Lessons learned from an attempted randomized-controlled feasibility trial on “WIDeCAD” - An internet-based depression treatment for people living with coronary artery disease (CAD)

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Abstract
Background: Despite the high prevalence of comorbid depression in people living with coronary artery disease (CAD), uptake of psychological treatment is generally low. This study was designed to investigate the feasibility of an internet-based cognitive-behavioral (iCBT) depression intervention for people with CAD and depressive symptoms. Methods: People with CAD and depressive symptoms (PHQ-9 ≥ 5) were randomly assigned to the eight modules comprising iCBT (N = 18), or waitlist-control (N = 16). Measures were taken at baseline (t1) and at post-treatment (eight weeks after randomization, t2). Feasibility-related outcomes were recruitment strategy, study attrition, intervention dropout, satisfaction, negative effects as well as the potential of the intervention to affect likely outcomes in a future full-scale trial (depression, anxiety, quality of life, fear of progression). Data analyses were based on intention-to-treat principles. Linear regression models were used to detect between group differences. Linear Mixed Models were used to model potential changes over time. Results: This trial was terminated prior to a-priori defined sample size has been reached given low recruitment success as well as high intervention dropout (88%) and study attrition (23%). On average, participants in the intervention group completed M = 2.78 (SD = 3.23) modules. Participants in the waitlist control group barely started one module (M = 0.82, SD = 1.81). The satisfaction with the intervention was low (M = 20.6, SD = 0.88). Participants reported no negative effects attributed to the iCBT. Differences between groups with regard to depression, anxiety, fear of progression and quality of life remained non-significant (p > 0.05). Conclusion: This trial failed to recruit a sufficient number of participants. Future work should explore potential pitfalls with regards to the reach and persuasiveness of internet interventions for people living with CAD. The study gives important indications for future studies with regard to the need for new ideas to reach and treat people with CAD and depression.

1. Introduction
Coronary artery disease (CAD) is the leading cause of death worldwide (Naghavi et al., 2015). Advances in medical treatment have resulted in a decrease of mortality rates (Mensah et al., 2017; Lopez and Adair, 2019), subsequently resulting in an increase in years lived with CAD (Vos et al., 2017; James et al., 2018). Besides the need of medical treatment, CAD is often accompanied by depression and anxiety.
Depression can be considered as a recurrent all-cause mortality (Lett et al., 2004) and is associated with cardiovascular morbidity and mortality (Härter et al., 2007; Baumeister et al., 2010, 2011, 2015; Haschke et al., 2012; Watkins et al., 2013; Smith and Kneebone, 2016; Stemman et al., 2016). Depression can be considered as a recurrent risk factor for CAD events (Brown et al., 2005; Dhar et al., 2016).

Research on comorbid depression reveals serious implications for individuals with regard to individual functioning and quality of life (Dickens et al., 2012; Palacios et al., 2016) as well as hampering health-related outcomes (Meijer et al., 2011; Tully and Baker, 2012; Pedersen et al., 2017; Palacios et al., 2018).

Internet Interventions could be a flexible approach for patients and might help to overcome various barriers in a cost-effective way by delivering low-threshold healthcare offers on a large scale and wide rollout (Bendig et al., 2018). Internet interventions are (guided) self-help programs, provided on a website (Barak et al., 2009) and can be complemented by mobile-based features. Recent meta-analyses indicate, that guided internet interventions can be as effective in treating mental and somatic disorders as face-to-face psychotherapy (Carlbom et al., 2018). Guidance refers to the extent of human support by eCoaches (e.g. psychologist/physician) (Barak et al., 2009), with at least a minimum of guidance shown to be a beneficial feature of internet interventions (Baumeister et al., 2014).

There is a growing body of well-conducted research on internet interventions for the treatment of depression in cardiovascular populations (e.g. Lundgren et al., 2016; Habilhowe et al., 2017). However, overall research is still scarce on the interface of cardiovascular disease and psychological depression treatment in general (Nygårdh et al., 2017; Johansson et al., 2019) and even more scarce at the interface of internet interventions for people living with CAD and depression.

There are two studies which investigated a CBT-based IMI (iCBT) in people with a recent acute coronary event (Norlund et al., 2018; Schneider et al., 2020). Norlund and colleagues (Norlund et al., 2018) investigated a 14-week iCBT (“U-CARE”) in comparison to a treatment-as-usual control-group (CG) in people who have had a recent (<3 month ago) myocardial infarction and symptoms of depression and/or anxiety (HADS >7) (N = 239). Primary outcome was depression and anxiety (HADS). There were no significant differences between groups (beta = −0.47, 95% CI -1.95 to 1.00, p = 0.53). Schneider and colleagues (Schneider et al., 2020) investigated an iCBT (“U-Card well being course”) for depression and anxiety in people who experienced an acute coronary event in the last 24 month (unstable angina or myocardial infarction). Authors planned to recruit N = 70 participants, but ended up with N = 53 participants. Results showed significant between-group improvements for the intervention group (n = 25) compared to the control-group (n = 28) on general anxiety (Cohen’s d = 1.62 95% CI 1.00 to 2.24) and depression (Cohen’s d = 1.09 95%CI 0.51 to 1.66).

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People with CAD and depression are seemingly not only difficult to reach, but also partly challenging to keep engaged. The U-Care study (Norlund et al., 2018) reported low intervention adherence rates with only 15.4% of participants in the IG completed more than the introductory module (Wallin et al., 2018). Adherence was investigated in depth by the help of machine learning algorithms (Waller et al., 2018). Adherent participants were more frequently female with a higher level of cardiac-related anxiety (Waller et al., 2018). Schneider and colleagues (Schneider et al., 2020) reported a good intervention adherence rate with 92% of participants completing at least four of eight modules. Also Johansson et al. (Johansson et al., 2019) found good adherence rates in a population with different cardiovascular diseases (heart failure, CAD, atrial fibrillation). A total of 60% (n = 43) of the iCBT group completed all seven modules (Johansson et al., 2019). As reasons for greater intervention adherence than in previous studies, authors discussed that iCBT contents were adapted for cardiovascular diseases and feedback was provided from medical staff (Johansson et al., 2019).

