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PhD thesis:

Heart and mind: The use of screening and digital health innovations

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Papers included in the thesis and additional relevant publications

Paper 1:

Systematic screening for anxiety and depression in cardiac rehabilitation – are we there yet?
Charlotte Helmark, Alex Harrison, Susanne S. Pedersen, Patrick Doherty. *Int J of Cardiol* (2022): doi: 10.1016/j.ijcard.2022.02.004

Paper 2:

Internet-based treatment of anxiety and depression in patients with ischaemic heart disease attending cardiac rehabilitation: a feasibility study (eMindYourHeart).
Charlotte Helmark, Robert Ahm, Christina M. Andersen, Søren J. Skovbakke, Robin Kok, Uffe K. Wiil, Thomas Schmidt, Jacob Hjelmborg, Lisbeth Frostholm, Ditte H. Frydendal, Tina B. Hansen, Ann-Dorthe Zwisler and Susanne S. Pedersen. *European Heart Journal - Digital Health* (2021). doi.org/10.1093/ehjdh/ztab037

Paper 3:

A web-based intervention for patients with an implantable cardioverter defibrillator – a qualitative study of nurses' experiences (Data from the ACQUIRE-ICD study).
Charlotte Helmark, Cecilie L Egholm, Nina Rottmann, Søren J Skovbakke, Christina M Andersen, Jens B Johansen, Jens C Nielsen, Charlotte E. Larroudé, Sam Riahi, Carl J. Brandt, Susanne S Pedersen. *Submitted to Patient Education and Counselling Innovation – IN REVIEW*

Additional papers published during the PhD - not included in the thesis:

Nurses' perceptions of feedback from cardiac rehabilitation registries: a qualitative study across the UK and Denmark.
Helmark C, Egholm CL, Kousgaard MB, Zwisler AD, Doherty P. *Br J of Cardiac Nurs* (2019). doi: org/10.12968/bjca.2018.0029

"Struggling with practices" - A qualitative study of factors influencing the implementation of clinical quality registries for cardiac rehabilitation in England and Denmark.
Egholm CL, Helmark C, Doherty P, Nilsen P, Zwisler AD, Bunkenborg G. *BMC Health Serv Res* (2019). doi: 10.1186/s12913-019-3940-5.

Efficacy and cost-effectiveness of a therapist assisted web-based intervention for depression and anxiety in patients with ischemic heart disease attending cardiac rehabilitation [eMindYourHeart trial]: randomised controlled trial protocol.
Pedersen SS, Andersen CM, Ahm R, Skovbakke SJ, Kok R, Helmark C, Wiil UK, Schmidt T, Olsen KR, Hjelmborg J, Zwisler AD, Frostholm L. *BMC Cardiovasc Disord.* (2021). doi: 10.1186/s12872-020-01801-w

Return to work: does cardiac rehabilitation make a difference? Danish nationwide register-based study.
Pedersen SM, Kruse M, Zwisler AD, Helmark C, Pedersen SS, Olsen KR. *Scand J Public Health* (2021). doi: 10.1177/14034948211062656.

Effects of screening for anxiety and depression in patients with ischaemic heart disease – a nationwide Danish register study.
Kruse M, Laudicella M, Olsen KR, Zwisler AD, Helmark C, Pedersen SS. *Scand J Public Health* (2022). doi: 10.1177/14034948221074972

Implementation of systematic screening for anxiety and depression in cardiac rehabilitation: Real world lessons from a longitudinal study.
Egholm CL, Helmark C, Rossau HK, Munkehøj P, Brøndum S, Pedersen SS, Zwisler AD. *J. Psychosom. Res.*(2022). doi:org/10.1016/j.jpsychores.2022.110909

Preface

This PhD thesis has been conducted while being employed at Department of Cardiology at Zealand University Hospital in the period 2019-2022.

Conducting the PhD has been a wild roller-coaster ride, as I have been obtaining invaluable research knowledge, skills, and great networking possibilities, while simultaneously having to deal with the break-out of a pandemic and a personal loss.

I am grateful to each and everyone who have supported me in any way, overcoming minor and major challenges throughout this PhD journey, I could not have done this without your support! Unfortunately, I am not able to mention you all, but to some people I would explicitly like to express my gratitude.

First of all, I would like to thank my main supervisor, Susanne Schmidt Pedersen, for tremendous support. You have patiently shared academic knowledge, generously invited me into your research networks, trusted me to find my own way in the world of research while at the same time being ready to guide me and listen to all my ups and downs. While fellow PhD students experienced long delays in response from their supervisors, I nearly experienced the opposite 😉. I always received fast and respectful feedback on my numerous inquiries, making it possible to move on in my various processes with no delay – even at times like Christmas. I cannot thank you enough!

I would also like to thank my two co-supervisors. First Tina B. Hansen, who made this PhD possible as she needed PhD students to supervise in her academic career pathway, opening this opportunity for me. Despite finding a new career path halfway through my PhD, I owe Tina many thanks for multiple academic discussions - also in the years prior to my PhD - and for showing the way in nursing research. To Christina Maar Andersen, for being supportive all the way through this journey, contributing with valuable feedback and practical experiences of the psychological treatment in the studies, and for always spotting the little errors in the tables.

I would like to thank the whole NACR team for their always friendly support and making a research stay in gorgeous York possible, as COVID-19 restrictions eventually diminished. Especially, I owe Professor Patrick Doherty many thanks for being so supportive and allowing me to follow a research idea, and for always being ready for academic discussions and a nice chat. Big thanks to Alex Harrison for good discussions, very patient guidance throughout the statistical work, and support in setting up the IT connection from Denmark to University of York. This made access to the NACR data possible, as I had to do all statistical analysis remotely because of the COVID-19 restrictions. Thanks to Jess Hemmingway, Nerina Onion, and Corinna Petre – you are all doing a tremendous job.

To Søren Skovbakke Jensen and Robert Ahm at Department of Psychology, SDU: Thanks to both of you for hours of networking, plenty of fruitful discussions, cake eating, and basically making my life as a PhD student more fun – I have very much appreciated the collaborating with you!

In times of trouble, I was so fortunate to have Cecilie Lindström Egholm to lean on. Thank you ever so much for your support, for opting in on the qualitative study, and for sharing drinks along the way when needed, it is ALWAYS a great pleasure to collaborate with you.

I owe thanks to the Department of Cardiology at Zealand University Hospital for supporting me in many ways. Especially thanks to head nurse Jytte Hykkelbjerg Bruhn, who are struggling to make nursing research become an integrated part of our department. Thanks to Bianca F. Bernth and Rikke L. Storkegård at the front office for always being extremely helpful with both smaller and bigger issues of all sorts, it means a lot! Many thanks to Gitte E. Ingwersen for exchanging endless opinions over the years, being helpful and sharing plenty experiences both inside and outside our office.

Many other persons have cheered along the way, such as Birgitte Blume, Bibi Hølge-Hazelton, Birgitte Sjöberg, Ann-Dorthe Zwisler, Karin Johansen, along with friends and family – thank you for that.

Last, but not least, I owe massive thanks to my three children, Karoline, Ida, and Malthe - you have supported me in so many ways along this PhD journey. Especially by helping with plenty IT-related practicalities such as designing figures and fine-tuning of documents. Having grown-up children is certainly not a bad thing when doing a PhD. But most of all, thank you for just being there and understanding that from time to time “mum is a BIT busy” 😊. Your support means the world!

Lotte Helmark
May 2022

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1. Introduction

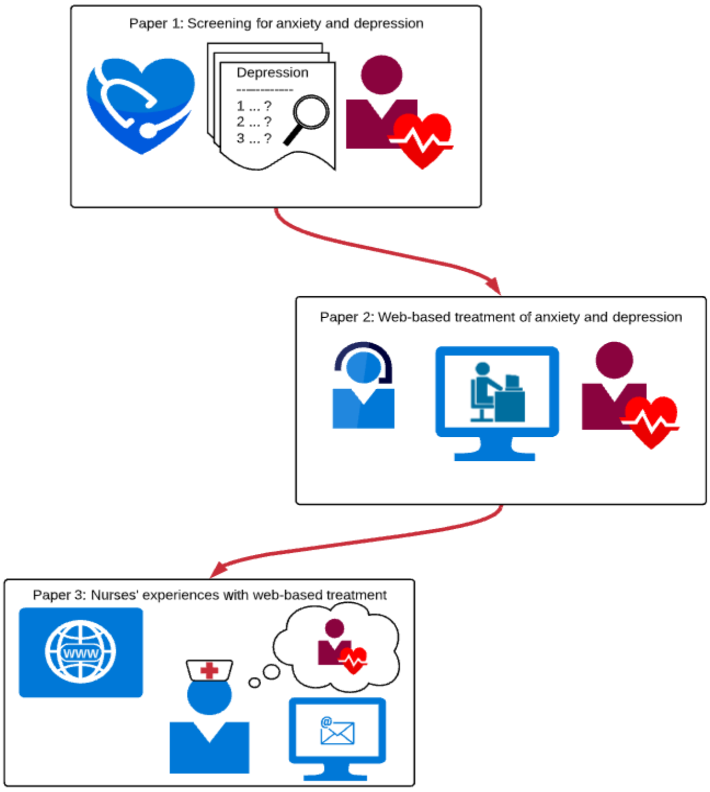
The crossfield between cardiology and psychology has always been the main topic of my interest as a nurse, as I have met so many cardiac patients in clinical practice who have struggled with different levels of psychological distress after being diagnosed with a cardiac disease.

I find the health care system excellent for treating cardiac diseases, as well as developing and investing in new innovative treatments as for instance medication and technology. But somehow the psychological dimension of being a patient with a cardiac disease has not obtained the same attention in the health care system as the underlying somatic disease. These patients must adapt to life with a chronic cardiac disease and tackle this situation for the rest of their lives, which for some patients are relatively easy to manage while many other patients struggle to obtain psychological wellbeing and an acceptable quality of life (QoL).

This thesis is structured around three papers with different aspects of psychological distress in cardiac patients and how the health care system can improve assessment and management of this for the benefit of the patients.

In very brief, the scope of the three papers is illustrated in Figure 1: (1) Screening for anxiety and depression in cardiac patients; (2) Web-based treatment of anxiety and depression among cardiac patients; (3) Cardiac nurses' experiences with web-based treatment.

FIGURE 1. ILLUSTRATION OF THE THREE PAPERS INCLUDED IN THE THESIS



The term cardiac disease covers a wide range of specific cardiac diagnosis, and this term will be used in the thesis whenever the text does not refer only to a specific cardiac diagnosis.

Digital health is a broad term which entails a large variety of concepts such as telerehabilitation, telemonitoring, electronic health records, artificial intelligence, and mobile health applications. In this thesis the digital health innovations in the papers are related to web-based psychological treatment and cardiac nurses' experiences with a web-based model of telerehabilitation.

1.1 Guidance with respect to reading the thesis

The thesis is built upon the three mentioned papers, each based on different data sets and carried out using different research methodologies. All three papers are inserted as appendices. Part 2 of the thesis presents the background and the relevance of the three research projects and how they are interlinked. Part 3 of the thesis describes each study separately, with presentation of the study design and theoretical framework followed by the methodologies used, key results, discussion, and limitations of the individual papers. Part 4 comprises the main discussion, including insights learned from the conducted research. Part 5 contains summaries in English and Danish, respectively.

2. Background

2.1 Cardiac disease and cardiac rehabilitation

More than 108 million people are living with cardiovascular disease in Europe, placing a substantial burden on both the individual person as well as society [1]. Patients with ischemic heart disease (IHD) is the largest group with a prevalence of 34.9 million cases and an incidence of 3.6 million per year in the 54 member countries of the European Society of Cardiology (ESC) [1]. Moreover, cardiovascular diseases are responsible for 3.9 million deaths annually in Europe, equivalent to 45% of all deaths [2]. The burden of cardiovascular diseases is not only related to health, but also to the challenge of increased healthcare costs which is estimated to be €210 billion per year in Europe [1,2]. Given the high prevalence and incidence of cardiovascular diseases, it is paramount to provide evidence-based cardiac rehabilitation (CR) in the most effective way.

The World Health Organization has defined CR as: *"The sum of activities required to influence favourably the underlying cause of the disease, as well as to provide the best possible physical, mental and social conditions, so that the patients may, by their own efforts, preserve or resume when lost as normal a place as possible in the community."* [3].

CR is a complex evidence-based multidisciplinary intervention, consisting of a range of components including patient assessment, management and control of cardiovascular risk factors, exercise training, dietary advice, and psychosocial support [4]. Evidence-based CR is shown to reduce morbidity, mortality, and healthcare costs, improve QoL and to be cost-effective [5-7]. Still, CR is underutilized despite the highest-ranking recommendations from the ESC (Class 1 level A) [4,8,9], where simple lack of referral might be a barrier for participation [10].

2.2 Prevalence and implications of anxiety and depression in patients with cardiac diseases

The global INTERHEART case-control study was the first to report that depression and perceived stress accounted for 32.5% of the population attributable risk for myocardial infarction, across continents, sex, and age [11], implying that these psychological conditions should be recognised and modified where possible. A bidirectional relationship between depression and IHD has been evidenced, pointing at both IHD being associated with depression and depression being associated with IHD [12], however the mechanisms linking these two conditions are not fully understood [13]. Anxiety and depression are well-known in patients with cardiac diseases [14], and with a significantly higher prevalence than in the general population [15]. The prevalence of anxiety and depression has some variation across cardiac diagnoses, for instance a review on patients with heart failure found a prevalence of clinically relevant depression of 21.5% [16], while another review found that 36% of females and 29% of males reported symptoms of depression after a myocardial infarction [17]. In general, the prevalence of anxiety disorders among patients with cardiac diseases is estimated to be approximately 30% [15,18], and for depression, 15-25% of patients with a cardiac disease meet the criteria for major depression with an even higher proportion of the patients having clinically relevant symptom levels of depression [14,19]. Anxiety and depression are not temporary conditions, as studies have found persistent high prevalences for both conditions up to one-year follow-up [20-22]. Anxiety and depression are not always present at the time of the cardiac event but might also occur at later points of time in the cardiac treatment pathway [23-24].

Anxiety and depression in cardiac patients are associated with poor QoL and poor health outcomes, including increased risk of recurrent cardiac events, morbidity, and mortality [14]. In addition, depression in cardiac patients is also associated with increased societal costs [25-26]. Anxiety and depression act as barriers to behaviour change and adherence to CR [4,27], which is a paradox since participation in CR at the same time is shown to reduce anxiety and depression [9]. Predictors for anxiety and depression in cardiac patients are multiple, and consist of patient characteristics such as female gender, living alone, having a high number of comorbidities, low educational level, living in areas of social deprivation, high body mass index, physical inactivity, and smoking [18,28-29].

2.3 Assessment of comorbid anxiety and/or depression in patients with cardiac diseases

The gold standard for assessing clinical depression is a diagnostic interview [13]. Due to restrained resources in the healthcare system, alternative assessments can be standardised questionnaires, where patient-reported outcomes (PROs) are used to assess symptoms of anxiety and depression [14]. Commonly used PRO questionnaires within cardiology are for instance the Hospital Anxiety and Depression Scale (HADS) [30], the Patients Health Questionnaire (PHQ-9) [31] and the Generalized Anxiety Disorder (GAD-7) [32]. These questionnaires entail various numbers of questions, leading to a cumulated score where cut-off scores indicate whether a patient is at risk or not. The questionnaires are all validated and found suitable to use in routine CR when clinicians are screening for anxiety and depression [19].

Identifying patients with comorbid anxiety and/or depression are crucial to improve health outcomes of this vulnerable subgroup, and professional societies have recommended screening for anxiety and depression in CR for more than a decade [33-34]. A recent position paper from the European Association of Preventive Cardiology, emphasizes that assessment and management of psychosocial issues - including anxiety and depression – is a core component of CR across cardiac diagnoses [4]. Also, a scientific statement from the American Heart Association concludes that the cardiac disease should not be treated in isolation, but mind, heart and body should be treated as a hole [35], leading to a more holistic approach to patients with cardiac diseases. The European

Association of Preventive Cardiology has developed a programme for accreditation of CR delivery, and this programme includes a quality indicator requiring a >10% improvement in anxiety and depression scores to achieve accreditation [36]. Despite these initiatives, the literature shows a gap between clinical guidelines and clinical practice [37-39], indicating an unsystematic approach to screening for anxiety and depression in routine CR.

2.4 Management of anxiety and depression in patients with cardiac diseases

Obviously, identifying anxiety and depression is not sufficient. To improve health outcomes and QoL in cardiac patients these modifiable psychological risk factors need to be recognised and managed during CR as they are risk modifiers of cardiac diseases [4,14]. Evidence-based treatment for reducing symptoms of anxiety and depression in cardiac patients includes psychotropic medication, psychological interventions, and exercise-based CR [13,40-42]. The literature shows that anxiety and depression in cardiac patients are undertreated [18,39], and in a national survey among incident Danish cardiac patients, the patients reported lack of psychosocial healthcare [43]. A Cochrane review found that psychological interventions improved psychological symptoms and reduced cardiac mortality in patients with coronary heart disease, however, the extent of efficacy was questioned due to clinical heterogeneities of the included studies [44]. Challenges in this review include complex psychological interventions with poor reporting of the intervention components making it difficult to understand the active ingredient [44]. However, in clinical care patients are complex with different needs and preferences, also indicating that psychological interventions might have to be differentiated to be effective as the one-size-fits-all approach might not be the right approach for the individual patient [27]. This suggests that research is still warranted to explore the right dose and the right components for effective psychological management of anxiety and depression in patients with cardiac diseases.

At the patient level, barriers in the general population for seeking help for mental health issues include fear of stigma [45] and low level of education [46]. Among patients with cardiac diseases, lack of information and reluctance to uptake of mental health care are reported as perceived barriers, alongside with practical barriers such as costs and transportation [47]. Timing of screening and referral is also reported as barriers for seeking help related to mental health issues, with patients preferring longer time for follow-up on mental health issues as they experienced these often worsened over time [47]. This is in alignment with a previous study, which identified new onset of anxiety and depression up till 24 months post-implant of an implantable cardiac defibrillator (ICD) [23], suggesting that screening once in the patient treatment pathway is not sufficient.

2.5 Digital health interventions to patients with cardiac disease and comorbid anxiety and/or depression

Digital health solutions for patients with cardiac diseases have been developed, tested, and discussed for years, also prior to the coronavirus disease 2019 (COVID-19) pandemic [48]. Even so, the COVID-19 pandemic induced a need for accelerated implementation of remotely delivered health care interventions due to a reduction in in-person healthcare [49-51].

With respect to delivery of psychological digital health interventions, a systematic review found small to moderate effect of internet-based cognitive behavioural therapy (ICBT) for treatment of anxiety and depression in patients with a chronic disease [52]. Studies on ICBT in cardiac populations are sparse and results heterogenous. Two randomized controlled trials (RCTs) reported no either short-term or long-term effect on anxiety and depression in patients with acute myocardial infarction [53-54], and no effect on depression in patients with heart failure, respectively [55]. Contrasting this, two other RCTs reported positive effects of ICBT on anxiety and depression in patients with an acute coronary event [56], and both short-term and long-term effect on depression in patients with cardiovascular diseases, respectively [57-58]. Potential explanations for these heterogenous results can be the complexity of the interventions, with for instance different levels of adherence to the treatment, different numbers and content of the treatment modules, and different professional backgrounds of the involved therapists (cardiac nurses versus psychologists). This indicates that ICBT holds a potential for treating anxiety and depression in cardiac patients, but further research is warranted to identify the right content and dose to achieve the optimal effect for the individual patient.

Transitioning from in-person health care to digital health care also entails a shift in the role of health care professionals [48], which may be challenging for the involved health care professionals when implementing digital mental health care in routine care [59]. Barriers and facilitators for digital health in terms of telerehabilitation are studied more widely from the perspective of cardiac patients [60], while literature on cardiac health care professionals' perspectives on telerehabilitation are limited. One study on barriers and facilitators for digital lifestyle support found that health care professionals in cardiac care recognized the potential advantage of digital health solutions but also perceived a range of barriers [61]. Thus, further research is needed to better understand the health care professionals' experiences and beliefs, as incorporating their needs and values might enhance uptake of digital health innovations for the benefit of the cardiac patients.

2.6 Objectives of the thesis

The objectives of the thesis are:

a) To investigate if the likelihood that patients with acute coronary syndrome (ACS) are screened for anxiety and depression - as part of routine CR - is associated with patient- and provider level characteristics.
b) To examine the feasibility of an eHealth intervention targeting anxiety and depression in patients with IHD - integrated in routine CR - as a precursor to an RCT.
c) To explore cardiac nurses' experiences with a web-based telerehabilitation model for patients with an implantable cardioverter defibrillator (ICD).

3. Theory, methodology, key results, and discussions of papers

3.1 Study 1: An observational study of screening for anxiety and depression in routine CR (Paper 1)

3.1.1. Study design

The quantitative study "Systematic screening for anxiety and depression in cardiac rehabilitation – are we there yet?" was conducted using an observational retrospective design [62]. The context of the study was execution of routine CR in the United Kingdom (UK), using clinical quality data collected as part of the National Audit of Cardiac Rehabilitation (NACR) [63]. The clinical quality data were explored for determinants of patient- and provider level characteristics associated with screening for anxiety and depression.

3.1.2. Theoretical framework

RCTs are - based on their high level of control - considered the gold standard of quantitative research and are most appropriate to use when testing hypotheses and causation [64]. However, the aim of this study was to explore associations between screening procedure and patient- and provider characteristics without conclusion of causation. Due to this aim, an observational study was appropriate despite the lower ranking in the evidence hierarchy and the risk of confounding factors [64].

The use of observational registry data collected in routine care has the advantage that these data are closer to "real-life" cardiac care, and thus represents the population to a broader extent. The analysis and findings that can be gained from this methodology benefit from including representation from patient groups that may be excluded in RCTs, such as patients with older age or comorbidities, due to restricted eligibility criteria [8]. NACR contains a large number of cases, increasing the generalisability and statistical power. Despite these large numbers, data in NACR must still be considered incomplete since not all eligible patients are enrolled in CR [8] and some data on various variables are missing in the reported cases (Paper 1) [62]. In addition, not all CR settings in the UK report to NACR as this is voluntary, increasing the risk of selection bias.

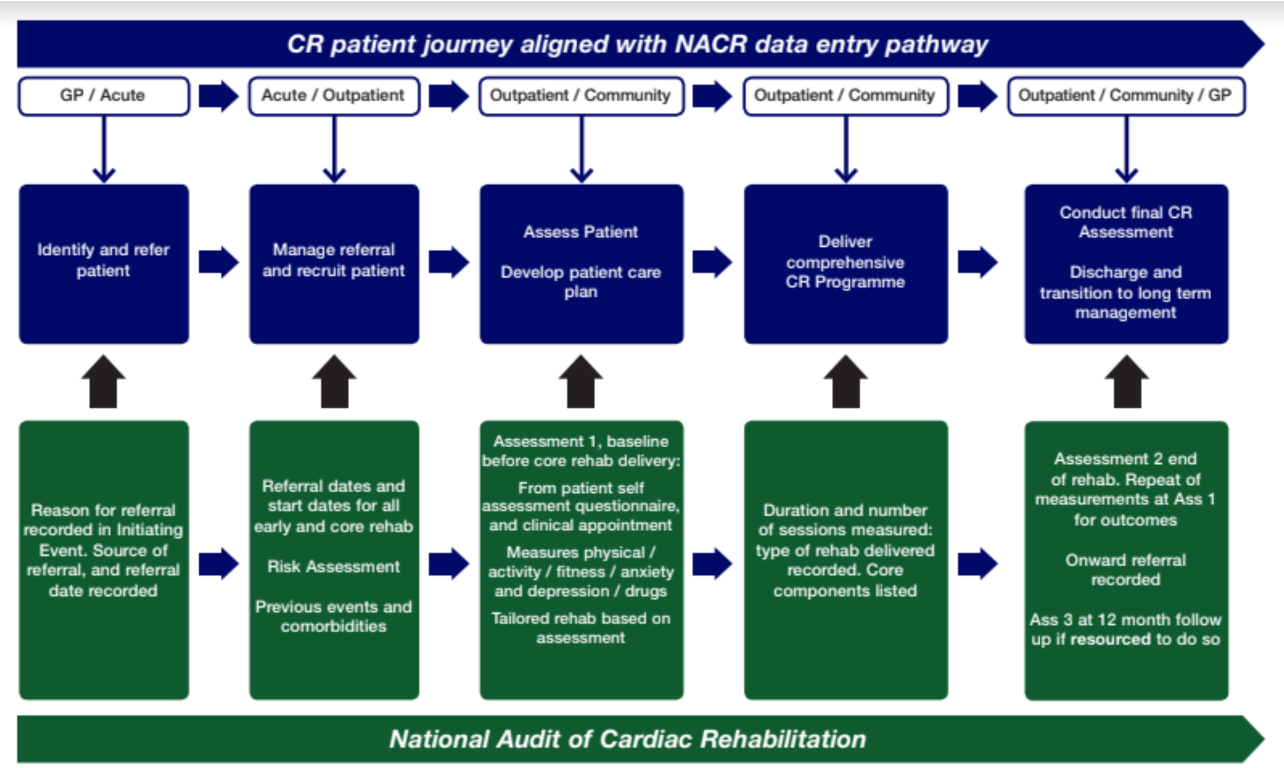
3.1.3. Participants and data collection

Data were collected in routine CR in the UK, anonymised, and transferred to University of York who hosts the NACR data [63]. NACR aims to monitor the quality of CR both on local and national levels, identify inequalities in CR delivery and support quality improvements in CR for the benefit of all eligible patients.

