TITLE

Promoting Activity, Independence and Stability in early dementia and mild cognitive impairment (PrAISED): A randomised controlled trial

AUTHORS

Rowan H Harwood [1], ORCID: 0000-0002-4920-6718

Professor of Palliative and End of Life Care, consultant geriatrician

Rowan.harwood@nottingham.ac.uk

Sarah E Goldberg [1], ORCID: 0000-0001-5109-798X

Professor of Older Persons' Care

Sarah.goldberg@nottingham.ac.uk

Andrew Brand [3], ORCID: 0000-0002-6942-0404

Trial statistician

a.brand@bangor.ac.uk

Veronika van Der Wardt [4], ORCID: 0000-0003-3995-7056

Senior Research Fellow

v.vanderwardt@uni-marburg.de

Vicky Booth [2], ORCID: 0000-0002-5338-0196

Clinical lecturer, physiotherapist

Victoria.booth@nottingham.ac.uk

Claudio Di Lorito [2], ORCID: 0000-0002-8953-0117

Senior Research Fellow

Claudio.dilorito@nottingham.ac.uk

Zoe Hoare [3], ORCID: 0000-0003-1803-5482

Senior Lecturer, Principal Trial Statistician

z.hoare@bangor.ac.uk

Jennie Hancox [6], ORCID: 0000-0001-5938-5265

Lecturer in psychology

j.hancox@lboro.ac.uk

Rupinder Bajwa [2], ORCID: 0000-0002-9551-2409

Research Assistant

Rupinder.bajwa@nottingham.ac.uk

Clare Burgon [2], ORCID: 0000-0002-4910-9969

Research Assistant

clare.burgon@nottingham.ac.uk

Louise Howe [2], ORCID: 0000-0002-0861-3042

Research occupational therapist

louise.howe@nottingham.ac.uk

Alison Cowley [2], ORCID: 0000-0001-6858-475X

Senior Research Fellow, physiotherapist

alison.cowley@nottingham.ac.uk

Trevor Bramley [15], ORCID: 0000-0002-0553-7849

Research occupational therapist

trevor.bramley@nottshc.nhs.uk

Annabelle Long [2], ORCID: 0000-0003-2220-6774

Research physiotherapist

Annabelle.Long1@nottingham.ac.uk

Juliette Lock [2], ORCID: 0000-0003-2028-6889

Research Assistant

juliette.lock@nottingham.ac.uk

Rachael Tucker [1], ORCID: 0000-0001-8133-1909

Research physiotherapist

Rachael.Tucker1@nottingham.ac.uk

Emma Adams [1], ORCID: 0000-0002-5444-6951

Senior Research Fellow

emma.adams@nottingham.ac.uk

Rebecca O'Brien [1], ORCID: 0000-0003-0300-8430

Senior Research Fellow

rebecca.obrien@nottingham.ac.uk

Fiona Kearney [5], ORCID: 0000-0003-0081-5958

Consultant geriatrician

Fiona.kearney@nuh.nhs.uk

Katarzyna Kowalewska [2], ORCID: 0000-0001-5018-9559

Research project administrator

katarzyna.kowalewska@nottingham.ac.uk

Maureen Godfrey [7]

PPI representative

maureengodfrey47@gmail.com

Marianne Dunlop [7]

PPI representative

mariannedunlop@icloud.com

Kehinde Junaid [8], ORCID: 0000-0001-5986-395X

Consultant psychiatrist

Kehinde.junaid@nottshc.nhs.uk

Simon Thacker [9], ORCID: 0000-0002-3203-1392

Consultant psychiatrist

simon.thacker@nhs.net

Carol Duff [10]; ORCID: 000-0002-6810-1786

Senior lecturer, Consultant occupational therapist

carol.duff3@nhs.net

Tomas Welsh [11]; ORCID: 0000-0002-2619-5032

Medical and research director, consultant geriatrician

tomas.welsh@nhs.net

Annette Haddon-Silver [12], ORCID: 0000-0002-6743-6496

Research occupational therapist

annette.haddon-silver@oxfordhealth.nhs.uk

John Gladman [2], ORCID: 0000-0002-8506-7786

Professor of Medicine in Older People, consultant geriatrician

john.gladman@nottingham.ac.uk

Pip Logan [2], ORCID: 0000-0002-6657-2381

Professor of Rehabilitation Research, occupational therapist

pip.logan@nottingham.ac.uk

Kristian Pollock [1], ORCID: 0000-0002-6836-8595

Professor of Medical Sociology

kristian.pollock@nottingham.ac.uk

Kavita Vedhara [13], ORCID: 0000-0002-9940-7534

Professor of Health Psychology

kavita.vedhara@nottingham.ac.uk

Victoria Hood [15], ORCiD: 0000-0002-4738-2427

Senior Research Fellow, physiotherapist

vicky_hood@hotmail.com

Roshan Das Nair [16], ORCiD: 0000-0001-8143-7893

Senior research scientist, professor of neuropsychology

roshan.nair@sintef.no

Helen Smith [15], ORCiD: 0000-0003-0380-1420

Programme Director, physiotherapist

helen.smith@nottshc.nhs.uk

Rhiannon Tudor-Edwards [17], ORCID: 0000-0003-4748-5730

Professor of Health Economics

r.t.edwards@bangor.ac.uk

Ned Hartfiel [17], ORCID: 0000-0001-9976-4294

Research Officer in Health Economics

ned.hartfiel@bangor.ac.uk

Victory Ezeofor [17], ORCiD: 0000-0002-4211-8942

Mathematical modeller in Health Economics

v.ezeofor@bangor.ac.uk

Robert Vickers [2], ORCID: 0000-0002-3031-2940

Research fellow

Robert.vickers@nottingham.ac.uk

Martin Orrell [14], ORCID: 0000 0002 1169 3530

Professor and Director of the Institute of Mental Health, consultant psychiatrist

m.orrell@nottingham.ac.uk

Tahir Masud [5], ORCID: 0000-0003-1061-2898

Consultant geriatrician

tahir.masud@nuh.nhs.uk

1. School of Health Sciences, University of Nottingham, Queen's Medical Centre, Nottingham NG7 2HA
2. School of Medicine, University of Nottingham, Queen's Medical Centre, Nottingham NG7 2HA
3. North Wales Organisation for Randomised Trials in Health, Y Wern, Normal Site, Holyhead Road, Bangor University, Bangor, Gwynedd LL57 2PZ
4. Abteilung für Allgemeinmedizin, Präventive und Rehabilitative Medizin, Philipps-Universität Marburg Karl-von-Frisch-Straße 4 35032 Marburg, Germany
5. Nottingham University Hospitals NHS Trust, Queen's Medical Centre, Nottingham NG7 2UH
6. School of Sport, Exercise and Health Sciences, Loughborough University, Epinal Way Loughborough Leicestershire LE11 3TU
7. Patient and Public Involvement contributor
8. Mental Health Services for Older People, Nottinghamshire Healthcare NHS Foundation Trust, Highbury Hospital, Highbury Rd, Nottingham NG6 9DR
9. Centre for Research and Development, Derbyshire Healthcare NHS Foundation Trust, Kingsway Hospital, Derby DE22 3LZ
10. Lincolnshire Partnership NHS Foundation Trust, Welton house, Lime Kiln Way, Lincoln, LN2 4WH
11. The RICE Centre, Research Institute for the Care of Older People, Royal United Hospital, Bath BA1 3NG
12. Oxford Health NHS Foundation Trust, Research & Development, Warneford Hospital, Oxford OX3 7JX
13. Centre for Academic Primary Care, Lifespan and Population Health, University of Nottingham, Applied Health Research Building, University Park, Nottingham, NG7 2RD
14. Institute for Mental Health, University of Nottingham, University of Nottingham Innovation Park, Triumph Road, Nottingham NG7 2TU
15. Nottinghamshire Healthcare NHS Foundation Trust, South Nottinghamshire Place Based Partnership, Lings Bar Hospital, Beckside, Gamston, Nottingham NG2 6PR
16. SINTEF (Stiftelsen for Industriell og Teknisk Forskning), P.O. Box 4760 Torgarden, NO-7465 Trondheim, Norway
17. Centre for Health Economics & Medicines Evaluation, College of Health and Behavioural Sciences, Bangor University, Ardudwy, Normal Site, Bangor, Gwynedd LL57 2PZ

Correspondence to:

Prof Rowan H Harwood

School of Health Sciences, University of Nottingham, Queen's Medical Centre, Nottingham NG7 2HA

Rowan.harwood@nottingham.ac.uk

The corresponding author is guarantor.

