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Balance on the Brain: a randomised controlled trial evaluating the effect of a multimodal exercise programme on physical performance, falls, quality of life and cognition for people with mild cognitive impairment—study protocol

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ABSTRACT

Introduction Exercise and physical activity have been shown to improve cognition for people living with mild cognitive impairment (MCI). There is strong evidence for the benefits of aerobic exercise and medium evidence for participating in regular strength training for people with MCI. However, people living with MCI fall two times as often as those without cognitive impairment and the evidence is currently unknown as to whether balance training for people with MCI is beneficial, as has been demonstrated for older people without cognitive impairment. The aim of this study is to determine whether a balance-focused multimodal exercise intervention improves balance and reduces falls for people with MCI, compared with a control group receiving usual care.

Methods and analysis This single blind randomised controlled trial (Balance on the Brain) will be offered to 396 people with MCI living in the community. The multimodal exercise intervention consists of two balance programmes and a walking programme to be delivered by physiotherapists over a 6-month intervention period. All participants will be followed up over 12 months (for the intervention group, this involves 6-month intervention and 6-month maintenance). The primary outcomes are (1) balance performance and (2) rate of falls. Physical performance, levels of physical activity and sedentary behaviour, quality of life and cognition are secondary outcomes. A health economic analysis will be undertaken to evaluate the cost-effectiveness of the intervention compared with usual care.

Ethics and dissemination Ethics approval has been received from the South Metropolitan Health Service Human Research Ethics Committee (HREC), Curtin University HREC and the Western Australia Department of Health HREC; and approval has been received to obtain data for health costings from Services Australia. The results will be disseminated through peer-review publications, conference presentations and online platforms.

Trial registration number ACTRN12620001037998; Australian New Zealand Clinical Trials Registry (ANZCTR).

Strengths and limitations of this study

- ► To our knowledge, this is the first randomised controlled trial for people living with mild cognitive impairment (MCI) that will evaluate the effect of exercise on improving balance and reducing falls.
- ► An economic evaluation from a healthcare perspective allows for potential future implementation should the intervention be effective.
- ► Participants will be monitored regularly with monthly follow-up phone calls collecting physical activity, health and falls data.
- ► The study is statistically powered for both primary outcomes (ie, balance and falls), baseline and outcome assessors are blinded to group allocation.
- ► A limitation may be convenience sampling (ie, one state) rather than population-based sampling (ie, multistate), which may not be representative of the Australian MCI population.

INTRODUCTION

The prevalence of mild cognitive impairment (MCI) varies between 20% for those aged 70+ years in USA,[1] 12.2%–15.5% in China for those aged 55 and 60 and over, respectively,[2 3] between 6.8% and 22.5% in Latin America and Caribbean populations over 50 years of age,[4] up to 37% for Australians aged 70–90 years,[5] and leads to an increased risk of dementia.[6] According to the

International Working Group on MCI, the core features of MCI include: evidence of deterioration in cognition either objectively measured over time and/or through self-report or by an informant reporting cognitive deficits beyond that expected for age and education level; the person not presenting with dementia and activities of daily living being preserved, although there may be some mild impairment in complex activities.[7 8]

People with MCI are more likely to fall than those of the same age without cognitive impairment.[9] This is often due to a decrease in motor function and balance, which may be associated with age-related change in white matter.[10] MCI can also affect specific gait parameters, and falls risk is increased particularly when a person with MCI is cognitively challenged or during dual-tasking.[11 12] The average age of the population is also increasing; therefore, MCI and falls are likely to affect thousands more people, including Australians as they age. This will not only negatively affect individuals and their families but will have a significant impact on health budgets over the coming decades unless successful interventions are developed and implemented widely (ie, Australian fall-related costs estimated at AUS$648 million in 2007–2008,[13] and falls are the leading cause of injury-related hospitalisations in Australia,[14] with age standardised rates increasing at >2% per annum).[15]

For older people living in the community without cognitive impairment, balance exercise programmes that mainly contain balance and functional training components have been shown to be one of the most effective measures for decreasing the risk and rate of falling.[16] Balance exercises may also benefit people living with MCI; however, the current evidence is less clear. Eight randomised controlled trials (RCTs)[17–24] have been conducted with people with MCI, which have included measuring falls or fear of falling; however, none has specifically used a balance exercise programme, nor followed participants for a long period of time (up to 12 months) with falls being the primary outcome.

