The effectiveness of structured physical activity on agitation in people with dementia: a rapid review

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Abstract

Objectives Managing agitation and other behaviours that challenge is a significant dementia care challenge. The priority is to find effective non-pharmacological interventions as drug treatments can have significant side effects. This review evaluates the effectiveness of structured physical activity on agitation in dementia.

Methods Our rapid review searched four electronic databases, Cochrane CENTRAL, MEDLINE, CINAHL and Embase, for interventional studies using a structured physical activity programme in people with dementia and studied the effect of this activity on behaviours that challenge. Study quality was assessed using CASP criteria and data was narratively synthesised.

Results We included 13 studies in this review (four rated as high quality), involving a total of 1546 participants. Results were analysed according to exercise type, frequency and intensity of the intervention. Exercise is effective in reducing agitation and studies with higher adherence to exercise demonstrated more positive effects on agitation and behaviours that challenge.

Conclusions Physical activity can be effective in reducing agitation in older adults with dementia. Further research is needed to clarify the type of intervention that is most beneficial. Strategies to make physical activity more acceptable and available to people with dementia need to be established.

Keywords dementia, behaviours that challenge, agitation, physical activity, exercise

Introduction

The number of people living with dementia worldwide is rising rapidly due to increased longevity and in the UK is predicted to surpass 1.6 million by 2040 (Wittenberg et al, 2019). Although the most prevalent symptom in dementia is memory loss, agitation is common and very distressing occurring under the umbrella of behaviours that challenge. Around 46% of people with moderate to severe dementia demonstrate clinically significant agitation (Laybourne et al, 2019) and more than 75% of those remain significantly clinically agitated over 6 months (Savva et al, 2009).

Agitation in people living with dementia has been reported as one of the most distressing behaviours to cope with for carers (Fauth and Gibbons, 2014). It impedes relationships, function and activities, leading to poor quality of life (Wetzels et al, 2010), more nursing home admissions (Gaugler et al, 2009) and increased mortality risk (Bransvik et al, 2021). In addition, the estimated mean excess cost associated with agitation for people with Alzheimer's disease in the UK equates to £2billion a year (Morris et al, 2015) and agitation accounts for 44% of the annual health care costs of dementia for people living in care homes (Panca et al, 2019).

Within care homes agitation is associated with functional impairments, social isolation, communication impairments and high levels of psychotropic medication use (Draper et al, 2000). Psychotropic medications are sometimes used for treating behavioural and psychological symptoms of dementia. Their use increases the incidence of stroke and mortality (Gustafsson et al, 2013), and among people living with dementia, results in 1800 deaths per annum in the UK (Banerjee, 2009). National guidance is that non-pharmacological approaches should be the primary method for managing behaviour that challenges in people with dementia (NICE, 2018). Furthermore, people living with dementia in long term care are mainly inactive (Portegijs et al, 2023) and less physically active than those living in the community (Van Alphen et al, 2016). It has been shown that physical activity can benefit other behaviours that challenge and symptoms such as mood and disorientation (Boolani et al, 2021) and therefore it would be prudent to examine if increasing structured physical activity could also benefit behavioural disturbances such as agitation. Evidence about the benefit of physical activity on agitation has been conflicting, with some suggesting the evidence is inconclusive (Thune-Boyle et al, 2012; Barreto et al, 2015; Junge et al, 2020) and others stating exercise is beneficial in managing behavioural symptoms (Brett et al, 2015;

Fleiner et al, 2017; Rodrigues et al, 2021; Kouloutbani et al, 2022). All these reviews identify methodological shortcomings in many of the studies and to improve this there is a need for future research to focus on exercise intervention with a reduction in behaviours that challenge as the primary outcome. Therefore, this review focuses solely on intervention studies that aimed to assess the effect on agitation in response to a specified physical activity intervention. In addition, all stages of dementia were included and interventions in any setting. Our rapid review aims to address the following research question: does structured physical activity reduce agitation in older adults living with dementia relative to usual care?

Methods

This rapid review follows the Cochrane rapid review guidance (Garritty et al, 2020) and uses PRISMA guidelines for systematic reviews (Page et al, 2021). A rapid review was chosen due to time limitations in synthesising knowledge on this topic. The evidence established being used to help develop a forthcoming fellowship grant application. Rapid reviews aim to inform clinical or policy decisions in a timely and resource efficient manner (Moons et al, 2021). They can provide adequate information on which to base clinical decisions and direct comparison of findings from full systematic reviews and rapid reviews showed that conclusions were not markedly different (Watt et al, 2008). The protocol for the rapid review was registered with PROSPERO https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=392894.

Information sources – a systematic literature search was conducted using the following electronic databases Cochrane CENTRAL, MEDLINE, CINHAL and EMBASE. Each database was searched from inception to 1st March 2023. Searches were conducted between 1st February 2023 to 1st March 2023.

Literature Search Strategy

The strategy was based on a search matrix divided into three blocks of search terms including MESH terms and text words covering dementia, physical activity and agitation. Each term in each block was combined with Boolean operators and no filters were applied. Reference lists of articles were also checked for any relevant studies. An example of the full search strategy is provided (Supplementary information –appendix one).

Eligibility criteria

Full text articles and abstracts in English and published in international, peer reviewed journals were considered for inclusion in the review. The PICO framework (Richardson et al, 1995) was used to guide the study inclusion and exclusion criteria:

Inclusion Criteria

-Population: adults with diagnosis of dementia

-Intervention: specified structured physical activity intervention

-Comparison: usual care which may or may not include non-structured activities both physical and non-physical

-Outcome: studies include measurement of agitation or behaviours that challenge using a validated outcome measure

-Study Design: randomised controlled studies, non-randomised intervention studies, pre/post intervention studies

-Language: English only

-Date: All dates

Exclusion Criteria

-Population: adults without diagnosis of dementia

-Intervention: no specified structured physical activity intervention

-Outcome: no measurement of agitation or other behaviours that challenge or no use of a validated outcome measure

-Study design: systematic reviews, cohort studies, non-intervention studies

-Language: any language other than English

Study Selection

The main author reviewed the initial search results and applied the inclusion criteria to screen for relevant articles and remove duplicates. Two individual authors then independently reviewed each article by title and abstract using Rayyan software (Ouzzani et al, 2016). The full text of any relevant articles was then independently reviewed by the same authors.

Consensus was reached on all decisions, with a third reviewer being available in case of disagreement.

Data Extraction and Analysis

Data were extracted using JBI SUMARI software (Munn et al, 2019) and tables created comprising the following characteristics: author, year of publication, country where the study was conducted, sample size, study design, description of physical activity intervention, primary outcomes, secondary outcomes, and main findings.

