseases) is different from geriatric rehabilitation after an acute event,

such as a hip fracture or stroke. Besides focussing on functional recovery and improvement of body structures and body functions, rehabilitation after an 'acute-on-chronic' event should also be aimed at improving self-management strategies (i.e. educate the patient how to live well with a chronic disease) and should also integrate palliative care aspects into the rehabilitation plan.

In **Chapter 2** we described the palliative care aspects of the GR_COPD program. The palliative care needs of patients with advanced chronic organ failure can be divided into five domains: 1) symptoms, 2) care dependency, 3) family caregiving, 4) co-morbidities. and 5) advance care planning.[25] Although all of these domains were implemented into the structure of the GR_COPD program, this was not carried out in a standardized systematic way in daily practice. Implementation of a more standardized systematic assessment of the five palliative care needs defined by Janssen et al might be beneficial to patients and could improve outcomes of the GR_COPD program. Therefore, a validated instrument for the assessment of multidimensional symptom burden, and specific interventions aimed at optimal control of specific symptoms (such as pain, fatigue and insomnia), are needed. An intervention that facilitates implementation of advance care planning into daily practice was recently developed and evaluated, and should be implemented into practice.[26]

Interprofessional processes

Interprofessional processes support the care process and outcomes, and encompass team functioning and improvement processes. However, since evaluating the quality of the interprofessional process of the GR_COPD program was beyond the aims of this research project, this element is not addressed in detail. Nevertheless, the design of the GR_COPD program does meet all the conditions that define good quality of team functioning in postacute rehabilitation, such as deliberate care planning (e.g. multidisciplinary treatment plans), care coordination (e.g. weekly interdisciplinary team meetings), team leadership (e.g. coordination of interdisciplinary care by the elderly care physician) and sociologic factors (e.g. rehabilitation climate as part of organizational culture).

Structure of the GR_COPD program

Organizational management

When the GR_COPD program was first developed, geriatric rehabilitation was part of a government-guided long-term care reimbursement system without financial incentive for efficient or high-quality geriatric rehabilitation. In 2011, a bundled payment system was introduced to improve the quality of service delivery and, ultimately, the quality of care. Considering the process of service delivery, develop-

ing structured care pathways was one of the main goals. However, this requires effective collaboration between different stakeholders, e.g. nursing homes with specialized nursing facilities (SNF), specialized rehabilitation centres and hospitals. Although the GR_COPD program was developed in close collaboration with the pulmonary department of the adjacent hospital (secondary care), structural collaboration with a pulmonary rehabilitation centre (tertiary care) or general practitioners and other primary care stakeholders was not part of the developmental process. Moreover, structural cooperation in daily practice on a patient, outcome and quality level was only present between the SNF and the adjacent hospital. Developing and implementing cooperation on a large scale with multiple healthcare providers and stakeholders from different domains of the healthcare system is challenging, especially in a changing external healthcare environment.[27,28] Nevertheless, from a patient's and evidence-based perspective, integrated care pathways that cover all domains of healthcare should always be pursued, as they improve quality of care and contribute to deliverance of the right type of care, at the right moment, in the right setting, for the right patient.

Patient centeredness

In the PAC quality framework, patient-focussed quality definitions are considered to be of key importance and, therefore, the patient is placed in the centre of the framework. First, a patient-centred rehabilitation process, with alignment with patients' care needs, values and perspectives, is crucial, Second, patients can be seen as co-creators of their own rehabilitation process and directly influence outcomes and quality of care. Therefore, involvement of the patient (and family/caregiver) in the rehabilitation process, mediated by individual goal setting, shared decision-making, improvement of self-management and context-based care, is needed.[11] This process should be fostered by healthcare providers. Recently, patients are increasingly involved in the development of patient- reported outcome measures (PROMs), also in line with value-based healthcare.[29,30] The GR_COPD program was developed as a patient-centred program. The treatment plan is based on a thorough individual assessment that includes the patient's preferences, needs and goals, also in the context of psychosocial status and participation. Furthermore, the program is aimed at improving self-management and disease-specific health status, using a disease-specific PROM (i.e. the CCQ) as outcome. Nevertheless, processes that actually constitute patient centeredness were not yet transparent and, thus, the quality of implementation cannot be objectively measured and evaluated. This calls for implementation of innovative techniques that, ideally, facilitate and foster patient centeredness (e.g. goal setting and self-management), improve the quality of the process (i.e. ensure that patient centeredness was indeed part

of daily practice) and improve (macro) outcomes (i.e. are (cost)-effective). An innovative technique that has the potential to combine these outcomes, is eHealth.[31] eHealth can be defined as the use of information and communication technologies for health and can, when integrated into usual care (i.e. blended eHealth), improve self-management in patients with chronic diseases, such as COPD.[32] Developing and implementing blended eHealth interventions aimed at improving, facilitating and monitoring patient centeredness in geriatric rehabilitation, can be seen as a new and important field of interest, both from a practice and evidence-based perspective.