Recently developed physical activity guidelines for older Australians with MCI or subjective cognitive decline (SCD),[25] recommended the same amount of aerobic, strength and balance exercise per week as the guidelines for all older adults (ie, 150 min moderate intensity aerobic activity, plus two strength and balance sessions per week[26]). The evidence for participating in aerobic activity is strong for people living with MCI and shows significant benefits to their brain health and function.[25] However, there is a lack of evidence to make specific recommendations for this population on balance recommendations.[7 25] The guidelines noted that there were no research trials specifically examining balance interventions in older adults with MCI and SCD and, therefore, their current recommendations were extrapolated from studies of older adults with no cognitive impairment.[25] A systematic review by Burton *et al*[27] also showed that few balance interventions have been undertaken to reduce falls for people living with dementia. Maintaining balance as one ages is critical for participating in everyday activities, staying mobile, living independently and reducing the risk of falling.[28]

Despite a number of additional RCTs evaluating exercise interventions in people with MCI since the publication of these recommendations, there remains a gap in the research and a critical need to better understand whether balance can be improved for people with MCI living in the community and if so, whether improved balance is translated into fewer falls. This project provides an opportunity to address these important research gaps and assist people with MCI, their caregivers, healthcare providers and potentially reduce the cost of healthcare into the future.

The aims of this research are to determine whether a balance-focused multimodal exercise intervention improves balance and reduces the rate of falls for people with MCI, compared with a control group (receiving usual care and a health promotion flyer). The study also aims to evaluate the cost-effectiveness of the intervention compared with usual care. Secondary aims include evaluating the effect of the intervention on physical performance, falls efficacy and quality of life and reducing cognitive decline.

It is hypothesised that older adults with MCI participating in the balance-focused multimodal exercise intervention, when compared with the usual care group (control), will (during the intervention and for the following 6 months) achieve:

1. Improved balance (improvement on four-square step test[29]).
2. A decrease in falls rate (using monthly calendar and phone calls) and improved falls efficacy (improvement on Falls Efficacy Scale—International[30]).
3. Improved physical performance (improvement in the Short Physical Performance Battery (SPPB),[31] timed-up-and-go (TUG),[32] 6 min walk test (6MWT)[33]) and physical activity (increase in step count using activPAL4 accelerometers).
4. Improved quality of life (improvement on Quality of Life—Alzheimer's Disease (QOL-AD).[34 35]
5. A reduction in rate of cognitive decline (Montreal Cognitive Assessment (MoCA)[36]).

It is also hypothesised that the exercise programme will be cost-effective compared with usual care, defined as having an incremental cost-effectiveness ratio (ICER) of less than AUD$50,000/QALY gained. In addition, the cost per fall will be evaluated.

METHODS AND ANALYSIS

Study design

This will be a single-blind RCT, comparing a balance-focused multimodal exercise intervention to a usual care control group for people with MCI (see figure 1). The Consolidated Standards of Reporting Trials (CONSORT) statement[37] has been used as a framework for developing the project methodology. The study recruitment and

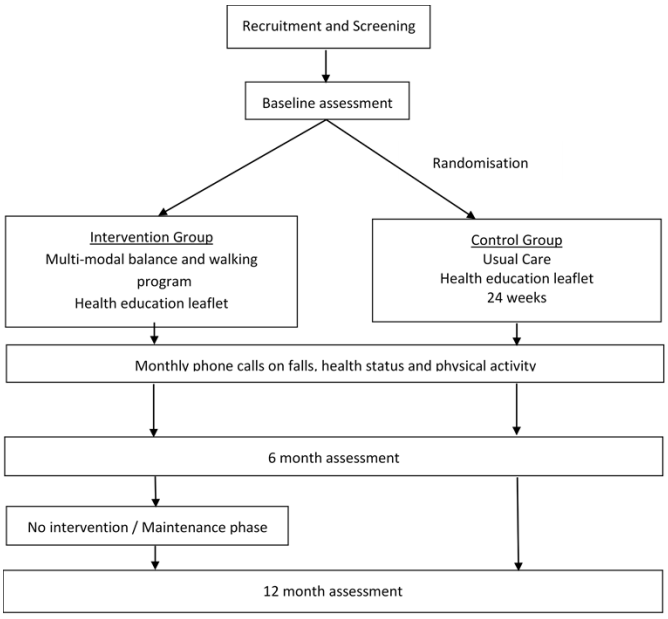

Figure 1 Study design.

data collection will be undertaken from the start of 2021 through to the end of 2024.

