

Study Protocol

**Internet based cognitive behavioural therapy for
depression in patients with Cardiovascular disease - The
DOHART Study**

Abstract

In patients with cardiovascular disease (CVD), depression is a common cause of decreased wellbeing, and increased morbidity and mortality. The World Health Organisation has found that treatment programs focusing depressive symptoms for patients with somatic illnesses are lacking and recommends that healthcare organisations prioritise the development and implementation of such programs. However generic depression programs may not be optimal for patients with chronic diseases since such programs are not adapted to the context of the disease. Tailored internet-based cognitive behavioural therapy (I-CBT) is a new innovative and person-centred method that may be used to decrease depressive symptoms, but has not yet been implemented in the clinical care of patients with CVD.

The main purpose of this study is therefore to evaluate the effects a tailored nine week I-CBT program on reducing depressive symptoms and other patient reported outcomes in patients with CVD and to explore factors related to implementation of the I-CBT program in clinical cardiac care.

A randomised controlled study will be performed aimed to evaluate the short- and long-term effects the nine-week I-CBT program on depressive symptoms in CVD patients. Qualitative methods will be used to evaluate the effectiveness of the I-CBT program to reduce depressive symptoms. Quantitative and qualitative methods will be used to explore factors that, among CVD patients, healthcare personnel and policymakers can act as barriers or facilitators to the implementation of I-CBT in the clinical care of patients with CVD.

In Sweden there are approximately 1.4 million CVD patients and of these 20-40 % (i.e. between 280.000 and 580.000 patients) have depressive symptoms. Thus, this study will have a large impact and is expected to contribute on the quality of care. If found effective, I-CBT can be implemented in cardiac care and be provided to a large number of patients at a low cost, who at present might not have an adequate treatment for depressive symptoms.

Purpose and aims

Tailored internet-based cognitive behavioural therapy (I-CBT) is a new innovative and person-centred method that is promising that may be used to decrease depression in CVD patients. In patients with cardiovascular disease (CVD), depressive symptoms is a common co-morbidity leading to decreased wellbeing, and increased morbidity and mortality. Depressive symptoms are both underdiagnosed and undertreated in CVD patients. Earlier studies have demonstrated the efficiency of cognitive behavioural therapy (CBT) for many psychiatric conditions, but few studies have evaluated CBT in patients with CVD.

The purpose of this study is to evaluate the effects of the tailored I-CBT program on reducing depressive symptoms and other patient reported outcomes in patients with cardiovascular disease (CVD) and to explore factors related to implementation of the I-CBT program in clinical cardiac care.

Aims of the study

- To evaluate the effects of the tailored I-CBT depression program on depressive symptoms, sleep, anxiety and quality of life.
- To evaluate factors that can influence the I-CBT programs effect on depressive symptoms.
- To gain knowledge about the I-CBT program, as perceived by patients and health care professionals.
- To explore facilitators and barriers to the implementation of the I-CBT program in clinical practice from the perspectives of patients, health care professionals and policymakers.

Survey of the field

Background: The World Health Organisation (WHO) has estimated that CVD and depressive symptoms will in the near future become the two most common causes of disability.¹ Depressive symptoms, according to the WHO, produces greater decrements in health than other chronic physical diseases and a comorbid depression significantly worsens the health of patients with such diseases.²

In Europe, CVD is the major cause of hospital discharges and accounts for 43% of all deaths at all ages (i.e., > 4 million deaths annually).³ Depressive symptoms is highly prevalent in patients with CVD (20%–40%)⁴ and it significantly worsens the health of CVD patients. Depressed CVD patients experience poorer quality of life,⁵ more frequent rehospitalisation,⁶ higher healthcare costs and a shorter life expectancy than CVD patients without depression.⁶ Both biological and behavioural mechanisms can explain the negative effects of depressive symptoms in CVD. With regard to the biological mechanisms, our own and other studies have shown that depressive symptoms increases plasma levels of stress hormones and inflammatory activity, which may speed up the progression of atherosclerosis and impairment of cardiac function.^{4,7} Regarding behaviour, depressive symptoms can influence non-adherence to medication, development of a sedentary lifestyle and poorer self-care performance.^{4,8}

The WHO states that our ‘traditional care approaches’ such as primary care centres or outpatient clinics do not offer enough support or treatment to patients with a chronic disease and depressive symptoms, such as those with CVD.² The WHO emphasises that the implementation of interventions targeting depression in healthcare should thus be prioritised.² In line with this recommendation, our proposed study will contribute to the development,

feasibility testing, and evaluation of the effectiveness of an internet-based cognitive behavioural therapy treatment program (I-CBT) aimed at treating depressive symptoms in CVD patients.

