

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	PartnerCARE – a psycho-oncological online intervention for partners of patients with cancer: Study protocol for a randomized controlled feasibility trial
<b>AUTHORS</b>	Bodschwinna, Daniela; Lorenz, Inga; Bauereiss, Natalie; Gündel, Harald; Baumeister, Harald; Hoenig, Klaus

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Miriam Noonan College of Medicine and Health University of Exeter United Kingdom
<b>REVIEW RETURNED</b>	26-Nov-2019

<b>GENERAL COMMENTS</b>	<p>Spelling: Line 1, line 24 –Extent Line 30: Routes</p> <p>Re-phrase this sentence as difficult to read:</p> <p>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.</p> <p>Re-phrase this sentence (bold section) as difficult to read:</p> <p>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]</p> <p>Introduction: Suggest a sentence on the difficulty determining how much the partner is involved in interventions (i.e. formally included or just happen to be there in the appointment) which makes it difficult to determine how/whether interventions that have been designed to include them actually make any difference.</p> <p>Rephrase the following sentence: Conduct a confirmatory effectivity evaluation of the intervention.</p> <p>Inclusion and exclusion criteria Does the partner need to be living with the patient? Ability to use internet/computer/smart phone? Or will people receive training in this if required?</p>
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	<p>Intervention Mention any specific theories which informed the intervention development</p> <p>Patient and public involvement More explanation needed as to why no patient and public involvement in the design of the pilot trial</p> <p>Other: Will partner health status be recorded?</p>
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<b>REVIEWER</b>	maru barrera SickKids Hospital Canada
<b>REVIEW RETURNED</b>	02-Jan-2020

<b>GENERAL COMMENTS</b>	<p>BMJ Open- PartnerCARE- a psycho-oncological online intervention for partners of patients with cancer: study protocol for a randomized controlled feasibility trial.</p> <p>This is an ongoing study examining the feasibility of an on-line intervention for partners of adult patients with any type of cancer, using a two arm parallel group randomized controlled trial with an intervention and a waitlist control group. Authors aim to enroll 60 partners (although it is not clearly stated, I assume this number refers to the total sample, rather than per group) using diverse recruit sources (e.g., support groups, social media) and at any stage of the patient's treatment (this is not stated in the manuscript). PartnerCARE intervention includes psychoeducation, cognitive-behavioural and imagery components and consist of 6 online structured sessions, a booster session and optional sessions addressing topics such as healthy sleep, relationship with own children, sexuality and existential burden. The primary outcomes are recruitment rates, study procedure, acceptance, and satisfaction of intervention, possible negative effects and drop-out rates. Secondary outcomes are: quality of life, distress, depression and anxiety symptoms, caregiver burden, and fear of progression, social support, self-efficacy, coping and loneliness. Measures will be completed online at baseline, 2 and 4 months after randomization. Data analyses will be conducted based on intent to treat.</p> <p>The study is interesting and the methodology is sound. My main criticisms are primarily related to omissions, organization of the manuscript and tables, as well as the terminology, definition of concepts and sentence structure, which may reflect translation errors, from German to English. Below I list specific points in order of presentation in the manuscript.</p> <ol style="list-style-type: none"> <li>1. Abstract needs to include some information about the intervention structure and content (e.g., number of session, issues covered, e-process)</li> <li>2. Study recruitment started in April, 2019 and it is said to be ongoing 'until the target sample is reached.' The reader needs to have an idea of whether the study will eventually be closed, even if the target sample is not reached. This too will be important information for assessing feasibility.</li> <li>3. In the randomization section it is unclear: what the authors meant by 'Permuted block randomization with randomly arranged block sizes (2 to 4) with an allocation ration of 1:1 is performed.' The rationale for block randomization needs to be spelled out.</li> <li>4. Table 1, over view of caregivers' needs, could be better re-organized, (e.g., information about patient illness and treatment, and</li> </ol>
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	<p>how to provide care; information about available resources: hospital, community, etc.). Also the table format needs improvement following guidelines for publication.</p> <p>5. Table 2 also needs re-organization and revision, e.g., Session 1: Identification of Caring Burdens; Aims: list personal burdens and Plan: list specific actions to deal with each burden.</p> <p>6. Also in Table 2 the main focus of each session is not always clear. For example in session 2, 'inner drivers', do you mean personal goals and expectations as a caregiver?</p> <p>7. The description of the PartnerCARE needs to be expanded and revised. I think that the meaning of some of the concepts might have been lost in the translation. The role of the e-coach is not clear. Do you mean to say that for each training module session, three videos are included depicting caregiver partners demonstrating how partners cope with a specific situation? The reader does not get a good idea of how an electronic module-session runs. I appreciate that the authors took about a year in developing the online program and that the feedback they received came from 4 psycho-oncologists (psychologists? Social workers?) and that such feedback was used to improve the program. However, without a clear description of the components of the program it is difficult to get a good understanding of what the caregivers are learning in the program.</p> <p>8. Incidentally, the last step of each session: 'imagination exercise' do the authors mean: a 'guided imagery exercise'? Can you describe the purpose of this exercise? Is it a mindfulness exercise?</p> <p>9. Description of the primary outcomes need to be better organized and described. I counted 11 outcomes in the first paragraphs of this section (page 11, lines 27-36) but not all are described in the following paragraphs.</p> <p>10. Secondary outcomes, not all questionnaires are adequately described (e.g., some list the number of items, some do not).</p> <p>11. The PHQ-8 as a measure of depression symptoms. Please be careful with how you describe this screening questionnaire; it should not be considered a diagnostic questionnaire of depression, but as an indicator of current depression symptoms.</p> <p>12. The description of the RAND 12-item, in page 12, line 39, is not a complete sentence.</p> <p>13. Discussion. In page 14 the authors use the term 'efficacy' in the context of assessing the program, but in the following page they refer to 'effectiveness', they do not mean the same thing.</p> <p>14. Discussion. References are needed to support the statements regarding reasons for low utilization of face-to-face psychosocial care (Page 15, lines 9-13).</p> <p>15. Discussion. The point regarding gender differences needs to be revised.</p> <p>16. Discussion. Recruitment rates being low needs to be mentioned in the introduction first and referred to it in the methodology as part of the justification for using different recruitment strategies.</p> <p>17. Discussion. In page 15 it is said that e-coach use will be measured, but is not described in the methodology.</p> <p>18. Finally, if the protocol described in this manuscript consist of a two arm trial and the study is ongoing, what is the scientific basis for proposing a three arm trial as the next step?</p>
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## VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Miriam Noonan

