Development and evaluation of a tailored and person-centered internet-based CBT program with the aim of relieving stress, anxiety and depression in persons with cardiovascular disease

Purpose and aims

In persons with cardiovascular disease (CVD) (i.e. ischemia, heart failure or arrhythmia), mental illness such as stress, anxiety and depressive symptoms are common, contributing to reduced well-being, increased health-care consumption and increased mortality. A challenge is that healthcare systems due to a shortage of trained staff, have difficulty meeting these persons' care needs and own wishes regarding support and treatment of mental illness. One possible innovative solution might be remote treatment via internet-based cognitive behavioural therapy (I-CBT) where the content can be tailored to whether it is stress, anxiety and/or depressive symptoms that are treated. At the same time such programs may be person-centered (i.e. the person becomes an active part of his or her own care) by allowing the person with CVD themselves to determine the design of the content of the I-CBT program (i.e. person-determined) and when support and feedback are desired (i.e. person-controlled support and feedback). Today we have a knowledge gap regarding the effects and experiences of such tailored and person-centered I-CBT programs in persons with CVD.

The purpose: to develop and evaluate a nine-week tailored and person-centred I-CBT program that can be directed towards stress, anxiety and depressive symptoms in persons with CVD. The purpose is also to examine the persons' experiences of designing their own I-CBT program and determining when support and feedback should be obtained.

Specific aims:

1. To evaluate the effect at 9 weeks as well as 6 and 12 months after completion of treatment through a tailored and person-centered I-CBT program on stress, anxiety, depressive symptoms, quality of life, adherence to I-CBT, self-care behaviors and health-economy.
2. To investigate factors such as age, gender, levels of stress, anxiety and depressive symptoms that can mediate or moderate the I-CBT program effect on stress, anxiety, depressive symptoms, quality of life, adherence to I-CBT, self-care behaviors and health-economy.
3. To investigate the impact of person-centered care on adherence to the I-CBT program and the exploitation of the therapist.
4. To explore how persons with CVD experience participation in the adapted and person-centered I-CBT program.

State of the art

Cardiovascular disease and mental illness: About 20-40 % of persons with cardiovascular disease (CVD) have mental illness such as stress, anxiety and/or depressive symptoms. This is 2 to 3 times higher than the normal population.[1] Compared to persons with CVD and without mental illness, we know that stress, anxiety and/or depressive symptoms in CVD leads to poorer self-care behaviors, quality of life, increased health care consumption and premature death.[1-4] However, less is known on how to best manage mental illness in CVD[5], this despite that European Society of Cardiology Prevention guidelines point out that persons with CVD should be offered support and treatment for mental illness.[6] Of importance is that persons with CVD themselves also want support and treatment for mental illness.[7]

Cognitive behavioural therapy in cardiovascular disease. Possibilities- and challenges: Cognitive behavioral therapy (CBT) is currently first-hand treatment of stress, anxiety or depressive symptoms.[8] A meta-analysis has shown that CBT in CVD can reduce

both anxiety and depressive symptoms.[9] In the majority of these studies, CBT was given "face to face" (a therapist meets a patient) and was run by CBT therapists.

A challenge with face to face CBT is the treatment gap, i.e. there is not enough trained staff to offer face to face CBT to the extent requested. This has attracted the attention of the World Health Organization (WHO), which stresses that healthcare must increase access to support and treatment of mental illness in patients with chronic somatic diseases, such as those with CVD.[10] To meet these demands, one possible solution could be remote treatment via internet based-CBT (I-CBT). In younger and middle-aged populations without CVD, I-CBT has proven as effective as regular CBT in the treatment of stress, anxiety and depression.[11] Furthermore, I-CBT has the advantage that it can be led by health-care professionals with only a short introduction in CBT, such as nurses, and without decreasing the effect of the treatment.[12] I-CBT also enables the person with CVD to receive support and treatment for mental illness at a lower cost and at home.

