PARTICIPANT & COMPANION INFORMATION STATEMENT

Project Title

Brain enhancement study (BES): Can optimising biochemical parameters (targets) via participation in a multi-modal lifestyle-based intervention improve cognition in amnestic MCI.

Invitation

You are invited to take part in a study that is investigating the effectiveness of a personalised multi-modal intervention to improve cognition, behavioural function and mood, in individuals who have mild but measurable declines in memory (i.e. who have mild cognitive impairment; MCI).

Before you decide whether or not to take part, either as a participant or companion, it is important to understand why the research is being conducted and what it will involve. Please take the time to read the following information carefully and discuss it with each other, your family and friends.

This study is being conducted by:

A/Prof. Ross Grant Australasian Research Institute, Sydney Adventist Hospital 0409 122 814 rossg@sah.org.au	Dr Jade Berg Australasian Research Institute, Sydney Adventist Hospital, 0410 434 707 jade.berg@sah.org.au

1. What is the purpose of the study?

Mild cognitive impairment (MCI) is the stage between the expected cognitive decline of normal aging and the severe reductions observed in dementia, including Alzheimer's Disease (AD). In one year, between 10 to 15% of those with MCI develop AD. Over six years this figure increases to approximately 80%. Of concern, despite decades of research, no drug has been found which effectively prevents the progression of the disease. Fortunately, emerging evidence indicates that multi-modal, lifestyle based interventions, may at least stabilise cognition.

Therefore the purpose of this study is to evaluate the effectiveness of a 6 month, personalised, lifestyle based, multi-modal intervention to stabilise or improve cognition in those with MCI.

2. Why have you been invited to participate?

We are asking individuals, aged 65 to 85 years, who suspect they have MCI, or who are diagnosed with MCI, to consider taking part in this vital research as a "*participant*", together with a close *"companion"*.

3. Who is eligible to be a participant ? – *The Screening Process*

We will need to conduct a number of assessments to determine if a potential participant is eligible to take part in this study. These are outline in Table 1 below.

Table 1: Eligibility assessments

Method	What is being assessed	Who completes the assessment	Location	Time (min)
Online Survey	Change in cognition over time	Companion	Home or other suitable location	15
	Background, medical history, medication use	Participant		30
	Sleep apnoea	Participant		10
	Functional capacity	Companion		15
Interview	Participant mood	Companion	Home or other suitable location	30 each
Computer Assisted	Cognition	Participant	Research Institute or other suitable location	60
Fasting blood sample (5-10 mL)	Biochemical markers of: - diabetes - hyper/hypothyroidism	Participant	blood collection centre	30
Physical Assessments	Blood Pressure	Participant	Home or other suitable location	15
	Medical Cert. for exercise	Participant (& companion if desired)	GP clinic	30
			Total Participant Time	2 hr 55 min
			Total Companion Time	1 hr

As indicated in Table 1 above, to determine eligibility potential participants will be asked to:

- complete a series of online surveys,
- undergo an interview,
- complete a number of cognitive assessments,
- have their blood pressure measured,
- provide one 5 – 10 mL, 12 hour fasting blood sample and
- provide a medical certificate indicating it is safe for them to exercise.

To provide their 12 hour fasting blood sample, potential participants will need to:

i. Consume no food or drink, except *water,* within 12 hours of their blood test. Thus, if blood is scheduled for collection at 8:00 AM, no food or liquid can be ingested after 8:00 PM the previous evening.
ii. Present with their request form to any Sonic Healthcare or Laverty Pathology collection centre (other blood collection centres may be used as appropriate and arranged by researchers).

The blood sample provided at this time will be analysed to determine the presence of poorly controlled diabetes and/or thyroid problems.
During Screening, companions will be requested to complete an online questionnaire and will be asked questions in an interview about the potential participants mood.

In total, these Screening assessments will take about 3 hrs for the potential participant to complete and about 1 hour for the companion to complete. To reduce any strain this may cause, assessments can be completed over a period of up to five days.

4. Who is eligible to be a companion?
There are no assessments to determine companion eligibility. The only stipulation is that companions be able and willing to support participants during the six month study. This will include taking part in a number of activities. A change in lifestyle, paralleling that of the participant, is highly desired. Companions should also be close enough to the participant to competently answer questions about mood and changes in cognition over time. Preferably they will be living with the participant.

If companions would like to take part in physical activity sessions, a medical certificate will need to be provided.

5. What does this study involve for those eligible to take part?
If eligible to take part in this study, both the participant and their companion will be randomly allocated, as a pair, to one of two groups; the Intervention or the Control. For every five pairs entering the study, three will randomly allocated to the Intervention and two will be randomly allocated to the Control. Please note, after participation in the Control Group individuals will have the opportunity to take part in the Intervention if they choose.

