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Leisure Activities and the Risk of Dementia

A Systematic Review and Meta-analysis

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Abstract

Background and Objectives

Leisure activities are major components of modifiable and healthy lifestyles and are proposed to help prevent the development of dementia. This study aimed to assess the effects of different types of leisure activities, including cognitive, physical, and social activities, on the incidence of all-cause dementia (ACD), Alzheimer disease (AD), and vascular dementia (VD).

Methods

We performed a systematic review and meta-analysis of the Cochrane, PubMed, Embase, and Web of Science databases to identify longitudinal studies that examined associations between leisure activities and dementia. Relative risks (RRs) and 95% CIs were pooled using random-effects meta-analysis. Subgroup analyses were used to estimate potential effect modifiers. The study was registered with PROSPERO (CRD42019116857).

Results

A total of 38 longitudinal studies, with 2,154,818 participants at baseline, 74,700 ACD cases, 2,848 AD cases, and 1,423 VD cases during follow-up, were included in the meta-analysis. The subgroup analyses showed that physical (RR 0.83, 95% CI 0.78–0.88), cognitive (RR 0.77; 95% CI 0.68–0.87), and social (RR 0.93; 95% CI 0.87–0.99) activities were associated with a decreased incidence of ACD. In addition, physical (RR 0.87; 95% CI 0.78–0.96) and cognitive (RR 0.66; 95% CI 0.52–0.85) activities were related to a reduced risk of AD. Physical activity (RR 0.67; 95% CI 0.53–0.85) was associated with a lower incidence of VD.

Discussion

Our findings suggest that leisure activities are inversely associated with a risk of ACD, AD, and VD.

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Glossary

ACD = all-cause dementia; **AD** = Alzheimer disease; **BDNF** = brain-derived neurotrophic factor; **CA** = cognitive activity; **FNDC5** = fibronectin type III domain-containing protein 5; **HR** = hazard ratio; **NOS** = Newcastle-Ottawa Scale; **OR** = odds ratio; **PA** = physical activity; **RR** = relative risk; **SA** = social activity; **VD** = vascular dementia; **WHO** = World Health Organization.

Dementia is one of the most prevalent health issues. It is the fifth leading cause of death, affecting 50 million people worldwide in 2018 according to the World Health Organization (WHO).[1,2] As life expectancy increases, the number of people with all-cause dementia (ACD) is expected to reach approximately 152 million by 2050, of which Alzheimer disease (AD) and vascular dementia (VD) are the 2 main subtypes.[2,3] Although numerous new treatments are being investigated, no treatments can cure dementia or alter its pathologic progression. The WHO recommends risk reduction to reduce the global burden of dementia.[4] Evidence-based prevention programs are needed to decrease or delay the onset of dementia.

Leisure activities, including physical activity (PA), cognitive activity (CA), and social activity (SA), are major components of modifiable and healthy lifestyles and are beneficial to cognition.[5-8] Previous studies showed that leisure activities were associated with various health benefits, such as a lower cancer risk,[9] a reduction of atrial fibrillation,[10] and subjective well-being.[11] However, evidence of the role of leisure activities in the prevention of dementia is conflicting. Some studies indicated that engagement in leisure activities may be a potential protective factor against the risk of cognitive impairment and dementia.[5,12] Other studies found no significant relationship between leisure activities and the progression of dementia or AD pathophysiology.[13,14] Furthermore, AD and VD have different etiologies. Unclear are the specific subtypes of dementia that may benefit from leisure activities or the ways in which different types of leisure activities can influence the risk of incident dementia. For example, several studies found that PA was related to a reduced risk of AD,[15,16] but other studies showed that PA was associated with a lower risk of VD but not AD.[17,18] CA also exerted contradictory effects on incident dementia.[19,20] To develop effective strategies to protect against dementia, detailed associations between different types of leisure activities and dementia and its subtypes need to be identified.

This study systematically reviewed studies of the role of leisure activities in the development of dementia and performed meta-analyses. We assessed the effect of PA, CA, and SA on the incidence of ACD, AD, and VD and discussed the potential mechanisms of these associations and proposed strategies to prevent incident dementia.