Participants consisted of patients with a pre-CR assessment (Assessment 1 in Figure 2) and a diagnosis of ACS, who had started CR in the period from 1st January 2016 to 31st December 2019 (n=138,018). We abstained from including patients participating in CR during 2020 since CR delivery was severely impacted by the COVID-19 breakout [63], and therefore could have skewed the results.

NACR collects data from different points of the CR patient journey as illustrated in Figure 2. The white boxes indicate where in the CR journey the patient is treated, while the blue boxes indicate the provider level CR tasks, and the green boxes indicate which type of data is collected. In this study, we have extracted individual patient level data from the first three collection points in Figure 2. In addition, data used for certification of CR centres are collected through the patient journey. Certification requirements consist of fulfilment of the seven key performance indicators (listed in Appendix IV), decided by the British Association of Cardiovascular Prevention and Rehabilitation (BACPR) [65].

FIGURE 2. THE PATIENT CR JOURNEY ALIGNED WITH COLLECTION OF NACR DATA



Permission to use the figure in the thesis is obtained from NACR.

The outcome of the study was constructed as a binary variable where patients were characterized as either screened for anxiety and depression or not. Patients were identified as screened if both domains of the HADS or both the PHQ-9 and GAD-7 were reported to NACR. Exposure measures consist of sociodemographic, clinical variables, and provider-level variables which are described in detail in Paper 1 [62].

3.1.4. Statistical analysis

Descriptive statistics were used to present baseline characteristics as counts with percentages and means applying standard deviation and range. To explore baseline differences between the groups of screened versus non-screened patients, we used Student's t-test for continuous variables and the Chi^2 test for categorical variables.

A logistic regression model is suitable to predict the likelihood of an event happening – and in this case the event is screening for depression. To explore the association between the outcome (screening for depression as the dependent variable) and the exposures (the independent variables), we conducted a multivariate logistic regression based on variables identified in the literature [66] and expert opinions since literature were sparse. Odds-ratios (OR) were applied to assess the magnitude of association with the included variables, with OR>1 indicating higher odds for the event to happen and OR<1 indicating lower odds for the event to happen [67]. NACR data contains 18 comorbidities [29] but we chose to remove erectile dysfunction as this is a male only condition and a sensitivity analysis showed it would have skewed the results. Comorbidities included anxiety and depression which we beforehand chose to keep in the regression model, as previous anxiety and depression are well-known predictors for recurrence of these conditions [28] and we wanted to explore if this was reflected in screening practice. For the remaining 15 comorbidities we conducted a stepwise backward selection. This meant removal of further eight comorbidities because of statistical insignificance (angina, arthritis, cancer, rheumatism, emphysema, claudication, family history of cardiovascular disease, and dyslipidaemia), leading to the inclusion of n=9 comorbidities in the final regression model (anxiety, depression, osteoporosis, chronic back problems, asthma, chronic obstructive pulmonary disease, diabetes, stroke, and hypertension).

As multivariate logistic regression models only include cases with complete data, missing data could potentially impact the results and therefore should be tested. We used a stepwise forward selection for test of impact, starting with core variables (age, gender, anxiety, and depression) followed by groups of variables on sociodemographic, clinical data, and provider level data, respectively. Despite reduction of cases, the significance levels of the variables did not change in these first four steps. The final step was inclusion of the variable Index of Multiple Deprivation (IMD) which impacted gender and marital status, so they were no longer significant. This suggests that living in areas of multiple deprivation overrides these two factors in determining the likelihood for being screened for anxiety and depression. Since previous studies have shown a strong association between IMD and psychosocial burden [14] as well as mortality [68], we chose to keep this variable in the model. The full dataset is presented in the Supplements of Paper 1 [62]. Another approach that could have been used to handle missing data was multiple imputation which is a statistical technique that estimates plausible values for the missing data [69]. However, as our approach showed satisfactory robustness, we chose not to impute data.

Furthermore, we examined prevalence of anxiety and depression in this population by applying the commonly used clinical cut off score of eight [30], indicating that patients with HADS anxiety scores ≥8 were categorized as having clinically relevant anxiety and patients with HADS depression scores ≥8 were categorized as having clinically relevant depression. HADS scores were reported as means with standard deviations and range and prevalence as counts with percentages. We also stratified the prevalence on IMD, to test if these conditions were evenly distributed across the population. We did not include data from PHQ-9 and GAD-7 in this stratification as they were sparsely used and had different cut-off scores than HADS.

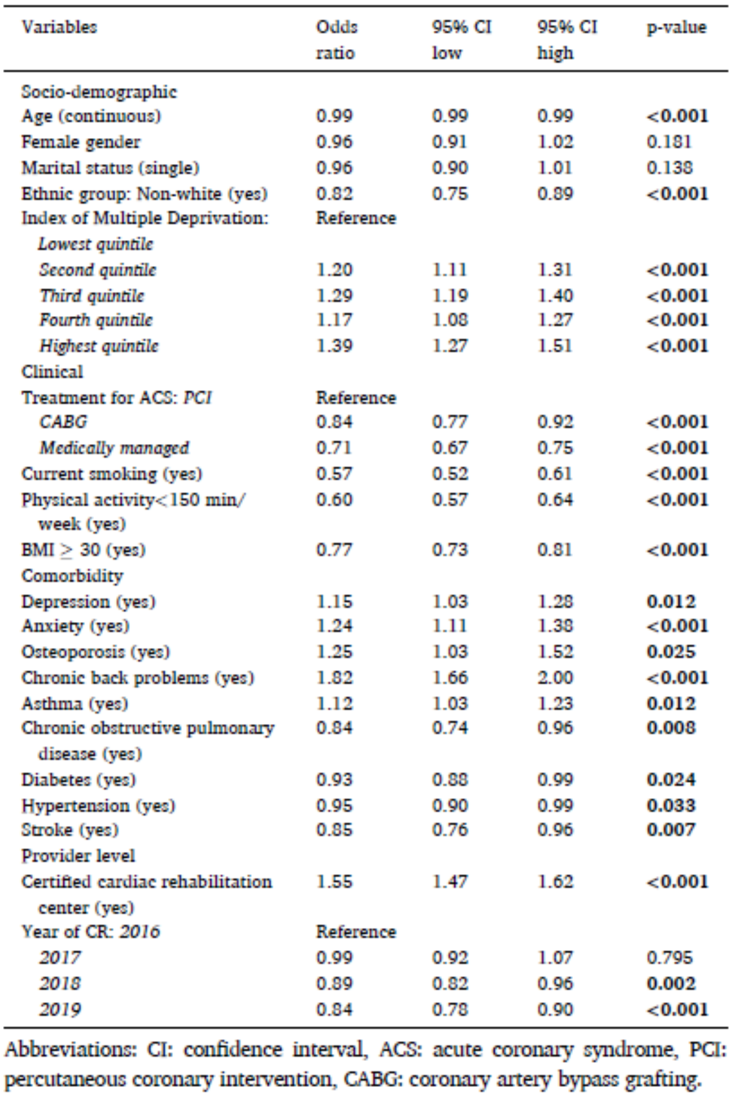
All analyses were performed using Stata version 16, and we applied a statistical significance level of 5%.

3.1.5. Key results

The study population consisted of n=138,018. Out of these, 59.8% were screened for anxiety and depression and 40.2% were not. We found a p-value<0.001 for the difference between screened versus non-screened patients on all baseline characteristics, as shown in Paper 1 [62].

The multivariate logistic regression model included 44,119 cases and is illustrated in Table 1. On patient-level variables, we found that younger patients and patients with non-white ethnicity were less likely to be screened for anxiety and depression, while there was no association between being screened and gender and marital status, respectively. Patients living in the most deprived areas were less likely to be screened compared to patients living in the least deprived areas. Patients treated for ACS with coronary artery bypass grafting or conservative treatment (i.e., medically managed) were less likely to be screened compared with patients treated with percutaneous coronary intervention. We found that patients who were current smokers, were physically active <150 minutes per week or had a body mass index ≥30 were less likely to be screened. Regarding comorbidities we found a mixed picture, with patients having comorbid depression, anxiety, osteoporosis, chronic back problems, or asthma were more likely to be screened, while patients with comorbid chronic obstructive pulmonary disease, diabetes, stroke, or hypertension were less likely to be screened. On provider-level variables we found that certified CR centres were more likely to screen for anxiety and depression compared to uncertified centres, and in the years from 2016 to 2019 we found a negative trend in the likelihood of screening practice.

Table 1. Multiple adjusted odds-ratios for screening for anxiety and depression (n=41,119)



Variables	Odds ratio	95% CI low	95% CI high	p-value
Socio-demographic				
Age (continuous)	0.99	0.99	0.99	**<0.001**
Female gender	0.96	0.91	1.02	0.181
Marital status (single)	0.96	0.90	1.01	0.138
Ethnic group: Non-white (yes)	0.82	0.75	0.89	**<0.001**
Index of Multiple Deprivation: *Lowest quintile*	Reference			
Second quintile	1.20	1.11	1.31	**<0.001**
Third quintile	1.29	1.19	1.40	**<0.001**
Fourth quintile	1.17	1.08	1.27	**<0.001**
Highest quintile	1.39	1.27	1.51	**<0.001**
Clinical				
Treatment for ACS: *PCI*	Reference			
CABG	0.84	0.77	0.92	**<0.001**
Medically managed	0.71	0.67	0.75	**<0.001**
Current smoking (yes)	0.57	0.52	0.61	**<0.001**
Physical activity< 150 min/ week (yes)	0.60	0.57	0.64	**<0.001**
BMI ≥ 30 (yes)	0.77	0.73	0.81	**<0.001**
Comorbidity				
Depression (yes)	1.15	1.03	1.28	**0.012**
Anxiety (yes)	1.24	1.11	1.38	**<0.001**
Osteoporosis (yes)	1.25	1.03	1.52	**0.025**
Chronic back problems (yes)	1.82	1.66	2.00	**<0.001**
Asthma (yes)	1.12	1.03	1.23	**0.012**
Chronic obstructive pulmonary disease (yes)	0.84	0.74	0.96	**0.008**
Diabetes (yes)	0.93	0.88	0.99	**0.024**
Hypertension (yes)	0.95	0.90	0.99	**0.033**
Stroke (yes)	0.85	0.76	0.96	**0.007**
Provider level				
Certified cardiac rehabilitation center (yes)	1.55	1.47	1.62	**<0.001**
Year of CR: *2016*	Reference			
2017	0.99	0.92	1.07	0.795
2018	0.89	0.82	0.96	**0.002**
2019	0.84	0.78	0.90	**<0.001**

Abbreviations: CI: confidence interval, ACS: acute coronary syndrome, PCI: percutaneous coronary intervention, CABG: coronary artery bypass grafting.

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With respect to stratification of prevalence on anxiety and depression on IMD, we found statistically significant trends for both conditions with increasing prevalence for more deprived areas (p<0.001).

3.1.6. Ethical considerations

The study has been conducted in alignment with the Helsinki declaration [70]. The use of observational patient level data for research might not be considered a personal risk for the individual patient, however patients are entitled to know what their health data are being used for and confidentiality of these sensitive data need to be protected. The NACR data are securely hosted at University of York through approval from the UK National Health System (NHS Digital). Through annually renewed agreements between these two parts, the use of anonymised NACR data is allowed for quality improvement purposes without needing individual consent from patients or any specific ethical approval. The patients have the right to withdraw their data from the NACR at any time. Even though consent is not required, the NACR encourages clinicians to inform patients of the purpose of collecting these data and the details of how data are used is described in the patient assessment questionnaires [71].

3.1.7. Discussion of Paper 1

The rationale for focusing on screening for anxiety and depression in CR in this study, was to explore if we could identify any determinants for the likelihood of being screened, and thereby seek to inform and thus improve quality of care within CR. As we did identify determinants and thereby inconsistency in screening for anxiety and depression, with this paper we aimed both to inform and support the clinical staff in improvement of screening procedures and to inform decision-makers of potential gaps in the quality of CR delivery.

The benefit of screening for depression in CR has been debated during the past years, as no effects of screening are shown on cardiac outcomes [72-73]. One RCT found that systematic screening in patients with ACS did not result in statistically significant changes in quality-adjusted life-years or depression-free days [74]. However, this could be caused by low acceptability and low adherence to treatment for depression in that specific study [47,74], and given this is only one study and it did not assess cardiac outcomes, further research is needed to potentially alter clinical guidelines on systematic screening in CR.

The most remarkable results of the current study were the low level of screening in patient subgroups with high risk of anxiety and depression. For instance, modifiable risk factors such as smoking, being physically active<150 minutes per week, and having a body mass index≥30 are all associated with elevated risk of anxiety and depression [28], yet patients with these risk factors had reduced odds for being screened. From a clinical perspective it is hard to imagine that patients were deliberately selected for non-screening based on these risk factors, but a possible explanation could be the severe impact of psychosocial burden. We found an increasing prevalence of both anxiety and depression for more deprived areas, and risk factors such as smoking, reduced physical activity, and high body mass index are likewise more prevalent in areas of multiple deprivation [75]. So, we can speculate if clustering of these risk factors means that CR clinicians in deprived areas are in high need of prioritizing restrained clinical time, in case of managing multiple risk factors at the same time in patients with ACS, leading to reduced resources to conduct the screening procedure and possibly the reporting of data to NACR [76]. However, no causation can be drawn based on these observational data [64], so further research is needed to gain an in-depth understanding of this.

In addition to this, with the prevalence of anxiety and depression being higher in the most deprived areas, and at the same time patients were less likely to be screened in these areas, the true prevalence could potentially be even higher in the most deprived areas and the distributing of anxiety and depression across IMD even more uneven. A recent Danish study among patients with

IHD found that low income, low level of education and a high comorbidity burden were negatively correlated with being screened for anxiety and depression in CR [39], so this supports our findings and suggests that inequity in CR delivery happens across countries.

One way to monitor screening for anxiety and depression in CR is the use of clinical quality registries [77]. Clinical quality registries such as the NACR [63] and the Danish Cardiac Rehabilitation Database [78] aim to monitor and improve the quality of CR, and the data collected in routine care can be used to showcase for instance inequity in CR delivery. From a global health perspective, the new International CR Registry (ICRR) has also been developed for low-resource settings aiming to harmonize CR assessment across countries and to improve quality of CR delivery in low- and middle-income countries [79]. Barriers for data entry to clinical quality registries are previously reported [76,80], so data from the registries are dependent on either well-functioning data capture from electronic health records or registries and/or reliable data entry from the CR settings to be considered trustworthy [77].

Given the high volume of data in this study and knowing the study population have attended CR, we consider the results representative, with the limitations of potential selection bias in terms of (1) a suboptimal reporting of screening results to NACR and (2) a minority of UK CR centres do not report data to the NACR.

To sum up, we identified inconsistency in screening for anxiety and depression in routine CR and our results indicates that quality improvement is needed especially in high-risk groups and that action is needed to mitigate inequity in CR delivery. Clinicians are encouraged to reflect upon their screening procedures and potentially the data entry process. Equally important, decision makers are encouraged to ensure sufficient resources and incentives for systematic screening for anxiety and depression in CR to improve outcomes for this vulnerable subgroup of patients with ACS and comorbid anxiety and/or depression.

3.2 Study 2. A feasibility study of internet-based treatment of anxiety and depression among patients with IHD in routine CR (Paper 2)

3.2.1. Study design

This mixed-methods study “Internet-based treatment of anxiety and depression in patients with ischaemic heart disease attending cardiac rehabilitation: a feasibility study (eMindYourHeart)” was conducted using a prospective interventional design [81]. The context of the study was an online psychological intervention to patients with IHD and comorbid anxiety and/or depression, recruited from nine CR centres across Denmark. The study was a precursor to a larger RCT [82], and the feasibility was assessed with respect to drop-out rate, changes in HADS scores, utility and use of intervention, and evaluation of the experiences of patients and CR nurses with the intervention, respectively.

3.2.2. Theoretical framework

The purpose of a feasibility study is to assess important parameters that may have a bearing on a larger main study, such as an RCT [83]. There is no gold standard for a feasibility study, thus the chosen design and outcomes are based on key features around the main study, such as feasibility to recruit patients or patients' adherence to the intervention [83,84]. A feasibility study can be a small RCT or not, depending on the purpose of the study, and there is no gold standard with respect to sample size [83]. Hence, it is important to decide which features are critical in the main study and apply sample size and outcomes according to this. For instance, even though evaluation of efficacy is part of the main RCT study due to a control group and the necessary statistical power, limited efficacy can be a key focus area in a feasibility study in order to evaluate if the intervention appears promising [84].

3.2.3. Participants and data collection

Quantitative part

The participants in the psychological intervention consisted of n=29 Danish patients with IHD, participating in routine CR, who had screened positive for anxiety and/or depression (HADS≥8) at the start of CR. Patients were recruited consecutively from nine CR centres across Denmark. In- and exclusion criteria are described in detail in Paper 2 [62].

Self-reported data (sociodemographic, HADS scores pre- and post-intervention, and the utility questionnaire) were collected and entered into the Research Electronic Data Capture database (REDCap) [85], while clinical data were extracted from the Danish Cardiac Rehabilitation Database [78]. Data on drop-out were also entered in REDCap, while data on patients' engagement with the intervention such as number of logins and time spend on the treatment platform were collected from the General Data Protection Regulation (GDPR) secure treatment platform.

Qualitative part

The participants in the two separate evaluations consisted of: (1) All patients who had completed the intervention (n=22) were invited, and n=14 patients agreed to provide feedback on the intervention and their experiences; (2) All CR nurses involved in the recruitment process (n=24) were invited and n=14 CR nurses across all nine participating CR centres agreed to evaluate their experiences with the procedures around the intervention.

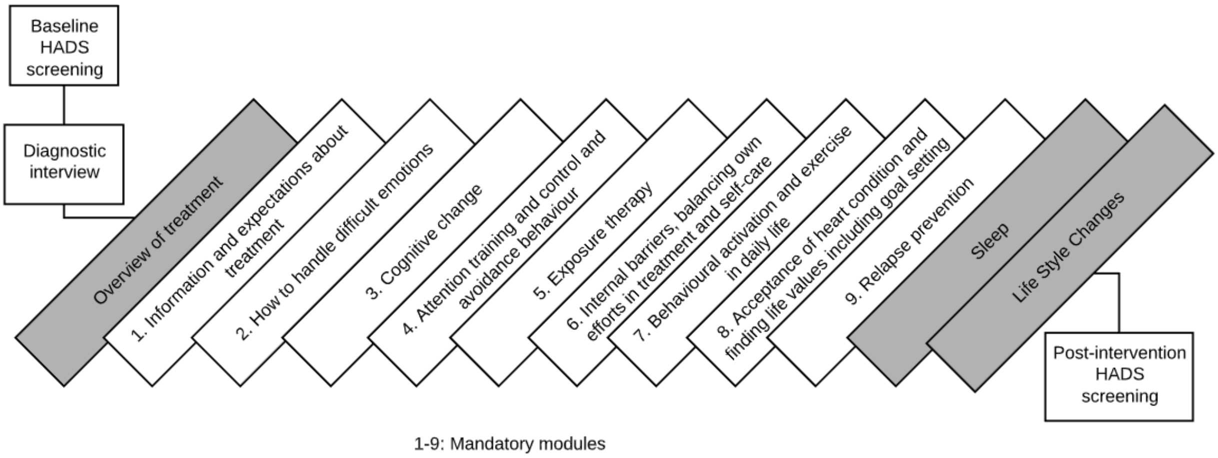
Both evaluations consisted of written purpose-designed open-ended questions. Participants received an email, containing a link to the designated questionnaire in REDCap. Answers were collected in open text to allow for broad feedback and to enable participants to provide supplementary comments in case the questions did not capture all their experiences. The evaluations were pilot tested on both respective target populations. For both evaluations, all participants were given the possibility to evaluate by phone interview if preferred, but no one chose this option.

3.2.4. The eMindYourHeart intervention

The intervention was delivered through a GDPR compliant platform hosted by the Research Clinic for Functional Disorders and Psychosomatics at Aarhus University Hospital in Denmark. Patients accessed the platform using two-factor authentication including a personal digital signature issued by the Danish authorities (NemID).

Prior to the feasibility study, a participatory design study had been conducted to engage the target population in the development of the intervention to make it as meaningful for patients as possible [86]. The intervention consisted of 12-week therapist-supported ICBT, covering the psychological components described in Figure 3. The intervention is described in detail in Paper 2 [81]. Alongside with working through their written assignments in the modules, patients had four scheduled phone contacts with their therapist (including the diagnostic interview). Patients could send and respond to messages in asynchronous chats with their therapist at any time they preferred, with the therapist responding within 2 working days. Further phone contact could be assigned in case the patient expressed a need.

FIGURE 3. OVERVIEW OF THE EMINDYOURHEART INTERVENTION



Reprint from Helmark et al. 2021 [81] *with permission from Oxford University Press. The unnumbered modules are voluntary.*

3.2.5. Analysis

Quantitative analysis

All analyses were performed using descriptive statistics and the statistical software Stata version 16. The drop-out rate was the primary outcome of the study, and the criteria for success was decided a priori as a drop-out rate <25%. This was based on a systematic review that found a drop-out rate of 28% across 40 studies for therapist-guided web-based ICBT for depression [87]. There is no gold standard for measuring adherence in ICBT [88], hence we chose that a minimum of five mandatory modules had to be finalised for a patient to be considered non-drop-out, as this would ensure patient engagement in multiple components of the psychological intervention (Figure 3). Secondary outcomes included changes in HADS scores and use and utility of the intervention. HADS scores were collected pre- and post the 12-week intervention and reported as means with standard deviations (SD) and range. The use of the intervention was likewise presented as means with SD and range and reported for completed patients by number of logins and the total time that patients spent on the platform. In addition, the number of contacts between patient and provider, and the duration of intervention reported in weeks. We divided the time of the logins into "inside" versus "outside" ordinary office hours to assess patients' preferences of when to engage in the intervention. Inside office hours was defined as Monday-Friday from 8 am to 4 pm, excluding public holidays. Regarding utility of the intervention, this was evaluated using six generic questions from the Internet Evaluation and Utility Questionnaire [89], as these specific questions were considered relevant for the context of this study.