CONTROL GROUP (Complete assessments only)
As part of the Control Group, both the participant and their companion will be asked to complete a number of assessments. This will occur at two time points, over a period of 24 weeks (i.e. 6 months). The types of assessments participants and companions of the Control Group will be asked to complete are described in Point 6 (pg. 7) and Point 7 (pg. 10) respectively. Assessment timing is described in Point 8 (pg. 11).

At the end of the study, a copy of assessment results will be provided. At this time, participants and companions of the Control Group will have the opportunity to immediately commence the Intervention, as detailed below, if they choose.

INTERVENTION GROUP (Intervention + Assessments)

INTERVENTION
Pairs allocate to the Intervention Group will be asked to complete the Intervention as detailed below.
The Intervention runs for 24 weeks (i.e. 6 months) and is divided into three phases (Figure 1, pg. 7).

Phase 1: Preparation (14 days)
The purpose of Phase 1 is to help the participant (and companion), gradually adjust to the changes in

lifestyle commencing in Phase 2. To achieve this, during Phase 1 we will ask the participant to a) reduce intake of meat, coffee and alcohol, b) increase intake of fruit and vegetables and c) cease consumption of non-prescribed supplements. If not already partaking in regular physical activity, the participant will also be asked to commence light levels of activity as appropriate for their health (e.g. walking). It is highly desirable and helpful if the companion chooses to make the same lifestyle adjustments at this time.

Phase 2: Intensive (5 ½ days)

The purpose of Phase 2, is to help the participant adopt brain healthy behaviours. We will ask and assist the participant, with the support of their companion, to reach the goals listed in Table 2 below. Some of these, including Nutrition and Cognitive training, are anticipated to be achieved almost immediately. Other, including Physical activity and Optimised biorhythms may take longer.

Table 2. Intervention focus areas and ultimate goals

Area	Ultimate Goal
Nutrition	Consumption of a dietician approved, brain healthy, plant-based diet.
Cognitive training	30-minutes each day, 5 days per week.
Optimised biorhythms	Between 7.5 and 8.5 hours of non-fragmented sleep each night.
Physical activity	30-60 min of moderate-intensity activity, 5 days/wk. Resistance exercises, at least 2 days/wk. Flexibility exercises, at least 2 days/wk.

To start progress towards these goals, during the Intensive both the participant and companion will need to visit the Australasian Research Institute, another location (i.e. office space or clinical rooms), or have research staff visit their home, for 5 ½ consecutive days. During this time, the participant will be asked to take part in the activities listed in Table 4 on the following page. It is important that the companion accompany the participant to each activity, even if direct involvement is not possible.

An evidence based, dietician approved, brain healthy, plant-based diet will be modelled through the provision of ALL meals to both the participant and companion during this Phase. Participants will also be asked to commence the daily consumption of a novel supplement (*BES*up) This includes various nutrients, scientifically validated to promote brain health. Please refer to Table 3 to view the ingredients. Please check that you, as a potential participant, are not allergic to any of these.

Table 3. Ingredients

Table 4. Activities to complete/commence during Phase 2- Intensive

Activity	Quantity	Time (min)	Description
Cooking Class 	1	60	During the Intensive, participants and companions will be asked to take part in one Cooking Tutorial. This will be supplemented with an additional three tutorials during Phase 3. In these tutorials the preparation of simple, whole food, plant-based meals from easily obtainable ingredients will be demonstrated. One breakfast, main meal, light meal and dessert will be taught.
Exercise 	5	60	During the Intensive participants and companions (who have provided a medical certificate) will take part in five, one-hour, group physical activity sessions. These sessions will be run by an exercise physiologist (EP) or qualified personal trainer (PT).
Brain Training 	5	30 – 60	During the Intensive the participant will commence a course of Computer based Cognitive Remediation Therapy (i.e. brain training). This will involve completing a series of exercises, like computer games, designed by scientists to improve various aspects of cognition. The difficulty of each exercise will fluctuate depending on individual performance. Starting in the Intensive, participants will be asked to train 30-min per day, 5 days per week for the duration of the study.
Lecture Series 	9	60	Participants and companions will commence the viewing of nine, approximately one-hour educational lectures. Topics covered include: 1. Welcome, Our Amazing Brain, MCI, Study Overview 2. CCRT; Your Brains Gym 3. Nutrition Part 1 4. Nutrition Part 2 5. Supplements: What is There Place? 6. What's Next? 7. The Importance of Keeping Active 8. The Importance of a Good Night's Rest 9. The Impact of Stress and Stress Management Techniques

Phase 3: Home Implementation

Part A (4 weeks)

During Home Implementation Part A, a Study Coach will visit the participant's home 1-3 times per week. The number of weekly visits will be decided by the participant and companion.

The purpose of these visits is to help implement within the home, the changes in behaviour initiated during the Intensive. The Study Coach may help the participant and companion, as desired, to;

- remove/replace unhealthy food,
- locate healthy food items in store,
- assist with food label reading,
- demonstrate cooking techniques,
- adapt recipes to suit personal tastes and study guidelines,
- answer basic/technical questions regarding the Exercise Plan (see below),
- answer technical questions regarding brain training.