Due to heterogeneity of the included studies full meta-analysis was not possible, so data was synthesised narratively (McKenzie & Brennan, 2023). This included tabulating the data, exploring relationships within and between the data and finally assessing the robustness of the synthesis (Popay et al, 2006).

For the studies appropriate for meta-analysis, we evaluated the pooled intervention effects by comparing mean post-intervention total NPI scores separately for community and care settings using a random-effects model in SPSS (IBM SPSS Statistics v. 28). We evaluated the effect size in accordance with Cohen's criteria (Cohen, 1988): small (d = 0.2), medium (d = 0.5), and large (d = 0.8). The direction of the effect size was defined according to the methodology utilized in the measurement of each outcome. To be included in the meta-analysis, the same needed to appear in two or more studies. The I^2 statistic was used to present statistical heterogeneity.

Quality Assessment

CASP criteria for randomised controlled trials (CASP, 2022) were used to evaluate the quality of the studies. A score was allocated based on the overall assessment of the methodological rigour of the study with points given to any answer marked yes. Risk of Bias for the eleven randomised controlled studies was assessed using the ROB2 tool (Sterne et al, 2019)

Results

Study Selection

Overall, 13 studies were included in the review with articles being published between 2007 and 2021. All articles were written in English. Figure 1 displays the flowchart of article selection in the different phases of screening.

Characteristics of included studies

Main characteristics of included studies are detailed in Table 1. Of these 10 were conducted in Europe (one each in Germany, Spain, Netherlands, Denmark, UK, Finland, France, Portugal, Norway and Italy) and three from the rest of the world (one each in USA, Taiwan and Brazil). Sample size varied from 27 to 200, with a total of 1546 participants in the included studies. Eleven studies were randomised controlled trials (Rolland et al, 2007; Stella et al, 2011; Lowery et al, 2014; Telenius et al, 2015; Cancela et al, 2016; Hoffmann et al, 2016; Ohman et al, 2017; Chen et al, 2017; Fleiner et al, 2017; Venturelli et al, 2017; Henskens et al, 2018) and two were quasi experimental studies (Aman & Thomas, 2009; Sampaio et al, 2021). Eight studies were undertaken in care homes (Rolland et al, 2007; Stella et al, 2011; Telenius et al, 2015; Cancela et al, 2016; Chen et al, 2017; Venturelli et al, 2017; Henskens et al, 2018; Sampaio et al, 2021), four were community-based (Lowery et al, 2014; ; Hoffmann et al, 2016; Ohman et al, 2017) and one conducted in an inpatient hospital setting (Fleiner et al, 2017). All participants were diagnosed with dementia, with most participants having mild dementia severity in one study (Hoffmann et al, 2016) moderate dementia in 8 studies (Stella et al, 2011; Lowery et al, 2014; Telenius et al, 2015; Hoffmann et al, 2016; Ohman et al, 2017; Fleiner et al, 2017; Venturelli et al, 2017; Sampaio et al, 2021), moderate/severe in 1 study (Henskens et al, 2018) severe in 3 studies (Rolland et al, 2007; Aman & Thomas, 2009; Chen et al, 2017) and a range of severity in one study (Cancela et al, 2016).

Intervention Characteristics

Appendix 3 describes the exercise intervention and the control groups demonstrating that the most common approach was multicomponent training e.g., two or more exercise types grouped together in the same session. Eight of the studies were randomised to interventions (Rolland et al, 2007; Lowery et al, 2014; Telenius et al, 2015; Cancela et al, 2016; Hoffmann et al, 2016; Ohman et al, 2017; Fleiner et al, 2017; ; Henskens et al, 2018), four were not (Aman & Thomas, 2009 Aman & Thomas, 2009; Chen et al, 2017; Sampaio et al, 2021) and one was unclear on the method of allocation (Venturelli et al, 2017). The nature of the

studies meant blinding was not possible for participants allocated to the treatment arm or for researchers providing the intervention. However eight of the studies did blind the outcome assessors (Rolland et al, 2007; Lowery et al, 2014; Cancela et al, 2016; Hoffmann et al, 2016; Fleiner et al, 2017; ; Henskens et al, 2018; Chen et al, 2017; Sampaio et al, 2021) while two did not (Stella et al, 2011; Cancela et al, 2016) and three were unclear (Aman & Thomas, 2009; Telenius et al, 2015; Ohman et al, 2017). Ten studies control groups followed usual care (Rolland et al, 2007; Aman & Thomas, 2009; Lowery et al, 2014; Hoffmann et al, 2016; Ohman et al, 2017; Fleiner et al, 2017; Chen et al, 2017; Stella et al, 2011; Henskens et al, 2018; Sampaio et al, 2021) and three had recreational social-type activities (Telenius et al, 2015; Cancela et al, 2016; Fleiner et al, 2017).

For people identified as leading the exercise sessions in the study, six were qualified physiotherapists (PT) (Telenius et al, 2015; Cancela et al, 2016; Hoffmann et al, 2016; Ohman et al, 2017; Fleiner et al, 2017; Venturelli et al, 2017), one an occupational therapist (OT) (Rolland et al, 2007), two were "exercise professionals" (Lowery et al, 2014; Sampaio et al, 2021), one a "qualified movement teacher" (Henskens et al, 2018), one an "expert on physical education" (Stella et al, 2011), one a trained volunteer (Chen et al, 2017) and the remaining study did not specify who conducted the exercise programme (Aman & Thomas, 2009).

Outcome measurements

Ten studies used the neuropsychiatric inventory (NPI) a well validated outcome measure encompassing a range of neuropsychiatric symptoms (NPS) including agitation (Rolland et al, 2007; Stella et al, 2011; Lowery et al, 2014; Telenius et al, 2015; Cancela et al, 2016; Chen et al, 2017; Ohman et al, 2017; Stella et al, 2011; Henskens et al, 2018; Sampaio et al, 2021) . Only three studies using the NPI specifically reported the agitation subscale (Stella et al, 2011; Telenius et al, 2015; Fleiner et al, 2017) and all showed reduction in agitation. Of the remaining seven studies, one used an additional agitation specific measure (Venturelli et al, 2017) while the others reported overall NPI score. Three studies used the Cohen Mansfield Agitation Inventory (CMAI) (Aman & Thomas, 2009; Fleiner et al, 2017; Henskens et al, 2018), one used the Pittsburgh Agitation Scale (PAS) (Aman & Thomas, 2009) and one used the Agitated Behaviour Scale (ABS) (Venturelli et al, 2017). These are all agitation specific outcome measures. One study each used the Cooperative Study –Clinical Global Impression

of Change (ADCS-CGIC) (Fleiner et al, 2017) and the Clifton Assessment Procedures for the Elderly –Behaviour Rating Scale (CAPE-BRS) (Chen et al, 2017).

