

# Cognitive behavioural therapy targeting cardiac anxiety post-myocardial infarction: results from two sequential pilot studies

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Received 21 November 2024; revised 17 January 2025; accepted 28 February 2025; online publish-ahead-of-print 7 March 2025

Handling Editor: Maciej Banach

#### **Aims**

Cardiac anxiety, which is cardiac-related fear and avoidance behaviours, is common following myocardial infarction (MI) and has been associated with increased risk for cardiovascular events. However, there are currently no treatments specifically designed to target cardiac anxiety. The aim of the two pilot studies was to evaluate an exposure-based cognitive behavioural therapy protocol (MI-CBT) targeting cardiac anxiety following MI, assessing feasibility, acceptability, and the intervention's potential for reducing cardiac anxiety and improving health-related quality of life (QoL).

# Methods and results

A series of two sequential, uncontrolled pilot studies were conducted. In Pilot Study 1 (n = 15), MI-CBT was delivered via face-to-face videoconference, while Pilot Study 2 (n = 23) was delivered online. Patients with a history of MI ( $\geq 6$  months before assessment, type 1 ST- or non-ST-segment elevation MI, and elevated cardiac anxiety as per clinical interview) were included. The interventions lasted 8 weeks and were therapist-led, with key components including exposure to cardiac-related symptoms and reduction of avoidance behaviours. Participants completed self-rated assessments, including the Cardiac Anxiety Questionnaire (CAQ) and the 12-Item Short Form Health Survey (SF-12), at baseline, post-treatment, and 6-month follow-up. Treatment adherence and satisfaction were high. Cognitive behavioural therapy led to a large reduction in cardiac anxiety, as measured by the CAQ (P < 0.001), and significant improvements in health-related QoL, as measured by the SF-12 (P < 0.001), in both pilot studies.

#### Conclusion

These studies suggest that exposure-based CBT is a feasible, acceptable, and promising approach to reduce cardiac anxiety and improve QoL following MI. A randomized controlled trial should be conducted to evaluate the efficacy of the intervention.

# Lay summary

In these two studies, we wanted to see if 8 weeks of cognitive behavioural therapy for heart-related anxiety after a heart attack could be a viable treatment approach, and whether it could help reduce the anxiety related to the heart and improve quality of life.

Key findings:

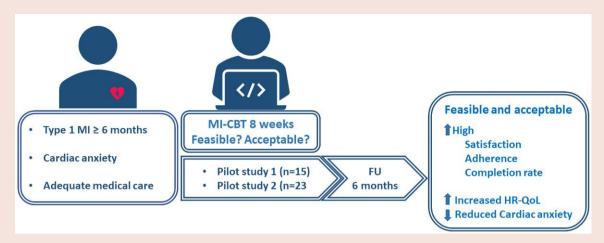
- Participants were satisfied with the treatment and reported that they had less anxiety related to the heart, as well as improved
  quality of life
- Cognitive behavioural therapy targeting heart-related anxiety may be a promising way of treating anxiety related to the heart following a heart attack.

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# **Graphical abstract**



**Keywords** 

Myocardial infarction • Cognitive behavioural therapy • Online cognitive behaviour therapy • Cardiac anxiety • Quality of life

# Introduction

Myocardial infarction (MI) is an acute cardiovascular event associated with adverse health outcomes and mortality. Following MI, it is common to experience psychological distress, with approximately one-third of patients developing clinically significant anxiety, depression, and cardiac-related fear and avoidance behaviours, i.e. cardiac anxiety. Psychological distress is a well-known risk factor for adverse cardiovascular outcomes and has been linked to pathophysiological pathways including sympathetic activation, autonomic dysregulation and systemic inflammation. Psychological distress is also linked to behavioural risk factors such as an unhealthy lifestyle including smoking, poor diet and low levels of exercise, incompliance with medical recommendations, and reduced participation in cardiac rehabilitation.

More specifically, cardiac anxiety has been shown to increase the risk for recurrent cardiovascular events post-MI (hazard ratio = 1.77)<sup>8,9</sup> and is associated with elevated depressive symptoms. <sup>9</sup> This association suggests that the relationship may arise from secondary effects of cardiac anxiety, such as avoidance behaviours and reduced quality of life, which contribute to the development of depressive symptoms. Cardiac anxiety specifically refers to distress about the heart's function, hypervigilance towards cardiac-related symptoms, and related avoidance behaviours.<sup>10</sup> This is distinct from general anxiety, which encompasses a broader range of worry themes; panic disorder, which centres on fear of panic attacks<sup>11</sup>; or health anxiety, characterized by a persistent fear of having or developing a serious illness and may include but is not limited to cardiac-related fears. 12 A potential behavioural pathway is that fear of cardiac-related symptoms (e.g. chest pain, increased heart rate, palpitations, shortness of breath) and fear of recurrent MI following the cardiac event lead to hypervigilance and avoidance behaviours 10 (e.g. avoidance of physical activity or being alone), which creates a self-reinforcing vicious cycle. Cardiac anxiety, unlike general anxiety and depression, offers a disease-specific framework for understanding the unique psychological challenges post-MI, allowing for more targeted interventions to address specific fears and avoidance behaviours associated with the cardiac event.

Exposure-based cognitive behaviour therapy (CBT) targets the cycle of anxiety, avoidance behaviour, and associated impairments <sup>13</sup> and has been shown to effectively alleviate psychological distress related to somatic disorders. <sup>14,15</sup> CBT can be effectively administered online, achieving treatment outcomes that are similar to those of traditional face-to-face therapy, while also increasing scalability. <sup>16</sup> CBT post-MI has shown promising results in reducing anxiety, depression, <sup>17</sup> and mitigating adverse cardiac outcomes <sup>18</sup>. However, no CBT protocol has been specifically designed with an exposure-based approach to address cardiac anxiety following an MI, emphasizing the need for a scalable clinical intervention.

Given how cardiac anxiety may affect the patient's ability to recover post-MI, there is a clinical need to develop and evaluate a CBT protocol, which specifically targets cardiac anxiety. We have previously developed an exposure-based CBT protocol targeting cardiac anxiety in patients with atrial fibrillation (AF)<sup>15,19,20</sup> demonstrating significant improvements in cardiac anxiety and disease-specific Quality of Life (QoL). In these two pilot studies, we adapted the previously evaluated CBT protocol to specifically address cardiac anxiety in post-MI patients, incorporating patient-reported experiences and clinical observations.

The primary aim of the two sequential non-randomized pilot studies was to evaluate the feasibility and acceptability of an exposure-based CBT protocol targeting cardiac anxiety post-MI (MI-CBT). Secondary aims were to investigate if MI-CBT potentially leads to reduction in cardiac anxiety and improvement in QoL, and to investigate cardiac anxiety as a putative mediator of treatment effect on health-related QoL.

# **Methods**

# Study design

Two sequential uncontrolled pilot studies were conducted at the Karolinska University Hospital in Stockholm, Sweden. In Pilot study 1 (n=15), MI-CBT was delivered face-to-face via video conference, while Pilot study 2 (n=23) used a text-based internet-delivered format. To assess aspects as feasibility, acceptability and patient safety, and enhance treatment

development, we conducted a stepwise evaluation of the MI-CBT by starting with a face-to-face format, and then moving to an internet-based format. Both studies employed a pretest-posttest design and included a 6-month follow-up and shared the same study design, recruitment, and inclusion procedures.

