The effects and experiences of internet-delivered cognitive behavioural therapy
The perspectives of patients with non-cardiac chest pain and healthcare professionals in the emergency and cardiac care

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The effects and experiences of internet-delivered cognitive behavioural therapy

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Magda Eriksson-Liebon
Till
Desirée och Noah
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ABSTRACT

Background
Non-cardiac chest pain (NCCP) is a common issue, accounting for roughly half of all emergency department visits related to chest pain. Patients afflicted with NCCP often endure cardiac anxiety, misinterpreting the pain as heart-related and fearing it, despite the absence of any life-threatening cardiac issues. This anxiety often leads to the avoidance of physical activities, negatively impacting their quality of life. Cognitive behavioural therapy (CBT) has been shown to be effective in managing psychological distress such as anxiety and depression. CBT is a structured process that helps patients identify and restructure their negative thoughts, get a corrected and more realistic perception of their symptoms, and learn to manage their thoughts about chest pain. Despite its effectiveness, CBT is resource-intensive, and therefore internet-delivered cognitive behavioural therapy (iCBT) may be an alternative as it increases accessibility and is more cost-effective compared to traditional therapy methods. However, there is a lack of research on the effectiveness of this treatment approach for patients with NCCP and cardiac anxiety. Moreover, digital care technologies are still relatively unfamiliar in clinical practice, particularly in emergency departments, and the successful implementation of iCBT relies on healthcare professionals' acceptance and integration of digital care into clinical practice.

Aim
The overall aim of this dissertation was to evaluate the short- and long-term effects of a nurse-led iCBT program on psychological distress in patients with NCCP, and to explore their experiences participating in the iCBT program. In addition, the study aimed to describe healthcare professionals' perceptions of digital care in the emergency and cardiac care for patients with NCCP.

Methods
This dissertation comprises two quantitative and two qualitative studies. A randomised clinical trial (RCT) (studies I, II, and III) was conducted to evaluate cardiac anxiety, measured with the Cardiac Anxiety Questionnaire...
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(2CAQ); and secondary outcomes such as fear of body sensations, measured with The Body Sensations Questionnaire (BSQ); depressive symptoms, assessed with the Patient Health Questionnaire-9 (PHQ-9); health-related quality of life (HRQoL), measured using the EuroQol Visual Analog Scale (EQ-VAS); and chest pain frequency with a self-developed question. The RCT cohort consisted of 109 patients who had at least two healthcare consultations for NCCP in the past 6 months, experienced cardiac anxiety (CAQ score ≥24), and were randomised into a 5-week iCBT program (n=54) or psychoeducation (n=55). An intention-to-treat analysis was conducted, and linear mixed model analysis was used to assess between-group differences in primary and secondary outcomes. The iCBT program included psychoeducation, mindfulness, and exposure to physical activity, with weekly homework assignments and feedback, while the control (psychoeducation) group received readable psychoeducation program aimed to increase knowledge about their mental health, symptoms, and the strategies that can be used to manage chest pain and improve their well-being. Study I was a short-term follow-up with a three-month duration. Study III was a longitudinal study with a 12-month follow-up. Additionally, factors impacting the treatment effect of iCBT on cardiac anxiety were also explored. Study II was a semi-structured qualitative study utilising an inductive approach with content analysis following Patton (2015). Face-to-face interviews were conducted with 16 participants from the iCBT group. Study IV was a qualitative descriptive study involving individual, digital/face-to-face semi-structured interviews with 17 licensed healthcare professionals (physicians and nurses) working in emergency care or cardiology. Data were analysed using inductive thematic analysis based on Braun and Clarke (2006).

Result

In Study I, no significant differences were found between the iCBT and control (psychoeducation) groups regarding cardiac anxiety or any of the secondary outcomes in terms of the interaction effect of time and group over the 3-month follow-up. iCBT demonstrated a small effect size on cardiac anxiety (Cohen’s d=0.31). A positive change score (≥11 points on the CAQ) was reported by 16 patients in the iCBT group (36%) compared to 13 patients (27%) in the control (psychoeducation) group, indicating a slightly greater improvement in cardiac anxiety in the iCBT group. However, the difference between the groups was non-significant (p=.213). Within-group analysis showed significant improvement in cardiac anxiety (p=.037) at the
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3-month follow-up compared to the 5-week follow-up in the iCBT group, but not in the control (psychoeducation) group.

In Study III, there was no statistically significant interaction effect of time and group between the iCBT and control (psychoeducation) groups regarding cardiac anxiety over the 12-month follow-up. However, there was a statistically significant interaction effect of time and group ($p=.009$) regarding chest pain frequency for the iCBT group and a group effect on health-related quality of life ($p=.03$) for the iCBT group. Furthermore, the regression analysis showed that higher scores of "avoidance" on the CAQ at baseline were associated with improvement in cardiac anxiety at the 12-month follow-up in both groups.

In Study II, participants described their experiences, leading to three main categories: "driving factors for participation in the iCBT program", "the program as a catalyst" and "learning to live with chest pain." Participants described how pain impacted their lives, the struggle that led them to participate in the program, and how they found the program helpful, trustworthy, and viewed it as a tool for gaining the strength and skills they needed to live a normal life despite chest pain.

In Study IV, healthcare professionals described their perception of digital care, resulting in four themes: "new ground to walk on", "a challenge for the current healthcare system", "digital care has its potential" and "prerequisites for use in clinical practice". These themes describe healthcare professionals' knowledge and experience with digital care, the challenges associated with implementing digital care in the current healthcare system, the opportunities it presents, and identify facilitators for the implementation of digital care in clinical practice.

Conclusions

In studies I and III, iCBT was not superior to psychoeducation in reducing cardiac anxiety in patients with NCCP. However, both iCBT and psychoeducation have demonstrated utility as interventions for reducing cardiac anxiety in these patients. Moreover, patients with an increased propensity to avoid activities or situations they believe may trigger cardiac-related symptoms, were found to have reduced cardiac anxiety. Patients generally perceived the iCBT program positively, viewing it as a tailored and effective tool for confronting fears and restoring normalcy in their lives.
Healthcare professionals express a mixture of caution and optimism towards digital care, emphasising the importance of clear leadership, education, technical competence, and positive attitudes to ensure successful implementation and maximise benefits for patients with NCCP.

Keywords
Cardiac anxiety, cognitive behavioural therapy, internet-delivered, non-cardiac chest pain, patient experience, psychological distress, randomised controlled trial, qualitative design.
**SVENSK SAMMANFATTNING**

**Bakgrund**

Icke-kardiell bröstsmärta (Non-cardiac chest pain - NCCP) är ett vanligt problem och utgör ungefär hälften av alla besök på akutmottagningen relatade till bröstsmärta. Patienter som besväras av NCCP upplever ofta hjärtrelaterad ångest då de tolkar smärtan som hjärtspecific, trots att ingen livshotande hjärtsjukdom konstateras. Hjärtrelaterad ångest leder ofta till att de undvik fysisk aktivitet eller sociala situationer på grund av rädsla för att förvärra symtom eller uppleva komplikationer, vilket påverkar livskvaliteten negativt. Kognitiv beteendeterapi (KBT) har visat sig vara effektiv för att hantera psykisk ohälsa såsom ångest och depression. KBT är en strukturerad process som hjälper patienter att identifiera och omstrukturer sig sina negativa tankar, få en korrigerad och mer realistisk uppfattning om sina symtom och lära sig att hantera sina tankar om bröstsmärta. Trots sin effektivitet är KBT resurskrävande och därför kan internetbaserad kognitiv beteendeterapi (iKBT) vara ett alternativ eftersom den ökar tillgängligheten och är mer kostnadseffektiv jämfört med traditionell KBT. Dock saknas det forskning kring effekten av denna behandlingsform för patienter med NCCP och hjärtrelaterad ångest. Dessutom är digitala vårdteknologier fortfarande relativt okända inom kliniska miljöer, särskilt på akutmottagningar, och en framgångsrik implementering av digitala behandlingsformer, såsom iKBT beror till stor del vårdpersonalens acceptans och integration av digital vård i klinisk praxis.

**Syfte**

Det övergripande syftet med denna avhandling var att utvärdera kort- och långsiktiga effekter av ett sjukspöteskelett iKBT-program på psykisk ohälsa hos patienter med NCCP, samt att utforska deras erfarenheter av att delta i iKBT-programmet. Dessutom syftade studien till att beskriva sjukvårdpersonals uppfattningar om digital vård inom akut- och hjärtspårjorden för patienter med NCCP.
Metod

Denna avhandling består av två kvantitativa och två kvalitativa studier. En randomiserad klinisk prövning (RCT), som var grunden för studie I, II och III, genomfördes för att utvärdera effekter av iKBT på hjärtrelaterad ångest, mätt med Cardiac Anxiety Questionnaire (CAQ); och sekundära utfall såsom rädska för kroppsliga förnimmelser, mätt med The Body Sensations Questionnaire (BSQ); depressiva symptom, bedömda med Patient Health Questionnaire-9 (PHQ-9); hälsorelaterad livskvalitet (HRQoL), mätt med EuroQol Visual Analog Scale (EQ-VAS); och bröstsmärtfrekvens mätt med en självutvecklad fråga avseende smärtfrekvens.


Resultat

Resultat i studie I visade på inga signifikanta skillnader mellan iKBT- och psykoedukationsgruppen gällande hjärtrelaterad ångest eller de övriga sekundära utfallsmätten, med hänsyn till interaktionseffekten av tid och grupp över 3-månadersuppföljningen. iKBT uppvisade en liten effekststorlek på hjärtrelaterad ångest (Cohens d=0.31). En positiv förändringspoäng
Svensk sammanfattning

(≥11 poäng på CAQ) rapporterades av 16 patienter i iKBT-gruppen (36%) jämför med 13 patienter (27%) i psykoeduktionsgruppen, vilket indikerar en något större förbättring av hjärtrelaterad ångest i iKBT-gruppen. Dock var skillnaden mellan grupperna inte signifikant (p=.213). Inomgruppsanalysen visade signifikant förbättring av hjärtrelaterad ångest (p=.037) vid 3-månadersuppföljningen jämfört med 5-veckorsuppföljningen i iKBT-gruppen, men inte i psykoeduktionsgruppen.

I studie III fanns ingen statistiskt signifikant interaktionseffekt av tid och grupp mellan iKBT- och psykoeduktionsgruppen beträffande hjärtrelaterad ångest över 12-månadersuppföljningen. Dock fanns det en statistiskt signifikant interaktionseffekt av tid och grupp (p=.009) för bröstsmärtfrekvens hos iKBT-gruppen och en gruppeffekt på hälsorelaterad livskvalitet (p=.03) för iKBT-gruppen. Dessutom visade regressionsanalysen att högre poäng på "undvikande" på CAQ vid baslinjen var associerade med förbättring av hjärtrelaterad ångest vid 12-månadersuppföljningen i båda grupperna.

I studie II beskrev deltagarna sina erfarenheter av att delta i iKBT-programmet. Detta resulterade i tre huvudkategorier: "drivkrafter för deltagande i iKBT-programmet", "programmet som katalysator" och "att lära sig att leva med bröstsmärten." Deltagarna beskrev smärtans påverkan på deras liv, kampen som ledde dem till att delta i programmet och hur de uppfattade programmet som hjälpsamt, pålitligt och såg det som ett verktyg för att finna styrka och färdigheter till att leva ett normalt liv trots bröstsmärten.

Slutligen, i studie IV beskrev sjukvårdspersonalens uppfattning om digital vård, vilket resulterade i fyra teman: "ny mark att gå på", "en utmaning för det nuvarande vårdsystemet", "digital vård har potential" och "förutsättningar för användning i klinisk praxis". Dessa teman beskrev sjukvårdspersonalens kunskap och erfarenhet av digital vård, de utmaningar som är förknippade med implementering av digitala verktyg i det nuvarande sjukvårdsystemet, de möjligheter implementeringen innebär, samt de faktorer som kan främja implementeringen av digital vård i klinisk praxis.

Slutsats

iKBT var inte bättre än psykoedukation på att minska hjärtrelaterad ångest hos patienter med NCCP. Dock har både iKBT och psykoedukation visat sig vara användbara som interventioner för att minska hjärtrelaterad ångest hos dessa patienter. Dessutom visade sig att patienter med en ökad benä-
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genhet att undvika aktiviteter eller situationer som de tror kan utlösa hjärt-relaterade symtom, får minskad hjärtrelaterad ångest. Överlag, patienterna som intervjuades om sina erfarenheter av iKBT-programmet, uppfattade det positivt och såg programmet som ett användbart och effektivt verktyg för att konfrontera sina rädslor och återfå normalitet i sina liv. Vårdpersonal uttryckte en blandning av försiktighet och optimism gentemot digital vård och betonade vikten av tydligt ledarskap, utbildning, teknisk kompetens och positiva attityder för att lyckas med framgångsrik implementering av digital vård och för att maximera fördelarna för patienter med NCCP.
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<td>Acute Myocardial Infarction</td>
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<td>BSQ</td>
<td>Body Sensations Questionnaire</td>
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<td>EQ-VAS</td>
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<td>GAD</td>
<td>Generalised Anxiety Disorder</td>
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<td>GERD</td>
<td>Gastroesophageal Reflux Disease</td>
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<td>HRQoL</td>
<td>Health-Related Quality of Life</td>
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<td>Heart-Focused Avoidance</td>
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The effects and experiences of internet-delivered cognitive behavioural therapy
I won’t be able to tell you about a patient or an encounter that changed my life, because that’s not how my research journey began.

My research journey started with a desire for change.

I have my roots in emergency care. As a newly graduated nurse, I started at the emergency department (ED) at Vrinnevisjukhuset i Norrköping, Sweden, in April 2011 and immediately felt that I was in the right place. Every shift involved dozens of patient encounters, different life stories, and the opportunity to help and change someone’s life, which made me grow in my role as a nurse. I enjoyed working at the clinic and had no thoughts of changing jobs. On the contrary, I wanted to develop and learn more about emergency care, which after a few years, resulted in a master’s degree in emergency care, and three years later a master’s degree in nursing science with a focus on care in high-tech and pre-hospital environments. During this time, I was involved and responsible for several projects and improvement work at my clinic. However, I often felt that I lacked the knowledge to take my projects further, because although they were implemented in the clinical practice at ED, it usually stopped there, and I wanted that knowledge to be out there, visible, and made available for others.

When I wrote my master’s thesis in 2018, I contacted a Research and Development (FoU) supervisor at NSÖ in Region Östergötland, Susanne Roos, who had been involved in one of my previous projects. I wanted help with publishing my thesis. Through Susanne, I came into contact with Ghassan Mourad, who recently had started his project on internet-delivered CBT for patients with non-cardiac chest pain. I didn’t know much about internet-delivered CBT, but I was familiar with the patient group. Moreover, Ghassan was so passionate and enthusiastic about the program, so I wanted to give it a shot. I was employed in the project as a research assistant and quality assessor at 20-30% for one year to assist with data collection. I reviewed patient lists and based on the study criteria, I selected the patients who were suitable to participate in the study, sent them the information package and contacted them by phone to provide more information about the study. It was then, I got a completely different perspective of this group of patients, not only based on the acute context when they visit the ED, but also their everyday life affected by the chest pain. At the same time, I got to be part of the research group and learn how the ”real research” was conducted.
When Ghassan, after a few months, gave me the opportunity to join the project as a doctoral student, I never hesitated. I saw this fantastic opportunity to learn and develop, while still having my clinical position at the ED to lean on and feel confident in.

In February 2020, I was enrolled in the doctoral program. Even though this journey was not straightforward, I’m glad I dared to take the step.
INTRODUCTION

Today’s healthcare system is facing major challenges with an aging population, an increase in chronic diseases, staff shortages, rising costs for medical devices, and increased patient expectations for access to high-quality care, in where patients can participate actively. This requires healthcare that is more efficient and available to residents on equal terms, regardless of conditions or geographical location. Innovative solutions, including digital tools and telemedicine, are needed to improve the accessibility and efficiency of healthcare while ensuring a fair distribution of resources and quality of care for all citizens (1).

One of most common patient groups in emergency departments (ED) are patients with chest pain. The primary diagnostic consideration is acute coronary syndrome, which encompasses various coronary artery pathologies, including unstable angina, non-ST segment elevation myocardial infarction, and ST-segment elevation myocardial infarction (2). Chest pain is a symptom that may indicate a life-threatening condition, leading to fear, as well as cardiac anxiety. Generally, chest pain has a strong impact on the patient. There is an association between the initial intensity of reported chest pain and anxiety, as well as chest pain after hospital admission. However, in many cases, no cardiac cause is found for the patient’s chest pain despite careful investigation (3), which creates cardiac anxiety, increases stress, and can lead to uncertainty for both the patient and the caregiver. Living with chest pain without a clear explanation or effective treatment can negatively affect the quality of life and well-being of patients (4), while also posing a challenge for healthcare system. Therefore, these patients need help and support to reduce cardiac anxiety and learn how to handle their non-cardiac chest pain (NCCP). During the 1990s, there was an increase in research on NCCP, but it then declined for a while. In recent years, interest and research on NCCP have increased again, likely due to heightened awareness, new technology, and the need for improved diagnostics and treatment. However, at the start of this dissertation, there were only one pilot RCT (5) evaluating iCBT in patients with NCCP and cardiac anxiety.

It is known that cognitive behavioural therapy (CBT) has proven to be an effective treatment for patients with NCCP and anxiety. However, because it is resource-intensive, questions are raised about whether iCBT, in line with WHO's "Global Strategy on Digital Health 2020–2025" (6) and the "Vision eHealth 2025" presented by the Swedish Association of Local Authorities and Regions (7), could offer a viable solution for these patients. E-health aims to improve
healthcare outcomes and promote equal access to services through digitalisation. This involves enhancing accessibility and suitability, providing continuous care and follow-up, and promoting participation and empowerment via patient portals, reducing waiting times, personalising care, and enhancing medical compliance. The adoption of digital care solutions has increased substantially over the past decade (8), and is expected to reduce the burden on primary and emergency care by creating a healthcare environment that is more tailored to patients' individual needs and enabling them to take a more active role in their own care (6, 7). In this case, it could also alleviate the burden on patients with NCCP and psychological distress, and on the healthcare system.
BACKGROUND

NCCP - a challenge in healthcare

Definition and symptoms of NCCP
Non-cardiac chest pain (NCCP) is defined as persistent chest pain without any identifiable cardiac pathology (9, 10). The differential diagnoses for chest pain are broad and, initially, it is necessary to exclude acute, life-threatening aetiologies, such as acute coronary syndrome, pneumothorax (10), pulmonary embolism or aortic dissection (11). In the literature, NCCP is also described as non-specific (11), unexplained (12), atypical (13), or functional chest pain (14), but also as “chest pain with normal coronary angiogram”, “cardiac syndrome x”, “microvascular dysfunction” and “microvascular angina” (12, 15), which can lead to additional difficulties in defining the condition (16). The term "non-cardiac chest pain” will be used in this dissertation.

