**Study Title:** **Personalised Music Therapy to improve Behavioural and Psychological Symptoms in Dementia and Delirium in older hospital inpatients.**

***Short Title:* *Personalised Music Therapy to improve outcomes for hospitalised patients with dementia.***

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**STATEMENT OF COMPLIANCE**

This document is a protocol for a clinical research study. The study will be conducted in compliance with all stipulations of this protocol, the conditions of ethics committee approval, the NHMRC National Statement on Ethical Conduct in Human Research (2007) and the Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95)

**PROTOCOL SYNOPSIS**

|  |  |
| --- | --- |
| **Title** | **Personalised Music Therapy to improve outcomes for hospitalised patients with dementia** |
| Objectives | Primary: Improvement in BPSD; Feasibility (and acceptability) of incorporating intervention into Standard care.  Secondary: Reduction in the use of psychotropic medications; Reduction in the number of critical incidents; Reduction in average hospital Length of Stay (LOS); Perceived reduction in caregiver distress/burden; Improvement in delirium severity. |
| Study Design | Historically controlled study (quantitative);  Feasibility (qualitative). |
| Study sites | Prince of Wales Hospital |
| Planned Sample Size | Target total 120 participants:   * Target 40 intervention patients; * Target 40 historical control patients; * Up to 40 healthcare staff users (questionnaire completed by a staff caregiver for each intervention patient. One staff participant may complete a questionnaire for more than one patient participant). |
| Selection Criteria | Intervention group: Patients aged ≥ 65 years admitted to hospital under the care of a geriatrician, with a diagnosis of dementia and presence of behavioural and psychological symptoms of dementia (BPSD) +/- delirium.  Appropriate written consent from the patient and/or Person Responsible.  Appropriate written consent from a staff participant to collect data generated from a questionnaire for each intervention patient.  Historical control group will comprise recently admitted patients of similar characteristics to intervention group.  Appropriate telephone consent from the patient and/or Person Responsible to access and collect data from the patient’s electronic medical record (EMR). |
| Study Procedures | Screening for recruitment (daily, Monday-Friday during study duration) by the PI or AIs (ie. the study investigators).  The PI will obtain written informed consent for intervention participants.  Healthcare staff administering the intervention will be approached to complete a questionnaire. An opt-in approach will also occur via invitations to participate through department-wide emails and through departmental meetings eg. case conference, grand rounds.  A more junior member of the study team will obtain written consent from healthcare staff participants.  A more junior member of the study team will obtain phone consent for historical control patients.  Study ID allocated to each participant by the PI for de-identified data input.  Introductory session to gather participant’s music preferences and compile an individualised digital profile and music library.  Personalised music therapy available to participant at any time during their admission (via portable speaker or headphones) and to be offered throughout the day (and evenings if appropriate).  Neuropsychiatric Inventory Questionnaire (NPI-Q) to be recorded pre-study commencement and then **at least twice a week** upon commencement (if possible, one recording prior to music therapy session on the day and the second being post-music therapy session, though these may occur on different days).  Frequency of intervention use, duration of sessions and associated activity (eg. during mealtimes, personal care administration, Allied Health sessions) to be recorded.  Delirium, where present, will have severity recorded (DRS-98) before study commencement and then at the conclusion of the intervention period.  Patient demographic data, diagnoses (reason for admission, dementia and delirium), BPSD measures (NPI-Q), psychotropic medications use, critical incidents and average hospital LOS to be collected for all patient participants (intervention and control groups).  Ongoing monitoring for potential adverse events related to the intervention by attending healthcare staff will occur throughout the intervention period and appropriate action/reporting to be undertaken.  Qualitative survey to be completed by the caregiver (staff participant) and patient participant (and/or Person Responsible) at the conclusion of the intervention period for that patient. Ensure written informed consent from the Staff participant for the collection of data generated by the questionnaire.  Data to be entered into REDCap by the PI.  Data cleaning and analysis. |
| Statistical Procedures | Sample Size Calculation:  A sample population of 40 for the intervention group was considered a realistic enrolment target for a 6 month period. This was considered a sufficient period to demonstrate feasibility of the intervention.  Taking into account an expected participation rate of 90% and attrition rate of 5%, up to 48 patients may need to be approached ie. 48 x 0.9= 43.2 and 43 x 0.95= 40.85 (40 patients).  A historical control group of 40 was considered a realistic target for patients admitted over the period November 2022- April 2023 with similar characteristics (and during which time sufficient NPI-Q data would be available).  Taking into account an expected participation rate of 95%, up to 43 patients may need to be contacted ie. 43 x 0.95= 40.85 (40 patients).  Analysis Plan:  Biostatistician support from Stats Central.  Statistical analysis will be conducted using IBM SPSS Statistics software.  Quantitative  Baseline characteristics, reason for admission, dementia diagnoses, NPI-Q results, psychotropic medication usage (type and dosage), critical incidents (eg. Code Blacks, falls) and hospital Length of Stay (LOS) will be collected for the intervention group and historical control group for comparison.  The historical control group will comprise recently admitted patients of similar characteristics.  A mixed effects model will be used to compare between the intervention and control groups for BPSD (presence/absence, total number of symptoms, severity of the symptoms, and associated distress); psychotropic medication usage (type and dosage), number of critical incidents (eg. Code Blacks, falls) and average hospital Length of Stay (LOS).  Effect of the intervention based on duration/frequency of usage (eg. number of sessions per week; hours used per day) may be examined though large variability may limit detailed analysis.  Effect of the intervention between subtypes and severity of dementia will also be examined though small numbers may limit the power of observations.  Effect of the intervention on delirium severity in the intervention group, where present, will also be described though small numbers may limit the power of observations and temporal bias may act as a confounder.  Qualitative  Feasibility (and acceptability) of incorporating the intervention into Standard care will be described using the Staff Participant and Patient Participant/Person Responsible questionnaires. |
| Duration of the study | 6 months (intervention period)  2 months (data cleaning and analysis) |

