PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	HOMESIDE: Home-based family caregiver-delivered music and reading interventions for people living with dementia: Protocol of a randomised controlled trial.
AUTHORS	Baker, Felicity; Bloska, Jodie; Braat, Sabine; Bukowska, Anna; Clark, Imogen; Hsu, Ming; Kvamme, Tone; Lautenschlager, Nicola; Lee, Young-Eun; Smrokowska-Reichmann, Agnieszka; Sousa, Tanara; Stensaeth, Karette; Tamplin, Jeanette; Wosch, Thomas; Odell-Miller, Helen

VERSION 1 - REVIEW

REVIEWER	Suzanne B. Hanser, EdD, MT-BC, Chair Emerita, Prof. Music Therapy Department Berklee College of Music 1140 Boylston Street Boston, MA 02215
REVIEW RETURNED	08-May-2019

GENERAL COMMENTS	This is an excellent and interesting paper about a creative intervention for an important clinical condition. The international collaboration is particularly noteworthy. Please note minor editorial issue: Page 3, line 41, add "trial" to randomized controlled ... Also, I recommend that authors add more research studies as background, particularly some of the relevant music therapy literature from the USA e.g., Hanser, S.B., Butterfield-Whitcomb, J., Kawata, M.,& Collins, B. (2011). Home-based music strategies with individuals who have dementia and their family caregivers, Journal of Music Therapy, 48(1), 2-27. I recommend publication.

REVIEWER	Teppo Särkämö University of Helsinki Finland
REVIEW RETURNED	16-May-2019

GENERAL COMMENTS	This planned large-scale multicentre (and multicountry) RCT focuses on determining the impact of a previously developed, home-based and caregiver-implemented music intervention on the behavioural and psychological symptoms of dementia and the

	emotional well-being and quality of life of persons with dementia and their caregivers. By focusing on caregiver-implemented interventions, the study follows the recent developments in the field (where there is a push towards earlier and more home-based methods) very well; there is a major demand exactly for this kind of trial at the moment. The general design of the study, using a 3-arm parallel group RCT comparing caregiver-implemented music intervention plus standard care to an active control intervention (caregiver-implemented reading) plus to standard care and to standard care alone, is balanced and carefully thought out. The objectives are clearly defined and also achievable and realistic with the outlined implementation and protocol of the study. The targeted sample size (n=495) is well justified based on power calculations, and also feasible given that 5 countries are involved. The outcome measures are chosen well from among the most established and widely used clinical measures available. Overall, the RCT protocol is sound and robust, but there are a number of smaller methodological issues that still require some clarification (the page numbers below refer to the page numbering of the entire pdf): Page 9, line 38: “dyads (cohabiting) who are close in relationship”. Does this broad definition mean that the CG can also be a sibling, child, or other relative (or even friend)? Page 9, line 44: “dyads where the PwD has a Neuropsychiatric Inventory-Questionnaire (NPI-Q) Score of >6”. Is this the Severity score (max. 36)? How was this cut-off derived? Is the trial aimed for all levels of dementia severity, starting from MCI stage (although these persons might not fulfill the first criterion of having dementia diagnosis yet) and including also in severe stage dementia? Page 9, line 55: “dyads where the CG employs paid carers for more than 5 hours per day on at least 5 days per week.” How about those dyads where the PwD is in an interval care situation (living some weeks at home and some weeks in a nursing home)? Also, if the PwD is in a public (government-ran) nursing home, then technically the CG is not “employing” the carers. Given that there is quite a bit of variability across countries in the provision and organization of dementia care services, does this criterion work in each country included in the study? Page 10, Music & reading intervention –paragraphs: The training, instructions etc. for the music and reading interventions are clearly explained, but it is unclear where the dyads get the material required in the interventions (e.g., music records, players, songbooks, reading material). Is this provided to them by the study personnel / therapist (free of charge) or are they assumed to possess the needed material upon recruitment? If the latter holds true, then the participation is not egalitarian in this regard and could bias the results also. Page 11, lines 19-21: “Standard Care. Dyads randomly allocated to this condition will not be trained in either MI or RI but will be instructed to care for the PwD in their usual manner.” What exactly constitutes SC here? Does it mean different care activities provided by the CG at home (ranging from caring for basic ADL functions to arranging activities that are more social / cognitively

