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HOMESIDE: A home-based family caregiver-delivered music intervention for people living with dementia: protocol of a randomised controlled trial.

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Abstract:

Introduction: Pharmacological interventions to address behavioural and psychological symptoms of dementia (BPSD) can have undesirable side effects, therefore non-pharmacological approaches to managing symptoms may be preferable. Past studies show that music therapy can reduce BPSD, and other studies have explored how formal caregivers use music in their caring roles. However, no randomised study has examined the effects on BPSD of music interventions delivered by informal caregivers (CGs) in the home setting. Our project aims to address the need for improved informal care by training cohabitating family CGs to implement music interventions that target BPSD, and the quality of life (QoL) and wellbeing of people with dementia (PwD), and of CGs.

Methods and analysis: A large international 3-arm parallel-group randomized controlled will recruit a sample of 495 dyads from Australia, Germany, UK, Poland and Norway. Dyads will be randomised equally to standard care (SC), a home-based music program plus SC, or a home-based reading program plus SC for 12 weeks. The primary outcome is BPSD of PwD (measured using the Neurospychiatric Index). Secondary outcomes will examine relationship quality between CG and PwD, depression, resilience, competence, QoL for CG, and QoL in PwD. Outcomes will be collected at baseline, at the end of the 12-week intervention and at 6-months post randomisation. Resource Utilization in Dementia will be used to collect economic data across the life of the intervention and at 6-month follow-up. We hypothesize that the music program plus SC will generate better results than SC alone (primary comparison), or the reading program plus SC (secondary comparison).

Ethics and dissemination: Ethical approval will be obtained for all countries. Results will be presented at national and international conferences and published in scientific journals and disseminated to consumer and carer representatives and the communty.

Strengths and Limitations of this study

- As a multinational trial, this study will provide internationally generalisable results concerning the effects of music intervention delivered by trained family caregivers on the behavioural and psychological symptoms of people living with dementia.
- Based on pilot data, this trial will have adequate power to determine the effects on the person with dementia.
- The trial will determine whether caregiver-delivered music intervention improve quality of life for and wellbeing of the carer reduce healthcare costs for the caregiver and society.
- A comprehensive set of core outcomes will be measured, including long-term effects in key variables, with assessor blinding.
- As participants cannot be blinded, a limitation of the study is that they may provide biased responses on their self-report measures.

BACKGROUND

Family caregivers (CG) play a vital role in providing care for a person living with dementia (PwD) in the home-setting,[1]. This personalised care not only directly benefits the PwD by keeping them at home in a familiar environment but represents a significant economic contribution to society. CGs often find caregiving satisfying and rewarding, however the task of managing the challenging behavioural and psychological symptoms of dementia (BPSD) can override their capacity to cope, leading to negative physical and mental health including fatigue, depression, burnout, and illness,[2-3]. A deterioration in CG wellbeing may have a negative flow-on effect on the wellbeing of the PwD. A negative spiral may develop until the CG can no longer sustain the caring role, and the PwD moves into residential care earlier than desired.

The 2015 global cost of dementia was estimated to be US$818 billion, and this figure will continue to increase as the number of people with dementia rises,[1]. Nearly 85% of costs are related to family and social, rather than medical care. With this increase and the escalating costs of care, it is time-critical that CG-directed home-based interventions are developed and tested. The 2017 Lancet Commission on Dementia,[1] suggests that pharmacological treatment of BPSD should be restricted to those with very severe symptoms and highlights music therapy as a non-pharmacological intervention that reduces BPSD (p.30).

Systematic reviews indicate that the majority of CG-directed interventions adopted cognitive-behavioural or psychoeducational approaches to address CG coping, depression and BPSD management,[4-5]. Adherence to programs was poor because CGs could not commit to the regular program attendance requirements,[4-5].[4,5] Drawing on social exchange theory, apathy and other BPSD lead to diminished reciprocity between CG and PwD, creating imbalances in the relationship,[6]. Therefore, the convenience of a home-based CG-delivered program that can manage BPSD and address relationship reciprocity is more likely to be adhered to, and more effective in promoting both PwD and CG wellbeing.

Music therapy is a registered psychosocial National Health Service (NHS in the UK) intervention that meets the current recommendations for addressing the individual needs of those with dementia. HOMESIDE (HOME-based caregiver-delivered music intervention for people living with dementia) uses a purposefully developed music intervention (MI) (described later) informed by previous meta-analyses that demonstrate

the effectiveness of music therapy in reducing BPSD,[9-11]. The MI is a translation of the research evidence to a home-care context and, instead of being delivered directly by qualified music therapists, they will train CGs to deliver the MI. The MI incorporates Kitwood's model of personhood for PwD,[12], which is essential to effective dementia care and underpins the philosophy of the 2018 Alzheimer's Association Dementia Care Practice Recommendations. The person-centred dementia care embedded in the MI emphasizes communication and relationships, recognising that dementia is best understood as an interplay between neurological impairment and psychosocial factors (e.g. health, individual psychology), and the environment,[13].

Small scale studies that have tested the effectiveness of MI training programs for informal and formal CGs have had positive findings to date. Results of a cluster RCT with formal CGs showed the MI to be a practicable and acceptable intervention, with PwD showing treatment-related improvements, and staff reporting enhanced skills in caregiving,[7]. Although based on a small sample (N=17), large effects in BPSD (Cohen's *d*=2.32) were found between standard care (SC) and MI from baseline to 7-months. A home-based feasibility RCT determined acceptability of the MI, assessed burden associated with delivering the MI, and tested appropriateness of the measures,[14]. BPSD scores decreased from baseline to post-test in the MI group but increased in the SC group and mixed results were shown for the comparative reading group.

The conceptual framework underpinning the MI intervention incorporates the responses of the PwD, the ensuing moment to moment interaction between the PwD and the CG, and the CGs' responses to the PwD and moments of interaction (Figure 1). The MI is grounded in the established knowledge that music-induced emotions and memories are often retained in PwD because of the relative preservation of medial frontal and limbic areas,[9, 15]. MI are effective when the music selected for use is chosen by the PwD (or CG),[9, 11]. When music facilitates moment to moment interactions, emotional and social engagement, and autobiographical recall, imbalances in reciprocity are diminished. CGs' positive experience of seeing "the person behind the dementia" via this music-induced response evokes CG experiences of pleasure, feelings of competence in the CG, and fosters their resilience and coping. Ultimately the enhanced wellbeing of CGs will lead to more effective care and better wellbeing outcomes for both CGs and PwD (Figure 1).

<<INSERT FIGURE 1 ABOUT HERE

Figure 1. Mechanisms of action underpinning the music intervention>>

The comparative conditions in this trial are SC only (control) and a reading intervention plus SC (RI, active control). The RI was included because studies have shown preliminary evidence that reading to and with PwD can have positive impacts on BPSD,[19-21]. We anticipate that the RI will lead to a small positive effect but that MI is expected to be superior as music has been shown to be a social connector and a trigger of autobiographical recall, is non-reliant on intact verbal comprehension or expression, and can be used to regulate emotion and behaviour,[7, 9-11, 15-18].

Trial Design

A large, pragmatic, blinded, international 3-arm parallel-group RCT design is planned with a 1:1:1 allocation ratio. Cohabiting dyads where one member of each dyad has a diagnosis of dementia will be randomised to one of three conditions: 1) MI plus SC; 2) RI plus SC; and 3) SC only (Figure 2). CG in MI and RI groups will receive a 2-hour training session on how to deliver the MI or RI and will then engage the PwD in a 5x weekly CG-directed home-program for 12 weeks. Two additional training sessions will be provided at 3-weeks and 6-weeks post allocation. Fifteen-minute fortnightly phone calls will be scheduled to support the CG, and encourage adherence to the protocol. Data will be collected at baseline and at the end of the 12-week intervention, and at 3-month follow-up (6-months post-randomization). The SC group will not receive any training sessions. This trial is framed as a superiority trial where we hypothesise that the MI will be superior to SC (primary) and RI plus SC (secondary) regarding BPSD of PwD at 12-weeks post-randomisation.

<<INSERT FIGURE 2 ABOUT HERE

Figure 2. HOMESIDE illustration of study design >>

Objectives

The primary aim is to demonstrate the effectiveness of the 12-week HOMESIDE MI plus SC on the short-term BPSD at the end of intervention of PwD living at home and being cared for by a cohabiting CG compared to SC (primary), and to evaluate the effectiveness of MI plus SC compared to RI plus SC (secondary). Other secondary objectives are as follows:

- Evaluate the maintenance of the effect of the MI plus SC on longer-term (6 months post-randomization) BPSD compared to SC and RI plus SC.
- Evaluate the effectiveness of the MI plus SC on short- and long-term levels of depression and quality of life of PwD compared to SC and RI plus SC.
- Evaluate the effectiveness of the MI plus SC on short- and long-term levels of depression, resilience, sense of competence, and quality of life of the CG compared to SC and RI plus SC.
- Evaluate the effectiveness of the MI plus SC on the short- and long-term perceived quality of the relationship between PwD and CG compared to SC and RI plus SC.
- Compare the cost-effectiveness of a CG-delivered MI plus SC on PwD and CG outcomes compared to SC and RI plus SC, using quality of life for both PwD and CG.

METHODS AND ANALYSIS

Participants

The trial will be conducted in people's homes located in metropolitan cities in Australia, Germany, Poland, Norway, and the United Kingdom.

Inclusion criteria:

- dyads (cohabiting) who are close in relationship and where one member has a diagnosis of dementia (Alzheimer's Disease [AD], Frontotemporal Dementia, Vascular Dementia [VD], Lewy Body Disease, or mixed dementia) as determined by a clinician experienced in diagnosising dementia,[8].
- dyads where the PwD has a Neuropsychiatric Inventory-Questionnaire (NPI-Q) Score of ≥6. There will be no restrictions on including PwD with mild cognitive impairment (MMSE scores ≤24) as research indicates that NPI-Q scores ≥6 occur in PwD who have high Mini Mental State Examination Scores,[22].

Exclusion criteria:

- dyads where the CG employs paid carers for more than 5 hours per day on at least 5 days per week. There will be no further exclusions.

Interventions

Music Intervention. Dyads randomly allocated to the MI will receive a 2-hour home-based MI training session that aims to engage the PwD during and following the MI. A music therapist will instruct the CG on methods and strategies for using music to assist the PwD to become calmer (if agitated) or more energised (if apathetic). CGs will be instructed on how to choose music and engage the PwD in effective and respectful discussions with the aim of evoking autobiographical memories and sharing meaningful experiences,[23]. Strategies to engage PwD and create opportunities for meaningful dialogue with the PwD will be provided, as well as training CGs to notice the PwD's positive and negative responses to music. The activities to be taught comprise: a) singing familiar/preferred songs followed by CG-facilitated discussions about the meaning of the songs for the dyad, the PwD, and significant others, and any associated memories,[16, 24]; b) movement to music (e.g. upper body and arms imitating familiar dance movements to music) to assist in regulating arousal,[11]; c) playing instruments (or using household items to make rhythmic sounds) while listening to music; and d) listening to familiar/preferred relaxing or enlivening music dependent upon BPSD present at the time to assist in regulating arousal,[16]. CGs are then instructed to deliver the MI at least 5x per week for approximately 30 mins over a 12-week period. After each MI session, they will diarise their experiences, including documenting which activities were used, session time and duration, and any positive or negative responses during and after the session. Such data (number of times per week, average duration, activities adopted) will be used to monitor and improve adherence to the protocol. At 3-weeks and 6-weeks post allocation, the MI trainer will return to the dyad's home for a second and third training session (Figure 2). These sessions aim to further extend CG knowledge and skills, troubleshoot any issues, and improve protocol adherence. Fortnightly phone conversations with CGs will be used to support the CG and remind them to complete the diaries (to mitigate risk and maximise participant engagement, retention, and protocol adherence).

Reading Intervention (active control). Dyads randomly allocated to the RI group will receive a 2-hour RI instruction session which aims to engage the PwD during and following the RI. The reading activities to be taught are based on RI methods commonly used with PwD including: a) CG reading aloud to PwD; b) PwD reading aloud (or reciting poems, prayers, prose, short stories, fairy tales, when unable to read) to CG; and c) discussion of the text and personal responses,[19-21]. Strategies to engage the PwD and create opportunities for meaningful dialogue with the PwD will be provided as well as guidance on selecting reading material accessible to the PwD's level of cognitive impairment. CGs are then instructed to deliver RI at least 5x per

week for 30 mins over 12-weeks and diarise their reading activities to record activity and adherence. Diaries will serve as a mechanism to monitor adherence to the protocol. At 3-weeks and 6-weeks post allocation, as per the MI condition, the RI trainers will return to the dyad's home for a second and third training session with the intention of further extending CG knowledge and skills and to monitor and improve intervention protocol adherence. Fortnightly phone conversations with CGs will be used to support the CG and remind them to complete the diaries (to mitigate risk of noncompletion). Like the MI condition, phone calls also aim to maximise participant engagement, retention, and protocol adherence.

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.

Discontinuing or Modifying Interventions. Where there is a significant deterioration in the health of the PwD and/or the CG that leads to hospital admission or care home admission, the MI or RI will be discontinued. If there is a change in primary CG partway through the study, the dyad will be withdrawn from the study.

*Training and assessment of fidelity***.** Given the MI and RI will be delivered in five different countries with different healthcare philosophies and practices, a careful plan for fidelity of the study design, treatment integrity, treatment differentiation, treatment receipt, and treatment enactment will be developed. A standardised manual for MI and RI has been developed and agreed upon by all countries prior to implementation. Fidelity in this study is complex as it will involve assessing fidelity of the MI and RI training session, but also fidelity of the CG-directed program. Delivery of MI and RI training by research staff will be videorecorded and a randomised selection of 20% of recordings from every country will be reviewed by members of the research team and cross-checked with the MI and RI protocol manuals using a customed fidelity checklist. Individualised supervision and monitoring of intervention trainers will be employed to minimise "drift" in trainer differences and control for differences in trainer styles. CG diaries will be used to determine whether the MI and RI protocols have been adhered to and the success of treatment enactment.

Outcomes

At baseline, demographic data (age, gender, and dyad history) of both CG and PwD will be collected as well as diagnostic information of PwD.

