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What do we know about the effects of physical exercise on dementia, without alzheimer's? systematic review of international clinical trials

¿Qué sabemos sobre los efectos del ejercicio físico en la demencia, excluyendo el alzheimer? una revisión sistemática de ensayos clínicos internacionales

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Abstract. Dementia is characterized by a progressive decline in cognitive and physical functions beyond that expected in normal aging affecting the quality of life and that of those close to them. Except for Alzheimer's, few studies have summarized exercise results in dementia. Thus, the aim of the study was to analyze the effects of physical exercise (PE) on dementia in older adults, not including Alzheimer's. This systematic review of the literature followed the recommendations of PRISMA and was conducted in September 2022 in the databases: Scopus, Web of Science, PubMed, and EBSCO. The search was performed without restriction regarding the date of publication. Experimental studies that analyzed people with dementia submitted to PE were included. In total, 17 studies met the inclusion criteria, with eight of them from the Asian continent. The studies showed that PE, especially aerobic exercise, benefits physical and cognitive aspects of older people with dementia. However, better results were seen when PE was associated with cognitive therapies. Most of the studies evaluated older people who were at different stages of the disease. Aerobic exercise was present in 70.58% of studies. The intervention periods ranged from four to 65 weeks, with combined exercises three times a week in five studies, and the intensities varied according to the type of PE. The benefits showed improvements in the performance of daily activities and cognitive functions. However, some studies have low methodological quality, which could interfere with the results. Further research is required on PE and dementia in older adults.
Keywords: Dementia, Exercise, Elderly, Cognition, Systematic Review.

Resumen. La demencia se caracteriza por un deterioro progresivo de las funciones cognitivas y físicas más allá de lo esperado en el envejecimiento normal, lo que afecta la calidad de vida tanto de los afectados como de quienes les rodean. Excepto por el Alzheimer, pocos estudios han resumido los resultados del ejercicio en la demencia. Por lo tanto, el objetivo del estudio fue analizar los efectos del ejercicio físico (EF) en los adultos mayores con demencia, excluyendo el Alzheimer. Esta revisión sistemática de la literatura siguió las recomendaciones de PRISMA y se llevó a cabo en septiembre de 2022 en las bases de datos: Scopus, Web of Science, PubMed y EBSCO. La búsqueda se realizó sin restricciones en cuanto a la fecha de publicación. Se incluyeron estudios experimentales que analizaron a personas con demencia sometidas a EF. En total, 17 estudios cumplieron con los criterios de inclusión, de los cuales ocho eran del continente asiático. Los estudios mostraron que el EF, especialmente el ejercicio aeróbico, beneficia los aspectos físicos y cognitivos de las personas mayores con demencia. Sin embargo, se obtuvieron mejores resultados cuando el EF se combinó con terapias cognitivas. La mayoría de los estudios evaluaron a personas mayores en diferentes etapas de la enfermedad. El ejercicio aeróbico estuvo presente en el 70,58% de los estudios. Los períodos de intervención variaron de cuatro a 65 semanas, con ejercicios combinados tres veces a la semana en cinco estudios, y las intensidades variaron según el tipo de EF. Los beneficios mostraron mejoras en el desempeño de las actividades diarias y las funciones cognitivas. Sin embargo, algunos estudios presentaron baja calidad metodológica, lo que podría interferir en los resultados. Se requiere investigación adicional sobre el EF y la demencia en adultos mayores.
Palabras clave: Demencia, Ejercicio, Personas mayores, Cognición, Revisión sistemática.

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Introduction

Population aging is a phenomenon that is observed all over the world (UN, 2017), and as a result, the number of disorders and diseases inherent to aging, such as dementia, is growing. Dementia is characterized by a progressive decline in cognitive and physical functions beyond what is expected in normal aging, affecting attention, learning, memory, language, and motor function (American Psychiatric Association, 2013; Liu et al., 2020; Logiudice & Warson, 2014). This makes simple daily tasks, such as remembering names, important dates, or how to perform everyday activities, a constant challenge. This loss of cognitive ability affects independence and self-esteem, contributing to a decrease in the quality of life (Aggarwal; Chaware; Aggarwal, 2022; Swinnen et al., 2021). Furthermore, dementia often leads to behavioral and emotional changes. Elderly individuals with dementia may experience agitation, apathy, depression, anxiety, and aggression, among other symptoms (Aggarwal; Chaware; Aggarwal, 2022; Lamb et al., 2018). These alterations can be perplexing and distressing for both them and their caregivers, further impacting their quality of life.

Due to the complications caused by the disease, in 2012 the World Health Organization (WHO) declared that the treatment of dementia should be a priority in public health, as it generates great economic, family, and social impacts (WHO, 2019). It is estimated that the world annual economic cost of treating dementia is approximately $818 billion, equivalent to 1.1% of global gross domestic product. In addition, the more severe the progression of symptoms, the greater the incapacity of the older adult, generating loss of autonomy and independence, thus, identity is impaired, as these individuals are unable to exercise their family and social role (Kolanowski et al., 2017; Okamura et al.,

2018). In this way, dementia directly affects the family structure and especially the caregiver, because, in addition to changes in the daily routine, there are physical, emotional, and financial overloads (Kolanowski et al., 2017).

It has been observed that dementia is more common among women, due to their longer life expectancy (Liu et al., 2020) and in the coming years, it is estimated that the number of individuals with dementia will increase considerably, from 50 million in 2017 to approximately 152 million by 2050 (WHO, 2019). Currently, approximately 5 to 8% of the population aged 60 years and over have dementia and in individuals between 85 and 90 years, the outlook increases to almost 50% (Alzheimer's Disease International, 2019).

As Alzheimer's is the most prevalent and the most widely studied dementia among older adults (Alzheimer's Disease International, 2019), the other forms of dementia that affect both mental and physical health and socialization end up being underestimated, which demonstrates the need for specific studies, analyzing possible treatment strategies and minimizing symptoms. Among the other forms of dementia, we can mention vascular dementia, dementia with Lewy bodies, and frontotemporal dementia (Fymat, 2021; Alzheimer's Disease International, 2019; Ienca et al. 2018).