# Study Management

* 1. **Coordinating Principal Investigator and Principal Investigator for Prince of Wales Hospital**

# Dr Thi Yen Hill

# Geriatrician

# Email: [Thiyen.hill@health.nsw.gov.au](mailto:Thiyen.hill@health.nsw.gov.au)

# Ph: (02) 9382 4252; 0402 096 925

# Department of Aged Care

# Prince of Wales Hospital

# Barker St, Randwick. NSW 2031

Affiliations:

Conjoint Lecturer- University of New South Wales.

Associate researcher- Neuroscience Research Australia (NeuRA).

*[Role: Study design, recruitment, data collection and analysis, report writing]*

* 1. **Associate Investigators**

|  |  |
| --- | --- |
| Ms Anika RobertsonClinical Nurse ConsultantDepartment of Aged CarePrince of Wales HospitalBarker St, Randwick. NSW 2031Ph.(02) 9382 4252Email: [Anika.Robertson@health.nsw.gov.au](mailto:Anika.Robertson@health.nsw.gov.au)*[Role: Recruitment, data collection and analysis, report writing].* | Dr Kylie Radford  Senior Research Scientist and Group Leader Neuroscience Research Australia139 Barker StreetRandwick NSW 2031Ph. 02 9399 1269Email: [k.radford@neura.edu.au](mailto:k.radford@neura.edu.au) *[Role****:*** *study design, analysis, report writing]****.*** |
| Prof Kim DelbaereSenior Principal Research ScientistFalls, Balance and Injury Research CentreNeuroscience Research Australia139 Barker StreetRandwick NSW 2031Ph. 02 9399 1066Email: [k.delbaere@neura.edu.au](mailto:k.delbaere@neura.edu.au)*[Role: study design, analysis, report writing].* |  |

**OTHER PERSONNEL**

* VeraProTM personnel.
  + Conflict-of Interest Statement: VeraProTM personnel will be involved in training healthcare staff in the Vera TM application and providing technical support. Their role during the study will involve training and/or supportive with regards to the practical usage of the technology. They will have no role in study design or data analysis (though the Results will be shared with them). VeraProTM may be consulted during report-writing for publication but only to confirm accurate description of their technology and its application.
* Hospital care staff involved in administering intervention ie. Medical Officers, Nursing staff, Allied Health (physiotherapist, occupational therapist, social worker, volunteers).
* Hospital care staff involved in qualitative analysis (questionnaires) ie. Medical Officers, Nursing staff, Allied Health (physiotherapist, occupational therapist, social worker, volunteers). These staff will be included as research participants (Staff participant) if they complete a questionnaire for analysis. Written informed consent will be obtained to collect the data generated by the questionnaire.
* Hospital care staff involved in data collection ie. Advanced Trainee in Geriatrics (Registrar) working with the PI.
  1. **Statistician (if applicable)**

Luz Palacios-Derflingher

Biostatistician

UNSW Stats Central

Mark Wainwright Analytical Centre

* 1. **Sponsor**

South Eastern Sydney Local Health District (SESLHD).

* 1. **Funding and resources**

This Project will be funded from the Prince of Wales Foundation.

* Expected number of users over 6 months =40. Expected cost $14,000.

# INTRODUCTION AND BACKGROUND

# INTRODUCTION

This study will evaluate the impact of digitalised music therapy during a hospital admission for patients living with dementia. Each participant will receive a personalised library of music that they can access throughout their stay via headphones and/or speaker. It is anticipated that patients will experience improvement in behavioural and psychological symptoms associated with dementia (BPSD), with subsequent benefits including a reduction in the use of psychotropic medication, hospital length of stay (LOS) and critical incidents1. Delirium, where present, may also improve during the intervention. The technology used to deliver the music therapy is novel in this care environment so feasibility and acceptability of incorporating this intervention into standard care will also be evaluated.

* 1. **Background Information**

Behavioural and Psychological Symptoms associated with Dementia (BPSD) represent a heterogenous group of symptoms and behaviours occurring in patients living with dementia. These include agitation, irritability, depression, delusions, hallucinations, aberrant motor behaviour, anxiety, apathy, disinhibition and sleep or appetite changes. BPSD is estimated to affect up to 90% of all patients with dementia over the course of their illness and is independently associated with poor outcomes, including misuse of medication, long term hospitalisation and increased health care costs2.

Unsurprisingly, BPSD is highly prevalent in hospitalised patients with dementia (76%), with frequency increasing with dementia severity (67% in mild dementia; 76% in moderate and 88% in severe dementia)3. BPSD is associated with increased nursing and caregiver distress, as well as complications in care, such as falls, physical harm through aggressive behaviours (to self or others), malnutrition and dehydration (through refusal of food and fluids).