The knowledge gap about I-CBT in cardiovascular disease: Since persons with CVD often are older and can be affected by their disease this may also affect the feasibility and effectiveness of I-CBT in CVD. Today there is a lack of studies regarding I-CBT in CVD.[13] However, own research, funded by the Swedish Research Council (dnr. 2015-02600), has recently shown that a 9 week I-CBT depression program and managed by nurses, had a good effect on depressive symptoms.[12] From secondary analyses of these data and own previous study[14] we have learned that an I-CBT depression program has a weaker effect on anxiety. This may be explained by the need for different CBT techniques to treat different types of mental illness. Thus, of importance to understand is that a CBT program designed for depression is not as effective on anxiety or stress. Indicating a need for an I-CBT program for persons with CVD that can be tailored to whether it is stress, anxiety and/or depressive symptoms that are treated. Studies conducted on younger or middle-aged patients without CVD have shown that I-CBT programs that can be tailored to anxiety or depression have positive effects on both anxiety and depression.[15] However, knowledge regarding the feasibility and effectiveness of tailored I-CBT programs in CVD is missing.

In future care, patients will make ever-increasing demands on sharing in designing their own care, i.e. increased need for implementing person-centered care[16] In I-CBT it is usually the therapist who determines the design of the I-CBT treatment and when support and feedback should be given. However, the patients should be seen as a resource in the design of their own care and this highlights the need to develop and evaluate person-centered I-CBT programs. In I-CBT, person-centering could mean that the participant themselves determines the content of their own I-CBT program (i.e. person-determined content) and/or self-determine when support and feedback should be provided (person-controlled support and feedback). A pilot study on middle-aged particpants without CVD showed that an I-CBT program, in which the participants themselves determine the content, reduced both depression and anxiety.[17] Person controlled support and feedback has in another I-CBT study, performed on middle-aged participants without CVD, been conceptualized as person-centered care.[18] They reported equal effect on depression and anxiety regardless whether feedback and support were controlled by participants or therapist.[18] Studies evaluating person-centered I-CBT programs in CVD have been requested[13] but are still lacking.

Thus, in CVD there is a need of studies that evaluate I-CBT programs that is tailored to stress, anxiety and depressive symptoms and at the same time is person-centered. However, today we have a knowledge gap regarding the effects and experiences of such a tailored and person-centered I-CBT program on stress, anxiety and/or depressive symptoms in persons with CVD.

Significance and novelty: The study is of significance since it is in alignment with WHO[10], who wants healthcare providers to prioritize the development and implementation of support and treatment programs against mental illness in chronic somatic disease[10], such as those

with CVD. The study is also in alignment with the Swedish Government's E-health vision 2025 and the Nordic Welfare Center's work to increase the implementation of healthcare that is provided through digital solutions.[19,20] The study is also of significance since implementation of I-CBT increases the ability for healthcare systems to provide the many persons with CVD support and treatment that can be tailored and directed toward either stress, anxiety and/or depressive symptoms and based from their own needs and desires. The novelty lies in this being the first study to evaluate the effectiveness of tailored and person-centered I-CBT program aimed to relieve stress, anxiety and/or depressive symptoms in those with CVD. Thus, we are the first researchers to fill the knowledge gap in CVD regarding:

- the effects of a tailored and person-centered I-CBT program on stress, anxiety, depressive symptoms, self-care behaviors, quality of life, health-economy and adherence to I-CBT.
- how person-centered designed I-CBT programs can affect stress, anxiety, depressive symptoms, self-care behaviors, quality of life, and adherence to I-CBT.
- how different factors such as age, gender, levels of stress, anxiety and depressive symptoms can affect the effect of -and adherence to tailored and person-centered I-CBT programs.
- experiences of participating in a person-centered I-CBT program, both in terms of determining the content of the I-CBT program and patient-controlled support and feedback.