The current study was designed to evaluate the feasibility and potential effectiveness of an iCBT for people living with CAD and depression (Web- and mobile-based Intervention for Depression in people with CAD “WIDeCAD”) in a German-speaking population (Germany, Switzerland, and Austria). Thereby, the trial aimed to test a wide range of recruitment strategies that can be considered fruitful (e.g. multipliers (=persons who contribute to the dissemination of information) in clinics and self-help organizations, advertisements of heart institutions, social media) (Treweek et al., 2013). An already existing ICBT, Icare Prevent (Weisel et al., 2019) was adapted to the population. The ICBT is optimized for desktop/notebook applications but also runs on mobile-based applications like smartphones/tablets. WIDeCAD aims at reducing depression, applies mechanisms to foster adherence, comprises highly personalizable contents and can be individually tailored to individual preferences of participants. Moreover, it targets anxiety symptoms, which are frequently present in people with CAD and depression (Rudisch and Nemeroff, 2003; Lett et al., 2004; Rothenbacher et al., 2007; Air et al., 2016). Specifically, the WIDeCAD study aimed to:

1. Explore the feasibility of the iCBT, specifically recruitment, dropout and satisfaction with the intervention.
2. Examine potential negative effects of the iCBT.
3. Examine if the intervention potentially affects depression and other intended outcomes of a future full-scale trial.

2. Materials and methods

2.1. Participants

Participants were eligible to take part in this study if they were 18
years of age or older, had a self-reported lifetime diagnosis of CAD and depressive symptoms (PHQ-9 ≥ 5) (Kroenke and Spitzer, 2002; Johansson et al., 2019), internet access, sufficient German language skills and provided informed consent. Participants received the consent forms after expressing their interest to participate digitized or printed and had to send them back signed. Exclusion criteria comprised increased suicidality (PHQ-9 item 9: “Thoughts that you would rather be dead or want to harm yourself” on more than half of the days) or lifetime diagnoses of a psychotic, schizophrenic or bipolar disorder.

2.2. Study design and assessment

This parallel group randomized-controlled feasibility trial was conducted from June 2017 to July 2019. The intervention group (IG), which received the guided iCBT, was compared to a waitlist control group (CG) which started the unguided iCBT 8 weeks after randomization.

This trial was conducted in compliance with the Declaration of Helsinki and good scientific practice. The trial is registered at the WHO International Clinical Trials Registry Platform via the German Clinical Trials Register Trial DRK5: DRKS00012546 (date of registration: 17.07.2017). All procedures involved in the study are consistent with the generally accepted standards of ethical practice approved by the ethics committee of the Friedrich-Alexander University Erlangen-Nuremberg (No. 46.17 B). The present study was reported in accordance with the CONSORT 2010 guidelines for RCTs (Eldrege et al., 2016) and the guidelines for executing and reporting internet interventions research (Barak et al., 2009).

All surveys were conducted online via the “Unipark” platform (www.unipark.de). Data was collected at baseline (t1) and after 8 weeks after randomization (posttreatment; t2). Data obtained from the online-platform included: number of modules completed and number of intervention completers. Outcomes, measurements and points of assessment are shown in Table 2.

2.3. Recruitment

Recruitment took place in German-speaking countries (Germany, Switzerland and Austria). Various recruitment strategies and methods to improve recruitment were applied (Treweek et al., 2013). We recruited via 1) medical specialists in clinics (departments for internal medicine/cardiology), 2) volunteers in heart foundations 3) waiting rooms of cardiac specialists’ practices, 4) self-help organizations for people living with CAD, 5) cardiac groups 6) heart institutions and foundations 7) social media (specialized groups/information websites) 8) talks and workshops on conferences for cardiologists 9) articles in cardiology patient magazines as well as 10) advertisements directly on the landing page for trial recruitment. Interested people approached through these channels signed up on the landing page or expressed their interest via E-Mail. Those who met inclusion criteria and provided informed consent were randomly allocated to one of the two groups. All participants had full access to treatment-as-usual care during the study. For an overview of applied channels see Table 2.

2.4. Randomization

Randomization was performed on an individual level by a not otherwise in the study involved university staff (Tim Dreitzler, TD). There was no way that researchers involved in the study could foresee allocation of individual participants. Not otherwise to the study associated staff enrolled and assigned participants (Laura Simmelbauer, LS and Karolin Bauer, KB). A permuted block randomization with 2 and 4-block size and an allocation ratio of 1:1 was used. The randomization list was created by an automated web-based program, sealed envelope (https://www.sealedenvelope.com).

2.5. Intervention

2.5.1. Development and central elements

The iCBT was adapted on the basis of the already evaluated ICARE prevent-intervention (Weisel et al., 2019). Originally, Weisel and colleagues (Weisel et al., 2019) built on evidence-based modules from a range of internet interventions which have shown to be effective in treating depression (e.g. Buntrock et al., 2016; Ebert et al., 2017). Weisel and colleagues (Weisel et al., 2018) then further developed ICARE prevent contents alongside the results of a small-scale study. ICARE prevent was designed as a transdiagnostic intervention (Weisel et al., 2018). The contents of the modules focus on depression and also include contents on symptoms of anxiety. Central elements of the iCBT are addressing needs (module 1), where treatment motivation, goals, the cognitive triangle and activity plans are addressed. Behavioral activation (module 2) comprises mood stabilizing, reinforcing positive activities and dealing with difficulties with achieving planned activities. Psychoeducation (module 3) includes information on depression and anxiety with the aim to mediate a better understanding for these mental aspects in participants. Cognitive Restructuring (module 4) and Problem solving (module 5) include basic CBT-based techniques and skills as well as exercises on structured behavioral analyses. In the last module (Future Plans) participants are supported to reflect on the past modules and to focus on strategies for the maintenance of learned techniques in the future. A Booster session (module 8) addresses the implementation efforts and successes so far and again focusses on the maintenance of learned techniques. More detailed descriptions of central elements can be found elsewhere (Weisel et al., 2019).

