Evaluation of a Telehealthcare Intervention for Patients with COPD

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BY
PERNILLE HEYCKENDORFF LILHOLT

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AALBORG UNIVERSITY
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CV

Pernille Heyckendorff Lilholt completed her Bachelor´s degree in Nursing (BN) at the University College of Northern Denmark in 2010. Subsequently, she received her Master of Science (MSc) degree in Clinical Science and Technology in 2012 from Aalborg University. Her Master's thesis was developed within the Teledi@log research and innovation project, in which she collaborated with various clinicians, companies, and associations to develop a telerehabilitation technology for cardiac patients. In her Master´s thesis, she focused on stratifying patients with different heart diseases to the telerehabilitation technology by creating a stratification tool that could be used by clinicians for decision support.

Along with her studies, Pernille Heyckendorff Lilholt has worked as a temp nurse at various somatic and psychiatric wards. In 2013, Pernille Heyckendorff Lilholt enrolled in the Doctoral School at the Faculty of Medicine, Aalborg University, under the supervision of Ole K. Hejlesen and Lars H. Ehlers.

ABBREVIATIONS AND DEFINITIONS

This PhD thesis should be of interest to academia but also to the industry, e.g., telehealthcare developers, decision makers in telehealth implementation, health care providers, policy makers, and others who have an interest in this matter. The Vancouver reference system will be used in this thesis.

ABBREVIATIONS

CAT	COPD Assessment Score
COPD	Chronic Obstructive Pulmonary Disease
FEV_1	Forced Expiratory Volume
FEV_1/FVC	Tiffeneau-Pinelli Index
FVC	Forced Vital Capacity
GOLD	The Global Initiative for Chronic Obstructive Lung Disease
GP	General Practitioner
GSM	Global System for Mobile Communications
HRQoL	Health-related Quality of Life
ICER	Incremental Cost-effectiveness Ratio
ISO	International Organization for Standardization
MCS	Mental Component Score
MRC	Medical Research Council Dyspnea Scale
PCS	Physical Component Score
QALY	Quality-adjusted Life Years
QoL	Quality of Life
RCT	Randomized Controlled Trial
SF-36	The Short-Form (36) Health Survey
SF-36v2	The Short-Form (36) Health Survey, Version 2
WHO	World Health Organization
WSD	Whole System Demonstrator Project

DEFINITIONS

District nurses	The term refers to the nurses working in the primary care. In the TeleCare North trial, these nurses monitored the patients' data and provided the patients with telephone advice
Effectiveness	The term refers to whether a given intervention obtains the intended outcomes and encompasses issues such as: "*Does the intervention work?" and "Who will benefit from its use?"* (1)

Health Literacy	Health literacy can be defined as: *"the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand, and use information in ways which promote and maintain good health"* (2)
Health-related Quality of Life	The term encompasses the core components: *physical, functional, social, and emotional well-being of an individual* (3)
Patient	The term relates throughout this thesis to people enrolled in the TeleCare North trial. These people are all residing in the North Denmark Region and diagnosed with COPD
Patient Empowerment	Patient empowerment is in total defined as: "*the acquisition of motivation (self-awareness and attitude through engagement) and ability (skills and knowledge through enablement) that patients might use to be involved or participate in decision-making, thus creating an opportunity for higher levels of power in their relationship with professionals"* (4)
Telehealthcare	Telehealthcare is defined as: "*the provision of personalized health care from a distance"* (5)
Telekit	The term refers to the telehealthcare system used in the TeleCare North trial. The Telekit system guides the patients in managing their disease during exacerbations
Usability	The term is by ISO defined as: "*Extent to which a system, product or service can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use*" (6)
User experiences	The conceptualization of user experiences is as follows: *"a person's perceptions and responses that result from the use and/or anticipated use of a product, system or service"* (7)

ENGLISH SUMMARY

[Introduction] The healthcare system is currently facing challenges in the treatment of chronic obstructive pulmonary disease (COPD), which has created the need for alternative ways to treat these patients. Telehealthcare could be this alternative. A range of studies have been conducted to evaluate the effectiveness of telehealthcare, but they generally conclude that there is a need for more large-scale studies to obtain sufficient evidence.

[Objectives] Taking this into consideration, the main aim of this PhD study was to evaluate a telehealthcare intervention for patients suffering from COPD. This thesis had a more specific focus on the following: I) developing a study protocol for the Danish, large-scale trial, TeleCare North; II) evaluating the trial's telehealthcare system (coined Telekit) in terms of its usability and patient experiences; and III) evaluating the trial's primary outcome, health-related quality of life (HRQoL). These focus areas have been addressed in seven papers.

[Paper I] A study protocol was developed in which the TeleCare North trial's research design and intervention were described. In total, 1,225 COPD patients were included in the cluster randomized, controlled trial to either telehealthcare with usual practice or only usual practice, depending on the municipality in which the patients resided. Telehealthcare consisted of an online data exchange between the patient and the healthcare provider. Usual practice involved the existing health care services without telehealthcare. The primary outcome was changes in HRQoL at the individual level from baseline to 12-month follow-up and the incremental cost-effectiveness ratio (ICER) measured as the cost per quality-adjusted life year (QALY) gained from baseline to 12-month follow-up. The secondary outcomes were changes in mortality and physiological parameters from baseline to 12-month follow-up.

[Paper II-VI] Telekit's usability and the COPD patients' satisfaction and user experiences were evaluated through a series of usability studies. Satisfaction and user experiences were assessed using a non-validated questionnaire that was developed for the purpose. Various usability evaluation methods were performed on Telekit to explore the system's user-friendliness. The findings of the usability studies indicated that the system needed improvement but overall was user-friendly and matched the patients' needs. The findings of the usability studies served as input for design improvements and led to significant changes to the Telekit system.

[Paper VII] Changes in the primary outcome, HRQoL, of the TeleCare North trial's intervention were evaluated. The Short-Form (36) Health Survey was distributed to the COPD patients at baseline and after 12 months. Analyses of HRQoL were performed using linear mixed models. The findings showed that the changes in

HRQoL between groups and subgroups were not statistically significantly different from baseline to 12 months. However, the subgroup analysis indicated a trend towards a positive effect on HRQoL among certain subgroups of the intervention group compared to usual practice.

[Conclusion] This PhD thesis demonstrated that the telehealthcare system was user-friendly and that the patients experienced freedom, security, control, and greater awareness of COPD symptoms. Poorer HRQoL was not found when the whole intervention group was compared to usual practice. Identifiable positive effects may exist among subgroups of the intervention group. Further research should be conducted to assess the effectiveness of the intervention e.g., by evaluating other clinical outcomes and by dividing the patients in subgroups.

DANSK RESUMÉ

[Introduktion] Sundhedsvæsenet står i øjeblikket over for udfordringer i behandlingen af kronisk obstruktiv lungesygdom (KOL), hvilket skaber behovet for alternative måder at behandle disse patienter på. Telehealthcare kunne være dette alternativ. En række studier er blevet udført for at evaluere effekten af telehealthcare, men de konkluderer generelt, at der er behov for flere studier i stor skala for at opnå tilstrækkelig evidens.

[Formål] Taget dette i betragtning, var hovedformålet med dette ph.d.-studie at evaluere en telehealthcare intervention for patienter, der lider af KOL. Denne afhandling havde mere specifikt fokus på: I) at udvikle en studieprotokol for det danske stor-skala studie, TeleCare Nord; II) at evaluere studiets telehealthcare-system (kaldet Telekit) i form af dets brugervenlighed og patientoplevelser; og III) at evaluere studiets primære resultat, helbredsrelateret livskvalitet. Disse fokusområder er blevet behandlet i syv artikler.

[Artikel I] En studieprotokol blev udviklet hvori TeleCare Nords forskningsdesign og intervention blev beskrevet. I alt blev 1.225 KOL-patienter inkluderet i det klynge-randomiserede, kontrollerede studie til enten telehealthcare i tillæg til sædvanlig praksis, eller kun til sædvanlig praksis afhængig af, hvilken kommune patienterne hørte til. Telehealthcare bestod af online dataudveksling mellem patienten og den sundhedsprofessionelle. Sædvanlig praksis involverede det eksisterende sundhedsvæsen uden telehealthcare. Det primære resultat var ændringer i helbredsrelateret livskvalitet på det individuelle niveau fra baseline til 12 måneders opfølgning og den inkrementelle omkostningseffektivitet målt som pris pr. kvalitetsjusterede leveår fra baseline til 12 måneders opfølgning. De sekundære resultater var ændringer i dødelighed og fysiologiske parametre fra baseline til 12 måneders opfølgning.

[Artikel II-VI] Telekits brugervenlighed og KOL-patienternes tilfredshed og brugeroplevelser blev evalueret gennem en række usability-studier. Tilfredshed og brugeroplevelser blev vurderet ved hjælp af et ikke-valideret spørgeskema, som blev udviklet til formålet. Forskellige usability-evalueringsmetoder blev udført på telehealthcare-systemet for at undersøge systemets brugervenlighed. Resultaterne af usability-studierne indikerede, at systemet skulle forbedres men generelt var brugervenligt og matchede patienternes behov. Resultaterne af studierne fungerede som input til designforbedringer og førte til væsentlige ændringer i Telekit-systemet.

[Artikel VII] Ændringer i det primære resultat, helbredsrelateret livskvalitet, af TeleCare Nords intervention blev evalueret. Short-Form (36) Health Survey blev udleveret til patienterne ved baseline og efter 12 måneder. Analyser af helbredsrelateret livskvalitet blev udført ved anvendelse af lineære mixed modeller. Resultaterne viste, at ændringerne i helbredsrelateret livskvalitet mellem grupper og

subgrupper ikke var statistisk signifikante fra baseline til 12 måneder. Dog indikerede subgruppeanalysen en tendens til en positiv effekt på helbredsrelateret livskvalitet blandt visse subgrupper af interventionsgruppen sammenlignet med sædvanlig praksis.

[Konklusion] Denne afhandling demonstrerede, at telehealthcare-systemet var brugervenligt, og at patienterne oplevede øget kontrol, frihed, tryghed, og større opmærksomhed på KOL-symptomer. Dårligere livskvalitet blev ikke fundet, når hele interventionsgruppen blev sammenlignet med sædvanlig praksis. Identificerbare positive effekter kan eksisterer blandt subgrupper af interventionsgruppen. Der bør udføres yderligere forskning for at kunne vurdere effekterne af interventionen, fx ved at evaluere andre kliniske resultater og ved at inddele patienterne i subgrupper.

PUBLICATION LIST

THESIS PUBLICATIONS

This thesis consists of the following seven papers, which in the thesis will be referred to by their Roman numerals, I-VII:

Paper I
Udsen, Flemming Witt; Lilholt, Pernille Heyckendorff; Hejlesen, Ole; Ehlers, Lars Holger (2014).
Effectiveness and cost-effectiveness of telehealthcare for chronic obstructive pulmonary disease: study protocol for at cluster randomized controlled trial
Published in Trials, 2014
DOI: 10.1186/1745-6215-15-178

Paper II
Lilholt, Pernille Heyckendorff; Jensen, Morten Hasselstrøm; Hejlesen, Ole (2015).
Heuristic Evaluation of a telehealth system from the Danish TeleCare North trial
Published in International Journal of Medical Informatics, 2015
DOI: 10.1016/j.ijmedinf.2015.01.012

Paper III
Lilholt, Pernille Heyckendorff; Heiden, Sisse; Hejlesen, Ole (2014).
User satisfaction and experience with a telehealth system for the Danish TeleCare North trial: a think-aloud study
Proceedings of MIE2014, 31 August-3 September 2014, Istanbul, Turkey. IOS Press, 2014. s. 900-904 (Studies in Health Technology and Informatics; Vol. 205)
DOI: 10.3233/978-1-61499-432-9-900

Paper IV
Lilholt, Pernille Heyckendorff; Schaarup, Clara; Hejlesen, Ole (2016).
An iterative, mixed usability approach applied to the Telekit system from the Danish TeleCare North trial
Submitted to International Journal of Telemedicine and Applications, 2016

Paper V
Lilholt, Pernille Heyckendorff; Hæsum, Lisa Korsbakke Emtekær; Hejlesen, Ole (2015).
Exploring user experience of a telehealth system from the Danish TeleCare North trial
Proceedings of MIE2015, 27-29 May 2015, Madrid, Spain. IOS Press, 2015. s. 301-305 (Studies in Health Technology and Informatics; Vol. 210)
DOI: 10.3233/978-1-61499-512-8-301

Paper VI
Lilholt, Pernille Heyckendorff; Hæsum, Lisa Korsbakke Emtekær; Ehlers, Lars Holger; Hejlesen, Ole (2016).
Specific technological communication skills and functional health literacy have no influence on self-reported benefits from enrollment in the TeleCare North trial
Published in International Journal of Medical Informatics, 2016
DOI: 10.1016/j.ijmedinf.2016.04.010

Paper VII
Lilholt, Pernille Heyckendorff; Udsen, Flemming Witt; Ehlers, Lars Holger; Hejlesen, Ole (2016).
Telehealthcare for patients suffering from COPD: Effects on health-related quality of life – results from the Danish "TeleCare North" cluster-randomised trial
Submitted to the British Medical Journal Open, 2016

RELATED PUBLICATIONS

Journal papers
Udsen, Flemming Witt; Lilholt, Pernille Heyckendorff; Hejlesen, Ole; Ehlers, Lars Holger (2016).
Cost-effectiveness of telehealthcare to patients suffering from chronic obstructive pulmonary disease: Results from the Danish "TeleCare North" cluster-randomized trial
Submitted to British Medical Journal Open, 2016

Stausholm, Mads Nibe; Egmose, Andreas; Dahl, Simon Christian; Cichosz, Simon L; Lilholt, Pernille Heyckendorff; Hejlesen, Ole K (2016).
Stratification of telehealthcare for patients with chronic obstructive pulmonary disease using a predictive algorithm as decision support: a pilot study
Published in Journal of Telemedicine and Telecare, 2016
DOI: 10.1177/1357633X16644129

Conference papers

Bonderup, Morten Algy; Hangaard, Stine Veje; Lilholt, Pernille Heyckendorff; Johansen, Mette Dencker; Hejlesen, Ole (2011).
A pilot assessment of why patients choose not to participate in self-monitoring oral anticoagulant therapy. Proceedings of MIE2011, 28-31 August 2011, Oslo, Norway. IOS Press, 2011. s 43-47 (Studies in Health Technology and Informatics; Vol.169).
DOI: 10.3233/978-1-60750-806-9-43.

Hangaard, Stine Veje; Bonderup, Morten Algy; Lilholt, Pernille Heyckendorff; Johansen, Mette Dencker; Hejlesen, Ole (2014).
Instructional video reduces errors in home blood pressure management
Proceedings of MIE2014, 31 August-3 September 2014, Istanbul, Turkey. IOS Press, 2014. s. 1188 (Studies in Health Technology and Informatics; Vol. 205).
DOI: 10.3233/978-1-61499-432-9-1188

Bonderup, Morten Algy; Hangaard, Stine Veje; Lilholt, Pernille Heyckendorff; Johansen, Mette Dencker; Hejlesen, Ole (2012).
Patient support ICT tool for hypertension monitoring
Proceedings of MIE2012, 26-29 August 2012, Pisa, Italy. IOS Press, 2012. s. 189-193 (Studies in Health Technology and Informatics; Vol. 180).
DOI: 10.3233/978-1-61499-101-4-189

Conference abstracts

Lilholt, Pernille Heyckendorff; Jensen, Morten Hasselstrøm; Hejlesen, Ole (2013).
A heuristic evaluation of a telehealth solution from the Danish TeleCare North large scale randomized trial
Proceedings of SHI2013, 20 August 2013, Copenhagen, Denmark. Linköping University Electronic Press, 2013. s. 93 (Linköping Electronic Conference Proceedings; Vol. 91).
http://www.ep.liu.se/ecp_article/index.en.aspx?issue=091;article=022

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On this day, I am writing notes of thanks as the finishing touch on my thesis. My PhD study has been a journey of challenges and learning experiences, both at a scientific level and a personal level. Through these acknowledgments, I express my gratitude to all the people who have been associated with this thesis and have supported me throughout this period.