Rationale for the intervention: Why should CBT be chosen for this purpose? Antidepressant medication seem to have limited effect on depressive symptoms in CVD patients.⁴ Furthermore, adding anti-depressant to the existing complex medical treatment for CVD may be perceived as burdensome and also increase the risk of developing side effects. CVD patients with depression prefer ‘talking’ therapies.⁹ There are other psychotherapies, but rarely, if ever, do they result in better outcomes than CBT.¹⁰ However, earlier studies of CBT in CVD patients’ only reports small effects on depressive symptoms. One probable reason is that most studies only used a single CBT component, such as psychoeducation alone, problem-solving therapy alone, relaxation alone or behavioural activation alone.¹¹ A program that combines different CBT components has been suggested to improve treatment efficacy.¹² Moreover, generic CBT programs may not be optimal for targeting depression in patients with chronic diseases since these programs are not adapted to the context of the disease,¹³ for example, by acknowledging the association between CVD and depression. We therefore believe that a CBT program that (I) includes different CBT components and (II) tailored to fit the context of CVD has the potential to improve the effect of CBT on depressive symptoms. This might also prevent the progression of CVD as well as improve quality of life and survival.

Implementation: There are three main barriers to the implementation of CBT in current CVD care. One is a shortage of personnel who can perform face-to-face treatment (a therapist meeting with a patient). A second barrier is a shortage of time.¹⁴ An approach that may overcome these barriers of implementation of CBT in clinical practice is its provision over the internet (I-CBT). I-CBT has proved to be effective in patients with depression.¹⁵ A major advantage is that I-CBT, compared with face-to-face CBT, can be provided to a large number of patients at a low cost.¹⁴ A second advantage is that healthcare personnel with only brief training in CBT can perform I-CBT with good treatment results.¹⁴ Another advantage of I-CBT is that, via the internet, patients can access CBT in their own homes and at a time that is suitable to them; thus, they do not need to travel to healthcare centres. These qualities suggest that I-CBT could be a promising method suitable for implementation in clinical cardiac care. A third barrier is patients and providers acceptability of the I-CBT program.¹⁶ We therefore will perform studies that explore patients, health-care personnel and policymakers’ perceptions of the I-CBT program and its content as well as perceptions on how to provide and receive care by the internet. This will add valuable knowledge that will contribute to further improvements of the I-CBT program as well as to gain knowledge of factors that can act as barriers or facilitators for implementation of I-CBT programs in clinical practice.

To summarize the state of the science no studies have developed and tested I-CBT programs for depressive symptoms in patients with CVD. Moreover, no studies have explored facilitators and barriers to the implementation of I-CBT as perceived by important stakeholders (i.e., CVD patients, healthcare professionals, decision-makers). Such knowledge is crucial for promoting the implementation of I-CBT programs in clinical cardiac care. We therefore aimed to evaluate the effects of the tailored I-CBT program on reducing depressive symptoms in patients with cardiovascular disease and other patient reported outcomes (CVD) and to explore factors related to implementation of the I-CBT program in clinical cardiac care.

Project description

The study has the following research questions:

- What are the short- (nine weeks) and long-term (six and twelve months) effects of a nine-week I-CBT program on depressive symptoms, anxiety, sleep and quality of life in patients with CVD and depressive symptoms.
- How does characteristics of the patient, anxiety, sleeping problems and quality of life at baseline influence the short- and long-term outcomes of the nine-week I-CBT program in patients with CVD and depressive symptoms?
- What are the patients' perceptions of participating in the nine-week I-CBT program, as well as their perceptions of the content in the CBT program?
- What are the healthcare professionals' and policymakers perceptions of delivering CBT via the internet and what are the factors healthcare professionals believe need be improved before I-CBT program can be implemented in daily care.