Participants

Three hundred and ninety-six participants living with MCI will be recruited across the Perth and Rockingham metropolitan areas of Western Australia (WA). Participants will be included if they meet the following criteria: aged over 50 years; living in the community with a diagnosis of MCI consistent with the Petersen criteria,[38] including self-reported memory complaint, a Clinical Dementia Rating[39] (CDR) of 0.5 and Standardised Mini-Mental State Examination[40] (SMMSE) Score of 24 or above. Other inclusion criteria are: not meeting Australian physical activity guidelines (ie, <150 min of moderate-intensity physical activity a week self-reported) and not participating in balance training regularly (ie, <two times a week).

Participants will be excluded if they have an unstable medical condition, terminal illness, diagnosis of significant cognitive impairment and/or chronic mental illness (eg, schizophrenia), severe sensory impairment affecting mobility, live in residential aged care, drink more than four standard alcoholic drinks per day (ie,>28/week), score >6 for the Geriatric Depression Scale-15 item (GDS-15)[41] or have a lack of fluency in written and spoken English.

Recruitment and screening

Participants will be recruited from the community via nine memory cafes that are held throughout Perth and organised by Alzheimer's WA, advertisements in the local media including CurtinFM radio, The Senior and Have a Go newspapers, and where possible through news segments on television. Alzheimer's WA will also forward enquiries from people with MCI who wish to participate. A Facebook page providing up to date information about the project will be developed and advertisements sent out promoting the study. Memory clinics at Armadale Hospital, Fremantle Hospital, Sir Charles Gairdner Hospital, the Royal Perth Cognitive Disorder Clinic, the Aged Care Rehabilitation Clinics, at Rockingham General Hospital, the Aged Care Assessment Team, the Regional Assessment Service (RAS) and the Neurosciences Unit will all assist with recruitment.

The research team will contact potential participants by telephone to check the suitability of the person in accordance with the inclusion and exclusion criteria using a screening protocol. The telephone screen includes a description of the study, questions about memory, current physical activity levels, living situation, availability over the following 6-month period, cognitive screen (ie, Modified Telephone Interview for Cognitive Status (TICS-M)), health screening (ie, vision, hearing, medical conditions), alcohol consumption, not participating in drug trials and the GDS-15. The GDS-15 is included in the screening to determine the presence of clinically relevant symptoms of depression. If the participant reports a medical diagnosis of depression, they will not be required to complete the GDS-15. The full phone screening tool is available from the corresponding author and takes approximately 45 min to complete. The contact details of the participant and their general practitioner (GP) will also be collected.

To complete the screening process, the research officer will meet with the potential participant face-to-face at a location comfortable for both parties and complete the questions required to determine a diagnosis of MCI for this study (see inclusion criteria). This includes a self-reported memory complaint, completing the CDR and receiving a score of 0.5 and the SMMSE with a score of ≥24 or diagnosis from medical specialist (eg, Geriatrician, Neurologist). If these criteria are met, participants will be asked if they have read the participant information sheet and consent form (if not they will be asked to read it then) and have any questions about participation in the trial answered. Prior to commencing in the study, each participant will provide written consent.

Outcomes and assessments

An overview of the primary and secondary outcomes and assessment tools to measure each outcome are presented in table 1. All assessments are valid, reliable and have been trialled with people with MCI. Participants will be closely supervised during all balance and mobility assessment tasks, as is routine practice when using these assessment items. To ensure standardisation of procedures, the Research Officers collecting the data will be trained by the same chief investigator who has a background in exercise science.