Delirium is defined as a disturbance in mental status (with a fluctuating course), attention, and thinking or consciousness. It is an acute confusional state that is extremely common in hospitalised adults over the age of 65, with approximately 18% of this population having delirium at the time of admission 4. A further similar percentage will develop delirium during their admission and an even higher number will develop delirium following an operation (15-50%) 5. Delirium prevalence rates of up to 50% also occurs in hospital patients with pre-existing dementia6.

Delirium can manifest as a hyperactive form (eg. agitation, aggression, psychotic symptoms, anxiety) or hypoactive (eg. Drowsiness, low mood, poor engagement), with the latter form conferring a poorer prognosis5.

Delirium is more common amongst older hospital inpatients, with dementia being a strong predisposing risk factor for developing delirium7. In turn, the development of delirium is a risk factor for incident dementia and further cognitive decline8. Other sequelae of delirium include prolonged hospitalisation, higher mortality rates and hospital-acquired complications such as falls and pressure injuries9.

Thus, in both delirium and BPSD, disturbances in behaviour can lead to many adverse outcomes.

Despite a lack of strong evidence for the use of psychotropic medications to effectively manage BPSD and delirium, these medications are invariably used. In general, antipsychotic medications are associated with an increased risk of sedation, motor and gait disturbances, falls, cardiac rhythm abnormalities, central nervous system adverse events, exacerbation of cognitive impairment and death (amongst other complications)10.

The first-line approach to managing BPSD and delirium should be person-centered, psychosocial based and multidisciplinary, with antipsychotic medications used only to target symptoms (ie. psychosis) and when psychosocial therapies have failed or there is severe risk of harm11.

This study is designed to incorporate these core principles, utilising music (psychosocial) therapy that is individualised (person-centered) and multidisciplinary (able to be facilitated by any number of caregivers and made available during leisure time, mealtimes, personal care tasks, physical therapy, and family visits).

The preservation of Procedural Memory (PM), which may include music, dancing and other activities learned and engrained in early life is thought to occur in dementia, even as Explicit Memory (EM) deteriorates. Thus, musical perception, musical emotion and musical memory can potentially out-survive other cognitive functions12.

A systematic review in 2018, which included 22 randomised controlled trials involving patients with dementia, found that music-based interventions may improve emotional wellbeing and quality of life, and reduce anxiety, depressive symptoms and overall behaviour problems.13

Most previous studies published on music therapy have occurred in other environments (ie. home or in residential aged care facilities) or utilised different modes of delivery (ie. group sessions or live musicians). Although benefit has been shown, most trials have only included small numbers of participants or did not have robust study designs.

Further, the use of live musicians or specialised musical therapists may present cost barriers. As ‘external visitors’, these facilitators would also potentially be prohibited from continuing therapy in a pandemic or ‘lockdown’ situation.

This study will focus on a hospital inpatient population, where the incidence of distressing symptoms associated with dementia is particularly high, with a high risk of adverse outcomes.

Previous attempts at music therapy at this site have included volunteer staff playing live instruments and personalised music for patients using their own CDs/tapes or that provided by staff. Where deliverable, there was a perceived reduction in patients’ BPSD but ongoing therapy was dependent on the availability of volunteer staff and/or music sources.

This study is novel in that it will utilise a digitalised application (VeraTM Music Health) that can be individualised for each participant. VeraTM is a music-based intervention tool that enables the creation of a digital profile for each user, including a curated musical library. Each personalised library will be readily accessible for the user, from a tablet device kept at the nursing station, to be played on a portable speaker or headphones.

This user-friendliness is anticipated to increase caregiver uptake of the therapy and facilitate easy integration into standard hospital care.

* 1. **Research Question**

**2.2 (a)** Does personalised, digitalised music therapy (delivered via VeraTM) lead to an improvement in behavioural and psychological symptoms associated with dementia (BPSD) and outcomes in hospitalised patients with dementia?

# HYPOTHESIS

HA: Personalised, digitalized music therapy reduces BPSD; delirium severity; the use of psychotropic medication; critical incidents; hospital LOS and/or perceived caregiver stress.

H0: Personalised, digitalized music therapy does not reduce BPSD; delirium severity; the use of psychotropic medication; critical incidents and/or perceived caregiver stress.

**2.2 (b)** Ispersonalised, digitalised music therapy (delivered via VeraTM) a feasible and acceptable intervention to incorporate into standard care for hospitalised patients with dementia?

# HYPOTHESIS

HA: Personalised, digitalized music therapy (delivered via VeraTM) is a feasible and acceptable intervention to incorporate into standard care for hospitalised patients with dementia.

H0: Personalised, digitalized music therapy (delivered via VeraTM) is not a feasible and acceptable intervention to incorporate into standard care for hospitalised patients with dementia.

* 1. **Rationale for Current Study**

As detailed above, dementia is a prevalent condition in the community and in hospitalised older patients. It is commonly associated with distressing behaviours and psychological symptoms, which invariably increase with hospital admission. Not only do these symptoms lead to adverse outcomes for the patient (and caregivers) but the management of these symptoms in hospital (including chemical restraints) also lead to negative sequelae.

It is imperative that novel non-pharmacological, person-centered approaches be explored and rigorously tested to improve the care of hospitalised older patients with dementia.