During this phase participants will also start their personalised exercise plan. This plan will help participants safely progress to the level of physical activity listed in Table 2. It is highly desirable for companions to join participants in their exercise routine if safe to do so (as stipulated by their doctor).

Participants and their companion will also be asked to join fellow study members in one group exercise session per week. This will be run by the Study Exercise Physiologist or Personal Trainer.

Part B (19 weeks)

During Home Implementation Part (B), in person visits by the Study Coach will be replaced by weekly phones calls and/or online meetings.

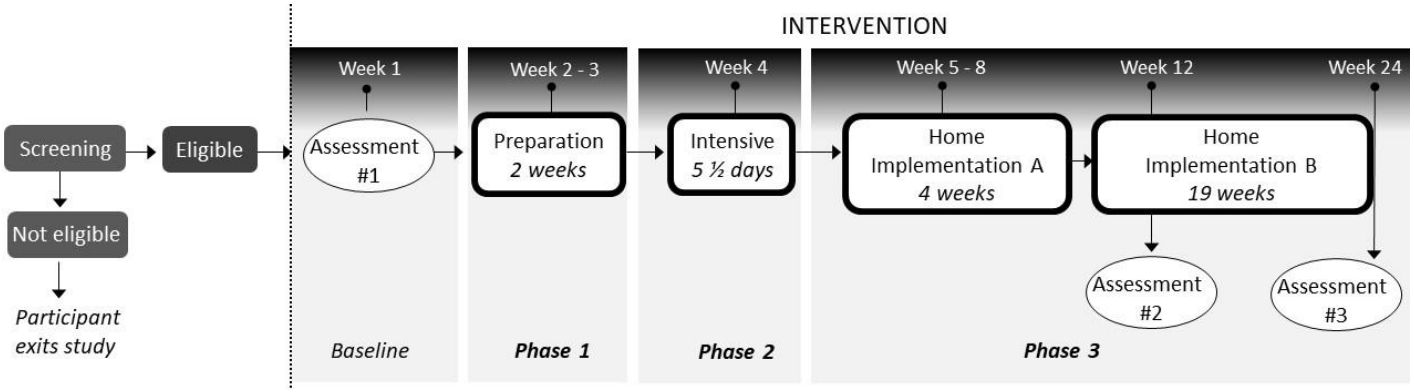
Participants, and their companions, will be asked to continue their personalised exercise plan and weekly group exercise session. The exercise plan will be updated at least twice during this period.

Throughout Phase 3, the Study Coach and Chief Investigators will have weekly meetings to discuss the progress of participants and any issues/concerns/complex questions raised by either the participant or companion. This will occur in consultation with the Study Doctor or Exercise Physiologist/Personal Trainer as appropriate.

ASSESSMENTS

Participants and companions of the Intervention Group will be asked to undergo a series of assessments. The information gained from these assessments will be used to personalise the Intervention and determine its effectiveness. Assessment results, and any personalised recommendations, will be discussed with both the participant and companion after each of the three assessment time points. This consultation may occur online or in person and may take up to one hour. The assessments to be completed are described in Point 6 (pg. 7) and Point 7 (pg. 10) respectively. Assessment timing is described in Point 8 (pg. 11).

Figure 1. Intervention Group Study Schedule



6. What assessments will I, as a <u>participant</u>, be asked to complete?

The types of assessments participants will be asked to complete are outlined below. These are the same, regardless of group allocation (i.e. Control or Intervention Group).

a. *Cognition & Functional Capacity*

Assessment of functional capacity and various aspects of cognition will involve completing a number of interactive, problem solving tasks on a computer and tablet. See Figure 2.

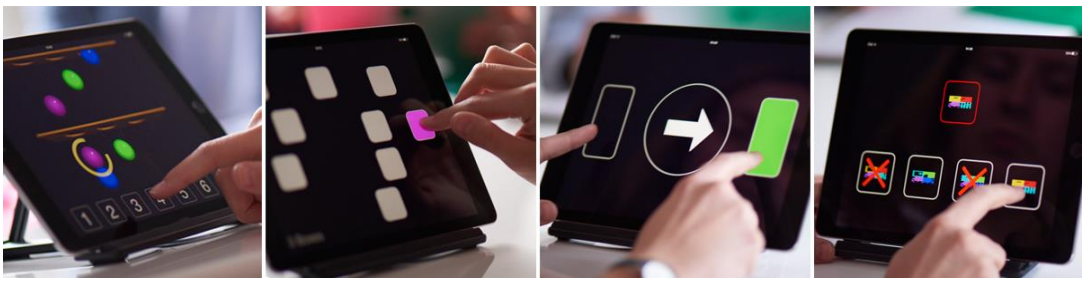


Figure 2. Assessment of Cognition

b. *Estimate of Prior Intelligence*

Prior intelligence will be assessed by a simple reading test. The participant will be shown and asked to pronounce 70 irregularly spelled words.

