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PartnerCARE – a psycho-oncological online intervention for partners of patients with cancer: Study protocol for a randomized controlled feasibility trial

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Abstract

Introduction: Cancer burdens not only the patient, but also the partner to a comparable extend. Partners of patients with cancer are highly involved in the caring process by providing physical care, treatment administration and emotional support. Therefore, they often experience distress and report a low quality of life. Interventions for supporting partners are scarce. Existing ones are rarely used by partners because they are often time consuming *per se* and offer only limited flexibility with regard to schedule and location. The online intervention PartnerCARE has been developed on the basis of caregiver needs and consists of tailored support combining psycho-educational, cognitive-behavioural and imaginative elements. The aim of the study is to evaluate feasibility and acceptance of the online intervention PartnerCARE and of the trial process as well as to gain first insights of the putative effectiveness of PartnerCARE.

Methods and analysis: A two arm parallel group randomized controlled trial (RCT) will be conducted to compare the PartnerCARE online intervention with a waitlist control group. The study aims to recruit n=60 partners of patients with any type of cancer across different access paths (e.g. university medical centres, support groups, social media). Congruent with feasibility study objectives, the primary outcome comprises recruitment process, study procedure, acceptance and satisfaction with the intervention (CSQ-I), possible negative effects (INEP) and drop-out rates. Secondary outcomes include quality of life, distress, depression, anxiety, caregiver burden, fear of progression, social support, self-efficacy, coping and loneliness. Online measurements will be performed by self-assessment at three time points (baseline/pre-randomization, 2 months and 4 months after randomization). Data analyses will be based on intention-to-treat principle.

Ethics and dissemination: Ethics approval has been granted. Results from this study will be disseminated to relevant healthcare communities, in peer-reviewed journals and at scientific and clinical conferences.

Keywords: cancer, caregiver, partner, spouse, distress, quality of life, caregiver burden, e-health

Trial Registration number: DRKS00017019. Registered on 08 April 2019.

Strengths and limitations of this study

- Randomized controlled feasibility trial of a novel online intervention specifically tailored to the care needs of partners of patients with cancer
- The PartnerCARE Online intervention integrates evidence-based psychological support including psycho-educational, cognitive-behavioural and imaginative components
- Low-threshold intervention for partners with low utilization of psychosocial services due to time and logistic limitations, low self-awareness of own care needs as well as gender-related concerns (e.g. male partners)
- Possible adverse effects of the intervention will be monitored
- Challenges of the trial comprise the diverse target group (regarding e.g. age, diagnosis of the patient, progress of the disease) and technical comprehension of the participants

Introduction

Family members, particularly the partners, are increasingly involved in care of individuals with cancer [1]. They support the patient in daily life (e.g. manage treatment appointments, additional tasks in the household, manage medication, provide emotional support) and are often not aware of their own needs [2,3]. The disease and the corresponding challenging situation can lead to a great impact on the partner's wellbeing and health. Partners are at high risk to suffer from various types of problems including social and emotional problems [4]. Hence caregivers of cancer patients reported significant more impairments than non-caregivers regarding work productivity, activity and quality of life [5]. Whereas the physical quality of life of partners is similar to a norm population, their reported mental quality of life is significantly lower [6]. Caregivers have also a significant higher occurrence of stress-related comorbidities like depression (OR=1.50), anxiety (OR=1.97) or insomnia (OR=2.01) compared to non-caregivers [5] and similar prevalence of depression (RR=1.01) and anxiety (RR=.71) compared to the patients [7,8]. Concurrently specific burden of caregivers often stays invisible, due to the fact that the health care system focus on the patient and partner's supportive care needs are often neglected or not reported proactive from partners [9]. Male partners as caregivers are a particularly under-recognized and under-supported group [10].

Several psychosocial interventions have been designed to address the needs of cancer caregiver. The interventions differ regarding to their aim (e.g. reduce caregiver burden, improve quality of life), the underlying approaches (e.g. psychoeducation, cognitive-behavioural therapy, existential therapy), delivering format (e.g. face-to-face, online, telephone and group therapy, dyadic, individual) and addressed participants (e.g. couple, patient alone). Systematic reviews have shown that these interventions have small to medium positive effects on multiple outcomes for caregivers [11–13], but interventions relying solely on cognitive behavioural therapy have only negligible effects on caregivers [14]. In general intervention studies often lack of reporting how to implement the interventions into practice [15]. Online interventions move into focus since the last decade and they are broadly perceived as suitable, acceptable and helpful for cancer caregivers [16–18]. Advantages of online interventions over other treatment delivering formats are easy and quick accessibility, flexibility regarding time and location independency and allowance for caregivers privacy while seeking for information and support [19,20]. Furthermore nearly a half of the caring partners are interested in using online interventions and would prefer an intervention that takes less than 1 hour per week, lasts minimum five weeks, is addressed to the partner only and contains information and peer support [21,22].

In the context of the German National Cancer Plan the Federal Ministry of Health requests appropriate psycho-oncological care for all patients and caregivers in need [23,24] irrespective of

inpatient or outpatient treatment. A recent report on the psycho-oncological care in Germany recommends to develop and promote innovative offers like e-health programs [25]. Despite the structures and recommendations a lot of patients and caregivers receive no or no promptly and no low-threshold psycho-oncological care in Germany [26].

Already developed or planned online interventions for caregivers address couples [27,28], informal caregivers in general (including partners, child, parent) [29,30] or male caregivers/caregivers of patients with a specific type of cancer [31,32], while only one hitherto known intervention particularly addresses partners [33]. None of them is available in German. The results from online interventions for caregivers are rare, because to date most of them did only publish study protocols [32,33] or promising trend results from feasibility studies [27–31].

Aim

The present study has two aims. First, we want to evaluate the feasibility of the online intervention PartnerCARE and the extend of participants' satisfaction with the intervention. Second, the potential effectiveness of PartnerCARE on the partner's wellbeing will be investigated compared to the waitlist control group post treatment and over 4-month follow-up. The results of this study will be used to optimize the online intervention via participant feedback and to plan and conduct a confirmatory effectivity evaluation of the intervention.

Methods

Study design

This is a two arm, parallel randomized controlled trial comparing the online intervention PartnerCARE (intervention group, IG) with a waitlist control group (CG). Participants of the intervention group receive the guided version (with individual feedback from an e-coach) of PartnerCARE. The control group receives no intervention during the study. After a waiting period of 4 months participants of the control group get the opportunity to work on the unguided version (with automatic feedback) of PartnerCARE. Assessments of the primary and secondary outcomes take place at baseline (T0), 2 months after randomization (post-treatment, T1) and 4 months after randomization (follow-up, T2).

This clinical trial has been approved by the ethics committee of Ulm University (No. 390/18) and will be conducted and reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) Statement for pilot RCTs [34] as well as the guidelines for executing and reporting internet intervention research [35]. The study protocol is reported according to the SPIRIT

(Standard Protocol Items: Recommendations for Interventional Trials) 2013 Statement [36]. This study is registered in the German clinical trial register under DRKS00017019.

Inclusion and exclusion criteria

The primary inclusion criterion for participation is to be in a relationship with a partner who is diagnosed with any type of cancer (initial diagnosis or relapse, regardless of the onset of the disease). Participants are required (1) to be age 18 or above, (2) have an internet access and an appropriate device, (3) provide the study team an e-mail address for contact reasons and (4) sign an informed consent. Participants will be excluded if the partner with cancer has died before the start of the study. Inclusion and exclusion criteria will be checked at the first online assessment (T0) via self-report.

Recruitment

Recruitment took place online and offline in the complete German-speaking area (includes Germany, Austria and Switzerland). Participants are recruited in relevant social media groups (e.g. groups for caregivers of patients with cancer), in online communities, via flyers and circular emails in university medical centres, links on clinic homepages, online and offline support groups, cancer counselling centres and comprehensive cancer centres (CCCs). All recruitment routs lead to the PartnerCARE study homepage (www.esano.klips-ulm.de/de/trainings/krebserkrankung/partnercare/), where potential participants get information and can register for the study via contact form or sending an e-mail to the study team. Recruitment started in April 2019 and is still ongoing until the target sample size will be reached.

Study Procedure

After initial contact via study homepage or e-mail interested partners receive an e-mail from the study team including a PDF with detailed participation information and an informed consent form attached. After given informed consent (via e-mail, fax or mail), participants get an invitation to the online baseline assessment (T0) and will be randomized afterwards either to the intervention group (immediately access to the guided version of PartnerCARE) or to the waitlist control group (access to the unguided version of PartnerCARE after about 4 months according to the follow-up assessment). Participants are informed via e-mail about group affiliation. 2 months and 4 months after randomization all participants receive an invitation for post-treatment and follow-up assessment (Figure 1).

**** Please insert figure 1 about here****

Randomization

Randomization and allocation of participants to two groups is conducted by an independent researcher, who is not involved in other processes of the study, using an automated online randomization program (www.sealedenvelope.com). Permuted block randomization with randomly arranged block sizes (2 and 4) with an allocation ratio of 1:1 is performed.

Intervention

Development of the intervention

The development of PartnerCARE was inspired by a therapy manual for a structured group intervention about psychoeducation with cancer patients [37] and internet intervention standards established by the research group [e.g. 38]. This group intervention was adapted to an individually online format and to the specific needs of caregivers. A literature search was conducted, focusing on current reviews, qualitative and quantitative research about needs of cancer caregivers. An overview of caregiver needs is listed in Table 1. The most relevant topics out of the caregiver needs are included into the PartnerCARE intervention and some topics that may only be relevant to some are provided as optional additional sessions (e.g. sexuality, death and dying). As PartnerCARE is an offer to partners of patients with any kind of cancer, we abstained from putting detailed information about specific cancer disease and treatment into the intervention to avoid an overload of the single sessions. Instead a list of relevant websites with further information and help services is provided in the 6th session.

In order to ensure participant motivation several persuasive elements were integrated in the design of PartnerCARE [39–41]. The reduction principle is used by providing a weekly activity plan where participants record small activities for each day to learn in small and simple steps to improve self-care. At the beginning of each session the experience with the activities are queried (rehearsal principle). The tunneling principle is implemented by guiding the participants through the intervention with feedback after each session from the e-coach. Reminders are sent if the weekly session is exceeded 2 days. Three exemplary partners are specifically developed regarding the similarity and social learning principle by telling their story, giving exemplary answers on exercises and accompany the participants through the sessions. The exemplary partners are also provided to show participants that they are not alone with their burdens. The online intervention is offered through Minddistrict (www.minddistrict.com), an e-health platform where a secure access to the online intervention and a secure exchange between participant and e-coach is granted. The internet platform and the intervention are available 24 hours a day and 7 days a week.

The first version of PartnerCARE (main sessions) was evaluated by 4 independent psycho oncologists who were not involved in the development process. Each psycho oncologist valued one session via the think aloud method [42]: while they were working on the session they were encouraged to vocalize what they are thinking at the moment. Participant comments were collected on a list and used to further develop PartnerCARE regarding user friendliness (e.g. insert of progress bars on each page), text formulations (e.g. incomprehensible and too psychological phrases verbalized more generally understandable) and content adjustments (e.g. connections to previous sessions). The overall development process lasted from January 2018 until February 2019.

**** Please insert table 1 about here****

Content of the intervention

The content of the online intervention PartnerCARE (Table 2) is composed of different empirically evaluated and clinically established manuals [e.g 37,43]. In the intervention we combined content of different reliable approaches, which are shown to be effective for caregivers [e.g.12]: psycho-education, cognitive behavioural therapy and imagination elements. Therefore, the intervention focuses on activating resources, positive activities, communication skills, improving self-care and self-help strategies to manage caregiver burdens. In addition to psycho-educative text the intervention contains visual and audio materials to enhance understanding and readability as well as to increase adherence and efficacy [44]. Practical exercises, the 3 exemplary partners and imagination exercises make the intervention interactive. To create a transfer of the learned content and strategies into daily life, examples and exercises for home practice between the lessons are contained. PartnerCARE consists of one introduction session, six main consecutive sessions, four optional additional sessions with specific content and one booster session. The optional sessions are presented at the third main session and can be selected by the participant. Duration of each session varies from 30 to 60 minutes, but there is no time limit. Participants can take breaks within a session whenever and how often they want. It is recommended to work on one session each week to have enough time between the sessions for practicing. Therefore, at the end of each session participants are asked to set an appointment for working on the next session.

To have a clear structure over the whole intervention, every session follows the same process:

1. Today's feeling: rating on a burden thermometer from 0 ("no burden") to 10 ("high burden") and describing the current feeling
2. Report of home practice from the last week
3. Basic information: psychoeducation about the topic of the lesson
4. Practical exercises: During the session or for practice between the sessions

5. Preview of the main topic from the next session
6. Imagination exercise: audio imagination of approximately 10 minutes with different topics

*** Please insert table 2 about here***

Guidance

For participants of the intervention group, who receive the guided version of PartnerCARE, every session is accompanied by an e-coach through written feedback. The feedbacks are partly standardized and will be individualized dependent on entries from the participant, encouraging them to stay motivated working on the intervention. Since it is aimed that e-coaches need about 10 minutes in average for writing a feedback due to time efficiency, the actual feedback time is measured. Participants receive the feedback within the next two weekdays after completing a session. Participants can also write a personal message to the e-coach via the Minddistrict platform if they have for example questions or technical problems. Guidance in online intervention is used to increase efficacy, adherence and decrease dropout [45,46].

Text Message Coach

Participants can choose in session 1 if they want to be supported additionally with two SMS per week during the intervention (at no charge for the participant). SMS are sent via online platform MessageBird (www.messagebird.com). The Text Message Coach is thematically matched with the intervention and accompanies each session with two messages and after the main sessions one message per week until the booster session (in total 15 SMS). The text messages include motivational quotes, mini-tasks and reminder of positive activities or exercises, for example "Before you go to bed tonight, look back on your day. Remember: What beautiful moments have you experienced today?". It has been shown that SMS support may have the effect to enhance the intervention effect [47].

Control condition

Participants of the waitlist control group receive no intervention during the study phase but they are free to use other treatment options in standard care. Four months after randomization and after completing the follow-up questionnaire (T2) they get access to the unguided version of PartnerCARE. The intervention is the same as in the intervention group, but instead of individualized feedback they receive a short automatic feedback after each session and the possibility to choose the Text Message Coach in session 1 as well.

Sample size/power calculation

Since with this study the practicality and feasibility of PartnerCARE will be evaluated as the primary outcome, a formal sample size calculation is not required. A sample size of n= 60 was chosen as a recommendation for pilot trials [48]. Part of the feasibility study is to explore the feasibility of recruitment and rating of the different recruitment strategies.

Assessments

All Assessments take place at the online survey platform Unipark (www.unipark.de). Table 3 shows all outcomes and time points. Socio demographic variables include age, sex, marital status, nationality, education, occupational situation and number of children. In addition, clinical characteristics from the diseased partner are assessed with single questions: cancer diagnosis, date of diagnosis, phase of the disease and current medical treatments. Participants will be reminded via email to complete surveys if they do not respond to invitation email.

Primary Outcome

Primary Outcome of this pilot RCT study is the feasibility of the PartnerCARE online intervention. To characterize the different aspects of feasibility a variety of questionnaires is used. The measurement of feasibility is composed of satisfaction with the online intervention, possible negative effects, attitudes toward psychological online interventions, participant flow, drop-out rates, duration of the intervention, processing duration of the lessons, effort from the e-Coaches, evaluation of the SMS-Coach, technical difficulties and individual feedback from participants.

User Satisfaction with web-based health interventions is measured with the *Client Satisfaction Questionnaire adapted to Internet-based interventions (CSQ-I)* [49]. Eight items are rated on a four-point Likert-Scale from 1 (“does apply to me”) to 4 (“does totally apply to me”) which leads to a sum score range from 8 to 32. The scale demonstrated good reliability and construct validity. The CSQ-I is being only submitted to the IG post treatment and follow up.

Possible negative effects of the online intervention are assessed with an online adapted version of the *Inventory for the Assessment of Negative Effects in Psychotherapy (INEP)* [50]. The original 21 items were adapted at the online setting by modifying text (“online intervention” instead of “therapy”) and replacing items about the relationship between participant and therapist with items about the e-coach. The adjusted inventory consists of 8 items with a 7-step bipolar format (-3 = definitely a negative effect; 0 =unchanged; +3 = definitely a positive effect) and 14 items with a 4-step unipolar format (from 0 (“strongly disagree”) to 3 (“fully agree”). Additionally, the first 17 items record whether any negative effect is attributed on the online intervention or on other circumstances in life. For the last 5 items there is an open question in what way the statement applies. The internal consistency for the original INEP was good (α=.86).