Although there is no cure, several studies have developed actions to alleviate and even delay the symptoms of dementia, such as pharmacological treatments, cognitive therapies, and physical exercise (PE) (Lamb et al., 2018; Okamura et al., 2018). Drug treatment, despite being commonly used, is not efficient in improving all health conditions. In addition to being an expensive treatment, interactions between drugs for dementia and other comorbidities can occur, causing serious side effects (Sönnerstam et al., 2019). Cognitive therapy, on the other hand, has been widely used in older people with dementia because it helps to stabilize the condition or results in small improvements in cognitive and functional declines, in addition to being an easy-to-apply method with low financial cost (Carrion et al., 2018; Tay et al., 2016). Like cognitive therapy, PE is a treatment that has no side effects, is easy to implement, and benefits many aspects of health. PE is already being used as a treatment in several populations such as patients with fibromyalgia (Andrade, Sieczkowska, & Villarino, 2019; Andrade, Steffens, et al., 2020; Sieczkowska et al., 2020; Sieczkowska et al., 2019), Parkinson's (Rawson et al., 2019), and multiple sclerosis (Rooney, Albalawi, & Paul, 2020); demonstrating effectiveness in improving symptoms of depression (Andrade et al., 2017), mood states (Andrade, et al., 2019), sleep disturbance (Andrade; Vilarino; & Bevilacqua, 2017; Curi et al., 2018; Andrade; Vilarino et al., 2020), Obesity (Ceballos-Gurrola et al. 2020; Berelleza et al. 2021) and strength and functionality (Dittus et al., 2019).

However, the scientific literature still does not present a consensus regarding the benefits of PE practice on dementia in older adults. Studies show that aerobic exercise can increase the volume of the hippocampus and promote cerebral angiogenesis, increasing memory performance (Bossers et al., 2015; Groot et al., 2016; Karssemeijer et al., 2017) and improving brain vitality, in addition to reducing the risk of developing dementia in healthy older adults (Karssemeijer et al., 2017; Norton, et al., 2014). However, the systematic review carried out by Forbes et al. (2015) found that PE alone is not able to improve the clinical framework of patients with dementia. This result differs in parts from that presented by Lamb et al. (2018), where aerobic exercise and resistance exercise improved physical health but were not able to reduce the cognitive deficit in older people with mild and moderate dementia. Thus, there are gaps in the literature on the effect of PE in older people with dementia that need further investigation.

Although the current evidence on the isolated practice of PE does not show positive results in terms of dementia in older adults, the differences between PE modalities and the protocols used have not been investigated. In this way, systematic review studies can help to better understand the use of PE as an aid in the treatment of dementia, identifying the main benefits, best modality, which protocol should be used (intensity, volume, and frequency), and the effects in relation to the stages of dementia. Thus, the aim of this study is to analyze the effects of physical exercise on dementia in older adults, not including Alzheimer's.

Methods

This systematic review was performed following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2015). It was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under number CRD42020197554.

Search Strategy

The literature search was carried out in September 2022 in the electronic databases: Scopus, Web of Science, PubMed, and EBSCO. The search terms used by the researchers were obtained after consulting the Medical Subject Headings (Table 1).

Table 1.
Search strategies in databases

Terms	Descriptors
1. Elderly	Elderly OR Aged OR Aging OR "Aged, 80 and over" OR Senescence OR "Oldest Old" OR "Old Adults" OR Nonagenarian* OR Octogenarian* OR Centenarian*'
2. Disease	"Dementia*" OR "Vascular Dementia" OR "Lewy Body Dementia" OR "Frontotemporal Dementias" OR "Senile Paranoid Dementia*"
3. Exercise	"Exercise*" OR "Physical Activity*" OR "Physical Exercise*" OR "Exercise Training" OR "Training, Endurance" OR "Resistance training" OR "Strength Training" OR "Aerobic Exercise" OR "Circuit Based Exercise" OR "Physical Endurance" OR "High Intensity Interval Training"
4. Study desing	"Randomized controlled trials" OR "Controlled clinical trial" OR "Random allocation" OR "Double-blind method" OR "Single-blind method" OR "Clinical trial" OR "Prospective study" OR "Crossover study" OR "Crossover design" OR "Experimental study" OR "Follow up study" OR "RCT" OR Intervention
Combination	#1 AND #2 AND #3 AND #4

Study selection

Two researchers (LNNS and GTV) independently selected the studies, and in the case of disagreement, a third researcher was consulted (AA). After excluding duplicate articles, the titles were read, then the abstracts were analyzed, and finally, the full texts of the studies that met the eligibility criteria were read.

Eligibility criteria

Eligibility for the study selection was determined according to the PICOS criteria (Moher et al., 2015), and is detailed in table 2.

Table 2.
Criteria for inclusion and exclusion of studies selected for review.

		Inclusion Criteria	Exclusion Criteria
P	Participate	Elderly with dementia	Elderly without dementia, Elderly with Alzheimer disease; animals
I	Intervention	Physical exercise	-
C	Comparison	Elderly without dementia, sedentary control, healthy subjects	-
O	Outcomes	Effects of physical exercise on dementia	Results not related to dementia
S	Study	Randomized Control Trial, Non Randomized Clinical Trial and pilot studies	Systematic review, case report and cross-sectional studies, book chapters or editorials

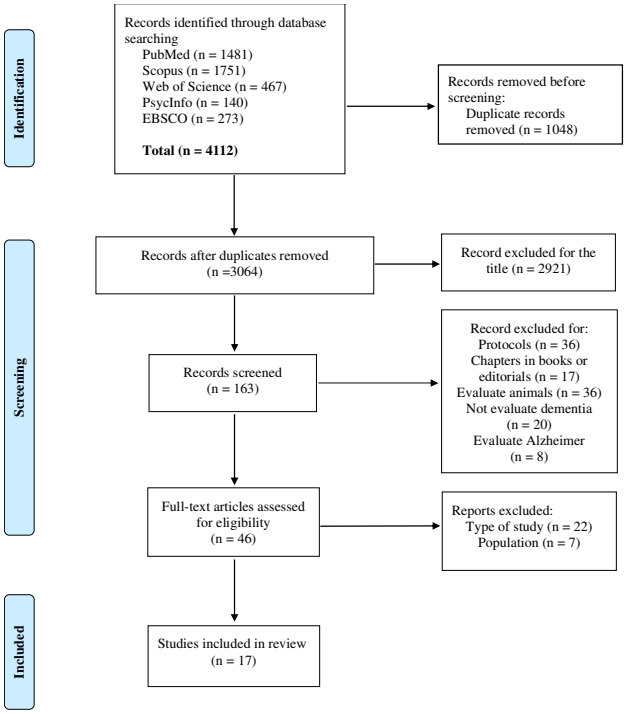

Figure. 1. Flowchart of the selection process of articles for the review.

