

Original Paper

# The Effect of Internet-Delivered Cognitive Behavioral Therapy Versus Psychoeducation Only on Psychological Distress in Patients With Noncardiac Chest Pain: Randomized Controlled Trial

Ghassan Mourad<sup>1</sup>, RN, PhD; Magda Eriksson-Liebon<sup>1,2</sup>, RN, MSc; Patric Karlström<sup>1,3</sup>, MD, PhD; Peter Johansson<sup>1,4</sup>, RN, PhD

<sup>1</sup>Department of Health, Medicine and Caring Sciences, Linköping University, Linköping, Sweden

<sup>2</sup>Department of Emergency Medicine in Norrköping, and Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden

<sup>3</sup>Department of Internal Medicine, Ryhov County Hospital, Region Jönköping County, Jönköping, Sweden

<sup>4</sup>Department of Internal Medicine in Norrköping, and Department of Health, Medicine and Caring Sciences, Linköping University, Linköping, Sweden

**Corresponding Author:**

Ghassan Mourad, RN, PhD

Department of Health, Medicine and Caring Sciences

Linköping University

Linköping

Sweden

Phone: 46 +46736209582

Email: [ghassan.mourad@liu.se](mailto:ghassan.mourad@liu.se)

## Abstract

**Background:** Patients with recurrent episodes of noncardiac chest pain (NCCP) experience cardiac anxiety as they misinterpret the pain to be cardiac related and avoid physical activity that they think could threaten their lives. Psychological interventions, such as internet-delivered cognitive behavioral therapy (iCBT), targeting anxiety can be a feasible solution by supporting patients to learn how to perceive and handle their chest pain.

**Objective:** This study aims to evaluate the effects of a nurse-led iCBT program on cardiac anxiety and other patient-reported outcomes in patients with NCCP.

**Methods:** Patients with at least two health care consultations because of NCCP during the past 6 months, and who were experiencing cardiac anxiety (Cardiac Anxiety Questionnaire score  $\geq 24$ ), were randomized into 5 weeks of iCBT ( $n=54$ ) or psychoeducation ( $n=55$ ). Patients were aged 54 (SD 17) years versus 57 (SD 16) years and were mainly women (32/54, 59% vs 35/55, 64%). The iCBT program comprised psychoeducation, mindfulness, and exposure to physical activity, with weekly homework assignments. The primary outcome was cardiac anxiety. The secondary outcomes were fear of bodily sensations, depressive symptoms, health-related quality of life, and chest pain frequency. Intention-to-treat analysis was applied, and the patients were followed up for 3 months. Mixed model analysis was used to determine between-group differences in primary and secondary outcomes.

**Results:** No significant differences were found between the iCBT and 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  $d=0.31$ ). In the iCBT group, 36% (16/44) of patients reported a positive reliable change score ( $\geq 11$  points on the Cardiac Anxiety Questionnaire), and thus an improvement in cardiac anxiety, compared with 27% of (13/48) patients in the psychoeducation group. Within-group analysis showed further significant improvement in cardiac anxiety ( $P=.04$ ) at the 3-month follow-up compared with the 5-week follow-up in the iCBT group but not in the psychoeducation group.

**Conclusions:** iCBT was not superior to psychoeducation in decreasing cardiac anxiety in patients with NCCP. However, iCBT tends to have better long-term effects on psychological distress, including cardiac anxiety, health-related quality of life, and NCCP frequency than psychoeducation. The effects need to be followed up to draw more reliable conclusions.

**Trial Registration:** ClinicalTrials.gov NCT03336112; <https://www.clinicaltrials.gov/ct2/show/NCT03336112>

**KEYWORDS**

cardiac anxiety; cognitive behavioral therapy; health-related quality of life; internet delivered; noncardiac chest pain; psychological distress

## Introduction

### Background

Approximately 50% of patients seeking acute care because of chest pain have noncardiac chest pain (NCCP) [1-5], which is equivalent to approximately 80,000 people annually in Sweden [6]. Despite recurrent chest pain, many patients are discharged without a clear explanation regarding the underlying cause of their chest pain [7,8], and a large proportion of them continue to experience chest pain [8-10]. Wertli et al [11], in a retrospective study of 1341 emergency department admissions among patients with NCCP, concluded that there is an uncertainty among physicians regarding how to approach these patients after ruling out the cardiac causes. In fact, many of these patients are still not convinced by their negative cardiac diagnosis several years after the primary assessment, and they worry about heart disease, avoid activities that they think might be harmful to their heart, and repeatedly seek medical help [12,13]. Physical activity has been shown to be associated with a lower risk of experiencing NCCP. Therefore, avoidance of such activities has negative effects on these patients [14]. This situation seems to cause functional impairment, psychological distress, and impaired quality of life in these patients [4,15-18]. Studies have also suggested that patients with NCCP use outpatient health care to the same extent as patients with myocardial infarction [4,17,19] and incur high costs for the health care system and society [1,6,20-22].

Cardiac anxiety has been found to be highly prevalent in these patients and is strongly associated with health care use [9,18]. An explanation is that cardiac anxiety may worsen the chest pain and create a *vicious circle*, leading to the maintenance of both anxiety and chest pain. Psychological interventions targeting anxiety can be a feasible way of breaking the vicious circle and improving patient outcomes by supporting patients in learning how to perceive and handle their chest pain. This is also warranted by the World Health Organization, which emphasizes the need for the implementation of interventions targeting psychological distress in patients with somatic diseases [23].

There is strong support for cognitive behavioral therapy (CBT) in the treatment of mild and moderately severe states of anxiety and depressive disorders [24-27]. CBT is a structured and collaborative process aiming to help individuals evaluate the accuracy and usefulness of their thoughts [28]. A Cochrane review found CBT useful and moderately successful, despite the multifaceted etiology in NCCP, and stressed the need for further randomized controlled trials of psychological interventions for NCCP with long follow-up periods [29]. However, a problem is that there are some barriers to the use of face-to-face CBT [30]. In addition to being time consuming, there is a lack of trained health care professionals who can deliver CBT, leading to a treatment demand gap; thus, the

number of patients in need of CBT is higher than the number being offered CBT [29,31]. A possible solution is to use the internet to deliver CBT (internet-delivered CBT [iCBT]), as it does not differ from face-to-face CBT regarding the effects among young and middle-aged people [32-35], requires less therapist involvement, can be given to more patients, is cheaper, and is not time or room dependent [30].

However, few studies have evaluated the effects and experiences of iCBT in patients with both somatic disease and psychological distress [36,37]. However, in a recent study, iCBT provided by nurses, with a brief introduction in iCBT, to patients with cardiac disease and depressive symptoms was shown to reduce depressive symptoms and improve the quality of life [38]. This implies that health care professionals, such as nurses within somatic health care, could use iCBT as a tool for treating patients, which could increase the access to CBT for psychological distress among patients with somatic diseases, such as NCCP. Furthermore, no studies have been undertaken concerning patients with NCCP, apart from our previous pilot study that tested the feasibility of iCBT in patients with NCCP and cardiac anxiety. Our piloted iCBT program was perceived as feasible by the patients [39]. Thus, there is a knowledge gap regarding the effects of iCBT programs guided by health care professionals, such as nurses, on cardiac anxiety and other patient-reported outcomes in patients with NCCP.

### Objective

The aim of this study is to evaluate the effects of a nurse-led iCBT program on cardiac anxiety and other patient-reported outcomes in patients with NCCP.

## Methods

### Design and Ethics

This was a randomized controlled trial and was registered at ClinicalTrials.gov (NCT03336112). The study was approved by the regional ethical review board in Linköping, Sweden (code 2017/343-31).

### Study Participants

Patients were eligible for participation if they were aged  $\geq 18$  years, had at least two health care consultations because of NCCP (International Classification of Diseases-10 codes R07.2, R07.3, R07.4, and Z03.4) during the past 6 months, and screened positive for cardiac anxiety (score  $\geq 24$  on the Cardiac Anxiety Questionnaire [CAQ]). Patients were excluded if they had no access to a computer or tablet with internet connection; were not able to perform physical activity because of physical constraints; did not speak or understand Swedish; or experienced severe depression, as measured by the Patient Health Questionnaire-9 (PHQ-9), cognitive impairment, or newly diagnosed cancer requiring treatment (according to medical records).