# STUDY OBJECTIVES

* 1. **Primary Objective**

To evaluate whether personalised, digitalised music therapy:

* Leads to animprovement in behavioural and psychological symptoms associated with dementia during hospital admission and when compared to a control group with similar characteristics.
* Is a feasible and acceptable inpatient intervention for this population of patients and can be incorporated into standard care.
  1. **Secondary Objectives**

To evaluate whether personalised, digitalised music therapy leads to:

* A reduction in the use of psychotropic medication during hospital admission and when compared to a control group with similar characteristics.
* A reduction in the number of critical incidents (IIMs reports) when compared to a control group with similar characteristics.
* A reduction in the average hospital LOS when compared to a control group with similar characteristics.
* A perceived reduction in caregiver distress or burden (via the Staff Participant questionnaire).
* An improvement in delirium severity, where present.

# STUDY DESIGN

* 1. **Type of Study**

It is predicted that the intervention will do more good than harm, hence it would be unethical to carry out a strict randomised control trial, where control participants would miss out on the intervention.

Further, as has been our experience, patients (or more so, their families) are often keen to try new non-pharmacological interventions and would view the possibility of being randomised into a control group as unsatisfactory.

* Historically controlled trial (quantitative)
  + Following screening, recruitment and consent, intervention participants will receive music therapy (delivered via the VeraTM program) throughout their hospital admission. The therapy will not be time limited and can be offered by care staff at any time, though use during potentially distressing activities will be encouraged (eg. mealtimes, personal care administration, Allied Health sessions). Frequency of intervention use, duration of sessions and associated activity (eg. during mealtimes, personal care administration, Allied Health sessions) are to be recorded.
  + Demographic data, diagnoses (reason for admission, dementia and delirium, including severity), NPI-Q (for BPSD), medication use, critical incidents and hospital LOS will be recorded for comparison with a historical control group.
  + The control group will be recent inpatients from the Acute Aged Care Extended (AACE) Unit (specific ward for dementia patients with BPSD and/or delirium) at the Prince of Wales Hospital. Although standard management and therapeutics is consistent across all hospital geriatric wards, the AACE unit is the only ward which routinely collects NPI-Q data as part of standard care. These patients will have similar characteristics to the intervention group and will be drawn from a period spanning November 2022- March 2023, to ensure minimal differences in standard management and therapeutics over time. Demographic data, diagnoses, medication use, NPI-Q, critical incidents, and hospital LOS are available for this group as part of their Electronic Medical Record (EMR).
  + Retrospective consent to utilise EMR data will be sought from the patients and/or Persons Responsible by phone. As these patients have generally undergone longer hospital admissions (due to dementia and behavioural symptoms), strong therapeutic relations and rapport have already been established with the PI and study investigator/s. We do not anticipate any difficulty with obtaining retrospective consent for the control group.
* Feasibility study (qualitative)
  + A questionnaire will be completed by intervention Patient participants (and/or Persons Responsible) as well as Staff participants involved in delivering the intervention to assess its feasibility and acceptability to be incorporated into standard care for hospital inpatients.
  1. **Study Design**

**Recruitment of participants**

**Intervention group**

* All hospital inpatients aged ≥ 65 years admitted under a geriatrician to the Aged Care acute or subacute ward will be screened for eligibility, as determined by the Inclusion and Exclusion criteria.
* Standard practice for clinical handover between senior medical staff in the Department of Aged Care at Prince of Wales is a group email (health.nsw.gov.au accounts only) advising of all new admissions. Thus, this will be the source to identify potential participants.
* The study investigator/s will review admissions each day (Monday to Friday, with patients admitted over weekends or public holidays to be screened on the next working day).Potential participants and/or their Person Responsible (where necessary and available) will be approached by the PI to obtain informed, written consent. This will include a semi structured assessment of the patient’s capacity to consent to research (see below in Consent section).
* Time for the participant/Person Responsible to consider participation will be up to 3 days.
* As this is a non-pharmacological intervention and through previous experience in introducing novel non-drug therapies, the proportion expected to agree to participate will be high.

**Historical control group**

* These participants will be drawn from recent inpatient records from the AACE Unit from November 2022- April 2023 and phone consent gained from the patient and/or Person Responsible by a study team member other than the PI (whose pre-existing relationship with the patients may influence their decision to participate). This will likely be the clinical nurse consultant (CNC) or registrar (Advanced Trainee). Otherwise, the same Inclusion and Exclusion criteria as the intervention group will apply for eligibility.

All participants (intervention and control) will be assigned an arbitrary Study ID by the CPI/PI for data input using Research Electronic Data Capture (REDCap) Software ie:

* + Intervention participants- VPI-001; VPI-002 etc (in order of study entry)
  + Control participants- VPHC-001; VPHC-002 etc (in order of recruitment)

**Staff participants**

* Healthcare staff who have administered the intervention and who agree to complete a questionnaire at the end of a patient intervention period will be consented for collection of the questionnaire data. Consent will be obtained by a study team member other than the PI (whose seniority may influence the staff member’s decision to participate). This will be a more junior member of the study team, likely the clinical nurse consultant (CNC) or registrar (Advanced Trainee).
* Further, opportunities to opt-in will be provided by communicating to staff about the study ie. through department-wide email and at department meetings such as case conferences, journal clubs and grand rounds.
* Staff name and other identifying data will not be recorded.
* Questionnaire data will be entered corresponding to the relevant Patient participant under their Study ID.

**Study procedures**

Prior to study commencement

* VeraTM Onboarding: *VeraPro* is the company infrastructure to support nurses, carers and allied healthcare professionals.
  + *VeraPro* will conduct a 45 minute in-person (or webinar) training session with the study investigator/s and healthcare staff leading to an accreditation.
  + An online, self-serve accreditation facility (e-learning module) will also be available that can be completed independently and takes approximately 30 minutes.
  + *VeraPro* may provide ongoing technical support for the duration of the study but will not have access to confidential participant information, including Study ID numbers.