Methods

Search Strategy

We performed a systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines (eTable 1, links.lww.com/WNL/C200)[21] and the Meta-analyses of Observational Studies in Epidemiology Checklist (eTable 2)[22] guidelines. The study was registered with PROSPERO (CRD42019116857). The Cochrane, PubMed, Embase, and Web of Science databases were searched for relevant studies up to May 8, 2021. Longitudinal studies that were published in English and assessed the role of leisure activities in incident ACD, AD, and VD were included. The following search terms (eTable 3) were used: ("leisure activities" OR "recreation" OR "cognitive activities" OR "cognitive stimulation" OR "intellectual activities" OR "mental activities" OR "exercise" OR "physical activities" OR "social activities") AND ("dementia" OR "Alzheimer's disease" OR "vascular dementia") AND ("cohort studies" OR "longitudinal studies" OR "prospective studies" OR "nested case control studies").

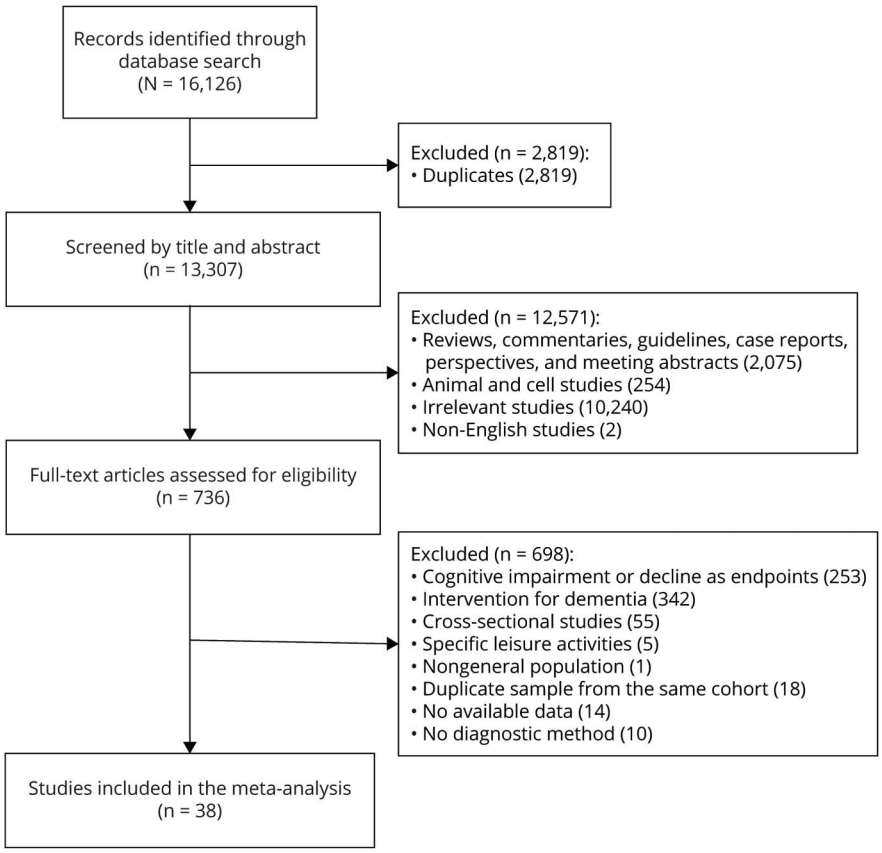
Selection Criteria

Three authors (S.S., L.S., and Y.Z.) independently screened the titles and abstracts for the eligibility of studies and reviewed the full-text articles using the Endnote X9 software. Studies were included if they met the following criteria: (1) evaluated associations between leisure activities and the incident dementia in the general population, (2) diagnosed dementia based on international diagnostic criteria, (3) used a longitudinal design (cohort studies and nested case-control studies), (4) ascertained leisure activities via questionnaires, or interviews, and (5) provided sufficient data to calculate odds ratios (ORs), relative risks (RRs), or hazard ratios (HRs) with 95% CIs based on multivariate adjustment. The following exclusion criteria were applied: (1) case reports, commentaries, conference abstracts, reviews, and cross-sectional studies, (2) studies that presented cognitive function as a continuous variable without available ORs, RRs, or HRs, and (3) studies for which the outcome measure was not ACD, AD, or VD.