## Procedures

Study participants were recruited after discharge from the emergency units at 3 regional hospitals and 1 university hospital in southeast Sweden. Recruitment of patients to the study was conducted between January 2018 and August 2020. At the start of the study, we only recruited patients from 2 hospitals; however, to allow for faster recruitment, we expanded to 2 more hospitals from April 2019. Eligible participants were identified by registers and sent a packet, which included study information, an informed consent form, and a prestamped envelope by post. After some days, patients were contacted by phone by the study team and informed verbally about the study. Patients interested in participation and who sent back a signed written informed consent form were screened for cardiac anxiety using an encrypted web-based survey tool provided by Linköping University and requiring both username and password to log in. Patients fulfilling the criteria were randomized in a 1:1 ratio into either iCBT or psychoeducation using a randomization table provided by a statistician. Masking of patients was not possible as the intervention was a CBT program. Participating in the study (in both the iCBT and psychoeducation groups) did not oppose seeking or receiving other inpatient or outpatient treatments.

The intervention was delivered through a website specifically developed for the study by the first author (GM). The website was accessible only to those who received the website URL and log-in details. In addition to username and password, 2-factor authentication was applied using an SMS text messaging one-time password to ensure security.

## iCBT Group

The iCBT group received a 5-session/week-long nurse-led iCBT program that was developed based on our previous pilot study [39]. This pilot study contained 4 sessions and was extended by 1 week to give patients more time to work on the content for better effects. The program comprised psychoeducation, mindfulness, and exposure to physical activity, with weekly homework assignments. The psychoeducation part was aimed at teaching patients about chest pain and its impact on daily life and how avoidance and safety behaviors can maintain or exacerbate chest pain. A chest pain diary and exposure plan were set up by the patients to help them learn about their chest pain and not be afraid of exposing themselves to physical activity that many patients normally avoid. The mindfulness part, comprising both information and different exercises to perform daily, was intended to raise awareness of what is going on in the body, emotions, and sensations and to be more in the present despite chest pain to learn how to handle the chest pain. The physical activity part comprised information and recommendations regarding physical activity based on national guidelines [40]. The goal of this part was to enable patients to learn that their hearts tolerate physical activity and to reduce cardiac anxiety and avoidance of physical activity.

The patients had various weekly assignments to accomplish and send in for feedback. They then received feedback and advice from the same nurse once per week at the same time to allow them to plan their time and engagement in the program. The participants were fully aware of this procedure. The entire

treatment was conducted through the study website. Reminders and encouraging messages were sent to motivate the patients to complete the program. The iCBT program accounted for the main part of the treatment. The guidance and feedback part took approximately a mean of 8 (SD 4) minutes per patient and week.

## Psychoeducation Group

Patients with NCCP can be seen as a forgotten group as they usually have no regular follow-ups regarding their chest pain. Thus, their care as usual is equivalent to no care at all. Therefore, comparing iCBT with care as usual is equivalent to comparing with nothing, and therefore, the effect of iCBT could be overestimated, as it would be difficult to evaluate if the effect only depended on iCBT or partly on the attention of being in a study [41]. It is also recommended that control patients in iCBT studies receive an active control [36]. Furthermore, it is, for ethical reasons, better to offer patients with different problems some kind of intervention than nothing at all when randomizing them to the control arm [41]. On the basis of this, our active control group received psychoeducation (ie, containing the same information that the iCBT group received as part of their psychoeducation but without any assignments or feedback). This information was divided into 5 sessions, and patients accessed 1 session per week through the same website as the iCBT group. The active control group received a message from the therapist every week when a new session was made available.

## Data Collection

Data were collected at baseline before randomization; at the end of the intervention (ie, 5 weeks from baseline), and at 3, 6, and 12 months after the end of the intervention. In this study, data from the 6- and 12-month follow-ups were not included. Medical data were provided via medical records, and the rest were self-reported. All self-reported data were collected using the encrypted web-based survey tool provided by Linköping University. As all questions were mandatory to be able to submit the questionnaires, this resulted in no missing values among those who chose to answer the questionnaires. In total, participants received 2 reminders every 2 weeks if they did not complete the questionnaires.

The primary outcome was cardiac anxiety. The secondary outcomes were fear of bodily sensations, depressive symptoms, health-related quality of life (HRQoL), chest pain frequency, health care use, and health care costs. Data on health care use and health care costs will be published separately.

## Data Measurement

### Cardiac Anxiety

Cardiac anxiety was measured by the CAQ. This measurement comprises 18 items, with scores ranging from 0 to 72. Higher scores indicate greater cardiac anxiety [42]. In this study, we used a median score of 24 from one of our previous studies [18] as the cutoff score for cardiac anxiety. In addition to the total score obtained from the 18 items, the CAQ comprises three subscales: fear, avoidance, and heart-focused attention. However, these subscales are not presented in this study. The total scale has demonstrated adequate reliability and validity

[42]. Cronbach  $\alpha$  coefficients of .79 to .89 were confirmed in this study at the different measurement points.

### **Fear of Bodily Sensations**

The Body Sensations Questionnaire (BSQ) was used to assess the fear of bodily sensations, such as palpitations, dizziness, and sweating. The BSQ comprises 17 items, with scores between 17 and 85. Higher scores indicate greater fear of bodily sensations [43]. The BSQ has been proven to be reliable and valid [13,18,43]. In this study, the Cronbach  $\alpha$  coefficients were .92 to .94.

### **Depressive Symptoms**

The prevalence and severity of depressive symptoms were assessed using the PHQ-9. This measurement comprises 9 items, with a score range between 0 and 27. Scores between 5 and 9 indicate mild depressive symptoms, 10 and 14 indicate moderate depressive symptoms, 15 and 19 indicate moderately severe depressive symptoms, and 20 and 27 indicate severe depressive symptoms. In this study, we used a cutoff score of 10 for depressive symptoms. The PHQ-9 is a reliable instrument [44], and in this study, the Cronbach  $\alpha$  coefficients were .87 to .89.

### **Chest Pain Frequency**

Data on chest pain frequency were collected with the following self-developed question: *During the last month, how often have you experienced NCCP?*

### **HRQoL Measure**

The EuroQol visual analog scale (EQ-VAS), which is a part of EuroQol, was used to measure HRQoL. This EQ-VAS scores range between 0 (worst imaginable health state) and 100 (best imaginable health state). The EQ-VAS provides a quantitative measure of the patient's perception of their overall health and is a frequently used instrument [45].

### **Statistical Analysis**

The SPSS (version 25; IBM Corp) was used for data analysis. The level of  $P < .05$  was set for significance. According to our power calculation that was based on results from our previous pilot study [39], 53 participants needed to be included in each group to reach a 20% improvement (approximately an effect size of 0.5) in cardiac anxiety (95% CI and 80% power). This was used as there is no established score for a clinically significant improvement in this measurement. This sample size is comparable with similar CBT studies [32]. Intention-to-treat analysis was applied, and patients were followed up even if they were inactive or dropped out from the study. This method was chosen to preserve the integrity of the randomization and minimize the risks of bias related to differences in groups following attrition or nonadherence [46].

Frequencies, percentages, mean values, and SDs were used to describe and compare the study variables. Chi-square test or 2-tailed Student  $t$  test was used depending on the level of the data to compare differences between iCBT and psychoeducation groups regarding demographic variables.

To compare the iCBT and psychoeducation groups regarding changes in cardiac anxiety, bodily sensations, depressive symptoms, HRQoL, and NCCP frequency over the 3 different measurement points (ie, baseline and 5-week and 3-month follow-ups), a mixed model analysis was performed. As we had little missing data (in total, 8% at 5-week follow-up and 16% at 3-month follow-up), we chose to base our analysis on the original data; however, we also ran a mixed model analysis based on multiple imputation as a sensitivity analysis to ensure the accuracy of our results. Multiple imputation was based on the consideration of data being missing at random (the Little missing completely at random test;  $P = .99$ ) [47]. According to this method, missing values depend on the observed data and are replaced by values based on the complete data set [48]. In this model, 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. The results from the mixed model analysis based on multiple imputation did not differ from the analysis that was based on the original data; therefore, these results are not presented in this study.

Relationships between demographic variables, disease and psychological burden, treatment activity (such as number of log-ins and sessions performed), and change score in cardiac anxiety between baseline and 3-month follow-up in the groups were determined using the Pearson correlation coefficient. As there were no significant correlations, no further regression analysis was performed.

