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A systematic review and meta-analysis of randomized controlled trials on the effect of serious games on people with dementia

3 Abstract Background: An increase in dementia prevalence has been accompanied by increasing interest 4 in new rehabilitation methods, such as serious games. Serious games hold the potential to 5 6 postpone functional and cognitive declines in people with dementia by increasing their independence and engagement; however, the efficacy of serious games remains underexplored. 7 This review was conducted to quantify the effects of serious games in people with dementia, 8 9 including several newly published trials, with the hopes of contributing to evidence-based practice by offering support for clinical decision-making. 10 Methods: Only randomized controlled trials (RCTs) assessing the impacts of game-based 11 intervention programs compared with conventional therapy on cognitive function, instrumental 12 and non-instrumental activities of daily living, or depression among people with dementia were 13 14 included in this review. Meta-analyses were performed to determine the pooled standardized mean difference (SMD) of each outcome using a random-effects model. 15 **Results:** The final search identified 12 studies that met our criteria. Overall, serious games were 16 17 found to improve cognitive function (pooled SMD: 0.34; 95% CI: 0.07 to 0.61) and alleviated depression (pooled SMD: -0.131; 95% CI: -1.85 to -0.77) in people with dementia. 18 19 **Conclusions:** Serious games improve cognitive function and reduce depression in people with 20 dementia. Future studies in this field should aim to evaluate and determine the long-term effect of 21 these games.

Keywords: Serious games, non-pharmacology intervention, rehabilitation, people with dementia,
 meta-analysis

3 **1. Introduction**

Dementia is a major cause of disability and is characterized by a progressive decline in 4 cognitive abilities that interferes with independent daily functioning (Gale et al., 2018; 5 6 Livingston et al., 2020). More than 55 million people are currently estimated to live with 7 dementia worldwide, and approximately 10 million cases of dementia are diagnosed each year, 8 with a new case identified every 3 seconds (Hand, 2019; WHO, 2021). The prevalence of 9 dementia is likely to triple by 2050, which will increase the need for additional rehabilitation resources (Nichols et al., 2022). People with dementia may suffer from memory loss, 10 disorientation, and behavior disorders that impact their functioning abilities (Emmady and Tadi, 11

12 2022; McIntyre et al., 2019).

There have been many recent developments in treatments for managing dementia symptoms, 13 14 and non-pharmacological interventions have provided a range of viable options (Berg-Weger and Stewart, 2017; Gupta et al., 2021). These include rehabilitation, which is currently recommended 15 for improving patient independence and involvement, postponing functional and cognitive 16 17 decline, and improving well-being (Cations et al., 2018; Laver et al., 2020). Conventional rehabilitation includes gait and balance rehabilitation (with or without the use of assistive 18 19 devices), fall prevention strategies, high-volume physical exercises, cognitive stimulation, and 20 psychological, behavioral, and occupational therapy (Cations et al., 2018). In recent years, the 21 rise in prevalence of dementia has resulted in a growing need for more effective treatments, and 22 the interest in new rehabilitation methods, such as serious games, has increased (Lau and Agius, 23 2021; Ning et al., 2020).

Serious games can be defined as games that have the primary purpose of learning and 1 education rather than entertainment (Landers, 2014; Robert et al., 2014). The mechanisms of 2 3 serious games rely on specific cognitive, social, and behavioral skills that can be improved by increasing playing time and challenge difficulty (Jacobs, 2020; Krath et al., 2021). These skills 4 5 include perception-attention motor skills, working memory management, memory for content, 6 and the ability to reason, plan, problem solve, and interact socially (Argasiński and Wegrzyn, 7 2019). In stroke and geriatric rehabilitation, for example, serious games are usually combined 8 with virtual reality, robotic devices, and tablets to facilitate motor and cognitive relearning by 9 delivering playful, interactive, multisensorial, and challenging interventions (Hocine et al., 2015). These technological assets have the added advantage of being able to permanently 10 measure objective parameters (reaction time, number of errors, movement smoothness, 11 compensation, and linearity, etc.) during the rehabilitation of people with dementia (Gago et al., 12 2016; Seo et al., 2017; Wiedenroth and Jauch, 2019). These measurements can be used to 13 14 improve patient motivation and engagement by automatically adapting game difficulty, cues, and sensorial feedback to patients' motor and cognitive performances (Tziraki et al., 2017; 15 Wiedenroth and Jauch, 2019). 16

Several systematic reviews with meta-analyses have demonstrated the effectiveness of serious games for stroke patients with impaired motor function and activity and suggested its potential for use in neurorehabilitation (Doumas et al., 2021; Karamians et al., 2020; Maier et al., 2019). Serious games can confer greater benefits in the areas of cognition, activities of daily living, and depression than commercial video games and conventional therapy. Serious games have been shown to result in favorable social effects, offer the possibility of tailoring

rehabilitation, improve social engagement, and could be used to deliver sensorial feedback as 1 2 needed (Bonnechère et al., 2020; Kleschnitzki et al., 2022; Sun et al., 2006; Tziraki et al., 2017). 3 However, to date, there is insufficient research assessing the effect of serious games programs on people with dementia, and their efficacy continues to be a subject of debate. For 4 example, a recent review suggested that video games are safe and more effective for improving 5 6 cognitive function in people with dementia than no intervention or conventional rehabilitation; 7 however, video games were not found to significantly improve memory or attention (Ferreira-8 Brito et al., 2021). Another review found that brain games did not improve cognitive function, 9 memory, or activities of daily living and did not reduce depression in people with dementia (Kletzel et al., 2021). These inconclusive results are likely to be attributed to the use of games 10 that were not specifically developed for rehabilitative purposes. However, no meta-analysis has 11 assessed the effects of serious games that have been specifically designed for rehabilitation in 12 people with dementia. In addition, whether dementia severity and cultural differences influence 13 14 the efficacy of serious games among people with dementia remains unknown. The inconclusive outcomes of past studies and the broad selection criteria used by previous 15 systematic reviews and meta-analyses has resulted in a lack of supportive evidence for the effects 16 17 of serious gaming therapies among people with dementia, warranting further examination that includes newer studies and a narrower focus on serious games. Clear evidence regarding the 18 19 efficacy of serious games and their outcomes remains necessary to improve clinical decision-20 making. This study reviewed and assessed the effectiveness of serious games-based programs for 21 improving global cognition, ADL, instrumental ADL (IADL), and depression in people with 22 dementia to determine how best to meet the needs of people with dementia in the digital era.

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1 2. Materials and Methods

The papers included in this study were subjected to thorough review and meta-analysis. The
Preferred Reporting Items for Systematic Study and Meta-Analysis (PRISMA) standards for
systematic reviews and meta-analyses were adhered to in the reporting (Page et al., 2021) (see
Supplementary document 3). The study protocol was assigned the International Prospective
Register of Systematic Review (PROSPERO) registration number CRD42022337759.

7 2.1 Literature search

8 A comprehensive literature search was carried out across 6 databases: CINAHL,

9 COCHRANE library, EMBASE, MEDLINE, PubMed, and Web of Science. Information from 10 the databases was taken from the date of their establishment until June 1, 2022. The framework for dementia includes Alzheimer's disease, mild cognitive impairment, Parkinson's disease, 11 vascular dementia, dementia with Lewy bodies (DLB), frontotemporal dementia, and other 12 cognitive syndromes, according to the guidelines developed by the International Classification of 13 14 Disease version 10 (ICD-10) (World Health Organization, 1992), the National Institute on Aging 15 and Alzheimer's Association (NIA-AA) (McKhann et al., 2011), and the Alzheimer's Disease 16 Association (Alzheimer's Association, 2019). The serious games criteria suggested by Ning et al. 17 (Ning et al., 2020) and a prior literature review of dementia-related serious games (McCallum and Boletsis, 2013) were applied. The following MeSH terms were utilized in the search 18 19 strategy: people with dementia OR dementia* OR Alzheimer's disease OR vascular dementia 20 OR Parkinson's disease OR dementia with Lewy body OR DLB OR mixed dementia OR 21 cognitive impairment OR MCI OR frontotemporal dementia AND board games OR tabletop 22 games OR go game OR video games OR computer games OR gaming OR online games OR 23 internet games OR online gaming OR virtual reality games OR exergames OR exergaming AND

randomized controlled trial OR RCT OR randomized control trial OR controlled trial OR
 randomization (see Supplementary document 1).