NCCP is usually described as angina-like (3, 17) squeezing, or burning pain that is localised around the sternum, with no evidence of cardiovascular origin (3), with radiation to the jaws, neck, back, and arms, and is difficult to distinguish from cardiovascular chest pain (18). The episodes of pain can last from a few seconds to hours and can radiate down into the lower extremities (19). The most common underlying reasons are gastroesophageal reflux disease (GERD), musculoskeletal, pulmonal, and psychological distress (3, 18, 20-23).

Patient characteristics
NCCP can affect individuals of all ages, although its prevalence seems to decrease with age and there is no gender difference (17, 24). Those who seek medical care tend to have more complaints, experience greater social detraction, and suffer more from GERD, compared to those who do not seek medical care. Gastrointestinal symptoms such as sore throat, dysphagia, and regurgitation are also more common among NCCP patients (25). However, generally they do not differ from those with cardiac chest pain in terms of demographics. Risk factors associated with NCCP include being overweight, experiencing reflux, smoking, using aspirin or non-steroidal anti-inflammatory drugs, having a neurotic personality trait, and experiencing anxiety (17, 26).
In patients with NCCP and psychological comorbidity, more women than men suffer from depression and anxiety. Women also smoke more than men, and generally more than the general population. More men report regular exercise compared to women, but overall, patients with NCCP exercise less than the rest of the Swedish population. Patients with NCCP also experience more constant stress at work and at home, and women report more stress at home and relationship difficulties compared to men (27). Finally, the entire patient group tends to assess their health-related quality of life lower compared to the normative population (28).

**Prevalence of NCCP**
A lifetime prevalence in general population for NCCP ranges from 20% to 40%, which means that about one-third of the population will experience NCCP at some point in their lifetime (10, 29, 30). NCCP is commonly found in clinical settings (17, 18, 31, 32). In primary health care, approximately 70%–80% of patients presenting with chest pain are determined to have pain of a non-cardiac origin, a proportion that extends to 50%–80% in ED and rapid chest pain clinics (10, 33).

Approximately 5% of all visits to ED, are due to chest pain, making it one of the leading reasons to seek emergency medical care (16, 32). Furthermore, the number of patients who have been diagnosed with NCCP at ED visits is estimated to be more than 50% of all patients presenting with chest pain in the ED (30, 34, 35). In addition, within 6 months of their initial visit to the ED for chest pain, 69% of patients have contacted primary care, while 28% have returned to seek care in the ED (36).

**Management of NCCP in emergency care**
The management of acute chest pain in the ED primarily focuses on identifying patients with life-threatening conditions, which creates a significant challenge when dealing with patients experiencing NCCP (37). Chest pain is considered a more urgent issue compared to other symptoms. In fact, it is directed towards immediate or emergency evaluation 2–3 times more often than other medical concerns (10). To make a diagnosis, a range of checks and tests are performed, including vital signs, such as blood pressure measurements, oxygen saturation or respiratory rate, and body temperature, but also ECG, blood analyses, and troponin tests (32).

However, there is an uncertainty and lack of clinical guidelines to assessing and treating patients with NCCP after an acute coronary syndrome has been
ruled out (32). Moreover, emergency physicians may find it difficult to identify psychological distress as the cause of somatic symptoms in patients with NCCP. Misdiagnosis of cardiovascular disease (CVD) as psychological distress, can lead to major consequences, which may explain caution in diagnosing with psychological diagnoses (37), as well as the delay in diagnosis (16).

Patients with NCCP are often inadequately or inconsistently informed about their symptoms and usually receive no further treatment beyond the assurance that there is nothing physically wrong. They experience anxiety about the diagnostic process, and negative test results are often not reassuring. Moreover, it is not empirically supported that simply informing patients that the testing has shown no abnormalities, is sufficient to reassure patients that they don’t have a medical problem. While extensive examinations can be misleading, even if the results are negative, can it reinforce patient perception that something is being missed, which in turn leads to even more anxiety and fear (37).

**Aspects of living with NCCP**

Patients with NCCP report negative impacts on their everyday lives, including problems with sleep, stress in the home and work environment, experience of more negative life events, and lower health-related quality of life (28, 38). Additionally, chest pain often becomes chronic despite the underlying cause of the pain usually remaining unknown (19). However, physical symptoms are not the only ones. Physical status and mental health are linked to each other (38). Higher anxiety levels in patients have also been shown to affect patients’ social lives. The affected social life and sick leave related to chest pain is the same in patients with NCCP as in patients with ischemic chest pain (39). A study by Mourad et al. (40) shows that patients admitted to hospital for acute NCCP show a greater tendency to suffer from psychological distress than patients with ischemic heart disease. Statistics show that almost 50% of these patients have seen a specialist, mainly a cardiologist, but only 2% of these patients were referred to a psychiatrist, despite the fact that 35%–40% of patients in the ED would present with at least one psychiatric disorder (36, 41).

Patients with NCCP repeatedly seek medical care for their symptoms. It is also demonstrated that experiencing one or more episodes of NCCP per month is associated with a 49% increase in the expected number of medical consultations. This finding further reinforces the notion that recurrent NCCP episodes without a clear diagnosis increase the likelihood of seeking medical consultation for the same issue. It also suggests a strong association with cardiac anxiety, which was the main variable examined in the study (36). However, in a study by
Israel et al. (42) targeting cardiac anxiety in patients with NCCP, significant correlations were found between cardiac-related fear, cardiac-related avoidance, and the interference of pain with daily functioning. This implies that individuals who experience cardiac-related fear and avoidance behaviours are more likely to experience a higher degree of disruption in their daily activities (42). This in turn, suggests that their disabilities, which are related to cardiac anxiety, are increasing further.

Although 1-year mortality for patients with NCCP is 2.3% (43), almost 90% of patients continue to complain of continued symptoms and reduced quality of life even four years after the first episode of chest pain (44). Although coronary angiography shows normal findings, nearly half of these patients continue to worry about underlying heart disease. The primary focus of ruling out CVD can often lead to patients being over-tested, and yet their confidence in healthcare remains low, which means that they continue to seek care for the same symptoms (45). NCCP leads to consequences for both the individual and society. Lack of explanation for their symptoms, difficulties in diagnosis and the experience of falling between the cracks affect the patients in different ways. Additionally, psychological distress is common among NCCP patients (38).

**Psychological distress in patients with NCCP**

Psychological distress, such as depression and anxiety, is one of the main causes of global and societal burdens, has a large impact on public health, and contributes to a substantial economic burden (46). Also, in patients with NCCP, depressive symptoms and anxiety are common and lead to impaired quality of life and interruption of everyday life (16, 47-52). Moreover, patients with NCCP and psychological distress show more frequent complaints of chest pain and less effective treatment compared to patients without psychological distress (53). In this context, recurrent chest pain without a clear explanation for the chest pain is a primary source of psychological distress in patients with NCCP, especially anxiety (54).

**Depression**

Depression is a complex and multifaceted mental health disorder characterised by persistent feelings of sadness, low mood, and a lack of interest or pleasure in
daily activities. It goes beyond the normal fluctuations in mood and can significantly impact a person’s thoughts, emotions, and physical well-being (55). Globally, depression is a leading cause of ill-health, productivity loss, and disability, exacerbating the prognosis of physical illnesses and diminishing overall health and quality of life in 4.4% of world’s population (56). Among patients with NCCP, over half had a depressive disorder, with a lifetime prevalence of major depression at approximately 20% (57). Depression is associated with the persistence of chest pain in NCCP patients. The relationship between psychological factors, including depression, and the perception of pain is complex and can contribute to the chronicity of symptoms (44). In addition, according to Watson (58), symptoms of depression such as sadness, loss of interest, psychomotor disorder, worthlessness/guilt, and cognitive impairment are strongly correlated with each other and with core features of GAD, such as worry and anxious mood. These symptoms primarily encompass a significant component of general distress and negative affectivity. This dissertation focuses on the concept of depressive symptoms.

**Anxiety disorders**

Anxiety disorders are highly prevalent worldwide (59). Individuals with anxiety disorders demonstrate excessive fear, anxiety, or avoidance triggered by perceived threats, whether external (such as social situations or unfamiliar places) or internal (such as unusual bodily sensations). Fear and anxiety are prevalent experiences in daily life. However, for a diagnosis of an anxiety disorder, these feelings must be significantly excessive or disproportionate to the actual threat, persistent over time, and accompanied by impairments in social, occupational, or other important areas of functioning. Essentially, anxiety disorders involve intense and prolonged fear or anxiety that significantly interferes with an individual’s ability to function normally in various aspects of life (60).


**Distress disorders**

The first, distress disorders, include disorders consistently associated with anxious-misery, and common features for distress disorders are pervasive subjective anxiety and non-specific negative affectivity (61).
The most common distress disorder is generalised anxiety disorder (GAD), which is characterised by an overwhelming and unmanageable worry about upcoming events or activities (63). Typical for GAD is that a patient has an unfocused worry and anxiety, not connected to recent stressful events, even if aggravated by certain situations. GAD is characterised by feelings of threat, restlessness, irritability, sleep disturbance, tension, and symptoms such as sweating, dry mouth, and palpitations (64). In addition, GAD is related to depression (58).

Fear disorder
The second, fear disorders, includes disorders that are consistently associated with fear, such as phobias (58). Kinesiophobia is a fear of movement, which is an issue in chronic pain patients. Unlike typical phobias, individuals with kinesiophobia often believe avoiding movement is justified, worsening their condition. This fear promotes hypervigilance and worsens disability, exacerbating pain sensations. Assessing and addressing kinesiophobia is crucial, especially since it hinders adherence to rehabilitation treatments that rely on physical exercise (65).

Cardiac anxiety
A fear disorder that is common in patients with NCCP is cardiac anxiety—a term related to heart-focused anxiety (HFA), an anxiety disorder characterised by fear and anxiety linked to cardiac-related stimuli and sensations (57, 66). Fear contributes to the complexity and persistence of symptoms in these patients [45]. Increased fear and anxiety are based on patients’ previously experienced events, where they perceived cardiac-related events such as palpitations or increased heart rate as unpleasant or dangerous, leading to anxiety. The person may interpret these sensations as signs of a heart attack or other potentially life-threatening conditions, despite the lack of medical confirmation that current symptoms are due to cardiac disease. Cardiac anxiety is a psychological factor that is more specific than other factors associated with the development and maintenance of anxiety issues, like anxiety sensitivity (66). While anxiety sensitivity refers to a general fear of symptoms related to anxiety, driven by the belief that they have harmful effects, cardiac anxiety involves the fear of events, sensations, and functioning related to the heart. Cardiac anxiety involves also vigilance of bodily sensations, especially those concerning the chest and heart (67). Therefore, cardiac anxiety is limited to anxiety about cardiac-related events rather than encompassing sensations throughout the entire body, making it a subset of anxiety sensitivity.
Pain-related fear is also linked to anxiety sensitivity (68) and leads to decreased activity participation, greater perceived disability, increased sick leave (69), decreased physical health (70), and is predictive of higher healthcare utilisation in NCCP (71). Patients with NCCP, driven by high levels of fear of body symptoms (57), may avoid physical activity due to the perceived threat to life and health (72). This avoidance, related to interpreting physical activity as triggering somatic symptoms like hyperventilation and palpitations (73), may negatively impact daily living, contribute to disability, maintain pain, and potentially lead to chronic pain, especially when associated with pain-related fear (69). Fear of pain is not only associated with restricted physical performance and disability levels in chronic pain patients, but also plays a central role in chronic musculoskeletal pain (74). Despite reassurance from healthcare providers, up to 80% of NCCP patients continue to experience chest pain, functional limitations, and psychological issues, underscoring the need for effective management strategies addressing both physical and psychological aspects (36, 75). Inadequately managed NCCP can lead to cardiac anxiety and depressive symptoms, with somatisation contributing to increased healthcare utilisation (40, 50).

Fear-avoidance model in relation to NCCP

The fear-avoidance model, as described by Vlaeyen (76, 77) may be a theoretical framework that illustrates how fear and avoidance affect pain and contribute to a vicious cycle in patients with NCCP and cardiac anxiety. Negative assessments, catastrophic thinking, negative affectivity, and anxiety sensitivity are precursors to pain-related fear. High negative affectivity makes individuals more vulnerable to developing specific fears, leading to pain-related fear and subsequent avoidance behaviours (78). While this avoidance may be beneficial in acute pain because it allows for healing, long-term avoidance of activity can lead to impairments such as decreased participation in work and leisure activities, increased negative emotions such as depression, and increased levels of disability due to disuse syndrome and worsening physical condition (79).

However, pain-related fear is not always associated with avoidance; contextual factors, and competing life goals also influence the individual’s behaviour. Negative emotional states enhance pain control engagement, while positive emotions and optimism promote prioritisation of valuable life goals (77). Exposure to perceived threatening situations, when avoidance behaviour is reduced, can lead to the formation of new non-threat associations to conditioned stimuli (76). The crucial part in the fear-avoidance model cycle is the prospective and stepwise relationships between catastrophic thoughts, fear, avoidance, and pain-related disability, as well as the role of fear as a common tool needed for
recovery (78). The experience of severe pain consists of both pain sensation and emotional reaction. How the patient reacts to pain and how pain is interpreted affects how the patient will deal with its pain (80).

When a patient with NCCP experiences pain, he/she responds with two types of responses: confrontations of the pain or avoidance of it (69, 81); See Figure 1. While confrontation makes it possible to face the fear and reduce it, avoidance leads to the maintenance and exacerbation of fear (69). A patient with NCCP who experiences chest pain without feeling fear of the pain, has a positive emotional state regarding the pain. This, in turn, allows the patient to confront their fear and promotes healing and progress to move on. This kind of positive interpretation, perceiving acute pain as non-threatening, does not hinder daily activities (69, 82).

Figure 1. The fear-avoidance model inspired by a model by Vlaeyen & Linton (77)

However, if the patient perceives fear of the pain experience, they may catastrophise the situation. Catastrophising the pain can be interpreted as extremely threatening, leading to pain-related fear and safety-seeking behaviours like avoidance (69, 82), and can result in both physical and psychological disability (83). Catastrophising symptoms can be reinforced by other negative associations or experiences. Catastrophising pain leads to pain-related fear, creating safety behaviours such as avoidance, marked by an extremely threatening interpretation of pain, and is associated with physical and psychosocial disability
Background

(83). Avoidance behaviours reinforce the perception that certain activities are harmful to the patient’s heart and health, which may be reflected in the reduction of activities to decrease the risk of pain recurrence. Patients with NCCP often avoid physical activity because they believe it may be harmful to their heart and health. It can also be linked to fear of physical symptoms (84) that may normally occur during physical activity (tachycardia, hyperventilation, palpitations, and sweating (73), which patients catastrophise as dangerous and manage through avoidance.

That, in turn, leads to disability, interference, and negative emotional states such as irritation, frustration, and depression. Additionally, cognitive functioning is disrupted, and patients have difficulty shifting attention away from pain-related information, affecting everyday problem-solving. Furthermore, attention to possible threat signals and hyperalgesia increases (85). This means that the patient is more alert, aware, and sensitive to potential threats or dangers, and more sensitive to pain. Moreover, prolonged avoidance of physical activity can have negative effects on musculoskeletal and cardiovascular systems, potentially worsening the pain problem and leading to ‘disuse syndrome’, increasing vulnerability to pain. Impaired physical and psychological function, hypervigilance, and avoidance behaviour lead to worsened chest pain or the onset of new chest pain. This creates a vicious cycle, where fear of pain leads to disability, maintenance of pain, and contributes to chronic pain (69).

Management of psychological distress in patients with NCCP

Treatment of psychological distress in patients with NCCP can include medication or psychological treatment. Medical treatment usually consists of anti-secretory drugs, anxiolytics, antidepressants, nitrates, and calcium channel blockers, and has been applied to alleviate symptoms and improve quality of life for some NCCP patients (86, 87). In cases where generalised anxiety is present, a combination of antidepressants followed by anxiolytics may be employed (88). On the other hand, psychological approaches such as Cognitive Behavioural Therapy (CBT) and psychodynamic therapy, are considered suitable interventions for NCCP, cause they take a holistic approach to treatment, considering thoughts, emotions behaviours and physical symptoms, teaching coping skills and managing the pain (87). In addition, physiotherapy and lifestyle changes have also been shown to be sufficient for the patient group (89). However, for patients with NCCP rooted in psychological distress, alternatives such as CBT, hypnotherapy, or biofeedback could be beneficial (22, 87). There is substantial support
for the effectiveness of CBT in treating anxiety, depressive symptoms (90-92), and specifically NCCP (81). A Cochrane review found CBT useful and moderately successful, despite the multifaceted aetiology of NCCP, and highlighted the need of further RCT of psychological interventions for NCCP with long follow-up periods (87).

**Cognitive Behaviour Therapy**

CBT is often used as an umbrella term that encompasses various psychological interventions (93). CBT is a structured, skills-focused, and collaborative approach aimed to help individuals assess the accuracy and usefulness of their thoughts, behaviours, or both. The goal is to shift cognitive appraisals from unhealthy and maladaptive to evidence-based and adaptive (94, 95).