Recruitment for Pilot study 1 started on 7 December 2020 and ended on 26 January 2021, and the last data were collected on 10 December 2021. Recruitment for Pilot study 2 started on 29 October 2021 and ended on 1 March 2022, and the last data were collected on 5 December 2022. Trial protocols were pre-registered at ClinicalTrials.gov: NCT04649307 (Pilot study 1) and NCT05128981 (Pilot study 2); and approved by the Swedish Ethical Review Authority no: 2020-05466 (Pilot study 1) and 2021-04488 (Pilot study 2).

# **Participants**

Eligibility criteria for participation in the studies included the following: (A) MI  $\geq 6$  months before assessment (type 1 ST- or non-ST-segment elevation MI); (B) elevated cardiac anxiety causing significant distress or limitation in daily activities [Cardiac Anxiety Questionnaire (CAQ); score  $\geq 20]^{21}$ ; (C) medical care as deemed adequate by the discretion of the study cardiologist and in accordance with current clinical guidelines  $^{22}$ ; (D) able to read and write in Swedish; (E) age 18–69 years (face-to-face CBT) or age 18–75 years (online CBT). Exclusion criteria were: (F) heart failure with severe systolic dysfunction, an ejection fraction at 35% or under; (G) significant valvular disease; (H) planned or recently performed coronary artery bypass surgery or other invasive treatment; (I) other severe medical illness; (J) any medical restriction to physical exercise; (K) severe psychiatric disorder, severe depression, or risk of suicide; or (L) alcohol dependence.

Trial participants were asked to refrain from engaging in any concurrent psychological treatment until the conclusion of CBT. Additionally, participants were advised to continue their current pharmacological therapy unless clinical adjustments were deemed necessary. The age range of 18–69 as an inclusion criterion in the first pilot study was influenced by the ongoing COVID-19 pandemic, as we needed to adhere to the social distancing guidelines for age groups 70 and older set forth by the Public Health Agency of Sweden during this period. See the Supplementary material online for a more detailed description of the measures taken due to the ongoing COVID-19 pandemic during Pilot Study 1.

# Recruitment and determination of eligibility

Patients in the respective studies were recruited nationally via self-referral in response to advertisements in social media, and information directed to cardiology practices. Applicants registered via a secure webpage and completed online screening, including informed consent, medical history, demographics, the CAQ,<sup>21</sup> the Alcohol Use Disorders Identification Test (AUDIT),<sup>23</sup> and the Patient Health Questionnaire-9 (PHQ-9).<sup>24</sup> The eligibility criteria (A–J) were assessed based on the screening data, medical records, and a telephone interview by a study cardiology nurse (E.Ó). Subsequently eligibility criteria B, K, and L were assessed via a structured telephone-based clinical interview by a licensed psychologist (J.S, B.E.L.) or last year clinical psychologist student (L.M., I.B.), under supervision by the last author (J.S.). The MI diagnosis, medical history, medical records, pharmacology treatment, and cardiac parameters were reviewed by the study cardiologist (H.S, L.G.M., S.K.) before decision on inclusion was made.

## **Procedures**

Assessments in both of the studies were completed online at baseline, weekly during treatment, post-treatment, and 6 months follow-up, with no interference of study personnel. After inclusion in the study, participants completed baseline assessment online and started treatment within 4 days.

## Intervention

The intervention was based on a CBT protocol targeting cardiac anxiety in patients with AF, developed by Särnholm et al.  $^{15,19,20}$  previously evaluated in a series of clinical trials. The CBT protocol (MI-CBT) was developed and tailored to the clinical presentation of MI patients by the lead author (J.S.) and underwent further development and refinement before the second study, during which the online manual was finalized. The MI-CBT intervention was therapist lead (see Therapist support below), lasted for 8 weeks and was

delivered face-face or via the internet, respectively, in eight interactive treatment modules. The treatment targets cardiac anxiety i.e. fear and hypervigilance towards cardiac-related symptoms, fear or recurrent MI and cardiac-related avoidance behaviour and includes the following treatment components: (i) psychoeducation on common emotional and behavioural reactions following MI and on cardiac anxiety and avoidance behaviours' impact on QoL. Education on benign vs. acute cardiac symptoms and when to seek medical care; (ii) labelling exercise (i.e. labelling of cardiac-related symptoms, thoughts, imagery, feelings, and behavioural impulses) to practice a more neutral stance towards bodily sensations and reduce fear and hypervigilance; (iii) interoceptive exposure to cardiac-related symptoms such as an increase in heart rate, palpitations, or shortness of breath. Participants were instructed to induce these sensations through various exercises, such as running on the spot, lying on their left side while placing a hand on their heart, or hyperventilating; (iv) systematic in-vivo exposure to avoided activities and situations (such as engaging in physical activity, going for a walk alone or planning activities for the future); (v) reduction of cardiac-related avoidance- and control behaviours (such as constantly monitoring the heart or excessive healthcare seeking); (vi) relapse prevention strategies to manage symptoms such as of chest pain or external stressors, and how to maintain treatment gains. Participants were encouraged to use components 1–5 in conjunction to enhance the effect of exposure. For example, going for walks alone, increase the heart rate and label their cardiac-related symptoms and emotional reactions while refraining from engaging in control behaviours, such as checking their pulse. See Box 1 for an overview of the treatment.

# Patient safety measures

Education on common benign cardiac related symptoms (e.g. palpitations from physical activity, chest tightness due to musculoskeletal pain) vs. acute cardiac symptoms and when to seek medical care (e.g. chest pain over 30 min unresponsive to nitro-glycerine, chest pain/pressure with shortness of breath and cold sweats) was provided in the first module. This aimed to help participants distinguish between manageable symptoms and those requiring medical attention. Physical activity, as recommended by clinical guidelines,<sup>25</sup> posed no risks for MI patients in the two pilot studies. However, participants were advised to stop the exposure exercise and inform their physician if they experienced exercise-induced chest pain or fainting sensations. Treating therapists could also consult the study nurse and cardiologist throughout the treatment if concerns arose about participants' well-being or if they needed advice on adapting exposure exercises to medical needs. Both the study nurse and the cardiologist were also able to access the platform to give written feedback and supervision to the treating psychologist.

#### Therapist support

The first pilot study comprised of 8 weekly face-to-face videoconference sessions with a licensed psychologist (B.L, B.E.L., J.S.). Text modules and weekly homework assignments were delivered online in conjunction with the session. The second pilot study consisted of eight interactive text-based treatment modules delivered via the internet over 8 weeks. The treatment was guided by licensed psychologist (J.S.) or last year clinical psychologist student under supervision (L.G.M., I.B.). The therapists gave feedback on weekly homework assignments, and guided the participants through the treatment. All study therapist received training on how to deliver MI-CBT by senior author (J.S.) and on the medical aspects of MI by the study cardiologist (H.S., L.G.M.). Fidelity to the MI-CBT protocol was monitored weekly by the senior author (J.S.) in both studies, and no deviations from the treatment protocol were identified.