3 2.2 Eligibility criteria

The PICOS (Population, Intervention, Comparison, Outcome, and Study design) method was 4 5 used to define the inclusion criteria for studies included in this meta-analysis and systematic 6 review (Amir-Behghadami and Janati, 2020). The following inclusion criteria were used: (P) 7 participants included adults with dementia, Alzheimer's disease, Parkinson's disease, cognitive 8 impairment, and other forms of dementia (no restrictions on age, sex, ethnicity, or deficits); (I) 9 adults in the intervention group participated in serious games-based intervention programs, including board games, video games, computer games, or virtual reality games (no restrictions 10 on dose, intensity, duration, route of administration, or timing); (C) adults in the control group 11 received usual care or conventional therapy (therapy recommended by the most recent guidelines 12 and usually provided for adults with dementia); (O) outcomes included cognitive function (Mini-13 14 Mental State Examination or Montreal Cognitive Assessment), ADLs (Basic ADL, Katz Index or Activities of Daily Living scale), IADL (Instrumental Activities of Daily Living scale or Hong 15 16 Kong Lawton Instrumental Activities of Daily Living Scale), and depression (Geriatric 17 Depression Scale, Cornell Scale for Depression in Dementia, or Center for Epidemiological Studies Depression); and (S) the study was a randomized controlled trial (RCT). Studies were 18 19 excluded if the data format prohibited computation of continuous outcomes "before" and "after," 20 if they were protocol trials, or if they did not define the target population or intervention. 21 2.3 Study selection and data items

Two investigators (IDS and GE) evaluated citation titles and abstracts according to the
 qualifying criteria. Differences in opinion were resolved by mutual consent with the support of a

third investigator (BOL), to reach a final decision. Two investigators independently extracted
data from citations that met the full-text screening inclusion criteria, such as study citation, study
design, participant characteristics (number of participants, mean and standard deviation of
participants' ages, types of dementia), intervention characteristics (intervention providers,
serious games procedure, control group activity, intervention frequency, duration, and followup), and outcomes.

7 2.4 Methodology assessment and GRADE evidence

An updated version of the ROB 2 instrument for trials with 6 domains was used to assess the 8 9 risk of bias in the trials included in this study (Sterne et al., 2019). The domains were: risk of bias from the randomization procedure, variations from the influence of intervention assignment, 10 missing outcome data, outcome evaluation, selection of the reported result, and overall risk of 11 bias. Two investigators assessed the risk of bias in the included studies, with differences resolved 12 by mutual assent, before reaching a final decision with the support of a third investigator. The 13 14 GRADE (grading of recommendation, assessment, development, and evaluation) methodology was then used to assess the quality of the pooled analyses (GRADEpro GDT | Cochrane 15 GRADEing). 16

1 2.5 Statistical analysis

The standardized mean difference (SMD) was calculated by combining continuous data from
variables with diverse measurement methods to generate one result (Lin and Aloe, 2021; Murad
et al., 2019), which was comprised of mean changes observed before and after the intervention,
the raw score of standard deviation, and the number of intervention and control group
participants (Lipsey and Wilson, 2001).
The DerSimonian and Laird random effects model was used to pool the SMD and analyze

the heterogeneity for each outcome (Borenstein et al., 2010). The Higgins I² was used to measure
heterogeneity, with 25% representing low heterogeneity, 50% representing moderate
heterogeneity, and > 75% representing high heterogeneity (Higgins and Thompson, 2002). The
forest and funnel plots were displayed for the meta-analyses. Furthermore, the Egger regression
test was also employed to investigate the influence of publication bias on each result (Egger et
al., 1997). Stata 16 was used for the meta-analysis (version 16.0: StataCorp LP, College Station,
TX, USA).

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16 **3. Results**

17 *3.1 Search yield*

Six database searches produced a total of 1,958 citations, and one additional study was obtained by Google scholar. The automatic duplication removal tool in EndNote 9 deleted 351 studies. A total of 1,521 studies were deemed ineligible because the population of the study was not people with dementia (n = 751); the intervention did not implement serious games (n = 579); or the study was not an intervention study (i.e., review, qualitative, protocol, observational study; n = 191). The full text of 87 studies was reviewed, with 77 being excluded because they did not

include the population of interest (n = 6), did not apply serious games (n = 28), or were not an
intervention study (i.e., review, qualitative, protocol, or observational study; n = 43). Ultimately,
12 studies, including 2 trials retrieved from prior reviews, were included in the final analysis
(Cavallo et al., 2016; Galante et al., 2007; Hagovská and Olekszyová, 2016; Karssemeijer et al.,
2019; Lee et al., 2013; Liu et al., 2022; Miller et al., 2013; Padala et al., 2012; Park and Park,
2018; Swinnen et al., 2021; Thapa et al., 2020; van Santen et al., 2020) (see Figure 1).

7 *3.2 Study characteristics*

8 The studies under consideration were published between 2007 and 2022. Two studies each 9 were conducted in Italy, the Netherlands, the United States, and South Korea, while one each was conducted in Belgium, China, Slovakia, and Taiwan. A total of 760 patients with mean ages 10 (and SD) ranging from 66.95 (4.10) to 84.70 (5.60) years in the intervention group, and 65.90 11 (6.20) to 85.30 (6.50) years in the control group were reported from the 12 studies. Of the 12 12 included studies, 4 studies included people with Alzheimer's disease, 4 studies included 13 14 participants with mild cognitive impairment, and 4 studies did not provide information on the types of dementia. One study identified participants with mild to severe dementia, whereas the 15 remaining 11 studies did not provide information regarding the dementia stage. Trials that 16 17 included information about the intervention provider stated that the serious games were delivered to people with dementia by a neuropsychologist (n = 2), physiotherapist (n = 1), trained student 18 19 or research assistant (n = 1), occupational therapist (n = 2), tai chi coach (n = 1), physical 20 therapist (n = 2), or an exercise specialist, physical therapist, and nutritionist (n = 1). 21 The intervention group received a variety of serious games, including exergame-22 computerized exercise with cognitive training, a computerized cognitive-aerobic bicycle, a 23 computer-assisted errorless learning program, exergame-based modified tai chi training, and

virtual reality games with cognitive training. The control group was allocated normal tasks or
participated in other activities, such as reading electronic newspaper articles, interviews and
reminiscence about their lives, watching and listening to music videos, or receiving general
health care education. The intervention lasted 1 to 6 months, with frequency varying from 2 to 5
times a week for 30 to 60 minutes each session. Interventions underwent follow-up from postintervention to 6 months afterward (see Table 1).

7 3.3 Risk of bias in studies and GRADE evidence

8 The quality of the 12 studies was assessed using the ROB 2. No studies were omitted due to a 9 significant likelihood of bias. However, publication bias could occur in some domains: the 10 allocation sequence may be concealed until participants are enrolled and assigned to interventions, or participants/carers/others delivering the intervention may be aware of the 11 assigned intervention during the trial (see Supplementary document 2). Furthermore, the 12 GRADE approach (Table 2) revealed that the quality of each result was very low (IADL), low 13 14 (ADL), or moderate (depression and cognitive functions). Consistency was reduced as heterogeneity was greater than 30%; precision was reduced as the SMD confidence interval 15 overlapped between experimental and control treatments. The number of observations was less 16 17 than 400, which also contributed to the lower quality of evidence (see Table 2). 3.4 Effects of serious games on patients with dementia 18 19 Cognitive function. Seven trials (Cavallo et al., 2016; Hagovská and Olekszyová, 2016; Lee et 20 al., 2013; Liu et al., 2022; Swinnen et al., 2021; Thapa et al., 2020; van Santen et al., 2020),

totaling 426 people with dementia, were pooled to investigate the effect of serious games on

22 cognitive function. The pooled estimate suggested that individuals who engaged in serious

23 games showed significant improvement in their cognitive function (SMD = 0.34, 95% CI

(confidence interval) 0.07 to 0.61, p = 0.01, see Figure 2.1). The trials were found to have a low 1 degree of heterogeneity ($\tau^2 = 0.05$, O = 10.51, df = 6, $I^2 = 42.92\%$). 2 **ADL.** Four trials (Galante et al., 2007; Karssemeijer et al., 2019; Padala et al., 2012; Swinnen et 3 al., 2021), totaling 154 people with dementia, were pooled to investigate the effect of serious 4 5 games on ADL. The pooled estimate found no significant differences in ADL performance between the intervention and control groups (SMD = -0.23, 95% CI -0.58 to 0.11, p = 0.19, see 6 Figure 2.2). A low level of heterogeneity was observed between the trials ($\tau^2 = 0.01$, Q = 3.29, 7 8 $df = 3, I^2 = 8.89\%$). 9 **IADL.** Four trials (Galante et al., 2007; Lee et al., 2013; Lin et al., 2016; Padala et al., 2012),

totaling 67 people with dementia, were pooled to investigate the effect of serious games on

11 IADL. The pooled estimate revealed that no significant differences were observed in IADL

performance between the intervention and control groups (SMD = -0.69, 95% CI -1.62 to 0.24,

13 p = 0.15, see Figure 2.3). Moderate heterogeneity was observed between the trials ($\tau^2 = 0.60$, Q 14 = 9.30, df = 3, I² = 67.75%).