Where possible, core outcomes (www.comet-initiative.org) for psychosocial intervention research in dementia care were selected,[25]. For the PwD, the following measures were selected:

- Behavioural and Psychological Symptoms of Dementia - The NPI-Q is the most highly regarded and used measure for determining the severity of BPSD in clinical trials. The 12-item scale is used to assess the behaviour of PwD across 12 domains of commonly displayed BPSD. The scale has been translated into more than 40 languages, has been cross-validated against the NPI as the gold standard (r=0.73) and has demonstrated good validity (sensitivity = 74.1%, specificity = 79.5%), internal reliability (α= 0.783) and excellent test-retest reliability (r = 0.99),[26-27]. Total severity scores range from 0 to 36; higher values are indicative of higher severity. Distress scores range from 0 to 60; higher values represent higher levels of distress.
- Despression – The Montgomery Asberg Depression Rating Scale,[28] (MADRS) will be used to assess the severity of depression. The 10-item scale with each item's scores ranging from 0 (no symptoms) –6 (severe symptoms) is determined by an interview with the PwD and/or proxy. Total score ranges from 0 to 60 with higher scores indicating more severe depression. MADRS has been found to have good constructive validity, internal reliability (α= 0.84), and test-retest reliability (ICC=0.78). The scale has been widely used in clinical trials,[28].
- Quality of Life (QoL) – The QoL of PwD will be determined by administering the Quality of Life-Alzheimer's Disease (QoL-AD),[29] scale. The QoL-AD is recommended by the COS,[25] for use in clinical trials. It is a simple 13-item self-report measure, which is rated on a 4-point scale, within the structure of a verbally delivered interview. Total scores range from 13 (no quality of life) to 52 (excellent quality of life in all areas). Studies indicate that the measure can demonstrated sensitivity to psychosocial intervention, correlates with health-utility measures,[30], has excellent interrater reliability ($\kappa > 0.70$) and internal consistency ($\alpha = 0.82$). The QoL-AD is reliable when used with people with MMSE scores of $\geq$10. Both a proxy and a self-report will be collected at the 3-timepoints. If the PwD is able to complete the MMSE at all time points, then their response will be included in the analysis. If not, then the proxy version at all time points will be used.

- Cognition - The Mini-Mental State Examination (MMSE) will be administered pre and post intervention (Time 1 and Time 2) to monitor any change in the PwD's cognition and to examine the relationship between cognitive decline, BPSD, depression and response to different conditions. The MMSE is a 30-point questionnaire used to estimate the severity and progression of cognitive impairment and to follow the course of cognitive changes in an individual over time,[31]. The MMSE tests for orientation, attention, memory, language and visual-spatial skills. It is reliable and valid for both diagnosis and longitudinal assessment. Higher scores indicate better cognitive capacity with scores of 24-30 indicating no cognitive impairment; 19-23 indicating mild cognitive impairment; 10-18 indicating moderate cognitive impairment; and scores <10 indicating severe cognitive impairment.

For the CG, the following measures were selected:

- Symptoms of depression – CG depression will be measured using the Patient Health Questionnaire–9 (PHQ-9),[32]. The 9-item questionnaire asks the participant about how often they experience the descriptors over the last 2 weeks. Each item is scored from 0 (not at all) to 3 (nearly every day). Total scores range from 0 to 27. The PHQ–9 has comparable sensitivity and specificity to other depression measures; high internal reliability (α = 0.89), and test-retest reliability (r =0.84).
- Resilience – CG resilience will be measured using the 14-item Resilience Scale (RS-14),[33]. Total scores range from 14 to 98, with higher scores indicative of higher resilience. The measure has been tested and has good concurrent validity, good internal reliability (α = 0.8 – 0.90), good construct validity, test-retest reliability (r=0.67 to 0.84) and has been translated into 36 languages,[34].
- Competence - CG competence will be measured using the Short Sense of Competence Questionnaire (SSCQ),[35]. The 7-items cover 3 main domains; self-reported feelings about how the caregiver role impacts the CG's personal life, satisfaction with their performance as a CG, and their satisfaction with how the PwD responds to the CG. Total scores ranged from 7 to 35 with higher scores indicative of a stronger sense of competence. The measure has been cross-validated with the longer 35-item standard Sense of Competence Questionnaire (r = 0.88) and has been shown to have high reliability (Cronbach's α = 0.76).

- CG Quality of Life – QoL of the CG will be assessed using the Assessment of Quality of Life-6D instrument (AQoL-6D),[35] Each item asks participants to describe their situation over the past week by ticking the box (from 4 to 6 choices) that best reflects their situation. The psychometric property testing found the instrument to be reliable and and valid, and has greater sensitivity to the psychosocial dimensions of QoL than other utility instruments,[36-37].
- Relationship quality – CG perception quality of the CG and PwD relationship will be captured by asking the CG to complete the Quality of Caregiver-Patient Relationship (QCPR),[38]. This 14-item measures aims to capture the strength of the quality of relationship between the PwD and CG, from the CG's perspective. Total scores range from 14 to 70, with higher scores indicating a higher quality relationship. The measure has demonstrated acceptable internal consistency ($\alpha = 0.82$) and concurrent validity.
- Adherence will be measured through CG completed diaries. CGs are deemed adherent to the protocol if they have provided >2 sessions of MI or RI per week, for at least 30minutes in total.

To evaluate the cost-effectiveness of MI compared to RI and SC on PwD and CG, the outcomes will be measured using:

- Quality Adjusted Life-Years – The EuroQol instrument (EQ-5D-5L),[39] is a generic quality of life measure that is internationally used to determine the quality-adjusted life-years (QALYs) and used for clinical and economic appraisal,[39]. The measure is not cognitively demanding and quick to complete. Scores from the five items are not combined arthimetically but using preference weights which arrive at an overally quality of life score. These range from lower than 0 (worse than death) to 1 (best possible). CGs will complete the measure as a proxy for the PwD and for their own health status,[25, 41-43].
- Resource Utilization in Dementia (RUD) - The RUD is a standardized instrument for resource use data collection in dementia, designed to collect data from formal and informal care across different countries. The RUD assesses resource use of both PwD and CG, including time expended in different daily tasks, and consists of baseline and a follow-up assessment,[44].

<<INSERT FIGURE 3 ABOUT HERE

Figure 3. Schedule of enrolment, interventions, and assessments >>

Sample size

A total of 165 dyads in each arm of the study, or 495 in total, are needed to detect a difference of 3-points in NPI-Q total severity score (primary outcome) between the MI plus SC and SC arm (primary comparison) at 12-weeks (primary time point). This assumes 90% power, a two-tailed significance level of 5%, equal standard deviation (SD, 7.5 points) in the groups, no correlation between baseline and 12 weeks (conservative), and 20% attrition. A 3-point change from baseline in NPI-Q total severity score is considered a clinically meaningful difference,[45]. A conservative SD of 7.5 points is based on that observed in 1026 community-living participants across eight European countries with mild to severe dementia (SD 5.9 to 6.5 points),[46-47]. A conservative drop-out proportion (e.g. withdrawn by CG, physician, or death) of 20% is based on a reported 5.6% (95% CI [1.8%, 12.6%]) drop-out at 3 months in 89 in-patients with mild to moderate dementia in Finland participating in a three-arm RCT of singing, music, or usual care,[24].

Recruitment

Randomisation will aim to be distributed equally across five countries (Australia, United Kingdom, Norway, Germany, and Poland) to support between-country analyses. Participants will be recruited through established partner organisations in each country who coordinate CG support groups. Staff from the partner organisations will introduce the trial to potential participants and invite them to participate in the study.They will be given an information sheet explaining the main aspects of the trial and provided with contact details of the research team who will be available to answer further questions.

Randomization, Allocation Concealment, and Blinding

The randomization schedule will be computer-generated by an independent statistician and allocation will be carried out through a centralised randomization service. Stratified block permuted randomization will be used for each country, so that treatment balance within country is achieved. Dyads who meet the inclusion criteria and none of the exclusion criteria will be randomized 1:1:1 into MI, RI, or SC. Randomization will occur after the eligibility checking, informed consent, and baseline assessment have been completed. The study

coordinator in each country will be informed of the allocation and will inform dyads of their group allocation by post, phone, or email.

Participant dyads cannot be fully blinded due to the active nature of the interventions however, we will avoid publicizing our hypothesis that MI may be superior to RI. Plain language statements and consent forms will use neutral wording to maintain equipoise and to avoid expectancy effects. Blinded assessors will collect participants' data at baseline, post-intervention, and follow-up. Diaries will be returned in sealed envelopes to minimise risk of assessors becoming unblinded. The success of assessor blinding will be checked following the collection of follow-up data for each dyad by asking each of the assessors whether they inadvertendlty discovered the dyad's allocation. The independent statistician will not reveal the allocation codes to any of the study team except for the study coordinators of each country in charge of group allocation. All other investigators and the study statistician will remain blinded until the database has been cleaned, a blinded data review has taken place, and the database is ready for analysis.

Analysis

Analyses will be performed on an intention-to-treat basis including all randomised dyads in their allocated study arm. The primary outcome (NPI-Q severity total score) will be analysed using a constrained longitudinal data analysis (cLDA) model,[48] with response consisting of all scores (baseline, 12 weeks and 6-months) and the model including factors representing intervention, time, intervention by time interaction, and country with the restriction of a common baseline mean score across interventions. The absolute difference between MI and SC and MI and RI in mean change from baseline will be estimated (including two-sided 95% confidence interval) at 12 weeks (primary time point). A hierarchical fixed sequence testing procedure will allow testing of MI versus RI at 12 weeks at 5% if the comparison of MI versus SC at 12 weeks has a p-value < 0.05. Secondary analyses will consist of a model adjusted for potential confounders (forms of dementia and gender). The cLDA model provides valid inference if the missing data mechanism is at most missing at random. In addition to the intention-to-treat effect we will obtain the complier average causal effect by making use of the collected adherence data,[49]. Analyses similar to the primary outcome will be applied to the secondary outcomes for PwD and CGs. Heterogeneity of the intervention effect across subgroups (gender of the PwD/CG,

forms of dementia, country) will be assessed by means of interaction tests. The number and percentage of PwDs and CGs with adverse events will be summarized by intervention group.

Cost-effectiveness analysis in a societal perspective will be performed separately for each country using the utilities generated by EQ-5D-5L for both PwD and CG and country-specific weights, to estimate a combined QALY score using a generalized linear model adjusted by the baseline. Health and informal care resources consumed by PwD will be assessed using the RUD and unit cost by country. A generalized linear mixed model will be used to estimate the main predictors of the total costs in the MI, RI and SC groups. Incremental cost-effectiveness ratio (ICER) will be calculated using the cost and effect estimates comparing MI with RI and SC. The uncertainty around the ICER will be estimated using bootstrapping (1000 replications) adjusting to control variables.

Patient and public involvement

All countries have involved user and advocacy organisations in the development and design of the study. The UK, Australia, and Germany have been piloting work with formal and informal CGs of PwD for many years. CGs and PwD have been involved designing the diaries which capture adherence data. It was imperative that the diary be user-friendly, not burdensome on the CG, and yet enabled them to document both the positive and negative aspects of the session. Several iterations of the diary were constructed prior to arriving at the final structure. Pilot work in Australia,[14] involved interviews post-intervention to identify strengths, limitations, challenges, and experiences in delivering the MI and RI?, as well as recommendations for suggested modifications to the intervention training. Representatives of advocacy groups and end users from all countries will be represented on an international Participant and Public Involvement Committee.

Monitoring and Oversight

A Trial Operations Committee (TOC) will comprise the principal investigator, chief investigators and clinical trial managers from each of the 5 countries, the biostatistician, health economist, and a consumer representative. The TOC will meet at least 6-weekly, and will oversee all aspects of the trial delivery including strategies to support efficient and effective recruitment and retention, reviewing completeness of datasets, monitoring intervention fidelity, management of timelines and milestones, review of country-by-

country progress, public and patient involvement or actions, and publication and dissemination plans. The role of the members of the TOC is to bring country-specific issues to the international team for discussion to ensure the study is being monitored and delivered according to the agreed protocols. Protocol deviations and any changes or amendments to the operational processes of the trial will be discussed and decisions made by the TOC.

A Trial Steering Committee (TSC) will comprise of members independent of the clinical trial as well as members and representating consumers and other relevant advocacy organisations. The trial Principal Investigator (or a proxy in her absence) will also sit on the committee as a non-voting member. The Committee will meet biannually (or more often when needed) to review and monitor all aspects of the study delivery. The committee will take careful note of recruitment and retention rates and identify potential modifications to protocols to mitigate risk of slow recruitment and attrition. They will draw on reports provided to them by the Data and Safety Monitoring Committee (DSMC) and make recommendations to the PI and TOC about whether further actions are required.

A DSMC will meet biannually (prior to the TSC) to review the cumulative study data to evalute the safety, study conduct, and scientific validity and integrity of the trial. The committee consist of at least four people with strong methodological, biostatistical, and clinical expertise who are independent of the project and an end user representative. The DSMC will be provided with data on recruitment, intervention uptake, any unforeseen and/or adverse events, and review serious adverse events. The meetings will consist of an open and a closed part. In the open part, the general progress of the trial will be discussed with the principal investigator. In the closed part, the DSMC will discuss any safety concerns and if considered required, the DSMC will make recommendations to the TSC for appropriate action.

Pilot testing in Australia will be undertaken to test the intervention fidelity, recruitment rates and retention, assessment processes, test the suitability of the developed database, and test the data monitoring systems. The data of the pilot cohort will be included in the main trial; no statistical adjustments are made because the decision depends only on feasibility, no group comparisons will be made.

Study data will be collected and managed using REDCap® electronic data capture tools hosted at the University of Melbourne,[50]. The Data Management Coordinating Center will oversee the intra-study data sharing process, with input from the Data Management Subcommittee. We will develop a data management manual detailing data collection protocols and provide comprehensive training of those members of the research team who collect, check and enter study data. The Principal Investigator, biostatistician, and health economist from the University of Melbourne will be given access to the cleaned data sets. Country specific lead investigators will only have acces to their own country's cleaned data sets. All data sets will be password-protected. To ensure confidentiality, data dispersed to project team members will have any identifying information removed.

Risk management

Processes have been put in place to mitigate risks. One of the most significant risks associated with the project is slow recruitment. To offset the risk of slow recruitment, data is being collected across five countries. If some countries have less difficulty than others in recruiting, then these countries will recruit greater numbers to ensure the required sample size is obtained. Another risk identified is the heterogeneity of intervention delivery. The inclusion of a detailed manual, regular supervision with interventionists, and monitoring the effectiveness of interventionist training will mitigate the risk of poor intervention fidelity.

Relevance and Benefit to Society

As the majority of PwD live in the community and not in residential care settings, quality informal care for PwD is crucial for managing BPSD and enhancing QoL. This protocol details the process for testing the effectiveness and cost-effectiveness of a CG-directed music intervention and reading intervention designed to manage the BPSD of PwD, the sense of burden and wellbeing of the CG, and provide meaningful possibilities to maintain the relationship between PwD and their CGs. We expect that with support and training, the MI will be easily implemented in the family home by CGs. With the increasing number of people living with dementia and the stress this will place on countries' economies, our project aims to test an intervention designed to keep people living at home with family CGs for as long as possible, reducing the burden for society and caregivers. Our study will be able to estimate the ICER between MI and RI, MI and

SC, and RI and SC. Data may support aged care policy recomendations and as the interventions will be delivered in five different countries, results will be broadly generalisable.

