

# A Randomized Controlled Trial of Adherence to a 24-Month Home-Based Physical Activity Program and the Health Benefits for Older Adults at Risk of Alzheimer's Disease: The AIBL Active-Study

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## Abstract.

**Background:** Previous studies have demonstrated that physical activity (PA) interventions can improve physical and cognitive outcomes in older adults, but most have been relatively short in duration (<1 year) with a few having specifically targeting individuals at risk of developing Alzheimer's disease.

**Objective:** To examine adherence and physical health outcomes in a 24-month home-based PA intervention in older adults at risk of Alzheimer's disease.

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**Methods:** Participants 60 years and older with mild cognitive impairment (MCI) or subjective memory complaints (SMC) with at least 1 cerebrovascular risk factor recruited from The Australian Imaging Biomarkers and Lifestyle Flagship Study of Aging (AIBL) were randomized to a PA or control group ( $n = 106$ ). The control group continued with their usual lifestyle. The PA group received a 24-month home-based program with a target of 150 minutes/week of moderate PA and a behavioral intervention. Retention (participants remaining) and PA adherence (PA group only, percent PA completed to the PA prescribed) were determined at 6, 12, 18, and 24 months. Assessments at baseline, 6, 12, and 24 months included, PA; fitness; body composition and fat distribution. Key outcome measures were PA adherence and PA.

**Results:** The 24-month retention rate (97.2%) and the median PA adherence 91.67% (Q1–Q3, 81.96, 100.00) were excellent. In the long-term the intervention group achieved significantly better improvements in PA levels, leg strength, fat mass and fat distribution compared to the control.

**Conclusion:** This study demonstrates that in this target group, long-term PA adherence is achievable and has physical health benefits.

**Keywords:** Adherence, cerebrovascular disease, mild cognitive impairment, physical activity, subjective memory complaints

**Trial Registration:** Australia New Zealand Clinical Trials Registry ACTRN12611000612910

## INTRODUCTION

Physical activity (PA) interventions resulting in increased PA and/or aerobic fitness have demonstrated an improvement in cognition in individuals with mild cognitive impairment (MCI) or subjective memory complaints (SMC) who are at increased risk of Alzheimer's disease (AD) [1, 2]. PA interventions have been shown to also provide improvements in fitness, function, mobility, and strength [3–5] in individuals with MCI or AD. Cerebrovascular risk factors (CVR) including physical inactivity, obesity, hypertension, heart disease, type II diabetes, smoking, and hypercholesterolemia, have been associated with increased risk for AD and may be additive [6, 7]. Mid-life adiposity and central obesity have been associated with a greater risk of dementia in older age ( $\geq 65$  years) [8, 9] with higher obesity being associated with greater dementia risk [10]. Physical inactivity and mid-life obesity have been identified as modifiable risk factors for AD [11]. Increasing PA has the potential to reduce fat mass and increase muscle mass and may be an effective lifestyle modification in preserving cognitive function in older age. Identifying effective PA interventions may have additional advantages of not only reducing the risk of AD from inactivity but also from obesity. The effect of PA on these outcomes depends on adherence to the PA program however there is a lack of evidence as to what strategies are effective in increasing adherence to PA interventions in populations at risk [12].

Few PA intervention studies have been long-term, with most ranging from 9 weeks to 12 months [5]. A recent systematic review concluded that supervised

multi-modal exercise for 60 min 2–3 days a week can improve physical function (strength, mobility, walking endurance/cardiovascular fitness) in individuals with various levels of cognitive impairment [5]. However, it is not known if unsupervised or home-based programs can achieve the same results in physical function. We have previously reported good short-term adherence and short and long-term improvements in PA levels with a 6-month home-based PA program in participants with MCI and SMC [1, 13]. Lam et al. [5] reported that functional improvements diminished from 9 weeks to 9 months after the completion of the intervention supporting the view that PA programs need to be continued to maintain improvements. It is unknown if PA programs can be sustained in the long-term to maintain the improvements in function and health initiated in short-term interventions in this target group.

To our knowledge, no other group has investigated in a group at increased risk of AD with CVR factors if they can be motivated to increase their PA, and if this confers fitness, body weight, and body composition benefits in the short and/or long-term. This study addresses the problems of an increase in physical inactivity with age, an increase in obesity, a decline in muscle mass and the increased risk of AD, frailty, and functional fitness. It highlights the challenges of motivating older adults with cognitive concerns or difficulties to maintain beneficial PA levels.

Thus, the aim of the current study was to investigate whether individuals with cognitive problems and additional CVR factors could increase their PA and maintain adherence to a PA program over 24 months. Furthermore, the aim was to evaluate the effects of

the PA program on functional fitness, body weight and body composition of individuals at risk of AD.

## METHODS

### *Study design*

The methods of this parallel single-blind randomized controlled trial have been previously published in detail [14]. The CONSORT statement was used as the framework for development of the methodology for this trial. The main outcome of the study was the change in white matter hyperintensities on MRI in the brain after the 24-month intervention. To achieve a medium effect size of 0.5, 80% statistical power, and a two-sided alpha error level of 0.05, it was estimated that 65 participants would be needed for each group. With an estimated 15% loss to follow-up the aim was to recruit 78 participants per group.

This paper reports the results for the secondary outcomes of retention, PA adherence, PA, fitness, body mass, and body composition measures. Protocols relevant to this paper are described briefly below.

Participants gave informed written consent and the study was approved by the Melbourne Health Human Research Ethics Committee. The project complies with the Declaration of Helsinki 1975.

### *Participants*

#### *Recruitment and screening*

Men and women, aged 60 years and older, with MCI or subjective memory complaints (SMC) and at least 1 CVR factor (physical inactivity, obesity, hypertension, heart disease, type II diabetes, smoking, hypercholesterolemia), were recruited from the Melbourne cohort of the observational study The Australian Imaging Biomarkers and Lifestyle Flagship Study of Ageing (AIBL) [15] to participate in the AIBL Active trial. Potential participants were identified for inclusion and then invited to undertake a telephone-screening interview. The phone screening included the 15-item Geriatric Depression Scale (GDS-15) [16] to establish the presence of clinically relevant symptoms of depression. Those with a score of 6 and higher were excluded. Participants' general practitioners were asked to consent to their patients' involvement in the study. In addition to the above criteria participants were included in the study if they were community dwelling, and understood written and spoken English. All participants had a subjective memory complaint, e.g., all answered yes

to the question "do you have any problems with your memory?". A standardized procedure was used for classification of MCI, which included use of a neuropsychology measure (the Consortium to Establish a Registry for Alzheimer's disease (CERAD) battery) and a global clinical measure (the Clinical Dementia Rating (CDR) scale). The CERAD battery has been shown to be one of the more sensitive tests for detecting MCI [17] and was completed as part of the test battery. The CDR was scored by NL an experienced old age psychiatrist, and a total score of 0.5 was required for classification of MCI.

Participants were excluded if they: a diagnosis of dementia or a Standardized Mini-Mental State Examination score (SMMSE) <24 [18]; were unable to have MRI scans; had a self-reported harmful use of alcohol; had an unstable or life-threatening medical condition; had a medical condition that contra-indicated PA; had severe visual or hearing impairment; or were participating in another randomized controlled trial.

### *Assessments*

Physical activity, physical fitness, body weight, body composition, health, lifestyle, and cognitive outcomes were assessed at baseline, 6, 12, and 24 months. PA adherence was measured at 6, 12, 18, and 24 months.

### *Measurements*

#### *Retention*

Retention was defined as the number of participants remaining in the study at each time-point, 6, 12, 18, and 24 months.

#### *Adherence*

Adherence to the prescribed PA in the PA group only was assessed from self-reported PA diaries that recorded type, frequency, duration, and intensity of the PA. Participants were given diaries in a simplified calendar format with the prescription of individualized PA sessions itemized on the relevant day for completion. The participants marked off the PA session when completed and recorded the perceived intensity on the Borg perceived rate of exertion scale [19]. Any changes to the prescribed PA were also noted and taken into account for the calculation of adherence. The diaries were returned by prepaid mail at the end of each month. Weekly program sheets were also given to participants to place in a

192 prominent place to remind them of their sessions.  
 193 Adherence was calculated as the number of minutes  
 194 of moderate PA completed relative to the prescribed  
 195 150 min/week expressed as a percentage. This was  
 196 determined for 4 stages of the 24-month interven-  
 197 tion period and the total 24-month period; Stage  
 198 1:0–6 months; Stage 2:6–12 months; Stage 3:12–18  
 199 months; Stage 4:18–24 months. Two measures of  
 200 adherence were calculated; AIBL Active adherence  
 201 (AIBLADH) calculated from the PA prescribed for  
 202 the study and total adherence (TotADH) which was  
 203 the calculated from the PA already being done at base-  
 204 line plus the amount of PA prescribed for the study.  
 205 The latter measure was included to minimize and  
 206 monitor any replacement of study PA for habitual PA.