CBT is a psychotherapeutic approach that combines cognitive therapy and behaviour therapy (96). CBT consist of various strategies and techniques focused on overcoming avoidance and engage in prosocial behaviour to participate in self-care and to improve psychological distress (95). The most-used strategies in previous CBT studies aimed to treat patients with NCCP and cardiac anxiety are:

**Psychoeducation** is about giving the person with NCCP sufficient knowledge about chest pain, how the pain affects them, and how therapy can improve their health, but also informing about the therapeutic process and the skills and strategies that are included in CBT. The goal of psychoeducation is to improve patients' understanding of their thoughts, feelings, and behaviours and to provide them with knowledge that can facilitate positive change (97).

**Exposure therapy**, where exposure is defined as systematic contact with a feared stimulus or reduction in the conditioned fear response to conditioned stimuli that pose a threat, is particularly used in the treatment of anxiety disorders. Exposure therapy involves gradually facing and confronting feared situations. This helps individuals reduce anxiety, overcome avoidance behaviours, and gain more adaptive appraisals of the feared situation. Exposure can be *in vivo*, by actual contact with a feared stimulus or situation; *imaginal* when it is unethical or infeasible to simulate actual fear, and a patient imagines feared consequences of contact with this stimulus or situation; and *interoceptive* exposure is used for patients who experience fear of anxiety, related to physical sensations or symptoms associated with anxiety itself, common in panic disorders or health anxiety (98).
Problem-solving is an approach that involves training individuals to use effective problem-solving skills. Patients learn to break down problems into manageable components, generate solutions, and implement action plans. This problem-solving approach consists of defining problems, brainstorming solutions without judgment, analysing options, and implementing and certifying the chosen solution (98).

Mindfulness and relaxation techniques, such as meditation and deep breathing, are integrated to increase awareness of the present moment and reduce stress (97). These techniques encourage the acceptance of thoughts and emotions without judgment, fostering a non-critical and open-minded approach. It also helps to manage intense emotions, reduce avoidance of internal stimuli, control self-focused attention, facilitate effective thinking, and increase awareness of thoughts and feelings (98).

Behavioural activation is encouraging individuals to engage in positive and rewarding activities to counteract feelings of depression or anxiety (98). It focuses on increasing activities that bring a sense of accomplishment, pleasure, and contribution to their lives. The fundamental idea is that individuals derive the most substantial antidepressant benefits when their behaviours are in harmony with their deeply held values and principles (97).

Cognitive restructuring is a process that involves identifying and challenging negative thought patterns by helping the patient to recognise, evaluate, and if needed, modify maladaptive or unhelpful thoughts and replace them with more balanced and realistic ones (98).

Homework assignments in CBT extend and generalise the positive effects of therapy beyond the therapy sessions. By assigning specific tasks between sessions, the patient has the opportunity to practice and reinforce the new skills and insights learned during therapy (99). These homework assignments also facilitate the practical application of changed behavioural patterns and thought processes, promoting long-term change and increasing the patient’s independence (97).

Face-to-face approach is most common form of CBT. However, there are some barriers for the use of face-to-face CBT. Traditional, face-to-face CBT is time consuming, expensive, and there is a lack of healthcare professionals that can deliver CBT to patients. A potential solution to improve access to CBT for patients suffering from both somatic diseases and psychological distress such as NCCP is to offer CBT via the internet (100).
The effects and experiences of internet-delivered cognitive behavioural therapy

Internet-based Cognitive Behavioural Therapy

Internet-based cognitive behavioural therapy (iCBT) also referred to as computer-based or web-based CBT, is a form of CBT delivered using digital technology. iCBT was incepted in the late 1990s, designed to address a variety of psychological and physical health conditions. Many iCBT programs involve therapist guidance through secure email communication, which in general has shown greater effects than unguided iCBT programs. Most often these programs are text-based, however, they also include elements like streamed videos, audio files, and interactive features, requiring more back-and-forth communication between the therapist and the patient. The length of these programs generally spans 6–15 modules, resembling the sessions in traditional face-to-face therapy (101). iCBT programs usually follows a structured format. It starts with educational elements such as psychoeducation and ends with relapse prevention or termination. In the middle, the treatment consists of modules that are based on treatment tailored to specific disorders. These modules can vary in length, ranging from short summaries to comprehensive texts of more than 20 pages. Illustrations and case examples are usually used, as are homework assignments, such as relaxation training and exposure exercises (102).

Guided iCBT

Generally, effects are greater in guided iCBT than in unguided iCBT (103), and therapist support is linked to positive effects on symptom reduction, adherence to treatment, and dropout rates. The therapist may play an important role in an internet-delivered intervention by providing guidance and support to the patient and detecting any deterioration (104). In a study by Holländare et al. (105) the therapists who were conducting iCBT for depressive symptoms were found to encourage, affirm, guide, and urge patients frequently, but they also clarified the framework, informed patients about modules, emphasised patient responsibility, confronted the patient, and made self-disclosures. However, the role and function of the therapist in iCBT can vary, because treatment programs differ from each other (106). Research also shows that other professions, such as nurses, can advantageously guide patients in iCBT after completing a brief therapist training (104).

Usually, communication between the therapist and the patient occurs via email within the treatment platform (107), but sometimes guidance can also be provided through brief scheduled phone calls, video conferencing, real-time chat-based internet therapy (102), or personal conversations (108, 109). Additionally, it’s common for therapists to send encouraging short text messages approximately once a week (107). The weekly communication takes approximately 10-15 minutes per patient per week during the treatment period (101).
Internet interventions without therapist contact often encounter challenges related to low adherence and high dropout rates (110). The comparable adherence rates with face-to-face CBT emphasise the effectiveness of the therapeutic approaches (111). This becomes particularly relevant when considering iCBT as a tool to support self-care, where iCBT provides patients with accessible and effective psychological support, even in situations with limited therapeutic engagement.

**Pros and Cons of iCBT**

An advantage with iCBT is overcoming traditional barriers associated with face-to-face CBT. Geographical limitations, mobility issues, and time constraints are effectively managed, allowing patients to access therapy at their own convenience. Moreover, iCBT helps diminish the stigma often linked to seeking psychological treatment (112). The online format of iCBT is particularly advantageous, enabling patients to engage in therapy lessons at a time and location that best suits their schedules, increasing accessibility, but also has the potential to foster a sense of self-efficacy among patients who successfully complete the program (113). Furthermore, iCBT proves to be a time-efficient and resource-effective approach. The burden on therapists is notably reduced, with an average weekly commitment between 10 (108) and 20 minutes per patient per week, which benefits both therapists and patients, making mental health support more accessible and manageable (112). Guided internet-delivered interventions have demonstrated substantial positive treatment effects on treatment response and remission post-treatment, as highlighted by Karyotaki et al. (114). Consequently, these interventions have the potential to complement existing services for psychological distress and bridge the gap between the increasing need for evidence-based treatments and their provision. Overall, leveraging iCBT, especially when guided by healthcare professionals, could be a valuable tool in enhancing psychological support for patients with both somatic diseases and psychological distress, e.g., those with NCCP.

There are also some negative effects associated with iCBT. Difficulty in implementing treatment strategies and completing recommended assignments or activities can contribute to feelings of pressure and dissatisfaction among participants. Technical issues navigating the treatment platform (115) and concerns about the security of digital care treatment can also be seen as a barrier (116). Furthermore, possessing adequate computer skills is necessary to effectively participate in digital care, which may exclude some individuals from accessing care (115, 116). Experiencing worsening of symptoms or developing new ones during treatment can create anxiety and frustration, and the uncertainty of managing these. Additionally, lacking motivation or energy to engage in internet-delivered therapy and perceiving it as a burden are also common challenges.
(115). Moreover, participants may perceive lack of support from their therapists, which can exacerbate feelings of frustration and hopelessness, while meaningful and frequent interaction with therapists is considered crucial (115, 116).

Use of digital care in clinical practice

Ensuring effective healthcare delivery requires that healthcare professionals have up-to-date competence and skills in using digital health technologies within their work environments (117). However, in addition to technical skills, healthcare professionals’ attitudes toward digital care play a crucial role in the successful integration of new treatment approaches in clinical practice. Research emphasises that healthcare professionals’ engagement and acceptance are crucial factors in implementing innovative treatments (118). Challenges in embracing new technology, reluctance, and strong opinions that are not supported by evidence can act as inhibiting factors for the acceptance of digital care. It’s important to realise that attitude itself may not always be the only obstacle. The reactions of healthcare professionals to changes can also have a significant impact on the implementation of new practices in healthcare (119). Furthermore, lack of knowledge or negative experiences can contribute to resistance to digital care technologies (120). Addressing these challenges requires a comprehensive approach. Therefore, it is important to understand how healthcare professionals perceive implementation of digital care in their clinical care settings.
Rationale

Psychological distress such as fear, anxiety, and depression are common in patients with NCCP. It is both a societal problem, as those patients use a large amount of healthcare resources, and this entails high costs for the healthcare system, as well as an individual health problem. From the individual's perspective, psychological distress leads to an increased symptom burden, interruption of daily activities, and impaired quality of life. Therefore, those patients need help and support to evaluate their thoughts and to learn how to manage their chest pain. Psychological interventions can be helpful in treating patients with NCCP, especially those who also have anxiety, depression, hypochondria, or panic disorders. An intervention that focuses on cardiac anxiety can be a way to gain new knowledge and break the habits. CBT has been shown to reduce psychological distress in patients with NCCP, but is resource-intensive, which is why other alternatives to CBT are needed. iCBT is more accessible and has been effective in mild and moderate anxiety and depressive disorders; however, there is a knowledge gap regarding the effectiveness of iCBT on patients with NCCP and cardiac anxiety. One hypothesis for this study was that iCBT would prove to be more effective than a psychoeducation only, in reducing psychological distress among patients with NCCP and cardiac anxiety. Additionally, it is also important to explore NCCP patients' experiences of participating in a nurse-led internet-delivered program, i.e., iCBT, that aims to reduce cardiac anxiety, since several of these patients do not consider themselves to suffer from psychological distress. Finally, more knowledge is needed about how healthcare professionals involved in the treatment of patients with NCCP, at ED or cardiology departments, perceive digital care as a form of treatment for their patients, and their views on the implementation of new digital care technologies in their workplace. This new knowledge may streamline and enhance care for patients with NCCP and cardiac anxiety and demonstrate the support healthcare professionals require to enable digital care for these patients.
The effects and experiences of internet-delivered cognitive behavioural therapy
Aim

Overall aim
The overall aim of this dissertation was to evaluate the effects of a nurse-led iCBT program on psychological distress in patients with NCCP, and to explore their experiences participating in the iCBT program. In addition, to describe healthcare professionals’ perceptions of digital care in the emergency and cardiac care for patients with NCCP.

Specific aims of included studies:

Study I: To evaluate the effects of a nurse-led iCBT program on cardiac anxiety and other patient-reported outcomes in patients with NCCP.

Study II: To explore the experiences of patients with NCCP and cardiac anxiety regarding their participation in the nurse-led iCBT program.

Study III: To evaluate the effects of a nurse-led iCBT program on cardiac anxiety and secondary outcomes, such as bodily sensations, depressive symptoms, health-related quality of life, and chest pain frequency in patients with NCCP at 6- and 12-month follow-ups, and to explore predictors that can have impact on the effects of the iCBT program on psychological distress.

Study IV: To describe healthcare professionals’ perceptions of digital care in clinical practice for patients with NCCP.
The effects and experiences of internet-delivered cognitive behavioural therapy
METHOD

Design
This dissertation comprises two quantitative studies (I & III) and two qualitative studies (II & IV). An overview of the design and study samples is presented in Table 2, and a flow chart with a time aspect of the study period will be shown in Figure 2.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Measurements</th>
<th>Data collection</th>
<th>Instruments</th>
<th>Data analysis</th>
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<tbody>
<tr>
<td>I</td>
<td>Quantitative study, RCT</td>
<td>109 patients with NCCP and cardiac anxiety</td>
<td>Sociodemographic data, cardiac anxiety, fear of body sensations, depressive symptoms, health-related quality of life, chest pain frequency</td>
<td>Questionnaire data collected at baseline, 5 weeks, and 3 months</td>
<td>CAQ, BSQ, PHQ-9, EQ-VAS, self-developed question regarding chest pain frequency</td>
<td>Linear mixed models analyses</td>
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<tr>
<td>II</td>
<td>Qualitative inductive, descriptive study</td>
<td>16 patients with NCCP and cardiac anxiety who participated in the iCBT program</td>
<td>Participants’ experiences of participation in iCBT</td>
<td>Face-to-face interviews &lt; 3 months after completed iCBT</td>
<td>Interview guide</td>
<td>Content analysis</td>
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<tr>
<td>III</td>
<td>Quantitative longitudinal study of an RCT</td>
<td>109 patients with NCCP and cardiac anxiety</td>
<td>Sociodemographic data, cardiac anxiety, fear of body sensations, depressive symptoms, health-related quality of life, chest pain frequency</td>
<td>Questionnaire data collected at baseline, 5 weeks, 3 months, 6 months, and 12 months</td>
<td>CAQ, BSQ, PHQ-9, EQ-VAS, self-developed question regarding chest pain frequency</td>
<td>Linear mixed models and multiple regression analyses</td>
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<tr>
<td>IV</td>
<td>Qualitative inductive, descriptive study</td>
<td>17 healthcare professionals from emergency and cardiology clinics</td>
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<td>Interview guide</td>
<td>Thematic analysis</td>
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RCT—Randomised controlled trial, iCBT—internet-delivered cognitive behavioural therapy, NCCP—Non-cardiac chest pain, CAQ—Cardiac Anxiety Questionnaire, BSQ—The Body Sensations Questionnaire, PHQ-9—Patient Health Questionnaire 9, EQ-VAS—EuroQol visual analogue scale
The effects and experiences of internet-delivered cognitive behavioural therapy

Figure 2. A flowchart with a time aspect of the study period.

Description of randomised controlled study (I & III)

Studies I and III use a randomised controlled design (RCT), registered at www.clinicaltrials.gov/(NCT03336112) and conducted between January 2018 and October 2021. The RCT was delivered and processed via a website that was created for the study by the study’s I first author (GM) (121).

iCBT program

The iCBT program, IKSIT, was developed based on a pilot study by Mourad et al. (5). The pilot and the final program were developed and reviewed by cardiac nurses, a cardiologist, a psychologist, a psychiatrist, a physiotherapist, a general practitioner, and two patients with long experience of NCCP. There was also access to a computer technician who could support the research team in the event of technical problems. Access to the website was restricted to individuals who received the designated URL and login details. In addition to requiring a username and password for entry, an extra layer of security was implemented through two-factor authentication, which involved the use of SMS one-time passwords.

The intervention – iCBT group

The intervention was a nurse-led iCBT program consisting of five sessions during five weeks. The participants of the intervention group received pre-made modules which they worked on weekly. As the participants progressed through the modules and submitted reports, the next modules were unlocked. The iCBT program included psychoeducation, modification of thoughts, exposure to physical activity, and mindfulness training with associated exercises and homework assignments; See Figure 3 for an overview of the content.
**Figure 3.** Overview of the content in the intervention and psychoeducation program.

<table>
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<tr>
<th>iCBT</th>
<th>Psychoeducation</th>
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<tr>
<td>1</td>
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<tr>
<td>• Study information</td>
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<td>• Information about intervention content and setup</td>
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<td>• Introduction week 1</td>
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<td>• Goal setting</td>
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<td>• Psychoeducation: Chest pain and related psychological aspects (text, figures and video)</td>
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<td>• Home assignments: Chest pain diary</td>
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<td>• Summary week 1</td>
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<td>• Introduction week 2</td>
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<tr>
<td>• Psychoeducation: Mindfulness (text, audio and video)</td>
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<td>• Home assignments: Chest pain diary and mindfulness training</td>
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<td>• Summary week 2</td>
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<td>• Introduction week 3</td>
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<tr>
<td>• Psychoeducation: Physical activity (text and video)</td>
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<td>• Home assignments: Chest pain diary, mindfulness training and physical activity</td>
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<td>• Summary week 3</td>
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<td>• Introduction week 4</td>
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<tr>
<td>• Psychoeducation: Avoidance and exposure (text and figures)</td>
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<td>• Home assignments: Chest pain diary, mindfulness training, physical activity and formulation of exposure plan</td>
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<td>5</td>
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<td>• Summary week 4</td>
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<td>• Introduction week 5</td>
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<tr>
<td>• Home assignments: Chest pain diary, mindfulness training, physical activity and performance of exposure plan</td>
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<tr>
<td>• Goal evaluation</td>
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<td>• Program evaluation</td>
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<td>• Psychoeducation: Chest pain and related psychological aspects (text)</td>
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<td>• Psychoeducation: Avoidance and exposure (text)</td>
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The effects and experiences of internet-delivered cognitive behavioural therapy

The psychoeducation component aimed to educate patients about the impact of chest pain on daily life, emphasising how avoidance and safety behaviours can maintain or exacerbate chest pain; See Figure 4 for screenshot from the internet platform. Patients were also asked to reflect on how chest pain limited them in everyday life, and what thoughts, feelings, and reactions it created, as well as what they did to deal with the pain. As a homework assignment, patients kept a chest pain diary where they were asked to write down the frequency, duration, location, character, intensity, and situation in which chest pain occurred in order to get to know their chest pain. This chest pain diary was sent to the therapist weekly for feedback.

Figure 4. Screenshot from the internet platform.

The mindfulness segment included informative content and daily exercises to increase awareness of bodily sensations and emotions, help patients remain present despite chest pain, and develop effective coping strategies. The participants were given a few text- and audio-based mindfulness exercises to choose from, some shorter or longer, which they were recommended to perform on a daily basis. The homework assignment was to send a detailed description of their mindfulness training each week by filling out a form.

The physical activity component provided information and recommendations in line with national guidelines (122), encouraging patients to realise the heart’s tolerance for physical activity. This part aimed to reduce cardiac anxiety
and address avoidance tendencies related to physical activity. This section consisted of both written information about the positive effects of physical activity on their health, and also videos with a physiotherapist with information and recommendations on physical activity; See figure 5 for screenshot from the internet platform. According to the National Board of Health and Welfare’s guidelines (90), patients were recommended to perform moderate physical activity for at least 30 minutes and 5 days a week during the course of the study. The homework assignment was to send in a detailed description of physical activity every week, as well as reflect on their thoughts and emotions about being exposed to physical activity.