Participants of the IG receive the online adapted version of the INEP (INEP-On) post treatment and follow up. In contrast, participants of the CG receive an abridged and adjusted INEP version with 14 items (INEP-CG) about the participation in the study and whether any negative effect is attributed on the participation in the study or on other circumstances in life post treatment and follow- up. Both questionnaires include the question "Since or during the online intervention/participation of the study I had suicidal thoughts/intentions for the first time.". Participants who score with 1 ("agree a little bit") receive automatically an email with information about available health care services in case of emergency. They are advised to seek for help if the symptoms increase. Participants who score 2 or 3 ("agree partly" or "fully agree") receive likewise the automatically emergency email and additionally a psychotherapist of the study management call the participant to clarify if they distance themselves from suicidal ideation.

The attitude towards online interventions is assessed with the *Attitudes towards Psychological Online Interventions Questionnaire (APOI)* [51]. The APOI consist of 16 five-step items (from 1 "totally agree" to 5 "totally disagree") which can integrate into four subscales: Scepticism and Perception of Risks (SCE), Confidence in Effectiveness (CON), Technologization Threat (TET) and Anonymity Benefits (ABE), with a theoretical range of 4 to 20 for each subscale. The total sum score ranges from 16 to 80 whereas higher scores imply a positive attitude towards online interventions. The medians of the scales can be used to classify the scores (56 for the total sum score, 9 for SCE, 16 for CON, 12 for TET and 12 for ABE). Cronbach's' alpha with α=.77 shows an acceptable to good internal consistency. The APOI is given to all participants at all three measurement points.

The SMS Coach is evaluated with three items at post treatment from participants of the IG: "The SMS Coach was helpful.", "The content of the SMS was pleasant." and "The SMS Coach was motiving.". The items are scored on a five-point scale from 1 ("never") to 5 ("always").

After each finished PartnerCARE lesson at the Minddistrict platform the participants have the possibility to give individual feedback to the lesson. First, they can rate the lesson from 1 ("did not like at all") to 10 ("did like very much"). One question is about the scope of the lesson ("too extensive", "too short", "just right"). Then four open questions ask about which exercise was most helpful, what was positive, what could be improved and how long took it to complete the lesson.

Secondary Outcomes

The *NCCN Distress Thermometer (DT)* which has been developed by the National Comprehensive Cancer Network (NCCN) is a valid and reliable measure of psychological distress [52,53]. It consists of a single item with a scale from 0 ("no distress") to 10 ("extreme distress"), illustrated by a thermometer and a list of 36 potential problems which can cause distress

(rationed into five categories: practical problems, family problems, emotional problems, spiritual/religious concerns and physical problems; all rated with yes/no). A cut off value of 5 or higher is recommended for a clinically significant level of distress.

The German version of the *Patient Health Questionnaire (PHQ-8)* is a reliable and valid self-report tool for assessing depression [54]. Given that the online intervention is preventive and does not focus on depression or suicidality, the PHQ-8 is used instead of the PHQ-9 to assess depressive symptoms are as secondary outcome. In this case the PHQ-8 is an acceptable alternative to the PHQ-9. The sensitivity, specificity and positive predictive value of the PHQ-8 is comparable to the PHQ-9 [55]. The questionnaire asks about impairments of the last two weeks and the items are scored on a 4-point Likert scale from 0 ("not at all") to 3 ("nearly every day") with a total range from 0 to 24. Higher values indicate increased severity of symptoms and a cut-off point of ≥10 is defined for a current depression [54].

The *Generalized Anxiety Disorder Questionnaire (GAD-7)* is a valid and efficient tool for assessing generalized anxiety disorder [56]. Items are scored on a 4-point Likert scale from 0 ("not at all") to 3 ("nearly every day"), a total score from 0 to 21 is possible. Like for the PHQ-8 a cut-off point of ≥10 is recommended to screen for generalized anxiety disorder. The reported internal consistency in a German sample is Cronbach α=.89 [57].

Quality of life is assessed with the *Veterans RAND 12-Item Health Survey (VR-12)*, an abbreviated version of the Veterans RAND 36 Items Health Survey (VR-36) which was developed on the basis of the validated SF-36 (Short form 36 health survey) questionnaire [58,59]. The VR-12 consists of different scaled questions (3 point-scale, 5 point-scale and 6 point-scale) with different rating descriptions. The 12 Items can be into two scores: Physical and Mental Health. Standard norms of the summary scores are available for the U.S. population: Mean for physical health summary M=48.60 (SD=11.1) and for mental health summary M=51.01 (SD=10.0) [60].

The *Short Version of the Burden Scale for Family Caregivers (BSFC-s)* is used to assess the amount of burden in caregivers [61,62]. The ten items are rated on a scale from 0 ("strongly disagree") to 3 ("strongly agree"). The score can range from 0 to 30, where higher scores indicate greater caregiver burden. For interpreting the BSFC-s scores a classification system was developed: 0-4 means "none to low" burden, 5-14 means "moderate" burden and 15-30 means "severe to very severe" burden [62]. Cronbach's alpha for the complete scale is with α=.92 very high [61].

Fear of Progression in spouse caregivers is assessed with the German Version of the *Fear of Progression in Partners of Chronically Ill Patients (FoP-Q-SF/P; German: PA-F-P-KF)* [63]. The 12 items are responded on a five-point Likert Scale from 1 ("not at all") to 5 ("very much"). The scale

will be evaluated through addition of the items, whereupon higher values shows higher fear of progression. A cut-off with 34 or higher indicates dysfunctional fear of progression. The internal consistency of the complete scale is high (Cronbach α=.87).

The *ENRICHED Social Support Inventory (ESSI)* is a short questionnaire to assess the perceived emotional social support [64,65]. The five items are measured with a five-point scale (1="at no time" to 5="always") with a minimum of 5 and a maximum of 25. The internal consistency of the scale is α=.89. For the definition lack of social support, the value of 18 was appointed.

The received social support is assessed with the three-item *Oslo social support scale (OSS-3)* [66]. The questionnaire consists of three questions with a four-point scale and two five-point scales with different descriptions. The evaluation is based on the sum score of the raw scores (3 to 14). A score of 3-8 can be interpreted as 'poor support', 9-11 as 'moderate support' and 12-14 as 'strong support' respectively. The internal consistency with α=.64 is acceptable considering the number of items [67]. While loneliness can be an important challenge for caregivers [68], we added one question about loneliness to this questionnaire: 'How lonely do you feel at the moment?' with a five-point-scale from 1="not at all" to 5="very much".

The German version of the *Generalized Self-Efficacy scale (GSE, German: SWE)* measures the perceived self-efficacy [69]. This one-dimensional scale was primary developed for students and teachers, but is also used in cancer context [70,71]. The 10 Items had a response range from 1 ("not at all true") to 4 ("exactly true"). The internal consistency is α=.86 and the validity is confirmed by numerous findings [72].

Coping is assessed with the German Version of the *BriefCOPE (Brief Coping Orientation to Problems Experienced) Inventory* [73,74]. It consists of 28 items which are rated on a four-point Likert-Scale ranged from 1 ("not at all") to 4 ("very much"). The questionnaire is divided in 14 subscales, each represented by two items. The internal consistency for the subscales range from α=.50 to α=.90.

**** Please insert table 3 about here****

Patient and public involvement

Psycho oncologists were involved by valuing the main sessions of PartnerCARE. Patients or public were not further involved in design or procedure of the study. Feedback from participants of the feasibility study will be used to further optimize the online intervention for the following effectivity evaluation study. We intend to disseminate the main results of the feasibility study with a short report at suitable platforms where partners of patients with cancer are reached (e.g. online communities).

Statistical analysis

Demographic data will be reported using descriptive statistics. A chart of participant flow during the whole study will be plotted. Quantity of drop-out and reasons for drop-out will be displayed. With basic psychometric analyses the scale structure and internal consistency of the used questionnaires will be verified. Chi-square (for categorical variables) and t-tests will be performed to analyse whether randomization lead to comparable groups with no significant differences at baseline. Before starting with the analyses, we examine if the data is normally distributed, else we will use a non-parametric test. The significance level for all analyses will be $p \leq .05$.

All statistical analyses will be performed based on the intention-to-treat principle with multiple imputations to replace missing data. Per-protocol analyses for the considerably completers will be additionally conducted to investigate the influence of intervention attrition on study results.

Qualitative individual feedback from participants via the Minddistrict platform regarding to the feasibility and acceptance of the online intervention will be summarized. Feasibility measurements from the online questionnaire will be analysed descriptive (INEP-On; drop-out) and with t-test (APOI; CSQ-I (only in IG)).

To test a potential intervention effect, i.e. an indication for the potential efficacy of PartnerCARE, continuous outcome parameters at post-treatment (T1) will be analysed using an analyses of covariance (ANCOVA), controlling for the baseline measurement (T0) and further covariates (e.g. age, sex). For follow-up (T2) effects a repeated measure analyses of covariance will be conducted with time as the within-subject factor (baseline vs. post-treatment vs. follow-up) and group as the between subject-factor (IG vs. CG). In the case of a significant main effect, post hoc tests will be conducted to analyse between which measurement points the significant differences exist. Cohen's d will be calculated to report effect sizes (effect sizes smaller than .32 are considered small, .33-.55 are considered moderate, and those larger than .56 are considered large [75]).

Discussion

Partners of patients with cancer are confronted with a variety of challenges and new, additional tasks regarding the disease, resulting in a decrease of mental health. These burdens are often overlooked and psycho-oncological support or specific interventions for partners are rare. The online intervention PartnerCARE was developed to provide tailored support for partners of patients with cancer. The main propose of the feasibility study is to evaluate the feasibility and acceptance of PartnerCARE and of the study process itself through a randomized controlled trial. Furthermore, we aim at gaining first preliminary evidence for the potential efficacy of the online

intervention which is hoped to pave the way for a comprehensive effectivity evaluation study. An online intervention is, from our point of view, particularly suitable for partners because of the flexibility (time and place independency), easy accessibility, possible anonymity and low-threshold format. We expect that the online intervention facilitates access to psychosocial services for partners with hitherto low utilization of conventional face-to-face psychosocial care (e.g. because of logistic and time reasons, discomfort or other objections towards psychosocial services or gender-related reasons). Although to date there is evidence that the majority of online intervention users are female [16], we assume that online interventions could suit particularly for male caregivers, because of their tendency to have to be strong (no public searching for help) and their potential difficulties to express their concerns and emotions (could be easier for them in an online setting) [10]. Definitely more research is needed to investigate to better reach male participants for online interventions.

Recruitment of partners of patients with cancer can be challenging due to the fact that partners are often busy and therefore not reached at the clinic, recruitment via patient is not always effective (information is not passed to the partner) and there are not many typical areas where partners can be reached. Recruitment rates for caregivers of cancer patients tended to be poor and varied from 20% to 66% [17]. To overcome the challenges of recruitment we try to use a wide variety of online and offline recruitment strategies and will evaluate their adequacy.

PartnerCARE is the first online interventions for partners of patients with cancer available in German language. The newly developed online intervention for partners of patients with cancer is adjusted to the needs of cancer caregivers and takes several persuasive principles into account. The online intervention uses a variety of different elements (relevant topics, varying exercises, practical tips, audio imaginations) to motivate participants to go on with the intervention. If the pilot study verifies the feasibility and acceptance of PartnerCARE it is conceivable to translate PartnerCARE in different languages and evaluate the online intervention in further studies worldwide.

With this pilot study we will initiate a continuous development and evaluation process of the online intervention PartnerCARE. During the online intervention we assess satisfaction, positive and negative estimations of the intervention via written feedback. These insights from partners of persons with cancer will be used to improve and further develop PartnerCARE to an even more user tailored intervention. We also will assess possible negative effects in our RCT, to evaluate potential side effects of the online intervention for partners. The measurement of e-coach time for feedback every week and quantity of sent reminders will give a first insight in the estimation of costs for the online intervention for implementation in usual health care. If the following effectivity evaluation study (with a planned three-arm trial: guided PartnerCARE vs. automatic

guided PartnerCARE vs. CG) may show that automatic feedback is similar effective than human feedback, PartnerCARE could be even more easily offered and with lower cost for the health care system. But there will be still the need for an intervention manager with an overview over all processes and an alert if suicidal ideation is expressed from participants. Additionally, more research about effects of unguided interventions in RCTs vs. effects of unguided interventions in real world is needed [76].

A few limitations need to be taken into consideration. As all outcomes are assessed via self-report and the contact with participants is only online, there is uncertainty regarding the identity of the participants. With signed informed consent and control questions with automatic premature termination at the first online assessment this problem will be reduced. Online interventions in general and online interventions specifically for caregivers have to face with high dropout rates (29% to 38%) [77,78]. To reduce a potential adherence problem and to enhance motivation the participants of the intervention group are accompanied by an e-coach with feedback and reminders [46,79] and the development of the online design includes persuasive elements [41]. As participation in the study is only possible with access to internet and some technical affinity, we designed the online intervention as simple and intuitive as possible and offer technical use basics at the introduction session. Furthermore, it has been discussed that including a waitlist control condition leads to an overestimation of the effect sizes compared to a no treatment or psychological placebo condition [80]. However, all participants in our study are free to use care as usual and they receive a list of other treatment options like cancer counselling centres if they are interested. In addition, we are able to have a look on possible long-term effects (4-month follow up), but this leads to a long waiting time for the waitlist control group. While the feasibility study used guided feedback in the IG and automated feedback in the CG, further research is needed to investigate whether guided, automatic guided or unguided versions of online interventions have different impacts on the participant's outcomes. Two studies show that human and automated support accomplish similar participant adherence and effectiveness of the online intervention [81,82]. To further investigate this effect, the following effectivity evaluation study could be a three-arm randomized trial with PartnerCARE with human feedback, PartnerCARE with automated feedback and a treatment as usual (TAU) control group. In addition, our online intervention for partners could not cover all relevant topics: A recent study showed 'home care interventions', 'impact of financial demands on caregiver, 'impact of health reforms, programs and policies on caregivers' as some of the most important topics for caregivers [83]. The further development of PartnerCARE should take these insights into account.

Regarding the future outlook, PartnerCARE could be included into the health care routine: by the time a patient becomes diagnosed with cancer, also the partner should be screened for psycho-social and physical burdens. PartnerCARE can also provide a communicative benefit for health

care professionals with enhanced awareness of caregivers and the opportunity of having a special offer for partners. If needed, PartnerCARE could be immediately offered as a tool for partners to work on their burdens regardless of where and when. It can also be used to overcome the waiting time for partners until a local psycho-oncological treatment is available.

Abbreviations

ABE: Anonymity Benefits (Subscale of APOI); ANOVA: Analysis of Variance; APOI: Attitudes towards Psychological Online Interventions Questionnaire; BriefCOPE: Brief Coping Orientation to Problems Experienced Inventory; BSFC-s: Short Version of the Burden Scale for Family Caregivers; CCC: Comprehensive Cancer Center; CG: Waitlist control group; CON: Confidence in Effectiveness (Subscale of APOI); CONSORT: Consolidated Standards of Reporting Trials; CSQ-I: Client Satisfaction Questionnaire adapted to Internet-based interventions; DT: National Comprehensive Cancer Network Distress Thermometer; ESSI: ENRICHED Social Support Inventory; FoP-Q-SF/P: Fear of Progression in Partners of Chronically ill Patients; GAD-7: Generalized Anxiety Disorder Questionnaire; GSE: Generalized Self-Efficacy scale; IG: Intervention group; INEP-On/-CG: Inventory for the Assessment of Negative Effects in Psychotherapy – Online/-Control group; NCCN: National Comprehensive Cancer Network; OSS-3: Oslo social support scale; PHQ-8/9: Patient Health Questionnaire; RCT: Randomized controlled trial; SCE: Scepticism and Perception of Risk (Subscale of APOI); SF-36: Short form 36 health survey questionnaire; SMS: Short Message Service; SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials; TAU: Treatment as usual; TET: Technologization Threat (Subscale of APOI); VR-12: Veterans RAND 12-Item Health Survey; VR-36: Veterans RAND 36 Items Health Survey

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the University of Ulm (no. 390/18) and was registered in the German Clinical Trials Register (DRKS00017019) on 08 April 2019. In case of important protocol modifications, trial registration will be updated. All participants receive written information about study process, data security and voluntariness of participation. Prior to the involvement into the study participants have to confirm understanding of the given information with written consent. Data collection occur pseudonymized by giving every participant a personal ID and data is stored password protected. Access to study data will only be given to authorized study members. After data collection all personal information of participants will be deleted.

Consent for publication

Not applicable.