### 207 *Physical activity*

208 *Pedometer:* Participants wore a pedometer (Digi-  
 209 Walker SW-200, Yamax Inc., Tokyo, Japan) for five  
 210 weekdays and the weekend and were requested to  
 211 keep to their usual activities during that week. They  
 212 were given instructions on how (above the right hip  
 213 on a belt worn around the waist) and when (all wak-  
 214 ing hours except when showering or partaking in  
 215 water-based activity) to wear the pedometer, and to  
 216 also record step counts in a 7-day pedometer diary.  
 217 When the pedometer was not worn the time off and  
 218 all activities done during this time were recorded. The  
 219 pedometer and diary were returned by mail.

220 *CHAMPS* (physical activity questionnaire for older  
 221 adults): The pedometer provides an objective mea-  
 222 sure of ambulatory PA but it does not provide any  
 223 information about the intensity of the PA. As we  
 224 were also interested in the intensity and duration of  
 225 different intensities of PA we used the CHAMPS  
 226 questionnaire in addition to the pedometer. This self-  
 227 reported PA questionnaire, designed for older adults,  
 228 collects information on various types of PA, their  
 229 intensity (low, moderate, high, and very high), fre-  
 230 quency, and duration recalled for a typical week over  
 231 the past 4 weeks [20].

### 232 *Physical performance battery*

233 *6-minute Walk Test:* This test assesses cardiovas-  
 234 cular fitness with the participant walking as far as  
 235 possible around a standardized course in 6 min and  
 236 the distance measured in meters [21]. Heart rate is  
 237 recorded every minute, peak heart rate determined  
 238 (Polar FS3c Heart Rate Monitor, Polar Electro Oy,  
 239 Kempele, Finland), and rate of perceived exertion  
 240 (RPE) measured at the end of the test [19].

241 *Sit-to-Stand Test:* A test of functional lower limb  
 242 or leg strength. The participant sits in a standard chair  
 243 and stands up and down 5 times as quickly as possible  
 244 while being timed [22].

245 *Step Test* (balance): A dynamic balance test with  
 246 the participant stepping one foot on then off a 7.5 cm  
 247 high step as many times as possible in 15 s without  
 248 using hand support [23].

249 *Timed Up and Go Test* (TUG): The participant is  
 250 timed in seconds (s) while standing up from a stan-  
 251 dard chair, walking three meters and then returning  
 252 to sit again in the chair [24]. The TUG assesses leg  
 253 strength and agility.

254 *Grip strength:* Measured in kilograms (kg) on both  
 255 dominant and non-dominant hands with a Smedleys  
 256 hand dynamometer [25].

### 257 *Injury and musculoskeletal conditions*

258 All participants were asked to self-report any  
 259 injuries or musculoskeletal conditions, including the  
 260 type, location of the injury, and if this was caused by  
 261 PA on the demographic and lifestyle questionnaire.

### 262 *Body mass, body composition, and body fat 263 distribution*

264 All measures were taken in light clothing and  
 265 without shoes. Height was measured using a fixed  
 266 stadiometer. Body mass, fat mass, %fat, fat free mass,  
 267 and body mass index (BMI) were measured with bio  
 268 impedance using the Tanita Body Composition Ana-  
 269 lyzer (Tanita TBF-300, Japan). Body fat distribution  
 270 was assessed via waist and hip girths. Waist girth  
 271 was measured at the minimum circumference at waist  
 272 level and hip girth was the maximum circumference at  
 273 the level of the greatest posterior protuberance of the  
 274 buttocks. Girths were measured in centimeters (cm)  
 275 3 times using a steel tape (Lufkin, W606PM Cooper  
 276 industries SC, USA) with the median measure used  
 277 as the score.

### 278 *Demographic and lifestyle questionnaire*

279 Participants completed a questionnaire providing  
 280 information about demographic characteristics, self-  
 281 reported medical history, current medications, dietary  
 282 habits (serves/day vegetables, fruit, protein), alco-  
 283 hol consumption, and any injuries or musculoskeletal  
 284 complaints associated with PA. They were asked to  
 285 maintain their usual lifestyle except for the change in  
 286 PA prescribed to the intervention group.

### 287 *Verification of CVR factors*

288 For the CVR factors and related medications a  
289 physician-researcher (ML) adjudicated on the medi-  
290 cal records obtained from each participant's doctor.

### 291 *Program and content evaluation*

292 At 6 months, participants completed question-  
293 naires designed specifically for this study about  
294 aspects of the program as a whole including, enjoy-  
295 ment (e.g., "How enjoyable did you find the physical  
296 activity program?"); understanding (e.g., "Did you  
297 find it easy to follow the program we set out for  
298 you?"); as well as on specific components of the  
299 program and the resources (e.g., "How helpful did  
300 you find the following items that we provided?", for  
301 example: worksheets; newsletters; phone calls; "Did  
302 you enjoy reading the manual and completing the  
303 worksheets?"). They answered "yes" or "no" and/or  
304 rated the item on a scale 1–5 with 1 being the least  
305 and 5 the highest score.

### 306 *Randomization and blinding*

307 At the completion of baseline assessments  
308 participants were randomized to study groups.  
309 Randomization was undertaken in blocks of six par-  
310 ticipants (three in each of the treatment arms). The  
311 blocks were generated in STATA 10 (StataCorp,  
312 TX, USA). An investigator not directly involved in  
313 the recruitment or assessment of participants per-  
314 formed the allocation of participants to a PA program  
315 (intervention) or usual care (control), concealed in  
316 envelopes. This was a single blind study in which the  
317 research staff involved in the collection of the main  
318 outcome variables were not made aware of group  
319 allocation. In this type of study, it is not practical  
320 to blind participants to the intervention and due to  
321 logistical difficulties a sham PA program was not  
322 employed. Blinding, however, was supported by the  
323 allocation of cognitive and physical assessments to  
324 different locations and explicit instructions to partic-  
325 ipants and research staff not to discuss issues related  
326 to PA during the assessments.

### 327 *Physical activity intervention*

#### 328 *Intervention*

329 The intervention package comprised three compo-  
330 nents; the PA program, the behavioral intervention  
331 package, and phone monitoring. The 24-month inter-  
332 vention period was divided into 4 stages. Stage

1:0–6 months; Stage 2:6–12 months; Stage 3:12–18  
333 months; Stage 4:18–24 months. The PA prescription  
334 and type of activity was reviewed at the end of each  
335 stage. Intervention participants attended an individ-  
336 ual PA workshop within 2 to 4 weeks of their baseline  
337 visit. During this 60-min session, the program manual  
338 was given to participants and they received instruc-  
339 tions on their PA program, recording and the use of  
340 the behavioral intervention material.  
341

#### 342 *Physical activity program*

343 The PA program was individualized for each par-  
344 ticipant by the addition of minutes of moderate PA to  
345 their baseline habitual PA with a final target of at least  
346 150 min/week of moderate intensity PA [26]. Partic-  
347 ipants not doing any moderate to vigorous intensity  
348 PA (MVPA) at baseline (defined as 'inactive') were  
349 prescribed the standard walking program (SWP);  
350 150 min/week of moderate walking completed pre-  
351 dominantly as 3, 50-min sessions/ week (with the  
352 option of 5, 30-min sessions/week) [13]. Partici-  
353 pants doing some PA but not reaching the target  
354 were prescribed two additional sessions/week. Those  
355 achieving the target at baseline had one session added  
356 to their PA. Sessions and the rating of perceived exer-  
357 tion (RPE) [19] were recorded in diaries returned by  
358 mail each month. If walking was not appropriate other  
359 moderate intensity activities (RPE 10–12) were pre-  
360 scribed taking into account health problems or other  
361 limitations, for example swimming or cycling. The  
362 PA started slowly and progressed gradually taking 8  
363 weeks to reach the target amount and intensity.

#### 364 *Behavioral intervention*

365 Educational material and recommendations for  
366 a healthy lifestyle (excluding PA information),  
367 were given to both groups. Intervention participants  
368 received a manual containing the PA program and  
369 the behavioral intervention (BI). The BI was based  
370 on the Stages of Change model modified for PA [27]  
371 which we have used previously [13, 28] and further  
372 modified to include the personal regulation of goal  
373 directed behavior or performance [29, 30]. Modifica-  
374 tions included a greater emphasis on identifying and  
375 setting goals, self-monitoring, giving relevant feed-  
376 back, review of progress, and identifying action steps  
377 to enhance self-regulation skills.

378 These strategies were introduced during the work-  
379 shop and supported over the 24-month intervention  
380 with 17 newsletters containing additional motivat-  
381 ing material mailed at regular intervals (4-weekly in  
382 Stage 1, 6-weekly Stages 2–4) and reinforced with

18 phone calls (week 2 then 4-weekly in Stage 1, 6-weekly Stages 2–4). The 15-min standardized and structured calls were used to monitor and give feedback on the participant’s progress and encourage their continuing adherence.