ICBT contents were personalizable and tailored to individual specific needs throughout the intervention. Participants could choose which psychoeducational contents they wanted to intensify and which skills and exercises they wanted to enhance (e.g. further practice and strengthen problem solving skills and/or practicing with fear-inducing stimuli). Moreover, participants were able anytime to choose if they wanted to read text passages themselves or if contents should be read to them. An overview of contents can be seen in Table 1.

Participants were able to choose additional modules in accordance to specific needs. Additional modules comprised e.g. healthy sleep, self-worth, rumination and worries, alcohol consumption and affect regulation or acceptance (detailed information on additional modules can be found elsewhere (Weisel et al., 2019).

Case vignettes (i.e. written patient narratives) underpinned iCBT contents for a variety of clinical purposes like psychoeducation, building relationships, support, decision making and problem solving. Different exercises and tasks based on CBT-techniques are integrated with the aim to support the transfer of knowledge and CBT-based strategies into the people’s daily lives.

The iCBT incorporates a high degree of mechanisms to foster adherence. This includes a high level of interactive material like tasks and quizzes. Contents are illustrated by multi-media components, e.g.

### Table 1

| Module title                  | Module content                                      |
|------------------------------|-----------------------------------------------------|
| 1 Addressing needs           | Treatment motivation, goals, cognitive triangle, activity plans adapted to people living with CAD |
| 2 Behavioral activation      | Mood stabilizing, reinforcing positive activities, difficulties with achieving planned activities |
| 3 Psychoeducation            | Structured information on depression and anxiety    |
| 4 Cognitive restructuring    | CBT-techniques and skills, structural behavioral analyses |
| 5 and 6 Problem solving      | Problem solving skills and optional exposition practice with fear-inducing stimuli |
| 7 Future plans               | Reflection and maintenance strategies               |
| 8 Booster session            | Implementation efforts and successes, maintenance of learned strategies and techniques |

Notes. CAD=coronary artery disease.
text, audio, video. After each module, participants of the IG receive feedback on tasks and contents from an eCoach. As soon as the participants read the feedback, they were enabled to continue with the next module. An optional SMS-coach was integrated to foster intervention adherence. The SMS-coach sent motivational messages to the mobile device of participants.

2.5.2. WIDeCAD version

Modifications were made to the original iCBT (Weisel et al., 2019), including 1) disease-specific information and psychoeducative elements as well as case vignettes of people living with CAD and depression. 2) Longer text passages of the original iCBT were structurally simplified and shortened. The iCBT in the WIDeCAD study consisted of seven modules and a booster session.

The iCBT was delivered on the online-platform Minddistrict®. If participants did not process through the next module within one week and did not react to reminder per Email, they were telephone reminders up to three times. Processing through a module was conceptualized to last approximately 45–60 min. However, there was no time limit and participants could take breaks, whenever they wanted and were encouraged to do so. Participants were recommended to complete one module per week. Four weeks after completing the seventh module, participants could process through a refresher module to repeat contents and support the participants to transfer learned contents and strategies into daily routines (Weisel et al., 2019).

2.6. Procedure

For participants in the IG, an account on the online-platform minddistrict® was created and an eCoach was assigned to the participant by KB or LS. Next, an automated E-mail was sent to the participant with the link for account activation. After creating a personal password, participants were enabled to login and start with the first module. The eCoach received a message whenever the participant finished a module. Within two working days, the eCoach provided a standardized feedback on the minddistrict®-platform. The feedback consists of standardized, pre-defined and minimally personalized text modules. Participants could start the next module after reading the feedback. Participants who missed to process through their next module within the following week were reminded three times. If the participant did not answer the third reminder, the current module was disabled by the eCoach. Participants were told that they can reactivate their module by messaging the eCoach.

In module 1, all participants (IG and CG) could choose if they wanted to be supported by none, three or five automated daily short messages (SMS). These SMS were standardized and had motivating and supportive content (tiny-tasks corresponding to intervention contents, reminders to practice).

Participants of the CG received the unguided iCBT eight weeks after randomization. All procedures were the same as for the IG but participants processed through the intervention without receiving feedback. Participants were a-priori informed about this difference between IG and CG and were able to contact their assigned eCoach anytime if they had any questions.

Throughout the intervention, participants were encouraged to apply newly learned strategies and supported by tasks (keeping a sleep-, activity-, thought-, challenge-, or alcohol consumption-diary). All eCoaches were Master’s level students in clinical psychology that received a training for eCoaching from EB, supervised by HB. All eCoaches used a detailed manualized protocol throughout the intervention for all processes: Giving feedback to participants, reminding participants to move on with the intervention or complete measurements, plot and react when emergencies occur. All eCoaches were regularly (at least once a month) inter- (EB) and supervised (HB) and were regularly encouraged to ask questions whenever there were insecurities, irregularities or signs of suicidality in participants.

2.7. Outcome: feasibility

2.7.1. Recruitment, dropout and satisfaction with the intervention

To answer the research questions, we investigated study flow and recorded access routes. In order to learn about characteristics of the population reached by the recruitment strategies, we assessed demographic variables (age, gender, nationality, marital status and former psychotherapy/counselling experiences) and recorded the severity of the CAD (New York Heart Association (NYHA) classification). Study attrition was operationalized by missing questionnaire data for one or both points of assessment. Every person who did not complete the intervention (module 1 to 7) was defined as intervention dropout. Participants who dropped out from the intervention where called and asked to give reasons for not continuing with the intervention.