## Measures

#### Feasibility and adherence to treatment

Treatment satisfaction was measured by the Client Satisfaction Questionnaire (CSQ-8)<sup>26</sup> at post-treatment. The total score ranges from 8 to 32, with a higher score indicating a higher level of satisfaction with the intervention. Adherence to treatment was assessed by the number of completed treatment modules over the 8-week treatment period. Treatment completion was defined as the completion of four modules, as the main treatment content is covered in the initial four modules and

#### **Treatment overview** Box 1

Module 1—Introduction and psychoeducation.

- · Common emotional reactions following MI
- The interaction between cardiac anxiety and avoidance behaviour
- Setting goals
- · Mapping of avoidance- and control-behaviours
- Module 2—Interoceptive exposure
- · Exposure to physical sensations to reduce associated fear
- Module 3—Introduction to
- · Self-observation through labelling
- exposure in-vivo
- · Introduction of gradual exposure to situations, places and activities
- Module 4—Cardiac related anxiety and thoughts
- Reduction of avoidance- and control-behaviours
- Modules 5, 6, 7—Continuing exposure and reclaiming activities
- · Introduction and rationale on strategies to manage thoughts and worries
- Module 8—Summary and

relapse prevention

- · Continuous work with gradual interoceptive and in vivo exposure
- · Combining the treatment strategies
- · Summary of treatment
- · Identifying risk situations
- · Plan for future work towards goals

participants have commenced exposure exercises. Adverse events related to the CBT-treatment were assessed weekly during treatment, at posttreatment and at 6-month follow-up. Adverse events related to the treatment were rated from a mild negative effect to a very negative effect, range 1-3, as well as the short- and long-term impact of the adverse event.

# **Continuous outcomes**

The primary outcome for both studies was health-related QoL, measured by the 12-Item Short-Form Health Survey (SF-12). 28 SF-12 consists of eight domains covering different life areas, such as physical functioning, bodily pain, general health and mental health. The eight domains are summarized into a Mental Health Summary score (SF-12 MCS) and Physical Health Summary score (SF-12 PCS), ranging from 0 to 100, with a higher score indicating better QoL. Secondary outcomes included: Cardiac anxiety (CAQ),<sup>21</sup> fear of bodily symptoms (body Schauser, BSQ),<sup>29</sup> physical activity (The Godin Leisure-time Exercise Questionnaire; (Tarabas Scale for Kinesiophobia Heart; 1 fear of bodily symptoms (Body Sensation Questionnaire; GSLTPAQ),<sup>30</sup> fear of movement (Tampas Scale for Kinesiophobia Heart; TSK Heart), 31 depressive symptoms (Patient Health Questionnaire-9; generalized anxiety (Generalized Anxiety disorder 7; GAD-7)<sup>32</sup> and perceived stress (Perceived Stress Scale-4; PSS-4).<sup>33</sup> (See the Supplementary material online for detailed descriptions of the secondary outcomes.) Other outcomes included in Pilot study 2 are reported in the Supplementary material online.

# Power analysis

The first pilot study aimed to include 20 participants to achieve 80% power for observing a standardized mean difference of at least d = 0.65 between pre-treatment and post-treatment, corresponding to an NNT = 3. However, recruitment was concluded at 15 participants because the principal aim of investigating the feasibility and acceptability of the intervention was deemed to have been achieved. Similarly, the initial aim for the second study was to include 30 participants, but recruitment concluded at 23 participants because we observed feasibility and acceptability and preliminary analysis of data from the first pilot study indicated that a within-group effect size of at least d = 0.8 could be expected, meaning that 20 participants were needed to achieve 90% power.

#### **Analysis**

Within-group changes were investigated using within-group t-test where we compared baseline assessment with the post-treatment and 6-month follow-up assessment, respectively. Cohen's d effect sizes were calculated as the within-group average change divided by the baseline standard deviation of the respective measure, and 5000 bootstrap replications were used to obtain 95% confidence intervals (Cls) for the effect sizes. Because only one participant in each study failed to complete posttreatment or 6-month follow-up assessment, no method of missing data handling was employed.

The potential mediating effects of cardiac anxiety (CAQ) on the treatment's effect on the primary outcome measure (SF-12) were analysed using exploratory mediation analysis. The mediation analyses were conducted based on the 8 weekly measurements of CAQ and SF-12 collected during the treatment. In Pilot study 1, we also included weekly measures of the perceived stress measure PSS-4 and physical activity measure GSLTPAQ. which were also investigated as potential mediators. See Supplementary material online for a more detailed description of the mediation analysis.

# **Results**

# Sample

The baseline characteristics of the samples of both studies are displayed in Table 1. The sample in Pilot study 1 (MI-CBT, face-to-face via video conference) consisted of 15 participants [mean age  $56.5 \pm 2.5$ , 11 (73%) males,  $1.9 \pm 1.4$  years since MI] and Pilot study 2 (internetdelivered MI-CBT) included 23 participants [mean age 62 ± 7.8, 14 (61%) males,  $3.9 \pm 4.2$  years since MI]. The majority of the participants had no prior MI [0 (0%) in Pilot study 1 and 4 (83%) in Pilot study 2]. Body mass index (BMI) in both studies indicated overweight (Pilot study 1 26.5  $\pm$  5.4, Pilot study 2 27.3  $\pm$  5.2). Insomnia was the most prevalent psychological condition in both studies, affecting 80% of participants in Pilot Study 1% and 43% in Pilot Study 2. Based on the baseline GSLTPAQ scores, participants in both pilot studies were classified as physically active. The average baseline CAQ score corresponded to clinical significant cardiac anxiety, 39.7 ± 8.7 in Pilot study 1 and  $35.1 \pm 9.1$  in Pilot study 2. Figure 1A and 1B outlines the steps involved in evaluating eligibility and tracking follow-up throughout the studies.

## Recruitment and retention

The recruitment goal in Pilot study 1 was achieved in 2, 4 months and in 5 months in Pilot study 2, respectively. The retention was high in both studies with 93.4% completing all outcome measures in Pilot study 1% and 95.7% in Pilot study 2.

# Treatment activity and satisfaction with the treatment

Treatment satisfaction according to CSQ-8<sup>26</sup> was high, with an average of 29.7 ( $\pm 4.1$ ) out of 32 points in Pilot study 1 and 28 ( $\pm 4.6$ ) in Pilot study 2. This corresponds to 'very satisfied' with the treatment. We observed high adherence and treatment completion in both studies. In Pilot study 1 all participants were considered treatment completers (n = 15; 100%), and participants completed on average 7.8 modules  $(\pm 0.8, \text{ range}, 5 \text{ to } 8)$ . In Pilot study 2, a majority (n = 17, 74%) were considered treatment completers, with an average completion rate of 5.9 modules among all participants (± 2.4, range, 1 to 8). In Pilot study 2, one participant reported progression of cardiac disease and discontinued the treatment after completing the first module.