First, I would like to thank Aalborg University (The Department of Health Science and Technology) and the North Denmark Region (The TeleCare North trial) for ensuring the financial framework for this PhD study. I extend my thanks to the staff of the TeleCare North trial for their cooperation and their sharing of essential knowledge about the trial. Without their active involvement, it would not have been possible to gain access to the research data and participants. Therefore, special thanks to all the COPD patients, who were, in one way or another, included in the PhD study's data archive. Without them, this research would not exist.

Many thanks to my supervisors, Professor Ole K. Hejlesen and Professor Lars H. Ehlers. Their sound ideas and guidance helped me at all times of the research and writing of this thesis. I would like to express my sincere gratitude to my main supervisor, Ole K. Hejlesen, for his immense knowledge, positive mind, continuous support, and caring. Ole K. Hejlesen allowed me to work in my way and made me believe more in myself, and when everything did not go as planned, he asked me to think about the phrase "never mind." I am also very grateful for the cooperation of the co-authors of my papers: *Flemming Witt Udsen, Lisa Korsbakke Emtekær Hæsum, Sisse Heiden, Clara Schaarup, and Morten Hasselstrøm Jensen for their willingness to help and for reading the drafts. Furthermore, I owe thanks to Mads Nibe Stausholm and Lasse Mark for their technical assistance in data extraction.*

In my daily work, I have been surrounded by friendly and helpful colleagues from the Medical Informatics Research Group. A special thanks to my office colleagues for all the fun we had in the last three and a half years. However, two individuals deserve special recognition. My sincere appreciation goes to my colleagues and friends, Lasse Lefevre Samson and Isabel Pino Peña. I thank them for the stimulating discussions and for making this time enjoyable.

Last but definitely not least, I would like to thank my friends and family for the support they have provided me throughout my entire life. In particular, my lovely boyfriend, Anders Secher has always cheered me up and been behind me at all times. Without his patience, love, and encouragement, it would not have been possible for me to complete this PhD study.

PREFACE

This PhD thesis is submitted to Aalborg University in fulfillment of the requirement for the degree of Doctor of Philosophy. The thesis presents the results of the scientific work that I have carried out in the period from 2013-2016 at the Department of Health Science and Technology, Aalborg University, Denmark. The PhD thesis is based on original work, except where references are represented. The PhD study was supervised by Professor Ole K. Hejlesen and co-supervised by Professor Lars H. Ehlers.

My motivation for this work comes from my general interest in the healthcare field and my experiences of working as a nurse. I started working within the telehealthcare area during my Master´s program and found a particular interest in helping to optimize the yield of various technological advances by identifying and documenting the need for new technologies. When I started my PhD, I was very enthusiastic about making a mark on telehealthcare to optimize the healthcare services and provide better treatment for patients.

During the period of my PhD, I had the opportunity to meet other fellow researchers and to present my research at Conferences in Madrid (Spain), Copenhagen (Denmark), Aalborg (Denmark), and Istanbul (Turkey). I also enjoyed supervising students in their projects in Medicine, Industrial Medicine, Biomedical Engineering, and Clinical Science and Technology.

This PhD study is based on a large-scale, Danish trial, named TeleCare North, which was launched in the North Denmark Region in January 2012. The trial aimed to develop and implement a telehealthcare system, Telekit, for patients suffering from COPD. The TeleCare North trial was funded by the North Denmark Region; the municipalities in the North Denmark Region; the Obel Family Foundation; the Danish Agency for Digitalization Policy and Strategy; and the European Social Fund. Four PhD activities were affiliated with the trial: a health economics PhD scholarship (Flemming Witt Udsen); a health literacy-based PhD scholarship (Lisa Korsbakke Emtekær Hæsum); an organizational theory PhD scholarship (Jannie Kirstine Bang Christensen); and a health- and patient-related PhD scholarship (Pernille Heyckendorff Lilholt).

All data for this PhD study are obtained from the TeleCare North trial. I began by gathering information about the conception of the TeleCare North trial and by determining the choice of appropriate methods and tools to evaluate the trial's intervention. Inclusion and exclusion criteria for patient selection were established in cooperation with the trial's Administration Office and other health professionals. Baseline data were measured by clinicians, and PhD students (including myself) were responsible for the data collection and data processing in the trial's assessment

period. During my PhD study, I evaluated the trial's telehealthcare system through an iterative process and provided feedback regarding Telekit's usability to the system developers. The trial's protocol and statistical analysis have been carried out through collaboration with Flemming Witt Udsen, who has a strong background in statistics.

The content of the thesis consists of seven papers that were written during my PhD studies. In addition to these papers, this thesis is divided into seven chapters with the following contents:

Chapters 1-2: Introduction and background to the research topic

Chapter 3: Overview of the structure of the PhD thesis supplemented with research aims and questions

Chapter 4: Summary of each paper's aim, methods, results, and discussion/conclusion

Chapter 5: The seven papers in full text

Chapter 6: General interpretation and discussion of the main findings of the PhD thesis in which the strengths and weaknesses are considered together with suggestions for future research

Chapter 7: Conclusion that summarizes the main results of the PhD thesis

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CHAPTER 1. INTRODUCTION

1.1. RATIONALE FOR THIS PHD STUDY

The healthcare system is under pressure due to demographic changes that indicate that the population is getting older and living longer (8,9). As a consequence, the number of chronic diseases in the population is increasing, which results in a growing need for more health services and thus rising healthcare costs and increased workload for the healthcare system (10).

To address some of these challenges, other alternatives have been considered to undertake the treatment and care of chronic patients (11). Policy makers and healthcare stakeholders have high expectations for telehealthcare as a central component of establishing a capable and more efficient health care system that can meet some of the challenges the health care system will have to face in the future. Telehealthcare can be a significant component of how care will be managed in the future, but it has yet to be widely accepted as a sustainable choice due to the lack of evidence regarding its effectiveness and cost-effectiveness (12). Reviews (13,14) have noted that the benefits of telehealthcare are not yet proven, and limited evidence is available concerning its use-value, which calls for larger scale studies.

The lack of large-scale Danish studies on telehealthcare has for many years been a barrier to the implementation of telehealth in Denmark. In 2012, the Government, Danish Regions, and Local Government Denmark created an ambitious National Action Plan for the Dissemination of Telemedicine (15,16). The Action Plan (15,16) should support and spread initiatives that could provide valuable experiences regarding the use of telehealth in chronic diseases. One of these initiatives included the establishment of a large-scale trial, TeleCare North in the northern part of Denmark. TeleCare North was implemented in the North Denmark Region between 2012 and 2015 to improve the body of evidence and to serve as a national standard for implementing telehealthcare in Denmark. TeleCare North intended to provide evidence of the effectiveness and cost-effectiveness of telehealthcare in patients suffering from COPD [Paper I].

This PhD study was compiled in association with the TeleCare North trial. The research presented in this thesis contains a description of the TeleCare North trial's intervention and an evaluation of its outcomes regarding health-related quality of life (HRQoL), usability and patients' experiences. This PhD thesis includes: I) a description of the TeleCare North trial's research design and intervention; II) a usability evaluation of the telehealthcare system adopted in the TeleCare North trial; and III) an outcome evaluation of the TeleCare North intervention assessing the changes in HRQoL.

CHAPTER 2. BACKGROUND

In this chapter, relevant background information will be presented about COPD and telehealthcare. This information is followed by a description of the current evidence on telehealthcare, how telehealthcare interventions can be evaluated regarding effectiveness and usability, and the TeleCare North trial. The chapter ends with a summary of the background that will lead to the scope of this PhD study.

2.1. CHRONIC OBSTRUCTIVE PULMONARY DISEASE

2.1.1. EPIDEMIOLOGY

COPD is a very common, progressive condition – both worldwide and in Denmark. The prevalence of COPD is estimated to be 11.7% worldwide (17) and 7% in Denmark (18). Approximately 436,000 Danes have COPD, of whom 166,000 have mild COPD, 230,000 have moderate COPD, and 40,000 have severe COPD (18). The high prevalence and the nature of the disease lead to, in Denmark (annual means from 2010-2012), 17,000 admissions, 3,400 emergency department visits, 65,000 out-patient visits, and 490,000 extra visits at the general practitioner (GP) (19). COPD is costly for the Danish healthcare system and costs up to 3 billion Danish crowns annually in hospital expenditures (exclusively medical expenses), equivalent to 10% of the total expenditure for individuals over 40 years. Furthermore, the expenditure for COPD is larger than those of other chronic diseases (20).

The disease is one of the leading causes of morbidity and mortality because many people suffer from COPD for years and die prematurely from the illness or its complications (21). More than 3 million people died of COPD worldwide in 2005 (22), and COPD is annually the cause of 3,500 deaths in Denmark (23). At present, the disease is the fourth leading course of deaths worldwide and is predicted to be the third leading cause of death in 2030 (24).

2.1.2. CHARACTERISTICS OF COPD

COPD is an umbrella term that describes progressive lung diseases including chronic bronchitis and emphysema. COPD is characterized by a persistent airflow limitation that is usually progressive and associated with an increased chronic inflammatory response in the airways and the lungs to noxious particles or gasses (21). COPD is a progressive disease in which the symptoms are slowly expressed without the patient necessarily noticing them in everyday life. The patients become accustomed to the symptoms leading to the illness often being diagnosed at an advanced stage (25). The common symptoms of COPD include chronic progressive dyspnea, cough, and sputum production. Many patients with COPD experience

variations in their symptoms throughout the day. Others experience discomfort most of the time (26).

2.1.3. ETIOLOGY

Smoking tobacco (including second-hand or passive exposure) is the primary cause of COPD in high- and middle-income countries. Risk factors also include indoor air pollution such as biomass fuels for cooking and heating and long-term exposures to dust, toxic gases, and chemicals. These risk factors often occur in low-income countries as a result of poorly ventilated homes and poor working conditions (27). Some genetic factors can also increase the vulnerability of the lungs to developing COPD. The most important is a hereditary condition in which there is insufficient production of the protein alpha-1-antitrypsin. Alpha-1-antitrypsin provides a natural defense mechanism against the persistent lung inflammation that can lead to emphysema and COPD. People who suffer from this condition can develop severe COPD within 40 years of age if they smoke (28). Another risk factor involves frequent lung infections in early childhood, which can lead to impaired development of the lungs and predispose individuals to an increased risk of COPD as an adult. There are a number of other factors in addition to lung infections in childhood such as low birth weight that predispose individuals to COPD in adulthood, and low social status is also associated with an increased risk of COPD (27).

2.1.4. PATHOLOGY AND PATHOPHYSIOLOGY

In COPD, changes in the lung tissue are identified in the large and small airways that jointly cause a variety of signs and symptoms that characterize the disease. COPD patients have different degrees of pathological changes in the airways (chronic bronchitis) and the alveoli (emphysema). The considerable variation in these changes among the various patients partly explains the different clinical manifestations of COPD (29).

In COPD, there is constriction of the airway lumen and obstruction not only due to the airway inflammation and an accumulation of secretion but also because of the destruction of the small terminal airways. The inflammation of the respiratory tract extends from the epithelium through the entire wall, with more goblet cells in the epithelium, more mucus-producing glands, hypertrophy of the smooth muscle cells, infiltration of the mucosa with inflammatory cells and fibrosis (30).

Destruction of the alveoli leads to the loss of lung tissue connections to the respiratory tract and contributes to the collapse of the bronchioles due to the lack of sufficient elasticity to keep the airways open – this observed particularly during expiration (31). Parallel to the chronic airway inflammation is the identified atrophy of the pulmonary vessels and capillaries. These changes can lead to pulmonary hypertension and cor pulmonale in severe cases. The process of inflammation may

be complicated by bronchiectasis, trachea-bronchomalacia and fibrotic changes in the airways and the lung parenchyma (32). The pathological changes result in reduced FEV1 (forced expiratory volume) over time and the following physiologic abnormalities and symptoms: airway limitations and air trapping, gas exchange abnormalities, mucus hypersecretion, pulmonary hypertension, exacerbations, and systemic features (21). This PhD thesis does not focus on the COPD pathology and pathophysiology, which is why they are not further described.

Exacerbations

Patients with COPD in the advantaged stage of the disease experience exacerbations that are an acute worsening of usual symptoms and often require hospitalization and changes in the patient's standard treatment (21). The symptoms that are often present during exacerbations include increased dyspnea, productive cough, fever, and increased sputum with changes in color (33). The causes of these exacerbations are mostly viral or bacterial infections, which are especially frequent in COPD patients because of the reduced capacity of their lungs to remove mucus. However, other causes such as environmental pollutants, psychological influences or unknown factors can also lead to exacerbations (34,35).

Exacerbations are strongly linked to worse health, more depressive symptoms and accelerations in the decline of lung function. Furthermore, exacerbations are strongly associated with mortality and morbidity. Early treatment of exacerbations is important for the possible outcome of the patient. Approximately 50% of all exacerbations have been estimated to be reported to the healthcare system. This under-estimation could be due to the patients' differing perceptions of the implications of an exacerbation (25).

Comorbidities

Among patients with COPD, there is an increased incidence of other diseases, i.e., comorbidities, which can affect their prognosis, quality of life (QoL), exacerbations, and treatment (36). The most important comorbidities include cardiovascular diseases, musculoskeletal disorders, osteoporosis, lung cancer, and mental illnesses such as depression and anxiety (37). The comorbid conditions increase the occurrence of exacerbations, the risk of hospital stays for COPD, and have a strong influence on mortality. Thus, comorbidities increase the difficulty of managing COPD and should therefore be treated routinely and appropriately (38,39).

2.1.5. DIAGNOSIS OF COPD

The COPD diagnosis is established based on smoking and medical history, symptoms, risk factors, and spirometry results. The lung function test, spirometry, is the cornerstone of the diagnosis, monitoring, and staging of COPD, as well as of the exclusion of the main differential diagnosis, asthma. The spirometry test measures

values of forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), and the FEV1/FVC ratio of these measures.

COPD is defined by an impaired lung function of the obstructive type, i.e., forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) < 70%, which is not entirely reversible (21). The FEV1/FVC ratio is between 0.70 and 0.80 in healthy adults (40). The FEV1 value in terms of the % of the predicted FEV1 value is determined based on age, sex, height, and race and is used to classify the severity (mild, moderate, severe, and very severe) of COPD. The staging is used to determine the treatment strategy (21).

In addition to spirometry, other various clinical examinations are used to assess the diagnosis of COPD. These examinations will not be further described but include, for example, chest x-ray, sputum culture, arterial puncture for blood gas analysis, CT scan of the thorax, and pulse oximetry (41).

2.1.6. COPD ASSESSMENT TOOLS

In addition to the spirometric diagnosis and the other clinical examinations, it is important to consider patient-reported symptoms to obtain an adequate overview of the COPD patient's condition. The assessment of COPD is based on the patients' symptoms, the risk of exacerbations, the degree of airflow limitation (spirometry), and the identification of comorbidities (42).

Medical Research Council Dyspnea Modified Scale

Patients' symptoms can be measured using the Medical Research Council modified scale (mMRC), which is a validated tool that has been translated into Danish. The scale is of use in clinical practice, and the scores accurately express the patient's prognosis and the necessity of medication and rehabilitation. The mMRC scale is based on the patients' description of their degree of shortness of breath (21,43,44). Table 1 shows the mMRC scale, which comprises five statements of the extent of breathlessness related to activity.

Table 1: The mMRC scale includes five statements that quantify the disability associated with breathlessness (21).

The mMRC Breathlessness Scale	
mMRC 0	I only get breathless with strenuous exercise
mMRC 1	I get short of breath when hurrying on the level or walking up a slight hill
mMRC 2	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level
mMRC 3	I stop for breath after walking about 100 meters or after a few minutes on the level
mMRC 4	I am too breathless to leave the house, or I am breathless when dressing and undressing

The COPD Assessment Test

The COPD Assessment Test (CAT) is an 8-item questionnaire that measures the level of health status impairment in COPD. The questionnaire is suitable for all patients with COPD and should be used in the clinical assessment of patient's COPD to achieve the optimal management of the disease. The CAT score ranges from 0-40, with higher scores denoting a more severe impact of COPD on a patient's life (45).