To measure treatment satisfaction, we used the Client Satisfaction Questionnaire (CSQ-8; Schmidt and Nübling, 2002). Participants rated their satisfaction with the WIDeCAD intervention on a 4-point Likert-scale for each of the 8 items. Higher scores indicate higher satisfaction. For psychosomatic contexts, a mean of $M = 23.5$ SD = 5.0 is reported (Kriz et al., 2008). Values $>23$ are being classified as good treatment satisfaction (Kriz et al., 2008).

2.7.2. Negative effects and potential of the intervention to affect intended outcomes

To assess experienced negative effects due to the intervention, the 15-item version of the Inventory for the Assessment of Negative Effects of Psychotherapy (INEP; Ladwig et al., 2014) was employed. Items are rated on a 4-point Likert scale (0 = “no agreement” to 3 = “total agreement”) or a bipolar 7-point scale. The INEP also allows to inquire whether participants attribute changes to the intervention or other life circumstances (e. g. “Since I attended WIDeCAD I feel better (+3)... worse (-3)”). Topics are negative effects in the social environment, intrapersonal factors or work-related situations.

To assess the potential for the intervention to affect likely outcomes in a future definitive RCT, we measured depression (PHQ-9), anxiety (GAD-7), quality of life (AQoL-8D) and fear of progression (FOP-Q-SF).

2.7.2.1. Depressive symptoms. Depressive symptoms are recorded by the Patient Health Questionnaire (PHQ-9; Kroenke and Spitzer, 2002). Nine items are rated on a 4-point Likert scale (0 = “not at all” to 3 = “almost every day”). There is an additional item which asks if functionality is limited in daily life. A meta-analysis concluded that scores of more than ten points indicate increased depressiveness and values over seven points at least a mild depressive episode (Manea et al., 2012).

2.7.2.2. Anxiety symptoms. The Generalized Anxiety Disorder 7-item Scale (GAD-7) measures anxiety symptoms or disorders (Spitzer et al., 2006). There are seven items to rate on a 4-point Likert scale (0 = “never” to 3 = “almost every day”). A sum score is computed. Sum scores of fifteen points or higher at severe anxiety symptoms.

2.7.2.3. Quality of life. We measured quality of life with the Assessment of Quality of Life scale (AQoL-8D) (Richardson et al., 2014). The AQoL-8D measures 8 dimensions of quality of life (independent living, senses, pain, mental health, happiness, self-worth, coping and relationships), that result in overall physical and psychosocial quality of life scores. The total score ranges between 35 and 176 points with higher values indicating lower quality of life.

2.7.2.4. Fear of progression. The short form of the Fear of Progression Questionnaire (FOP-Q-SF) worries and fear of disease progression can be captured within people with chronic diseases (Mehnert et al., 2006). The response to twelve items is documented on a 5-point-Likert scale (1 = “never” to 5 = “very often”).
2.8. Data analysis

The data was analyzed by means of SPSS 26 and R (Core Team, 2017) software and Excel. Qualitative data were analyzed by means of descriptive statistics (frequency, percentage, mean, standard deviation).

The present analyses follow the ITT principle. To handle missing values multivariate imputation by chained equations were performed to create 20 complete datasets (Enders, 2010). Missing data was assumed to be missing at random (van Buuren et al., 1999). Predictive mean matching was used as imputation method (van Buuren and Groothuis-Oudshoorn, 2011). Imputation models were defined following the recommendations by van Buuren and colleagues (van Buuren et al., 1999; van Buuren and Groothuis-Oudshoorn, 2011). Imputation models include variables defined for the primary analysis and auxiliary variables. Analyses were conducted for each imputed dataset and pooled using Rubin’s rule (Rubin, 1996, 2004).

Potential group differences were explored by linear regression models. Baseline values were defined as predictors in regression models (van Buuren and Groothuis-Oudshoorn, 2011). For these computations, mean, standard deviation, standardized regression coefficient, and the corresponding 95% CI as well as Cohen’s d (corrected for small sample size, \( d = \frac{M_1 - M_2}{S_p \sqrt{\frac{n_1 n_2}{n_1 + n_2}} \cdot \frac{1}{n_1} + \frac{1}{n_2} \) (Cohen, 1977; Durlak, 2009)), were reported. These cross-sectional analyses were enriched by longitudinal analyses. Linear mixed models consider that assessments are nested within persons and the resulting dependency between variables. In this study, the repeated measurements (level 1) are nested within person (level 2) (Luke, 2004; Nezlek et al., 2006). For all analyses the significance level was set to \( p < 0.05 \).

3. Results

3.1. Recruitment, dropout and satisfaction with the intervention

3.1.1. Recruitment

In total, \( N = 72 \) people living with CAD expressed their interest to participate in the study and were invited for the screening. \( N = 62 \) participants were screened for eligibility. \( N = 34 \) people (55%) fulfilled the inclusion criteria and provided informed consent during the 25-month recruitment period. The main reasons for exclusion was not providing informed consent (53%, \( n = 18 \)). Post-assessment was completed by \( n = 26 \) (76%) participants, with a higher percentage of completers in the control group (\( n = 13 \), 81%) compared with the intervention group (\( n = 13 \), 72%). An overview of recruitment channels can be seen in Table 2. Participant flow can be seen in Fig. 1.