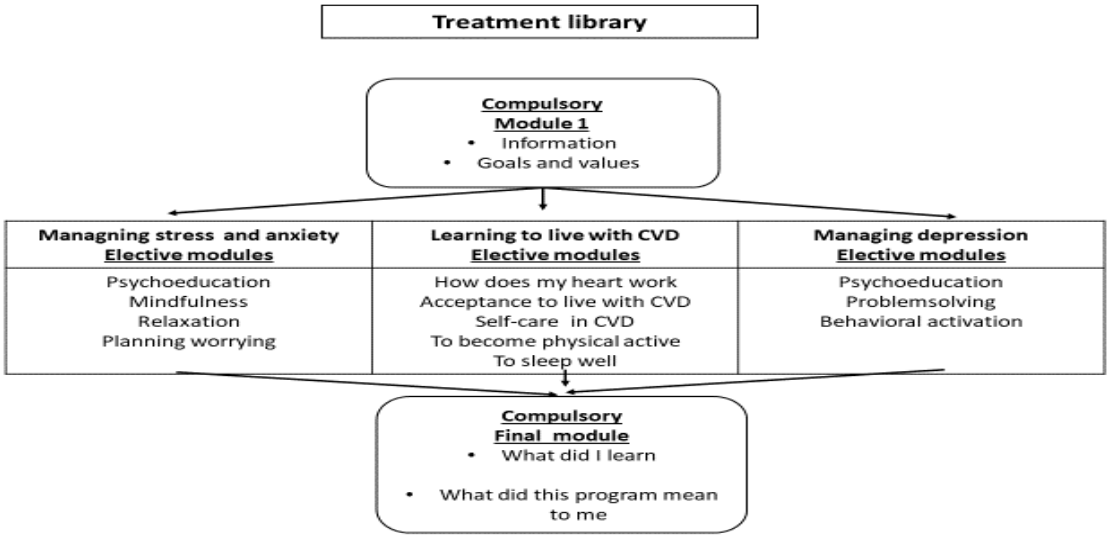
Preliminary findings: We have in previous studies developed I-CBT programs for persons with CVD and depressive symptoms and evaluated these in proof of concept-, pilot- and full randomized controlled studies.[12,14,21] We have found that I-CBT can be used to treat depressive symptoms and to improve quality of life in persons with CVD and of both genders.[12,14,21] In qualitative studies we have also found that persons with CVD experience I-CBT as a challenging but effective tool for self-management of health problems.[13] Furthermore, we have recently found that I-CBT in CVD may improve self-care behaviors.[22] In an ongoing interview study, the participants suggests the I-CBT program to be more person-centered by having the possibility to receive support and feedback when desired. Thus, these findings have given our research group knowledge and experience necessary to continue to pursue the development and evaluation of a tailored and person-centered I-CBT program against stress, anxiety and depressive symptoms in CVD.

Description of the project

Theory and method: CBT theory in short, CBT aims to enable the participant to change and manage negative and stressful thoughts and behaviors that affect how they feel and behave. An important aspect of CBT is that the participant actively works with exercises and home tasks that are then given feedback by a therapist.[23] Of importance is that different CBT techniques are needed to treat stress, anxiety or depressive symptoms. In our study tailored means that the content of I-CBT program can be applied to whether it is stress, anxiety and/or depressive symptoms that are treated.[23] Person-centered care means that the patient is not a passive target of an intervention but instead is involved as an active part his in his or her care and the decision-making process.[16] A possibility for the person with CVD to become an active part in their I-CBT treatment could be to allow them to decide the content of their own I-CBT program (i.e. person-determined content) and/or self-determine when support and feedback should be provided (person-controlled support and feedback). We are aware of that tailored and person-centered can be interpreted as same concepts. But in our study, tailored I-CBT means that the focus is on which type of mental illness to be treated while person-centered means that the focus is to allow the person with CVD to become an active part in their own I-CBT treatment.