Availability of data and materials

All principal investigators will be given full access to the data sets. Data set will be stored on password-protected servers of Ulm University with restricted access. External researches may get access to the final trial dataset on request depending on to be specified data security and data exchange regulation agreements. To ensure confidentiality, data dispersed to any investigator or researcher will be blinded of any identifying participant information.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

DB, HG, HB and KH contributed to the study design. DB and IL compiled the content of the intervention sessions. The online design and structure of the intervention was carried out from DB building on prior online interventions of the department of Clinical Psychology and Psychotherapy (HB). Intervention development was supervised by HG, HB and KH. DB is responsible for recruitment and coordination of the study. DB drafted the manuscript. All authors provided critical revision and approved the final manuscript.

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Appendix

Table 1 Overview of needs of cancer caregivers

Needs of caregivers	Literature
Information (e.g. illness and treatment, providing care, death and dying)	[8,22,84,85]
Comprehensive cancer care (e.g. contact with healthcare professionals, knowledge of available services, help in patients' care)	[8,20,84,85]
Emotional and psychological support (e.g. sleep disturbances, depression, anxiety, fatigue, weight gain)	[8,22,84,86]
Impact in daily life (e.g. financial, uncertainty, looking after own health, balance own needs with needs of patient)	[8,20,22,84–86]
Relationship (e.g. communication, sexuality)	[8,22,84]
Spirituality	[84,86]
Optional peer support	[22]

Figure 1 Flow diagram of the study procedure

See separate File "PartnerCARE_Figure 1 Flow diagram.docx"

Table 2 Structure and content of the PartnerCARE sessions

Sessions	**Content**	**Aim**
Introduction	- technical issues/functions - overview of the training	
Main sessions		
1. Specific burdens	- specific burdens of partners - identification of resources - plan for positive activities	- awareness of burdens and own resources
2. Inner drivers	- identification, interpretation and meaning of personal drivers - giving yourself permissions	- recognizing and down-scaling of excessive expectations on the own person to facilitate daily life
3. Partnership communication	- basic rules of successful communication (non-verbal, gender differences) - communication in the context of disease	- improve open communication between partner and patient
4. Handling negative feelings	- focus on anxiety - mindfulness as strategy to deal with anxiety	- reduction of dysfunctional coping and regain of control
5. Control and acceptance	- discrimination between things which are controllable or should be accepted - enjoyment in everyday life	- awareness of dysfunctional control - awareness of little positive things in everyday life
6. Paths and goals	- further support offers - reflection of the training - outlook: next steps / goals	- motivation of the partner to be his own trainer
Booster session	- repetition of two basis elements of the training:	- consolidation of training content

	activity plan and open communication	
Optional additional sessions		
Support of own children	- burdens of children - suggestions for a conversation about the disease/situation	- support with communication with children
Healthy sleep	- rules for healthy sleep - sleeping problems - relaxation exercises	- support with sleep problems
Closeness and sexuality	- open communication about sexuality - relaxation/massage exercises	- removal of taboos regarding communication about sexuality - encouragement to try something new
Existential burdens	- thinking about end of life - hope, farewell, grief	- removal of taboos regarding thinking and talking about death

Table 3 Overview of the assessments

Instruments	Aim	Time of measurement		
		T0	T1	T2
Primary Outcome - feasibility				
CSQ-I[a]	Participant satisfaction		✓	✓
INEP-On/INEP-CG	Negative effects online Interventions/participation in study (CG)		✓	✓
APOI	Attitudes psychological interventions	✓	✓	✓
Dropout rate	Participant adherence		✓	✓
Secondary Outcome				
DT	Distress	✓	✓	✓
PHQ-8	Depression	✓	✓	✓
GAD-7	Anxiety	✓	✓	✓
VR-12	Quality of life	✓	✓	✓
BSFC-s	Caregiver burden	✓	✓	✓

PA-F-P-KF	Fear of progression	✓	✓	✓
ESSI	Perceived emotional social support	✓	✓	✓
OSS-3	Received social support	✓	✓	✓
SWE	General self-efficacy expectation	✓	✓	✓
Brief COPE	Coping	✓	✓	✓
Loneliness	Feeling lonely	✓	✓	✓
Other assessments				
Socio-demographics	Age, sex, occupation, children	✓		
Clinical characteristics partner	Diagnosis, onset, disease phase, current treatment	✓		
Psychotherapy (yes/no, how long)		✓	✓	✓

T0: Baseline, T1: 2 months, T2: 4 months; [a] Recorded in intervention group only
CSQ-I: Client Satisfaction Questionnaire adapted to internet-based interventions, INEP-On/INEP-CG: Inventory of negative effects in psychotherapy – online/-control group, APOI: Attitudes towards Psychological Online Interventions Questionnaire, DT: Distress Thermometer, PHQ-8: Patient Health Questionnaire, GAD-7: Generalized Anxiety Disorder, VR-12: Veterans RAND 12-item Health Survey, BSFC-s: Short version of the Burden Scale for family caregivers, PA-F-P-KF: Fear of progression questionnaire for partners, ESSI: ENRICHD-Social-Support-Instrument, OSS-3: Oslo social support scale, SWE: general self-efficacy expectation scale, Brief COPE: abbreviated version of the COPE (Coping Orientation to Problems Experienced) Inventory

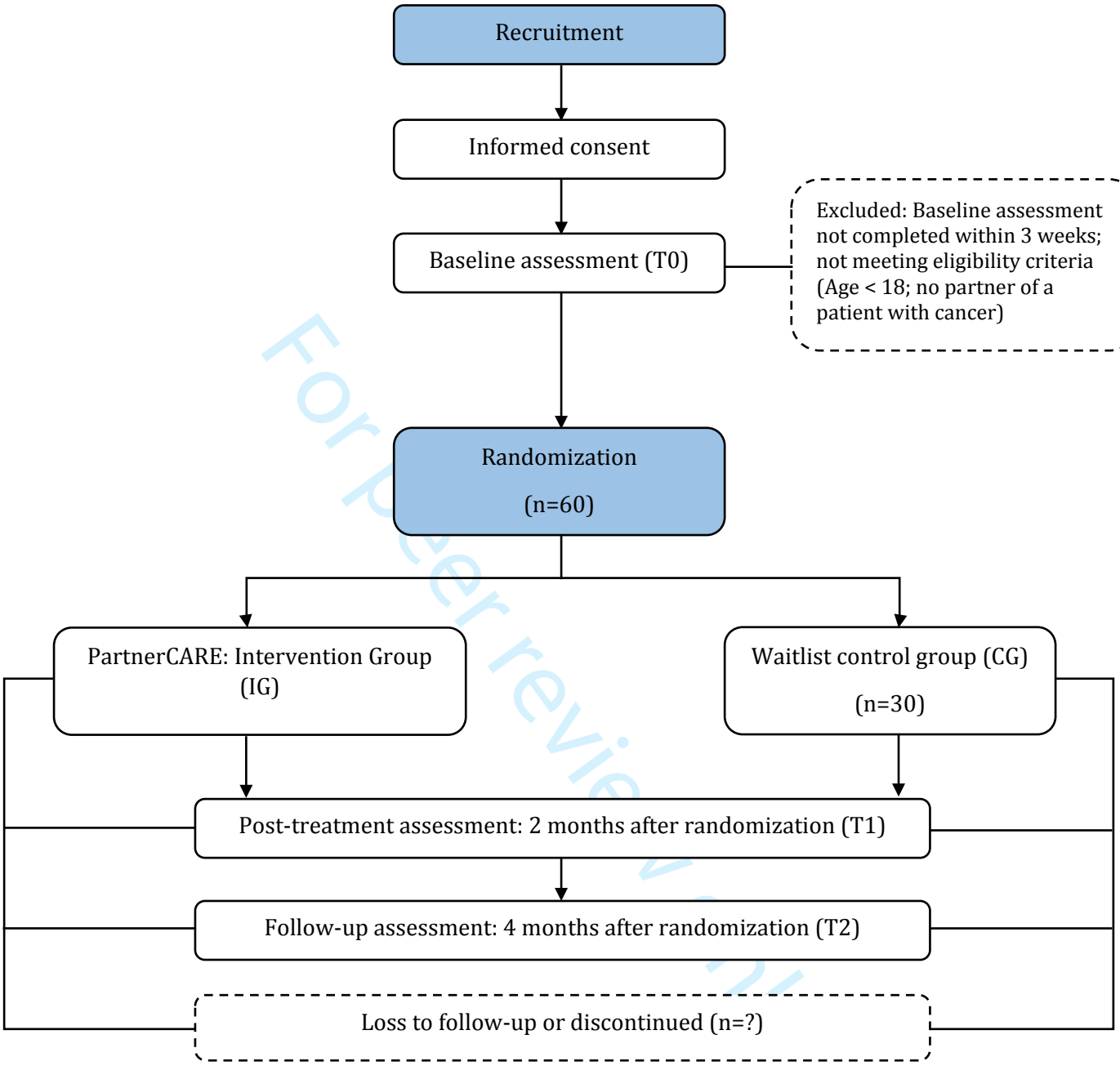

Figure 1 Flow diagram of the study procedure

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2, 17
	2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	18
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	-
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	17-18
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	-

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	9
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5-6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	-
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	7,9
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	-
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10-13
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	6, Fig. 1 (Flowchart)

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	10
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6-7
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	-
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	-
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10-13
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10, 13

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	6, 10, 18
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	-
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	-
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	-
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	10-11
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	-
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	17
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	17

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6, 18
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	-
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	6, 10,18
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	18
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	18
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	2
	31b	Authorship eligibility guidelines and any intended use of professional writers	-
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	-
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	-
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.

BMJ Open

PartnerCARE – a psycho-oncological online intervention for partners of patients with cancer: Study protocol for a randomized controlled feasibility trial

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PartnerCARE – a psycho-oncological online intervention for partners of patients with cancer: Study protocol for a randomized controlled feasibility trial

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Abstract

Introduction: Cancer burdens not only the patient, but also the partner to a comparable extent. Partners of patients with cancer are highly involved in the caring process and therefore often experience distress and report a low quality of life. Interventions for supporting partners are scarce. Existing ones are rarely used by partners because they are often time consuming *per se* and offer only limited flexibility with regard to schedule and location. The online intervention PartnerCARE has been developed on basis of caregiver needs and consists of six consecutive sessions and four optional sessions, which are all guided by an e-coach. The study aims to evaluate feasibility and acceptance of the online intervention PartnerCARE and the related trial process. In addition, first insights of the putative efficacy of PartnerCARE should be gained.

Methods and analysis: A two arm parallel group randomized controlled trial (RCT) will be conducted to compare the PartnerCARE online intervention with a waitlist control group. The study aims to recruit in total n=60 partners of patients with any type of cancer across different access paths (e.g. university medical centres, support groups, social media). Congruent with feasibility study objectives, the primary outcome comprises recruitment process, study procedure, acceptance and satisfaction with the intervention (CSQ-I), possible negative effects (INEP) and drop-out rates. Secondary outcomes include quality of life, distress, depression, anxiety, caregiver burden, fear of progression, social support, self-efficacy, coping and loneliness. Online measurements will be performed by self-assessment at three time points (baseline/pre-randomization, 2 months and 4 months after randomization). Data analyses will be based on intention-to-treat principle.

Ethics and dissemination: Ethics approval has been granted by the Ethics Committee of the University of Ulm (No. 390/18). Results from this study will be disseminated to relevant healthcare communities, in peer-reviewed journals and at scientific and clinical conferences.

Keywords: cancer, caregiver, partner, spouse, distress, quality of life, caregiver burden, e-health

Trial Registration number: DRKS00017019. Registered on 08 April 2019.

Strengths and limitations of this study

- Randomized controlled feasibility trial of a novel online intervention specifically tailored to the care needs of partners of patients with cancer
- The PartnerCARE online intervention integrates evidence-based psychological support including psycho-educational, cognitive-behavioural and guided imagery components
- Low-threshold intervention for partners with low utilization of psychosocial services due to time and logistic limitations, low self-awareness of own care needs as well as gender-related concerns (e.g. male partners)
- Possible adverse effects of the intervention will be monitored
- Challenges of the trial comprise the diverse target group (regarding e.g. age, diagnosis of the patient, progress of the disease) and technical comprehension of the participants

Introduction

Family members, particularly the partners, are increasingly involved in care of individuals with cancer [1]. They support the patient in daily life (e.g. manage treatment appointments, additional tasks in the household, manage medication, provide emotional support) and are often not aware of their own needs [2,3]. The disease and the corresponding challenging situation can lead to a great impact on the partner's wellbeing and health. Partners are at high risk to suffer from various types of problems including social and emotional problems [4]. Hence caregivers of cancer patients reported significant more impairments than non-caregivers regarding work productivity, activity and quality of life [5]. Whereas the physical quality of life of partners is similar to a norm population, their reported mental quality of life is significantly lower [6]. Caregivers have also a significant higher occurrence of stress-related comorbidities like depression (OR=1.50), anxiety (OR=1.97) or insomnia (OR=2.01) compared to non-caregivers [5] and similar prevalence of depression (RR=1.01) and anxiety (RR=.71) compared to the patients [7,8]. Concurrently specific burden of caregivers often stays invisible, due to the fact that the health care system focus on the patient and partner's supportive care needs are often neglected or not reported proactive from partners [9]. Male partners as caregivers are a particularly under-recognized and under-supported group [10].

Several psychosocial interventions have been designed to address the needs of cancer caregiver. The interventions differ regarding their aim (e.g. reduce caregiver burden, improve quality of life), the underlying approaches (e.g. psychoeducation, cognitive-behavioural therapy, existential therapy), delivering format (e.g. face-to-face, online, telephone and group therapy, dyadic, individual) and addressed participants (e.g. couple, caregiver alone). Systematic reviews have shown that these interventions have small to medium positive effects on multiple outcomes for caregivers [11–13], but interventions relying solely on cognitive behavioural therapy have only negligible effects on caregivers [14]. Especially in couple interventions the effects for caregivers have to be considered critically, because numerous interventions focus on patient care and caregivers are only involved as support resource [11]. In general intervention studies often lack of reporting how to implement the interventions into practice [15]. There are two main challenges about interventions for caregivers: First, the target group is difficult to reach, which is evident from low recruitment rates [12,16]. Second, the existing face-to-face interventions are rarely used by caregivers (e.g. too time-consuming, caregivers are unaware of own needs) [17,18]. Therefore, online interventions move into focus since the last decade and they are broadly perceived as suitable, acceptable and helpful for cancer caregivers [16,17,19]. Online interventions have several advantages over other treatment delivering formats: online interventions are easy and quick accessible, flexible regarding time and location independency and allow caregivers privacy

while seeking for information and support [20,21]. Furthermore nearly a half of the caring partners are interested in using online interventions and would prefer an intervention that takes less than 1 hour per week, lasts minimum five weeks, is addressed to the partner only and contains information and peer support [22,23].

In the context of the German National Cancer Plan the Federal Ministry of Health requests appropriate psycho-oncological care for all patients and caregivers in need [24,25] irrespective of inpatient or outpatient treatment. A recent report on the psycho-oncological care in Germany recommends to develop and promote innovative offers like e-health programs [26]. Despite the structures and recommendations a lot of patients and caregivers receive no or no promptly and no low-threshold psycho-oncological care in Germany [27].

Already developed or planned online interventions for caregivers address couples [28,29], informal caregivers in general (including partners, children, parents) [30,31] or male caregivers and caregivers of patients with a specific type of cancer [32,33], while only one hitherto known intervention particularly addresses partners [34]. None of them is available in German. The results from online interventions for caregivers are rare, because to date most of them did only publish study protocols [33,34] or promising trend results from feasibility studies [28–32].

Aim

The present study has two aims. First, we want to evaluate the feasibility of the online intervention PartnerCARE and the extent of participants' satisfaction with the intervention. Second, the potential efficacy of PartnerCARE on the partner's wellbeing will be investigated compared to the waitlist control group post treatment and over 4-month follow-up. The results of this feasibility study will be used to optimize PartnerCARE via participant feedback. Subsequently a comprehensive efficacy evaluation of the online intervention is planned.

Methods

Study design

This is a two arm, parallel randomized controlled trial comparing the online intervention PartnerCARE (intervention group, IG) with a waitlist control group (CG). Participants of the intervention group will receive the guided version (with individual feedback from an e-coach) of PartnerCARE. The control group will receive no intervention during the study. After a waiting period of 4 months participants of the control group will get the opportunity to work on the unguided version (with automatic feedback) of PartnerCARE. Assessments of the primary and

secondary outcomes will take place at baseline (T0), 2 months after randomization (post-treatment, T1) and 4 months after randomization (follow-up, T2).

This clinical trial has been approved by the ethics committee of Ulm University (No. 390/18) and will be conducted and reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) Statement for pilot RCTs [35] as well as the guidelines for executing and reporting internet intervention research [36]. The study protocol is reported according to the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) 2013 Statement [37]. This study is registered in the German clinical trial register under DRKS00017019.