Data extraction

Data extraction was performed by two independent researchers (LNNS and GTV), and discrepancies were resolved by a third evaluator (AA). For the analysis and discussion of the results, the following data were extracted: author and study design, sample characteristics (age, sex, level of dementia), type of exercise, duration of intervention, intensity, and results on dementia.

Quality appraisal

This systematic review evaluated the quality of the included studies and the risk of bias using the Cochrane Collaboration Risk of Bias tool (Higgins et al., 2011), which includes criteria to identify bias in the selected studies that could interfere with the interpretation and conclusion. The bias analysis is divided into seven categories: generation of random sequence, concealment of allocation, blinding of participants, blinding of evaluators, incomplete outcomes, selective outcome reporting, and other biases. Bias risk assessment was performed by two researchers (LNNS and GTV). The kappa concordance index (Cohen, 1960) between the reviewers for each of the criteria was determined, and differences were resolved by consulting a third reviewer (AA) for a final opinion.

Results

Identification and selection of studies

The first stage of the database search identified 2536 studies, of which 700 duplicated studies were excluded. One hundred and thirteen studies were selected after reading the titles. In the review of abstracts, 78 studies were excluded, of these 30 were protocols, 17 were chapters in books or editorials, 16 evaluated animals, and 15 did not evaluate dementia. In the fourth stage, 35 articles were read in full, 22 were excluded because they were not clinical trials, and five did not evaluate older adults. Thus, 11 studies were selected for analysis, as shown in figure 1.

Bibliometric analysis

The studies were carried out in 15 countries, with the majority being published in Asia and the European continent. There were no studies developed in the African continent or in central America (Figure 2).

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Figure. 2. Global geographical distribution of studies related to dementia and physical exercise in older adults.

From the analysis of keywords, the 15 most frequent in the studies were identified, with the term "Dementia" being the most cited, present in 16 studies, followed by "Exercise" in 14, "Elderly" in 11, and "Randomized

controlled trial" in nine. The study by Lamb et al. (2018) does not provide information about the keywords. The other words are illustrated in Figure 3 through a word cloud.

Figure. 3. Keywords used in the articles selected for analysis.

Characteristics of included studies

Of the seventeen articles included in this review, the oldest was published in 2006 (Stevens e Killeen, 2006) and the most recent were published in 2021 (Swinnen et al., 2021; Tanaka, Yamagami, & Yamaguchi, 2021). The study with the lowest mean age was that by Styliadis, Kartsidis, Paraskevopoulos, Ioannides e Bamidis (2015) with 70.42 ± 6.63 years, while the study by Tanaka et al. (2021) had the highest mean age with 88.10 ± 8.10 years. The total sample consisted of 65.7% of women (n=1054) aged ≥60 years. Most of the studies evaluated older people who were at different stages of the disease: all stages (Tanaka et al., 2021; Henskens, Nauta, Van Eekeren, & Scherder, 2018; Lamb et al., 2018; Okamura et al., 2018; Cancela, Ayán, Varela, & Seijo, 2016), mild to moderate phases (Swinnen et al., 2021; Trautwein et al., 2020), and moderate to severe phases (Higuti, Barbosa, Corrêa, Izzo, & Ansai, 2020; Karssemeijer et al., 2019), and seven studies evaluated a sample of older people at the same stage: early (Tay et al., 2016), mild (Ho et al., 2020; Lee, Joung, & Shin, 2019; Cheng et al., 2014; Burgener, Yang, Gilbert, & Marsh-Yant, 2008), and moderate (Liu et al. 2020; Styliadis et al., 2015; Stevens, & Killeen, 2006). These and other characteristics can be seen in table 3.

Table 3.
Characteristics and results of experimental clinical studies with physical exercise in dementia elderly

Reference	*Sample*	*Interventions*	*Analyzed variables*
Swinnen et al. (2021) RCT	45 elderlies; Age: 85.0±6.0 years (35 women and 10 men) Mild and moderate dementia	*Exercise and Combination therapy* exergaming-training group	Gait speed, balance, strength of the lower limbs, step reaction time, cognitive function, depression, quality of life, ADL
Tanaka, Yamagami &Yamaguchi (2021) quasi-RCT	31 elderlies; Age: 88.1±8.10 years (18 women and 13 men) All stages of dementia	*Exercise and Combination therapy* Strength, aerobic exercise and cognitive stimulation - training group	social activity in daily behavior, cognitive function, apathy, muscle and grip strength, independence of ADL, life-space, and objective quality of life (QOL).
Higuti et al. (2020)	17 elderlies; Age: 79.6±9.3 years (9 women and 8 men) Moderate and severe dementia	*Exercise and Combination therapy* Mobility exercise - training group Mobility exercise with music - training group	Functional capacity, cognitive function
Ho et al. (2020)	166 elderlies; Age: 79.0±8.0 years (134 women and 32 men) Mild dementia	*Exercise* Dance movement therapy (DMT)- training group Body movement-training group	Loneliness, depression, mood, ADL, cognitive function, and cortisol
Trautwein et al. (2020)	163 elderlies; Age 85.0±7.0 years (137 women and 26 men) Mild and moderate dementia	*Exercise and Combination therapy* Exercise Program (strength, balance, endurance, flexibility) and cognitive stimulation -training group	Gait performance, Balance, mobility, strength, and function of lower limb, cognitive function
Liu et al. (2020) RCT	61 elderlies; Age: 85.7±6.9 years (11 women and 50 men) Mild and moderate dementia	*Exercise* Strength exercise-training group stationary bicycle-training group	Cognitive function, Depression, BDNF, plasma MCP-1, and plasma IGF-1
Karssemeijer et al. (2019) RCT	115 elderlies; Aged: 79.2±6.9 years; (53 women and 62 men) Moderate and severe dementia	*Exercise* exergaming-training group stationary bicycle -training group	Executive function, psychomotor speed, episodic memory and working memory
Lee, Joung & Shin (2019)	45 elderlies; Aged: 79.2±6.9 years; (22 women and 13 men) Mild dementia	*Exercise* Exercise Program (Fumanet exercise) – training Group	Cognitive function, Depression, gait performance
Henskens et al. (2018) RCT	87 elderlies; Age: uninformed (67 women and 20 men) All stages of dementia	*Exercise and Combination therapy* Strength and walking-training group Activities of daily living - training group Strength, walking, and Activities of daily living - training group	Cognitive function, Physical function (Physical Endurance, Functional Mobility, Balance and Muscle Strength) Mood, behavior, and ADL
Lamb et al. (2018) Prospective cohort study	415 elderlies; Age: 77±7.9 years (163 women and 252 men) All stages of dementia	*Exercise* Strength and stationary bicycle -training group	Cognitive function, neuropsychiatric symptoms, ADL, Physical fitness, and quality of life
Okamura et al. (2018) RCT	100 elderlies; Age: 82.4±8.0 (70 women and 30 men) All stages of dementia	*Exercise and Combination therapy* Arm ergometer cycle and visual exercise stimulation - training group visual exercise stimulation - training group	Cognitive function, selective and continuous attentive function, ADL
Cancela et al. (2016)	189 elderlies; Age: 80.63 ± 8.32 (126 women and 63 men) All stages of dementia	*Exercise* Stationary bicycle -training group	Cognitive function, memory, depression, functional independence (functional mobility and ADL) and neuropsychiatric disturbances.
Tay et al. (2016) Prospctive cohort study	39 elderlies; Age: 79±6.2 years (17 women and 22 men) Early dementia	*Exercise and Combination therapy* Strength, walking and cognitive stimulation -training group	Cognitive function, ADL, iADL, walking speed
Styliadis et al. (2015) Longitudinal study	70 elderlies; Age: 70.80±5.67 years (45 women and 25 men) Moderate dementia	*Exercise and Combination therapy* Exergaming - training group Auditory processing and working memory - training group Exergaming and auditory processing, working memory - training group	Status and Cognitive function.
Cheng et al. (2014) RCT	110 elderlies; Age: uninformed (71 women and 39 men) Mild dementia	*Exercise and Combination therapy* Tai Chi - training group Mahjong - training group	Cognitive function. Depression, Immediate/delayed recall, categorical fluency, and digit span