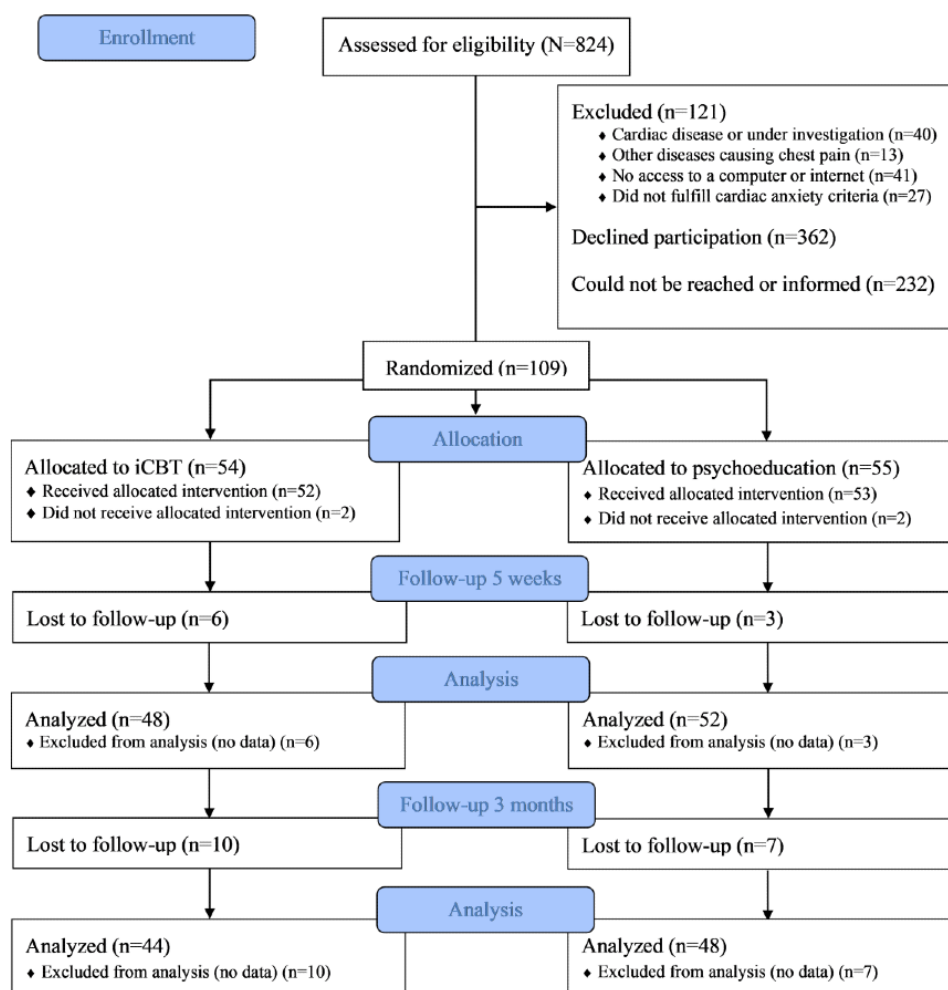
Cohen  $d$  was used to measure the effect sizes of the intervention. Effect sizes  $< 0.20$  were considered trivial, 0.20 to 0.49 were considered small, 0.50 to 0.79 were considered moderate, and  $\geq 0.80$  were considered large [49]. As there is no established score for a clinically significant improvement in CAQ, we calculated a reliable change index score according to the study by Christensen et al [50] using the baseline SD of 8.6 and baseline reliability score of 0.79 in our groups. On the basis of these values, a reliable change was deemed to be a change score of approximately 11 points per participant. The chi-square test was used to examine the difference between groups in the number of patients with a change score  $\geq 11$ .

Within-group differences over the 3 different measurement points were analyzed using paired  $t$  tests.

## **Results**

### **Study Participants**

In total, 824 patients were assessed for eligibility and invited to participate in the study (Figure 1). After screening, 13.2% (109/824) of patients who fulfilled the inclusion and exclusion criteria and consented to participate were randomized into iCBT (54/109, 49.5%) or psychoeducation (55/109, 50.4%). Study participants included a higher proportion of women than nonparticipants (715/824, 86.8%; 67/109, 61.5% vs 354/715, 49.5%;  $P = .02$ ).

**Figure 1.** The CONSORT (Consolidated Standards of Reporting Trials) flowchart. iCBT: internet-delivered cognitive behavioral therapy.

The demographic data for the iCBT and psychoeducation groups are presented in [Table 1](#).

Patients in these groups had a mean age of 54 (17) years versus 57 (SD 16) years and were mainly women (32/54, 59% vs 35/55, 64%) and in a relationship (45/54, 83% vs 38/55, 69%). Approximately 33% (18/54) in the iCBT group and 27% (15/55) in the psychoeducation group had previous heart disease, 43% (23/54) in the iCBT group, and 34% (19/55) in the psychoeducation group reported previous problems with psychological distress (such as anxiety, panic, or depression), and more than half reported troubles with musculoskeletal pain. Furthermore, approximately half of them (iCBT 23/54, 43% vs psychoeducation 25/55, 45%) had been treated with psychotropic drugs. No significant differences were found between the groups for any of the demographic variables.

Among the participants, the attrition rates at the 5-week follow-up were 11% and 5% for the iCBT and psychoeducation groups, respectively. Patients in the iCBT group who were lost

to the 5-week follow-up, that is, did not fill in the questionnaires, were more often on sick leave ( $P=.02$ ). In addition, they had low or no engagement in the program; that is, they completed a mean of 1 session compared with 4.2 in those who continued their participation ( $P<.001$ ). In the psychoeducation group, those lost to follow-up were more often single and living alone ( $P=.008$ ). As for the iCBT group, those in the psychoeducation group who were lost to the 5-week follow-up had low or no engagement in the program, that is, completed a mean of 0.33 sessions compared with 4.0 in those who continued their participation ( $P<.001$ ). The corresponding attrition rates of iCBT and psychoeducation groups for the 3-month follow-up were 19% and 13%, respectively, compared with baseline. The only differences between those who continued their participation and those lost to the 3-month follow-up was a lower number of completed sessions in the latter group (a mean of 4.1 vs 2.8 sessions,  $P=.02$ , in the iCBT group and a mean of 4.2 vs 1.6 sessions,  $P<.001$ , in the psychoeducation group).

**Table 1.** Demographic data of study patients at baseline (N=109).

Characteristics	iCBT <sup>a</sup> (n=54)	Psychoeducation (n=55)	<i>P</i> value
Age (year), mean (SD)	54.3 (16.5)	56.8 (15.5)	.42
<b>Sex, n (%)</b>			.64
Women	32 (59)	35 (64)	
Men	22 (41)	20 (36)	
<b>Marital status, n (%)</b>			.08
In a relationship	45 (83)	38 (69)	
Single	9 (17)	17 (31)	
Salary (US \$), mean (SD)	3564 (5742)	4018 (5486)	.69
<b>Economic situation, n (%)</b>			.46
Very good	5 (9)	7 (13)	
Good	42 (78)	38 (69)	
Problematic	7 (13)	10 (18)	
<b>Educational level, n (%)</b>			.89
Compulsory school	7 (13)	8 (15)	
High school	23 (43)	25 (45)	
University	24 (44)	22 (40)	
<b>Occupational status, n (%)</b>			.30
Working	20 (37)	27 (49)	
Retired	20 (37)	19 (35)	
On sick leave	6 (11)	5 (9)	
Unemployed	2 (4)	3 (5)	
Student	6 (11)	1 (2)	
<b>Smoking, n (%)</b>			.97
Nonsmoker or previous smoker	49 (91)	48 (87)	
Smoker	5 (9)	7 (13)	
<b>Alcohol consumption, n (%)</b>			.58
Never or seldom	28 (52)	25 (45)	
≤9 glasses/week	24 (44)	30 (55)	
>9 glasses/week	2 (4)	0 (0)	
Exercise ≥30 minutes (days/week), mean (SD)	2.5 (2.1)	3.0 (2.2)	.24
<b>Origin, n (%)</b>			.36
Sweden	45 (85)	42 (76)	
Another Nordic country	2 (4)	3 (6)	
Another country within Europe	5 (9)	5 (9)	
South America	1 (2)	1 (2)	
Asia	0 (0)	4 (7)	
Charlson Comorbidity Index, mean (SD)	2.2 (2.4)	2.5 (2.1)	.57
Previous heart disease, n (%)	18 (33)	15 (27)	.49
Acid reflux, n (%)	9 (17)	9 (16)	.97
Muscle pain, n (%)	29 (54)	26 (47)	.50
Joint or skeletal pain, n (%)	32 (59)	31 (56)	.76
Psychological disorder, n (%)	23 (43)	19 (34)	.39

Characteristics	iCBT <sup>a</sup> (n=54)	Psychoeducation (n=55)	<i>P</i> value
Psychological treatment, n (%)	8 (15)	5 (9)	.36
Treatment with psychotropic drugs, n (%)	23 (43)	25 (45)	.76
Number of log-ins per week, mean (SD)	13.7 (12.8)	5.4 (2.5)	<.001
<b>Sessions performed, n (%)</b>			.06
0	2 (4)	2 (4)	
1	5 (9)	4 (7)	
2	7 (13)	4 (7)	
3	5 (9)	9 (16)	
4	1 (2)	10 (18)	
5	34 (63)	26 (47)	

<sup>a</sup>iCBT: internet-delivered cognitive behavioral therapy.