Study commencement

* Recruitment and consent of participants as detailed above.

**Intervention group**

* Study checklist to be completed by study investigator/s.
* Interview with study investigator/s to introduce the VeraTM music program and gather information on preference/music tastes to compile a personalised music library (approximately 30 minutes).
* Each participant is provided with a portable speaker and/or headphone set which will be labelled with their name and remain theirs to use for the duration of the study intervention.
* Each participant profile (and their music library) will be stored on a tablet device kept at the ward nursing station. The music selection can be ‘cast’ to the portable speaker or headphone to deliver the intervention. The tablet will be controlled by hospital care staff (medical, nursing and Allied Health).
* Music therapy will be available and offered to the participant throughout each nursing shift and can be utilised at any time on participant request. Time using the program is not limited: duration and frequency is to be recorded and considered in the analysis. Healthcare staff are to document in the electronic medical record (EMR) whether VeraTM was used during care administration or therapy sessions. It will be recommended that VeraTM be used at least during one activity daily that is potentially distressing for patients e.g during personal care.
* Data collection:
  + Patient demographics
  + Diagnoses including reason for admission, dementia diagnosis (subtype and severity).
  + NPI-Q (for BPSD) is to be recorded before study commencement, then at least twice-weekly (Monday and Thursday, or other appropriate working day) and at the conclusion of the intervention period. Timing of NPI-Q scoring is to be recorded to facilitate potential correlation with intervention if delivered on the same day.
  + Delirium, where present, will have severity recorded (DRS-98) before study commencement and then at the conclusion of the intervention period.
  + Psychotropic medication usage (type and dosage).
* Patient/Substitute Experience survey at the conclusion of the intervention period for each patient participant.
* Healthcare staff questionnaire at the conclusion of the intervention period for each patient participant (with appropriate written consent to collect data from questionnaire).
* All participant data collected by study investigators will be collated by the PI who will have exclusive access to corresponding Study IDs.
* The PI will transfer data collected for Study IDs to REDCap.
* Any devices (ie. speakers, headphones) utilised by the participant are to be cleaned/disinfected prior to being used by the next study participant.

**Control group**

* Demographic data, diagnoses (reason for admission, dementia and delirium, including severity), NPI-Q (for BPSD), medication use, critical incidents and hospital LOS will be collected from patient’s EMR.
* All participant data collected by study investigators will be collated by the PI who will have exclusive access to corresponding Study IDs.
* The PI will transfer data collected for Study IDs to REDCap.
  1. **Number of Participants**

Target total 120 participants:

* 40 participants undergoing intervention;
* 40 historical control participants; and
* 40 staff participants (though information collected here will be input as data for the relevant intervention participant).

For the Intervention group: taking into account an expected participation rate of 90% and attrition rate of 5%, up to 48 patients may need to be approached ie. 48 x 0.9= 43.2 and 43 x 0.95= 40.85 (40 patients).

For the Historical control group: taking into account an expected participation rate of 95%, up to 43 patients may need to be contacted ie. 43 x 0.95= 40.85 (40 patients).

* 1. **Study sites**

Prince of Wales Hospital, Randwick. NSW.

Principal Investigator- Dr Thi Yen Hill

Expected number of participants is 120 (40 intervention, 40 control, 40 staff participants).

* 1. **Expected Duration of Study**

6 months intervention period: expected start May 2023; expected end November 2023.

Historical control group will be drawn from inpatient records from November 2022- April 2023.

Recruitment will occur throughout the study ie. no separate ‘recruitment phase’.

Longer lasting benefits (ie. beyond hospital admission time) will not be analysed, therefore there will be no ‘follow up phase’ of the study.

2 Months is the time estimated for data cleaning and analysis.

* 1. **Primary and Secondary Outcome Measures**

**Primary Outcome Measures**

* Animprovement in behavioural and psychological symptoms associated with dementia, as recorded by any improvement in the NPI-Q (Cummings RL, 1994), collected at least twice a week for the duration of the study intervention. This may include eliminating the presence of a neuropsychiatric symptom (from ‘Yes’ to ‘No’); reducing the number of BPSD symptoms; reducing the symptom severity; or reducing the level of distress associated with the symptom.
* Feasibility and acceptability of incorporating this intervention into standard care for this population of patients will be assessed via questionnaires, completed by Staff participants involved in the delivery of the intervention, at the end of the intervention period for each patient, as well as Patient participants (and/or their Person Responsible).

**Secondary Outcome Measures**

* A reduction in psychotropic medication use (including type and dosage) during the hospital admission and when compared to the control group. Medication usage will be recorded in the participant’s EMR, as per standard practice.
* A reduction in the number of critical incidents (IIMs reports) when compared to the control group. Critical incidents during the participant’s admission will be recorded in the participant’s EMR, as per standard practice.
* A reduction in the average hospital LOS when compared to the control group. This data is available in the participant’s EMR.
* Perceived impact on caregiver distress or burden will be measured via the Staff participant questionnaire at the end of the intervention period for each patient.
* Improvement in delirium severity (where present) in the intervention group. Delirium screening already occurs as part of standard practice using the 4AT rapid assessment test for delirium. This is the validated tool utilised in the Prince of Wales Hospital and across the SESLHD.