The Global Initiative for COPD

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) is a collaboration between the National Heart, Lung, and Blood Institute, National Institutes of Health, USA, and the World Health Organization. GOLD has produced some guidelines to support healthcare providers and clinicians in the treatment, stratification, and assessment of COPD (21). Table 2 illustrates GOLD's Spirometric Assessment Classification that stratifies patients according to their degree of airflow limitation. This spirometric classification (I-IV) was used in Paper VII to categorize the patients from the TeleCare North trial based on their disease severity.

Table 2: GOLD's Spirometric Assessment Classification, which classifies people with COPD based on their degree of obstruction (21).

Stages of COPD	Fixed ratio	Severity of airflow limitation
Mild (I)	FEV1/FVC < 70%	FEV1 ≥ 80% predicted
Moderate (II)	FEV1/FVC < 70%	50% ≤ FEV1 < 80% predicted
Severe (III)	FEV1/FVC < 70%	30% ≤ FEV1 < 50% predicted
Very Severe (IV)	FEV1/FVC < 70%	FEV1 < 30% predicted

GOLD has since updated its guidelines and suggested other COPD staging criteria because the spirometric classification (I-IV) only considers the patients' degree of airflow limitation and does not account for other symptoms and factors. FEV1 is a poor predictor of disease status alone, which has led to GOLD's development of combined risk assessment scores that include the patients' symptoms, breathlessness, spirometric assessments, and/or risk of exacerbations (21). Table 2 shows GOLD's Combined COPD Assessment Classification, which categorizes patients into four groups (A-D) according to disease severity.

Table 3: GOLD's Combined COPD Assessment Classification, which categorizes patients based on symptoms, exacerbation history, and airflow obstruction (21).

Stages of COPD	Combined assessment of COPD
Low risk, low symptom burden (A)	Low symptom burden (mMRC 0-1 OR CAT > 10) AND FEV1% ≥ 50 AND Low exacerbation rate (0-1/year)
Low risk, higher symptom burden (B)	Higher symptom burden (mMRC ≥ 2 OR CAT ≥ 10) AND FEV1% ≥ 50 AND Low exacerbation rate (0-1/year)

High risk, low symptom burden (C)	Low symptom burden (mMRC 0-1 OR CAT < 10) AND FEV1% < 50 AND/OR high exacerbation rate (≥ 2/year)
High risk, higher symptom burden (D)	Higher symptom burden (mMRC ≥ 2 OR CAT ≥ 10 AND FEV1% < 50 AND/OR high exacerbation rate (≥ 2/year)

Vital signs

Measuring vital signs such as blood pressure, heart rate, oxygen saturation, and weight is also important in assessing disease progression in COPD. These vital signs can be measured at home, in clinical settings or elsewhere by different devices such as pulse oximeters and blood pressure monitors. If the vital signs differ from the usual, this may indicate progression of COPD (46,47).

Relevant markers and tools other than those mentioned in this thesis are available for the assessment of COPD (48). The above assessment tools were used to measure a set of inclusion criteria for the TeleCare North trial. This trial will be presented later in this chapter of the thesis.

2.1.7. TREATMENT OF COPD IN DENMARK

In Denmark, the entity responsible for the detection, diagnosis, treatment, and follow-up of COPD patients is to a large extent general practice, particularly in patients with mild to moderate COPD. Usually, patients' GPs follow them throughout the course of the disease and act as the patients' coordinators. Patients have to be referred by their GP to consult a pulmonologist at the hospital, but all have equal access to health care services, including being examined and treated by a GP or at a public hospital. People can use health services regardless of their financial situation or insurance conditions because the healthcare system is almost 100% publicly financed through taxes (49). In many other countries, health benefits are not tax-financed and are payable by individuals when using a service. In the TeleCare North trial, the patients allocated to the control group received the existing healthcare treatment.

Pulmonary rehabilitation is well-documented as an effective component of the treatment of COPD (50). The aim is to provide the individual COPD patient the opportunity to achieve the highest possible functional capacity and quality of life. Pulmonary rehabilitation is indicated by an MRC score ≥ 3, and the rehabilitation should include the following elements (51):

Nicotine replacement therapy: Patients are offered a motivational conversation and assistance in stopping smoking as well as information about the damage caused by tobacco consumption. Smoking cessation is the most effective intervention against COPD to prevent disease progression and reduce future health care costs (51).

Exercise training: Patients are advised of the importance of physical exercise, especially aerobic training, as a part of rehabilitation. Patients' functional levels decrease concurrently with the progression of the disease, resulting in a more sedentary lifestyle and poor conditioning, with deterioration in respiratory symptoms. The purpose of the exercise is to provide patients with the best possible starting point to account for this progression (51).

Pharmacological therapy: Medical treatment is a prerequisite for the rehabilitation of COPD, and its purpose is to improve the patient's health conditions and minimize their symptoms of COPD. The treatment varies depending on the severity of the disease and whether the patient is in a stable or acute phase of illness. In the stable phase, all patients regardless of their severity of COPD receive vaccination against influenza and short-acting bronchodilators as needed to reduce their short-term symptoms. Patients with moderate to severe COPD are permanently treated with long-acting bronchodilators, while patients with severe to very severe COPD are offered steroid inhalants if repeated exacerbations are experienced. Oxygen therapy is offered to patients with severe COPD. A distinction is made between short- and long-term oxygen therapy. Long-term therapy is used in connection with acute exacerbation of COPD during hospitalization at a hospital or in the ensuing weeks. Long-term oxygen therapy is permanent, continuous oxygen therapy (at least 15 hours a day). Treatment leads to improved survival and enhances patients' quality of life; they are more energetic and awake and can manage several activities (51).

Education on COPD: COPD patients are taught with the aim of strengthening their autonomy, action competence, and quality of life by providing information about the disease itself and its corresponding prevention and rehabilitation. The effects of minimal exposures to risk factors, especially tobacco consumption, are emphasized, and the patient is informed about management of acute exacerbations. The education helps patients to participate actively in the treatment and rehabilitation of their disease in collaboration with the healthcare system and allows patients to take responsibility for their illness (51).

Emotional support: COPD is associated with social isolation, anxiety, and depression. Emotional support aims to prevent the development of mental disorders. The risk of anxiety and depression increases with the progression of the disease and increased shortness of breath. The patient's psychosocial conditions are attempted to be assessed, and appropriate support and relief measures are offered such as specialist referrals, patient associations or family support (51).

Nutrition counseling: The aim of nutrition counseling is to ensure that the patient maintains an optimal nutritional status and an adequate weight relative to their disease condition. Patients who are underweight receive individual guidance and nutritional therapy to increase their body weight. In contrast, patients who are obese

are recommended to reduce their body weight and are offered diet and regular weight control strategies (51).

2.1.8. THE CONSEQUENCES OF COPD

The global burden of COPD could increase due to demographic changes that indicate that the average life expectancy will increase in the future. These changes would lead to an increase in the number of elderly needing care and an increase in the number of chronic diseases, which ultimately also implies significant increases in health care expenditures (52). The socio-economic costs are associated with the treatment and care of COPD and the society's loss of production due to COPD patients' untimely deaths and withdrawal or absence from the labor market (27,53,54). The patient-related costs are related to the discomfort or disability that the disease causes, with reduced quality of life as a consequence (55). Consequently, the disease constitutes a major health challenge for the individual and for society. The growing elderly population with several chronic diseases causes an increased demand on the healthcare system and thus the need for more efficient treatments. Additionally, it appears that the costs of COPD will increase in the future, which make it appropriate to prevent and treat COPD for both human and economic reasons (56).

2.2. TELEHEALTH AS A POTENTIAL SOLUTION

The healthcare challenges described above can be addressed by making better use of resources and by delivering health services in new ways. COPD is treated with the aim of reducing symptoms and preventing disease progression and exacerbations. The identification and treatment of the disease before any exacerbations occur may lower the morbidity, mortality, comorbidity, healthcare utilization, and costs and improve health- and patient-related outcomes (56). Telehealth is a potential answer to providing efficient and safe healthcare by using it as a service in the management of COPD (57,58); some feasibility studies have already assumed that telehealth has a favorable value concerning quality of life compared to standard care (59–63).

Different terminologies

The term "telehealth" does not have a consistent definition across the literature and is often used interchangeably with the terms "telemedicine", "telecare" and "eHealth" (64,65). However, there exist certain substantial differences between the terms (66):

The World Health Organization (WHO) defines telehealth as follows:

> "*the delivery of health care services, where patients and providers are separated by distance. Telehealth uses ICT for the exchange of information*

> *for the diagnosis and treatment of disease and injuries, research and evaluation, and for the continuing education of health professionals. Telehealth can contribute to achieving universal health coverage by improving access for patients to quality, cost-effective, health services wherever they may be. It is particularly valuable for those in remote areas, vulnerable groups and aging populations"* (67)

In the Whole System Demonstrator Project (WSD), the English physician and expert in Health Informatics, Stanton Newman, adopts the following detailed definition of telehealth:

> *"Telehealth requires active participation of patients to measure vital signs using peripheral devices whereas telecare monitors without the need for patient input"* (68)

> *"Telehealth differs in that it allows the remote exchange of data between a patient (at home) and health care professionals (at a Monitoring Centre) to assist in the management of existing long-term conditions (chronic obstructive pulmonary disease, diabetes, heart failure)"* (68)

"Telehealth" is especially often used in connection with "telecare," as these two concepts complement each other.

Stanton Newman defines telecare as:

> "*TeleCare describes a system that allows remote and automatic monitoring that does not require any active involvement of individuals' personal health and safety (e.g. mobility, falls) and home environment (e.g. floods, fires) in order to manage the risks of independent living or provide prompt emergency responses*" (68)

"Telehealthcare" is composed of the two concepts, "telehealth" and "telecare", and the conceptualization of telehealthcare defined by Doctor Susannah McLean is as follows:

> *"the provision of personalized health care from a distance"* (5)

This description comprises the following key considerations:

> *"Information is obtained from individual patients, for example, in the form of a symptom score, oxygen saturation level, pulse rate"* (5)

> *"These data are transmitted over a distance by information and communication technology"* (5)

> *"A healthcare professional then exercises their clinical skills and judgment in interpreting this information and actively provides the patient with personalized feedback"* (5)

This PhD research preferentially uses the term "telehealthcare" throughout the thesis because the telehealthcare system utilized in the TeleCare North trial involves active patient participation, with COPD patients measuring their vital signs using an asynchronous application with peripheral devices. The TeleCare North trial and its system will be described later in this chapter.

Types of telehealthcare

Telehealthcare can be divided into three main types of applications covering store-and-forward, remote monitoring, and real-time interactive services:

Real-time services: This type is also known as synchronous telehealth, in which information is sent from the originating site to the receiving site as it occurs, rather than being stored for later transmission. Real-time telehealth services are used to consult, diagnose or treat patients and require the involved individuals to be present at the same time (69,70).

Store-and-forward services: This type is also known as asynchronous telehealth; in it, the transmission of information can be sent to the specialist at a suitable time for evaluation offline. The information can be stored in a specific format and sent to healthcare providers for a diagnosis, a confirmatory or second opinion or any other reason. This type of application does not require the involved individuals to be present at the same time, and the transmission typically occurs in one direction. An asynchronous telehealthcare application was used in the TeleCare North trial (69,70).

Remote monitoring services: This type is also called self-monitoring and relies on the patients using these various forms of technologies to test and monitor themselves from their home. Remote monitoring is often used in the treatment of chronic conditions, such as COPD and heart disease (69,70).

Advantages and disadvantages of telehealthcare

Telehealthcare's main benefit is its possibility of providing consultations between healthcare providers and patients without any geographic boundaries. Telehealthcare has many other potential benefits such as the following:

- Decreased travel time or distance and removal of travel barriers
- Enhanced access to health care services
- Early detection of disease processes or health issues
- Better communication between providers
- Ownership of healthcare and feelings of empowerment
- Long-term health and independence

- Caregiver reassurance
- Patient satisfaction with health care (71,72)

Despite the several advantages of telehealthcare, some potential drawbacks also deserve to be mentioned:

- A disintegrated relationship between healthcare providers and patients
- A disintegrated relationship between healthcare providers
- Concerns about the quality of health information
- Complications of organizational and bureaucratic character (73)

Despite telehealthcare's many potential advantages in managing chronic conditions, the evidence regarding its benefits, costs, and acceptance seems not to be determined yet.

2.2.1. CURRENT EVIDENCE ON TELEHEALTHCARE

A number of systematic reviews and meta-analyses suggest that telehealthcare can be effective in improving quality of life and health outcomes and may also result in cost reductions (5,74). However, there seems to be some degree of agreement that the evidence on the effects of telehealthcare remains limited and that there is still a need for further robust research within this field (14,75–79). The evidence is questioned due to the large number of pilot studies and mixed quality trials with diverse outcomes and limited numbers of patients. Most reviews claim that clinical heterogeneity is present in most outcomes of interest, which is primarily due to the different study populations (e.g., variation in diseases, disease severity, age), different interventions, different technologies, and different study designs (e.g., RCTs versus observational studies), which make it difficult to determine the effects of telehealthcare based on these outcomes (80–82).

The reviews address the methodological limitations of the current studies and provide suggestions for strengthening the evidence base, both regarding cost-effectiveness and effectiveness (83–86). The reviews generally conclude that more evidence is needed from large RCTs of appropriate rigor and quality (80). Studies with longer follow-up periods are necessary to gain knowledge about the long-term effects and the sustainability of telehealthcare (87). Some reviews discuss the need for studies to include technical, ethical, organizational, and economic effects in addition to clinical effectiveness (74,86,88–90). More knowledge is also necessary to identify which patient groups are most likely to benefit from telehealthcare (91,92), and what types of devices or services are most effective (93). Thus, the answer to whether telehealthcare is effective remains uncertain (5).

2.2.2. EVALUATION OF TELEHEALTHCARE

Effectiveness of telehealthcare

Evaluations of interventions can provide evidence regarding the effectiveness of telehealthcare and support stakeholders and policy makers in decision-making regarding best practices. Effectiveness addresses issues such as "*Does the intervention work?" and "Who will benefit from its use?"* (1) Telehealthcare might be a solution to the management of chronic illnesses but as with all types of health technologies, it is required that the technologies demonstrate user usefullness, effectiveness, and cost-effectiveness before telehealthcare can be fully implemented (94). Telehealthcare has been reported to produce the same or even better clinical outcomes compared with existing conventional care, but we do not know whether these reports are true. An evaluation of the outcomes of care delivered through telehealthcare compared with the outcomes delivered through conventional treatment will provide information about the effectiveness of telehealthcare.

In Medical Informatics, the gold standard for research and evaluation is the randomized controlled trial (RCT) (1,95,96). In the RCT design, subjects are randomly allocated to intervention or control groups and, if possible, are blinded to the treatment procedure. RCTs are considered the most robust method to establish cause and effect relationships (97). A cluster-RCT is a type of RCT in which groups of subjects, rather than individuals, are randomized to an intervention and control group (98). A cluster-RCT was chosen as the research design of the TeleCare North trial.

In the evaluation of telehealthcare interventions, a range of reliable and validated outcomes may be selected, with the goal of establishing evidence of the value of telehealthcare (99). These outcomes can be based on clinical effectiveness, patient perspectives, economic and organizational aspects, etc. (100). The goal of caring for chronically ill patients with COPD is not to cure them but rather to increase their quality of life. Thus, QoL can be a suitable outcome measure for assessing whether telehealthcare is the same as or is better than existing treatments for COPD patients (101,102). Many validated, generic or disease-specific QoL outcome tools have been developed. A patient-reported QoL outcome tool that is commonly used to evaluate health-related quality of life (HRQoL) is the Short-Form Health Survey (SF-36) (103,104). HRQoL includes four core domains (3), which are depicted in Figure 1.