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Promoting Activity, Independence and Stability in Early Dementia and mild cognitive impairment (PrAISED): A randomised controlled trial

Abstract

Background: Dementia is associated with frailty leading to increased risks of falls and hospitalisations. Interventions are required to maintain functional ability, strength and balance.

Design: Multi-centre parallel group randomised controlled trial, with embedded process evaluation. Procedures were adapted during the COVID-19 pandemic.

Participants: People with mild dementia or mild cognitive impairment (MCI), living at home, and a family member or carer.

Objectives: To determine the effectiveness of an exercise and functional activity therapy intervention compared to usual care.

Intervention: A specially-designed dementia-specific rehabilitation programme focussing on strength, balance, physical activity and performance of ADL, which was tailored, progressive, addressed risk and the psychological and learning needs of people with dementia, providing up to 50 therapy sessions over 12 months. The control group received usual care plus a falls risk assessment.

Main outcome measure: The primary outcome was the informant-reported Disability Assessment for Dementia (DAD) 12 months after randomisation. Secondary outcomes were: self-reported ADL, cognition, physical activity, quality of life, frailty, balance, functional mobility, fear of falling, mood, carer strain and service use (at 12 months) and falls (between months 4 and 15).

Results: 365 people were randomised, 183 to intervention and 182 to control. Median age of participants was 80 years (range 65-95), median Montreal Cognitive Assessment score 20/30 (range 13-26), 58% were men. Participants received a median of 31 (IQR = 22-40) therapy sessions out of a possible maximum of 50. Participants reported completing a mean 121 minutes/week of PrAISED activity outside of supervised sessions. Primary outcome data were available for 149 (intervention) and 141 (control) participants. There was no difference in DAD scores between groups: adjusted mean difference -1.3/100, 95% Confidence Interval (-5.2 to +2.6); Cohen's d effect size -0.06 (-0.26 to +0.15); p=0.5. Upper 95% confidence intervals excluded small to moderate effects on any of the range of secondary outcome measures. Between months 4 and 15 there were 79 falls in the intervention group and 200 falls in the control group, adjusted incidence rate ratio 0.78 (0.5 to 1.3); p= 0.3.

Conclusion: The intensive PrAISED programme of exercise and functional activity training did not improve ADLs, physical activity, quality of life, reduce falls or improve any other secondary health status outcomes even though uptake was good. Future research should consider alternative approaches to risk reduction and ability maintenance.

Trial registration: ISRCTN15320670. *Funding*: National Institute for Health and Care Research

What is already known

- Dementia is associated with progressive loss of functional ability, including activities of daily living and mobility, and a high risk of falls

- Exercise programmes and rehabilitation therapies may improve ability, or slow the rate of decline, but evidence from trials and systematic reviews is equivocal

What this study tells us

- We developed an intensive dementia-specific exercise and functional activity rehabilitation programme, lasting 12 months, taking account of motivation, learning needs and context, in particular the need to engage carers, and evaluated it in a randomised controlled trial

- The programme was very well received by participants and therapists, but had no effect on activities of daily living, physical activity, quality of life, falls, cognition or any other health status outcome

- We are unlikely to be able to change rate of loss of ability in dementia through exercise or functionally orientated rehabilitation therapy.

- We need different ways of defining wellbeing after a dementia diagnosis.

INTRODUCTION

Dementia causes progressive loss of ability in activities of daily living (ADL) and physical activity. Multiple mechanisms lead to functional loss, including cognitive and neurological decline, co-morbidities, acute illness, injuries, delirium, inactivity, deconditioning and restriction of opportunities, especially if the person suffers stigma or family members are concerned for safety. Dementia (and a possible precursor state, mild cognitive impairment, MCI) confers an increased risk of crises, including acute physical illness and a twofold increased risk of falls. Sixty to 80% of people living with dementia fall each year [1-5].

Dementia prevalence increases exponentially with age, affecting 20% of 80-year-olds. A similar number again have MCI [6,7]. Prevalence in the population will double in the next 30 years [8]. Dementia is one of the main drivers of dependency (the need for help from other people). It creates high levels of demand on health and social care services, families and other informal carers [9]. The English National Dementia Strategy emphasised the importance of early diagnosis and the goal of living well with dementia [10]. Reasons to diagnose dementia include access to cognitive enhancing drugs and cognitive stimulation therapy, however their effects are small [11,12]. Commentators have highlighted a relative lack of available therapeutic interventions [13]. Exercise has been proposed as a way of preventing or slowing the progression of dementia [14], but in trials, has been shown to have little effect on global cognition [15-18]. Some evidence suggests that exercise might slow the decline in ADL performance or prevent falls [15,18,19].

We hypothesised that exercise-based, functionally-directed rehabilitation would improve physical reserve, promote safe performance of activities, reduce falls, enhance recovery from intercurrent illness or injury, and hence improve ADL. We undertook a programme of research to develop and evaluate this approach [20]. We developed a dementia-specific therapy intervention, called Promoting Activity, Independence and Stability in Early Dementia and mild cognitive impairment (PrAISED) [21]. The target population was those with relatively mild impairment who might retain capacity to learn, change behaviour and develop new routines. We conducted a 3-arm feasibility trial with 60 participants, comparing the PrAISED intervention delivered with 12 months supervision, a reduced schedule of 3 months supervision, and a control condition, in which we demonstrated that intervention delivery and research were feasible and found benefits in balance and mobility outcomes, but most participants required ongoing supervision to sustain adherence [21-23]. The aim of this definitive trial was to determine the effectiveness of the PrAISED intervention on ADL, falls, physical activity and quality of life, among other outcomes.

METHODS

Study design

We performed a multi-centre, individually 1:1 randomised, stratified, pragmatic, parallel group, randomised controlled trial [24]. The trial was impacted by the COVID-19 pandemic. Recruitment was paused and delivery adaptations instituted between March and September 2020.

Study setting

Participants were recruited by trained researchers from five sites in England via secondary care memory clinics (dementia diagnostic services), general practice registers, dementia support groups, and the NIHR *Join Dementia Research* register. The intervention was delivered in participants' homes and local communities.

Participants

Patient participants were aged over 65 years, had a diagnosis of MCI or dementia, a Montreal Cognitive Assessment (MoCA) score of 13-25 (out of 30), a family member or carer who knew the participant and had a minimum of 1-hour weekly contact in person or by telephone/internet, and was willing to act as an informant. Participants had to be able to walk without human help, communicate in English, have adequate sight, hearing, and dexterity to complete neuropsychological tests, mental capacity to give consent as assessed by a study researcher, and consented to participate. Carers participated in their own right, and separate consent was taken.

Exclusion criteria included a diagnosis of Dementia with Lewy Bodies, a comorbidity preventing participation (such as severe breathlessness, pain or severe neurological disorder), anticipated unavailability over the next year (e.g., relocation, prolonged holiday) or life expectancy less than a year.

Baseline data

The study dataset included multiple health status measures, as appropriate for a complex intervention trial [25-30]. The rationale was to measure a range of credible predictor, mediator, intermediate and distal health status outcomes, including ADL, balance, mobility, frailty, executive function, mood, carer strain and quality of life.