All participants will be assessed at baseline, 6 months (ie, completion of the intervention period) and 12 months. This study will have two primary outcomes:

1. balance: measured using the four-square step test
2. Falls rate: measured using monthly calendars and follow-up phone call. A fall will be defined as 'an

Table 1 Assessments and timelines for Balance on the Brain

Measure	Outcome(primary/secondary)	Phone/home screen	Baseline	6 months	12 months
Geriatric Depression Scale—15 Item		X			
Modified Telephone Interview for Cognitive Status		X			
Standardised Mini-Mental State Examination		X			
Cognitive Dementia Rating		X			
Balance: Four Square Step Test[29 55]	Primary		X	X	X
Primary falls: collected using a monthly call and calendar	Primary		Monthly phone call and calendar		
Physical performance: Short Physical Performance Battery Test[31 56 57]	Secondary		X	X	X
Physical performance: Timed Up and Go Test[32]	Secondary		X	X	X
Physical performance: 6 Minute Walk Test[33]	Secondary		X	X	X
Physical activity: Accelerometer worn for 7 days (ActivPAL4) (step count and time spent in moderate to vigorous physical activity)	Secondary		X	X	X
Physical activity: Physical Activity Scale for the Elderly administered a week after each assessment (at accelerometer pick up)[45 47 58]	Secondary		X+1 week	X+1 week	X+1 week
Quality of Life: Quality of Life—Alzheimer's Disease[34 35]	Secondary		X	X	X
Cognition: Montreal Cognitive Assessment Test[36]	Secondary		X	X	X
Secondary falls: number of fallers, injurious falls	Secondary		Monthly phone call and calendar		
Falls efficacy: Falls Efficacy Scale—International [30]	Secondary		X	X	X

An injurious fall will be defined as a fall where the participant sought 'medical advice'. Data will also be collected on any injury sustained such as bruising, laceration, fracture, loss of consciousness or if the participant reports ongoing pain.[59 60]

unexpected event in which the individual comes to rest on the ground, floor or lower level'[42] as recommended by the Prevention of Falls Network Europe.

The four-square step test (dynamic standing balance) uses four walking sticks/poles/PVC pipes to create four squares (ie, quadrants).[29] To complete the test, the participant steps both feet into each quadrant in a clockwise direction, then in an anti-clockwise direction back to the starting position, without touching the poles.[29] Two full trials are completed and the fastest time is reported.

All study participants will be asked to complete a monthly calendar that includes falls information (ie, fall and date occurred), changes to health and self-reported physical activity. This will be followed up each month with a phone call to collect these data (ie, falls, changes to health, physical activity). At each monthly call, participants will be reminded to keep their calendar in a place they view often, as a reminder to complete it and will also be asked if they had any falls not recorded in the calendar. Falls data collected during the phone call will include number of falls, where they occurred, injuries, medical attention required etc.

The SPPB groups a number of physical performance measures such as gait speed, chair stand and balance tests into one test.[43] It has been used to monitor function in older people and those with MCI as well as predict possible disability, risk for mortality and residential aged care admission. Scores range from 0 (worst performance) to 12 (best performance).

The TUG test is used to not only measure a person's mobility but also includes the ability to stand up from a chair, walk three metres, turn, walk back and sit down in the chair.[32] The participant will be timed using a stop watch. Each participant will be given a practice trial that is not timed and then asked to complete the TUG.

6MWT is a submaximal exercise test used to assess walking endurance and aerobic capacity.[33] Participants will walk around a circuit which is at least 12 m long for 6 min with the distance calculated at the end of this time. The circuit will be marked by using bright coloured cones.

Physical activity will be measured using ActivPAL4 accelerometers. The activPAL is currently considered the most accurate field-based measure of sitting time and sit-to-stand transitions.[44] The accelerometers will be worn, and data collected over a 7-day period at baseline, 6 and 12-month data collection. ActivPAL data will be converted to event level files using propriety PAL Technologies software. The following variables will be derived from the accelerometer data across the 7 days: step count, time spent in sedentary, upright and stepping activities, stepping intensity (cadence) and duration of lying, sitting, standing and stepping activities. The activPAL4 will be worn on the thigh, is waterproof and does not need to be removed for the 7 days. The accelerometer will be applied by research staff using a Tegaderm dressing and removed by the research staff on return. Each device is small (23.5×43×5 mm) and weighs 9 g

The Physical Activity Scale for the Elderly (PASE) is a 12-item self-report instrument designed to assess physical activity levels in older people over a 1-week period.[45] It combines physical activity information during leisure, household and occupational activity.[46] A score is calculated based on activity frequency and an activity-weighted score multiplied by frequency.[47] The higher the PASE score, the more physically active a person is, with PASE scores ranging from 0 to 400.

