PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Sexual counselling for patients with cardiovascular disease: protocol for a pilot study of the CHARMS sexual counselling intervention.
AUTHORS	Murphy, Patrick; McSharry, Jenny; casey, dympna; Doherty, Sally; Gillespie, Paddy; Jaarsma, Tiny; Murphy, Andrew; Newell, John; O'Donnell, Martin; Steinke, Elaine; Toomey, Elaine; Byrne, Molly

VERSION 1 - REVIEW

REVIEWER	Richard Lange, Md, MBA Texas Tech Univ Health Sciences Center El Paso
REVIEW RETURNED	19-Feb-2016

GENERAL COMMENTS	This is a methods manuscript providing details regarding a multi center pilot study for the Cardiac Health and Relationship Management and Sexuality (CHARMS) intervention. The manuscript is very well written (among the best I've seen). The study justification, design, recruitment, intervention, statistical analysis and outcomes are all presented. I have 2 minor issues: 1. The authors are enrolling patients referred for cardiac rehabilitation, but they do not state that they are limiting the study to individuals with partners. Please clarify, as it doesn't seem worthwhile/fruitful to enroll patients who are single. 2. There are a few misspellings that need to be corrected: enrol and enrolment (page 10, second paragraph) and practising (page 13, last paragraph).

REVIEWER	Heather Tulloch University of Ottawa Heart Institute
REVIEW RETURNED	11-Mar-2016

GENERAL COMMENTS	In general, I think this paper and the work proposed is excellent. However, I am not convinced that a publication of a protocol for a pilot study is required. I encourage the authors to re-submit for publicaton when results are available. I very much look forward to seeing the results! The article “sexual counseling for patients with cardiovascular disease: protocol for a pilot study of the CHARMS sexual counseling intervention” describes a well-planned pilot intervention aimed to address the often-neglected area of sexual health among cardiac patients. This study is being led by a strong team with an impressive

	research program in an important area for further development. It is well-written and, for the most part, quite comprehensive. The authors were diligent to include many methods to ensure high standards of intervention and measurement. Nonetheless, I am not convinced a protocol for a pilot study is necessary. Instead, I would encourage the authors to publish once pilot data is available; however, I leave that final decision to the editor. Please find detailed, minor comments below. Minor comments: -p.3, line 7 - remove “on” -excellent use of intervention development guide (Michie et al) -p. 6, line 24-30 provide more ‘exact’ data from baseline study (e.g., % of those who were had their sexual concerns addressed in CR) -p. 6, lines 45-50 - provide findings in brief -p. 7, lines19-25 - Many readers will appreciate more information in the current paper, removing the need to search for other articles to get more detail on the intervention described. I encourage the authors to provide additional details so that the reader does not have to refer to another source, especially when it is one that is not yet published. -good rationale for conducting pilot studies -p. 8, The authors include a description of the planned, but exploratory, efficacy analyses for the primary outcome in the analysis section. I suggest that they add this question with the others on page 8. -p.8, The research questions are reasonable, but the authors should provide some objective criteria to answer their questions (e.g., what is the cut off for “acceptability” by patients – mean score of X on Y; % of participants in FU interview felt it was acceptable). - p.9, line 8 - define MRC (or put in acronym at earlier use) -p.9, line 17 – the intervention will be implemented in 2 centres, but there is no control. As the authors are attempting to recruit many sites, it is recommended that they choose 2 additional, matched sites that they might uses as a control and assess on knowledge, QoL, and other pre-post intervention measures so they might *explore* the efficacy of their intervention. -p.10, line21-26 – Although I agree that the authors would not need to confirm diagnosis of cardiac disease, I would encourage them to record type of cardiac diagnosis as this may affect the results of the intervention (e.g., less invasive treatment such as PCI, may have less impact on sexual activity which, in turn, may result in reduced impact of the CHARMS intervention)