Table 1 Participants characteristics at baseline

	Pilot study 1 (n = 15)	Pilot study 2 (n = 23)
Mala	11 /739/\	14 ((19/)
Male	11 (73%)	14 (61%)
Age, yr	56,5 ± 2,5	62.01 ± 7.8
Employment status	11 (730/)	12 (529/)
Employment	11 (73%)	12 (52%)
Sick leave	1 (7%)	0 (0%)
Retired	3 (20%)	9 (39%)
Unemployed	0 (0%)	2 (9%)
Highest completed education	4 (70/)	2 (420/)
Primary	1 (7%)	3 (13%)
Secondary education	1 (7%)	5 (13%)
Tertiary	11 (74%)	25 (65%)
Other	1 (7%)	0 (0%)
Most recent MI		
Years since MI	1.9 ± 1.4	$3.9 \pm 4.2$
Type of MI	NSTEMI, 9 (60%)	NSTEMI, 10 (43%)
		STEMI, 10 (43%)
	STEMI, 6 (40%)	Unspecified, 3
		(13%)
PCI	15 (100%)	17 (74%)
CABG	0	5 (22%)
Conservative treatment	0	1 (4%)
Medical history		
Smoker	0 (0%)	1 (4%)
Diabetes	1 (7%)	2 (9%)
Previous stroke	2 (13%)	0 (0%)
Angina pectoris	2 (13%)	3 (13%)
Atrial fibrillation	1 (7%)	0 (0%)
Hypertension	7 (47%)	15 (65%)
Previous MI	0 (0%)	4 (17%)
Mental health characteristics		
Insomnia	12 (80%)	10 (43%)
Depressed mood	7 (47%)	6 (26%)
Any anxiety disorder	6 (40%)	6 (26%)
Baseline characteristics	, ,	,
BMI	$26.5 \pm 5.4$	$27.3 \pm 5.2$
Blood pressure systolic, mmHg	124.5 ± 12.1	$128.8 \pm 13.4$
Blood pressure diastolic, mmHg	78.7 ± 7.9	$77.4 \pm 8.3$
Heart rate, bpm	$64.8 \pm 8.8$	$61.4 \pm 8.6$
Ejection fraction, %	$49.9 \pm 14.7$	$52.39 \pm 5^{a}$
Current medication	., <u>-</u>	32.37 _ 3
Beta blocker	11 (73%)	16 (70%)
ACEi/ARB	11 (73%)	20 (87%)
Calcium channel blocker	3 (20%)	4 (17%)
Lipid-lowering agents	15 (100%)	22 (96%)
ASA	10 (67%)	17 (74%)
DAPT	8 (53%)	6 (26%)
	` '	` '
SSRI Apprioration (as pooded)	2 (13%)	1 (4%)
Anxiolytics, 'as needed'	0 (0%)	1 (4%)
Sleep medication	1 (7%)	5 (22%)

Continued

Table 1 Continued

	Pilot study 1 (n = 15)	Pilot study 2 (n = 23)
Cardiac rehabilitation		
Currently attending	1 (7%)	2 (9%)
Attended in past	6 (40%)	14 (61%)
Was not offered	5 (33%)	3 (13%)
Discontinued due to	3 (20%)	4 (17%)
COVID-19		

Values are mean  $\pm$  SD or n (%).

BMI, body mass index; PCI, percutaneous coronary intervention; bpm, beats per minute; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid; DAPT, dual antiplatelet therapy; SSRI, selective serotonin reuptake inhibitor.

<sup>a</sup>Five datapoints missing from the sample and not included in the calculation.

## **Adverse events**

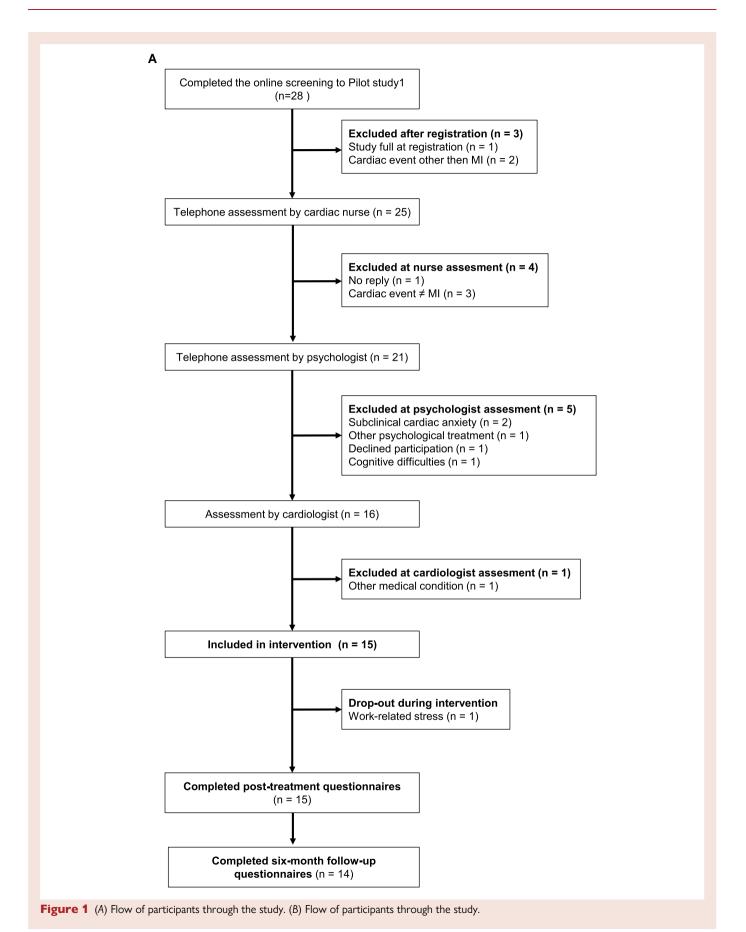
There were no serious adverse events or medical incidents reported in either of the studies. The majority of adverse events were rated as mild and transient and related to discomfort during exposure exercises, increased cardiac-related attention, or stress due to participating in the study. In Pilot study 1, seven adverse events were reported by four participants (27%) over the treatment, and in Pilot study 2, four adverse events were reported by four participants (17%). No adverse events were reported post-treatment or at 6 months follow-up in either of the pilot studies.

