BMJ Open

Impact of type, intensity, frequency, duration and volume of physical activity on dementia and mild cognitive impairment in older adults: protocol for a systematic review and meta-analysis

Ana Lúcia Junger [iD] ,[1,2] Amanda Maria de Sousa Romeiro,[1] Matias Noll,[1,2] Cesar de Oliveira,[3] Erika Aparecida Silveira [iD] [1,3]

[1]Postgraduate Program in Health Sciences, Faculty of Medicine, Federal University of Goiás, Goiania, Brazil
[2]Public Health, Instituto Federal Goiano, Ceres, Brazil
[3]Department of Epidemiology & Public Health, University College London, London, UK

Correspondence to
Dr Cesar de Oliveira;
c.oliveira@ucl.ac.uk,
Dr Matias Noll;
matias.noll@ifgoiano.edu.br and
Dr Erika Aparecida Silveira;
erikasil@terra.com.br

ABSTRACT

Introduction Worldwide, the prevalence of degenerative diseases such as dementia and mild cognitive impairment (MCI) is increasing with population ageing and increasing life expectancy. Both conditions share modifiable risk factors. Physical inactivity is one of these modifiable risk factors, and research points to the protective effect of physical activity on the incidence of dementia and MCI. However, this association tends to change according to type, intensity, frequency, duration and volume of physical activity. Furthermore, it remains unclear which of these characteristics offers the greatest protective effect. Therefore, this study aims to evaluate the impacts of different types, intensities, frequencies, duration and volume of physical activity on dementia and cognitive decline in older adults.

Methods and analysis The search will be carried out from October 2023, using the following databases: PubMed, Embase, Scopus, CINAHL and Web of Science. Cohort studies with a follow-up time of 1 year or longer that have investigated the incidence of dementia and/ or MCI in older adults exposed to physical activity will be included. There will be no limitations on the date of publication of the studies. Studies published in English, Spanish or Portuguese will be analysed. Two researchers will independently screen the articles and extract the data. Any discrepancies will be resolved by a third reviewer. Association measures will be quantified, including OR, HR, relative risk and incidence ratio, with a 95% CI. If the data allow, a meta-analysis will be performed. To assess the methodological quality of the selected studies, the Grading of Recommendations, Assessment, Development and Evaluations instrument, and the Downs and Black instrument to assess the risk of bias, will be used.

Ethics and dissemination Ethical approval is not required. The results will be submitted for publication in a peer-reviewed journal.

PROSPERO registration number CRD42023400411.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This systematic review will highlight the characteristics of physical activity that could be protective or risk factors for cognitive dysfunction.
⇒ The review will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations, and the article selection and data extraction will be carried out by independent investigators, ensuring critical appraisal of the studies and data extraction.
⇒ The data presented in the included studies may show high variability and heterogeneity in the sensitivity and specificity of the different measurement tools, so the results may need to be interpreted with caution.
⇒ The evidence base may be limited, particularly from some parts of the world, given the costs involved in conducting cohort studies.

INTRODUCTION

The increased life expectancy worldwide is accompanied by a worrying fact, that is, an increase in the prevalence of neurodegenerative disorders. Globally, the older age group (aged 60 years and over) comprised 13% of the world's population in 2017. This population is growing at a rate of 3% per year, and projections suggest that it will double by 2050. The phenomenon of population ageing is currently observed in both developed and developing countries.[1] This increase in life expectancy may result in a greater risk of most chronic diseases,[2] such as mild cognitive impairment (MCI) and dementia.[3]

MCI is the clinical state in which the individual has impaired cognition, but their activities of daily living have not been impacted. People with worsening MCI can progress to dementia. These conditions result in deficiencies in social and cognitive abilities, hindering the execution of tasks and reducing the independence and autonomy of older people.[4] Dementia is a growing concern worldwide,

with the number of diagnosed cases increasing exponentially over the last 30 years. In 1990, there were 20.2 million cases, but in 2022, this number rose to 55 million. Experts predict that by 2050, there will be a staggering 152 million cases worldwide.[5 6] Sadly, mortality rates associated with dementia have also increased by 100% in older adults between 1990 and 2019, making it the fourth leading cause of death in people aged 70 years or older.[3] This highlights the significance of dementia as a public health issue, especially in later life.