Depression. Three trials (Galante et al., 2007; Lee et al., 2013; Swinnen et al., 2021), totaling 66
people with dementia, were pooled to investigate the effect of serious games on depression
status. The pooled estimate found that those who applied serious games had a significant
reduction in depression symptoms compared to the control group (SMD = -1.31, 95% CI -1.85
to -0.77, p < 0.001, see Figure 2.4). No heterogeneity was observed between the trials (τ² =

20 0.00, O = 1.07, df = 2, $I^2 = 0.00\%$).

1 *3.5 Sensitivity analysis*

Leave-one-out ran a sensitivity analysis for each result to identify the most impactful studies.
The findings showed that the outlier study had no effect on the overall stability of the SMD
estimate in the meta-analysis (Chi² = 0.49, p = 0.48).

5

6 4. Discussion

7 This study found that serious games significantly improved cognitive function and reduced 8 depression in people with dementia. ADL and IADL did not significantly differ between the 9 groups, which could be due to a small sample size, variability in the types of therapies offered, 10 participant characteristics, or differences in outcome assessment. Overall, the feasibility of 11 employing serious games as an intervention for improving memory function or daily physical 12 activity in people with dementia warrants further investigation.

Our results were consistent with previous review studies, further supporting the use of 13 14 serious games to improve cognitive performance in dementia patients (Ferreira-Brito et al., 2021a; Zhao et al., 2020). Previous studies found that serious games could be designed for 15 16 cognitive rehabilitation and provided an enjoyable and participative experience for people with 17 dementia (Ning et al., 2020; Tong et al., 2017). When serious games are played in conjunction with entertainment video games, patients benefit from constructive learning at a neurological 18 19 level, resulting in improved cognitive function (Kuil et al., 2018; Martins et al., 2019; Ong et al., 20 2021). The games provided to patients (including those with dementia) for rehabilitation 21 purposes incorporate systematic computerized cognitive training with a variety of activities to 22 stimulate thinking, visual perception, attention, and memory. Technological advancement 23 enables gaming activities to be merged with computerized training and connected to a television

screen or mobile television, which helps to improve cognitive engagement, user-friendliness, and 1 2 safety for people with dementia and results in cognitive enhancement (Bonnechère et al., 2020; 3 Hill et al., 2016). Furthermore, serious games are typically followed by a structural activity or cycle (i.e., defining the aim, planning, action, and assessment), which is constructed and 4 5 customized to patients' cognitive needs and includes some fascinating components (i.e., music, 6 or sound or visual effects) (Dietlein et al., 2018; Ning et al., 2020). The structured activity 7 employed in serious games stimulates initiative and encourages patients to think, do, and feel in 8 order to connect fully with the game's dynamic (Craven and Fabricatore, 2016). However, it 9 should be noted that, although serious games have been found to improve cognitive function, this study was unable to group the studies into subgroups based on the optimal frequency, duration, 10 or follow-up of serious games for people with dementia. More rigorous RCTs (with pre-11 determine frequency, duration, or intervention follow-up designed to identify long-term effects) 12 are therefore required to provide data for future review studies on cognitive performance for 13 14 patients with dementia and other memory-related conditions. The pooled result revealed that integrating serious games was beneficial for alleviating 15 depression in people with dementia (Chu et al., 2022; Ferreira-Brito et al., 2021a; van Santen et 16 17 al., 2018; Wang et al., 2017). Mental health improvement can be attributed to the game design used in serious games. Serious games are intended to be recreational, meaningful, and enjoyable 18 19 activities that encourage novelty exposure and provide participants with instant gratification, 20 resulting in prolonged activity engagement and mood improvement (Drazich et al., 2020; 21 Moholdt et al., 2017). Furthermore, previous research has indicated that playing games, 22 including for therapeutic purposes, has favorable social effects that can help to improve mood 23 (Huang et al., 2017; Li et al., 2018a). Playing serious games can stimulate beta-endorphin

neurons, which are known to reduce stress hormone synthesis and provide analgesia and a sense 1 of well-being. This results in an improvement in mood status, including the reduction of 2 3 depressive symptoms (Li et al., 2018b; Sarkar and Zhang, 2013). Serious games are therefore recommended for therapeutic purposes in people with dementia (Ning et al., 2020; Tziraki et al., 4 2017). Further research on the influence of serious games on depressive symptoms in dementia 5 6 patients is required to better understand the mechanism behind the results and guide future 7 interventions. Based on these results, healthcare practitioners should develop serious games that 8 combine exercise rehabilitation with cognitive training. Interesting activities and a user-centered 9 design could encourage participation, enjoyment, accessibility, and usability. Serious games have been demonstrated to be potentially useful for dementia rehabilitation purposes. However, the 10 challenges remain that may prevent the implementation of serious games for use among people 11 with dementia. For example, video games and virtual reality games come with high costs, can be 12 difficult to use, and require specific technologies to facilitate game delivery, which may prevent 13 14 their adoption. Alternative strategies, such as board games that do not require access to technology, can provide rehabilitative effects even in the absence of access to technology. 15 An interdisciplinary team (including, for example, a neuropsychologist, physiotherapist, 16 17 physical therapist, nurse, dietitian, and research assistant) may collaborate on the development and administration of serious games for dementia patients (Bamidis et al., 2015; Zhao et al., 18 19 2020). Selecting a group of healthcare practitioners with a diverse but interrelated body of 20 expertise will contribute to the development of a clear protocol to guide the use of serious games 21 in dementia patients (Ning et al., 2020; Tong et al., 2017). This protocol should be as 22 comprehensive as possible and include more well-targeted dementia treatments, such as MINWii

to enhance cognitive function (Benveniste et al., 2012) or Wii Fit to promote physical health
 (Padala et al., 2012; Tripette et al., 2017).

3 Serious games were developed across a wide variety of fields. They may be used in accordance with the various symptoms of dementia that emerge at a level of difficulty 4 appropriate to the cognitive function of the patient and different stages of the disease (Ning et al., 5 6 2020; Wang et al., 2016). People with early-stage or mild dementia experience relatively mild 7 impairments in memory and cognitive skills, with symptoms that can include memory lapses 8 (i.e., forgetting common words or locations), becoming easily confused with familiar 9 surroundings, and being more easily upset or irritable, which can be difficult to distinguish from changes common to normal aging (Alzheimer's Association, 2019; World Health Organization, 10 2021). The rapid detection of cognitive declines is essential during the early stages, and serious 11 games primarily geared toward screening, training, and emotional development can be useful for 12 both detecting symptoms and slowing progression at this stage (Ning et al., 2020). By delivering 13 14 engaging, amusing, and motivating games as interventions for people with dementia, they may be able to improve their activity, postponing and counterbalancing functional and cognitive 15 deterioration (Abd-Alrazaq et al., 2022; Lau and Agius, 2021). For example, the 'Kitchen and 16 17 Cooking' Game was shown to improve object identification and attentiveness (Manera et al., 2015), and the COSMA game improves memory skills, object identification, navigational 18 19 abilities, and emotional state (Bojan et al., 2021). 20 As the disease progresses to a moderate stage, symptoms become more prominent, and

walking (Alzheimer's Association, 2019; World Health Organization, 2021). As a result, treating

numerous physical abnormalities emerge, such as sleep alterations and increasing difficulty