Burgener et al. (2008)	43 elderlies; Age: 77,9±7,9 years (20 women and 23 men) Mild dementia	*Exercise and Combination therapy* Tai Chi and Cognitive therapy - training group	Cognitive function, Physical function (balance, strength, and measure of physical illness), depression, and self-esteem
Stevens & Killeen (2006) RCT	75 elderlies; Age: 80.5 years (56 women and 19 men) Moderate dementia	*Exercise* Body movement-training group	ADL, progression of dementia

Legend: *BDNF*: Brain-derived neurotrophic factor; *iADL*: instrumental activities of daily living; *ADL*: activities of daily living; *IGF-1*: insulin-like growth factor-1; *MCP-1:* monocyte chemotactic protein-1.

Characteristics of interventions (Physical Exercises)

It is noteworthy that only seven studies used PE as a single intervention (Ho et al., 2020; Liu et al., 2020; Karssemeijer et al., 2019; Lee et al., 2019; Lamb et al., 2018; Cancela et al., 2016; Stevens, & Killeen, 2006), while another five studies combined PE and cognitive therapy (Swinnen et al., 2021; Tanaka et al., 2021; Okamura et al. 2018; Tay et al., 2016; Styliadis et al., 2015; Cheng et al., 2014; Burgener, Yang, Gilbert, & Marsh-Yant, 2008). Higuti et al. (2020) associated PE practice with music and Henskens et al. (2018) used the combination of PE and activities of daily living. Regarding the types of PE, aerobic exercise, in walking, exergaming, and cycling modalities, in isolation or combined with resistance exercise was used in almost all studies, except in the studies by Cheng et al. (2014) and Burgener et al. (2008) which investigated Tai Chi (Table 3) and the studies by Higuti et al. (2020) and by Lee et al. (2019) which investigated mobility exercises.

When analyzing the intervention protocol, six studies submitted patients to intervention three times a week (Swinnen et al., 2021; Karssemeijer et al., 2019; HenskenS et al., 2018; Cheng et al., 2014; Burgener et al., 2008, Stevens, & Killeen, 2006), four studies to once a week (Higuti et al., 2020; Lee et al., 2019; Okamura et al., 2018; Tay et al., 2016), three studies to twice a week (Tanaka et al., 2021; Ho et al., 2020; Trautwein et al., 2020), two studies to five interventions a week (Liu et al., 2020; Styliadis et al., 2015), and one study to daily sessions (Cancela et al., 2016). Regarding the intervention time, the shortest study lasted four weeks (Liu et a., 2020), while the longest studies lasted 65 (Cancela et al., 2016) and 40 weeks (Burgener et al., 2008) (Table 4).