Delirium severity will be measured with the Delirium Rating Scale (DRS-R 98) (Trzepacz et al. 1988), collected prior to study commencement and then at intervention completion for each patient.

1. **PARTICIPANT ENROLLMENT AND RANDOMISATION**
   1. **Recruitment (as outlined in Section 4.2)**

There is no randomisation required for this study.

**Intervention group**

* All hospital inpatients aged ≥ 65 years admitted under a geriatrician to the Aged Care acute or subacute ward will be screened for eligibility, as determined by the Inclusion and Exclusion criteria.
* Standard practice for clinical handover between senior medical staff in the Department of Aged Care at Prince of Wales is a group email (health.nsw.gov.au accounts only) advising of all new admissions. Thus, this will be the source to identify potential participants.
* The study investigator/s will review admissions each day (Monday to Friday, with patients admitted over weekends or public holidays to be screened on the next working day).Potential participants and/or their Person Responsible (where necessary and available) will be approached by the PI to obtain informed, written consent. This will include a semi structured assessment of the patient’s capacity to consent to research (see below in Consent section).
* Time for the participant/Person Responsible to consider participation will be up to 3 days.
* As this is a non-pharmacological intervention and through previous experience in introducing novel non-drug therapies, the proportion expected to agree to participate will be high.

**Historical control group**

* These participants will be drawn from recent inpatient records from the AACE Unit from November 2022- April 2023 and phone consent gained from the patient and/or Person Responsible by a study team member other than the PI (whose pre-existing relationship with the patients may influence their decision to participate). This will likely be the clinical nurse consultant (CNC) or registrar (Advanced Trainee).. Otherwise, the same Inclusion and Exclusion criteria as the intervention group will apply for eligibility.

All participants (intervention and control) will be assigned an arbitrary Study ID by the CPI/PI for data input using Research Electronic Data Capture (REDCap) Software ie:

* + Intervention participants- VPI-001; VPI-002 etc (in order of study entry)
  + Control participants- VPHC-001; VPHC-002 etc (in order of recruitment)

**Staff participants**

* Healthcare staff who have administered the intervention and who agree to complete a questionnaire at the end of a patient intervention period will be consented for collection of the questionnaire data. Consent will be obtained by a study team member other than the PI (whose seniority may influence the staff member’s decision to participate). This will be a more junior member of the study team, likely the clinical nurse consultant (CNC) or registrar (Advanced Trainee).
* Further, opportunities to opt-in will be provided by communicating to staff about the study ie. through department-wide email and at department meetings such as case conferences, journal clubs and grand rounds.
* Staff name and other identifying data will not be recorded.
* Questionnaire data will be entered corresponding to the relevant Patient participant under their Study ID.
  1. **Eligibility Criteria**
     1. **Inclusion Criteria**

**Intervention group**

* Patients aged ≥ 65 years admitted under a geriatrician to the Aged Care acute or subacute ward;
* Diagnosis of all-cause dementia (new or pre-existing);
* Presence of neuropsychiatric symptoms of dementia +/- delirium; and
* Appropriate written consent from the patient and/or Person Responsible if the patient does not have decisional capacity to consent to clinical research.

**Historical Control group**

* Patients aged ≥ 65 years admitted under a geriatrician to the Acute Aged Care Extended Unit (AACE) from November 2022- April 2023;
* Diagnosis of all-cause dementia (new or pre-existing);
* Presence of neuropsychiatric symptoms of dementia +/- delirium; and
* Appropriate telephone consent from the patient and/or Person Responsible if the patient does not have decisional capacity to consent to clinical research (in this case, access and collection of data from the patient’s EMR).

**Staff participant group**

* Staff member has participated in delivering and/or facilitating the intervention for participant in question (at least once); and
* Appropriate written consent from the staff member to collect data from the questionnaire.
  + 1. **Exclusion Criteria**
* Disturbed behaviour due to primary psychiatric illness (not dementia).
* Unable to obtain written consent from patient or Person Responsible.
* Unable to obtain phone consent from patient or Person Responsible for historical control group.
* Unable to obtain written consent from Staff participant.

# Informed Consent Process

**Intervention group**

Those patients screened as eligible will be approached on the ward by the PI to gain informed, written consent.

As this is a vulnerable population, the severity of cognitive impairment as well as decisional capacity to consent to research will be considered. The severity of cognitive impairment will be recorded as part of demographic data collection ie. Clinical Dementia Rating scale (CDR) and cognitive screening test (where available), though it is noted that dementia severity (in and of itself) does not determine capacity/incapacity. The consent process will involve the PI (a senior staff specialist geriatrician) conveying the necessary study information and using semi-structured questioning to establish decisional capacity to consent to research based on:

* *Understanding* ie. comprehension of the nature of the study and study materials;
* *Reasoning* ie. the ability to compare the consequences of research involvement or non-involvement.
* *Appreciation* (that the goals of research may not include direct personal benefits); and
* The ability to express a logical choice.

The “arm’s length” principle will be employed, to ensure there is voluntary agreement to participate, free from coercion.

If the participant’s decisional capacity is questionable the investigator will offer to contact a nominated Person Responsible who may act as a surrogate decision maker. The Person Responsible may also be contacted if requested by the participant for any reason. The Person Responsible will only be contacted with consent from the patient.

A hard copy of the PISCF will be provided to the participant/Person Responsible after consent is gained, including the section for Withdrawal of Consent.