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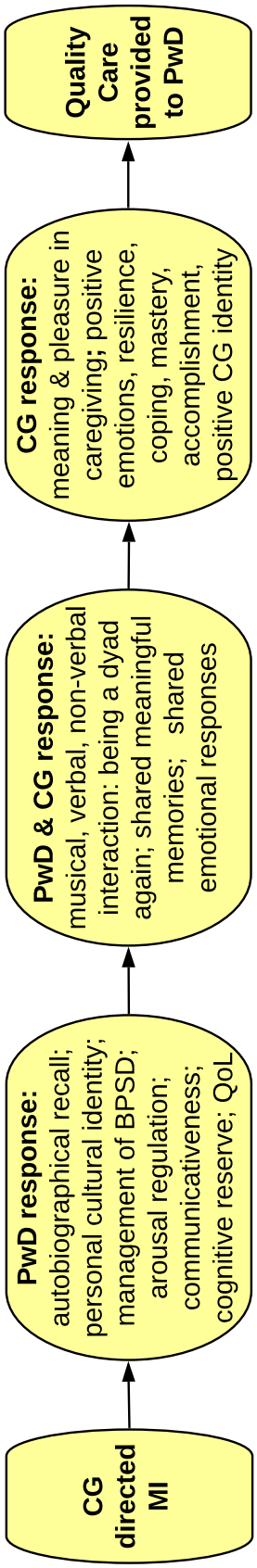
CG directed MI
PwD response: autobiographical recall; personal cultural identity; management of BPSD; arousal regulation; communicativeness; cognitive reserve; QoL
PwD & CG response: musical, verbal, non-verbal interaction: being a dyad again; shared meaningful memories; shared emotional responses
CG response: meaning & pleasure in caregiving; positive emotions, resilience, coping, mastery, accomplishment, positive CG identity
Quality Care provided to PwD

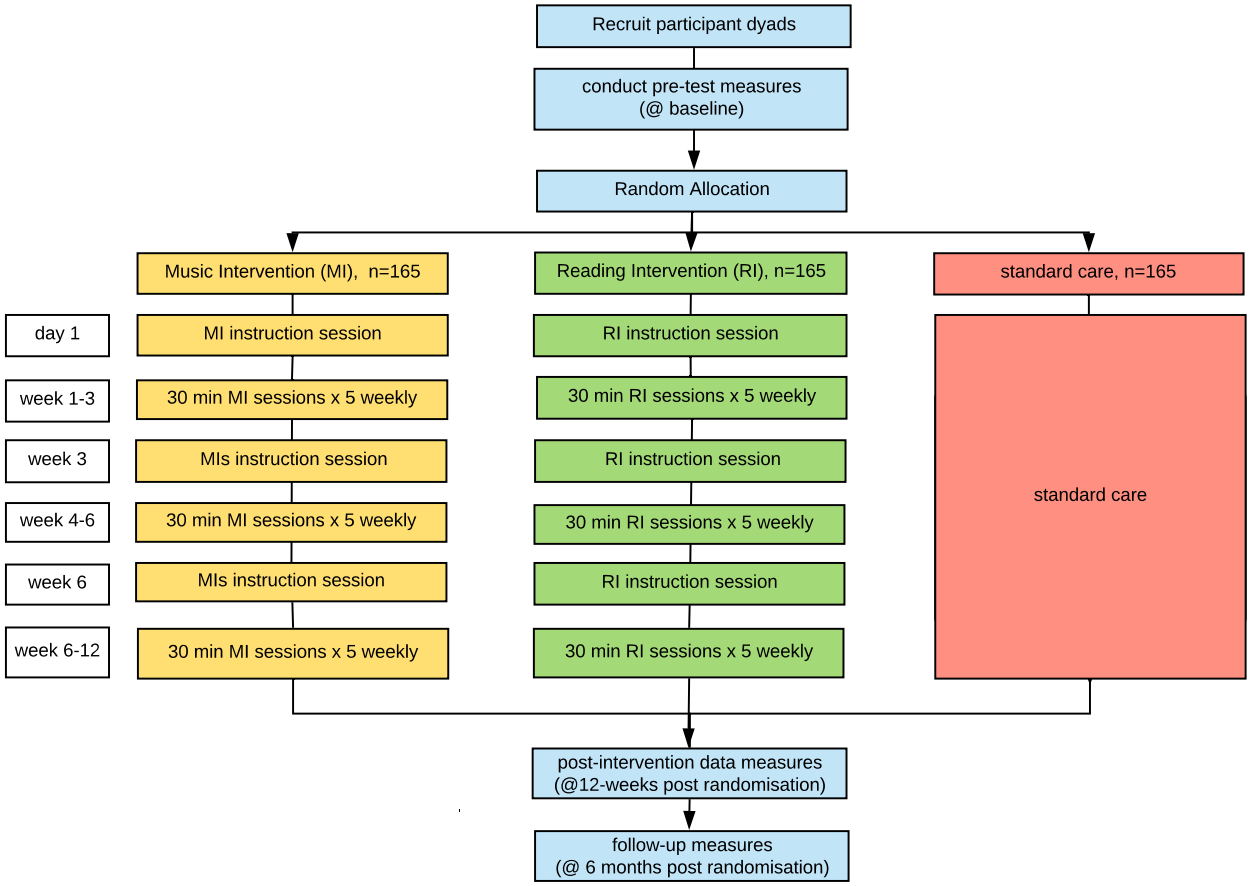

Figure 2. HOMESIDE Trial Design
Note, MI and RI are in addition to standard care.

	Enrolment	Allocation	Intervention				Follow-up
TIMEPOINT	***-1day*** (-7- -1 days)	**0**	***1day*** (+/- 7 days)	***Day 21*** (+/- 7 days)	***Day 42*** (+/- 7 days)	***Day 90*** (+/- 7 days)	***Day 180*** (+/- 7 days)
ENROLMENT:							
Eligibility screen	X						
Informed consent (or assent)	X						
Dyad: allocation		X					
INTERVENTIONS:							
Music Intervention Training			X	X	X		
Reading Intervention Training			X	X	X		
ASSESSMENTS:							
PERSON WITH DEMENTIA sociodemographic information	X						
MMSE (self)	X					X	
dementia diagnosis (proxy)	X						
NPI-Q (proxy)	X					X	X
MADRS *(proxy)*	X					X	X
QoL-AD *(proxy or self)*	X					X	X
EQ-5D-5L *(self and proxy)*	X					X	X
Adverse events; death, hospitalisation, death of caregiver			X	X	X	X	X
CAREGIVER *sociodemographic information*	X						
PHQ-9	X					X	X
RS-14	X					X	X
SSCQ	X					X	X
QPCR	X					X	X

AQoL-6D	X					X	X
EQ-5D-5L *(self)*	X					X	X
RUD	X					X	X
Interviews						X	
Diary (5xweekly diary entries for MI and RI)			X	X	X	X	
Adverse events; death, hospitalisation							

Figure 3. Schedule of enrolment, interventions, and assessments

RUD - Resource Utilization in Dementia, MMSE -MiniMental State Examination Score; ICD-10 – International Classification of Diseases-10; NPI-Q – Neuropsychiatric Inventory; MADRS - Montgomery Asberg Depression Rating Scale; QoL-AD - Quality of Life-Alzheimer's Disease; PHQ-9 - Patient Health Questionnaire–9; RS - Resilience Scale; SSCQ - Short Sense of Competence Questionnaire; AQoL-6D - Assessment of Quality of Life-6D instrument; QCPR - Quality of Caregiver-Patient Relationship; Quality Adjusted Life-Years – EQ-5D-5L The EuroQol instrument

BMJ Open

HOMESIDE: Home-based family caregiver-delivered music and reading interventions for people living with dementia: Protocol of a randomised controlled trial.

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Title: HOMESIDE: Home-based family caregiver-delivered music and reading interventions for people living with dementia: Protocol of a randomised controlled trial.

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Abstract:

Introduction: Pharmacological interventions to address behavioural and psychological symptoms of dementia (BPSD) can have undesirable side effects, therefore non-pharmacological approaches to managing symptoms may be preferable. Past studies show that music therapy can reduce BPSD, and other studies have explored how formal caregivers use music in their caring roles. However, no randomised study has examined the effects on BPSD of music interventions delivered by informal caregivers (CGs) in the home setting. Our project aims to address the need for improved informal care by training cohabiting family CGs to implement music interventions that target BPSD, and the quality of life (QoL) and wellbeing of people with dementia (PwD) and of CGs.

Methods and analysis: A large international 3-arm parallel-group randomised controlled trial will recruit a sample of 495 dyads from Australia, Germany, UK, Poland and Norway. Dyads will be randomised equally to standard care (SC), a home-based music program plus SC, or a home-based reading program plus SC for 12 weeks. The primary outcome is BPSD of PwD (measured using the Neurospychiatric Inventory-Questionnaire). Secondary outcomes will examine relationship quality between CG and PwD, depression, resilience, competence, QoL for CG, and QoL in PwD. Outcomes will be collected at baseline, at the end of the 12-week intervention and at 6-months post randomisation. Resource Utilization in Dementia will be used to collect economic data across the life of the intervention and at 6-month follow-up. We hypothesize that the

music program plus SC will generate better results than SC alone (primary comparison) and the reading program plus SC (secondary comparison).

Ethics and dissemination: Ethical approval will be obtained for all countries. Results will be presented at national and international conferences and published in scientific journals and disseminated to consumer and caregiver representatives and the community.

Strengths and Limitations of this study

- As a multinational trial, this study will provide internationally generalisable results concerning the effects of music intervention delivered by trained family caregivers on the behavioural and psychological symptoms of people living with dementia.
- Based on pilot data, this trial will have adequate power to determine the effects on the person with dementia.
- The trial will determine whether caregiver-delivered music interventions improve quality of life and wellbeing of the caregiver, and reduce healthcare costs for the caregiver and society.
- A comprehensive set of core outcomes will be measured, including long-term effects in key variables, with assessor blinding.
- As participants cannot be blinded, a limitation of the study is that they may provide biased responses on their self-report measures.

BACKGROUND

Family caregivers (CG) play a vital role in providing care for a person living with dementia (PwD) in the home-setting [1]. This personalised care not only directly benefits the PwD by keeping them at home in a familiar environment but represents a significant economic contribution to society. CGs often find caregiving satisfying and rewarding, however the task of managing the challenging behavioural and psychological symptoms of dementia (BPSD) can override their capacity to cope, leading to negative physical and mental health including fatigue, depression, burnout, and illness,[2-3]. A deterioration in CG wellbeing may have a negative flow-on effect on the wellbeing of the PwD. A negative spiral may develop until the CG can no longer sustain the caring role, and the PwD moves into residential care earlier than desired.

The 2015 global cost of dementia was estimated to be US$818 billion, and this figure will continue to increase as the number of people with dementia rises,[1]. Nearly 85% of costs are related to family and social, rather than medical care. With this increase and the escalating costs of care, it is time-critical that CG-directed home-based interventions are developed and tested. The 2017 Lancet Commission on Dementia,[1] suggests that pharmacological treatment of BPSD should be restricted to those with very severe symptoms and highlights music therapy as a non-pharmacological intervention that reduces BPSD (p.30).

Systematic reviews indicate that the majority of CG-directed interventions adopted cognitive-behavioural or psychoeducational approaches to address CG coping, depression and BPSD management,[4-5]. Adherence to programs was poor because CGs could not commit to the regular program attendance requirements,[4-5]. Drawing on social exchange theory, apathy and other BPSD lead to diminished reciprocity between CG and PwD, creating imbalances in the relationship,[6]. Therefore, the convenience of a home-based CG-delivered program that can manage BPSD and address relationship reciprocity is more likely to be adhered to, and more effective in promoting both PwD and CG wellbeing.

Music therapy is a registered psychosocial National Health Service (NHS in the UK) intervention that meets the current recommendations for addressing the individual needs of those with dementia,[7]. HOMESIDE (HOME-based caregiver-delivered music intervention for people living with dementia) uses a purposefully developed music intervention (MI) (described later) informed by previous meta-analyses that demonstrate

the effectiveness of music therapy in reducing BPSD,[8-11]. The MI is a translation of the research evidence to a home-care context and, instead of being delivered directly by qualified music therapists, they will train CGs to deliver the MI. The MI incorporates Kitwood's model of personhood for PwD,[12], which is essential to effective dementia care and underpins the philosophy of the 2018 Alzheimer's Association Dementia Care Practice Recommendations. The person-centred dementia care embedded in the MI emphasizes communication and relationships, recognising that dementia is best understood as an interplay between neurological impairment and psychosocial factors (e.g. health, individual psychology) and the environment,[13].

Small scale studies that have tested the effectiveness of MI training programs for informal and formal CGs have had positive findings to date. Results of a cluster RCT with formal CGs showed the MI to be a practicable and acceptable intervention, with PwD showing treatment-related improvements, and staff reporting enhanced skills in caregiving,[8]. Although based on a small sample (N=17), large effects in BPSD (Cohen's *d*=2.32) were found between standard care (SC) and MI from baseline to 7-months. A home-based feasibility RCT determined acceptability of the MI, assessed burden associated with delivering the MI, and tested appropriateness of the measures,[14]. BPSD scores decreased from baseline to post-test in the MI group but increased in the SC group and mixed results were shown for the comparative reading group. A study involving eight family CGs who were trained to deliver home-based music programs for their care recipient with dementia, 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 drawing 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 in comparison with care recipients. Findings suggested that CGs enjoyed partaking in the reminiscing and shared musical activities with their loved ones,[15].

The conceptual framework underpinning the MI incorporates the responses of the PwD, the ensuing moment to moment interaction between the PwD and the CG, and the CGs' responses to the PwD and moments of interaction (Figure 1). The MI is grounded in the established knowledge that music-induced emotions and

memories are often retained in PwD because of the relative preservation of medial frontal and limbic areas,[9, 16]. MIs are effective when the music selected for use is chosen by the PwD (or CG),[9, 11]. When music facilitates moment to moment interactions, emotional and social engagement, and autobiographical recall, imbalances in reciprocity are diminished. CGs' positive experience of seeing "the person behind the dementia" via this music-induced response evokes CG experiences of pleasure, feelings of competence in the CG, and fosters their resilience and coping. Ultimately the enhanced wellbeing of CGs will lead to more effective care and better wellbeing outcomes for both CGs and PwD (Figure 1).

<<INSERT FIGURE 1 ABOUT HERE

Figure 1. Mechanisms of action underpinning the music intervention>>

The comparative conditions in this trial are SC only (control) and a reading intervention plus SC (RI, active control). The RI was included because studies have shown preliminary evidence that reading to and with PwD can have positive impacts on BPSD,[17-18]. We anticipate MI to be superior to SC only. In addition, we postulate that the RI will lead to a small positive effect but that MI is expected to be superior as music has been shown to be a social connector and a trigger of autobiographical recall, is non-reliant on intact verbal comprehension or expression, and can be used to regulate emotion and behaviour,[7, 9-11, 16, 19-22].