It has been estimated that almost half of the global cases of dementia can be attributed to risk factors that can be modified.[7] These risk factors include low education level, hypertension, obesity, diabetes, smoking, excessive alcohol consumption, physical inactivity, depression, low social contact, hearing loss, traumatic brain injuries and air pollution. It is important to note that physical activity and an active lifestyle can significantly improve cognitive function by regulating neurotoxic and neurotrophic factors, increasing blood flow to the brain and reducing inflammatory markers such as the brain-derived neurotrophic factor (BDNF).[8] BDNF plays a crucial role in various aspects of adult brain development and plasticity, which include neuronal proliferation, differentiation, survival, neurogenesis, synaptic plasticity and cognitive function. It also helps in preventing or managing chronic diseases like hypertension, diabetes and depression.[9] When it comes to healthy ageing, physical activity is one of the most significant modifiable risk factors.

With regard to systematic reviews and meta-analyses of observational studies on the association between physical activity and the incidence of dementia in older adults, seven studies have been published.[10–16] In one study, physical inactivity was not associated with dementia,[11] while in the others, physical activity had a protective effect.[10 12 13 15 16] Out of the studies analysed, five did not assess the type of physical activity.[10 11 13 14 16] Three studies did not assess the intensity of physical activity[10 13 14] and three did not assess its quantity in terms of volume, duration or frequency.[10 11 13] One study did not assess the affected cognitive functions,[13] while two studies only examined the incidence of dementia.[12 16]

Studies have revealed that physical activity can help protect against dementia and cognitive decline in old age. However, the extent of this effect varies depending on the duration or age of the study population. Additionally, there is no agreement on the optimal level of physical activity that can minimise the risk of MCI and dementia. It is important to note that currently, there has been no investigation into the specific type of physical activity that offers the greatest protection against the incidence of MCI and dementia. It is crucial to conduct further research to determine the characteristics (type, intensity, frequency, duration and volume) of physical activity that have a greater protective effect on the incidence of dementia and MCI. It is also important to identify which cognitive domains are most impacted by these activities

and whether variables such as sex and age can modify this association.

Given the controversial evidence and gaps found in observational studies and literature reviews, we propose this systematic review and potential meta-analysis. It is important to gather conclusive findings that will help to clarify the association between physical activity and its characteristics with the incidence of dementia and cognitive decline in older adults from different age groups since these variables can significantly alter this association. Therefore, the present study intends to describe a systematic review protocol that aims primarily to assess the risk of dementia and MCI in older adults who practise physical activity according to the type, intensity, frequency, duration and volume, and to analyse possible interference caused by factors such as age and gender. Secondarily, in case this information is available in the included articles, our study also aims to measure the impacts of physical activities on the cognitive domains: memory, attention, spatial–temporal and visuospatial orientation, verbal command, reading and praxis.

METHODS AND ANALYSIS
Protocol and registration

This systematic review will be reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol criteria.[17] This protocol was written using scientific writing methods[18] to improve the technical quality of the article.

We will adopt the PECO structure[19] defined as follows: population (P), consisting of older adults of both sexes without a diagnosis of dementia or presence of symptoms of cognitive decline at baseline; exposure (E), individuals who practise physical activity; control (C), individuals who do not practise physical activity; outcome (O), occurrence of dementia or symptoms of cognitive decline.

The present study intends to investigate, as a primary outcome condition, the occurrence of dementia or symptoms of cognitive decline in older adults who practise physical activity. As an additional outcome, we intend to analyse the particularities observed by exposure to different types, intensities, frequencies, duration and volume of physical activities.

The current study protocol is registered in the International Prospective Register of Systematic Reviews (PROSPERO) under code CRD42023400411. Any modifications made to this protocol during the study will be reported in PROSPERO and the final manuscript.

Dementia

Dementia is a progressive syndrome characterised by a significant decline in at least one of the cognitive domains, including executive function, complex attention, language, learning, memory, perceptual–motor and social cognition, interfering with the individual's autonomy and activities of daily living. The diagnostic criteria are derived from a meticulous medical history

and physical examination, biomarker analysis, as well as assessments of cognitive and motor functions.[20 21] The most common types of dementia are Alzheimer's disease and vascular dementia.[22]

Mild cognitive impairment

MCI is a transitional stage between normal cognitive decline associated with ageing and dementia.[23] People with MCI experience more severe cognitive deficits than those typically observed in the natural ageing process. They show objective and subjective memory impairment that is inconsistent with their age, but their global cognitive functioning and performance in cognitive domains remain normal.[24] The diagnosis of MCI can be confirmed through clinical diagnosis or specific tests for cognitive decline.