c. *Quality of Life & Pain*

Quality of life and pain levels will be assessed by completion of an online questionnaire.

d. *Blood Pressure*

Blood pressure will be measured after a 10 hour, overnight fast. To do this a cuff will be placed on the upper right arm. The participant will then be asked to rest for 15 minutes, lying down. The cuff will then inflate and blood pressure will be measured using a semi-automatic instrument. As blood pressure is influenced by talking, conversation should be avoided during this time. A minimum of four recordings will be taken.

e. Pulse Wave Velocity (PWV)

Figure 3. *Pulse Wave Velocity*

PWV is a measure of blood vessel health. It is safe, painless and non-invasive. Before completing this test both strenuous physical activity and alcohol should be avoided for 24 hours and a 10 hour fast will be required. On the morning of the assessment only water should be consumed. This includes refraining from supplement intake.

The assessment will take place between 6:00 and 10:00 AM. While lying down, an inflatable cuff will be placed on the upper leg and the distance between the cuff and various anatomical locations measured. The participant will then be asked to rest for 15-minutes. During this period, blood pressure will be measured as described in point (e) below.

Following the rest period, a transducer (a small microphone-like device) will be placed on the neck. The leg cuff will simultaneously inflate putting pressure on the leg. A number of clicks will then be heard while the computer measures the speed of the pulse as it travels from the neck to upper leg. Three measurements will be taken. See Figure 3.

f. Hand Grip Strength

The grip strength of both the left and right hand will be measured. This involves squeezing a device called a dynamometer as hard as possible. Two trials on each hand will be conducted. See Figure 4.

Figure 4. *Hand Grip Strength*

g. Body Shape

We will measure height and weight using a height stick and scale. To do this, shoes, socks and any heavy objects from pockets will need to be removed. In addition to weight, the scale will simultaneously measure muscle, bone, water and total fat mass as well as visceral fat (i.e. fat that's stored within the abdominal cavity).

Figure 5. *Eye Scan for Antioxidants*

h. Eye Antioxidants

The level of eye antioxidant pigments will be assessed. This will involve looking into an instrument at a stimulus light. The participant will be asked to press a button when they see a light flicker. See Figure 5.

i. Diet

Research staff will help the participant download the Research Food Diary App onto either their smartphone or the smartphone of their companion. Using this software, at each assessment time point all food and liquids consumed for three days will be recorded. This will include two weekdays and one weekend day. Companions may help participants complete this task if need be.

j. Sleep & Physical Activity

We will collect sleep and physical activity data using a sleep/activity tracker. The tracker used in the study is a light, slimline device that should be worn on the non-dominate wrist. It is waterproof and can be worn in the shower and while swimming. Participants will be asked to wear the tracker continuously for 7 days. During this period the tracker will log information about sleep, physical activity and heart rate. See Figure 6.

Figure 6. *Activity Tracker*

k. Physical ability

Participants will be asked to perform six tasks to assess physical ability. These are illustrated Figure 7.