Methodological quality

Four studies scored over 10 using CASP guidelines and were considered higher quality papers (Telenius et al, 2015; Hoffmann et al, 2016; Henskens et al, 2018; Sampaio et al, 2021) while seven studies were of moderate quality, scoring between 8 and 9 (Rolland et al, 2007; Aman & Thomas, 2009; Lowery et al, 2014; Cancela et al, 2016; Chen et al, 2017; Fleiner et al, 2017; Venturelli et al, 2017). Risk of bias assessment using ROB2 showed that five had low risk of bias (Rolland et al, 2007; Lowery et al, 2014; Cancela et al, 2016; Hoffmann et al, 2016; Henskens et al, 2018), six had some concerns of bias (Stella et al, 2011; Telenius et al, 2015; Fleiner et al, 2017; Ohman et al, 2017; Venturelli et al, 2017; Sampaio et al, 2021) and one had high risk of bias (Chen et al, 2017). Two of the randomised controlled trials had low scores for quality on CASP assessment and some concerns of bias on ROB2 (Stella et al, 2011; Ohman et al, 2017). For Ohman et al (2017) it was unclear whether all participants were accounted for at the end of the study or if outcome assessors were blinded. Stella et al (2011) did not randomise their sample due to the very small sample size (intervention group n=16, control n=11) and reported they wanted to ensure two groups with similar physical activity levels. Their outcome assessors were not blinded leading to potential benefit bias and did not report confidence intervals.

Effectiveness of physical activity in reducing agitation

From the thirteen studies, seven showed significant reductions in total NPS score (Aman & Thomas, 2009; Stella et al, 2011; Cancela et al, 2016; Hoffmann et al, 2016; Chen et al, 2017; Fleiner et al, 2017; Venturelli et al, 2017), one showed a trend towards agitation being a lesser problem in the exercise group, but this did not reach significance (Telenius et al, 2015) and the remainder did not show these positive effects. In relation to agitation specifically, Aman & Thomas (2009) reported a multicomponent 3-week programme in care homes with a sample size of 50 undertaking 15 minutes of walking outside and 15 minutes of resistance and balance exercises, 3 days per week. They observed significant reductions in agitation measured by PAS ($p=0.034$) and even more so in subjects who were agitated at baseline ($p<0.001$) but not by CMAI ($p=0.843$). Another multicomponent training programme conducted by Stella et al (2011) taking place over 60 minutes, three times per week on non-consecutive days with a small sample of 27 participants. They reported significant reductions

in the NPI agitation subscale (p=0.02) as well as overall NPI score (p=0.01). In addition, Venturelli et al (2016) whose approach was purely aerobic exercise with 40 care home residents, walking at moderate intensity with a caregiver for 60 minutes three times per week, also reported significant reduction in agitation as measured by the ABS ($p<0.05$). Fleiner et al (2017) conducted the only inpatient study included in this review and used a unique exercise carousel program of four 20 minutes sessions per day, 3 days per week. Exercise consisted of strengthening exercises with weights and endurance exercise on seated ergometers over a 2-week period with 70 participants. They confirmed a significant reduction in verbal agitation in those undergoing exercise using both the NPI (p=0.04) and CMAI (p=0.01). Telenius et al (2015) reported a trend towards reduction of agitation through high intensity functional exercise focusing on strength and balance through twice a week session lasting 60 minutes but this did not reach significance (p=0.07). In contrast the only study using CMAI as the sole measure of agitation (Henskens et al, 2018) reported on a double parallel RCT comparing ADL training and exercise training with control and the exercise component consisted of alternating strength and aerobic sessions, three times per week for 6 months with a group of 87 participants in total. They did not report any significant reduction in agitation (p=0.89).

Five studies using a qualified physiotherapist or occupational therapist, reported significant reductions in NPS (Telenius et al, 2015; Cancela et al, 2016; Hoffmann et al, 2017; Fleiner et al, 2017; Venturelli et al, 2017) while from those studies using other instructors three from the five reported no effect on NPS (Lowery et al, 2014; Henskens et al, 2018; Sampaio et al, 2021).

Effectiveness of different types of intervention components in reducing agitation

Seven studies reported on multicomponent intervention which was a mixture of aerobic, strengthening and balance exercises, with three reporting significant improvements in NPS (Aman & Thomas, 2009; Stella et al, 2011; Fleiner et al, 2017). However, of the four that focused on aerobic exercise three reported significant reduction in NPS (Cancela et al, 2016; Hoffmann et al, 2016; Venturelli et al, 2017). Two studies focused purely on strengthening exercises or a combination of strengthening and balance exercises and both reported improvements in behavioural problems (Telenius et al, 2015; Chen et al, 2017). Regards intensity, four studies were not specific on intensity and described it as individualised to the patient or self-selected by the patient (Cancela et al, 2016; Chen et al, 2017; Fleiner et al,

2017; Ohman et al, 2017); seven reported moderate intensity (Rolland et al, 2007; Aman & Thomas, 2009; Stella et al, 2011; Lowery et al, 2014; Venturelli et al, 2017; Henskens et al, 2018; Sampaio et al, 2021); one moderate to high (Hoffman et al, 2016) and one high intensity (Telenius et al, 2015). Three moderate intensity interventions resulted in significant effects (Aman & Thomas, 2009; Stella et al, 2011; Venturelli et al, 2017) and both the moderate to high intensity and high intensity both had effective interventions on NPS (Telenius et al, 2015; Hoffmann et al, 2016). Three studies that were non-specific about intensity all reported significant benefits of exercise on NPS (Cancela et al, 2016; Chen et al, 2017; Fleiner et al, 2017).