Physical activity

Physical activity is defined as the movement of skeletal muscles, resulting in energy expenditure that exceeds that of the resting state.[10] The intensity can be considered according to the energy expenditure of a given activity and the energy expenditure can be measured in kilocalories.[25 26] Physical activity in daily life can be categorised into occupational, sporting, conditioning, household and other activities.[25] The WHO recommends that older adults should engage in at least 150–300 min per week of moderate aerobic exercise or 75–150 min of vigorous aerobic exercise. Additionally, they should perform muscle-strengthening exercises of moderate or greater intensity that involve all major muscle groups on 2 or more days per week, as these provide additional health benefits. It is also recommended performing varied physical activities that emphasise functional balance and strength training of moderate or greater intensity on 3 or more days a week to increase functional capacity and prevent falls.[27]

Search strategy

The research is scheduled in October 2023, in the following databases: PubMed (National Library of Medicine, USA), Embase, Scopus and Web of Science. The terms will be searched in a standardised manner in the three databases according to the combinations shown in box 1. In the case of the PubMed database, Medical Subject Headings terms will also be used to cover the search for more results. The complete search strategy results used in all databases can be seen in the online supplemental material and will be complemented by manual searches of the reference list of the included studies and previously published systematic reviews.

Selection of studies

For our study, we will only consider (1) prospective cohort studies; (2) articles published in English, Spanish or Portuguese; (3) studies conducted with community-dwelling older adults aged 60 years or above who have been exposed to physical activity; (4) studies with a follow-up time longer than 1 year; (5) studies with clear

---

> **Box 1 Terms that will be used for the main search strategy of the systematic review**
>
> ⇒ #1 Exercise OR Gymnastics OR "Resistance Training" OR Walking OR "Physical Fitness" OR "Sedentary Behavior" OR "Physical Activity" OR "Physical Exercise" OR "Training"
> ⇒ #2 Aged OR "Age groups" OR Aging OR Elderly OR Ageing OR "Old adult" OR "Older adult" OR "Older adults" OR Geriatric
> ⇒ #3 dementia OR "dementia, vascular" OR "frontotemporal dementia" OR "Alzheimer disease" OR "neurocognitive disorders" OR "cognition disorders" OR "cognitive dysfunction" OR "Lewy body disease"
> ⇒ #4 "Cohort Studies" OR "Follow-Up Studies" OR "Longitudinal Studies" OR "Prospective Studies" OR "Observational Studies"
> ⇒ #5 = #1 AND #2 AND #3 AND #4

definitions and measurement of dementia and MCI; (6) studies that present data on type, intensity, volume, duration or frequency of physical activity at baseline; (7) studies that analyse the association between physical activity and dementia or MCI; and (8) studies that include a population without a diagnosis of dementia or MCI at baseline.

The following will be excluded: (1) articles that do not include prospective cohort studies; (2) experimental studies; (3) articles without criteria for evaluating dementia or MCI; (4) articles with no data on physical activity (type, intensity, volume, duration or frequency) at baseline; and (5) publications such as commentaries, letters to the editor, protocols and opinion articles. There will be no limitations on the date of publication of the studies.

Reviewer training

The authors in charge of the eligibility and selection stages of the articles (ALJ and AMdSR) will undergo training to apply the inclusion and exclusion criteria and test their skills in the first 100 articles. The authors will also receive training in the application of the instruments to assess the risk of bias. The selection steps will be performed using EndNote and Rayyan software.[28–32]

Review process

After the search strategy, duplicate articles will be deleted using EndNote software. Two reviewers (ALJ and AMdSR) will independently remove articles that do not match the inclusion criteria based on titles and abstracts read using the Rayyan software. Disagreements on the inclusion of manuscripts will be resolved by a third reviewer (EAS). The remaining articles will be read in full and evaluated to determine their eligibility for this systematic review. In addition, article reference lists will be checked to identify additional studies missed by the database searches. Eligible articles will be included and relevant data according to our objectives will be extracted. Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol statement, we have included a flow chart of the process of identification, selection,

Table 1 Data extraction template

Author/country/year	Population		Follow-up time	Incidence of dementia and MCI	Diagnostic criteria (dementia, MCI)	Cognitive domains	PA measurements (type, frequency, intensity, volume and duration)	Association measure	Variables of adjustment
	Age, sample size sex	Ethnic groups and level of education							

MCI, mild cognitive impairment; PA, physical activity.

data extraction and analysis in the online supplemental material.

Data extraction

Data will be extracted from the documents included in the review by two independent reviewers (ALJ and AMdSR). To extract data from the articles, a standardised form prepared by the authors will be used. The following aspects will be considered: author, year, country, study population (age group, sample size, sex, ethnic groups and level of education), follow-up time, incidence and diagnostic criteria for dementia and MCI, cognitive domains, measures of physical activity (type, frequency, intensity, volume and duration), association (relative risk, OR or HR) and variables of adjustment. Refer to the data extraction shown in table 1.