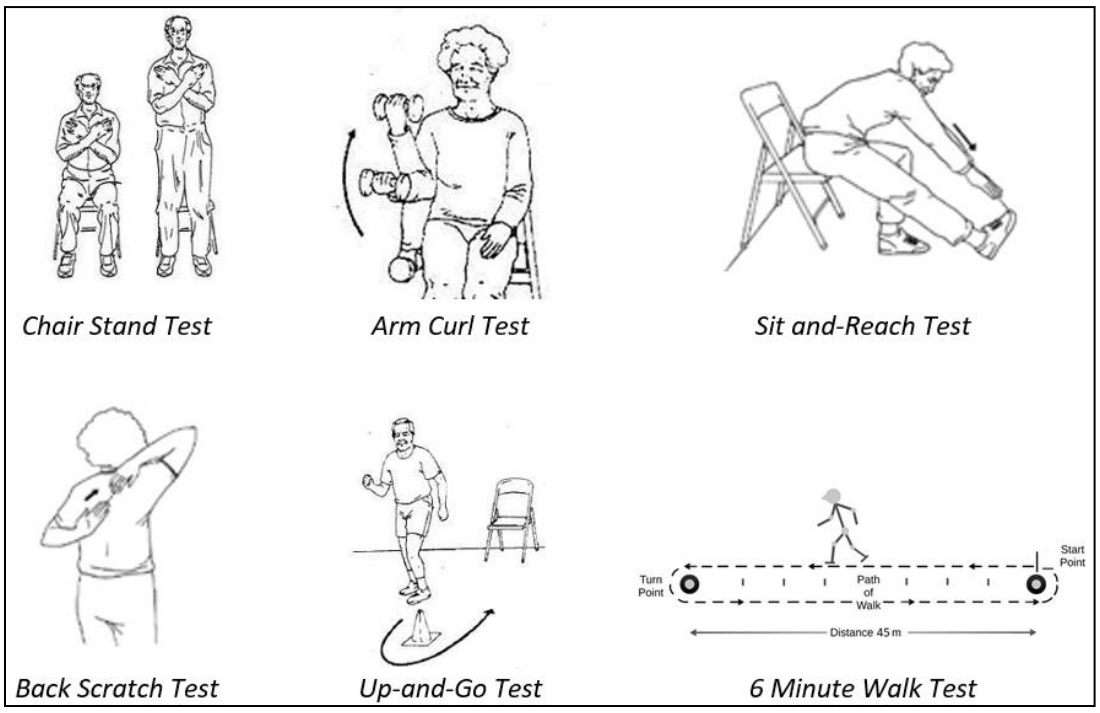


Figure 7. *Physical Ability Tests*

m. Blood Biomarkers

In addition to a Screening blood sample, participants of the Intervention Group will be asked to provide a further 3 separate blood samples. Participants in the Control Group will be asked to provide a further 2 separate blood samples. The volume of each sample will be about 35 mL or 2 1/3 tablespoons.

Each time a blood sample is required participants will need to:

i. Consume no food or drink, except *water,* within 12 hours of their blood test. Thus, if blood is scheduled for collection at 8:00 AM, no food or liquid can be ingested after 8:00 PM the previous evening.

ii. Present with their request form to any Sonic Healthcare or Laverty Pathology collection centre (other blood collection centres may be used as appropriate and arranged by researchers).

The blood samples will be analysed for the markers listed in Table 4. Please note that not all of the markers listed will be analysed in every sample provided.

Table 4. Blood biomarkers to be analysed

Category	Associated Biomarkers
Vascular health	Triglycerides
	Cholesterol
	Homocysteine
Sugar regulation	HbA1c
	HOMA2
	Insulin
Inflammation	hsCRP
	White blood cells
	Erythrocyte Sedimentation Rate
	Kynurenine/ Tryptophan ratio
	Tumour necrosis factor receptor-1
Oxidation potential	Total antioxidant Capacity
	Hydroperoxides
Iron studies	Iron
	Ferritin
	Transferrin
	Transferrin Saturation
Nutrition	Omega-3 Index
	Vitamin B12
	Folate
	Vitamin D
Cell energy	NAD+
Brain health	Neurofilament light chain
	Phosphorylated tau
	β-Amyloid
Genes linked to Alzheimer's	APOE genetic status

7. What assessments will I, as a <u>companion</u>, be asked to complete?

The assessments companions will be asked to complete are outlined below. These are the same, regardless of group allocation (i.e. Control or Intervention Group).

a. *Activities of Daily Living*

Companions will be asked to fill out an online questionnaire about how well the participant performs normal activities of daily living, such as household duties, catching public transport or shopping.

b. *Mood*

A member of the research team will talk to the companion about various aspects of the participants mood, including their experience of anxiety and sadness.

The companion will also be asked to assist the participant in completing some of their assessments as needed and appropriate.

8. When, and how often, will I be assessed?

As indicated in Table 5 and 6, the number of assessments participants and companions will need to complete, and when, will depend on their Group allocation. Please note, these tables also include assessments performed during Screening, discussed in Point 3 above.

At each time point assessments may be completed over a period of up to 5 days as convenient for the participant and companion. This will occur regardless of group allocation.

Assessments may be completed either at the participants home, the Australasian Research Institute or another suitable location such as a clinic or office.

Table 5. <u>INTERVENTION GROUP</u> assessment schedule for participant & companion

Participant Assessments	Assessment Time Points			
	Screening	Baseline	Week 12	Week 24
Cognition	✓	✓	.	✓
Quality of Life & Pain	.	✓	.	✓
Background	✓	.	.	.
Sleep Apnoea	✓	.	.	
Mood	✓	✓	(if indicated)	✓
Pulse Wave Velocity	.	✓		✓
Blood Pressure	✓	✓	✓	✓
Med Cert. for exercise	✓	.	.	.
Hand Grip Strength	.	✓	.	✓
Body Shape	.	✓	✓	✓
Eye Antioxidants	.	✓	✓	✓
Diet	.	✓	✓	✓
Sleep & Physical Activity	.	✓	✓	✓
Physical Ability	.	✓	✓	✓
Blood Biomarkers	✓	✓	✓	✓
~Total Participant Time	2 hrs 55 min	5 hrs 5 min	2 hrs 45 min	5 hrs 55 min

Companion Assessments	Assessment Time Points			
	Screening	Baseline	Week 12	Week 24
Change in Cognition	✓	.	.	.
Activities of Daily Living	✓	.	.	✓
Mood	✓	✓	(if indicated)	✓
~Total Companion Time	1 hr	30 min	0*	1 hr 15 min