Methodological consideration

When interpreting the results of this thesis, some important limitations should be considered. We discuss these limitations in relation to the three study designs that were used.

Limitations of the feasibility study

The first and most important limitation of the feasibility study (designed as a real-life study describing a consecutive series of patients all receiving the GR_COPD program, but with no control group) is population bias due to the selection procedure, which was not based on strict inclusion criteria and might negatively affect generalizability. The lack of a control group, although self-evident when considering the design and aims of this study, can be seen as a second limitation: it is plausible that those that received usual care also experienced significant improvement. Thirdly, when considering the guidelines on conducting feasibility studies, one important recommended objective was not incorporated into this study: we could not report on recruitment rate, as data from patients that were indicated but not motivated for the program, were not collected.

Limitations of the systematic review and meta-analysis

First, because our review was the first systematic review study on pain in patients with COPD, at the time of performing the search strategy the literature on this topic was scarce; only 14 studies on pain and symptom burden in patients with COPD could be included and, of these, only 11 reported on the prevalence of pain in COPD. Also, because the included studies showed considerable heterogeneity in design, setting, patient characteristics and pain measurement instruments used, this probably affected the validity and reliability of our results. As a consequence, the estimated prevalences of pain in patients with COPD showed a large range (21-

72% overall; 32-60% in high-quality studies). Furthermore, the appropriateness of including data from quality of life instruments that included a separate pain domain is debatable. Because our search strategy did not include 'quality of life' as a keyword, we included only those studies on quality of life that mentioned the keyword 'pain' in the abstract. This implies that our data on pain as a subdomain of quality of life are probably incomplete. However, there has been a recent increase in studies specifically focussing on pain in COPD; this allows to more accurately determine the prevalence of pain in COPD, and helps the development and implementation of treatment interventions that specifically target pain in patients with COPD.

Limitations of the GR_COPD study

The design of the GR_COPD study is an important limitation. Because randomization was considered unethical, lack of comparability in outcome risk factors between the GR_COPD and control group might have led to confounding. Therefore, we chose to use propensity scores (PS) analysis and included sensitivity analysis for unmeasured confounding. PS analysis is recommended when conducting observational real-life studies that evaluate treatment benefits and harms in older adults. Although an additional sensitivity analysis showed similar results, confounding cannot be fully excluded as we did not perform other recommended strategies to address unmeasured confounding (e.g. active comparator design). Another important limitation is the generalizability to other patients with COPD; although positively influenced by the fact that this was a real-life study and lenient exclusion criteria were applied, this influence may have been limited due to selection bias caused by the indication criteria applied. Moreover, patients willing to participate might have been a selective group, even though no differences were found in demographics and baseline CCQ and HADS scores between the included and not included patients. Finally, results from both the feasibility study and the GR_COPD study question the appropriateness and relevance of the instruments used to measure functional status (i.e. the Barthel Index and the 6MWT). This limitation was mainly reflected in the observed ceiling effect of the Barthel Index and the wide range in values of the 6MWT combined with a relatively high amount of missing data (40%). Furthermore, since no valid set of outcome measures for this group of patients and setting is available, this makes it difficult to compare our results on functional status with other studies in general.

Conclusion, implications and recommendations

Based on the results of the work in this thesis we conclude that a disease-specific geriatric rehabilitation program that integrates rehabilitation with palliative care aspects (the GR_COPD program) is needed, is feasible, and shows beneficial effects on disease-specific health status and exacerbation rate, in older patients with COPD hospitalized for an acute exacerbation. These results imply that the GR_COPD program should be available to all patients within this specific group.