The differences between reviewers during the screening of studies will be resolved by a senior reviewer (EAS). The authors of the articles will be contacted to request missing or additional data when necessary.

Quality assessment and risk of bias

To determine the quality of the evidence presented by the articles included in the study, we will be using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE)[33] system online. Each article will be classified according to the preferred method into one of the following four levels: high, moderate, low and very low.[34] GRADE-pro GDT software will be used.

The risk of bias in the included articles will be estimated using the Downs and Black instrument,[35] which consists of a score that aims to assess the methodological quality and is specially designed to contemplate randomised and non-randomised studies and presents 27 scoring items. A summary quality score (0–27 points) will be calculated for each manuscript, and the number of conforming items will be expressed as a total percentage. A score >70% will be used to define a low risk of bias.

For articles with missing data, an attempt will be made to talk to the author to make the unpublished data available. The heterogeneity of included articles will be assessed using the I² statistic with cut-offs of low (25%), moderate (50%) and high (75%). Results of meta-analyses for outcomes will be summarised using forest plots showing the estimated summary effects of physical activity and MCI/dementia. Egger's asymmetry regression test will be used to assess publication bias.

Evidence synthesis and statistical analyses

If the data extracted from different studies are homogeneous, they will be combined in a meta-analysis. The association between physical activity and research outcomes will be analysed according to what the studies report: HR and relative risk.

Subgroup analysis will be performed using different types, volume, intensities, duration and frequencies of physical activity. If the data are sufficient, we intend to analyse the subgroups as well as the demographic data of

the participants, that is, sex and age group, stratified by ethnic group and level of education.

Patient and public involvement

None.

ETHICS AND DISSEMINATION

Ethical approval is not required. The results will be submitted for publication in a peer-reviewed journal.

DISCUSSION

As there is no cure, the most effective approach to managing MCI and dementia is prevention through lifestyle changes. Physical activity is a recommended healthy habit by specialists as it improves flexibility, strength, balance and endurance, which can delay motor degeneration caused by various types of dementia. However, no valid inferences have been found to support the potential protective effects of these measures.[34] Therefore, it is vital to conduct a comprehensive review that covers various aspects of physical activity associated with MCI and dementia.

To date, observational studies that have investigated the association between physical activity and the risk of dementia or MCI in older adults have found inconsistent results. Furthermore, studies with a longer follow-up period tend not to observe a significant association between physical activity and the incidence of dementia in older adults, while shorter-term cohorts point to the protective action of physical activity for dementia, depending on the type and/or intensity of the activity and the age group of the older adults.[36–40]

This review aims to examine the primary protective factors of physical activity for the elderly population with MCI or dementia. Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidance will be used to ensure that the results are reported appropriately and objectively, despite the possible heterogeneity and variability of the data resulting from different methods of variable measurement in different studies. Cohort studies will be included to observe these factors' effects over time. However, the evidence base may be limited, particularly from some parts of the world, given the costs involved in conducting cohort studies.

Investigating the physical activity profile that would have the greatest protective effect against dementia and MCI is of paramount importance for science, public health policy and society. Dementia is a syndrome with several modifiable risk factors, and there is an urgent need for protocols and measures capable of reducing its incidence or even postponing its onset, and, ultimately, mitigating its impacts on the economy, public health and individuals' lives.

ORCID iDs
Ana Lúcia Junger http://orcid.org/0000-0002-1526-7440
Erika Aparecida Silveira http://orcid.org/0000-0002-8839-4520

REFERENCES

1 United Nations Departament of Economic and Social Affairs, Population Divisions. World population ageing 2020 highlights: living arrangements of older persons; 2020.
2 Rodrigues LP, de Oliveira Rezende AT, Delpino FM, *et al*. Association between multimorbidity and hospitalization in older adults: systematic review and meta-analysis. *Age Ageing* 2022;51.
3 GBD 2019 Collaborators. Global mortality from dementia: application of a new method and results from the global burden of disease study 2019. *Alzheimers Dement (N Y)* 2021;7.
4 Kelley BJ, Petersen RC. Alzheimer's disease and mild cognitive impairment. *Neurol Clin* 2007;25:577–609.
5 WHO. Dementia. 2022. Available: https://www.who.int/news-room/fact-sheets/detail/dementia
6 Lisko I, Kulmala J, Annetorp M, *et al*. How can dementia and disability be prevented in older adults: where are we today and where are we going? *J Intern Med* 2021;289:807–30.
7 Huang T, Larsen KT, Ried-Larsen M, *et al*. The effects of physical activity and exercise on brain-derived neurotrophic factor in healthy humans: a review. *Scand J Med Sci Sports* 2014;24:1–10.
8 Silveira EA, Mendonça CR, Delpino FM, *et al*. Sedentary behavior, physical inactivity, abdominal obesity and obesity in adults and older adults: a systematic review and meta-analysis. *Clin Nutr ESPEN* 2022;50:63–73.
9 Izquierdo M, Merchant RA, Morley JE, *et al*. International exercise recommendations in older adults (ICFSR): expert consensus guidelines. *J Nutr Health Aging* 2021;25:824–53.
10 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.
11 Kivimäki M, Singh-Manoux A, Pentti J, *et al*. Physical inactivity, cardiometabolic disease, and risk of dementia: an individual-participant meta-analysis. *BMJ* 2019;365:l1495.
12 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.