Inclusion and exclusion criteria

The primary inclusion criterion for participation is to be in a relationship with a partner who is diagnosed with any type of cancer (initial diagnosis or relapse, regardless of the onset of the disease or stage of the patient's treatment). Participants are required (1) to be age 18 or above, (2) have an internet access and an appropriate device, (3) provide the study team an e-mail address for contact reasons and (4) sign an informed consent. Participants do not have to live with the patient, but participants will be excluded if the partner with cancer has died before the start of the study. Inclusion and exclusion criteria will be checked at the first online assessment (T0) via self-report.

Recruitment

To overcome the challenge of recruiting cancer caregivers, recruitment take place in a multiplicity of online and offline fields in the complete German-speaking area (includes Germany, Austria and Switzerland). Participants are recruited in relevant social media groups (e.g. groups for caregivers of patients with cancer), in online communities, via flyers and circular emails in university medical centres, links on clinic homepages, online and offline support groups, cancer counselling centres and comprehensive cancer centres (CCCs). All recruitment routes lead to the PartnerCARE study homepage (www.esano.klips-ulm.de/de/trainings/krebserkrankung/ partnercare/), where potential participants get information and can register for the study via contact form or sending an e-mail to the study team. Recruitment started in April 2019 and is still ongoing until the target sample size will be reached. Due to further project plans and financial reasons recruitment will be closed after 18 months, even if the target sample size could not be reached.

Study Procedure

After initial contact via study homepage or e-mail interested partners will receive an e-mail from the study team including a PDF with detailed participation information and an informed consent form attached. After given informed consent (via e-mail, fax or mail), participants will get an invitation to the online baseline assessment (T0) and will be randomized afterwards either to the

intervention group (immediately access to the guided version of PartnerCARE) or to the waitlist control group (access to the unguided version of PartnerCARE after about 4 months according to the follow-up assessment). Participants will be informed via e-mail about group affiliation. 2 months and 4 months after randomization all participants will receive an invitation for post-treatment and follow-up assessment (Figure 1).

**** Please insert figure 1 about here****

Randomization

Randomization and allocation of participants to two groups will be conducted by an independent researcher, who is not involved in other processes of the study, using an automated online randomization program (www.sealedenvelope.com). Permuted block randomization with randomly arranged block sizes (2 and 4) with an allocation ratio of 1:1 (allocation to intervention and waitlist control condition will be equally distributed in each block) will be performed. This results in a preferably balanced group distribution and that the data collector is not able to forecast the allocation of participant.

Intervention

Development of the intervention

The development of PartnerCARE was inspired by a therapy manual for a structured group intervention about psychoeducation with cancer patients [38] and internet intervention standards established by the research group were used [e.g. 39]. Thus, the intervention is based on various concepts which are widely used in cancer context: psychoeducation, behavioural therapy, supportive therapy and guided imagery [12]. The group intervention was adapted to an individually online format and to the specific needs of caregivers. A literature search was conducted, focusing on current reviews, qualitative and quantitative research about needs of cancer caregivers. An overview of caregiver needs is listed in Table 1. The most relevant topics out of the caregiver needs are included into the PartnerCARE intervention and some topics that may only be relevant to some are provided as optional additional sessions (e.g. sexuality, death and dying). As PartnerCARE is an offer to partners of patients with any kind of cancer, we abstained from putting detailed information about specific cancer disease and treatment into the intervention to avoid an overload of the single sessions. Instead a list of relevant websites with further information and help services is provided in the 6th session.

In order to ensure participant motivation several persuasive elements were integrated in the design of PartnerCARE [40–42]. The reduction principle is used by providing a weekly activity plan where participants record small activities for each day to learn in small and simple steps to improve self-care. At the beginning of each session the experience with the activities are queried

(rehearsal principle). The tunneling principle is implemented by guiding the participants through the intervention with feedback after each session from the e-coach. Reminders are sent if the weekly session is exceeded 2 days. Three exemplary partners are specifically developed regarding the similarity and social learning principle by telling their story, giving exemplary answers on exercises and accompany the participants through the sessions. These exemplary partners are introducing themselves in the first session via picture and written text. In all following sessions participants can click on the picture of the exemplary partners and read their exemplary answers to various exercises. The exemplary partners are provided to show participants that they are not alone with their burdens. The online intervention is offered through Minddistrict (www.minddistrict.com), an e-health platform where a secure access to the online intervention and a secure exchange between participant and e-coach is granted. The internet platform and the intervention are available 24 hours a day and 7 days a week.

The first version of PartnerCARE (main sessions) was evaluated by 4 independent psycho oncologists (three psychologists, one psychiatrist) who were not involved in the development process. Each psycho oncologist valued one session via the think aloud method [43]: while they were working on the session they were encouraged to vocalize what they are thinking at the moment. Participant comments were collected on a list and used to further develop PartnerCARE regarding user friendliness (e.g. insert of progress bars on each page), text formulations (e.g. incomprehensible and too psychological phrases verbalized more generally understandable) and content adjustments (e.g. connections to previous sessions). The overall development process lasted from January 2018 until February 2019.

Table 1 Overview of needs of cancer caregivers

Needs of caregivers		**Literature**
Information	about illness and treatment, how to provide care	[8,23,44,45]
Comprehensive cancer care	contact with healthcare professionals, knowledge of available services like e.g. peer support	[8,21,23,44,45]
Emotional and psychological support	sleep disturbances, depression, anxiety, fatigue, weight gain	[8,23,44,46]
Impact in daily life	financial, uncertainty, looking after own health, balance own needs with needs of patient	[8,21,23,44–46]
Relationship	communication, sexuality	[8,23,44]
Spirituality		[44,46]

Content of the intervention

The content of the online intervention PartnerCARE (Table 2) is composed of different empirically evaluated and clinically established manuals [e.g 38,47]. In the intervention we combined content of different reliable approaches, which are shown to be effective for caregivers [e.g.12]: psycho-education, cognitive behavioural therapy, supportive therapy and guided imagery elements. Therefore, the intervention focuses on activating resources, positive activities, communication skills, improving self-care and self-help strategies to manage caregiver burdens. In addition to psycho-educative text the intervention contains visual and audio materials to enhance understanding and readability as well as to increase adherence and efficacy [48]. Practical exercises and the three exemplary partners make the intervention interactive. The guided imagery exercises facilitate awareness of inner-soul processes and they are used for relaxation. To create a transfer of the learned content and strategies into daily life, examples and exercises for home practice between the sessions are contained. PartnerCARE consists of one introduction session (overview of the intervention, introduction in technical handling of the intervention), six main consecutive sessions, four optional additional sessions with specific content and one booster session. The optional sessions are presented at the third main session and can be selected by the participant. Duration of each session varies from 30 to 60 minutes, but there is no time limit. Participants work on their own and can take breaks within a session whenever and how often they want. It is recommended to work on one session each week to have enough time between the sessions for practicing. Therefore, at the end of each session participants are asked to set an appointment for working on the next session.

To have a clear structure over the whole intervention, every session follows the same process:

1. Today's feeling: rating on a burden thermometer from 0 ("no burden") to 10 ("high burden") and describing the current feeling
2. Report of home practice from the last week
3. Basic information: psychoeducation about the topic of the session
4. Practical exercises: During the session or for practice between the sessions
5. Preview of the main topic from the next session
6. Guided imagery exercise: guided audio imagination of approximately 10 minutes with different topics

Table 2 Structure and content of the PartnerCARE sessions

Sessions	Content	Example exercise
Introduction	- technical issues and functions - overview of the training	*Aim:* train the ability to use the online intervention
Main sessions		
1. Specific burdens	- specific burdens (e.g. from partners - identification of own resources (e.g. - plan for positive activities	We ask the partner to write down their story and how they cope with it. *Aim:* awareness of burden and perception of how to deal with the burden using existing resources
2. Inner drivers	- identification, interpretation and meaning of personal drivers (e.g. 'be perfect', 'please others') and their possible impact in caregiver context - giving yourself permissions	Partners identify their inner drivers via questionnaire and are asked to phrase self-permissions. *Aim:* recognizing and down-scaling of excessive expectations on the own person to facilitate daily life
3. Partnership communication	- basic rules of successful communication (non-verbal, gender differences) - communication in the context of disease	Partners are asked to write down their communication problems. Afterwards they should plan a conversation with implementing the learned communication rules. *Aim:* improve open communication between partner and patient
4. Handling negative feelings	- focus on anxiety - mindfulness as strategy to deal with anxiety	Partners are encouraged to try different mindfulness exercises. *Aim:* reduction of dysfunctional coping and regain of control

5. Control and acceptance	- discrimination between things which are controllable or should be accepted - enjoyment in everyday life	Partners are asked which actuality they want to accept because it's not controllable. Furthermore, they learn how to enjoy little things. *Aim:* awareness of dysfunctional control and awareness of little positive things in everyday life
6. Paths and goals	- further support offers - reflection of the training - outlook: next steps / goals	We ask the partner what was helpful and what they want to continue. *Aim:* motivation of the partner to be his own trainer
Booster session	- repetition of two basis elements of the training: activity plan and open communication	Partners are asked how they have fared in the past two weeks and which exercises they continued. *Aim:* reminder and consolidation of training content
Optional additional sessions		
Support of own children	- burdens of children - suggestions for a conversation about the disease/situation	Partners are asked to write down their experience with their children and they get conversation examples. *Aim:* support with communication with children
Healthy sleep	- rules for healthy sleep - sleeping problems - relaxation exercises	Quiz about healthy sleep and sleeping problems. *Aim:* support with sleep problems
Closeness and sexuality	- open communication about sexuality - relaxation/massage exercises	Partners learn about other types of sexuality e.g. relaxation and closeness through massage exercises. *Aim:* removal of taboos regarding communication

			about sexuality and encouragement to try something new
Existential burdens	-	thinking about end of life	Partners can write about their thoughts about the end of life and they are encouraged to write about the sense of the time together with their spouse. *Aim:* removal of taboos regarding thinking and talking about death
	-	hope, farewell, grief	

Online Intervention Process and guidance

After baseline assessment (T0) participants of the intervention group will get immediately access to PartnerCARE. Therefore, they will receive an e-mail with log in information for the Minddistrict platform. After log in the participant can start directly with the introduction session. At the end of each session the participant clicks on a send button and the e-coach receive a note that a session was finished. Afterwards the e-coach log in to Minddistrict, read the filled in text fields from the participant and write a feedback. The participant also receives a note via e-mail when feedback on a session is available.

The feedbacks from the e-coach will be partly standardized and individualized dependent on entries from the participant, encouraging them to stay motivated working on the intervention. Since it is aimed that e-coaches need about 10 minutes in average for writing a feedback due to time efficiency, the actual feedback time is measured. Participants will receive the feedback within the next two weekdays after completing a session. Participants can also write a personal message to the e-coach via the Minddistrict platform if they have questions or technical problems. The communication between participant and e-coach will be asynchronous. Guidance in online intervention is used to increase efficacy, adherence and decrease dropout [49,50].

Text Message Coach

Participants can choose in session 1 if they want to be supported additionally with two SMS per week during the intervention (at no charge for the participant). SMS will be sent via online platform MessageBird (www.messagebird.com). The Text Message Coach is thematically matched with the intervention and accompanies each session with two messages and after the main

sessions one message per week until the booster session (in total 15 SMS). The text messages include motivational quotes, mini-tasks and reminder of positive activities or exercises, for example "Before you go to bed tonight, look back on your day. Remember: What beautiful moments have you experienced today?". It has been shown that SMS support may have the effect to enhance the intervention effect [51].

Control condition

Participants of the waitlist control group will receive no intervention during the study phase but they are free to use other treatment options in standard care. Four months after randomization and after completing the follow-up questionnaire (T2) they will get access to the unguided version of PartnerCARE. The intervention is the same as in the intervention group and participants will have the possibility to choose the Text Message Coach in session 1 as well. But instead of individualized feedback they will receive a short automatic feedback after each session.

Sample size/power calculation

Since with this study the practicality and feasibility of PartnerCARE will be evaluated as the primary outcome, a formal sample size calculation is not required. A total sample size of n= 60 (30 partners per arm) was chosen as a recommendation for pilot trials [52]. Part of the feasibility study will be to explore the feasibility of recruitment and rating of the different recruitment strategies.

Assessments

All Assessments will take place at the online survey platform Unipark (www.unipark.de). Table 3 shows all outcomes and time points. Socio demographic variables include age, sex, marital status, nationality, education, occupational situation and number of children. In addition, clinical characteristics from the diseased partner will be assessed with single questions: cancer diagnosis, date of diagnosis, phase of the disease and current medical treatments. Participants will be reminded via email to complete surveys if they do not respond to invitation email.

Primary Outcome

Primary Outcome of this pilot RCT study is the feasibility of the PartnerCARE online intervention. To characterize the different aspects of feasibility a variety of questionnaires will be used. The measurement of feasibility will be composed of satisfaction with the online intervention, possible negative effects, attitudes toward psychological online interventions, evaluation of the SMS-Coach, individual feedback from participants, processing duration of the sessions (via feedback from participants), participant flow, drop-out rates, duration of the intervention, effort from the e-Coaches and technical difficulties.

User Satisfaction with web-based health interventions will be measured with the *Client Satisfaction Questionnaire adapted to Internet-based interventions (CSQ-I)* [53]. Eight items are rated on a four-point Likert-Scale from 1 ("does apply to me") to 4 ("does totally apply to me") which leads to a sum score range from 8 to 32. The scale demonstrated good reliability and construct validity. The CSQ-I is being only submitted to the IG post treatment and follow up.

Possible negative effects of the online intervention will be assessed with an online adapted version of the *Inventory for the Assessment of Negative Effects in Psychotherapy (INEP)* [54]. The original 21 items were adapted at the online setting by modifying text ("online intervention" instead of "therapy") and replacing items about the relationship between participant and therapist with items about the e-coach. The adjusted inventory consists of 8 items with a 7-step bipolar format (-3 = "definitely a negative effect"; 0 = "unchanged"; +3 = "definitely a positive effect") and 14 items with a 4-step unipolar format (from 0= "strongly disagree" to 3= "fully agree"). Additionally, the first 17 items record whether any negative effect is attributed on the online intervention or on other circumstances in life. For the last 5 items there is an open question in what way the statement applies. The internal consistency for the original INEP was good (α=.86). Participants of the IG will receive the online adapted version of the INEP (INEP-On) post treatment and follow up. In contrast, participants of the CG will receive an abridged and adjusted INEP version with 14 items (INEP-CG) about the participation in the study and whether any negative effect is attributed on the participation in the study or on other circumstances in life post treatment and follow- up. Both questionnaires include the question "Since or during the online intervention/participation of the study I had suicidal thoughts/intentions for the first time.". Participants who score with 1 ("agree a little bit") receive automatically an email with information about available health care services in case of emergency. They are advised to seek for help if the symptoms increase. Participants who score 2 or 3 ("agree partly" or "fully agree") receive likewise the automatically emergency email and additionally a psychotherapist of the study management call the participant to clarify if they distance themselves from suicidal ideation.

The attitude towards online interventions will be assessed with the *Attitudes towards Psychological Online Interventions Questionnaire (APOI)* [55]. The APOI consists of 16 five-step items (from 1 ="totally agree" to 5 ="totally disagree") which can be integrated into four subscales: Scepticism and Perception of Risks (SCE), Confidence in Effectiveness (CON), Technologization Threat (TET) and Anonymity Benefits (ABE), with a theoretical range of 4 to 20 for each subscale. The total sum score ranges from 16 to 80 whereas higher scores imply a positive attitude towards online interventions. The medians of the scales can be used to classify the scores (56 for the total sum score, 9 for SCE, 16 for CON, 12 for TET and 12 for ABE). Cronbach's' alpha with α=.77 shows an acceptable to good internal consistency. The APOI is given to all participants at all three measurement points.

The SMS Coach will be evaluated with three items at post treatment from participants of the IG: "The SMS Coach was helpful.", "The content of the SMS was pleasant." and "The SMS Coach was motiving.". The items are scored on a five-point scale from 1 ("never") to 5 ("always").

After each finished PartnerCARE session at the Minddistrict platform the participants will have the possibility to give individual feedback to the session. First, they can rate the session from 1 ("did not like at all") to 10 ("did like very much"). One question is about the scope of the session ("too extensive", "too short", "just right"). Then four open questions ask about which exercise was most helpful, what was positive, what could be improved and how long took it to complete the session.

Participant flow and drop-out rates will be recorded during the study period. Duration of the intervention for each participant, effort from the e-coach (needed time for written feedback and quantity of sent reminders) and technical difficulties are collected by the e-coach.