	stimulating) or more broadly any activities that the PwD participates in at home or in the community (including participation in day centre activities, cultural or sports events, etc)? Is direct (medical) care also included in SC? How is the amount of SC (no matter how narrowly or broadly defined) kept track of during the study to make sure that the groups are comparable in this regard? The same question also stands for the amount of musical and reading leisure activities that are not part of the intervention protocol(s). Page 15, lines 55-57: "Stratified block permuted randomization will be used for each country". For which exact variables is the randomization stratified for (e.g., dementia severity, etiology, age, gender, CG type etc.) and how is the stratification done in practice (can be difficult if many variables are included)? Page 15, lines 59-61: "Randomization will occur after the eligibility checking, informed consent, and baseline assessment have been completed." How does the informed consent protocol work for PwDs who are not able to provide it in written format (e.g., due to the severity of cognitive, sensory, or motor deficits)? In these cases, is the informed consent obtained then proxy from the CG (or legal guardian) and how is it verified (and documented) that the PwD him/herself wants to participate. Or are these PwDs excluded? How about cases where the PwD initially is able to give informed consent but loses this ability during the course of the study e.g., due to sudden progression of illness? Page 16, lines 12-14: "Blinded assessors will collect participants' data at baseline, post-intervention, and follow-up." If I understood correctly, the primary outcome measure of the trial (Neuropsychiatric Inventory-Questionnaire, NPI-Q) is given to the caregivers as a self-report questionnaire, not filled by the researchers based on an interview of the PwD and CG. As the CGs are delivering the interventions, the data collection is therefore not blinded at all in this regard, and there is a high likelihood of a responder bias. It would be good to clarify for all the outcome measures, are they based on (i) self-reports of the PwD and CG, (ii) informant-reports of the CG, or (iii) ratings done by clinician / researcher based on interviews of the PwD and CG. Also it would be good to mention if the CGs receive any instructions / training on how to fill the scales, both in more concrete terms on how to actually fill the forms (which can be difficult for some) and in more abstract terms on how to avoid the bias in one's responses. Page 16, line 41: "…the restriction of a common baseline mean score across interventions" What does this mean exactly?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

5) Please leave your comments for the authors below

Please note minor editorial issue:

Page 3, line 41, add "trial" to randomized controlled ...

RESPONSE: amended

6) Also, I recommend that authors add more research studies as background, particularly some of the relevant music therapy literature from the USA e.g., Hanser, S.B., Butterfield-Whitcomb, J., Kawata, M.,& Collins, B. (2011). Home-based music strategies with individuals who have dementia and their family caregivers, Journal of Music Therapy, 48(1), 2-27.

RESPONSE: Thank-you for drawing our attention to this publication. It has been added into the literature review. We have added:

A study involving eight family caregivers who were trained to deliver home-based music programs with the person with dementia they were caring for, found that both CGs and PwD improved in self-reported relaxation, comfort, and happiness from baseline to post-test. Music activities taught to CGs comprised music listening with reminiscence, movement to music, music and progressive muscle relaxation, drawing and discussing drawings to music, singing, percussion instrument playing, and strategic use of music for use while performing activities of daily living. CGs seemed to derive the most benefit from the program. Findings suggested that CGs enjoyed partaking in the reminiscing and shared musical activities with their loved ones. [15]

Reviewer: 2

7) Page 9, line 38: “dyads (cohabiting) who are close in relationship”. Does this broad definition mean that the CG can also be a sibling, child, or other relative (or even friend)?

RESPONSE: Yes that is correct. We have made this clearer by adding:

“Close in relationship refers to a CG who may be a sibling, spouse, adult child, friend, niece or nephew or any person who has a close relationship to the PwD, that is, anyone who is not a formal paid caregiver.”

8) Page 9, line 44: “dyads where the PwD has a Neuropsychiatric Inventory-Questionnaire (NPI-Q) Score of >6”. Is this the Severity score (max. 36)? How was this cut-off derived? Is the trial aimed for all levels of dementia severity, starting from MCI stage (although these persons might not fulfill the first criterion of having dementia diagnosis yet) and including also in severe stage dementia?

RESPONSE: Thank-you for this comment. Yes this is the severity score (max 36), it is derived through the screening process whereby the assessor completes the NPI-Q to determine eligibility for the study. Participants with a formal diagnosis of dementia at all levels of dementia severity are included and MMSE will be captured at baseline and now at post-test. The new text states:

• dyads where the PwD has a Neuropsychiatric Inventory-Questionnaire (NPI-Q) Score of >6 (from a maximum score of 36) and MMSE scores <24 as research indicates that NPI-Q scores >6 occur in PwD who have high Mini Mental State Examination Scores [22]. NPI-Q will form part of the screening process, with a trained assessor administering the NPI-Q in the dyad's home prior to enrolment in the study.

9) Page 9, line 55: "dyads where the CG employs paid carers for more than 5 hours per day on at least 5 days per week." How about those dyads where the PwD is in an interval care situation (living some weeks at home and some weeks in a nursing home)? Also, if the PwD is in a public (government-ran) nursing home, then technically the CG is not "employing" the carers. Given that there is quite a bit of variability across countries in the provision and organization of dementia care services, does this criterion work in each country included in the study?

RESPONSE: Thank-you, this is an excellent comment. We have revised and make this clearer:

"dyads where the CR receives professional care for more than 5 hours per day on at least 5 days per week during the planned 12-week intervention period. There will be no further exclusions."

10) Page 10, Music & reading intervention –paragraphs: The training, instructions etc. for the music and reading interventions are clearly explained, but it is unclear where the dyads get the material required in the interventions (e.g., music records, players, songbooks, reading material). Is this provided to them by the study personnel / therapist (free of charge) or are they assumed to possess the needed material upon recruitment? If the latter holds true, then the participation is not egalitarian in this regard and could bias the results also.

RESPONSE: an excellent point. Yes we have taken this into consideration. We have added this into the manuscript.