13 Sofi F, Valecchi D, Bacci D, *et al*. Physical activity and risk of cognitive decline: a meta-analysis of prospective studies: physical activity and risk of cognitive decline. *J Intern Med* 2011:107–17.

14 Hamer M, Chida Y. Physical activity and risk of neurodegenerative disease: a systematic review of prospective evidence. *Psychol Med* 2009;39:3–11.

15 Lü J, Fu W, Liu Y. Physical activity and cognitive function among older adults in China: a systematic review. *J Sport Health Sci* 2016;5:287–96.

16 Iso-Markku P, Kujala UM, Knittle K, *et al*. 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.

17 Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:71.

18 Aparecida Silveira E, Maria de Sousa Romeiro A, Noll M. Guide for scientific writing: how to avoid common mistakes in a scientific article. *Jhgd* 2022;32:341–52.

19 Morgan RL, Whaley P, Thayer KA, *et al*. Identifying the PECO: a framework for formulating good questions to explore the association of environmental and other exposures with health outcomes. *Environ Int* 2018;121:1027–31.

20 Gale SA, Acar D, Daffner KR. Dementia. *Am J Med* 2018;131:1161–9.

21 Emmady PD, Schoo C, Disorder TP. *Major Neurocognitive disorder (dementia)*. Treasure Island (FL): StatPearls Publishing, 2023. Available: http://www.ncbi.nlm.nih.gov/books/NBK557444/

22 Miller DI, Taler V, Davidson PSR, *et al*. Measuring the impact of exercise on cognitive aging: methodological issues. *Neurobiol Aging* 2012;33:622.

23 Jia L, Du Y, Chu L, *et al*. Prevalence, risk factors, and management of dementia and mild cognitive impairment in adults aged 60 years or older in China: a cross-sectional study. *Lancet Public Health* 2020;5:e661–71.

24 McCleery J, Abraham RP, Denton DA, *et al*. Vitamin and mineral supplementation for preventing dementia or delaying cognitive decline in people with mild cognitive impairment. *Cochrane Database Syst Rev* 2018;11.

25 Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* 1985;100:126–31.

26 Marques R da S, Rezende A de O, Junger AL, *et al*. What is the relationship between physical activity and chronic pain in older adults? A systematic review and meta-analysis protocol. *BMJ Open* 2022;12:e062566.

27 WHO. Guidelines on physical activity and sedentary behaviour; 2020.

28 Noll M, Wedderkopp N, Mendonça CR, *et al*. Motor performance and back pain in children and adolescents: a systematic review and meta-analysis protocol. *Syst Rev* 2020;9:212.

29 Ferreira ADB, Filho RRDS, Rodrigues LP, *et al*. Association between sarcopenia and hospitalization in community-dwelling older adults, using the SARC-F and SARC-calf methods: a systematic review protocol. *Physical Therapy Reviews* 2021;26:391–7.

30 Fernandes M da SV, Mendonça CR, da Silva TMV, *et al*. The relationship between depression and quality of life in students and the academic consequences: protocol for a systematic review with meta-analysis. *IJEDRO* 2021;109:101812.

31 Ouzzani M, Hammady H, Fedorowicz Z, *et al*. Rayyan-a web and mobile app for systematic reviews. *Syst Rev* 2016;5:210.

32 Rodrigues LP, Rezende AT de O, Moura L de ANE, *et al*. What is the impact of multimorbidity on the risk of hospitalisation in older adults? A systematic review study protocol. *BMJ Open* 2021;11:e049974.

33 Balshem H, Helfand M, Schünemann HJ, *et al*. GRADE guidelines: 3 rating the quality of evidence. *J Clin Epidemiol* 2011;64:401–6.