Trial Design

A large, pragmatic, single-blinded, international 3-arm parallel-group RCT design is planned with a 1:1:1 allocation ratio. Cohabiting dyads where one member of each dyad has a diagnosis of dementia will be randomised to one of three conditions: 1) MI plus SC; 2) RI plus SC; and 3) SC only (Figure 2). CGs in MI and RI groups will receive a 2-hour training session on how to deliver the MI or RI and will then engage the PwD in a 5x weekly CG-directed home-program for 12 weeks. Two additional training sessions will be provided at 3-weeks and 6-weeks post allocation. Fifteen-minute fortnightly phone calls will be scheduled to support the CG, and encourage adherence to the protocol. Data will be collected at baseline, at the end of the 12-week intervention, and at 3-month follow-up (6-months post-randomisation). The SC group will not receive any training sessions. This trial is framed as a superiority trial where we hypothesise that the MI will

be superior to SC (primary) and RI plus SC (secondary) regarding BPSD of PwD at 12-weeks post-randomisation.

<<INSERT FIGURE 2 ABOUT HERE

Figure 2. HOMESIDE illustration of study design >>

Objectives

The aim is to demonstrate the effectiveness of the 12-week HOMESIDE MI plus SC on the short-term BPSD at the end of intervention of PwD living at home and being cared for by a cohabiting CG compared to SC (primary), and to evaluate the effectiveness of MI plus SC compared to RI plus SC (secondary). Other secondary objectives are as follows:

- Evaluate the maintenance of the effect of the MI plus SC on longer-term (6 months post-randomisation) BPSD compared to SC and RI plus SC.
- Evaluate the effectiveness of the MI plus SC on short- and long-term levels of depression and quality of life of PwD compared to SC and RI plus SC.
- Evaluate the effectiveness of the MI plus SC on short- and long-term levels of depression, resilience, sense of competence, and quality of life of the CG compared to SC and RI plus SC.
- Evaluate the effectiveness of the MI plus SC on the short- and long-term perceived quality of the relationship between PwD and CG compared to SC and RI plus SC.
- Compare the cost-effectiveness of a CG-delivered MI plus SC on PwD and CG outcomes compared to SC and RI plus SC, using quality of life for both PwD and CG.

METHODS AND ANALYSIS

Participants

The trial will be conducted in people's homes located in metropolitan cities and adjoining rural areas, in Australia, Germany, Poland, Norway, and the United Kingdom.

Inclusion criteria:

- dyads (cohabiting) who are close in relationship and where one member has a diagnosis of dementia according to ICD-10 criteria (Alzheimer's Disease [AD], Frontotemporal Dementia, Vascular

Dementia [VD], Lewy Body Disease, or mixed dementia) as determined by a clinician experienced in diagnosing dementia,[7]. 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.

- 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,[23]. 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.

Exclusion criteria:

- dyads where either or both the CR or PwD have significant hearing impairments that are not resolved through the use of a hearing aid device and limit their capacity to enjoy musical experiences. There will be no further exclusions.

Interventions

Music Intervention. Dyads randomly allocated to the MI will receive a 2-hour home-based MI training session that aims to engage the PwD during and following the MI. Using a carefully prepared and detailed intervention manual, a qualified music therapist will instruct the CG on methods and strategies for using music to assist the PwD to become calmer (if agitated) or more energised (if apathetic). CGs will be instructed on how to choose music and engage the PwD in effective and respectful discussions with the aim of evoking autobiographical memories and sharing meaningful experiences,[24]. Strategies to engage the PwD and create opportunities for meaningful dialogue with the PwD will be provided, as well as training CGs to notice the PwD's positive and negative responses to music. The activities to be taught comprise: a) singing familiar/preferred songs followed by CG-facilitated discussions about the meaning of the songs for the dyad, the PwD, and significant others, and any associated memories,[20, 25]; b) movement to music (e.g. upper body and arms imitating familiar dance movements to music) to assist in regulating arousal,[11]; c) playing instruments (or using household items to make rhythmic sounds) while listening to music; and d) listening to familiar/preferred relaxing or enlivening music dependent upon BPSD present at the time to assist in regulating arousal,[20]. CGs are then instructed to deliver the MI at least 5x per week for approximately 30 mins over a 12-week period. After each MI session,

they will diarise their experiences, including documenting which activities were used, session time and duration, and any positive or negative responses during and after the session. Such data (number of times per week, average duration, activities adopted) will be used to monitor and improve adherence to the protocol. At 3-weeks and 6-weeks post allocation, the MI trainer will return to the dyad's home for a second and third training session (Figure 2). These sessions aim to further extend CG knowledge and skills, troubleshoot any issues, and improve protocol adherence. Fortnightly phone conversations with CGs will be used to support the CG and remind them to complete the diaries (to mitigate risk and maximise participant engagement, retention, and protocol adherence).

Reading Intervention (active control). Dyads randomly allocated to the RI group will receive a 2-hour RI instruction session which aims to engage the PwD during and following the RI. The reading activities will be taught by a qualified practitioner, following a carefully prepared and detailed intervention manual. These activities are based on RI methods commonly used with PwD including: a) CG reading aloud to PwD; b) PwD reading aloud (or reciting poems, prayers, prose, short stories, fairy tales, when unable to read) to CG; c) listening to audio books and d) discussion of the text and personal responses,[17-19]. Strategies to engage the PwD and create opportunities for meaningful dialogue with the PwD will be provided as well as guidance on selecting reading material accessible to the PwD's level of cognitive impairment. CGs are then instructed to deliver RI at least 5x per week for 30 mins over 12-weeks and diarise their reading activities to record activity and adherence. Diaries will serve as a mechanism to monitor adherence to the protocol. At 3-weeks and 6-weeks post allocation, as per the MI condition, the RI trainers will return to the dyad's home for a second and third training session with the intention of further extending CG knowledge and skills and to monitor and improve intervention protocol adherence. Fortnightly phone conversations with CGs will be used to support the CG and remind them to complete the diaries (to mitigate risk of noncompletion). Like the MI condition, phone calls also aim to maximise participant engagement, retention, and protocol adherence.

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.

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. This consists of receiving medical, therapeutic and personal care, as well as participating in usual leisure activities.

Discontinuing or Modifying Interventions. Where there is a significant deterioration in the health of the PwD and/or the CG that leads to hospital admission or care home admission, the MI or RI will be discontinued. If there is a change in primary CG partway through the study, the dyad will be withdrawn from the study.

*Training and assessment of fidelity***.** Given the MI and RI will be delivered in five different countries with different healthcare philosophies and practices, a careful plan for fidelity of the study design, treatment integrity, treatment differentiation, treatment receipt, and treatment enactment has been developed. A standardised manual for MI and RI has been developed and agreed upon by all countries prior to implementation. Fidelity in this study is complex as it will involve assessing fidelity of the MI and RI training session, but also fidelity of the CG-directed program. Delivery of MI and RI training by research staff will be videorecorded and a randomised selection of 20% of recordings from every site will be reviewed by members of the research team and cross-checked with the MI and RI protocol manuals using a custom fidelity checklist. Individualised supervision and monitoring of intervention trainers will be employed to minimise "drift" in trainer differences and control for differences in trainer styles. CG diaries will be used to determine whether the MI and RI protocols have been adhered to and the success of treatment enactment.

Outcomes

At baseline, demographic data (age, gender, and dyad history) of both CG and PwD will be collected as well as diagnostic information of PwD (ICD-10).

Where possible, core outcomes (www.comet-initiative.org) for psychosocial intervention research in dementia care were selected,[26]. For the PwD, the following measures were selected:

- Behavioural and Psychological Symptoms of Dementia - The NPI-Q is the most highly regarded and used measure for determining the severity of BPSD in clinical trials. The 12-item scale is used to assess the behaviour of PwD across 12 domains of commonly displayed BPSD. The scale has been translated

into more than 40 languages, has been cross-validated against the NPI as the gold standard (r=0.73) and has demonstrated good validity (sensitivity = 74.1%, specificity = 79.5%), internal reliability (α= 0.783) and excellent test-retest reliability (r = 0.99),[27-28]. Total severity scores range from 0 to 36; higher values are indicative of higher severity. Distress scores range from 0 to 60; higher values represent higher levels of distress. CGs will self-complete the NPI-Q with guidance from the research assessor if required.

- Depression – The Montgomery Asberg Depression Rating Scale,[29] (MADRS) will be used to assess the severity of depression. The 10-item scale with each item's scores ranging from 0 (no symptoms) –6 (severe symptoms) is determined through an assessor-led interview with the proxy, in this study, the CG. Total score ranges from 0 to 60 with higher scores indicating more severe depression. MADRS has been found to have good constructive validity, internal reliability (α= 0.84), and test-retest reliability (ICC=0.78). The scale has been widely used in clinical trials,[29].
- Quality of Life (QoL) – The QoL of PwD will be determined by administering the Quality of Life-Alzheimer's Disease (QoL-AD),[30] scale. The QoL-AD is recommended by the COS,[26] for use in clinical trials. It is a simple 13-item self-report measure, which is rated on a 4-point scale, within the structure of a verbally delivered interview. Total scores range from 13 (poor quality of life) to 52 (excellent quality of life in all areas). Studies indicate that the measure can demonstrate sensitivity to psychosocial intervention, correlates with health-utility measures,[31], has excellent interrater reliability ($\kappa > 0.70$) and internal consistency ($\alpha = 0.82$). The QoL-AD is reliable when used with people with MMSE scores of $\geq$10. Both a CG proxy and PwD self-report (if possible) will be collected at the 3-timepoints. If the PwD is able to complete the MMSE at all time points, then their response will be included in the analysis. If not, then the proxy version at all time points will be used.
- Cognition - The Mini-Mental State Examination (MMSE) will be administered pre and post intervention (Time 1 and Time 2) to monitor any change in the PwD's cognition and to examine the relationship between cognitive decline, BPSD, depression and response to different conditions. The MMSE is a 30-point questionnaire used to estimate the severity and progression of cognitive impairment and to follow the course of cognitive changes in an individual over time,[32]. The MMSE tests for orientation, attention, memory, language and visual-spatial skills. It is reliable and valid for both diagnosis and longitudinal assessment. Higher scores indicate better cognitive capacity with scores of 24-30 indicating

no cognitive impairment; 19-23 indicating mild cognitive impairment; 10-18 indicating moderate cognitive impairment; and scores <10 indicating severe cognitive impairment. MMSE scores will be determined through assessor-led interviews with PwD participants.

For the CG, the following measures were selected:

- Symptoms of depression – CG depression will be measured using the Patient Health Questionnaire–9 (PHQ-9),[33]. This self-completed 9-item questionnaire asks the participant about how often they experience the descriptors over the last 2 weeks. Each item is scored from 0 (not at all) to 3 (nearly every day). Total scores range from 0 to 27. The PHQ–9 has comparable sensitivity and specificity to other depression measures; high internal reliability ($\alpha = 0.89$), and test-retest reliability ($r = 0.84$).
- Resilience – CG resilience will be measured using the self-completed 14-item Resilience Scale (RS-14),[34]. Total scores range from 14 to 98, with higher scores indicative of higher resilience. The measure has been tested and has good concurrent validity, good internal reliability ($\alpha = 0.8 – 0.90$), good construct validity, test-retest reliability (r=0.67 to 0.84) and has been translated into 36 languages,[35].
- Competence - CG competence will be measured using the self-completed Short Sense of Competence Questionnaire (SSCQ),[36]. The 7-items cover 3 main domains; self-reported feelings about how the caregiver role impacts the CG's personal life, satisfaction with their performance as a CG, and their satisfaction with how the PwD responds to the CG. Total scores ranged from 7 to 35 with higher scores indicative of a stronger sense of competence. The measure has been cross-validated with the longer 35-item standard Sense of Competence Questionnaire ($r = 0.88$) and has been shown to have high reliability (Cronbach's $\alpha = 0.76$).
- CG Quality of Life – QoL of the CG will be assessed using the self-completed Assessment of Quality of Life-6D instrument (AQoL-6D),[37] Each item asks participants to describe their situation over the past week by ticking the box (from 4 to 6 choices) that best reflects their situation. The psychometric property testing found the instrument to be reliable and valid, and has greater sensitivity to the psychosocial dimensions of QoL than other utility instruments,[37-38].
- Relationship quality – CG perception quality of the CG and PwD relationship will be captured by asking the CG to self-complete the Quality of Caregiver-Patient Relationship (QCPR),[39]. This 14-

item measure aims to capture the strength of the quality of relationship between the PwD and CG, from the CG's perspective. Total scores range from 14 to 70, with higher scores indicating a higher quality relationship. The measure has demonstrated acceptable internal consistency ($\alpha = 0.82$) and concurrent validity.

- Adherence to the MI/RI intervention will be measured through CG completed diaries. CGs are deemed adherent to the protocol if they have provided >2 sessions of MI or RI per week, for at least 30minutes in total. Data on the general use of reading and music by all dyads (including SC) will be collected at post-test. For each diary entry, CGs will be asked to record the date, start and stop time of MI/RI engagement, types of activities used, their experiences during the session (negative, neutral, positive, unsure), effects from the intervention for the remainder of the day until the PwD goes to bed for the evening sleep (negative, neutral, positive, unsure), and any comments. This data will be used in qualitative analyses to gain more nuanced understandings of how the activities are perceived and how these may change over the course of the intervention period.

To evaluate the cost-effectiveness of MI compared to RI and SC on PwD and CG, the outcomes will be measured using:

- Quality Adjusted Life-Years – The EuroQol instrument (EQ-5D-5L),[40] is a generic quality of life measure that is internationally used to determine the quality-adjusted life-years (QALYs) and used for clinical and economic appraisal,[40]. The measure is not cognitively demanding and quick to complete. Scores from the five items are not combined arithmetically but using preference weights which arrive at an overall quality of life score. These range from lower than 0 (worse than death) to 1 (best possible). CGs will complete the measure as a proxy for the PwD and self-report their own health status,[26, 41-44].
- Resource Utilization in Dementia (RUD) - The RUD is a standardized instrument for resource use data collection in dementia, designed to collect data from formal and informal care across different countries. The RUD assesses resource use of both PwD and CG, including time expended in different daily tasks, and consists of baseline and a follow-up assessment,[45]. The RUD will be completed through assessor-led interviews with CGs.

CGs will be provided with a set of guidelines as to how to complete the diary and all self-report and proxy measures. The schedule for enrolment, baseline assessments, all outcome measures, and intervention trainings is outlined in Figure 3.

<<INSERT FIGURE 3 ABOUT HERE

Figure 3. Schedule of enrolment, interventions, and assessments >>

Sample size

A total of 165 dyads in each arm of the study, or 495 in total, are needed to detect a difference of 3-points in NPI-Q total severity score (primary outcome) between the MI plus SC and SC arm (primary comparison) at 12-weeks (primary time point). This assumes 90% power, a two-tailed significance level of 5%, equal standard deviation (SD, 7.5 points) in the groups, no correlation between baseline and 12 weeks (conservative), and 20% attrition. A 3-point change from baseline in NPI-Q total severity score is considered a clinically meaningful difference,[46]. A conservative SD of 7.5 points is based on that observed in 1026 community-living participants across eight European countries with mild to severe dementia (SD 5.9 to 6.5 points),[47-48]. A conservative drop-out proportion (e.g. withdrawn by CG, physician, or death) of 20% is based on a reported 5.6% (95% CI [1.8%, 12.6%]) drop-out at 3 months in 89 in-patients with mild to moderate dementia in Finland participating in a three-arm RCT of singing, music, or usual care,[25].