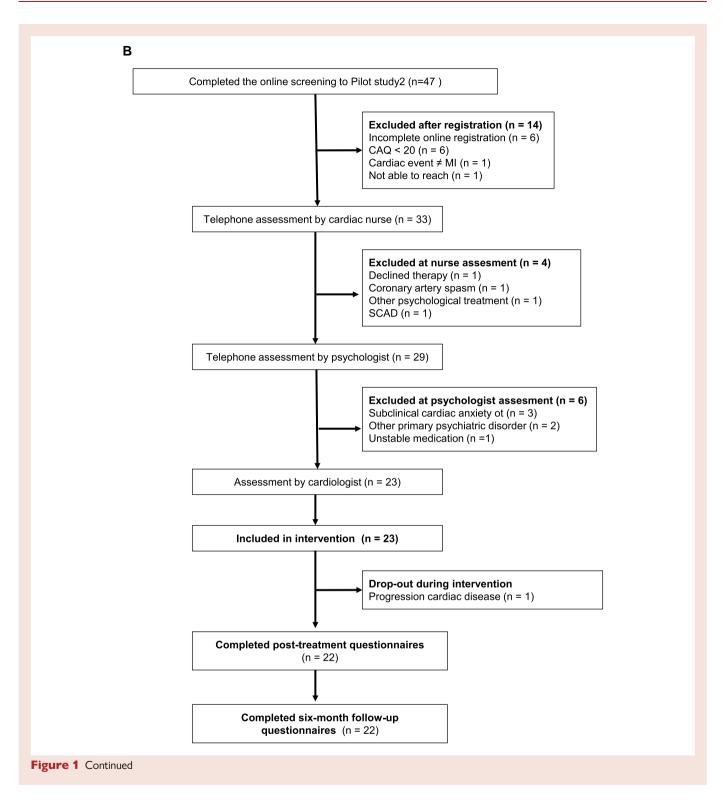
# Primary and secondary outcomes

Table 2 displays the estimated within-group mean changes. At posttreatment, compared with baseline, health-related QoL was significantly improved on both mental QoL (SF-12 MCS, P-value: < 0.001 for both studies) and physical QoL (SF-12 PCS, P-value: 0.036 for Pilot study 1, P-value: 0.008 for Pilot study 2). The improvements in mental QoL from baseline remained significant at the 6-month follow-up in both studies, whereas physical QoL (SF-12 PCS) was only significant in Pilot study 1 at the 6-month follow-up. We also observed a large and significant reduction in cardiac anxiety (CAQ) in both pilot studies (P-value: < 0.001 for both studies). These results were maintained at the 6-month followup. The results on the majority of outcome measures showed a consistent pattern. Fear of bodily symptoms (BSQ), depression (PHQ-9), general anxiety (GAD-7), and perceived stress (PSS-4) all, except PSS-4 in Pilot study 2, showed statistically significant improvement in estimated mean changes from baseline to post-treatment in both studies, although improvements in PSS-4 were not statistically significant at the 6-month follow-up in Pilot study 2. There were no significant effects on physical activity (GSLTPAQ) in either study. For effect size calculations, see Supplementary material online, *Table S1*.

# **Mediation analysis**

In Pilot study 1, we started with single-mediator analysis and retained significant mediators in a multiple mediator analysis. For the SF-12 MCS subscale as outcome, GSLTPAQ was not found to mediate change (data not shown) whereas both PSS-4 and CAQ were found to mediate change (data not shown) and were included in the multiple mediator analysis. In the multiple mediation analysis on SF-12 MCS, PSS-4 was still a significant mediator, ab = 0.86, 95% CI [0.52, 1.35], whereas CAQ was not a mediator, ab = 0.23, 95% CI [-0.24, 0.73].





For the SF-12 PCS subscale, neither GSLTPAQ nor PSS-4 where significant single mediators (data not shown) and we therefore only report the single mediator analysis with CAQ, which was statistically significant, ab = 1.15, 95% CI [0.50, 2.08].

In Pilot study 2, only CAQ was measured weekly together with SF-12 and therefore only single mediator analysis could be performed. Cardiac Anxiety Questionnaire was a significant mediator of change on both the SF-12 MCS subscale,  $ab=1.00,\,95\%$  CI [0.77, 1.24] and the SF-12 PCS subscale,  $ab=0.77,\,95\%$  CI [0.44, 1.36].

# Changes in cardiac health and medication

In Pilot study 1, one participant reported perceived worsening of cardiac symptoms in the post-treatment period (increased AF), while five participants (33%) reported perceived deterioration of cardiac symptoms at the 6-month follow-up assessment. In Pilot study 2, one participant reported a perceived worsening post-treatment (onset of AF), and four participants (17%) reported perceived deterioration of cardiac symptoms at the 6-month follow-up assessment. The reported

Table 2 Estimated between-group differences in mean change at post-treatment (8 wk) and at 6 months follow-up

Pilot study 1							
	Observed mean outcomes		Change from baseline to post-treatment		Change from baseline to 6-month follow-up		
Outcome	Baseline	Post-treatment	6-month follow-up	Mean change (95% CI)	P-value	Mean change (95% CI)	P-value
SF-12 PCS	40.3 ± 7.0	46.7 ± 11.8	$45.7 \pm 9.7$	6.4 (0.5 to 12.3)	0.036	6.5 (1.1 to 11.9)	0.021
SF-12 MCS	$39.3 \pm 8.2$	$50.9 \pm 10.2$	$49.5 \pm 10.7$	11.6 (6.1 to 17.1)	< 0.001	9.5 (2.3 to 16.7)	0.014
CAQ	$39.7 \pm 8.7$	19.8 ± 8.3	$21.8 \pm 7.6$	-19.9 (-24.9 to -15.0)	< 0.001	-18.6 (-24.0 to -13.3)	< 0.001
BSQ	$45.1 \pm 12.6$	$32.8 \pm 9.8$	$33.4 \pm 10.9$	-12.3 (-17.8 to -6.8)	< 0.001	-12.5 (-18.4 to -6.7)	< 0.001
TSK heart	$39 \pm 8.7$	$32.9 \pm 5.5$	$32.9 \pm 4.3$	-6.07 (-9.8 to -2.3)	0.004	-7.0 (-11.7 to -2.3)	0.007
PSS-4	$7.9 \pm 2.5$	$3.5 \pm 2.9$	$4.3 \pm 2.5$	-4.4 (-6.5 to -2.3)	< 0.001	−3.4 (−4.9 to −2.0)	< 0.001
GSLTPAQ	$56.4 \pm 38.9$	61.9 ± 44.7	$60.8 \pm 35.5$	5.5 (-17.0 to 28.1)	0.607	2.1 (-25.9 to 30.2)	0.872
GAD-7	$8.07 \pm 3.4$	3.1 ± 3.4	$3.2 \pm 3.6$	-4.9 (-7.1 to -2.7)	< 0.001	-4.7 (-6.7 to -2.7)	< 0.001
PHQ-9	$10.2 \pm 5.0$	$4.6 \pm 2.5$	$4.7 \pm 3.6$	-5.6 (-8.2 to -3.0)	< 0.001	-5.0 (-7.3 to -2.8)	<0.001

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	Observed mean outcomes			Change from baseline to post-treatment		Change from baseline to 6-month follow up	
Outcome	Baseline	Post-treatment	6-month follow-up	Mean change (95% CI)	P-value	Mean change (95% CI)	P-value
SF-12 PCS	44.5 ± 9.9	49.7 ± 8.9	$48.8 \pm 9.3$	4.8 (1.4 to 8.2)	0.008	3.9 (-0.5 to 8.3)	0.077
SF-12 MCS	41.4 ± 10.5	51.7 ± 8.6	$50.6 \pm 9.0$	9.7 (5.2 to 14.2)	< 0.001	0.8 (0.4 to 1.3)	< 0.001
CAQ	35.1 ± 9.1	15.6 ± 11.4	18.1 ± 11.4	-19.0 (-24.0 to -14.0)	< 0.001	-16.5 (-21.4 to -11.6)	< 0.001
BSQ	40.3 ± 11.2	$29.4 \pm 12.2$	$27.7 \pm 9.9$	-10.8 (-14.8 to -6.8)	< 0.001	-12.5 (-16.3 to -8.7)	< 0.001
TSK heart	$34.7 \pm 5.4$	$31.8 \pm 5.0$	$30.6 \pm 4.4$	-2.6 (-5.6 to 0.4)	0.087	−3.8 (−6.2 to −1.3)	0.004
PSS-4	$5.2 \pm 3.1$	$3.6 \pm 3.0$	$4 \pm 3.4$	-1.3 (-2.6 to -0.1)	0.039	-1.0 (-2.6 to 0.7)	0.231
GSLTPAQ	95.8 ± 177.5	$127.3 \pm 200.7$	$60.6 \pm 79.3$	28.6 (-9.5 to 86.8)	0.318	-38.1 (-103.1 to 26.8)	0.236
GAD-7	$8.8 \pm 5.5$	$2.6 \pm 3.2$	$2.7 \pm 2.9$	-6.0 (-8.3 to -3.7)	< 0.001	-6.0 (-8.5 to -3.4)	< 0.001
PHQ-9	$9.0 \pm 5.7$	$3.5 \pm 3.7$	$4.3 \pm 4.4$	−5.0 (−7.0 to −3.0)	< 0.001	-4.2 (-6.3 to -2.1)	< 0.001