Institution and Country: College of Medicine and Health, University of Exeter, United Kingdom

Please state any competing interests or state 'None declared': None declared

1. Spelling: Line 1, line 24 –Extent

Line 30: Routes

Reply: Thank you. We corrected the misspellings.

2. Re-phrase this sentence as difficult to read: “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.”

Reply: We thank the reviewer for pointing out the difficult readability of the sentence. We agree and revised the sentence as follows: 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.

3. Re-phrase this sentence (bold section) as difficult to read: “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]”

Reply: We also rephrase this sentence as follows: 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.

4. Introduction: Suggest a sentence on the difficulty determining how much the partner is involved in interventions (i.e. formally included or just happen to be there in the appointment) which makes it difficult to determine how/whether interventions that have been designed to include them actually make any difference.

Reply: Thank you for addressing this important point. We totally agree with you, that it is difficult to determine the involvement of partners in interventions and therefore is not reported in detail in articles. We included the following sentence: 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].

5. Rephrase the following sentence: Conduct a confirmatory effectivity evaluation of the intervention.

Reply: Thank you for the recommendation to rephrase the sentence. We have modified it as follows: 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.

6. Inclusion and exclusion criteria: Does the partner need to be living with the patient?

Reply: No, living together with the patient is not required. We added the following sentence at the inclusion and exclusion paragraph: Participants do not have to live with the patient,

7. Ability to use internet/computer/smart phone? Or will people receive training in this if required?

Reply: In our invitation email to the online intervention, a point-to-point explanation how to log in to the online intervention is included. Furthermore, at the introduction session of PartnerCARE an introduction in technical handling of the intervention is given. If there are any other technical questions, participants can write an e-mail to the PartnerCARE study team or the technical-support team of the research group.

8. Intervention: Mention any specific theories which informed the intervention development

Reply: Thank you for this comment. We specified the theories which took part in the development process: Thus, the intervention is based on various concepts which are widely used in cancer context: psychoeducation, behavioural therapy, supportive therapy and guided imagery.

9. Patient and public involvement: More explanation needed as to why no patient and public

involvement in the design of the pilot trial

Reply: We added a more detailed explanation to the patient and public involvement paragraph: 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.

10. Other: Will partner health status be recorded?

Reply: Yes, the mental health status is recorded with secondary outcomes like PHQ-8, GAD-7, etc. of the partner but not of the patient.