** An additional 60 min may be required to complete mood related interview if indicated*

Table 6. <u>CONTROL GROUP</u> assessment schedule for participant & companion

Participant Assessments	Assessment Time Points		
	Screening	Baseline	Week 24
Cognition	✓	✓	✓
Quality of Life & Pain		✓	✓
Background	✓		
Sleep Apnoea	✓		
Mood	✓	✓	✓
Pulse Wave Velocity		✓	✓
Blood Pressure	✓	✓	✓
Med Cert. for exercise	✓		
Hand Grip Strength		✓	✓
Body Shape		✓	✓
Eye Antioxidants		✓	✓
Diet		✓	✓
Sleep & Physical Activity		✓	✓
Gut Bacteria		✓	✓
Physical Ability		✓	✓
Blood Biomarkers	✓	✓	✓
Total Participant Time	2 hrs 55 min	5 hrs 5 min	5 hrs 55 min

Companion Assessments	Assessment Time Points		
	Screening	Baseline	Week 24
Change in Cognition	✓		
Activities of Daily Living	✓		✓
Mood	✓	✓	✓
Total Companion Time	1 hr	30 min	1 hr 15 min

9. What are the risks/discomforts?

The majority of assessments conducted in this study are non-invasive and pose no risk. Over the course of the study we will however ask the participant to provide up to 4 blood samples. Blood will be collected by a qualified phlebotomist using best practice techniques. A small degree of pain from the needle insertion will likely be felt, and a small bruise may develop.

The DNA in one blood sample will be analysed to determine what forms of APOE (genotype) are present. The APOE gene exists in three different forms – e2, e3, and e4. APOE e4 has been associated with an increased risk of Alzheimer Disease (AD). It is important to note, in terms of lifetime risk, most APOE e4 individuals will never develop AD and there are many people with AD who are e4 negative. On the Consent Form (last page), there is a space to indicate whether or not a participant would like to know their APOE gene status. If YES is indicated and an APOE e4 positive result is found, a genetic counsellor will contact the participant and companion to disclose the result and discuss its implications.

As part of this study we may detect other adverse findings of physical and/or clinical relevance. If this occurs the study doctor will advise participants of the most appropriate next course of action which may be to consult a General Practitioner, to whom a copy of the relevant results will be supplied.

Please be aware that the companion will be asked a number of questions about the participant's mood. While not diagnostic, results may suggest the presence of anxiety or depression. If results indicate the presence of severe anxiety, we will advise the participant of the most appropriate action, which may be to seek help from their General Practitioner. Participants will be able to continue taking part in the study. However, if *severe* depression is indicated during Screening, potential participants will not be eligible to take part in either the Intervention or Control. Further if *severe* depression develops throughout the study, participants will be asked to discontinue their involvement. In each instance we will advise the participant of the most appropriate action, which may be to seek help from a General Practitioner.

Please note, regardless of group allocation, involvement in this study as either a participant or companion requires the commitment of a significant quantity of time. If allocated to the Intervention Group, involvement as a participant will also require a major change in lifestyle for the study duration (i.e. 6 months). Participants, with the support of their companion will be asked to do their best to work towards the goals listed in Table 2, pg.4. Please take the time to consider likely effects and discuss this with members of your family/friends who may be impacted.

The following risk/discomforts apply if randomised the Intervention Group only

As part of the recommended change in lifestyle, participants allocated to the Intervention Group will be asked to consume *BES*up, a nutritional supplement, each day (refer to Section???). All ingredients in this product are approved for consumption by the Australian Therapeutic Goods Association. Please double check that as a potential participant, you are not allergic to any of the ingredients listed in Table 3. Importantly consumption of this product may result in the following side effects:

- fishy body odour
- excessive sweating
- excessive salivation
- dizziness
- reflux
- nausea
- diarrhoea
- abdominal pain/cramping
- bloating
- belching
- vomiting
- thirst
- increased urine output
- transitory skin flushing
- transitory skin burning
- yellow urine
- skin yellowing

If allocated to the Intervention Group participants will be asked, and companions encouraged, to follow a diet that likely significantly differs from their usual food intake. As the body adapts to this change, *headaches, bloating, diarrhoea or constipation, irritability and fatigue* may be experienced. These side effects may take 1 to 2 weeks to reside.

Participants in the Intervention Group will also be asked to increase their levels of physical activity. There exists the remote possibility during exercise of adverse changes including, but not limited to, *abnormal blood pressure, fainting, dizziness, disorders of heart rhythm, and in very rare instances heart attack, stroke, or even death*. There also exists the *risk of bodily injury* including, but not limited to, injuries to muscles, ligaments, tendons, and joints. Every effort will be made to minimise these occurring.

10. Will I be reimbursed/paid for taking part in this study?

Participation in this study is voluntary; there is no payment for taking part.

Participants of both the Intervention and Control will however get a report of their assessment results. Each report is valued at approximately ??? Those in the Control Group will also have the option of later taking part in the Intervention.

Participants and companions may be reimbursed for travel costs. If you would like reimbursement for travel/parking, please keep any parking or public transport tickets/receipts as well as a record of kilometres travelled by car.