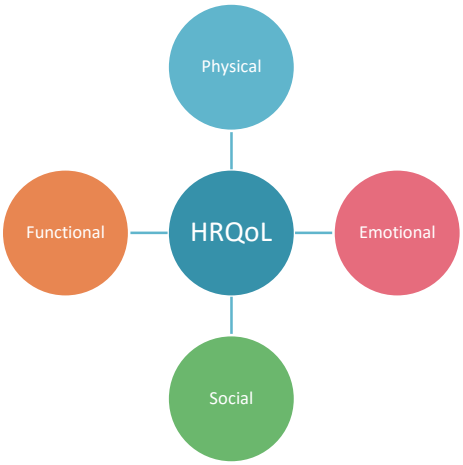

Figure 1: The core domains included in the assessment of multi-dimensional HRQoL (3).

The SF-36 is a generic 36-item questionnaire that is not addressed to a specific age group, disease group or treatment group. The survey measures eight domains that cover functional health and well-being from the patients' perspective. The eight domains include physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain and general health. An aggregated percentage score that ranges from 0% (lowest HRQoL) to 100% (highest HRQoL) is produced for each of the eight domains. Two summary scores of physical HRQoL (Physical component summary score; PCS) and emotional HRQoL (Mental component summary score; MCS) can also be generated by calculating the mean average of all of the physically relevant questions and all of the emotionally relevant questions, respectively. The SF-36 is a useful indicator of change in HRQoL over time and during treatment, with an increase in scores indicating an improvement in HRQoL (104). The questionnaire was used as the primary outcome measure of effectiveness in the evaluation of the TeleCare North trial.

Usability in telehealthcare

Usability is an essential element in the successful implementation of telehealthcare and can contribute to the effectiveness of such interventions and to ensuring the benefits of telehealthcare technologies (105). The International Organization for Standardization (ISO) defines usability as follows:

> *"The extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency, and satisfaction in a specified context of use"* (6)

Poor usability reduces the acceptance of telehealthcare systems, and the potential benefits of telehealthcare could fail if the users cannot easily or efficiently use these systems to meet their needs (106). Therefore, usability in telehealthcare is important but has frequently been ignored by designers and evaluators. Much attention has been paid to the technical aspects of telehealthcare, and less focus has been on its usability aspects. Most often, the design of telehealthcare systems has been limited by the requirements of the clinical users, healthcare providers, and the equipment vendor (107). System development requires the involvement of all users, with their physical limitations, environments, activities, abilities, and skills being taken into account (108). The following requirements should be fulfilled by telehealthcare according to Botsis and Hartvigsen (109): telehealthcare should be simple to use, operate without interruptions and provide computer security and data confidentiality (109).

The design of telehealthcare systems should be usable and acceptable, and ensuring usability can be challenging because it is typically elderly people with limited functional status and skills who will be using these technologies (110,111). As telehealthcare systems might be challenging, especially for older people who may have limited capabilities, it is important to explore their use of and experiences with these types of technologies (112,113). The ISO defines user experiences as:

> *"A person's perceptions and responses that result from the use and/or anticipated use of a product, system or service"* (7)

User experiences can be measured with psychometric questionnaires (114) and by the system's usability and can be verified and tested through tests and evaluations to ensure that the users remain central to the design process of a system and that usability is designed into the system (115). The two standard methods of measuring usability are inspection methods performed by experts and empirical testing conducted by representative users (116,117). The telehealthcare system used in the TeleCare North trial was evaluated by using both types of usability testing methods (see Paper II-VI) to assess the user-friendliness of the system.

2.3. PRESENTATION OF THE TELECARE NORTH TRIAL

In 2012, the Government, Danish Regions, and Local Government Denmark framed an ambitious National Action Plan for Dissemination of Telemedicine (15,16). The Action Plan included five initiatives (projects) that were intended to ensure that telemedicine was tested in a large-scale context and in areas of the healthcare service in which there was sparse documentation of the effects of this form of care. A total of DKK 80 million (Approx. 11 million EUR) were invested to finance these five initiatives of the Action Plan to establish a better framework for telemedicine (15,16). One of these five initiatives was the Danish TeleCare North trial (www.telecarenord.dk), which was expected to acquire the experiences of

implementing telehealthcare at a large scale. The ambition was that given the TeleCare North trial, it would be possible to establish common national models and strategies for how telehealthcare solutions, both technically and cross-organizationally, should be implemented and organized (118).

In this section, the TeleCare North trial will be briefly presented. For more detailed information about the trial, see the trial protocol (Paper I) or Chapter 3 (Section 3.1.: Context of the PhD study).

The TeleCare North trial was implemented between 2012 and 2015 and was established as a cross-sectional cooperation between the North Denmark Region, Aalborg University, and the municipalities, hospitals and general practitioners in the Region [Paper I]. The TeleCare North trial was based on the results of small pilot studies such as the previous Danish research project, TeleKat, which was targeted to patients with COPD (119). TeleKat showed that telerehabilitation had both positive patient-related and economic effects, with a reduction observed in hospital admissions, number of out-patient visits, home care services and average length of stay (120). An improvement was found in patient empowerment (121) and their achievement of feeling safe at home (92).

The TeleCare North trial was the first pragmatic, randomized, controlled large-scale trial in Denmark. The trial had two main purposes: 1) to evaluate the effectiveness and cost-effectiveness of telehealthcare in comparison with usual practice and 2) to obtain knowledge about the management and organizational implications of telehealthcare at a large scale (119). In total, 1,225 (578 intervention, 647 control) COPD patients were randomly allocated to either telehealthcare in addition to usual practice or only usual practice. The intervention patients were assigned to the telehealthcare system (coined Telekit), and the control group was assigned to the existing conventional treatment of COPD. Figure 2 illustrates the research design of the TeleCare North trial using a basic flow diagram.

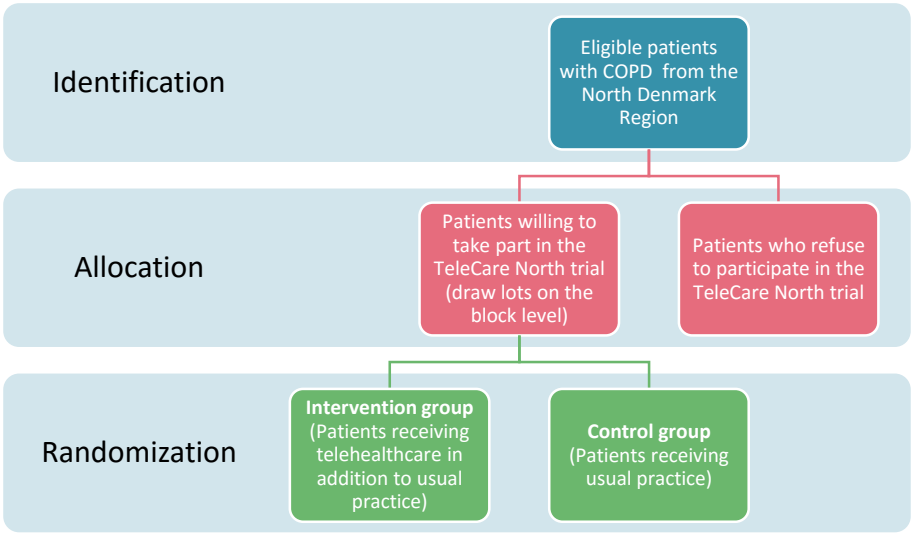

Figure 2: The TeleCare North trial's research design with the process of identification, allocation, and randomization of patients.

2.3.1. THE TELEHEALTHCARE SYSTEM, TELEKIT

The telehealthcare system, Telekit, was developed by Silverbullet, Aarhus, Denmark (http://opentele.silverbullet.dk) with the aim of supporting patients in coping with their chronic disease. The basic logic behind the system was that by improving the patients' disease-specific knowledge, it would be possible to enhance patient empowerment, resulting in an improved quality of life and prediction of the onset of an exacerbation. The Telekit system was installed by a technician in the patients' home, and if the patients experienced various technical problems with the equipment or for other reasons desired to return the system, it was collected again by the technician who calibrated the equipment.

The Telekit operated on an open source platform, OpenTele, which has been used to remotely monitor different patient groups in addition to COPD, including those with diabetes, hypertension, asthma, congestive heart failure, and pregnancy, in Denmark (122). The Telekit system was delivered to the patients in the TeleCare North trial in an iterative and dynamic process. Thus, in this PhD study, several usability tests were conducted to assess whether Telekit was a useful system (See Papers II-IV).

Telekit consists of a Samsung Galaxy tablet (Samsung Galaxy TAB 2, 10.1, Samsung Electronics, Seoul, South Korea) (123), a fingertip pulse oximeter (Nonin, Onyx II% SpO2, A&D Medical, Tokyo, Japan) (124), a blood pressure monitor (Model UA-767, plus BT-C, Nonin Medical, Minnesota, USA) (125), a precision

health scale (UC-321PBT-C, A&D Medical, Tokyo, Japan) (125), a tablet pen, and a user guide [Paper I]. The Telekit system can be observed in Figure 3.

Figure 3: The telehealthcare system, Telekit, consists of a tablet, a blood pressure monitor, a fingertip pulse oximeter, and a weight.

The Telekit tablet has two apps. The first app, OpenTele, contains questionnaires that collect patients' answers regarding their respiratory symptoms. The app also collects vital signs measured through Telekit's devices via Bluetooth. Additionally, the patients have access to their measurements and access to a message function to initiate a conversation with the healthcare providers. This message function is for non-acute messages. The second app is a support app that contains a digital version of the instruction guide, several videos that illustrate how Telekit and the various devices can be used, and a training video targeted to patients with COPD (126).

The COPD patients measured their respiratory symptoms and vital signs (heart rate, blood pressure, oxygen saturation, and weight) weekly through the Telekit system (see Figure 4). Patients' data were monitored asynchronously and sent via wireless internet connection through the tablet to a platform that was viewed by district nurses in the municipalities. Patients had access to their data on the tablet or via the public health portal (www.sundhed.dk).

Figure 4: A patient with COPD is using the Telekit system to measure his vital signs.

The GPs also had access to the health portal (www.sundhed.dk). The district nurses viewed the data from a web portal, OpenTele, on scheduled days in the week. These nurses manually interpreted the data based on color codes: green (normal values – no threshold values are exceeded); yellow (providers should be aware of the condition of patients – one or more threshold values are exceeded); and red (the patient's condition is at risk, probably due to an exacerbation – one or more threshold values are exceeded and have not previously been recorded).The threshold values for the patients' conditions were specified by the patients' GPs. These color codes constituted a recommended order of reviewing the submitted data and were managed in accordance with the compiled instructions. The patients were contacted if their values fell outside these threshold values to establish further treatment. The intervention patients were able to keep the Telekit system and the control patients were offered the system after trial completion. The district nurses' web portal and the telehealthcare system architecture are depicted in Figures 5 and 6, respectively.

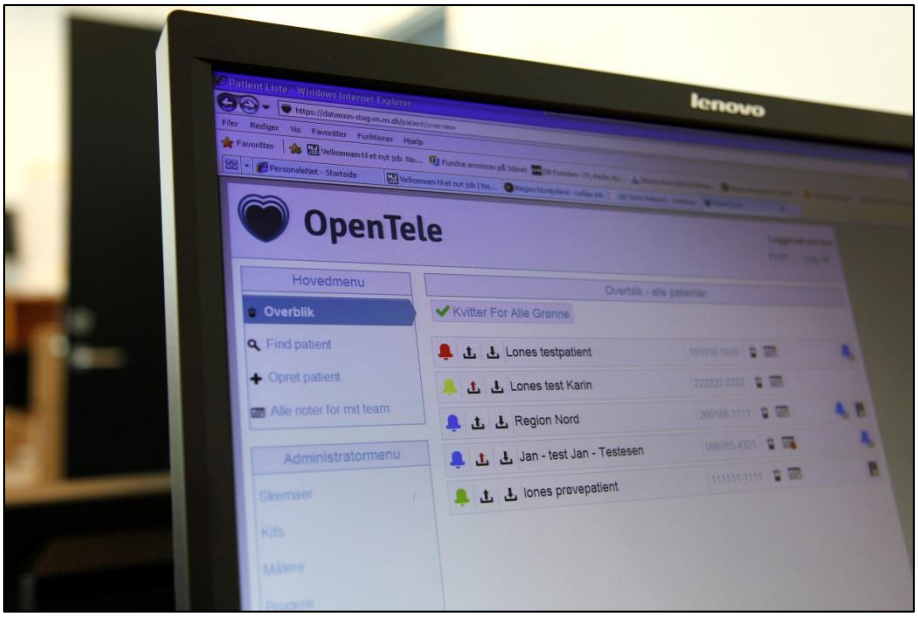

Figure 5: The district nurses view the patient measurements from the web portal, OpenTele.

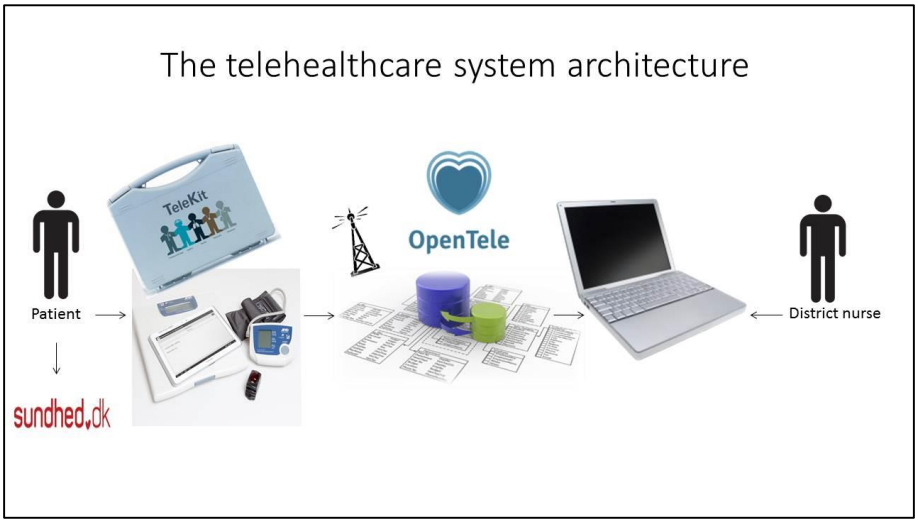

Figure 6: The Telekit system framework. At home, patients were guided through their measurements using a tablet application. Devices used to measure the patients' vital signs were connected to the tablet through Bluetooth. Patients could view their measurements via the tablet or the public health portal (www.sundhed.dk). The data were sent by patients to a central server, OpenTele, which stores data and ensures data exchange between relevant entities. District nurses could view the data from the web portal, OpenTele, and contacted the patients if deviations in their measurements occurred.

Instructional videos of the Telekit system and its connected devices can be viewed by visiting the following links (the videos are only recorded in Danish):

Instructions on the use of the tablet: http://www.rn.dk/Sundhed/Til-sundhedsfaglige-og-samarbejdspartnere/TeleCare-Nord/Instrukser-KOL/Instruktionsvideoer/Instruktion-i-brug-af-tablet

Instructions on the use of the blood pressure monitor: http://www.rn.dk/Sundhed/Til-sundhedsfaglige-og-samarbejdspartnere/TeleCare-Nord/Instrukser-KOL/Instruktionsvideoer/Instruktion-i-brug-af-blodtryksmaaler

Instructions on the use of the fingertip pulse oximeter: http://www.rn.dk/Sundhed/Til-sundhedsfaglige-og-samarbejdspartnere/TeleCare-Nord/Instrukser-KOL/Instruktionsvideoer/Instruktion-i-brug-af-iltmaaler

Instructions on the use of the weight: http://www.rn.dk/Sundhed/Til-sundhedsfaglige-og-samarbejdspartnere/TeleCare-Nord/Instrukser-KOL/Instruktionsvideoer/Instruktion-i-brug-af-vaegt

2.4. SUMMARY OF THE BACKGROUND

In this chapter, it was outlined that chronic obstructive pulmonary disease and other chronic diseases are responsible for a growing burden on the healthcare system. The burden of COPD has led to a need to develop other approaches to facilitate the treatment and care of these chronic patient groups. In recent years, technology has advanced exponentially, which has brought innovation into focus. Many health organizations are implementing health information technologies to reduce the incidence of hospitalizations and to prevent deterioration of chronic diseases.