Reviewer: 2

Reviewer Name: maru barrera

Institution and Country: SickKids Hospital, Canada

Please state any competing interests or state 'None declared': none

This is an ongoing study examining the feasibility of an on-line intervention for partners of adult patients with any type of cancer, using a two arm parallel group randomized controlled trial with an intervention and a waitlist control group. Authors aim to enroll 60 partners (although it is not clearly stated, I assume this number refers to the total sample, rather than per group) using diverse recruit sources (e.g., support groups, social media) and at any stage of the patient's treatment (this is not stated in the manuscript). PartnerCARE intervention includes psychoeducation, cognitive-behavioural and imagery components and consist of 6 online structured sessions, a booster session and optional sessions addressing topics such as healthy sleep, relationship with own children, sexuality and existential burden. The primary outcomes are recruitment rates, study procedure, acceptance, and satisfaction of intervention, possible negative effects and drop-out rates. Secondary outcomes are: quality of life, distress, depression and anxiety symptoms, caregiver burden, and fear of progression, social support, self-efficacy, coping and loneliness. Measures will be completed online at baseline, 2 and 4 months after randomization. Data analyses will be conducted based on intent to treat. The study is interesting and the methodology is sound. My main criticisms are primarily related to omissions, organization of the manuscript and tables, as well as the terminology, definition of concepts and sentence structure, which may reflect translation errors, from German to English. Below I list specific points in order of presentation in the manuscript.

Reply: We thank Maru Barrera for her encouraging statement and the work she put into the manuscript. We think the protocol improved substantially through her helpful comments. To make the sample size clearer, we added explanations at the abstract and at the sample size chapter as follows: A total sample size of  $n=60$  (30 partners per arm). We also supplement to the inclusion chapter that partners are included independent of the stage of the patient's treatment.

1. Abstract needs to include some information about the intervention structure and content (e.g., number of session, issues covered, e-process)

Reply: Thank you to call our attention to the missing information in the abstract. We added the information as follows: 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.

2. Study recruitment started in April, 2019 and it is said to be ongoing 'until the target sample is reached.' The reader needs to have an idea of whether the study will eventually be closed, even if the target sample is not reached. This too will be important information for assessing feasibility.

Reply: Thank you to call our attention to the missing information in the recruitment section. We agree that an eventually closing of recruitment should be considered. We added the following sentence: 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.

3. In the randomization section it is unclear: what the authors meant by 'Permuted block

randomization with randomly arranged block sizes (2 to 4) with an allocation ratio of 1:1 is performed.' The rationale for block randomization needs to be spelled out.

Reply: We will use a permuted block randomization with randomly arranged block sizes to get a balanced group distribution as well as data collectors are not able to forecast the allocation of participant to one of the two groups. We added the following to the randomization section: 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.

4. Table 1, over view of caregivers' needs, could be better re-organized, (e.g., information about patient illness and treatment, and how to provide care; information about available resources: hospital, community, etc.). Also the table format needs improvement following guidelines for publication.

Reply: We reorganized table 1 under the aspect of clarity and economy/aggregation. Furthermore we placed the tables in the main text as recommended in the guidelines from BMJ.

5. Table 2 also needs re-organization and revision, e.g., Session 1: Identification of Caring Burdens; Aims: list personal burdens and Plan: list specific actions to deal with each burden.

Reply: We also reorganized table 2 and insert example exercises for each session to give more insights to the content of PartnerCARE.

6. Also in Table 2 the main focus of each session is not always clear. For example in session 2, 'inner drivers', do you mean personal goals and expectations as a caregiver?

Reply: Inner drivers mean the concept of inner motivations like every person has in a different intensity (e.g. be perfect). These personal inner drivers can also have an impact at the way caregivers operate. Therefore, we try to make the partners aware of their inner drivers and to learn how to respond appropriately.

7. The description of the PartnerCARE needs to be expanded and revised. I think that the meaning of some of the concepts might have been lost in the translation. The role of the e-coach is not clear. Do you mean to say that for each training module session, three videos are included depicting caregiver partners demonstrating how partners cope with a specific situation? The reader does not get a good idea of how an electronic module-session runs. I appreciate that the authors took about a year in developing the online program and that the feedback they received came from 4 psycho-oncologists (psychologists? Social workers?) and that such feedback was used to improve the program. However, without a clear description of the components of the program it is difficult to get a good understanding of what the caregivers are learning in the program.

Reply: Thank you for your comments on the description of the online intervention. We revised the sections about the intervention and added some sentences to clarify the role of the e-coach, the three exemplary partners, and which background the psycho oncologists had. In addition, we insert a section about the process of the online intervention to make it clearer what happens after a participant is randomized into the intervention group: 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 a 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 communication between participant and e-coach is asynchronous.

8. Incidentally, the last step of each session: 'imagination exercise' do the authors mean: a 'guided imagery exercise'? Can you describe the purpose of this exercise? Is it a mindfulness exercise?