### Control group

The control group continued with their usual PA for the 24-month study period. In addition to the educational material, the control group (usual care) participants received newsletters containing generic non-PA information and were contacted by phone at the same frequency as the intervention group with conversation limited to everyday topics with no discussion about PA. This was to ensure that the control and intervention group had similar study contact. The control group were offered A PA workshop at the end of the study.

### Statistical analysis

All analyses were conducted using Stata 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC) and alpha was set at 0.05. Data were summarized using counts and proportions, means and standard deviations (sd), means and 95% confidence intervals (CI), or median and quartiles (Q1-Q3) as appropriate. The distributions of continuous outcomes were investigated for indications of deviation from normality and if found were log transformed when this produced an improvement. Random effects linear regression with maximum likelihood estimation was employed to test for differences in continuous outcomes over time between intervention and control groups using the interaction of time and group. Time was treated as a factor (categorical) variable. All random effects linear regressions were bootstrapped to ensure p values were robust to any remaining departures from normality. In order to investigate potential differences in the frequency of exercise at different intensity levels (from the CHAMPS questionnaire) between groups over time, a negative binomial random effects regression was applied using a three-way interaction of time, group and intensity (low versus moderate, high and very high combined). Differences in the number of minutes (<150 versus  $\geq$ 150 min) of physical activity between groups over time was investigated in a mixed effects logistic regression model with a three-way interaction of time, group, and intensity. Models were run with and without adjustment for age, sex, and baseline BMI. The selection of

co-variables was based on evidence from the literature and previous experience with PA intervention studies. Body composition models were run with and without adjustment for age and sex. As the adjusted models did not change the result the unadjusted models are reported. In the intervention group, only adherence to the intervention was analyzed using quantile regression due to persistent skew in the distribution. Quantile regression generates estimates based on quantiles, by default the median, rather than the mean which will be biased when the distribution is skewed. A per person cluster variance adjustment was applied to account for the lack of independence between observations over time within participant. The effects of being inactive at baseline, cognitive status (MCI/SMC), and sex on PA adherence were also examined in these regressions.

Differences in the change in the number of serves of fruit, vegetables and protein between groups were analyzed using mixed effects ordinal logistic regression after combining the first two or last two categories where numbers were small. The assumption of proportional odds was assessed using the Brant test.

## RESULTS

### Baseline characteristics

Baseline characteristics in the two groups for the 106 participants who started the study are shown in Tables 1 and 2. The groups were well balanced for baseline characteristics, except that the control group appear to have more retirees, participants on blood pressure medication, and higher alcohol intake. Fifty-seven (53.8%) of the participants were women; 67% ( $n=71$ ) were overweight or obese and 28.3% were diagnosed with MCI ( $n=30$ ). Mean age was 73.16 (5.84) years; were well educated 14.16 (3.59) years; 45.8% ( $n=48$ ) were married or co-habiting; 73.6% ( $n=78$ ) were retired from paid employment; 56.5% ( $n=61$ ) and 31.5% ( $n=34$ ) were classified as ‘low active’ or ‘sedentary’, respectively, based on their pedometer score [31].

### Retention

The participant flow over 24 months is shown in Fig. 1. The overall retention rates were 99.1% (6 months), 98.1% (12 months), 98.1% (18 months), and 97.2% (24 months). There was no significant between-group difference in retention rate. The

Table 1  
Baseline demographic and physical activity characteristics of participants in the 2 study groups in the AIBL Active study conducted in Melbourne, Australia 2011–2014

	Control Group (n = 51)	Intervention Group (n = 55)
Age (y)	70.10 (5.97)	72.29 (5.64)
Sex (n, % female)	28 (52.8%)	29 (52.7%)
Education (y)	14.24 (3.58)	14.09 (3.62)
MCI (N, % of group)	16 (31.4%)	14 (25.5%)
Married/co-habit (n, % of group)	21 (42%)	27 (49.1%)
Retired (n, % of group)	41 (80.4%)	37 (67.3%)
SMMSE	28.78 (1.56)	28.56 (1.63)
Body Mass Index (kg·m <sup>-2</sup> )	26.47 (4.31)	27.46 (4.03)
Overweight/Obese (n, % of group)	31 (60.8%)	40 (72.7%)
Smokers (n, % of group)	2 (3.9%)	2 (3.6%)
Blood pressure medication (n, % of group)	21 (41.2%)	14 (25.5%)
Cholesterol medication (n, % of group)	18 (35.3%)	26 (47.3%)
<sup>a</sup> Vascular risk factors (n)	2.00 (0, 4)	1.00 (0, 6)
<sup>a</sup> Alcohol consumed (gms/week ethanol)	77 (14.90, 121.10)	12.60 (0, 75.70)
Low Active (n, % of group)	29 (54.7%)	32 (58.2%)
Falls history last 6 months (n (%))	21(41.2%)	14 (25.5%)

Values are mean and (SD), <sup>a</sup>median and (Q1–Q3) unless described otherwise. MCI, mild cognitive impairment; SMMSE, Standardized Mini-Mental State Examination score. Vascular risk factors include: physical inactivity, obesity, hypertension, heart disease, type II diabetes, smoking, and hypercholesterolemia. ‘Low active’ was defined as <7500 steps/day for the pedometer score [37].

Table 2  
Adherence to the prescribed and total physical activity program over 24-months for the intervention group in the AIBL Active study conducted in Melbourne, Australia 2011–2014

Adherence	Stage 1 0–6 Months (n = 48)	Stage 2 6–12 Months (n = 46)	Stage 3 12–18Months (n = 40)	Stage 4 18–24 Months (n = 40)	Total 0–24 Months	Change over time <i>p</i> value
AIBLADH (Median, Q1–Q3)	91.67 (83.12, 100.00)	93.17 (80.83, 100.00)	93.33 (82.77, 100.00)	92.48 (80.98, 100.00)	91.67 (81.96, 100.00)	0.90
TotADH (Median, Q1–Q3)	81.46 (68.88, 92.56)	81.10 (74.02, 92.13)	86.25 (71.42, 94.25)	82.41 (59.90, 90.08)	81.83 (69.38, 92.29)	0.30

AIBLADH denotes (%Prescribed adherence), TotADH denotes, (%Total PA adherence). Values are median scores and (Q1–Q3). The *p* value reflects the interaction *p* value that tests for a difference over time within the intervention group with adjustment for sex, MCI status, and baseline ‘inactive’.

479 control participant who withdrew did so before  
480 the start of the intervention and the two interven-  
481 tion participants withdrew at 46 and 94 weeks into  
482 the 96-week intervention. Reasons why participants  
483 (n = 3) withdrew from the study are also shown in  
484 Fig. 1.

#### 485 Physical activity adherence

486 Two participants declined the intervention after  
487 baseline and did not receive a PA program. Fifty-three  
488 (96.3%) attended the workshop session; however,  
489 a further 5 did not start the intervention but they  
490 returned for some follow-up assessments. Of the 7  
491 who did not start the PA intervention, 4 were already  
492 active at baseline and 3 were inactive. Forty-eight

(87.2%) participants recording at least 1 session are  
included in the adherence results. Fourteen partici-  
pants (26.4%) not engaged in PA at baseline were  
prescribed the standard walking program (SWP). For  
the 24-month intervention period, the median scores  
for the prescribed PA (AIBLADH) and the total  
PA (TotADH) were 91.67% (Q1–Q3, 81.96, 100.00)  
and 81.83% (69.38, 92.99), respectively. The median  
adherence scores for the 4 intervention stages and  
the overall 24-month period are shown on Table 2.  
There was no evidence of a significant variation in  
either of these adherence measures over time. Fur-  
ther, sex, MCI status, or baseline inactivity did not  
change these results. The mean RPE (PA intensity)  
over the 24 months was 11.39 (11.22, 11.56) with no  
evidence of a variation in the pattern of change over