**Note:** Raw scores are presented as mean ± SD. Estimated differences are presented with 95% confidence intervals.

CI, confidence interval; SF-12 PCS, Short-Form Health Survey SF-12 Physical Health Summary score; SF-12 MCS, Short-Form Health Survey Mental Health Summary score; CAQ, Cardiac Anxiety Questionnaire; BSQ, Body Sensation Questionnaire; TSK heart, Tampas Scale for Kinesiophobia Heart; PSS-4, Perceived Stress Scale-4; GSLTPAQ, The Godin Leisure-time Exercise Questionnaire, PHQ-9, Patient Health Questionnaire.

changes in cardiac health at 6-month follow-up in both studies included progression of AF, increase of cardiac-related symptoms, e.g. chest pains and shortness of breath. There were no invasive cardiac procedures, cardiac events, or recurrent MIs reported at post-treatment in either of the studies. At 6-month follow-up, one participant in Pilot study 1 reported having undergone an ablation due to AF, and one participant reported a recurrent MI. There were few changes in medication reported (See Supplementary material online, *Table* S2).

# **Discussion**

These two pilot studies evaluated a CBT protocol targeting cardiac anxiety following MI, with regards to the feasibility, acceptability, and the intervention's potential for reducing cardiac anxiety and improving QoL. The results suggest that the MI-CBT intervention, both in a face-to-face via video conference and through online CBT, is both feasible and acceptable. Both formats showed high participant retention, high completion rates and adherence to the treatment, satisfactory clinical safety, and overall satisfaction with the intervention. We

observed significant improvements, with similar results between face-to-face and online CBT, across multiple domains, including both mental and physical health-related QoL and cardiac anxiety. Similar patterns were noted for other outcomes, such as fear of bodily symptoms, symptoms of depression, and general anxiety. The treatment effects were largely sustained at the 6-month follow-up.

The results are consistent with our research group's previous studies on online exposure-based CBT for AF and premature ventricular extra beats, <sup>15,19,20,34</sup> as well as exposure-based CBT for other somatic conditions. <sup>27,35</sup> The results also align with other CBT studies targeting general anxiety and depression in patients with coronary heart disease. <sup>36–38</sup> Moreover, we now demonstrate that CBT focusing on exposure can be beneficial for patients experiencing anxiety following MI. The findings of these two pilot studies suggest that addressing cardiac anxiety could be a pathway in mitigating the psychological aftermath following an MI. The mediation analyses suggested that reduced cardiac anxiety was associated with increased physical QoL in both studies. In Pilot study 1, perceived stress was a dominant mediator of change in mental QoL compared to cardiac anxiety, which was a somewhat

unexpected result. This result could not be replicated in Pilot study 2 because PSS-4 was not included among the weekly measurements. It is possible that cardiac anxiety has a more pronounced effect on physical limitation, whereas the exposure treatment may have improved patients' sense of being able to cope with daily stressors, which in turn improved their general mental health. Importantly, Pilot study 2 suggests that the internet-based format appears viable for the target population, although the results need to be replicated in a larger trial. This approach may offer a cost-effective and scalable intervention, <sup>34</sup> as indicated in our previous study on exposure-based CBT for AF, minimal therapeutic time was required, and a reduction in AF-specific healthcare seeking was observed. <sup>15</sup>

Strengths of the studies include the interdisciplinary collaboration, with comprehensive psychological and cardiac assessments conducted before enrolment, as well as supervision by a nurse and cardiologist during treatment. These measures ensured patient safety and that participants were able to fully engage in exposure strategies during treatment. Exposure-based approaches are often underused in psychological treatment, <sup>39</sup> potentially more so in cardiac patients due to patient-safety concerns. This interdisciplinary collaboration is both valuable and pivotal, serving as a pilot for a method of delivering exposure-based CBT to patients following MI. Other strengths include that the samples in both studies were broadly similar to the general MI population in key baseline characteristics such as sex (60–70% male participants), BMI (indicating overweight), 40 and around 20-40% of participants reporting depression and other anxiety.<sup>2</sup> This similarity enhances the potential generalizability of the findings to the broader population of MI patients. However, the primary outcome measure, SF-12, serves as a general assessment of health-related quality of life and may have been too broad to effectively evaluate QoL in this specific target group. Therefore, future studies should consider using a diseasespecific QoL measure to more directly assess cardiac-related aspects.

There are several limitations that need to be considered. As uncontrolled pilot studies, the results we observed are based on within-group comparisons, which limit internal validity compared to a randomized between-group design. Causality cannot be inferred, and the outcomes may have been influenced by external factors such as the passage of time, caregiver attention, or participants' expectations of improvement. The studies were limited by small sample sizes, making it difficult to draw broad conclusions, and the mediation analysis was further constrained by the use of different mediators in each study. In addition, simultaneous participantion in cardiac rehabilitation (one participant in Pilot study 1 and two participants in Pilot study 2) could potentially have influenced the outcomes. Future studies should explore how CBT and cardiac rehabilitation interact and influence each other's effects.

# **Conclusions**

The studies show that exposure-based CBT targeting cardiac anxiety post-MI was both feasible and acceptable. The findings suggest that addressing cardiac anxiety may be a promising approach in alleviating psychological distress and improving quality of life following an MI. However, additional research and a larger randomized controlled are necessary to validate these findings and further explore the impact of intervening on cardiac anxiety in post-MI recovery.

# Data availability

The datasets generated and analysed in this study are not publicly available due to the inclusion of sensitive patient information, which is protected under the General Data Protection Regulation (GDPR).

# Supplementary material

Supplementary material is available at European Heart Journal Open online.

# **Authors' contribution**

A.J.: Writing original draft and revising the manuscript, data curation, formal analysis and interpretation of data. B.L.: Study conceptualization, treating psychologist in Pilot study 1, data collection, formal analysis and interpretation of data, writing and revising the manuscript, resources and funding. B.E.L.: Treating psychologist in Pilot study 1, data collection, review and editing of the manuscript. H.S.: Study cardiologist in Pilot study 1, data collection, review and editing of the manuscript. L.M.: Treating psychologist in Pilot study 2, data collection and curation, review and editing of the manuscript. I.B.: Treating psychologist in Pilot study 2, data collection, review and editing of the manuscript. E.Ó.: Study nurse in Pilot study 1 and 2, supervising nurse, data collection, review and editing of the manuscript. S.K.: Study cardiologist in Pilot study 2, data collection, review and editing of the manuscript. F.B.: Supervising study cardiologist in Pilot study 1, study conceptualization, review and editing of the manuscript. L.G.M.: Supervising study cardiologist in Pilot study 2, study conceptualization, review and editing of the manuscript. I.S.: Study conceptualization, treatment development and adaptation, supervising psychologist, treating psychologist, data collection, formal analysis and interpretation of data, writing original draft and revising the manuscript.