Data Extraction

The data were independently extracted from eligible articles by 3 authors (S.S., L.S., and Y.S.) who subsequently cross-checked the data, and additional information was obtained by contacting authors. Discrepancies were resolved by discussion until a consensus was reached. The following information was

Figure 1 Flowchart of the Identification of Eligible Studies



extracted from each study: (1) first author, (2) publication year, (3) study design, (4) research site (country), (5) total number of participants at baseline and dementia cases during follow-up, (6) characteristics of baseline participants, such as sex ratio and age distribution, (7) follow-up time, (8) methods of ascertainment and operationalization of leisure activities, (9) type, duration, frequency, and intensity of leisure activities, (10) clinical tools used for dementia diagnosis, (11) effect estimates (ORs, RRs, or HRs) with 95% CIs, and (12) covariates that were used for adjustment.

Quality Assessment

Three authors (S.S., L.S., and X.H.) assessed the quality of individual studies using the Newcastle-Ottawa Scale (NOS).[23] The following items were considered: selection of the study groups, comparability of groups, and ascertainment of outcome measure for cohort studies with a sufficiently long follow-up time (≥5 years). A study could have a maximum quality score of 9. Studies with 7–9 points were of high quality. Studies with 4–6 points were of medium quality. Studies with 0–3 points were of low quality.

Definitions

Leisure activities, including CA, PA, and SA, were defined as activities in which individuals engaged for enjoyment or well-being.[24] CA mainly consisted of conscious and intellectual activities and included, but were not limited to, reading books, magazines, or newspapers, watching television, listening to the radio, writing for pleasure or calligraphy, playing games (e.g., cards, checkers, crossword puzzles, or other puzzles), playing musical instruments, using a computer or browsing the Internet, painting, and engaging in handicrafts. Physical activities included, but were not limited to, walking for exercise, hiking or excursions, jogging or running, swimming, stair climbing, bicycling, using exercise machines, playing ballgames or racket sports, participating in group exercises, performing Qigong or Yoga, performing calisthenics, and dancing. Social activities mainly referred to activities that involved communication with others and included, but were not limited to, attending an interest class, joining a social center, participating in volunteer work, meeting relatives or friends, attending religious activities, and participating in organized group discussions.[5,20,24,25]

In this study, ACD, AD, and VD were diagnosed based on the *Diagnostic and Statistical Manual of Mental Disorders*, *International Statistical Classification of Diseases* and Related Health Problems, National Institute of Neurological Disorders and Stroke and Alzheimer's Disease and Related Disorders Association criteria, National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherche et l'Enseignement en Neurosciences criteria,