Methods

Design of the study

Both quantitative and qualitative methods will be used to answer the research questions. The effects of the I-CBT program will be evaluated in a randomised controlled study (RCT). Issues related to implementation of the I-CBT program will be evaluated from the perspectives of patients, health care professionals and policymakers.

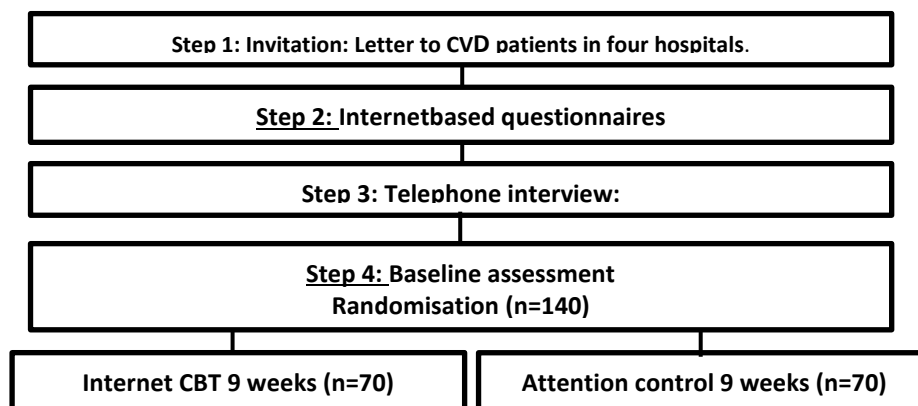
1. RCT

Enrolment of study participants in the RCT

For the RCT study, 140 patients will be recruited. Enrolment of the patients will be performed in four steps (Figure 1).

Power calculation: A recent published meta-analysis¹⁵ of studies evaluating the effect of internet based CBT on depression, that will be the primary outcome in the study, reported the effect size in studies including patients with depression to vary between 0.56-1.26 (mean 0.89), the mean number of patients in these studies was 107. Own power calculation: Effect size=0.5, alpha=0.05 (Z=1.96), Power 0.80 (Z -0.84) = 122 participants. Due to drop-outs or deaths the size of the study population for the RCT study was decided to n=140.

Figure 1. Description of the enrolment and randomisation of study participants



Step 1. Screening for participants. All CVD patients who received care at the department of cardiology the last 12 months in four hospitals in southeast of Sweden will be contacted by a letter with information about the study. Approximately 20% of CVD outpatients are depressed. Of these, we estimate that 50%-75% will not accept participation or do not have computer and/or access to internet. To be able to enrol 140 patients, we estimate that approximately 2500 patients will be needed to be contacted by a letter.

Step 2. Patients interested in participating will be requested to visit our website (www.heading-cbt.se) for more information, registration and the provision of informed consent. After registration, the participants will respond to questions on the website (see figure 1). Inclusion or exclusion will be assessed by a board consisting of a cardiologist, a psychologist, a cardiology nurse specialists and a psychiatric nurse specialist.

Inclusion

- age > 18 years
- treatment for CVD according to European Society of Cardiology guidelines
- stable CVD (NYHA class I–III) and not having been hospitalised for CVD in the last four weeks.
- depressive symptoms (Patient Health Questionnaire-9¹⁷ (PHQ-9) > 5 points)

Exclusion

- severe CVD (NYHA IV) or another severe chronic life-threatening disease
- severe depression assessed as requiring acute treatment
- not being able to dedicate 3-4 hours to participate in the program

Step 3. Before final inclusion and randomisation, eligible participants will be contacted for a telephone interview held by the psychiatric nurse specialist. Mini International Neuropsychiatric Interview (MINI) will be used to assess depression at this stage.

Step 4 Included (n=140) patients will, on our website (www.heading-cbt.se) complete the baseline study questionnaires and then be randomised to nine weeks of internet-based CBT (n=70) or nine weeks in an attention control group (n=70) where the patients will participate in an internet based discussion group. As suggested by the ethical committee, those in the attention-control group will be offered I-CBT treatment after the termination of the study.