The QOL-AD tool is a 13-item measure designed to obtain a rating of quality of life.[34 35] Each question is rated on a four point scale, 1 being poor and 4 being excellent, total scores range between 13 and 52.[34 35] It was specifically designed for people with cognitive impairment.

Cognition will be assessed using the MoCA, which assesses eight cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations and orientation.[36] The total maximum score is 30 points and the research staff will administer it face-to-face.[36]

The Falls Efficacy Scale—International is a 16-item tool used to measure 'concerns about falling' and is recommended to be administered face-to-face for people with cognitive impairment.[48] Participants will be asked to answer each question on a Likert scale from 'not at all concerned' (1) through to 'very concerned' (4), based on whether they think they would be concerned about falling while participating in the activities, for example, *How concerned are you about falling while cleaning the house (eg, sweeping, vacuuming or dusting)?*

Randomisation and blinding

A concealed, computer-generated sequence of randomly selected permuted blocks (block size=6) in a 1:1 ratio will be generated by a statistician not involved in the study. A staff member (external to the study) from Curtin University's Clinical Trials Data Management Centre will enter the randomisation codes into the REDCap project data management system, minimising bias by concealing randomisation. Once a participant has been recruited and they provide written consent to participate, baseline data collection will be undertaken by one of three research officer staff. After baseline data collection is completed and has been entered into REDCap by a research officer, the lead researcher will then press the randomisation button (which will allocate that participant to the intervention or control group). An email will be automatically sent by the REDCap project system (for intervention, participants only) to the lead researcher (independent, not involved in assessments or intervention) who will allocate the intervention participant to a physiotherapist delivering the intervention. This email will include the contact details (ie, name, phone number and address) of the participant allocated to the intervention group, to allow the physiotherapist to contact them directly.

The research officers who enrol the participants, collect and enter baseline, 6 and 12-month data will be blinded to group allocation throughout the study (figure 1). Those delivering the intervention (ie, physiotherapists) will not be involved in any study outcome data collection after randomisation has occurred (except for the process evaluation of the intervention delivery—separate study, methods not reported in this paper). Participants cannot be fully blinded to receiving the intervention. Participants will be reminded at each outcome assessment (ie, baseline, 6 months and 12 months) not to divulge their group assignment to research staff or other participants (ie, who may attend the same memory cafe).

Intervention

The intervention period will be 24 weeks and the data collection/follow-up periods 6 and 12 months postbaseline. The intervention will be delivered by qualified physiotherapists, with a background in working with older adults and those living with cognitive impairment. The physiotherapists will also complete two half days of training prior to delivering the intervention. The balance-focused multimodal exercise intervention group will participate in the Balance Yourself (a book)[49] and Clock Yourself programmes (exergame App or compact disc (CD))[49] and in discussion with the physiotherapist progress (where appropriate) to walking 30 min per day, 5 days a week in a safe environment. Both balance programmes are safe and have been delivered by experienced physiotherapists for over 5 years to approximately 500 older adults, including some individuals with stroke, Parkinson's disease, MCI or early-stage dementia. These complementary programmes aim to build a person's capacity to prevent falls. The Balance Yourself programme aims to

improve balance, whereas the Clock Yourself programme aims to improve stepping reactions in all directions in the event that a person should lose their balance. Each programme starts slowly and progresses over time through levels of increasing difficulty in accordance with each participants' ability. The Balance Yourself book, which has been adjusted specifically for people with MCI, guides the user to practise evidence-based balance exercises, which are introduced in a progressively challenging sequence. The standing balance exercises involve standing still and are progressed in difficulty with narrowing foot positions and then introducing head movements, reaching outside the base of support, closing eyes and dual tasking. The dynamic balance exercises involve stepping or walking in various directions and with narrowing foot positions, for example, sideways, backwards, tandem, figure of 8.

The Clock Yourself programme is presented as a brain game to help people think faster on their feet. It is a volitional stepping method designed to progressively improve physical agility and stepping reaction times while a person's attention is divided. The programme is deliverable by either an app (low-tech) or a set of audio CDs (no-tech). To cater for heterogeneity in tech-literacy and to promote self-efficacy with the exercise, participants can choose whichever tool they are most confident with. A guidebook is also available to assist participants to navigate the app or the CDs. Participants will be asked to progress throughout the 24-week intervention to participating in 60 min of the Balance Yourself programme and Clock Yourself programme per week, for a total of 120 min of balance exercise per week (ie, 20 min/day). Where required, carers will be asked to support the participants to carry out the exercise programmes, for example, guiding them with safe set up or providing reminders.