On average, participants were \( M = 56.4 \) years of age (SD = 10.2), 35% (\( n = 12 \)) were woman. The highest education level of 50% (\( n = 17 \)) of participants was secondary school level, 50% (\( n = 17 \)) indicated A-levels. With regard to employment status, 21% (\( n = 7 \)) indicated to work full-time. About one third indicated absenteeism (permanently unable to work, \( n = 6 \), 18%; or currently in sick leave, \( n = 5 \), 15%), 23% (\( n = 8 \)) were retired. Net household income was \(<60.000 \text{ €} \) in 82% (\( n = 28 \)) of participants. Nearly half of the participants have had prior experiences with psychotherapy (41%, \( n = 14 \)), whilst 21% (\( n = 7 \)) currently received psychotherapy and \( n = 3 \) (9%) were on a waiting-list for psychotherapy. One third (29%, \( n = 10 \)) never received any psychotherapeutic treatment. One third of participants (32%, \( n = 11 \)) was taking antidepressant medication, with \( n = 6 \) in the IG and \( n = 5 \) in the CG. With regard to risk factors, 21% (\( n = 7 \)) indicated to have an arterial hypertension, 24% (\( n = 8 \)) indicated a lipometabolic disorder, 18% (\( n = 6 \)) indicated to have diabetes type 2, 50% (\( n = 17 \)) indicated to live with any additional chronic disease. More than half of the participants identified as smoking formerly, but currently absent (53%, \( N = 18 \)), 12% (\( n = 4 \)) were smokers. With regard to the self-reported severity of CAD (New York Heart Association (NYHA) classification), 27% (\( n = 9 \)) indicated Stadium I (No restrictions on physical performance), 50% (\( n = 16 \)) Stadium II, 18% (\( n = 6 \)) Stadium III and 6% (\( n = 2 \)) Stadium IV. Average BMI was \( M = 31 \), SD = 6.66. For further details see Table 3.

3.1.2. Study attrition, intervention dropout and satisfaction

Intervention dropout was high (88%, \( n = 16 \)), with 41% (\( n = 7 \)) of the intervention group not completing the introductory module, 18% (\( n = 3 \)) completing the introductory module only, and 30% (\( n = 5 \)) completing additional modules. Furthermore, only 18% (\( n = 3 \)) adhered to the treatment by completing all modules within eight weeks. On average, participants in the intervention group completed \( M = 2.78 \) (SD = 3.23) modules. Participants in the waitlist control group barely started one module (\( M = 0.82 \), SD = 1.81). Nearly one quarter of questionnaire data was missing (23%, \( n = 8 \)). Participants’ satisfaction with the intervention (CSQ-8) was low with \( M = 20.6 \), SD = 0.88. Interested participants who provided informed consent but did not start the intervention (\( n = 7 \)) most often indicated (71%, \( n = 5 \)) that other life circumstances kept them from participation. Participants which discontinued the intervention most often indicated that the contents were too difficult to understand/involved too much text (\( n = 7 \) of \( n = 11 \) participants indicated dropout reasons) or that they did not feel that the intervention was helpful to them/provided additional support (\( n = 4 \)).

3.2. Negative effects and potential of the intervention to affect intended outcomes

At post-measurement (t2) effects on depression (\( \beta = -0.40 \), 95% CI -1.07 to 0.27, \( p = 0.24 \)), anxiety (\( \beta = 0.03 \), 95% CI -0.60 to 0.66, \( p = 0.91 \)), fear of progression (\( \beta = 0.12 \), 95% CI -0.55 to 0.78, \( p = 0.72 \)) and on quality of life (\( \beta = -0.05 \), 95% CI -0.82 to 0.72, \( p = 0.89 \)) were statistically insignificant (Table 4).

Longitudinal analyses revealed no significant change over time in anxiety, depression, quality of life and fear of progression (\( p > 0.05 \)). The intervention had no main effect on the outcomes (\( p > 0.05 \)) and there was no significant effect on the change over time (all interaction effects: \( p > 0.05 \)).

None of the participants reported negative effects attributed to the intervention (t2). One participant indicated suicidal thoughts and plans (participant indicated that he or she would kill her/himself if she/he could) but did not attribute these thoughts to the iCBT but to other life circumstances.

### Table 2

| Addressed recruitment channels. | \( N \) contacted | \( N \) shared information/accepted posts* |
|---------------------------------|------------------|-----------------------------------------|
| German heart institutions/organizations | 35 | 15 |
| Austrian heart institutions/organizations | 17 | 2 |
| Swiss heart institutions/organizations | 2 | 1 |
| Self-help organizations | 26 | 12 |
| Facebook groups | 23 | 11 |
| Facebook sites | 6 | 4 |
| Cardiological practices | 6 | 2 |
| Clinics | 25 | 9 |
| Forums for self-help | 7 | 4 |
| Heart training group | 1 | 1 |
| Conference workshops on WIDeCAD and talks on cardiological conferences | 3 | n.a. |
| Specialized patient magazines | 4 | 0 |
| Psychologists in cardiac clinics | 2 | 1 |
| Psychocardiologists | 1 | 0 |
| Volunteers which are committed to a heart foundation | 10 | 2 |
| Banner on CAD informational web pages/landing page | 5 | 4 |

* Numbers from organizations etc. we know for sure (through feedback) that they have forwarded information on WIDeCAD/helped recruiting by means of sharing flyers, clinics sending follow-up letters to their patients and included information on the WIDeCAD study.
4. Discussion

In this RCT, we evaluated the feasibility of a guided, tailored iCBT compared to a waitlist control-group in participants living with CAD and depressive symptoms. On average, participants in the intervention group completed $M = 2.78$ ($SD = 3.23$) modules. Participants in the waitlist control group barely started one module ($M = 0.82$, $SD = 1.81$). Intervention adherence was comparatively low in comparison to meta-analytically evaluated studies on iCBT for depression and anxiety (Pasarelu et al., 2017) indicating a high percentage of participants allocated to the iCBT received a small intervention dosage. The satisfaction with the intervention was low ($M = 20.6$, $SD = 0.88$, CSQ-8). Participants reported no negative effects attributed to the intervention. Differences between groups with regard to depression, anxiety, fear of progression and quality of life remained non-significant ($p > 0.05$).