Telehealthcare could be a potential solution for managing COPD, but the evidence regarding its effects has yet to be determined. Another important factor to be addressed is the usability of telehealthcare and the user experiences with these telehealthcare technologies. Thus, large-scale trials are needed to provide evidence on the effectiveness of telehealthcare. A large-scale trial in Denmark, TeleCare North, was established to improve this lack of evidence by testing the effects of telehealthcare in patients suffering from COPD.

CHAPTER 3. AIMS AND OVERVIEWS OF THE PHD STUDY AND PAPERS

In this chapter, the context, research questions, aims, and overview of the PhD study will first be described. This description is followed by a presentation of the specific purpose of each paper included in the PhD study. Finally, the chapter provides an overview of the thesis paper's design/methods, subjects, and primary aims.

3.1. CONTEXT OF THE PHD STUDY

The PhD study was affiliated with the TeleCare North trial, the telehealthcare trial for COPD patients in the North Denmark Region. The population in the North Denmark Region is estimated to consist of approximately 45,000 COPD patients, and the number is growing. Of these, nearly 4,500 have severe or very severe COPD (127). The North Denmark Region is one of the five Danish regions and is divided into 11 municipalities with ten hospitals and approximately 350 GPs spread across 200 medical practices (128).

Four PhD students conducted an evaluation of the TeleCare North trial's intervention with the following scholarships:

- A health-economics PhD scholarship from the Danish Centre for Healthcare Improvements, Aalborg University
- A health-related/patient-oriented PhD scholarship from the Department of Health Science and Technology, Aalborg University
- An organizational theory PhD scholarship from the Centre for Organization, Management and Administration, Aalborg University
- A health literacy-based PhD scholarship from the Department of Health Science and Technology, Aalborg University.

Figure 7 provides an overview of the four scholarships including their respective research areas.

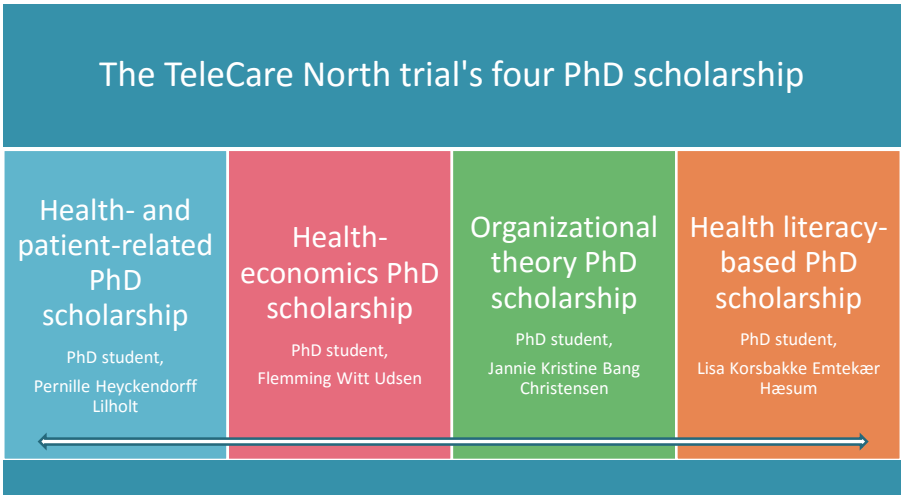

Figure 7: The evaluation of the TeleCare North trial was carried out by four PhD students each in their specific research area.

3.2. AIMS AND RESEARCH QUESTIONS OF THE PHD STUDY

The overall aim of this PhD study was to evaluate a telehealthcare intervention for patients suffering from COPD. The focus areas of this PhD thesis were to provide a description of the TeleCare North trial's intervention and to evaluate its outcomes regarding health-related quality of life (HRQoL), usability, and patient experiences.

In particular, this thesis had a more specific focus on the following objectives with their corresponding research questions (Figure 8):

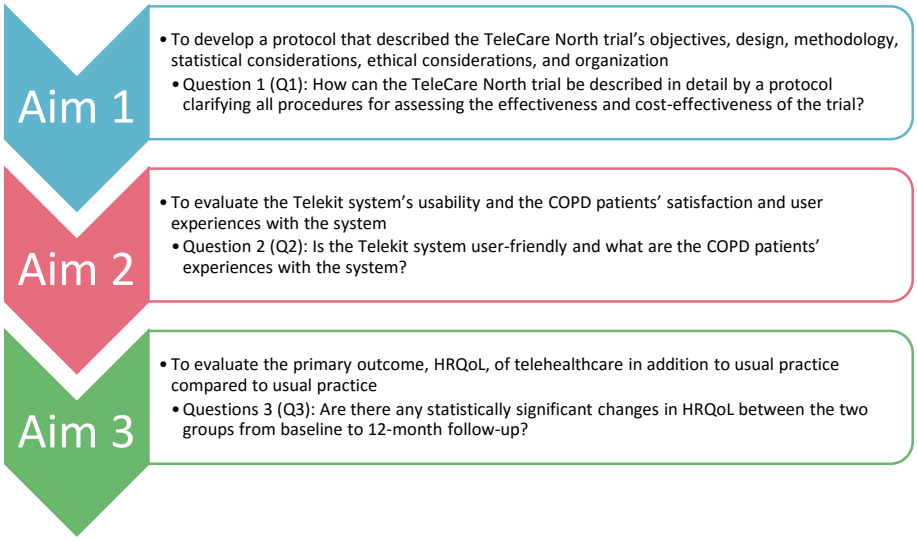

Figure 8: The PhD thesis aims and research questions.

The research questions, depicted in Figure 8 will be considered and responded to through seven thesis papers (the answers to Q1-Q3 are presented in Chapter 6: General discussion and Chapter 7: Conclusion).

3.3. OVERVIEW OF THE PHD STUDY

The research in this PhD study was conducted in three phases. The first phase of the research process consisted of the development of TeleCare North trial´s protocol. The second phase comprised an evaluation of the telehealthcare system's usability and the COPD patients' user experiences. The final phase contained an evaluation of the TeleCare North trial's primary outcome, HRQoL. Figure 9 illustrates the three phases with their related papers.

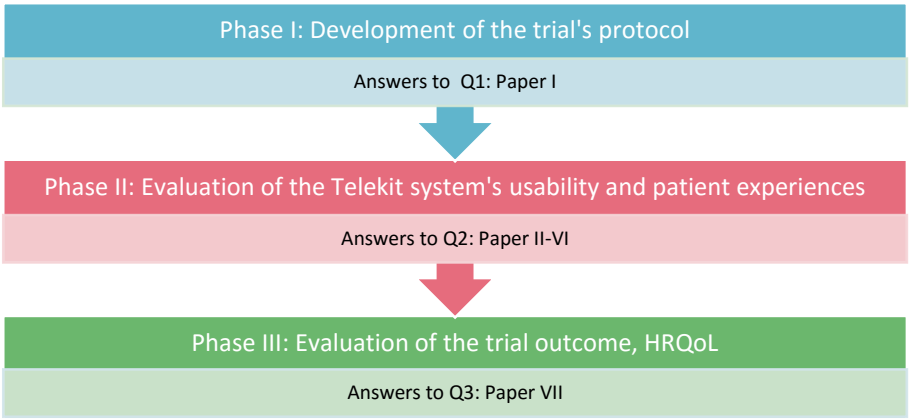

Figure 9: This PhD study was divided into three phases with associated papers. These papers provided answers to the three thesis research questions (Q1-Q3).

3.4. SPECIFIC AIMS OF THE PAPERS

Paper I: The aim was to evaluate the effectiveness and cost-effectiveness of a telehealthcare intervention for patients suffering from COPD compared to usual practice.

Paper II: The aim was to evaluate the usability of the design of the telehealthcare system, named Telekit, early in the design process to assess potential problems and limitations that could hinder its user-friendliness and its successful implementation.

Paper III: The aim was to evaluate the COPD patients' satisfaction and user experiences with a revised version of the Telekit system.

Paper IV: The aim was to evaluate Telekit's usability using an iterative, mixed usability approach.

Paper V: The aim was to explore the COPD patients' user experiences with the Telekit in relation to increased control, freedom, security and greater awareness of their COPD symptoms.

Paper VI: The aim was to examine the association between COPD patients' use of Telekit and their functional health literacy and the association between their use of the Telekit system and their specific technological communication skills.

Paper VII: The aim was to assess the effect of telehealthcare compared to usual practice based on an assessment of HRQoL in patients suffering from COPD.

3.5. OVERVIEW OF THE PAPERS

The seven thesis papers' design/methods, subjects and primary aims are illustrated in Table 4.

Table 4: The seven papers included in the PhD study are listed below with information about the design/methods, subjects, and primary aim of each paper.

Papers	Design/methods	Subjects	Primary aim
Paper I	Protocol/cluster randomized trial	COPD patients from the North Denmark Region	To evaluate the effectiveness and cost-effectiveness of telehealthcare compared to usual practice (cost-effectiveness is not addressed in this thesis)
Paper II	Heuristic evaluation	5 usability experts	To evaluate the usability of Telekit's design early in the design process to assess potential problems that could affect the outcome of its implementation
Paper III	Think aloud test	6 COPD patients from the intervention group	To evaluate the COPD patients' satisfaction and user experiences with a revised version of the Telekit system
Paper IV	Iterative, mixed usability approach	10 usability experts, 11 COPD patients from the intervention group	To evaluate Telekit's usability using an iterative, mixed usability approach
Paper V	Non-validated questionnaire	60 COPD patients from the intervention group	To explore the COPD patients' user experiences with the Telekit system in relation to increased control, freedom, security and greater awareness of their COPD symptoms
Paper VI	TOFHLA test/Non-validated questionnaire	60 COPD patients from the intervention group	To examine I) the association between COPD patients' use of the telehealthcare system, Telekit, and their functional health literacy and II) the association between their use of the telehealthcare system, Telekit, and their specific technological communication skills

Paper VII	Short Form (36) Health Survey	1225 (n=578 intervention; n=647 controls) COPD patients	To assess the effect of telehealthcare compared to usual practice based on an assessment of HRQoL in COPD patients at the individual level

CHAPTER 4. SUMMARY OF PAPERS

This chapter is divided into the three phases of the PhD study and their associated papers. The chapter includes a summary of each paper's aim, methods, results, and discussion/conclusion. A more detailed description of the papers' contents can be found in each paper separately.

4.1. PHASE I: DEVELOPMENT OF THE TRIAL'S PROTOCOL

4.1.1. SUMMARY OF PAPER I

Effectiveness and cost-effectiveness of telehealthcare for chronic obstructive pulmonary disease: study protocol for a cluster randomized controlled trial

Aim: The objective of the TeleCare North trial was two-fold: 1) To evaluate the effectiveness in terms of HRQoL in patients with COPD and 2) to evaluate the cost-effectiveness of implementing telehealthcare. The second part of the objective is not addressed in this thesis, as it is covered by another PhD student, Flemming Witt Udsen.

Methods: TeleCare North was a cluster-randomized, pragmatic, controlled trial with 12 month follow-up. We cluster-randomized 26 (with between 1 and 5 districts per municipality) matched municipality districts in the North Denmark Region. The municipalities were matched in terms of the municipality district's size, population, unemployment rate, and the proportion of COPD > 40 years of age.

The hospitals and the GPs in the North Denmark Region were responsible for including patients in the trial. GPs from the Region recruited patients from a list of potentially eligible patients in their practices. The COPD patients received detailed information about the study via brochures from the trial's Administration Office and the GPs. Additionally, 30-minute appointments with GPs were established with each eligible patient, consisting of a conversation that was based on the forwarded brochure and patients' baseline measurements. At this appointment, the COPD patients also signed written consent for participation. GPs transferred the threshold values of the baseline measurements for each patient to the municipalities electronically when the patients were included. Additionally, the GPs sent a return envelope with the baseline measurements and written consent to the trial's Administration Office. Patients were eligible for inclusion if they were diagnosed with COPD, verified by spirometry ($FEV_1/FVC < 70\%$). Patients were excluded if they had problems understanding Danish, did not have telephone- or Global System for Mobile Communications (GSM) coverage, or had cognitive disabilities. The inclusion and exclusion criteria are listed in detail in Paper I.

The intervention included COPD patients receiving telehealthcare supplemented with existing usual practice. The compared alternative was patients receiving the existing usual practice and no form of telehealthcare. The existing usual practice involved treating, monitoring, and caring throughout the study period. The intervention patients were instructed on how to take the relevant measurements and how to use the telehealthcare system by appointments with their health care provider (district nurses). Patients were informed about taking daily vital sign measurements (blood pressure, heart rate, oxygen saturation, and weight) for the first 14 days after receiving the Telekit system and thereafter on a weekly basis after agreement with their GPs. District nurses from the municipalities reviewed patient measurements based on predefined threshold values on fixed weekdays. The district nurses followed up with a phone call when there were diverging measurements and planned patients' next actions with the patients. The background section of this thesis and Paper I include more specific information regarding the trial's design and intervention.

The primary outcome was effectiveness defined by change in HRQoL at the individual level from baseline to 12-month follow-up. The primary outcome for cost-effectiveness was the incremental cost-effectiveness ratio (ICER) at the individual and cluster level measured from baseline to 12-month follow-up. The secondary outcomes for effectiveness were changes in mortality and vital signs from baseline to 12-month follow-up. An intention-to-treat principle was applied in the statistical analysis of the outcomes. See Paper VII for the evaluation of the primary outcome. The secondary outcomes of effectiveness and the outcomes concerning cost-effectiveness are not incorporated in this thesis or any of the thesis papers.

Discussion: The TeleCare North trial aimed to improve the body of international evidence on the effectiveness and cost-effectiveness of telehealthcare in COPD patients by establishing a large-scale, cluster-randomized trial. The changes in outcomes were evaluated from baseline to 12-month follow-up. After the trial period, all recruited patients were offered telehealthcare. The trial outcomes were expected to be used as a Danish national standard for a technological platform and as a telehealthcare implementation model if the findings were favorable.

The trial protocol was developed to increase the transparency of the TeleCare North trial. The protocol was registered at clinicaltrials.gov under trial no. NCT01984840 before trial initiation.

4.1. PHASE II: EVALUATION OF THE TELEKIT SYSTEM'S USABILITY AND PATIENT EXPERIENCES

4.1.1. SUMMARY OF PAPER II

Heuristic evaluation of a telehealth system from the Danish TeleCare North trial

Aim: In this paper, the usability of the telehealthcare system's design was evaluated early in the design process to assess potential problems that could affect the outcome of its implementation.

Methods: Five usability experts performed a heuristic evaluation of the Telekit system from the Danish TeleCare North trial. The experts evaluated Telekit's interface for any problems using Jakob Nielsen's ten heuristics and Rolf Molich's severity classification. The experts evaluated the system based on designed scenarios, and whenever problems were identified, they were categorized into heuristics and given a score of severity. A debriefing session was carried out after all the experts had individually completed the heuristic evaluations. In this forum, all experts were gathered to discuss the positive and negative aspects of the system. The data from the heuristic evaluations were analyzed through simple bar charts to compare the experts' identified problems.

Results: The usability experts identified 152 problems through the heuristic evaluation, of which 86 (57%) were unique problems. Each expert documented between 22 and 40 problems with Telekit. The three most commonly used heuristics were "*Match between system and the real world*" (32%), "*Consistency and standards*" (13%), and "*Aesthetic and minimalist design*" (13%). The problems included in these heuristics were associated with the Telekit's inability to speak the users' language with words and phrases that were understandable and its ability to inform users about how measurements were to be obtained. The problems were most often given severity grades of "*Improvement*" (40%) and "*Minor problem*" (43%).

The positive and negative aspects of the Telekit system were discussed during the debriefing. The three most positive aspects were the Telekit's navigation system, its simple design, and its feedback. The three most serious aspects were the system's lack of integrated help functions, lack of consistency in the design and content, and its failure to meet tablet standards.

