

Physical activity: a neglected therapy for dementia

Atividade física: um tratamento negligenciado para demência

Actividad física: un tratamiento descuidado para la demencia

*Natan Feter*¹
*Jayne Feter*²
*Gustavo S. Silva*¹
*Maria Inês Schmidt*²
*Airton José Rombaldi*¹

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Introduction

Dementia is a leading cause of dependence and disability worldwide^{1,2,3}. The number of dementia cases worldwide is projected to increase from 57.4 million in 2019 to 152.8 million by 2050, with a new case of dementia being diagnosed every three seconds^{4,5}. In the last four decades, a great and continuous effort has led to the discovery of different pharmacological treatments to attenuate the symptoms and slow disease progression. For example, aducanumab and lecanemab are monoclonal antibodies directed against aggregated amyloid beta approved by the FDA (U.S. Food and Drug Administration), with findings indicating a reduction in amyloid-beta accumulation and slower cognitive decline through follow-up^{6,7}. However, these treatments are largely unavailable at the population level due to their high estimated annual cost⁸.

A robust body of literature has established an association between physical activity and reduced risk of cognitive decline and dementia^{9,10,11,12,13,14,15}. Consequently, governmental and nongovernmental organizations have advocated the role of physical activity in mitigating the risk of dementia¹⁶. For example, the World Health Organization's (WHO) global action plan on dementia² recommends a minimum of 150 minutes of physical activity per week to prevent dementia. Similarly, national dementia plans, which are designed to reduce the current and projected burden of dementia in each country, endorse the role of physical activity as an essential preventive strategy. However, few studies have addressed the extent to which physical activity is recommended as a complementary treatment for dementia.

Exercise as a prescription for people with dementia

Physical activity is a safe and effective nonpharmacological strategy to preserve cognition and functionality in people with intact cognitive function, mild cognitive impairment, and dementia^{9,17,18}. In a rapid search on PubMed combining dementia, physical activity or exercise, and meta-analysis keywords, a total of 278 records were identified in November 2023. By searching only meta-analysis with randomized controlled trials (RCTs) employing physical activity protocols in people with dementia, 12 studies were found^{19,20,21,22,23,24,25,26,27,28,29,30}. Also, three umbrella reviews of meta-analyses

¹ Escola Superior de Educação Física, Universidade Federal de Pelotas, Pelotas, Brasil.
² Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brasil.

Correspondence

N. Feter
Escola Superior de Educação Física, Universidade Federal de Pelotas.
Rua Luís de Camões 625, Pelotas, RS 96055-630, Brasil.
natanfeter@hotmail.com



revealed that exercise could improve cognitive function in people with dementia ^{9,31,32}, with an effect size (ES) similar to that found by pharmacological studies (physical activity: standardized mean differences – SMD = 0.41, 95% confidence interval – 95%CI: 0.24-0.58; pharmacological studies: SMD ≤ 0.51, 95%CI: 0.35-0.67) ^{9,33}. The umbrella reviews acknowledged some limitations in the current evidence restricting our knowledge of the most effective exercise characteristics to improve physical and mental symptoms in people with dementia. However, there is sufficient evidence to state that older adults with dementia benefit from physical activity ²⁸.

A network meta-analysis showed that aerobic, resistance, and mind-body exercises could improve cognitive function in people with mild cognitive impairment and dementia ²⁶. The authors also showed that resistance training was the most effective intervention for people with dementia compared to aerobic, multicomponent, and mind-body exercises ²⁶. Moreover, another meta-analysis showed that home-based physical exercise could improve cognitive function (ES = 0.71; 95%CI: 0.43-0.99) and functional capacity (ES = 2.24; 95%CI: 1.80-2.68) and reduce neuropsychiatric symptoms (ES = 0.37; 95%CI: 0.17-0.57) and caregivers' burden (ES = 0.63; 95%CI: 0.32-0.94) ³⁰. Finally, a systematic review with meta-analysis showed that aerobic (SMD = 0.24) and resistance (SMD = 0.18) training could improve physical function in older adults in residential care ³⁴. Moreover, a moderate-to-high effect was observed in studies including older adults with cognitive impairment (SMD = 0.44), with dependence in activities of daily living (SMD = 0.40), and in older adults with pre-frailty or frailty (SMD = 0.65) ³⁴.