Figure 5. Screenshot from the internet platform.

Patients submitted their homework assignments weekly during the course of the study for feedback. The same nurse, in this study called a therapist, provided feedback and advice once a week at a predetermined time, allowing patients to plan their engagement effectively. This process was transparent to the participants. The entire treatment and contact med participants were administered through the study’s website, with reminders and motivational messages sent to
encourage completion of the program. The iCBT program constituted the primary treatment, with the guidance and feedback part requiring an average of 8 (±4) minutes per patient per week.

The control – psychoeducation group

To control in RCT, an active control group was chosen and provided with psychoeducation. This psychoeducation contained identical text-based information as the information presented to the intervention group, yet it lacked any accompanying assignments or feedback components. The psychoeducational content was divided into five sessions, with participants accessing one session each week via the same website used by the intervention group. The therapist sent out a notification to participants each week when a new session became available; See Figure 4 for overview of the content.

Description of qualitative studies (II & IV)

Both studies design, are descriptive interview studies with inductive approach, analysis with content analysis (II) according to Patton (123), and semantic thematic approach (IV) based on Braun and Clarke (124). The inductive approach in Study II was employed due to the lack of prior studies on the experiences of participants in iCBT program for patients with NCCP. Similarly, the inductive approach in Study IV was utilized due to the lack of research on perceptions and attitudes towards digital care and offering iCBT among healthcare professionals in emergency care and cardiac care.
Participants and procedure of recruitment

Participants of RCT (I – III)

Participants in studies I and III are the same patients who were recruited at the same time and followed up for one year. Patients were recruited following their discharge from the ED at three regional hospitals and one university hospital in Southeast Sweden. The recruitment process took place from January 2018 to August 2020. Initially, patients were recruited only from two hospitals, however, in April 2019, due to recruitment problems, recruitment was expanded, and two additional hospitals were included. Identification of eligible participants was done through registers. To be eligible for participation, patients needed to be ≥18 years and must have had at least two healthcare consultations due to NCCP (ICD 10-codes: R07.2 – Precordial pain; R07.3 – Other chest pain; R07.4 – Chest pain, unspecified; and Z03.4 – Observation for suspected cardiovascular condition) during the last 6 months.

Those patients who met the inclusion criteria were sent a package by post containing study information, an informed consent form, and a pre-stamped envelope. Subsequently, the study team contacted patients within a week by phone, to provide verbal information about the study and answer questions about participation. Patients who expressed interest and returned a signed written informed consent were then assessed for cardiac anxiety using an encrypted web-based survey tool. Patients who screened positive for cardiac anxiety (score ≥24 on the Cardiac Anxiety Questionnaire) were randomly assigned in a 1:1 ratio to either the intervention or the control group, using a randomisation table provided by a statistician; See Figure 6.

Patients were excluded if they had no access to computer/tablet with an internet connection, were not able to perform physical activity due to physical constraints, did not speak/understand Swedish, or suffered from severe depression measured by the Patient Health Questionnaire-9 (PHQ-9), had cognitive impairment, or newly diagnosed cancer requiring treatment (according to medical records).

Participants in study II are 16 of 54 participants in the intervention group. To avoid impacting patients’ activity in the iCBT program, patients in the intervention group were invited to participate in study II upon completing the iCBT program. They were asked to share their experiences through interviews, irrespective of the number of sessions they had completed. Firstly, the intention was to interview all participants in the iCBT group, but the outbreak of the COVID-19 pandemic hindered the face-to-face interviews from being completed.
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Figure 6. The CONSORT flowchart of patient inclusion to RCT in studies I and III.
Healthcare professionals (IV)
Participants in study IV are licensed healthcare professionals (physicians and nurses) working at ED or cardiology departments, which was the only criteria for participation in the study. Recruitment to this study started with obtaining approval from the managers at four ED and two cardiology clinics at one university and two regional hospitals in Southeast Sweden. Thereafter, contact was made with the research managers at these clinics for distribution of research information to physicians and nurses. Most clinics were visited in person by the author (MEL) to provide detailed information about the study. A random sampling approach was used. The healthcare professionals who showed interest in participating in the interview, fulfilled the inclusion criteria (physicians and nurses working in emergency and cardiac care), and gave their consent to participate, were contacted by the author (MEL) for oral information and to schedule an appointment for an interview. They were consecutively selected in the order in which they expressed interest in participating in the study.

Data collection

Measurements (I & III)
Data were collected at three points is study I; i.e., at baseline before randomisation, 5 weeks from baseline (after the end of the intervention), and at 3 months after the end of the intervention. In study III, data were collected at five points, which, in addition to the previous points in study I, also included 6 months and 12 months after the end of the intervention. Medical data, obtained from medical records, was complemented by self-reported information. All self-reported data were collected using an encrypted web-based survey tool, Survey & Reports, provided by Linköping University. Participants in iCBT group were sent two reminders every two weeks if they had not filled out the questionnaires.

The primary outcome in the RCT was cardiac anxiety, while the secondary outcomes encompassed fear of body sensations, depressive symptoms, health-related quality of life (HRQoL), and chest pain frequency.
Cardiac Anxiety Questionnaire

The Cardiac Anxiety Questionnaire (CAQ) is a self-report assessment tool designed to measure cardiac anxiety levels associated with sensations in the chest. Developed and evaluated by Eifert et al. (66), the CAQ is applicable to patients with or without heart disease. The instrument covers various aspects of cardiac anxiety, including attention to heartbeats, avoidance of physical activities, and fear of cardiac-related sensations. This questionnaire consists of three subscales (fear, 8 items; avoidance, 5 items; and attention, 5 items), where each item is rated on a 5-point Likert scale ranging from 0 (never) to 4 (always). CAQ comprises 18 items with a score range between 0 and 72, where the higher scores indicate greater cardiac anxiety. The total CAQ score is derived by calculating the mean of the relative frequency ratings for each of the 18 items. This is achieved by summing up the responses for individual items and dividing the mean total by 18. Subscale scores, reflective of different aspects of cardiac anxiety (fear, avoidance, and attention), are similarly computed by determining the mean of the ratings for each item within the respective subscale. The CAQ does not have any specific cut-off values that define clinically significant levels of cardiac anxiety, so in this study, we used the median score of 24 from a previous study by Mourad et al. (52).

The validity and reliability of CAQ has been measured in a study in Swedish post-myocardial infarction patients (125). CAQ showed good internal consistency with a Cronbach’s α coefficient of 0.89 for the full questionnaire and similarly high internal consistency for fear (α = 0.86) and avoidance (α = 0.87). Despite slightly lower internal consistency for attention (α = 0.67), this measure indicates that all items within the CAQ and its subscales reliably measure the construct of cardiac anxiety. The study found also good test-retest reliability for the CAQ total score (ρ = 0.75), indicating that CAQ present consistent results when administered to the same individuals on separate occasions, indicating its reliability over time. Convergent validity was demonstrated by showing significant correlations between the CAQ total score and other anxiety measures (HADS Anxiety, PCL-C), as well as depressive measures (HADS Depression, BADS, MADRS-S), suggesting that the questionnaire effectively captures symptoms of anxiety. While discriminant validity was indicated by weaker correlations between the CAQ and measures of depression compared to measures of anxiety. Finally, both exploratory and confirmatory factor analysis confirmed the validity of the 3-factor structure, suggesting that the items within the CAQ, cluster together and form distinct factors representing different aspects of cardiac anxiety and by that supporting its construct validity (125).

The Cronbach’s α coefficients in both studies I and III were .79 to .89 for the iCBT, and the control (psychoeducation) groups.
Body Sensations Questionnaire
Fear of bodily sensations was measured with The Body Sensations Questionnaire (BSQ) (126). The BSQ is a 17-items scale that is a valid and reliable measurement for assessment of dimensions of fear of body sensations (e.g., fear of panic attacks, heart palpitations, mental illness, and fainting). Higher scores indicate greater fear of bodily sensations. This questionnaire has demonstrated good psychometric properties. In this RCT, the Cronbach’s α coefficients were .92 to .94 for the iCBT and the control (psychoeducation) groups.

Patient Health Questionnaire-9
The prevalence and severity of depressive symptoms were measured with the Patient Health Questionnaire-9 (PHQ-9). This instrument consists of 9-items with a score range between 0 and 27. Scores between 5 and 9 indicate mild depressive symptoms, 10–14 indicate moderate depressive symptoms, 15–19 moderately severe depressive symptoms, and 20–27 severe depressive symptoms. For this RCT-study, a cut-off score of 10 was employed to identify individuals with at least moderate depressive symptoms. The PHQ-9 is recognised as a reliable instrument (127), and in the present study, it demonstrated Cronbach’s α coefficients ranging from 0.87–0.89 for the iCBT and the control (psychoeducation) groups.

EuroQol Visual Analog Scale
Health-related quality of life (HRQoL) was measured with The EuroQol visual analogue scale (EQ-VAS). The scale ranges between 0–100, where 0 is the worst imaginable health state and 100 is the best imaginable health state. This questionnaire, provides a quantitative measure of patients’ perception of their overall health (128).

Chest pain frequency
Chest pain frequency was measured with a self-developed question: During the last month, how often have you experienced NCCP? Participants responded by provide a number of times they had experienced chest pain in the past month.
Interviews (II & IV)

Qualitative data were collected by individual interviews with participants in the iCBT program (II), and healthcare professionals (IV). Sensitivity of the topic, particularly in study II, and ethical considerations meant that individual interviews were considered to be the most suitable for collecting data on patients' experiences of the treatment that they have undergone. An overview of data collection in those studies is presented in Table 3.

<table>
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<th>Table 3. Overview of data collection in the qualitative studies.</th>
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<td><strong>Study</strong></td>
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| II        | May 2018–January 2020 | Face-to-face | Participants’ homes, offices or the interviewers’ workplace | 16 | 47 min (20–86 min) | 3 | Yes, without any further changes | "Why did you choose to participate in this study?" "Can you tell us about your experience of receiving care online?" "How did you experience the content and structure of the program?" "How do you feel your expectations of the therapist were met?"
| IV        | December 2021–Mars 2023 | Video (15) and face-to-face (2) | by Teams, in 2 cases when face-to-face, at participants’ offices | 17 | 38 min (22–55 min) | 2 | Yes, without any further changes | “Can you share your experience offering internet-delivered treatment?” “In what way do you think the introduction of internet-delivered treatment, such as iCBT, can affect your work?” “What fears or advantages do you see with internet-delivered treatment for patients with NCCP?”

In study II, data were collected through face-to-face interviews. Participants had the opportunity to select the time and location convenient for them. The interviews occurred at participants’ homes, offices, or the interviewers’ workplace, based on the preferences of the participants. Only the interviewers and participants were present during the interviews. In study IV, the data of 15 participants were collected by video interviews using Microsoft Teams, however,
some participants preferred face-to-face interviews, which resulted in 2 interviews performed at participants' workplaces. According to Peasgood et al. (129), video interviews are preferred by a larger percentage of participants than face-to-face interviews, but by allowing participants to choose the interview option that is most convenient for them, the chances increase that more participants will attend the interview. The use of video interviews does not decrease data quality (129), and have advantages from financial, opportunistic, and environmental perspectives (130).

The interview guide was developed and utilized to ensure consistency and standardization (123), employing semi-structured questions. The objective of the interviews was to gather participants' viewpoints on the subject. Patton suggests six overarching categories that can aid in framing the study's aim by posing more specific and intentional questions. These general categories encompass questions regarding experience and behaviour, opinions and values, emotions, knowledge, sensory perceptions, and background and demographic information. These categories were integrated into the design of the interview questions to facilitate the exploration of various types of responses during the interview process. Probes were also employed to elicit more comprehensive and insightful answers (123). Examples of interview questions in study II and study IV are presented in Table 2.

A pilot interview was performed in both studies, and because it required no further adjustments, both pilot interviews were included in the analysis. Participants received verbal information about the interviewers when scheduling the interviews and before the start of interview. All interviews were audio-recorded and transcribed verbatim by the author of this dissertation.

Data in the interview studies were collected by a total of four interviewers. In study II, interviews were conducted with three interviewers, two PhDs and one PhD student, all with previous experience in qualitative interviewing. In study IV, interviews were conducted by two interviewers, one PhD and one PhD student, also with previous experience of qualitative interviewing.
Data analysis

Statistical analysis (I & III)

The IBM SPSS version 25 was used for data analysis in study I and IBM SPSS 28 in study III. To describe the background variables, frequencies, percentages, mean values, and SDs were used. Chi-square tests or Student’s t-tests were used depending on the data, for comparison between groups regarding demographic variables.

The level of p < .05 was set for significance. Based on power calculations derived from findings in the pilot study (5), each group in the RCT (study I) should include 53 participants to achieve a 20% improvement (approximately an effect size of 0.5) in cardiac anxiety (95% CI and 80% power).

To assess improvement in cardiac anxiety, a reliable change index score was calculated in the study I, as CAQ lacks an established cut-off score indicating prevalence or severity of cardiac anxiety (121). The selected sample size aligns with those in comparable CBT studies (109). To preserve the integrity of randomisation and minimise bias risks associated with attrition or non-adherence, intention-to-treat analysis was applied, ensuring follow-up for patients even if they became inactive or dropped out of the study (131).

To compare the iCBT and control (psychoeducation) groups regarding changes in cardiac anxiety, bodily sensations, depressive symptoms, HRQoL, and NCCP frequency, a linear mixed model analysis was performed in both study I and study III. The comparison was performed at three different measurement points in study I, and at five different measurement points in study III; See Table 4.

| Table 4. Overview of measurement points in study I and study III. |
|-------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
|                  | Baseline | 5 weeks (end of intervention) | 3 months (end of intervention) | 6 months (end of intervention) | 12 months (end of intervention) |
| Study I           | X        | X                             | X                           |                             |                             |
| Study III         | X        | X                             | X                           | X                           | X                           |
In study I, 8% of the total data were missing at the 5-week follow-up and 16% at the 3-month follow-up. To ensure the accuracy of our results, a mixed model analysis based on multiple imputation was performed as a sensitivity analysis, in addition to mixed model analysis based on original data. The multiple imputation was conducted under the assumption that the data were missing at random (Little’s MCAR test \( p = 1.0 \)) (132). In this approach, missing values were assumed to depend on the observed data and were replaced with values generated from and based on the complete dataset (133). A total of 40 imputations were calculated based on the outcome and demographic variables that showed a significant correlation with the primary outcome at baseline. Since the results of mixed model analysis, based on original data, did not differ from the results based on multiple imputations, only the results from the original data were presented in that study.

In study III, 15% of the participants had missing data at both the 6-month and 12-month follow-ups. All longitudinal analysis was performed on original data and imputation of missing data was not performed. Baseline chest pain frequency data were not normally distributed, but a mixed model analysis is considered a robust approach that can handle non-normally distributed data. Furthermore, a standardised value (z-value) for chest pain frequency was calculated, however the outcomes did not deviate from the mixed model results obtained from the original data, which is why these z-value outcomes are not presented in the results.

In study I, the Pearson correlation coefficient was used to determine the relationships between demographic variables, disease, and psychological burden, treatment activity (including metrics like the number of logins and performed sessions), and the change score in cardiac anxiety between the measurement points.

In study III, a multiple regression analysis was used to explore factors that had an impact on the treatment effect of iCBT on cardiac anxiety. Change score (changes in CAQ score between baseline and 12-month follow-up) were used as the dependent variable. An exploratory approach was used because we did not know which factors could impact the treatment effect of iCBT on cardiac anxiety, therefore all variables from Table 5 were tested. To find possible exploratory variables, a two-step algorithm was used. First, to find variables that could be included in a multiple regression model, a univariate analysis of variance was performed. That, to explore the relationship between demographic and medical variables and the change score in CAQ between baseline and 12-month follow-up. Consistent with Altman’s recommendation (134), variables were chosen
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based on a lax criterion, e.g., \( p < .20 \) or higher, due to unforeseen ways in which the variables may contribute to a multiple regression model, due to complex relationships among them. Variables with a significance level of \( p < .20 \) were deemed suitable as exploratory variables for the multiple regression analysis. Additionally, baseline scores of the CAQ total and the subscales (fear, avoidance, and heart-focused attention), BSQ, PHQ-9, EQ-VAS, and chest pain frequency were also included in the univariate analysis of variance. Selected variables, i.e., psychotropic treatment, CAQ total baseline, CAQ avoidance baseline, and CAQ attention baseline were simultaneously entered into the multiple regression analysis. Non-significant variables (\( p > .05 \)) were removed from the analysis and re-examined until the final model comprised only statistically significant variables. The final model met the criterion of excluding multicollinear variables, demonstrated as a variance inflation factor <10.

Effect sizes from the intervention were assessed using Cohen’s d, with interpretations of <0.20 considered trivial, 0.20–0.49 as small, 0.50–0.79 as moderate, and ≥0.80 as large (135). Due to lack of a defined cut-off for clinically significant improvement in CAQ, a reliable change index score according to Christensen and Mendoza (136) was calculated. This was done by dividing the baseline SD score of 8.6 by the Cronbach’s \( \alpha \) coefficient score of 0.79 within study groups, a reliable change was defined as a change score of approximately 11 points per participant. To explore differences between groups in the number of patients with a change score ≥11 at all measurement points, the chi-square test was employed.

Qualitative analysis (II & IV)

Content analysis

The analysis of study II was performed according to Patton's (123) qualitative data content analysis method, focusing on identifying patterns and regularities within the data to be organised into categories. The study was carried out using an inductive approach, indicating that the content analysis followed a conventional method aimed at describing a particular phenomenon. A benefit of using the conventional approach to content analysis is its flexibility in adapting to diverse and dynamic datasets. Without predefined categories or theoretical frameworks, researchers have the freedom to explore emerging themes and patterns in the data. This adaptability ensures that the analysis remains responsive to the richness and complexity of the information provided by study participants, fostering a more comprehensive understanding of the studied phenomenon (137).
Each text consists of a manifest and a latent content. The manifest content is about the textual and obvious and is expressed at a descriptive level in the form of categories. The latent, on the other hand, is about the underlying meaning of the text, or what is said between the lines and expressed at the interpretive level in the form of themes (123).