Baseline data comprised demographics, medications, medical and falls history, ADL (Disability Assessment for Dementia, DAD [31]; Nottingham Extended ADL scale, NEADL [32]); cognition (MoCA [33]); animal-naming verbal fluency; Cambridge Neuropsychological Test Automated Battery,

CANTAB [34]); mood (Hospital Anxiety and Depression Scale, HADS [35]); Apathy Evaluation Scale [36]; physical activity (Longitudinal Aging Study of Amsterdam Physical Activity Questionnaire, LAPAQ [37,38]); step count (Misfit Shine accelerometer); self and proxy-assessed quality of life (DEMQOL [39], DEMQOL-U [40], EuroqoL EQ-5D-3L [41]); fear of falling (short Falls Efficacy Scale-International, FES-I [42]); frailty (SHARE index [43]); balance (Berg Balance Scale [44]); mobility and ability in divided attention (Timed Up and Go, TUG, dual-task TUG [45]); hand grip strength (Camry EH101 Electronic Hand Dynamometer); health and social care resource use for patient and carer (Client Service Receipt Inventory, CSRI [46]); carer strain (Caregiver Strain Index, CSI [47]); carer health-related quality of life (EQ-5D-5L). Verbal fluency, apathy and CANTAB measures were intended as markers of executive function, which is associated with risk of falls, and has been reported to improve with exercise interventions [48-51].

Intervention

The intervention was delivered by National Health Service (NHS) and other local healthcare providers, according to a manual [52](TIDieR checklist, Appendix 1). Clinicians were trained by centrally-based research therapists, including a two-day initial course, a mid-point refresher conference, and weekly teleconferences to discuss problems and difficult scenarios.

The development and content of the PrAISED intervention have been published [21,52,53]. Participants in the intervention arm received an individually tailored programme comprising physical exercises (i.e., progressive strength, balance, and dual task training [54-58]; functional activities (i.e., ADL with an element of physical activity, such as going out shopping)[59, 60]; inclusion in community life (e.g., through signposting physical exercise classes and exercise facilities); risk enablement (positive risk-taking); [61] and environmental assessment (accessibility and safety issues at home). Participants received up to 50 home therapy sessions over 12 months from a multidisciplinary team comprising physiotherapists, occupational therapists and rehabilitation support workers (associate practitioners). Sessions were intended to teach and supervise exercise and functional activities, monitor progress and adjust and progress the programme. Delivery used a specifically developed behaviour change model [23, 62-67]. The intervention was tailored to individual abilities, co-morbidities, interests, and goals using a stratification tool to determine the frequency of intervention to enable participants to sustain the programme [52]. Participants were encouraged to perform their programme for a minimum of three hours per week based on previous research findings for improvements in falls and executive function [48-50, 68, 69]. Family members or carers were encouraged to support or participate where possible. The amount of supervision was 'tapered' (became progressively less frequent over time) to encourage habit formation and promotion of self-

directed exercise and activity between supervised sessions and after the programme had finished. Therapy sessions were intended to be delivered in-person.

The control intervention consisted of a falls prevention assessment and advice and was modelled on usual falls prevention care. This consisted of an initial therapy visit for assessment and up to two further visits by a study therapist to review actions, give advice, and refer on to their general practitioner (GP) or local services, if needed. These visits lasted up to 90 minutes. The control participants were seen by the same therapists who delivered the active intervention.

Both study groups were assessed using the Guide to Action falls risk factor assessment tool [70]. Advice was offered based on the findings including further clinical assessment, assessment for equipment, and medication review by their GP, if necessary. Any non-study intervention was permitted in both study arms including cognitive stimulation therapy, use of acetylcholine inhibitor or memantine drugs, or referrals to mental health, medical, rehabilitation or falls prevention services.

Outcome evaluation

Each participant took part for 15 months. A brief postal follow up, with telephone support if needed, was undertaken with a carer after 6 months. The main follow up was completed at 12 months (+/- 4 weeks) when participating dyads were visited at home by two researchers to collect outcome data by interviewing the participant and carer separately (table 1). This follow up was undertaken remotely via telephone or video-calls during the COVID-19 lockdown.

Falls, PrAISED activities done independently, service use and hospitalisations were ascertained using monthly self-completed calendars between months 0 and 15 with telephone prompts and support by researchers not involved in delivery of the intervention, where necessary. Injurious falls were adjudicated by two clinicians based on details provided on calendars.

Study outcomes

At 6 months, quality of life (EQ-5D-3L, DEMQOL-U) and service use (short CSRI) were collected.

The primary outcome was carer-informant-rated disability in ADLs, measured by the DAD, after 12 months. Secondary outcomes at 12 months were the self-reported NEADL; falls, rate of falling and injurious falls; cognition (MoCA, verbal fluency, apathy evaluation scale and CANTAB); quality of life (DEMQOL, EQ5D); activity (LAPAQ, accelerometers); frailty (SHARE Index); Berg Balance Scale, functional mobility (single and dual task TUG test), hand grip strength; fear of falling (FES-I); mood (HADS); carer strain (CSI) and carer quality of life (table 1).

Harm and Adverse events

Adverse events were classified as serious (death, life-threatening events, hospitalisation, significant incapacity), or potentially related to the intervention or to PrAISED exercises undertaken independently. Adverse events were ascertained by participants or their carer reporting them to the study or intervention delivery teams or through monthly calendars. The intervention group had more exposure to study therapists, and consequently more opportunity to report adverse events, resulting in an ascertainment (information) bias. To compare the safety of the intervention we considered deaths, hospital admissions and falls to be core adverse events. To investigate the possibility of an early falls hazard associated with increased activity, we analysed falls in the first three months separately.

Impact of the Covid-19 pandemic

Following UK Government guidance for strict social distancing and the requirement to remain at home, all non-essential face-to-face contact ceased on 17th March 2020. At this time, 64 participants had completed the study, 187 were in process and 27 had been recruited but had not commenced therapy. A series of mitigating measures was undertaken and PrAISED therapists were provided with guidance (Appendix 2). A protocol amendment to adapt trial procedures was approved, including delivery of the intervention via telephone or videocall [71]. Follow up assessments were conducted remotely, meaning we could not complete measures requiring physical contact. We removed some outcome measures to reduce burden on participants (Table 1). Participants within 6 weeks of the end of their programme had their final assessment brought forward. An additional interim outcome data collection point was introduced for all other remaining participants, in case no further trial activity became possible. Recruitment and in-person therapy and data collection recommenced after 1st September 2020, if participants were willing, using personal protective equipment, and excluding assessments that required close personal contact or sharing of equipment (including CANTAB cognitive measures and accelerometers). Some remote assessment continued after this time if requested by the participant.

Sample size

An initial calculation based on parameters from published literature suggested a sample size of 368 participants (184 per group), with a 23% attrition rate, had 80% power to detect changes in disability outcome (DAD), with an effect size of 0.5 (11 points on a baseline of 70, standard deviation 22) [19, 72]. A minimum clinically important difference has not been defined for the DAD, but a natural history study in Alzheimer's disease suggested the loss of about one point per month over 12 months [73]. Following the feasibility study, a recalculation suggested that a sample size of 248 was

sufficient. The original sample size was maintained, with the agreement of the data monitoring and steering committees, in the light of uncertainties in estimates.

In the event, with the COVID-19 pandemic, this proved prescient. Recalculation of sample sizes in July 2020, prior to restarting the trial, under a range of feasible impacts on intervention effect size, primary outcome standard deviation and withdrawal rates, suggested that the sample size of 368 had adequate power to answer the research question.

Randomisation

Randomisation was performed after baseline assessment and consent. A secure internet-based system using a dynamic, adaptive allocation algorithm, accessed by a secure web portal held at the North Wales Organisation for Randomised Trials in Health Clinical Trials Unit, Bangor University was used to randomise individuals, 1:1, minimised by site, presence of a co-resident, and history of previous falls [74]. The randomisation system was maintained by a statistician independent of the analysis and research teams. Allocation was later emailed to the intervention delivery teams, who arranged for the first clinical assessment.

Blinding

Blinding of participants and therapists was not possible due to the nature of the intervention. Researchers collecting outcome data were not blinded as participants almost always inadvertently unblinded the researcher during the feasibility study [22]. Analysis was blinded.