Study recruitment was difficult. Additionally, one third of the few people who signed up for screening were excluded due to not providing informed consent. Based on these findings, the administered study procedures and iCBT cannot be deemed feasible to be investigated in a full-scale trial in the present form.

This trial failed to achieve higher uptake and intervention adherence albeit self-referral, adaption of already evaluated contents and enhanced mechanisms to foster adherence. In the following we will discuss possible reasons and solutions for both uptake and intervention adherence as lessons learned from this trial.

Findings are in line with previous trials on depression in people with CAD with a low uptake rate (Messerli-Bürgy et al., 2012; Norlund et al., 2018; Schneider et al., 2020). Based on prior trials we aimed at a broad recruitment strategy in order to examine ways of reaching people living with CAD. However, neither of the online and on-site recruitment strategies (Table 2) proved their value. Various reasons could explain this.

First, there could be a need to address certain subgroups within the population of people living with CAD. Recent studies suggest that people with mild depressive symptoms do often not need additional support shortly after an cardiac index event like MI (Herrmann-Lingen et al., 2016) or implantable cardioverter defibrillator implantation (Habibović et al., 2017) whilst there might be other subpopulations which do. Relevant subpopulations could comprise e.g. people with persisting depressive symptoms after a cardiac event (Davidson et al., 2010).

Second, 53% of the people who expressed their interest did not provide informed consent. The informed consent process could have been too complicated or the described requirements for study participation might have been perceived as too demanding (7 weekly modules, 2 measurements, 1 booster module, technical demands). However, these
Sociodemographic characteristics.

Table 3

| Variable | N  | %  |
|----------|----|----|
| Relationship status |    |    |
| Single | 4  | 11.8% |
| In a relationship | 6  | 17.6% |
| Married (living together) | 22 | 64.7% |
| Married (living apart) | 1  | 2.9% |
| Divorced | 1  | 2.9% |
| Children |    |    |
| Yes | 20 | 58.8% |
| No | 14 | 41.2% |
| Highest educational level (ISCED-97-level) |    |    |
| Level 2 (secondary education first stage) | 17 | 50.0% |
| Level 3 (secondary education second stage) | 6  | 17.6% |
| Level 4 (post-secondary non tertiary education) | 1  | 0.03% |
| Level 5 (first stage of tertiary education) | 9  | 26.5% |
| Level 6 (second stage of tertiary education) | 1  | 0.03% |
| Employment |    |    |
| Yes | 7  | 20.6% |
| No | 7  | 20.6% |
| Income |    |    |
| <1300€ | 4  | 11.8% |
| 1300€ - 2600€ | 10 | 29.4% |
| 2600€ - 5000€ | 7  | 20.6% |
| 5000€ - 18,000€ | 4  | 11.8% |
| Not specified | 2  | 5.9% |
| Details on the CAD condition |    |    |
| Myocardial infarction |    |    |
| Yes | 12 | 35.3% |
| No | 22 | 64.7% |
| NYHA classification |    |    |
| Stadium I: no limitation of physical capacity | 9  | 26.5% |
| Stadium II: complaints in case of increased physical strain | 17 | 50.0% |
| Stadium III: complaints during light physical strain | 6  | 17.6% |
| Stadium IV: complaints at rest | 2  | 5.9% |
| Treatment |    |    |
| Treatment completed | 11 | 32.4% |
| Currently under treatment | 20 | 58.8% |
| Treatment is paused | 3  | 8.8% |
| Implantable defibrillator converter |    |    |
| Yes | 9  | 26.5% |
| No | 25 | 73.5% |
| Operation |    |    |
| No | 11 | 32.4% |
| Yes | 11 | 32.4% |
| Bypass surgery | 11 | 32.4% |
| Percutaneous coronary intervention | 12 | 35.3% |
| Psychotherapy or -intent |    |    |
| Yes | 7  | 20.6% |
| Treatment more than 3 months ago | 14 | 41.2% |
| Currently on waiting list | 3  | 8.8% |
| No | 10 | 29.4% |
| Cardiac rehabilitation |    |    |
| Yes | 23 | 67.6% |
| No and none planned | 8  | 23.5% |
| Currently not, but planned | 3  | 8.8% |
| Antidepressants |    |    |
| Yes, stable dose for at least 3 months | 10 | 29.4% |
| Yes, dose was changed in the last 3 months | 1  | 2.9% |
| No | 23 | 67.6% |
| Somatic (risk) factors |    |    |
| Arterial hypertension | 7  | 20.6% |
| Lipometabolic disorders (cholesterol) | 8  | 23.5% |
| Coagulation disorders | 2  | 5.9% |
| Unknown | 5  | 14.7% |
| Type 2 diabetes | 6  | 17.6% |
| Cancer | 1  | 2.9% |
| Other chronic conditions | 17 | 50.0% |
| No other somatic problems | 15 | 44.1% |
| Nutrition (Fruit and vegetables in the last month) |    |    |

Table 3 (continued)

| Variable | N  | %  |
|----------|----|----|
| >5× a day | 1  | 2.9% |
| 4–5× a day | 2  | 5.9% |
| 5–6× per week | 6  | 17.6% |
| 3× a day | 5  | 14.7% |
| 3–4× per week | 1  | 2.9% |
| 2× a day | 13 | 38.2% |
| 1–2× per week | 2  | 5.9% |

Risk behavior

Alcohol consumption (Alcoholic drinks in the last month)

| Variable | N  | %  |
|----------|----|----|
| Never | 13 | 38.2% |
| 1–2× per month | 10 | 29.4% |
| 1–2× per week | 7  | 20.6% |
| 3–4× per week | 3  | 8.8% |
| 5× per week | 1  | 2.9% |

Physical activity

| Variable | N  | %  |
|----------|----|----|
| Never | 3  | 8.8% |
| 1–2× per week | 10 | 29.4% |
| 3–4× per week | 9  | 26.5% |
| Daily | 12 | 35.5% |