Although evidence supports the benefits of exercise for people with dementia, it is essential to acknowledge specific gaps in our understanding. For example, the significant heterogeneity observed in meta-analyses concerning exercise interventions and sample characteristics limits our knowledge regarding the most effective exercise program in intensity, frequency, and type. A recent meta-analysis suggested two to three weekly sessions of multi-component and aerobic training, each session lasting 60 minutes, to improve cognitive and physical capacity in people with dementia ³⁵.

Additionally, most RCTs have been conducted in high-income countries, requiring further studies in cognitively diverse populations to better comprehend the impact of exercise on cognitive function. Given the heterogeneity of disease stages observed across meta-analyses on exercise in people with dementia, exploring the effects of exercise for each stage of the disease may enhance our understanding.

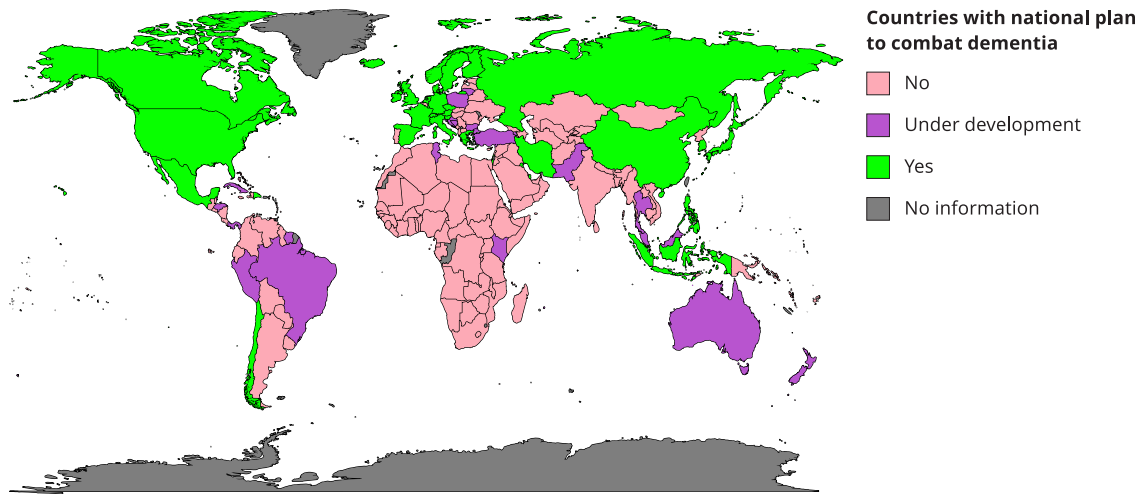
Considering the evidence, governments are expected to promote physical activity as a complementary therapy for people with dementia via public health initiatives, including a national plan to combat dementia. Instead of generic recommendations, national plans to combat dementia can address dementia-related issues, respecting each country's culture and sociodemographic characteristics.

We reviewed national plans to combat dementia worldwide to identify the presence of initiatives to promote physical activity for people with dementia. After retrieving the national plans, we systematically searched for any mention of physical activity as a nonpharmacological and complementary therapy for people with dementia. To keep focus on national plans that promote physical activity for people with dementia, we did not include documents in which physical activity was only mentioned as a preventive strategy. For national plans published in languages other than English, Spanish, or Portuguese, online tools were used to identify the most appropriate terms for physical activity, exercise, and walking.