Tailoring of the I-CBT program: The tailored 9-week I-CBT program is created from a library consisting of different types of treatment text modules (i.e. different CBT techniques) (Figure 1) which can be directed towards stress, anxiety and/or depressive symptoms. The first and final modules in the library are compulsory (Figure 1). This is because the first module contains important information for working in the program as well as establishing goals and identifying values. In the last module it is important that the participant summarizes their participation and establishes an action plan for handling possible future mental illness. In a previous I-CBT study, we showed that persons with CVD found content adapted to the CVD context particularly positive and facilitating.[7] In the planned study, all text and figures in the treatment modules will therefore also be designed to fit the context of persons with CVD.

Figure 1. Overview of the treatment library, with examples of elective treatment modules, that forms the tailored I-CBT program.



Person-centering of the I-CBT program: In this study we will evaluate two types of person-centered designs of the tailored I-CBT program: *person-determined CBT content* and *person-controlled support and feedback*. The person-determined content will be compared to a therapist determined I-CBT program. The person-controlled support and feedback will be compared to therapist-controlled support and feedback. A motive for not using a traditional control group is that I-CBT has proven more effective against not getting anything at all but also compared to active control such as a discussion group.[14]

The person-determined I-CBT treatment: When determining their own I-CBT program, the participants in this study will be allowed to choose from the library of treatment modules (Figure 1). Each treatment module will include a description of content and function. We believe that those who use a self-determined I-CBT program may become more motivated to be involved and pursue their treatment compared to those who receive a therapist determined program. This may contribute to an increased self-care behavior, adherence to the program as well as effect on stress, anxiety and/or depressive symptoms. The therapist-determined I-CBT program will follow others and own previous studies.[12,24] In this project, members of the research group, consisting of psychologists and nurses with experience of I-CBT in CVD, will determine the content of the I-CBT program. This is done after assessment of the participant based on responses from questionnaires on stress, depressive symptoms and anxiety and telephone interviews. The content will be selected from the treatment library (Figure 1).

The person-controlled support and feedback: In our study person- controlled support and feedback means that the participant will be able to contact the therapist when support and feedback is desired whereas therapist controlled support and feedback are given weekly and in a structured manner.[18] Therapist controlled support have by participants been described

as burdensome and to disrupt everyday tasks and thus may be poorly adapted to the persons needs and hence increases the risk of attrition.[25] We believe that person-controlled support and feedback can counteract perceived load[22], decrease attrition, increase adherence and thus the effectiveness of the I-CBT program. In our study feedback and support, regardless of person controlled or therapist-controlled support and feedback, will be provided by nurses with experience in cardiac care. The rationale for this is that we in own previous CVD studies we have shown that I-CBT programs where support and feedback was provided was effective to decrease depression.[7,12] These nurses will have the opportunity to consult psychologist and a cardiac specialist.

Method

Study design: Both quantitative and qualitative methods will be used to evaluate the specific aims of the study. The development and evaluation of the tailored and personal centered I-CBT program will take place in two stages.

Stage 1. Feasibility and preparation and of the tailored and person-centered I-CBT program. We have in previous studies shown that I-CBT is feasible and effective to treat depression in CVD.[12,14,21] To prepare the tailored I-CBT program, we will develop our I-CBT depression program[12] (i.e. treatment library) by adding treatment modules that can be directed towards stress and anxiety and that are adapted to fit the context of CVD. As far as person-centering is concerned, participants from our project organisation (PJ, GA, JL) are now conducting a pilot study where the participants can determine their own CBT program and patient-controlled support and feedback. The experiences from the pilot study will be used to make any adjustments to the I-CBT program.