Tobacco use

| Variable | N  | %  |
|----------|----|----|
| Yes | 4  | 11.8% |
| No, but smoked in the past | 18 | 52.9% |
| No, never smoked | 12 | 35.3% |

Screening for psychosocial aspects

Following European guidelines (Piepoli et al. (2016)/German translation of Albus et al. (2018), multiple answers possible)

Critical life events just before problems with the heart occurred

| Variable | N  | %  |
|----------|----|----|
| Death of a loved one | 4  | 11.7% |
| Divorce | 1  | 0.03% |
| Serious illness in the family | 6  | 17.6% |
| Job loss | 4  | 11.7% |
| No | 16 | 47.0% |
| Other critical life events | 10 | 29.4% |

Bond between parents and children

| Variable | N  | %  |
|----------|----|----|
| Yes | 21 | 61.8% |
| No | 8  | 23.5% |
| Unknown | 5  | 14.7% |
| Social support |    |    |
| Yes | 14 | 41.2% |
| Rather yes | 10 | 29.4% |
| Rather no | 8  | 23.5% |
| No | 2  | 5.9% |

Do you often feel annoyed by the habits of other people?

| Variable | N  | %  |
|----------|----|----|
| Yes | 25 | 73.5% |
| No | 9  | 26.5% |

Do you often get annoyed about little things?

| Variable | N  | %  |
|----------|----|----|
| Yes | 25 | 73.5% |
| No | 9  | 26.5% |

Chronic diseases in the family (multiple answers possible)

| Variable | N  | %  |
|----------|----|----|
| Coronary artery disease | 24 | 70.6% |
| Type 2 diabetes | 10 | 29.4% |
| Cancer | 16 | 47.1% |
| Other chronic conditions | 7  | 20.6% |

Notes.

a International Standard Classification of Education (ISCED).

obstacles to successful clinical trials in patients with somatic diseases and depression were also present in other trials of the present research group using similar interventions (Nobis et al., 2015; Bauereiß et al., 2017; Baumeister et al., 2020; Sander et al., 2020). All of these trials have been successfully completed and showed mostly promising results regarding uptake and effectiveness (Nobis et al., 2015; Bauereiß et al., 2017; Baumeister et al., 2020; Sander et al., 2020). Thus, whilst the informed consent process has likely an impact on uptake, this alone does not explain the recruitment problems seemingly specific to psychotherapy trials on patients with CAD.

A third reason for low uptake could be that the target group might be unaware of or ambivalent towards opportunities and necessities of mental health care (Pols et al., 2018). In people with CAD the focus might rather be on the management of the somatic symptoms (Scherer et al., 2007), subordinating the role of psychological aspects, sometimes perceived as stigmatizing (Pols et al., 2018). It has been only a few
decades since “psychocardiology” as an emerging field at the interface between cardiology, psychiatry and psychology is becoming more prominent in the clinical field (Halaris, 2013; Koch, 2013). Researchers call it a challenge of our time to bring different disciplines together to optimize the treatment of CAD towards a more holistic understanding and treatment of disease (Davidson et al., 2018). Thereby, attitudes of both patients and health care providers might need to be tackled (Magaard et al., 2018; Pols et al., 2018) in order to reach patients with CAD and depression. Attitudes and mental health literacy regarding psychological aspects and their treatment in CAD could be subject of future research. This might be even more important for women as the health literacy regarding cardiovascular disease seems generally lower (e.g. Merz et al., 2017) and different (Bucciarelli et al., 2020) than in men. A promising, holistic approach is the collaborative care model (Katon et al., 2010). It integrates services of somatic and mental health professionals (Katon et al., 2010; Tully and Baumeister, 2015). The approach can be feasible and effective as a depression treatment in CAD (Katon et al., 2010; Tully and Baumeister, 2015). So far, there is insufficient evidence to determine the superiority of one of the depression treatments in CAD (standalone psychological or pharmacological or collaborative care) (Tully et al., submitted). To combine advantages of treatment approaches, future studies could investigate an internet intervention like WIDeCAD in a collaborative care framework.

Fourth, our approach did possibly not sufficiently address the social and economic characteristics of the target population. The sample deviates from usual sampling characteristics in the sector of internet intervention utilization, where well educated middle-aged women are often overrepresented (Andersson and Titov, 2014; Karyotaki et al., 2017). Characteristics in the present sample are related to a lower educational level, lower income and complex disease (multi-morbidity, often overrepresented (Andersson and Titov, 2014; Karyotaki et al., 2017). Characteristics in the present sample are related to a lower educational level, lower income and complex disease (multi-morbidity, often overrepresented (Andersson and Titov, 2014; Karyotaki et al., 2017). This finding concords with prior research, documenting a socioeconomic gradient in CAD with income populations (Janati et al., 2011). Thus, this could play an important role in driving health disparities as a whole, suggesting that we need to increase our efforts of tackling the difficult to reach difficult to treat people in need of mental health care.

These considerations raise the question of underlying mechanisms of utilization behavior in psychological interventions for people with CAD. A limited action-control belief (Hoebel et al., 2013; Fournier, 2020; Green et al., 2020) or more existential needs than the future mental health of the intervention was insufficiently engaging. The text comprehensibility of the iCBT at hand could have been too complex, as some participants stated problems with intervention contents. This could have reduced task-related self-efficacy (Schwarzer, 1992). Future studies could examine whether there are associations between perceived text comprehensibility (e.g. readability index), self-efficacy and adherence in people living with CAD.

Second, participants had to complete 7 weekly modules of 45–60 min duration each within 8 weeks to meet the criteria for intervention adherence. This might have been challenging and difficult to integrate into the peoples’ daily lives. As intervention usage can continue beyond post-treatment, it is possible that the number of processed modules could rise with further measurement points. Future studies could explore if a pragmatic intervention usage over a longer time period beyond the post-assessment could be more appropriate (Braun et al., 2020). A corresponding operationalization of adherence might then be indicated.