### The Effects of iCBT Compared With Psychoeducation on Cardiac Anxiety

The mixed model analysis showed no significant differences between the iCBT and psychoeducation groups regarding cardiac anxiety in terms of the interaction effect of time and group over the 3-month follow-up (Table 2). However, as shown in Figure 2, the iCBT group continued to show improvements in cardiac anxiety at the 3-month follow-up, which was not the case for the psychoeducation group. The analysis showed a small effect size in favor of iCBT (Cohen  $d=0.31$ ). Looking at the time effect, there were statistically significant differences in cardiac anxiety at both the 5-week and 3-month follow-ups compared with baseline ( $P<.001$ ).

In the iCBT group, 36% (16/44) of patients had a positive reliable change score between 11 and 34 points, indicating

improvement in cardiac anxiety, whereas 2% (1/44) of patients had a negative reliable change score, showing a deterioration in cardiac anxiety. The corresponding numbers in the psychoeducation group were 27% (13/48) of patients with a positive reliable change score and 2% (1/48) of patients with a negative reliable change score. However, the difference between the groups was nonsignificant ( $P=.21$ ).

Within-group analysis showed that both iCBT and psychoeducation groups improved significantly with respect to cardiac anxiety from baseline to 5-week follow-up ( $P<.001$ ). The iCBT group had an improved mean score from 35.8 to 29.0, whereas the psychoeducation group had an improved score from 36.3 to 30.8. In addition, at the 3-month follow-up, the mean score in the iCBT group was 26.6, which was significantly lower than both baseline ( $P<.001$ ) and the 5-week follow-up ( $P=.04$ ).

**Table 2.** Mixed model analysis of the effect of internet-delivered cognitive behavioral therapy (iCBT) compared with psychoeducation on cardiac anxiety and secondary outcomes, presented in estimated marginal means.

Variables	Time effect		Group effect			Interaction effect			Effect size (Cohen <i>d</i> )
	Value, mean	<i>P</i> value <sup>a</sup>	iCBT	Psychoeducation	<i>P</i> value	iCBT	Psychoeducation	<i>P</i> value <sup>a</sup>	
<b>CAQ<sup>b</sup></b>			31.3	32.4	.96				
Baseline	36.4	N/A <sup>c</sup>				36.3	36.4	N/A	N/A
5 weeks	30.3	<.001				29.7	30.8	.46	N/A
3 months	28.9	<.001				27.9	29.9	.28	0.31
<b>BSQ<sup>d</sup></b>			39.3	39.5	.62				
Baseline	42.7	N/A				43.3	42.1	N/A	N/A
5 weeks	38.1	<.001				37.1	39.1	.10	N/A
3 months	37.4	<.001				37.5	37.4	.55	0.15
<b>PHQ-9<sup>e</sup></b>			7.2	6.6	.76				
Baseline	7.8	N/A				8.0	7.6	N/A	N/A
5 weeks	7.0	.54				7.6	6.4	.32	N/A
3 months	5.9	.005				6.0	5.8	.87	0.10
<b>EQ-VAS<sup>f</sup></b>			60.4	63.4	.03				
Baseline	62.5	N/A				58.5	66.4	N/A	N/A
5 weeks	61.4	.49				60.4	62.3	.12	N/A
3 months	61.9	.32				62.5	61.5	.10	0.57
<b>Chest pain frequency</b>			13	7.9	.006				
Baseline	12.0	N/A				15.1	8.9	N/A	N/A
5 weeks	11.1	.60				14.1	8.1	.93	N/A
3 months	8.3	.005				9.7	6.8	.20	0.21

<sup>a</sup>In comparison with baseline.

<sup>b</sup>CAQ: Cardiac Anxiety Questionnaire.

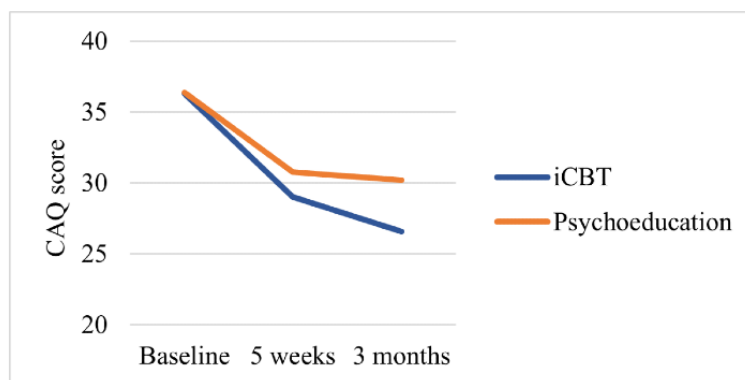
<sup>c</sup>N/A: not applicable.

<sup>d</sup>BSQ: Body Sensations Questionnaire.

<sup>e</sup>PHQ-9: Patient Health Questionnaire-9.

<sup>f</sup>EQ-VAS: EuroQol visual analog scale.

**Figure 2.** Changes in cardiac anxiety over time between internet-delivered cognitive behavioral therapy (iCBT) and psychoeducation groups. CAQ: Cardiac Anxiety Questionnaire.



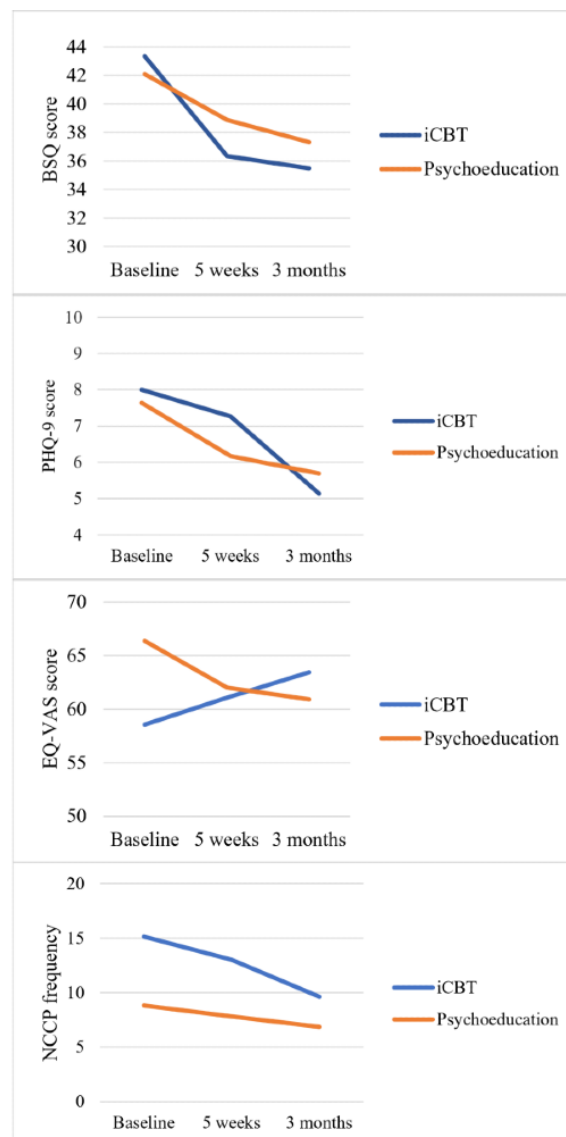


### The Effects of iCBT Compared With Psychoeducation on Secondary Outcomes

No significant interaction effect of time and group was found in any of the secondary outcomes (ie, fear of bodily sensations, depressive symptoms, HRQoL, and chest pain frequency) over the 3-month follow-up in the iCBT and psychoeducation groups (Table 2 and Figure 3). Table 3 displays the number of patients with depressive symptoms  $\geq 10$  in the iCBT and psychoeducation groups. In the iCBT group, only 11% (6/54) of patients reported depressive symptoms at the 3-month follow-up compared with 39% (21/54) of patients at baseline. For the psychoeducation