	-nice urban/ rural stratification -p.12, line 57 – at minimum, the researchers should track the demographics, including age, gender and profession of the refusers. Similar tracking should be applied to patient/partners who refuse to participate. -p.13, line10 – I am concerned that patient recruitment will be low by mail, and the sample will not be representative. I am confused as to why the cardiac coordinator could not recruit and provide the questionnaires in person. -p. 14, line 9-10 - Again, a sentence or two that describes key concepts would be appreciated here and below (line 39). -p. 14 line 33 - Is there a minimum % of partner enrollment that you are expecting for it to be considered feasible or acceptable? For the larger study, it will be important to also consider how you will handle data from patients whose spouse does not participate. -p.15, line 31 – More detailed descriptions of all the measures are absolutely necessary. Including a measure of anxiety is recommended. -p. 15, line 54 - As noted earlier, will diagnosis and treatment be tracked? -The use of objective fidelity checks is a real strength. -please explain if the intervention follows an “open workshop” style or if patients are given an appointment time. This would be important to track regarding up-take and acceptability of the program. -p. 20, line 50 - Please explain the method of purposive sampling more clearly – what is the sampling criteria based on the measures? (e.g., those in certain ranges?) -ref #13 appears incomplete…a book?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Richard Lange, Md, MBA
Institution and Country: Texas Tech Univ Health Sciences Center El Paso, USA Competing Interests: None
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This is a methods manuscript providing details regarding a multi center pilot study for the Cardiac Health and Relationship Management and Sexuality (CHARMS) intervention.

The manuscript is very well written (among the best I've seen). The study justification, design, recruitment, intervention, statistical analysis and outcomes are all presented.

I have 2 minor issues:

Comment: 1. The authors are enrolling patients referred for cardiac rehabilitation, but they do not state that they are limiting the study to individuals with partners. Please clarify, as it doesn't seem worthwhile/fruitful to enroll patients who are single.

Response: Patients without a partner will not be excluded from the study, as sexual self-satisfaction is an important part of sexual health for all people, regardless of relationship status. A sentence to clarify this has been added to the section 'Inclusion Criteria for Cardiac Rehabilitation Patients'.

Comment: 2. There are a few misspellings that need to be corrected: enrol and enrolment (page 10, second paragraph) and practising (page 13, last paragraph).

Response: 'Enrol' and 'enrolment' may appear to be misspellings to those more familiar with American English, but they are in fact standard spellings in British English, which we felt was more appropriate for this journal (http://www.oxforddictionaries.com/definition/english/enrolment). Also, 'practising' is used as a verb in the given context, so the spelling is appropriate.

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Reviewer: 2
Reviewer Name: Heather Tulloch
Institution and Country: University of Ottawa Heart Institute Competing Interests: None declared
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Comment: Please see attached file. In general, I think this paper and the work proposed is excellent. However, I am not convinced that a publication of a protocol for a pilot study is required. I encourage the authors to re-submit for publicaton when results are available. I very much look forward to seeing the results!

The article "sexual counseling for patients with cardiovascular disease: protocol for a pilot study of the CHARMS sexual counseling intervention" describes a well-planned pilot intervention aimed to address the often-neglected area of sexual health among cardiac patients. This study is being led by a strong team with an impressive research program in an important area for further development. It is well-written and, for the most part, quite comprehensive. The authors were diligent to include many methods to ensure high standards of intervention and measurement. Nonetheless, I am not convinced a protocol for a pilot study is necessary. Instead, I would encourage the authors to publish once pilot data is available; however, I leave that final decision to the editor. Please find detailed, minor comments below.

Response: We thank the reviewer for the compliments regarding this paper and the programme of research. We would hope that the reviewer may become convinced of the value of publishing a protocol for a pilot study. The publication of protocols is a powerful method of: (1) reducing publication bias, (2) ensuring duplicate studies are not funded, and (3) early dissemination to interested researchers 1. These benefits apply to pilot studies as much as they apply to full randomised controlled trials. We also note that the editors of BMJ Open have chosen to publish protocols of many pilot studies to date, which we take to be an indication that they share our views of this matter.

Minor comments:

Comment: -p.3, line 7 - remove "on"

Response: We have removed the word "on" as requested.