34 Jongsiriyanyong S, Limpawattana P. Mild cognitive impairment in clinical practice: a review article. *Am J Alzheimers Dis Other Demen* 2018;33:500–7.

35 Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998;52:377–84.

36 Sabia S, Dugravot A, Dartigues J-F, *et al*. Physical activity, cognitive decline, and risk of dementia: 28 year follow-up of whitehall II cohort study. *BMJ* 2017;357.

37 Aarsland V, Borda MG, Aarsland D, *et al*. Association between physical activity and cognition in Mexican and Korean older adults. *Arch Gerontol Geriatr* 2020;89:104047.

38 Kunutsor SK, Laukkanen JA, Kauhanen J, *et al*. Physical activity may not be associated with long-term risk of dementia and Alzheimer's disease. *Eur J Clin Invest* 2021;51:e13415.

39 Dupré C, Helmer C, Bongue B, *et al*. Associations between physical activity types and multi-domain cognitive decline in older adults from the three-city cohort. *PLoS One* 2021;16:e0252500.

40 Osuka Y, Kojima N, Sasai H, *et al*. Exercise types and the risk of developing cognitive decline in older women: a prospective study. *J Alzheimers Dis* 2020;77:1733–42.

Supplementary material

Table 1 – Search strategy

PubMed
1.	((((((((((((((((((((((((((dementia[MeSH Terms]) OR ("dementia, vascular"[MeSH Terms])) OR ("frontotemporal dementia"[MeSH Terms])) OR ("Alzheimer disease"[MeSH Terms])) OR ("neurocognitive disorders"[MeSH Terms])) OR ("cognition disorders"[MeSH Terms])) OR (amnesia[MeSH Terms])) OR ("neurodegenerative diseases"[MeSH Terms])) OR ("cognitive dysfunction"[MeSH Terms])) OR ("Lewy body disease"[MeSH Terms])) OR (cognition[MeSH Terms])) OR (dementia[Title/Abstract])) OR ("dementia vascular"[Title/Abstract])) OR ("frontotemporal dementia"[Title/Abstract])) OR ("Alzheimer disease"[Title/Abstract])) OR ("neurocognitive disorders"[Title/Abstract])) OR ("cognition disorders"[Title/Abstract])) OR (amnesia[Title/Abstract])) OR ("neurodegenerative diseases"[Title/Abstract])) OR ("neurodegenerative disease"[Title/Abstract])) OR ("cognitive dysfunction"[Title/Abstract])) OR ("cognitive impairments"[Title/Abstract])) OR ("Alzheimer dementia"[Title/Abstract])) OR ("vascular dementia"[Title/Abstract])) OR ("Lewy body disease"[Title/Abstract])) OR ("Lewy body dementia"[Title/Abstract])) OR ("Cognitive function"[Title/Abstract])) OR (cognition[Title/Abstract])) OR ("Cognitive Symptoms"[Title/Abstract])) OR ("Cognitive Symptom"[Title/Abstract])
2.	(((((((((((((Aged[MeSH Terms]) OR ("Age groups"[MeSH Terms])) OR (Aging[MeSH Terms])) OR (Aged[Title/Abstract])) OR ("Age groups"[Title/Abstract])) OR (Aging[Title/Abstract])) OR (Elderly[Title/Abstract])) OR (Ageing[Title/Abstract])) OR ("Old adult"[Title/Abstract])) OR ("Old adults"[Title/Abstract])) OR ("Older adult"[Title/Abstract])) OR ("Older adults"[Title/Abstract])) OR (Geriatric[Title/Abstract])) OR ("Senior citizen"[Title/Abstract])
3.	((((((((((((((((((((((((((((((((Exercise[MeSH Terms]) OR ("Cool-Down Exercise"[MeSH Terms])) OR (Gymnastics[MeSH Terms])) OR ("Muscle Stretching Exercises"[MeSH Terms])) OR ("Physical Conditioning, Human"[MeSH Terms])) OR ("Circuit-Based Exercise"[MeSH Terms])) OR ("Endurance Training"[MeSH Terms])) OR ("High-Intensity Interval Training"[MeSH Terms])) OR ("Resistance Training"[MeSH Terms])) OR (Running[MeSH Terms])) OR (Jogging[MeSH Terms])) OR (Swimming[MeSH Terms])) OR (Walking[MeSH Terms])) OR ("Nordic Walking"[MeSH Terms])) OR ("Stair Climbing"[MeSH Terms])) OR (Exercise[Title/Abstract])) OR ("Cool-Down Exercise"[Title/Abstract])) OR (Gymnastics[Title/Abstract])) OR ("Muscle Stretching Exercises"[Title/Abstract])) OR ("Physical Conditioning, Human"[Title/Abstract])) OR ("Circuit-Based Exercise"[Title/Abstract])) OR ("Endurance Training"[Title/Abstract])) OR ("High-Intensity Interval Training"[Title/Abstract])) OR ("Resistance Training"[Title/Abstract])) OR (Running[Title/Abstract])) OR (Jogging[Title/Abstract])) OR (Swimming[Title/Abstract])) OR (Walking[Title/Abstract])) OR ("Nordic Walking"[Title/Abstract])) OR ("Stair Climbing"[Title/Abstract])) OR ("Physical Fitness"[Title/Abstract])) OR (Sports[Title/Abstract])) OR