group, of the 55 patients, the corresponding numbers were 9 (16%) patients at the 3-month follow-up and 13 (24%) at baseline. The effect sizes of the iCBT group on the secondary outcomes were trivial to moderate (Cohen *d* between 0.10 and 0.57) compared with those of the psychoeducation group. There were statistically significant differences regarding the time effect in bodily sensations at both 5-week and 3-month follow-ups ( $P < .001$ ) and in depressive symptoms and chest pain frequency at the 3-month follow-up ( $P = .005$ ) compared with baseline. Comparing the groups without considering the time effects, there were significant differences in HRQoL ( $P = .03$ ) and chest pain frequency ( $P = .006$ ) in favor of iCBT.

**Figure 3.** Changes in bodily sensations, depressive symptoms, EuroQol visual analog scale (EQ-VAS), and noncardiac chest pain (NCCP) frequency over time between internet-delivered cognitive behavioral therapy (iCBT) and psychoeducation groups. BSQ: Body Sensations Questionnaire; PHQ-9: Patient Health Questionnaire-9.



**Table 3.** Changes in the number of patients with depressive symptoms  $\geq 10$  between baseline and 3-month follow-up in the internet-delivered cognitive behavioral therapy (iCBT) and psychoeducation groups.

Measurement point	Patients with depressive symptoms, n (%)	
	iCBT (n=54)	Psychoeducation (n=55)
Baseline	21 (39)	13 (24)
5-week follow-up	15 (28)	9 (16)
3-month follow-up	6 (11)	9 (16)

## Discussion

### Principal Findings

To our knowledge, this is the first randomized controlled iCBT study targeting cardiac anxiety in patients with NCCP. In this study, we compared a 5-week-long nurse-led iCBT program comprising psychoeducation, mindfulness, and exposure to physical activity, with psychoeducation only to evaluate the effects on psychological distress, including cardiac anxiety, and other patient-reported outcomes in patients with NCCP. Our findings showed that iCBT was not superior to psychoeducation in decreasing cardiac anxiety in these patients. We found that one-third of the patients who received iCBT reported decreased anxiety levels compared with one-fourth of those who received psychoeducation, that is, a reliable change score of at least 11 points on the CAQ. Another important aspect is that only one of the patients in each group reported increased cardiac anxiety scores at the 3-month follow-up, indicating that the program was safe.

Although no significant interaction effect of time and group was found between the groups, iCBT seems to have better long-term effects on cardiac anxiety than psychoeducation, as within-group analysis showed that patients in the iCBT group had improved further at the 3-month follow-up ( $P=.04$ ), which the psychoeducation group did not. In addition, patients who received iCBT tended to show long-term improvement in all reported variables (Figures 2 and 3), whereas those in the psychoeducation group did not change further. We also found a possible interaction effect of time and group regarding HRQoL in favor of the iCBT group with a moderate effect size. The patients improved over the measurement points (EQ-VAS increased from 58.5 at baseline to 65.5 at the 3-month follow-up), whereas the psychoeducation group deteriorated (EQ-VAS decreased from 66.4 at baseline to 61.5 at the 3-month follow-up).

These findings point to the fact that results related to changes in psychological distress and HRQoL may take more time to appear and that our intervention might be too short to detect such changes. A systematic review and meta-analysis by Reavell et al [51] showed a significant reduction in anxiety in long CBT interventions but not in short- to medium-term interventions compared with controls. These interventions were performed in patients with cardiovascular disease, and patients might need a longer time to adjust to their cardiac diagnosis and handle their anxiety compared with patients with NCCP. Previous studies in patients with NCCP using short interventions have reported inconsistent results [13,25,52,53]. Jonsbu et al [13] used a 3-session CBT intervention and reported significant

effects in favor of CBT on fear of bodily sensations, avoidance of physical activity, depression, and some domains of HRQoL, and these effects lasted up to 12 months. However, cardiac anxiety was not studied. In a study by van Beek et al [25], positive effects on anxiety were found 24 weeks following a 6-session CBT intervention compared with usual treatment in patients with NCCP and panic disorder. Mulder et al [52] reported significantly lower health anxiety scores at 3 months but not at 12 months in patients who received 3 to 4 sessions of CBT compared with care as usual. The authors suggested booster sessions or longer interventions for more sustained improvement. Tyrer et al [53] failed to present any significant differences between iCBT and standard care at both 6- and 12-month follow-ups. Their CBT intervention comprised 4 to 10 sessions (mean 5.7) during a mean period of 14.3 weeks. They concluded that these results were mainly because of the study being underpowered. In an 8-year follow-up of CBT on health anxiety [54], the authors reported sustained improvement in health anxiety symptoms, especially among patients with cardiac diseases, and this improvement was greatest in nurse-led CBT. However, different length and follow-up periods for the interventions were used in these studies, which also used face-to-face CBT, compared with passive controls, which makes these studies difficult to compare with our study. This suggests that CBT is valuable to medical patients, including NCCP, with anxiety; however, the key is to find the right duration and type of CBT modality.

Furthermore, we believe that we could not find significant differences as iCBT was compared with an active control. In addition to the possible placebo effect of being in a trial and having their symptoms recognized, receiving psychoeducation, which our control group did, seems to have had effects on both primary and secondary outcomes, which could explain the minor and nonsignificant differences between the iCBT and psychoeducation groups [41]. Psychoeducation makes it easier for patients to understand what therapeutic tools to use and facilitates the motivation for behavior change and finding different ways of thinking in relation to their condition [55]. This can be compared with other studies comparing iCBT with usual care or waiting list instead of an active control and reporting significant improvement in anxiety and depression in favor of iCBT [25,30]. Studies with passive controls, such as waiting list or standard care, often report better outcomes in favor of the intervention compared with those with active controls [56]. An important aspect to consider is how long the effects of psychoeducation last and whether more psychological tools, such as cognitive restructuring and behavioral change strategies, are needed to maintain long-term results.

In the iCBT group, a larger proportion (21/54, 39% vs 13/55, 24%) of patients had at least moderate levels of depressive symptoms at baseline, although the mean values in the group did not differ significantly from those in the psychoeducation group. Although the study was not designed to target depressive symptoms, the iCBT program had significant effects on depressive symptoms in most of these patients, as 71% (15/21) reported lower scores on the PHQ-9 (ie, <10) than was reported in patients who received psychoeducation, in which only 31% (4/13) reduced depressive symptom levels. On the basis of our previous findings revealing that depressive symptoms have strong effects on cardiac anxiety in patients with NCCP, we believe that the effects of iCBT targeting cardiac anxiety might have been limited by the higher proportion of patients with depressive symptoms in this group [57]. Another affecting aspect could be that the length of our program was too short to lead to improvement, as comorbid depressive symptoms need longer treatments than if patients only have anxiety [58].

### Strengths and Limitations

Of the 824 patients assessed, only 109 (13.2%) took part in the study. This could indicate that the population in this study may not be representative of patients with NCCP in general. Patients were included based on high levels of anxiety, as the program was designed to target anxiety. As the CAQ lacks a cutoff score for anxiety, we used the median value in our previous study. This might have been too high, as many patients who perceived themselves to have cardiac anxiety did not come up to this cutoff and were, therefore, excluded from the study. As we had little missing values, we chose to report the original data; however,

we also provided a mixed model analysis with multiple imputed data to ensure the accuracy of our results. Regardless of the type of statistical analysis, our result proved to remain. Some patients could not join the study because of a lack of computer or internet access or perceive themselves as having difficulties in handling such interventions. However, we are aware that internet interventions cannot fit all patients, partly because of technical aspects but mainly because of preferences for face-to-face therapies [30]. We had difficulties recruiting patients to the study and had to expand our recruitment sites during the study. This could be as many patients with NCCP are not motivated to receive psychological treatment as they perceive their pain to be physical. As stated previously, the iCBT program accounted for the main part of the treatment effect, and the guidance and feedback part mainly aimed at confirming patients' work and progress and encouraging them to reflect on different issues and take on new challenges. The guidance and feedback were mainly provided by the first author (GM) and, in some cases, by the second author (MEL), who was mentored by the first author. This indicates that feedback can be provided by different health care professionals with a short introduction to iCBT.