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23 symptoms rather than detecting them is recommended at this stage (Ning et al., 2020). A variety

1	of serious games designed to improving abilities, such as a planting game, a pet-type robot, Wii,
2	or Wii Fit, may be offered to improve cognitive and memory functions, observational skills, and
3	communication abilities (Ning et al., 2020; Toshimitsu et al., 2008; Tseng et al., 2020).
4	Exergame-based computers or Kinect-based virtual games and other assistive technology
5	systems can be provided to enhance physical abilities, such as balance, muscular strength, motor
6	response, and sleep (Cavallo et al., 2016; Pu et al., 2021; Sáenz-de-Urturi et al., 2014).
7	Individuals with late-stage dementia experience substantial cognitive and memory impairments,
8	accompanied by near-complete dependency and immobility (World Health Organization, 2021).
9	Serious games are not suitable interventions for patients with late-stage dementia, as these
10	patients may be unable to follow the rules, grasp the goals, or have the necessary physical
11	strength required to complete the intervention (Ning et al., 2020).
12	This study has several limitations that should be considered. Certain pooled results, such as
13	IADL and cognitive function, showed substantial heterogeneity. This phenomenon can be
14	attributed to the wide variety of participants' circumstances (e.g., age and dementia types) and
15	intervention settings (e.g., types of games used, frequency and duration of games provided, and
16	intervention follow-up). The pooled analyses conducted in this study had relatively small sample
17	sizes, preventing the performance of subanalyses according to participant characteristics (i.e.,
18	age, type of dementia, or severity of dementia) or intervention characteristics (i.e., intervention
19	provider, types of serious games, frequency, duration, or follow-up intervention); according to
20	the Cochrane review, at least 10 studies are required to conduct a subgroup analysis [9.6.5.1
21	Ensure that there are adequate studies (cochrane.org)]. Small sample sizes can affect the reported
22	within-study variances, which should not be accepted as true variances, and sampling errors
23	should be acknowledged clearly in such meta-analyses. Last, the GRADE results were found to

be low to moderate for all included studies, primarily affected by the low number of patients 1 included in studies assessing ADL and IADL, the effect sizes of the results, and study 2 heterogeneity. To improve the global certainty of evidence regarding the outcomes of 3 interventions using serious games (particularly the effects on ADL), larger and well-conducted 4 5 RCTs should be undertaken among people with dementia. To reduce between-study 6 heterogeneity, future studies should better describe their population characteristics (dementia 7 severity, county, etc.) and the parameters of their interventions. To improve the comparability of 8 RCT results, gold-standard assessments should be identified, and a consensus regarding the 9 definitions of "conventional therapy" and "usual care" should be established for the rehabilitation of patients with dementia. 10

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12 **5.** Conclusion

In summary, the results of our meta-analysis indicated that serious games can enhance 13 14 cognitive performance and alleviate depression in patients with dementia. Our findings are clinically significant, as cognitive impairment and mental health issues are major predictors of 15 poor health outcomes in dementia patients, and improvements in cognitive function or 16 17 depression may lead to better overall health. Serious games should therefore be included in rehabilitation programs for dementia care in this demographic. However, the impact of these 18 19 games on physical function warrants additional examination, and more research is required to 20 confirm the long-term effects and practicality of using serious games in a clinical setting. Funding: This research did not receive any specific grant from funding agencies in the public, 21 22 commercial, or not-for-profit sectors.

23 Competing interest: The authors have no conflict of interest

1	Availability of data, code, and materials: Data sharing is not applicable to this article as no
2	new data were created or analyzed in this study.
3	References
4	Abd-Alrazaq, A., Alajlani, M., Alhuwail, D., Toro, C.T., Giannicchi, A., Ahmed, A., Makhlouf,
5	A., Househ, M., 2022. The Effectiveness and Safety of Serious Games for Improving
6	Cognitive Abilities Among Elderly People With Cognitive Impairment: Systematic
7	Review and Meta-Analysis. JMIR Serious Games 10, e34592.
8	Alzheimer's Association, 2019. 2019 Alzheimer's disease facts and figures. Alzheimer's &
9	dementia 15, 321-387.
10	Amir-Behghadami, M., Janati, A., 2020. Population, Intervention, Comparison, Outcomes and
11	Study (PICOS) design as a framework to formulate eligibility criteria in systematic
12	reviews. Emerg Med J 37, 387.
13	Argasiński, J.K., Węgrzyn, P., 2019. Affective patterns in serious games. Future Generation
14	Computer Systems 92, 526-538.
15	Bamidis, P.D., Fissler, P., Papageorgiou, S.G., Zilidou, V., Konstantinidis, E.I., Billis, A.S.,
16	Romanopoulou, E., Karagianni, M., Beratis, I., Tsapanou, A., Tsilikopoulou, G.,
17	Grigoriadou, E., Ladas, A., Kyrillidou, A., Tsolaki, A., Frantzidis, C., Sidiropoulos, E.,
18	Siountas, A., Matsi, S., Papatriantafyllou, J., Margioti, E., Nika, A., Schlee, W., Elbert, T.,
19	Tsolaki, M., Vivas, A.B., Kolassa, I.T., 2015. Gains in cognition through combined
20	cognitive and physical training: the role of training dosage and severity of neurocognitive
21	disorder. Front Aging Neurosci 7, 152.

1	Benveniste, S., Jouvelot, P., Pin, B., Péquignot, R., 2012. The MINWii project: Renarcissization
2	of patients suffering from Alzheimer's disease through video game-based music therapy.
3	Entertainment Computing 3, 111-120.
4	Berg-Weger, M., Stewart, D.B., 2017. Non-Pharmacologic Interventions for Persons with
5	Dementia. Mo Med 114, 116-119.
6	Bojan, K., Stavropoulos, T., Lazarou, I., Nikolopoulos, S., Kompatsiaris, I., Tsolaki, M.,
7	Mukaetova-Ladinska, E., Christogianni, A., 2021. The Effects of playing the COSMA
8	Cognitive Games in Dementia. International Journal of Serious Games 8.
9	Bonnechère, B., Langley, C., Sahakian, B.J., 2020. The use of commercial computerised cognitive
10	games in older adults: a meta-analysis. Sci Rep 10, 15276-15276.
11	Borenstein, M., Hedges, L.V., Higgins, J.P., Rothstein, H.R., 2010. A basic introduction to fixed-
12	effect and random-effects models for meta-analysis. Research synthesis methods 1, 97-
13	111.
14	Cations, M., Laver, K.E., Crotty, M., Cameron, I.D., 2018. Rehabilitation in dementia care. Age
15	and Ageing 47, 171-174.
16	Cavallo, M., Hunter, E.M., van der Hiele, K., Angilletta, C., 2016. Computerized Structured
17	Cognitive Training in Patients Affected by Early-Stage Alzheimer's Disease is Feasible
18	and Effective: A Randomized Controlled Study. Archives of Clinical Neuropsychology 31,
19	868-876.
20	Chu, C.H., Quan, A.M.L., Souter, A., Krisnagopal, A., Biss, R.K., 2022. Effects of Exergaming
21	on Physical and Cognitive Outcomes of Older Adults Living in Long-Term Care Homes:
22	A Systematic Review. Gerontology.
23	Craven, M., Fabricatore, C., 2016. Game Features of Cognitive Training.