Effectiveness of exercise frequency, duration and adherence of intervention in reducing agitation

Six studies carried out their intervention 3 times per week (Aman & Thomas, 2009; Stella et al, 2011; Hoffmann et al, 2016; Fleiner et al, 2017; Chen et al, 2017; Henskens et al, 2018) but the others varied from twice to seven days a week. The duration of each exercise intervention varied from 15-80 minutes a day with a mean of 51 minutes. Three out of the four studies of shorter duration (2 times per week) did not demonstrate significant effect on NPS, while Telenius et al, (2015) did show effect and was the only study of high intervention (which may have compensated for the less frequent intervention. The length of study intervention ranged from 2 weeks to 15 months. The shortest intervention period being 2 weeks (Fleiner et al, 2017) was the inpatient study, which was able to provide a more intensive intervention (four 20-minute sessions daily) which still resulted in favourable effects on NPS. There were four studies of 12 months or longer duration (Rolland et al, 2007; Cancela et al, 2016; Chen et al, 2017; Ohman et al, 2017) and two demonstrated significant benefits of exercise on NPS (Cancela et al, 2016; Chen et al, 2017). Of the seven studies between 3 and 6 months in duration four showed benefit of exercise on NPS (Stella et al, 2011; Lowery et al, 2014; Telenius et al, 2015; Venturelli et al, 2017).

Adherence to interventions varied from 19% to 96.9%, with one study not reporting adherence (Aman & Thomas, 2009). Eight studies reported adherence above 70% (Stella et al, 2011; Telenius et al, 2015; Cancela et al, 2016; Hoffmann et al, 2016; Chen et al, 2017; Ohman et al, 2017; Venturelli et al, 2017; Sampaio et al, 2021) six had positive results of exercise on NPS (Stella et al, 2011; Telenius et al, 2015; Cancela et al, 2016; Hoffmann et al, 2016; Chen et al, 2017; Venturelli et al, 2017). The lowest reported adherence was just over

30% which Lowery et al, (2014) acknowledged limited their results, but they did not explain possible reasons for this poor adherence. Henskens et al (2019) showed reasonable adherence of 55% and identified reasons for non-attendance as most commonly illness, clash with other activities and lack of motivation.

Meta-analysis

Of the 13 studies included in the review, 7 were excluded from the meta-analysis because they did not provide usable data for computing the required effect sizes. Therefore, data from 6 studies (2 community-based and 4 nursing home-based) including 646 participants in total were subject to a meta-analysis.

Figures 2 and 3 show the overall effect size of the interventions on post total NPI scores in the community and nursing home-based studies. Regarding the former, we performed a meta-analysis of 2 RCTs (Stella et al, 2011; Hoffman et al, 2016) involving 232 community-dwelling participants which showed that physical activity had a large positive albeit nonsignificant effect on post-intervention NPI scores (mean difference = −0.81; 95% CI: -1.98 to 0.36; $I^2 = 0.88$). The latter meta-analysis involved 414 nursing home participants in 4 RCTs (Telenius et al, 2015; Venturelli et al, 2016; Fleiner et al, 2017; Rolland et al, 2017) and showed that physical activity had small and nonsignificant effects on total NPI scores post intervention (mean difference = -0.15; 95% CI: -0.46 to 0.16; $I^2 = 0.55$).

Discussion

The main objective of this review was to determine the effectiveness of structured physical activity on agitation in people living with dementia. Most of the included studies agree that physical exercise is a promising intervention in the management of behaviours that challenge. This is supported by the meta-analysis which demonstrates, in the community studies, a large positive effect on post-intervention NPI scores, despite not reaching statistical significance. The effect in the care home studies was smaller, but still positive and this may indicate differences between settings that need considering for future study design. This could be that care home residents are likely to be more significantly cognitively impaired and may have more challenging behaviour than those still living at home. Overall, the studies included in this review showed significant heterogeneity in exercise interventions, outcome measures and sample number and most studies being of moderate quality due to methodological issues and so the results should be interpreted with caution.

Aerobic exercise interventions provide the best evidence to support the use of physical activity in reducing agitation (Cancela et al, 2016; Hoffmann et al, 2016; Venturelli et al, 2017) but there is also some support for strengthening regimes (Telenius et al, 2015; Chen et al, 2017). This is important as aerobic exercise can be incorporated into most lifestyles without the need for specialist equipment. Multicomponent exercise for older adults in general has been shown to impact positively on physical activity, falls and physical functioning (Pinheiro et al, 2022). These same benefits are also extended to older adults with dementia (Pitkala et al, 2013), which suggests for overall benefits to health it is appropriate to consider both aspects when designing interventions.

As expected, better adherence to exercise programmes appears to offer more benefit in terms of reducing behavioural symptoms in dementia. It is essential to understand what factors influence adherence to an exercise programme and to make these programmes accessible to all. Perceived benefits, enjoyment and being with other people are all suggested facilitators to adherence (van Alphen et al, 2016; van der Wardt et al, 2017) however it is unclear how facilitators influence the level of adherence of an individual (Hancox et al, 2019). Therefore, time and resources should be spent exploring the reasons for poor adherence to plan programmes effectively and make their success more likely. Low staffing levels and experience contribute to physical inactivity in care home settings (Smit et al, 2017; Douma et al, 2017) as well as physical and cognitive limitations (Van Alphen et al, 2016) and

environmental factors (Portegijs et al, 2023). Gebhard & Mir (2021) investigated barriers to physical activity in people living with dementia and found that physical activity programmes need to be adapted to different mobility levels, tailored to individuals, offer activity in small groups and promote social cohesion. They also suggested meaningful music based on participants individual music preferences is likely to increase adherence and the use of the outdoor environment to undertake physical activity will also help.

There were some side effects reported (Table 2) but most were not considered related to the intervention itself and the most common side effects that were attributed to the physical activity were musculoskeletal in nature or falls. Therefore, this suggests that physical activity programmes are safe for most patients who have undergone appropriate risk assessment by a professional prior to commencement.

Most studies included used the NPI which is a well validated scale (Cummings et al, 1994). Although most measured overall behavioural symptoms, the agitation subscale was not always reported. The non-reporting of NPI agitation subscale means it is difficult to identify specifically how agitation was reduced. Instead, the findings demonstrate the overall impact the physical activity programme have in reducing behaviours that challenge of which agitation is a common feature.

Limitations of the review

This investigation consists of a rapid review. A fuller systematic review of the literature may have found additional studies and there is a need to be cautious with interpreting the evidence presented. The studies are generally very heterogenous in nature and generalisation of the findings to a wider population cannot be made confidently. However, the 13 studies included, were mostly of moderate quality, comprised a total of 1546 participants and provided evidence that physical activity can effectively reduce agitation. A more thorough meta-analysis could have been completed if full data had been available for all of the RCT's included in the review. This could have had further implications on the review and recommendations made.