11. Can I find out what the researchers learn?

We need to collect and analyse data from lots of people before we can draw meaningful conclusions. This can take many years. As such group results from this study will be made known through the media and/or scientific publications. If interested, participants or companions can however directly contact Chief Investigator, Dr Ross Grant on 0419 288 492 or Dr Jade Berg on 0410 434 707, who will provide group results if/when available.

12. What happens if I do not take part or wish to withdraw from this study?

Participation in this study is completely voluntary. Your decision will in no way affect future relations with your health care provider, the Australasian Research Institute, the Sydney Adventist Hospital, Avondale University or Vitality Works.

If, at any time, a participate finds their involvement is becoming too difficult, they *can cease their involvement without reason*.

If this occurs, with the participants permission, we will keep all previously collected information. If permission is not provide, all identifiable information will be destroyed.

13. What will you do with my results?

Participant and companion assessment results will be combined into a database containing the results from others who have also taken part. This data will be analysed statistically to determine if the everyday function, cognition, mood and biomarkers of brain health of people who completed the Intervention improved compared to those who did not.

14. How will my privacy be protected?

The privacy of both participants and companions is very important to us. All results (i.e. data) will be handled in accordance with applicable Australian federal and state privacy laws. This involves the enforcement of a number of physical and technical safeguards.

<u>Technical Safeguards</u>

All online programs used in the study comply with the Health Insurance Portability and Accountability Act (HIPPA), amongst others. Data will be stored, in an encrypted format, in a secure data centres.

'Online' data will be periodically exported into a local excel file. This will only be accessible by the Chief Investigators and will be protected using unique user IDs and passwords.

Physical Safeguards

With the exception of the Consent Form, where possible information provided by participants and companions will only be identified using a unique, random, computer generated code. Some assessments however will initially generate individually identifiable results, due to either the nature of the assessment or the information required by assessment specific software (for the calculation of scores). In such instances identifiers will be removed as soon as possible for storage.

While standard pathology results will be accessible by laboratory staff, as is routine, only the Chief Investigators will have unrestricted access to results linked to the identity of participants and companions. The Study Doctor, Exercise Physiologist/Personal Trainer and Study Coach will only be provided information that is required for them to fulfil their role.

Apart from the Consent Form, only the participants/companions ID number and initials will be recorded on any hard copy documents generated as part of the study. These, and the Consent Form, will be held in separate locked cabinets by the Chief Investigator.

Any information that is obtained in connection with this study and that can be identified with either the participant or companion will remain confidential and will be disclosed only with their permission, except as required by law or in case of an exceptional emergency.

At the end of the study de-identified study documents will be stored in password protected files on a hard-drive, and/or in a locked unit in the Chief Investigators Archives, for 15 years as required by law.

We plan to publish the results of this study in relevant scientific/medical journals so that others may benefit from our findings. We may also make a public statement in the popular media following analysis of the group data. In any publication, information will be presented in such a way that individuals can not be identified.

15. What happens if I am physically injured on site?

If a participant or companion is injured on site, either at the Australasian Research Institute, the Sydney Adventist Hospital, Avondale University or a collaborating clinic, office or gym, we will advise that a GP be consulted. If the injury is serious we will call the ambulance for assistance. We will also complete an incident report form and review any aspects of OH&S as necessary.

It is the recommendation of the independent ethics committee responsible for the review of this study/investigation that the participant/companion seek independent legal advice.

16. What happens if I'm partaking in illicit activities?

If a member of the Research Team becomes aware that a participant or companion is partaking in an illicit activity that has criminal implications, legal advice will be sought; this may involve contacting the NSW Police.

17. What should I do if I want to discuss this study further before I decide?

We encourage interested individuals to discuss with family/friends their potential involvement in this study, and what will be required of them if they take part. We also encourage interested individuals to discuss their potential involvement with their general practitioner (GP).

If you have any questions please feel free to contact the Chief Investigators:

- Dr Ross Grant: 0419 288 492 OR rossg@sah.org.au
- Dr Jade Berg: 0410 434 707 OR jade.berg@sah.org.au

18. Who should I contact if I have concerns about the conduct of this study?

This study has been approved by the Bellberry Limited Human Research Ethics Committee.
Written complaints and concerns may be directed to;

Bellberry Limited
129 Glen Osmond Road
Eastwood SA 5063
Email: bellberry@bellberry.com.au

Any complaint you make will be treated in confidence and investigated.

Thank you for taking the time to consider this study.

If you wish to take part, please sign the appropriate Consent Form on the following pages and return ????.

CONSENT FORM - PARTICIPANT

Brain enhancement study (BES): Can optimising biochemical parameters (targets) via participation in a multi-modal Lifestyle-based intervention improve cognition in amnestic MCI.

I _____(participant name) the undersigned hereby voluntarily consent to my involvement in the research project as titled above.