Secondary Outcomes

The *NCCN Distress Thermometer (DT)* which has been developed by the National Comprehensive Cancer Network (NCCN) is a valid and reliable measure of psychological distress [56,57]. It consists of a single item with a scale from 0 ("no distress") to 10 ("extreme distress"), illustrated by a thermometer and a list of 36 potential problems which can cause distress (rationed into five categories: practical problems, family problems, emotional problems, spiritual/religious concerns and physical problems; all rated with yes/no). A cut off value of 5 or higher is recommended for a clinically significant level of distress.

The German version of the *Patient Health Questionnaire (PHQ-8)* is a reliable and valid self-report tool for assessing current depression symptoms [58]. Given that the online intervention is preventive and does not focus on depression or suicidality, the PHQ-8 will be used instead of the PHQ-9 to assess depressive symptoms are as secondary outcome. In this case the PHQ-8 is an acceptable alternative to the PHQ-9. The sensitivity, specificity and positive predictive value of the PHQ-8 is comparable to the PHQ-9 [59]. The questionnaire consisting of eight items asks about impairments of the last two weeks and the items are scored on a 4-point Likert scale from 0 ("not at all") to 3 ("nearly every day") with a total range from 0 to 24. Higher values indicate increased severity of symptoms and a cut-off point of ≥10 is defined for current depression symptoms [58].

The *Generalized Anxiety Disorder Questionnaire (GAD-7)* is a valid and efficient tool for assessing symptoms of a generalized anxiety disorder [60]. The seven items are scored on a 4-point Likert scale from 0 ("not at all") to 3 ("nearly every day"), a total score from 0 to 21 is possible. Like for the PHQ-8 a cut-off point of ≥10 is recommended to screen for symptoms of a

generalized anxiety disorder. The reported internal consistency in a German sample is Cronbach α=.89 [61].

Quality of life will be assessed with the *Veterans RAND 12-Item Health Survey (VR-12)*, an abbreviated version of the Veterans RAND 36 Items Health Survey (VR-36) which was developed on the basis of the validated SF-36 (Short form 36 health survey) questionnaire [62,63]. The VR-12 consists of different scaled questions (3 point-scale, 5 point-scale and 6 point-scale) with different rating descriptions. The 12 Items can be separated into two scores: Physical and Mental Health. Standard norms of the summary scores are available for the U.S. population: Mean for physical health summary M=48.60 (SD=11.1) and for mental health summary M=51.01 (SD=10.0) [64].

The *Short Version of the Burden Scale for Family Caregivers (BSFC-s)* will be used to assess the amount of burden in caregivers [65,66]. The ten items are rated on a scale from 0 ("strongly disagree") to 3 ("strongly agree"). The score can range from 0 to 30, where higher scores indicate greater caregiver burden. For interpreting the BSFC-s scores a classification system was developed: 0-4 means "none to low" burden, 5-14 means "moderate" burden and 15-30 means "severe to very severe" burden [66]. Cronbach's alpha for the complete scale is with α=.92 very high [65].

Fear of Progression in spouse caregivers will be assessed with the German Version of the *Fear of Progression in Partners of Chronically Ill Patients (FoP-Q-SF/P; German: PA-F-P-KF)* [67]. The 12 items are responded on a five-point Likert Scale from 1 ("not at all") to 5 ("very much"). The scale will be evaluated through addition of the items, whereupon higher values shows higher fear of progression. A cut-off with 34 or higher indicates dysfunctional fear of progression. The internal consistency of the complete scale is high (Cronbach α=.87).

The *ENRICHED Social Support Inventory (ESSI)* is a short questionnaire to assess the perceived emotional social support [68,69]. The five items are measured with a five-point scale (1="at no time" to 5="always") with a minimum of 5 and a maximum of 25. The internal consistency of the scale is α=.89. For the definition lack of social support, the value of 18 was appointed.

The received social support will be assessed with the three-item *Oslo social support scale (OSS-3)* [70]. The questionnaire consists of one question with a four-point scale and two questions with a five-point scales with different descriptions. The evaluation is based on the sum score of the raw scores (3 to 14). A score of 3-8 can be interpreted as 'poor support', 9-11 as 'moderate support' and 12-14 as 'strong support' respectively. The internal consistency with α=.64 is acceptable considering the number of items [71]. While loneliness can be an important challenge

for caregivers [72], we added one question about loneliness to this questionnaire: 'How lonely do you feel at the moment?' with a five-point-scale from 1("not at all") to 5 ("very much").

The German version of the *Generalized Self-Efficacy scale (GSE, German: SWE)* measures the perceived self-efficacy [73]. This one-dimensional scale was primary developed for students and teachers, but is also used in cancer context [74,75]. The 10 Items had a response range from 1 ("not at all true") to 4 ("exactly true"). The internal consistency is α=.86 and the validity is confirmed by numerous findings [76].

Coping will be assessed with the German Version of the *BriefCOPE (Brief Coping Orientation to Problems Experienced) Inventory* [77,78]. It consists of 28 items which are rated on a four-point Likert-Scale ranged from 1 ("not at all") to 4 ("very much"). The questionnaire is divided in 14 subscales, each represented by two items. The internal consistency for the subscales ranges from α=.50 to α=.90.

Table 3 Overview of the assessments

Instruments	Aim	Time of measurement		
		T0	T1	T2
Primary Outcome - feasibility				
CSQ-I[a]	Participant satisfaction		✓	✓
INEP-On/INEP-CG	Negative effects online Interventions (IG) /participation in study (CG)		✓	✓
APOI	Attitudes psychological interventions	✓	✓	✓
Dropout rate	Participant adherence		✓	✓
Evaluation SMS-Coach[a]	SMS-Coach satisfaction		✓	
Secondary Outcome				
DT	Distress	✓	✓	✓
PHQ-8	Depression	✓	✓	✓
GAD-7	Anxiety	✓	✓	✓
VR-12	Quality of life	✓	✓	✓
BSFC-s	Caregiver burden	✓	✓	✓
PA-F-P-KF	Fear of progression	✓	✓	✓

ESSI	Perceived emotional social support	✓	✓	✓
OSS-3	Received social support	✓	✓	✓
SWE	General self-efficacy expectation	✓	✓	✓
Brief COPE	Coping	✓	✓	✓
Loneliness	Feeling lonely	✓	✓	✓
Other assessments				
Socio-demographics	Age, sex, occupation, children	✓		
Clinical characteristics patient	Diagnosis, onset, disease phase, current treatment	✓		
Psychotherapy (yes/no, how long)		✓	✓	✓

T0: Baseline, T1: 2 months, T2: 4 months; [a] Recorded in intervention group only
CSQ-I: Client Satisfaction Questionnaire adapted to internet-based interventions, INEP-On/INEP-CG: Inventory of negative effects in psychotherapy – online/-control group, APOI: Attitudes towards Psychological Online Interventions Questionnaire, DT: Distress Thermometer, PHQ-8: Patient Health Questionnaire, GAD-7: Generalized Anxiety Disorder, VR-12: Veterans RAND 12-item Health Survey, BSFC-s: Short version of the Burden Scale for family caregivers, PA-F-P-KF: Fear of progression questionnaire for partners, ESSI: ENRICHD-Social-Support-Instrument, OSS-3: Oslo social support scale, SWE: general self-efficacy expectation scale, Brief COPE: abbreviated version of the COPE (Coping Orientation to Problems Experienced) Inventory

Patient and public involvement

Before start of the feasibility trial, psycho oncologists and partners of cancer patients were invited to value the main sessions of PartnerCARE. Since only four psycho oncologists responded to the request, only the feedback from these four psycho oncologists could be included in the development process. As a subsequent step, feedback from participants of the feasibility study will be used to further optimize the online intervention for the following efficacy evaluation study. We intend to disseminate the main results of the feasibility study with a short report at suitable platforms where partners of patients with cancer are reached (e.g. online communities).

Statistical analysis

Demographic data will be reported using descriptive statistics. A chart of participant flow during the whole study will be plotted. Quantity of drop-out and reasons for drop-out will be displayed. With basic psychometric analyses the scale structure and internal consistency of the used questionnaires will be verified. Chi-square (for categorical variables) and t-tests will be performed to analyse whether randomization lead to comparable groups with no significant differences at baseline. Before starting with the analyses, we will examine if the data is normally

distributed, else we will use a non-parametric test. The significance level for all analyses will be $p \leq .05$.

All statistical analyses will be performed based on the intention-to-treat principle with multiple imputations to replace missing data. Per-protocol analyses for the considerably completers will be additionally conducted to investigate the influence of intervention attrition on study results.

Qualitative individual feedback from participants via the Minddistrict platform regarding to the feasibility and acceptance of the online intervention will be summarized. Feasibility measurements from the online questionnaire will be analysed descriptive (INEP-On; drop-out) and with t-test (APOI; CSQ-I (only in IG)).

To test a potential intervention effect, i.e. an indication for the potential efficacy of PartnerCARE, continuous outcome parameters at post-treatment (T1) will be analysed using an analyses of covariance (ANCOVA), controlling for the baseline measurement (T0) and further covariates (e.g. age, sex). For follow-up (T2) effects a repeated measure analyses of covariance will be conducted with time as the within-subject factor (baseline vs. post-treatment vs. follow-up) and group as the between subject-factor (IG vs. CG). In the case of a significant main effect, post hoc tests will be conducted to analyse between which measurement points the significant differences exist. Cohen's d will be calculated to report effect sizes (effect sizes smaller than .32 are considered small, .33-.55 are considered moderate, and those larger than .56 are considered large [79]).

Discussion

Partners of patients with cancer are confronted with a variety of challenges and new, additional tasks regarding the disease, resulting in a decrease of mental health. These burdens are often overlooked and psycho-oncological support or specific interventions for partners are rare. The online intervention PartnerCARE was developed to provide tailored support for partners of patients with cancer. The main propose of the feasibility study is to evaluate the feasibility and acceptance of PartnerCARE and of the study process itself through a randomized controlled trial. Furthermore, we aim at gaining first preliminary evidence for the potential efficacy of the online intervention which is hoped to pave the way for a comprehensive efficacy evaluation study. An online intervention is, from our point of view, particularly suitable for partners because of the flexibility (time and place independency), easy accessibility, possible anonymity and low-threshold format. We expect that the online intervention facilitates access to psychosocial services for partners with hitherto low utilization of conventional face-to-face psychosocial care (e.g. because of logistic and time reasons, discomfort or other objections towards psychosocial services or gender-related reasons)[17,18]. Although to date there is evidence that the majority of online

intervention users are female [17] and female caregivers are more negatively affected by the caregiving process [1], male caregivers should not be neglected. We assume that online interventions could suit particularly for male caregivers, because of their tendency to have to be strong (no public searching for help) and their potential difficulties to express their concerns and emotions (could be easier for them in an online setting) [10]. There is recent research about an online intervention especially for male caregivers [33], but definitely more research is needed to investigate specific needs of male caregivers and how to better reach male participants for online interventions.

Recruitment of partners of patients with cancer can be challenging due to the fact that partners are often busy and therefore not reached at the clinic, recruitment via patient is not always effective (information is not passed to the partner) and there are not many typical areas where partners can be reached. Recruitment rates for caregivers of cancer patients tended to be poor and varied from 20% to 66% [16]. To overcome the challenges of recruitment we try to use a wide variety of online and offline recruitment strategies and will evaluate their adequacy.

PartnerCARE is the first online interventions for partners of patients with cancer available in German language. The newly developed online intervention for partners of patients with cancer is adjusted to the needs of cancer caregivers and takes several persuasive principles into account. The online intervention uses a variety of different elements (relevant topics, varying exercises, practical tips, guided imagery exercises) to motivate participants to go on with the intervention. If the pilot study verifies the feasibility and acceptance of PartnerCARE it is conceivable to translate PartnerCARE in different languages and evaluate the online intervention in further studies worldwide.

With this pilot study we will initiate a continuous development and evaluation process of the online intervention PartnerCARE. During the online intervention we assess satisfaction, positive and negative estimations of the intervention via written feedback. These insights from partners of persons with cancer will be used to improve and further develop PartnerCARE to an even more user tailored intervention. We also will assess possible negative effects in our RCT, to evaluate potential side effects of the online intervention for partners. The measurement of e-coach time for feedback every week and quantity of sent reminders will give a first insight in the estimation of costs for the online intervention for implementation in usual health care.

A few limitations need to be taken into consideration. As all outcomes will be assessed via self-report and the contact with participants is only online, there is uncertainty regarding the identity of the participants. With signed informed consent and control questions with automatic premature termination at the first online assessment this problem will be reduced. Online interventions in general and online interventions specifically for caregivers have to face with high

dropout rates (29% to 38%) [80,81]. To reduce a potential adherence problem and to enhance motivation the participants of the intervention group will be accompanied by an e-coach with feedback and reminders [50,82] and the development of the online design includes persuasive elements [42]. As participation in the study is only possible with access to internet and some technical affinity, we designed the online intervention as simple and intuitive as possible and will offer technical use basics at the introduction session. Furthermore, it has been discussed that including a waitlist control condition leads to an overestimation of the effect sizes compared to a no treatment or psychological placebo condition [83]. However, all participants in our study will be free to use care as usual and they receive a list of other treatment options like cancer counselling centres if they are interested. Furthermore, we will be able to have a look on possible long-term effects (4-month follow up), but this leads to a long waiting time for the waitlist control group. In addition, our online intervention for partners could not cover all relevant topics: A recent study showed 'home care interventions', 'impact of financial demands on caregiver, 'impact of health reforms, programs and policies on caregivers' as some of the most important topics for caregivers [84]. The further development of PartnerCARE should take these insights into account.

Regarding the future outlook, PartnerCARE could be included into the health care routine: by the time a patient becomes diagnosed with cancer, also the partner should be screened for psycho-social and physical burdens. PartnerCARE can also provide a communicative benefit for health care professionals with enhanced awareness of caregivers and the opportunity of having a special offer for partners. If needed, PartnerCARE could be immediately offered as a tool for partners to work on their burdens regardless of where and when. It can also be used to overcome the waiting time for partners until a local psycho-oncological treatment is available.

Abbreviations

ABE: Anonymity Benefits (Subscale of APOI); ANOVA: Analysis of Variance; APOI: Attitudes towards Psychological Online Interventions Questionnaire; BriefCOPE: Brief Coping Orientation to Problems Experienced Inventory; BSFC-s: Short Version of the Burden Scale for Family Caregivers; CCC: Comprehensive Cancer Center; CG: Waitlist control group; CON: Confidence in Effectiveness (Subscale of APOI); CONSORT: Consolidated Standards of Reporting Trials; CSQ-I: Client Satisfaction Questionnaire adapted to Internet-based interventions; DT: National Comprehensive Cancer Network Distress Thermometer; ESSI: ENRICHED Social Support Inventory; FoP-Q-SF/P: Fear of Progression in Partners of Chronically ill Patients; GAD-7: Generalized Anxiety Disorder Questionnaire; GSE: Generalized Self-Efficacy scale; IG: Intervention group; INEP-On/-CG: Inventory for the Assessment of Negative Effects in Psychotherapy – Online/-Control group; NCCN: National Comprehensive Cancer Network; OSS-3: Oslo social

support scale; PHQ-8/9: Patient Health Questionnaire; RCT: Randomized controlled trial; SCE: Scepticism and Perception of Risk (Subscale of APOI); SF-36: Short form 36 health survey questionnaire; SMS: Short Message Service; SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials; TAU: Treatment as usual; TET: Technologization Threat (Subscale of APOI); VR-12: Veterans RAND 12-Item Health Survey; VR-36: Veterans RAND 36 Items Health Survey

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the University of Ulm (no. 390/18) and was registered in the German Clinical Trials Register (DRKS00017019) on 08 April 2019. In case of important protocol modifications, trial registration will be updated. All participants receive written information about study process, data security and voluntariness of participation. Prior to the involvement into the study participants have to confirm understanding of the given information with written consent. Data collection occur pseudonymized by giving every participant a personal ID and data is stored password protected. Access to study data will only be given to authorized study members. After data collection all personal information of participants will be deleted.

Consent for publication

Not applicable.

Availability of data and materials

All principal investigators will be given full access to the data sets. Data set will be stored on password-protected servers of Ulm University with restricted access. External researches may get access to the final trial dataset on request depending on to be specified data security and data exchange regulation agreements. To ensure confidentiality, data dispersed to any investigator or researcher will be blinded of any identifying participant information.

Competing interests

The authors declare that they have no competing interests.

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in data collection, analyses, decision to publish or preparation of future papers regarding the PartnerCARE project.

Author contributions

DB, NB, HG, HB and KH contributed to the study design. DB and IL compiled the content of the intervention sessions. The online design and structure of the intervention was carried out from DB building on prior online interventions of the department of Clinical Psychology and Psychotherapy (HB). Intervention development was supervised by NB, HG, HB and KH. DB is responsible for recruitment and coordination of the study. DB drafted the manuscript. All authors provided critical revision and approved the final manuscript.