### Conclusions

iCBT was not superior to psychoeducation in decreasing cardiac anxiety in patients with NCCP. However, iCBT tends to have better long-term effects on psychological distress, including cardiac anxiety, HRQoL, and NCCP frequency than psychoeducation. Better conclusions may be drawn based on further follow-ups.

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### Authors' Contributions

GM, PK, and PJ contributed to the conception and design of the study. GM, MEL, and PK collected data. GM, MEL, and PJ performed statistical analyses and interpretation of the data and contributed to the drafting of the manuscript.

### Conflicts of Interest

None declared.

### Multimedia Appendix 1

CONSORT-eHEALTH (V1.6.1)

[\[PDF File \(Adobe PDF File\), 722 KB-Multimedia Appendix 1\]](#)

### References

1. Mol KA, Smoczynska A, Rahel BM, Meeder JG, Janssen L, Doevendans PA, et al. Non-cardiac chest pain: prognosis and secondary healthcare utilisation. *Open Heart* 2018 Oct 15;5(2):e000859 [FREE Full text] [doi: [10.1136/openhrt-2018-000859](https://doi.org/10.1136/openhrt-2018-000859)] [Medline: [30364505](https://pubmed.ncbi.nlm.nih.gov/30364505/)]
2. McDevitt-Petrovic O, Kirby K, Shevlin M. The prevalence of non-cardiac chest pain (NCCP) using emergency department (ED) data: a Northern Ireland based study. *BMC Health Serv Res* 2017 Aug 09;17(1):549 [FREE Full text] [doi: [10.1186/s12913-017-2493-8](https://doi.org/10.1186/s12913-017-2493-8)] [Medline: [28793910](https://pubmed.ncbi.nlm.nih.gov/28793910/)]
3. Campbell KA, Madva EN, Villegas AC, Beale EE, Beach SR, Wasfy JH, et al. Non-cardiac chest pain: a review for the consultation-liaison psychiatrist. *Psychosomatics* 2017 May;58(3):252-265 [FREE Full text] [doi: [10.1016/j.psych.2016.12.003](https://doi.org/10.1016/j.psych.2016.12.003)] [Medline: [28196622](https://pubmed.ncbi.nlm.nih.gov/28196622/)]

4. Webster R, Norman P, Goodacre S, Thompson A. The prevalence and correlates of psychological outcomes in patients with acute non-cardiac chest pain: a systematic review. *Emerg Med J* 2012 Apr 27;29(4):267-273. [doi: [10.1136/emered-2011-200526](https://doi.org/10.1136/emered-2011-200526)] [Medline: [22034535](https://pubmed.ncbi.nlm.nih.gov/22034535/)]
5. Bjørnsen LP, Naess-Pleyrn LE, Dale J, Grenne B, Wiseth R. Description of chest pain patients in a Norwegian emergency department. *Scand Cardiovasc J* 2019 Feb 26;53(1):28-34. [doi: [10.1080/14017431.2019.1583362](https://doi.org/10.1080/14017431.2019.1583362)] [Medline: [30760035](https://pubmed.ncbi.nlm.nih.gov/30760035/)]
6. Mourad G, Alwin J, Strömberg A, Jaarsma T. Societal costs of non-cardiac chest pain compared with ischemic heart disease--a longitudinal study. *BMC Health Serv Res* 2013 Oct 09;13(1):403 [FREE Full text] [doi: [10.1186/1472-6963-13-403](https://doi.org/10.1186/1472-6963-13-403)] [Medline: [24107009](https://pubmed.ncbi.nlm.nih.gov/24107009/)]
7. Reid S, Wessely S, Crayford T, Hotopf M. Medically unexplained symptoms in frequent attenders of secondary health care: retrospective cohort study. *Br Med J* 2001 Mar 31;322(7289):767 [FREE Full text] [doi: [10.1136/bmj.322.7289.767](https://doi.org/10.1136/bmj.322.7289.767)] [Medline: [11282861](https://pubmed.ncbi.nlm.nih.gov/11282861/)]
8. Spalding L, Reay E, Kelly C. Cause and outcome of atypical chest pain in patients admitted to hospital. *J R Soc Med* 2003 Mar 01;96(3):122-125 [FREE Full text] [doi: [10.1258/jrsm.96.3.122](https://doi.org/10.1258/jrsm.96.3.122)] [Medline: [12612112](https://pubmed.ncbi.nlm.nih.gov/12612112/)]
9. Tremblay M, Denis I, Turcotte S, Fleet RP, Archambault P, Dionne CE, et al. Heart-focused anxiety and health care seeking in patients with non-cardiac chest pain: a prospective study. *Gen Hosp Psychiatry* 2018 Jan;50:83-89. [doi: [10.1016/j.genhosppsych.2017.10.007](https://doi.org/10.1016/j.genhosppsych.2017.10.007)] [Medline: [29120733](https://pubmed.ncbi.nlm.nih.gov/29120733/)]
10. TEW R, Guthrie EA, Creed FH, Cotter L, Kisely S, Tomenson B. A long-term follow-up study of patients with ischaemic heart disease versus patients with nonspecific chest pain. *J Psychosom Res* 1995 Nov;39(8):977-985. [doi: [10.1016/0022-3999\(95\)00065-8](https://doi.org/10.1016/0022-3999(95)00065-8)]
11. Wertli MM, Dangma TD, Müller SE, Gort LM, Klausner BS, Melzer L, et al. Non-cardiac chest pain patients in the emergency department: do physicians have a plan how to diagnose and treat them? A retrospective study. *PLoS One* 2019 Feb 1;14(2):e0211615 [FREE Full text] [doi: [10.1371/journal.pone.0211615](https://doi.org/10.1371/journal.pone.0211615)] [Medline: [30707725](https://pubmed.ncbi.nlm.nih.gov/30707725/)]
12. Bass C, Mayou R. Chest pain. *Br Med J* 2002 Sep 14;325(7364):588-591 [FREE Full text] [doi: [10.1136/bmj.325.7364.588](https://doi.org/10.1136/bmj.325.7364.588)] [Medline: [12228139](https://pubmed.ncbi.nlm.nih.gov/12228139/)]
13. Jonsbu E, Dammen T, Morken G, Moum T, Martinsen EW. Short-term cognitive behavioral therapy for non-cardiac chest pain and benign palpitations: a randomized controlled trial. *J Psychosom Res* 2011 Feb;70(2):117-123. [doi: [10.1016/j.jpsychores.2010.09.013](https://doi.org/10.1016/j.jpsychores.2010.09.013)] [Medline: [21262413](https://pubmed.ncbi.nlm.nih.gov/21262413/)]
14. Castonguay J, Turcotte S, Fleet RP, Archambault PM, Dionne CE, Denis I, et al. Physical activity and disability in patients with noncardiac chest pain: a longitudinal cohort study. *Biopsychosoc Med* 2020 Jun 30;14(1):12 [FREE Full text] [doi: [10.1186/s13030-020-00185-9](https://doi.org/10.1186/s13030-020-00185-9)] [Medline: [32612673](https://pubmed.ncbi.nlm.nih.gov/32612673/)]
15. Goodacre S, Mason S, Arnold J, Angelini K. Psychologic morbidity and health-related quality of life of patients assessed in a chest pain observation unit. *Ann Emerg Med* 2001 Oct;38(4):369-376. [doi: [10.1067/mem.2001.118010](https://doi.org/10.1067/mem.2001.118010)] [Medline: [11574792](https://pubmed.ncbi.nlm.nih.gov/11574792/)]
16. Eslick G, Talley NJ. Non-cardiac chest pain: predictors of health care seeking, the types of health care professional consulted, work absenteeism and interruption of daily activities. *Aliment Pharmacol Ther* 2004 Oct 15;20(8):909-915 [FREE Full text] [doi: [10.1111/j.1365-2036.2004.02175.x](https://doi.org/10.1111/j.1365-2036.2004.02175.x)] [Medline: [15479363](https://pubmed.ncbi.nlm.nih.gov/15479363/)]
17. Mourad G, Jaarsma T, Hallert C, Strömberg A. Depressive symptoms and healthcare utilization in patients with noncardiac chest pain compared to patients with ischemic heart disease. *Heart Lung* 2012 Sep;41(5):446-455. [doi: [10.1016/j.hrtlng.2012.04.002](https://doi.org/10.1016/j.hrtlng.2012.04.002)] [Medline: [22652167](https://pubmed.ncbi.nlm.nih.gov/22652167/)]
18. Mourad G, Strömberg A, Johansson P, Jaarsma T. Depressive symptoms, cardiac anxiety, and fear of body sensations in patients with non-cardiac chest pain, and their relation to healthcare-seeking behavior: a cross-sectional study. *Patient* 2016 Feb 4;9(1):69-77. [doi: [10.1007/s40271-015-0125-0](https://doi.org/10.1007/s40271-015-0125-0)] [Medline: [25840677](https://pubmed.ncbi.nlm.nih.gov/25840677/)]
19. Eslick GD. Health care seeking behaviors, psychological factors, and quality of life of noncardiac chest pain. *Dis Mon* 2008 Sep;54(9):604-612. [doi: [10.1016/j.disamonth.2008.06.004](https://doi.org/10.1016/j.disamonth.2008.06.004)] [Medline: [18725002](https://pubmed.ncbi.nlm.nih.gov/18725002/)]
20. Eslick G, Coulshed DS, Talley NJ. Review article: the burden of illness of non-cardiac chest pain. *Aliment Pharmacol Ther* 2002 Jul;16(7):1217-1223 [FREE Full text] [doi: [10.1046/j.1365-2036.2002.01296.x](https://doi.org/10.1046/j.1365-2036.2002.01296.x)] [Medline: [12144570](https://pubmed.ncbi.nlm.nih.gov/12144570/)]
21. Forberg JL, Henriksen LS, Edenbrandt L, Ekelund U. Direct hospital costs of chest pain patients attending the emergency department: a retrospective study. *BMC Emerg Med* 2006 May 04;6(1). [doi: [10.1186/1471-227x-6-6](https://doi.org/10.1186/1471-227x-6-6)]
22. Groarke J, O'Brien J, Go G, Susanto M, Owens P, Maree AO. Cost burden of non-specific chest pain admissions. *Ir J Med Sci* 2013 Mar 3;182(1):57-61. [doi: [10.1007/s11845-012-0826-5](https://doi.org/10.1007/s11845-012-0826-5)] [Medline: [22552895](https://pubmed.ncbi.nlm.nih.gov/22552895/)]
23. Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. *Lancet* 2007 Sep;370(9590):851-858. [doi: [10.1016/s0140-6736\(07\)61415-9](https://doi.org/10.1016/s0140-6736(07)61415-9)]
24. The Swedish National Board of Health and Welfare. Vård vid depression och ångestsyndrom. Stöd för styrning och ledning. 2019. URL: <https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/nationella-riktlinjer/2019-5-13.pdf> [accessed 2022-01-13]
25. van Beek M, Voshaar R, Beek A, van Zijderveld G, Visser S, Speckens A, et al. A brief cognitive-behavioral intervention for treating depression and panic disorder in patients with noncardiac chest pain: a 24-week randomized controlled trial. *Depress Anxiety* 2013 Jul 26;30(7):670-678. [doi: [10.1002/da.22106](https://doi.org/10.1002/da.22106)] [Medline: [23625592](https://pubmed.ncbi.nlm.nih.gov/23625592/)]