The walking component will be individually tailored to each participants' abilities, with emphasis on walking environments to maximise safety. Participants will be encouraged to progress to walking 30 min a day, 5 times a week over the 24-week intervention.

The physiotherapists will deliver the intervention approximately 7–10 days after group allocation (ie, to intervention group), they will return for further home visits in weeks 2, 8, 12, 17 and 20 of the intervention to provide advice on technique, use of the intervention tools and progressing through the levels of exercise. Motivational phone calls will be made by the physiotherapist in weeks 3, 6, 10 and 14 of the intervention (see figure 2). These phone calls will include progress of the participant since the last home visit, problem solving should any issues arise, questions on confidence of the participant to increase and/or progress activities and any assistance they may need. Each intervention participant will be asked to practice the balance and walking programmes progressing over time to 5–7 days a week (or up to 120 min for the week for the balance programmes, plus a minimum of 30 min/walking).

Control group

The usual care group will receive a health promotion education leaflet, after completing baseline data collection. This will include documentation on the current physical activity recommendations for people with MCI and healthy eating and drinking recommendations. The intervention group will also receive the same education leaflet.

Sample size

The sample size was calculated separately for the two primary outcomes: (1) balance, based on the four-square

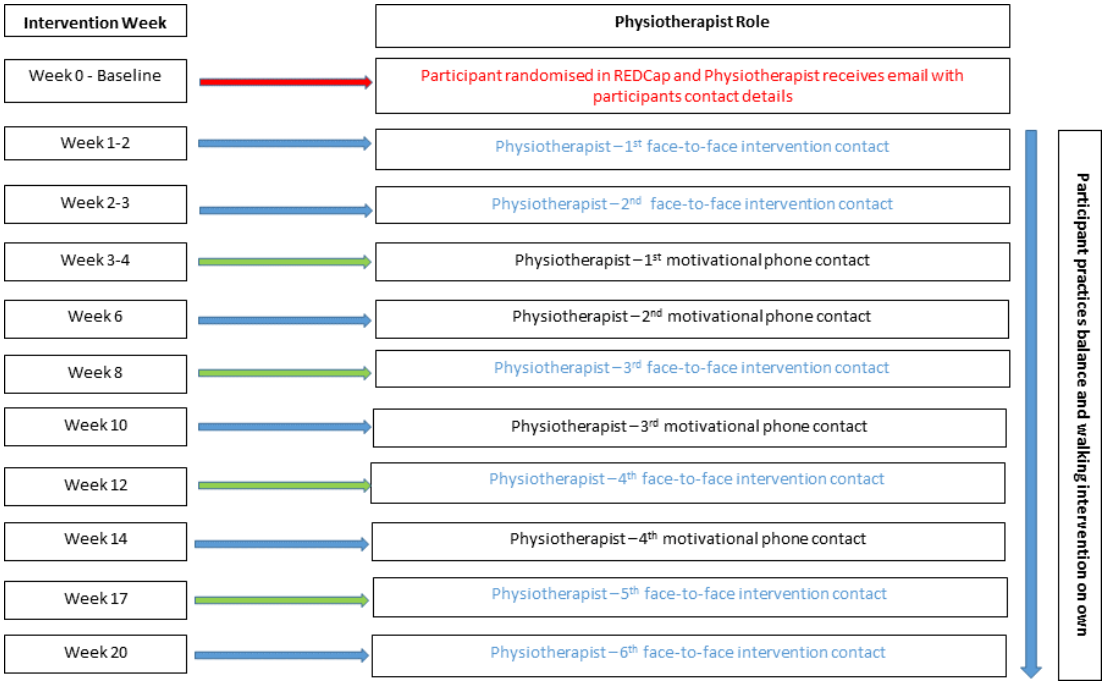

Figure 2 Timeline of intervention delivery by physiotherapists.

step test and (2) falls rate. The sample size for the balance outcome was calculated based on detecting a minimum effect size difference of 0.18[50] over 3 time points between intervention and control groups, with 80% power and alpha=0.05. After assuming a 20% withdrawal rate over the 24-week intervention, and a further 15% loss to follow-up over the following 6-month follow-up, consistent with other similar studies,[51] a total of 212 participants (106 per group) are required.