Recruitment

Randomisation will aim to be distributed equally across five countries (Australia, United Kingdom, Norway, Germany, and Poland) to support between-country analyses. Participants will be recruited through established partner organisations in each country who coordinate CG support groups. Staff from the partner organisations will introduce the trial to potential participants and invite them to participate in the study. They will be given an information sheet explaining the main aspects of the trial and provided with contact details of the research team who will be available to answer further questions.

Randomisation, Allocation Concealment, and Blinding

The randomisation schedule will be computer-generated by an independent statistician and allocation will be carried out through a centralised randomisation service. Block permuted randomisation with stratification by participating site will be used, so that treatment balance within site is achieved. Dyads who meet the inclusion criteria and none of the exclusion criteria will be randomised 1:1:1 into MI, RI, or SC. Randomisation will occur after the eligibility checking, informed consent, and baseline assessment have been completed. Informed consent/assent will be obtained by a blinded assessor prior to the baseline assessment. The study coordinator in each country will be informed of the allocation and will inform dyads of their group allocation by post, phone, or email.

Participant dyads cannot be fully blinded due to the active nature of the interventions however, we will avoid publicizing our hypotheses that MI may be superior to SC only and RI. Plain language statements and consent forms will use neutral wording to maintain equipoise and to avoid expectancy effects. Blinded assessors will collect participants' data at baseline, post-intervention, and follow-up. Diaries will be returned in sealed envelopes to minimise risk of assessors becoming unblinded. The success of assessor blinding will be checked by asking the assessor to guess the treatment assignment (or say "I do not know") after the post-intervention and follow-up periods. This treatment guess will then be compared against the actual treatment and the blinding index derived. The independent statistician will not reveal the allocation codes to any of the study team except for the study coordinators of each country in charge of group allocation. All other investigators and the study statistician will remain blinded until the database has been cleaned, a blinded data review has taken place, and the database is ready for analysis.

Analysis

Analyses will be performed on an intention-to-treat basis including all randomised dyads in their allocated study arm. The primary outcome (NPI-Q severity total score) will be analysed using a constrained longitudinal data analysis (cLDA) model,[49] with response consisting of all scores (baseline, 12 weeks and 6-months) and the model including factors representing intervention, time, intervention by time interaction, and site with the restriction of a common baseline mean score across interventions. This refers to the assumption that at baseline there are no differences between the interventions in the mean score, thus assuming the randomisation was effective. This assumption will be enforced statistically in the statistical model. The absolute difference between MI and SC and MI and RI in mean change from baseline will be estimated (including two-sided 95%

confidence interval) at 12 weeks (primary time point). A hierarchical fixed sequence testing procedure will allow testing of MI versus RI at 12 weeks at 5% if the comparison of MI versus SC at 12 weeks has a p-value < 0.05. Secondary analyses will consist of a model adjusted for potential confounders (types of dementia and gender). The cLDA model provides valid inference if the missing data mechanism is at most missing at random. In addition to the intention-to-treat effect we will obtain the complier average causal effect by making use of the collected adherence data,[50]. Analyses similar to the primary outcome will be applied to the secondary outcomes for PwD and CGs. Heterogeneity of the intervention effect across subgroups (gender of the PwD/CG, types of dementia, severity of dementia, time of onset dementia, length of time having dementia, relationship between PwD and CG, country) will be assessed by means of interaction tests. The number and percentage of PwDs and CGs with adverse events will be summarized by intervention group.

Cost-effectiveness analysis in a societal perspective will be performed separately for each country using the utilities generated by EQ-5D-5L for both PwD and CG and country-specific weights, to estimate a combined QALY score using a generalized linear model adjusted by the baseline. Health and informal care resources consumed by PwD will be assessed using the RUD and unit cost by country. A generalized linear mixed model will be used to estimate the main predictors of the total costs in the MI, RI and SC groups. Incremental cost-effectiveness ratio will be calculated using the cost and effect estimates comparing MI with RI and SC. The uncertainty around the incremental cost-effectiveness ratio will be estimated using bootstrapping (1000 replications) adjusting to control variables.

Patient and public involvement

All countries have involved user and advocacy organisations in the development and design of the study. The UK, Australia, and Germany have been piloting work with formal and informal CGs of PwD for many years. CGs and PwD have been involved designing the diaries which capture adherence data. It was imperative that the diary be user-friendly, not burdensome on the CG, and yet enabled them to document both the positive and negative aspects of the session. Several iterations of the diary were constructed prior to arriving at the final structure. Pilot work in Australia,[14] involved interviews post-intervention to identify strengths, limitations, challenges, and experiences in delivering the MI, as well as recommendations for suggested

modifications to the intervention training. Representatives of advocacy groups and end users from all countries will be represented on an international Participant and Public Involvement Committee.

Monitoring and Oversight

A Trial Operations Committee (TOC) will comprise the principal investigator, chief investigators and clinical trial managers from each of the 5 countries, the study statistician, health economist, and a consumer representative. The TOC will meet at least 6-weekly, and will oversee all aspects of the trial delivery including strategies to support efficient and effective recruitment and retention, reviewing completeness of datasets, monitoring intervention fidelity, management of timelines and milestones, review of country-by-country progress, public and patient involvement or actions, and publication and dissemination plans. The role of the members of the TOC is to bring country-specific issues to the international team for discussion to ensure the study is being monitored and delivered according to the agreed protocols. Protocol deviations and any changes or amendments to the operational processes of the trial will be discussed and decisions made by the TOC.

A Trial Steering Committee (TSC) will comprise of members independent of the clinical trial as well as members and representating consumers and other relevant advocacy organisations. The trial Principal Investigator (or a proxy in her absence) will also sit on the committee as a non-voting member. The Committee will meet biannually (or more often when needed) to review and monitor all aspects of the study delivery. They will draw on reports provided to them by the TOC and make recommendations to the PI and TOC about whether further actions are required.

A DSMC will review the cumulative study data to evalute the recruitement, safety, study conduct, and scientific validity and integrity of the trial. The committee consists of at least five people with strong methodological, biostatistical, and clinical expertise who are independent of the project and an end user representative. The DSMC will be provided with data on recruitment, intervention uptake, any unforeseen and/or adverse events, and review serious adverse events. The meetings will consist of an open and a closed part. In the open part, the general progress of the trial will be discussed with the principal investigator. In the closed part, the DSMC will discuss any safety concerns and if considered required, the DSMC will make recommendations to the TOC for appropriate action.

Study data will be collected and managed using REDCap® electronic data capture tools hosted at the University of Melbourne,[51]. The Data Management Coordinating Center will oversee the intra-study data sharing process between countries?, with input from the Data Management Subcommittee. We will develop a data management manual detailing data collection protocols and provide comprehensive training of those members of the research team who collect, check and enter study data. The Principal Investigator, study statistician, and health economist from the University of Melbourne will be given access to the cleaned data sets. Country specific lead investigators will only have acces to their own country's cleaned data sets. All data sets will be password-protected. To ensure confidentiality, data dispersed to project team members will have any identifying information removed.

Risk management

Processes have been put in place to mitigate risks. One of the most significant risks associated with the project is slow recruitment. To offset the risk of slow recruitment, data is being collected across five countries. If some countries have less difficulty than others in recruiting, then these countries will recruit greater numbers to ensure the required sample size is obtained. Another risk identified is the heterogeneity of intervention delivery. The inclusion of a detailed manual, regular supervision with interventionists, and monitoring the effectiveness of interventionist training will mitigate the risk of poor intervention fidelity.

Ethics and Dissemination Plan

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.
- National and International rules on data protection will be followed. that the participating countries in HOMESIDE within the EU and EEA (UK, Germany, Poland and Norway) also relate to the General Data Protection Regulation (GDPR)(Regulation (EU) 2016/679), designed to harmonize data privacy laws across Europe, to protect and empower all EU citizens data privacy, and to reshape the way organizations across the region approach data privacy. The HOMESIDE partners have also signed a consortium agreement where they consent to follow national and international rules on collaboration, ethics and data protection.

The report on the main, pre-planned analyses of the primary endpoint and up until the 6-month follow-up will be submitted to a leading medical journal. Further publications may focus on issues such as recruitment and retention strategies for home-based programs. Publications based on qualitative interviews and video analyses will focus on barriers and facilitators for implementation and promotion of adherence to home-based programs; experiences of caregivers in delivering the programs; and the development of best practice training guidelines. In addition to publications in academic journals, a number of policy briefing papers for Government and aged care/dementia advocacy groups are planned as well as the development of training manuals and guidelines for dissemination.

Data Sharing

In accordance with the Australian Code for Responsible Conduct of Research (Universities Australia, 2018), all data will be retained for retrieval and re-use in future research where participant permission is granted. Following project completion, de-identified anonymised data (with participant consent) will be available on the Australian Data Archive https://ada.edu.au and listed on Research Australia's https://researchaustralia.org website to facilitate access for future research. Data made available will include individual-level deidentified participant data, reports on adverse events, and deidentified interview transcripts. According to the GDPR, the consortium have agreed to the reuse of data for 10 years post project completion.

Relevance and Benefit to Society

As the majority of PwD live in the community and not in residential care settings, quality informal care for PwD is crucial for managing BPSD and enhancing quality of life. This protocol details the process for testing the effectiveness and cost-effectiveness of a CG-directed music intervention and reading intervention designed to manage the BPSD of PwD, the sense of burden and wellbeing of the CG, and provide meaningful possibilities to maintain the relationship between PwD and their CGs. We expect that with support and training, the MI will be easily implemented in the family home by CGs. With the increasing number of people living with dementia and the stress this will place on countries' economies, our project aims to test an intervention designed to keep people living at home with family CGs for as long as possible, reducing the burden for society and caregivers. Our study will be able to estimate the incremental cost-effectiveness ratio between MI and RI, MI and SC, and RI and SC. Data may support aged care policy recomendations and as the interventions will be delivered in five different countries, results will be broadly generalisable.

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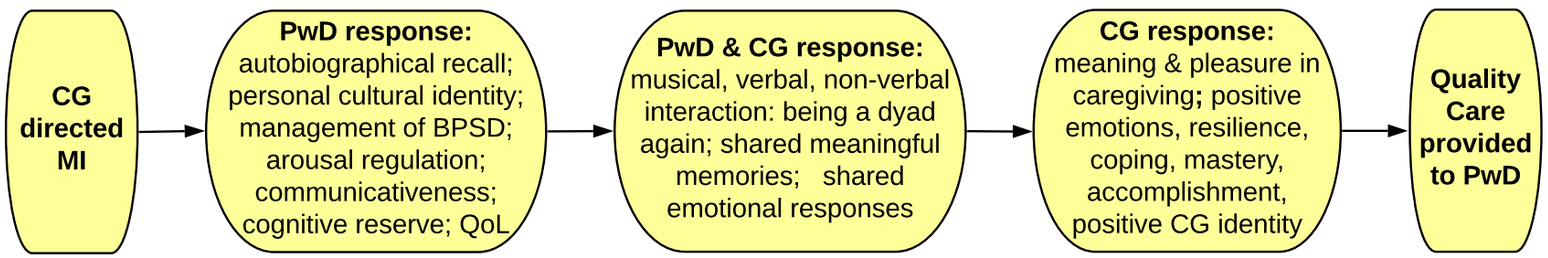
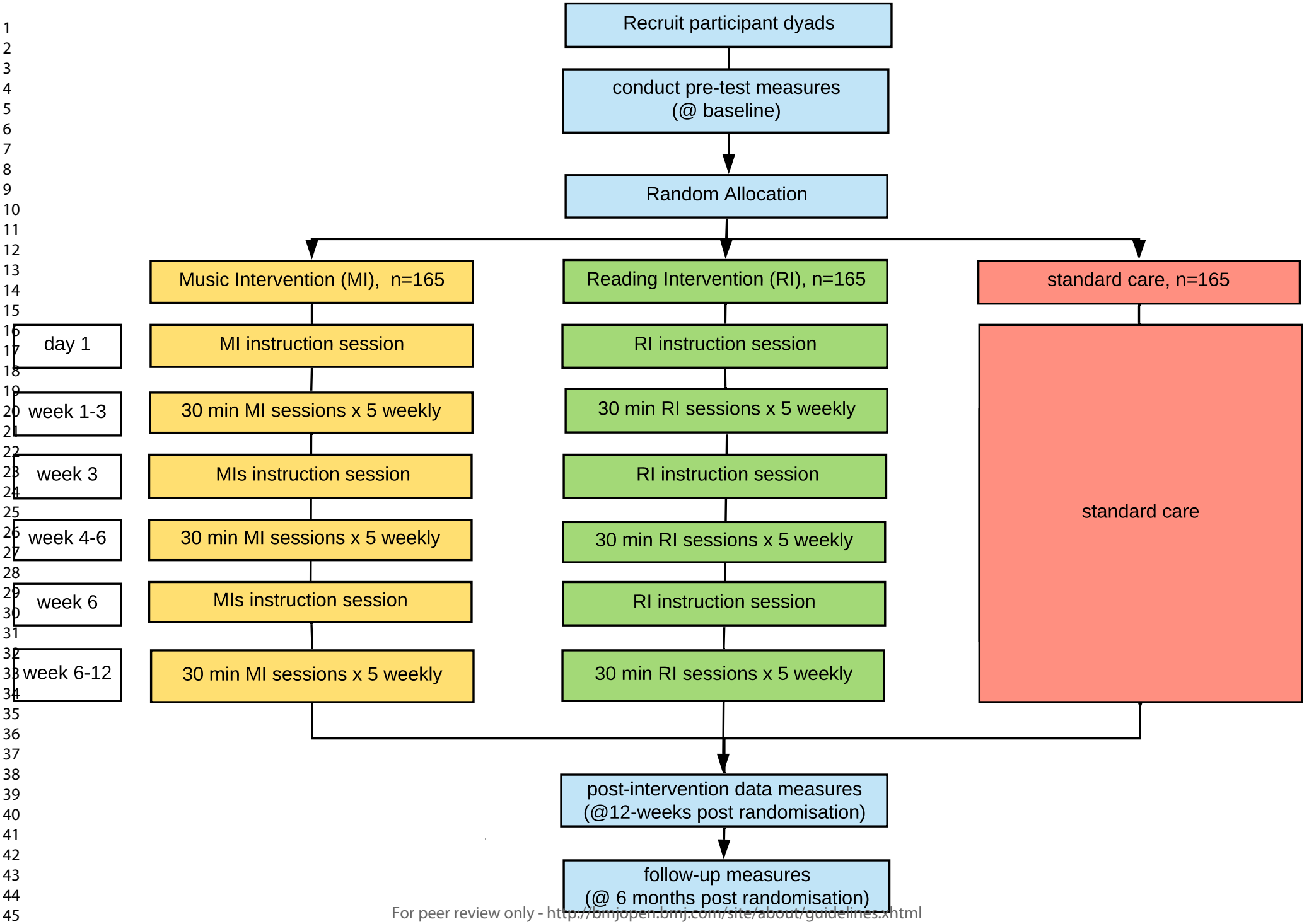