# **Acknowledgements**

The authors would like to thank the participants in the study.

# Funding

This study was supported by a Research and Development Grant from Karolinska University Hospital, Stockholm Sweden. The funding body had no involvement in the design of the study, data analysis, or interpretation of the results.

**Conflict of interest:** F.B. declares personal fees for trial committee participation and lectures by Medtronic, Biotronik, Biosense Webster, Impulse Dynamics, Novartis, Orion, Boehringer and Pfizer. H.S. declares lecture fees from Novo Nordisk and Astra Zeneca. B.L. has co-authored a Swedish self-help book on exposure-based cognitive behaviour therapy for health anxiety and owns the rights to a self-help manual for irritable bowel syndrome, not currently published. L.G.M. declares lectures, consulting and clinical trials fees to her institution from Amarin, Amgen, Astra Zeneca, Bayer AG, Boehringer-Ingelheim Janssen, Novartis, NovoNordisk, Sanofi. No other disclosures were reported.

#### References

- 1. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, Barengo NC, Beaton AZ, Benjamin EJ, Benziger CP, Bonny A, Brauer M, Brodmann M, Cahill TJ, Carapetis J, Catapano AL, Chugh SS, Cooper LT, Coresh J, Criqui M, DeCleene N, Eagle KA, Emmons-Bell S, Feigin VL, Fernández-Solà J, Fowkes G, Gakidou E, Grundy SM, He FJ, Howard G, Hu F, Inker L, Karthikeyan G, Kassebaum N, Koroshetz W, Lavie C, Lloyd-Jones D, Lu HS, Mirijello A, Temesgen AM, Mokdad A, Moran AE, Muntner P, Narula J, Neal B, Ntsekhe M, Moraes de Oliveira G, Otto C, Owolabi M, Pratt M, Rajagopalan S, Reitsma M, Ribeiro ALP, Rigotti N, Rodgers A, Sable C, Shakil S, Sliwa-Hahnle K, Stark B, Sundström J, Timpel P, Tleyjeh IM, Valgimigli M, Vos T, Whelton PK, Yacoub M, Zuhlke L, Murray C, Fuster V. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. J Am Coll Cardiol 2020; 76:2982–3021.
- Karami N, Kazeminia M, Karami A, Salimi Y, Ziapour A, Janjani P. Global prevalence of depression, anxiety, and stress in cardiac patients: a systematic review and meta-analysis. Affect Disord 2023;324:175–189.
- Hohls JK, Beer K, Arolt V, Haverkamp W, Kuhlmann SL, Martus P, Waltenberger J, Rieckmann N, Müller-Nordhorn J, Ströhle A. Association between heart-focused anxiety, depressive symptoms, health behaviors and healthcare utilization in patients with coronary heart disease. J Psychosom Res 2020;131:109958.
- Flygare O, Boberg J, Rück C, Hofmann R, Leosdottir M, Mataix-Cols D, de la Cruz LF, Richman P, Wallert J. Association of anxiety or depression with risk of recurrent cardiovascular events and death after myocardial infarction: a nationwide registry study. *Int J Cardiol* 2023;381:120–127.

- Van Beek MHCT, Zuidersma M, Lappenschaar M, Pop G, Roest AM, Van Balkom AJLM, Speckens AEM, Oude Voshaar RC. Prognostic association of cardiac anxiety with new cardiac events and mortality following myocardial infarction. Br J Psychiatry 2016;209: 400–406
- Levine GN, Cohen BE, Commodore-Mensah Y, Fleury J, Huffman JC, Khalid U, Labarthe DR, Lavretsky H, Michos ED, Spatz ES, Kubzansky LD. Psychological health, well-being, and the mind-heart-body connection: a scientific statement from the American Heart Association. Circulation 2021;143:e763–e783.
- Rao A, Zecchin R, Newton P, Phillips J, DiGiacomo M, Denniss A, Hickman LD. The prevalence and impact of depression and anxiety in cardiac rehabilitation: a longitudinal cohort study. Eur J Prev Cardiol 2020;27:478

  –489.
- Leissner P, Held C, Humphries S, Rondung E, Olsson EMG. Association of anxiety and recurrent cardiovascular events: investigating different aspects of anxiety. Eur J Cardiovasc Nurs 2024;23:720–727.
- van Beek MHCT, Mingels M, Voshaar RCO, van Balkom AJLM, Lappenschaar M, Pop G, Speckens AEM. One-year follow up of cardiac anxiety after a myocardial infarction: a latent class analysis. J Psychosom Res 2012;73:362–368.
- Eifert GH, Zvolensky MJ, Lejuez CW. Heart-focused anxiety and chest pain: a conceptual and clinical review. Clin Psychol (New York) 2000;7:403

  –417.
- 11. Szuhany KL, Simon NM. Anxiety disorders: a review. JAMA 2022;328:2431–2445.
- Österman S, Axelsson E, Forsell E, Svanborg C, Lindefors N, Hedman-Lagerlöf E, Ivanov VZ. Effectiveness and prediction of treatment adherence to guided internet-based cognitive behavioral therapy for health anxiety: a cohort study in routine psychiatric care. *Internet Interv* 2024;38:100780.
- 13. Craske MG, Treanor M, Conway CC, Zbozinek T, Vervliet B. Maximizing exposure therapy: an inhibitory learning approach. *Behav Res Ther* 2014;**58**:10–23.
- Axelsson E, Kern D, Hedman-Lagerlöf E, Lindfors P, Palmgren J, Hesser H, Andersson E, Johansson R, Olén O, Bonnert M, Lalouni M, Ljótsson B. Psychological treatments for irritable bowel syndrome: a comprehensive systematic review and meta-analysis. Cogn Behav Ther 2023;52:565–584.
- Särnholm J, Skúladóttir H, Rück C, Axelsson E, Bonnert M, Bragesjö M, Venkateshvaran A, Ólafsdóttir E, Pedersen SS, Ljótsson B, Braunschweig F. Cognitive behavioral therapy improves quality of life in patients with symptomatic paroxysmal atrial fibrillation. J Am Coll Cardiol 2023;82:46–56.
- 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;47:1–18.
- Li YN, Buys N, Ferguson S, Li ZJ, Sun J. Effectiveness of cognitive behavioral therapybased interventions on health outcomes in patients with coronary heart disease: a meta-analysis. World J Psychiatry 2021;11:1147–1166.
- Magán I, Jurado-Barba R, Casado L, Barnum H, Jeon A, Hernandez AV, Bueno H. Efficacy of psychological interventions on clinical outcomes of coronary artery disease: systematic review and meta-analysis. J Psychosom Res 2022;153:110710.
- Särnholm J, Skúladóttir H, Rück C, Klavebäck S, Ólafsdóttir E, Pedersen SS, Braunschweig F, Ljótsson B. Internet-delivered exposure-based therapy for symptom preoccupation in atrial fibrillation: uncontrolled pilot trial. JMIR cardio 2021; 5:e24524.
- Särnholm J, Skúladóttir H, Rück C, Pedersen SS, Braunschweig F, Ljótsson B. Exposure-based therapy for symptom preoccupation in atrial fibrillation: an uncontrolled pilot study. *Behav Ther* 2017;48:808–819.
- Eifert GH, Thompson RN, Zvolensky MJ, Edwards K, Frazer NL, Haddad JW, Davig J.
  The cardiac anxiety questionnaire: development and preliminary validity. Behav Res
  Ther 2000;38:1039–1053.
- 22. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimsky P. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2017;39:119–177.
- Saunders JB, Aasland OG, Babor TF, De la Fuente JR, Grant M. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. Addiction 1993;88: 791–804
- Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;16:606–613.
- Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, Claeys MJ, Dan G-A, Dweck MR, Galbraith M, Gilard M, Hinterbuchner L, Jankowska EA, Jüni P, Kimura T, Kunadian V, Leosdottir M, Lorusso R, Pedretti RFE, Rigopoulos AG, Rubini Gimenez M, Thiele H, Vranckx P, Wassmann S, Wenger NK, Ibanez B, Halvorsen S, James S, Abdelhamid M, Aboyans V, Marsan NA, Antoniou S, Asteggiano R, Bäck M, Capodanno D, Casado-Arroyo R, Cassese S, Čelutkienė J, Cikes M, Collet J-P,