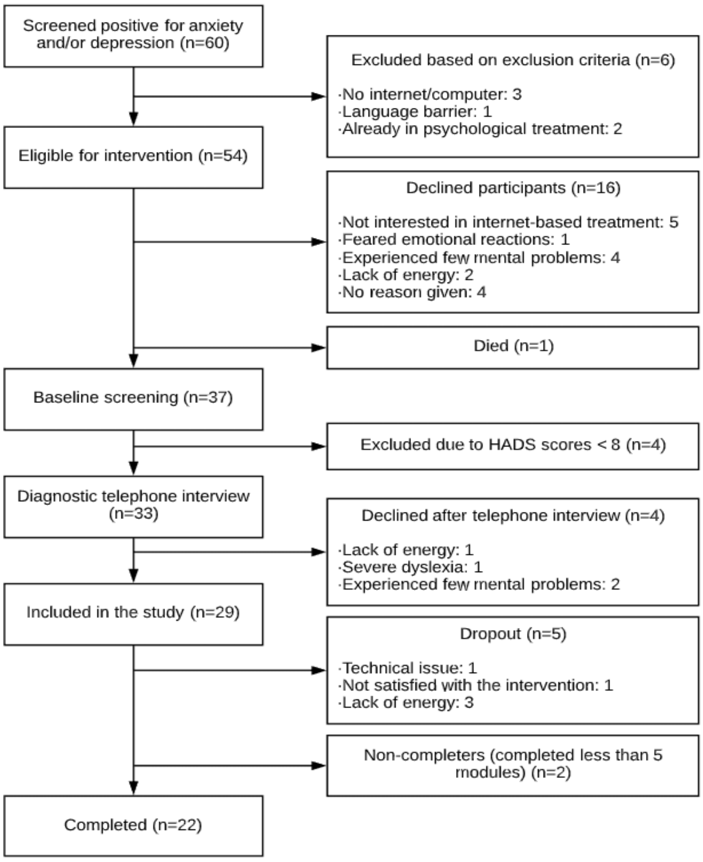
Qualitative analysis

Both evaluations were analysed using thematic analysis, inspired by the methodology described by Braun and Clarke [90]. The process is described in detail in Paper 2 [81] but includes stepwise stages in terms of reading the text repeatedly, systematic manual coding of the text, combining codes into categories and themes, while reflecting and going back and forth throughout this creative process, looking for patterns of meaning. We strived to take an inductive approach in this data-driven analysis, hence no theory or framework was chosen to guide the analysis [90]. Choosing to conduct the evaluations in writing was based on the reasons that (1) these were minor parts of the feasibility study, and a full-scale qualitative study would require much more resources. (2) We had been inspired by a conference presentation in 2019 from "Improving Access to Psychological Therapies (IAPT)", which is an English health service that provides evidence-based psychological therapy to people with anxiety disorders and depression [91]. The IAPT presentation described successful use of written evaluations, however, we have since not been able to identify the publication reporting on what was presented during the conference. (3) We were not looking for in-depth experiences with the intervention and the procedures at this stage, but more interested in how we could improve the structure of these matters to optimize recruitment and adherence.

3.2.6. Key results

The primary outcome was drop-out rate. Out of 54 eligible patients, 29 were included in the study (Figure 4). Of these 29 patients, 22 completed the intervention according to our criteria, leading to a drop-out rate of 24.1% (7/29).

FIGURE 4. FLOWCHART OF THE STUDY POPULATION



Reprint from Helmark et al. 2021 [81] *with permission from Oxford University Press*

Regarding changes in HADS scores, we found mean improvements of 5.5 (SD 4.6) points for anxiety scores and 4.6 (SD 5.1) for depression scores, respectively. With respect to the use of the intervention, patients who completed the intervention had a mean of 8.0 (SD 3.9) phone calls, a mean of 19.7 (SD 22.6) written messages and spent a mean of 10.96 hours (SD 6.5) on the treatment platform. The intervention lasted on average 13.3 (SD 2.8) weeks. Patients were on average logging on to the platform 33.5 (SD 13.4) times, with 59.4% of the logins being within office hours. Concerning utility of the intervention, the majority of patients who completed the intervention reported that the intervention was easy to use, it kept their interest, was useful and easily understood. Also, the majority reported not being worried about their privacy when engaging in the intervention, however, a few were “somewhat” or “mostly” worried.

From the thematic analysis of patients’ evaluation, four themes were derived: treatment platform, intervention, communication with therapist, and personal experience. The patients generally experienced the treatment platform as user-friendly, but few experienced the logon procedure cumbersome. Patients were overall highly satisfied with the intervention, but some found the workload too high. All patients were highly satisfied with the communication with their therapist. With respect to personal experiences, all patients reported a variety of positive experiences, such as better understanding of own feelings and reactions, being positively surprised of the concept, and obtainment of tools to cope with difficult thoughts and feelings. Still, some patients found it difficult with insufficient time to work through the modules and a high workload.

With respect to the nurses' experiences, three themes were identified: intervention, inclusion procedures, and collaboration with study team. The nurses were all positive towards the intervention, basically just happy about having a psychological treatment to offer to their patients. Nevertheless, they experienced that some patients were reluctant to engage in an online treatment or that for some patients the offer came too soon in the CR pathway. Concerning inclusion of patients into the study, nurses experienced being well introduced to the procedures, however, they still found it burdensome as it was an additional task on top of an already busy clinical practice. All nurses felt well supported by the study team and that the collaboration worked well.

3.2.7. Ethical considerations

This study was approved by the Danish Data Protection Agency (17/41433) and the Regional Committee of Health Research Ethics for Southern Denmark (S-20180024) and was conducted according to the Helsinki declaration [70]. To protect confidentiality most study data were collected and entered into the REDCap database, an international GDPR-secure platform for data management of research data [85], while the remaining data were collected and kept at the GDPR-secure treatment platform at Aarhus University Hospital. Both patients and CR nurses received information about the purpose of the study and gave informed written consent, giving them the right to withdraw their consent at any time without consequences. In combination with the diagnostic interview prior to inclusion, patients were informed more in-depth about the practical elements of the intervention. This resulted in four patients declining participation (Figure 4), however this was found more ethical than pursuing an intervention with reluctant or incapable patients. As patients received a psychological intervention, all (including drop-out patients) were monitored closely by their individual therapist to ensure no harm from the intervention were done to these potentially vulnerable patients. Out of the 22 patients who completed the intervention, three reported worse outcomes on the HADS post intervention due to personal conditions outside the intervention. Two of these were granted a prolongation of the intervention period, resulting in clinically relevant improvements in HADS scores. The third patient was highly affected by COVID-19 induced social isolation and was supported by extra phone calls by the therapist and guidance in how to deal with the situation.

3.2.8. Discussion of Paper 2

The primary outcome of the feasibility study was drop-out rate, which was 24.1%, and thus below the a priori determined threshold of 25%. This suggests acceptable patient adherence to the intervention, which is important as low adherence is previously reported in an ICBT study in cardiac patients [53], and could potentially dilute the efficacy of the intervention in the RCT.

With respect to changes in HADS scores, we found the improvements encouraging, while being aware of the limited efficacy in an uncontrolled feasibility study [84].

Reported negative patient experiences with ICBT are – among others – complicated log-in procedures, time-consuming, and too little time to work on the modules [92]. Even though we have tried to accommodate this by involving patients in the development of the intervention [86], these negative experiences were also reported in our feasibility study. This may suggest that an even more patient-centred approach is necessary as some patients might find ICBT burdensome no matter the extent of assignments. Noticeably, these patients enrolled in ICBT have comorbid anxiety and/or depression – some severely – such that for some patients even a minimal effort could be perceived as very burdensome and thus might impact adherence. Cardiac patients from a previous study [92] had 19 suggestions for improvements of ICBT, and among these were: (1) allow longer time for working on the modules perceived relevant by patients, (2) offer telephone calls with therapists, (3) make the outcome questionnaires easier to understand, and (4) make the intervention more fun. Regarding (1), this was in alignment with the findings from our feasibility study. In the eMindYourHeart RCT, patients will have access to the modules six months post intervention, giving patients the opportunity to spend extra time afterwards on modules which they find meaningful [82]. This does not solve the problem that some patients prefer the intervention prolonged to have enough time for each individual module, however, from a research perspective this was the best possible choice as the purpose of the eMindYourHeart RCT was to evaluate efficacy and cost-effectiveness of a 12-week intervention. However, further research is needed to explore if specific modules are perceived particularly burdensome, or if some patient subgroups need more time than estimated to optimise adherence, e.g., patients with low level of eHealth literacy [93]. Regarding (2), offering telephone calls with therapists, this component was part of our intervention and much appreciated by the patients as it helped building a therapeutic alliance. As reported in Paper2 [81], the mean number of phone calls was higher than expected in our study (n=8.0), which could be potentially problematic in the RCT study when estimating cost-effectiveness, as this would mean increased costs. However, we included the last patient in the study concurrently with the first national lockdown in Denmark due to the COVID-19 outbreak. The lockdown compromised a large part of in-person CR activities globally [94], including Denmark, and the involved therapists of our intervention reported many COVID-19 related contacts from worried patients who had most CR activities cancelled, in line with reporting in the literature [51]. To accommodate this, we integrated targeting COVID-19 related worries in the intervention, and thereby hoped to reduce the mean number of phone calls in the RCT. With respect to patient suggestion (3) – making the outcome questionnaires easier to understand – this is challenged by the requirement for using validated assessment tools in research. This issue may be solved by involving the patients in the choice of questionnaires where possible, so it becomes more meaningful for them to respond. For instance, the patients participating in the development of the eMindYourHeart intervention chose a disease-specific questionnaire instead of a generic questionnaire for assessment of anxiety, as they found it more relevant [86]. Another solution might be in combination with suggestion (4), make the intervention more fun, which is also requested by patients with HIV-associated non–acquired immunodeficiency syndrome [95]. Including innovative elements such as gamification in a CR eHealth intervention might also be one solution to optimize adherence and keep the patients interested [96]. Research experts might have divergent opinions to patients of the optimal interface of an intervention [95], hence involving the end-users in for instance font size and visualization design might enhance adherence and thereby patient outcomes.

Methodological considerations for the qualitative part were that we managed to obtain a good variety of patient experiences in writing. This helped us to confirm the quality of the intervention and enabled us make improvements, such as a more personalised approach to the assignments in the modules. Limitations were the risk of selection bias, as only 14 out of 22 completed patients accepted the invitation to participate in the evaluation, which potentially could be the most resourceful patients. In addition, we failed to invite drop-out patients to participate even though they could have contributed with valuable knowledge. With respect to the nurses' evaluation, we did not assess the risk of selection bias as high since all key CR nurses across all participating centres took part in the evaluation, nevertheless, further participants may have led to broader views. Email interviews are found to be trustworthy alternatives to in-person interviews [97] but have limitations as for example voice mode and non-verbal communication are absent, and there is no possibility for immediate follow-up questions. This means, we may have generated broader or other experiences from the participants by doing in-person or telephone interviews but given the purpose of the feasibility study we found our chosen approach most cost-effective.

Taken together, the eMindYourHeart feasibility study showed an acceptable drop-out rate, encouraging changes in HADS scores, satisfactory use and utility of the intervention, and gave us valuable feedback from patients and CR nurses. This meant that with a range of minor adjustments, we could move on to the RCT [82] and found this exciting, as there is still only few RCT studies published on ICBT within the cardiac population.

3.3 Study 3. A qualitative study of cardiac nurses' experiences with a web-based intervention to patients with an ICD (Paper 3)

3.3.1. Study design

The study "A web-based intervention for patients with an implantable cardioverter defibrillator – a qualitative study of nurses' experiences (Data from the ACQUIRE-ICD study)" was descriptive and carried out using qualitative methodology [98]. It was based on semi-structured interviews with nine cardiac nurses involved in the delivery of a web-based intervention for patients with an ICD.

The acronym ACQUIRE-ICD stands for: AdvanCe the QualIty of life and caRE of patients with an ICD [99].

3.3.2. Theoretical framework

Qualitative methodology is appropriate to use when exploring in-depth understandings of a complex phenomenon as experienced by the involved individuals. Different qualitative approaches can be undertaken such as phenomenology, grounded theory, and narrative analysis, even though some of these approaches might be used interchangeably [100]. We were inspired by the methodology of qualitative content analysis in this study, since it is found useful for exploring the field of nursing, as well as areas with limited knowledge [100-102], and thereby relevant for the objective of this study.

Qualitative content analysis

The qualitative content analysis aims to obtain a condensed and broad description of a phenomenon, and to systematically build a model of the content [102]. There is no gold standard for execution of content analysis [102], but by striving to be transparent throughout the research processes, trustworthiness of the study can be enhanced [101]. In content analysis, one can focus on either the latent or the manifest content of the data [101]. We chose to focus on the latent content, interpreting the underlying meaning of the text in-depth, in contrast to analysing the obvious concepts from the visible transcription text [101]. This decision was based on dealing with a new and complex phenomenon (i.e., cardiac nurses' experiences with a complex web-based intervention) and relatively few participants. An inductive approach is useful when there is sparse knowledge of the studied phenomenon, as is the case with this study. Therefore, we chose this inductive approach, coding the text openly and creating subcategories and categories during a non-linear creative process without trying to fit the data with for example a predefined theory as done in a deductive approach [102].

Consolidated Framework for Implementation Research (CFIR)

This meta-theoretical framework was used to provide a theoretical understanding of the findings in the discussion part in Paper 3 [98]. CFIR contains five main domains including: (1) characteristics of the intervention that is to be implemented; (2) inner setting; (3) outer setting; (4) characteristics of the involved individuals; and (5) the implementation process [103]. Each domain covers a broad menu of constructs that may either facilitate or hinder implementation of the intervention [103]. Multiple implementation frameworks exist [104], however the CFIR framework was chosen as it is multifaceted, found useful in complex interventions and includes the domain "characteristics of individuals" which was particularly relevant in this context of exploring individual experiences [103].

Pre-understanding

Within qualitative methodology it is commonly recognised that the research process will be influenced by the researchers' prior understandings of the studied phenomenon, including for instance assumptions, beliefs, and ideas [105]. It is probably impossible to disclose the full scale of a person’s pre-understandings but striving to describe the most obvious may enhance trustworthiness. For me – as the interviewer and researcher – I have routine in interviewing and was able to establish a positive relationship with the participants, as we shared the same backgrounds as experienced clinical cardiac nurses with mutual understandings of busy clinical practice, specific care to cardiac patients, and being employed in the context of a department of cardiology in Denmark. I knew some of the interviewed nurses beforehand but have never worked closely with any of them. I have positive attitudes towards eHealth, but believe it is necessary to conduct further research in eHealth delivery, so that as many cardiac patients as possible can benefit from this mode of CR delivery. As the second author (CL) and I have previously used CFIR in research [76], there was a risk that this could influence the analytical process for instance in creation of categories. However, we actively tried to counterbalance this by involving a qualitative expert with no prior knowledge of CFIR or other implementation frameworks (NR).

3.3.3. Participants and data collection

The participants were strategically recruited across the five cardiac sites participating in the ACQUIRE-ICD RCT in Denmark [99]. Cardiac nurses currently involved in the intervention were identified by the ACQUIRE-ICD project team and invited by email. The invitation consisted of an information letter describing the purpose of the study and an informed consent. All invited nurses accepted (n=9), thus we had a complete sample of possible informants.

An interview guide was developed (Appendix V), focusing on letting the participants describe their experiences with the intervention. The guide was developed using empirical and theoretical knowledge, including CFIR [103]. We strived to keep the questions open-ended to not steer the participants in any pre-defined direction and had follow-up questions prepared in case guidance or exemplification was needed. It was pilot-tested on two nurses from the target group and minor modifications were made based on their feedback. For instance, we added a follow-up question about experiences with differences in patients’ engagement in the intervention, depending on if the patient had suffered a cardiac arrest or not. This was added since both nurses from the pilot interviews mentioned the topic spontaneously and regarded it important.

The gold standard of generating an interview is in-person as it entails direct verbal and non-verbal communication with no technical interference [97]. However, due to COVID-19 restrictions we could not conduct the semi-structured interviews in-person. The participants could instead choose between telephone or video interviews, which are considered trustworthy alternatives and have the advantage of using considerably less resources in terms of travel time and transportation costs [97]. Video interviews were offered to enhance the social connection between the interviewer and the participant, but it was only audio-recorded. Most participants preferred telephone interviews for simple convenience, as they did not need to find and pre-book an undisturbed room with a computer that had a web-cam installed. Two chose video-interviews. By request from a participant, one interview was generated in-person as we were on the same premises on the day of the interview and were able to comply with current COVID-19 restrictions. The interviews were audio-recorded using a digital USB device which ensured that we could transfer the recorded interview files directly to a secure site (SharePoint) and thereby optimize protection of the research data.

3.3.4. The ACQUIRE-ICD intervention

The multi-component ACQUIRE-ICD intervention is described in Table 2.

Table 2. Components of the ACQUIRE-ICD intervention.

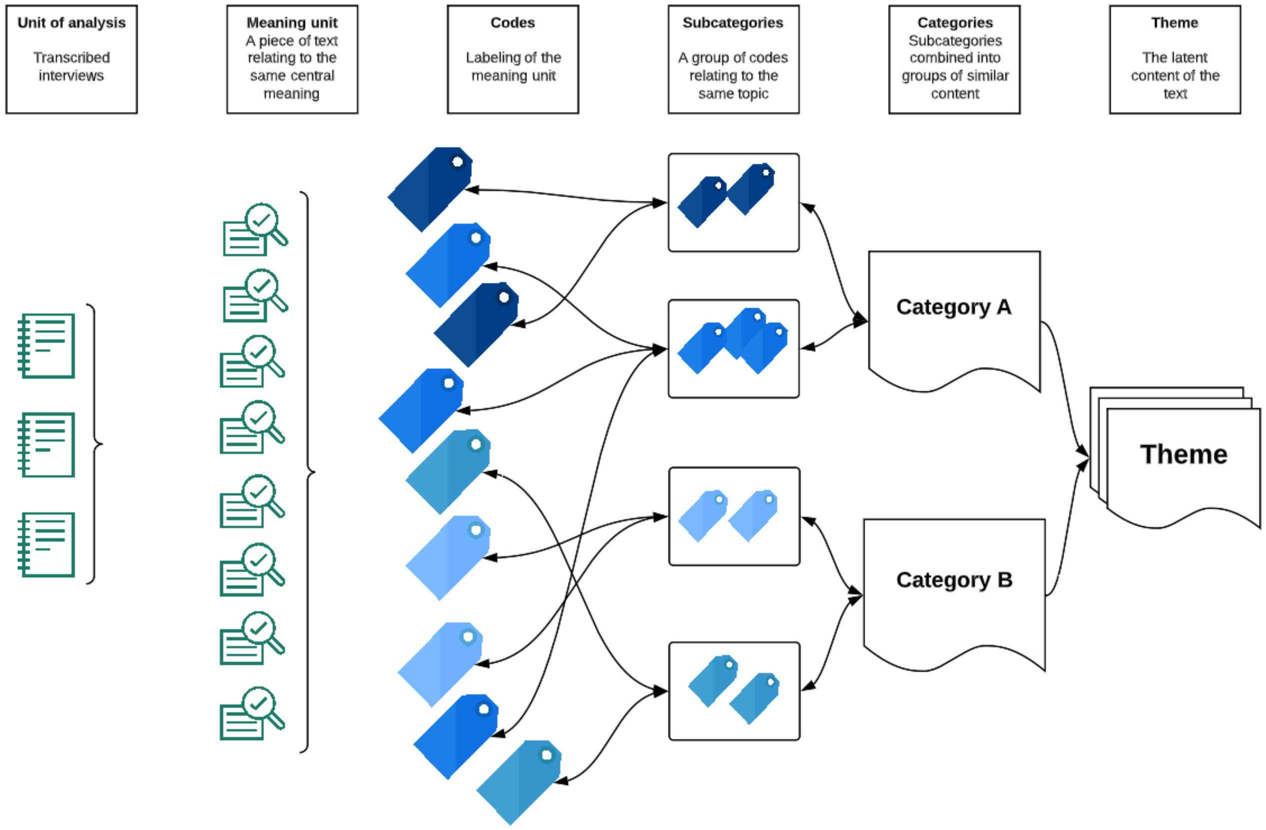
Table 2. Overview of the components of the 12 months ACQUIRE-ICD intervention	
Written communication with cardiac nurses on the platform	Weekly 1-3 months post ICD implant (nurse-initiated) Monthly 4-12 months post ICD implant (nurse-initiated) Extra dialogue possible, both written and by telephone (could be nurse- or patient initiated)
Information provision and patient education	Toolbox of material distributed to patients at regular intervals (see above). For instance, material on ICD-related topics, anxiety, depression, behavioural change, sleep, relaxation training, quizzes, podcasts with cardiac patients and health professionals.
Monitoring of anxiety, depression, and self-rated health	Monthly (tools were GAD-7 for anxiety, PHQ-9 for depression and EQ-VAS for self-rated health)
Referral for psychological treatment in case of elevated scores for anxiety and/or depression	Cognitive behavioural therapy delivered by psychologists
Goal-setting for behavioural change	Minimum one goal was required upon entrance to the platform, with no upper limit of goals (e.g., improvement in activity level, smoking cessation, or diet change). This action was a requirement from the chosen platform.
Online patient forum.	Patient-to-patient communication - no moderation by health professionals (the data manager could access the forum and redirect in case of negative conversation).
Abbreviations: *ICD* Implantable cardioverter defibrillator; *GAD* Generalized Anxiety Disorder scale; *PHQ* Patient Health Questionnaire; *EQ-VAS* EuroQol visual analogue scale.	

This Table is modified from Helmark et al. 2022 [98].

3.3.5. Qualitative analysis

The complex phenomenon we explored was the cardiac nurse's experiences of the web-based intervention. The analysis was conducted stepwise and inspired by the approach suggested by Graneheim and Lundman [101] and illustrated in Figure 5.

FIGURE 5. ILLUSTRATION OF THE QUALITATIVE CONTENT ANALYSIS INSPIRED BY GRANEHEIM AND LUNDMAN.

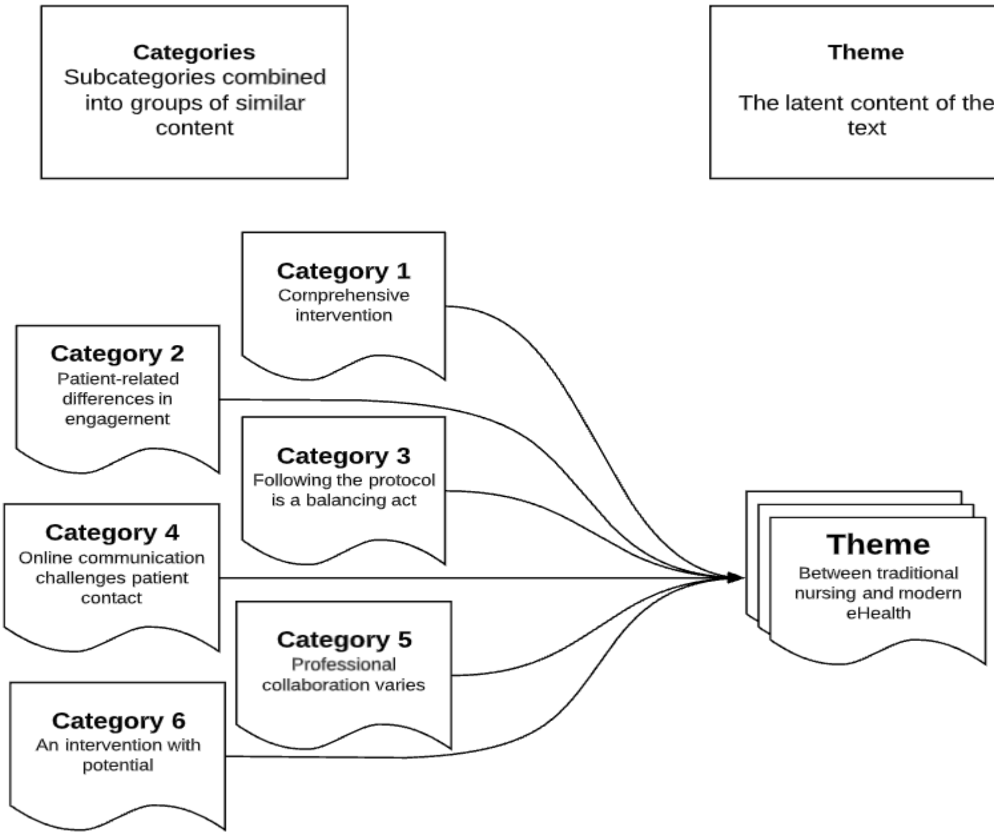


The audio-recorded interviews were transcribed verbatim, and the interviews were read individually several times by two authors (CH & CL), taking notes along the process of reading to obtain a sense of the whole. Using researcher triangulation, three different interviews were coded separately, and the codes discussed in-depth until consensus was reached. We deliberately chose three interviews from three different sites to optimize chances of a variety of views, leading to a broad variety of codes as well. After reaching consensus the remaining interviews were coded. The codes were discussed and reflected upon and to improve trustworthiness, we included further two authors (NR & SSP), combining codes into subcategories and categories, going back and forth several times. Upon decision on the final model, a theme was discussed and derived, which expressed the latent content of all interviews. Examples of the analysis are displayed in Appendix VI.