Table 1 Summary of Longitudinal Studies Included in the Meta-analysis

Study	Study design	Country	Total sample	Female, %	Age at baseline, y	Method of leisure activities	Leisure activity types	Follow-up duration, y	Diagnosis of dementia	Participants with dementia
Akbaraly et al., 2009[6]	Cohort study	France	5,698	60.87	73.7 ± 5.4	Questionnaire	Cognitive, physical, social	4	ACD: *DSM-4*, AD: NINCDS-ADRDA	ACD: 161 (AD: 105)
Blasko et al., 2014[7]	Cohort study	Austria	399	61.14	75.8 ± 0.5	Interview	Cognitive, physical	5	AD: NINCDS-ADRDA, VD: NINDS-AIREN, Frontotemporal lobe dementia: the Manchester-Lund criteria; dementia with Lewy bodies: the revised Criteria of Consortium for Dementia with Lewy bodies	ACD: 117
Chang et al., 2010[27]	Cohort study	Iceland	4,945	57.67	51.1 ± 6.7	Interview	Physical	25.8	*DSM-4*	ACD: 184
de Bruijn et al., 2013[28]	Cohort study	Netherlands	4,406	59.00	72.7 ± 7.2	Questionnaire	Physical	8.8	ACD: *DSM-3R*, AD: NINCDS-ADRDA	ACD: 583 (AD: 490)
Floud et al., 2020[29]	Cohort study	United Kingdom	1,136,846	100.00	56 ± 5	Interview	Physical	18	*ICD-10*	ACD: 30,957
Floud et al., 2021[30]	Cohort study	United Kingdom	851,307	100.00	60 ± 5	Interview	Leisure	16	*ICD-10*	ACD: 31,187
Gelber et al., 2012[31]	Case-control study nested in a prospective cohort	United States	3,468	0.00	Mean 52	Interview	Physical	25	ACD: *DSM-3R*, AD:NINCDS-ADRDA, VD: criteria of California Alzheimer's Disease Diagnostic and Treatment Centers	ACD: 223 (AD: 117, VD: 78)
Grasset et al., 2017[32]	Cohort study	France	3,670	58.01	75.3 ± 6.8	Questionnaire	Physical	11.6	*DSM-3R*	ACD: 168
Hansson et al., 2019[18]	Cohort study	Sweden	20,639	60.00	57.5 (51.0–63.8)	Questionnaire	Physical	15	*DSM-5*	ACD: 1,375 (AD: 300, VD: 834)
Hughes et al., 2010[33]	Cohort study	United States	942	66.45	75.8 ± 5.1	Interview	Cognitive	6.07	Modified CERAD and Pittsburgh Alzheimer Disease Research Center assessment protocols	ACD: 111
Kishimoto et al., 2016[34]	Cohort study	Japan	803	61.30	74 ± 6.8	Questionnaire	Physical	11.5	ACD: *DSM-3R*, AD: NINCDS-ADRDA, VD: NINDS-AIREN	ACD: 291 (AD: 165, VD: 93)
Larson et al., 2006[35]	Cohort study	United States	1,740	60.34	74.4 ± 5.7	Questionnaire	Physical	6.2	ACD: *DSM-4*, AD: NINCDS-ADRDA	ACD: 158 (AD: 107)
Laurin et al., 2001[36]	Cohort study	Canada	4,615	60.33	≥65	Questionnaire	Physical	5	*DSM-4*	ACD: 285 (AD: 169; VD: 54)
Lee et al., 2018[20]	Cohort study	China	15,582	63.90	74 (71–77)	Questionnaire	Cognitive, social, physical	5	*ICD-10R*	ACD: 1,349
Llamas-Velasco et al., 2015[37]	Cohort study	Spain	3,105	56.60	73.2 ± 6.3	Interview	Physical	3.2	ACD: *DSM-4*	ACD: 134

Continued

Table 1 Summary of Longitudinal Studies Included in the Meta-analysis *(continued)*