For both the MI and RI, at screening, the assessors will determine the music and reading resources already available to the dyads. Should they require resources (for example large print books, mp3 players/speakers, downloadable music), the research team will loan these resources for the dyads, free of charge.

11) Page 11, lines 19-21: "Standard Care. Dyads randomly allocated to this condition will not be trained in either MI or RI but will be instructed to care for the PwD in their usual manner." What exactly constitutes SC here? Does it mean different care activities provided by the CG at home (ranging from caring for basic ADL functions to arranging activities that are more social / cognitively stimulating) or more broadly any activities that the PwD participates in at home or in the community (including participation in day centre activities, cultural or sports events, etc)? Is direct (medical) care also included in SC? How is the amount of SC (no matter how narrowly or broadly defined) kept track

of during the study to make sure that the groups are comparable in this regard? The same question also stands for the amount of musical and reading leisure activities that are not part of the intervention protocol(s).

RESPONSE: Thank-you for this useful comment. We are assuming the groups would normally be relatively equal at baseline and we have included at baseline, questions about what they usually do during the week, with specific questions also asking them about their use of music and reading as an activity prior to enrolment in the study. We do not discourage them from continuing those activities, we will introduce strategies that aim to enhance the quality of any existing music or reading activities. We have added additional information.

12) Page 15, lines 55-57: “Stratified block permuted randomization will be used for each country”. For which exact variables is the randomization stratified for (e.g., dementia severity, etiology, age, gender, CG type etc.) and how is the stratification done in practice (can be difficult if many variables are included)?

RESPONSE: Thank-you for this comment. We have revised this text to now read:

Block permuted randomization with stratification by country will be used, so that treatment balance within country is achieved.

We will not stratify by severity, etiology etc, but will undertake sub-group analyses. We have added a paragraph in the data analysis section to make this clear.

13) Page 15, lines 59-61: “Randomization will occur after the eligibility checking, informed consent, and baseline assessment have been completed.” How does the informed consent protocol work for PwDs who are not able to provide it in written format (e.g., due to the severity of cognitive, sensory, or motor deficits)? In these cases, is the informed consent obtained then proxy from the CG (or legal guardian) and how is it verified (and documented) that the PwD him/herself wants to participate. Or are these PwDs excluded? How about cases where the PwD initially is able to give informed consent but loses this ability during the course of the study e.g., due to sudden progression of illness?

RESPONSE: We have added a section on ethics to the manuscript. We have added the following text.

All research and clinical activities carried out for the HOMESIDE project will be in compliance with fundamental ethical principles including those reflected in the Oviedo convention and the Convention for the Protection of Human Rights and Fundamental Freedoms and legal requirements (Directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data; and Directives 2001/20/EC, 2005/28/EC relating to the implementation of good clinical practice in the conduct of clinical trials). Ethical conduct will be managed in the following ways:

- The clinical trial coordinator in each country will implement the research in full respect of European /national/ institutional legal and ethical requirements and codes of practice.

- Ethics approvals in each country must be obtained prior to commencement of the trial.

- Informed consent from the PwD's guardian must be obtained prior to enrolling a participant in the study. Assent from the PwD will always be sought prior to enrolment in the study. In the case of cognitive deterioration prohibiting ongoing assent from the PwD, assent will be assumed if the PwD continues to comply with the assessment and intervention.

- National and International rules on data protection will be followed.

14) Page 16, lines 12-14: "Blinded assessors will collect participants' data at baseline, post-intervention, and follow-up." If I understood correctly, the primary outcome measure of the trial (Neuropsychiatric Inventory-Questionnaire, NPI-Q) is given to the caregivers as a self-report questionnaire, not filled by the researchers based on an interview of the PwD and CG. As the CGs are delivering the interventions, the data collection is therefore not blinded at all in this regard, and there is a high likelihood of a responder bias.

RESPONSE: No, the NPI-Q is administered by the assessor who is blinded. Indeed all the measures are presented to the PwD and CG by the assessor. Although the NPI-Q is designed to be a self-administered questionnaire, Cummings et al (1994) indicate that it should be administered as part or entirely as a semi-structured interview to clarify and review responses.

15) It would be good to clarify for all the outcome measures, are they based on (i) self-reports of the PwD and CG, (ii) informant-reports of the CG, or (iii) ratings done by clinician / researcher based on interviews of the PwD and CG. Also it would be good to mention if the CGs receive any instructions / training on how to fill the scales, both in more concrete terms on how to actually fill the forms (which can be difficult for some) and in more abstract terms on how to avoid the bias in one's responses.

RESPONSE: A detailed manual of processes and procedures (caregiver guidelines) has been developed which explain how to complete the forms, particularly the diary. We have added the following statement:

CGs will be provided with a set of guidelines as to how to complete the diary and all self-report and proxy measures.

16) Page 16, line 41: "…the restriction of a common baseline mean score across interventions" What does this mean exactly?

RESPONSE: This refers to the assumption that at baseline there are no differences between the interventions in the mean score, thus hereby assuming the randomisation worked. This assumption will be enforced statistically in the statistical model.