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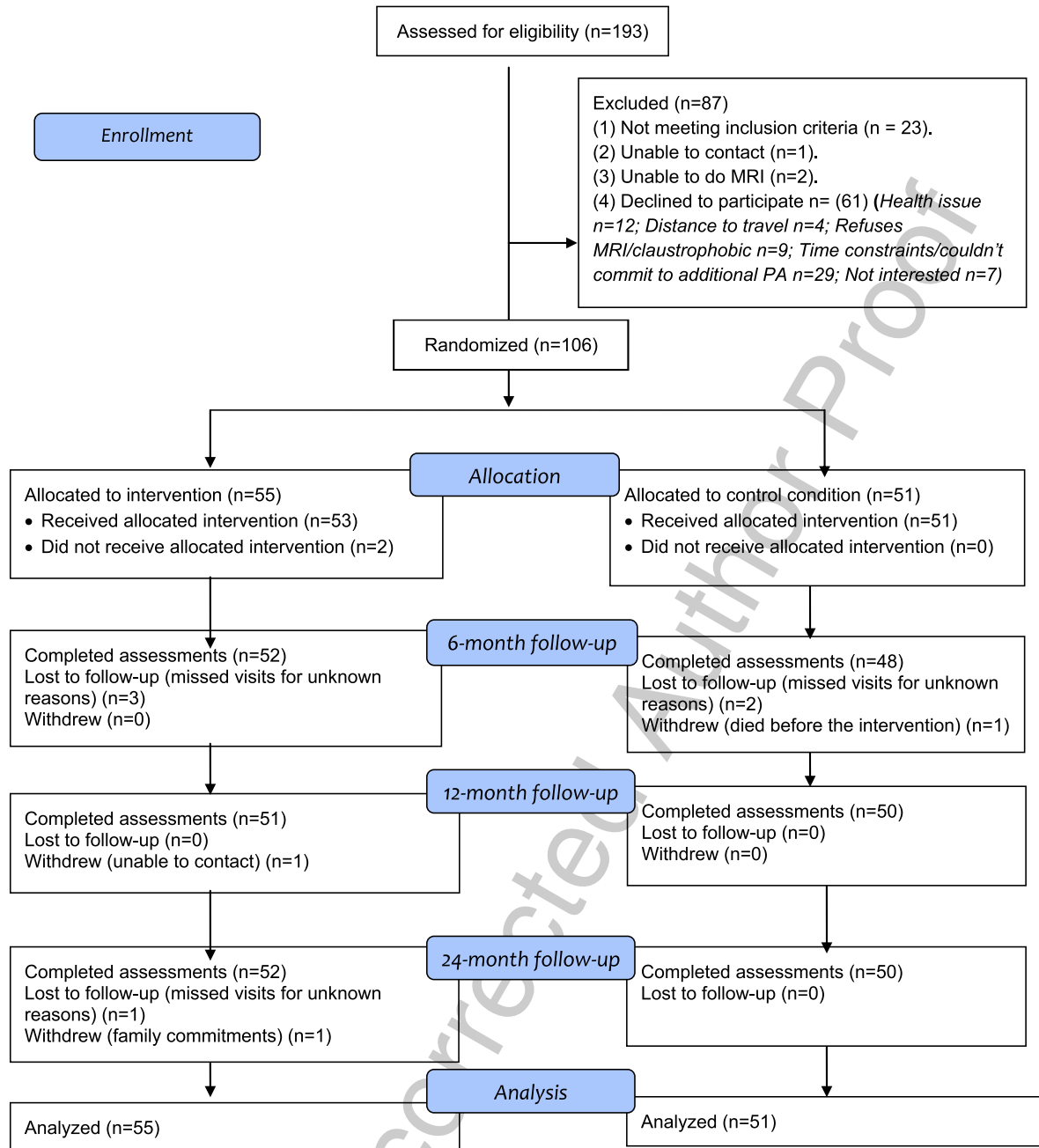


Fig. 1. AIBL Active study participant flow from recruitment to the end of the 24-month follow-up. Note: Some participants missed visits for unknown reasons at an earlier follow-up but returned for the assessment at a later follow-up.

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time ( $p = 0.36$ ) which was within the target range of 10–12. Walking was the most frequent PA type, with 79.7% ( $n = 39$ ) with an additional 4.1% ( $n = 2$ ) for each of swimming/water walking, circuit gym and cycling and an additional 2% for aerobics, social dance, tennis, and croquet.

#### Physical activity level

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#### Pedometer scores

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The PA measured by pedometer in steps/day for the 24 months is shown in Table 3a and Fig. 2. The difference in the pattern of change over time

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518

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Table 3

(a) Daily pedometer steps over 24 months, (b) Minutes/week of all physical activity over 24-months (c) number of participants self-reporting 150minutes/week of moderate or higher intensity PA (CHAMPS questionnaire) for the control and intervention groups in the AIBL Active study conducted in Melbourne, Australia 2011–2014

	0 Months (n = 51) (n = 55)	6 Months (n = 48) (n = 52)	12 Months (n = 50) (n = 50)	24 Months (n = 50) (n = 52)	Change over time p value
(a) Pedometer PA (steps/day)					
Control	6708.91 (5966.29,7544.12)	6318.39 (5363.53, 7443.19)	5642.61 (4774.15, 6692.70)	5906.79 (5111.04,6826.43)	0.04
Intervention	6244.20 (5331.47,7313.20)	7134.05 (5954.52, 8547.22)	6729.03 (5708.24,7927.65)	6290.61 (5397.23,7331.86)	
(b) Self-reported PA (CHAMPS) (min/week)					
Control (Median, Q1–Q3)	750 (540, 1035)	705 (532.5, 937.5)	810 (555, 1020)	900 (660, 1050)	0.12
Intervention (Median, Q1–Q3)	780 (495, 1065)	832.5 (577.5, 1147.5)	802.5 (585, 1050)	772.5 (547.5, 1125)	
(c) Self-reported > moderate PA ≥ 150 mins/week					
Control (n, (%))	32 (62.75)	29 (56.86)	39 (76.47)	38 (74.51)	0.18
Intervention (n, (%))	35 (63.64)	43 (78.18)	40 (72.73)	40 (72.73)	

(a) Values are geometric mean (95% CI), (b) Values are median scores and (Q1–Q3), (c) Values are number (n) of participants and % of group. The p value reflects the interaction p value that tests for a difference between groups over time. (b) When adjusted for sex, MCI status, and baseline 'inactive' the result was similar. (a) and (c) When adjusted for age, sex, and BMI the result was similar.

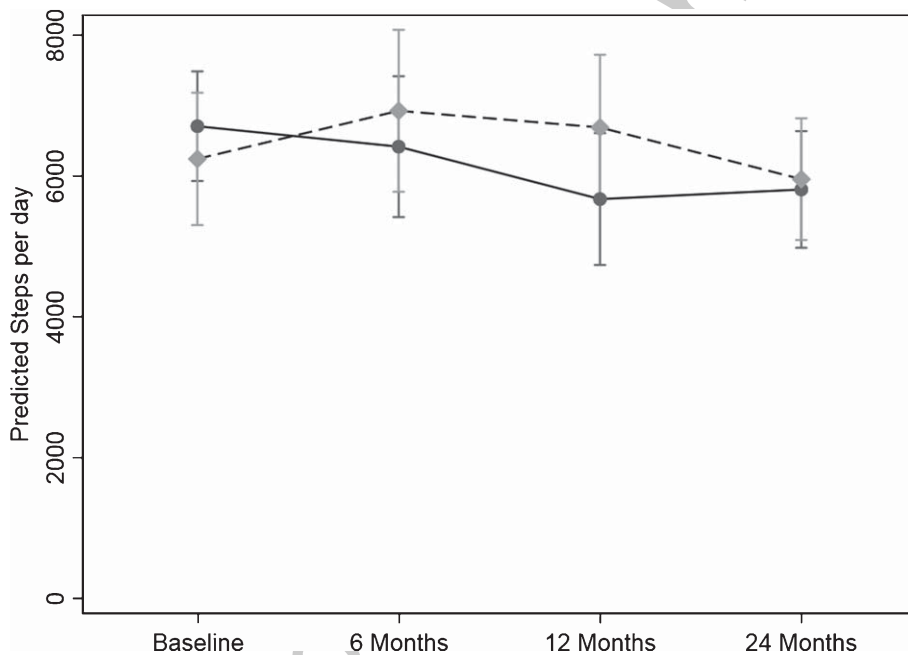


Fig. 2. Change in physical activity over the 24-months study measured as steps/day from the pedometer scores. Values are geometric mean and 95% margins. Control Group —; Intervention Group - - -. There was a significant difference in the pattern of change in physical activity (steps/day) over time between the control and intervention group ( $p=0.04$ ). The  $p$  value reflects the interaction  $p$  value that tests for a difference between groups over time.

520 between the two groups was significant ( $p=0.04$ ).  
 521 There was a significant 15.4%, 1035.85 steps/day  
 522 reduction for the control group from baseline to  
 523 12 months ( $p=0.008$ ) with the decline persisting to  
 524 24 months with a 13.4%, 899.70 steps/day reduc-  
 525 tion from baseline to 24 months ( $p=0.004$ ). The

intervention group maintained their steps/day over  
 time.