This review also demonstrated the inconsistencies between outcome measures reporting on agitation and has been some reports on the reasons for this. The CMAI and NPI are validated tools however they are both proxy rated by the caregiver and therefore liable to bias (Sano et al, 2018) and although a clinician rated version of the NPI has been developed (NPI-C) this has not yet been widely used in studies. A European task force report suggested for future

studies that either the NPI or CMAI be used to give the caregiver perspective but included alongside the NPI-C to give a more reliable assessment (Sano et al, 2018). Previous issues reported with the psychometric properties of the CMAI were its lack of simplicity (Aman & Thomas, 2009) and lack of sensitivity (Fleiner et al, 2017).

Implications for practice and research

The findings of this review suggest that physical activity can be beneficial to reducing agitation in people living with dementia which could have a positive impact on their quality of life, reduce mortality risk and reduce healthcare costs. Therefore, it is recommended that clinicians look to methods to include regular exercise into these individuals' weekly routines, particularly those with known behavioural symptoms who may benefit the most.

The inconsistent use of outcome measures and variability in physical activity intervention design and length need to be addressed in future studies to allow for better comparison between studies and for more detailed meta-analysis. It is also essential that feasibility for application of physical activity into real life situations for people with dementia is investigated, as it has been shown that better adherence improves outcomes. Exploring the key factors in engaging people with dementia in physical activity on an ongoing basis is an essential component of achieving good outcomes for this group.

For future research the use of recommended and validated scales should be followed to provide more homogeneity in outcome measures. The NPI is considered the gold standard tool for neuropsychiatric assessment but may have less sensitivity in the milder stages of cognitive impairment and presence of milder NPS (Konig et al, 2021). In addition, researchers need to agree on common components of physical activity interventions to allow comparisons between studies.

As well as identifying interventions that can help reduce agitation and other symptoms, it is also key to try to identify causative factors and manage these to prevent behavioural symptoms arising in the first place. It has been suggested that anxiety could be a key trigger of agitated behaviour (Mintzer et al, 1996; Twelftree et al, 2006; Kwak et al, 2017) and therefore identifying this early in the disease journey could reduce behavioural issues. Furthermore, sleep disturbances, sensory impairments, acute illness and pain can all generate agitated behaviour (Frederiksen et al, 2017) and thorough, comprehensive examination is therefore required for patients with these types of presentation.

Conclusions

This review demonstrates the growing evidence for the benefit of physical activity on behaviours that challenge but there is a need for better quality studies focusing on physical activity and measuring agitation specifically as a primary outcome measure. Further studies are needed to identify the optimum timing and length of intervention as well as which individuals are most likely to benefit and at what stage of their disease.

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Conflicts of Interest

Authors have no conflicts of interest to declare

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Figure 1 – Process of screening and selecting studies for inclusion in the rapid review (Page et al, 2021)