3.3.6. Key results

Based on six categories, the analysis resulted in an overall theme which we named “Between traditional nursing and modern eHealth” (Figure 6). The theme covered the cardiac nurses’ reflections of having positive attitudes towards web-based treatment and believing in this being a future mode of CR delivery and at the same time being challenged by lacking face-to-face contact for assessment of patient's psychological wellbeing and worried about consequences for less resourceful patients.

FIGURE 6. ILLUSTRATION THE SIX CATEGORIES AND THE DERIVED THEME.



The six categories are described in detail in Paper 3 [98], but hereby briefly presented: (1) "Comprehensive intervention" relates to the content of the ACQUIRE-ICD intervention, which the nurses experienced as comprehensive but also with too many tasks for some of the patients. There were opposite opinions of having a non-moderated online patient forum. (2) "Patient-related differences in engagement" relates to the participants engagement with the intervention, where the nurses experienced a large variety mostly depending on patients' individual resources and individual adjustments to life with an ICD. (3) "Following the protocol is a balancing act" is a category that relates to the processes of the intervention. Due to different modes of organization locally, there were inter-site variability in adherence to the protocol. Most nurses strived to deliver materials to patients as planned but experienced they were challenged with the tasks of keeping the patient adherent to the intervention. (4) The category "Online communication challenges patient contact" covers that most nurses found it difficult assessing patients' psychological wellbeing as they could not interpret the patients' verbal and non-verbal communication as traditionally done within nursing. They lacked in-person contact to establish a personal connection with patients they supported in the intervention. They were in doubt of how much to chase the patients despite having a protocol, because they on one hand worried about non-respondent patients and on the other hand did not want to appear overzealous. In addition, they experienced that they lacked training in online written communication with patients (chat) to achieve a balance between personalised messages with for instance emojis and professional documentation. (5) "Professional collaboration varies" relates to the social context of the study, where the nurses experienced that the ACQUIRE-ICD had a low priority compared to other concurrent studies in their departments and that the possibilities for networking were suboptimal. All nurses were confident that patients had fast access to cardiac care in case needed, and all experienced good support from the project team. (6) "An intervention with potential" relates to the nurse's belief in the intervention. All nurses found the intervention innovative, and that it entails a great potential. They experienced that many patients were ready for this transition to eHealth, especially towards the end of the study where the COVID-19 emerged, and some patients having tried for instance video consultations with their general practitioner.

3.3.7. Ethical considerations

This study complies with the Helsinki Declaration with all participants providing written informed consent [70]. The study was approved through the Data Protection Agency at the University of Southern Denmark (11.380) and the Research Ethics Committee at the University of Southern Denmark approved ethics of the study (21/27575). We considered telephone and video interviews to be ethically appropriate, as the contents of the interviews were not too personal. We also expected that participants possess the required skills to engage in telephone and video interviews [97], as they were experienced cardiac nurses with routine in research processes and thereby highly capable of understanding the informed consent and the consequences of participation. In addition, we aimed to reduce the potential perceived burden of participation by letting them choose the format of the interview. The identities of the participants were protected by not reporting age, sex, and names of hospitals in the paper [98].

3.3.8. Discussion of Paper 3

The overarching theme of the qualitative content analysis was "Between traditional nursing and modern eHealth", and this theme covers the "red thread" that unifies the six categories.

All cardiac nurses were in general positive towards telerehabilitation and eHealth, and believed it is here to stay and very likely to increase. They believed that the specific ACQUIRE-ICD intervention holds a great potential, but that adjustments of the intervention are required to better fit patients' needs for care and nurses' need for assessment of the psychological dimension of patients. The nurses experienced that specific training is needed to optimise web-based communication with patients, which is in alignment with previous findings [48]. Especially with respect to communication about psychological wellbeing, the nurses experienced difficulties, as patients were challenged with respect to expressing themselves in writing. Nurses were also challenged by not being able to interpret patients' verbal and non-verbal communication, which they are trained to do in clinical practice. Brandt et al. found that building an empathic relationship between patient and health professional was a crucial driver for successful eHealth coaching with respect to lifestyle changes, including face-to-face meetings [106]. This indicates that integrating a face-to-face option in the intervention could be valuable to patients and nurses, as it enables use of verbal and non-verbal communication and thereby enhances the building of an empathetic relationship with patients. This was neither practically nor legally an option on the chosen intervention platform for ACQUIRE-ICD at the start of the study in 2017, but with rapid development of eHealth solutions, integrating this option should be considered in case of future implementation in clinical practice.

Involving patients in the development of new interventions through Patient and Public Involvement (PPI) strategies has become mainstream, as patients are the obvious and most important end-users of the intervention [86,107-108]. For the ACQUIRE-ICD study, the web-based intervention was originally targeting to patients with heart failure and as such, a PPI study was conducted [109]. Difficulties with recruitment of patients with heart failure due to competing studies resulted in changing the focus to patients with an ICD as target population. The contents of the intervention were adjusted accordingly, although not through a state-of-the art and published PPI study but with health professionals with expertise with ICD patients and focus group interviews with patients. Nevertheless, involvement of other key stakeholders in the development - including the cardiac nurses delivering the intervention – may enhance successful implementation [103]. As stated in CFIR all involved individuals carry organizational, professional, and individual mind-sets and through a dynamic interplay they will seek to find a meaning with the intervention and try to improve or adjust it [103], mirroring the findings of our study [98]. Thus, also involving the key staff delivering the intervention in the development phase might be important to optimise fidelity to the intervention and the chance of later wide-spread implementation. As suggested in Paper 3, another recommendation could be to offer regular webinars to cardiac nurses to counter local deviations from the protocol and discuss cases and experienced challenges.

All nurses worried about the appropriateness of the intervention for less resourceful patients, especially elderly patients, due to potentially low eHealth literacy. eHealth literacy is often defined as *"the ability to seek, find, understand, and appraise health information from electronic sources and apply the knowledge gained to addressing or solving a health problem"* [110]. As eHealth interventions are increasing, the understanding of eHealth literacy is paramount. Fortunately, research in eHealth literacy is growing [111]. In one study of a cardiovascular risk population, there was no association between sociodemographic factors and eHealth literacy, but spending >1 hour daily on the internet was associated with high level of eHealth literacy [111]. Another study of eHealth literacy among patients undergoing percutaneous coronary interventions found only a weak correlation with age [112]. A third study on cardiac patients' experience with CR telerehabilitation did not find an association between age and eHealth literacy, but that the web-based intervention improved patients' eHealth literacy [113]. This indicates that health professionals should not refrain from including patients in cardiac telerehabilitation due to older age. Another solution could be to tailor the web-based interventions to meet cardiac patients' individual needs and preferences by for instance developing user-friendly interfaces or differentiate the content to various age groups. In addition, nurses who are delivering the web-based intervention should receive specific training of in how to handle for instance elderly patients' CR online. Still, these results on eHealth literacy should be interpreted with caution as eHealth evolves very rapidly, such as launching of health information on websites, social media, and new mobile health applications, potentially making it challenging to conduct up-to-date assessments of eHealth literacy [114].

With respect to methodological considerations, the concepts used for evaluating the quality of qualitative research differs from quantitative research. In quantitative research the concept generalisability refers to the extent to which the results are transferrable to a wider population, based on a statistical approach. In qualitative research the concept generalisability refers to analytical generalisability, meaning the extent to which the findings can be generalized to other contexts under similar theoretical conditions, such as time, place, persons, and the social context [115]. When using qualitative content analysis as done in the current study, Graneheim and Lundman suggest using the concepts credibility, dependability, and transferability as measures for evaluating the quality of the research, described as the *trustworthiness* of a study [101]. Credibility covers the research processes, including selection of participants, data collection, and the creation of categories. In our study, we included all cardiac nurses who were involved in the delivery of the intervention in the ACQUIRE-ICD study. Hence, we could not have gained further insights by including more participants. Nevertheless, we believe we gained broad insights into the research question as the participants represented five different hospitals with five different modes of work division and support. Regarding data collection, we acknowledge that in-person interviews with direct interaction and the possibility to create a more personal relationship [97] could have led to richer insights. Given the circumstances of the COVID-19 restrictions and that the participants could choose between video and telephone interview, we believed that we chose the most appropriate method for data collection. In the analytical process of creating codes, categories, and themes, we actively used researcher triangulation to maximise credibility by involving researchers with different professional backgrounds and various expertise in qualitative methods. This meant, that we could interpret the findings with different perspectives and the dialogues contributed to agreement of the credibility of the results and thereby the trustworthiness. The concept dependability refers to the level of alterations in the study design and data collection over time, with the risk of inconsistency in the findings. As our data collection was conducted within few months and by the same researcher, we believe our dependability to be trustworthy. The last concept – transferability – relates to the extent that the findings are transferrable to similar populations or contexts. As described in Paper 3 [98], a limitation of the study is that the findings might have limited external validity with respect to routine CR as the context of our research lies within the interventional arm of an RCT. The staffing, the nurses' skills, priorities of managers, and resources may well differ, and comparing with telerehabilitation implemented in routine clinical care is difficult as – to our knowledge – no studies are published on this yet [116]. Still, our findings mirrored other results from the literature on eHealth in the cardiac field and we therefore consider our results transferable to the context of development of eHealth interventions. Concluding on trustworthiness, we have sought to maximise trustworthiness by being transparent throughout the research processes, and by reporting our interpretations and findings using thick descriptions, however we acknowledge that having applied a different qualitative approach might have led to other interpretations.

Taken together, in this qualitative study of cardiac nurses' experiences with a web-based intervention for patients with an ICD, we found that nurses experienced that they were in a crossfield between having positive attitudes towards web-based interventions, while at the same time being challenged by the lack of in-person contacts with patients. Involving the cardiac nurses – who deliver the intervention – in the development of web-based interventions in the future may enhance fidelity and thereby the efficacy of an intervention.

4. Main discussion

The overall scope of the three studies in this PhD was to investigate different aspects of assessment and management of psychological distress in CR, as illustrated in Figure 1 in the Introduction. This led to new insights, where we found inconsistencies in screening for anxiety and depression in CR. We found a person-centred ICBT intervention - targeting anxiety and depression in patients with IHD - feasible for further testing in an RCT. Finally, we found that cardiac nurses were positive towards web-based treatment, but also lacked face-to-face contact in communication with patients, especially concerning psychological health. These results will be discussed in the following section.

In Study 1 entitled "*Systematic screening for anxiety and depression in cardiac rehabilitation – are we there yet?*" we identified a range of patient- and provider level characteristics that were associated with the likelihood of patients being screened for anxiety and depression. These results are important, as we need to identify patients with symptoms of anxiety and depression as the first step. Then follows delivery of evidence-based psychological interventions to this vulnerable high-risk group of patients with cardiac disease and comorbid anxiety and/or depression in order to improve patients' health outcomes [14]. Around 60% of the study population were screened, but data from the four included years indicated a decrease in assessment of psychological health within CR in the UK [62]. We only analysed these data on an aggregated level, meaning that the results might be impacted by inter-site variation in the included CR settings. Comparing to a recent Danish study, this showed that the national proportion of CR patients being screened for depression in hospitals improved slightly from 60% in 2016 to 63% in 2020, however the inter-site variability varied from 0-100% at both time points [117]. This large inter-site variability suggests that systematic screening for anxiety and depression in CR may be affected by local individual beliefs in the value of screening, rather than the attempt to follow guidelines on screening [117]. **Hence, from a clinical perspective, CR sites are encouraged to revise their screening procedures and evaluate potential barriers for screening for the benefit of cardiac patients.** Study 1 showed that certified CR centres are significantly more likely to screen for anxiety and depression compared to uncertified CR centres [62], despite this component not being one of the seven key performance indicators of the BACPR certification requirements [65] (Appendix IV). This indicates that a certification system may push quality improvements in other areas as well. This could possibly be through higher awareness of guidelines or additional supporting initiatives in CR centres striving for certification through high level of performance. In Denmark, a national certification of CR is not planned yet, but for instance the new ICRR has developed a certification program for international sites using this registry [79], aiming for future harmonisation and quality improvement across countries.

The results of Study 1 also show the impact of living in areas of multiple deprivation, with higher prevalences of anxiety and depression, while at the same time less patients being screened as compared to patients from less deprived areas [62]. Other cardiac risk factors such as smoking, high BMI, and low level of physical activity are at the same time are more prevalent in areas of multiple deprivation [75]. This could indicate that patients from more deprived areas have a need for more extensive support in their CR pathway, as they might have a higher number of risk factors to tackle. As behavioural change is complex and influenced by the context of the patient's environment [118], it may demand additional resources for CR settings to assess, treat, and support patients from multiple deprived areas to achieve the goals outlined in the guidelines, including goals for psychological health. Area deprivation is also a predictor of mortality [68] and not easily targeted by the CR settings. **Thus, from a public health perspective, decision makers are encouraged to ensure that CR settings in multiple deprived areas have sufficient resources to support patients with more complex cardiac risk profiles and thereby seek to mitigate inequity in health care delivery**. A recent observational study reported that a high level of patient-reported psychosocial healthcare was associated with statistically significant reductions in readmissions and mortality [119], suggestion that prioritising psychosocial components in CR could potentially reduce societal costs of readmissions and adverse events for cardiac patients.

As Study 1 is based on an observational study design, no causation can be drawn – neither with respect to the unsystematic approach to screening nor the association with the identified determinants in the study [64]. **From a research perspective, gaining an in-depth understanding of the inconsistency in screening for anxiety and depression in CR could be valuable for improved implementation in clinical practice and obtained using qualitative methodology.** For instance, an interview-based study based on implementation science could lead to a broader understanding of multi-level barriers and facilitators for screening for anxiety and depression in CR [104].

With respect to Study 2, *"Internet-based treatment of anxiety and depression in patients with ischaemic heart disease attending cardiac rehabilitation: a feasibility study (eMindYourHeart)",* the overall satisfactory results from this feasibility study meant that after a range of minor adjustments the eMindYourHeart RCT could commence [82]. At the time of writing 130/188 (69%) patients have been randomized. In a feasibility study, different areas of focus can be relevant depending on the context [84]. One of the focus areas in Study 2 was the acceptability within the CR settings with respect to the perceived need for the intervention. From our evaluations with the CR nurses [81] and through feedback via regular webinars with the involved CR staff, we learned that the possibility of offering cardiac a psychological intervention to cardiac patients was perceived as very meaningful in clinical practice. Clinical practice is busy, and the CR nurses experienced that recruitment is an extra burden on top of other clinical tasks, but still all CR centres recruiting for the feasibility study also chose to participate in the RCT and even an additional centre joined. **Thus, from a clinical perspective, having a psychological intervention to refer to as an integrated part of CR appears meaningful for CR staff**. In addition, we were approached by some heart failure clinics who wanted their patients to participate in the study. Unfortunately, this was not possible as the eMindYourHeart intervention was specifically developed for and with patients with IHD. However, this suggests that easy-access psychological interventions as part of CR are lacking for patients across cardiac diagnoses.

Feasibility studies are useful for assessing if an intervention is appropriate for further testing for efficacy and cost-effectiveness in an RCT [84]. As such, feasibility studies are important precursors that also help ensure that limited research resources are not wasted on non-feasible studies due to e.g., low acceptability among patients or staff or challenges and barriers in the clinical setting. Anxiety and depression in cardiac patients are associated with increased societal costs [25,26], as well as increased readmissions and mortality [27]. **From a public health perspective, developing an evidence-based and cost-effective web-based psychological intervention may reduce societal costs and adverse health outcomes in future cardiac patients.**

The literature on efficacy and cost-effectiveness of web-based psychological interventions to cardiac patients is still sparse and results heterogenous [58]. An RCT reporting long-term effects of ICBT on depression found that patients with heart failure were less likely to improve their depression scores [58]. This does not necessarily mean that ICBT is less effective within in patients with heart failure but could suggest that tailoring and user-friendliness of ICBT could be tried adjusted to better target the needs of patients with a heart failure diagnosis. By involving the target patients in the development of the intervention from start and prioritizing their needs, the end-users' needs become central [120]. Hence, by involving patients with IHD in a PPI study [86] and conducting the feasibility study [81], we have sought to make the eMindYourHeart intervention patient-centred and meet their needs which hopefully will enhance the efficacy of the intervention [48]. **From a research perspective, the results of the eMindYourHeart RCT will add to the increasing body of evidence on web-based psychological interventions for cardiac patients, and hopefully highlight the potential for remote digital health solutions for cardiac patients.**

In Study 3, entitled *"A web-based intervention for patients with an implantable cardioverter defibrillator – a qualitative study of nurses' experiences (Data from the ACQUIRE-ICD study)"*, we identified the theme "Between traditional nursing and modern eHealth". This illuminates the crossfield between rapid evolving digital health innovations in cardiac care on the one hand [49,120-121], and the need for training of the involved health care professionals on the other hand [48]. In the new ESC Textbook of Cardiovascular Nursing, it is stated that despite concerns *"technology should be embraced as an adjunct to human interaction between the nurse and patient and an aide to the nurse providing care"* [118]. Our findings suggest that cardiac nurses recognise the potential of digital health technology - here in terms of telerehabilitation - but lack training in online communication [98]. Building a strong relationship between patient and health care provider is an important driver for sustainable behavioural change [106,122]. The possibility of integrating a face-to-face option in the ACQUIRE-ICD intervention [99] may be the missing link that would improve the relationship with patients and be perceived as an aide for the cardiac nurses. **From a clinical perspective, cardiac nurses acknowledge the large potential of the ACQUIRE-ICD intervention but the shift from in-person care to telerehabilitation requires specific training of the involved nurses.**

An important finding in Study 3 was that the nurses experienced differences in patient engagement, depending on resources and needs of the individual patient. Due to the COVID-19 pandemic and the following lack of sustained delivery of in-person CR, a large need for cardiac telerehabilitation emerged to be able to deliver core components of CR [49,121]. However, the digital divide between resourceful patients and less resourceful patients should be considered, to ensure that these interventions are efficient across patient subgroups, including elderly patients and patients with low level of eHealth literacy [123]. As these and other subgroups are already associated with low participation and adherence to CR, the transition from in-person to remotely delivered CR calls for surveillance regarding inequity in care [124]. One-size does not fit all in CR delivery, as CR patients are potentially diverse with different individual needs and preferences [8], with the possibility that effectiveness of interventions may vary across subgroups. **From a public health perspective, it is important to ensure provision of evidence-based cardiac telerehabilitation across all subgroups, to maintain the benefits of CR for all eligible patients.** Another point is, that telerehabilitation simply might not be the right choice for all patients, as some will prefer in-house CR e.g., to meet other patients in-person [125].

In Study 3 the cardiac nurses especially experienced challenges with communication related to patients' mental issues, which made them insecure of the psychological wellbeing of the patients [98]. Previous studies identified on cardiac health care professionals' experiences with eHealth delivery are limited to the area of behavioural change [61,106,122]. Hence, the focus areas may be different from the ACQUIRE-ICD intervention where the focus area is a comprehensive intervention targeted to increase device-acceptance of the ICD [99]. The cardiac nurses experienced that the patients had difficulties with expressing themselves in writing concerning their mental health. Therefore, needs and preferences of both patients and cardiac nurses might differ to some degree across interventions, including the need for venting mental issues. **From a research perspective, further research is needed to explore how telerehabilitation can best support the dialogues around mental health.** One study reported that patients participating in remote CR experienced more improvement in their mental health compared to patients participating in in-person CR [126]. However, the remote CR intervention included telephone consultations and the possibility for videoconferences with patient education, giving patients the possibility to express themselves orally. This indicates that telerehabilitation with face-to-face possibilities could support the psychological aspects of patients attending CR. Although, by contrast, a recent study found that patients participating in hybrid CR experienced less improvements in symptoms of depression, compared to patients receiving in-person or virtual CR [127]. These contradictory results may in part be explained by the use of an observational study design during the COVID-19 pandemic in two different contexts (Australia versus California), with rapid decisions being a necessity instead of carefully planning of studies [126-127]. Other possible explanations could be the use of different tools for measuring mental health outcomes (the Short Form Health Survey versus PHQ-9), or differences in either CR populations with respect to socio-demographics and cardiac diagnosis or the content of the delivered CR interventions. Taken together, this suggests that we still lack knowledge of evidence-based telerehabilitation delivery with respect to dialogue on mental health issues with patients and improvement of psychological health outcomes.

4.1 Perspectives on future digital health solutions in CR

Cardiac care and CR have changed considerably over the last decades [128] and since the COVID-19 pandemic globally impacted CR delivery severely. One can speculate about lessons learned from times of COVID-19 quarantine and how future CR will be delivered [50,123,126]. Already prior to the pandemic, there was a high awareness towards transition to use of digital health solutions in cardiology [121,129]. With respect to the included studies in this thesis, digital health solutions are highly relevant.

A paper by Redfern et al. have described the history of CR and included recommendations for contemporary CR in 2022 [128]. For contemporary CR, Redfern et al. for instance recommend systematic digital incorporation of CR performance indicators [128], such as screening for anxiety and depression. This performance indicator is already a part of the Danish CR Database [78], however with 63% of CR patients screened nationally in Denmark we are still far from the required standard of 80% sat by the Danish CR Database [117]. An initiative by the Danish Health Data Authorities is currently establishing a national system for digital reporting of a range of PROs in CR, including measures of anxiety and depression [130]. This initiative may increase the screening rate as the intention is to send the PRO questionnaires digitally to patients prior to pre- and post CR assessments. Thus, patients fill out the PROs digitally before attendance, with the possibility to use patients' perceptions of own health both in a dialogue between patient and health care professional and as an outcome measure. The intention is also to transfer relevant PROs digitally to the Danish CR Database, to reduce the burden of manual data-entry.

Redfern et al. also recommend comprehensive risk factor management that include psychosocial issues [128]. Integrating ICBT such as the eMindYourHeart intervention in CR may be a future digital solution which could ensure cardiac patients with anxiety and depression fast access to psychological treatment and potentially reduce CR drop-out and adverse events. Patient-related benefits are many and include autonomy of when and where to engage in the treatment, reduced stigma, no transportation, and continuation of treatment in times of quarantine related to pandemics [82].

Also, Redfern et al. recommend performing scientific evaluations of evidence for digital health innovations in CR [128]. The eMindYourHeart and the ACQUIRE-ICD studies are performed in alignment with the highest ranking of the evidence-hierarchy, the RCT [64]. In addition to this, the concurrent qualitative study of cardiac nurses' experiences with the ACQUIRE-ICD intervention can contribute with knowledge of the cardiac nurses' perspective. These insights are important as it is stated that health care providers need specific training when transitioning from in-person to remote delivery of care [48], and that delivery of digital mental health care requires different competencies than traditional in-person delivery [59]. However, further research on the content of the mentioned "specific training" is warranted, to give cardiac nurses the competencies they experienced were lacking, especially when communicating about mental health issues.

Reviews on both quantitative and qualitative research on telerehabilitation are recently conducted, pointing at both advantages and challenges with this mode of delivery [60,121]. Probably telerehabilitation is here to stay. Hence, as researchers we need to keep striving to develop and improve cost-effective solutions for the benefit of the cardiac patients. Maybe we, as researchers and health care professionals, need to think more "out of the box" in the future. We could for instance engage more with gamification experts and patients, to make CR eHealth solutions feel more fun and personalised for patients, and thereby seek to improve participation and adherence. This could potentially lead to a more holistic approach to cardiac care and improve health outcomes for cardiac patients, including psychological outcomes.