Table 4.
Characteristics and results of the intervention with physical exercises

Reference	*Protocol of intervention*	*Protocol of exercises*	*Conclusions*
Swinnen *et al.* (2021)	Duration: 8 weeks; Weekly frequency: 3; EA 15'	AE: Exergaming: Stepping movements Intensity: mild to moderate (RPE)	Exergame training improves lower extremity functioning, cognitive functioning and step reaction time, and symptoms of depression in inpatients with dementia.
Tanaka, Yamagami & Yamaguchi (2021)	Duration: 8 weeks; Weekly frequency: 2; ER + EA 15'	Multi-component exercise training AE: Not informed Intensity: mild to moderate (RPE) RE: Not informed Intensity: mild to moderate (RPE)	Group-based combined intervention for dementia is effective for maintaining social activity and QOL in a geriatric health service facility.
Higuti et al. (2020)	Duration: 12 weeks; Weekly frequency: 1; Mobility 25-30'	Mobility: Body movements (extension, flexion, adduction, abduction, rotation and elevation) Intensity: light (Not informed unit of measurement)	Listening to music combined with physical exercise training did not exert an effect on functional or cognitive performance in institutionalized older adults with moderate to advanced dementia.
Ho et al. (2020)	Duration: 12 weeks; Weekly frequency: 2; EA 60' each	AE: Dance Intensity: light to moderate (Not informed unit of measurement) Mobility: stretching and joint movements and exercising with towels Intensity: light to moderate (Not informed unit of measurement)	DMT, instead of intervention with physical exercise, has therapeutic effects on the ADL psychosocial and neuroendocrine functioning of elderly people with cognitive disabilities.
Trautwein et al. (2020)	Duration: 16 weeks; Weekly frequency: 2; EP: 45'	Multi-component exercise training EP: strength, balance, endurance, and flexibility) Intensity: moderate (RPE)	a combined exercise program is not effective in reducing decline in gait performance among elderly people with dementia.
Liu et al. (2020)	Duration: 4 weeks; Weekly frequency: 5; ER 2x12 EA 30'	AE: stationary bicycle Intensity: moderate (RPE) RE: Biceps, triceps, and pectoralis major. gluteus and quadriceps muscles Intensity: 40-50% 1RM	Both exercises bring a significant benefit to patients with dementia, while the serum brain-derived neurotrophic factor and plasma monocyte-1 chemotactic protein have been improved through aerobic training.
Karssemeijer et al. (2019)	Duration: 12 weeks; Weekly frequency: 3; Exergame 30-50'/w EA 30-50'/w	AE: Exergaming: cycling training (combined cognitive-aerobic bicycle training) Intensity: 65-75% of maximum HR AE: stationary bicycle Intensity: 65-75% of maximum HR	Both exergaming and AE can improve psychomotor speed. But no effects were found on executive function, episodic memory and working memory in older adults with dementia.
Lee, Joung & Shin (2019)	Duration: 8 weeks; Weekly frequency: 1; Fumanet 60'	Mobility: Body movements performed in a net of squares Intensity: Not informed	The Fumanet exercise is an effective nursing intervention to improve gait ability among older adults with mild dementia.
Henskens et al. (2018)	Duration: 6 weeks; Weekly frequency: 3; Sessions were alternated weekly (1st week: 1 ER 2 EA; 2nd weeks: 2 ER and 1 EA). ER: 3x8 EA: 500 meters or 1 kilometer 14 participants per group	Multi-component exercise training AE: outdoor walking sessions. Intensity: Not informed RE: chest press, side and front raises, triceps/biceps curl, seated row, seated leg extension, standing rear leg raise, hip abduction Intensity: moderate to strong	ADL training appears to be effective for the elderly with moderately dementia serious. It is not yet clear whether physical training is an effective type of stimulation.
Lamb et al. (2018)	Duration: 16 weeks; Weekly frequency: 2 ER: 3x20 EA: 25' 6-8 participants per group	Multi-component exercise training EA: static cycling; Intensity: moderate to strong (RPE) RE: Biceps exercise (For more able individuals: shoulder front raise,	Aerobic and strength exercises do not decrease cognitive impairment in people with mild to moderate dementia

		lateral raise, or press exercises) sit-to-stand exercise; Intensity: moderate to Strong (RPE) Home based exercise: Don't described.	
Okamura et al. (2018)	Duration: 6 weeks; Weekly frequency: 1; EA: 5'	Arm ergometer exercise Intensity: Not informed	The combined system is effective for increasing attention and concentration and improving cognitive function and activities of daily living in elderly people with dementia;
Cancela et al. (2016)	Duration: 65 weeks; Weekly frequency: diary sessions; EA: 15'	AE: bicycle; Intensity: light (Not informed unit of measurement)	EA improves cognitive functioning behavior and functional mobility in the individual with dementia.
Tay et al. (2016)	Duration: 16 weeks; Weekly frequency: 1; 45 min of exercise 10 participants per group	Multi-component physical exercise program AE: walking Intensity: light (Not informed unit of measurement) RE: sit to stand exercises and flexion/extension exercises Intensity: Not informed	Physical and cognitive rehabilitation improves dual task walking in early dementia, which can be contributed by improving cognitive performance
Styliadis et al. (2015)	Duration: 8 weeks; Weekly frequency: 5; Exergaming: 1 h/d 14 participants per group	The games' scenarios targeted body flexibility, balance, and strength as well as physical endurance through aerobic training. AE: 20' of aerobic exercises, RE: 8–10 exercises, Flexibility: 10' and a set of balance targeted exercises.	Combined physical and cognitive training improves cognitive function in patients with mild cognitive impairment.
Cheng et al. (2014)	Duration: 12 weeks; Weekly frequency: 3; Tai Chi (Yang stayle) 12 participants per group	Simpler versions of Tai Chi (8 or 12 forms.) Each form is practiced on its own with repetitions until it is sufficient. Intensity: Not informed	Mahjong and tai chi can preserve functioning or slow down the decline in certain cognitive domains, even those with significant cognitive impairment.
Burgener et al. (2008)	Duration: 40 weeks; Weekly frequency: 3; Tai Chi (Qigong style) 12 participants per group	Simpler versions of Tai Chi (7 forms.) Each form is practiced on its own with repetitions until there is sufficient. Intensity: Not informed	Combined physical and cognitive training stabilized physical illness and depression, but there was no improvement in dementia at the end of the intervention, more tests needed
Stevens & Killeen (2006)	Duration: 12 weeks; Weekly frequency: 3; EA: 30' 30 participants per group	Joint and large muscle group movement. Intensity: light (Not informed unit of measurement)	Exercise appears to affect the progress of dementia and improve capacity in activities of daily living for elderly people with dementia.

Legend: *RPE*: Rated Perceived Exertion; *AE*: Aerobic Exercise; *RE*: Resistance Exercise; *6MWT*: 6 Minute Walk Test; EP: Exercise Program

In three studies, the intensity used for aerobic exercise was mild (Tay et al., 2016; Cancela et al., 2016; Stevens, & Killeen, 2006), another three studies used mild to moderate intensities (Swinnen et al*.,* 2021; Tanaka et al., 2021; Ho et al., 2020) and two studies used moderate to high intensities (Karssemeijer et al., 2019; Henskens et al., 2018; Lamb et al., 2018). Four articles used the Rating of Perceived Exertion (RPE) as a unit of measurement (Swinnen et al*.,* 2021; Tanaka et al., 2021; Liu et al., 2020; Lamb et al., 2018), and one study used the maximum heart rate (Karssemeijer et al., 2019). The other studies do not mention the unit of measurement of the intensity of aerobic exercise (Ho et al., 2020; Henskens et al., 2018; Tay et al., 2016; Cancela et al., 2016; Stevens, & Killeen, 2006).

Resistance training consisted of exercises with machines and free weights that worked the large and small muscle groups, but only the study by Liu et al. (2020) specified how they determined the training load. In that study, the authors chose to work with an intensity between 40-50% 1RM. Exercise intensity was not reported in seven studies (Tanaka et al., 2021; Henskens et al., 2018; Okamura et al., 2018; Tay et al., 2016; Styliadis et al., 2015; Cheng et al., 2014; Burgener et al., 2008).