CHAMPS questionnaire

Table 3b shows the minutes of self-reported  
 'all physical activity' recorded from the CHAMPS

526  
 527  
 528  
 529  
 530

Table 4

Cardiovascular fitness, mobility, leg strength, grip strength and balance results over the 24-month period for the control and intervention groups in the AIBL Active study conducted in Melbourne, Australia 2011–2014

	0 Months (n = 51)	6 Months (n = 48)	12 Months (n = 49)	24 Months (n = 48)	Change ver time p value
Control					
Intervention					
Walk distance (m)					
Control	499.56 (468.21, 524.92)	504.16 (476.92, 531.40)	509 (481.49, 538.05)	497.10 (466.48, 527.72)	0.61
Intervention	488.0 (465.09, 510.90)	507.32 (480.80, 533.84)	511.95 (484.61, 539.31)	514.54 (488.29, 540.80)	
TUG (s)					
Control	6.57 (5.92, 7.23)	6.60 (6.10, 7.11)	6.82 (6.22, 7.43)	6.88 (6.31, 7.45)	0.68
Intervention	6.39 (6.00, 6.78)	6.43 (5.95, 6.91)	6.32 (5.88, 6.76)	6.49 (5.97, 7.01)	
Sit to Stand (s)					
Control	11.03 (10.06, 12.00)	11.04 (10.10, 11.98)	11.24 (10.25, 12.23)	11.38 (10.64, 12.13)	0.02
Intervention	11.68 (10.80, 12.57)	11.24 (10.39, 12.10)	10.25 (9.58, 10.91)	10.68 (9.90, 11.47)	
Grip Strength (kg) (Dominant hand)					
Control	30.52 (27.91, 33.14)	29.96 (26.95, 32.97)	30.48 (27.74, 33.21)	29.11 (26.33, 31.89)	0.83
Intervention	33.51 (31.13, 35.90)	32.52 (29.98, 35.07)	32.86 (30.27, 35.46)	31.00 (28.48, 33.53)	
Grip Strength (kg) (Non-dominant)					
Control	28.48 (25.84, 31.11)	27.86 (25.15, 30.56)	27.67 (24.82, 30.52)	26.33 (23.66, 28.99)	0.94
Intervention	31.06 (28.85, 33.27)	29.96 (27.61, 32.30)	30.02 (27.56, 32.47)	28.39 (25.97, 30.81)	
Step Test (steps)					
Control	15.07 (14.07, 16.08)	14.81 (13.65, 15.96)	15.28 (14.10, 16.45)	14.96 (13.88, 16.03)	0.88
Intervention	15.25 (14.91, 16.31)	15.41 (14.37, 16.45)	15.95 (14.72, 17.19)	15.66 (14.35, 16.97)	

Values are mean and (95% CI). The *p* value reflects the interaction *p* value that tests for a difference between groups over time. When adjusted for age, sex, and BMI the result was unchanged.

questionnaire at each assessment over the 24 months. There was no significant difference in the pattern of minutes over time between the 2 groups ( $p=0.12$ ) and after adjustment for age, sex, and BMI the result was unchanged. The number of participants self-reporting more than 150 min/week of moderate intensity or higher PA over the 24 months is shown in Table 3c. Similarly, there was no significant difference in the pattern of change over 24 months. The pattern of change over time between the 2 groups for frequency of activities and the energy expended in PA was not significant (results not shown).

### Physical performance

The fitness test battery results are shown on Table 4. When age, sex, and BMI were included in the regression analyses the results were unaltered so the reported results are unadjusted values.

### Cardiovascular fitness

For walk distance (cardiovascular fitness) the difference in the pattern of change over time between the groups was not significant. For the control group the pattern of change over time in walk distance was not significant. In the intervention group the pattern of change over time for walk distance increased from baseline by 17.80 (−1.69, 37.29) m ( $p=0.074$ ), 16.80

(−3.78, 37.39) m ( $p=0.110$ ), and 18.22 (2.60, 33.84) m ( $p=0.022$ ) at 6, 12, and 24 months, respectively. This significant change from baseline to 24 months in the intervention group represents an increase of 3.73% in cardiovascular fitness.

### Leg strength

There was a significant difference in the pattern of change over time between the control and intervention group for the sit to stand test (s) the measure of leg strength ( $p=0.016$ ) (Fig. 3). There was no evidence for a change over time in sit to stand time in the control group. There were significant changes over time for sit to stand time in the intervention group. Compared to the control group the reduction the test time for the intervention group from baseline to 6, 12 and 24 months was 0.43 (95%CI: (1.11, 0.24) s ( $p=0.209$ ), 1.19 (2.01, 0.37) s ( $p=0.004$ ), and 0.83 (1.52, 0.14) s ( $p=0.017$ ), respectively. This represents a 10.2% and 7.1% improvement in leg strength in the intervention group at 12 and 24 months.

### Balance

There was no significant difference in the pattern of change over time for balance (step test) between the control and intervention group. Further, there was no evidence of any change over

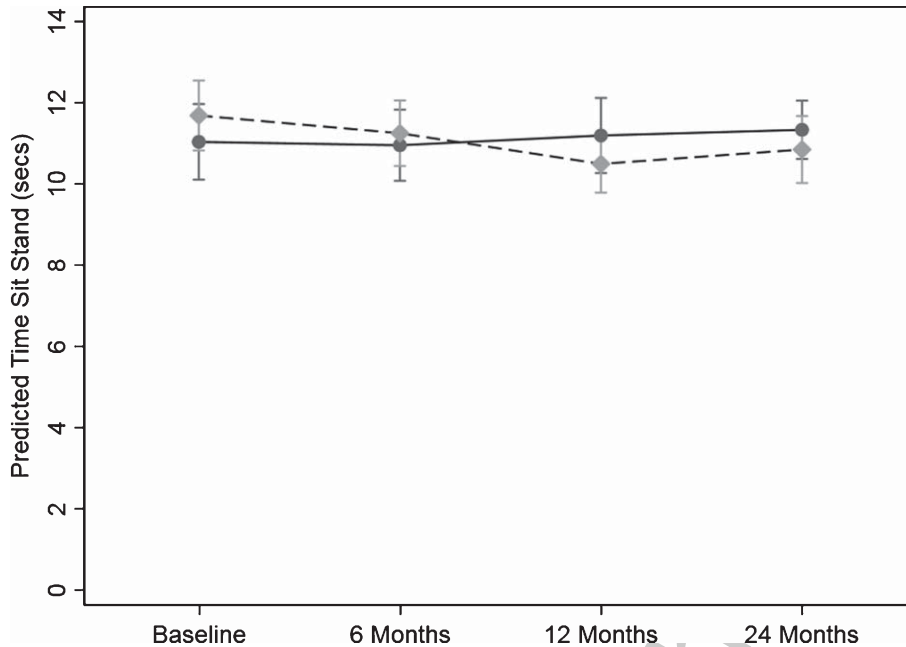


Fig. 3. Change in timed sit to stand test (leg strength) over the 24-months study. Values are predicted mean (seconds) and 95% margins. A reduction in time indicates an increase in leg strength. Control Group —; Intervention Group - - -. There was a significant difference in the pattern of change over time for leg strength between the control and intervention group ( $p=0.02$ ). The  $p$  value reflects the interaction  $p$  value that tests for a difference between groups over time. Compared to the control group the reduction in the test time for the intervention group from baseline to 6, 12, and 24 months was 0.43 (95%CI: (1.11, 0.24) s ( $p=0.209$ ), 1.19 (2.01, 0.37) s ( $p=0.004$ ), and 0.83 (1.52, 0.14) s ( $p=0.017$ ), respectively.

time in balance scores for the control or intervention group.

#### Mobility

There was no evidence of a significant difference in the pattern of change over time for the 2 groups in mobility (TUG). Nor were there any significant changes over time for the TUG score for the control or intervention group.

#### Grip strength

The difference in the pattern of change over time between the control and intervention group in grip strength for either the dominant or non-dominant hand was not significant ( $p=0.83$  and  $p=0.94$ ), respectively.

#### Injury and musculoskeletal conditions

Over the 24 months, 8.4% ( $n=9$ ) of participants reported an injury or musculoskeletal condition related to PA. The incidence was similar for both groups 8% ( $n=4$ ) and 9% ( $n=5$ ) for the control and intervention group, respectively. The most reported injury was knee tendonitis or arthritis ( $n=4$ ) with 2 out of 3 reports for the intervention group related to exacerbation of pre-existing conditions. Foot fasci-

itis was reported by 2 participants, although this was attributed to work and household PA as well as recreational PA; hip muscle soreness ( $n=2$ ) and calf strain ( $n=1$ ) accounted for the other reported conditions.

#### Body mass and body composition

Body mass, body composition, BMI, waist and hip circumference results are shown on Table 5. Figure 4 shows the pattern of change in body mass, fat mass, and fat-free mass over the 24-months.

#### Body mass and BMI

There was no significant difference in the pattern of change over time in body mass between the control and the intervention group ( $p=0.14$ ). When the analysis was adjusted for sex and age the results did not change.

The results for BMI were similar with no significant difference in pattern of change over time in BMI ( $p=0.11$ ).