**Historical control group**

A study team member other than the PI will contact the patient and/or person Responsible (if the patient does not have decisional capacity to consent to clinical research) to gain phone consent for the access and collection of data from the patient’s EMR.

A similar process of questioning as described above will be adopted to ascertain capacity.

The study team member will ask the questions on the consent form and sign to confirm that the participant (or Person Responsible) has been given all necessary information pertaining to the study and has been given opportunity to ask questions.

A hard copy of the PISCF will be sent to the participant/Person Responsible after consent is gained, including the section for Withdrawal of Consent.

**Staff Participants**

Healthcare staff willing to complete a questionnaire will be consented (written) by a study team member other than the PI (whose seniority may influence the staff member’s decision to participate). This will be a more junior member of the study team, likely the clinical nurse consultant (CNC) or registrar (Advanced Trainee)..

A hard copy of the PISCF will be provided to the Staff participant after consent is gained, including the section for Withdrawal of Consent.

**Waiver of Consent -** Not applicable

* 1. **Participant Withdrawal**
     1. **Reasons for withdrawal**

Possible circumstances for early termination of the study or withdrawal of the participant may include:

* Severe, critical illness arising where administration of music therapy may not be practicable eg. admission to Intensive Care Unit (ICU).
* Distress associated with music therapy (despite efforts to personalise music library with positive-association selections).

Participants may withdraw at any time without giving a reason.

Any withdrawal or early study termination will not damage any therapeutic relationships nor affect the ongoing delivery of best practice care.

# STUDY VISITS AND PROCEDURES SCHEDULE

Flow schedule:



* All study visits will occur on the hospital ward during the participants’ admission.

# ADVERSE EVENT REPORTING

Potential risks/adverse events include:

* Distress associated with music therapy (despite efforts to personalise music library with positive-association selections).
  + Mitigation/management strategy- Healthcare staff to cease intervention and notify the study investigator/s of possible adverse event at earliest possible time. Team doctor and/or PI to review the participant to ascertain whether a particular music selection is causing distress and remove from the participant’s digital library. In the event all songs compiled for the participant causes distress the intervention will be terminated for that participant.
* Irritation from headphone use.
  + Mitigation/management strategy- Healthcare staff to cease intervention and notify the study investigator/s of possible adverse event at earliest possible time. Team doctor and/or PI to review and examine the participant to ascertain the source of irritation ie. from the headphone itself (uncomfortable material, incorrect size, volume setting, fidelity of sound, interference or dropout) or due to patient factors (hearing aid interference, ear discomfort or infectious/inflammatory pathology). Circumstances that can be remedied will be addressed immediately and music therapy suspended or delivered via speakers in the interim. In the event of persistent irritation the intervention will be terminated.
* Irritation from speaker use.
  + Mitigation/management strategy- Healthcare staff to cease intervention and notify the study investigator/s of possible adverse event at earliest possible time. Team doctor and/or PI to review and examine the participant to ascertain the source of irritation ie. from the speaker itself (volume setting, fidelity of sound, interference or dropout) or due to patient factors (hearing aid interference, anxiety or fear triggered by sound coming from a speaker). Circumstances that can be remedied will be addressed immediately and music therapy suspended or delivered via headphones in the interim. In the event of persistent irritation the intervention will be terminated.

Although this Non-Therapeutic Goods Trial is not expected to result in any adverse events, the CPI is committed to:

a) Capture and assess all adverse events that occur at the site.

b) Report Serious Adverse Events (SAEs) to the sponsor within 24 hours.

c) Report any Urgent Safety Measures (USMs) to the sponsor within 24 hours.

d) Act on all verbal or written reports of Significant Safety Issues (SSIs) from the sponsor to ensure any implications for trial participants are managed appropriately.

e) Report to the Research Governance Office (RGO) as soon as possible, and in any case no later than 72 hours, all SSIs and SAEs arising from the local site.

f) Ensure that any research-related events that meet the definition of an incident are processed in keeping with any organisation-wide reporting of incidents relating to patient safety, in accordance with the Incident Management Policy.

The CPI is ultimately responsible for supervising any individual or party to whom they have delegated intervention delivery, safety monitoring or reporting duties or functions.

The CPI will ensure that any members of the trial team are appropriately qualified and trained to undertake those activities.

# STATISTICAL METHODS

* 1. **Sample Size Estimation**

A sample population of 40 for the intervention group was considered a realistic enrolment target for a 6 month period. This was considered a sufficient period to demonstrate feasibility of the intervention.

Taking into account an expected participation rate of 90% and attrition rate of 5%, up to 48 patients may need to be approached ie. 48 x 0.9= 43.2 and 43 x 0.95= 40.85 (40 patients).

A historical control group of 40 was considered a realistic target over the period November 2022- March 2023 ie. a recent time frame and during which sufficient NPI-Q data would be available.

Taking into account an expected participation rate of 95%, up to 43 patients may need to be contacted ie. 43 x 0.95= 40.85 (40 patients).

* 1. **Statistical Analysis Plan**

Biostatistician support from Stats Central: consultation and collaboration with abovenamed biostatistician has commenced and will be ongoing.

Statistical analysis will be conducted using IBM SPSS Statistics software.

Quantitative

Baseline characteristics, reason for admission, dementia diagnoses, NPI-Q results, psychotropic medication usage (type and dosage), critical incidents (eg. Code Blacks, falls) and hospital Length of Stay (LOS) will be collected for the intervention group and historical control group for comparison.