Stage 2. Evaluation of the tailored and person-centered I-CBT program: A randomized controlled trial (RCT) with a 2x2 factorial design will be used. A more detailed overview of the factorial design is described in Figure 2. Factorial design is considered a good method for evaluating the individual effect and interaction between different interventions (i.e. factors) while the number of participants in each factor does not have to be so large in order to provide "statistical power".[26] **Factor 1** concerns the design of the I-CBT program and is divided into person-determined CBT content (i.e. person-centered) or therapist determined I-CBT content. **Factor 2** regards control of support and feedback and is divided into person-controlled support and feedback (i.e. person-centred) and therapist -controlled Since we do not use a control group but two active groups in each factor, we have to evaluate "non-inferiority" and we will use the confidence interval method to assess non-inferiority. **Power analysis**. In our own I-CBT study[12] and the study that evaluated therapist vs. person controlled of support and feedback[18] the mean scores and standard deviations (SD) on the primary measures of depression and anxiety at follow-up was approximately 6 and 5 respectively. The latter study[18] reported a power to detect a 35 % difference in scores between the two groups (i.e. 6 x 0.35= score of 2.1). Using a mean difference of 2.1, SD of 5, β=90 % and alpha =5 %, a total of 98 participants per group will be needed to detect if the different interventions are similar. Our factorial design contain four groups and we will therefore recruit 400 participants to the study.

Figure 2. Specific description of the factorial design

I-CBT program tailored for stress, anxiety and/or depressiva symtoms in patients with CVD n=400			
		Factor 1 Determination of the I-CBT content	
		A Person-determined	**B Therapist-determined**
Factor 2 Controlled support and feedback	**C Person-controlled**	n=100	n=100
	D Therapist-controlled	n=100	n=100

Evaluation of study outcomes: Table 1 below describes the quantitative primary and secondary outcomes in the study. We expect many of the participants to have combinations of stress, anxiety and depressive symptoms. As a primary measure of effect, we will therefore use a composite score based on the changes in stress, anxiety and depressive symptoms measured with General Anxiety Questionnaire (GAD) [27], Patient Health-Questionnaire-9 (PHQ-9)[28] and Perceived Stress Scale (PSS).[29] The disadvantage with this is that we can lose specific information regarding changes in stress, anxiety and depressive symptoms. We will therefore also analyze these variables separately (i.e. change in stress, anxiety and depressive symptoms). The questionnaires measuring the primary outcomes are valid and reliable and have been used in CVD as well as in I-CBT studies.

*Table 1. Overview of the study's primary and secondary outcome measures and how and when data should be collected***.**

	Data collection	**Follow-up**		
		9-weeks	**6-months**	**12-months**
Primary outcomes				
Anxiety Depressive symptoms Stress	General Anxiety Questionnaire[27] Patient Healt-Questionnaire-9[28] Percieved stress scale-10[29]	X X X	X X X	X X X
Secondary Outcomes				
Quality of life and self-care behaviour	Short Form-12[30] Euro-QoL-5D[31] Self-care of chronic illness inventory[32]	X X X	X X X	X X X
Health-economy	The Care Data Warehouse, which is a population-based diagnose-related administrative database.		X	X
Exploitation of therapist: -Frequency and time	Data will be collected on the study treatment internet site.	X		
Adherence to treatment: -Satisfaction with treatment -Completion of modules -Attrition	The client satisfaction questionnaire[33] Data collected on the study treatment internet site.	X X		

Data analysis and statistics (Specific aims 1, 2 and 3): Data analysis will begin with a descriptive description of the variables (such as frequencies, mean values and standard deviations, medians and interquartiles). The RCT study will be analyzed according to the "intention to treat principle" and data loss are handled with multiple imputation. Through the 2x2 factorial design, we will analyze the 2 factors using mixed models. In the first factor, person-determined I-CBT content (i.e. person-centered) is compared to therapist determined I-CBT program (In Figure 2, group A (n=200) vs. group B (n=200) and in the second factor, person-controlled support and feedback (i.e. person-centered) is compared to therapist controlled support and feedback (In Figure 2, group C (n=200) vs. group D). The study's factorial design also allows subgroup analysis where we can analyze the groups that received the combination of *person-determined/person-controlled support and feedback* (AC, n=100) compared to *therapist determined/therapist-controlled support and feedback* (BD, n=100). Multivariate statistics will be used to investigate mediators and moderators (for example age, gender, levels of stress, anxiety and depressive symptoms) that can affect the primary and secondary outcomes (Table 1) of the I-CBT program.