#### Fat mass and % body fat

There was a significant difference in the pattern of change over time in fat mass between the

Table 5  
 BMI, body mass, body composition, and waist and hip circumference results over the 24-month period for the control and intervention groups in the AIBL Active study conducted in Melbourne, Australia 2011–2014

	0 Months (n = 51)	6 Months (n = 48)	12 Months (n = 50)	24 Months (n = 50)	Change over time p value
BMI (kg/m <sup>2</sup> )					
Control	26.47 (25.25, 27.68)	26.56 (25.22, 27.90)	26.67 (25.39, 27.91)	26.61 (25.22, 27.99)	0.11
Intervention	27.46 (26.37, 28.55)	26.80 (25.73, 27.87)	27.18 (26.04, 28.31)	27.10 (25.99, 28.20)	
Body Mass (kg)					
Control	71.71 (67.51, 74.84)	71.00 (67.07, 74.94)	71.27 (67.62, 74.91)	71.25 (67.41, 75.09)	0.14
Intervention	76.15 (72.02, 80.27)	73.98 (70.15, 77.82)	75.42 (71.10, 79.73)	75.16 (71.00, 79.33)	
Fat Mass (kg)					
Control	21.92 (19.64, 24.20)	22.40 (20.07, 24.74)	22.78 (20.12, 25.43)	22.16 (19.74, 24.57)	0.03
Intervention	24.25 (21.80, 26.69)	22.73 (20.36, 25.10)	23.73 (21.22, 26.24)	23.48 (21.03, 25.93)	
% Body Fat					
Control	30.61 (28.33, 32.9)	31.97 (29.51, 34.43)	31.54 (29.15, 33.93)	31.09 (28.82, 33.35)	0.07
Intervention	31.34 (29.07, 33.61)	30.36 (28.02, 32.70)	31.13 (28.84, 33.41)	30.88 (28.58, 33.19)	
Fat-free Mass (kg)					
Control	48.27 (45.61, 51.08)	47.63 (44.92, 50.50)	47.52 (45.01, 50.17)	47.93 (45.31, 50.70)	0.85
Intervention	50.87 (48.19, 53.70)	49.99 (47.49, 52.63)	50.29 (47.56, 53.17)	50.34 (47.56, 53.27)	
Waist circumference (cm)					
Control	88.88 (85.39, 92.37)	88.27 (84.71, 91.83)	89.77 (86.24, 93.30)	89.61 (85.81, 93.42)	0.47
Intervention	91.46 (87.77, 95.15)	89.65 (86.15, 93.15)	90.34 (86.47, 94.22)	91.49 (87.85, 95.13)	
Hip circumference (cm)					
Control	102.28 (99.59, 104.96)	102.66 (99.95, 105.37)	102.93 (100.21, 105.64)	102.10 (99.23, 104.95)	0.02
Intervention	104.98 (102.42, 107.55)	102.96 (100.54, 105.38)	103.01 (100.43, 105.59)	102.21 (99.73, 104.68)	

Values are mean and (95% CI) Value for fat-free mass is geometric mean and (95% CI). The *p* value reflects the interaction *p* value that tests for a difference between groups over time. When adjusted for age, sex, and BMI the result was unchanged.

control and intervention ( $p=0.03$ ). From baseline to 6 months there was a significant change in the intervention group of  $-1.12$  ( $-1.80, -0.43$ ) kg ( $p=0.001$ ) with no significant change over time in the control group which constituted a difference between the two groups of  $1.33$  ( $0.44, 2.23$ ) kg.

For %body fat there was no significant difference in the change over time between the groups ( $p=0.078$ ).

#### Fat-free mass

There was no significant difference between groups in change over time in fat-free mass ( $p=0.857$ ). Further, there was no significant change over time in fat-free mass within either group for any stage.

#### Waist circumference

For waist circumference, the pattern of change over time between the two groups was not significant.

#### Hip circumference

For hip circumference there was a significant difference in the pattern of change over time between the control and intervention group ( $p=0.020$ ) (Table 5 and Fig. 5).

In the intervention group, the change over time from baseline to 6, 12, and 24 months in hip circumference was  $1.72$  ( $0.24, 3.20$ ) cm, ( $p=0.022$ ),  $2.44$  ( $0.75, 4.13$ ) cm, ( $p=0.005$ ), and  $2.22$  ( $0.60, 3.83$ ) cm ( $p=0.007$ ) lower than the control group, respectively. The result was unchanged when adjusted for age and sex.

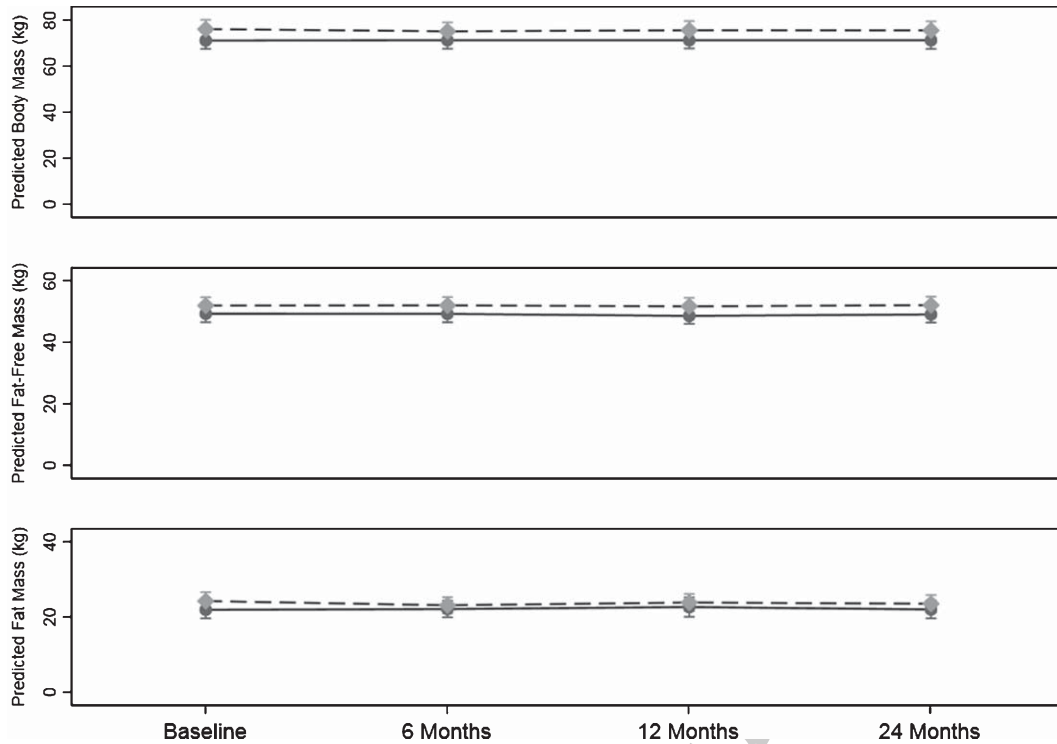


Fig. 4. Change body mass, fat mass and fat-free mass over the 24-month study. Values are predicted mean (kg) and 95% margins. Control Group —; Intervention Group - - -. There was a significant difference in the pattern of change over time for fat mass (kg) between the control and intervention group ( $p=0.03$ ). The  $p$  value reflects the interaction  $p$  value that tests for a difference between groups over time.

### 655 Dietary habits

656 No significant difference in the change over time  
 657 was detected for fruit, vegetable or protein intake  
 658 ( $p=0.33$ ,  $p=0.31$ , and  $p=0.55$ , respectively).

### 659 Program evaluation

660 At 6 months 91% and 85% of control and interven-  
 661 tion participants completed the program evaluation.  
 662 In the intervention group enjoyment of the PA pro-  
 663 gram was high (97.8%). The newsletters and phone  
 664 calls were rated as “helpful – extremely helpful” by  
 665 (94.3%) and (96.6%) of participants, respectively.  
 666 The workbook was rated as “helpful – extremely  
 667 helpful” by 97.7% of the intervention group with  
 668 78% stating that they enjoyed completing the BI  
 669 worksheets.

## 670 DISCUSSION

671 We have demonstrated that in this group of older  
 672 adults at risk of AD and having at least 1 CVR factor,  
 673 participants achieved excellent study retention and

674 adherence to a moderate intensity PA program which  
 675 was maintained for 24 months. Further, the PA pro-  
 676 gram participants achieved an improved health profile  
 677 with sustained PA levels, improved leg strength,  
 678 lower fat mass and hip circumference in the long-term  
 679 and short-term improvements in body mass, when  
 680 compared to control participants. The results of the  
 681 program evaluation demonstrated that the program  
 682 was enjoyable, and acceptable.