	("Motor Activity"[Title/Abstract])) OR ("Sedentary Behavior"[Title/Abstract])) OR (Exercises[Title/Abstract])) OR ("Physical Activity"[Title/Abstract])) OR ("Physical Activities"[Title/Abstract])) OR ("Physical Exercise"[Title/Abstract])) OR ("Physical Exercises"[Title/Abstract])) OR ("Isometric Exercises"[Title/Abstract])
4.	(((((((((((("Cohort Studies"[MeSH Terms]) OR ("Follow-Up Studies"[MeSH Terms])) OR ("Longitudinal Studies"[MeSH Terms])) OR ("Prospective Studies"[MeSH Terms])) OR ("Cohort Studies"[Title/Abstract])) OR ("Follow-Up Studies"[Title/Abstract])) OR ("Longitudinal Studies"[Title/Abstract])) OR ("Prospective Studies"[Title/Abstract])) OR ("Cohort Study"[Title/Abstract])) OR ("Incidence Studies"[Title/Abstract])) OR ("Incidence Study"[Title/Abstract])
5.	#1 AND #2 AND #3 AND #4

| Embase	
1.	'exercise'/exp OR exercise OR gymnastics:ti,ab,kw OR 'resistance training':ti,ab,kw OR walking:ti,ab,kw OR fitness:ti,ab,kw OR 'sedentary lifestyle':ti,ab,kw OR 'physical activity':ti,ab,kw OR 'physical activity scale for the elderly':ti,ab,kw OR training:ti,ab,kw
2.	'aged'/exp OR aged OR 'groups by age':ti,ab,kw OR aging:ti,ab,kw OR aged:ti,ab,kw OR 'older adults':ti,ab,kw OR 'older people':ti,ab,kw OR 'older adult':ti,ab,kw OR 'geriatric patient':ti,ab,kw
3.	'dementia'/exp OR dementia OR 'alzheimer disease':ti,ab,kw OR 'frontotemporal dementia':ti,ab,kw OR 'multiinfarct dementia':ti,ab,kw OR 'disorders of higher cerebral function':ti,ab,kw OR cognition:ti,ab,kw OR 'cognitive defect':ti,ab,kw OR 'diffuse lewy body disease':ti,ab,kw
4.	'cohort analysis'/exp OR 'cohort analysis' OR 'follow up':ti,ab,kw OR 'longitudinal study':ti,ab,kw OR 'prospective study':ti,ab,kw OR 'observational study':ti,ab,kw
5.	#1 AND #2 AND #3 AND #4

Scopus	
1.	(TITLE-ABS-KEY (exercise) OR TITLE-ABS-KEY (gymnastics) OR TITLE-ABS-KEY ("resistance training") OR TITLE-ABS-KEY (walking) OR TITLE-ABS-KEY ("physical fitness") OR TITLE-ABS-KEY ("sedentary behavior") OR TITLE-ABS-KEY ("physical activity") OR TITLE-ABS-KEY ("physical exercise") OR TITLE-ABS-KEY ("training"))
2.	(TITLE-ABS-KEY (aged) OR TITLE-ABS-KEY ("age groups") OR TITLE-ABS-KEY (aging) OR TITLE-ABS-KEY (elderly) OR TITLE-ABS-KEY (ageing) OR TITLE-ABS-KEY ("old adult") OR TITLE-ABS-KEY ("older adult") OR TITLE-ABS-KEY ("older adults") OR TITLE-ABS-KEY (geriatric))
3.	(TITLE-ABS-KEY (dementia) OR TITLE-ABS-KEY ("dementia, vascular") OR TITLE-ABS-KEY ("frontotemporal dementia") OR TITLE-ABS-KEY ("alzheimer disease") OR TITLE-ABS-KEY ("neurocognitive disorders") OR TITLE-ABS-KEY ("cognition disorders"))