- Ducrocq G, Falk V, Fauchier L, Geisler T, Gorog DA, Holmvang L, Jaarsma T, Jones HW, Køber L, Koskinas KC, Kotecha D, Krychtiuk KA, Landmesser U, Lazaros G, Lewis BS, Lindahl B, Linhart A, Løchen M-L, Mamas MA, McEvoy JW, Mihaylova B, Mindham R, Mueller C, Neubeck L, Niebauer J, Nielsen JC, Niessner A, Paradies V, Pasquet AA, Petersen SE, Prescott E, Rakisheva A, Rocca B, Rosano GMC, Sade LE, Schiele F, Siller-Matula JM, Sticherling C, Storey RF, Thielmann M, Vrints C, Windecker S, Wiseth R, Witkowski A, El Amine Bouzid M, Hayrapetyan H, Metzler B, Lancellotti P, Bajrić M, Karamfiloff K, Mitsis A, Ostadal P, Sørensen R, Elwasify T, Marandi T, Ryödi E, Collet J-P, Chukhrukidze A, Mehilli J, Davlouros P, Becker D, Guðmundsdóttir II, Crowley I, Abramowitz Y, Indolfi C, Sakhov O, Elezi S, Beishenkulov M, Erglis A, Moussallem N, Benlamin H, Dobilienė O, Degrell P, Balbi MM, Grosu A, Lakhal Z, ten Berg J, Pejkov H, Angel K, Witkowski A, De Sousa Almeida M. Chioncel O. Bertelli L. Stoikovic S. Studenčan M. Radšel P. Ferreiro IL. Ravn-Fischer A, Räber L, Marjeh MYB, Hassine M, Yildirir A, Parkhomenko A, Banning AP, Prescott E, James S, Arbelo E, Baigent C, Borger MA, Buccheri S, Ibanez B, Køber L, Koskinas KC, McEvoy JW, Mihaylova B, Mindham R, Neubeck L, Nielsen JC, Pasquet AA, Rakisheva A, Rocca B, Rossello X, Vaartjes I, Vrints C, Witkowski A, Zeppenfeld K. 2023 ESC guidelines for the management of acute coronary syndromes: developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC). Eur Heart | 2023;44: 3720-3826.
- Attkisson CC, Zwick R. The client satisfaction questionnaire: psychometric properties and correlations with service utilization and psychotherapy outcome. Eval Program Plann 1982:5:233–237.
- 27. Ljótsson B, Hesser H, Andersson E, Lackner JM, El Alaoui S, Falk L, Aspvall K, Fransson J, Hammarlund K, Löfström A, Nowinski S, Lindfors P, Hedman E. Provoking symptoms to relieve symptoms: a randomized controlled dismantling study of exposure therapy in irritable bowel syndrome. Behav Res Ther 2014;55:27–39.
- Gandhi SK, Salmon JW, Zhao SZ, Lambert BL, Gore PR, Conrad K. Psychometric evaluation of the 12-item short-form health survey (SF-12) in osteoarthritis and rheumatoid arthritis clinical trials. Clin Ther 2001;23:1080–1098.
- 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;52:1090–1097.
- Amireault S, Godin G. The godin-shephard leisure-time physical activity questionnaire: validity evidence supporting its use for classifying healthy adults into active and insufficiently active categories. Percept Mot Skills 2015;120:604–622.
- Bäck M, Jansson B, Cider Å, Herlitz J, Lundberg M. Validation of a questionnaire to detect kinesiophobia (fear of movement) in patients with coronary artery disease. J Rehabil Med 2012;44:363–369.
- 32. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006;166:1092–1097.
- Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav 1983;24:385–396.
- Liliequist BE, Särnholm J, Skúladóttir H, Ólafsdóttir E, Ljótsson B, Braunschweig F. Cognitive behavioral therapy for symptom preoccupation among patients with premature ventricular contractions: nonrandomized pretest-posttest study. JMIR Cardio 2024; 8:e53815.
- 35. Hedman-Lagerlöf M, Gasslander N, Ahnlund Hoffmann A, Bragesjö M, Etzell A, Ezra S, Frostell E, Hedman-Lagerlöf E, Ivert C, Liliequist B, Ljótsson B, Hoppe JM, Palmgren J, Spansk E, Sundström F, Särnholm J, Tzavara G, Buhrman M, Axelsson E. Effect of exposure-based vs traditional cognitive behavior therapy for fibromyalgia: a two-site single-blind randomized controlled trial. PAIN 2024; 165:1278–1288.
- Gulliksson M, Burell G, Vessby B, Lundin L, Toss H, Svärdsudd K. Randomized controlled trial of cognitive behavioral therapy vs standard treatment to prevent recurrent cardiovascular events in patients with coronary heart disease: secondary prevention in Uppsala primary health care project (SUPRIM). Arch Intern Med 2011; 171:134–140.
- Schneider LH, Hadjistavropoulos H, Dear B, Titov N. Efficacy of internet-delivered cognitive behavioural therapy following an acute coronary event: a randomized controlled trial. Internet Interv 2020;21:100324.
- Norlund F, Wallin E, Olsson EMG, Wallert J, Burell G, von Essen L, Held C. Internet-based cognitive behavioral therapy for symptoms of depression and anxiety among patients with a recent myocardial infarction: the U-CARE heart randomized controlled trial. J Med Internet Res 2018;20:e88.
- Hamlett GE, Foa EB, Brown LA. Exposure therapy and its mechanisms. Curr Top Behav Neurosci 2023;64:273–288.
- SWEDEHEART, Vasko P, Alfredsson J, Bäck M, Erlinge D, Ernkvist M, Friberg Ö, Hagström E, Hultqvist H, Settergren M, Svensson A. SWEDEHEART annual report 2023. https://www.ucr.uu.se/swedeheart/dokument-sh/arsrapporter-sh SWEDEHEART; 2024, May. 293p.