Comment: -excellent use of intervention development guide (Michie et al)

Response: We thank the reviewer for this compliment.

Comment: -p. 6, line 24-30 provide more 'exact' data from baseline study (e.g., % of those who were had their sexual concerns addressed in CR)

Response: More exact data (% and n) have been provided in the section The CHARMS Baseline Study

Comment: -p. 6, lines 45-50 - provide findings in brief

Response: The findings have been provided in brief (see paragraph 3 of the section The CHARMS Baseline Study)

Comment: -p. 7, lines19-25 - Many readers will appreciate more information in the current paper, removing the need to search for other articles to get more detail on the intervention described. I encourage the authors to provide additional details so that the reader does not have to refer to another source, especially when it is one that is not yet published.

Response: The process of intervention development was complex, and its description required significant resources. We feel it is appropriate to refer readers to another article for full details regarding this. However, more information about the finalised intervention components (including the staff intervention, the patient intervention, the patient booklet, and the study poster) is provided in the section Intervention Procedures, and we have included an online supplementary file containing an example mapping of BCTs and intervention components. We have added a sentence indicating that additional information about the intervention components is provided later in the paper.

Comment: -good rationale for conducting pilot studies

Response: We thank the reviewer for this compliment.

Comment: -p. 8, The authors include a description of the planned, but exploratory, efficacy analyses for the primary outcome in the analysis section. I suggest that they add this question with the others on page 8.

Response: We have added this question to the others on page 8 as suggested.

Comment: -p.8, The research questions are reasonable, but the authors should provide some objective criteria to answer their questions (e.g., what is the cut off for "acceptability" by patients – mean score of X on Y; % of participants in FU interview felt it was acceptable).

Response: The likely effect size for the primary outcome and the optimal number of clusters and participants needed for a definitive cluster RCT will be objectively assessed using the statistical analyses described. However, feasibility and acceptability will be assessed primarily using qualitative methods. We will not have a mean "acceptability" score as there is no quantitative "acceptability" measure. To reduce qualitative data to percentages of participants would be to lose the power of qualitative methods. Judgements of feasibility and acceptability will be therefore be subjective, but given the thoroughness of the planned qualitative analysis, those judgements will be absolutely rigorous.

Comment: - p.9, line 8 - define MRC (or put in acronym at earlier use)

Response: We have defined the acronym MRC (Medical Research Council) at first usage (in the section The CHARMS Pilot Study).

Comment: -p.9, line 17 – the intervention will be implemented in 2 centres, but there is no control. As the authors are attempting to recruit many sites, it is recommended that they choose 2 additional, matched sites that they might uses as a control and assess on knowledge, QoL, and other pre-post intervention measures so they might explore the efficacy of their intervention.

Response: We have closely followed the MRC guidance in the design of our protocol 2. This guidance specifies that pilot studies should be concerned with testing procedures and feasibility, estimating recruitment and retention, and determining sample size. Only once pilot work has been conducted should effectiveness be evaluated by the comparison of intervention and control centres. Therefore we feel it is appropriate to defer recruitment of control centres to the evaluation stage.

Comment: -p.10, line21-26 – Although I agree that the authors would not need to confirm diagnosis of cardiac disease, I would encourage them to record type of cardiac diagnosis as this may affect the results of the intervention (e.g., less invasive treatment such as PCI, may have less impact on sexual activity which, in turn, may result in reduced impact of the CHARMS intervention)

Response: We agree with the reviewer on this point, and the medical information collected for each participant will include a self-report of cardiac diagnosis. This has been clarified in the expanded description of the patient questionnaire (see below).

Comment: -nice urban/ rural stratification

Response: We thank the reviewer for this compliment.

Comment: -p.12, line 57 – at minimum, the researchers should track the demographics, including age, gender and profession of the refusers. Similar tracking should be applied to patient/partners who refuse to participate.

Response: Unfortunately, ethically do we not have access to any demographic information about staff or patients/partners who refuse to participate.