1	Dietlein, C., Eichberg, S., Fleiner, T., Zijlstra, W., 2018. Feasibility and effects of serious games
2	for people with dementia: A systematic review and recommendations for future research.
3	Gerontechnology 17, 1-17.
4	Doumas, I., Everard, G., Dehem, S., Lejeune, T., 2021. Serious games for upper limb rehabilitation
5	after stroke: a meta-analysis. Journal of NeuroEngineering and Rehabilitation 18, 100.
6	Drazich, B.F., LaFave, S., Crane, B.M., Szanton, S.L., Carlson, M.C., Budhathoki, C., Taylor, J.L.,
7	2020. Exergames and Depressive Symptoms in Older Adults: A Systematic Review.
8	Games Health J 9, 339-345.
9	Egger, M., Davey Smith, G., Schneider, M., Minder, C., 1997. Bias in meta-analysis detected by
10	a simple, graphical test. Bmj 315, 629-634.
11	Emmady, P.D., Tadi, P., 2022. Dementia.
12	Ferreira-Brito, F., Ribeiro, F., Aguiar de Sousa, D., Costa, J., Caneiras, C., Carriço, L., Verdelho,
13	A., 2021. Are Video Games Effective to Promote Cognition and Everyday Functional
14	Capacity in Mild Cognitive Impairment/Dementia Patients? A Meta-Analysis of
15	Randomized Controlled Trials. J Alzheimers Dis 84, 329-341.
16	Gago, M.F., Yelshyna, D., Bicho, E., Silva, H.D., Rocha, L., Lurdes Rodrigues, M., Sousa, N.,
17	2016. Compensatory Postural Adjustments in an Oculus Virtual Reality Environment and
18	the Risk of Falling in Alzheimer's Disease. Dementia and Geriatric Cognitive Disorders
19	Extra 6, 252-267.
20	Galante, E., Venturini, G., Fiaccadori, C., 2007. Computer-based cognitive intervention for
21	dementia: Preliminary results of a randomized clinical trial. Giornale italiano di medicina
22	del lavoro ed ergonomia 29, B26-32.

1	Gale, S.A., Acar, D., Daffner, K.R., 2018. Dementia. The American Journal of Medicine 131,
2	1161-1169.
3	Gupta, A., Prakash, N.B., Sannyasi, G., 2021. Rehabilitation in Dementia. Indian J Psychol Med
4	43, S37-S47.
5	Hagovská, M., Olekszyová, Z., 2016. Impact of the combination of cognitive and balance training
6	on gait, fear and risk of falling and quality of life in seniors with mild cognitive impairment.
7	Geriatr Gerontol Int 16, 1043-1050.
8	Hand, M.D., 2019. Every Three Seconds: A Review of an Innovative Documentary on Research
9	and Stigma Surrounding Dementia Across the Globe. J Gerontol Soc Work 62, 369-373.
10	Higgins, J.P., Thompson, S.G., 2002. Quantifying heterogeneity in a meta-analysis. Stat Med 21,
11	1539-1558.
12	Hill, N.T.M., Mowszowski, L., Naismith, S.L., Chadwick, V.L., Valenzuela, M., Lampit, A., 2016.
13	Computerized Cognitive Training in Older Adults With Mild Cognitive Impairment or
14	Dementia: A Systematic Review and Meta-Analysis. American Journal of Psychiatry 174,
15	329-340.
16	Hocine, N., Gouaïch, A., Cerri, S.A., Mottet, D., Froger, J., Laffont, I., 2015. Adaptation in serious
17	games for upper-limb rehabilitation: an approach to improve training outcomes. User
18	Modeling and User-Adapted Interaction 25, 65-98.
19	Huang, HC., Wong, MK., Yang, YH., Chiu, HY., Teng, CI., 2017. Impact of Playing
20	Exergames on Mood States: A Randomized Controlled Trial. Cyberpsychology, Behavior,
21	and Social Networking 20, 246-250.
22	Jacobs, R.S., 2020. Serious games: Play for change, The video game debate 2. Routledge, pp. 19-
23	40.

1	Karamians, R., Proffitt, R., Kline, D., Gauthier, L.V., 2020. Effectiveness of Virtual Reality- and
2	Gaming-Based Interventions for Upper Extremity Rehabilitation Poststroke: A Meta-
3	analysis. Arch. Phys. Med. Rehabil. 101, 885-896.
4	Karssemeijer, E.G.A., Bossers, W.J.R., Aaronson, J.A., Sanders, L.M.J., Kessels, R.P.C., Rikkert,
5	M., 2019. Exergaming as a Physical Exercise Strategy Reduces Frailty in People With
6	Dementia: A Randomized Controlled Trial. Journal of the American Medical Directors
7	Association 20, 1502-+.
8	Kleschnitzki, J.M., Grossmann, I., Beyer, R., Beyer, L., 2022. Modification in the Motor Skills of
9	Seniors in Care Homes Using Serious Games and the Impact of COVID-19: Field Study.
10	JMIR Serious Games 10, e36768.
11	Kletzel, S.L., Sood, P., Negm, A., Heyn, P.C., Krishnan, S., Machtinger, J., Hu, X.L., Devos, H.,
12	2021. Effectiveness of Brain Gaming in Older Adults With Cognitive Impairments: A
13	Systematic Review and Meta-Analysis. Journal of the American Medical Directors
14	Association 22, 2281-+.
15	Krath, J., Schürmann, L., Von Korflesch, H.F., 2021. Revealing the theoretical basis of
16	gamification: A systematic review and analysis of theory in research on gamification,
17	serious games and game-based learning. Computers in Human Behavior 125, 106963.
18	Kuil, M.N.A.v.d., Visser-Meily, J.M.A., Evers, A.W.M., Ham, I.J.M.v.d., 2018. A Usability Study
19	of a Serious Game in Cognitive Rehabilitation: A Compensatory Navigation Training in
20	Acquired Brain Injury Patients. Front. Psychol. 9.
21	Landers, R.N., 2014. Developing a Theory of Gamified Learning: Linking Serious Games and
22	Gamification of Learning. Simulation & Gaming 45, 752-768.

1	Lau, SY.J., Agius, H., 2021. A framework and immersive serious game for mild cognitive
2	impairment. Multimedia Tools and Applications 80, 31183-31237.
3	Laver, K.E., Crotty, M., Low, LF., Clemson, L., Whitehead, C., McLoughlin, J., Swaffer, K.,
4	Cations, M., 2020. Rehabilitation for people with dementia: a multi-method study
5	examining knowledge and attitudes. BMC Geriatrics 20, 531.
6	Lee, G.Y., Yip, C.C.K., Yu, E.C.S., Man, D.W.K., 2013. Evaluation of a computer-assisted
7	errorless learning-based memory training program for patients with early Alzheimer's
8	disease in Hong Kong: a pilot study. Clinical interventions in aging 8, 623-633.
9	Li, J., Erdt, M., Chen, L., Cao, Y., Lee, SQ., Theng, YL., 2018a. The Social Effects of
10	Exergames on Older Adults: Systematic Review and Metric Analysis. Journal of medical
11	Internet research 20, e10486-e10486.
12	Li, J., Theng, YL., Foo, S., Xu, X., 2018b. Exergames vs. traditional exercise: investigating the
13	influencing mechanism of platform effect on subthreshold depression among older adults.
14	Aging & mental health 22, 1634-1641.
15	Lin, F., Heffner, K.L., Ren, P., Tivarus, M.E., Brasch, J., Chen, DG., Mapstone, M., Porsteinsson,
16	A.P., Tadin, D., 2016. Cognitive and Neural Effects of Vision-Based Speed-of-Processing
17	Training in Older Adults with Amnestic Mild Cognitive Impairment: A Pilot Study. Journal
18	of the American Geriatrics Society 64, 1293-1298.
19	Lin, L., Aloe, A.M., 2021. Evaluation of various estimators for standardized mean difference in
20	meta-analysis. Stat Med 40, 403-426.

21 Lipsey, M.W., Wilson, D.B., 2001. Practical meta-analysis. SAGE publications, Inc.

1	Liu, C.L., Cheng, F.Y., Wei, M.J., Liao, Y.Y., 2022. Effects of Exergaming-Based Tai Chi on
2	Cognitive Function and Dual-Task Gait Performance in Older Adults With Mild Cognitive
3	Impairment: A Randomized Control Trial. Front Aging Neurosci 14, 761053.
4	Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., Brayne, C., Burns,
5	A., Cohen-Mansfield, J., Cooper, C., 2020. Dementia prevention, intervention, and care:
6	2020 report of the Lancet Commission. The Lancet 396, 413-446.
7	Maier, M., Rubio Ballester, B., Duff, A., Duarte Oller, E., Verschure, P.F.M.J., 2019. Effect of
8	Specific Over Nonspecific VR-Based Rehabilitation on Poststroke Motor Recovery: A
9	Systematic Meta-analysis. Neurorehabilitation and Neural Repair 33, 112-129.
10	Manera, V., Petit, P.D., Derreumaux, A., Orvieto, I., Romagnoli, M., Lyttle, G., David, R., Robert,
11	P.H., 2015. 'Kitchen and cooking,' a serious game for mild cognitive impairment and
12	Alzheimer's disease: a pilot study. Front Aging Neurosci 7, 24.
13	Martins, F., Fernandes, F., Naves, E., 2019. Serious Games in Neurorehabilitation for People with
14	Intellectual and Cognitive Impairments: A Systematic Study, pp. 359-364.
15	McCallum, S., Boletsis, C., 2013. Dementia Games: A Literature Review of Dementia-Related
16	Serious Games.
17	McIntyre, A., Harding, E., Yong, K.X., Sullivan, M.P., Gilhooly, M., Gilhooly, K., Woodbridge,
18	R., Crutch, S., 2019. Health and social care practitioners' understanding of the problems of
19	people with dementia-related visual processing impairment. Health & Social Care in the
20	Community 27, 982-990.
21	McKhann, G.M., Knopman, D.S., Chertkow, H., Hyman, B.T., Jack, C.R., Jr., Kawas, C.H.,
22	Klunk, W.E., Koroshetz, W.J., Manly, J.J., Mayeux, R., Mohs, R.C., Morris, J.C., Rossor,
23	M.N., Scheltens, P., Carrillo, M.C., Thies, B., Weintraub, S., Phelps, C.H., 2011. The