683 To our knowledge, no other study has achieved  
 684 these levels of PA adherence over a 24-month period.  
 685 The median adherence score of 91.6% over the 24-  
 686 month period was in-line with the 87% that we  
 687 previously reported for a similar 6-month PA inter-  
 688 vention in older adults with and without memory  
 689 concerns [13], but higher than 71% for a 12-month  
 690 center-based walking program [32] and 79.2% for  
 691 a 12-month multicomponent exercise program [33].  
 692 Even though 12.7% ( $n=7$ ) participants allocated to  
 693 the PA intervention failed to start the program this  
 694 was better than the non-start rate for other studies.  
 695 We previously reported a 22% non-start rate [20].  
 696 van Uffelen et al. [32] reported 32% non-start and  
 697 a range of non-response rates of 21%–90% has been

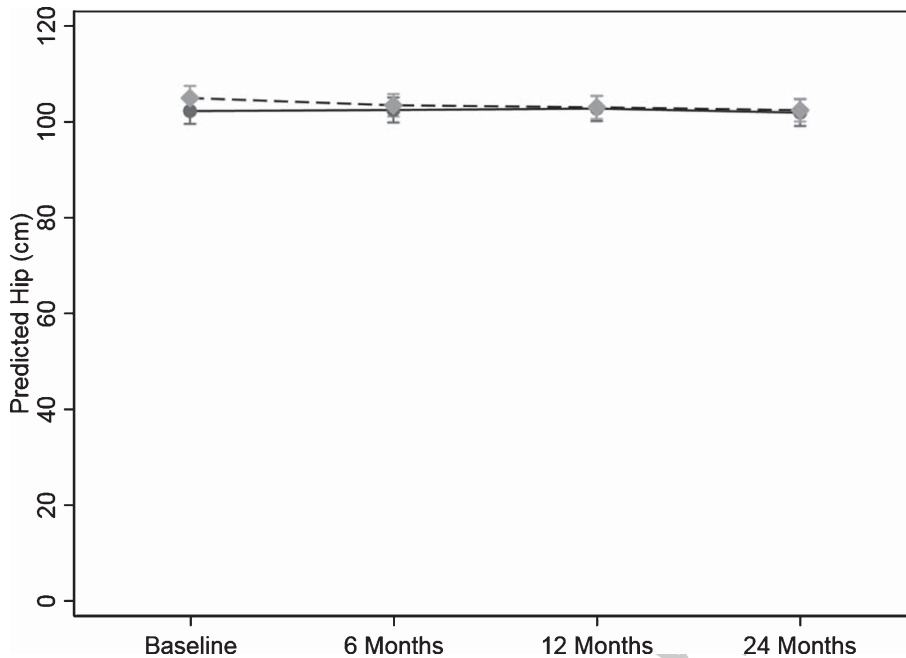


Fig. 5. Change hip circumference over the 24-month study. Values are predicted mean (cm) and 95% margins. Control Group —; Intervention Group - - -. There was a significant difference in the pattern of change over time for hip circumference (cm) between the control and intervention group ( $p=0.02$ ). The  $p$  value reflects the interaction  $p$  value that tests for a difference between groups over time.

698 reported for home and group-based PA [34]. The reasons for not starting the PA program are unknown and the numbers are too few to speculate. It is noted, however, that non-responders were from both the active and inactive categories at baseline. This highlights the problem of motivating older adults to firstly, initiate a PA program and underscores the need to find strategies to tackle this ongoing challenge in this target group.

701 We did not observe any difference between the sexes in the uptake and maintenance of PA at any stage. This is in contrast to our previous study in which men achieved a 14% higher adherence to the prescribed PA during the 6-month intervention period [13]. The number of PA related injuries reported in this study was low and mostly due to previous conditions. This is consistent with our previous trial [13] demonstrating that older adults can engage a moderate intensity, predominantly walking PA program safely.

718 The observation of a significant reduction in PA measured by the pedometer control group over the 24 months was not unexpected as PA declines with age highlighting the need for PA to continue to be promoted during older age. The 15.4% and 13.4% reduction translates into approximately 73 and 63 min/week less moderate intensity PA (3 METS) at

725 12 and 24 months for the control group [35]. The magnitude of the reduction is substantial given it is approximately the mean of 1 day/week of PA at baseline and nearly 50% of the 150 min/week of moderate intensity PA recommended for good health [36]. Even though the increase in PA by the intervention group did not reach statistical significance, the difference between the two groups in the pattern of change over time was statistically significant, which supports a finding of successful maintenance of PA in the intervention group. The inability to show a significant difference in the intervention group is most likely due to the relatively small group numbers and lack of power. This maintenance of PA levels over the 24-month period in the intervention group was achieved with a home-based program employing a BI, and although this was supported by mail-outs and phone calls it was of low intensity. These results underscore the importance of developing appropriate strategies for this target group that achieve good adherence [12] and persist in the long-term. Further, this suggests that to achieve significant increases in PA levels approaches may need to be more intensive.

748 PA measured via the CHAMPS questionnaire did not show an increase in PA when compared to the control group. That was not the case with the objective measure using the pedometer. As this questionnaire

752 relies on the recall of PA in a typical week over the  
753 past month in this target group of individuals with  
754 memory concerns it is possible that the result was a  
755 consequence of inaccurate recall. Thus highlighting  
756 the need for PA interventions in this target group to  
757 use objective measures of PA.

758 While cardiovascular fitness did not differ in the  
759 pattern of change between the two groups over the  
760 period of the intervention, this is not surprising.  
761 Previous studies have similarly failed to observe a  
762 difference between control and intervention in fitness  
763 [37]. Further, this sample included some participants  
764 who were already doing some moderate intensity  
765 PA at baseline which limited the amount of PA that  
766 could be added to the participant's PA program. Only  
767 the 'inactive' group at baseline (26.4%) were pre-  
768 scribed the amount recommended to improve health  
769 and fitness of 150 min/week of moderate intensity PA.  
770 Since the magnitude of change in fitness is related to  
771 baseline levels and the PA load, then the expected  
772 change would be small in magnitude. Thus limit-  
773 ing our ability to achieve higher levels of change  
774 in cardiovascular fitness. Further, the control group  
775 continued with their habitual PA again limiting our  
776 ability to show a large relative change between the  
777 two groups. However, it was encouraging to note that  
778 the relative increase from baseline to 24 months in the  
779 distance walked for the intervention group of 18.22 m  
780 was close to the range (19–22 m) considered to be a  
781 clinically relevant increase in fitness [38] and was  
782 similar in magnitude to that reported by Lamb et al.  
783 [39].

784 The improvement in leg strength with the home-  
785 based PA program was consistent with the results  
786 of a meta-analysis of center-based supervised PA  
787 interventions in people with cognitive impairment  
788 [5]. This is an important result as the specificity  
789 of the training is important for improved outcomes  
790 [5]. Although our PA program was predominantly  
791 walking and not strength training based, we achieved  
792 improvements similar to those that were mostly mul-  
793 timodal or resistance training programs. This finding  
794 of a 7% improvement in leg strength over the 24  
795 months in the intervention group is relevant demon-  
796 strating that a walking program has the potential to  
797 not only reduce the decline in strength with age but to  
798 increase leg strength, thus potentially improving bal-  
799 ance and physical function [39]. This is very salient,  
800 as individuals with MCI are reported to have higher  
801 levels of motor dysfunction than other older adults  
802 [40, 41]. In the current study we did not observe a  
803 difference between the groups on the balance test

804 even though leg strength improved which is a finding  
805 that has been previously reported [42]. The lack of  
806 finding of a difference between the control and inter-  
807 vention group in grip strength was not unexpected  
808 as the PA program utilized walking which uses lower  
809 leg muscles whereas grip strength involves hand mus-  
810 cles and improvements with training are seen to be  
811 related to specificity of training [5]. Similarly, the lack  
812 of improvement in mobility (TUG) with the PA pro-  
813 gram was not surprising as even though both the TUG  
814 and PA program involve walking the performance of  
815 the TUG also requires leg strength and reaction time  
816 (in getting up and down from a chair), fast walking  
817 speed and agility in changing direction. The walk-  
818 ing program engaged in by our participants did not  
819 specifically target these skills thus it is not surpris-  
820 ing that we did not demonstrate an improvement in  
821 mobility. Improvements in physical function are spe-  
822 cific to the type of training, and need to be of sufficient  
823 frequency and/or duration to improve, balance, hand  
824 strength and mobility [5]. These authors also reported  
825 in their systematic review of exercise training and  
826 physical function in MCI and AD participants that  
827 studies including community-based participants only  
828 reported no significant results. They suggested that  
829 their higher baseline values in these functional out-  
830 comes means they have less room for improvement.  
831 In the current study, the inability to show a significant  
832 difference between groups may also have been due to  
833 the relatively small group size and lack of power.