We used the PAC quality framework to structure implications for daily practice and recommendations for research. *First*, considering the macro outcomes of the program, it is recommended to use the CCQ as primary patient-related outcome measure (PROM), in clinical practice and in research. PROMs related to activity and participation (macro outcome) and to functional recovery (intermediate outcome) for this specific group of patients are needed, because integration of personal goals on the level of activity, participation and functional recovery into the treatment plan is important. There is evidence that using the USER and USER-p as outcome measures on an intermediate and macro level is promising, and further research should focus on evaluating the validity, reliability and responsiveness of these instruments in geriatric rehabilitation. Furthermore, measurement of patients' and caregivers' experience with the program is important and should be implemented into practice and used as an outcome measure in studies on geriatric rehabilitation.

Second, within the process-outcome interface, it is recommended to use the three-domain model with a specific focus on self-management (Figure 2) in disease-specific geriatric rehabilitation programs for patients that suffer from acute exacerbations of chronic ('acute-on-chronic') diseases. Furthermore, palliative care aspects should be integrated into the treatment plan by incorporating standardized symptom assessment and advance care planning methods. Research should focus on developing a valid multidimensional symptom assessment instrument for patients with COPD or, more generally, for patients with chronic organ failure. Specific interventions aimed at optimal symptom control (e.g. pain, fatigue and insomnia) and facilitating implementation of advance care planning into practice, should be developed and tested. *Third*, research should focus on obtaining more knowledge about the effectiveness of specific interventions of the GR_COPD program, especially concerning self-management and palliative care. This requires development of a conceptual approach to the complex interaction between motivation, psychological status and self-management in this specific group of patients and setting. *Fourth*, on an organizational level, models of cooperation between multiple healthcare providers and stakeholders that cover all domains of rehabilitation medicine (community and hospital care, tertiary (pulmonary) reha-

bilitation centres) on a patient, outcome and quality level, should be developed and implemented into practice. *Finally*, eHealth is a novel but promising field of interest with considerable potential in terms of improving patient centeredness, quality of care and saving costs. Therefore, future research should also focus on development, implementation and evaluation of blended eHealth interventions in geriatric rehabilitation.

References

1. Jesus TS, Hoenig H. Postacute rehabilitation quality of care: toward a shared conceptual framework. Archives of physical medicine and rehabilitation. 2015;96(5):960-969.
2. McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews. 2015(2).
3. Lanken PN, Terry PB, Delisser HM, et al. An official American Thoracic Society clinical policy statement: palliative care for patients with respiratory diseases and critical illnesses. American journal of respiratory and critical care medicine. 2008;177(8):912-927.
4. Janssen DJ, McCormick JR. Palliative care and pulmonary rehabilitation. Clinics in chest medicine. 2014;35(2):411-421.
5. Spruit MA, Singh SJ, Garvey C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. American journal of respiratory and critical care medicine. 2013;188(8):e13-64.
6. Puhan MA, Gimeno-Santos E, Cates CJ, Troosters T. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. The Cochrane database of systematic reviews. 2016;12:Cd005305.
7. Carrasco Garrido P, de Miguel Diez J, Rejas Gutierrez J, et al. Negative impact of chronic obstructive pulmonary disease on the health-related quality of life of patients. Results of the EPIDEPOC study. Health and quality of life outcomes. 2006;4:31.
8. Aaron SD. Management and prevention of exacerbations of COPD. BMJ (Clinical research ed). 2014;349:g5237.
9. Post MW, van der Zee CH, Hennink J, Schafrat CG, Visser-Meily JM, van Berlekom SB. Validity of the utrecht scale for evaluation of rehabilitation-participation. Disability and rehabilitation. 2012;34(6):478-485.
10. de Graaf JA, van Mierlo ML, Post MWM, Achterberg WP, Kappelle LJ, Visser-Meily JMA. Long-term restrictions in participation in stroke survivors under and over 70 years of age. Disability and rehabilitation. 2018;40(6):637-645.
11. Wattel EM, Position Paper Geriatric Rehabilitation - a research agenda for geriatric rehabilitation in the Netherlands , Consortium Geriatric Rehabilitation, Utrecht, 2017 https://www.actiz.nl/stream/position-paper-grz
12. Black N, Jenkinson C. Measuring patients' experiences and outcomes. BMJ (Clinical research ed). 2009;339:b2495.
13. Janssen DJ, Spruit MA, Uszko-Lencer NH, Schols JM, Wouters EF. Symptoms, comorbidities, and health care in advanced chronic obstructive pulmonary disease or chronic heart failure. Journal of palliative medicine. 2011;14(6):735-743.
14. Vestbo J, Hurd SS, Agusti AG, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. American journal of respiratory and critical care medicine. 2013;187(4):347-365.
15. Janssen DJ, Wouters EF, Parra YL, Stakenborg K, Franssen FM. Prevalence of thoracic pain in patients with chronic obstructive pulmonary disease and relationship with patient characteristics: a cross-sectional observational study. BMC pulmonary medicine. 2016;16:47.