Study	Study design	Country	Total sample	Female, %	Age at baseline, y	Method of leisure activities	Leisure activity types	Follow-up duration, y	Diagnosis of dementia	Participants with dementia
Luck et al., 2014[38]	Cohort study	Germany	2,492	64.70	81.1 ± 3.5	Interview	Cognitive, physical	4.5	ACD: *DSM-4*, AD: NINCDS-ADRDA	ACD: 278 (AD: 184)
Marioni et al., 2015[39]	Cohort study	France	2,854	59.00	77.0 ± 6.8	Interview	Social	9.4	*DSM-3R*	ACD: 783
Marseglia et al., 2019[40]	Cohort study	Sweden	2,648	62.95	73.6 ± 10.5	Interview	Leisure	6.4	*DSM-4*	ACD: 246
Morgan et al., 2012[41]	Cohort study	United Kingdom	1,005	0.00	56	Questionnaire	Physical	16	NINDS-AIREN	ACD: 72
Nabe-Nielsen et al., 2021[42]	Cohort study	Denmark	4,721	0.00	49.0 ± 5.3	Interview	Physical	29.3	*ICD-8* in 1970-1993 and *ICD-10* in 1994 onwards	ACD: 697
Najar et al., 2019[16]	Cohort study	Sweden	800	100.00	47.2 ± 4.5	Interview	Cognitive, physical	44	ACD: *DSM-3R*, AD: NINCDS-ADRDA, VD: NINDS-AIREN	ACD: 194 (AD: 102, VD: 27)
Neergaard et al., 2016[43]	Cohort study	Denmark	5,512	100.00	70.6 ± 6.5	Questionnaire	Physical	11.9	*ICD-10*	ACD: 592 (AD: 250, VD: 43)
Paganini-Hill et al., 2016[44]	Cohort study	United States	587	Not reported	93 ± 2.6	Questionnaire	Leisure	3	*DSM-4*	ACD: 268
Palta et al., 2019[45]	Cohort study	United States	10,705	55.95	59.9 ± 5.67	Questionnaire	Physical	17.4	*DSM-5*	ACD: 1,063
Podewils et al., 2005[46]	Cohort study	United States	3,375	59.10	74.8 ± 4.9	Questionnaire	Physical	5.4	AD:NINCDS-ADRDA, VD: Alzheimer's Disease Diagnostic and Treatment Centers criteria	ACD: 479 (AD: 245, VD: 213)
Ravaglia et al., 2008[17]	Cohort study	Italy	749	53.50	73.2 ± 6.0	Questionnaire	Physical	3.9	ACD: *DSM-4*, AD: NINCDS-ADRDA, VD: NINDS-AIREN	ACD: 86 (AD: 54, VD: 27)
Sabia et al., 2017[47]	Cohort study	United Kingdom	10,308	33.11	45.0 ± 6.0	Questionnaire	Physical	26.6	*ICD-10*	ACD: 329
Scarmeas et al., 2001[48]	Cohort study	United States	1,772	68.12	75.64 ± 6.30	Interview	Leisure	2.9	ACD: *DSM-3R*	ACD: 207
Scarmeas et al., 2009[15]	Cohort study	United States	1,880	69.00	77.2 ± 6.6	Questionnaire	Physical	5.4	NINCDS-ADRDA	AD: 282
Sommerladet al., 2020[49]	Cohort study	United Kingdom	6,050	30.70	55.9 ± 6.0	Questionnaire	Leisure	18	*ICD-10*	ACD: 247
Sorman et al., 2014[19]	Cohort study	Sweden	1,475	56.67	73.7 ± 6.9	Questionnaire	Cognitive, social	6.3	*DSM-4*	ACD: 357