4.2 Conclusions

Based on the objectives of the thesis, the following conclusion can be drawn from the three studies:

a) Both patient- and provider level determinants of screening for anxiety and depression in CR exist. Especially high-risk groups of cardiac patients were less likely to be screened, indicating social inequity in CR delivery. Both CR settings and decision-makers should make efforts to quality ensure screening for anxiety and depression to all eligible patients.

b) Based on drop-out rate, mean improvements in HADS anxiety and depression scores, patients' use of the intervention and qualitative evaluations from patients and involved CR nurses, the eMindYourHeart feasibility study showed readiness for an RCT after minor adjustments.

c) Cardiac nurses were positive towards the ACQUIRE-ICD intervention and telerehabilitation in general, but lacked face-to-face contact with patients, especially with respect to patients' mental health. The value of web-based interventions might be enhanced from cardiac nurses' perspective by ensuring face-to-face contact. Specific training in eHealth communication seems necessary as web-based care entails a shift in the role of the nurse and requires different competencies compared to traditional in-person communication.

4.3 Future research

While the conducted studies - in our opinions - add important findings to the field of psychological health in CR, they also disclose areas where further research is warranted.

One area where further research is needed is related to the lack of systematic screening for anxiety and depression in CR. As previously mentioned, an in-depth exploration of the inconsistencies in screening procedures may contribute with new and broader understandings of barriers and facilitators for screening for anxiety and depression in CR. This could be obtained using qualitative methodology, potentially adding a survey in a mixed-methods study.

A study on the effect of the national digital PRO initiative in Denmark could contribute with knowledge of whether such national concepts could improve screening rates of anxiety and depression in CR. In addition, a qualitative study on how patients and cardiac nurses experience digital PROs with respect to psychological health and communication could inform us, if this is a suitable approach or if further development is needed to meet patients' needs in CR.

Another area where further research is warranted is cardiac telerehabilitation. A considerable number of studies in cardiac telerehabilitation have been conducted, but - to our knowledge - studies on implementation of telerehabilitation in clinical practice in CR are lacking. This is necessary to assess whether research results are transferrable when transitioned to clinical practice, where contexts vary from limited research contexts in terms of "real-world" CR populations and contexts.

Research on how relevant eHealth competencies for health care professionals are best acquired is warranted to improve the value of telerehabilitation from the perspective of health care professionals, which may help improve the quality of cardiac telerehabilitation delivery.

5. Summaries

5.1 English summary

The overall scope of the three studies in this PhD was to investigate different aspects of assessment and management of psychological health in the cardiac rehabilitation (CR) setting.

More than 108 million people are living with a cardiovascular disease in Europe, placing a substantial burden on both the individual person as well as society. Comorbid anxiety and depression are prevalent in approximately 20% of cardiac patients, and are associated with poor health outcomes, including increased risk of recurrent cardiac events, morbidity, and mortality. It is therefore crucial to identify and treat this vulnerable subgroup of patients.

Screening for anxiety and depression in cardiac patients is recommended in national and international guidelines to identify patients with need for psychological support. The screening procedure is reported to be suboptimal in CR, but it is unknown whether there are any patient- or provider level characteristics associated with the likelihood of being screened.

Despite guideline recommendations for evidence-based management of anxiety and depression in CR, patients are undertreated. However, new person-centred web-based solutions, including internet-delivered cognitive behavioural therapy, may show efficacy and cost-effectiveness for cardiac patients, although more research on this topic is warranted.

Telerehabilitation is found beneficial for cardiac patients, but little is known about cardiac nurses' experiences with delivery of web-based care. Their experiences could potentially influence the delivery of web-based care, as transition from in-person care to web-based care requires different competencies.

The aim of the first study was to investigate if the likelihood that patients with acute coronary syndrome were screened for anxiety and depression - as part of routine CR - was associated with patient characteristics and quality of provider level. For this observational retrospective study, data from the National Audit of Cardiac Rehabilitation (NACR) in the United Kingdom were used. A multivariate logistic regression analysis was performed to identify predictors for being screened for anxiety and depression. Based on the statistical analysis, we found that 60% of the CR population had been screened. We found inconsistencies in routine screening in CR, with identification of a range of patient- and provider level characteristics determining the likelihood of being screened. From this study, we concluded there was inconsistency in systematic screening for anxiety and depression. We recommend that CR centres should reflect on screening procedures, but also that decision makers should ensure support and resources for screening, for the benefit of patients participating in CR.

The aim of the second study was to examine the feasibility of a web-based intervention targeting anxiety and depression in patients with ischemic heart disease that is integrated in routine CR. For this interventional prospective feasibility study, we used a mixed-method approach. Patients (n=29) were recruited consecutively from routine CR settings in nine Danish CR centres. Regarding quantitative methods, descriptive statistics were used for assessing drop-out rate, changes in anxiety and depression scores, and usage and utility of the intervention. Regarding qualitative methods, thematic analysis was used for analysing evaluations of the experiences of patients and CR nurses with the intervention and the procedures. We found a drop-out rate<25%, positive changes in anxiety and depression scores, and acceptable use and utility of the intervention. Patients (n=14) and CR nurses (n=14) were in general positive towards the intervention. The conclusion of this study was that a randomized controlled trial on web-based treatment of anxiety and depression in CR seems feasible, and that this will be the next step to assess the efficacy and cost-effectiveness of the intervention.

In the third study, we explored the experience of cardiac nurses with respect to using a web-based intervention for patients with an implantable cardioverter defibrillator. This prospective qualitative study was interview-based using qualitative content analysis. We interviewed nine cardiac nurses across the five Danish university hospitals implanting ICDs, who delivered the web-based intervention. The results showed that cardiac nurses were positive towards the web-based intervention and believe it holds a large potential. However, they felt challenged by not having in-person and face-to-face contact with patients, which they found valuable for assessing patients' wellbeing and especially psychological distress. From this study we concluded that as web-based communication entails a shift in the nursing role, it requires specific training to obtain adequate competences.

The overall conclusion of this PhD is that screening for anxiety and depression in CR should be optimised, and that the use of digital health solutions in CR holds great potential for management of psychological health. However, further research is needed to identify the most effective solutions for delivery of holistic web-based care to cardiac patients and what works for whom.

5.2 Dansk resume (Danish summary)

Det overordnede omdrejningspunkt, for de tre studier i denne PhD, var at undersøge forskellige områder af vurdering og behandling af det psykiske helbred blandt hjertepatienter der deltager i hjerterehabilitering.

I Europa lever over 108 millioner mennesker med en hjertesygdom, hvilket er en stor byrde for både det enkelte menneske og for samfundet. Samtidig angst eller depression er forekommende blandt ca. 20% af alle patienter med hjertesygdom, og er associeret med dårligere helbred som for eksempel øget risiko for nye hjertetilfælde, andre sygdomme samt dødelighed. Det er derfor afgørende at identificere og behandle denne sårbare gruppe af patienter.

Screening af hjertepatienter for angst og depression er anbefalet i både nationale og internationale guidelines med henblik på at identificere patienter med behov for psykologisk støtte og behandling. Studier har vist at screening foregår suboptimalt i hjerterehabilitering, men det er uvist om der findes specifikke patient eller organisations faktorer der har betydning for sandsynligheden for at patienter screenes.

På trods af anbefalingerne i guidelines om behandling af angst og depression i hjerterehabilitering, viser studier, at patienter underbehandles. Nye personcentrerede og web-baserede løsninger kan vise sig effektive til behandling af patienter med hjertesygdom, men forskning er nødvendig for at vurdere dette.

Studier har vist at telerehabilitering er gavnlig for patienter med hjertesygdom. Men der er begrænset viden om hvordan hjertesygeplejersker oplever at arbejde med telerehabilitering, selvom disse oplevelser potentielt kan påvirke behandlingen da det kan kræve andre kompetencer end traditionel hjerterehabilitering.

Formålet med det første studie var at undersøge om sandsynligheden for at patienter screenes for angst og depression i hjerterehabilitering, er associeret med patient- eller organisations faktorer. Studiet blev udført som et retrospektivt observationsstudie, og med anvendelsen af kliniske kvalitetsdata fra den Britiske hjerterehabiliteringsdatabase, The National Audit of Cardiac Rehabilitation. Hovedanalysen bestod af en multivariat logistisk regressions model, med henblik på identifikation af prædiktorer for screening for angst og depression. Baseret på de statistiske analyser fandt vi, at ca. 60% af patienter der deltog i hjerterehabilitering, blev screenet. Vi fandt inkonsistens i screening og identificerede en række patient- og organisationsfaktorer der var associeret med screening. På baggrund af resultaterne konkluderede vi at der var inkonsistens i forhold til systematisk screening. Vi anbefaler at hjerterehabiliteringscentre bør optimere deres screeningsprocedurer samtidigt med at beslutningstagere bør sikre rammerne for screening.

Formålet med det næste studie var at undersøge gennemførligheden (feasibility) af en web-baseret psykologisk behandling af angst og depression til patienter med iskæmisk hjertesygdom, som et led i hjerterehabilitering. Dette prospektive interventionsstudie blev udført ved hjælp af et mixed-methods design. Patienterne (n=29) blev rekrutteret konsekutivt fra 9 danske hjerterehabiliteringscentre. Til de kvantitative analyser anvendte vi deskriptiv statistik til at beskrive frafald, ændringer i niveau af angst og depression, og brug af interventionen. De kvalitative analyser var baseret på evalueringer fra patienter og hjerterehabiliteringssygeplejersker. Vi anvendte tematisk analyse til at analysere henholdsvis patienters og sygeplejerskers oplevelser med intervention og procedurer. Resultaterne viste, at <25% af patienterne frafaldt interventionen, at der var positive ændringer i forhold til niveau af angst og depression, og at patienterne brugte interventionen som forventet. Patienter (n=14) og sygeplejersker (n=14) var generelt positive overfor interventionen. Konklusionen på dette studie blev, at det efterfølgende er muligt at gennemføre et randomiseret kontrolleret studie der skal vurdere effekt og kost-effekt af web-baseret psykologisk behandling til patienter med iskæmisk hjertesygdom.

I det tredje studie undersøgte vi hjertesygeplejerskers oplevelser af at arbejde med en web-baseret model for telerehabilitering målrettet patienter med en implanterbar cardioverter defibrillator (ICD). I dette interview-baserede studie anvendtes kvalitativ indholdsanalyse som metode. Vi interviewede de ni hjertesygeplejersker der deltog i afprøvning af modellen, på tværs af fem danske universitetshospitaler. Resultaterne viste, at hjertesygeplejerskerne var positive overfor den web-baserede model og mener den har et stort potentiale. Modsat oplevede de også udfordringer med ikke at kunne se patienterne i kommunikationen, da de er oplært i at bruge nonverbal kommunikation til at vurdere patienterne, specielt i forhold til psykisk velbefindende. Konklusionen blev at det kræver speciel oplæring og kompetencer at arbejde med web-baseret kommunikation, da dette fordrer en ny måde at arbejde på.

Den overordnede konklusion på denne PhD afhandling er, at screening for angst og depression bør optimeres indenfor hjerterehabilitering, og at digitale løsninger har et stort potentiale for håndtering af den psykologiske dimension blandt patienter med hjertesygdom. Yderligere forskning er dog nødvendig for at kunne identificere de mest effektive løsninger for en holistisk web-baseret hjerterehabilitering.

6. Abbreviations

ACQUIRE-ICD	AdvanCe the QualIty of life and caRE of patients with an ICD
ACS	Acute coronary syndrome
BACPR	British Association of Cardiovascular Prevention and Rehabilitation
COVID-19	Coronavirus disease 2019
CR	Cardiac rehabilitation
IESC	European Society of Cardiology
GAD-7	General Anxiety Disorder
GDPR	General Data Protection Regulation
HADS	Hospital Anxiety and Depression Scale
ICBT	Internet-delivered Cognitive Behavioural Therapy
ICD	Implantable cardioverter defibrillator
ICRR	International Cardiac Rehabilitation Registry
IHD	Ischemic Heart Disease
IMD	Index of Multiple Deprivation
NACR	National Audit of Cardiac Rehabilitation
PHQ-9	Patient Health Questionnaire
PPI	Patient and Public Involvement
PRO	Patient-reported outcomes
QoL	Quality of life
RCT	Randomized Controlled Trial
REDCap	Research Electronic Data Capture
SD	Standard deviation
UK	United Kingdom

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APPENDICES

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Appendix I

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Systematic screening for anxiety and depression in cardiac rehabilitation – are we there yet?[☆]

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ABSTRACT

Background: Anxiety and depression are prevalent in 20% of patients with acute coronary syndrome (ACS) and associated with poor outcomes. Guidelines recommend screening for these conditions in cardiac rehabilitation (CR) however, clinical practice is inconsistent. Sparse knowledge exists on determinants for screening.
Methods: This observational study used data from the National Audit of Cardiac Rehabilitation from January 2016–December 2019. A multivariate logistic regression model was performed to analyze patient- and provider level determinants for screening for anxiety and depression among patients with ACS.
Results: The population consisted of 138,018 patients, where 82,507 (59.8%) were screened and 55,511 (40.2%) were not. Younger age, non-white ethnicity, living in areas of social deprivation, current smoking, body mass index>30, and physical activity<150 min per week were negatively correlated with patients being screened. Compared to patients having a percutaneous coronary intervention, patients undergoing coronary artery bypass grafting or medical treatment were less likely to be screened. History of anxiety, depression, osteoporosis, chronic back problems, and asthma were positively correlated with screening, while chronic obstructive pulmonary disease, diabetes, hypertension, and stroke were negatively correlated with screening. Regarding provider level, certification of CR centers was positively associated with screening, while looking over time data showed an incremental negative trend in screening from 2016 to 2019.
Conclusion: We found both patient and provider level determinants of screening for anxiety and depression. Clinical practice is still inconsistent especially for high-risk groups. We recommend systematic screening to enable tailored interventions which in turn may mitigate inequity in health outcomes.

1. Introduction

In Europe alone, more than 108 million people are estimated to be living with a cardiac disease, including acute coronary syndrome (ACS) [1]. Approximately 20% of patients with ACS suffer from symptoms of comorbid anxiety and/or depression, increasing their risk of both morbidity and mortality [2,3]. Therefore, it is important to identify and treat patients for both their underlying cardiovascular disease alongside symptoms of anxiety and depression [4–6].

Cardiac rehabilitation (CR) is an evidence-based multidisciplinary intervention consisting of a range of core components, including screening for anxiety and depression [7]. Clinical guidelines have recommended screening for anxiety and depression as part of comprehensive CR for years [8,9]. Nevertheless, a small number of studies suggest clinical practice is still far from implementing systematic screening in CR [10–12]. Anxiety and depression have been shown to act as barriers to treatment adherence and life-style changes which may reduce the effect of CR [7,13]. Hence, identifying these psychosocial risk factors in patients are crucial in order to improve clinical and patient-reported outcomes. Several factors associated with anxiety and depression in patients with ACS have been investigated. Younger age, living alone, living in an area of high social deprivation, increased number of comorbidities, high body mass index (BMI), physical inactivity, and smoking are all associated with increased prevalence of anxiety and/or

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[☆] All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.
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depression [14,15].

While several studies have investigated the association between anxiety and/or depression and ACS, we know little about whether subgroups of patients with ACS are less likely to be systematically screened for anxiety and/or depression in routine CR as compared to other patients. One study conducted in the general population in the United States found that calendar year, female gender, physician specialty, metropolitan location, geographical region, and time spent with the physician were significantly associated with performing screening for depression [16]. Even though the latter study is not conducted in patients with ACS, the findings raise the question if there might be similar patient or provider level characteristics, determining if ACS patients are screened for anxiety and depression as part of routine CR. Understanding what factors might be associated with a tendency to refrain from screening in patients with ACS and elevated risk of anxiety and/or depression may help to improve the quality of CR services with respect to patients' psychosocial burden. Thus, the aim of the current study was to investigate if the likelihood that patients with ACS are screened for anxiety and depression, as part of routine practice CR, is associated with patient characteristics and service quality at the provider level.

2. Methods

We used an observational study design and the STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology) [17] for reporting the results.

2.1. Data collection

All data were collected in routine CR in the United Kingdom (UK). The National Audit of Cardiac Rehabilitation (NACR) collects a large variety of data at both patient and provider level to maintain and improve the quality of CR [18]. Data includes sociodemographic, clinical variables and outcomes at the patient level, as well as service level variations at the provider level according to the British Association for Cardiac Prevention and Rehabilitation (BACPR) standards [19]. The NACR is hosted by NHS Digital, and data are collected and monitored under NHS data requirements. NACR has permission to use anonymized data for quality purposes without needing separate ethical approval or individual informed consent.

2.2. Participants

The study population consisted of patients from the NACR database with ACS and a pre-CR assessment in the period from 1st January 2016 to 31st December 2019 ($n = 138.018$). Due to the large variation in patient presentation, entry into CR as well as the service change throughout the COVID-19 pandemic, all data from 2020 was excluded [18] [20].

2.3. Variables of interest

2.3.1. Outcome measure

Screening for anxiety and depression is a core component of CR which should be executed using a validated tool [7]. Within NACR it is possible to register data with respect to screening for anxiety and depression based on three validated patient-reported questionnaires: the Hospital Anxiety and Depression Scale (HADS) [21], the Generalized Anxiety Disorder (GAD-7) [22] and the Patient Health Questionnaire (PHQ-9) [23]. A composite binary outcome was generated from these questionnaires, so either both domains of the HADS or both the GAD-7 and the PHQ-9 had to be reported in NACR for a patient to be considered screened for anxiety and depression.

2.3.2. Screening tools

The HADS consists of 14 items with seven items covering the domains anxiety and depression, respectively. The HADS is widely used in the CR settings [4] and is reliable and valid for the assessment of cardiac patients [21]. GAD-7 consists of seven items on general anxiety, while PHQ-9 consists of 9 items on depression. All questionnaires are scored on a scale from 0 to 3, with higher scores indicating more symptoms. Hence, HADS and GAD-7 scores will be in a range from 0 to 21, while PHQ-9 scores will have a score range of 0–27.

2.3.3. Exposure measures

Variables selected for adjustment were chosen a priori based on the literature on factors associated with psychosocial wellbeing and expert opinions, since the literature on the topic is sparse. Regarding sociodemographic variables, age was used as a continuous variable while gender was categorized as male or female. Marital status was categorized as single (single/widowed/separated) or partnered (married/partnered), and ethnic group as white or non-white. Index of multiple deprivation (IMD) is a measure that classifies the relative deprivation of a small area in England [24]. Seven domains of deprivation are weighted differently and aggregated into one single score. We categorized the IMD score into quintiles. With respect to clinical variables, we categorized treatment for ACS as either percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG) or medically managed. We used current smoking (yes/no), physical activity <150 min pr week (yes/no), and BMI ($\text{BMI} < 30$ versus $\text{BMI} \geq 30$) as binary variables. Data on comorbidity was collected from patients' medical history, which was verified by CR clinicians. We used depression, anxiety, diabetes, stroke, osteoporosis, hypertension, chronic obstructive pulmonary disease, asthma, and chronic back problems as binary variables (yes/no). Concerning provider level data, we used these as an indicator for quality of CR services. We categorized the CR programs as certified or not, according to the National Certification Program for Cardiac Rehabilitation in the UK [12,18,19]. To be classified as certified, the individual program had to meet all seven key performance indicators. To assess improvement over time we included year of CR.

2.4. Statistical analysis

Descriptive statistics were used to summarize the baseline characteristics in terms of means, standard deviations, and percentages. For comparing baseline characteristics between groups of screened versus non-screened, we used Student's *t*-test for continuous variables and Chi^2-test for categorical variables. For analysis of determinants for screening for anxiety and depression, we used a multivariate logistic regression model, applying odds-ratios. Since NACR contains a wide range of comorbidities ($n = 18$) we conducted a stepwise backward selection of these and chose beforehand to remove erectile dysfunction as it is a male only condition. Further eight comorbidities were removed in this process due to statistical insignificance.

The impact of missing cases in the multivariate analysis was tested using a forward stepwise selection of groups of core variables. Inclusion of variables did not alter the results in the first four steps, while the final step with inclusion of IMD led to change of significance level in gender and marital status. We chose to keep IMD in the main model as previous studies have shown a strong association with psychosocial burden [4] as well as mortality [25]. The full dataset is presented in the supplementary material (Supplementary material A).

Furthermore, we investigated the prevalence of anxiety and depression using the commonly clinical cut-off scores of HADS [21] and reported as numbers and percentages. We analyzed if anxiety and depression were evenly distributed across the five levels of IMD. We only included HADS scores in these sub analyses, as the scores represented the overall majority of the population and scoring range as well as cut-off scores differ from HADS in the remaining questionnaires.

A statistical level of <0.05 was applied to the analyses. All statistical analyses were conducted using STATA version 16.

3. Results

3.1. Study population

The total study population consisted of 440,405 patients entered in the NACR database during a 4-year period (Fig. 1). Out of these, 138,018 had both assessment 1 and a diagnosis of ACS and constituted the study population. We found that 59.8% of the study population were screened for anxiety and depression at start of CR, while the remaining 40.2% were not. Among the screened patients, 91.3% ($n = 75{,}315$) were screened with HADS, while 8.9% ($n = 7333$) were screened with GAD-7 plus PHQ-9, and 0.2% ($n = 141$) with both combinations.

3.2. Baseline characteristics

Table 1 describes the study population, comparing screened with non-screened for anxiety and depression. At baseline the two groups differed in terms of statistical significance on all characteristics ($p < 0.001$ for all). The subgroups more likely to be screened were those with younger age, being male, being partnered, white ethnicity, living in the least deprived areas, treated with PCI or CABG, non-smoking, physically active>150 min weekly, and having a BMI < 30. Regarding comorbidities, patients with depression, anxiety, osteoporosis, chronic back problems, and asthma were more likely to be screened than patients without the comorbidities. Patients with chronic obstructive pulmonary disease, diabetes, stroke, and hypertension were less likely to be screened than patients without these comorbidities. At the provider level, we found that certified CR centers were more likely to screen for anxiety and depression compared to uncertified CR centers. For development over time, we found that patients were less likely to be screened in 2016 compared to the following years.

3.3. Logistic regression model

Table 2 shows the adjusted odds-ratios (OR) for being screened for anxiety and depression, with the inclusion of 44,119 cases. In relation to socio-demographics, younger patients (OR 0.99; 95% CI: 0.99–0.99; $p < 0.001$) and patients with non-white ethnicity (OR 0.82; 95% CI: 0.75–0.89; p < 0.001) were less likely to be screened for anxiety and depression. Patients living in the least deprived areas were more likely to be screened for anxiety and depression, compared to the most deprived area (OR 1.39; 95% CI: 1.27–1.55; p < 0.001). We found no statistically significant associations between being screened and gender and marital status, respectively.

With respect to the clinical variables, treatment with CABG or medically managed patients were less likely to be screened for anxiety and depression compared to patients treated with PCI (OR 0.84; 95% CI: 0.77–0.92; $p < 0.001$) (OR 0.71; 95% CI: 0.67–0.75; p < 0.001). Patients who were currently smoking (OR 0.57; 95% CI: 0.52–0.61; p < 0.001), were physically active<150 min/week (OR 0.60; 95% CI: 0.57–0.64; $p < 0.001$), had a BMI ≥ 30 (OR 0.77; 95% CI: 0.73–0.81; p < 0.001) were less likely to be screened.

We found five comorbidities that were positively associated with screening for anxiety and depression. These were depression (OR 1.15; 95% CI: 1.03–1.28; $p = 0.012$), anxiety (OR 1.24; 95% CI: 1.11–1.38; $p < 0.001$), osteoporosis (OR 1.25; 95% CI: 1.03–1.52; $p = 0.025$), chronic back problems (OR 1.82; 95% CI: 1.66–2.00; p < 0.001), and asthma (OR 1.12; 95% CI: 1.03–1.23; $p = 0.012$). We also found four comorbidities that were negatively associated with screening for anxiety and depression, including chronic obstructive pulmonary disease (OR 0.84; 95% CI: 0.74–0.96; p = 0.012), diabetes (OR 0.93; 95% CI: 0.88–0.99; $p = 0.024$), hypertension (OR 0.95; 95% CI: 0.90–0.99; $p = 0.033$), and stroke (OR 0.85; 95% CI: 0.76–0.96; $p = 0.007$).