I acknowledge that the nature, purpose and risks of the research project and alternatives to participation have been fully explained to my satisfaction by _____.

Specifically, the details of the procedure(s) proposed and the anticipated length of time it will take, the frequency with which the procedure(s) will be performed and an indication of any discomfort that may be expected have been explained to me.

- I freely agree to take part in this research project as a participant, according to the conditions in the Information Statement which I confirm has been provided to me.
- I understand that my involvement in this study may not be of any direct benefit to me.
- I understand that I may be randomly assigned to either the Intervention or Control Group, the later receiving standard care.
- I understand that if I am randomly to the Intervention Group I will be asked, with my companion, to attend the Australasian Research Institute, another suitable location or have research staff visit my home for 5 ½ consecutive days.
- I understand that if assigned to the Intervention Group, participation will likely involve significant changes to my lifestyle and agree to do my best to work towards any recommended changes in lifestyle.
- I understand that involvement in this study will take a considerable amount of time.
- I understand that in order to take part in this study, I need a study companion.
- I have been given the opportunity to have a member of my family or another person present while the study is explained to me and have been encouraged to discuss the research project with someone I trust.
- I have been told that no information linked to me will be divulged to unauthorised third parties and the results of any tests involving me will not be published so as to reveal my identity.
- I understand that my results may be accessed for quality assurance, auditing and in the event of a adverse event and I consent to this access.
- I understand that I am free to withdraw from the study at any stage without prejudice.
- I declare that all my questions have been answered to my satisfaction.
- I have read and I understand the Information Statement, version 1, dated 24/02/2022

Do you want to know your APOE gene status? ○ Yes: I would like to know the form of my APOE gene

○ No: I would like the form of my APOE gene kept from me and my companion

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I confirm that I have no known allergies to the ??? ingredients listed in Table 3. ○ Yes ○ No

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Do you consent for left over blood samples to be stored and potentially analysed for markers not outlined in this document to further this research, for which approval by a Human Research Ethics Committee will be sought? ○ Yes ○ No

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…… …… ……/…./……

Participant Name **Participant Signature** **Date**

Participant Contact Number (mobile) ……

…… ……. ……/…./……

Name of Witness **Witness Signature** **Date**

……...

Witness Address

Declaration by Principal Investigator (PI) or Co-Investigator (CI):

A verbal explanation of the research project, its procedures and risks has been given to the participant and parent/guardian of the participants and I believe that both have understood that explanation**.**

…… …… ……/…./……

Name of PI or CI **PI or CI Signature** **Date**

Office use only
Participant Identification #

……..

CONSENT FORM - COMPANION

Brain enhancement study (BES): Can optimising biochemical parameters (targets) via participation in a multi-modal Lifestyle-based intervention improve cognition in amnestic MCI.

I _____(companion name) the undersigned hereby voluntarily consent to my involvement in the research project as titled above.

I acknowledge that the nature, purpose and risks of the research project and alternatives to taking part have been fully explained to my satisfaction by _____.

Specifically, the details of the procedure(s) proposed and the anticipated length of time it will take, the frequency with which the procedure(s) will be performed and an indication of any discomfort that may be expected have been explained to me.

- I freely agree to take part in this research project as a "companion", according to the conditions in the Information Statement which I confirm has been provided to me.
- I understand that my involvement in this study may not be of any direct benefit to me or the participant who is known to me.
- I understand that I may be randomly assigned, with the participant who is known to me, to either the Intervention or Control Group and that if assigned to the Control Group, the participant who is known to me will receive standard care.
- I understand that if randomly to the Intervention Group I will be asked, with the participant that is known to me, to attend the Australasian Research Institute, another suitable location or have research staff visit my/the participants home for 5 ½ consecutive days.
- If assigned to the Intervention, I agree to do my best to support the participant who is known to me, work towards any recommended changes to their lifestyle. I understand that these are likely significant.
- I understand that involvement in this study will take a considerable amount of time, both for myself and the participant who is known to me.
- I have been encouraged to discuss the research project with someone I trust.
- I have been told that no information linked to me or the participant who I know, will be divulged to unauthorised third parties and the results of any tests involving me will not be published so as to reveal my identity.
- I understand that information I provide may be accessed for quality assurance, auditing and in the event of a serious adverse event and I consent to this access.
- I understand that I, and the participant who I know, are free to withdraw from the study at any stage without prejudice.
- I declare that all my questions have been answered to my satisfaction.
- I have read and I understand the Information Statement, version 1, dated 24/02/2022

…… …… ……/…./……
Companion Name **Companion Signature** **Date**

Companion Contact Number (mobile) ……

Declaration by Principal Investigator (PI) or Co-Investigator (CI):
A verbal explanation of the research project, its procedures and risks has been given to the participant and parent/guardian of the participants and I believe that both have understood that explanation**.**

…… …… ……/…./……
Name of PI or CI **PI or CI Signature** **Date**

Office use only
Companion Identification #

……..