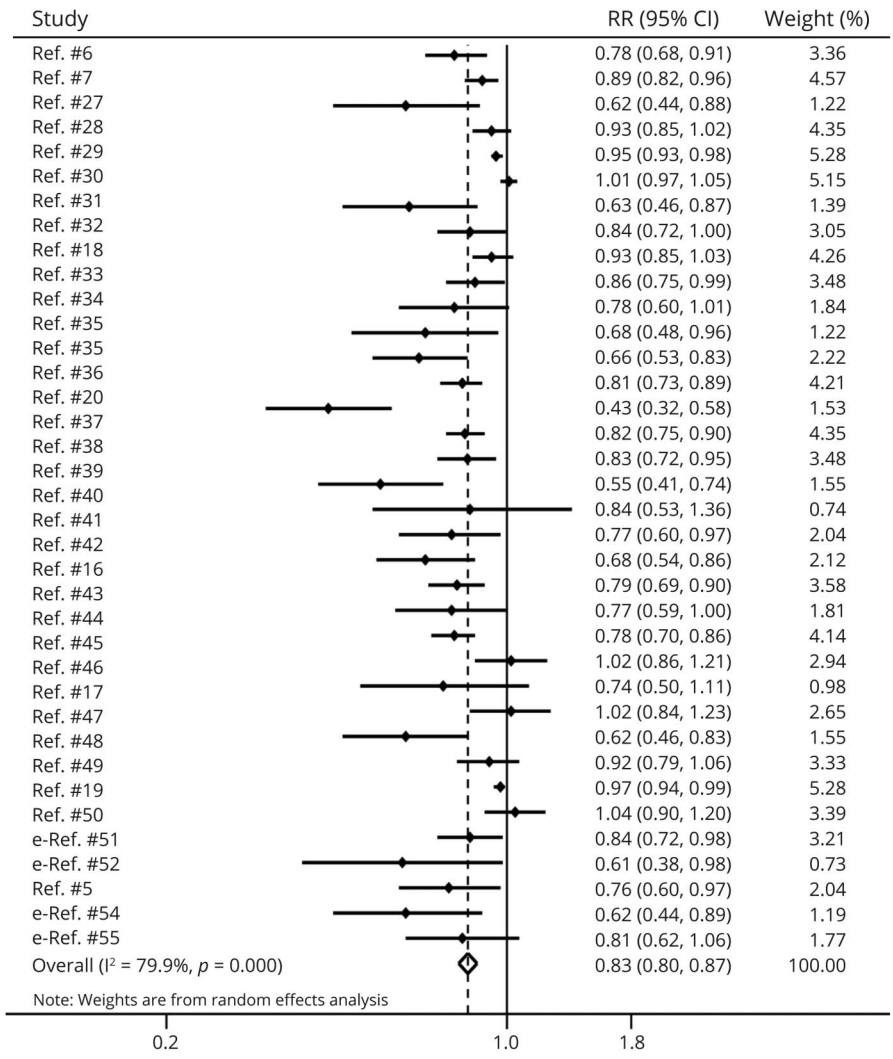
Continued

Table 1 Summary of Longitudinal Studies Included in the Meta-analysis *(continued)*

Study	Study design	Country	Total sample	Female, %	Age at baseline, y	Method of leisure activities	Leisure activity types	Follow-up duration, y	Diagnosis of dementia	Participants with dementia
Tan et al., 2017[50]	Cohort study	United States	3,714	54.44	70.5 ± 7.0	Questionnaire	Physical	7.5	ACD: *DSM-4*, AD: NINCDS-ADRDA	ACD: 236 (AD: 188)
Tolppanen et al., 2015[e51]	Cohort study	Finland	3,559	56.50	51.2 ± 6.0	Questionnaire	Physical	24.4	ACD: *DSM-4*	ACD: 544
Verdelho et al., 2012[e52]	Cohort study	Not reported	639	55.00	74.1 ± 5	Interview	Physical	3	AD: NINCDS-ADRDA, VD: NINDS-AIREN	ACD: 90 (VD: 54)
Verghese et al., 2003[5]	Cohort study	Canada	469	64.06	79.1 ± 3.1	Questionnaire	Cognitive, physical	5.1	*DSM-3R*/*DSM-3*	ACD: 124
Wilson et al., 2007[e53]	Cohort study	United States	775	75.36	80.4 ± 7.4	Questionnaire	Cognitive	3.5	NINCDS-ADRDA	AD: 90
Wu et al., 2020[e54]	Cohort study	China	1,648	54.50	71.5 ± 7.4	Questionnaire	Physical	5.3	*DSM-4*	ACD: 166
Zotcheva et al., 2018[e55]	Cohort study	Norway	28,916	50.20	53.4	Questionnaire	Physical	15.2	*ICD-10*	ACD: 359

Abbreviations: ACD = all-cause dementia; AD = Alzheimer disease; CERAD = Consortium to Establish a Registry for Alzheimer Disease; *DSM-3 = Diagnostic and Statistical Manual of Mental Disorders, Third Edition*; *DSM-3R = Diagnostic and Statistical Manual of Mental Disorders, Third Edition Revised; DSM-4 = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; ICD-8 = International Statistical Classification of Diseases, Eighth Edition; ICD-10 = International Statistical Classification of Diseases, 10th Edition*; *ICD-10R = InternationalStatistical Classification of Diseases,10th Revision*; NINCDS-ADRDA = National Institute of Neurological and Communicative Diseases and Stroke and the Alzheimer's Disease and Related Disorders Association; NINDS-AIREN = National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences criteria.
Age at baseline (years): mean ± SD/median (interquartile range) years.