834 The finding of a difference between groups in the  
835 change fat mass over the 24-months with a reduc-  
836 tion of fat mass in the intervention group and this  
837 taken in conjunction with a preservation of fat-free  
838 mass is important and relevant for this target group as  
839 weight loss has been shown to often precede AD [43].  
840 This 'obesity paradox' raises the question if increas-  
841 ing PA results in a reduction in body weight does this  
842 reduction potentially increase the risk of AD in older  
843 adults already at increased risk? Exercise is often an  
844 adjunct to energy restriction in weight loss programs  
845 as reducing energy intake alone results in both fat loss  
846 and loss of fat-free mass [44]. The major component  
847 of fat-free mass is muscle mass. Preserving muscle  
848 mass is important as we age. The loss of skeletal mus-  
849 cle and strength with age is reported to be around 2%  
850 per year after the age of 60 years and this loss can  
851 affect daily activities [45–47]. This gradual loss of  
852 muscle mass and function known as 'sarcopenia' has  
853 also been associated with cognitive impairment [48].  
854 Further, higher levels of sarcopenia and frailty in indi-  
855 viduals with AD and CVR are associated with adverse

856 outcomes such as falls, disability and mortality [49].  
857 A supervised moderate intensity, walking program in  
858 combination with diet-induced weight loss has been  
859 shown to attenuate the loss of muscle mass [50]. In  
860 the current study, we did not have robust dietary mon-  
861 itoring and, although we cannot be certain that the fat  
862 loss was due to the walking program and not a reduc-  
863 tion in energy intake, taken together with the lack of  
864 a reduction in fat-free mass it is likely that PA was the  
865 major contributor. Further, as we demonstrated a sig-  
866 nificant difference between the two groups in PA but  
867 not the 6-minute walk test this highlights the possi-  
868 bility that the changes in body composition were due  
869 to the amount of the PA over the duration of the trial  
870 rather than the intensity of the PA which is needed  
871 to improve fitness. That is, the energy expenditure  
872 achieved by more steps over a longer period resulted  
873 in energy output that was sufficient to reduce fat mass  
874 but may not have been of sufficient intensity to stimu-  
875 late an increase in fitness. Even though the magnitude  
876 of the reduction in fat mass of 1.12 kg is not large,  
877 this translates into an even larger amount of weight  
878 lost. Given that an increase in weight of 0.5 kg/year  
879 is associated with an increase in all-cause mortality  
880 [51], our findings are clinically meaningful.

881 Further, taken together with the reduction in hip  
882 circumference and the increase in leg strength in the  
883 intervention group this suggests that the loss of fat  
884 could have been from buttocks region but with preser-  
885 vation of the gluteal muscle mass which play a major  
886 role in the sit to stand task. Although we were not  
887 able to determine if this was the case, preservation of  
888 lower limb fat-free mass determined by dual-energy  
889 x-ray absorptiometry, 'leaner' thigh muscle deter-  
890 mined by CT and muscle fiber size determined by  
891 muscle biopsy has been reported with a walking inter-  
892 vention in older adults [50]. This novel finding is  
893 important, as it demonstrates that this PA interven-  
894 tion of moderate intensity walking has the potential  
895 to slow down the loss of muscle mass and strength  
896 seen with sarcopenia in this target group.

897 We were not able to demonstrate a significant  
898 difference in central obesity (waist circumference)  
899 a recognized CVR factor between the control and  
900 intervention group. This may have been due to  
901 measurement variation as the waist circumference  
902 measure taken at the level of the minimum width,  
903 is subject to more observer error than the hip cir-  
904 cumference that has a reference of an anatomical  
905 landmark.

906 One of the strengths of our study is that we inves-  
907 tigated the effects of a home-based PA intervention

908 over a long-term period with 4 assessment periods  
909 which is rare in healthy older populations, and to our  
910 knowledge a first in this target group. We have been  
911 able to demonstrate that such programs can increase  
912 PA and that this increase is maintained. The excel-  
913 lent retention and adherence to the prescribed amount  
914 of PA enabled us to demonstrate a beneficial effect  
915 on PA, leg strength, and body composition that are  
916 not always apparent in the short-term. These results  
917 highlight the need to develop effective strategies that  
918 lead to sustained PA levels if the inclusion of mod-  
919 est amounts of PA is to be translated into community  
920 programs and have a meaningful effect on health sta-  
921 tus. The utilization of the pedometer as an objective  
922 measure PA rather than relying on participant recall  
923 in a group who has memory concerns adds to the  
924 strength of the study. The pedometer is limited how-  
925 ever in the ability to determine the intensity of the  
926 PA. A further strength is the relatively large number  
927 of participants in a 24-month trial that was adequate  
928 for some outcomes but for some outcomes even with  
929 these numbers, we had limited power to be able to  
930 detect a significant difference between groups. We  
931 simplified the recording of the PA for the intervention  
932 group by providing individualized diaries to record  
933 their activity and supported both groups through-  
934 out the 24 months with newsletters and phone calls  
935 to enhance retention and adherence. The inclusion  
936 of participants who may have already been doing  
937 some moderate intensity PA limited the amount of  
938 PA that could be prescribed, thus reducing our ability  
939 to demonstrate an effect as the amount of PA pre-  
940 scribed depended upon the baseline PA and this varied  
941 within the intervention group. For those with higher  
942 baseline PA levels the effects on some measures may  
943 have been limited due to a ceiling effect. However,  
944 the inclusion of non-sedentary participants does not  
945 limit the generalizability of the results of this trial as  
946 the PA classifications of our participants were similar  
947 to those of Australians in the same age range [52]

948 Even though participants were asked not to change  
949 other lifestyle habits and we only collected basic self-  
950 reported dietary information and not detailed diet  
951 records, we cannot be sure that the body composition  
952 changes were not at least in part due to some change  
953 in diet and a possible reduction in energy intake. We  
954 used practical field measures for some outcomes such  
955 as fitness and body composition and while these have  
956 the advantage of being implemented and translated  
957 for use in a community setting they have limitations.  
958 Limitations in terms of the robustness and variability  
959 of the measures may have reduced the ability of this



960 trial to detect small changes between groups. Another  
961 limitation of this study is that we have reported several  
962 secondary outcomes in this paper and as the analyses  
963 have not been adjusted for multiple comparisons it  
964 is possible that some results may be subject to type  
965 1 error (false positives). However, it is also possible  
966 that by not reporting the unadjusted results there is  
967 the risk of a type 2 error where we report that there  
968 is no significant difference when there is one.

969 The results of this trial have several implications  
970 for implementation in a community and clinical set-  
971 ting. Firstly, the PA regime of moderate intensity,  
972 predominantly walking, is achievable by older adults  
973 without major health conditions and this was demon-  
974 strated in this group of older adults with MCI and  
975 at least 1 CVR factor. Secondly, being home-based  
976 means that PA can be undertaken with minimal or no  
977 cost, overcomes the potential barrier of transporta-  
978 tion, and can be done at the individual's convenience.  
979 Further, the low incidence of PA program related  
980 injury or musculoskeletal conditions and no major  
981 adverse events means that it can be engaged in safely.  
982 It also supports the findings of Hamer et al. [53] in  
983 older adults that sustained PA has health benefits but  
984 that these benefits are apparent even if PA is not  
985 taken up until later in life. In a longitudinal aging  
986 study, two-thirds of MCI cases were reported to be  
987 physically frail or pre-frail largely due to low muscle  
988 mass, slow gait speed, balance and gait impairment  
989 [54]. The improvement in leg strength, fat mass,  
990 and preservation of lean body mass reported in this  
991 study, if repeated in future trials, highlights the poten-  
992 tial of this modest, easily accessible, and acceptable  
993 walking program to be used in programs targeting  
994 older adults, in particular those with MCI or SMC  
995 to achieve improved health status and the preven-  
996 tion of disability. Importantly, the uptake of PA needs  
997 to be maintained, underscoring the need for salient  
998 strategies to motivate this target group to sustain their  
999 PA.

1000 In conclusion, in this target group at risk of AD and  
1001 having a co-existing CVR factor long-term PA adher-  
1002 ence is achievable, acceptable, and has health benefits  
1003 in terms of fitness, body composition, and potentially  
1004 attenuating sarcopenia and risk of disability.

1005 Our novel results of high retention rates and excel-  
1006 lent long-term adherence to a PA intervention are  
1007 important for the global efforts to reduce dementia  
1008 risk. To date there are no effective pharmacological  
1009 treatments available for the prevention of cognitive  
1010 decline AD or dementia. This makes the modifi-  
1011 cation of lifestyle that reduces risk factors such as

1012 physical inactivity, cognitive inactivity, mid-life obe-  
1013 sity, hypertension, heart disease, diabetes, smoking,  
1014 and hypercholesterolemia a crucial strategy. This  
1015 is underscored by the estimate that a third of AD  
1016 cases worldwide may be attributed to modifiable risk  
1017 factors. Recently it was reported that with a 10%  
1018 reduction in each risk factor each decade, by 2050 the  
1019 estimated reduction in the prevalence of AD would  
1020 be 8.3% [11]. We have previously identified a need  
1021 for targeted, effective, and viable PA intervention in  
1022 order to achieve a reduction in the risk from inac-  
1023 tivity [55]. The current study demonstrates that such  
1024 PA interventions are not only achievable and effec-  
1025 tive in increasing PA long-term but are acceptable  
1026 to the target group. Further the observed increase  
1027 in leg strength and favorable improvements in fat  
1028 mass and body fat distribution highlight the additional  
1029 health benefits of PA interventions and the potential  
1030 to reduce other risk factors for dementia. The moder-  
1031 ate intensity PA intervention undertaken in this study  
1032 was low risk, easily accessible, and possible for most  
1033 older adults at minimal or no cost making it easily  
1034 adaptable and available on a global scale. Hence high-  
1035 lighting the potential for PA interventions to have a  
1036 potent impact as a global strategy for the prevention  
1037 of dementia. Future research needs to concentrate on  
1038 finding successful strategies for the implementation  
1039 of PA programs into the community.

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