CG directed MI
PwD response: autobiographical recall; personal cultural identity; management of BPSD; arousal regulation; communicativeness; cognitive reserve; QoL
PwD & CG response: musical, verbal, non-verbal interaction: being a dyad again; shared meaningful memories; shared emotional responses
CG response: meaning & pleasure in caregiving; positive emotions, resilience, coping, mastery, accomplishment, positive CG identity
Quality Care provided to PwD



	Enrolment	Allocation	Intervention			Post-Intervention	Follow-up
TIMEPOINT	***-1day*** (-7- -1 days)	**0**	***1day*** (+/- 7 days)	***Day 21*** (+/- 7 days)	***Day 42*** (+/- 7 days)	***Day 90*** (+/- 7 days)	***Day 180*** (+/- 7 days)
ENROLMENT:							
Eligibility screen	X						
Informed consent (or assent)	X						
Dyad: allocation		X					
INTERVENTIONS:							
Music Intervention Training			X	X	X		
Reading Intervention Training			X	X	X		
ASSESSMENTS:							
PERSON WITH DEMENTIA sociodemographic information	X						
MMSE (self)	X					X	
dementia diagnosis (proxy)	X						
NPI-Q (proxy)	X					X	X
MADRS *(proxy)*	X					X	X
QoL-AD (proxy and self)	X					X	X
EQ-5D-5L *(self and proxy)*	X					X	X
Adverse events; death, hospitalisation, death of CG			X	X	X	X	X
CAREGIVER *sociodemographic information*	X						
PHQ-9	X					X	X
RS-14	X					X	X
SSCQ	X					X	X
QPCR	X					X	X
AQoL-6D	X					X	X
EQ-5D-5L*(self)*	X					X	X
RUD	X					X	X
Interviews						X	
Diary (5xweekly diary entries for MI and RI)			X	X	X	X	
Adverse events; death, hospitalisation			X	X	X	X	X

Figure 3. Schedule of enrolment, interventions, and assessments

RUD - Resource Utilization in Dementia, MMSE -MiniMental State Examination Score; ICD-10 – International Classification of Diseases-10; NPI-Q – Neuropsychiatric Inventory; MADRS - Montgomery Asberg Depression Rating Scale; QoL-AD - Quality of Life-Alzheimer's Disease; PHQ-9 - Patient Health Questionnaire–9; RS - Resilience Scale; SSCQ - Short Sense of Competence Questionnaire; AQoL-6D - Assessment of Quality of Life-6D instrument; QCPR - Quality of Caregiver-Patient Relationship; Quality Adjusted Life-Years – EQ-5D-5L The EuroQol instrument

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	1
	2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	3	Date and version identifier	n/a original
Funding	4	Sources and types of financial, material, and other support	1
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	1-2
	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	n/a
	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)	16-17

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	4-6
	6b	Explanation for choice of comparators	6
Objectives	7	Specific objectives or hypotheses	7
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)	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	7-8
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)	7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
	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)	10
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8-9, 13
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7-9
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)	Fig. 3

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	14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	17
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	14
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	14
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	14
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	14-15
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
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	N/A

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	16-18
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	15-16
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	15-16
	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)	15-17
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	17
	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	N/A 17
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, 17
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	16-17
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	18
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)	16-18
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	14

	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
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	17-18
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	2
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	18-19
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	N/A
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	18-19
	31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	19
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
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	19

*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

HOMESIDE: Home-based family caregiver-delivered music and reading interventions for people living with dementia: Protocol of a randomised controlled trial.

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Title: HOMESIDE: Home-based family caregiver-delivered music and reading interventions for people living with dementia: Protocol of a randomised controlled trial.

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Abstract:

Introduction: Pharmacological interventions to address behavioural and psychological symptoms of dementia (BPSD) can have undesirable side effects, therefore non-pharmacological approaches to managing symptoms may be preferable. Past studies show that music therapy can reduce BPSD, and other studies have explored how formal caregivers use music in their caring roles. However, no randomised study has examined the effects on BPSD of music interventions delivered by informal caregivers (CGs) in the home setting. Our project aims to address the need for improved informal care by training cohabiting family CGs to implement music interventions that target BPSD, and the quality of life (QoL) and wellbeing of people with dementia (PwD) and of CGs.

Methods and analysis: A large international 3-arm parallel-group randomised controlled trial will recruit a sample of 495 dyads from Australia, Germany, UK, Poland and Norway. Dyads will be randomised equally to standard care (SC), a home-based music program plus SC, or a home-based reading program plus SC for 12 weeks. The primary outcome is BPSD of PwD (measured using the Neurospychiatric Inventory-Questionnaire). Secondary outcomes will examine relationship quality between CG and PwD, depression, resilience, competence, QoL for CG, and QoL in PwD. Outcomes will be collected at baseline, at the end of the 12-week intervention and at 6-months post randomisation. Resource Utilization in Dementia will be used to collect economic data across the life of the intervention and at 6-month follow-up. We hypothesize that the

music program plus SC will generate better results than SC alone (primary comparison) and the reading program plus SC (secondary comparison).

Ethics and dissemination: Ethical approval will be obtained for all countries. Results will be presented at national and international conferences and published in scientific journals and disseminated to consumer and caregiver representatives and the community.

Strengths and Limitations of this study

- As a multinational trial, this study will provide internationally generalisable results concerning the effects of music intervention delivered by trained family caregivers on the behavioural and psychological symptoms of people living with dementia.
- Based on pilot data, this trial will have adequate power to determine the effects on the person with dementia.
- The trial will determine whether caregiver-delivered music interventions improve quality of life and wellbeing of the caregiver, and reduce healthcare costs for the caregiver and society.
- A comprehensive set of core outcomes will be measured, including long-term effects in key variables, with assessor blinding.
- As participants cannot be blinded, a limitation of the study is that they may provide biased responses on their self-report measures.

BACKGROUND

Family caregivers (CG) play a vital role in providing care for a person living with dementia (PwD) in the home-setting [1]. This personalised care not only directly benefits the PwD by keeping them at home in a familiar environment but represents a significant economic contribution to society. CGs often find caregiving satisfying and rewarding, however the task of managing the challenging behavioural and psychological symptoms of dementia (BPSD) can override their capacity to cope, leading to negative physical and mental health including fatigue, depression, burnout, and illness,[2-3]. A deterioration in CG wellbeing may have a negative flow-on effect on the wellbeing of the PwD. A negative spiral may develop until the CG can no longer sustain the caring role, and the PwD moves into residential care earlier than desired.

The 2015 global cost of dementia was estimated to be US$818 billion, and this figure will continue to increase as the number of people with dementia rises,[1]. Nearly 85% of costs are related to family and social, rather than medical care. With this increase and the escalating costs of care, it is time-critical that CG-directed home-based interventions are developed and tested. The 2017 Lancet Commission on Dementia,[1] suggests that pharmacological treatment of BPSD should be restricted to those with very severe symptoms and highlights music therapy as a non-pharmacological intervention that reduces BPSD (p.30).

Systematic reviews indicate that the majority of CG-directed interventions adopted cognitive-behavioural or psychoeducational approaches to address CG coping, depression and BPSD management,[4-5]. Adherence to programs was poor because CGs could not commit to the regular program attendance requirements,[4-5]. Drawing on social exchange theory, apathy and other BPSD lead to diminished reciprocity between CG and PwD, creating imbalances in the relationship,[6]. Therefore, the convenience of a home-based CG-delivered program that can manage BPSD and address relationship reciprocity is more likely to be adhered to, and more effective in promoting both PwD and CG wellbeing.

Music therapy is a registered psychosocial National Health Service (NHS in the UK) intervention that meets the current recommendations for addressing the individual needs of those with dementia,[7]. HOMESIDE (HOME-based caregiver-delivered music intervention for people living with dementia) uses a purposefully developed music intervention (MI) (described later) informed by previous meta-analyses that demonstrate

the effectiveness of music therapy in reducing BPSD,[8-11]. The MI is a translation of the research evidence to a home-care context and, instead of being delivered directly by qualified music therapists, they will train CGs to deliver the MI. The MI incorporates Kitwood's model of personhood for PwD,[12], which is essential to effective dementia care and underpins the philosophy of the 2018 Alzheimer's Association Dementia Care Practice Recommendations. The person-centred dementia care embedded in the MI emphasizes communication and relationships, recognising that dementia is best understood as an interplay between neurological impairment and psychosocial factors (e.g. health, individual psychology) and the environment,[13].

Small scale studies that have tested the effectiveness of MI training programs for informal and formal CGs have had positive findings to date. Results of a cluster RCT with formal CGs showed the MI to be a practicable and acceptable intervention, with PwD showing treatment-related improvements, and staff reporting enhanced skills in caregiving,[8]. Although based on a small sample (N=17), large effects in BPSD (Cohen's *d*=2.32) were found between standard care (SC) and MI from baseline to 7-months. A home-based feasibility RCT determined acceptability of the MI, assessed burden associated with delivering the MI, and tested appropriateness of the measures,[14]. BPSD scores decreased from baseline to post-test in the MI group but increased in the SC group and mixed results were shown for the comparative reading group. A study involving eight family CGs who were trained to deliver home-based music programs for their care recipient with dementia, 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 drawing 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 in comparison with care recipients. Findings suggested that CGs enjoyed partaking in the reminiscing and shared musical activities with their loved ones,[15].

The conceptual framework underpinning the MI incorporates the responses of the PwD, the ensuing moment to moment interaction between the PwD and the CG, and the CGs' responses to the PwD and moments of interaction (Figure 1). The MI is grounded in the established knowledge that music-induced emotions and

memories are often retained in PwD because of the relative preservation of medial frontal and limbic areas,[9, 16]. MIs are effective when the music selected for use is chosen by the PwD (or CG),[9, 11]. When music facilitates moment to moment interactions, emotional and social engagement, and autobiographical recall, imbalances in reciprocity are diminished. CGs' positive experience of seeing "the person behind the dementia" via this music-induced response evokes CG experiences of pleasure, feelings of competence in the CG, and fosters their resilience and coping. Ultimately the enhanced wellbeing of CGs will lead to more effective care and better wellbeing outcomes for both CGs and PwD (Figure 1).

<<INSERT FIGURE 1 ABOUT HERE

Figure 1. Mechanisms of action underpinning the music intervention>>

The comparative conditions in this trial are SC only (control) and a reading intervention plus SC (RI, active control). The RI was included because studies have shown preliminary evidence that reading to and with PwD can have positive impacts on BPSD,[17-18]. We anticipate MI to be superior to SC only. In addition, we postulate that the RI will lead to a small positive effect but that MI is expected to be superior as music has been shown to be a social connector and a trigger of autobiographical recall, is non-reliant on intact verbal comprehension or expression, and can be used to regulate emotion and behaviour,[7, 9-11, 16, 19-22].

Trial Design

A large, pragmatic, single-blinded, international 3-arm parallel-group RCT design is planned with a 1:1:1 allocation ratio. Cohabiting dyads where one member of each dyad has a diagnosis of dementia will be randomised to one of three conditions: 1) MI plus SC; 2) RI plus SC; and 3) SC only (Figure 2). CGs in MI and RI groups will receive a 2-hour training session on how to deliver the MI or RI and will then engage the PwD in a 5x weekly CG-directed home-program for 12 weeks. Two additional training sessions will be provided at 3-weeks and 6-weeks post allocation. Fifteen-minute fortnightly phone calls will be scheduled to support the CG, and encourage adherence to the protocol. Data will be collected at baseline, at the end of the 12-week intervention, and at 3-month follow-up (6-months post-randomisation). The SC group will not receive any training sessions. This trial is framed as a superiority trial where we hypothesise that the MI will

be superior to SC (primary) and RI plus SC (secondary) regarding BPSD of PwD at 12-weeks post-randomisation.

<<INSERT FIGURE 2 ABOUT HERE

Figure 2. HOMESIDE illustration of study design >>

Objectives

The aim is to demonstrate the effectiveness of the 12-week HOMESIDE MI plus SC on the short-term BPSD at the end of intervention of PwD living at home and being cared for by a cohabiting CG compared to SC (primary), and to evaluate the effectiveness of MI plus SC compared to RI plus SC (secondary). Other secondary objectives are as follows:

- Evaluate the maintenance of the effect of the MI plus SC on longer-term (6 months post-randomisation) BPSD compared to SC and RI plus SC.
- Evaluate the effectiveness of the MI plus SC on short- and long-term levels of depression and quality of life of PwD compared to SC and RI plus SC.
- Evaluate the effectiveness of the MI plus SC on short- and long-term levels of depression, resilience, sense of competence, and quality of life of the CG compared to SC and RI plus SC.
- Evaluate the effectiveness of the MI plus SC on the short- and long-term perceived quality of the relationship between PwD and CG compared to SC and RI plus SC.
- Compare the cost-effectiveness of a CG-delivered MI plus SC on PwD and CG outcomes compared to SC and RI plus SC, using quality of life for both PwD and CG.

METHODS AND ANALYSIS

Participants

The trial will be conducted in people's homes located in metropolitan cities and adjoining rural areas, in Australia, Germany, Poland, Norway, and the United Kingdom.

Inclusion criteria:

- dyads (cohabiting) who are close in relationship and where one member has a diagnosis of dementia according to ICD-10 criteria (Alzheimer's Disease [AD], Frontotemporal Dementia, Vascular

Dementia [VD], Lewy Body Disease, or mixed dementia) as determined by a clinician experienced in diagnosing dementia,[7]. 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.

- 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,[23]. 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.

Exclusion criteria:

- dyads where either or both the CR or PwD have significant hearing impairments that are not resolved through the use of a hearing aid device and limit their capacity to enjoy musical experiences. There will be no further exclusions.

Interventions

Music Intervention. Dyads randomly allocated to the MI will receive a 2-hour home-based MI training session that aims to engage the PwD during and following the MI. Using a carefully prepared and detailed intervention manual, a qualified music therapist will instruct the CG on methods and strategies for using music to assist the PwD to become calmer (if agitated) or more energised (if apathetic). CGs will be instructed on how to choose music and engage the PwD in effective and respectful discussions with the aim of evoking autobiographical memories and sharing meaningful experiences,[24]. Strategies to engage the PwD and create opportunities for meaningful dialogue with the PwD will be provided, as well as training CGs to notice the PwD's positive and negative responses to music. The activities to be taught comprise: a) singing familiar/preferred songs followed by CG-facilitated discussions about the meaning of the songs for the dyad, the PwD, and significant others, and any associated memories,[20, 25]; b) movement to music (e.g. upper body and arms imitating familiar dance movements to music) to assist in regulating arousal,[11]; c) playing instruments (or using household items to make rhythmic sounds) while listening to music; and d) listening to familiar/preferred relaxing or enlivening music dependent upon BPSD present at the time to assist in regulating arousal,[20]. CGs are then instructed to deliver the MI at least 5x per week for approximately 30 mins over a 12-week period. After each MI session,

they will diarise their experiences, including documenting which activities were used, session time and duration, and any positive or negative responses during and after the session. Such data (number of times per week, average duration, activities adopted) will be used to monitor and improve adherence to the protocol. At 3-weeks and 6-weeks post allocation, the MI trainer will return to the dyad's home for a second and third training session (Figure 2). These sessions aim to further extend CG knowledge and skills, troubleshoot any issues, and improve protocol adherence. Fortnightly phone conversations with CGs will be used to support the CG and remind them to complete the diaries (to mitigate risk and maximise participant engagement, retention, and protocol adherence).