From 194 countries, we identified 35 (18%) with national dementia plans: 20 (57.1%) in Europe, 10 (28.6%) in Asia, three (8.6%) in North America, and two (5.7%) in South America and the Caribbean (Figure 1). Only the following eight (22.9%) countries, all high-income countries, recommended physical activity for people with dementia: Chile, Denmark, France, Luxembourg, Norway, Singapore, Sweden, and the United States. For example, the Chilean plan reinforces the pivotal role of physical activity in preventing and managing disease ³⁶. The Norwegian document ³⁷ also highlights the importance of good architecture and planning to stimulate physical activity. Also, starting in January 2020, cities should offer activities for people with dementia living at home, including physical activity, as part of an inclusion strategy that contributes to mastery, meaningfulness, and good experience for these individuals ³⁷. The Singaporean dementia plan promoted the Peer-to-Peer Support Group, where Zoom videoconferences with music, social engagement, health education, and exercise were offered to minimize the harmful consequences of social distancing restrictions on health ³⁸.

Figure 1

Countries with national plan to combat dementia.



Source: data was collected from the World Health Organization ³⁹ and the Alzheimer's Disease International ⁴⁰.

Generally, the literature indicates that physical activity is a safe and effective complementary therapy for people living with dementia. In contrast, only 35 high-income countries designed national dementia plans that recommend physical activity for this population. This finding mirrors the small number of RCTs with physical activity in people with dementia in low- and middle-income countries and those with varying cognitive reserves. We do not intend to imply that exercise or any form of physical activity can replace traditional and innovative therapeutic methods for dementia. Instead, we emphasize the importance of promoting physical activity for this population. Older individuals with mild cognitive impairment and dementia often bear multiple comorbidities, such as cardiovascular disease and diabetes. Therefore, prescribing physical activity as a therapeutic intervention can target various therapeutic goals while minimizing side effects, and it can be tailored to individual preferences, akin to pharmacotherapy.

Contributors

N. Feter contributed with the study conceptualization, data analysis, and writing; and approved the final version. J. Feter contributed with the study conceptualization, writing, and review; and approved the final version. G. S. Silva contributed with the study conceptualization, writing, and review; and approved the final version. M. I. Schmidt contributed with the writing and review; and approved the final version. A. J. Rombaldi contributed with the study conceptualization, writing, and review; and approved the final version.

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Additional information

ORCID: Natan Feter (0000-0001-6295-9792); Jayne Feter (0000-0002-4612-7301); Gustavo S. Silva (0009-0006-9380-8982); Maria Inês Schmidt (0000-0002-3837-0731); Airton José Rombaldi (0000-0002-6707-814X).

References

- Nichols E, Szeoke CEI, Vollset SE, Abbasi N, Abd-Allah F, Abdela J, et al. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019; 18:88-106.
- World Health Organization. Global action plan on the public health response to dementia 2017-2025. <https://www.who.int/publications/i/item/global-action-plan-on-the-public-health-response-to-dementia-2017---2025> (accessed on 09/Jun/2024).
- World Health Organization. Dementia: a public health priority. <https://apps.who.int/iris/handle/10665/75263> (accessed on 09/Jun/2024).
- Global Burden of Diseases. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. *Lancet Public Health* 2022; 7:e105-25.
- Wortmann M. Dementia: a global health priority-highlights from an ADI and World Health Organization report. *Alzheimers Res Ther* 2012; 4:40.
- Budd Haerberlein S, Aisen PS, Barkhof F, Chalkias S, Chen T, Cohen S, et al. Two randomized phase 3 studies of aducanumab in early Alzheimer's disease. *J Prev Alzheimers Dis* 2022; 9:197-210.
- van Dyck CH, Swanson CJ, Aisen P, Bateman RJ, Chen C, Gee M, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med* 2022; 388:9-21.
- Sinha P, Barocas JA. Cost-effectiveness of aducanumab to prevent Alzheimer's disease progression at current list price. *Alzheimers Dementia (N Y)* 2022; 8:e12256.
- López-Ortiz S, Lista S, Valenzuela PL, Pinto-Fraga J, Carmona R, Caraci F, et al. Effects of physical activity and exercise interventions on Alzheimer's disease: an umbrella review of existing meta-analyses. *J Neurol* 2023; 270:711-25.
- Blondell SJ, Hammersley-Mather R, Veerman JL. Does physical activity prevent cognitive decline and dementia? A systematic review and meta-analysis of longitudinal studies. *BMC Public Health* 2014; 14:510.
- Guure CB, Ibrahim NA, Adam MB, Said SM. Impact of physical activity on cognitive decline, dementia, and its subtypes: meta-analysis of prospective studies. *Biomed Res Int* 2017; 2017:9016924.
- Yin S, Nie H, Xu Y. Physical activity and dementia: a meta-analysis of prospective studies. *J Chem Pharm Res* 2013; 5:235-9.