1	diagnosis of dementia due to Alzheimer's disease: recommendations from the National
2	Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for
3	Alzheimer's disease. Alzheimers Dement 7, 263-269.
4	Miller, K.J., Dye, R.V., Kim, J., Jennings, J.L., O'Toole, E., Wong, J., Siddarth, P., 2013. Effect
5	of a Computerized Brain Exercise Program on Cognitive Performance in Older Adults. The
6	American Journal of Geriatric Psychiatry 21, 655-663.
7	Moholdt, T., Weie, S., Chorianopoulos, K., Wang, A.I., Hagen, K., 2017. Exergaming can be an
8	innovative way of enjoyable high-intensity interval training. BMJ Open Sport & amp; amp;
9	Exercise Medicine 3, e000258.
10	Murad, M.H., Wang, Z., Chu, H., Lin, L., 2019. When continuous outcomes are measured using
11	different scales: guide for meta-analysis and interpretation. BMJ (Clinical research ed.)
12	364, k4817-k4817.
13	Nichols, E., Steinmetz, J.D., Vollset, S.E., Fukutaki, K., Chalek, J., Abd-Allah, F., Abdoli, A.,
14	Abualhasan, A., Abu-Gharbieh, E., Akram, T.T., Al Hamad, H., Alahdab, F., Alanezi,
15	F.M., Alipour, V., Almustanyir, S., Amu, H., Ansari, I., Arabloo, J., Ashraf, T., Astell-
16	Burt, T., Ayano, G., Ayuso-Mateos, J.L., Baig, A.A., Barnett, A., Barrow, A., Baune, B.T.,
17	Béjot, Y., Bezabhe, W.M.M., Bezabih, Y.M., Bhagavathula, A.S., Bhaskar, S.,
18	Bhattacharyya, K., Bijani, A., Biswas, A., Bolla, S.R., Boloor, A., Brayne, C., Brenner, H.,
19	Burkart, K., Burns, R.A., Cámera, L.A., Cao, C., Carvalho, F., Castro-de-Araujo, L.F.S.,
20	Catalá-López, F., Cerin, E., Chavan, P.P., Cherbuin, N., Chu, DT., Costa, V.M., Couto,
21	R.A.S., Dadras, O., Dai, X., Dandona, L., Dandona, R., De la Cruz-Góngora, V.,
22	Dhamnetiya, D., Dias da Silva, D., Diaz, D., Douiri, A., Edvardsson, D., Ekholuenetale,
23	M., El Sayed, I., El-Jaafary, S.I., Eskandari, K., Eskandarieh, S., Esmaeilnejad, S., Fares,

1	J., Faro, A., Farooque, U., Feigin, V.L., Feng, X., Fereshtehnejad, SM., Fernandes, E.,
2	Ferrara, P., Filip, I., Fillit, H., Fischer, F., Gaidhane, S., Galluzzo, L., Ghashghaee, A.,
3	Ghith, N., Gialluisi, A., Gilani, S.A., Glavan, IR., Gnedovskaya, E.V., Golechha, M.,
4	Gupta, R., Gupta, V.B., Gupta, V.K., Haider, M.R., Hall, B.J., Hamidi, S., Hanif, A.,
5	Hankey, G.J., Haque, S., Hartono, R.K., Hasaballah, A.I., Hasan, M.T., Hassan, A., Hay,
6	S.I., Hayat, K., Hegazy, M.I., Heidari, G., Heidari-Soureshjani, R., Herteliu, C., Househ,
7	M., Hussain, R., Hwang, BF., Iacoviello, L., Iavicoli, I., Ilesanmi, O.S., Ilic, I.M., Ilic,
8	M.D., Irvani, S.S.N., Iso, H., Iwagami, M., Jabbarinejad, R., Jacob, L., Jain, V., Jayapal,
9	S.K., Jayawardena, R., Jha, R.P., Jonas, J.B., Joseph, N., Kalani, R., Kandel, A., Kandel,
10	H., Karch, A., Kasa, A.S., Kassie, G.M., Keshavarz, P., Khan, M.A.B., Khatib, M.N.,
11	Khoja, T.A.M., Khubchandani, J., Kim, M.S., Kim, Y.J., Kisa, A., Kisa, S., Kivimäki, M.,
12	Koroshetz, W.J., Koyanagi, A., Kumar, G.A., Kumar, M., Lak, H.M., Leonardi, M., Li, B.,
13	Lim, S.S., Liu, X., Liu, Y., Logroscino, G., Lorkowski, S., Lucchetti, G., Lutzky Saute, R.,
14	Magnani, F.G., Malik, A.A., Massano, J., Mehndiratta, M.M., Menezes, R.G., Meretoja,
15	A., Mohajer, B., Mohamed Ibrahim, N., Mohammad, Y., Mohammed, A., Mokdad, A.H.,
16	Mondello, S., Moni, M.A.A., Moniruzzaman, M., Mossie, T.B., Nagel, G., Naveed, M.,
17	Nayak, V.C., Neupane Kandel, S., Nguyen, T.H., Oancea, B., Otstavnov, N., Otstavnov,
18	S.S., Owolabi, M.O., Panda-Jonas, S., Pashazadeh Kan, F., Pasovic, M., Patel, U.K.,
19	Pathak, M., Peres, M.F.P., Perianayagam, A., Peterson, C.B., Phillips, M.R., Pinheiro, M.,
20	Piradov, M.A., Pond, C.D., Potashman, M.H., Pottoo, F.H., Prada, S.I., Radfar, A., Raggi,
21	A., Rahim, F., Rahman, M., Ram, P., Ranasinghe, P., Rawaf, D.L., Rawaf, S., Rezaei, N.,
22	Rezapour, A., Robinson, S.R., Romoli, M., Roshandel, G., Sahathevan, R., Sahebkar, A.,
23	Sahraian, M.A., Sathian, B., Sattin, D., Sawhney, M., Saylan, M., Schiavolin, S., Seylani,