NVivo software was used for data management. All data were transcribed by the author (MEL), who later listened to all the recordings to ensure that they matched the transcriptions. Subsequently, multiple readings of the transcripts were conducted for content familiarisation. To enhance the study’s trustworthiness, three interviews were randomly selected and individually coded by all authors. A collaborative discussion among the authors lead to the development of a comprehensive coding scheme. The remaining transcripts were then systematically coded by MEL, including new codes into the scheme and adjusting existing ones for better content description, as needed (123). After completing the coding, the codes were organised into distinguishable patterns within sub-categories and categories. Approval of these categories occurred through a collective discussion involving all authors before proceeding to write the results. The results were strengthened with quotations extracted directly from the raw data, which were translated into English for publication, adhering to guidelines by Patton (123). This rigorous process ensures a comprehensive and reliable content analysis, underscoring the importance of systematic coding, collaborative validation, and the use of direct quotations to support the study’s results (123).

Thematic analysis

The data analysis in study IV used an inductive thematic approach, following Braun and Clarke’s (124) methodology. This inductive strategy aimed to identify themes from patterns in the data, interpreting and exploring underlying meanings to unveil insights not previously addressed by existing theories, thereby fostering a more comprehensive understanding. The analysis adopted a semantic approach, prioritising explicit meanings in the data to give voice to the participants, without looking beyond what has been written (138).

The analysis was developed in six phases. Initially, the author (MEL) immersed herself in the data through transcription of all audio material and then repeated readings of all transcripts, establishing an initial coding system to preserve context. To increase the credibility of the study, five interviews were selected randomly for individual coding by all authors. Subsequently, the focus shifted to identifying broader themes, with the authors collectively organising codes into potential thematic categories. A coding scheme was jointly developed by all authors to guide and define coding, which served as a tool to facilitate interpretation (124). Building on the established coding scheme, the remaining
transcripts were systematically coded by MEL. Subsequently, themes underwent a thorough review and refinement process to accurately represent the data. The iterative nature of this process ensured that the final description captured the nuances and depth of the identified themes.

Quality of research

Validity and reliability (I & III)

The concepts of validity and reliability were evaluated in studies I and III. The definition of validity refers to the extent to which study design and methods accurately measure what they are intended to measure and whether the study results can be trusted and applied to the target population (139). The concept of reliability refers to the consistency and stability of the measurements or observations used in the study, and assesses whether the results would be consistent if the same study were conducted again under similar conditions (134).

Trustworthiness (II & IV)

The trustworthiness was assessed in the qualitative studies, II and IV. Criteria such as credibility, transferability, confirmability, and dependability, according to Lincoln & Guba (140), were used to ensure the study being trustworthy. The concept of credibility refers to the authenticity of research findings and the extent to which results accurately reflect the experiences and perspectives of participants in the study. Transferability refers to the extent to which the study findings can be applied or transferred to other contexts or settings outside the specific sample. Transferability aims to apply study findings to similar contexts or situations and is essential for determining the relevance and usefulness of the findings beyond the immediate study setting. Dependability refers to transparency and thoroughness in the description of methods, as well as consistency and reliability in research findings over time. The concept of confirmability refers to the degree to which the findings are derived subjectively from data, rather than from the researcher’s biases or presumptions. Findings should be confirmable or verifiable by others and not solely a reflection or subjective interpretation of the authors (140).
Ethical considerations

Studies I, II, and III were approved by the Regional Ethical Review Board in Linköping, Sweden (code 2017/343-31). In study IV, an ethical review was also applied, however, the application was rejected on the grounds that the study is not covered by the provisions of Sections 3–4 of the Ethical Review Act and therefore should not be ethically reviewed (ref. no. 2020-06358). Anyhow, the Ethical Review Board issued an advisory statement on the research project.

All studies were conducted according to the Helsinki Declaration (141), which is a fundamental ethical framework for medical research. It emphasizes respect for participants’ autonomy and dignity through requirements for informed consent. All participants in studies I-IV received both written and verbal information and signed a written consent form before being included in the studies. Risks and benefits for participants were carefully assessed. The benefits of the study were deemed to outweigh the potential risks, and vulnerable individuals were protected through careful consideration of inclusion and exclusion criteria. No conflicts of interest could be declared in the studies. Furthermore, thorough and honest reporting of the studies has been conducted, with all researchers being responsible for upholding ethical principles.

Moreover, all studies, I-IV were conducted in accordance with the Swedish Research Council’s (142) four fundamental ethical principles for research in the humanities: the information requirement, the consent requirement, the confidentiality requirement, and the use requirement. All data will be stored for 10 years on a secure server with no possibility for unauthorised access.

To compare treatment methods in the RCT, study I, and study III, active control group was chosen. Individuals who experience NCCP often feel inadequately or inconsistently informed about their symptoms, neglected and usually receive no further treatment beyond the assurance that there is nothing physically wrong (37). Comparing iCBT with such a minimal level of care could lead to an overestimation of the iCBT effect, making it challenging to discern whether the observed impact is solely due to iCBT or partially influenced by the attention received from participating in a study (143). It is advisable (144) and also recommended to have an attention control, such as psychoeducation, in order to conclude whether the effects are linked to the intervention (103). In addition, for ethical reasons, it is preferable to offer individuals facing various psychological problems some form of intervention rather than leaving them completely unsupported when assigned to the control group (132).
The participants in the RCT were those who met the criteria for participation and had sought care for chest pain on at least two occasions during a 6-month period. This meant that the patients had been examined by physicians at least twice and undergone examinations to rule out acute illness or heart disease as the reason for chest pain. These patients received no treatment or follow-up for their symptoms in routine care. Participation in the study did not affect the patients' ability to seek care. There was a risk that iCBT could arouse feelings and thoughts that could create discomfort in participants. Participants were given the opportunity and encouraged to contact and receive feedback on their thoughts and feelings from the study team. The study team had competence to handle such situations, and there was also a management plan for these patients. The research group consisted of a broad base of expertise that met the requirements for the intervention, including nurses, cardiologists, and psychologists. All had both clinical and theoretical experience with patients with NCCP and iCBT.

One factor that was discussed was that patients could feel both supported and neglected because they had sought care for a physical condition but were offered psychological treatment. However, despite this, the benefits of the study were considered to outweigh the negative aspects. Patients were generally satisfied that their issues had been acknowledged, as they usually feel overlooked by healthcare.

Another question raised was whether patients with pre-existing heart conditions should be included in the study. This was duly considered and discussed in the ethics application. According to a 20-year Swedish register study by Fagring et al. (145), there has been a significant improvement in the prognosis for patients with heart disease, including those with acute myocardial infarction (AMI), angina, and NCCP. Mortality rates have decreased, and for patients with angina or NCCP, mortality rates are similar to those of the general age-matched population. However, Holmberg et al. (146) suggests that patients with AMI are particularly vulnerable due to a lack of control over the situation, anxiety, and fear of death as a possible outcome. Van Beek's et al. (147) study shows that patients reporting higher levels of cardiac anxiety following an AMI are at an increased risk of adverse cardiac prognosis. The risk of new cardiac events increased with each point increase on the CAQ, primarily driven by avoidance behaviour related to cardiovascular stimuli. This association remained significant even after adjusting for parameters of disease severity, suggesting an independent prognostic effect of cardiac anxiety. The results of these studies underscore the importance of integrating psychological treatment as part of the care for patients with heart diseases. Treatment should focus on reducing cardiovascular
anxiety and avoidance behaviour, which can contribute to improved prognosis and quality of life for these patients (147).

The essence of the iCBT intervention in studies I and III, lay in empowering patients to monitor and manage their symptoms on their own. The knowledge and training aimed to allow them to learn to distinguish different characteristics of chest pain and pay attention to changes such as the nature of the pain, duration, radiation, or the appearance of additional symptoms that they experienced as abnormal. In addition, patients with persistent chest pain were strongly encouraged to seek immediate care for medical assessment and management of their symptoms. This proactive attitude aimed to ensure that patients received prompt and appropriate care, especially in cases where their chest pain was an indication of potential cardiac issues. Regarding the selection of participants for the study, individuals who had initially been invited to participate in the study but who were later, during follow-up telephone information, found to have un-investigated chest pain or ongoing diagnostic investigations for their symptoms were excluded from the study. This exclusion was implemented to maintain homogeneity in the study population and to ensure that participants were investigated for their chest pain before study inclusion. In addition, participants were informed at inclusion that participation in the study would in no way impede their ability to seek medical care. The information was provided to reduce concerns about how study participation would affect their access to health care.
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RESULTS

Sample

In studies I and III, a total of 824 patients were approached and invited to participate in the RCT study; See Figure 6. Following the screening process, 230 patients (28%) were assessed for eligibility and invited to the study, and of those, 109 (47%) who met the inclusion and exclusion criteria and provided their consent were randomly assigned to either iCBT (54/109, 49.5%) or psychoeducation (55/109, 50.4%). Demographic details for both the iCBT and control (psychoeducation) groups are outlined in Table 5. The mean age of participants was 56 years (SD 16), with a majority being women (62%, n=67), no working (51%, n=55), and married or in a relationship (76%, n=83). 30% (n=33) had a history of previous heart disease. Regarding of prior psychological distress treatment, 88% (n=96) had no prior experience with psychotherapy, and 56% (n=61) had not been prescribed psychotropic treatment. No significant differences were identified in baseline characteristics or medical data between patients assigned to iCBT or psychoeducation.

Participants in study II were patients who had been randomised to and had performed the iCBT intervention (study I). In total, 33 of 54 patients of iCBT group were invited and 16 (30%) of them agreed to participate in the interview. These 16 participants were aged 33–77 (mean 57, SD 17), equally divided between women and men (50%). The majority were married or in a relationship (88%), were working (56.3%), and half of them had a high school education (50%). The average number of sessions completed by the participants in the program was 4.4 sessions (SD 1.1); See Table 6.
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<th>Characteristics</th>
<th>iCBT (n=54)</th>
<th>Control (n=55)</th>
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<tbody>
<tr>
<td>Age year (mean ± SD)</td>
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<td>56.8±15.5</td>
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<tr>
<td>Sex, n (%)</td>
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<tr>
<td>Females</td>
<td>32 (59)</td>
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<td>.639</td>
</tr>
<tr>
<td>Males</td>
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<td>Marital status, n (%)</td>
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<tr>
<td>Married/cohabitants</td>
<td>45 (83)</td>
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<td>Single</td>
<td>9 (17)</td>
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<td>Economic situation, n (%)</td>
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<td>Good</td>
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<td>Problematic</td>
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<td>10 (18)</td>
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<tr>
<td>University</td>
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<td>Occupational status, n (%)</td>
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<td>Working</td>
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<tr>
<td>None/previous smoker</td>
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<td>48 (87)</td>
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<tr>
<td>Smoker</td>
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<td>7 (13)</td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption, n (%)</td>
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<tr>
<td>No drinking (0–4 glasses)</td>
<td>83 (45)</td>
<td>85 (47)</td>
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<tr>
<td>Drinking (&gt;5 glasses)</td>
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<td>18 (8)</td>
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<td>Charlson Comorbidity Index (mean ± SD)</td>
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<td>2.5 (2.1)</td>
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<tr>
<td>Previous heart disease, n (%)</td>
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<td>15 (27)</td>
<td>.496</td>
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<td>Psychotherapy, n (%)</td>
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<td>5 (9)</td>
<td>.357</td>
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<tr>
<td>Psychotropic treatment, n (%)</td>
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<td>25 (45)</td>
<td>.763</td>
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<td>Exercise ≥30 min, days/week (mean ± SD)</td>
<td>2.5 (2.1)</td>
<td>3.0 (2.2)</td>
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<td>Origin, n (%)</td>
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<tr>
<td>Sweden</td>
<td>46 (85)</td>
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<tr>
<td>Another Nordic country</td>
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<td>3 (6)</td>
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<tr>
<td>Another country within Europe</td>
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<tr>
<td>South America</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td></td>
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<tr>
<td>Asia</td>
<td>0 (0)</td>
<td>4 (7)</td>
<td></td>
</tr>
<tr>
<td>Acid reflux, n (%)</td>
<td>9 (17)</td>
<td>9 (16)</td>
<td>.966</td>
</tr>
<tr>
<td>Muscle pain, n (%)</td>
<td>29 (54)</td>
<td>26 (47)</td>
<td>.502</td>
</tr>
<tr>
<td>Joints/Skeletal pain, n (%)</td>
<td>32 (59)</td>
<td>31 (56)</td>
<td>.760</td>
</tr>
<tr>
<td>Psychological disorder, n (%)</td>
<td>23 (43)</td>
<td>19 (34)</td>
<td>.388</td>
</tr>
<tr>
<td>CAQ Total at baseline (mean ± SD)</td>
<td>36 (8)</td>
<td>36 (9)</td>
<td>.959</td>
</tr>
<tr>
<td>CAQ Fear at baseline (mean ± SD)</td>
<td>19 (4)</td>
<td>15 (5)</td>
<td>.901</td>
</tr>
<tr>
<td>CAQ Avoidance at baseline (mean ± SD)</td>
<td>8 (4)</td>
<td>8 (4)</td>
<td>.735</td>
</tr>
<tr>
<td>CAQ Attention at baseline (mean ± SD)</td>
<td>9 (4)</td>
<td>9 (3)</td>
<td>.460</td>
</tr>
<tr>
<td>BSQ at baseline (mean ± SD)</td>
<td>43 (14)</td>
<td>42 (12)</td>
<td>.624</td>
</tr>
<tr>
<td>PHQ9 at baseline (mean ± SD)</td>
<td>8 (6)</td>
<td>8 (6)</td>
<td>.755</td>
</tr>
<tr>
<td>EQ-VAS at baseline (mean ± SD)</td>
<td>59 (20)</td>
<td>66 (17)</td>
<td>.031</td>
</tr>
<tr>
<td>Chest pain frequency at baseline (mean ± SD)</td>
<td>15 (13)</td>
<td>9 (11)</td>
<td>.006</td>
</tr>
</tbody>
</table>

CAQ: cardiac anxiety questionnaire; BSQ: body sensations questionnaire; PHQ-9: Patient Health Questionnaire-9; EQ-VAS: EuroQol visual analogue scale.
Results

The participants in study IV were healthcare professionals working in emergency care (47%) or cardiology (53%). These 17 participants were aged 25–62 years (mean 41.5; SD 12) and were mostly women (88%). Both nurses (76%) and physicians (24%) were included in this study, and they had a mean of 11.8 years (SD 8.9) in their profession; See Table 7.

<table>
<thead>
<tr>
<th>Table 6. Characteristics of the sample, in study II.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics</strong></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td>Female, n (%)</td>
</tr>
<tr>
<td><strong>Age, years (mean ± SD)</strong></td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
</tr>
<tr>
<td>Married / in relationship, n (%)</td>
</tr>
<tr>
<td><strong>Educational level</strong></td>
</tr>
<tr>
<td>Compulsory school, n (%)</td>
</tr>
<tr>
<td>High school, n (%)</td>
</tr>
<tr>
<td>University, n (%)</td>
</tr>
<tr>
<td><strong>Occupational status</strong></td>
</tr>
<tr>
<td>Working, n (%)</td>
</tr>
<tr>
<td>Retired, n (%)</td>
</tr>
<tr>
<td>On sick-leave, n (%)</td>
</tr>
<tr>
<td>Unemployed, n (%)</td>
</tr>
<tr>
<td><strong>Interview duration, minutes (mean ± SD)</strong></td>
</tr>
<tr>
<td><strong>Number of sessions performed (mean ± SD)</strong></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 7. Characteristics of the sample, in study IV.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics</strong></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td>Female, n (%)</td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td><strong>Age, year (mean ± SD)</strong></td>
</tr>
<tr>
<td><strong>Workplace</strong></td>
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<tr>
<td>Emergency Department, n (%)</td>
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<tr>
<td>Department of Cardiology, n (%)</td>
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<tr>
<td><strong>Occupation</strong></td>
</tr>
<tr>
<td>Nurse, n (%)</td>
</tr>
<tr>
<td>Registered Nurse, n (%)</td>
</tr>
<tr>
<td>Specialist Nurse, n (%)</td>
</tr>
<tr>
<td>Master Specialist Nurse, n (%)</td>
</tr>
<tr>
<td>Physicians n (%)</td>
</tr>
<tr>
<td>Resident Physicians, n (%)</td>
</tr>
<tr>
<td>Specialist Physician, n (%)</td>
</tr>
<tr>
<td><strong>Years in the profession at workplace (mean ± SD)</strong></td>
</tr>
<tr>
<td><strong>Interview duration, minutes (mean ± SD)</strong></td>
</tr>
</tbody>
</table>
The effects and experiences of internet-delivered cognitive behavioural therapy

The short- and long-term effects of iCBT

Cardiac Anxiety (I & III)

The mixed model analysis showed no statistically significant interaction effect of time and group regarding cardiac anxiety in the short-term effect; i.e., 3 months, (I: \( p=.275 \); Cohen’s d=0.31) or the long-term effect, i.e., 12 months, (III: \( p=.256 \); Cohen’s d=0.31) between the iCBT and control (psychoeducation) groups; See Table 8.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Time effect</th>
<th>Group effect</th>
<th>Interaction effect</th>
<th>Effect size</th>
<th>Cohens’ d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>P-value(^a)</td>
<td>iCBT</td>
<td>Control</td>
<td>P-value(^b)</td>
</tr>
<tr>
<td>CAQ(^b)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>36.4</td>
<td>-</td>
<td>29.4</td>
<td>30.8</td>
<td>.959</td>
</tr>
<tr>
<td>5 weeks</td>
<td>30.3</td>
<td>(&lt;.001)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>29.0</td>
<td>(&lt;.001)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>28.1</td>
<td>(&lt;.001)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>26.8</td>
<td>(&lt;.001)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) In comparison with baseline

\(^b\) CAQ: cardiac anxiety questionnaire

Within-group analysis indicated significant improvements in cardiac anxiety for both the iCBT and control (psychoeducation) groups from baseline to the 12-month follow-up (\( p<.001 \)). In study I, the iCBT group demonstrated a reduction in their mean score from 36.3 at baseline, to 29.7 at 5 weeks’ follow-up and to 27.9 at 3 months’ follow-up. In control (psychoeducation) group, the mean score was 36.4 at baseline, reduced to 30.8 at 5 weeks’ follow-up and to 29.9 at 3 months’ follow-up.