Reply: Yes, we renamed the imagination exercise into guided imagery exercise. Thank you for that recommendation. The guided imagery exercises facilitate awareness of inner-soul processes and they are used for relaxation. Mindfulness exercises are only part of session 4, where participants get the possibility to try different mindfulness exercises.

9. Description of the primary outcomes need to be better organized and described. I counted 11 outcomes in the first paragraphs of this section (page 11, lines 27-36) but not all are described in the following paragraphs.

Reply: Thank you for pointing out this inconsistency. We restructured the enumeration of the primary outcomes and describe each in the same order in the following paragraphs. Therefore, we also added one paragraph for the missing description of these outcomes: 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.

10. Secondary outcomes, not all questionnaires are adequately described (e.g., some list the number of items, some do not).

Reply: Thank you for pointing out this inconsistency, too. We added the missing number of items at the correspondent questionnaires.

11. The PHQ-8 as a measure of depression symptoms. Please be careful with how you describe this screening questionnaire; it should not be considered a diagnostic questionnaire of depression, but as an indicator of current depression symptoms.

Reply: Thank you for the note. We change the sentence as follows: The German version of the Patient Health Questionnaire (PHQ-8) is a reliable and valid self-report tool for assessing current depression symptoms.

12. The description of the RAND 12-item, in page 12, line 39, is not a complete sentence.

Reply: Yes, thank you for your attention. The word 'separated' was missing.

13. Discussion. In page 14 the authors use the term 'efficacy' in the context of assessing the program, but in the following page they refer to 'effectiveness', they do not mean the same thing.

Reply: Yes, the wording was a mistake. We replaced effectiveness with efficacy.

14. Discussion. References are needed to support the statements regarding reasons for low utilization of face-to-face psychosocial care (Page 15, lines 9-13).

Reply: Thank you for the comment. We insert the missing references.

15. Discussion. The point regarding gender differences needs to be revised.

Reply: We revised the paragraph about gender differences as follows: 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.

16. Discussion. Recruitment rates being low needs to be mentioned in the introduction first and referred to it in the methodology as part of the justification for using different recruitment strategies.

Reply: Thank you for pointing out the missing mention in the introduction. We added the following sentences to the introduction: There are two main challenges about interventions for caregivers: First, the target group is often 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].

17. Discussion. In page 15 it is said that e-coach use will be measured, but is not described in the methodology.

Reply: The e-coach effort is assessed with time needed for feedback every week and the quantity of sent reminders. We added the detailed description also in the method section.

18. Finally, if the protocol described in this manuscript consist of a two arm trial and the study is ongoing, what is the scientific basis for proposing a three arm trial as the next step?

Reply: Thank you for pointing out this inconsistency. We have already taken a step further here by

giving a too big view into the future plans. For better intelligibility, we have removed this paragraph from the discussion.

### VERSION 2 – REVIEW

<b>REVIEWER</b>	Miriam Catherine Noonan College of Medicine and Health University of Exeter
<b>REVIEW RETURNED</b>	18-May-2020
<b>GENERAL COMMENTS</b>	Some minor grammatical corrections required throughout page 4  If participants engage in optional sessions how is this going to be measured and how in turn will this be comparable? Apart from support of own children, what is the rationale for the other topics to be included as optional/additional? Why not in the core programme?

### VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Miriam Catherine Noonan

Institution and Country: College of Medicine and Health, University of Exeter, United Kingdom

1. Some minor grammatical corrections required throughout page 4

Reply: Thank you. We corrected the grammatical errors.

2. If participants engage in optional sessions how is this going to be measured and how in turn will this be comparable? Apart from support of own children, what is the rationale for the other topics to be included as optional/additional? Why not in the core programme?

Reply: We will count the number of optional sessions finished by each participant (the e-coach enters the number in a list). Furthermore, we can count the total number of all optional sessions finished to get insights with regard to which are the most relevant ones for partners. The focus of the feasibility trial is to get to know how the online intervention is used and which topics are relevant. This information will be used to further improve and develop PartnerCARE.

The idea of including optional sessions was motivated by the fact that some information might be relevant to only a subset of the participants. For instance, “healthy sleep” was offered as an optional session because only some of the partners suffer from sleep problems. Similarly, only some of the partners suffer from problems regarding sexuality. “Existential burden” becomes increasingly more relevant in the progress of the disease. Due this dependency “existential burden” might be of minor concern in earlier phases of the disease (e.g. shortly after diagnosis) but become more and more important later on. Hence, we offered these additional sessions in order to get more information on which might be considered more relevant by the participants.