Theoretical underpinning for the CBT intervention

According to CBT theory¹⁸, depression arises from negative thoughts, emotions and behaviours that can be activated as a response to stressful life events, such as the development of CVD. Figure 2 shows a CBT model, inspired by Moorey¹⁹ of how CVD can cause depression. The inner circle of the model describes perceived losses, threats and stressful symptoms caused by CVD. This activate negative thoughts, emotions and behaviours, thus a process leading to development of depression (the outer circle). In the model, a vicious circle can be seen since the negative thoughts, emotions and behaviours in turn can worsen patients' perceived stress of CVD and thus both worsen depressive symptoms and CVD.

Intervention: With CBT the patients become active participants and perform exercises that enable them to become aware of, modify, as well as learn skills to cope with negative thoughts and unhelpful behaviours, which contributes to decrease negative emotions.¹⁸ CBT can help CVD patients to break the vicious circle. The nine-week tailored I-CBT program consists of the components of psychoeducation, relaxation, problem-solving and behavioural activation. Table 1 describes the I-CBT program and Figure 2 describes how the four components in the I-CBT will work to decrease depression. CBT usually includes some form of homework. Specifically, just seeing a therapist is insufficient, and change must be implemented in real life, which is achieved by collaborating with the patient and prescribing

homework. The present I-CBT program thus also has homework assignments (Table 1) and the patients are provided with weekly feedback on them by a nurse specialising in mental health care who is supported by a psychologist and can consult with a cardiologist as well as a specialist cardiac nurse. Feedback is delivered in writing and focuses on positive aspects of the patient's progress; support is also provided to help the patients proceed with the program.

Figure 2. A CBT model describing how CVD can cause depression. The figure also describes how the 4 components in the I-CBT program (1) psychoeducation, (2) problem solving, (3) behavioural activation and (4) relaxation can help to decrease depression by modification of negative thoughts, behaviours and emotions.