4.	((TITLE-ABS-KEY ('cohort AND studies') OR TITLE-ABS-KEY ('follow-up AND studies') OR TITLE-ABS-KEY ('longitudinal AND studies') OR TITLE-ABS-KEY ('prospective AND studies'))
5.	#1 AND #2 AND #3 AND #4

Web of Science	
1.	((((((((ALL=(exercise)) OR ALL=(Gymnastics)) OR ALL=("Resistance Training")) OR ALL=(Walking)) OR ALL=("Physical Fitness")) OR ALL=("Sedentary Behavior")) OR ALL=("Physical Activity")) OR ALL=("Physical Exercise")) OR ALL=("Training")
2.	((((((((ALL=(Aged)) OR ALL=("Age groups")) OR ALL=(Aging)) OR ALL=(Elderly)) OR ALL=(Ageing)) OR ALL=("Old adult")) OR ALL=("Older adult")) OR ALL=("Older adults")) OR ALL=(Geriatric)
3.	((((((((ALL=(dementia)) OR ALL=("dementia, vascular")) OR ALL=("frontotemporal dementia")) OR ALL=("Alzheimer disease")) OR ALL=("neurocognitive disorders")) OR ALL=("cognition disorders")) OR ALL=("cognitive dysfunction")) OR ALL=("Lewy body disease")
4.	(((((ALL=("Cohort Studies")) OR ALL=("Follow-Up Studies")) OR ALL=("Longitudinal Studies")) OR ALL=("Prospective Studies")) OR ALL=("Observational Studies")
5.	#1 AND #2 AND #3 AND #4

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only
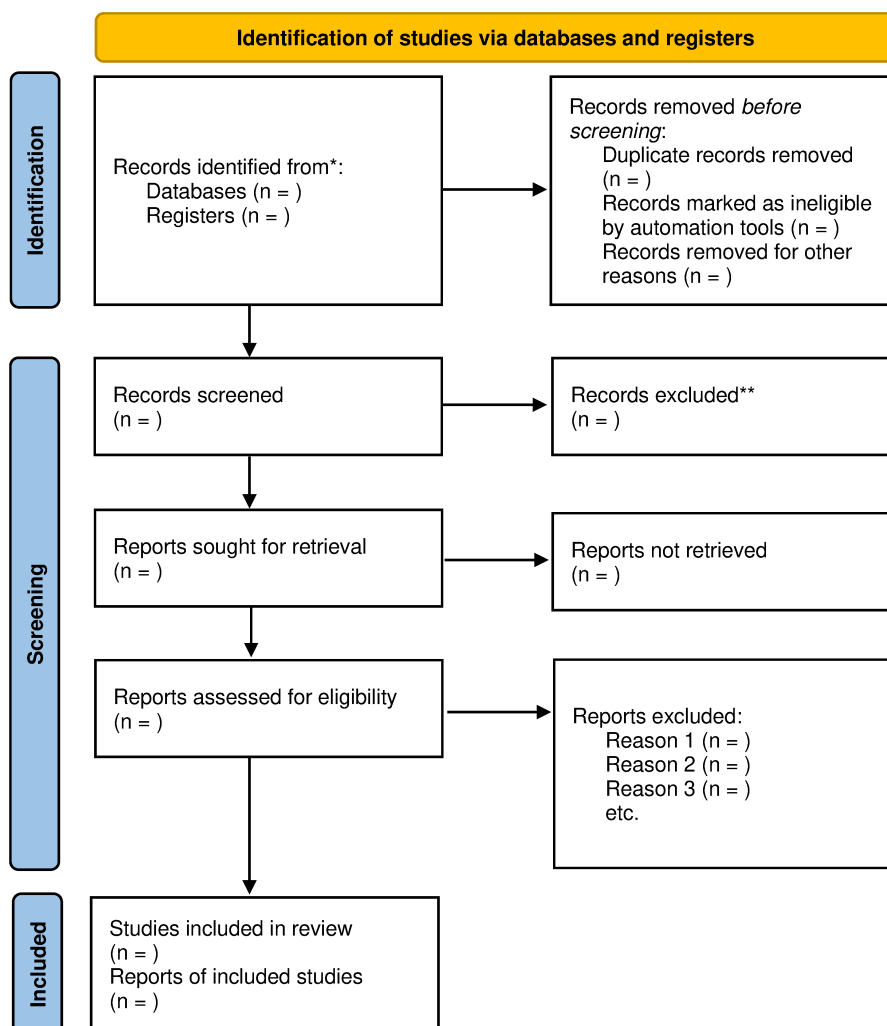
Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71