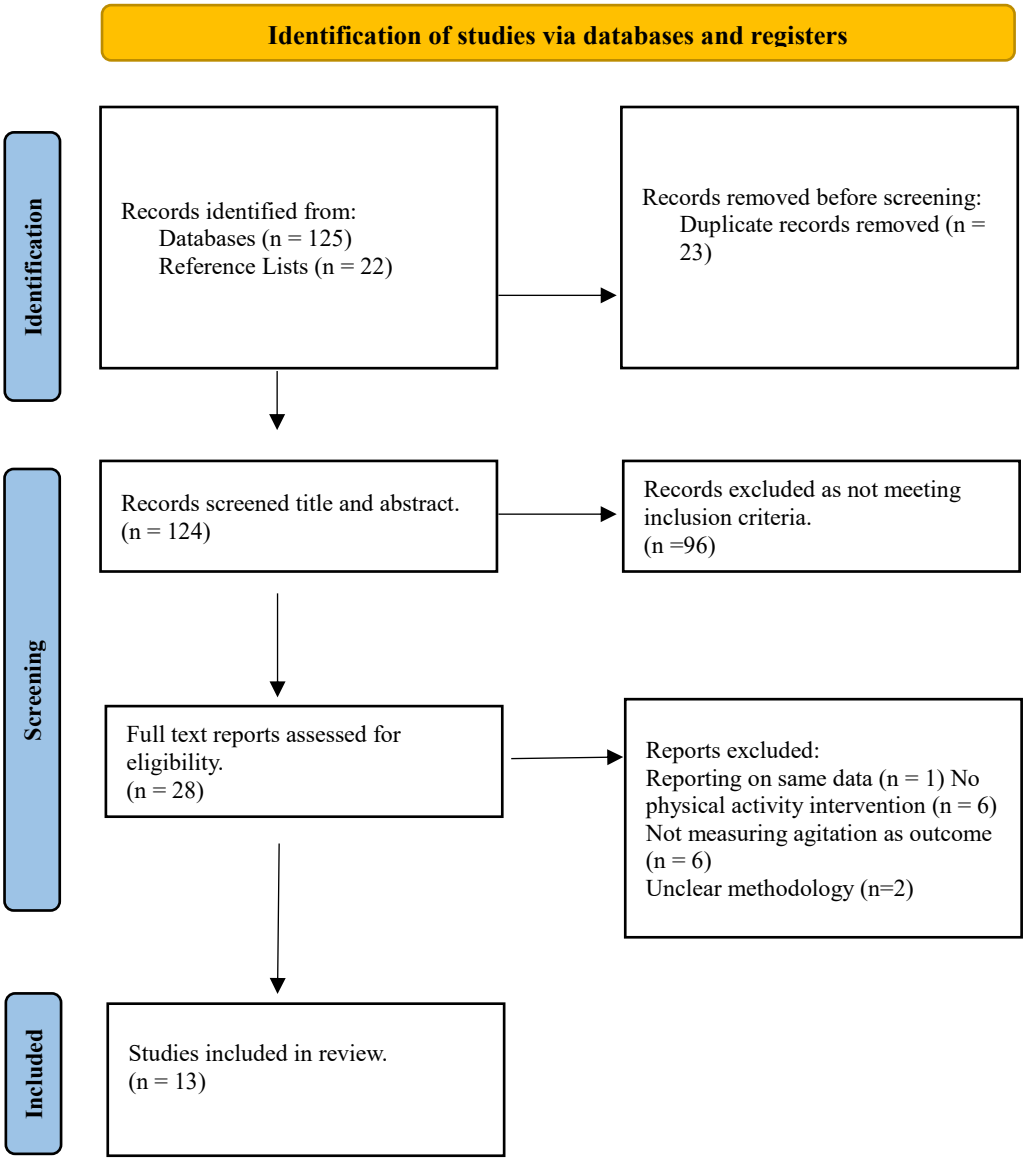
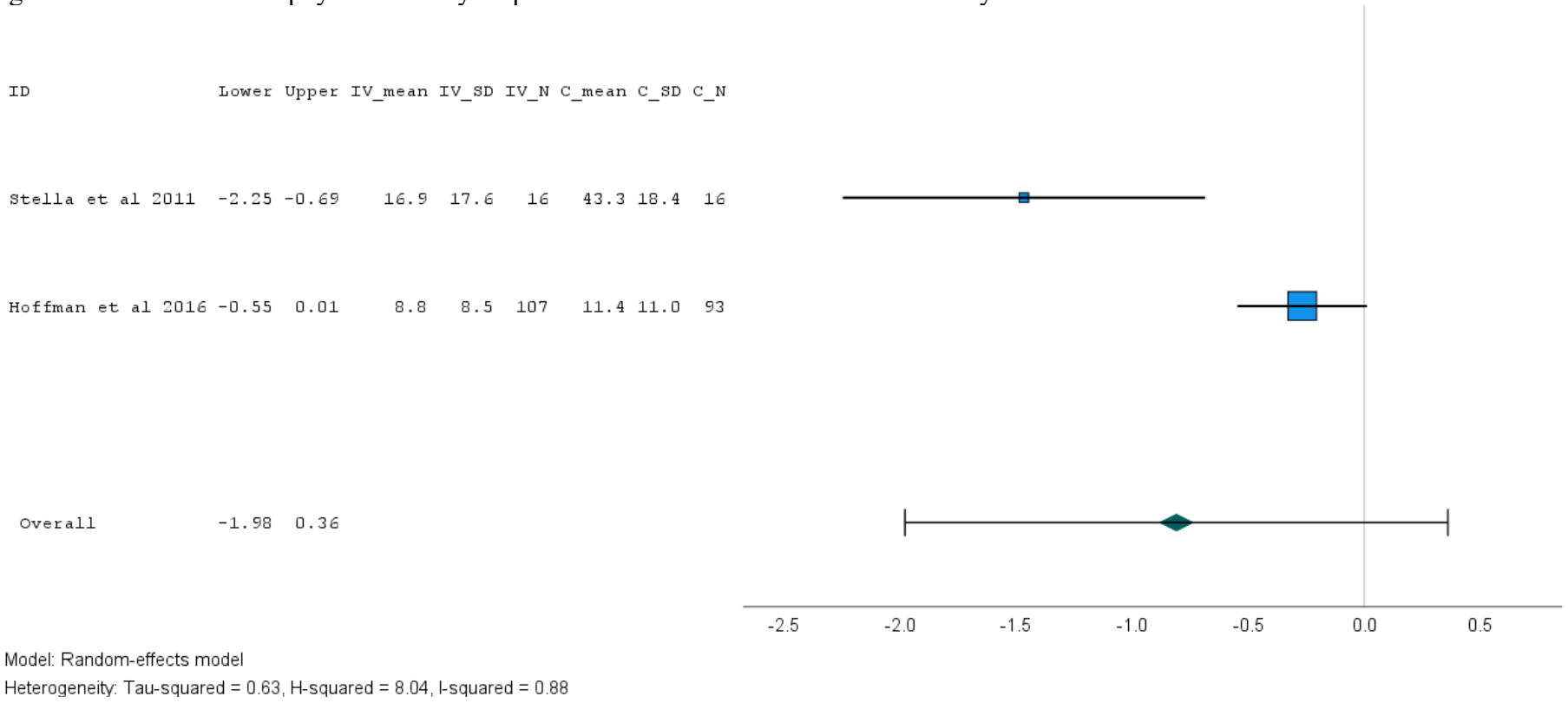
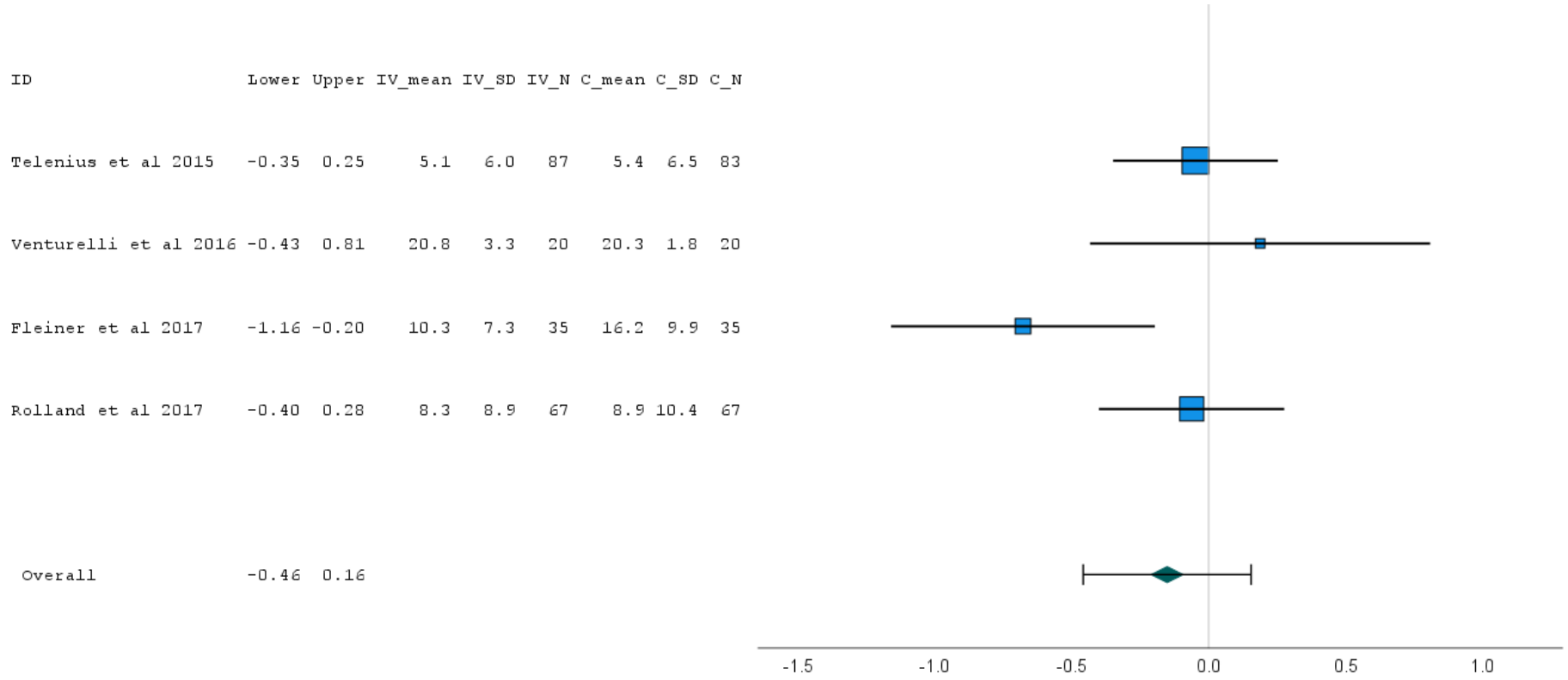


Figure 2. Pooled effects of physical activity on post-intervention NPI scores in community RCTs.