Reading Intervention (active control). Dyads randomly allocated to the RI group will receive a 2-hour RI instruction session which aims to engage the PwD during and following the RI. The reading activities will be taught by a qualified practitioner, following a carefully prepared and detailed intervention manual. These activities are based on RI methods commonly used with PwD including: a) CG reading aloud to PwD; b) PwD reading aloud (or reciting poems, prayers, prose, short stories, fairy tales, when unable to read) to CG; c) listening to audio books and d) discussion of the text and personal responses,[17-19]. Strategies to engage the PwD and create opportunities for meaningful dialogue with the PwD will be provided as well as guidance on selecting reading material accessible to the PwD's level of cognitive impairment. CGs are then instructed to deliver RI at least 5x per week for 30 mins over 12-weeks and diarise their reading activities to record activity and adherence. Diaries will serve as a mechanism to monitor adherence to the protocol. At 3-weeks and 6-weeks post allocation, as per the MI condition, the RI trainers will return to the dyad's home for a second and third training session with the intention of further extending CG knowledge and skills and to monitor and improve intervention protocol adherence. Fortnightly phone conversations with CGs will be used to support the CG and remind them to complete the diaries (to mitigate risk of noncompletion). Like the MI condition, phone calls also aim to maximise participant engagement, retention, and protocol adherence.

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.

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. This consists of receiving medical, therapeutic and personal care, as well as participating in usual leisure activities.

Discontinuing or Modifying Interventions. Where there is a significant deterioration in the health of the PwD and/or the CG that leads to hospital admission or care home admission, the MI or RI will be discontinued. If there is a change in primary CG partway through the study, the dyad will be withdrawn from the study.

*Training and assessment of fidelity***.** Given the MI and RI will be delivered in five different countries with different healthcare philosophies and practices, a careful plan for fidelity of the study design, treatment integrity, treatment differentiation, treatment receipt, and treatment enactment has been developed. A standardised manual for MI and RI has been developed and agreed upon by all countries prior to implementation. Fidelity in this study is complex as it will involve assessing fidelity of the MI and RI training session, but also fidelity of the CG-directed program. Delivery of MI and RI training by research staff will be videorecorded and a randomised selection of 20% of recordings from every site will be reviewed by members of the research team and cross-checked with the MI and RI protocol manuals using a custom fidelity checklist. Individualised supervision and monitoring of intervention trainers will be employed to minimise "drift" in trainer differences and control for differences in trainer styles. CG diaries will be used to determine whether the MI and RI protocols have been adhered to and the success of treatment enactment.

Outcomes

At baseline, demographic data (age, gender, and dyad history) of both CG and PwD will be collected as well as diagnostic information of PwD (ICD-10).

Where possible, core outcomes (www.comet-initiative.org) for psychosocial intervention research in dementia care were selected,[26]. For the PwD, the following measures were selected:

- Behavioural and Psychological Symptoms of Dementia - The NPI-Q is the most highly regarded and used measure for determining the severity of BPSD in clinical trials. The 12-item scale is used to assess the behaviour of PwD across 12 domains of commonly displayed BPSD. The scale has been translated

into more than 40 languages, has been cross-validated against the NPI as the gold standard (r=0.73) and has demonstrated good validity (sensitivity = 74.1%, specificity = 79.5%), internal reliability (α= 0.783) and excellent test-retest reliability (r = 0.99),[27-28]. Total severity scores range from 0 to 36; higher values are indicative of higher severity. Distress scores range from 0 to 60; higher values represent higher levels of distress. CGs will self-complete the NPI-Q with guidance from the research assessor if required.

- Depression – The Montgomery Asberg Depression Rating Scale,[29] (MADRS) will be used to assess the severity of depression. The 10-item scale with each item's scores ranging from 0 (no symptoms) –6 (severe symptoms) is determined through an assessor-led interview with the proxy, in this study, the CG. Total score ranges from 0 to 60 with higher scores indicating more severe depression. MADRS has been found to have good constructive validity, internal reliability (α= 0.84), and test-retest reliability (ICC=0.78). The scale has been widely used in clinical trials,[29].
- Quality of Life (QoL) – The QoL of PwD will be determined by administering the Quality of Life-Alzheimer's Disease (QoL-AD),[30] scale. The QoL-AD is recommended by the COS,[26] for use in clinical trials. It is a simple 13-item self-report measure, which is rated on a 4-point scale, within the structure of a verbally delivered interview. Total scores range from 13 (poor quality of life) to 52 (excellent quality of life in all areas). Studies indicate that the measure can demonstrate sensitivity to psychosocial intervention, correlates with health-utility measures,[31], has excellent interrater reliability ($\kappa > 0.70$) and internal consistency ($\alpha = 0.82$). The QoL-AD is reliable when used with people with MMSE scores of $\geq$10. Both a CG proxy and PwD self-report (if possible) will be collected at the 3-timepoints. If the PwD is able to complete the MMSE at all time points, then their response will be included in the analysis. If not, then the proxy version at all time points will be used.
- Cognition - The Mini-Mental State Examination (MMSE) will be administered pre and post intervention (Time 1 and Time 2) to monitor any change in the PwD's cognition and to examine the relationship between cognitive decline, BPSD, depression and response to different conditions. The MMSE is a 30-point questionnaire used to estimate the severity and progression of cognitive impairment and to follow the course of cognitive changes in an individual over time,[32]. The MMSE tests for orientation, attention, memory, language and visual-spatial skills. It is reliable and valid for both diagnosis and longitudinal assessment. Higher scores indicate better cognitive capacity with scores of 24-30 indicating

no cognitive impairment; 19-23 indicating mild cognitive impairment; 10-18 indicating moderate cognitive impairment; and scores <10 indicating severe cognitive impairment. MMSE scores will be determined through assessor-led interviews with PwD participants.

For the CG, the following measures were selected:

- Symptoms of depression – CG depression will be measured using the Patient Health Questionnaire–9 (PHQ-9),[33]. This self-completed 9-item questionnaire asks the participant about how often they experience the descriptors over the last 2 weeks. Each item is scored from 0 (not at all) to 3 (nearly every day). Total scores range from 0 to 27. The PHQ–9 has comparable sensitivity and specificity to other depression measures; high internal reliability ($\alpha = 0.89$), and test-retest reliability ($r = 0.84$).
- Resilience – CG resilience will be measured using the self-completed 14-item Resilience Scale (RS-14),[34]. Total scores range from 14 to 98, with higher scores indicative of higher resilience. The measure has been tested and has good concurrent validity, good internal reliability ($\alpha = 0.8 – 0.90$), good construct validity, test-retest reliability (r=0.67 to 0.84) and has been translated into 36 languages,[35].
- Competence - CG competence will be measured using the self-completed Short Sense of Competence Questionnaire (SSCQ),[36]. The 7-items cover 3 main domains; self-reported feelings about how the caregiver role impacts the CG's personal life, satisfaction with their performance as a CG, and their satisfaction with how the PwD responds to the CG. Total scores ranged from 7 to 35 with higher scores indicative of a stronger sense of competence. The measure has been cross-validated with the longer 35-item standard Sense of Competence Questionnaire ($r = 0.88$) and has been shown to have high reliability (Cronbach's $\alpha = 0.76$).
- CG Quality of Life – QoL of the CG will be assessed using the self-completed Assessment of Quality of Life-6D instrument (AQoL-6D),[37] Each item asks participants to describe their situation over the past week by ticking the box (from 4 to 6 choices) that best reflects their situation. The psychometric property testing found the instrument to be reliable and valid, and has greater sensitivity to the psychosocial dimensions of QoL than other utility instruments,[37-38].
- Relationship quality – CG perception quality of the CG and PwD relationship will be captured by asking the CG to self-complete the Quality of Caregiver-Patient Relationship (QCPR),[39]. This 14-

item measure aims to capture the strength of the quality of relationship between the PwD and CG, from the CG's perspective. Total scores range from 14 to 70, with higher scores indicating a higher quality relationship. The measure has demonstrated acceptable internal consistency ($\alpha = 0.82$) and concurrent validity.

- Adherence to the MI/RI intervention will be measured through CG completed diaries. CGs are deemed adherent to the protocol if they have provided >2 sessions of MI or RI per week, for at least 30minutes in total. Data on the general use of reading and music by all dyads (including SC) will be collected at post-test. For each diary entry, CGs will be asked to record the date, start and stop time of MI/RI engagement, types of activities used, their experiences during the session (negative, neutral, positive, unsure), effects from the intervention for the remainder of the day until the PwD goes to bed for the evening sleep (negative, neutral, positive, unsure), and any comments. This data will be used in qualitative analyses to gain more nuanced understandings of how the activities are perceived and how these may change over the course of the intervention period.

To evaluate the cost-effectiveness of MI compared to RI and SC on PwD and CG, the outcomes will be measured using:

- Quality Adjusted Life-Years – The EuroQol instrument (EQ-5D-5L),[40] is a generic quality of life measure that is internationally used to determine the quality-adjusted life-years (QALYs) and used for clinical and economic appraisal,[40]. The measure is not cognitively demanding and quick to complete. Scores from the five items are not combined arithmetically but using preference weights which arrive at an overall quality of life score. These range from lower than 0 (worse than death) to 1 (best possible). CGs will complete the measure as a proxy for the PwD and self-report their own health status,[26, 41-44].
- Resource Utilization in Dementia (RUD) - The RUD is a standardized instrument for resource use data collection in dementia, designed to collect data from formal and informal care across different countries. The RUD assesses resource use of both PwD and CG, including time expended in different daily tasks, and consists of baseline and a follow-up assessment,[45]. The RUD will be completed through assessor-led interviews with CGs.

CGs will be provided with a set of guidelines as to how to complete the diary and all self-report and proxy measures. The schedule for enrolment, baseline assessments, all outcome measures, and intervention trainings is outlined in Figure 3.

<<INSERT FIGURE 3 ABOUT HERE

Figure 3. Schedule of enrolment, interventions, and assessments >>

Sample size

A total of 165 dyads in each arm of the study, or 495 in total, are needed to detect a difference of 3-points in NPI-Q total severity score (primary outcome) between the MI plus SC and SC arm (primary comparison) at 12-weeks (primary time point). This assumes 90% power, a two-tailed significance level of 5%, equal standard deviation (SD, 7.5 points) in the groups, no correlation between baseline and 12 weeks (conservative), and 20% attrition. A 3-point change from baseline in NPI-Q total severity score is considered a clinically meaningful difference,[46]. A conservative SD of 7.5 points is based on that observed in 1026 community-living participants across eight European countries with mild to severe dementia (SD 5.9 to 6.5 points),[47-48]. A conservative drop-out proportion (e.g. withdrawn by CG, physician, or death) of 20% is based on a reported 5.6% (95% CI [1.8%, 12.6%]) drop-out at 3 months in 89 in-patients with mild to moderate dementia in Finland participating in a three-arm RCT of singing, music, or usual care,[25].

Recruitment

Randomisation will aim to be distributed equally across five countries (Australia, United Kingdom, Norway, Germany, and Poland) to support between-country analyses. Participants will be recruited through established partner organisations. Staff from the partner organisations will introduce the trial to potential participants and invite them to participate in the study. They will be given an information sheet explaining the main aspects of the trial and provided with contact details of the research team who will be available to answer further questions.

Randomisation, Allocation Concealment, and Blinding

The randomisation schedule will be computer-generated by an independent statistician and allocation will be carried out through a centralised randomisation service. Block permuted randomisation with stratification by participating site will be used, so that treatment balance within site is achieved. Dyads who meet the inclusion criteria and none of the exclusion criteria will be randomised 1:1:1 into MI, RI, or SC. Randomisation will occur after the eligibility checking, informed consent, and baseline assessment have been completed. Informed consent/assent will be obtained by a blinded assessor prior to the baseline assessment. The study coordinator in each country will be informed of the allocation and will inform dyads of their group allocation by post, phone, or email.

Participant dyads cannot be fully blinded due to the active nature of the interventions however, we will avoid publicizing our hypotheses that MI may be superior to SC only and RI. Plain language statements and consent forms will use neutral wording to maintain equipoise and to avoid expectancy effects. Blinded assessors will collect participants' data at baseline, post-intervention, and follow-up. Diaries will be returned in sealed envelopes to minimise risk of assessors becoming unblinded. The success of assessor blinding will be checked by asking the assessor to guess the treatment assignment (or say "I do not know") after the post-intervention and follow-up periods. This treatment guess will then be compared against the actual treatment and the blinding index derived. The independent statistician will not reveal the allocation codes to any of the study team except for the study coordinators of each country in charge of group allocation. All other investigators and the study statistician will remain blinded until the database has been cleaned, a blinded data review has taken place, and the database is ready for analysis.

Analysis

Analyses will be performed on an intention-to-treat basis including all randomised dyads in their allocated study arm. The primary outcome (NPI-Q severity total score) will be analysed using a constrained longitudinal data analysis (cLDA) model,[49] with response consisting of all scores (baseline, 12 weeks and 6-months) and the model including factors representing intervention, time, intervention by time interaction, and site with the restriction of a common baseline mean score across interventions. This refers to the assumption that at baseline there are no differences between the interventions in the mean score, thus assuming the randomisation was effective. This assumption will be enforced statistically in the statistical model. The absolute difference between MI and SC and MI and RI in mean change from baseline will be estimated (including two-sided 95%

confidence interval) at 12 weeks (primary time point). A hierarchical fixed sequence testing procedure will allow testing of MI versus RI at 12 weeks at 5% if the comparison of MI versus SC at 12 weeks has a p-value < 0.05. Secondary analyses will consist of a model adjusted for potential confounders (types of dementia and gender). The cLDA model provides valid inference if the missing data mechanism is at most missing at random. In addition to the intention-to-treat effect we will obtain the complier average causal effect by making use of the collected adherence data,[50]. Analyses similar to the primary outcome will be applied to the secondary outcomes for PwD and CGs. Heterogeneity of the intervention effect across subgroups (gender of the PwD/CG, types of dementia, severity of dementia, time of onset dementia, length of time having dementia, relationship between PwD and CG, country) will be assessed by means of interaction tests. The number and percentage of PwDs and CGs with adverse events will be summarized by intervention group.