26. Høifødt RS, Strøm C, Kolstrup N, Eisemann M, Waterloo K. Effectiveness of cognitive behavioural therapy in primary health care: a review. *Fam Pract* 2011 Oct 09;28(5):489-504. [doi: [10.1093/fampra/cmz017](https://doi.org/10.1093/fampra/cmz017)] [Medline: [21555339](https://pubmed.ncbi.nlm.nih.gov/21555339/)]
27. Hofmann SG, Asnaani A, Vonk IJ, Sawyer AT, Fang A. The efficacy of cognitive behavioral therapy: a review of meta-analyses. *Cognit Ther Res* 2012 Oct 01;36(5):427-440 [FREE Full text] [doi: [10.1007/s10608-012-9476-1](https://doi.org/10.1007/s10608-012-9476-1)] [Medline: [23459093](https://pubmed.ncbi.nlm.nih.gov/23459093/)]
28. Beck AT, Dozois DJ. Cognitive therapy: current status and future directions. *Annu Rev Med* 2011 Feb 18;62(1):397-409. [doi: [10.1146/annurev-med-052209-100032](https://doi.org/10.1146/annurev-med-052209-100032)] [Medline: [20690827](https://pubmed.ncbi.nlm.nih.gov/20690827/)]
29. Kisely S, Campbell LA, Skerritt P. Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy. *Cochrane Database Syst Rev* 2005 Jan 25;2015(1):CD004101. [doi: [10.1002/14651858.CD004101.pub2](https://doi.org/10.1002/14651858.CD004101.pub2)] [Medline: [15674930](https://pubmed.ncbi.nlm.nih.gov/15674930/)]
30. Health Quality Ontario. Internet-delivered cognitive behavioural therapy for major depression and anxiety disorders: a health technology assessment. *Ont Health Technol Assess Ser* 2019;19(6):1-199 [FREE Full text] [Medline: [30873251](https://pubmed.ncbi.nlm.nih.gov/30873251/)]
31. The Swedish National Board of Health and Welfare. Långvarig psykisk ohälsa en utmaning för vården. Socialstyrelsen. 2019. URL: <https://www.socialstyrelsen.se/om-socialstyrelsen/pressrum/press/langvarig-psykisk-ohalsa-en-utmaning-for-varden/> [accessed 2022-01-13]
32. Andrews G, Cuijpers P, Craske MG, McEvoy P, Titov N. Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis. *PLoS One* 2010 Oct 13;5(10):e13196 [FREE Full text] [doi: [10.1371/journal.pone.0013196](https://doi.org/10.1371/journal.pone.0013196)] [Medline: [20967242](https://pubmed.ncbi.nlm.nih.gov/20967242/)]
33. Johansson R, Andersson G. Internet-based psychological treatments for depression. *Expert Rev Neurother* 2012 Jul 09;12(7):861-870. [doi: [10.1586/ern.12.63](https://doi.org/10.1586/ern.12.63)] [Medline: [22853793](https://pubmed.ncbi.nlm.nih.gov/22853793/)]
34. Carlbring P, Andersson G, Cuijpers P, Riper H, Hedman-Lagerlöf E. Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: an updated systematic review and meta-analysis. *Cogn Behav Ther* 2018 Jan 07;47(1):1-18. [doi: [10.1080/16506073.2017.1401115](https://doi.org/10.1080/16506073.2017.1401115)] [Medline: [29215315](https://pubmed.ncbi.nlm.nih.gov/29215315/)]
35. Olthuis J, Watt MC, Bailey K, Hayden JA, Stewart SH. Therapist-supported internet cognitive behavioural therapy for anxiety disorders in adults. *Cochrane Database Syst Rev* 2015 Mar 05;3(3):CD011565. [doi: [10.1002/14651858.CD011565](https://doi.org/10.1002/14651858.CD011565)] [Medline: [25742186](https://pubmed.ncbi.nlm.nih.gov/25742186/)]
36. McCombie A, Geary R, Andrews J, Mikocka-Walus A, Mulder R. Computerised cognitive behavioural therapy for psychological distress in patients with physical illnesses: a systematic review. *J Clin Psychol Med Settings* 2015 Mar 11;22(1):20-44. [doi: [10.1007/s10880-015-9420-0](https://doi.org/10.1007/s10880-015-9420-0)] [Medline: [25666485](https://pubmed.ncbi.nlm.nih.gov/25666485/)]
37. Mehta S, Peynenburg VA, Hadjistavropoulos HD. Internet-delivered cognitive behaviour therapy for chronic health conditions: a systematic review and meta-analysis. *J Behav Med* 2019 Apr 01;42(2):169-187. [doi: [10.1007/s10865-018-9984-x](https://doi.org/10.1007/s10865-018-9984-x)] [Medline: [30387008](https://pubmed.ncbi.nlm.nih.gov/30387008/)]
38. Johansson P, Westas M, Andersson G, Alehagen U, Broström A, Jaarsma T, et al. An internet-based cognitive behavioral therapy program adapted to patients with cardiovascular disease and depression: randomized controlled trial. *JMIR Ment Health* 2019 Oct 03;6(10):e14648 [FREE Full text] [doi: [10.2196/14648](https://doi.org/10.2196/14648)] [Medline: [31584000](https://pubmed.ncbi.nlm.nih.gov/31584000/)]
39. Mourad G, Strömberg A, Jonsbu E, Gustafsson M, Johansson P, Jaarsma T. Guided Internet-delivered cognitive behavioural therapy in patients with non-cardiac chest pain - a pilot randomized controlled study. *Trials* 2016 Jul 26;17(1):352 [FREE Full text] [doi: [10.1186/s13063-016-1491-1](https://doi.org/10.1186/s13063-016-1491-1)] [Medline: [27456689](https://pubmed.ncbi.nlm.nih.gov/27456689/)]
40. Physical activity in the prevention and treatment of diseases. Swedish National Institute of Public Health. 2011. URL: <https://www.folkhalsomyndigheten.se/publicerat-material/publikationsarkiv/p/physical-activity-in-the-prevention-and-treatment-of-disease/> [accessed 2022-01-13]
41. Aycock DM, Hayat MJ, Helvig A, Dunbar SB, Clark PC. Essential considerations in developing attention control groups in behavioral research. *Res Nurs Health* 2018 Jun 14;41(3):320-328. [doi: [10.1002/nur.21870](https://doi.org/10.1002/nur.21870)] [Medline: [29906317](https://pubmed.ncbi.nlm.nih.gov/29906317/)]
42. Eifert GH, Thompson RN, Zvolensky MJ, Edwards K, Frazer NL, Haddad JW, et al. The Cardiac Anxiety Questionnaire: development and preliminary validity. *Behav Res Ther* 2000 Oct;38(10):1039-1053. [doi: [10.1016/s0005-7967\(99\)00132-1](https://doi.org/10.1016/s0005-7967(99)00132-1)]
43. Chambless DL, Caputo GC, Bright P, Gallagher R. Assessment of fear of fear in agoraphobics: The Body Sensations Questionnaire and the Agoraphobic Cognitions Questionnaire. *J Consult Clin Psychol* 1984 Dec;52(6):1090-1097. [doi: [10.1037/0022-006x.52.6.1090](https://doi.org/10.1037/0022-006x.52.6.1090)]
44. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001 Sep;16(9):606-613 [FREE Full text] [doi: [10.1046/j.1525-1497.2001.016009606.x](https://doi.org/10.1046/j.1525-1497.2001.016009606.x)] [Medline: [11556941](https://pubmed.ncbi.nlm.nih.gov/11556941/)]
45. EQ-5D. EuroQolGroup. 2017. URL: <https://euroqol.org/> [accessed 2022-01-13]
46. McCoy E. Understanding the intention-to-treat principle in randomized controlled trials. *West J Emerg Med* 2017 Oct 18;18(6):1075-1078 [FREE Full text] [doi: [10.5811/westjem.2017.8.35985](https://doi.org/10.5811/westjem.2017.8.35985)] [Medline: [29085540](https://pubmed.ncbi.nlm.nih.gov/29085540/)]
47. Jakobsen JC, Gluud C, Wetterslev J, Winkel P. When and how should multiple imputation be used for handling missing data in randomised clinical trials - a practical guide with flowcharts. *BMC Med Res Methodol* 2017 Dec 06;17(1):162 [FREE Full text] [doi: [10.1186/s12874-017-0442-1](https://doi.org/10.1186/s12874-017-0442-1)] [Medline: [29207961](https://pubmed.ncbi.nlm.nih.gov/29207961/)]
48. Little RA, Rubin DB. *Statistical Analysis with Missing Data*, Second Edition. Hoboken, New Jersey, United States: John Wiley & Sons; 2002.
49. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd Ed. New York: Routledge; 1988.