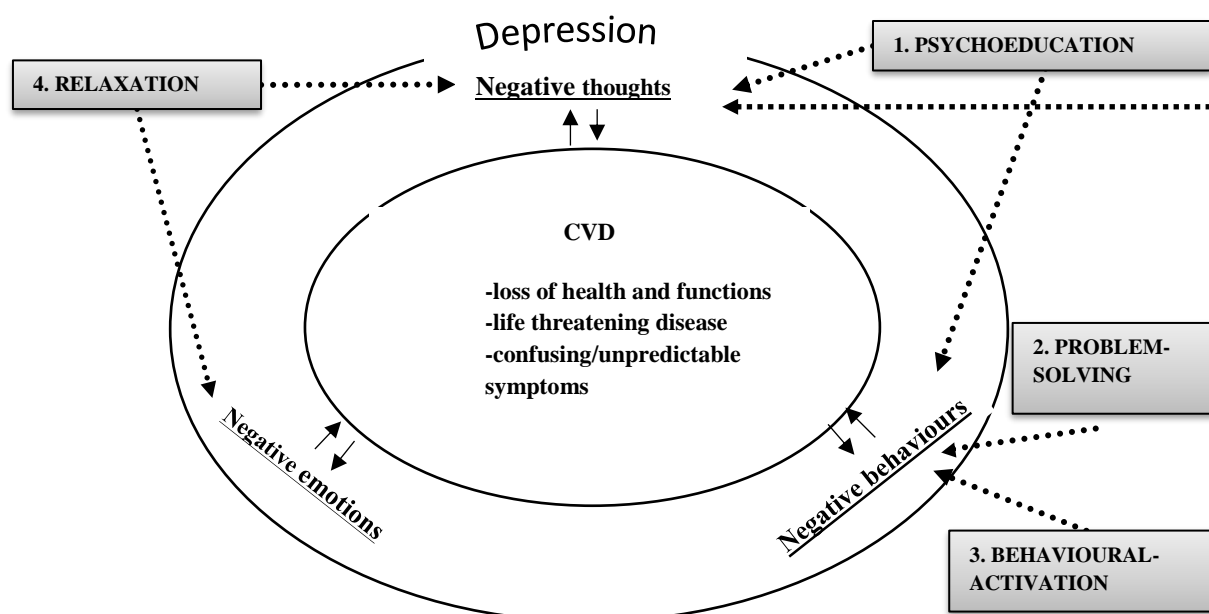


Table 1. A brief overview of the I-CBT program

CBT component/Content	Aim	Homework
Week 1: Psychoeducation Introduction	Inform and engage the participant. Goal setting.	Identify values and set up goals for the participation in the program
Week 2: Psychoeducation Living with CVD	To understand what CVD is and its impact on life.	Self-assessment of CVD symptoms. Identification of situations when symptoms occurs. Propose coping strategies.
Week 3 Psychoeducation Depression and CVD	To understand what depression is and its link to CVD.	Identify symptoms of depression, fear and worries Identify situations when symptoms affects the participant.
Week 3: Relaxation	To learn relaxation	Practice relaxation continuously during the CBT program.
Week 4 and 5: Behavioural activation	To identify behaviours that have negative and positive impacts on wellbeing.	Mapping activities in a week schedule. Making a list of desirable activities. Planning and implementing new activities
Week 6 and 7: Behavioural activation	To reduce negative behaviours and increase positive ones.	Eliminate or reduce negative activities. Increase number of positive activities.
Week 8: Problem-solving	To identify perceived problems. To solve or cope with a problem.	Practicing problem solving in accordance to the problem solving tool
Week 9: Final module	Learn strategies to maintain the changes achieved.	Set up a personal strategy that can be used if depressive symptoms re-occur.

Measurements to evaluate the RCT

The PHQ-9¹⁷ will be used to measure the primary outcome (i.e. depressive symptoms). The PHQ-9 is a valid and frequently used depression questionnaire. To detect depression a sensitivity of 88% and a specificity of 88% has been reported in primary care patients²⁰ whereas a sensitivity and specificity of 70 %r respectively 92% has been reported in patients with CVD.²¹ Table 2 gives an overview of the primary and secondary outcomes and the timing for measurements in the RCT.

Table 2. The different measurements and the timing for measurements in the study.

	Questionnaires	<u>Baseline</u>	<u>Post-CBT</u> 9 weeks, 6 and 12 months
<u>Primary outcome</u>			
Depressive symptoms	Patient Health Questionnaire-9 ¹⁷	X	X
<u>Secondary outcomes</u>			
Sleep	Insomnia Severity Index ²²	X	X
Anxiety	Cardiac Anxiety Questionnaire ²³	X	X
Quality of life	Short Form-12 ²⁴ Euro-QoL-5D ²⁵	X X	X X

Analysis of data collected in the RCT

Repeated measurement statistics, i.e. a two-way ANOVA with group (I-CBT and attention control) and follow-up (baseline and 9 weeks, 6 and 12 months) will be used to evaluate the short-term and long-term effects of the I-CBT program on depressive symptoms, anxiety, sleeping problems and quality of life. Multivariate statistics will be used to explore how characteristics of the patient, anxiety, sleeping problems and quality of life measured at baseline can impact prospective changes in depressive symptoms.

2. Implementation issues

Design of studies specifically investigating the implementation of the I-CBT program

1. **Patient experiences:** Aim to explore their perceptions of participating in the nine-week I-CBT program, as well as their perceptions of the content in the CBT program further. Semi structured interviews with 20 patients will be performed after the 12 months follow up and analysed with qualitative content analysis.²⁶ Strategically sampling, based on age and gender, variation in the primary outcome (i.e., depression) will be used to achieve maximum variations regarding perceptions. Patients' acceptability of the I-CBT program is pivotal for implementation in clinical care. The results from this study will add important knowledge on how to further improve and adapt the I-CBT program to fit the preferences of the CVD patients, and thus facilitate implementation of the I-CBT program.
2. **Perceptions of health-care personnel:** Aim to explore to perceptions of delivering I-CBT and factors need to be improved before an I-CBT program can be implemented in daily care. Semi structured interviews with 20 health care professionals (i.e., physicians, physiotherapists, nurses, and enrolled nurses) working with CVD patients at the four participating hospitals will be included. Strategically sampling, based on age, gender,

profession, years in the profession will be used to achieve maximum variations regarding perceptions. Interviews will be analysed with qualitative content analysis.²⁶ This study explores the acceptability of the CBT-program from the perspective of health-care personnel. This will gain knowledge of needs among health-care personnel when planning implementation of the I-CBT program into the routine cardiac care treatment.