Statistical Methods

For the primary outcome of difference in DAD score between groups, an analysis of covariance (ANCOVA) was conducted using stratification variables (site, co-resident carer and history of falls) and baseline DAD score as covariates. For secondary outcome measures, ANCOVAs were conducted, using the stratification and respective baseline measures as covariates. All analyses were conducted on an intention-to-treat basis. Multiple imputation using chained equations (MICE) was used in the main analysis when appropriate. Effect sizes were standardised as Cohen's d [75]. Minimum clinically important differences on scores were identified, where available. Adjusted mean differences, effect size estimates, 95% confidence intervals (CI) and p-values were reported for all analyses. A range of sensitivity analyses was performed, including a complete case analysis. Falls were analysed as the proportions of participants falling, the incidence rate ratio using a negative binomial regression, and time to first fall using a Cox proportional hazards regression. We anticipated that any impact of the PrAISED intervention on falls would not be immediate, so our pre-defined efficacy outcome was rate of falling between months 4 and 15. The statistical analysis plan is available [76].

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Process Evaluation

We undertook a process evaluation following Medical Research Council (MRC) guidelines [77-80]. We investigated reach, dose, fidelity and adaptations of training and intervention delivery. We recorded details of each session delivered, exercise undertaken independently via monthly calendars, and fidelity of delivery from analysis of a sample of 14 video-recorded sessions, in which evidence was sought of 14 key principles of the PrAISED intervention [52]. We conducted qualitative interviews with a sample of participants with dementia, carers and therapists to investigate how the intervention was received, as well as barriers and facilitators to participation.

Ethics and study monitoring

The study was approved by the Bradford-Leeds Research Ethics Committee (REC number 18/YH/0059). The trial was monitored by an independent steering committee and a data monitoring committee [81].

Patient and public involvement

Public and patient involvement (PPI) was integrated into every stage of the research cycle with the aim that the intervention had relevance and the research processes were acceptable to people with mild dementia and their carers. One of our co-investigators was a carer. PPI representatives were members of the programme management group and the trial steering committee. They worked in collaboration with the research team to develop the funding application and intervention, co-designed patient facing materials, participated in research interviews [82] and interpreting results.

RESULTS

Participant Flow

From 8th October 2018 to 23rd June 2022, 1540 potential patient participants were pre-screened, of whom 319 were ineligible and 746 did not wish to take part. Of 475 screened, 110 were not randomised: 61 were ineligible, 18 withdrew, 31 were lost (figure 1). 365 patient and 365 carer participants were randomised (84, 23% Bath; 79, 22% Derby; 60, 16% Lincoln; 23, 6% Oxford; 119, 33% Nottingham). Three protocol deviations involved failure to adjust baseline MoCA scores of 25/30 for duration of education.

Numbers analysed

Seventy-five participants (21%) did not complete 12-month follow up: 52 (14%) withdrew, 23 (6%) were lost. There was no difference in withdrawals between groups (26 vs 26, Fischer's Exact Test p=0.9). Available details for participants who withdrew were assessed by a blinded panel for whether they had 'meaningful' health-related outcomes, that is, had died, been admitted to a care home or withdrew due to deteriorating health. Twenty-seven withdrawals were meaningful, with no difference between groups (14 vs 13, p=1.0).

Baseline Data

Baseline characteristics were similar between groups, including those who withdrew (table 2). Patient participants had a median age of 80 years (range 65 to 95), 58% male, 98% white ethnicity, 68% married and 76% co-resident with their carer. A third (31%) completed a college or university degree. 19% had MCI, 39% Alzheimer's dementia, 19% vascular dementia, 16% mixed dementia, 7% other or unknown. Carer participants' median age was 70 years (range 20 to 94), mostly spouses (65%) and predominantly female (73%). A third (34%) of carers had a limiting long-term health condition.

Adherence and fidelity

The intervention was delivered largely as intended and participants engaged well, despite the disruption of the COVID-19 pandemic. Participants in the intervention group took part in a median of 31 therapy sessions (IQR=22 to 40). Participants in the control group took part in a median of one session (IQR=1 to 1). The mean length of sessions was 71 minutes (SD=30; range: 5 to 220). Two-thirds were delivered face-to-face (n=1,357; 68%). Fidelity of therapy delivery was 70% against PrAISED core principles rated from video-recordings. 4,040/4,863 (83%) expected calendars were returned from intervention participants. The intervention group participants recorded a mean of 482

minutes of PrAISED exercise per month (standard deviation=705; range: 0 to 5310; 121 minutes/week) (Appendix 2).

Outcomes

There was no difference between intervention and control on the primary ADL outcome, DAD: adjusted mean difference -1.3 (95% CI -5.2 to +2.6); effect size (d) -0.06, 95% CI -0.26 to 0.15, p=0.5, or on most secondary outcome measurements, including balance, functional mobility, physical activity or quality of life (tables 3 and 4). Upper 95% confidence intervals excluded small to moderate beneficial treatment effects. There were statistically significant small differences, in favour of the control group, on the dual task Timed Up and Go test (d=0.48, 95% CI 0.12 to 0.83, p=0.01) and (self-reported) DEMQOL (d=-0.26, 95% CI -0.47 to -0.06, p=0.01), but not DEMQOL proxy or Euroqol EQ5D quality of life measures.

The analyses of CANTAB cognitive measures were underpowered, but suggested statistically significant benefits for the PrAISED intervention, with a moderate effect size, on tests of multi-tasking (MTT, an executive function test assessing participants' ability to manage conflicting information) and Spatial Span (SSP, a test of visuo-spatial working memory capacity; tables 5 and 6).

Multiple sensitivity analyses showed no differences in results, including (i) complete cases, (ii) those completing the intervention before the COVID-19 pandemic, (iii) using the interim data collected in the early weeks of the pandemic, (iv) correcting for survivor bias, by assigning a DAD score of zero to participants who died, (v) excluding those who terminated the intervention early due to the pandemic, (vi) excluding three participants who had MoCA scores at baseline above the upper limit.

4.4% of participants reported a confirmed COVID-19 infection. 82% engaged in social distancing for a median 116 days (IQR=37 to 210) and 47% COVID-19 self-isolated for a median 71 (IQR=22 to 139) days. Results were no different for those reporting, or not reporting, a COVID-19 infection.

Falls

There were 796 falls in total, 375 in the intervention group and 421 in control group. 60% of participants in the intervention group had at least one fall in the trial compared with 57% participants in the control group, odds ratio, OR=1.1 (95% CI 0.71 to 1.8), p=0.6. There were 73 injurious falls in total, 38 in the intervention group, 35 in the control group. At least one injurious fall was reported by 15% of participants in the intervention and 16% in the control groups, OR=0.91 (0.51 to 1.6), p=0.8.

The falls efficacy outcome was falls in months 4-15. There were 279 falls recorded for participants who completed all the study calendars for these months, 79 in the intervention group, 200 in the control group. 59% of participants in the intervention group had at least one fall compared with 55% of participants in the control group, OR=1.2 (0.57 to 2.4), p=0.7. Falls incidence rate in the intervention group was 1.49 per person year compared with 2.47 per person years in the control group, Incidence Rate Ratio=0.78 (0.46 to 1.3), p=0.3, adjusted for site, co-resident carer and previous history of falls. A survival analysis showed median time to the first fall was 13 months for the intervention group, 12 months for the control group, adjusted Hazard Rate Ratio=0.85 (0.50 to 1.4), p = 0.5.

Harms (adverse events)

One hundred and sixty-seven adverse events were recorded: 59 in control and 108 in the intervention groups, involving 68 participants: 27 (15%) from control and 61 (33%) from intervention groups. There were 91 serious adverse events: 29 in control and 62 in intervention, involving 60 participants: 22 (12%) from control and 38 (21%) from intervention groups. None was treatment related. There were 13 deaths: 4 (2.2%) in control and nine (4.9%) in the intervention groups (OR = 2.3, 95% CI 0.70 to 8.7, p = 0.3). There were 7 new care home placements; 2 (1.1%) from control and 5 (2.7%) from intervention group (OR = 2.4, 95% CI 0.49 to 19, p = 0.5). There were 75 hospital admissions: 27 in control and 48 in intervention groups, involving 53 participants: 22 (12%) from control and 31 (17%) from intervention groups (OR = 1.5, 95% CI 0.82 to 2.7, p = 0.2).