Qualitative evaluation (Specific aim 4): Experiences of participating in the tailored and person-centered I-CBT program will be explored by using inductive content analysis according to Hsieh & Shannon.[34] The inductive method is used because we have no knowledge of how persons with CVD experience a tailored and person-centered I-CBT program. A total of 40 participants from the RCT (20 from factor 1 and 20 from factor 2) will be included and undergo semi-structural interviews. The interviews will be digitally recorded, transcribed verbatim and then be repeatedly read for an in-depth and increased

understanding of the text. During reading, codes are identified, which then will be formed to subcategories and categories depending on how the codes are related to each other and answer the purpose of the study. During analysis of data and for results to be credible, the research group will meet for regular discussions.

Enrolment of study participants: Our enrolment process is feasible and have been used in previous own I-CBT studies performed on persons with CVD.[12,14] Enrolment will be performed in four steps:

Step 1: Screening for participants. All persons diagnosed as CVD (i.e. diagnosis Ischemia (ICD-code I20., I25.), Heart Failure (ICD-code I50., I42.) or Arrhythmia (ICD-code I48, I49, DF016) and who received care in the last 12 months at hospitals in the south-east of Sweden will be contacted by letter with information about the study. Information on the study is sent out continuously until enough participants are recruited (n=400). We are aware of that this screening process is limited by the fact that not all persons with CVD have a mental illness or have visited a hospital the last year. However, we have learned that this screening process is a feasible method to approach and recruit participants with CVD and mental illness to I-CBT studies. If this recruitment process is slow, we also plan to recruit participants through newspapers and social media.

Step 2: Participants who are interested are invited to visit our website (www. xxxxxxx) for more information, registration and provision of informed consent. After registration, participants will respond to questions about demographics, medical history, stress, anxiety and depressive symptoms on the website. Inclusion or exclusion (see criteria´s below) will be assessed by a group consisting of a psychologist, a psychiatry specialist nurse and nurses with experience in cardiac care. A Cochrane study of psychosocial interventions in CVD showed weak effects on anxiety and depressive symptoms.[5] This due to floor effects because most of the studies had included persons with CVD patients regardless of the degree of anxiety and/or depressive symptoms. Thus, to avoid floor effects we will therefore only include persons with CVD who have increased levels of stress, anxiety and/or depressive symptoms.

Inclusion criteria

- age 18 years and above
- treatment for CVD according to European Society of Cardiology guidelines
- stable CVD (New York Heart Association class I–III) and not having been hospitalised for CVD in in the last four weeks.
- stress (Perceived Stress Scale (PSS)-10>13 points)[29] and/or
- anxiety (i.e. General Anxiety Disorder Scale (GAD) ≥ 5 points)[27] and/or
- depressive symptoms (Patient Health Questionnaire-9 [28] (PHQ-9) > 5 points)

Exclusion criteria

- severe CVD (New York Heart Association classification IV) or another severe chronic life-threatening disease
- severe stress, anxiety or depression assessed as requiring acute treatment
- not being able to dedicate 3-4 hours per week to participate in the program

Step 3: Before final inclusion and randomization, in order to provide information and answer question about the study as well as to assess severity of CVD, stress, anxiety and depression, eligible participants will be contacted for a telephone interview held by the study nurses.

Step 4: Included (n=400) participants will, on our website (www.xxxxxx), complete the baseline study questionnaires and then be randomised according to the factorial design as presented in Figure 2.

Time plan and implementation: Preparation of the I-CBT treatment modules and the pilot-study as described in Stage 1, are expected to be completed in 2020. Based on own experiences from previous I-CBT studies in CVD, we will be able to recruit and intervene about 200 participants per year. Thus, performance of the I-CBT intervention will take about 2 years and is planned to take place from February 2021 to May 2023. Recruitment and treatment of patients will not take place during the summer- or Christmas holidays. Data analysis may begin September 2023 and dissemination of results may begin in spring 2024. To facilitate and promote implementation of the I-CBT program, the results will be disseminated internationally and nationally to important stakeholders such as CVD patient organizations, CVD researchers, decision makers in healthcare as well as healthcare-professionals working in clinical cardiac care.