Provider level data showed that certification of CR centers was positively associated with screening for anxiety and depression (OR 1.55; 95% CI: 1.47–1.62; $p < 0.001$). With respect to changes in screening over time, the data showed an incremental negative trend

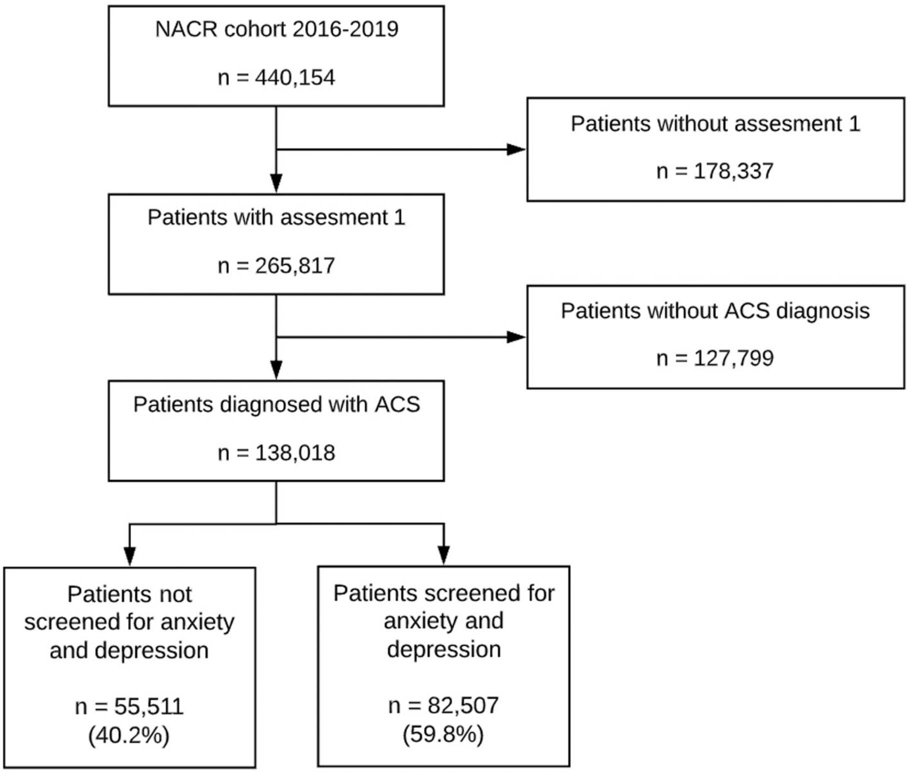

Fig. 1. Flowchart of the study population.

Table 1
Baseline characteristics of patients with acute coronary syndrome with first assessment in cardiac rehabilitation, stratified by screening for anxiety and depression (*p*-value between non-screened vs. screened).

Variables	Total	Non-screened	Screened	p-value*
Socio-demographics n (%)				
Age: mean (SD), range (n=138,018)	65.2 (12.3), 18-118	66.2 (13.0), 18-118	64.6 (11.7), 18-102	<0.001
Gender (n=136,408)				<0.001
Female	37,592 (27.6)	16,488 (43.8)	21,144 (56.2)	
Male	98,816 (72.4)	37,880 (38.3)	60,936 (61.7)	
Marital status (n=94,969)				<0.001
Single	24,334 (25.6)	9,430 (38.8)	14,904 (61.2)	
Partnered	70,635 (74.4)	24,246 (34.3)	46,389 (65.7)	
Ethnic group (n=112,379)				<0.001
Non-White	10,770 (9.6)	4,866 (45.2)	5,904 (54.8)	
White	101,609 (90.4)	38,178 (37.6)	63,431 (62.4)	
Index of Multiple Deprivation (n=114,104)				<0.001
Lowest quintile	21,314 (18.7)	10,559 (49.5)	10,755 (50.5)	
Second quintile	21,841 (19.1)	9,564 (43.8)	12,277 (56.2)	
Third quintile	23,273 (20.4)	9,143 (39.3)	14,128 (60.7)	
Fourth quintile	23,809 (20.9)	8,636 (36.3)	15,173 (63.7)	
Highest quintile	23,869 (20.9)	7,466 (31.3)	16,403 (68.7)	
Clinical data n (%)				
Treatment for ACS (n=138,018)				<0.001
Percutaneous coronary intervention	90,053 (65.2)	33,439 (37.1)	56,614 (62.9)	
Coronary artery bypass grafting	9,596 (7.0)	3,568 (37.2)	6,028 (62.8)	
Medically managed	38,369 (27.8)	18,504 (48.2)	19,865 (51.8)	
Smoking at start of CR (n=118,967)				<0.001
Yes	14,065 (11.8)	6,609 (47.0)	7,456 (53.0)	
No	104,902 (88.2)	33,656 (32.1)	71,246 (67.9)	
Physical activity<150 min/week (n=87,646)				<0.001
Yes	48,233 (55.0)	12,068 (25.0)	36,165 (75.0)	
No	39,413 (45.0)	5,808 (14.7)	33,605 (85.3)	
BMI (n=138,018)				<0.001
MI ≥ 30	63,327 (45.9)	32,687 (51.6)	30,640 (48.4)	
BMI < 30	74,691 (54.1)	22,824 (30.6)	51,867 (69.4)	
Comorbidities n (%) (n=107,580)				
Depression				<0.001
Yes	8,697 (8.0)	2,644 (30.4)	6,053 (69.6)	
No	98,883 (92.0)	37,675 (38.1)	61,208 (61.9)	
Anxiety				<0.001
Yes	8,043 (7.5)	2,317 (28.8)	5,726 (71.2)	
No	99,537 (92.5)	38,002 (38.2)	61,535 (61.8)	
Osteoporosis				<0.001
Yes	1,994 (1.9)	607 (30.4)	1,387 (69.6)	
No	105,586 (98.1)	39,712 (37.6)	65,874 (62.4)	
Chronic back problems				<0.001
Yes	9,937 (9.2)	2,146 (21.6)	7,791 (78.4)	
No	97,643 (90.8)	38,173 (39.1)	59,470 (60.9)	
Asthma				<0.001
Yes	9,178 (8.5)	3,203 (34.9)	5,975 (65.1)	
No	98,402 (91.5)	37,116 (37.7)	61.286 (62.3)	
Chronic obstructive pulmonary disease				<0.001
Yes	4,059 (3.8)	1,811 (44.6)	2,248 (55.4)	
No	103,521 (96.2)	38,508 (37.2)	65,013 (62.8)	
Diabetes				<0.001
Yes	24,018 (22.3)	9,957 (41.5)	14,061 (58.5)	
No	83,562 (77.7)	30,362 (36.3)	53,200 (63.7)	
Stroke				<0.001
Yes	4,822 (4.5)	2,152 (44.6)	2,670 (55.4)	
No	102,758 (95.5)	38,167 (37.1)	64,591 (62.9)	
Hypertension				<0.001
Yes	49,107 (45.7)	19,081 (38.9)	30,026 (61.1)	
No	58,473 (54.3)	21,238 (36.3)	37,235 (63.7)	
Provider level data n (%)				
CR Certification (n=138,017)				<0.001
Yes	76,176 (55.2)	25,523 (33.5)	50,652 (66.5)	
No	61,841 (44.8)	29,988 (48.5)	31,853 (51.5)	
Year of CR (n=138,018)				<0.001
2016	31,129 (22.6)	13,567 (43.6)	17,562 (56.4)	
2017	33,523 (24.3)	13,351 (39.8)	20,172 (60.2)	
2018	35,627 (25.8)	13,828 (38.8)	21,799 (61.2)	
2019	37.739 (27.3)	14,765 (39.1)	22,974 (60.9)	

Abbreviations: SD: standard deviation, ACS: acute coronary syndrome, CR: cardiac rehabilitation.
**p*-values are based on t-test for continuous variables and chi^2 test for categorical variables.

from 2016 to 2019 (OR 0.84; 95% CI: 0.78–0.90; $p < 0.001$).

3.4. Prevalence of anxiety and depression stratified by IMD

For both HADS anxiety and depression scores we found an incremental decrease in scores, from the lowest to the highest level of IMD (Table 3). We found that 33% (n = 24,910) of the population suffered from clinically relevant levels of anxiety (HADS anxiety scores 8–21), and 22% (n = 16,570) from clinically relevant levels of depression (HADS depression scores 8–21). When stratifying by IMD we found a statistically significant difference in prevalence for both anxiety and depression ($p > 0.001$). The prevalence of anxiety varied from 21.8% in the lowest quintile to 19.0% in the highest quintile. For depression, we found a prevalence of 23.7% in the lowest quintile and 17.9% in the highest quintile.

4. Discussion

This study showed that a range of both patient characteristics and the service quality at provider level determine the likelihood of patients

Table 2
Multiple adjusted odds-ratios for screening for anxiety and depression ($n = 41{,}119$).

Variables	Odds ratio	95% CI low	95% CI high	p-value
Socio-demographic				
Age (continuous)	0.99	0.99	0.99	**<0.001**
Female gender	0.96	0.91	1.02	0.181
Marital status (single)	0.96	0.90	1.01	0.138
Ethnic group: Non-white (yes)	0.82	0.75	0.89	**<0.001**
Index of Multiple Deprivation: *Lowest quintile*	Reference			
Second quintile	1.20	1.11	1.31	**<0.001**
Third quintile	1.29	1.19	1.40	**<0.001**
Fourth quintile	1.17	1.08	1.27	**<0.001**
Highest quintile	1.39	1.27	1.51	**<0.001**
Clinical				
Treatment for ACS: *PCI*	Reference			
CABG	0.84	0.77	0.92	**<0.001**
Medically managed	0.71	0.67	0.75	**<0.001**
Current smoking (yes)	0.57	0.52	0.61	**<0.001**
Physical activity<150 min/week (yes)	0.60	0.57	0.64	**<0.001**
BMI ≥ 30 (yes)	0.77	0.73	0.81	**<0.001**
Comorbidity				
Depression (yes)	1.15	1.03	1.28	**0.012**
Anxiety (yes)	1.24	1.11	1.38	**<0.001**
Osteoporosis (yes)	1.25	1.03	1.52	**0.025**
Chronic back problems (yes)	1.82	1.66	2.00	**<0.001**
Asthma (yes)	1.12	1.03	1.23	**0.012**
Chronic obstructive pulmonary disease (yes)	0.84	0.74	0.96	**0.008**
Diabetes (yes)	0.93	0.88	0.99	**0.024**
Hypertension (yes)	0.95	0.90	0.99	**0.033**
Stroke (yes)	0.85	0.76	0.96	**0.007**
Provider level				
Certified cardiac rehabilitation center (yes)	1.55	1.47	1.62	**<0.001**
Year of CR: *2016*	Reference			
2017	0.99	0.92	1.07	0.795
2018	0.89	0.82	0.96	**0.002**
2019	0.84	0.78	0.90	**<0.001**

Abbreviations: CI: confidence interval, ACS: acute coronary syndrome, PCI: percutaneous coronary intervention, CABG: coronary artery bypass grafting.

Table 3
Prevalence of anxiety and depression, measured by the Hospital Anxiety and Depression Scale (HADS), and stratified by Index of Multiple Deprivation.

HADS Scores	**HADS-Anxiety (n = 75,400)**	**HADS-Depression (n = 75.376)**
Mean (SD), range	6.0 (4.4), 0–21	4.7 (3.9), 0–21
Normal (0–7) n (%)	50,490 (67%)	58,806 (78%)
Clinically relevant anxiety and depression scores (8–21) n (%)	24,910 (33%)	16,570 (22%)
Proportion of patients with clinically relevant anxiety and depression scores, stratified on Index of Multiple Deprivation (HADS 8–21)		
Index of Multiple Deprivation	**HADS-Anxiety (n = 20,374)** * $p < 0.001$	**HADS-Depression (n = 13,486)** * $p < 0.001$
Lowest quintile n (%)	4445 (21.8%)	3190 (23.7%)
Second quintile n (%)	4196 (20.6%)	2869 (21.3%)
Third quintile n (%)	3950 (19.4%)	2576 (19.1%)
Fourth quintile n (%)	3915 (19.2%)	2440 (18.1%)
Highest quintile n (%)	3868 (19.0%)	2411 (17.9%)

[*] Missing cases due to missing data on Index of Multiple Deprivation.

with ACS being screened for anxiety and depression in routine CR. To our knowledge, this is the first study to investigate this within the cardiac field.

Regarding patient characteristics, we found three sociodemographic determinants that reduced the likelihood of being screened for anxiety and depression. These were younger age, non-white ethnicity, and living in areas of high social deprivation. One simple explanation for reduced screening in the non-white ethnicity group could be language barriers, as the screening tools are available only in English, however that is not likely to be the full explanation. Looking at the IMD, areas with high social deprivation are negatively associated with screening practice. At the same time, mean HADS scores were higher in areas with high social deprivation which is in alignment with the literature [4,15,26]. This signals that the prevalence of anxiety and depression might currently be underreported for these areas, as screening apparently is underperformed at the present time. We do not know if it is the low-risk patients who are not being screened for anxiety and depression in areas of high social deprivation. However, since the psychosocial burden is high and this is strongly associated with poor outcomes [4,25,27], further research is needed to investigate these associations in order to improve quality of care and the patients' health outcomes. Inequality in access to cardiac treatment has been reported previously [28], emphasizing the need for systematic quality improvements to ensure state-of-the-art CR across IMD, including screening for anxiety and depression.

Our results show that patients treated with PCI are more likely to be screened for anxiety and depression compared with patients treated with CABG or medically managed patients. This suggests that CR programs prioritize the patients differently depending on cardiac treatment, despite guidelines recommending screening of all patients with ACS [7]. In addition, we found that current smoking, low level of physical activity and high BMI are negatively associated with the screening practice. Although the presence of multiple modifiable risk factors at the same time is known to be associated with high prevalence of anxiety and depression [14,26] the current study indicates this was not associated with an increased likelihood of screening. We can only speculate if this may be attributed to CR staff prioritizing their sparse resources on supporting patients' somatic lifestyle changes, even though anxiety and depression act as barriers for successful behavioral change [29].

The literature shows that comorbidity is associated with increased prevalence of anxiety and depression in cardiac patients [14,15,30]. Previous anxiety and depression are well-known predictors for recurrent psychological distress [4], and we found that patients with these comorbidities have higher odds for being screened for anxiety and depression. This could point towards CR staff giving extra attention to these high-risk patients, but potentially CR staff might also be more prone to screen patients with signs of psychosocial distress [31], underlining the importance of systematic screening. Further results on comorbidities were mixed with no obvious explanation. Some chronic patient subgroups, such as ACS patients with diabetes might be screened for anxiety and depression during the diabetes treatment pathway, so we can speculate if this leads to CR staff refraining from repeated screening.

With respect to provider level, the European Association of Preventive Cardiology has described screening for anxiety and depression as part of their future CR accreditation, underlining the importance of this area [32]. On the bright side, we found that certification of a CR center is positively associated with screening for anxiety and depression. This indicates, that even though screening for anxiety and depression is not a key performance indicator of the BACPR certification [19], focus on quality of care through certification might enhance other areas of care within CR. On the other hand, we also found that the odds for being screened deteriorate over the included four years. Again, we can only speculate if decrease in screening might be associated with evolving sparse resources or competing tasks of the involved CR staff. Also, barriers for registration in NACR might be a contributing factor [33]. CR centers in areas with high social deprivation and large numbers of psychosocially complex patients may appear as low-performing, reducing motivation to engage in feedback-driven quality improvement initiatives as the NACR [34]. Since we only included data from the first assessment in the CR pathway, there might be patients who have been screened at a later timepoint, or patients where conducted screening was not reported in the NACR system due to suboptimal registration practice.

Overall, screening practices in routine CR are still far from optimal with only 60% of patients with ACS being screened for anxiety and depression, and inconsistency in the procedure across patient characteristics. A gap between guidelines and clinical practice regarding screening is previously reported [10,11,30] but results from this study illuminates the importance of implementing systematic screening procedures across all subgroups to mitigate inequity in CR delivery. Clinical implications include reflection on and adjustment of screening procedures locally. In addition, decision makers are called upon to allocate the necessary resources to safeguard the possibilities for screening for anxiety and depression in CR, as these conditions increases risk of both morbidity and mortality for cardiac patients [2,3].

In this study, we included patients with ACS at start of CR, but since anxiety and depression might also occur at a later point in time, more than one screening is required to identify patients at risk [6]. Pre-and post-screening in CR is warranted on both patient and provider level in order to be able to assess changes, and continuously support the individual patient, and to assess and improve the quality of care in CR [18,27].

Screening patients with ACS for anxiety and depression is crucial to identify this vulnerable subgroup, but obviously this is not sufficient. Collopy et al. points at a need for information provision in health care settings, to support cardiac patients in seeking help for mental health problems [35]. It is paramount that the CR center has an evidence-based treatment to offer to patients who screen positive for anxiety or depression [4,35]. Therefore, we find it important that CR centers reflect on procedures for referral to treatment for anxiety and depression, to best support the patient and tackle barriers [35]. Treatment could for instance be delivered onsite [36] or as an eHealth intervention, safeguarding treatment in times of the COVID-19 pandemic [37]. Here again, decision makers have a responsibility to help CR centers ensure available evidence-based treatment options.

4.1. Strengths and limitations

Observational data from clinical practice are appropriate to use when exploring associations, with the limitation that no causality can be inferred [38]. However, a strength of using routinely collected data from clinical practice in this study is the possibility of examining a broader population, as no patients are excluded e.g. to age-criteria as in controlled studies [39]. Another strength of this study is the high volume of patients, despite missing cases.

Limitations include the accessible variables in NACR, where other factors could possibly be co-existing determinants. As the vast majority of CR centers in the UK report to NACR, we consider the results to be representative, however patterns of screening practice might be different in the remaining CR centers with a risk of selection bias. Further research is needed to investigate if the results can be generalized to other cardiac populations or countries with different modes of CR delivery.

4.2. Conclusion

We found both patient and provider level determinants of screening for anxiety and depression. However, clinical practice is inconsistent in respect of patient assessment especially for high-risk groups. We recommend that clinicians should systematically screen patients to enable tailored interventions which in turn may mitigate inequity in CR delivery and thereby health outcomes of the patients.

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Declaration of Competing Interest

None

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2022.02.004.

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Appendix II

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European Heart Journal Digital Health
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ORIGINAL ARTICLE

Internet-based treatment of anxiety and depression in patients with ischaemic heart disease attending cardiac rehabilitation: a feasibility study (eMindYourHeart)

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Aims Anxiety and depression are prevalent in 20% of patients with ischaemic heart disease (IHD); however, treatment of psychological conditions is not commonly integrated in cardiac rehabilitation (CR). Internet-based psychological treatment holds the potential to bridge this gap. To examine the feasibility of an eHealth intervention targeting anxiety and depression in patients with IHD attending CR.

Methods and results We used a mixed-methods design, including quantitative methods to examine drop-out and change in anxiety and depression scores, and qualitative methods (thematic analysis) to evaluate patients' and nurses' experiences with the intervention. The therapist-guided intervention consisted of 12 modules provided via a web-based platform. The primary outcome was drop-out, with a drop-out rate <25% considered acceptable. Patients were considered as non-drop-out if they completed ≥5 modules. Out of 60 patients screened positive for anxiety and/or depression, 29 patients were included. The drop-out rate was 24% (7/29). Patients had a mean improvement in anxiety and depression scores of 5.5 and 4.6, respectively. On average, patients had 8.0 phone calls with their therapist and 19.7 written messages. The qualitative analysis of patients' experiences identified four themes: treatment platform, intervention, communication with therapist, and personal experience. Patients were positive towards the intervention, although some found the assignments burdensome. From the nurses, we identified three themes: intervention, inclusion procedure, and collaboration with study team. The nurses were positive, however, due to limited time some struggled with the inclusion procedure.

Conclusion Integrating an eHealth intervention in CR is feasible and the drop-out rate acceptable.

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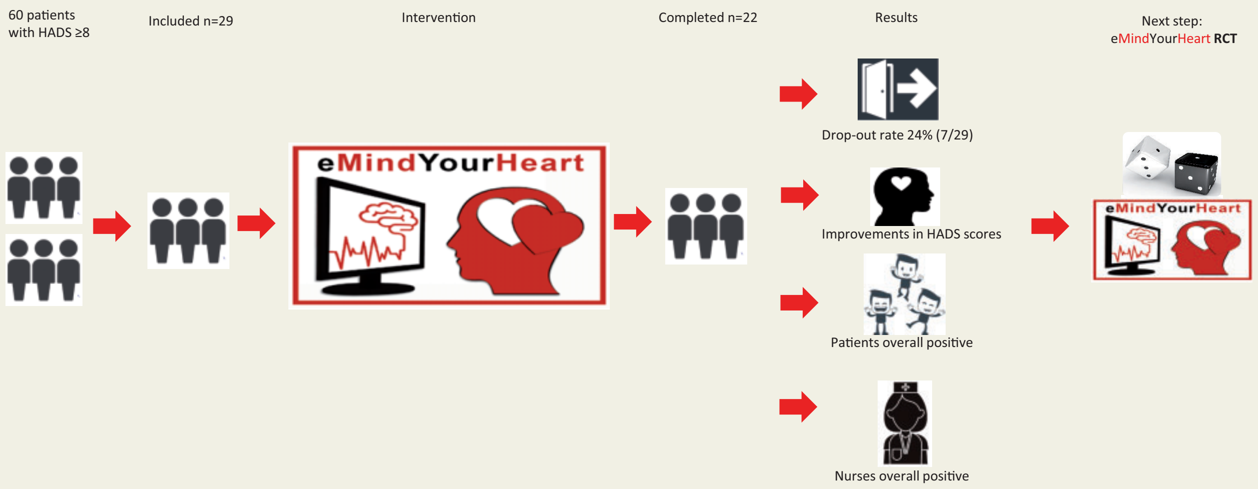
Graphical Abstract

Internet-based treatment of anxiety and depression in patients with ischemic heart disease attending cardiac rehabilitation:
The eMindYourHeart feasibility study



Keywords Anxiety • Cardiac rehabilitation • Depression • E-health • Internet-based cognitive behavioural therapy • Ischaemic heart disease

Introduction

More than 83.5 million people in Europe live with cardiovascular disease, including ischaemic heart disease (IHD).[1] Approximately 20% of patients with IHD have symptoms of anxiety or depression that warrant treatment.[2] Psychological conditions such as anxiety and/or depression act as barriers to treatment adherence of cardiac rehabilitation (CR). This increases the risk of adverse outcomes in this vulnerable subset of patients,[2] as evidence-based CR is shown to reduce cardiovascular mortality, rehospitalization,[3] and improve psychological distress.[4]

Clinical guidelines recommend screening for psychological distress in patients with IHD combined with psychological treatment if patients screen positive.[5] However, psychological treatment is not routinely offered as part of standard CR following screening.[6] Cognitive behavioural therapy (CBT) is an effective treatment for anxiety and depression in cardiac patients,[7] but lack of psychologists and challenged healthcare budgets hinder implementation of CBT in CR.[6,8,9]

Current technology has enabled the delivery of internet-based psychological treatment and internet-based CBT (ICBT) appear to be an equally effective treatment for anxiety and depression as face-to face therapy.[10] ICBT interventions are typically delivered on a weekly basis and contain structured written material, audios, and videos, resembling face-to face treatment.[11] ICBT is not geographically or timely confined, which enables patients with internet access to engage in the treatment from any place at any time of the day.[11] Further advantages include reducing delay to psychological treatment, enabling quick access to treatment.[11]

The widespread use of internet-enabled devices ensures the possibility of delivering ICBT to a broad population, including all socio-economic backgrounds.[12] However, implementing the service in routine care is challenging due to complex and fragmented healthcare systems, lack of funding, and limited stakeholder knowledge.[12] Therefore, it can be challenging for patients with IHD to obtain treatment, since there—at least in Denmark—are no automatic referral channels from the CR centres for ICBT or other psychological therapies. This means that patients with IHD besides dealing with their somatic disease must contact their general practitioner for guidance and referral to psychological treatment or seek help elsewhere.[2] For some patients, particularly those with depression, this may be an insurmountable task, with the risk that they never receive psychological treatment. In addition, psychological treatment might only be reimbursed under specific conditions and unaffordable for patients with e.g. low socio-economic status. Hence, integration of ICBT as part of CR has a considerable potential for the subset of patients with IHD suffering from anxiety and depression.