13. Lee J. The relationship between physical activity and dementia: a systematic review and meta-analysis of prospective cohort studies. *J Gerontol Nurs* 2018; 44:22-9.
14. Xu W, Wang HF, Wan Y, Tan C-C, Yu J-T, Tan L. Leisure time physical activity and dementia risk: a dose-response meta-analysis of prospective studies. *BMJ Open* 2017; 7:e014706.
15. Iso-Markku P, Kujala UM, Knittle K, Polet J, Vuoksima E, Waller K. Physical activity as a protective factor for dementia and Alzheimer's disease: systematic review, meta-analysis and quality assessment of cohort and case-control studies. *Br J Sports Med* 2022; 56:701-9.
16. Chen Y, Hou L, Li Y, Lou Y, Li W, Struble LM, et al. Barriers and motivators to promotion of physical activity participation for older adults with mild cognitive impairment or dementia: an umbrella review. *Int J Nurs Stud* 2023; 143:104493.
17. Hillman CH, Erickson KI, Kramer AF. Be smart, exercise your heart: exercise effects on brain and cognition. *Nat Rev Neurosci* 2008; 9:58-65.
18. Erickson KI, Hillman C, Stillman CM, Ballard RM, Bloodgood B, Conroy DE, et al. Physical activity, cognition, and brain outcomes: a review of the 2018 physical activity guidelines. *Med Sci Sports Exerc* 2019; 51:1242-51.
19. Livingston G, Kelly L, Lewis-Holmes E, Baio G, Morris S, Patel N, et al. A systematic review of the clinical effectiveness and cost-effectiveness of sensory, psychological and behavioural interventions for managing agitation in older adults with dementia. *Health Technol Assess* 2014; 18:1.
20. Zhang S, Zhen K, Su Q, Chen Y, Lv Y, Yu L. The effect of aerobic exercise on cognitive function in people with Alzheimer's disease: a systematic review and meta-analysis of randomized controlled trials. *Int J Environ Res Public Health* 2022; 19:15700.
21. Karamacoska D, Butt A, Leung IHK, Childs RL, Metri NJ, Uruthiran V, et al. Brain function effects of exercise interventions for cognitive decline: a systematic review and meta-analysis. *Front Neurosci* 2023; 17:1127065.
22. Sun Y, Ji M, Leng M, Li X, Zhang X, Wang Z. Comparative efficacy of 11 non-pharmacological interventions on depression, anxiety, quality of life, and caregiver burden for informal caregivers of people with dementia: a systematic review and network meta-analysis. *Int J Nurs Stud* 2022; 129:104204.
23. Santiago JA, Potashkin JA. Physical activity and lifestyle modifications in the treatment of neurodegenerative diseases. *Front Aging Neurosci* 2023; 15:1185671.
24. Luo G, Zhang J, Song Z, Wang Y, Wang X, Qu H, et al. Effectiveness of non-pharmacological therapies on cognitive function in patients with dementia – a network meta-analysis of randomized controlled trials. *Front Aging Neurosci* 2023; 15:1131744.
25. Kouloutbani K, Venetsanou F, Karteroliotis KE, Politis A. Physical exercise as a nonpharmacological intervention for the treatment of neuropsychiatric symptoms in persons with dementia: a meta-analysis of randomized controlled trials. *Alzheimer Dis Assoc Disord* 2023; 37:73-81.
26. Huang X, Zhao X, Li B, Cai Y, Zhang S, Wan Q, et al. Comparative efficacy of various exercise interventions on cognitive function in patients with mild cognitive impairment or dementia: a systematic review and network meta-analysis. *J Sport Health Sci* 2022; 11:212-23.