In study III, within-group analyses showed a reduction of mean score in iCBT-group from 36.3 at the baseline, to 29.8 at 5 weeks’ follow-up, 28.0 at 3 months’ follow-up, 26.8 at 6 months’ follow-up, and finally to 25.6 at 12 months’ follow-up. In control (psychoeducation) group, the mean score at baseline was 36.4, and was reduced to 30.9 at 5 weeks’ follow-up, 30.0 at 3 months’ follow-up, 29.1 at 6 months’ follow-up, and finally to 27.8 at 12 months’ follow-up. This was a significant improvement on cardiac anxiety during the 12 months’ follow-up (\( p<.001 \)) in both groups; See Figure 7 and Table 9.
Changes in cardiac anxiety between the groups

A reliable change score of ≥11 points, suggesting a clinical improvement in cardiac anxiety, was calculated and compared between the groups. Within the iCBT group in study I, 36% (16/54) of patients demonstrated a positive reliable change score, while 2% (1/54) exhibited a negative reliable change score, indicating a deterioration in cardiac anxiety at the 3-month follow up. In the control (psychoeducation) group, the corresponding numbers were 27% (13/55) of patients with a positive reliable change score and 2% (1/55) of patients with a negative reliable change score.

In study III, in the iCBT group, at the 12-month follow up, 46% (21/46) of patients had a positive reliable change score and 2% (1/46) had negative reliable change score, and corresponding numbers in the control (psychoeducation) group was 34% (16/47) of patients with positive reliable change score, and 2% (1/47) with a negative score. Nevertheless, the difference between the iCBT and control (psychoeducation) groups was not significant (p=.25).

Figure 7. Changes in cardiac anxiety over time between iCBT and control (psychoeducation) group.
Table 9. Within-group changes (Estimates of Fixed Effects from Linear Mixed Model Analysis) over the 12-month follow-up in the iCBT and control group (psychoeducation). Modified table from study III.

<table>
<thead>
<tr>
<th>Variable (Instrument)</th>
<th>Time</th>
<th>iCBT group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>Std. Error</td>
</tr>
<tr>
<td>Cardiac anxiety (CAQ)</td>
<td>0 Weeks</td>
<td>36.32</td>
<td>1.109</td>
</tr>
<tr>
<td></td>
<td>5 Weeks</td>
<td>29.81</td>
<td>1.229</td>
</tr>
<tr>
<td></td>
<td>3 Months</td>
<td>27.98</td>
<td>1.467</td>
</tr>
<tr>
<td></td>
<td>6 Months</td>
<td>26.82</td>
<td>1.400</td>
</tr>
<tr>
<td>Fear of bodily sensations (BSQ)</td>
<td>0 Weeks</td>
<td>43.33</td>
<td>1.943</td>
</tr>
<tr>
<td></td>
<td>5 Weeks</td>
<td>36.86</td>
<td>1.509</td>
</tr>
<tr>
<td></td>
<td>3 Months</td>
<td>37.76</td>
<td>1.756</td>
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<td></td>
<td>6 Months</td>
<td>37.72</td>
<td>1.944</td>
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<td></td>
<td>12 Months</td>
<td>35.43</td>
<td>1.665</td>
</tr>
<tr>
<td>Depressive symptoms (PHQ-9)</td>
<td>0 Weeks</td>
<td>8.00</td>
<td>.768</td>
</tr>
<tr>
<td></td>
<td>5 Weeks</td>
<td>7.83</td>
<td>.739</td>
</tr>
<tr>
<td></td>
<td>3 Months</td>
<td>6.29</td>
<td>.746</td>
</tr>
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<td></td>
<td>6 Months</td>
<td>6.08</td>
<td>.722</td>
</tr>
<tr>
<td></td>
<td>12 Months</td>
<td>5.13</td>
<td>.579</td>
</tr>
<tr>
<td>Health-related quality of life (EQ-VAS)</td>
<td>0 Weeks</td>
<td>58.54</td>
<td>2.760</td>
</tr>
<tr>
<td></td>
<td>5 Weeks</td>
<td>60.18</td>
<td>2.863</td>
</tr>
<tr>
<td></td>
<td>3 Months</td>
<td>62.70</td>
<td>3.209</td>
</tr>
<tr>
<td></td>
<td>6 Months</td>
<td>59.63</td>
<td>3.082</td>
</tr>
<tr>
<td></td>
<td>12 Months</td>
<td>64.66</td>
<td>2.895</td>
</tr>
<tr>
<td>Chest pain frequency (Self-developed question)</td>
<td>0 Weeks</td>
<td>15.15</td>
<td>1.704</td>
</tr>
<tr>
<td></td>
<td>5 Weeks</td>
<td>13.81</td>
<td>2.474</td>
</tr>
<tr>
<td></td>
<td>3 Months</td>
<td>9.25</td>
<td>2.000</td>
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<td></td>
<td>6 Months</td>
<td>8.90</td>
<td>1.636</td>
</tr>
<tr>
<td></td>
<td>12 Months</td>
<td>5.82</td>
<td>1.201</td>
</tr>
</tbody>
</table>

Abbreviations:
a: Used as time reference
CAQ: Cardiac Anxiety Questionnaire
BSQ: Body Sensations Questionnaire
PHQ-9: Patient Health Questionnaire-9
EQ-VAS: EuroQol Visual Analogue Scale
Secondary outcomes (I & III)

No significant short-term interaction effects of time and group were found when comparing the iCBT and control (psychoeducation) groups regarding any of the secondary outcomes over the 3-month follow-up (I); i.e., fear of body sensations ($p=0.55$; Cohen’s $d=0.15$), depressive symptoms ($p=0.87$; Cohen’s $d=0.10$), HRQoL ($p=0.10$; Cohen’s $d=0.57$), and chest pain frequency ($p=0.20$; Cohen’s $d=0.21$).

Also, the long-term (12 months’ follow-up; III) interaction effects of time and group were statistically non-significant regarding fear of bodily sensations ($p=0.09$; Cohen’s $d=0.40$), depressive symptoms ($p=0.55$; Cohen’s $d=0.07$), and health-related quality of life ($p=0.26$; Cohen’s $d=0.27$). However, the analysis showed a statistically significant interaction effect of time and group regarding chest pain frequency ($p=0.009$; Cohen’s $d=0.48$) in favour of the iCBT group at the 12-month follow-up; See Table 10.

| Table 10. Mixed model analysis of the effect of iCBT compared to control (psychoeducation) on secondary outcomes, presented in estimated marginal means. |
|---|---|---|---|---|---|
| Variables | Time effect | Group effect | Interaction effect | Effect size |
| BSQ | Baseline 42.7 | - | 38.2 | 38.5 | .618 | 0.40 |
| | 5 weeks 38.0 | <.001 | 37.0 | 39.1 | .092 |
| | 3 months 37.5 | <.001 | 35.7 | 37.3 | .664 |
| | 6 months 36.8 | <.001 | 37.6 | 35.9 | .872 |
| | 12 months 36.8 | <.001 | 35.3 | 38.3 | .086 |
| PHQ-9 | Baseline 7.8 | - | 6.6 | 6.3 | .752 | 0.07 |
| | 5 weeks 7.0 | .515 | 7.6 | 6.4 | .324 |
| | 3 months 5.9 | .005 | 6.0 | 5.8 | .901 |
| | 6 months 6.2 | .003 | 6.1 | 6.3 | .476 |
| | 12 months 5.4 | <.001 | 5.3 | 5.5 | .546 |
| EQ-VAS | Baseline 62.5 | - | 61.1 | 65.7 | .030 | 0.27 |
| | 5 weeks 61.2 | .579 | 60.0 | 62.3 | .139 |
| | 3 months 61.9 | .304 | 62.2 | 61.6 | .094 |
| | 6 months 64.9 | .629 | 60.0 | 69.9 | .642 |
| | 12 months 66.5 | .027 | 64.9 | 68.2 | .258 |
| Chest pain frequency | Baseline 12.0 | - | 10.6 | 6.7 | .005 | 0.48 |
| | 5 weeks 8.1 | .003 | 15.1 | 8.8 | - |
| | 3 months 6.8 | <.001 | 14.2 | 8.1 | .923 |
| | 6 months 5.2 | <.001 | 9.4 | 6.7 | .164 |

a) In comparison with baseline; c) BSQ: body sensations questionnaire; d) PHQ-9: Patient Health Questionnaire-9; e) EQ-VAS: EuroQol visual analogue scale
The effects and experiences of internet-delivered cognitive behavioural therapy

In study I, between group-analysis of short-term effects with regard to groups showed significant differences in HRQoL ($p=.031$) and chest pain frequency ($p=.006$) in favor of iCBT.

Considering the time effect, there was a significant difference in bodily sensations at both 5-weeks and 3-month follow-ups compared to baseline ($p<.001$). Additional time-related differences were also found in depressive symptoms ($p=.005$) and chest pain frequency at 3-month follow-up ($p=.005$), compared with baseline.

In study III, the between group-analysis of long-term effects of iCBT compared to psychoeducation found a group effect in health-related quality of life ($p=.03; \text{Cohen's } d=0.27$) and in chest pain frequency ($p=.005; \text{Cohen's } d=0.48$) favouring iCBT.

Regarding time effect, there were statistically significant differences in both groups regarding fear of body sensations at all outcome measure points; i.e., at 5 weeks, 3 months, 6 months, and 12-month follow-up compared to baseline ($p<.001$). There were also significant differences in both groups regarding depressive symptoms at 3-month follow-up ($p=.005$), at 6-month follow-up ($p=.003$), and at 12-month follow-up ($p<.001$), in health-related quality of life at 12-month follow-up ($p=.027$), and in chest pain frequency at 3-month follow-up ($p=.003$), and 6 and 12-month follow-up ($p<.001$); See Table 9 and Figure 8-11.

![Figure 8. Changes in bodily sensations over time between iCBT and control (psychoeducation) group.](image-url)
Results

Figure 9. Changes in depressive symptoms over time between iCBT and control (psychoeducation) group.

Figure 10. Changes in HRQoL over time between iCBT and control (psychoeducation) group.

Figure 11. Changes in chest pain frequency over time between iCBT and control (psychoeducation) group.
The effects and experiences of internet-delivered cognitive behavioural therapy

The number of patients with depressive symptoms ≥10 at baseline in the iCBT group was 21 (39%) and decreased to 9 (17%) at 12-month follow-up, representing an improvement by 57%. In the control (psychoeducation) group, the number of patients at baseline was 13 (24%) and decreased to 8 (14%) at 12-month follow-up, representing an improvement by 38%; See Table 11.

<table>
<thead>
<tr>
<th>Measurement point</th>
<th>Patients with depressive symptoms, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>iCBT (n=54)</td>
</tr>
<tr>
<td>Baseline</td>
<td>21 (39)</td>
</tr>
<tr>
<td>5-week follow-up</td>
<td>15 (28)</td>
</tr>
<tr>
<td>3-month follow-up</td>
<td>6 (11)</td>
</tr>
<tr>
<td>6-month follow-up</td>
<td>8 (15)</td>
</tr>
<tr>
<td>12-month follow-up</td>
<td>9 (17)</td>
</tr>
</tbody>
</table>

**Factors associated with changes in cardiac anxiety at 12-month follow-up**

A multiple regression analysis was performed in study III to find variables in the iCBT group that may be associated with changes in cardiac anxiety using CAQ at 12-month follow-up. By using univariate analysis of variance, four exploratory variables were found to be significant and were thereby included in the multiple regression analysis: psychotropic treatment (p=.065), CAQ total baseline (p=.035), CAQ avoidance baseline (p=.008), and CAQ attention baseline (p=.153). The exploratory variables that were not significant, and excluded in further analyses were: group (p=.410), age (p=.686), gender (p=.646), marital status (p=.805), socioeconomic status (p=.731), educational level (p=.331), occupational status (p=.564), smoking (p=.578), alcohol consumption (p=.439), Charlson Comorbidity Index (p=.922), previous heart disease (p=.950), psychotherapy (p=.991), CAQ fear baseline (p=.729), BSQ baseline (p=.417), PHQ-9 baseline (p=.739), EQ-VAS baseline (p=.459), and chest pain frequency baseline (p=.735). All four significant variables were entered simultaneously into the multiple regression model, and only CAQ avoidance at baseline was statistically significant (beta=0.355, p=.034). This result suggests that the more avoidance
Results

there is at baseline, the greater the likelihood of reduced cardiac anxiety at 12-month follow-up.

Experience and perception of iCBT and digital care

Experience of iCBT in patients with NCCP (II)

The study resulted in three categories and eight sub-categories. The first one, “driving factors for participation in the iCBT program”, described the impact of pain on patients’ lives and their struggle before participating in the program. The second, “the program facilitates change”, described how the program helped them make changes regarding pain, fear and anxiety. The last category, “learning to live with chest pain”, described the program as a tool for gaining the strength and skills needed to live a normal life despite chest pain; See Table 12.

<table>
<thead>
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<th>Table 12. Overview of categories and subcategories in study II.</th>
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<td><strong>Category</strong></td>
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<td>Driving factors for participation in the iCBT</td>
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<td>The program as a catalyst</td>
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<td>Learning to live with chest pain</td>
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Driving factors for participation in the iCBT program

The first category consists of two subcategories: "fear and anxiety in relation to chest pain" and "the desire for normalisation". In this category, the participants described their everyday life before treatment as characterised by fear, anxiety, and depression, which was the main driving factor for participating in the study. They described how their symptoms, which were
similar to those of the heart, led to negative thoughts and fear of death. They also described behavioural changes, such as avoidance of physical activities or social encounters, that left them feeling lonely and have a limited life. Being repeatedly discharged from ED, without getting answers on their symptoms, usually caused anxiety and/or fear of death, as well as loss of trust in the healthcare system.

The participant also described a desire to get back to a normal life, without feeling fear of pain. By participating in the study, they saw opportunities to make changes in their lives, where pain does not have a central place.

The program as a catalyst

The second category contains four subcategories: “the program felt trustworthy and provided safety”, “feeling commitment to the program”, “getting encouragement and confirmation through feedback” and “use of and access to the program”. This category describes their experiences with the iCBT program. They perceived the program as credible, obvious, reliable, and clearly related to their chest pains. The program gave them a sense of community and counteracted the feeling of being alone with their problems. Participants perceived the content as varied and promoted their abilities and different preferences. The knowledge, experience, and competence of the team behind the program made them perceive it as credible.

The presence of a therapist motivated participants to work on the program. The therapist was perceived as interested, curious, and encouraging, which increased participants’ engagement with the program. They felt that they were taken seriously when the therapist analysed, reflected on and answered their questions. Additionally, they described that the therapist had the courage to ask difficult questions, which created the opportunity to share thoughts, and receive understanding, patience and compassion, which strengthened the participants’ relationship with the therapist.

The weekly feedback was experienced as a confirmation and encouragement to continue working with the program. However, they were aware that active participation and personal responsibility were necessary to implement the program in their lives. A predetermined day and time when the feedback would come made the treatment more predictable, and easier to schedule. The feedback was also perceived as individual and as taking into account users’ disabilities and needs. Contact with the therapist was perceived as professional but not as rigid or mechanical.

Finally, the iCBT program was seen and used by many as a database, where facts and information were supplemented with exercises and contact.
with the therapist. The participants saw the therapist as a complement to the program. They appreciated the easy and unlimited accessibility to the materials, during the treatment period, and were free to make their own choices regarding the daily activities of the program. Participants were able to use the program as a safe space that gave them strength as they struggled with their symptoms. However, some participants were concerned that the program could awaken thoughts and fears that could be difficult to deal with on their own.

Learning to live with chest pain

The last category contains two subcategories: "challenging my fear and gaining strength" and "gaining new insights into my abilities". In these categories, participants stated that the program made them challenge their fears, which helped them accept and learn to live with their limitations due to chest pain. They saw the different strategies in iCBT as tools to help them expose things they perceived as threatening, despite fear of pain. The program taught them new coping skills to control their chest pain and fear and to continue dealing with situations that they perceived as dangerous. The program allowed them to improve their ability to focus on everyday life, and to normalise their problems by exposing them to situations that could cause pain.

Last, the program gave them insight into how common NCCP is, which made it easier to recognise themselves in the treatment and feel less alone. Their new knowledge had a calming effect on the anxiety associated with the pain. Participants found that they were able to implement these new skills in everyday life, even outside of the program. They acknowledged that mind-changing processes and new insights require long-term work, and at the same time, they saw participation in the program as the beginning of their new journey.

Perception of digital care among healthcare professionals (IV)

The study results show the healthcare professionals’ perceptions of digital care within clinical practice in emergency and cardiology care for patients with NCCP. Four themes and eleven subthemes were identified. The first theme, “new ground to walk on” describes healthcare professionals’ knowledge and experiences in digital care. The second theme: “a challenge to current healthcare system” describes digital care as a challenge for the current healthcare system. The third theme: “digital care has its potential”
The effects and experiences of internet-delivered cognitive behavioural therapy shows that a majority saw opportunities in using digital care. The fourth and last theme: “prerequisites for use in clinical practice” demonstrates facilitators for the introduction of digital care in clinical practice; See Figure 12.

Figure 12. Overview of themes and sub-themes in study IV.

New ground to walk on
This theme consists of two sub-themes: "limited knowledge about digital care" and "varying amounts of experience in digital care" which depict different healthcare professionals' experiences of digital care. Confusion of concepts, uncertainty about the form of treatment, lack of familiarity and knowledge about digital care, and uncertainty about one's own competence were also perceived by participants as obstacles. In addition, healthcare professionals expressed uncertainty about offering psychological treatment to patients seeking treatment for somatic symptoms, such as NCCP. Digital care was considered to be relatively new and unexplored, which was one explanation for their scepticism towards this form of treatment. Participants were aware of the potential risks of digital care, but also admitted that they felt that a lack of knowledge about digital care made it difficult for them to imagine how digital care could affect their work and tasks. The lack of knowledge about digital care was mainly due to the participants' limited experience of this form of treatment.
Most participants had no previous experience in digital care. A few healthcare professionals had limited hands-on experience with the implementation of digital care, while others had knowledge of these tools and referred patients to them. They were more likely to encourage their patients to use the program when they were familiar with the program’s design and components, which also improved their understanding of when patients deviated or discontinued the treatment plan. There were also some participants who had personal experiences with iCBT treatments. For them, the positive outcome of their treatment had created a positive association with this form of treatment.