A systematic review on ICBT in populations with a chronic disease showed significant improvements in anxiety and depressive symptoms, but further research in cardiac populations is suggested due to limited evidence.[13] Furthermore, this study points at exploring how to best integrate ICBT in routine care, as most studies have been conducted in research settings.[13] Results on effect of ICBT targeting anxiety and depression in cardiac patients are mixed and very limited. Two studies found no effects on symptoms of anxiety and depression in randomized controlled trials (RCTs) of patients with myocardial infarction[14] and heart failure,[15] respectively, while two other RCTs show positive effects on anxiety and depression in cardiac populations,[8,16] indicating a potential for ICBT in cardiac care. Thus, the high prevalence of anxiety and depression highlights the need to develop and evaluate the potential efficacy of ICBT models in CR.

The overall objective of the study was to examine the feasibility of an eHealth intervention targeting anxiety and depression in patients with IHD and integrated in standard CR as a precursor to an RCT.[17] Focus areas of the study were acceptability from patients and CR nurses to assess how the intervention were received and implementation of the intervention to test logistics before the RCT.[18] The specific aims were to evaluate (i) the dropout rate to assess acceptability, (ii) changes in anxiety and depression scores pre- and post-intervention to determine potential benefits and harms of the intervention, (iii) the extent of use of the treatment platform, (iv) the utility and experiences of the intervention from the patient's perspective, and (v) the logistics of the intervention from the CR nurses perspective.

Apart from dropout rate, the evaluations did not include predefined outcome targets as these parameters were conducted as proof of concept before the RCT.

Methods

Design

This feasibility study is part of the eMindYourHeart study[17] and was conducted using a prospective mixed-methods design to enhance the feasibility assessment of the intervention and the procedures.[19] The use of parallel research methods was chosen to obtain a broader view of the context of the study and to draw on strengths and mitigate weaknesses from each individual method. Quantitative methods included descriptive analysis of dropout, changes in anxiety and depression scores post-intervention (i.e. at 3 months of follow-up) and the extent of use of the treatment platform. Qualitative methods included thematic text analysis of written evaluations from patients about their experiences with the intervention and from CR nurses' their experiences with the inclusion procedures. The study is reported according to the CONSORT 2010 guideline (Consolidated Standards of Reporting Trials), using the checklist for feasibility trials.[20]

Participants

Participants in the intervention

We aimed to recruit 30 participants, which was a pragmatic choice and considered sufficient for the aims of the feasibility evaluation. Participants were Danish patients attending CR who screened positive on the Hospital Anxiety and Depression Scale (HADS)[21] as part of routine care. Inclusion criteria were age ≥18 years, diagnosis of IHD, HADS score ≥8 on depression and/or anxiety,[22] access to a computer or smartphone, ability to use computer or smartphone, proficient in the Danish language, and a signed informed consent. Exclusion criteria were severe psychiatric disorder (e.g. schizophrenia), severe cognitive difficulties (e.g. dementia), participation in other psychological intervention studies, seeing a psychologist or mental health professional for the treatment of depression and anxiety.

The participants were recruited consecutively from nine Danish CR centres. The centres were strategically chosen across all five Regions in Denmark and across hospitals and municipalities, to ensure variation with respect to logistics in the CR programmes and a variety in patient demographics. CR nurses recruited patients for the study when starting their CR programme and being routinely screened for anxiety and depression, as recommended by national[23] and European guidelines.[5]

Participants in the evaluations

All patients who completed the intervention and all CR nurses involved in recruitment of patients were invited to participate in an evaluation of the intervention.

Intervention

The intervention was developed using a participatory design.[24] This design was used to ensure the target patient group experienced the ICBT as relevant and useful. Psychologists and supervised graduate students of psychology (in their final year) with thorough training in mental health in cardiac patients guided the intervention as therapists. A CR nurse supervised the cardiac aspects when needed. The therapist contacted the patients within three workdays after completing the baseline questionnaire. The intervention began with a diagnostic telephone interview conducted by the therapist, using a brief purpose-designed interview protocol. The protocol was implemented to gain background information about patients' life situation, experiences with heart disease, motivation to participate in the intervention, understanding of the concepts of the ICBT intervention, sleep problems, use of alcohol and recreational drugs, previous experiences with anxiety, depression and psychological treatment, suicidal ideation, and prior trauma as well as building a therapeutic alliance. The 12-week ICBT intervention consisted of nine mandatory and three voluntary modules, covering topics like behavioural activation and cognitive restructuring (*Figure 1*; *Table 1*). All mandatory modules contained written assignments. Patients could access the treatment platform at any time of the day using smartphone, tablet, or computer.

Patients had a personal therapist assigned who supported them throughout the intervention, guiding them through the modules on a weekly basis by asynchronous written messages via the platform. Patients could use the written message function whenever they wanted, and the therapist would respond within two workdays. Furthermore, patients had four phone calls with the therapist during the intervention, including the diagnostic interview. In case patients had an additional need, further phone calls could be assigned.[25] The dropout rate was tried diminished by therapists supporting all patients with individual approaches depending on the patient's situation and the phone calls allowed for this individualization. Patients accessed the intervention platform by a GDPR-compliant website, using their NemID, a Danish national two-factor authentication solution.

Quantitative outcomes and statistics

The primary outcome was dropout rate where a rate <25% was considered a success, based on a systematic review of guided ICBT.[26] Treatment completion was defined a priori as five or more mandatory modules completed, since this would ensure that the patient had engaged in both psycho-educative and cognitive and behaviour change content. Secondary outcomes were changes in HADS scores, extent of use of the platform and utility of intervention. Utility was evaluated with six generic questions from the Internet Evaluation and Utility Questionnaire,[27] which were chosen as they fitted well with the context of the current intervention. Data on dropout and patient-reported outcomes were collected

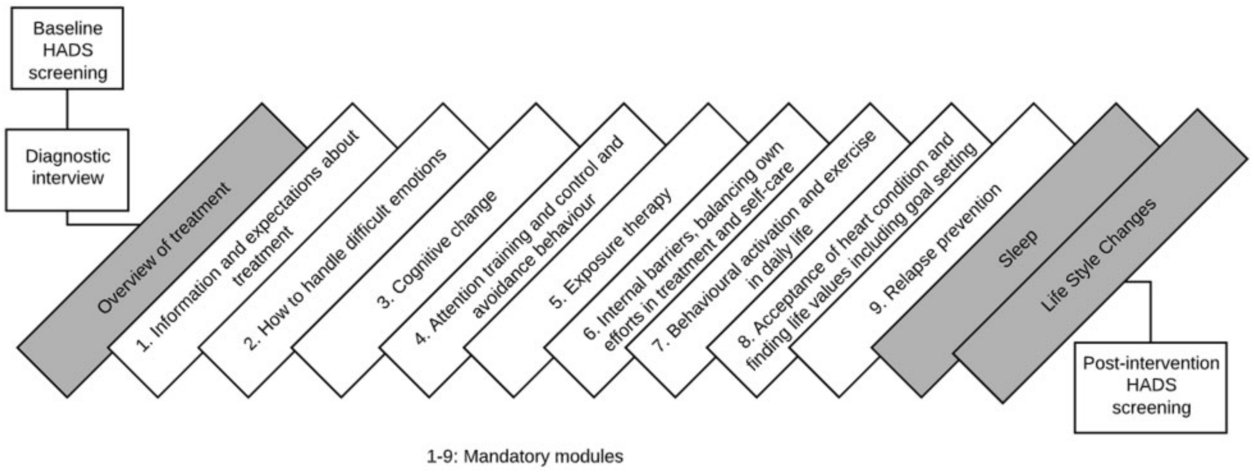


Figure 1 Overview of the intervention.

and managed electronically using the internationally recognized system for data management—Research Electronic Data Capture (REDCap)—via Odense Patient data Explorative Network (OPEN).[28] Patient-reported data were collected at baseline and at 3-month follow-up. Extent of use of the platform included duration spent on the treatment platform and frequency and time of login. These data were captured via the treatment platform. Demographics were collected in the baseline questionnaire and clinical data through the Danish Cardiac Rehabilitation Database.[29] Results were presented using descriptive statistics and reported with frequencies, percentages, means, range, and standard deviation where appropriate. All statistical analyses were conducted using Stata version 16.1.

Qualitative measurements

Data on patients' experiences with the intervention were generated through a purpose-designed questionnaire at 3 months of follow-up, divided into categories regarding experiences with the intervention. Patients gave written feedback on the questionnaire, which did not call for alterations. Data on CR nurse's perception of the intervention were likewise generated through a purpose-designed questionnaire divided into categories regarding logistics of the recruitment procedure. Two CR nurses gave written feedback on this, leading to minor adjustments. Both questionnaires were completed online using REDCap, and answered with open text, enabling the possibility of broad feedback. Both groups had the possibility to write issues beyond the predefined categories and give their evaluation by phone if preferred. The qualitative analysis processes were performed using thematic analysis, inspired by Braun and Clarke.[30] For each evaluation, two authors (C.H. and S.J.S.) repeatedly read and coded the data independently and afterwards discussed the coding until consensus was reached. The codes were then sorted into categories and mapped into themes. To optimize credibility the themes were discussed, analysed, and revised with the inclusion of further two authors (C.M.A. and S.S.P.). The trustworthiness of the qualitative analysis was tried accomplished by involving the end-users in the design of the questionnaires to optimize reliability, by using investigator triangulation in the coding process to gain credibility and by describing the context to show transferability.

Hospital Anxiety and Depression Scale (HADS)

The HADS was chosen as the screening tool for anxiety and depression, since it has shown to be a valid measure in cardiac patients[22,31] and is recommended in CR in the Danish national clinical guidelines.[23] HADS is a 14-item questionnaire with 7 items each contributing to the subscales anxiety and depression. Each item is scored on a Likert scale from 0 to 3 leading to a score range from 0 to 21 for both subscales, with higher scores indicating more severe symptoms. The commonly used cut-off score of ≥8 was applied to identify symptoms of anxiety and depression.[22]

Ethics

Permission to conduct the study was obtained from the Danish Data Protection Agency at Odense University Hospital (17/41433 on 24 November 2017) via the umbrella permission of the Region of Southern Denmark. Ethical approval was obtained from the Regional Committees on Health Research Ethics for Southern Denmark (S-20180024). The study complies with the Helsinki Declaration with all patients providing written informed consent.[32]

Results

Participants and drop-out rate

The participants were recruited and treated between November 2019 and July 2020. *Figure 2* outlines the flowchart of the study population. A total of 60 patients were identified with elevated HADS scores, of which six were excluded based on exclusion criteria, while 16 patients declined to participation and one died. After the baseline questionnaire and telephone interview, a further eight were excluded or declined. Thus, we included 29 participants in the feasibility study corresponding to 54% of eligible patients. Of the included patients, five dropped out and two did not complete the required five modules to be considered 'completer' of the intervention. This means we had a dropout rate of 24.1% (7/29), reaching the desired rate of <25%.

Table 1 **Description of the modules in the internet-based cognitive behavioural treatment**

Module	Content	Aim	Therapeutic components
Extra	Overview of treatment	Introduction to treatment + information about IHD.	Psychoeducation
1	Information and expectations about treatment	To give the patients a better understanding of their own psychological reactions.	Psychoeducation, motivation, and goals
2	How to handle difficult emotions	To help patients understand and manage their own emotions in a healthier way.	Psychoeducation, mentalization, self-compassion
3	Cognitive change (Introduction to cognitive diamond)	To give patients a better understanding about their own psychological patterns and concrete tools on how to manage difficult thoughts.	Psychoeducation, cognitive restructuring, cognitive diffusion
4	Attention training and control and avoidance and behaviour	To help patients to less attention on bodily anxiety symptoms which can be interpreted as IHD. Moreover, to help them identify their own safety and avoidance behaviours.	Psychoeducation, selective attention training
5	Exposure therapy	To help patients face their fears and overcome them.	Exposure therapy
6	Internal barriers, balancing own efforts in treatment and self-care	Patients identify and work with potential treatment barriers. Also benefits of self-compassion and exercises promoting self-compassion.	Cognitive restructuring, self-compassion
7	Behavioural activation and exercise in daily life	To activate depressive patients and to promote physical exercises, to lower depression and anxiety.	Behavioural activation
8	Acceptance of heart condition and finding life values	To promote acceptance of current situation, and a shift in focus away from limitations and towards possibilities.	Cognitive restructuring, life values
9	Relapse prevention	To ensure patients know how to spot early signs of relapse and know how to handle these.	Psychoeducation, cognitive restructuring
Extra	Sleep	Knowledge and tools on how to improve sleep.	Psychoeducation
Extra	Lifestyle changes	Information about living with IHD, e.g. where to get help quitting smoking.	Psychoeducation

Out of 54 eligible patients, 25 (46%) were not included in the study. For these 25 patients, data are missing for five since they did not provide informed consent. Of the remaining 20 patients, four patients (20%) were female, and the mean age was 59.7 (SD: 10.1), with a range of 33–76 years. The characteristics of the 29 included patients are presented in *Tables 2* and *3*.

Changes in anxiety and depression (measured with HADS)

We found a mean improvement for HADS anxiety scores at 5.5 points and a mean improvement for HADS depression scores at 4.6 points (*Table 4*). Among the 22 completed patients, three had missing HADS scores at follow-up. The minimal clinical important difference (MCID) reflects meaningful changes for the patient, and for HADS scores it is 1.8.[33] We found that 16 out of 19 (84%) patients achieved the MCID for anxiety and 15 out of 19 patients (79%) achieved the MCID for depression. Three reported worse outcomes post-intervention compared to pre-intervention, where one of these were clinically relevant according to the MCID.

Use of intervention

Patients who completed the intervention had a mean of 8 telephone calls and 19.7 written messages with their therapist during the intervention (*Table 5*). The diagnostic telephone interview is not included in these data. On average, patients spent 10.95 h on the treatment platform. Participants were automatically logged out after 5 min of inactivity, so the time consumption does not include patients who left the treatment platform unattended. For patterns of login, we found that patients logged on to the treatment platform a mean of 33.5 times, where 59.4% of the times took place during normal opening hours for CR centres, while 40.6% took place outside normal opening hours. The total time of the intervention from diagnostic interview to completion of the last module was on average 13.3 weeks.

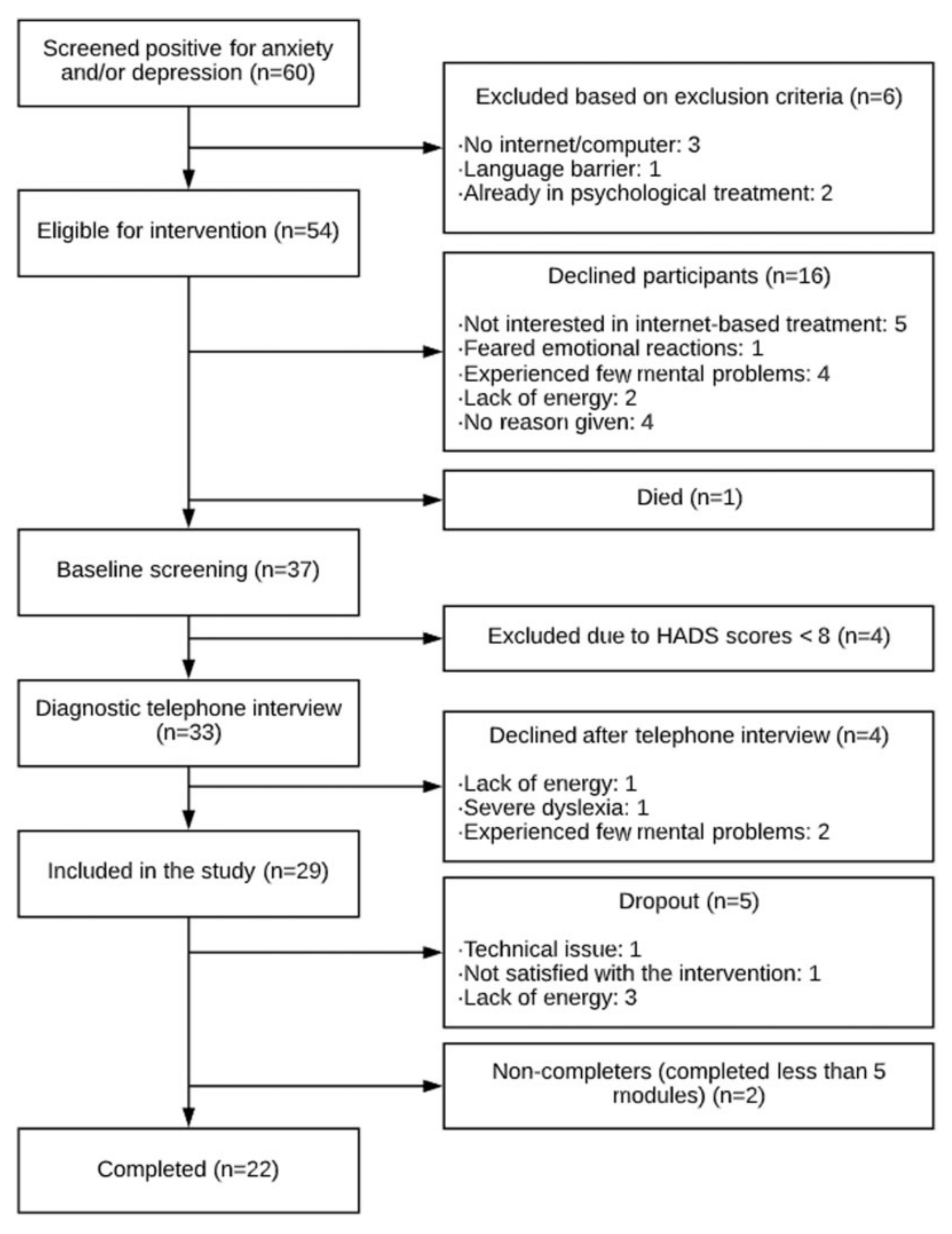


Figure 2 Flowchart of the study population.

Utility of the intervention

The same 19 patients who completed HADS also completed the utility questions post-intervention (*Figure 3*). The majority found the intervention easy to use, that the intervention kept their interest and attention, that the information was useful and easy to understand and were satisfied with the intervention. The majority were not worried about their privacy although one patient-reported being worried 'mostly'.

Patients' evaluation of the intervention

Of the 22 patients who completed the intervention, 14 agreed to provide an evaluation. The text analysis led to the identification of four themes: treatment platform; intervention; communication with therapist; and personal experience (*Table 6*). Patients experienced that accessing and navigating on the treatment platform was easy, however few found the logon procedure burdensome. Regarding the intervention, the patients were highly satisfied with the concept,

Table 2 **Characteristics of included patients ($n = 29$)**

	Completed participants ($n = 22$)	Non-completed participants ($n = 7$)
Age, mean (SD)	64.6 (11.2)	53.0 (10.0)
range	47–84	40–70
Female sex, *n* (%)	9 (41%)	2 (29%)
Living alone, *n* (%)	6 (27%)	4 (57%)
Employment status, *n* (%)		
Employed	9 (41%)	5 (71%)
Retired	12 (55%)	1 (14%)
Other	1 (4%)	1 (14%)
Highest completed education, *n* (%)		
Primary school/high school	3 (14%)	2 (29%)
Short education (≤3 years)	7 (31%)	5 (71%)
Bachelor's degree (3–4 years)	9 (41%)	0
Higher education (≥5 years)	3 (14%)	0
Body mass index, mean (SD)	28.1 (5.3)	30.2 (4.6)
range	20.6–40.9	23.3–37.2
Currently smoking, *n* (%)	2 (9%)	3 (43%)
Previously diagnosed with psychiatric disorder, *n* (%)	2 (9%)	1 (14%)
Physically active ≥150 min per week, *n* (%)	7 (32%)	2 (29%)

Table 3 **Clinical data from the Danish Cardiac Rehabilitation Database ($n = 18$)[a]**

Variable	*n* (%)	Missing *n* (%)
Primary indication for referral to cardiac rehabilitation		
ST-elevation myocardial infarction	5 (28)	2 (11)
Non-ST-elevation myocardial infarction	7 (39)	
Stable angina pectoris	4 (22)	
Primary cardiac procedure		
Percutaneous coronary intervention	11 (61)	0 (0)
Medically managed[b]	6 (33)	
Heart valve replacement	1 (6)	
Diabetes	1 (6)	0 (0)
Heart failure	1 (6)	0 (0)
Referred for exercise-based cardiac rehabilitation	16 (89)	1 (6)
Referred for group-based patient education	11 (6)	2 (11)

SD, standard deviation.

[a] Out of the 22 completed participants, 18 were identified in the Danish Cardiac Rehabilitation Database.

[b] These are classified as medically managed, as they are not registered as having undergone percutaneous coronary intervention or coronary artery bypass grafting.

Table 4 **Changes in anxiety and depression (measured with HADS) ($n = 19$)[a]**

	HADS pre-scores	HADS post-scores	Change
HADS A			
Mean (SD)	11.7 (3.1)	6.1 (4.4)	**−5.5 (4.6)**
Range	6–18	0–15	-16 to +4
HADS D			
Mean (SD)	9.5 (3.2)	4.9 (3.8)	**−4.6 (5.1)**
Range[b]	5–17	0–12	-15 to +5

HADS, Hospital Anxiety and Depression Scale; SD, standard deviation.

[a] Missing HADS data at follow-up, $n = 3$.

[b] Reported worse outcomes post-intervention, $n = 3$.

leaving them in control of time, place, and speed. Still, some found the written assignments inside some of the modules burdensome. All patients were highly satisfied with the communication with the therapist, appraising the competences of their personal therapist. The patients indicated that their personal motivation for participation was related to a need for help with worries, fear, anxiety, and loneliness, while some specified tools for coping. They experienced the intervention helped with better understanding and acceptance of difficult feelings, and the majority pointed at the cognitive diamond as particularly helpful. Some were positively surprised at the effectiveness of online intervention, and some found it a relief not having to engage in face-to-face treatment. The patients had individual patterns for when they engaged in the intervention based on energy levels, moods, convenience, and schedules.

Nurses' evaluation of the intervention

Among the involved CR nurses, 14 completed the evaluation, representing all nine centres. The text analysis led to three themes: intervention; inclusion procedures; and collaboration with study team (*Table 7*). Overall, the nurses were very positive towards the concept of ICBT, appreciating fast access to psychological treatment for their patients. The nurses experienced that patients do not want to or have the energy to contact their general practitioner seeking help for

Table 5 **Use of intervention for completed participants (*n* = 22)**

	Mean (SD)	Range
Number of contacts with therapist		
Telephone calls	8.0 (3.9)	3–22
Written messages on the treatment platform[a]	19.7 (22.6)	5–37
Time consumption on the treatment platform (h)	10.95 (6.5)	4.7–34.1
Number of log ons to the treatment platform[b]		
Total (100%)	33.5 (13.4)	12–69
Logins within normal opening hours[c] (59.4%)	19.9 (8.3)	4–34
Logins outside normal opening hour[c] (40.6%)	13.6 (7.3)	3–35
Total time of intervention including diagnostic interview (weeks)	13.3 (2.8)	10–20

SD, standard deviation.

[a] Combined written messages on the treatment platform from participant and therapist.

[b] Including training of participant, which included logging on twice.

[c] Opening hours defined as Monday to Friday from 8 a.m. until 4 p.m., public holidays excluded.

their anxiety and depression. They also experienced that some patients were not interested in online treatment, and for others it was offered to soon in the CR pathway. Regarding inclusion procedures, some were challenged by the additional task of including patients as part of clinical practice, but also that procedures gradually became less burdensome. Willingness to use clinical time on recruiting patients was in recognition of lack of psychological treatment within their CR centre. Sustainable support from the study team was highly appreciated, safeguarding motivation to participation in the study.

Discussion

This study examined the feasibility of integrating ICBT into routine CR in patients with IHD. We found a dropout rate from the ICBT intervention of 24%, which is below the a priori determined threshold. The study showed satisfactory improvements in anxiety and depression scores during the intervention. User patterns of the intervention showed a large variability. The evaluations revealed that patients were very positive towards the intervention, but some experienced the workload burdensome. The nurses were very positive about the concept of ICBT but stated that including patients was yet another task to manage in busy clinical practice.