There were 228 falls recorded for participants who completed the first three months' calendars, 96 falls in the intervention group and 132 falls in the control group. 32% of participants in the intervention group had at least one fall compared with 31% participants in the control group, OR = 1.1, 95% CI (0.64 to 1.8), p = 0.9.

DISCUSSION

Summary

The PrAISED intervention did not improve ADL, physical activity, quality of life or any other health status outcome, including balance and functional mobility, for people with mild dementia or MCI in the 12-month period after randomisation. There may have been a small reduction in rate of falling (22% relative risk, statistically uncertain), and improvement in some specific cognitive domains, in underpowered analyses, but these did not translate into functional gains. Delivery of the intervention was disrupted by COVID-19 pandemic restrictions.

Strengths and limitations

This was a high-quality multi-centred RCT. We followed MRC guidance to develop and evaluate the intervention [83]. We established the feasibility and acceptability of intervention delivery and trial processes before starting the trial [22]. A process evaluation established reasonable participant adherence and fidelity of intervention delivery. Our attrition and missing data rates were acceptable. In qualitative interviews, undertaken as part of the process evaluation, the trial intervention was overwhelmingly well-received by participants, carers and provider staff [80].

The intervention was systematically designed, and refined over several years, including during the feasibly trial [21,22,54]. It was intended to be practical and relevant to participants. It comprised predominantly resistance (strength and balance) exercises, in a home setting, linking to daily activities, explicitly addressing risk of falls and other safety concerns and encouraging outdoor mobility. Intervention was individualised (tailored, personalised). Exercise was not a standard prescription but was seen as subserving activities that participants needed or wanted to do. Close attention was paid to motivation, the learning needs of people with dementia, and contextual factors, especially involvement of family or other carers. It was delivered by trained and experienced physiotherapists and occupational therapists, who made assessments and plans and supervised trained rehabilitation support workers.

The intervention was about as intensive as could be credibly delivered by a public health service. In designing the trial, the funder, NIHR, on behalf of the UK National Health Service, was concerned that the intervention was unfeasibly intensive, and requested the inclusion of a briefer and less expensive intervention in the feasibility study. The feasibility study demonstrated the need for prolonged supervision, however [22]. In our main trial, we emphasised tailoring of supervision to individual needs. Although a median of 31 therapy sessions over a year might have been insufficiently intensive to change outcomes (compared, for example, with the FINALEX study [19]) it

was probably the maximum plausible dose in relation to NHS services and costs of delivery. We used 'tapering' of the intervention, with twice weekly visits in the first 3 months, reducing to monthly visits in the last 3 months to encourage independent undertaking of exercise. In the event, without direct supervision, this may simply have reduced adherence.

The patient population lacked diversity, being disproportionately well-educated, white men. The study enrolled people willing to agree to take part in research and perform prolonged exercise, who may have already been living healthy lifestyles and may have been the least likely to benefit.

The trial was disrupted by the COVID-19 pandemic, associated lockdown and social distancing restrictions. Clinical delivery teams were quick to move to remote delivery of the intervention and demonstrated great flexibility and innovation in doing so [71, 84], but this did not work for many participants, such as those with sensory impairments, lacking information technology hardware or internet connections, or a carer to help with telephone calls or videoconferencing. In this situation, progression of exercises was impossible to do safely, and access to community facilities diminished or ceased. Some follow-up interviews were conducted remotely, which might have affected data quality. Remote follow-up prevented us from collecting some secondary outcome measures. Sub-group analysis on participants followed-up prior to the COVID-19 pandemic did not suggest different results, however. Equally, it could be argued that the pandemic was challenging for all older people, our intervention could have mitigated this and shown exaggerated benefits [85,86].

We planned to objectively measure physical activities undertaken by participants in their own time using accelerometers but had to abandon this due to the pandemic [87]. We had no direct measure of participant independence, nor participant or carer satisfaction with the programme.

Research in context

There have been numerous reviews of non-pharmacological interventions in dementia. The evidence that exercise and physical activity can improve ADLs for people with dementia is inconclusive. A Cochrane review found no high-quality evidence [16]. A further review concluded that exercise and physical activity reduced disability and falls, but that the quality of evidence was low [88]. A recent meta-analysis found no effect of exercise on ADLs [89]. Two reviews considered a range of interventions designed to maintain functional activity in dementia. Both identified heterogeneity between studies, mixed evidence of effectiveness, generally low quality of evidence, but a greater effect when interventions were tailored to participants' interests and abilities, and delivered by registered therapists [90, 91]. The evidence for moderate to high intensity exercise preventing falls in cognitively intact older people is strong [92].

There have been a few adequately powered and high-quality individual trials. One trial of prolonged (12 months) and intensive (1 hour twice a week), physiotherapist-supervised, home exercise demonstrated a substantial reduction in rate of loss of ADL abilities and halved the rate of falling [19]. Two trials of exercise interventions for people with sarcopenia and frailty who were not cognitively impaired showed small but significant improvements in mobility disability incidence (20% risk reduction) and frailty markers with moderate intensity programmes [93-95]. Two 4-month trials of moderate to high intensity supervised group exercise for people with mild to moderate dementia showed no improvement in ADLs after six months [96,97]. Functionally orientated occupational therapy improved abilities and activity [60], but these findings were not replicated in two subsequent trials [98, 99]. The 'Journeying Through Dementia' trial of a bespoke, moderate-intensity, occupational therapy intervention was negative [100]. A trial of cognitive rehabilitation in mild to moderate dementia, focusing on functional activity, demonstrated that more goals were met in the intervention group, but no impact on health status measures such as ADL [101].

Interpretation

Dementia is a progressive condition with no cure. In recent years, there has been increasing interest in preventing dementia [14]. Secular trends in incidence suggest that dementia risk is not immutable [6], but good evidence for the effectiveness of interventions to reduce dementia risk is lacking. Protective factors such as physical activity are likely to act over decades rather than months. 'Secondary prevention' (of progression once dementia is diagnosed) through lifestyle interventions appears to be ineffective. A reduction in rate of falling remains possible, and may be valuable, but did not impact on preservation of ADLs or quality of life. The point estimate of falls risk reduction in our study was in line with estimates from meta-analyses [92].

Current health policy emphasises living well after a dementia diagnosis, through a combination of healthcare, psycho-social and societal changes, and adaptation of services to meet the particular needs of people living with dementia [10]. We, and others, have demonstrated that maintaining abilities is not likely to be possible. This does not mean that intervention may not have benefit in the psycho-social domain, including affirming personhood, inclusion, occupation, relationships, or carer support. Aspects such as social engagement, concern, hope, goal-achievement, information-giving (on a range of dementia-related topics), and therapeutic relationship-building appear to have been greatly valued [80]. In palliative care and mental health, therapeutic relationships are valued in their own right; the exercise may have been a means to an end.

The absence of measurable health gain makes it hard to argue for routine provision of this intervention. However, our observations could inform the development of future models of support.

There is a widespread perception of a 'service gap' for people after a dementia diagnosis and their carers. The healthcare background, knowledge and expertise of the therapists appears to have been relevant to delivering holistic and supportive intervention. What this means in terms of measurement and evaluation is yet to be defined, but our current paradigm may be missing something. Others have commented on the unsuitability of available outcome measures and the limitations of randomised controlled trials in evaluating interventions in this population [99, 100]. A Social Return on Investment analysis of our feasibility trial, a health economic methodology which attempts to identify, quantify and monetise a wide range of health, personal and social benefits from a public policy perspective, was strongly positive [102].