Regarding mobility exercises, only the study by Ho et al. (2020) specified the intensity (light to moderate) but did not inform the measurement unit. The training protocols used in each study are described in table 4.

Results on physical and cognitive aspects

Regarding physical variables, the analysis of results revealed that PE alone or combined with cognitive therapy is effective in improving performance in activities of daily living (Ho et al., 2018; Cancela et al., 2016; Lamb et al. 2018; Liu et al., 2020; Stevens, & Killeen, 2006; Okamura et al., 2018; TAY et al., 2016; Burgener et al. 2008), physical fitness (Lamb et al. 2018), and mobility (Trautwein et al., 2020; Cancela et al., 2016) in all stages of dementia in older adults.

With regard to cognitive aspects, it appears that PE alone (Liu et al., 2020; Cancela et al., 2016; Stevens, & Killeen, 2006) or combined with cognitive therapies (Swinnen et al. 2021; Cheng et al., 2014; Okamura et al., 2018; Styliadis et al., 2015; Tay et al., 2016) or interventions in activities of daily living (Henskens et al., 2018) increase cognitive performance, reducing the progression of dementia symptoms.

Positive changes in the biochemical markers for dementia, MCP-1, and IGF-1 were verified with the practice of aerobic and resistance exercises, both with moderate intensities (Liu et al., 2020). Improvements occurred in depressive symptoms with PE and interventions with activities of daily living (Henskens et al., 2018), in exergaming (Swinnen et al, 2021) in Dance Therapy (HO et al. 2018), and in tai chi (Burgener et al. 2008). Cheng et al. (2014) did not find beneficial effects of tai chi on depressive symptoms, but did find effects on memory, especially short-term memory. A similar result was found by Cancela et al., 2016, who observed significant improvements in memory functioning. On the other hand, Karsemeijer et al. (2019) found that both episodic memory, working memory, and executive functioning were not benefited by aerobic exercises (exergaming and stationary bicycle). However, these interventions were able to improve psychomotor speed, which is one of the most

important factors in predicting functional decline. The combination of aerobic exercise and cognitive stimulation positively affects attention and concentration at all stages of dementia. (Okamura et al., 2018).

Practical implications

The analysis of the results of the studies demonstrates that the practice of PE alone or combined with another therapy has important physical, psychological, and cognitive benefits in the lives of patients (Swinnen et al., 2021; Tanaka et al., 2021; Ho et al., 2020; Liu et al., 2020; Karssemeijer et al., 2019; Okamura et al., 2018; Tay et al., 2016; Cancela et al., 2016; Cheng et al., 2014; Burgener et al., 2008; Stevens, & Killeen, 2006). It should thus be recommended that patients perform aerobic and resistance exercises, as they have important practical implications such as improvement in clinical symptoms of the disease and performance improvement in daily tasks. The practical implications of each study analyzed are presented in table 5.

Table 5.
References and Practical implications of physical exercise interventions

Reference	Practical implications
Swinnen et al. (2021)	Exergame can improve physical and cognitive functioning in people with dementia residing in long-term care facilities.
Tanaka, Yamagami & Yamaguchi (2021)	*There was no exercise group* The combination of exercise and cognitive therapy is effective for socialization and quality of life for elderly people with dementia.
Higuti et al. (2020)	Exercise combined with music does not benefit physical aspects or cognition in institutionalized elderly people with dementia
Ho et al. (2020)	DMT improves psychosocial functioning, neuroendocrine daily performance in patients with dementia.
Liu et al. (2020)	Both exercises (AE and RE) improve the performance of activities of daily living, cognitive functions and biochemical markers for dementia (MCP-1 and IGF-1).
Karssemeijer et al. (2019)	Exergaming and AE improves psychomotor speed, as psychomotor speed is an important predictor of functional decline
Lee, Joung & Shin (2019)	The Fumanet exercise improve gait ability among older adults with mild dementia.
Henskens et al. (2018)	Exercise training (AE and RE) benefitted only grip strength of participants with mild-to-moderate cognitive impairment.
Lamb et al. (2018)	The exercise program (AE and RE) only improved physical fitness but not slow cognitive impairment in people with mild to moderate dementia.
Okamura et al. (2018)	*There was no exercise group* AE combined with cognitive therapy improved cognitive function, concentration, memory and activities of daily living
Cancela et al. (2016)	AE daily may slow cognitive decline as well as improve functional mobility, neuropsychiatric symptoms and memory function in institutionalized individuals with dementia, especially in severe cases of dementia.
Tay et al. (2016)	*There was no exercise group* EA and RE combined with cognitive stimulation improvements in cognitive performance and in dual task walking but not in single-task gait speed
Styliadis et al. (2015)	The isolated exercise (Exergaming) was not able to offer better cognitive.
Cheng et al. (2014)	Thai Chi improves cognitive performance, a short-term memory, but does not benefit long-term memory.
Burgener et al. (2008)	*There was no exercise group* Thai Chi combined Cognitive Therapy promotes physical improvement, self-esteem and depression.
Stevens & Killeen (2006)	EA decreases cognitive decline and promotes independence in daily activities

Legend: *IGF-1*: insulin-like growth factor-1; *MCP-1*: monocyte chemotactic protein-1; *EA*: Aerobic Exercise; *RE*: Resistance Exercise; *DMT*: Dance movement therapy

Quality of studies and Risk of Bias

According to the Cochrane Collaboration Risk of bias (Higgins et al., 2011), the Kappa agreement index between reviewers (LNNS and GTV) should be analyzed to assess the risk of bias in the studies. The agreement rate was greater than 85% for all criteria in the 17 studies. All studies presented a high risk of bias in criteria for allocation concealment, blinding of participants and professionals, and blinding of evaluators (figure 4). Although blinding of participants has been assessed with a high risk of bias, due to the nature of the interventions (EF), blinding of participants is impossible in some studies, a fact that does not affect the quality of the results.

Discussion

After analyzing the 17 studies included in the review, it appears that PE alone or combined with cognitive therapies improves medical, psychological, and cognitive conditions in older people with dementia, with both aerobic, mobility, and resistance exercises being recommended.