Acceptability and adherence

Among 54 eligible patients with high HADS scores, 29 were included in the study. Of the 25 eligible non-included patients, six experienced minor mental problems, four were excluded at baseline with HADS scores ≤8, 1 died, leaving 14 out of 54 eligible patients (26%) with symptoms of anxiety and depression who declined participation. Three of these patients reported lack of energy and for four patients we do not have information about reason for declining. We can only speculate that for some patients the timing of the intervention may have been too soon after the cardiac event. Others may be unwilling to engage in a psychological intervention e.g. due to stigma or being uncomfortable with online treatment. To our knowledge, only one other study on ICBT within cardiology included patients in routine care, and they reported 1359 out of 1946 eligible patients (70%) declined participation.[14] This indicates that this study has a satisfactory acceptability. To safeguard inclusion, additional nine CR centres are recruited for the RCT.

Only few studies on ICBT within cardiology are published. When comparing our findings with these, one RCT in patients with myocardial infarction found no effect of ICBT on symptoms of anxiety or depression.[14] The study had a low treatment adherence with 38.4% completing only the introductory module and 15.4% completing additional modules, making it difficult to evaluate the effect of the intervention. Another RCT of ICBT in patients with cardiovascular disease found a significant effect on depression and had 59 patients (82%) completing at least four out of seven modules.[8] A recent RCT in patients with acute coronary event also showed a positive effect of ICBT on both anxiety and depression where 92% completed at least four out of eight lessons.[16] This suggests that poor adherence to

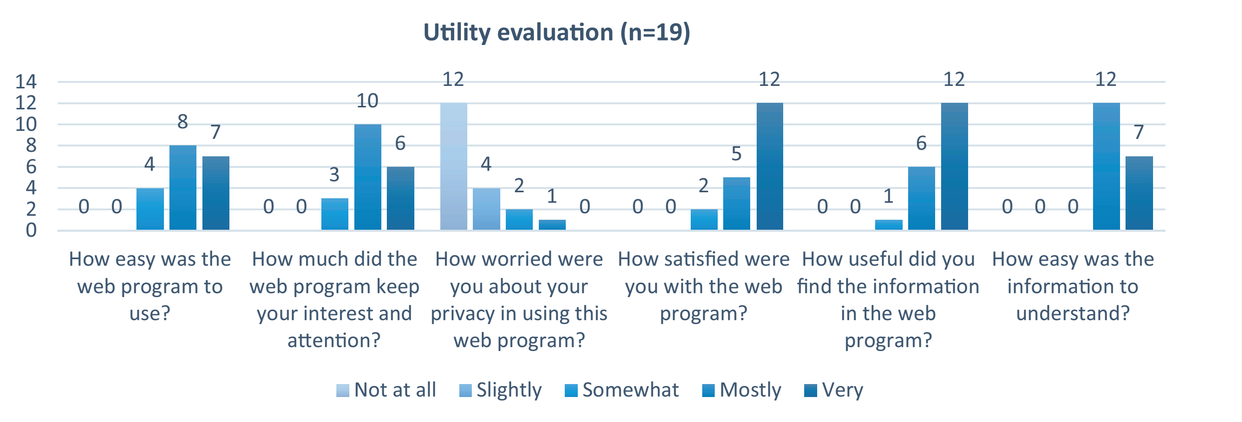


Figure 3 Utility of the intervention.

Table 6 **Summary of patient's experiences based on the written evaluations**

Theme	Findings	Quotes
Treatment platform	Pro: • Easy to access, navigate, and use Con: • Burdensome logon procedure • Miss possibility to follow progress in the modules and to print out pages	*'Nice, easy and clear. Miss possibility to print out on paper' (female, 73 years)*
Intervention	Pro: • In control of time and speed of the intervention • Very relevant content • Highly satisfied with the concept • Can participate from home • Fine balance between treatment elements • Length of intervention and amount of homework appropriate Con: • Length of time to intervention too short • Amount of homework too much	*'With online (treatment)—I decide for myself when to engage in the treatment' (female, 73 years)* *'It was nice that I did not have to leave home even though I needed help to live without anxiety' (male, 60 years)* *'Written assignments were a bit burdensome, especially when you have limited energy' (female, 52 years)*
Communication with therapist	Pro: • Highly satisfied with therapist • Therapist is competent • Sufficient time in phone calls Con: • None	*'100% okay. It is a really good idea that you can text with your therapist during the intervention' (female, 79 years)*
Personal experience	Pro: • Positively surprised of the concept • More relaxed and calm afterwards • Better acceptance of feelings • Better understanding of own reactions • Obtained various tools to cope with negative thoughts and feelings • No physical contact with therapist • Cognitive diamond helpful Con: • Not enough time to go through the modules • Too many written assignments	*'I liked to see my psychologist in person, which I have tried before. But I am positively surprised that this (online treatment) can work' (female, 64 years)* *'Actually this (online treatment) is an advantage when you are a bit of an "introvert" like me. I did not have to look anybody in the eyes' (male, 56 years)*

treatment is a barrier to dissemination of potentially effective treatments, even though a linear relationship is still fully uncovered[34] and the association was insignificant in the RCT by Lundgren *et al.*[15] It has been proposed from previous ICBT studies that a factor attributing to poor adherence might be a lack of customization of the ICBT treatment to fit the target population.[8,16,35] This is among the reasons

Table 7 **Summary of nurses' experiences based on the written evaluations**

Theme	Findings	Quotes
Intervention	Pro: • Online treatment is a valuable and important concept • Most patients were interested and positive • Free of charge for the patients • Fast track to psychological treatment Con: • Some patients had doubts or rejected the offer because treatment is online • Some patients might need the treatment later in the care pathway	*'The best part is to have an offer to our sad patients, and on top of that, that the patients can start the intervention so fast'*
Inclusion procedures	Pro: • Good introduction • Inclusion process became easier with routine Con: • Challenging on top of usual assessment tasks at start of CR • Too much project information to both patients and the nurses	*'Good project, but we also have to register in other databases, leaving less time for the patient'*
Collaboration with study team	Pro: • Personal introduction to the study • High level of information, feedback and availability of the team Con: • None	*'The best part is to feel that someone is passionate about this (psychological treatment)'*

why we decided using a participatory design for development of the intervention.[24] There are substantial differences in recruitment procedures, length of interventions as well as numbers and content of the modules in the mentioned studies, making comparisons difficult. In the current study, patients were considered 'completers' if they had completed at least five of the mandatory modules. Two patients did not accomplish the required five modules due to personal life situations but still benefitted from the intervention based on the treatment evaluation of their therapist, suggesting that our choice of five modules might be somewhat arbitrary. On these grounds, and since there is no gold standard for what comprises a 'completer' in ICBT, we have decided to change our definition in the eMindYourHeart RCT. Patients will be considered completers regardless of number of completed modules, if they follow the treatment plan agreed upon with their therapist. A patient can drop out of the treatment in two ways: (i) active drop out by communicating this decision to their therapist, or (ii) passive drop out, i.e. the patient stops responding to their therapist attempts to contact them and the contact is not re-established within the 12 weeks of treatment. We have extended the treatment manual and developed a stricter, therapist independent rating system for assessing if a module is completed, and which modules are relevant for the individual patient. This to secure a more personalized approach depending on the patient's individual situation and a high degree of interrater reliability.

Changes in anxiety and depression

Given the design of this uncontrolled study, we did not analyse the effectiveness of the intervention. With mean improvements in scores of 5.5 for anxiety and 4.9 for depression, the intervention indicated positive signs of obtaining the established MCID of 1.8.[33] Although these results could be due to chance, they are encouraging. At an individual level, 18/22 (82%) of those patients who completed the intervention reached the cut-offs for absence of anxiety and depression (HADS scores < 8). Schneider *et al.*[16] showed a range of recovery from anxiety and depression at 77%-85% that resembles our results. Regarding the three patients who had worsened HADS scores post-intervention, two had their treatment prolonged. Therefore, their follow-up HADS questionnaire was filled out before the intervention was completed, and in both cases, their therapist assessed clinical improvement at the end of the intervention. The third patient was severely impacted by COVID-19 and the associated social isolation. Out of the 22 completed patients, three stopped filling out the follow-up battery of questionnaires before they reached the HADS questionnaire, despite receiving two reminders. Since HADS will be the primary outcome of the eMindYourHeart RCT, HADS will be moved to the top of the follow-up questionnaire to safeguard this measure. In addition, the therapist will systematically encourage the patients to respond to this questionnaire at their last contact.

Use of intervention

Regarding use of intervention, Lundgren *et al.*[15] found that number of logins was associated with improvements in depression in the ICBT group. However, data on numbers of logins and range are not reported making comparison difficult. Our results somewhat resemble the results of Schneider *et al.*[16] in their RCT, as mean numbers of login were 33.5 (SD 13.4) vs. 26.4 (SD 16.6) and mean numbers of phone calls 8.0 (SD 3.9) vs. 4.8 (SD 3.1). The number of phone calls in this study was higher than expected which could be explained by the study design, testing, and adjusting procedures. Another explanation is the start of the COVID-19 pandemic in the trial period, which induced extra calls from patients. Our analysis showed that 40.6% of logins happened outside normal opening hours of CR services, which emphasizes that patients might prefer treatment at other timepoints than currently offered. One explanation could be that negative thoughts and emotions intrude at night-time when there is more time to think and ruminate. Concerning the duration of intervention, we found an average of 13.3 weeks that is longer than the stipulated 12 weeks. One reason is delay in time for some patients between the diagnostic interview and the start of first module, mostly caused by technical issues. Moreover, some patients requested extra time to complete the intervention due to personal situation. In the RCT, the length of the intervention will be monitored from start to end of the modules and the time kept to 12 weeks, making comparison easier.

Patient evaluation

A relatively high proportion of patients had a high educational level. We can only speculate if patients with low levels of education may be more reluctant to participate in ICBT or if CR staff are more reluctant to include patients with low levels of education, since this is seen in previous studies.[16,36] Since all included patients with high levels of education completed the current intervention, it could also mean that our intervention might not be properly adjusted to participants with lower levels of education, despite efforts in the participatory design study.[24] Some patients found the written assignments burdensome, signalling the need for personalized levels of the modules, which could potentially be related to level of education. Challenges with burden of assignments are also described previously.[36,37] Wallin *et al.*[36] argue for a more personalized ICBT approach, as some patients perceive text-based material strenuous and time-consuming. We have accordingly adjusted the one-size-fits-all approach to a more personalized model in the following RCT. Also consistent with the findings from Wallin *et al.*,[36] some of our patients found the two-step logon procedure burdensome but given the GDPR rules, this is the best possible solution momentarily. Conversely, it might give other patients a feeling that the platform is secure and trustworthy, which is previously reported.[37] Some patients expressed a preference to print out material from the platform. Previous studies have described this,[12] and e.g. the Mindspot Clinic in Australia are sending out hard copies of the material upon request.[38] Although this will not be possible in the RCT, since it will refrain us from collecting data on user activity on the platform, it should be considered if implementing into routine CR. Most patients found the intervention easily accessible and manageable and all were highly satisfied with their personal therapist and reported positive personal gains related to their mental condition. As one wrote: '*I have become myself again, this is pure happiness*'.

Nurses evaluation

The findings from the nurses' evaluations revealed strong support for the concept of ICBT integrated into CR, as this gives patients fast access to psychological treatment. They appreciated the high level of availability of the eMindYourHeart study team, which might have a positive impact on patient recruitment. Still, it is evident that the CR nurses have a high workload and they struggled with inclusion procedures as it takes clinical time from their patients, which suggests that implementation is a complex process.[39] It is therefore necessary to support the nurses to keep them engaged in recruiting patients, and in case of future implementation in routine care, a solid implementation plan is needed.

The European Society of Cardiology supports digital health as an innovative opportunity to improve the quality of care in secondary prevention.[9] Especially in the light of the COVID-19 pandemic, ICBT might be an effective solution to treat anxiety and depression in patients with IHD as an integrated part of CR.[40] Patients expressed high levels of gratefulness for the continuity of this intervention and the possibility to talk about their concerns related to COVID-19, while experiencing most elements of CR being cancelled. We managed to adapt the intervention to help also with concerns related to COVID-19, as it became obvious that this induced anxiety and worries among the patients.

Strengths and limitations

Strength of this study include the multicentre approach, testing of inclusion procedures in a large variety of CR models and centres across Denmark, and adaptations and optimisation of the intervention. Collaboration with the recruiting centres prior to the RCT also included a webinar for the CR staff (on their request) which is likely to be an advantage for successful recruitment in the RCT study. The study had following limitations: firstly, there were 16 patients declining to participate in the study, and since we only have sparse data on these patients, we are not able to examine if they differ from participating patients. Thus, there might be unidentified subgroups not willing to participate in ICBT. Declining patients are asked to fill out an informed consent to use of data in the RCT and due to the considerably higher volume in this study, these data might reveal important knowledge. Secondly, since the feasibility study were uncontrolled the positive changes in outcomes should be interpreted with great caution. In addition, clinical data from the Danish Cardiac Rehabilitation Database were rather incomplete, and other national registries will be considered for the RCT. We asked patients and nurses to evaluate their experiences with the intervention and procedures in writing, while oral interviews potentially could have led to deeper insights into barriers and facilitators of the intervention, as done by e.g. Wallin *et al.*[36] However, an in-depth qualitative analysis was not the scope of this study and would have required thorough elaboration.

Conclusion

This study demonstrated the feasibility of the eMindYourHeart study, based on drop-out rate, mean improvements in HADS scores, use of intervention and experiences from patients and CR nurses. The study was an essential prerequisite for a larger interventional study. Thus, the intervention will be adjusted according to the reported results and used in the following eMindYourHeart RCT.

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Conflict of interest: none declared.

Data Availability

The data from this article cannot be shared publicly due to the use of confidential health information.

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Authors

Biography: Charlotte Helmark is a PhD candidate employed at Zealand University Hospital and working in the crossfield between cardiology and psychology.

Appendix III

Note to Appendix III

Paper 3 is not included in this version, because it has not been published at the time of submission of the thesis.

Paper 3:

A web-based intervention for patients with an implantable cardioverter defibrillator – a qualitative study of nurses' experiences (Data from the ACQUIRE-ICD study).

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Submitted to Patient Education and Counselling Innovation – CURRENTLY IN REVIEW

Abstract

Objective: The aim of this study was to explore cardiac nurses' experiences with a web-based intervention for patients with an implantable cardioverter defibrillator, as it is a new way of delivering care to patients.

Methods: We conducted a qualitative study based on individual semi-structured interviews with 9 cardiac nurses from 5 Danish university hospitals.

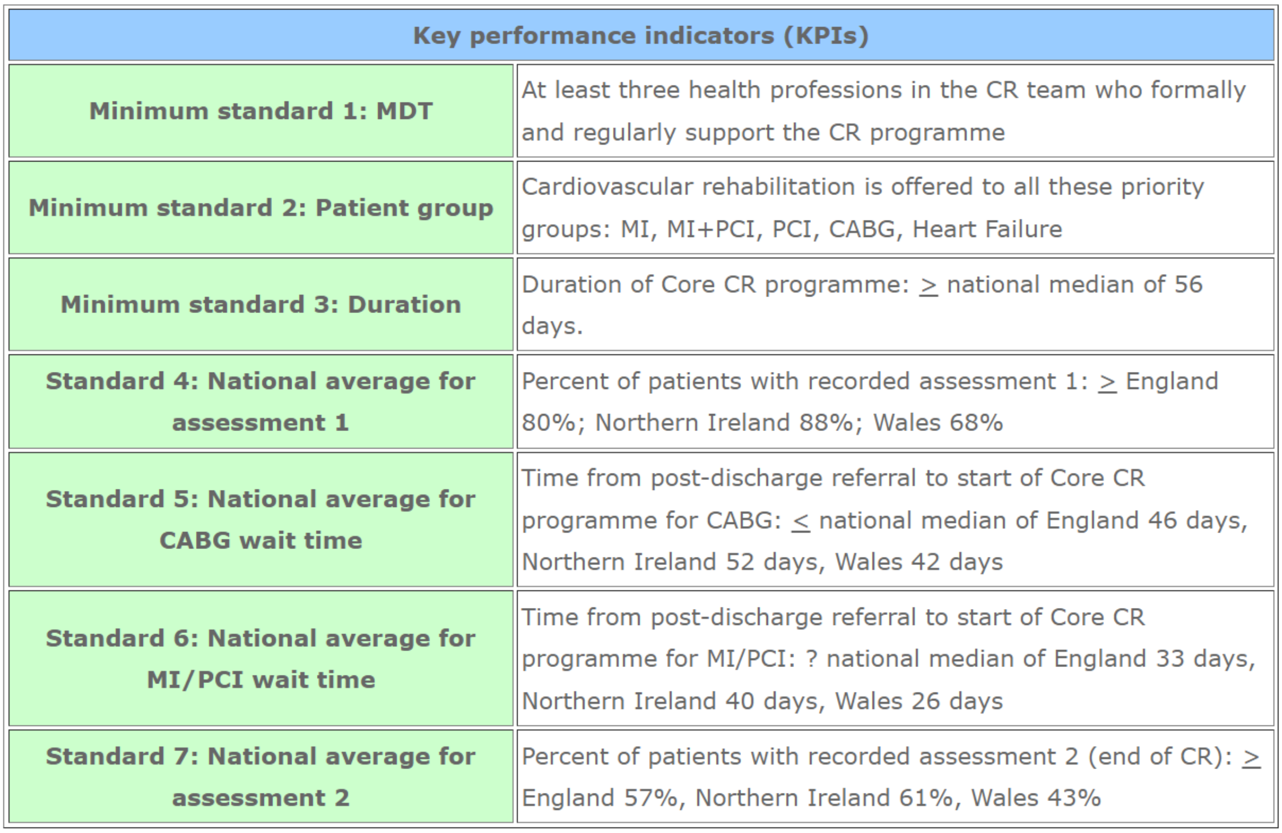
Results: We found one overall theme: "Between traditional nursing and modern eHealth". This theme was derived from the following six categories: (1) comprehensive intervention, (2) patient-related differences in engagement, (3) following the protocol is a balancing act, (4) online communication challenges patient contact, (5) professional collaboration varies, and (6) an intervention with potential. Cardiac nurses were positive towards the web-based intervention and believe it holds a large potential. However, they felt challenged by not having in-person and face-to-face contact with patients, which they found valuable for assessing patients' wellbeing and psychological distress.

Conclusion: Specific training in eHealth communication seems necessary as web-based care entails a shift in the nursing role and requires a different way of communication.

Innovation: Web-based health care is a new and innovative mode of delivering health care communication, but it also requires new competences to safeguard the quality of care.

Appendix IV

Table of the seven BACPR key performance indicators. Certification is achieved through meeting all seven indicators.



Key performance indicators (KPIs)	
Minimum standard 1: MDT	At least three health professions in the CR team who formally and regularly support the CR programme
Minimum standard 2: Patient group	Cardiovascular rehabilitation is offered to all these priority groups: MI, MI+PCI, PCI, CABG, Heart Failure
Minimum standard 3: Duration	Duration of Core CR programme: ≥ national median of 56 days.
Standard 4: National average for assessment 1	Percent of patients with recorded assessment 1: ≥ England 80%; Northern Ireland 88%; Wales 68%
Standard 5: National average for CABG wait time	Time from post-discharge referral to start of Core CR programme for CABG: ≤ national median of England 46 days, Northern Ireland 52 days, Wales 42 days
Standard 6: National average for MI/PCI wait time	Time from post-discharge referral to start of Core CR programme for MI/PCI: ? national median of England 33 days, Northern Ireland 40 days, Wales 26 days
Standard 7: National average for assessment 2	Percent of patients with recorded assessment 2 (end of CR): ≥ England 57%, Northern Ireland 61%, Wales 43%

Permission to use the table in the thesis is obtained from NACR. In Standard 6, the "?" should be replaced with "≤".

Appendix V

INTERVIEW GUIDE

Interview of nurses’ experiences with the ACQUIRE - ICD intervention

Subject	Interview questions	CFIR domain/notes
Introduction		
Presentation of interviewer and purpose of the interview Short presentation of the frame for the interview Presentation of informant: Role in relation to ACQUIRE-ICD	What role do you have/have you had in relation to ACQUIRE-ICD? - *How did you get this role?*	Ask, if you don’t understand the question Approx. 30 min, audio recorded *CFIR: Proces*
Before onset of the project		
	Try to remember back when you first heard about the project - what did you think about the idea of treating and communicating with patients online?	*CFIR: Characteristics of Individuals*
	What were your expectations to how the patients would respond to the project?	*CFIR: Outer Setting*
	How were you trained for the task? - *Did you feel well prepared for the task?*	*CFIR: Proces*
The execution of the intervention		
	How did the patients respond to the project? *(If the nurse has only included patients, this question is skipped)* How did you experience communicating with the patients online?	*CFIR: Proces*
	Have you had issues in the intervention which have been specifically	

	difficult or challenging? - *If yes – are there anything that have been supportive?* - *If yes – has the job been getting easier with routine?*	*CFIR: Characteristics of Individuals*
	If you compare with talking face-to-face with the patients, are there something which have been better or easier in ACQUIRE-ICD? - *Are there something which have been harder?*	*CFIR: Proces*
	How did you experience following the protocol for the project? - *Did you succeed with it?* - *Did you sometimes do more than/less than the described tasks? (e.g. goal-setting)* - *Can you give examples of what you did?*	*CFIR: Proces*
	How did you experience the patients' engagement with the intervention? - *Were you able to assess if the patients' benefitted from the intervention?* - *Can you give an example?* - *Did you experience any patient subgroups benefitted more than others? (e.g. patients who have had cardiac arrest)*	*CFIR: Outer Setting*
	Is there something you would like to change on the platform? - *E.g. technicalities or interface?*	*CFIR: Intervention Characteristics*
Support and interest from management and colleagues		
	What did your colleagues in the ICD team think of ACQUIRE-ICD? - *Are there - for instance - someone in the team who thinks that the psycho-educative element is part of/not part of the job for an ICD nurse?*	*CFIR: Intervention Characteristics* *CFIR: Inner Setting*
	How did your managers support the project?	*CFIR: Inner Setting*
	Which possibilities have you had for discussing issues or networking in relation to ACQUIRE-ICD? - *Have you lacked anything?*	*CFIR: Outer Setting*
	Did you have any experiences with interdisciplinary cooperation during the project?	*CFIR: Inner Setting*

	- *For instance, with medical doctors if you were insecure of programming of ICD/medication/other?*	
Perspectives of the future		
	How did you overall experience that the patients were coping with online treatment? - *Do you think the patients have lacked or missed anything?* - *In your opinion - are there subgroups of patients with an ICD who are not suitable for online treatment?*	*CFIR: Outer Setting*
	Have you lacked anything - as a nurse - in your online communication with the patients? - *If yes, can you describe it?*	*CFIR: Characteristics of Individuals*
	How do you see the potential for implementing ACQUIRE-ICD in the future? - *Potential barriers?* - *Do you see possibilities for improvement of ACQUIRE-ICD?* - *How about other kinds of online treatment for patients with an ICD?*	*CFIR: Inner Setting*
	Do you think ACQUIRE-ICD or similar online treatment could be used for other groups of cardiac patients? - *If yes – describe*	*CFIR: Outer Setting*
Debriefing/finishing of interview		
	We are about to finish the interview. Is there anything you would like to add before we stop? Can we contact you if we have further questions?	Thank you on behalf of the project team

Appendix VI

Appendix VI. Examples of codes, subcategories, categories, and the derived theme from analysis in Paper 3.

Theme	Between traditional nursing and modern eHealth			
Category	Online communication challenges patient contact		Comprehensive intervention	
Subcategory	Personal relation matters	Face-to-face is important	Toolbox of patient information and education is very good	Mixed perceptions of online patient network forum
Code	Patients benefit from personal contact	Online communication is a barrier	Materials in toolbox are good	Positive towards patient forum
Text	Now, had there been a phone contact with the nurse, I think it would have made a difference. Because I could see that the patient that the data manager called, she thought this was great.	I think sometimes in this study, which is much about psychological dimensions, you can miss out on things because you can´t see the patients or their body language, mimic and so on compared to when you have them face-to face.	About the vodcasts, my perception is that it has been very beneficial for the patients. Because you can watch them when it fits, and you are ready. And it is really nice that you can watch them with your spouse, and they can sit together and talk about it.	I believe it is smart with such a forum for ICD patients where they can write stuff, but I actually don’t know if they have used it.