Some specific aspects of our trial may explain negative results. The DAD is recommended as the most appropriate ADL outcome for dementia trials but can be difficult to complete. It distinguishes between 'initiation' and 'performance' of activities, and privileges activities undertaken without prompting. Whilst reasonable on a normative basis, this may not adequately ascertain 'supported performance' rather than independence. We undertook training in dual-task-activities, as impairment in this is a risk factor for falling, it is trainable and improved abilities can carry over between activities [56-58]. Our main index of ability in dual tasking was the dual task TUG test, which deteriorated in the intervention group. The test involved getting up, walking three metres, turning and sitting down again, whilst counting backwards. The instructions were cognitively demanding. Researchers reported that participants who had received active therapy sometimes misunderstood the task, for example trying to walk backwards, and may have confused the test with therapeutic tasks they had practiced during the intervention. Similarly, the DEMQOL quality of life scale asks if the participant is 'worried about' things related to their dementia. The therapy programme may have increased participants' awareness of their inabilities.

We can speculate whether control group participants, who get a diagnosis of dementia, and who are sufficiently able to volunteer for a research study, successfully adapt, drawing upon their existing resources and striking a balance that works for them in terms of activity and wellbeing. The objective of the trial was to introduce an intervention that did something different. Frequent involvement of health care professionals could disrupt normal adaption, draw attention to ill-health rather than well-being, encourage people to take greater risks than they would usually have done, and prompt greater involvement of health care services.

Implications and future work

We add to accumulating evidence that interventions to delay cognitive or functional decline in early dementia or MCI are ineffective. So far, drug therapies, cognitive stimulation, exercise, and rehabilitation therapies have, at best, a small impact on functional activities and quality of life, and do not appear to change the course of the disease.

We need to think again about how we support people with dementia to live well with the condition. A more supportive approach to care may be required. Healthcare interventions should focus on solving practical problems and crises. We should emphasise helping the person with dementia to live well, despite their limitations, minimise intervention burden, maintain personhood, inclusion and occupation, provide psychological and emotional support, and support family and other carers. Restoration of 'independence' in activities may be unrealistic, 'adapted' or 'supported' functioning (compensatory approaches) may be more achievable [103]. For example, a person may be assisted to cook or shop, in order that they remain active and included, rather than aiming for them to be able to do these tasks alone. We need outcome measures that reflect these. The value of therapeutic relationships may be underappreciated and may go beyond what might be expected from befriending, counselling or social prescribing. Exercise and physical activities should be promoted for enjoyment, occupation, inclusion and to enhance relationships.

To make a real impact on the course of dementia we are likely to need disease modifying drugs. Recent data on lecanemab provide proof of concept, but the ADL benefits over 18 months were very small (2 points on a 90-point scale) [104]. The failure of non-drug therapies justifies the continued search for new agents.

OTHER INFORMATION

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Ethical Approval: This study was approved by the Bradford-Leeds Research Ethics Committee (REC number 18/YH/0059, IRAS project identification 236099) and research governance departments in each organisation.

Data sharing: we are happy in principle to share our data. Please contact the corresponding author.

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Programme Steering Committee: S Iliffe (chair), L Allan, G Mountain, J Whitney, R Ogollah (statistician), M Lewis (statistician), P Riley (PPI), P Foster (PPI).

Data Monitoring Committee: J Treml (chair), D Howell (statistician), A Bishop, E Mioshi.

Authors contribution:

- Conception, design, funding: RH, TM, SG, VvdW, PL, HS, KP, VHM, KV, RdN, MG, ZH, RTE, JG, KP, MO
- Intervention development, training and delivery support: VB, PL, TB, LH, AC, RT, JH, CDL, HS, LB, AL, MG, MD, TM, RH
- Literature searching: CDL, VB, VvdW, JH, FK, SG, RH
- Recruitment, data collection: RB, CB, JL, AL, ST, KJ, CD, CDL, AHS, TW
- Statistics, CTU: ZH, AB, RH
- Process evaluation: CDL, VvdW, KP, MG, MD, VB, LH, RH
- Health economic evaluation: RTE, VE, NH
- Study management: SG, VvdW, ROB, EA, MG, MD, KK, RV, TM, RH
- Interpretation: RH, CDL, VvdW, SG, FK, PL, JG, KP, VB, LH, AC, EA, RdN, TW, HS, MO, MG, MD

- Paper drafting: RH, SG, FK, CDL
- All authors approved the final paper

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FIGURES

Figure 1: Consort Participant Flow Diagram
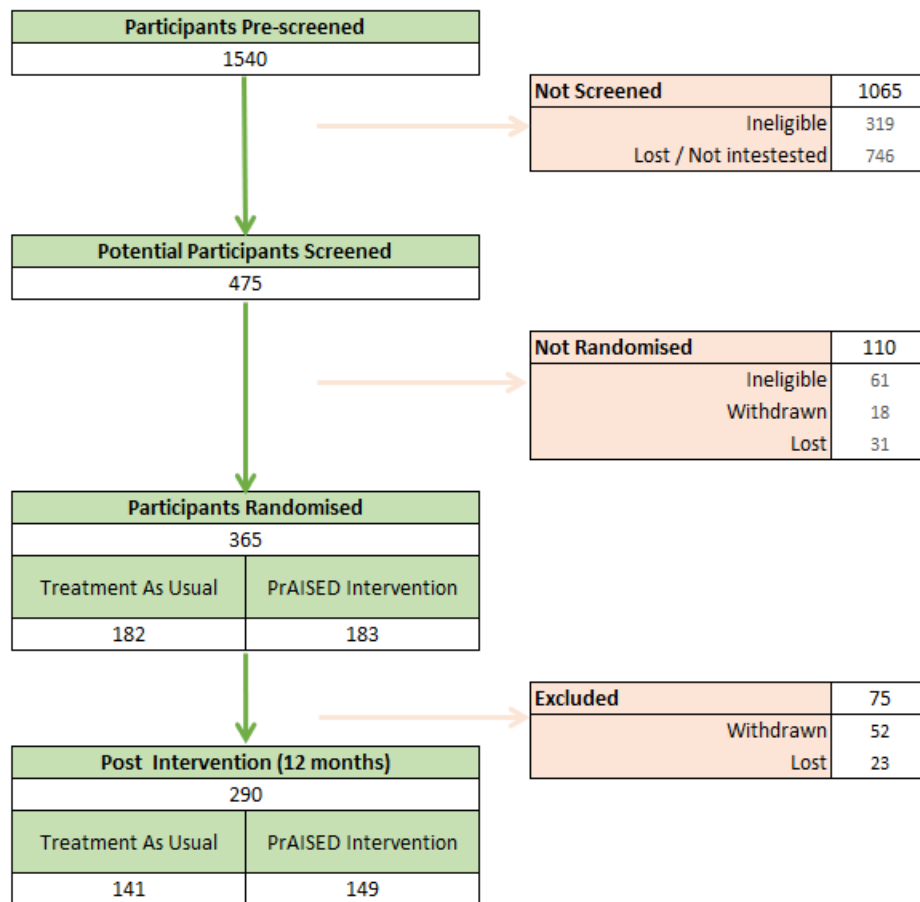
TABLES