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Figure 1 Flow diagram of the study procedure

See separate File "PartnerCARE_Figure 1 Flow diagram.pdf"

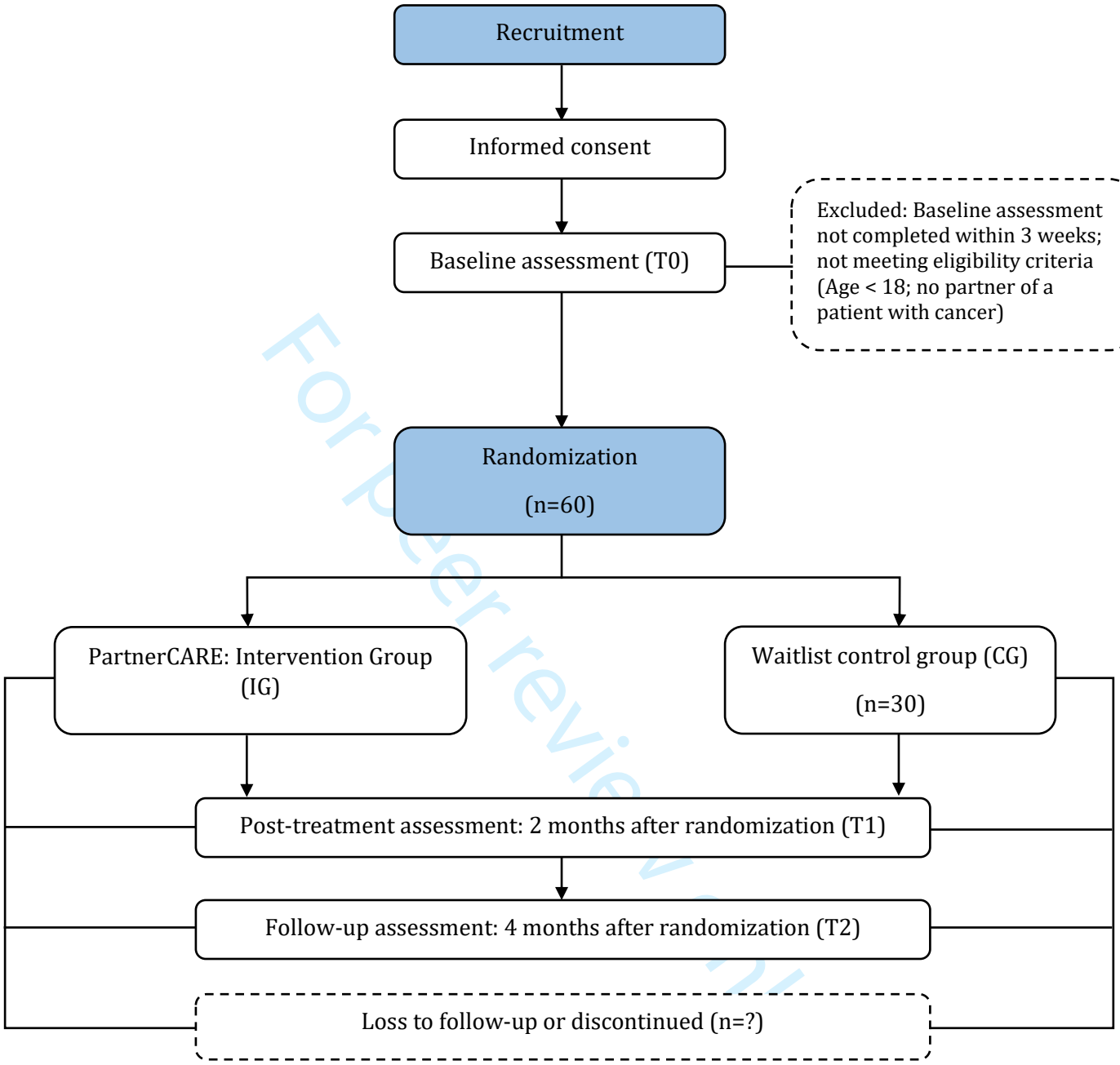

Figure 1 Flow diagram of the study procedure

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2, 22
	2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	-
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	22-23
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	-

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	13
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5-6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-12
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	-
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	7-9
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	-
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	13-18
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	7, Fig. 1 (Flowchart)

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	13
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6-7
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	-
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	-
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13-18
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13, 15

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	6, 13, 22
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	18-19
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	-
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	18-19
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	-
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	-
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	14
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	-
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	22
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	22

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6, 22
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	-
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	6, 13,22
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	22-23
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	22
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	2
	31b	Authorship eligibility guidelines and any intended use of professional writers	-
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	-
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	-
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.

BMJ Open

PartnerCARE – a psycho-oncological online intervention for partners of patients with cancer: Study protocol for a randomized controlled feasibility trial

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PartnerCARE – a psycho-oncological online intervention for partners of patients with cancer: Study protocol for a randomized controlled feasibility trial

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Abstract

Introduction: Cancer burdens not only the patient, but also the partner to a comparable extent. Partners of patients with cancer are highly involved in the caring process and therefore often experience distress and report a low quality of life. Interventions for supporting partners are scarce. Existing ones are rarely used by partners because they are often time consuming *per se* and offer only limited flexibility with regard to schedule and location. The online intervention PartnerCARE has been developed on basis of caregiver needs and consists of six consecutive sessions and four optional sessions, which are all guided by an e-coach. The study aims to evaluate feasibility and acceptance of the online intervention PartnerCARE and the related trial process. In addition, first insights of the putative efficacy of PartnerCARE should be gained.

Methods and analysis: A two arm parallel group randomized controlled trial (RCT) will be conducted to compare the PartnerCARE online intervention with a waitlist control group. The study aims to recruit in total n=60 partners of patients with any type of cancer across different access paths (e.g. university medical centres, support groups, social media). Congruent with feasibility study objectives, the primary outcome comprises recruitment process, study procedure, acceptance and satisfaction with the intervention (CSQ-I), possible negative effects (INEP) and drop-out rates. Secondary outcomes include quality of life, distress, depression, anxiety, caregiver burden, fear of progression, social support, self-efficacy, coping and loneliness. Online measurements will be performed by self-assessment at three time points (baseline/pre-randomization, 2 months and 4 months after randomization). Data analyses will be based on intention-to-treat principle.

Ethics and dissemination: Ethics approval has been granted by the Ethics Committee of the University of Ulm (No. 390/18). Results from this study will be disseminated to relevant healthcare communities, in peer-reviewed journals and at scientific and clinical conferences.

Keywords: cancer, caregiver, partner, spouse, distress, quality of life, caregiver burden, e-health

Trial Registration number: DRKS00017019. Registered on 08 April 2019.

Strengths and limitations of this study

- Randomized controlled feasibility trial of a novel online intervention specifically tailored to the care needs of partners of patients with cancer
- The PartnerCARE online intervention comprises evidence-based psychological support including psychoeducational, cognitive behavioural, and guided imagery components
- Low-threshold intervention for partners with low utilization of psychosocial services due to time and logistic limitations, low self-awareness of own care needs as well as gender-related concerns (e.g. male partners)
- Possible adverse effects of the intervention will be monitored
- Challenges of the trial comprise the diverse target group (regarding e.g. age, diagnosis of the patient, progress of the disease) and technical comprehension of the participants

Introduction

Family members, particularly partners, are increasingly involved in the care of individuals with cancer [1]. They support the patient in daily life (e.g. they manage treatment appointments, take over additional tasks in the household, manage medication, and provide emotional support) and are often not aware of their own needs [2,3]. The disease and the corresponding challenging situation can lead to a great impact on the partner's well-being and health. Partners are at high risk to suffer from various types of problems including social and emotional problems [4]. Hence, caregivers of cancer patients reported significant more impairments than non-caregivers regarding work productivity, activity and quality of life [5]. Whereas the physical quality of life of partners is similar to a norm population, their reported mental quality of life is significantly lower [6]. Compared to non-caregivers, caregivers show a significantly higher occurrence of stress-related comorbidities like depression (OR=1.50), anxiety (OR=1.97) or insomnia (OR=2.01) [5], and compared to patients they show a similar prevalence of depression (RR=1.01) and anxiety (RR=.71) [7,8]. Concurrently, caregivers' burden often stays invisible, due to the fact that the health care system focuses on the patient which leaves partners' supportive care needs often neglected or under-reported [9]. Male partners as caregivers are a particularly under-recognized and under-supported group [10].

Several psychosocial interventions have been designed to address the needs of cancer caregiver. The interventions differ regarding aim (e.g. reduce caregiver burden, improve quality of life), underlying approaches (e.g. psychoeducation, cognitive-behavioural therapy, existential therapy), delivering format (e.g. face-to-face, online, telephone and group therapy, dyadic, individual) and addressed participants (e.g. couple, caregiver alone). Systematic reviews have shown that these interventions have small to medium positive effects on multiple outcomes for caregivers [11–13]. Interventions exclusively relying on cognitive behavioural therapy had only negligible effects on caregivers [14]. Especially in couple interventions the effects for caregivers have to be considered critically, because numerous interventions focus on patient care and include caregivers only as support resources [11]. In general, intervention studies often lack of reporting how to implement the interventions into practice [15]. There are two main challenges about interventions for caregivers: First, the target group is difficult to reach, which is evident from low recruitment rates [12,16]. Second, the existing face-to-face interventions are rarely used by caregivers (e.g. they are too time-consuming, caregivers are unaware of own needs) [17,18]. As a result, online interventions have moved into focus over the last decade. They have broadly been perceived as suitable, acceptable and helpful for cancer caregivers [16,17,19]. Online interventions have several advantages over other treatment delivering formats: online interventions are easily and quickly accessible as well as flexible regarding time and location

independency, and they allow for caregivers privacy while seeking for information and support [20,21]. Furthermore nearly a half of the caring partners are interested in using online interventions and would prefer an intervention that takes less than 1 hour per week, lasts minimum five weeks, is addressed to the partner only and contains information as well as peer support [22,23].

In the context of the German National Cancer Plan the Federal Ministry of Health requests appropriate psycho-oncological care for all patients and caregivers in need [24,25] irrespective of inpatient or outpatient treatment. A recent report on the psycho-oncological care in Germany recommends to develop and promote innovative offers like e-health programs [26]. Despite the structures and recommendations a lot of patients and caregivers receive no or no promptly and no low-threshold psycho-oncological care in Germany [27].

Already developed or planned online interventions for caregivers address couples [28,29], informal caregivers in general (including partners, children, parents) [30,31] or male caregivers and caregivers of patients with a specific type of cancer [32,33], while only one hitherto known intervention particularly addresses partners [34]. None of them is available in German. The results from online interventions for caregivers are rare, because to date most of them did only publish study protocols [33,34] or promising trend results from feasibility studies [28–32].

Aim

The present study has two aims. First, we want to evaluate the feasibility of the online intervention PartnerCARE and the extent of participants' satisfaction with the intervention. Second, the potential efficacy of PartnerCARE on the partner's well-being will be investigated compared to the waitlist control group post treatment and over 4-month follow-up. The results of this feasibility study will be used to optimize PartnerCARE via participant feedback. Subsequently a comprehensive efficacy evaluation of the online intervention is planned.

Methods

Study design

This is a two arm, parallel randomized controlled trial comparing the online intervention PartnerCARE (intervention group, IG) with a waitlist control group (CG). Participants of the intervention group will receive the guided version (with individual feedback from an e-coach) of PartnerCARE. The control group will receive no intervention during the study. After a waiting period of 4 months participants of the control group will get the opportunity to work on the unguided version (with automatic feedback) of PartnerCARE. Assessments of the primary and

secondary outcomes will take place at baseline (T0), 2 months after randomization (post-treatment, T1) and 4 months after randomization (follow-up, T2).

This clinical trial has been approved by the ethics committee of Ulm University (No. 390/18) and will be conducted and reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) Statement for pilot RCTs [35] as well as the guidelines for executing and reporting internet intervention research [36]. The study protocol is reported according to the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) 2013 Statement [37]. This study is registered in the German clinical trial register under DRKS00017019.

Inclusion and exclusion criteria

The primary inclusion criterion for participation is to be in a relationship with a partner who is diagnosed with any type of cancer (initial diagnosis or relapse, regardless of the onset of the disease or stage of the patient's treatment). Participants are required (1) to be age 18 or above, (2) have an internet access and an appropriate device, (3) provide the study team an e-mail address for contact reasons and (4) sign an informed consent. Participants do not have to live with the patient, but participants will be excluded if the partner with cancer has died before the start of the study. Inclusion and exclusion criteria will be checked at the first online assessment (T0) via self-report.

Recruitment

To overcome the challenge of recruiting cancer caregivers, recruitment take place in a multiplicity of online and offline fields in the complete German-speaking area (includes Germany, Austria and Switzerland). Participants are recruited in relevant social media groups (e.g. groups for caregivers of patients with cancer), in online communities, via flyers and circular emails in university medical centres, links on clinic homepages, online and offline support groups, cancer counselling centres and comprehensive cancer centres (CCCs). All recruitment routes lead to the PartnerCARE study homepage (www.esano.klips-ulm.de/de/trainings/krebserkrankung/ partnercare/), where potential participants get information and can register for the study via contact form or sending an e-mail to the study team. Recruitment started in April 2019 and is still ongoing until the target sample size will be reached. Due to further project plans and financial reasons recruitment will be closed after 18 months, even if the target sample size could not be reached.

Study Procedure

After initial contact via study homepage or e-mail interested partners will receive an e-mail from the study team including a PDF with detailed participation information and an informed consent form attached. After given informed consent (via e-mail, fax or mail), participants will get an invitation to the online baseline assessment (T0) and will be randomized afterwards either to the

intervention group (immediately access to the guided version of PartnerCARE) or to the waitlist control group (access to the unguided version of PartnerCARE after about 4 months according to the follow-up assessment). Participants will be informed via e-mail about group affiliation. 2 months and 4 months after randomization all participants will receive an invitation for post-treatment and follow-up assessment (Figure 1).

**** Please insert figure 1 about here****

Randomization

Randomization and allocation of participants to two groups will be conducted by an independent researcher, who is not involved in other processes of the study, using an automated online randomization program (www.sealedenvelope.com). Permuted block randomization with randomly arranged block sizes (2 and 4) with an allocation ratio of 1:1 (allocation to intervention and waitlist control condition will be equally distributed in each block) will be performed. This results in a preferably balanced group distribution and that the data collector is not able to forecast the allocation of participant.

Intervention

Development of the intervention

The development of PartnerCARE was inspired by a therapy manual for a structured group intervention about psychoeducation with cancer patients [38] and internet intervention standards established by the research group [e.g. 39]. Thus, the intervention is based on various concepts which are widely used in cancer context: psychoeducation, behavioural therapy, supportive therapy and guided imagery [12]. The group intervention was adapted to an individually online format and to the specific needs of caregivers. A literature search was conducted, focusing on current reviews, qualitative and quantitative research about needs of cancer caregivers. An overview of caregiver needs is listed in Table 1. The most relevant topics out of the caregiver needs are included into the PartnerCARE intervention and some topics that may only be relevant to some are provided as optional additional sessions (e.g. sexuality, death and dying). As PartnerCARE is an offer to partners of patients with any kind of cancer, we abstained from putting detailed information about specific cancer disease and treatment into the intervention to avoid an overload of the single sessions. Instead a list of relevant websites with further information and help services is provided in the 6th session.

In order to ensure participant motivation several persuasive elements were integrated in the design of PartnerCARE [40–42]. The reduction principle is used by providing a weekly activity plan where participants record small activities for each day to learn in small and simple steps to improve self-care. At the beginning of each session the experience with the activities are queried

(rehearsal principle). The tunneling principle is implemented by guiding the participants through the intervention with feedback after each session from the e-coach. Reminders are sent if the weekly session is exceeded 2 days. Three exemplary partners are specifically developed regarding the similarity and social learning principle by telling their story, giving exemplary answers on exercises and accompany the participants through the sessions. These exemplary partners are introducing themselves in the first session via picture and written text. In all following sessions participants can click on the picture of the exemplary partners and read their exemplary answers to various exercises. The exemplary partners are provided to show participants that they are not alone with their burdens. The online intervention is offered through Minddistrict (www.minddistrict.com), an e-health platform where a secure access to the online intervention and a secure exchange between participant and e-coach is granted. The internet platform and the intervention are available 24 hours a day and 7 days a week.

The first version of PartnerCARE (main sessions) was evaluated by 4 independent psycho oncologists (three psychologists, one psychiatrist) who were not involved in the development process. Each psycho oncologist valued one session via the think aloud method [43]: while they were working on the session they were encouraged to vocalize what they are thinking at the moment. Participant comments were collected on a list and used to further develop PartnerCARE regarding user friendliness (e.g. insert of progress bars on each page), text formulations (e.g. incomprehensible and too psychological phrases verbalized more generally understandable) and content adjustments (e.g. connections to previous sessions). The overall development process lasted from January 2018 until February 2019.