Discussion/Conclusion: The heuristic evaluation aimed to identify problems that could present an obstacle to users. By identifying potential problems, these could be addressed so that users could more easily access the system. The method was effective in finding problems with the interface, and although most problems were categorized as minor problems, it was recommended by all the usability experts to resolve them. The system was characterized as unfinished, given its use of small

buttons and the absence of touchscreen feedback. However, the system was considered simple in the design and usable for individuals who were unfamiliar with technology in general. Regardless, experts agreed on the need for interface improvements to make the Telekit more user-friendly. The heuristic evaluation was performed by experts and not the potential users, i.e., COPD patients. Therefore, the system should in the future undergo user tests after improvements have been made by Silverbullet, the company responsible for the system's development (See Paper II for more detailed information about the heuristic evaluation of the Telekit system).

4.1.1. SUMMARY OF PAPER III

User satisfaction and experience with a telehealth system for the Danish TeleCare North trial: A think-aloud study

Aim: This paper aimed to evaluate the COPD patients' satisfaction and user experiences with a redesigned version of the Telekit system.

Methods: Six COPD patients (three women, three men) were randomly chosen to conduct a think-aloud test of the Telekit system. A heuristic evaluation had earlier been performed on the Telekit system to review the system for potential problems that could hinder its successful implementation (Paper II). The heuristic evaluation led to several changes to Telekit's interface, and the revised system was then ready for user testing involving the patients' satisfaction and user experiences with the system. The think-aloud test was performed in the patients' homes, where the COPD patients completed representative tasks through the system. These tasks comprised the following 1) to log into the Telekit tablet; 2-3) to measure vital signs; 4) to identify graphical images of their measurements; 5) to use the message function; and 6) to sign out of the Telekit tablet. Observations were made during the tests, and satisfaction was assessed using a developed questionnaire for this purpose.

Results: *The questionnaire* – The patients assessed the Telekit system as user-friendly, and there was consensus among patients that most people would be able to learn using the system. The time consumption varied among the patients, from using it on a weekly basis to even more frequently. Different technical assistance needs and the involvement of relatives in the utilization of the system were present. Some patients involved their healthcare provider or relatives, whereas others did not. In general, the patients were satisfied with the functionality of the Telekit system and were confident in using the system.

Think aloud test and observations – All tasks were accomplished. Difficulty initiating a reaction on the touchscreen display was observed among some women due to having long fingernails or cold fingers. Some of the patients also had trouble identifying buttons, remembering passwords, and taking measurements in the appropriate order. The problems prevented patients from continuing through the system and from sending measurements. Some patients commented that the textual material in the Telekit system application was too extensive, and they wished for less text to facilitate readability.

Discussion: Important knowledge was obtained during the test regarding the Telekit's user-friendliness and the patients' satisfaction. The patients were satisfied with the functionality of the Telekit system, and the feedback was mostly positive. However, different issues were identified concerning the textual material, interface design, and the need for a call center. The patients were all familiar with the Telekit

system before the tests took place, which could have meant they had acquired habits in using the system. Therefore, these patients could have been able to look past the problems that novices would have otherwise noticed. Valuable knowledge was obtained during the tests regarding the Telekit's user-friendliness and the patients' satisfaction. This knowledge is essential to improving current and future telehealthcare systems (See Paper III for more detailed information about the study).

4.1.1. SUMMERY OF PAPER IV

An iterative, mixed usability approach applied to the Telekit system from the Danish TeleCare North trial

Aim: The aim of this study was to evaluate Telekit's usability using an iterative, mixed usability approach

Methods: The study was carried out as an evaluation of the Telekit system and included a pre- and post-test. The former comprised a heuristic evaluation (HE1) and a think-aloud test (TA1), and the latter also comprised a heuristic evaluation (HE2) and a think-aloud test (TA2). In both heuristic evaluations, ten double usability experts (HE1: n= 5, HE2: n=5) participated, and 11 COPD patients from the TeleCare North trial took part in both think-aloud tests (TA1: n=6, TA2: n=5).

In the heuristic evaluations, the usability experts found usability problems and classified them using Jakob Nielsen's heuristics. The problems were also classified according to their severity based on Rolf Molich's scale from zero to four. During the think-aloud tests, patients were asked to express their perceptions and thoughts about the Telekit while they performed representative tasks through the system.

All four usability evaluations were carried out by a moderator and an observer and were recorded and audiotaped. The mixed usability approach produced both qualitative and quantitative data, which were combined and compared in the data analysis descriptively. The data were analyzed and compared as follows I) a pre- and post-test comparison of HE1 versus HE2, II) a pre- and post-test comparison of TA1 versus TA2, and III) a post-test comparison of HE2 versus TA2.

Results: *Comparison of HE1 versus HE2* – In HE1, 152 problems were identified, of which 86 (57%) were unique. In HE2, 195 problems were found, of which 101 (52%) were unique. See Paper IV for further details about the distribution of problems in the heuristics and the distribution of usability problems by the Rolf Molich's severity rating scale. More specific information about the findings of these two evaluations can be found in Paper IV.

Comparison of TA1 versus TA2 – A total of 12 themes were created based on the usability findings from the think-aloud tests: 1) Habits; 2) Lack of curiosity; 3) Information level; 4) The Telekit system – know how; 5) Comfort with the Telekit system; 6) Usability problems; 7) Learnability; 8) System feedback; 9) Content of the Telekit system; 10) Measurements; 11) The Telekit design, and 12) Relevance of the Telekit system. More themes with associated examples of usability problems were observed in TA2 compared with TA1. For further information about the content and presence of these twelve themes, see Paper IV.

Comparison of HE2 versus TA2 – Overall, the number of usability problems reported in HE2 was higher than the number of usability problems verbalized in TA2. In total, the experts identified the most (n=222), compared to the patients' comments (n=76) and researcher observations (n=40). More specific knowledge regarding the comparisons of HE2 and TA2 can be obtained in Paper IV.

Discussion/Conclusion: The Telekit system was evaluated through an iterative, mixed usability approach. The findings from the usability evaluations pointed to the importance of iteratively combining various methods. The findings from the study indicate that Telekit is suitable for supporting COPD patients in coping with their disease. The usability experts in HE1 generated substantial changes to the telehealthcare system, and new versions of the system were brought into operation. Subsequently, a think-aloud test, TA1, was carried out, in which patients verbalized their feelings and thoughts concerning the Telekit system. The post-test (HE2, TA2) was conducted approximately 12 months after.

The comparison of HE1 and HE2 in the pre- and post-test showed that more problems were found in the post-test, which was relatively surprising because it was expected that this test would identify fewer problems. The identification of the number of the greater number of problems could be explained by Silverbullet's (the company that developed Telekit) prioritization of the usability problems or by the different experts' views on the system.

The findings from the think-aloud tests, TA1 and TA2, indicated that most usability problems in the themes appeared in TA2. An explanation for this could be that Telekit's usability decreased after TA1 instead of trending in the other direction towards an improvement of the system.

A comparison of HE2 and TA2 was also performed and suggested that most usability problems were found through the heuristic evaluations versus the think-aloud tests. The COPD patients and experts agreed on many usability aspects, but they also had different views, which was considered an advantage. The COPD patients also included the positive aspects of the system, whereas the experts only focused on identifying problems with the system's functionality and design.

In this study, a large body of material representing the experts' and the patients' perspectives on the usability aspects of Telekit was collected. Jakob Nielsen's heuristics and Rolf Molich's severity classification were used in all heuristic evaluations to increase comparability. The findings from the study supported the relevance of testing the Telekit system iteratively and using mixed methods to elucidate as many perspectives on the system as possible.

The study was limited by the fact that not all experts had the opportunity to take part in both the pre- and post-test, which hindered the individual comparisons of the

results among experts. Another important limitation was the diverse versions of the Telekit system generated through the pre-test, which not could be avoided due to the corrections established in the system after the first heuristic evaluation, HE1. The findings of this study cannot be generalized to other telehealthcare systems that differ from the Telekit system.

In conclusion, the Telekit system is fully operational, but in the future the system should still be evaluated to improve the usability of the system. Other evaluation methods, such as eye tracking, would be appropriate to implement with the system to supplement problems that were not assessed by other evaluation methods.

4.1.1. SUMMERY OF PAPER V

Exploring user experience of a telehealth system for the Danish TeleCare North trial

Aim: The purpose of this study was to explore the COPD patients' user experiences with the Telekit System concerning increased control, freedom, security and greater awareness of their COPD symptoms.

Methods: A non-standardized questionnaire consisting of 14 questions was developed to explore the patients' user experiences with Telekit. The questionnaire was divided into three sections, with questions related to: I) the patients' health status/characteristics, II) the patients' use of specific technologies (computer, mobile phone, smartphone, and tablet), and III) the patients' user experiences with the Telekit system.

In total, 60 (27 women, 33 men) participants from the intervention group of the TeleCare North trial completed the questionnaire in the homes where a test responsible was present. The patients were all familiar with the Telekit system and had received instructions on the system by a healthcare provider two months before this study. The data from the patients' responses were quantified and descriptively analyzed.

Results: The majority of the patients (88%) considered the system simple to use. Most patients felt enhanced control (62%) and security (72%) by using the system. Half of the patients (50%) perceived greater awareness of their COPD symptoms. Finally, 27% of the patients answered positively to the question about experiencing enhanced freedom.

Discussion/Conclusion: The study explored patients' user experiences with Telekit to adjust the system to the COPD patients' needs and abilities. Overall, the patients had positive experiences with the system and expressed increased control, freedom, security and a high awareness of their symptoms. These findings are also consistent with previous results of usability studies on the Telekit system.

A weakness of this study was the small sample size, and it could have been more desirable to include the total number of patients from the intervention group in the survey. This study was also performed with patients who had possessed the Telekit for a relatively short amount of time, and as the patients' experiences might change over time, it might have been worthwhile to ask the patients the same questions again after a longer period had elapsed.

Regarding the study strengths, it should be mentioned that the patients were visited in their homes, which are assumed to provide a safe environment. The questionnaire was paper-based, which was believed to be beneficial because most of the COPD

patients were elderly individuals whose cognitive capabilities could be limited due to worsening disease.

To conclude, the findings of the study provided essential knowledge about patients' experiences, which also indirectly provided information about the implementation of the system and its success.

4.1.1. SUMMARY OF PAPER VI

Specific technological communication skills and functional health literacy have no influence on self-reported benefits from enrollment in the TeleCare North trial

Aim: This study's purpose was to investigate: I) the association between COPD patients' use of the telehealthcare system, Telekit, and their functional health literacy and II) the association between their use of the telehealthcare system, Telekit, and their specific technological communication skills.

Methods: A consecutive sample of the intervention group (n=60) in the TeleCare North trial participated in the study. The intervention patients had used the telehealthcare system for two months when this study was carried out.

Face-to-face interviews were conducted with each individual to obtain the following demographic data: gender, age, and educational level. All patients performed a Danish TOFHLA test, which measured their functional health literacy, and completed a non-standardized questionnaire about their health status, their use of the Telekit system, and their specific technological communication skills. The questionnaire included the following: seven questions about patients' health status, disease severity, and activity level; four questions about Telekit's ability to enhance patients' sense of freedom, security, control, and awareness of their COPD symptoms; one question about Telekit's ease of use; and two questions concerning the patients' use of communication technologies (e.g., tablet, mobile phone, etc.) and their specific skills (e.g., searching for information, paying bills, sending SMS/MMS, etc.) with these technologies. The questions were used for descriptive statistics, except for the last question, which was used to investigate the association between the patients' skills and their benefits from using the telehealth system. The questionnaire is presented in Paper VI as supplementary material.

Descriptive statistics and binary logistic regressions were suitable to investigate how functional health literacy and specific technological communication skills affected the use of the telehealthcare system by providing users an enhanced sense of freedom, security, control, and a greater awareness of COPD symptoms. The logistic regression models were investigated by calculating the odds ratios, and their respective 95% confidence intervals.

Results: *Participants' characteristics* – In total, 60 (28 women, 33 men) COPD patients with a mean age of 70 (SD: 8.37) years participated in the study. The majority of patients were skilled (45%) or were elementary school educated (35%). The mean functional health literacy score was 71.42; 14 (23%) of the patients were classified as having inadequate functional health literacy, 12 (20%) as having marginal, and 34 (57%) as having adequate literacy. See Paper VI for more detailed information about the descriptive characteristics of the patients.

Association between the use of the telehealthcare system and functional health literacy – The functional health literacy score had no statistically significant effect on the utilization of the telehealthcare system regarding its contribution to the users' experience of increased control, freedom, security, and greater awareness of symptoms.

Association between the use of the telehealthcare system and specific technological communication skills – The number of specific communication skills had no statistically significant effect on the utilization of the telehealthcare system regarding its contribution to the users' experience of increased control, freedom, security, and greater awareness of symptoms.

Discussion/Conclusion: This study investigated: I) the association between the use of the telehealthcare system and functional health literacy and II) the association between the use of the telehealthcare system and the number of specific communication skills. The majority of the participants felt enhanced security, control, freedom and greater awareness of their COPD symptoms, but no association between the benefit obtained from using the system, health literacy, and specific technological communication skills were identified.

This study took place in the patients' environment, and the investigator was present during the test to clarify questions and ensure a high response rate, which was considered an advantage of this study. A paper-based format of the questionnaire might be more favorable instead of the online format due to the assumption that chronic patients may have cognitive difficulties. The patients' own home was chosen to establish a pleasant atmosphere that created the least possible stress during the test situation – this should have led to an increased quality of the test and questionnaire responses. The generalizability of the study was considered high due to the diverse sample of patients. Nonetheless, these findings cannot be generalized to other telehealthcare studies using telehealthcare systems other than Telekit.

The study could be limited by the self-reported responses, which could give rise to social desirability bias and satisfying strategies because of the investigator's presence. Therefore, it is possible that the patients responded more positively than actually intended or chose a more neutral response option to complete the test and questionnaire quickly. The questionnaire was based on relevant literature to ensure content validity. Psychometric tests would have been preferable to perform on the non-standardized questionnaire to assure the questionnaire's validity and reliability.

In conclusion, the study demonstrated that functional health literacy and specific communication skills did not have any effects on the experience of using the telehealthcare system. Based on the findings, it is assumed that specific communication skills and functional health literacy are not preconditions for using the Telekit system (See Paper VI for more specific information about the study).

4.1. PHASE III: EVALUATION OF THE TRIAL OUTCOME, HRQOL

4.1.1. SUMMARY OF PAPER VII

Telehealthcare for patients suffering from COPD: Effects on health-related quality of life – results from the Danish "TeleCare North" cluster-randomised trial

Aim: The study aimed to evaluate the effect of telehealthcare in addition to usual practice compared with usual practice alone based on an assessment of HRQoL in COPD patients at the individual level.

Methods: This study was nested within the TeleCare North trial and was established in consensus with the trial protocol (Paper I). More detailed information about the study design can be obtained through the trial protocol (Paper I). The COPD patients (n=1225) in the intervention and control group received the Short-Form (36) Health Survey at baseline and after 12 months of follow-up. The survey measured the patients' HRQoL based on summary scores of physical (PCS) and mental component scores (MCS). The scores ranged from 0 (maximum disability) to 100 (no disability). The patients completed the questionnaire at home and were able to contact the study investigators for help in clarifying the questions. The importance of responding in the best possible manner and the importance of completing all the questions was made clear to the patients.

The study's primary outcomes were related to the patients' mean differences in HRQoL over time from baseline to the 12-month follow-up at the individual level. The primary outcome was the adjusted mean differences in the groups' summary component scores (PCS, MCS) from baseline to 12-month follow-up. The secondary outcomes were based on a subgroup analysis of the mean differences in summary scores (PCS, MCS) at the clustered level. The summary scores were calculated by using QualityMetric Incorporated (http://www.sf-36.org/). The effectiveness analysis followed the intention-to-treat principle. The data were analyzed using linear mixed models for continuous outcomes to evaluate the mean differences in scores between groups over the 12-month period.

Results: In total, 1225 (578 intervention, 647 controls) patients were included at baseline (see the CONSORT participant flow diagram in supplementary material, Paper VII). Socio-demographic characteristics and clinical characteristics were assessed at baseline and indicated no significant differences between groups, except for FVC% ($p<0.05$). The control groups' mean FVC% (74.34%) was slightly higher than of the intervention group.