Most of the studies were conducted in European and Asian countries, with only one study being conducted in South America and none in the African continent or Central America. The interest in studying diseases related to the aging process in these countries can be justified due to the large population of older people present in the European and Asian continents (Balachandran et al., 2020; WHO, 2017). Furthermore, the study samples were mostly composed of women (65.7%), who are the majority among older adults (He, Goodkind, & Kowal, 2016; WHO, 2017), and who, because they have a longer life expectancy due to greater health care, end up suffering more from aging-related diseases, such as dementia.

The gradual decline in cognitive function is the main symptom of dementia and is associated with loss of memory, attention, reasoning, and the ability to perform daily tasks, negatively affecting the autonomy and independence of individuals (Liu et al., 2019; WHO, 2019; Etnier, Shih & Piepmeier, 2015). A review by Groot et al. (2016) found that interventions with AE are beneficial for cognitive and physical function at any stage of dementia, with AE being able to promote neurobiological alterations that increase angiogenesis, synaptogenesis, and neurotransmitter synthesis in different brain structures and functions involved in cognition (Paillard, 2015; Di Liegro et al., 2019; Firth et al., 2018). Thus, in order to achieve a healthy old age, PE has been encouraged as a strategy to

reduce the loss of physical and cognitive abilities associated with age, with both aerobic and resistance exercises being used for this purpose.

In relation to AE, it was found that when performed in isolation it improves performance in daily tasks (Ho et al., 2020; Liu et al., 2020; Cancela et al., 2016; Stevens, & Killeen, 2006), cognitive function in general (Ho et al., 2020; Cancela et al., 2016; Karssemeijer et al., 2019; LIU et al., 2020; Stevens, & Killeen, 2006), and cognitive aspects (Karssemeijer et al., 2019), in addition to reducing levels of MCP-1 and increasing BDNF (Liu et al., 2020). AE, when used in conjunction with cognitive therapies, promotes neuroplasticity (Styliadis et al., 2015), and improves cognitive function (Swinnen et al., 2021; Styliadis et al., 2015; Okamura et al., 2018; Karssemeijer et al., 2019), attention and concentration (Okamura et al., 2018), and performance of daily activities (Swinnen et al., 2021; Styliadis et al., 2015; Okamura et al., 2018).

It was observed that there is no specific AE protocol for individuals with dementia, with different types of exercise, intensities, durations, and frequencies of training being used in different studies, which can produce different benefits. The study by Liu et al. (2020) subjected older people with dementia to stationary bicycle training at moderate intensity for 30 minutes a day and found improvements in cognitive function, while the study by Cancela et al. (2016) submitted patients to 15 minutes daily and the study by Karssemeijer et al. (2019) presented an intervention of 30 to 50 minutes 3 times a week. Despite the differences between the durations of the sessions, these studies demonstrate that AE was effective in improving cognitive function, alleviating dementia symptoms. It is also noteworthy that the results obtained in the study by Liu et al. (2020) occurred after just four weeks. Other AE modalities used were outdoor walks (Henskens et al 2018), arm ergometer (Okamura et al., 2018), dance therapy (Ho et al., 2020), and exergaming (Karssemeijer et al., 2019; Styliadis et al., 2015).

Although current recommendations for older adults include at least 150-300 minutes of moderate-intensity aerobic physical activity or 75-150 minutes of vigorous-intensity aerobic physical activity per week (WHO, 2010), some researchers believe this recommendation may not be appropriate for individuals with dementia, especially in the most severe stage (Forbes et al., 2015; Liu et al., 2020; Ho et al., 2020). This may justify the results of this review where the majority of studies opted for lower intensities (Ho et al., 2020; Cancela et al, 2016; Stevens, & Killeen, 2006). However, when referring to the literature, it appears that there is no consensus on the best AE intervention protocol for individuals with dementia. This probably occurs due to the different types and etiologies of this disease, which produce different symptoms at different times (Forbes et al., 2015; Karssemeijer et al., 2017).

Few studies have been published evaluating the effects of RE on older people with dementia. The limited number of studies is believed to have occurred because RE tends to improve physical components more than cognitive functions in cases of dementia (Tyndall et al., 2018; Ten Brinke et al., 2015; Liu-Ambrose, & Donaldson, 2009). Liu,6 & Donaldson. (2009) found that RE does not significantly improve cognition among older people with dementia, but can prevent cognitive declines among healthy older adults. According to this study, RE can reduce morbidity, improve sarcopenia, and, consequently, fractures and falls. Other studies suggest that RE decreases frailty (Yoon, Lee, & Song, 2018), balance (Cadore et al., 2014; Yoon et al., 2018), strength (Brown et al., 2015; Cadore et al., 2014; Yoon et al., 2018), and performance of daily activities (Chen et al., 2020; Bossers et al., 2016; Lee, & Don Kim, 2018). Although the physical benefits of RE are a consensus among researchers, some studies have shown that there may be benefits of this practice on cognitive function (Brown et al., 2015; Yoon et al., 2018).

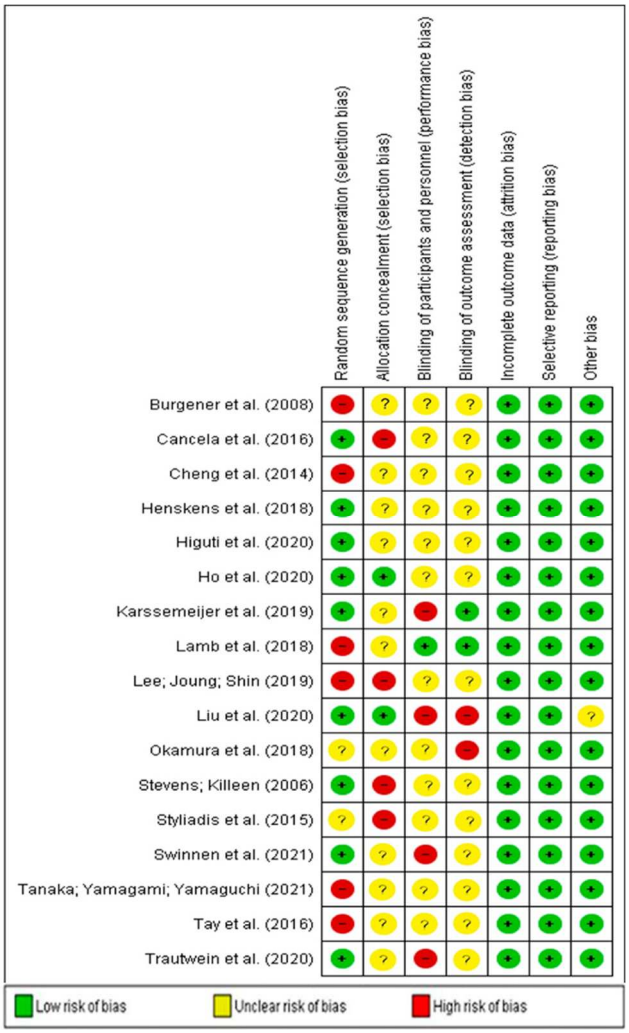

Figure. 4: Risk of bias in the studies analyzed.