3. **Policymakers opinions:** Aim to explore, factors that can act as facilitators and/or barriers for implementing of an I-CBT program into daily care, will be studied by using the critical incident technique.²⁷ Twenty strategically selected policymakers of different professions at different levels in the health care organisation (i.e., ward and department level, as well as hospital level) from the four participating hospitals will be recruited. Politicians' working with health care issues at the county council level, as well as in the House of Representatives will also be included in the sample. This study focuses acceptability of I-CBT from the perspective of policymakers'. The study will gain knowledge of factors that can facilitate or hinder I-CBT to be implemented as a part of the health care organisations standard care treatment for CVD patients.

Timing of the planned studies

The study is planned to involve one PhD student and one post-doc. Table 3 gives an overview of the project and the timing of the different studies.

Table 3. Overview for the timing and planned studie

	2016	2017	2018	2019	2020
Preparation of the I-CBT program	■				
Enrolment of patientes and start ICBT study		■			
Stop I-CBT study			■		
RCT data analysis				■	■
Study of patient experiences				■	■
Study of health-care professionals perceptions				■	■
Study of policy makers opinions				■	■
Analyses and writing of publications				■	■

Project organisation

Project leader: Peter Johansson Associate Prof, Nurse. Department of Cardiology and Medicine and Health Sciences, Linköping University will lead the project including supervision of PhD students and of post-doctors.

Co-workers.

- Gerhard Andersson, Professor, Psychologist. Linköping University, Sweden. International expert in internet-CBT. Will be active in development and preparation of the I-CBT program, enrolment of patients, and evaluation of the I-CBT program.
- Tiny Jaarsma, Professor, Nurse. Linköping University, Sweden. International researcher in the studies of patients with CVD. Will be active in development and preparation of the I-CBT program, and evaluation of the I-CBT program.
- Anders Broström, Professor, Nurse, Jönköping University, Sweden. Expertise in research of CVD patients and in qualitative methods. Will be active in development of the I-CBT program, and in the qualitative studies
- Urban Alehagen, Associate Prof. Cardiologist. Linköping University, Sweden. Expert in CVD research and statistics. Will be active in development of the I-CBT program, enrolment of patients, and evaluation of the I-CBT program.
- Per Nilsen Professor. Linköping University. Expert in studies of implementation of research into practice. Will be active in the studies that explores facilitators and barriers to the implementation of the I-CBT program in clinical practice.

Significance and clinical significance

CVD is a public disease affecting approximately 1.4 million Swedes.²⁸ Of these approximately 20-40%, or as much as between 280.000 to 580.000 thousands, also have comorbid depressive symptoms. CVD with comorbid depressive symptoms is a challenge for the patients themselves as well as for the healthcare system. To meet this challenge, the WHO recommends that healthcare system prioritise the development and implementation of depression treatment programs for patients with chronic somatic diseases. Our study focuses on: (I) the development, feasibility and effectiveness of an I-CBT program aimed at reducing depressive symptom in CVD and (II) exploring factors among important stakeholders that can facilitate or hinder its implementation. This can be seen to be in line with the above recommendation by the WHO. The knowledge obtained from this study will have a significant impact on large number of CVD patients with depressive symptoms and should contribute to improved quality of care. Thus, if found effective, implementation of I-CBT for depressive symptoms can be provided to a large number of CVD patients, who at present might not have an adequate treatment. I-CBT for depression can also be provided at a low cost without need for face-o-face meeting with health care professionals. It is also in line with person-centred care, since it is tailored to fit the individual with CVD. Another advantage is that patients can have access to CBT in their own homes at their own preferences of time.

Preliminary results of the I-CBT program

The I-CBT website (www.heading-cbt.se) and the nine-week I-CBT depression program and has been pilot-tested on seven patients with heart failure in order to establish feasibility. This pilot study showed that the depression score on the PHQ-9 was reduced from 11 to 5.5. The amount of time required for guidance and feedback was low, approximately 20 minutes per participant and week. The participants perceived that the I-CBT program provided them with knowledge about their health problems and what they could do about them, gave them

freedom of time disposition and to take the time needed when working with the CBT program. The participants spent between reported that they spent 3-4 hours per week working with CBT program. None of the patients' depression deteriorated and no one dropped out. (Paper resubmitted to Patient Education and Counselling February 2015)

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