Equipment : We will use the same I-CBT internet web-platform as in own previous studies.[12,14,21]

Need for infrastructure: By the Linköping University we have access to necessary infrastructures such as library and library service, statistical advisors and computer programs, secure data servers as well as regular research meetings.

International and national collaboration: We have an on-going discussion with researchers from the University of Genoa about to evaluate our I-CBT depression program for persons with CVD[12] in Italy. If this is successful, it is also possible that we can evaluate an Italian version of the tailored and person-centered I-CBT program as well.

Other applications or grants: I have a previous project funded from VR 2016-2019 as main applicant, dnr. 2015-02600. The main result from the project has been published.[12] This application is a further development based from the experiences of that previous VR project. I will be co-applicant in another I-CBT study, but that study concerns another group of patients and will not interfere the study in this application.

Independent line of research: This study is line with my independent line of research focusing the development and evaluation I-CBT program against mental illness in CVD. In previous studies, as a principal investigator, I have developed I-CBT programs for persons with CVD and depressive symptom and evaluated these in pilot- and RCT studies.[12,14,21] I have also conducted qualitative studies that examined persons with CVD an their experiences of participating I-CBT programs.[7] All these studies have given me knowledge and experiences necessary to the perform the present study that aims to evaluate a tailored and person-centered I-CBT program against mental illness in persons with CVD.

Project organisation. Professor and nurse Peter Johansson is the principal investigator and will be responsible for all parts of the study being carried out. Professor and psychologist Gerhard Andersson with world leading expertise in I-CBT is also a member of the organization. Gerhard Andersson and Peter Johansson have for the past 8 years worked closely together regarding development and evaluation of an I-CBT program for persons with CVD. Professor Andersson will participate in the preparation of the I-CBT program, performance of the I-CBT study, analyses of data and preparation of manuscripts.The group also includes collaboration with professors and nurses Anna Strömberg and Tiny Jaarsma, who both have expertise in cardiac research and E-technology. They will participate in preparation of the program and data analyses. Johan Lundgren PhD, specialist nurse in psychiatry with expertise in I-CBT in CVD and qualitative method will be post-doc in the study. Ghassan Mourad PhD, nurse, will contribute with expertise in I-CBT and in health-economic analysis. Patric Karlström PhD and cardiologist will add expertise in cardiology. Specialist nurses and PhD students Mats Westas, Kristina Nilsson and Magda Leibon will participate in the recruitment of participants and provide support and feedback in the I-CBT intervention. Computer technician George Vlaescu will be in charge of the I-CBT web platform. Main applicant and co-applicants have previous contributions from the Swedish Research Council, FORTE, Hjärt- och Lung-Fonden and Kamprad stiftelsen. To summarize,

our project organisation includes a collaboration between different clinical specialists (nurses, psychologist and cardiologist) and academic disciplines (caring, medicine and behavioural sciences) as well as a collaboration between senior- and junior researchers and PhD students.

Clinical implications: Approximately 2 million Swedes have CVD.[35] Of these, about 20-40% or as many as 400.000 to 800.000 have mental illness due stress, anxiety and/or depressive symptoms. This has a profound and negative impact on quality of life and prognosis in persons with CVD. Due to a lack of resources such as trained staff, healthcare systems today cannot provide specific and person-centered support and CBT treatment for stress, anxiety and/or depressive symptoms to all these persons. Thus, if the tailored and person centered I-CBT program is found to be effective, a large number of persons with CVD, who currently may not have adequate treatment for stress, anxiety and/or depressive symptoms, may get increased access to effective and person-centered treatment of mental illness, which can be provided at a low cost and in the persons home.

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