16. Lohne V, Heer HC, Andersen M, Miaskowski C, Kongerud J, Rustoen T. Qualitative study of pain of patients with chronic obstructive pulmonary disease. Heart & lung : the journal of critical care. 2010;39(3):226-234.
17. Clark N, Fan VS, Slatore CG, et al. Dyspnea and pain frequently co-occur among Medicare managed care recipients. Annals of the American Thoracic Society. 2014;11(6):890-897.
18. Lee AL, Harrison SL, Goldstein RS, Brooks D. Pain and its clinical associations in individuals with COPD: a systematic review. Chest. 2015;147(5):1246-1258.
19. Keating A, Lee A, Holland AE. What prevents people with chronic obstructive pulmonary disease from attending pulmonary rehabilitation? A systematic review. Chronic respiratory disease. 2011;8(2):89-99.
20. Cleutjens F, Spruit MA, Ponds R, et al. The Impact of Cognitive Impairment on Efficacy of Pulmonary Rehabilitation in Patients With COPD. Journal of the American Medical Directors Association. 2017;18(5):420-426.
21. Troosters T, Hornikx M, Demeyer H, Camillo CA, Janssens W. Pulmonary rehabilitation: timing, location, and duration. Clinics in chest medicine. 2014;35(2):303-311.
22. Ries AL, Bauldoff GS, Carlin BW, et al. Pulmonary Rehabilitation: Joint ACCP/AACVPR Evidence-Based Clinical Practice Guidelines. Chest. 2007;131(5 Suppl):4s-42s.
23. Levack WM, Weatherall M, Hay-Smith EJ, Dean SG, McPherson K, Siegert RJ. Goal setting and strategies to enhance goal pursuit for adults with acquired disability participating in rehabilitation. The Cochrane database of systematic reviews. 2015(7):Cd009727.
24. Waal DMd. Preliminary results of pilot studies on the feasibility of the COPM in geriatric rehabilitation. In. LUMC, Leiden, The Netherlands2018.
25. Janssen DJA. Palliative care needs of patients with advanced organ failure. Maastricht: Centre of expertise for chronic organ failure (CIRO) and the School for Public Health and Primary Care (CAPHRI), Maastricht University 2012.
26. Houben CH, Spruit MA, Wouters EF, Janssen DJ. A randomised controlled trial on the efficacy of advance care planning on the quality of end-of-life care and communication in patients with COPD: the research protocol. BMJ open. 2014;4(1):e004465.
27. Bouwstra H, Wattel LM, de Groot AJ, Smalbrugge M, Hertogh CM. The Influence of Activity-Based Funding on Treatment Intensity and Length of Stay of Geriatric Rehabilitation Patients. Journal of the American Medical Directors Association. 2017;18(6):549.e515-549.e522.
28. Holstege MS, Caljouw MAA, Zekveld IG, et al. Successful Geriatric Rehabilitation: Effects on Patients' Outcome of a National Program to Improve Quality of Care, the SINGER Study. Journal of the American Medical Directors Association. 2017;18(5):383-387.
29. Porter ME. What is value in health care? The New England journal of medicine. 2010;363(26):2477-2481.
30. Smit EB, Bouwstra H, van der Wouden JC, Wattel LM, Hertogh C. Patient-centred goal setting using functional outcome measures in geriatric rehabilitation: is it feasible? European geriatric medicine. 2018;9(1):71-76.
31. Talboom-Kamp EP, Verdijk NA, Harmans LM, Numans ME, Chavannes NH. An eHealth Platform to Manage Chronic Disease in Primary Care: An Innovative Approach. Interactive journal of medical research. 2016;5(1):e5.
32. Talboom-Kamp EP. eHealth in primary care. Leiden: Department of public Health and Primary Care, Leiden University Medical Centre; 2017.