Table 1 Overview of needs of cancer caregivers

Needs of caregivers		**Literature**
Information	about illness and treatment, how to provide care	[8,23,44,45]
Comprehensive cancer care	contact with healthcare professionals, knowledge of available services like e.g. peer support	[8,21,23,44,45]
Emotional and psychological support	sleep disturbances, depression, anxiety, fatigue, weight gain	[8,23,44,46]
Impact in daily life	financial, uncertainty, looking after own health, balance own needs with needs of patient	[8,21,23,44–46]
Relationship	communication, sexuality	[8,23,44]
Spirituality		[44,46]

Content of the intervention

The content of the online intervention PartnerCARE (Table 2) is composed of different empirically evaluated and clinically established manuals [e.g 38,47]. In the intervention we combined content of different reliable approaches, which are shown to be effective for caregivers [e.g.12]: psycho-education, cognitive behavioural therapy, supportive therapy and guided imagery elements. Therefore, the intervention focuses on activating resources, positive activities, communication skills, improving self-care and self-help strategies to manage caregiver burdens. In addition to psychoeducative text the intervention contains visual and audio materials to enhance understanding and readability as well as to increase adherence and efficacy [48]. Practical exercises and the three exemplary partners make the intervention interactive. The guided imagery exercises facilitate awareness of inner-soul processes and they are used for relaxation. To create a transfer of the learned content and strategies into daily life, examples and exercises for home practice between the sessions are contained. PartnerCARE consists of one introduction session (overview of the intervention, introduction in technical handling of the intervention), six main consecutive sessions, four optional additional sessions with specific content and one booster session. The optional sessions are presented at the third main session and can be selected by the participant. Duration of each session varies from 30 to 60 minutes, but there is no time limit. Participants work on their own and can take breaks within a session whenever and how often they want. It is recommended to work on one session each week to have enough time between the sessions for practicing. Therefore, at the end of each session participants are asked to set an appointment for working on the next session.

To have a clear structure over the whole intervention, every session follows the same process:

1. Today's feeling: rating on a burden thermometer from 0 ("no burden") to 10 ("high burden") and describing the current feeling
2. Report of home practice from the last week
3. Basic information: psychoeducation about the topic of the session
4. Practical exercises: During the session or for practice between the sessions
5. Preview of the main topic from the next session
6. Guided imagery exercise: guided audio imagination of approximately 10 minutes with different topics

Table 2 Structure and content of the PartnerCARE sessions

Sessions	Content	Example exercise
Introduction	- technical issues and functions - overview of the training	*Aim:* train the ability to use the online intervention
Main sessions		
1. Specific burdens	- specific burdens (e.g. from partners - identification of own resources (e.g. - plan for positive activities	We ask the partner to write down their story and how they cope with it. *Aim:* awareness of burden and perception of how to deal with the burden using existing resources
2. Inner drivers	- identification, interpretation and meaning of personal drivers (e.g. 'be perfect', 'please others') and their possible impact in caregiver context - giving yourself permissions	Partners identify their inner drivers via questionnaire and are asked to phrase self-permissions. *Aim:* recognizing and down-scaling of excessive expectations on the own person to facilitate daily life
3. Partnership communication	- basic rules of successful communication (non-verbal, gender differences) - communication in the context of disease	Partners are asked to write down their communication problems. Afterwards they should plan a conversation with implementing the learned communication rules. *Aim:* improve open communication between partner and patient
4. Handling negative feelings	- focus on anxiety - mindfulness as strategy to deal with anxiety	Partners are encouraged to try different mindfulness exercises. *Aim:* reduction of dysfunctional coping and regain of control

5. Control and acceptance	- discrimination between things which are controllable or should be accepted - enjoyment in everyday life	Partners are asked which actuality they want to accept because it's not controllable. Furthermore, they learn how to enjoy little things. *Aim:* awareness of dysfunctional control and awareness of little positive things in everyday life
6. Paths and goals	- further support offers - reflection of the training - outlook: next steps / goals	We ask the partner what was helpful and what they want to continue. *Aim:* motivation of the partner to be his own trainer
Booster session	- repetition of two basis elements of the training: activity plan and open communication	Partners are asked how they have fared in the past two weeks and which exercises they continued. *Aim:* reminder and consolidation of training content
Optional additional sessions		
Support of own children	- burdens of children - suggestions for a conversation about the disease/situation	Partners are asked to write down their experience with their children and they get conversation examples. *Aim:* support with communication with children
Healthy sleep	- rules for healthy sleep - sleeping problems - relaxation exercises	Quiz about healthy sleep and sleeping problems. *Aim:* support with sleep problems
Closeness and sexuality	- open communication about sexuality - relaxation/massage exercises	Partners learn about other types of sexuality e.g. relaxation and closeness through massage exercises. *Aim:* removal of taboos regarding communication

			about sexuality and encouragement to try something new
Existential burdens	-	thinking about end of life	Partners can write about their thoughts about the end of life and they are encouraged to write about the sense of the time together with their spouse. *Aim:* removal of taboos regarding thinking and talking about death
	-	hope, farewell, grief	

Online Intervention Process and guidance

After baseline assessment (T0) participants of the intervention group will get immediately access to PartnerCARE. Therefore, they will receive an e-mail with log in information for the Minddistrict platform. After log in the participant can start directly with the introduction session. At the end of each session the participant clicks on a send button and the e-coach receive a note that a session was finished. Afterwards the e-coach log in to Minddistrict, read the filled in text fields from the participant and write a feedback. The participant also receives a note via e-mail when feedback on a session is available.

The feedbacks from the e-coach will be partly standardized and individualized dependent on entries from the participant, encouraging them to stay motivated working on the intervention. Since it is aimed that e-coaches need about 10 minutes in average for writing a feedback due to time efficiency, the actual feedback time is measured. Participants will receive the feedback within the next two weekdays after completing a session. Participants can also write a personal message to the e-coach via the Minddistrict platform if they have questions or technical problems. The communication between participant and e-coach will be asynchronous. Guidance in online intervention is used to increase efficacy, adherence and decrease dropout [49,50].

Text Message Coach

Participants can choose in session 1 if they want to be supported additionally with two SMS per week during the intervention (at no charge for the participant). SMS will be sent via online platform MessageBird (www.messagebird.com). The Text Message Coach is thematically matched with the intervention and accompanies each session with two messages and after the main

sessions one message per week until the booster session (in total 15 SMS). The text messages include motivational quotes, mini-tasks and reminder of positive activities or exercises, for example “Before you go to bed tonight, look back on your day. Remember: What beautiful moments have you experienced today?”. It has been shown that SMS support may have the effect to enhance the intervention effect [51].

Control condition

Participants of the waitlist control group will receive no intervention during the study phase but they are free to use other treatment options in standard care. Four months after randomization and after completing the follow-up questionnaire (T2) they will get access to the unguided version of PartnerCARE. The intervention is the same as in the intervention group and participants will have the possibility to choose the Text Message Coach in session 1 as well. But instead of individualized feedback they will receive a short automatic feedback after each session.

Sample size/power calculation

Since with this study the practicality and feasibility of PartnerCARE will be evaluated as the primary outcome, a formal sample size calculation is not required. A total sample size of n= 60 (30 partners per arm) was chosen as a recommendation for pilot trials [52]. Part of the feasibility study will be to explore the feasibility of recruitment and rating of the different recruitment strategies.

Assessments

All Assessments will take place at the online survey platform Unipark (www.unipark.de). Table 3 shows all outcomes and time points. Socio demographic variables include age, sex, marital status, nationality, education, occupational situation and number of children. In addition, clinical characteristics from the diseased partner will be assessed with single questions: cancer diagnosis, date of diagnosis, phase of the disease and current medical treatments. Participants will be reminded via email to complete surveys if they do not respond to invitation email.

Primary Outcome

Primary Outcome of this pilot RCT study is the feasibility of the PartnerCARE online intervention. To characterize the different aspects of feasibility a variety of questionnaires will be used. The measurement of feasibility will be composed of satisfaction with the online intervention, possible negative effects, attitudes toward psychological online interventions, evaluation of the SMS-Coach, individual feedback from participants, processing duration of the sessions (via feedback from participants), participant flow, drop-out rates, duration of the intervention, effort from the e-Coaches and technical difficulties.

User Satisfaction with web-based health interventions will be measured with the *Client Satisfaction Questionnaire adapted to Internet-based interventions (CSQ-I)* [53]. Eight items are rated on a four-point Likert-Scale from 1 ("does apply to me") to 4 ("does totally apply to me") which leads to a sum score range from 8 to 32. The scale demonstrated good reliability and construct validity. The CSQ-I is being only submitted to the IG post treatment and follow up.

Possible negative effects of the online intervention will be assessed with an online adapted version of the *Inventory for the Assessment of Negative Effects in Psychotherapy (INEP)* [54]. The original 21 items were adapted at the online setting by modifying text ("online intervention" instead of "therapy") and replacing items about the relationship between participant and therapist with items about the e-coach. The adjusted inventory consists of 8 items with a 7-step bipolar format (-3 = "definitely a negative effect"; 0 = "unchanged"; +3 = "definitely a positive effect") and 14 items with a 4-step unipolar format (from 0= "strongly disagree" to 3= "fully agree"). Additionally, the first 17 items record whether any negative effect is attributed on the online intervention or on other circumstances in life. For the last 5 items there is an open question in what way the statement applies. The internal consistency for the original INEP was good (α=.86). Participants of the IG will receive the online adapted version of the INEP (INEP-On) post treatment and follow up. In contrast, participants of the CG will receive an abridged and adjusted INEP version with 14 items (INEP-CG) about the participation in the study and whether any negative effect is attributed on the participation in the study or on other circumstances in life post treatment and follow- up. Both questionnaires include the question "Since or during the online intervention/participation of the study I had suicidal thoughts/intentions for the first time.". Participants who score with 1 ("agree a little bit") receive automatically an email with information about available health care services in case of emergency. They are advised to seek for help if the symptoms increase. Participants who score 2 or 3 ("agree partly" or "fully agree") receive likewise the automatically emergency email and additionally a psychotherapist of the study management call the participant to clarify if they distance themselves from suicidal ideation.

The attitude towards online interventions will be assessed with the *Attitudes towards Psychological Online Interventions Questionnaire (APOI)* [55]. The APOI consists of 16 five-step items (from 1 ="totally agree" to 5 ="totally disagree") which can be integrated into four subscales: Scepticism and Perception of Risks (SCE), Confidence in Effectiveness (CON), Technologization Threat (TET) and Anonymity Benefits (ABE), with a theoretical range of 4 to 20 for each subscale. The total sum score ranges from 16 to 80 whereas higher scores imply a positive attitude towards online interventions. The medians of the scales can be used to classify the scores (56 for the total sum score, 9 for SCE, 16 for CON, 12 for TET and 12 for ABE). Cronbach's' alpha with α=.77 shows an acceptable to good internal consistency. The APOI is given to all participants at all three measurement points.

The SMS Coach will be evaluated with three items at post treatment from participants of the IG: "The SMS Coach was helpful.", "The content of the SMS was pleasant." and "The SMS Coach was motiving.". The items are scored on a five-point scale from 1 ("never") to 5 ("always").

After each finished PartnerCARE session at the Minddistrict platform the participants will have the possibility to give individual feedback to the session. First, they can rate the session from 1 ("did not like at all") to 10 ("did like very much"). One question is about the scope of the session ("too extensive", "too short", "just right"). Then four open questions ask about which exercise was most helpful, what was positive, what could be improved and how long took it to complete the session.

Participant flow and drop-out rates will be recorded during the study period. Duration of the intervention for each participant, effort from the e-coach (needed time for written feedback and quantity of sent reminders) and technical difficulties are collected by the e-coach.

Secondary Outcomes

The *NCCN Distress Thermometer (DT)* which has been developed by the National Comprehensive Cancer Network (NCCN) is a valid and reliable measure of psychological distress [56,57]. It consists of a single item with a scale from 0 ("no distress") to 10 ("extreme distress"), illustrated by a thermometer and a list of 36 potential problems which can cause distress (rationed into five categories: practical problems, family problems, emotional problems, spiritual/religious concerns and physical problems; all rated with yes/no). A cut off value of 5 or higher is recommended for a clinically significant level of distress.

The German version of the *Patient Health Questionnaire (PHQ-8)* is a reliable and valid self-report tool for assessing current depression symptoms [58]. Given that the online intervention is preventive and does not focus on depression or suicidality, the PHQ-8 will be used instead of the PHQ-9 to assess depressive symptoms are as secondary outcome. In this case the PHQ-8 is an acceptable alternative to the PHQ-9. The sensitivity, specificity and positive predictive value of the PHQ-8 is comparable to the PHQ-9 [59]. The questionnaire consisting of eight items asks about impairments of the last two weeks and the items are scored on a 4-point Likert scale from 0 ("not at all") to 3 ("nearly every day") with a total range from 0 to 24. Higher values indicate increased severity of symptoms and a cut-off point of ≥10 is defined for current depression symptoms [58].

The *Generalized Anxiety Disorder Questionnaire (GAD-7)* is a valid and efficient tool for assessing symptoms of a generalized anxiety disorder [60]. The seven items are scored on a 4-point Likert scale from 0 ("not at all") to 3 ("nearly every day"), a total score from 0 to 21 is possible. Like for the PHQ-8 a cut-off point of ≥10 is recommended to screen for symptoms of a generalized anxiety disorder. The reported internal consistency in a German sample is Cronbach α=.89 [61].

Quality of life will be assessed with the *Veterans RAND 12-Item Health Survey (VR-12)*, an abbreviated version of the Veterans RAND 36 Items Health Survey (VR-36) which was developed on the basis of the validated SF-36 (Short form 36 health survey) questionnaire [62,63]. The VR-12 consists of different scaled questions (3 point-scale, 5 point-scale and 6 point-scale) with different rating descriptions. The 12 Items can be separated into two scores: Physical and Mental Health. Standard norms of the summary scores are available for the U.S. population: Mean for physical health summary M=48.60 (SD=11.1) and for mental health summary M=51.01 (SD=10.0) [64].

The *Short Version of the Burden Scale for Family Caregivers (BSFC-s)* will be used to assess the amount of burden in caregivers [65,66]. The ten items are rated on a scale from 0 ("strongly disagree") to 3 ("strongly agree"). The score can range from 0 to 30, where higher scores indicate greater caregiver burden. For interpreting the BSFC-s scores a classification system was developed: 0-4 means "none to low" burden, 5-14 means "moderate" burden and 15-30 means "severe to very severe" burden [66]. Cronbach's alpha for the complete scale is with α=.92 very high [65].

Fear of Progression in spouse caregivers will be assessed with the German Version of the *Fear of Progression in Partners of Chronically Ill Patients (FoP-Q-SF/P; German: PA-F-P-KF)* [67]. The 12 items are responded on a five-point Likert Scale from 1 ("not at all") to 5 ("very much"). The scale will be evaluated through addition of the items, whereupon higher values shows higher fear of progression. A cut-off with 34 or higher indicates dysfunctional fear of progression. The internal consistency of the complete scale is high (Cronbach α=.87).

The *ENRICHED Social Support Inventory (ESSI)* is a short questionnaire to assess the perceived emotional social support [68,69]. The five items are measured with a five-point scale (1="at no time" to 5="always") with a minimum of 5 and a maximum of 25. The internal consistency of the scale is α=.89. For the definition lack of social support, the value of 18 was appointed.

The received social support will be assessed with the three-item *Oslo social support scale (OSS-3)* [70]. The questionnaire consists of one question with a four-point scale and two questions with a five-point scales with different descriptions. The evaluation is based on the sum score of the raw scores (3 to 14). A score of 3-8 can be interpreted as 'poor support', 9-11 as 'moderate support' and 12-14 as 'strong support' respectively. The internal consistency with α=.64 is acceptable considering the number of items [71]. While loneliness can be an important challenge for caregivers [72], we added one question about loneliness to this questionnaire: 'How lonely do you feel at the moment?' with a five-point-scale from 1("not at all") to 5 ("very much").

The German version of the *Generalized Self-Efficacy scale (GSE, German: SWE)* measures the perceived self-efficacy [73]. This one-dimensional scale was primary developed for students and teachers, but is also used in cancer context [74,75]. The 10 Items had a response range from 1 ("not at all true") to 4 ("exactly true"). The internal consistency is α=.86 and the validity is confirmed by numerous findings [76].

Coping will be assessed with the German Version of the *BriefCOPE (Brief Coping Orientation to Problems Experienced) Inventory* [77,78]. It consists of 28 items which are rated on a four-point Likert-Scale ranged from 1 ("not at all") to 4 ("very much"). The questionnaire is divided in 14 subscales, each represented by two items. The internal consistency for the subscales ranges from α=.50 to α=.90.