Unadjusted and adjusted primary outcomes - The unadjusted significant differences in HRQoL scores between groups showed a decline in scores from baseline to follow-up at 12 months. The mean difference in the intervention group's PCS score

was -2.62 (95% CI, -1.9238464 to -3.317276), and the control group's was -2.83 (95% CI, -2.16342096; -3.494888704). The mean difference in MCS score for the intervention group was -4.69 (95% CI, -3.76360248; -5.61360952) and was -5.31 (95% CI, -4.44201504; -6.17870496) for the controls. For both groups, the mean differences in scores combined were MCS: 0.3771 (95% CI, 1.7506; 2.5049) and PCS: 0.1813 (95% CI, 1.3848; 1.7474). The confidence intervals indicated a statistically nonsignificant difference in unadjusted mean HRQoL scores between the intervention and control groups.

The groups' adjusted mean differences in HRQoL from baseline to 12-month follow-up were PCS: 0.1399 (95% CI, -1.3689; 1.6496) and MCS: 0.3603 (95% CI, -1.6788; 2.3994). No statistically significant differences were found concerning the adjusted outcomes between groups.

To summarize, the mean differences in the summary scores through the trial period were larger for the control group, which might suggest a more rapid deterioration over the 12 months in the control group compared with the intervention group. The difference was largest in the MCS, which points to a slower decline in mental health for the telehealthcare group. However, no statistically differences were found between groups.

The secondary outcomes - A subgroup analysis defined as posteriori was also conducted in this study and indicated no statistically significant effect of the intervention in any of the defined subgroups.

Discussion/Conclusion: This study was conducted to improve the evidence on the HRQoL of patients suffering from COPD. HRQoL was assessed from baseline to follow-up at 12 months in both groups, and these values were compared against each other. The findings indicated no significant differences in HRQoL over time between groups and subgroups. However, there was a trend towards positive effects in HRQoL among certain subgroups.

The study was based on our knowledge of the largest studies that on an international level, tried to create better evidence for telehealthcare in one chronic disease, namely COPD. The SF-36v2 (the Short-Form (36) Health Survey, version 2) was used to evaluate HRQoL from baseline to follow-up. The SF-36v2 is a generic and validated questionnaire that is used for both healthy and sick individuals; however, it might not be sensitive enough to detect a change in HRQoL among COPD patients. A more disease-specific questionnaire such as the St. George Respiratory Questionnaire would have been desirable as a supplement to assess changes in quality of life over time.

A comparison of the baseline values of FVC% between groups indicated that the intervention group was sicker than the controls. The difference in FVC% might explain why there was no significant difference in HRQoL between groups over

time. The Hawthorne effect could also have affected the outcome and led to the lack of difference between groups. Some of the COPD patients could have enhanced their engagement and changed their behavior simply as a result of their enrollment in the study and the increased awareness of being observed by researchers and healthcare providers.

In the future, the focus should be on finding answers for this study's lack of proven effectiveness. The reason for the lack of effects might be due to the fact that some patients benefit more from telehealthcare than others or that some municipalities in the North Denmark Region have been better about implementing telehealthcare than others. The specific subgroups should also be considered in assessing which patients will most benefit from telehealthcare. Identifiable effects may exist among subgroups of the intervention group. Thus, a mixture of both qualitative and quantitative research is needed to gain a clearer understanding of the relationship between quality of life and telehealthcare. More studies on a larger scale are not advisable until this relationship has been further investigated. Policy makers and healthcare providers should be directed towards other indicators for implementing telehealthcare in practice such as reducing costs, reducing mortality or improving clinical outcomes.

In conclusion, this study has obtained more evidence for the effects of HRQoL in telehealthcare. Based on the study results, the telehealthcare intervention supplemented with patient education did not improve the COPD patients' HRQoL over 12 months. However, telehealthcare with existing care did not lead to poorer HRQoL compared with usual practice.

CHAPTER 5. PAPER CONTRIBUTION

The following chapter includes the seven scientific papers that constitute the core of this PhD thesis. The full version of the thesis includes the papers in full text.

5.1. PAPER I

Effectiveness and cost-effectiveness of telehealthcare for chronic obstructive pulmonary disease: study protocol for at cluster randomized controlled trial

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Published in: Trials, 2014, vol. 15, No. 178, DOI: 10.1186/1745-6215-15-178

5.2. PAPER II

Heuristic evaluation of a telehealth system from the Danish TeleCare North trial

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Published in: International Journal of Medical Informatics, 2015, vol. 84, p. 319-326, DOI: 10.1016/j.ijmedinf.2015.01.012

5.3. PAPER III

User satisfaction and experience with a telehealth system for the Danish TeleCare North trial: a think-aloud study

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Presented at: the 25th Medical Informatics European Conference, MIE 2014, Istanbul, Turkey

Published by: IOS Press Ebook – Studies in Health Technology and Informatics, vol 205: e-health – For Continuity of Care

5.4. PAPER IV

An iterative, mixed usability approach applied to the Telekit system from the Danish TeleCare North trial

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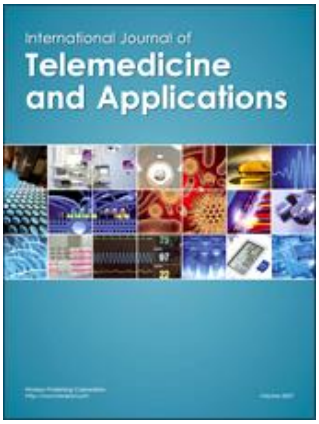
Submitted to: International Journal of Telemedicine and Applications, 2016



5.5. PAPER V

Exploring user experience of a telehealth system from the Danish TeleCare North trial

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Presented at: the 26th Medical Informatics European Conference, MIE 2015, Madrid, Spain

Published by: IOS Press Ebook – Studies in Health Technology and Informatics, vol 210: Digital Healthcare Empowering Europeans

5.6. PAPER VI

Specific technological communication skills and functional health literacy have no influence on self-reported benefits from enrollment in the TeleCare North trial

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5.7. PAPER VII

Telehealthcare for patients suffering from COPD: Effects on health-related quality of life - results from the Danish "TeleCare North" cluster-randomised trial

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CHAPTER 6. GENERAL DISCUSSION

In this chapter, an interpretation of the main findings derived from the three phases of the PhD study will be presented by providing answers to Q1-Q3. The interpretation of the main findings is followed by methodological considerations in which the strengths and limitations of the TeleCare North trial's intervention and outcomes regarding usability, user experiences, and HRQoL will be discussed. Finally, implications for practice will be discussed together with suggestions for future research.

This PhD study concerned COPD patients, a heavy burdened group of patients who incur high costs for both the patients and society (21,129). The increasing costs of care and the declining health resources create a need to change the management of COPD to one in which patients play a more active role in the treatment and care of their disease (57,58). Telehealthcare services have the potential to support user involvement and to promote higher professional, organizational and patient-perceived quality of overall healthcare, and they are being used increasingly to create more efficiency in healthcare (62,72,73). Implementing telehealthcare systems is often a costly expense that affects patients, clinicians, and other healthcare stakeholders, demonstrating the importance of choosing an adequate research design to evaluate interventions. Nevertheless, reviews have discussed the difficulty of making comparisons between telehealthcare and usual practice due to the lack of comparable research studies and evaluations (80–82). Consequently, there is still not enough evidence regarding the effects of telehealthcare (12,77,78), which has created a demand for large-scale studies, such as the TeleCare North trial, to evaluate such interventions.

The objective of this PhD study was to contribute to improving the body of evidence on telehealthcare by evaluating the TeleCare North trial's intervention. The PhD research had a more specific focus on: I) developing a trial protocol for the Danish, large-scale trial, TeleCare North; II) evaluating the trial's telehealthcare system regarding its usability and patient experiences; and III) evaluating the trial's outcome regarding health-related quality of life (HRQoL).

6.1. MAIN FINDINGS

The main findings of the PhD study will be described by providing answers to the following specific questions:

> *Q1: How can the TeleCare North trial be described in detail by a protocol clarifying all procedures for assessing the effectiveness and cost-effectiveness of the trial?*

Q2: Is the Telekit system user-friendly and what are the COPD patients' experiences with the system?

Q3: Are there any statistically significant changes in HRQoL between the two groups from baseline to 12-month follow-up?

6.1.1. PHASE I: DEVELOPMENT OF THE TRIAL'S PROTOCOL

How can the TeleCare North trial be described in detail by a protocol clarifying all procedures for assessing the effectiveness and cost-effectiveness of the trial?

The TeleCare North trial was among the biggest large-scale studies at the international level and was the first of its kind in Denmark to evaluate the effectiveness and cost-effectiveness of telehealthcare. The trial used a pragmatic cluster-randomized design to provide sufficient evidence on telehealthcare compared to usual practice in patients suffering from COPD. The effectiveness and cost-effectiveness were assessed by evaluating changes in health-related quality of life and costs from baseline to 12-month follow-up. The cost-effectiveness outcomes of the trial were not integrated into this PhD study, as the health economics domain pertained to another PhD student, Flemming Witt Udsen. The TeleCare North trial was carried out according to a research plan, more precisely a study protocol that contained all the steps (background, objectives of the study, study design, duration, participants, recruitment, randomization, intervention, outcomes, sample size, statistical, and ethical considerations) of the study.

Paper I comprised the fixed study protocol for the TeleCare North trial. The protocol was developed to clarify the trial procedure and to avoid poor scientific work with invalid data and incorrect statistical analyses. The TeleCare North trial was described according to the CONSORT Extension for Cluster Trials (130) to ensure transparency in the reporting process. The protocol was registered on www.clinicaltrials.gov before trial initiation and subsequently published in TRIALS.

COPD patients in the North Denmark Region were cluster-randomized to an intervention group or a control group. The control group received the existing usual practice, and the intervention group received telehealthcare along with the existing usual practice. The intervention group was provided the telehealthcare system, Telekit, and was trained in using the system by a healthcare provider at two planned appointments. Intervention group patients were instructed to measure their vital signs and to respond to questions on disease-related symptoms at home on fixed days after agreement with their respective GPs was reached.

The monitored data were reviewed by healthcare providers in the municipalities on scheduled days. The patients' data were transferred into risk profiles (red, yellow, green) based on threshold values to guide the healthcare providers in their identification and assessment of high-risk patients. The healthcare providers

contacted the patients if their data deviated from the normal threshold values with a risk of disease deterioration. The Telekit system was not an emergency service, and patients were therefore informed to consult their GPs or doctors in emergency services in case of exacerbations. After the TeleCare North trial's completion, the control group was also offered telehealthcare due to ethical considerations (see Paper I for further details about the TeleCare North trial's design and intervention).

6.1.2. PHASE II: EVALUATION OF THE TELEKIT SYSTEM'S USABILITY AND PATIENT EXPERIENCES

Is the Telekit system user-friendly and what are the COPD patients' experiences with the system?

The telehealthcare system, Telekit, used in the TeleCare North trial was developed with the purpose of improving patients' empowerment by involving the patients in caring for their illness and by increasing their coping skills through self-monitoring. Usability is a fundamental element to consider when offering telehealthcare to patients suffering from COPD (105,112,113). Living at home with a chronic disease can be very anxiety provoking and isolating (131,132), and COPD patients are typically elderly with limited cognitive and physical capabilities, highlighting the importance of striving to make telehealthcare as user-friendly as possible by modifying telehealthcare systems to the patients' needs (110,111). The current evidence points in general to positive user experiences with telehealthcare, but more knowledge within specific population groups is necessary, demonstrating the importance of testing the usability of telehealthcare systems (133).

Papers II-VI present the evaluation of Telekit's usability and the patients' experiences and satisfaction with the use of the system. In Paper II, a heuristic evaluation with five usability experts was performed to identify potential usability problems that could affect the success of the implementation of the Telekit system. The experts identified 152 usability problems, of which 86 were unique. Some of these problems were subsequently revised according to priorities to improve Telekit's design. The experts characterized the system as unfinished, but in general, there was consensus about the system's simple design and functionality, and the experts agreed that the system was suitable for COPD patients who were unfamiliar with technology. Subsequently, Telekit underwent improvements and was revised to address the usability problems in order of priority. However, the heuristic evaluation was not able to assess how the end users would interact with the system's interface, which called for more usability evaluations involving user testing.

In paper III, a think-aloud test was therefore performed in which six patients interacted with the Telekit system on the basis of constructed user scenarios. The patients were observed and asked to express their thoughts and feelings about the system as they performed the representative tasks. The think-aloud test resulted in

an evaluation of the Telekit's usability and the patients' satisfaction with the system. The findings confirmed that Telekit was user-friendly, as evidenced by the patients' satisfaction with the functionalities integrated in the system and by observing their interactions with the system.

An iterative, mixed usability approach was also conducted because the previous heuristic evaluations and think-aloud tests revealed that Telekit needed further design improvements. In Paper IV, the iterative approach encompassed a pre- and post-test, including the aforementioned heuristic evaluation and think-aloud test along with a new version of each test. These usability evaluations were compared and generated both qualitative and quantitative findings on the prevalence, severity, and content of the usability issues in Telekit. Most problems were identified in the post-test, which was surprising because it was assumed that fewer usability issues would occur after conducting more evaluations. The findings of Paper IV illustrated the importance of working iteratively and using mixed usability methods in the evaluation of telehealthcare systems.

In addition to the various usability tests, a survey, described in Paper V, was conducted in the patients' home to investigate more specifically the patients' self-reported benefits of using Telekit. These findings indicated that 53 (88%) perceived the system as easy to use. The patients experienced benefits regarding enhanced control (61.7%) and security (71.7%) after using the system. Additionally, 50% felt greater awareness of their COPD symptoms in responding to disease deterioration and some patients (26.7%) also perceived increased freedom. In Paper VI, associations were made between: I) the patient benefits of using Telekit and the patients' functional health literacy; and II) the patient benefits of using Telekit and their specific technological communication skills. These findings demonstrated that the patients' self-reported benefits attained by using the telehealthcare system were not associated with the patients' functional health literacy level and communication skills. Patients' communication skills and health literacy levels were revealed to not be prerequisites for the use of the Telekit system.

Overall, the series of usability evaluations from phase II showed that telehealthcare was an adequate service to help patients in their self-care. The Telekit system proved to be stable in operation and patients gained positive experiences from using the system. The Telekit system received criticism from several usability experts, who designated the system's app to be old-fashioned in design compared to newer apps. However, during the user tests, the patients expressed that they appreciated that the system was straightforward and easy to use. One noteworthy lesson derived from the series of usability studies was to keep the Telekit system as simple as possible (see Paper II-IV for further details about the series of usability studies).

6.1.3. PHASE III: EVALUATION OF THE TRIAL OUTCOME, HRQOL

Are there any statistically significant changes in HRQoL between the two groups from baseline to 12-month follow-up?

In Paper VII, an intention-to-treat analysis was carried out to evaluate the effects of HRQoL from baseline to 12-month follow-up. The primary outcome, HRQoL, of 1,225 COPD patients was evaluated, of whom 578 were in position of the Telekit system. The Short-Form (36) Health Survey, version 2, was distributed to patients at study enrollment and after 12 months to compare the two groups' HRQoL outcomes. The questionnaire contained 36 questions that measured patients' HRQoL based on a mental- (MCS) and a physical (PCS) summary score.

At baseline, the patients' mean age in the intervention group was 69.55 (9.36) years, and in the control group, it was 70.33 (9.11) years. The patients represented different degrees of disease severity, which were distributed as follows: GOLD I (6%), GOLD II (38%), GOLD III (39%) and GOLD VI (17%). No differences in baseline variables were found between the groups, except for a statistically significant difference in FVC% ($p < 0.05$).

The differences between the intervention and the control groups' HRQoL were compared, which indicated that telehealthcare compared to usual practice did not lead to poorer quality of life. A slower deterioration was observed among the intervention patients receiving telehealthcare. However, no statistically significant differences in HRQoL were identified between the intervention- and control group or between subgroups of the population.