1	A., Sha, F., Shaikh, M.A., Shaji, K.S., Shannawaz, M., Shetty, J.K., Shigematsu, M., Shin,
2	J.I., Shiri, R., Silva, D.A.S., Silva, J.P., Silva, R., Singh, J.A., Skryabin, V.Y., Skryabina,
3	A.A., Smith, A.E., Soshnikov, S., Spurlock, E.E., Stein, D.J., Sun, J., Tabarés-Seisdedos,
4	R., Thakur, B., Timalsina, B., Tovani-Palone, M.R., Tran, B.X., Tsegaye, G.W., Valadan
5	Tahbaz, S., Valdez, P.R., Venketasubramanian, N., Vlassov, V., Vu, G.T., Vu, L.G., Wang,
6	YP., Wimo, A., Winkler, A.S., Yadav, L., Yahyazadeh Jabbari, S.H., Yamagishi, K.,
7	Yang, L., Yano, Y., Yonemoto, N., Yu, C., Yunusa, I., Zadey, S., Zastrozhin, M.S.,
8	Zastrozhina, A., Zhang, ZJ., Murray, C.J.L., Vos, T., 2022. Estimation of the global
9	prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the
10	Global Burden of Disease Study 2019. The Lancet Public Health 7, e105-e125.
11	Ning, H., Li, R., Ye, X., Zhang, Y., Liu, L., 2020. A Review on Serious Games for Dementia Care
12	in Ageing Societies. IEEE J Transl Eng Health Med 8, 1400411-1400411.
13	Ong, D.S.M., Weibin, M.Z., Vallabhajosyula, R., 2021. Serious games as rehabilitation tools in
14	neurological conditions: A comprehensive review. Technol Health Care 29, 15-31.
15	Padala, K.P., Padala, P.R., Malloy, T.R., Geske, J.A., Dubbert, P.M., Dennis, R.A., Garner, K.K.,
16	Bopp, M.M., Burke, W.J., Sullivan, D.H., 2012. Wii-Fit for Improving Gait and Balance
17	in an Assisted Living Facility: A Pilot Study. Journal of Aging Research 2012, 597573.
18	Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer,
19	L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., Chou, R., Glanville, J., Grimshaw, J.M.,
20	Hróbjartsson, A., Lalu, M.M., Li, T., Loder, E.W., Mayo-Wilson, E., McDonald, S.,
21	McGuinness, L.A., Stewart, L.A., Thomas, J., Tricco, A.C., Welch, V.A., Whiting, P.,
22	Moher, D., 2021. The PRISMA 2020 statement: an updated guideline for reporting
23	systematic reviews. Bmj 372, n71.

1	Park, JH., Park, JH., 2018. Does cognition-specific computer training have better clinical
2	outcomes than non-specific computer training? A single-blind, randomized controlled trial.
3	Clinical rehabilitation 32, 213-222.
4	Pu, L., Moyle, W., Jones, C., Todorovic, M., 2021. The effect of a social robot intervention on
5	sleep and motor activity of people living with dementia and chronic pain: A pilot
6	randomized controlled trial. Maturitas 144, 16-22.
7	Robert, P., König, A., Amieva, H., Andrieu, S., Bremond, F., Bullock, R., Ceccaldi, M., Dubois,
8	B., Gauthier, S., Kenigsberg, PA., Nave, S., Orgogozo, J.M., Piano, J., Benoit, M.,
9	Touchon, J., Vellas, B., Yesavage, J., Manera, V., 2014. Recommendations for the use of
10	Serious Games in people with Alzheimer's Disease, related disorders and frailty. Frontiers
11	in Aging Neuroscience 6.
12	Sáenz-de-Urturi, Z., Zapirain, B.G., Zorrilla, A.M., 2014. Kinect-based virtual game for motor and
13	cognitive rehabilitation: a pilot study for older adults, Proceedings of the 8th International
14	Conference on Pervasive Computing Technologies for Healthcare, pp. 262-265.
15	Sarkar, D.K., Zhang, C., 2013. Beta-endorphin neuron regulates stress response and innate
16	immunity to prevent breast cancer growth and progression. Vitam Horm 93, 263-276.
17	Seo, K., Kim, Jk., Oh, D.H., Ryu, H., Choi, H., 2017. Virtual daily living test to screen for mild
18	cognitive impairment using kinematic movement analysis. PLOS ONE 12, e0181883.
19	Sterne, J.A.C., Savović, J., Page, M.J., Elbers, R.G., Blencowe, N.S., Boutron, I., Cates, C.J.,
20	Cheng, H.Y., Corbett, M.S., Eldridge, S.M., Emberson, J.R., Hernán, M.A., Hopewell, S.,
21	Hróbjartsson, A., Junqueira, D.R., Jüni, P., Kirkham, J.J., Lasserson, T., Li, T., McAleenan,
22	A., Reeves, B.C., Shepperd, S., Shrier, I., Stewart, L.A., Tilling, K., White, I.R., Whiting,

1	P.F., Higgins, J.P.T., 2019. RoB 2: a revised tool for assessing risk of bias in randomised
2	trials. Bmj 366, 14898.

- Sun, Z., Wang, J.R., Wang, Z.Y., Zhang, S.M., Wang, M.J., 2006. Implement of behavioral
 intervention taking need-driven dementia-compromised behavior pattern as theory frame
 in patients with vascular dementia. Chinese Journal of Clinical Rehabilitation 10, 40-42.
- 6 Swinnen, N., Vandenbulcke, M., de Bruin, E.D., Akkerman, R., Stubbs, B., Firth, J., Vancampfort,
- D., 2021. The efficacy of exergaming in people with major neurocognitive disorder
 residing in long-term care facilities: a pilot randomized controlled trial. Alzheimer's
 research & therapy 13, 1-13.
- Thapa, N., Park, H.J., Yang, J.-G., Son, H., Jang, M., Lee, J., Kang, S.W., Park, K.W., Park, H.,
 2020. The Effect of a Virtual Reality-Based Intervention Program on Cognition in Older
 Adults with Mild Cognitive Impairment: A Randomized Control Trial. Journal of Clinical
 Medicine 9.
- 14 Tong, T., Chan, J., Chignell, M., 2017. Serious Games for Dementia.
- Toshimitsu, H., Hiroki, O., Kazuya, I., Joji, M., Hisashi, O., Yoshihito, K., Tomomi, H., 2008.
 Robot therapy as for recreation for elderly people with dementia Game recreation using
 a pet-type robot, RO-MAN 2008 The 17th IEEE International Symposium on Robot and
 Human Interactive Communication, pp. 174-179.
- Tripette, J., Murakami, H., Ryan, K.R., Ohta, Y., Miyachi, M., 2017. The contribution of Nintendo
 Wii Fit series in the field of health: a systematic review and meta-analysis. PeerJ 5, e3600.
- 21 Tseng, W.S., Ma, Y.C., Wong, W.K., Yeh, Y.T., Wang, W.I., Cheng, S.H., 2020. An Indoor
- Gardening Planting Table Game Design to Improve the Cognitive Performance of the
 Elderly with Mild and Moderate Dementia. Int J Environ Res Public Health 17.

1	Tziraki, C., Berenbaum, R., Gross, D., Abikhzer, J., Ben-David, B.M., 2017. Designing Serious
2	Computer Games for People With Moderate and Advanced Dementia: Interdisciplinary
3	Theory-Driven Pilot Study. JMIR Serious Games 5, e16.
4	van Santen, J., Dröes, RM., Holstege, M., Henkemans, O.B., van Rijn, A., de Vries, R., van
5	Straten, A., Meiland, F., 2018. Effects of Exergaming in People with Dementia: Results of
6	a Systematic Literature Review. Journal of Alzheimer's disease : JAD 63, 741-760.
7	Wang, R., DeMaria Jr, S., Goldberg, A., Katz, D., 2016. A systematic review of serious games in
8	training health care professionals. Simulation in Healthcare 11, 41-51.
9	Wang, Y., Xiao, L.D., Ullah, S., He, G.P., De Bellis, A., 2017. Evaluation of a nurse-led dementia
10	education and knowledge translation programme in primary care: A cluster randomized
11	controlled trial. Nurse Educ Today 49, 1-7.
12	WHO, 2021. Dementia. World Health Organization, Geneva.
13	Wiedenroth, S., Jauch, C., 2019. Design and Development of a Tablet Based Serious Game for
14	People with Dementia.
15	World Health Organization, 1992. The ICD-10 classification of mental and behavioural disorders
16	: clinical descriptions and diagnostic guidelines. World Health Organization, Geneva.
17	World Health Organization, 2021. Global status report on the public health response to dementia.
18	Dementia (who.int)
19	Zhao, Y., Feng, H., Wu, X., Du, Y., Yang, X., Hu, M., Ning, H., Liao, L., Chen, H., Zhao, Y.,
20	2020. Effectiveness of exergaming in improving cognitive and physical function in people
21	with mild cognitive impairment or dementia: systematic review. JMIR Serious Games 8,
22	e16841.