Table 3 Overview of the assessments

Instruments	Aim	Time of measurement		
		T0	T1	T2
Primary Outcome - feasibility				
CSQ-I[a]	Participant satisfaction		✓	✓
INEP-On/INEP-CG	Negative effects online Interventions (IG) /participation in study (CG)		✓	✓
APOI	Attitudes psychological interventions	✓	✓	✓
Dropout rate	Participant adherence		✓	✓
Evaluation SMS-Coach[a]	SMS-Coach satisfaction		✓	
Secondary Outcome				
DT	Distress	✓	✓	✓
PHQ-8	Depression	✓	✓	✓
GAD-7	Anxiety	✓	✓	✓
VR-12	Quality of life	✓	✓	✓
BSFC-s	Caregiver burden	✓	✓	✓
PA-F-P-KF	Fear of progression	✓	✓	✓
ESSI	Perceived emotional social support	✓	✓	✓
OSS-3	Received social support	✓	✓	✓

SWE	General self-efficacy expectation	✓	✓	✓
Brief COPE	Coping	✓	✓	✓
Loneliness	Feeling lonely	✓	✓	✓
Other assessments				
Socio-demographics	Age, sex, occupation, children	✓		
Clinical characteristics patient	Diagnosis, onset, disease phase, current treatment	✓		
Psychotherapy (yes/no, how long)		✓	✓	✓

T0: Baseline, T1: 2 months, T2: 4 months; [a] Recorded in intervention group only
CSQ-I: Client Satisfaction Questionnaire adapted to internet-based interventions, INEP-On/INEP-CG: Inventory of negative effects in psychotherapy – online/-control group, APOI: Attitudes towards Psychological Online Interventions Questionnaire, DT: Distress Thermometer, PHQ-8: Patient Health Questionnaire, GAD-7: Generalized Anxiety Disorder, VR-12: Veterans RAND 12-item Health Survey, BSFC-s: Short version of the Burden Scale for family caregivers, PA-F-P-KF: Fear of progression questionnaire for partners, ESSI: ENRICHD-Social-Support-Instrument, OSS-3: Oslo social support scale, SWE: general self-efficacy expectation scale, Brief COPE: abbreviated version of the COPE (Coping Orientation to Problems Experienced) Inventory

Patient and public involvement

Before start of the feasibility trial, psycho oncologists and partners of cancer patients were invited to value the main sessions of PartnerCARE. Since only four psycho oncologists responded to the request, only the feedback from these four psycho oncologists could be included in the development process. As a subsequent step, feedback from participants of the feasibility study will be used to further optimize the online intervention for the following efficacy evaluation study. We intend to disseminate the main results of the feasibility study with a short report at suitable platforms where partners of patients with cancer are reached (e.g. online communities).

Statistical analysis

Demographic data will be reported using descriptive statistics. A chart of participant flow during the whole study will be plotted. Quantity of drop-out and reasons for drop-out will be displayed. With basic psychometric analyses the scale structure and internal consistency of the used questionnaires will be verified. Chi-square (for categorical variables) and t-tests will be performed to analyse whether randomization lead to comparable groups with no significant differences at baseline. Before starting with the analyses, we will examine if the data is normally distributed, else we will use a non-parametric test. The significance level for all analyses will be $p \leq .05$.

All statistical analyses will be performed based on the intention-to-treat principle with multiple imputations to replace missing data. Per-protocol analyses for the considerably completers will be additionally conducted to investigate the influence of intervention attrition on study results.

Qualitative individual feedback from participants via the Minddistrict platform regarding to the feasibility and acceptance of the online intervention will be summarized. Feasibility measurements from the online questionnaire will be analysed descriptive (INEP-On; drop-out) and with t-test (APOI; CSQ-I (only in IG)).

To test a potential intervention effect, i.e. an indication for the potential efficacy of PartnerCARE, continuous outcome parameters at post-treatment (T1) will be analysed using an analyses of covariance (ANCOVA), controlling for the baseline measurement (T0) and further covariates (e.g. age, sex). For follow-up (T2) effects a repeated measure analyses of covariance will be conducted with time as the within-subject factor (baseline vs. post-treatment vs. follow-up) and group as the between subject-factor (IG vs. CG). In the case of a significant main effect, post hoc tests will be conducted to analyse between which measurement points the significant differences exist. Cohen's d will be calculated to report effect sizes (effect sizes smaller than .32 are considered small, .33-.55 are considered moderate, and those larger than .56 are considered large [79]).

Discussion

Partners of patients with cancer are confronted with a variety of challenges and new, additional tasks regarding the disease, resulting in a decrease of mental health. These burdens are often overlooked and psycho-oncological support or specific interventions for partners are rare. The online intervention PartnerCARE was developed to provide tailored support for partners of patients with cancer. The main propose of the feasibility study is to evaluate the feasibility and acceptance of PartnerCARE and of the study process itself through a randomized controlled trial. Furthermore, we aim at gaining first preliminary evidence for the potential efficacy of the online intervention which is hoped to pave the way for a comprehensive efficacy evaluation study. An online intervention is, from our point of view, particularly suitable for partners because of the flexibility (time and place independency), easy accessibility, possible anonymity and low-threshold format. We expect that the online intervention facilitates access to psychosocial services for partners with hitherto low utilization of conventional face-to-face psychosocial care (e.g. because of logistic and time reasons, discomfort or other objections towards psychosocial services or gender-related reasons)[17,18]. Although to date there is evidence that the majority of online intervention users are female [17] and female caregivers are more negatively affected by the caregiving process [1], male caregivers should not be neglected. We assume that online

interventions could suit particularly for male caregivers, because of their tendency to have to be strong (no public searching for help) and their potential difficulties to express their concerns and emotions (could be easier for them in an online setting) [10]. There is recent research about an online intervention especially for male caregivers [33], but definitely more research is needed to investigate specific needs of male caregivers and how to better reach male participants for online interventions.

Recruitment of partners of patients with cancer can be challenging due to the fact that partners are often busy and therefore not reached at the clinic, recruitment via patient is not always effective (information is not passed to the partner) and there are not many typical areas where partners can be reached. Recruitment rates for caregivers of cancer patients tended to be poor and varied from 20% to 66% [16]. To overcome the challenges of recruitment we try to use a wide variety of online and offline recruitment strategies and will evaluate their adequacy.

PartnerCARE is the first online interventions for partners of patients with cancer available in German language. The newly developed online intervention for partners of patients with cancer is adjusted to the needs of cancer caregivers and takes several persuasive principles into account. The online intervention uses a variety of different elements (relevant topics, varying exercises, practical tips, guided imagery exercises) to motivate participants to go on with the intervention. If the pilot study verifies the feasibility and acceptance of PartnerCARE it is conceivable to translate PartnerCARE in different languages and evaluate the online intervention in further studies worldwide.

With this pilot study we will initiate a continuous development and evaluation process of the online intervention PartnerCARE. During the online intervention we assess satisfaction, positive and negative estimations of the intervention via written feedback. These insights from partners of persons with cancer will be used to improve and further develop PartnerCARE to an even more user tailored intervention. We also will assess possible negative effects in our RCT, to evaluate potential side effects of the online intervention for partners. The measurement of e-coach time for feedback every week and quantity of sent reminders will give a first insight in the estimation of costs for the online intervention for implementation in usual health care.

A few limitations need to be taken into consideration. As all outcomes will be assessed via self-report and the contact with participants is only online, there is uncertainty regarding the identity of the participants. With signed informed consent and control questions with automatic premature termination at the first online assessment this problem will be reduced. Online interventions in general and online interventions specifically for caregivers have to face with high dropout rates (29% to 38%) [80,81]. To reduce a potential adherence problem and to enhance motivation the participants of the intervention group will be accompanied by an e-coach with

feedback and reminders [50,82] and the development of the online design includes persuasive elements [42]. As participation in the study is only possible with access to internet and some technical affinity, we designed the online intervention as simple and intuitive as possible and will offer technical use basics at the introduction session. Furthermore, it has been discussed that including a waitlist control condition leads to an overestimation of the effect sizes compared to a no treatment or psychological placebo condition [83]. However, all participants in our study will be free to use care as usual and they receive a list of other treatment options like cancer counselling centres if they are interested. Furthermore, we will be able to have a look on possible long-term effects (4-month follow up), but this leads to a long waiting time for the waitlist control group. In addition, our online intervention for partners could not cover all relevant topics: A recent study showed 'home care interventions', 'impact of financial demands on caregiver, 'impact of health reforms, programs and policies on caregivers' as some of the most important topics for caregivers [84]. The further development of PartnerCARE should take these insights into account.

Regarding the future outlook, PartnerCARE could be included into the health care routine: by the time a patient becomes diagnosed with cancer, also the partner should be screened for psycho-social and physical burdens. PartnerCARE can also provide a communicative benefit for health care professionals with enhanced awareness of caregivers and the opportunity of having a special offer for partners. If needed, PartnerCARE could be immediately offered as a tool for partners to work on their burdens regardless of where and when. It can also be used to overcome the waiting time for partners until a local psycho-oncological treatment is available.

Ethics and dissemination

This study has been approved by the Ethics Committee of the University of Ulm (No. 390/18). Results will be published in peer-reviewed journals and presented on local, national, and international conferences.

Abbreviations

ABE: Anonymity Benefits (Subscale of APOI); ANOVA: Analysis of Variance; APOI: Attitudes towards Psychological Online Interventions Questionnaire; BriefCOPE: Brief Coping Orientation to Problems Experienced Inventory; BSFC-s: Short Version of the Burden Scale for Family Caregivers; CCC: Comprehensive Cancer Center; CG: Waitlist control group; CON: Confidence in Effectiveness (Subscale of APOI); CONSORT: Consolidated Standards of Reporting Trials; CSQ-I: Client Satisfaction Questionnaire adapted to Internet-based interventions; DT: National Comprehensive Cancer Network Distress Thermometer; ESSI: ENRICHED Social Support Inventory; FoP-Q-SF/P: Fear of Progression in Partners of Chronically ill Patients; GAD-7: Generalized Anxiety Disorder Questionnaire; GSE: Generalized Self-Efficacy scale; IG: Intervention

group; INEP-On/-CG: Inventory for the Assessment of Negative Effects in Psychotherapy – Online/-Control group; NCCN: National Comprehensive Cancer Network; OSS-3: Oslo social support scale; PHQ-8/9: Patient Health Questionnaire; RCT: Randomized controlled trial; SCE: Scepticism and Perception of Risk (Subscale of APOI); SF-36: Short form 36 health survey questionnaire; SMS: Short Message Service; SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials; TAU: Treatment as usual; TET: Technologization Threat (Subscale of APOI); VR-12: Veterans RAND 12-Item Health Survey; VR-36: Veterans RAND 36 Items Health Survey

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the University of Ulm (no. 390/18) and was registered in the German Clinical Trials Register (DRKS00017019) on 08 April 2019. In case of important protocol modifications, trial registration will be updated. All participants receive written information about study process, data security and voluntariness of participation. Prior to the involvement into the study participants have to confirm understanding of the given information with written consent. Data collection occur pseudonymized by giving every participant a personal ID and data is stored password protected. Access to study data will only be given to authorized study members. After data collection all personal information of participants will be deleted.

Consent for publication

Not applicable.

Availability of data and materials

All principal investigators will be given full access to the data sets. Data set will be stored on password-protected servers of Ulm University with restricted access. External researches may get access to the final trial dataset on request depending on to be specified data security and data exchange regulation agreements. To ensure confidentiality, data dispersed to any investigator or researcher will be blinded of any identifying participant information.

Competing interests

The authors declare that they have no competing interests.

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decision to publish or preparation of this manuscript. The German Cancer Aid will not be involved in data collection, analyses, decision to publish or preparation of future papers regarding the PartnerCARE project.

Author contributions

DB, NB, HG, HB and KH contributed to the study design. DB and IL compiled the content of the intervention sessions. The online design and structure of the intervention was carried out from DB building on prior online interventions of the department of Clinical Psychology and Psychotherapy (HB). Intervention development was supervised by NB, HG, HB and KH. DB is responsible for recruitment and coordination of the study. DB drafted the manuscript. All authors provided critical revision and approved the final manuscript.

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Figure 1 Flow diagram of the study procedure

See separate File "PartnerCARE_Figure 1 Flow diagram.pdf"

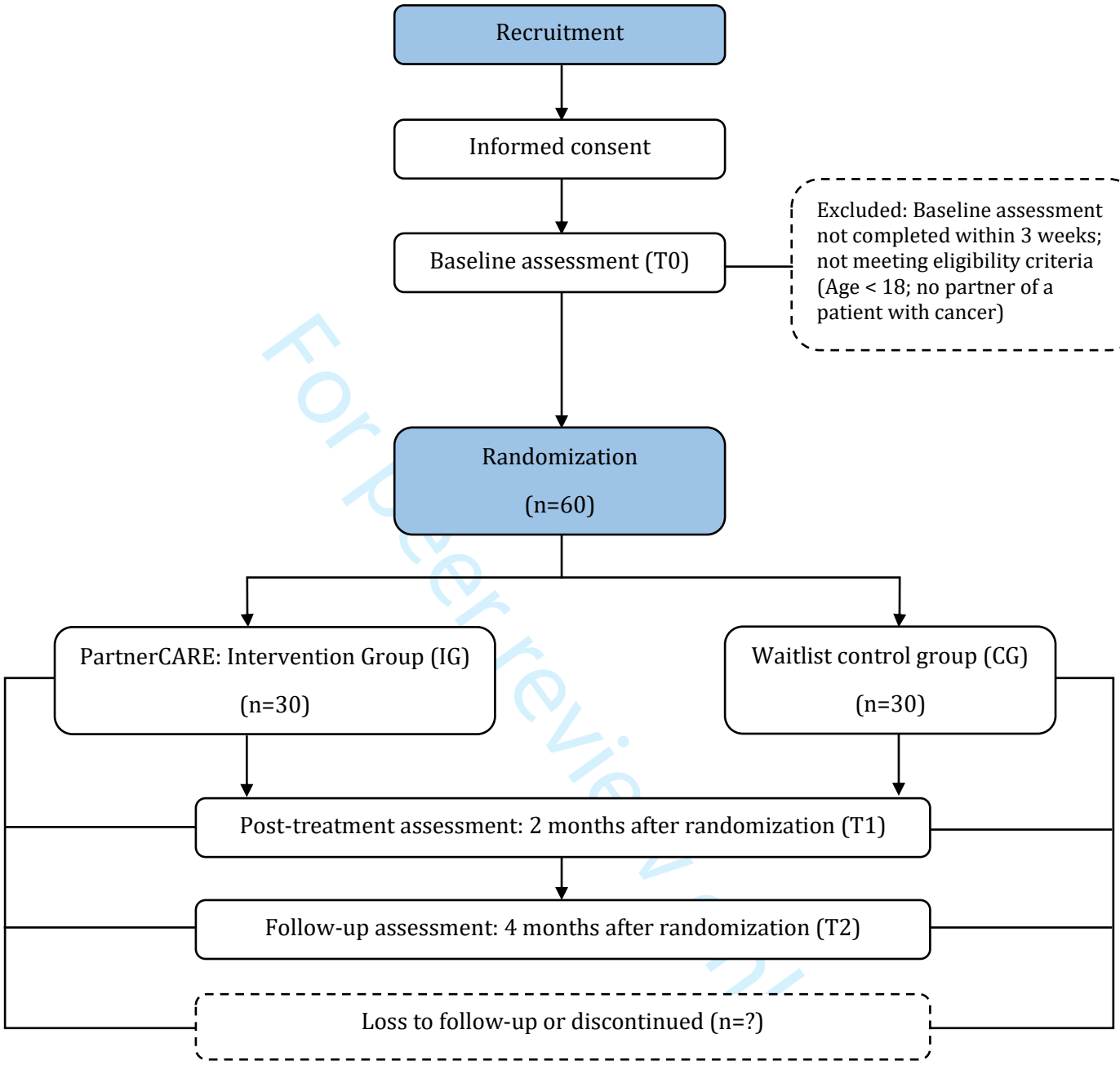

Figure 1 Flow diagram of the study procedure

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2, 22
	2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	-
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	22-23
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	-

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	13
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5-6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-12
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	-
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	7-9
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	-
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	13-18
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	7, Fig. 1 (Flowchart)

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	13
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6-7
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	-
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	-
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13-18
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13, 15

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	6, 13, 22
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	18-19
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	-
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	18-19
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	-
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	-
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	14
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	-
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	22
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	22

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6, 22
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	-
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	6, 13,22
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	22-23
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	22
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	2
	31b	Authorship eligibility guidelines and any intended use of professional writers	-
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	-
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	-
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.