27. Ding Z, Leung PY, Lee T-L, Chan AS. Effectiveness of lifestyle medicine on cognitive functions in mild cognitive impairments and dementia: a systematic review on randomized controlled trials. *Ageing Res Rev* 2023; 86:101886.
28. Zeng Y, Wang J, Cai X, Zhang X, Zhang J, Peng M, et al. Effects of physical activity interventions on executive function in older adults with dementia: a meta-analysis of randomized controlled trials. *Geriatr Nurs (Minneapolis)* 2023; 51:369-77.
29. Yan J, Li X, Guo X, Lin Y, Wang S, Cao Y, et al. Effect of multicomponent exercise on cognition, physical function and activities of daily life in older adults with dementia or mild cognitive impairment: a systematic review and meta-analysis. *Arch Phys Med Rehabil* 2023; 104:2092-108.
30. de Almeida SIL, Gomes da Silva M, Marques ASPD. Home-based physical activity programs for people with dementia: systematic review and meta-analysis. *Gerontologist* 2020; 60:e600-8.
31. Andrade A, Siqueira TC, D'Oliveira A, Dominiski FH. Effects of exercise in the treatment of Alzheimer's disease: an umbrella review of systematic reviews and meta-analyses. *J Aging Phys Act* 2021; 30:535-51.
32. Demurtas J, Schoene D, Torbahn G, Marengoni A, Grande G, Zou L, et al. Physical activity and exercise in mild cognitive impairment and dementia: an umbrella review of intervention and observational studies. *J Am Med Dir Assoc* 2020; 21:1415-22.e6.
33. Dou KX, Tan MS, Tan CC, Cao XP, Hou XH, Guo QH, et al. Comparative safety and effectiveness of cholinesterase inhibitors and memantine for Alzheimer's disease: a network meta-analysis of 41 randomized controlled trials. *Alzheimers Res Ther* 2018; 10:126.
34. Valenzuela PL, Saco-Ledo G, Morales JS, Gallardo-Gómez D, Morales-Palomo F, López-Ortiz S, et al. Effects of physical exercise on physical function in older adults in residential care: a systematic review and network meta-analysis of randomised controlled trials. *Lancet Healthy Longev* 2023; 4:e247-56.

35. Li Z, Guo H, Liu X. What exercise strategies are best for people with cognitive impairment and dementia? A systematic review and meta-analysis. *Arch Gerontol Geriatr* 2024; 124:105450.
36. Ministerio de Salud. Plan Nacional de Demencia. <https://www.minsal.cl/wp-content/uploads/2017/11/PLAN-DE-DEMENCIA.pdf> (accessed on 25/Jun/2023).
37. Norwegian Ministry of Health and Care Services. Dementia Plan 2025. <https://www.regjeringen.no/contentassets/b3ab825ce67f4d73bd24010e1fc05260/dementia-plan-2025.pdf> (accessed on 25/Jun/2023).
38. Dementia Colabs. Towards a dementia-inclusive Singapore. <https://www.aic.sg/resources/Documents/Brochures/Mental%20Health/Dementia%20Colabs%20Report.pdf> (accessed on 26/Jun/2023).
39. World Health Organization. Global Health Observatory. <https://www.who.int/data/gho> (accessed on 09/Jun/2024).
40. Alzheimer's Disease International. Dementia plans. <https://www.alzint.org/what-we-do/policy/dementia-plans/> (accessed on 09/Jun/2024).

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