Cost-effectiveness analysis in a societal perspective will be performed separately for each country using the utilities generated by EQ-5D-5L for both PwD and CG and country-specific weights, to estimate a combined QALY score using a generalized linear model adjusted by the baseline. Health and informal care resources consumed by PwD will be assessed using the RUD and unit cost by country. A generalized linear mixed model will be used to estimate the main predictors of the total costs in the MI, RI and SC groups. Incremental cost-effectiveness ratio will be calculated using the cost and effect estimates comparing MI with RI and SC. The uncertainty around the incremental cost-effectiveness ratio will be estimated using bootstrapping (1000 replications) adjusting to control variables.

Patient and public involvement

All countries have involved user and advocacy organisations in the development and design of the study. The UK, Australia, and Germany have been piloting work with formal and informal CGs of PwD for many years. CGs and PwD have been involved designing the diaries which capture adherence data. It was imperative that the diary be user-friendly, not burdensome on the CG, and yet enabled them to document both the positive and negative aspects of the session. Several iterations of the diary were constructed prior to arriving at the final structure. Pilot work in Australia,[14] involved interviews post-intervention to identify strengths, limitations, challenges, and experiences in delivering the MI, as well as recommendations for suggested

modifications to the intervention training. Representatives of advocacy groups and end users from all countries will be represented on an international Participant and Public Involvement Committee.

Monitoring and Oversight

A Trial Operations Committee (TOC) will comprise the principal investigator, chief investigators and clinical trial managers from each of the 5 countries, the study statistician, health economist, and a consumer representative. The TOC will meet at least 6-weekly, and will oversee all aspects of the trial delivery including strategies to support efficient and effective recruitment and retention, reviewing completeness of datasets, monitoring intervention fidelity, management of timelines and milestones, review of country-by-country progress, public and patient involvement or actions, and publication and dissemination plans. The role of the members of the TOC is to bring country-specific issues to the international team for discussion to ensure the study is being monitored and delivered according to the agreed protocols. Protocol deviations and any changes or amendments to the operational processes of the trial will be discussed and decisions made by the TOC.

A Trial Steering Committee (TSC) will comprise of members independent of the clinical trial as well as members and representating consumers and other relevant advocacy organisations. The trial Principal Investigator (or a proxy in her absence) will also sit on the committee as a non-voting member. The Committee will meet biannually (or more often when needed) to review and monitor all aspects of the study delivery. They will draw on reports provided to them by the TOC and make recommendations to the PI and TOC about whether further actions are required.

A DSMC will review the cumulative study data to evalute the recruitement, safety, study conduct, and scientific validity and integrity of the trial. The committee consists of at least five people with strong methodological, biostatistical, and clinical expertise who are independent of the project and an end user representative. The DSMC will be provided with data on recruitment, intervention uptake, any unforeseen and/or adverse events, and review serious adverse events. The meetings will consist of an open and a closed part. In the open part, the general progress of the trial will be discussed with the principal investigator. In the closed part, the DSMC will discuss any safety concerns and if considered required, the DSMC will make recommendations to the TOC for appropriate action.

Study data will be collected and managed using REDCap® electronic data capture tools hosted at the University of Melbourne,[51]. The Data Management Coordinating Center will oversee the intra-study data sharing process between countries?, with input from the Data Management Subcommittee. We will develop a data management manual detailing data collection protocols and provide comprehensive training of those members of the research team who collect, check and enter study data. The Principal Investigator, study statistician, and health economist from the University of Melbourne will be given access to the cleaned data sets. Country specific lead investigators will only have acces to their own country's cleaned data sets. All data sets will be password-protected. To ensure confidentiality, data dispersed to project team members will have any identifying information removed.

Risk management

Processes have been put in place to mitigate risks. One of the most significant risks associated with the project is slow recruitment. To offset the risk of slow recruitment, data is being collected across five countries. If some countries have less difficulty than others in recruiting, then these countries will recruit greater numbers to ensure the required sample size is obtained. Another risk identified is the heterogeneity of intervention delivery. The inclusion of a detailed manual, regular supervision with interventionists, and monitoring the effectiveness of interventionist training will mitigate the risk of poor intervention fidelity.

Ethics and Dissemination Plan

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.
- National and International rules on data protection will be followed. that the participating countries in HOMESIDE within the EU and EEA (UK, Germany, Poland and Norway) also relate to the General Data Protection Regulation (GDPR)(Regulation (EU) 2016/679), designed to harmonize data privacy laws across Europe, to protect and empower all EU citizens data privacy, and to reshape the way organizations across the region approach data privacy. The HOMESIDE partners have also signed a consortium agreement where they consent to follow national and international rules on collaboration, ethics and data protection.

The report on the main, pre-planned analyses of the primary endpoint and up until the 6-month follow-up will be submitted to a leading medical journal. Further publications may focus on issues such as recruitment and retention strategies for home-based programs. Publications based on qualitative interviews and video analyses will focus on barriers and facilitators for implementation and promotion of adherence to home-based programs; experiences of caregivers in delivering the programs; and the development of best practice training guidelines. In addition to publications in academic journals, a number of policy briefing papers for Government and aged care/dementia advocacy groups are planned as well as the development of training manuals and guidelines for dissemination.

Data Sharing

In accordance with the Australian Code for Responsible Conduct of Research (Universities Australia, 2018), all data will be retained for retrieval and re-use in future research where participant permission is granted. Following project completion, de-identified anonymised data (with participant consent) will be available on the Australian Data Archive https://ada.edu.au and listed on Research Australia's https://researchaustralia.org website to facilitate access for future research. Data made available will include individual-level deidentified participant data, reports on adverse events, and deidentified interview transcripts. According to the GDPR, the consortium have agreed to the reuse of data for 10 years post project completion.

Relevance and Benefit to Society

As the majority of PwD live in the community and not in residential care settings, quality informal care for PwD is crucial for managing BPSD and enhancing quality of life. This protocol details the process for testing the effectiveness and cost-effectiveness of a CG-directed music intervention and reading intervention designed to manage the BPSD of PwD, the sense of burden and wellbeing of the CG, and provide meaningful possibilities to maintain the relationship between PwD and their CGs. We expect that with support and training, the MI will be easily implemented in the family home by CGs. With the increasing number of people living with dementia and the stress this will place on countries' economies, our project aims to test an intervention designed to keep people living at home with family CGs for as long as possible, reducing the burden for society and caregivers. Our study will be able to estimate the incremental cost-effectiveness ratio between MI and RI, MI and SC, and RI and SC. Data may support aged care policy recomendations and as the interventions will be delivered in five different countries, results will be broadly generalisable.

Acknowledgements

Laura Blauth and Libby Flynn provided valuable comments on this protocol.

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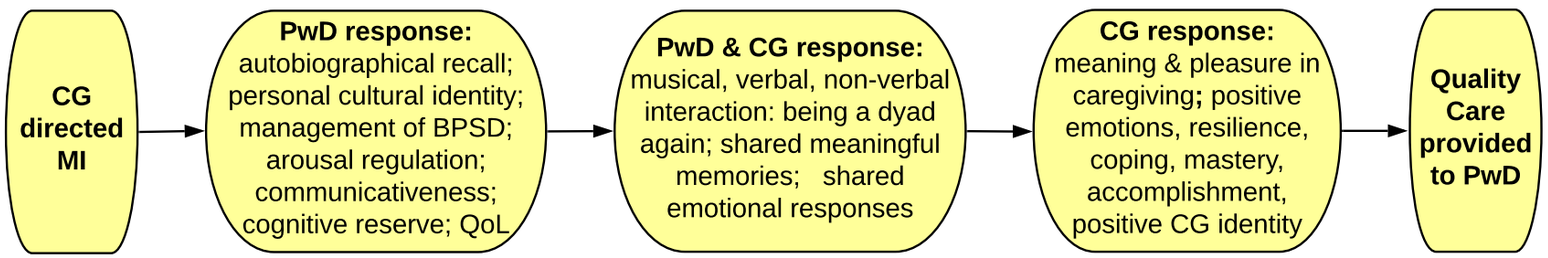
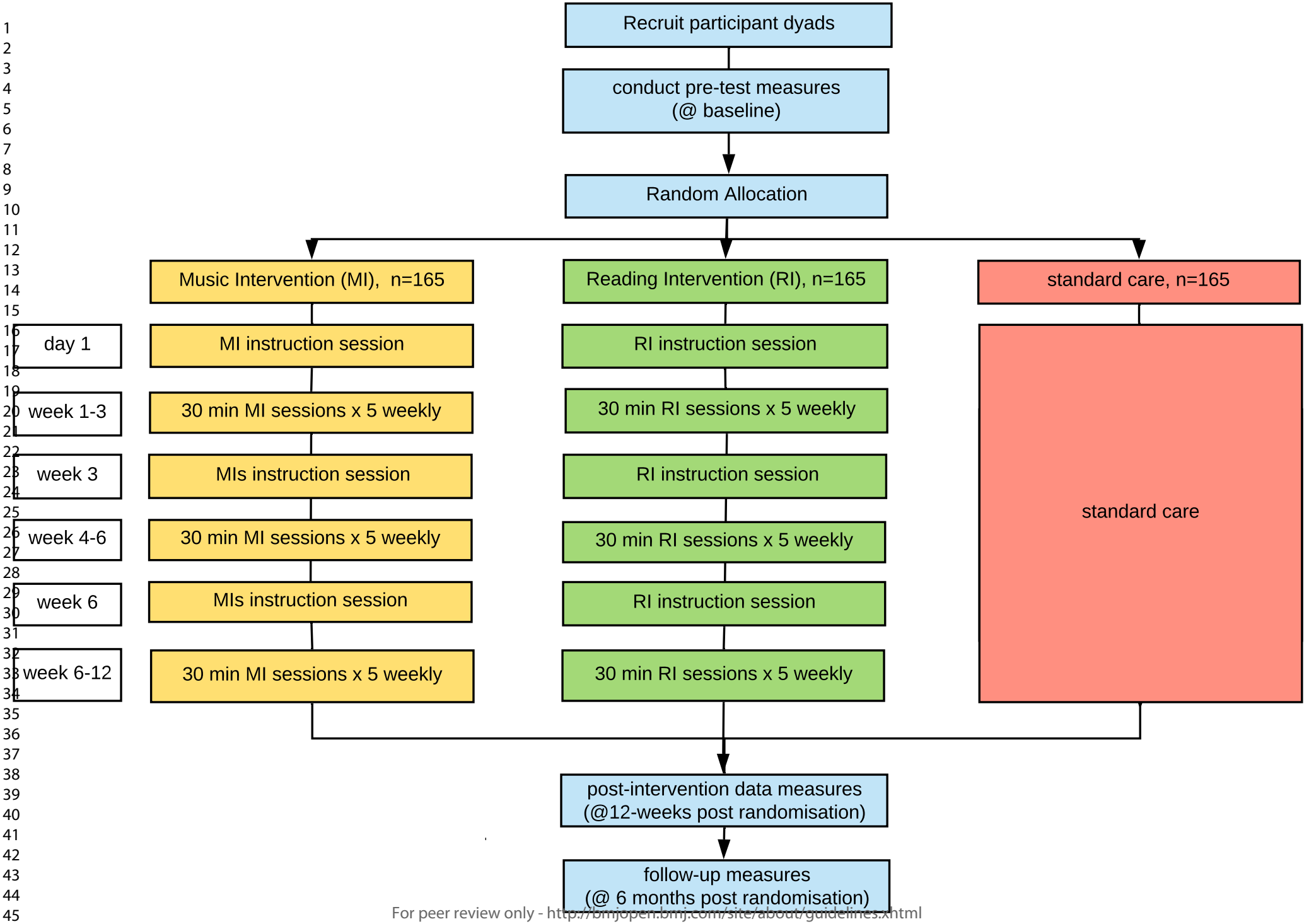

CG directed MI
PwD response: autobiographical recall; personal cultural identity; management of BPSD; arousal regulation; communicativeness; cognitive reserve; QoL
PwD & CG response: musical, verbal, non-verbal interaction: being a dyad again; shared meaningful memories; shared emotional responses
CG response: meaning & pleasure in caregiving; positive emotions, resilience, coping, mastery, accomplishment, positive CG identity
Quality Care provided to PwD



	Enrolment	Allocation	Intervention			Post-Intervention	Follow-up
TIMEPOINT	***-1day*** (-7- -1 days)	**0**	***1day*** (+/- 7 days)	***Day 21*** (+/- 7 days)	***Day 42*** (+/- 7 days)	***Day 90*** (+/- 7 days)	***Day 180*** (+/- 7 days)
ENROLMENT:							
Eligibility screen	X						
Informed consent (or assent)	X						
Dyad: allocation		X					
INTERVENTIONS:							
Music Intervention Training			X	X	X		
Reading Intervention Training			X	X	X		
ASSESSMENTS:							
PERSON WITH DEMENTIA sociodemographic information	X						
MMSE (self)	X					X	
dementia diagnosis (proxy)	X						
NPI-Q (proxy)	X					X	X
MADRS *(proxy)*	X					X	X
QoL-AD (proxy and self)	X					X	X
EQ-5D-5L *(self and proxy)*	X					X	X
Adverse events; death, hospitalisation, death of CG			X	X	X	X	X
CAREGIVER *sociodemographic information*	X						
PHQ-9	X					X	X
RS-14	X					X	X
SSCQ	X					X	X
QPCR	X					X	X
AQoL-6D	X					X	X
EQ-5D-5L*(self)*	X					X	X
RUD	X					X	X
Post-training Questionnaires			X	X	X		
Interviews						X	
Diary (5xweekly diary entries for MI and RI)			X	X	X	X	
Adverse events; death, hospitalisation			X	X	X	X	X

Figure 3. Schedule of enrolment, interventions, and assessments

RUD - Resource Utilization in Dementia, MMSE -MiniMental State Examination Score; ICD-10 – International Classification of Diseases-10; NPI-Q – Neuropsychiatric Inventory; MADRS - Montgomery Asberg Depression Rating Scale; QoL-AD - Quality of Life-Alzheimer's Disease; PHQ-9 - Patient Health Questionnaire–9; RS - Resilience Scale; SSCQ - Short Sense of Competence Questionnaire; AQoL-6D - Assessment of Quality of Life-6D instrument; QCPR - Quality of Caregiver-Patient Relationship; Quality Adjusted Life-Years – EQ-5D-5L The EuroQol instrument

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	1
	2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	3	Date and version identifier	n/a original
Funding	4	Sources and types of financial, material, and other support	1
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	1-2
	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	n/a
	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)	16-17

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	4-6
	6b	Explanation for choice of comparators	6
Objectives	7	Specific objectives or hypotheses	7
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)	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	7-8
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)	7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
	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)	10
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8-9, 13
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7-9
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)	Fig. 3

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	14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	17
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	14
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	14
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	14
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	14-15
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
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	N/A

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	16-18
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	15-16
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	15-16
	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)	15-17
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	17
	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	N/A 17
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, 17
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	16-17
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	18
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)	16-18
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	14

	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
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	17-18
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	2
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	18-19
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	N/A
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	18-19
	31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	19
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
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	19

*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.