As challenges regarding intervention adherence is already known from prior studies (e.g. Norlund et al., 2018), we used an iCBT developed to maximize intervention adherence. Moreover, participants had to sign up to the intervention themselves as research indicates that intervention adherence is higher in self-referral health care models compared to internet interventions integrated into primary care settings (Newby et al., 2013; Allen et al., 2016; Norlund et al., 2018). Furthermore, the iCBT contents were already evaluated in prior studies (Weisel et al., 2019, 2020) and adapted to the population with CAD, which was both discussed as reason for comparatively good intervention adherence in prior studies (Johansson et al., 2019; Schneider et al., 2020). Again, based on the low intervention adherence, we have to conclude that all these mechanisms and measures might still not be sufficient to treat people with CAD and depression.

Notes. Data are M (SD), regression coefficients and Cohen's d; SE = standard error; PHQ-9 = Patient Health Questionnaire-9; GAD-7 = Generalized Anxiety Disorder 7-item Scale; AQoL-8D = Assessment of Quality of Life scale; PA-F-KF = Fear of Progression Questionnaire.

### Table 4
Linear regression analysis of changes from pre- to post-treatment.

| Measurement | Baseline T1 IG M (SD) | Post-measurement IG M (SD) | Baseline CG M (SD) | Post CG M (SD) | Standardized coefficient β | SE β | 95% CI | p-Value | Cohen’s d |
|-------------|-----------------------|----------------------------|-------------------|---------------|---------------------------|------|--------|---------|----------|
| Depress., PHQ-9 | 11.61 (3.94) | 9.04 (5.16) | 10.69 (4.67) | 10.73 (5.31) | -0.40 | 0.33 | -1.078 to | 0.24 | 0.31 |
| Anxiety, GAD-7 | 10.00 (5.01) | 8.21 (5.52) | 10.38 (4.41) | 8.29 (4.72) | 0.03 | 0.30 | -0.5973 to | 0.91 | 0.02 |
| Quality of life, AQoL-8D | 61.27 (12.52) | 63.87 (16.43) | 60.06 (12.81) | 63.78 (14.42) | -0.05 | 0.36 | -0.8191 to | 0.89 | 0.00 |
| Fear of progression, Q-SF | 38.50 (10.22) | 39.54 (11.55) | 39.63 (12.16) | 39.00 (8.77) | 0.12 | 0.32 | -0.5467 to | 0.72 | 0.05 |

| | | | | | | | | | |

| | | | | | | | | | |
feasibility trial was neither designed to nor appropriately powered to test a hypothesis (Aarin et al., 2016; Shanyinde et al., 2011). Online assessment leads to a heterogeneous sample limiting the internal validity of findings. For example online assessments are associated with uncertainties concerning diagnostic status of participants as it was based on self-report. Including medical data and applying standardized clinical diagnostic interviews would have been desirable to clarify the mental and somatic status of participants. Additionally, the current sample does not reflect real-life uptake of patients already in the health care system. In order to investigate this a pragmatic trials would have to be conducted which systematically recruit participants from routine care settings like e.g. Johansson et al. (2019). Although generalizability of results is arguably limited, an important strength of this trial is the provision of deeper insights into often encountered difficulties regarding reach and engagement in this population. This might prove to be fruitful for future research in the field as it provides various starting points for future trials.

5. Conclusions

In a nutshell, there is a health policy mandate to provide interventions for people with CAD and depression (Dickens et al., 2012; Haschke et al., 2012; Naghavi et al., 2015). ICBT can be effective, but its reach is not always sufficient and its effectiveness at the patient level cannot yet be determined consistently (Messeri-Bürgy et al., 2012; Norlund et al., 2018; Schneider et al., 2020). It is from utmost importance to further investigate how interventions could effectively reach and support people living with CAD and depression (Nygard et al., 2017; Johansson et al., 2019). This is not the first CAD-trial that didn't succeed recruiting a sufficient number of participants (e.g. Messeri-Bürgy et al., 2012). Future trials on internet-based depression treatment could strive towards a better understanding of the people behind the diagnosis “CAD” in order to address them more effectively (Habibović et al., 2017; Herrmann-Lingen et al., 2016). One idea could be to use recommendations of The European Association of Cardiologists e.g. regarding psychosocial screening questions (Piepoli et al., 2016) to understand and involve the patients’ perspectives and needs more inherently. Then, further investigations regarding persuasive e-health design are needed, supporting people with uptake and regular use of interventions (Baumeister et al., 2019). Overall, new ideas are needed to reach and treat people with CAD and depression since the struggle is real.

Declaration of competing interest

HB received consultancy fees, reimbursement of congress attendance and travel costs as well as payments for lectures from Psychotherapy and Psychiatry Associations as well as Psychotherapy Training Institutes in the context of E-Mental-Health topics. He has been the beneficiary of study support (third-party funding) from several public funding organizations. DDE possess shares in the GET.On Institute GmbH, which works to transfer research findings on Internet- and mobile-phone-based health interventions into routine care. DDE has received payments from several companies and health insurance providers for advice on the use of Internet-based interventions. He has received payments for lectures from Psychotherapy and Psychiatry Associations and has been the beneficiary of third-party funding from health insurance providers.

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CRediT authorship contribution statement

HB and DDE had the idea to investigate the CBT-based intervention in people living with CAD and depression. Intervention contents were originally developed by the university of Erlangen-Nuremberg in cooperation with others (see Weisel et al., 2019). EB adapted contents to the target population. EB and HB planned and designed the study. HB supervised the study. EB operatively performed the study. EB drafted the manuscript, all other authors critically revised the work for important intellectual content. All authors approved the final version to be published and agree to be accountable for all aspects of the work.

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