Table 1 Summary of included studies

Table	e 1 Summary of includ	led studies	5											
				Participants characteris	stics		Intervention characteristics							
No	Citation/Country	Study design	Sample size (n)	Mean (SD) of age (intervention/control)	Dementia type and stage	Intervention provider	Serious games group	Control group	Frequancy and duration of intervention	Intervention and follow-up length (month)	Outcomes			
1	Cavallo, Hunter, van der Hiele, & Angilletta, 2016/ Italy	RCT	80	76.50 (2.88)/ 76.33 (3.83)	Alzheimer's disease	Neuropsychologist	Received exergame-computerized exercise with cognitive training in order to stimulate visual perception, auditory perception, attention, language, reading and writing, computations, logic and deduction, memory, and sensory motor abilities.	Read electronic newspaper articles or participate in other activities that interest the participants in control group	Three times a week for 30-45 minutes per seesion	12 weeks/ post- intervention and 6 weeks	Significant interaction effects were observed for the IG compared with the CG on the Rivermead Behavioural Memory Test immediate (F = 2.877, p = 0.03), digit span forward (F= 2.785, p = 0.03), and verbal fluency (F = 3.491, p = 0.004).			
2	Galante, Venturini, & Fiaccadori, 2007/ Italy	RCT	12	76.00 (6.00)	Alzheimer's disease	Neuropsychologist	Received exergame-based computerized exercise	Participated in an interview and reminisced about the participants' lives.	Three times a week for 60 minutes per seesion	4 weeks/ post interventions, 3 months, and 9 months	IG: The mean differences between baseline and post-intervention scores were -2.60 ± 2.15 for instrumental activities of daily living, 0.10 ± 0.90 for activities of daily living, and -0.50 ± 0.30 for depression. CG: The mean differences between baseline and post-intervention scores were 0.50 ± 0.71 for instrumental activities of daily living, -0.30 ± 0.79 for activities of daily living, and 0.30 ± 1.16 for depression.			
3	Hagovská & Olekszyová, 2016/ Slovakia	RCT	80	68.00 (4.40)/ 65.90 (6.20)	Mild cognitive impairment	Physiotherapist	Received computerized exergames with cognitive training with with subprograms Nback, Vismo and Pland	NA	Twice a week for 30 minutes per session	10 weeks/ baseline and 10 weeks	Significant differences recorded between the IG and CG after training on Cognitive function ($p = 0.04$), TUG dual task ($p = 0.01$), and quality of life ($p < 0.001$).			
4	Karssemeijer et al., 2019/ Netherlands	RCT	115	79.00 (6.90)/ 79.80 (6.50)	Mild to moderate dementia	Trained student or research assistant	Received computerized cognitive- aerobic bicycle connected to a television screen	Reveived relaxation and flexibility exercises	Three times a week for 30-50 minutes per seesion	12 weeks/ post interventions and 12 weeks	Higher adherence for the IG compared with the CG (87.3% vs 81.1%, p = 0. 05). Non-significant improvement in activities of daily living following IG intervention (mean difference scores: IG = -0.30 ± 3.3 ; CG = 0.80 ± 3.21).			
5	Lee, Yip, Yu, & Man, 2013/ China	RCT	19	77.70 (6.07)	alzheimer's disease	Occupational therapists	Received computer-assisted errorless learning program (CELP) using errorless memory programs	Received general cognitively challenging activities to perform	Twice a week for 30 minutes per session	6 weeks/ baseline, post intevrention, and 3 months	Significant improvements in activities of daily living ($p = 0.02$) and dementia severity ($p = 0.04$) were observed for the IG compared with the CG. No differences in cognitive performance ($p = 0.09$) or depression ($p = 0.05$) were observed across groups.			
6	Liu, Cheng, Wei, & Liao, 2022/ Taiwan	RCT	50	73.40 (6.50)/ 74.60 (6.10)	Mild cognitive impairment	Tai-Chi coach	Received exergame-based modified Tai Chi training, which included standing from a broad to a narrow base, body mass weight shifting, squats, and slow symmetrical to diagonal coordination arm-leg motions.	Usual care	Once a week for 50 minutes	12 weeks/ baseline and post intervention	The IG performed better than the CG in gait speed ($p < 0.001$) and cognitive function ($p = 0.002$).			
7	Miller et al., 2013/ USA	RCT	69	82.20 (4.40)/ 81.50 (7.60)	Dementia	NA	Received exergame-computerized exercise with cognitive training	Usual care	Five times a week for 20-25 minutes	8 weeks/ baseline, 2	Significant differences in Delayed Memory between the IG and the CG ($F = 4.7$, $p = 0.01$).			

8	Padala et al., 2012/ USA	RCT	22	79.30 (9.80)/ 81.60 (5.20)	Alzheimer's disease	Physical therapist.	Received Wii-Fit software exergames (i.e. strength training, yoga, and balance games) connected to a mobile television	NA	Five times a week for 30 minutes
9	Park & Park, 2018/ South Korea	RCT	78	66.95 (4.10)/ 67.64 (4.55)	Mild cognitive impairment	Occupational therapists	Received exergames (i.e. table tennis, sword play, and archery)-based virtual reality	Received cognitive training	Three days a week
10	Swinnen et al., 2021/ Belgium	RCT	55	84.70 (5.60)/ 85.30 96.50)	Dementia	Physical therapist.	Received exergames (i.e. grasp, walk)	Watched and listened to music video	Three times a week for 15 minutes
11	Thapa et al., 2020/ South Korea	RCT	68	72.60 (5.40)/ 72.70 (5.60)	Mild cognitive impairment	Exercise specialist, physical therapist and nutritionist	Received virtual reality games including several activities (i.e. pick a recipe, memorize the list, shooting game)	General health care health education was provided.	Three times a week for 100 minutes per sessions
12	van Santen et al., 2020/ Netherlands	RCT	112	79.00 (6.00)/ 79.00 (7.00)	Dementia	NA	Received exergame-cycling linked to a screen that simulates the feeling of riding outside, providing both physical and cognitive stimulation.	Attended varied activity program (i.e. arts and crafts, music, and physical exercise)	Five times a week for 60 minutes

CG (control group); IG (intervention group); and NA (Not Available)

1

months, and 6 months

8 weeks/ Baseline, 1 month, and 2 months

10 weeks/ baseline and 10 weeks

8 weeks/ baseline and post intervention

8 weeks/ baseline and post intervention

6 months/ baseline, 3 months, and 6 months Significant improvements in balance for the IG compared with the CG (p = 0.003). No significant differences between groups for activities of daily living (p = 0.55), instrumental activities of daily living (p = 0.36), or cognitive function (p = 0.55).

Significant improvement in cognitive function for the IG compared with the CG (mean difference scores IG: 9.31 ± 2.54 ; CG: 9.26 ± 4.38).

Significant interaction effects were observed for the IG compared with the CG on cognitive function (F = 24.4, p < 0.001), depression (F= 28.8, p < 0.001), quality of life (F = 6.9, p = 0.01), and activities of daily living (F = 7.7, p = 0.008).

Significant interaction effects were observed for the IG compared with the CG on gait speed (F = 0.14, p = 0.02).

Significant positive effects were observed for the IG compared with the CG on cognitive function (r = 2.30, 95% confidence interval [CI]: 0.65 to 3.96, p = 0.007), social functioning (r= 1.86, 95% CI: 3.56 to 0.17, p =0.03), and distress (r = -3.30, 95% CI: 6.57 to 0.03, p = 0.048).

Table 2 GRADE evidence 1

Question: Serious games programs compared to usual care for people with dementia 2

Bibliography: 3

			Certainty as	sessment			N₂ of pa	tients	Eff	ect	
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Serious games programs	usual care		Absolute (95% CI)	Importance

Global cognition 4

7	randomised trials	not serious	seriousª	not serious	not serious	none	231	195	-	SMD 0.34 SD higher (0.07 higher to 0.61 higher)	⊕⊕⊕⊖ Moderate	
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6

ADL

5

4	randomised trials	not serious	not serious	not serious	very serious ^{b,c}	none	79	75	-	SMD 0.23 SD lower (0.58 lower to 0.11 higher)	⊕⊕⊖O Low		
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7 8

4	randomised trials	not serious	seriousª	not serious	very serious ^{b,c}	none	35	32	-	SMD 0.69 SD lower	⊕⊖⊖⊖ _{Very low}	
										(1.62 lower to U.24 higher)		

Depression 9

Instrumental ADL

<u>10</u> CI: confidence interval; SMD: standardised mean difference

Explanations

a. Consistency was downgraded because the heterogeneity was superior to 30%
 b. Precision was downgraded because the SMD confidence interval overlaapped between experimental and control intervention
 c. Precision was downgraded as the number of observations was inferior to 400
 d. Precision was doubly downgraded as the number of observations was inferior to 200