Demonstrates a trend towards less agitation in the physical activity intervention group.

Figure 3. Pooled effects of physical activity on post-intervention NPI scores in nursing home RCTs.



Model: Random-effects model

Heterogeneity: Tau-squared = 0.05, H-squared = 2.22, I-squared = 0.55

Demonstrates a trend towards less agitation in the physical activity intervention group.

Table 1 - Characteristics of Included Studies of older adults with dementia

AUTHORS, YEAR AND COUNTRY	TYPE OF STUDY	SETTING/POPULATION	STUDY GROUPS AND SAMPLE SIZE	INTERVENTION LENGTH	OUTCOMES	ASSESSMENT TOOL
AMAN & THOMAS 2009. USA	Quasi Experimental Study	Nursing homes	EG n=40 No exercise group n=10	3wk	DS; agitation; ADL function	CSDD; PAS; CMAI; ADCS-ADL
CANCELA ET AL. 2016 SPAIN	RCT	Residential homes	EG n=73 CG n=116	15mth	CF; functional mobility; NPS; DS; immediate memory	MMSE; TUG; NPI; Katz Index; CSDD; FOME
CHEN ET AL. 2017. TAIWAN	RCT	Nursing homes	EG n=75 CG n=75	15mth	DS; behavioural problems	CSDD; CAPE-BRS
FLEINER ET AL. 2017. GERMANY	RCT	Inpatient hospital	EG n=35 Social stimulation (control) n=35	2wk	NPS	ADCS-CGIC; NPI; CMAI
HENSKENS ET AL, 2018 THE NETHERLANDS	RCT	Nursing homes	Exercise and ADL training n=22 ADL training n=21 EG n=22 CG n= 22	6mth	CF; Physical endurance; Functional Mobility; Balance; Muscle Strength; DS; Apathy; Agitation	MMSE, Severe Impairment Battery, 6MWT, TUG, Figure of 8 walk test, FICSIT-4, Timed chair stand test, Jamar hand dynamometer, CSDD, Apathy evaluation scale, CMAI
HOFFMANN ET AL. 2016. DENMARK	RCT	Community	EG n=107 CG n=93	16wk	Mental speed and attention; cognitive function; DS; NPS; QOL	SDMT; ADAS-Cog; MMSE; HAMD-17; ADCS-ADL; NPI; EQ-5D
LOWERY ET AL. 2014. UK	RCT	Community	EG n=67 CG n=64	12wk	BPSD	NPI; GHQ; DemQOL-Proxy; ZBI
ÖHMAN H ET AL. 2017. FINLAND	RCT	Community	Home exercise n=63 Group exercise n=57 CG n=59	12mth	NPS; DS; physical functioning; CF	NPI; CSDD; FIM; MMSE
ROLLAND ET AL. 2007. FRANCE	RCT	Nursing homes	EG n=67 CG n=67	12mth	ADL function; physical performance; nutritional status; behavioural disturbance; DS	Katz Index; 6MWT; TUG; One leg balance test; MNA; NPI; MADRS
SAMPAIO ET AL. 2021. PORTUGAL	Quasi-experimental study	Nursing homes	EG n=40 CG n=37	6mth	CF; physical fitness; functional capacity; QOL; BPSD	Senior Fitness Test; MMSE; Katz Index; QoL-AD; NPI

STELLA F ET AL 2011. BRAZIL	RCT	Community	EG n=16 CG n=16	6mth	CF; NPS	MMSE; NPI; CSDD
TELENIUS ET AL. 2015. NORWAY	RCT	Nursing homes	EG n=87 CG n=83	12wk	Balance; mobility; muscle strength; ADL function; CF; BPSD; DS; QOL	BBS; 6MWT; Chair stand test; Barthel Index; CDR; MMSE; NPI; CSDD; QUALID
VENTURELLI ET AL. 2016. ITALY	RCT	Nursing homes	EG n=20 Cognitive training group n=20 Exercise + cognitive training n=20 CG n=20	12wk	Salivary cortisol; NPS; CF	Salivary cortisol levels; NPI; ABS; MMSE

ABS- Agitated Behaviour Scale; ADAS-COG– Alzheimer's disease assessment scale – cognitive subscale; ADCS-ADL– Alzheimer's Disease Cooperative Study –Activities of Daily Living; ADCS-CGIC– Alzheimer's Disease Cooperative Study –Clinical Global Impression of Change; ADL- Activities of daily living; BBS- Berg Balance Scale; BPSD– behavioural and psychological symptoms of dementia; CAPE-BRS– Clifton Assessment Procedures for the Elderly –Behaviour Rating Scale; CDR– Clinical Dementia Rating Scale; CF– cognitive function; CG– control group; CMAI– Cohen Mansfield Agitation Inventory; CSDD– Cornell Scale for Depression in Dementia; d- days; DemQOL-Proxy– dementia quality of life proxy; DS– depressive symptoms; EG– exercise group; EQ5D– European Quality of Life 5 dimensions; FICSIT-4– Frailty and Injuries – Cooperative Studies of Intervention Techniques 4 scale; FIM– Functional Index Measure; FOME– Fuld Object Memory Evaluation; min – minutes; GHQ– general health questionnaire; HAMD-17– Hamilton Depression Rating Scale; MADRS– Montgomery Asberg Depression Rating Scale; MMSE– mini mental state examination; MNA– Mini Nutritional Assessment; mth– months; NPI– neuropsychological inventory; NPS– neuropsychiatric symptoms; PA– Physical activity; PAS– Pittsburgh Agitation Scale; QoL-AD– Quality of Life – Alzheimer's Disease; QUALID– Quality of life in late-stage dementia scale; QOL– quality of life; RCT– Randomised controlled trial; 6MWT– 6 minute walk test; SDMT– Symbol Digit Modalities Test; TUG– Timed up and Go; wk– weeks; ZBI– Zarit Caregiver Burden Inventory