A challenge for the current healthcare system

The second theme consists of three sub-themes; "worries and resistance to change", "concerns about miscalculations and exclusion of patients" and "concerns regarding unserious digital applications", which describe how digital care was seen as a challenge for today’s healthcare system. Most of participants expressed a positive perception of the implementation of digital care in their workplace, but they also saw the challenges associated with the implementation of new forms of treatment and new ways of working in healthcare. The fear of the unknown was tangible among healthcare professionals and could lead to a lack of commitment. Participants felt that it was important to involve healthcare professionals in the implementation process at an early stage to show that their experiences and concerns were valued.

Concerns about missing an acute illness were also expressed by several participants. They were worried about their own skills and the skills of their colleagues, and worried that they might neglect or overlook a serious condition that could have catastrophic consequences for the patient. Some healthcare professionals were concerned that it would be difficult to convince patients to try a treatment option that requires a certain amount of effort from them, and others worried that patients seeking help for somatic problems would feel neglected if they were offered a psychological treatment. The possible exclusion of older people or people with disabilities was also seen as an obstacle.

Concerns about rogue digital applications were mainly associated with healthcare apps or digital health centres, which led to some scepticism among individuals, often linked to concerns about unscrupulous for-profit
healthcare providers. Healthcare professionals were concerned about referring patients for treatments in which they lacked sufficient information or who promised unrealistic results. In addition, there were concerns about the lack of control over the care that patients actually received and the care that was paid for.

**Digital care has its potential**

This theme consists of the three sub-themes “cautious trust in digital care”, “positive experience generate trust”, and “possible benefit for young people and introverts” describe how the majority of participants felt that healthcare has a lot to learn from embracing digital care. They perceived digital care as an innovative approach and saw benefits in being able to offer it to different generations based on their unique needs and preferences. They admitted that they had noticed that digitalisation has become increasingly important in patients’ lives, and that much of healthcare today takes place digitally. They also saw that the shift to digital care offers many options that can modernise the process of seeking and delivering medical assistance.

Some participants admitted that they had not previously reflected on digital care, but they perceived digital care as an innovative approach and saw benefits in being able to offer it to different generations based on their unique needs and preferences. Patients’ perception of digital care also affected healthcare professionals’ attitudes. Healthcare professionals had also noticed an increased interest in online therapies following the COVID-19 pandemic. Younger people, in particular, were considered to be the main beneficiaries of digital care due to their natural familiarity with the digital world from a young age, making digital care feel more natural to them. The younger population was generally seen as more adaptable, making them well-suited to digital care. Even people who, for various reasons, prefer not to interact with others in person, e.g., introverts, were seen as a suitable target group for digital care.

**Prerequisites for use in clinical practice**

This last theme consists of three sub-themes, “leadership and contact person”, “technology and practical support”, and “information and training”,

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where participants identified several factors that can facilitate the introduction of digital care in clinical practice.

Leadership was perceived as an important prerequisite for participants to feel confident in introducing and offering digital care. Committed and interested leadership was necessary to create the conditions required for a successful implementation. Understanding how management views and plans for a new form of treatment, as well as when and how it should be implemented, was important for participants. Participants also saw the benefits of having a contact person who they could turn to for questions and concerns, and who would also play a key role in motivating and encouraging other healthcare professionals to embrace the new digital healthcare technology. Evaluation and quality assurance were also considered essential to ensure that digital healthcare technology met expectations and delivered the desired results.

Technical and practical assistance was another factor that was considered crucial. Digital healthcare technology needs to be easily accessible, secure, and provide a safe environment for users. In addition, participants wanted to be not only informed but also educated on how to get started with the treatment. Conditions such as increased numbers of healthcare professionals or the provision of necessary resources were also considered beneficial and highly desirable during the implementation process.

Another crucial prerequisite for a successful implementation of digital care was information and education. Healthcare professionals saw a need for both written and verbal information, with details about the treatment and practical issues such as costs and duration. They also wanted to gain access to the treatment website, to explore the treatment they would offer their patients. Competence was also seen as important. Healthcare professionals felt responsible for the treatment they referred or recommended to their patients and wanted to ensure that the treatment met patients' expectations.
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DISCUSSION

Discussion of the results

The overall aim of this dissertation was to evaluate the effects of a nurse-led iCBT program on psychological distress in patients with NCCP, and to explore their experiences participating in the iCBT program. In addition, to describe healthcare professionals’ perceptions of digital care in the emergency and cardiac care for patients with NCCP.

The overall findings of this dissertation show that cardiac anxiety was reduced in patients with NCCP, but iCBT was statistically not more effective than psychoeducation. Regarding secondary outcomes, iCBT was statistically not better than psychoeducation in decreasing fear of body sensations or depressive symptoms, but there was a significant positive change in health-related quality of life and number of chest pain episodes in favour of iCBT. However, despite randomisation, there were at baseline some differences in the number of chest pain episodes between groups which need to be taken into consideration. Within-group analysis shows a significant improvement in both groups during a 12-month time period. Moreover, patients with a high tendency to avoid activities or situations that they believe could trigger cardiac symptoms had better improvement in their cardiac anxiety. In interviews, patients described that they experienced the iCBT program as helpful, trustworthy, and useful, and saw the program as a tool to challenge their fear of chest pain and death, and gain strength and new insights into their ability to live a normal life. Looking at healthcare professionals’ perception of digital care, they were cautiously positive and hopeful about the implementation of digital care therapy for patients with NCCP. However, they also saw that certain factors must be met in order to successfully implement the treatment in a clinical practice.

Is iCBT more beneficial than psychoeducation?

The findings of study I and III shed light on the efficacy of iCBT compared to psychoeducation in reducing cardiac anxiety among patients with NCCP. Although iCBT has not been shown to be more effective than psychoeducation in reducing cardiac anxiety, some factors may have limited this change.
Possible limiting factors for change

An important aspect to consider is the differences in structure and content between the iCBT and psychoeducation programs. The iCBT program in study I and III offers a more varied and interactive treatment approach through various tools to support patients in changing their thought patterns. This includes exercises, homework assignments, and feedback mechanisms that promote active participation and learning. While, psychoeducation program only offers educational materials in the text form, which does not provide the same level of interaction and engagement from patients. This variation in treatment format may be a key factor contributing to iCBT being perceived as more beneficial as it allows for a more in-depth and engaging treatment. The importance of design, layout, structure, usability, and interactivity in maintaining user engagement in iCBT was described in previous research (148, 149) and also highlighted by participants of iCBT and described in study II.

Moreover, factors that may contribute to iCBT being more acceptable and effective may be due to the variety of tools and educational formats, which can cater to patients’ different preferences and stimulate different senses. In addition, the accessibility and flexibility of iCBT can increase adherence to treatment by offering patients the opportunity to participate in treatment when and where it suits them best.

Another important factor is the duration of the intervention. The fact that the iCBT program in study I and III did not prove to be superior to psychoeducation can partly be attributed to the relatively short treatment time. Meta-analysis of Reavell et al. (150), have shown significant reduction of anxiety in longer CBT interventions for patients with CVD, which was not observed in shorter interventions. This suggests that an extended iCBT intervention may yield better results for patients with NCCP by allowing more time for practice and learning, especially for cognitive changes that require time to be established.

The presence of comorbidity, particularly depression, is also an important factor to consider. Although all participants were randomized at baseline to either the iCBT or control (psychoeducation) group, 21 (39%) patients with depressive symptoms ended up in the iCBT group compared to 13 (24%) patients in the control group, which may have impacted the study outcome. Patients with depression often require longer treatment times and more tailored interventions. This is also confirmed by the systematic review and meta-analysis by Liu et al. (151) who concluded that patients suffering from anxiety and depression require longer treatment times and more frequent sessions, as depression can affect the length and
Discussion

intensity of treatment to achieve the desired results. Because of this, patients with higher levels of depressive symptoms in studies I and III may not fully benefit from iCBT for cardiac anxiety due to the relatively short and standardized intervention period and exposure not being optimal in treatment of depression. Considering comorbidities in the design of treatment programs and addressing them during study inclusion may be crucial for achieving better outcomes.

Active or passive treatment form

The comparison between iCBT and psychoeducation raises questions about the active versus passive nature of interventions. iCBT typically involves structured exercises, interactive modules, and homework assignments aimed at modifying maladaptive thoughts and behaviours. In contrast, psychoeducation often entails providing patients with information about their condition and coping strategies without requiring active participation. This is what it looked like in our RCT in study I and III as well. The meta-analysis by Donker et al. (152), suggests that passive psychoeducational interventions may have modest effect sizes in addressing symptoms of mental illness. While passive interventions are easier to implement and may be perceived as less stigmatising, they may not offer the same level of engagement as active interventions. Moreover, the study highlights the importance of considering patient preferences and treatment flexibility. It’s noted that not all patients prefer active involvement in their treatment process. Some may prefer receiving information passively, while others may prefer more hands-on, interactive, or physical approaches. This aligns with previous research suggesting that treatment acceptability and engagement can be influenced by patient preferences (153).

While iCBT may offer certain advantages such as structured interventions and active engagement, psychoeducation also proved to be effective. This could be attributed to its simplicity and passive nature, which may appeal to some patients. Understanding these factors and tailoring treatment approaches accordingly could enhance patient adherence and treatment outcomes. One possible limitation of this dissertation is the fact that only participants in the iCBT group were interviewed about their experiences regarding participation in the iCBT program (II). By also interviewing the control (psychoeducation) group, which received psychoeducation, other experiences could have been captured, creating a better overall picture of the experience of the psychoeducation program. This is particularly important, as psychoeducation, as a standalone treatment modality, has also been shown to be effective. It also raises questions about whether a passive
psychoeducation program might be sufficient as a treatment alternative in today's times when access to healthcare is reduced, and quick and cost-effective alternatives are demanded.

**Tailoring the program**

The possibility of receiving a tailored program, where patients have the opportunity to customise their treatment based on their needs and preferences, has been described in previous research (154–156). This was also described in interviews with participants of the iCBT program in study II. Availability and accessibility to information were crucial aspects for participants to incorporate treatment into their daily lives, for example, without needing to take time off from work. They found it easier to integrate treatment into their daily lives when they had control over when they could participate and how often. Free and easy access to the material was also of great importance to participants. The ability to log in late at night and access the support offered by the program was seen as a substantial advantage, which may factor that contributed to the positive view of iCBT in that study. These findings underscore the importance of tailored interventions for patients with NCCP, and align with previous research emphasising the benefits of personalised approaches in mental health treatment (154, 155, 157). In a study by Nissling et al. (154), findings indicate that participants in the patient-driven iCBT group showed significantly higher perceptions of control over their treatment compared to those receiving standard iCBT. Although the specific treatment choices made by the patient-driven iCBT group closely mirrored standard procedures, the mere opportunity to exercise autonomy in selecting treatment options appeared to enhance their perception of control. This suggests that offering patients a sense of agency in their treatment decisions can positively influence their treatment experience, even if the choices themselves don’t deviate significantly from standard protocols. Further, according to Williams et al. (157), most individuals had specific preferences regarding their treatment, such as the location of treatment, appointment times, therapist’s gender, language of therapy, and type of therapy. The authors in that study also observed that patients who reported unmet preferences were less likely to perceive therapy as helpful, particularly when their preferences for a specific type of therapy were not accommodated.

Although our iCBT program (I and III) was tailored with regard to the problems of the patients, all participants received the same standardised program and were unable to tailor the content. However, they were given the opportunity to choose when and where they wanted to engage with the
program, how much work they put into different parts of the content, as well as which type of physical activity and mindfulness exercises, they wanted to participate in. These options allowed participants to feel that they could influence their treatment, which may have contributed to the positive perception of iCBT described in the interviews in study II.

However, tailored web-based interventions are not always more effective than standardised web-based interventions, as in the meta-analysis of Martorella et al. (156), where effectiveness in interventions were compared to a passive control group and measured in terms of pain intensity, pain-related disability, anxiety, and depression. Additionally, there are also some challenges with tailored interventions that are important to take into consideration. According to Silfvernagel et al. (155), challenges in selecting treatment modules based on symptoms and preferences and without established reliability in the selection procedure, as well as the specificity of treatment effects and the difficulty in determining which components of the interventions drive the observed effects, may raise concerns. Additionally, the selection of outcome measures may not adequately capture the tailored nature of interventions, as tailored treatment approaches could benefit from tailored assessments. Therefore, it is important to consider these challenges in the design of tailored and patient preference-based interventions, as they can impact the interpretation of outcome effects.

To summarize, both iCBT and psychoeducation offer unique advantages and contribute to the treatment outcomes in patients with NCCP. iCBT provides an interactive approach with various tools such as exercises, homework assignments, support and feedback which foster active participation and learning. This can enhance patient engagement and thereby improve treatment outcomes. On the other hand, psychoeducation, that also is a part of our iCBT program, primarily offers educational material in textual form, which may be more passive but still valuable for some patients. The accessibility and flexibility of iCBT can enhance treatment adherence by allowing patients to participate according to their own preferences. However, the short duration of the intervention may limit its effectiveness, especially for patients with comorbid depression. To maximize outcomes, it may be preferable to tailor interventions to individual patient needs and preferences and effectively manage the comorbidities.

Thus, it is important to integrate both iCBT and psychoeducation into treatment plans to offer a flexible and effective approach for patients with NCCP. By combining different methods and tailor interventions, treatment
The effects and experiences of internet-delivered cognitive behavioural therapy

outcomes can be improved, and patients’ needs can be met in the best possible way.

**Therapeutic support and trust in iCBT**

An aspect described by participants in study II as important was therapeutic support in the program. Contact with the therapist was something that held great importance for participants, as the therapist's presence motivated them and made the program feel more alive, knowing there was a real person behind it rather than just a blank screen. What was surprising was the relationship participants developed with the therapist. They had never met, and had only spoken on the phone once when they were enrolled in the study, yet several participants felt a connection with the therapist. Some participants mentioned feeling spurred to work on the program when they knew the therapist would read their responses, which further motivated them to actively engage with the program. Having the therapist there to motivate and support them through the treatment became a way to assist participants in their transformation. Efficacy and benefits of personalised treatment have also been demonstrated in a meta-analysis by Karyotaki et al. (158) which showed that guided iCBT was associated with more effectiveness than unguided iCBT for individuals with moderate to severe depression.

In interviews in study II, participants expressed that they perceived treatment as the initial step in their journey toward learning to live with pain. They viewed the program as a tool to help them manage their fears. This awareness and willingness to change could be interpreted as a pivotal first step in breaking out of the vicious cycle. The next step can be supported by utilising tools in iCBT, such as psychoeducation and mindfulness, to counter pain catastrophising (159-161), like we did in study I. By conveying knowledge and awareness that pain in and of itself does not necessarily pose a threat, pain-related fear can be reduced. Through physical activity and exposure to situations that patients perceive as dangerous, individuals gain the opportunity to break avoidance patterns, thereby reducing disabilities and other negative effects (162, 163). Through gradual exposure to feared activities and engagement in physical rehabilitation, patients have the opportunity to regain control over their fear of pain and reduce the negative effects of pain and disabilities. The interesting aspect of this is the fact that the control group, which received psychoeducation, also demonstrated a similar effect, as presented in Figures 7-11 and Table 9. They received the material solely in text form, and despite awareness of being part of a control group, several participants were able to break the
vicious cycle on their own. This could be interpreted as the act of being noticed and receiving an invitation to participate in the study being sufficient to increase motivation and the desire for change, among these patients. Which further strengthens the need to pay attention to these patients in healthcare.

**Fear and avoidance in relation to NCCP**

Participants in studies I, II, and III experienced fear and anxiety, which has been evident in both the survey and interview responses. Both fear and cardiac anxiety have been measured using the BSQ and CAQ, but they have also been reflected in the interviews where they shared how their lives were affected by NCCP, and how it created fear and anxiety. The fear that their chest pain may be due to a serious heart condition can lead to behaviours such as avoiding physical activity and social interactions (76), which also was described by participants in study II. Avoidance behaviours and fear of pain have a substantial impact on their quality of life and well-being. Participants described also avoiding various activities and social interactions due to their fear of exacerbating their symptoms, which creates a sense of isolation and limitation in their lives, further deteriorating their mental health and quality of life, which also is described in study by Jonsbu et al. (84).

To address fear and avoidance behaviours in patients with NCCP, an integrated approach is necessary. iCBT can be a useful tool in supporting these patients, because it offers variety of tools to counter catastrophising thoughts associated with their pain and increase awareness that pain itself does not necessarily pose a threat (83). By gradually exposing patients to previously avoided activities and engaging them in physical rehabilitation, psychological interventions, such as iCBT can help break the vicious cycle of fear and avoidance behaviours, which in turn can lead to reduced disabilities and improved quality of life (28, 69). This versatility and flexibility of tools that iCBT offers can support patients in different ways, based on their preferences, as well as increase accessibility even further. However, psychoeducation as a treatment has also shown to be effective in studies I and III, as confirmed by the meta-analysis conducted by Donker et al. (152), which demonstrates that brief passive psychoeducational interventions for depression and psychological distress can reduce symptoms. Increased understanding and recognition of symptoms can help reduce anxiety and fear related to cardiac anxiety. Psychoeducation can also support patients in finding motivation and developing personal coping strategies.
(164). However, it raises the question of whether that motivation will be enough to create longtime life changes.