Comment: -p.13, line10 – I am concerned that patient recruitment will be low by mail, and the sample will not be representative. I am confused as to why the cardiac coordinator could not recruit and provide the questionnaires in person.

Response: We share the reviewer's concern. However, recruitment by post was deemed appropriate for two reasons. Firstly, it would not put undue pressure on patients to participate in a potentially sensitive study. Secondly, as staff will for the most part be unaware if individual patients are participating in the study, it will help to minimise any conscious or unconscious differences in the treatment of patients based on participation. We have clarified this rationale in the section Patient Recruitment.

Comment: -p. 14, line 9-10 - Again, a sentence or two that describes key concepts would be appreciated here and below (line 39).

Response: As above, we have included an online supplementary file containing an example mapping of BCTs and intervention components.

Comment: -p. 14 line 33 - Is there a minimum % of partner enrollment that you are expecting for it to be considered feasible or acceptable? For the larger study, it will be important to also consider how you will handle data from patients whose spouse does not participate.

Response: As detailed in the protocol, sample size calculations are specific only to patients, and therefore there is no minimum % of partner enrolment needed for feasibility or acceptability. As stated, partners will be invited to participate in line with sexual counselling guidance3, as excluding partners from sexual counselling activities would be an unreasonable restriction. However, we fully agree with the reviewer that the participation of partners will need to be reflected in the analysis for the larger study.

Comment: -p.15, line 31 – More detailed descriptions of all the measures are absolutely necessary. Including a measure of anxiety is recommended.

Response: Much more detail about the measures included in the staff and patients questionnaires has been provided. The primary outcome for the study (the Sexual Self-Perception and Adjustment Questionnaire) includes a measure of sexual anxiety. Anxiety/depression is also assessed by the EQ-5D-5L, and the PHQ-2.

Comment: -p. 15, line 54 - As noted earlier, will diagnosis and treatment be tracked?

Response: Yes, this has been clarified in the expanded description of the patient questionnaire measures.

Comment: -The use of objective fidelity checks is a real strength.

Response: We thank the reviewer for this compliment.

Comment: -please explain if the intervention follows an “open workshop” style or if patients are given an appointment time. This would be important to track regarding up-take and acceptability of the program.

Response: As stated in the protocol, the CHARMS patient intervention will be integrated into existing cardiac rehabilitation programmes, which consist of “twice-weekly supervised exercise and group-based educational sessions on various topics related to living with cardiovascular disease” (see the section Inclusion Criteria for Cardiac Rehabilitation Centres). To clarify this, we have specified that the patient intervention will be embedded as “an additional group-based educational session” in the section The CHARMS Patient Intervention. We note however that patients will also be invited “to request a one-to-one consultation”.

Comment: -p. 20, line 50 - Please explain the method of purposive sampling more clearly – what is the sampling criteria based on the measures? (e.g., those in certain ranges?)

Response: We have expanded on the method of purposive sampling as requested in the section Qualitative Evaluation of Feasibility, Acceptability, and Fidelity.

Comment: -ref #13 appears incomplete…a book?

Response: Apologies for the error. We have corrected this reference.

1. Skogvoll E, Kramer-Johansen J. Publication of clinical trial protocols – what can we learn? Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine 2013;21:12-12.

2. Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: The new Medical Research Council guidance. International Journal of Nursing Studies 2013;50(5):587-92.
3. Steinke EE, Jaarsma T, Barnason SA, et al. Sexual counselling for individuals with cardiovascular disease and their partners: a consensus document from the American Heart Association and the ESC Council on Cardiovascular Nursing and Allied Professions (CCNAP). Circulation 2013;128(18):2075-96.

VERSION 2 – REVIEW

REVIEWER	Heather Tulloch, PhD, C. Psych University of Ottawa Heart Institute, Prevention and Rehabilitation Centre, Ottawa, Canada
REVIEW RETURNED	12-Apr-2016

GENERAL COMMENTS	The authors have addressed all of my concerns. I espeically appreciated their comment regarding the rationale for publishing pilot protocols.