Table 1: Data collection time points

Scale or measure	Baseline	6 months	12 months	Discont-inued from March 2020	Not collected remotely	Completed by
Disability in dementia scale (DAD)	X		X			Carer participant
Nottingham Extended Activities of Daily Living Scale (NEADL)	X		X			Patient participant
Demographics	X					Carer participant
Past Medical History	X					Carer participant
Medications	X					Carer participant
Montreal Cognitive Assessment (MoCA)	X		X		X	Patient participant
Verbal fluency	X		X		X	Patient participant
Cambridge Neuropsychological Test Automated Battery (CANTAB)	X		X	X	X	Patient participant
Apathy Evaluation Scale	X		X			Carer participant
Berg Balance scale	X		X		X	Patient participant
Hand grip strength	X		X		X	Patient participant
Timed up and go (TUG) test and dual task TUG.	X		X		X	Patient participant
SHARE frailty instrument	X		X		X	Patient participant
Longitudinal Study of Aging Amsterdam Physical Activity Questionnaire (LAPAQ)	X		X			Carer participant
Step count over 7 days (accelerometer)	X		X	X	X	Patient participant
Euroqol EQ5D-3L self-completed quality of life	X		X			Patient participant
Euroqol EQ5D-5L proxy-completed quality of life	X	X	X			Carer participant
Dementia Quality of Life Scale (DEMQOL)	X		X			Patient participant
Dementia utility-weighted items (DEMQOL-U)	X	X				Carer participant
Dementia Quality of Life Scale (DEMQOL-proxy)	X		X			Carer participant
Hospital Anxiety and Depression Scales (HADS)	X		X			Patient participant
Falls Efficacy Scale – International (FES-I)	X		X			Patient participant
Carer strain index	X		X			Carer participant
Carer quality of life EQ5D-5L	X		X			Carer participant
Client Service Receipt Inventory	X	X	X			Carer participant

Calendars were collected monthly from randomisation to 15 months

Table 2: Baseline variables split by allocation group

	Control N= 182	Intervention N= 183	Withdrew n=52
PATIENT PARTICIPANTS			
Age median (IQR)/years	81(75-84)	80 (75-85)	80 (77-85)
Gender Female n (%)	73 (40%)	82 (45%)	23 (44%)
Ethnic Group White n (%)	179 (98%)	179 (98%)	52 (100%)
Married n (%)	123 (68%)	124 (68%)	34 (66%)
Living Alone n (%)	46 (25%)	43 (24%)	17 (33%)
Montreal Cognitive Assessment (MoCA) mean/30 (SD)	19.8 (3.1)	20.0 (3.2)	19.9 (3.2)
Higher education	54 (30%)	59 (32%)	12 (23%)
Diagnosed dementia	142 (78%)	151 (83%)	44 (85%)
Comorbidity count/23 Mean (SD)	4.0 (2.0)	3.9 (1.8)	3.9 (1.9)
Number of drugs Mean (SD)	6.1 (3.5)	6.1 (3.2)	6.1 (3.4)
Previous fall	95 (52%)	93 (53%)	26 (50%)
CARER PARTICIPANTS			
Husband/wife/partner	119 (65%)	117 (64%)	32 (62%)
Son/daughter	50 (28%)	55 (30%)	16 (31%)
Other	13 (7%)	11 (6%)	4 (8%)
Carer Gender Female	134 (74%)	131 (72%)	38 (73%)
Carer co-resident	136 (75%)	140 (76%)	38 (73%)
Carer long term medical condition	63 (35%)	61 (33%)	20 (39%)
Carer Age (median, IQR)/years	70 (58-77)	70 (58-78)	69 (58-78)

IQR Interquartile Range, SD standard deviation.

Table 3: Unadjusted scores on outcome measures according to randomisation group

Measure	Group	n	Baseline Mean (SD)	Follow Up Mean (SD)	Differ-ence	Interpretation
ADL DAD /100 Higher is superior	Control	125	77.8 (20.8)	66.4 (24.5)	-11.4	Deterioration
	Intervention	133	77.6 (20.1)	64.2 (25.7)	-13.4	Deterioration
NEADL Score/22 Higher is superior	Control	124	16.8 (3.9)	14.1 (4.8)	-2.7	Deterioration
	Intervention	129	16.2 (4.2)	13.9 (4.3)	-2.2	Deterioration
Physical Activity (LAPAQ) Higher is superior	Control	118	1483 (1608)	1293 (1430)	-189	Deterioration
	Intervention	130	1395 (1230)	1037 (1224)	-358	Deterioration
Accelerometer-Total Steps in 7 days Higher is superior	Control	22	21412 (20112)	21694 (17308)	282	Improvement
	Intervention	21	24410 (21081)	20584 (15226)	-3826	Deterioration
Berg Balance Scale/56 Higher is superior	Control	58	50.3 (5.5)	46.7 (10.6)	-3.6	Deterioration
	Intervention	66	46.8 (9.6)	46.3 (9.2)	-0.5	Deterioration
Timed Up and Go /seconds Higher is inferior	Control	69	13.9 (6.7)	14.0 (7.0)	+0.1	Deterioration
	Intervention	69	13.7 (4.5)	16.6 (12.6)	+3.0	Deterioration
Dual Task Timed Up and Go/seconds Higher is inferior	Control	62	18.4 (8.3)	20.8 (9.9)	+2.3	Deterioration
	Intervention	64	19.7 (11.7)	28.1 (20.0)	+8.4	Deterioration
DEMQOL/112 Higher is superior; MCID 6	Control	136	90.9 (11.4)	88.9 (14.9)	-2.0	Deterioration
	Intervention	140	89.2 (12.9)	83.7 (15.2)	-5.5	Deterioration
DEMQOL Proxy/124 Higher is superior; MCID 6	Control	135	95.6 (12.9)	90.7 (15.1)	-4.9	Deterioration
	Intervention	145	92.1 (13.3)	90.6 (13.3)	-1.5	Deterioration
DEMQOL-U (6 months) Higher is superior	Control	149	0.69 (0.1)	0.72 (0.13)	+0.03	Improvement
	Intervention	141	0.72 (0.1)	0.72 (0.13)	0	Deterioration
Self-reported Quality of life EQ-5D-3L/1.0 Higher is superior	Control	135	0.82 (0.18)	0.75 (0.25)	-0.07	Deterioration
	Intervention	138	0.81 (0.18)	0.75 (0.24)	-0.06	Deterioration
Proxy Quality of life EQ-5D-5L/1.0 Higher is superior	Control	130	0.80 (0.18)	0.71 (0.23)	-0.09	Deterioration
	Intervention	143	0.79 (0.17)	0.73 (0.19)	-0.07	Deterioration
Montreal Cognitive Assessment /30 Higher is superior	Control	77	20.0 (3.2)	17.5 (4.6)	-2.5	Deterioration
	Intervention	75	20.1 (3.5)	17.3 (5.2)	-2.8	Deterioration
Verbal fluency/words Higher is superior	Control	79	12.3 (4.7)	10.8 (4.8)	-1.5	Deterioration
	Intervention	76	12.0 (4.6)	10.0 (4.4)	-1.9	Deterioration
Apathy Evaluation Scale / 72 Higher is inferior	Control	121	40.3 (12.0)	44.6 (12.0)	+4.3	Deterioration
	Intervention	134	42.4 (12.4)	46.3 (13.0)	+3.9	Deterioration

Measure	Group	n	Baseline Mean (SD)	Follow Up Mean (SD)	Differ-ence	Interpretation
Falls Efficacy Scale – International/28 Higher is inferior	Control	134	10.3 (4.1)	10.9 (4.8)	+ 0.5	Deterioration
	Intervention	138	10.4 (3.9)	11.0 (4.5)	+0.6	Deterioration
HADS Anxiety/21 Higher is inferior	Control	133	3.7 (2.9)	4.2 (3.6)	+0.5	Deterioration
	Intervention	132	4.3 (3.0)	5.0 (3.3)	+0.7	Deterioration
HADS Depression/21 Higher is inferior	Control	132	3.9 (2.6)	4.8 (3.7)	+0.9	Deterioration
	Intervention	132	4.9 (2.7)	5.3 (3.0)	+0.4	Deterioration
SHARE Frailty Index Higher is inferior	Control	71	1.6 (1.6)	1.7 (1.8)	+0.1	Deterioration
	Intervention	72	1.7 (1.8)	1.7 (1.8)	0	Deterioration
Hand grip strength Right hand/kg Higher is inferior	Control	78	24.9 (10.8)	23.6 (9.6)	-1.3	Deterioration
	Intervention	76	22.4 (8.3)	20.9 (7.5)	-1.5	Deterioration
Carer Strain Index/13 Higher is inferior	Control	125	4.3 (3.3)	4.7 (3.5)	0.4	Deterioration
	Intervention	134	4.7 (3.3)	4.8 (3.5)	0.2	Deterioration
Carer EQ-5D-5L Index/1.0 Higher is superior	Control	132	0.88 (0.17)	0.86 (0.17)	-0.02	Deterioration
	Intervention	140	0.85 (0.18)	0.85 (0.16)	-0.01	Deterioration