The sample size for falls rate outcome was based on detecting a 30% minimum relative reduction in the falls rate (0.5 to 0.35) in the intervention group compared with the control group, with 80% power and alpha=0.05. After assuming a 20% withdrawal rate over the 24-week intervention, and a further 15% loss to follow-up over the following 6-month follow-up, a sample size of n=396 is required (198 per group). Therefore, a sample size of 396 participants will be required for the overall study (G*Power 3.1.9.2).

Statistical analysis

Continuous data will be summarised as means and SD or medians and IQRs and compared using t tests or Mann-Whitney U tests, depending on normality. Categorical data will be summarised using frequency distributions and compared using χ^2 tests. The primary outcomes will be analysed at baseline, 6 and 12 months using generalised linear mixed-effects models, which use Maximum Likelihood Estimation methods to account for data missing at random. Imputation methods will not be used as they lead to potential bias. The primary outcome of falls rate will be analysed using negative binomial regression, with adjustment for participant's observation time in the study and known confounding demographic factors with strong significant differences. Models will be summarised using predicted mean estimates, weighted mean differences and 95% CIs. All final measures, regardless of intervention participation or compliance, will be collected. Analysis will be performed on both intention-to-treat and per-protocol basis. Stata V.16.0 will be used for data analysis, with significance level set at 0.05.

Economic analysis

Two forms of economic analyses will be undertaken: (1) a cost-utility analysis using the QOL-AD to assess the incremental cost of quality-adjusted life years (QALYs) gained and (2) a cost-effectiveness analysis to assess the incremental cost per fall prevented. Both analyses will be undertaken from a healthcare system perspective

Given an RCT is being undertaken to determine the effectiveness of intervention, the economic evaluation will reflect a service substitution model without cost sharing or transfer. Costs of the programme will be evaluated using prospective data collection for each participant and will include the costs associated with the intervention and outcomes using a healthcare system perspective. Programme costs in addition to those for usual care will include:

- Training the physiotherapists to deliver the two balance programmes (ie, Balance Yourself and Clock Yourself) and the progressive walking programme.
- Physiotherapists salary to deliver the intervention
- Costs associated with outcomes for (all) participants (regardless of group) include:
  - Cost of emergency department (ED) visits.
  - Cost of in-patient hospitalisation.
  - Cost of ambulance use.
  - Cost of GP and other Medicare subsidised out-of-hospital services (Medicare Benefits Scheme: MBS).
  - Cost of Pharmaceutical Benefits Scheme (PBS) medication.

Inpatient costs will be calculated using Diagnostic-Related Group-based costings using the appropriate Independent Hospital Pricing Authority (IHPA) National Efficient Price Determination report. Cost of ED attendances will be based on urgency-related/disposition group (derived using Episode End Status, Type of Visit, Triage, Sex and Diagnosis Code) and costed using IHPA National Efficient Price Determination report or cost report.

Ambulance utilisation will be costed at $986 per service. The cost of MBS services will be ascertained directly from the data (schedule fee, actual fee paid). PBS-supported medication costs will be ascertained using the relevant PBS prescription charges (ie, for general and healthcare card beneficiaries).

Effectiveness of the intervention will be measured using the framework of a within trial cost utility analysis using the QOL-AD mapped across the EQ-5D-5L utility algorithm weighted for the Australian population to derive an overall index of the health state utility at each time point. Participant (ie, intervention and controls) health state utilities will be captured at baseline, 6 and 12 months post recruitment.