Few studies have been published evaluating the effects of RE on older people with dementia. The limited number of studies is believed to have occurred because RE tends to improve physical components more than cognitive functions in cases of dementia (Tyndall et al., 2018; Ten Brinke et al., 2015; Liu-Ambrose, & Donaldson, 2009). Liu,6 & Donaldson. (2009) found that RE does not

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Regarding RE, only one of the studies evaluated its effects in isolation, the study by Liu et al. (2020) compared RE with AE. The RE protocol consisted of exercises for the upper and lower limbs with 40-50% of 1RM. The results showed similar results on physical and cognitive variables between the two practices. Regarding sets and repetitions, the study by Liu et al. (2020) used 2 sets of 12, while Henskens et al. (2018) used 3 sets of 8 repetitions and Lamb et al. (2018) 3 sets of 20 repetitions, so it appears that there is no standardization in the number of sets, repetitions, and intensities.

In addition to the AE and RE, two articles used tai chi as an intervention (Cheng et al., 2014; Burgener et al., 2008) and three used mobility exercises (Higuti et al. 2020; Ho et al. 2020; Lee et al., (2019). Regarding tai chi, despite the interventions having the same weekly frequency (3 times a week) and different durations in the two studies (12 weeks versus 40 weeks, respectively), both found that this practice can alleviate the degenerative effects and symptoms in cases of moderate dementia. Similar studies suggest that in the early stages of the disease, tai chi can delay or slow cognitive degeneration (Anderson, et al., 2017; Lim et al., 2019; Nyman et al., 2019). Cheng et al. (2014) found that although tai chi improves memory components, the results do not differ from Mahjong practice. According to the authors, both practices preserve cognitive functioning and may delay declines from dementia, including depressive symptoms. Burgener et al. (2008) found 20 weeks of tai chi combined with cognitive training were sufficient to alleviate and delay the derogatory effects of dementia, reduce depression, and improve self-esteem, balance, and muscle strength. However, the authors found that from the twentieth week onwards there is stabilization of physical and cognitive symptoms. Even though it is not an expected result, stabilization can represent positive effects, as dementia is characterized by progressive declines in performance. The scientific literature still lacks a consensus on the best intervention protocol for older people with dementia to benefit from the practice of tai chi. In this review, it was found that short interventions can have good results, and tai chi, performed in the short or long term, has a positive impact on physical and cognitive health as well as on social life in patients at any stage of dementia (Yang et al., 2020; Liu et al., 2019).

With regard to mobility, although studies differ in the duration and frequency of the intervention, it was found that this modality, when performed alone, has little or no effect on physical and cognitive performance in older people with dementia. Ho et al. (2020) when comparing the effects of dance therapy and mobility exercises in older people with moderate dementia, observed that two sessions for 12 weeks were sufficient to improve loneliness, depression, mood, and performance of daily tasks in dance therapy practitioners. No positive effect on these variables was observed in the mobility exercises group. Higuti et al. (2020) found that interventions with mobility exercises alone or combined with music therapy, performed once a week for 12 weeks, did not improve cognitive function or functional capacity in patients with moderate and severe dementia. Although there were no gains, there was no loss of these functions during the intervention, suggesting some delay in the degeneration caused by the disease. In the study conducted by Lee et al. (2019), although the authors consider mobility exercises an effective intervention for locomotion and socialization, they did not benefit cognitive function or reduce depressive symptoms in mild cases of the disease.

Although PE, alone or in combination, provides physical and cognitive benefits in older people with dementia, some studies suggest that its practice is unable to prevent the progression of dementia (Trautwein et al., 2020; Hensken et al., 2018; Lamb et al., 2018). Henskens et al. (2018) and Lamb et al. (2018) found that the combination of resistance and aerobic exercises, performed at moderate to high intensities, is able to benefit physical fitness and handgrip strength only in mild and moderate cases of dementia. Neither study found any benefit from this intervention on other physical and cognitive functions, suggesting that this modality of PE does not reduce cognitive decline. Likewise, Trautwein et al. (2020) found that a combined PE program involving stretching, balance, flexibility, and resistance, performed for 16 weeks at moderate intensity, was not sufficient to promote motor or cognitive benefits in elderly people with dementia. Two reviews found results similar to these, verifying that the practice of physical exercise can have null effects on cognition, especially in the severe stage of the disease (Forbes et al., 2015; Groot et al., 2016).

Strengths and Limitations of the Study

Some limitations must be noted. The analysis of intervention protocols was limited due to the lack of data related to the intensity of the PE. In addition, due to the diversity of interventions and the low number of studies, it was not possible to conclude which type of exercise is most efficient for dementia in older adults.

However, this is one of the few studies to address dementia without focusing on Alzheimer's, since most of the research produced analyzes Alzheimer's disease and excludes other types of dementia. Investigating how physical exercise works in dementia in general can help health professionals and families to use physical exercise to

alleviate, delay, and even prevent negative events from this disease, in order to provide better quality of life for patients and their caregivers and close relatives.

Conclusion

The recommendation to incorporate PE as part of the treatment for elderly individuals with dementia is a highly valuable strategy that has been gaining increasing support from scientific evidence. Research in this field has shown promising results, pointing to significant improvements in daily functional capacity and cognitive skills in these patients. This underscores the importance of PE as an essential component of comprehensive care for individuals with dementia. It is crucial to understand that results may vary depending on the stage of the disease and the individual characteristics of each patient. Each person with dementia is unique, and therefore, it is important to tailor therapeutic approaches, including PE, to their specific needs. However, it is worth noting that some studies investigating the effects of PE on dementia patients have methodological limitations that may affect the reliability of their results. This highlights the pressing need for conducting more rigorous research in this area to fully understand how exercise can benefit elderly individuals with dementia and how these benefits can be optimized. Therefore, continuous research and the improvement of therapeutic strategies are essential to address this public health challenge more effectively.

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