Furthermore, in study III, we observed that the more avoidance behaviour a patient experiences at the baseline of the intervention, the higher the likelihood of reducing cardiac anxiety with the help of iCBT. Previous research on cardiac patients has shown that increased avoidance behaviour at baseline negatively impacts physical activity levels (165) and is linked to a heightened risk of major adverse cardiac events (147). This underscores the importance of physical activity as protective against disabilities associated with NCCP (166), as well as the importance of motivating and supporting patients to participate in physical activity. In the RCT study, both the iCBT and control (psychoeducation) groups were provided with information emphasising the importance of physical activities. However, the iCBT group received specific homework assignments focused on engaging in and reporting physical activity undertaken during the intervention. Furthermore, the therapist provided support and encouragement to participants to sustain physical activity levels. By delivering structured and tailored treatment along with continuous feedback and support, while also considering factors related to the fear-avoidance model in patients with NCCP, individuals can obtain tools and assistance to break the detrimental cycle of fear and avoidance behaviours, which was also described by some participants in study II. This, in turn, can lead to enhanced function and improved quality of life for these patients.

**iCBT as a tool to support self-care in patients with NCCP**

The various tools in the iCBT program are intended to support and encourage patients in different aspects of their self-care. By providing education, motivation, support, and involving patients in their own care, individuals can develop an understanding of the issues underlying their suffering. Individuals with NCCP need healthy behaviours and habits to support them in their daily lives, which are often overshadowed by concerns about chest pain. However, when anxiety takes over and affects patients’ daily lives and relationships, they may struggle to maintain their health. For patients with NCCP, this need is even greater, as they often lack a healthcare facility to turn to, and the majority do not receive a clear diagnosis or cause for their pain, and therefore do not receive any general management of their problems, which they described in study II. At this point, self-care becomes crucial. According to Riegel et al. (167), the middle-range theory of self-care of
chronic illness defines self-care as maintaining health processes by promoting health practices and managing illness (167), even without a clear diagnosis. Patients with chronic illness, e.g., chronic pain, have an outstanding need of self-care, because engaging in their own self-care makes patients active participants in the management of their illness. Jaarsma et al. (168), show that patients who report more effective self-care have better quality of life and lower mortality in comparison to those who report poorer self-care (168). However, it is crucial to remember that self-care is not the same for all patients, and some activities may be inappropriate for one patient but right for others (167), which shows the importance of person-centric treatments.

The maintenance, monitoring, and management of self-care empowers individuals to cope with their illness. Self-care maintenance in NCCP entails adopting behaviours that contribute to physical and emotional well-being. Behaviours to maintain physical and psychological stability include, among others, to stop isolating, be physically active (166), seek social support (169), maintain a healthy lifestyle (170), and deal with fears instead of avoiding them (71). The iCBT intervention and psychoeducation can augment traditional approaches by providing education on symptom recognition and promoting physical activity (171). By empowering individuals with knowledge and skills to manage their symptoms, iCBT enhances their self-care maintenance efforts. Self-care monitoring involves vigilant observation of symptoms and emotional states that are crucial for individuals with conditions like NCCP, where psychological distress can exacerbate symptoms. To monitor their symptoms and signs of changes, patients observe, recognise, and interpret data (i.e., frequency, duration, location, character, intensity, and situations when pain occurs). They also reflect on bodily symptoms and identifying negative thoughts. iCBT and psychoeducation may also equip individuals with tools to recognise somatic symptoms, monitor thought patterns related to chest pain, and track emotional responses (98). Through systematic monitoring facilitated by iCBT, patients gain insights into their condition, enabling them to implement coping strategies effectively. Finally, self-care management encompasses evaluating changes in symptoms and undertaking appropriate actions to alleviate distress, adapt physical activity and exposure, practice relaxation techniques, and ask for support. iCBT interventions offer education, motivate, support, and empower patients to proactively manage their symptoms (102).

By supporting self-care with iCBT, individuals with NCCP can gain autonomy in managing their condition despite the absence of a clear diagnosis. iCBT interventions provide structured support and education, enabling
patients to understand and address the factors contributing to their suffering [108]. As patients gain knowledge to monitor and manage their symptoms, they get the opportunity to experience a sense of empowerment, breaking the vicious cycle of psychological burden and promoting overall well-being (74, 173). However, there are several challenges and limitations that need to be considered. Patient engagement and adherence, frustration and uncertainty due to the absence of a clear diagnosis (174), scepticism towards online interventions or low health literacy (175), technical and geographical barriers, and implementation into existing healthcare systems may create some challenges (155).

**Implementation of digital care technologies in clinical practice**

Considering the generally limited experience in digital care technologies among participants in study IV, there was a significant perception in the context of potential implementation of iCBT for patients with NCCP. The implementation of digital care technologies in healthcare aims to improve patient care, enhancing efficiency, and optimising healthcare delivery processes. However, successful implementation requires careful consideration of various factors, including organisational readiness, healthcare professionals’ attitudes and behaviours, and the management of barriers and facilitators (176, 177).

Healthcare professionals who participated in study IV perceive that the successful implementation of digital care in clinical practice, e.g., iCBT for patients with NCCP, is dependent on various factors. Engaged and interested leadership, user-friendly technological usability, and adequate information and training was considered an essential prerequisite for participants to feel confident in introducing and offering digital care. In addition, they saw the importance of a positive implementation climate at the clinic.

However, implementation of new systems in healthcare practice is complex (178). According to previous research, successful programs depend on the availability of easy-to-use technology; organisational and clinician acceptance and use of the technology, which can vary across departments (179, 180) and hospitals (178); as well as an effective implementation strategy. Essentially, a comprehensive understanding of the unique challenges and needs of healthcare is essential for successful system implementation and improved patient care (176). According to Nilsen (181), one critical aspect highlighted in the implementation science is the importance of organisational enthusiasm and willingness for change. The concrete benefits that digital care technologies offer, such as improved patient care and
process efficiency, need to be recognised. Effective communication of these benefits is essential to gain support from healthcare professionals and stakeholders. Additional, implementation climates characterised by extensive educational support contribute to fostering positive attitudes toward evidence-based practice among healthcare professionals. According to Powell et al. (182), by providing opportunities for education and training, healthcare organisations can promote a culture that values evidence-based approaches and facilitates their effective implementation in clinical practice. Moreover, the perceived effort required to utilise these technologies needs to be minimalised to create acceptance and adoption among healthcare professionals (183). However, according to Bagot et al. (176), addressing barriers to implementation is another important factor in the successful implementation of digital care technologies into healthcare practice. Establishing a local contact person for troubleshooting and clarification of technical functions (176) and management support to provide necessary resources and guidance for optimising the implementation process (184).

Due findings in study IV and previous described research, successful implementation of digital healthcare technologies requires a combination of user-friendly technology, organisational support, and effective implementation strategies. By addressing challenges and promoting a culture that fosters evidence-based practice, there is a possibility to improve patient care and process efficiency.

**Methodological considerations**

**Recruitment and adherence to treatment**

Recruitment methods and adherence to treatment are critical factors that can have a significant impact on study results. In this RCT (I, II and III), participants were recruited through invitation to participate, according to two or more care visits related to NCCP over a six-month period. However, this recruitment method may not always interest only those individuals who are fully motivated to engage with the changes that iCBT can offer, which may affect their adherence to the treatment protocol. A meta-analysis by Romijn, et al. (185), suggests that differences in recruitment practices may affect study outcomes. Effective recruitment for studies to interventions such as iCBT for anxiety disorders involves different channels, collab-
oration with clinicians, clear eligibility criteria, but also balancing of exclusion criteria and providing adequate support, resources, and follow-up to improve adherence rates (185).

A study by Andrews et al. (186) regarding computer therapy for anxiety and depression disorders, showed that employing open recruitment methods and implementing stricter exclusion criteria for patients with depressive symptoms results in patients reporting higher levels of treatment adherence. Open recruitment allows motivated individuals who have confidence in psychological treatments to participate. In our RCT, 63% of participants in the iCBT group completed all five modules, which is comparable to findings from other studies (186). In contrast, 47% of participants in the control group completed all modules. This suggests that approximately half of all participants in both groups underwent the entire treatment, potentially impacting the measured outcomes.

The level of therapist involvement in the intervention can also significantly influence treatment adherence. Research conducted by Richards et al. (187) revealed that adherence to interventions among patients with depressive symptoms was three times higher in those receiving therapist-guided interventions compared to those receiving self-guided interventions, further supporting the effectiveness of therapist-led interventions. This finding was also described in study II and highlighted the positive impact of therapist involvement on participant engagement and activity within the intervention.

**Choice of control group**

Demonstrating the difference in efficacy between the iCBT group and the control (psychoeducation) group proved to be challenging. Previous research indicates that comparing treatments based on similar principles can make it difficult to detect improvements. This issue underscores the importance of carefully selecting the control group in studies. Mehta’s et al. (132) meta-analysis highlights the inadequacy of comparing treatments with ‘care as usual’ in RCTs, as this fails to provide an accurate comparison. Mehta et al. (132) suggests that any form of treatment in the intervention group is likely to yield better results than receiving no treatment at all. Therefore, the meta-analysis (132) recommends employing an active control group to ascertain whether observed effects are genuinely linked to the intervention rather than merely the result of receiving attention as part of a study. However, according to LaFave et al. (188), it can be difficult to dis-
Distinguish the benefits of a behavioural intervention between the benefits derived from the actual content of the intervention and the benefits derived from the attention and interaction that participants receive from the individuals who lead the intervention (intervention facilitators). This interaction itself can be beneficial and can influence participants’ outcomes regardless of the content of the intervention. Which means that it can be difficult to determine which specific parts of the intervention actually provide benefits, and which are due to the general attention and interaction from the facilitators.

Utilising an active control group offers several advantages. First, it helps reduce the placebo effect (189), especially when participants are unaware of which group they belong to. This alleviates the risk of overstated responses among those who know they are in the control group, however, it can be difficult to achieve in a CBT studies. Secondly, employing an active control group allows for a direct comparison between different treatments, enhancing the generalisability of the findings (132, 188). Additionally, using an active control group addresses ethical concerns, particularly regarding withholding potentially beneficial treatments from vulnerable patient groups.

Therefore, careful consideration of the control group is essential to minimise bias in study results. Selecting an active control group facilitates more accurate assessments of treatment efficacy and contributes to the overall robustness and validity of the research findings.

Validity and reliability

Maintaining the validity of studies I and III was crucial to ensuring the credibility and reliability of the study results. Different strategies were conducted: a RCT was chosen as the study design to ensure the rigor of the study, and participants were randomised into the study to reduce the risk of bias. Furthermore, outcome measures and instruments were carefully selected to improve the validity of the study. These factors were chosen to ensure the accuracy, reproducibility, and generalisability of the results.

Strategies used to ensure reliability in study I and III included using standardised measuring instruments tested for reliability, as well as basing RCT on a pilot study (5). Additionally, clear and transparent reporting of the study description was undertaken to ensure reproducibility and consistency of measurements and results. These concepts were utilised to minimise potential systematic and random errors in medical research (134).
**Trustworthiness**

To ensure trustworthiness in studies II and IV, credibility, transferability, confirmability, and dependability were applied (140).

The trustworthiness of the study results in study IV may have been affected by several factors, including the inclusion of different clinics for emergency care and cardiology care in the data collection. By expanding the sample to include cardiology clinics in addition to the planned emergency clinics, variations in patient populations and treatment practices may have been introduced. This could make the results more difficult to generalise or compare with previous studies that focused solely on emergency care.

**Credibility**

In study II, participants in the intervention program had direct experience of the phenomenon they were interviewed about. In study IV, participants described their perceptions of the phenomenon, which meant they could share their thoughts on the subjects. Triangulation was also used to strengthen credibility (140). In both studies, triangulation was employed during the analysis phase, where all authors independently analysed several transcripts before collectively agreeing on a coding scheme. Triangulation and the subsequent joint discussion aimed to ensure that individual experiences and perceptions did not influence the outcome and results. The studies were also described in detail, providing a rich description of the research context, methodology, participants, and results. This was done to enhance the trustworthiness of the interpretation and findings. Moreover, the concept of information power, as outlined by Malterud et al. (190), was used to guide adequate sample size in both qualitative studies. Information power refers to the size of the sample, which depends on the aim of the study, the specificity of the sample, the use of the established theory, the quality of the dialogue, and the analysis strategy. To achieve a sample size with sufficient information power in study II, one-third of the total population with experience of the phenomenon were interviewed, resulting in a rich dataset of 16 interviews with an average duration of 47 minutes. The study specifically focused on participation in the iCBT program, utilised content analysis by Patton (123), and employed an analysis strategy involving all authors participating in mutual discussions and the development of a coding scheme. In study IV, the mean duration of interviews was 38 minutes. Similarly, in this study, information power was applied through rich datasets, participants' specific knowledge of the subject, analysis of
data based on a reliable analysis method, and joint discussion and development of results by all authors.

Transferability
Enhancing transferability in studies II and IV was achieved through rich and detailed descriptions of the study context, methods, participants, and findings, facilitating the assessment of whether the findings might be relevant or applicable to similar contexts (140). The sampling strategy was also an important aspect to ensure transferability. By employing thoughtful sampling techniques, the most suitable participants could be selected for the studies to represent the experiences and perspectives relevant to the aims of the studies.

Dependability
It was crucial to establish standardised procedures for data collection, such as using interview guides in both study II and study IV. This aimed to minimise variations that could affect the reliability of the findings and ensured that the process remained consistent across different settings and researchers (140). Detailed documentation in all aspects of the study allowed for transparency and facilitated the replication of the study by other researchers. Additionally, involving multiple coders in data analysis was crucial to ensure the consistency of interpretations and the robustness and meaningfulness of the findings (123).

Confirmability
To ensure confirmability, authors acknowledged and reflected upon their own biases and assumptions, actively worked with an awareness of their own perspectives. The triangulation process, which was also used in both studies, helped minimise the impact of individual bias through individual and mutual data analysis to ensure that participants’ findings aligned with their experiences and perspectives (140).
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Clinical implications

Patients suffering from NCCP find themselves in a complex situation, where their pain lacks a clear medical explanation. This group of patients often experiences significant physical and psychological distress. Without a diagnosis or explanation for their pain, they live in a constant state of worry and fear, greatly affecting their quality of life and ability to function normally in everyday life. The experienced lack of understanding and support from healthcare exacerbates their sense of neglect and contributes to their suffering, diminishing their trust in the healthcare system.

This dissertation has the potential to shed light on this overlooked patient group and bring their suffering to the attention of healthcare professionals. By exploring the patients’ life situations caused by fear of pain, the dissertation can provide a deeper understanding of the challenges and difficulties these individuals face daily. Furthermore, the dissertation may also show a need of effective ways to reduce cardiac anxiety in these patients by offering psychological treatment and appropriate self-care.

The iCBT program has the potential to manage cardiac anxiety and improve quality of life for patients with NCCP. With the newfound knowledge, the program can be developed to be even more effective, more adaptable to participants’ preferences, and become more feasible and practically applicable in clinical practices. This dissertation can provide insights into how this can be achieved by investigating and addressing any barriers to the implementation of digital care methods. To facilitate the implementation of new treatments and improve care for patients with NCCP, it is also important to pay attention to and involve both healthcare professionals and management. By demonstrating the positive impact of providing adequate care and support to this patient group, the dissertation can help convince healthcare organisations of the importance of prioritising the needs of patients with NCCP and improving their care experience.
Future research

This dissertation has created new questions and ideas to further research work:

- Develop and evaluate a tailored education and support program aimed at improving quality of life in patients with NCCP, with a focus on patient-centred care and self-care.
- Develop and evaluate a tailored education and support program aimed at improving quality of life in spouses of patients with NCCP.
- Explore how pain sensitivity affects patients with NCCP.
- Investigate effects of digital care on healthcare quality and patient outcomes such as patient satisfaction, treatment results, and cost-effectiveness compared to traditional care methods.
- Investigate the effects of digital care and remote monitoring on managing NCCP symptoms and improving patient adherence to treatment plans.
- Compare the emotional and practical effects of chest pain between spouses of patients with NCCP and spouses of patients with cardiac conditions to reveal unique challenges specific to NCCP and offer a broader perspective on the overall impact of chest pain.
- Develop and evaluate a tailored intervention aimed at improving communication and mutual support within couples where one partner suffers from NCCP.
- Explore socioeconomic and cultural factors and their impact on the experience of NCCP and participation in digital care.
- Investigate gender differences in the experience and management of NCCP, including how societal perceptions of gender roles and expectations may influence symptom reporting, healthcare-seeking behaviour, and treatment outcomes.
CONCLUSIONS

A common conclusion was drawn based on four studies included in this dissertation.

Despite the hypothesis that iCBT was better than psychoeducation in reducing cardiac anxiety in patients with NCCP, both iCBT and psychoeducation have shown to be useful interventions in reducing cardiac anxiety and improving psychological well-being in patients with NCCP. Although iCBT did not prove to be superior to psychoeducation in reducing cardiac anxiety, long-term effects suggest that iCBT may be more advantageous in reducing psychological distress, including cardiac anxiety, health-related quality of life, and the frequency of NCCP. Additionally, patients with a high tendency to avoid activities or situations they believe may trigger cardiac symptoms seem to benefit more from psychological interventions targeting cardiac anxiety, which can increase their physical activity and thereby reduce psychological burden.

Patients with NCCP saw the invitation to the iCBT program as an opportunity to return to a life without limitations and disabilities. They found the iCBT program to be predominantly positive, perceived its benefits and felt that the program was tailored to their specific needs and concerns. They described the program as helpful, trustworthy, and useful, seeing it as a tool to help them confront their fears and resume a normal life without being hindered by fear and anxiety related to chest pains. Overall, the program was seen as an opportunity to regain a sense of normalcy.

Regarding healthcare professionals’ perceptions of digital care, there is a mixture of caution and optimism. There are concerns about resistance to change and the potential for harm if digital care is not handled correctly. However, healthcare professionals also see the potential and benefits of digital care for patients with NCCP and the healthcare in general. To maximise the benefits of digital care and ensure its effective implementation, clear leadership, education, technical competence, and positive attitudes from healthcare professionals are required for successful adoption and to avoid any potential negative consequences.
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I’m now at the end of this road, somehow ready to close this chapter and start a new one. However, first I want to acknowledge those who supported me on this journey.

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Papers

The papers associated with this thesis have been removed for copyright reasons. For more details about these see:

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The perspectives of patients with non-cardiac chest pain and healthcare professionals in the emergency and cardiac care

Magda Eriksson-Liebon