Abbreviations: DAD Disability Assessment for Dementia, NEADL, Nottingham Extended Activities of Daily Living (NEADL), DEMQOL Dementia Quality of Life, LAPAQ Longitudinal Ageing Study Amsterdam Physical Activity Questionnaire, AES Apathy Evaluation Scale, EQ5D-3L EuroQol five dimensions questionnaire - three levels (EQ5D-3L), EQ5D-5L EuroQol five dimensions questionnaire – five levels, CSI Care Strain Index, MoCA Montreal Cognitive Assessment; HADS Hospital Anxiety and Depression Scale; SHARE Survey of Health Ageing and Retirement in Europe, MCID minimum clinically important difference

Table 4: Analysis of Covariance and standardised effect size estimates for intervention group (with missing data imputed)

Measures	n	Adjusted mean difference (95% CI) *	Cohen's d effect Size (95%CI) *	p
DAD Score	365	-1.3 (-5.2; +2.6)	-0.06 (-0.26; 0.15)	0.51
NEADL Score	256	+0.2 (-0.7; 1.1)	+0.05 (-0.20; 0.29)	0.71
LAPAQ Physical Activity Score	365	-167 (-445; 112)	-0.14 (-0.35; 0.06)	0.25
Accelerometer- Number of Steps in 7 days	43	-4030 (-11028; 2969)	-0.37 (-0.98; 0.23)	0.25
Berg Balance Scale	145	+1.8 (-0.7; 4.2)	+0.15 (-0.08; 0.57)	0.15
Timed Up and Go	138	-2.7 (-5.9; +0.5)	-0.29 (-0.62; +0.05)	0.10
Dual Task Timed Up and Go	126	-7.3 (1.8; 12.8)	-0.48 (0.12; 0.83)	0.01
DEMQOL	365	-3.8 (-6.8; -0.8)	-0.26 (-0.47; -0.06)	0.01
DEMQOL Proxy	365	+2.4 (-0.3; 5.1)	+0.18 (-0.03; 0.38)	0.08
DEMQOL-U (6 months)	365	+0.01 (-0.01; 0.04)	+0.11 (-0.1; 0.3)	0.29
EQ-5D-3L Index self-reported	365	+0.02 (-0.04; 0.07)	+0.08 (-0.12; 0.29)	0.51
EQ-5D-5L Index proxy	365	+0.03 (-0.01; 0.07)	+0.15 (-0.05; 0.36)	0.16
MoCA	155	-0.4 (-1.5; 0.8)	-0.11 (-0.42; 0.21)	0.52
Verbal Fluency - Correct Words	155	-0.5 (-1.6; 0.5)	-0.16 (-0.48; 0.15)	0.32
Apathy Evaluation Scale	365	-0.6 (-2.7; 1.4)	-0.07 (-0.27; 0.14)	0.54
Falls Efficacy Scale-International, short	365	+0.2 (-0.7; 1.0)	+0.05 (-0.15; 0.26)	0.64
HADS Anxiety	275	+0.4 (-0.3; 1.1)	+0.15 (-0.09; 0.38)	0.23
HADS Depression	275	-0.1 (-0.8; 0.6)	-0.03 (-0.27; 0.20)	0.78
SHARE Frailty Index	149	-0.05 (-0.52; 0.42)	-0.04 (-0.36; 0.29)	0.56
Hand Grip Strength /kg	154	-0.9 (-2.9; 1.1)	-0.15 (-0.47; 0.16)	0.36
Carer Strain Index	365	-0.01 (-0.63; 0.62)	-0.04 (-0.25; 0.16)	0.69
Carer EQ5D5L Index	365	+0.01 (-0.01; 0.04)	+0.09 (-0.12; 0.29)	0.37

Note: Effect size Cohen's d interpretation: 0-0.2=no effect; 0.2-0.5=small; 0.5-0.8=moderate; >0.8=large
*Positive values show an effect in favour of intervention group

Abbreviations: DAD Disability Assessment for Dementia, NEADL, Nottingham Extended Activities of Daily Living (NEADL), DEMQOL Dementia Quality of Life, LAPAQ Longitudinal Ageing Study Amsterdam Physical Activity Questionnaire, AES Apathy Evaluation Scale, EQ5D-3L EuroQol five dimensions questionnaire - three levels (EQ5D-3L), EQ5D-5L EuroQol five dimensions questionnaire – five levels, CSI Care Strain Index, MoCA Montreal Cognitive Assessment; HADS Hospital Anxiety and Depression Scale; SHARE Survey of Health Ageing and Retirement in Europe, CI Confidence Interval

Table 5: CANTAB cognitive assessment results, unadjusted comparisons

Measure	Group	n	Baseline Mean (SD)	Follow-Up Mean (SD)	Difference	Interpretation
MTT RL median congruent/ms Higher is inferior	Control	24	930 (168)	953 (192)	22	Deterioration
	Intervention	26	904 (168)	894 (163)	-9	Improvement
MTT RL median incongruent /ms Higher is inferior	Control	24	1040 (193)	1038 (193)	-1	Improvement
	Intervention	26	1038 (173)	993 (159)	-44	Improvement
MTT RL median switching blocks/ms Higher is inferior	Control	24	1144 (246)	1081 (192)	-63	Improvement
	Intervention	26	1063 (240)	1036 (183)	-27	Improvement
PAL memory score Higher is superior	Control	27	3.5 (2.1)	2.7 (2.1)	-0.8	Deterioration
	Intervention	29	3.7 (3.4)	3.0 (2.7)	-0.7	Deterioration
PAL number of patterns Higher is superior	Control	27	4.9 (1.3)	4.3 (1.3)	-0.6	Deterioration
	Intervention	29	5.0 (1.5)	4.4 (1.6)	-0.6	Deterioration
PAL total errors Higher is inferior	Control	27	16.1 (7.4)	13.9 (5.8)	-2.2	Improvement
	Intervention	29	17.2 (7.3)	15.5 (8.7)	-1.7	Improvement
SSP Lengths forward Higher is superior	Control	28	4.1 (1.2)	3.8 (1.3)	-0.3	Deterioration
	Intervention	30	4.2 (1.2)	4.5 (1.5)	0.3	Improvement

MTT multi-tasking test (executive function); PAL paired associates learning (visual memory); SSP Spatial Span (visuospatial working memory); ES effect size, NS not statistically significant, CI confidence interval

Table 6: CANTAB cognitive assessment results, ANCOVA analysis

Measures	n	Adjusted mean difference (95% CI)	Effect Size (95%CI)	p-value	Interpretation (intervention)
MTT RL median congruent	50	-69 (-146; 7)	-0.58 (-1.14; +0.01)	0.07	Better, moderate ES, NS
MTT RL median incongruent	50	-79 (-159; 1)	-0.62 (-1.19; -0.05)	0.05	Better, moderate ES
MTT RL median switching blocks	50	-61 (-152; 30)	-0.43 (-0.99; + 0.14)	0.19	Better, small ES, NS
PAL memory score	56	0.10 (-1.19; 1.39)	0.05 (-0.48; +0.57)	0.87	Same
PAL number of patterns	56	0.09 (-0.67; 0.84)	0.07 (-0.46; +0.59)	0.82	Same
PAL total errors	56	1.22 (-3.1; 5.55)	0.16 (-0.37; +0.68)	0.57	Same
SSP lengths forward	58	0.81 (0.14; 1.48)	0.68 (+0.15; +1.2)	0.02	Better, moderate ES

MTT multi-tasking test (executive function); PAL paired associates learning (visual memory); SSP Spatial Span (visuospatial working memory); ES effect size, NS not statistically significant, CI confidence interval