The historical control group will comprise recently admitted patients of similar characteristics.

A mixed effects model will be used to compare between the intervention and control groups for BPSD (presence/absence, total number of symptoms, severity of the symptoms, and associated distress); psychotropic medication usage (type and dosage), number of critical incidents (eg. Code Blacks, falls) and average hospital Length of Stay (LOS).

Effect of the intervention based on duration/frequency of usage (eg. number of sessions per week; hours used per day) may be examined though large variability may limit detailed analysis.

Effect of the intervention between subtypes and severity of dementia will also be examined though small numbers may limit the power of observations.

Effect of the intervention on delirium severity in the intervention group, where present, will also be described though small numbers may limit the power of observations and temporal bias may act as a confounder.

Qualitative

Feasibility (and acceptability) of incorporating the intervention into Standard care will be described using the Staff Participant and Patient Participant/Person Responsible questionnaires.

# DATA MANAGEMENT

* 1. **Data Collection**
  2. **Data Storage**
  3. **Data confidentiality**

|  |  |  |  |
| --- | --- | --- | --- |
| Data collected  (including for Historical control group) | How | By whom | Data storage |
|
| Study ID (de-identified) | Arbitrary assignment | PI | SESLHD shared drive database |
| Demographic data | EMR (standard care) | Entered by hospital care staff (medical doctors, nursing staff, Allied Health) onto EMR for standard care data.  Entered onto study forms by study investigators (NPI-Q, DRS-98, questionnaires).  Extracted by Study investigator/s. | Collected data tabulated onto Participant data sheet and entered into  REDCap  by PI |
| Reason for admission | EMR (standard care) |
| Diagnoses (including dementia subtype and severity) | EMR (standard care) |
| BPSD presence | EMR (standard care) |
| NPI-Q | Intervention group:  Recorded on NPI-Q forms for study.  Control group:  EMR (standard care) |
| Delirium presence | EMR (standard care)  Screened with 4AT |
| Delirium severity | Intervention group:  Recorded on DRS-98 forms for study. |
| Medications used | EMR (standard care) |
| Intervention used (time, date, duration, activity). | Intervention group:  Recorded on EMR (standard care for new therapies) |
| Patient Participant Questionnaire | Intervention group:  Recorded on questionnaire form for study. |
| Staff Participant Questionnaire | Intervention group:  Recorded on questionnaire form for study. |

PI = Principal investigator

SESLHD = South Eastern Sydney Local Health District

EMR = Electronic medical record

BPSD = Behavioural and psychological symptoms of dementia

NPI-Q = Neuropsychiatric Inventory Questionnaire

The CPI/PI will maintain ultimate responsibility over data collection, storage and confidentiality.

Methods to reduce identifiability and the consequent risks include:

1. Minimising the number of variables collected for everyone.

(b) Separation and separate storage of identifiers and content information.

As this study will not be blinded to the investigators, they will have access to the source data (EMR is password protected and for privileged use of SESLHD employees only).

Any hard documents generated during data collection (eg. forms or surveys completed) will be separately stored (deidentified or appropriately redacted) in a locked filing cabinet in the locked office of the CPI (on-site at Prince of Wales Hospital).

The CPI will have sole access to participants’ Study IDs which will be kept in a secure, password protected SESLHD shared drive database and will not be used to re-identify participants for any purpose.

(c) Separating the roles of those responsible for management of identifiers and those responsible for analysing content.

The CPI will enter all relevant data collected into REDCap.

The biostatistician performing the analysis will not have access to any identifying information.

Data will remain de-identified throughout the study duration and any publication.

* 1. **Study Record Retention**

Research data will be retained in the abovementioned secure storage databases and filing cabinets for at least 15 years following trial completion (as per NHMRC guidelines).

Hard documents will be disposed of and shredded through the Prince of Wales Hospital Confidential Waste bins (locked).

Digitalised records will be disposed of with the assistance of the relevant Information Technology support service (eg. SESLHD Information Management).

# ADMINISTRATIVE ASPECTS

* 1. **Independent HREC approval**

In progress with the South Eastern Sydney Local Health District HREC.

* 1. **Amendments to the protocol**

Any amendments will be submitted via REGIS for review prior to implementation as per HREC guidelines.

* 1. **Participant reimbursement**

Not applicable.

* 1. **Financial disclosure and conflicts of interest**

Not applicable. No financial incentives or conflicts of interest to declare.

# USE OF DATA AND PUBLICATIONS POLICY

Results of the study will be disseminated to the sponsor (SESLHD), financier (Prince of Wales Hospital Foundation), VeraTM Music Health and submitted for publication in relevant peer-reviewed journals.

The CPI will take the lead with regards to report writing and publication articles and submissions (with assistance from study associate investigators and biostatistician).

Those to be acknowledged in publication include:

* The sponsor (SESLHD - Randwick Health and Innovation Precinct)
* The financier (Prince of Wales Hospital Foundation)
* VeraTM Music Health
* Design and development support from Neuroscience Research Australia (NeuRA); Mindgardens Neuroscience Network; and University of New South Wales.
* Healthcare staff involved in delivering the intervention and completing questionnaires.
* Study participants and their families/carers.

As part of routine clinical care, participants and carers may be notified of their response to the intervention. This feedback will not include information on any other trial participants.

An option for the Control group to receive more direct information about the efficacy of the intervention (if found), so that they may consider using Vera themselves in the future, has been included on their consent form.

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