Table 2 - Summary of Effects on Neuropsychiatric Symptoms of Included Studies

AUTHORS AND YEAR	EXERCISE INTERVENTION	PARTICIPANTS	ADVERSE EVENTS	RESULTS
AMAN & THOMAS 2009.	MCT: aerobic, strengthening and balance exercises	N=50	None reported	Reduction in agitation on PAS but not CMAI PAS: T0: 5.8; T1: 4.5 Effect size: NR, p=0.034 PAS Agitated subjects: T0: 9.1; T1: 6.1 Effect size NR, p<0.001 CMAI: T0: 51.7; T1: 52.4 Effect size NR, p=0.843
CANCELA ET AL. 2016	AE cycling on a recumbent bicycle	N=189	None attributable to the exercise program, all serious medical events related to pre-existing comorbidity	Reduction in all NPI domains except for depression NPI: T0: IG: 9.70/CG: 11.32; T1: IG: 3.24/CG: 14.2 Effect size: NR, p=0.01
CHEN ET AL. 2017.	Wheelchair bound senior elastic band programme including AE and stretching using resistance bands	N=150	None reported	Reduction in behavioural problems from 6-15 months of intervention CAPE-BRS: T0: IG: 7.5/CG: 8.0 CAPE-BRS 3mths IG: 7.5/CG: 7.7; 6mths: IG: 7.1/CG: 8.7; 9mths: IG: 7.0/CG: 9.3; 12mths: IG: 7.4/CG:9.8; 15mths: IG: 7.4/CG: 10.5 Effect size NR; p=0.55 (3mths); p=0.001 (6mths), p<0.001 (9-15mths)
FLEINER ET AL. 2017.	MCT: AE on seated ergometers, strengthening exercises with ankle or wrist weights	N=85	None in IG. Two in CG – severe hyponatraemia and cardiac decompensation. Assessed as not related to the study protocol	Reduction in agitation on all scales ADCS-CGIC emotional agitation. IG: p<0.001; psychomotor agitation IG: p=0.01. NPI Total: IG p=0.04; NPI behaviour symptoms p=0.04 Effect size 0.51 verbal aggression IG: p=0.04 Effect size 0.52 CMAI Total IG p=0.11 Effect size 0.40; verbally agitated behaviour p=0.01 Effect size 0.68
HENSKENS ET AL, 2018	MCT: alternating strength (seated upper and lower limb exercises with or without weights) and AE (walking outside)	N=87	None reported	No reduction in agitation, apathy or depression CMAI: T0: IG: 8.5/CG: 8.1; T1: IG: 8.6/CG: 6.7 Effect size: 0.1, p=0.89
HOFFMANN ET AL. 2016.	Moderate to high intensity AE using an ergometer bicycle, cross trainer and treadmill	N=200	58 adverse events and 13 serious adverse events reported. Majority not related to the study – 6 MSK problems related and 1 case of atrial fibrillation possibly related	Reduction in all NPI domains except depression NPI: T0: IG: 10.0/CG: 9.4; T1: IG: 8.8/CG: 11.4 Effect size NR, p=0.002
LOWERY ET AL. 2014.	AE: individually tailored regimen of walking deigned to become progressively more intensive	N=131	11 reported adverse events none deemed to be related to the study (6 falls and 5 deaths)	No significant reduction in NPI total score NPI: Mean 6wk IG: 26.6/CG: 25.7. p=0.76 Mean 12wk IG: 25.6/CG: 23.9. p=0.60

ÖHMAN H ET AL. 2017.	MCT: AE, strength training and balance exercises. HE group – individually tailored exercise regime. GE – similar components but assisted by gym equipment	N=179	None reported	No significant reduction in NPI total score NPI: T0: IG: (GE: 12.05, HE: 13.45)/CG: 16.56; T1: IG: (GE: 12.93, HE: 16.18)/CG: 17.2. Effect size: NR, p=0.41
ROLLAND ET AL. 2007.	MCT: AE (walking), strength (squats, sit to stand, toe raises), flexibility and balance training (step trial exercises, one or two leg balance exercises)	N=134	Five falls during exercise sessions Mean number of hospitalisations per patients significantly higher in exercise group at 6 and 12 months	No significant reduction in NPI total score NPI: T0: IG: 10.7/CG: 11.4; T1: IG: 8.2/CG: 9.2; T2: IG: 8.3/CG: 8.9 NPI 6mth p=0.47 NPI 12mth p=0.78 Effect size NR
SAMPAIO ET AL. 2021.	MCT: AE(15min), muscle strengthening, flexibility and balance exercises (15-20min) plus warm up and cool down	N=64	None reported	No significant reduction in NPI total score NPI: T0: IG: 15.92/CG: 21.5 Effect size NR
STELLA F ET AL 2011.	MCT: AE such as dancing and walking; stretching; muscular resistance; motor coordination; and balance exercises.	N=27	Five participants from control suffered severe clinical occurrences unrelated to the study	Significant reduction in NPI total score and agitation domain NPI: T0: IG: 40.3/CG: 39.6; T1: IG: 16.9/CG: 43.3 p=0.01 NPI Agitation: T0: IG: 2.4/CG: 2.7; T1: IG: 0.3/CG: 5 p=0.02 Effect size NR
TELENIUS ET AL. 2015.	High intensity functional exercise: strengthening exercises for lower limbs and balance exercises	N=170	No adverse effects of exercise	Trend in reduction of NPI agitation domain but not significant NPI: T0: IG: 5.8/CG: 4.8; T1: IG: 5.1/CG: 5.4 Effect size: 0.2, p=0.17 NPI Agitation: T0: IG: 1.7/CG: 1.3; T1: IG: 1.5/CG: 1.7 Effect size agitation: 0.2, p=0.07
VENTURELLI ET AL. 2016.	AE: walking at moderate intensity with a caregiver along the hallways of the care unit	N=80	No adverse events related to exercise or cognitive treatments	Significant reduction in ABS and NPI total score ABS $p<0.05$ in AE group at sundown NPI $p<0.05$ in AE group at sundown Effect size NR

ABS– Agitated Behaviour Scale; ADCS-CGIC– Alzheimer's Disease Cooperative Study -Clinical Global Impression of change; AE– aerobic exercise; CAPE-BRS- Clifton Assessment Procedures for the Elderly –Behaviour Rating Scale; CMAI– Cohen Mansfield Agitation Inventory; CG– Control Group; IG- Intervention Group; GE– Group Exercise; HE– Home Exercise; MCT– multicomponent training; NPI– Neuropsychological Inventory; NR– Not reported; PAS– Pittsburgh Agitation Scale