In comparison with other studies, Cartwright et al. (134) studied a similar intervention in the Whole System Demonstrator Project (WSD) and found no improvement in HRQoL as a result of telehealth. Other comparable studies, e.g., the Virtual Hospital trial (135) and the Telescot study (136), likewise found no significant differences in HRQoL among patients with COPD. Thus, the findings from the TeleCare North trial correspond well with the mentioned studies' results. The rationale behind the TeleCare North trial's intervention, specifically enhancing patient empowerment with patient education and strengthening the organizational focus on detecting disease deterioration, was found to not be able to improve the patients' HRQoL.

6.2. METHODOLOGICAL CONSIDERATIONS

6.2.1. THE TELECARE NORTH TRIAL

Strengths and limitations of the trial

Trial design: At the international level, the TeleCare North trial was among the largest large-scale studies. At the national level, the trial was the first of its kind in the Danish context. The TeleCare North trial was constructed as a pragmatic, cluster randomized controlled design. The trial's purpose was to evaluate the effectiveness and cost-effectiveness of telehealthcare in addition to usual practice compared with only usual practice in patients suffering from COPD. This type of research design is relevant for studying a large number of people (137) and was selected to increase the feasibility of implementing the study in a real-life operational context. Another reason for selecting the study design was to avoid contamination and recruitment bias (138) (see Paper I for further details).

However, there are some limitations to applying this design in the evaluation of telehealthcare. Some research cannot be adequately addressed by a randomized trial such as complex interventions. Telehealthcare interventions are more complex than other types of interventions because they are dependent on human behavior, participant engagement, and other contributing factors (139,140). The effectiveness of telehealthcare is not only related to the effects of the service itself but also to the effects of a combination of intervention and context. Utilizing a mixed method approach to evaluate effectiveness might have been a better choice in the evaluation of the TeleCare North trial's intervention (141). A mixture of RCTs and other research designs and methods are appropriate to assess fully complex interventions (142). Using both qualitative and quantitative evaluation methods are needed as a supplement to the gold standard to explain why and how an intervention actually works (143). Implementing telehealthcare in routine care is considered to be a complex intervention that involves a number of components: people, processes, infrastructure, and technologies, and the outcomes of these interventions therefore depend on these components. Using a mixed methods approach, it might be possible to achieve an understanding of the complex link between these components in the context of a given intervention.

The inclusion and exclusion criteria: The inclusion and exclusion criteria were similar to those used in other telehealthcare studies and those listed in the GOLD guidelines (21) to increase comparability. The broad range of COPD patients with different stages of COPD severity may have improved the trial's external validity. The external validity could lead to an understanding of the mechanisms that produce the effects (e.g., the interaction between intervention and context, including patients, relatives, and care personnel).

Patient recruitment: The recruitment of patients was delegated to GPs in the North Denmark Region from May 2013 to November 2013. To support the identification of patients for inclusion, patient lists with potential COPD patients were generated for each clinic/hospital. A conflict between the Danish Medical Association (www.læger.dk) and Danish Regions (www.regioner.dk) limited some GPs' motivation to include a sufficient number of patients, which also led to the hospitals' involvement in the enrolment process. However, the general practices referred approximately 900 patients and the hospitals approximately 300 patients during the inclusion period. According to the research protocol, the same inclusion criteria were used at the hospitals and in the practices.

Cluster randomization: The randomization was performed by an external person who was not affiliated with the trial. In contrast to WSD (134,144–147), the randomization of patients was not at the general practice level but rather at the municipality district level. In that way, we prevented healthcare providers in the same municipality district from providing care for patients in both groups. The randomization divided the patients into two comparable groups, in which no differences in case distribution between the two groups were found except for in FVC%. The intervention group's FVC% was slightly higher than that of the control group. Therefore, it can be argued that the patients in the telehealthcare group were sicker at baseline than the control group.

Study duration: The study duration was limited to 12 months due to ethical considerations and other reasons such as related costs. Patients in the control group should have received the same offer of telehealthcare after 12 months. A longer follow-up period would be desirable to examine the long-term effects. However, the timeframe of 12 months was considered appropriate to detect these long-term effects.

The effect size: The effect size was estimated by findings from a previous Norwegian study; (148) combined with an expected dropout rate of 10%, the estimated required total sample was 800 patients. The recruited sample of 1,225 patients was considered large enough to detect a minimal clinically important difference in HRQoL.

Instruction of patients on telehealthcare: The instructions provided to the patients were carried out in the municipalities in different ways because the training in the Telekit was completed by either the health care centers or the district nurses. Several municipalities had both individual and group training, and some of the municipalities might have been better at educating and organizing the telehealthcare services than others. However, all municipalities' instructions were based on the same training guidelines produced by the trial's Administration Office.

Data collection: The data analysis followed the intention-to-treat principle, in which all patients were analyzed according to the group to which they were randomly assigned to provide the strongest possible basis for inference about the treatment effects and to eliminate all risks of bias (149).

After the inclusion of patients in the trial, GPs electronically transferred threshold values based on baseline measurements for each patient to the municipalities and to the trial's Administration Office. Several of the baseline clinical measurements were not noted, which caused some missing values in the data analysis.

Loss to follow-up was also a cause of missing values in the data analysis. The most frequent reasons for dropout were deaths, relatives' deaths or disease deterioration, which affected the patients' abilities or resources to participate in the TeleCare North trial. Some patients withdrew due to a lack of cognitive function or emigration from the North Denmark Region. A small number of patients chose to leave the trial due to technical issues with the Telekit or due to disappointment in not belonging to the intervention group.

In Paper VII, the COPD patients were stratified into the four GOLD groups (I-IV) (21) based on their FEV1 value; this indicated that the majority of patients were in the moderate (II) to severe (III) stages of COPD. It would have been more desirable to use the updated GOLD classification (A-D) (21), which ranks patients based on other factors and symptoms in addition to their degree of airflow obstructions. In that way, it would have been possible to delineate more appropriate subgroups.

Effectiveness Outcomes: The primary outcome of effectiveness was change in HRQoL at the individual level from baseline to 12-month follow-up. The secondary outcomes were changes in mortality and physiological parameters from baseline to 12-month follow-up. The secondary outcomes still need to be evaluated, as some effects of the telehealthcare intervention might be observed among these outcomes. Other valid and reliable measures of outcomes of interest could have been used in the evaluation such as anxiety, depression, etc. However, HRQoL was selected as the primary outcome to enhance the comparability to other telehealthcare studies.

6.2.2. THE TELEKIT SYSTEM'S USABILITY AND PATIENT EXPERIENCES

Strength and limitations of the usability studies

The series of usability studies (Paper II-VI) performed on the Telekit system had some advantages and disadvantages.

First of all, the usability studies supported the process of the Telekit system CE being marked and approved as a medical device class II, which can be used for clinical decision support.

Second, all usability tests (Paper II-IV) were designed in collaboration with at least a second author of the paper to ensure credibility. The usability tests were recorded, and a plan for each test was developed before conducting the usability tests to help manage and organize the usability evaluations.

Third, the choice to use mixed usability evaluation methods iteratively elicited several perspectives on the use of the Telekit system. The experts and COPD patients focused on different aspects of usability. The experts paid attention to the system design and functionalities, whereas the patients focused on the meaning behind the use of the system. The overlooked usability issues that were not identified in one evaluation method could be discovered by repeating the test or by another evaluation method. The choice of using mixed evaluation methods is also supported by usability expert, Jakob Nielsen (150).

Lastly, the think aloud tests (Paper III, IV) were completed by real end users, which strengthens the representativeness. The usability tests (Paper III-VI) took place in the patients' home in real settings, which was assumed to provide a safer and more pleasant environment, which could expedite the patients' thoughts about the Telekit.

A limitation was that the COPD patients had received instructions on the system in advance, which could have led to the formation of habits in using the system. It would have been interesting to test inexperienced patients; however, the Telekit was not designed for use without instructions.

In Papers V and VI, a non-standardized self-reported questionnaire was used to explore the patients' user experiences with the Telekit. Psychometric tests were not performed on this questionnaire, but these tests could have enhanced the questionnaire's construction, reliability, and validity.

6.2.3. OUTCOME OF THE TELECARE NORTH TRIAL

Strength and limitations of the outcome evaluation

A generic validated questionnaire, the SF-36, version 2, was utilized in the evaluation of HRQoL, the outcome of the intervention. The SF-36 is validated and considered to be an appropriate measure to compare changes in HRQoL between groups (151). Nevertheless, it would have been optimal to use a disease-specific questionnaire as a supplement. The SF-36 may not be sensitive enough to detect changes in HRQoL among COPD patients, suggesting a disease-specific questionnaire would be suitable as an alternative (152). Reviews by Chen (152) and Engström et al. (153) have also confirmed the importance of using a combination of generic and disease-specific questionnaires. However, this combination was not chosen because it could encumber patients with yet another questionnaire and because of the risk of receiving fewer responses.

The lack of a significant difference could be due to the duration of the trial period. The 12-month follow-up was perhaps too short a period to identify a change in HRQoL. However, the sample size calculation was designed to detect differences in HRQoL between the groups, making this possibility more unlikely. The non-significant results could also be explained by the fact that telehealthcare was a new technology that required patients and healthcare providers to learn how to use the technology. COPD patients should learn to manage their disease condition in relation to its symptoms and the overall burden that comes with living with the disease. Another explanation that might have affected the patients' quality of life was that the Telekit system simply did not address all of the patients' needs.

The underlying mechanisms, including improved patient empowerment and increased organizational focus, failed to demonstrate effectiveness. These mechanisms were intended to provide effects, making it unclear what types of other factors have a decisive role in demonstrating detectable effects. A combination of the SF-36 questionnaire and qualitative interviews would have been preferable to obtain a more nuanced picture of the complex connection between quality of life and telehealthcare in patients with COPD.

The choice of primary outcome, HRQoL, used to evaluate the effectiveness can also be discussed. HRQoL was an appropriate measure because it is frequently used to assess the effects of such interventions and is a valid measure to assess QoL in the population (151). Other alternative outcome variables of clinical characteristics could have been selected, but due to time constraints, they were not included in this PhD study.

6.3. IMPLICATIONS FOR PRACTICE

The outcomes (Paper VII) of this trial suggest that telehealthcare in addition to usual practice did not improve the HRQoL of patients with COPD. However, some subgroups might experience potential benefits in HRQoL from using telehealthcare. The lack of a significant difference in effect between the intervention and control groups indicates that additional telehealthcare will not benefit all patients, nor the average COPD patient. Telehealthcare may provide patient satisfaction and enhanced security, freedom, control, and awareness of symptoms but not increased health (Papers II-VI).

Policymakers, stakeholders, and healthcare providers should consider the purposes and effects that define the underlying reasons for implementing telehealthcare, e.g., costs, clinical outcomes, or mortality. Additionally, stakeholders should identify strategies to direct telehealthcare to the COPD patients who are most likely to benefit from such interventions. This knowledge is essential in designing telehealthcare systems that are better tailored to the individual and the context of use.

6.4. FUTURE DIRECTIONS AND PERSPECTIVES

The TeleCare North trial's intervention has been integrated as a general offer for patients with COPD in the North Denmark Region. Policymakers and stakeholders in the Region have also decided to deploy a large-scale study in patients with heart failure. This new large-scale study will be implemented over a two-year period from December 2015 to November 2017.

Local Government Denmark has also decided to spread the use of telehealthcare to COPD patients nationwide. The national implementation will be based on the TeleCare North trial's gained experiences. In the national implementation, decision-makers considered the experiences and findings from the TeleCare North trial in the way that health gains existed for the subgroup with severe COPD, GOLD stage III (21). Therefore, telehealthcare will be deployed nationally for this group despite the fact that we have not actually demonstrated this assumption, and this should, therefore, be examined more specifically and preferably before national implementation.

There are also other unknown areas that should be investigated further, and future research still needs to address the following:

- The usability evaluations performed through this PhD study included only COPD patients as users. Future usability evaluations of the system should also consider the perspectives of other users, such as the healthcare providers, to adapt the system to their needs of monitoring patients' data.

- Usability is one factor that can promote satisfaction with telehealthcare systems such as Telekit. Other factors could also have been addressed to guarantee satisfaction such as organizational factors and patient factors. These factors should be considered in future studies.

- Future research should investigate the patients' user experiences in the TeleCare North trial after a longer follow-up period to explore whether their experiences change.

- Consideration should be given to integrating other functionalities in the Telekit system, such as motivating training functions.

- Building on the experiences learned from the TeleCare North trial, it could be useful to consider assessing whether the effects concerning HRQoL are distinct between patients suffering from COPD and those with heart disease.

- The underlying mechanisms and preconditions required to enhance patients' HRQoL need to be explored through qualitative research.

- A mixed research approach exploring patients' quality of life by combining the SF-36 with individual interviews might increase the understanding of this study's outcome.

- More research is needed to examine which patients benefit the most from telehealthcare because some patients may experience a greater benefit from telehealthcare than others. A priori-defined subgroup analyses for COPD using clinical outcomes should, therefore, be carried out.

- The possibility of standardizing the selection of patients based on a stratification decision support system that selects patients on the basis of telehealthcare outcomes combined with other socio-demographic and health characteristics should be investigated.

- Evaluations of the outlined secondary clinical outcomes of the TeleCare North trial have to be performed.

CHAPTER 7. CONCLUSION

In conclusion, this PhD thesis attempted to describe the TeleCare North trial's research design and to evaluate the Telekit system regarding HRQoL, usability, and patient experiences. In this chapter, the answers to the three research questions (Q1, Q2, Q3) of the PhD study are provided:

> *Q1: How can the TeleCare North trial be described in detail by a protocol clarifying all procedures for assessing the effectiveness and cost-effectiveness of the trial?*

Patients suffering from COPD in the North Denmark Region were asked to participate in the TeleCare North trial and randomized to telehealthcare in combination with usual practice or usual practice, alone. In the protocol, the research design of the TeleCare North trial and all the procedures used to assess effectiveness and cost-effectiveness were presented to ensure transparency (Paper I).

> *Q2: Is the Telekit system user-friendly and what are the COPD patients' experiences with the system?*

Telekit has proven to be capable of monitoring COPD at a distance. The usability evaluations of the system indicated that the Telekit system needed design and functionality improvements, but in general, the patients expressed positive user experiences and satisfaction with the system. There will be continuing need for evaluation of the telehealthcare system through an iterative process to adapt the system to the COPD patients' needs (Paper II-VI).

> *Q3: Is there any statistically significant changes in HRQoL between the two groups from baseline to 12-month follow-up*

The work presented in this thesis found no statistically significant differences in HRQoL between groups from baseline to the 12-month follow-up. Thus, based on these findings, the TeleCare North trial's telehealthcare intervention cannot be recommended as a potential service to enhance COPD patients' HRQoL. However, the telehealthcare intervention might have other clinical, economic or organizational effects that simply have not been addressed in this PhD study. These results have provided insights into the effects of telehealthcare on HRQoL. Although no significant differences between treatment groups and subgroups were found, a trend towards a slower disease deterioration in HRQoL was observed within certain subgroups of the intervention group when compared with those receiving usual care. This slower deterioration may indicate that at the least, telehealthcare does not lead to poorer HRQoL over time (Paper VII).

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SUMMARY

The healthcare system is facing challenges regarding the treatment of chronic obstructive pulmonary disease (COPD), which necessitating alternative ways to treat these patients. Telehealthcare could be this alternative. A range of studies have been conducted to evaluate the effectiveness of telehealthcare, but they generally conclude that there is a need for more large-scale studies to obtain sufficient evidence. In this context, a Danish large-scale trial (TeleCare North) was launched in the North Denmark Region in 2012 to enable the management of COPD from patients' home environments through telehealthcare. The overall aim of this dissertation was to evaluate the TeleCare North trial's intervention. The PhD thesis focused more specifically on I) developing a trial protocol for the Danish, cluster-randomized, large-scale trial, TeleCare North; II) evaluating the trial's telehealthcare system, Telekit, in terms of its usability and patient experiences; and III) evaluating the trial's outcomes regarding health-related quality of life (HRQoL). These focus areas were addressed in seven papers.

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