50. Christensen L, Mendoza JL. A method of assessing change in a single subject: an alteration of the RC index. *Behav Ther* 1986 Jun;17(3):305-308. [doi: [10.1016/s0005-7894\(86\)80060-0](https://doi.org/10.1016/s0005-7894(86)80060-0)]
51. Reavell J, Hopkinson M, Clarksmith D, Lane DA. Effectiveness of cognitive behavioral therapy for depression and anxiety in patients with cardiovascular disease: a systematic review and meta-analysis. *Psychosom Med* 2018;80(8):742-753. [doi: [10.1097/psy.0000000000000626](https://doi.org/10.1097/psy.0000000000000626)]
52. Mulder R, Zarifeh J, Boden J, Lacey C, Tyrer P, Tyrer H, et al. An RCT of brief cognitive therapy versus treatment as usual in patients with non-cardiac chest pain. *Int J Cardiol* 2019 Aug 15;289:6-11. [doi: [10.1016/j.ijcard.2019.01.067](https://doi.org/10.1016/j.ijcard.2019.01.067)] [Medline: [30770262](https://pubmed.ncbi.nlm.nih.gov/30770262/)]
53. Tyrer P, Tyrer H, Morriss R, Crawford M, Cooper S, Yang M, et al. Clinical and cost-effectiveness of adapted cognitive behaviour therapy for non-cardiac chest pain: a multicentre, randomised controlled trial. *Open Heart* 2017 May 16;4(1):e000582 [FREE Full text] [doi: [10.1136/openhrt-2016-000582](https://doi.org/10.1136/openhrt-2016-000582)] [Medline: [28674627](https://pubmed.ncbi.nlm.nih.gov/28674627/)]
54. Tyrer P, Wang D, Crawford M, Dupont S, Cooper S, Nourmand S, et al. Sustained benefit of cognitive behaviour therapy for health anxiety in medical patients (CHAMP) over 8 years: a randomised-controlled trial. *Psychol Med* 2020 Mar 16;51(10):1714-1722. [doi: [10.1017/s003329172000046x](https://doi.org/10.1017/s003329172000046x)]
55. Borza L. Cognitive-behavioral therapy for generalized anxiety. *Dialogues Clin Neurosci* 2017 Jul;19(2):203-208. [doi: [10.31887/dcms.2017.19.2/lorza](https://doi.org/10.31887/dcms.2017.19.2/lorza)]
56. LaFave SE, Granbom M, Cudjoe TK, Gottsch A, Shorb G, Szanton SL. Attention control group activities and perceived benefit in a trial of a behavioral intervention for older adults. *Res Nurs Health* 2019 Dec 24;42(6):476-482 [FREE Full text] [doi: [10.1002/nur.21992](https://doi.org/10.1002/nur.21992)] [Medline: [31647125](https://pubmed.ncbi.nlm.nih.gov/31647125/)]
57. Mourad G, Jaarsma T, Strömberg A, Svensson E, Johansson P. The associations between psychological distress and healthcare use in patients with non-cardiac chest pain: does a history of cardiac disease matter? *BMC Psychiatry* 2018 Jun 05;18(1):172 [FREE Full text] [doi: [10.1186/s12888-018-1689-8](https://doi.org/10.1186/s12888-018-1689-8)] [Medline: [29866125](https://pubmed.ncbi.nlm.nih.gov/29866125/)]
58. Liu J, Gill NS, Teodorczuk A, Li Z, Sun J. The efficacy of cognitive behavioural therapy in somatoform disorders and medically unexplained physical symptoms: a meta-analysis of randomized controlled trials. *J Affect Disord* 2019 Feb 15;245:98-112. [doi: [10.1016/j.jad.2018.10.114](https://doi.org/10.1016/j.jad.2018.10.114)] [Medline: [30368076](https://pubmed.ncbi.nlm.nih.gov/30368076/)]

## Abbreviations

- BSQ:** Body Sensations Questionnaire
- CAQ:** Cardiac Anxiety Questionnaire
- CBT:** cognitive behavioral therapy
- EQ-VAS:** EuroQol visual analog scale
- HRQoL:** health-related quality of life
- iCBT:** internet-delivered cognitive behavioral therapy
- NCCP:** noncardiac chest pain
- PHQ-9:** Patient Health Questionnaire-9

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