An incremental cost-utility analysis will be undertaken to compare the mean incremental cost and QALY profiles for each group according to intervention status. The QALY profile for each intervention participant will be calculated using area under the curve methods, where a significant difference occurs between the groups, an ICER for QALYs gained based on utilities derived from the mapped EQ-5D-5L will be calculated.[52] Using the average costs for the intervention and the mean QALYs gained for the intervention, the incremental cost of the intervention will be compared with the control group and calculated and then plotted on a cost-effectiveness plane.[53] To estimate a distribution around costs and QALYs gained, and to calculate the CIs around the ICERs to account for joint uncertainty in costs and QALYs gained, bootstrapping will be applied.[53] After conducting one-way and probabilistic sensitivity analysis incorporating all key variables, a cost-effectiveness acceptability curve will be plotted.[53] This will provide information as to whether the intervention is cost-effective, based on a decision-maker's willingness to pay for each additional QALY gained (ie, <$50 000/QALY gained).[53]

Cost-effectiveness will also be estimated by using measurement of the change in other outcomes (eg, falls rate, falls injuries), where a significant difference is observed between the intervention and control groups. CIs will be presented around the ICERs and cost-effectiveness acceptability curves for varying threshold values of cost-effectiveness will be presented. A 12-month time horizon will be used and a healthcare system perspective using within trial probabilities and costs will be undertaken. Assessment of the sensitivity of the results obtained to variation in measured effectiveness, healthcare resource use, intervention and usual care unit costs and participant groups will be undertaken using one-way and probabilistic sensitivity analysis, as per best practice guidelines.[54]

Data management

All data will be collected and stored in Curtin University's REDCap data management system (redcap.curtin.edu.au), which uses a secure-socket-layer to encrypt the web transport layer with two-step authentication (ie, email or mobile). Anyone accessing this project database must provide a valid username, password and code at each log in. Each data entry instance into the REDCap file is logged. All other electronic data and information connected to this study will be kept in a password-protected Curtin University R-Drive folder only accessible by the chief investigators and research staff.

Data monitoring

The project will be managed by a steering committee that includes the chief investigators and representatives of the associate investigators/advisory group. The steering committee will monitor (including audits) the conduct and progress of the research project and ensure that project milestones are being met; study procedures are being adhered to; data entered accurately (checking paper to electronic data) and provide guidance about the project implementation. The committee will meet and report half-yearly throughout the project. The committee will report to the appointed hospital representatives and the Ethics Committee Chairs where required. A Data Monitoring Committee (DMC) external to the study investigators will be formed and the committee will receive updates every 6 months (or earlier if applicable). The aim of the DMC is to safeguard the interests of the study participants and assess the safety and integrity of the intervention. The DMC will include a person with previous experience serving on a DMC and an experienced physiotherapist and/or researcher.

Harms

Adverse events will be documented across the 6-month intervention either by physiotherapists during intervention visits/phone calls or by research staff during monthly follow-up calls to participants to collect data about adverse events, possible falls and health issues from the preceding month documented in monthly calendars. Any significant adverse events will be reported to the Human Research Ethics Committee (HREC).

Patient and public involvement statement

Two consumer representatives living with memory issues have been involved with the project since it was funded. They have assisted with the language in the participant information and consent forms and all documentation that will be read or received by the Balance on the Brain participants. They have also provided feedback on completing the monthly calendar and will continue to provide their expertise and feedback across the duration of the project.

ETHICS AND DISSEMINATION

Ethics approval for this study has been granted by the South Metropolitan Health Service HREC, the Western Australian Department of Health HREC (for hospital and emergency data) and the Curtin University HREC. Governance has also been approved for the six hospitals and medical sites assisting with recruitment. Services Australia has also approved participant healthcare data to be accessed at the completion of the study.

All participants will be given a participant information sheet and two consent forms (one project consent form and one Services Australia consent form), with sufficient time to read it and ask questions prior to providing written consent. All participants will be required to provide written informed consent prior to participation and data collection commencing. Participants may refuse the right to participate or withdraw at any time from the research project up to the point that data are deidentified and analysed.

Data will be deidentified and participant confidentiality maintained at all times. It is expected that the results will be published in peer-review journals and presentations delivered to the community, industry and at academic conferences.

CONCLUSION

People living with MCI fall and experience fall injuries nearly two times as often as those living with no cognitive impairment.[9] To the authors' knowledge, no RCTs have evaluated the effect of a balance-focused multimodal exercise programme to improve balance and prevent falls for people with MCI over the long term (ie, 6 and 12 months). This study aims to address this current gap in the literature. We will also evaluate whether physical performance and quality of life are improved and determine whether there is a reduction in cognitive decline. Cost-effectiveness analyses will be undertaken and if effective, the results will provide governments and policymakers with an easy to administer, cost-effective community-based programme that will assist people living with MCI to live independently and reduce their risk of future falls.

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