Figure 2 Forest Plot of the Protective Role of Leisure Activities in the Risk of All-Cause Dementia



The results are expressed as RRs and 95% CIs. RR = relative risk.

California Alzheimer's Disease Diagnostic and Treatment Centers criteria, Consortium to Establish a Registry for Alzheimer Disease and Pittsburgh Alzheimer Disease Research Center assessment protocols, Manchester-Lund criteria, and other recognized diagnostic criteria.

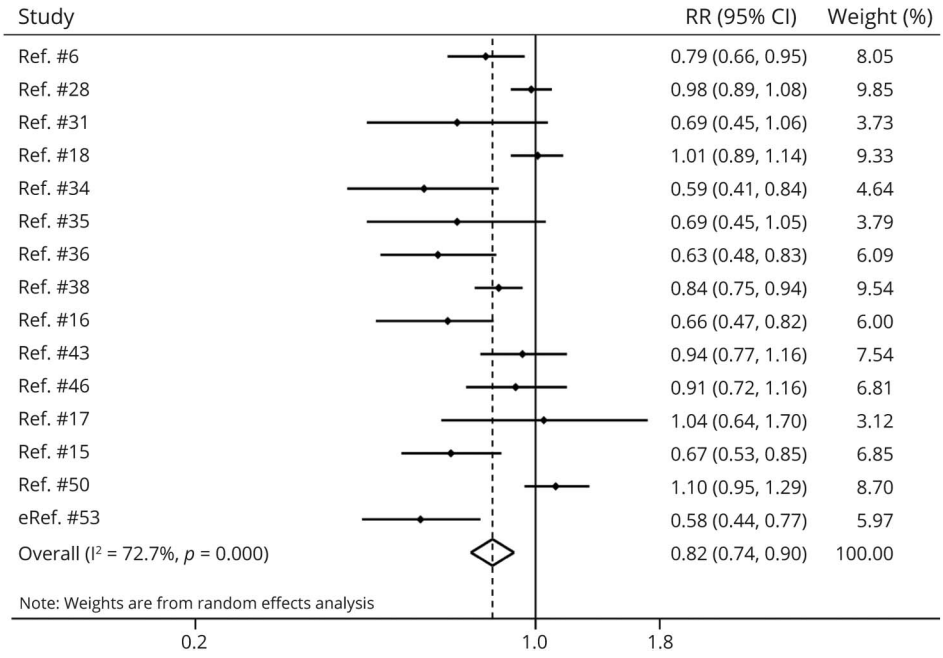
Statistical Analysis

The statistical analyses were performed using STATA 15 software. Because the incidence of dementia was very low, ORs, RRs, and HRs were treated equally.[26] The RRs and 95% CIs were used to indicate effect sizes. Heterogeneity was evaluated using the I^2 statistic (I^2 = 0%–60% [none to moderate] and I^2 > 60% [substantial statistical heterogeneity]). If no heterogeneity was found, a fixed-effect model was used, or the random-effect model was chosen to bolster the results. Subgroup analyses were conducted to explore the effects of PA, CA, and SA on incident ACD, AD, and VD. We used meta-regression to assess the effects of age, sex, years of follow-up, number of participants, and broad WHO regional classification (i.e., Africa, Americas, Asia, Europe, and Oceania) on study-specific effect estimates. Funnel plots were used to assess publication bias. Egger tests were used to estimate publication bias. Values of $p < 0.05$ were considered statistically significant. Sensitivity analyses were conducted to evaluate the influence of each study on the overall results.

Results

Figure 1 presents a flowchart of the identification of eligible studies. A total of 16,126 articles were retrieved. After excluding duplicate publications, there were 13,307 articles, of which 12,571 were irrelevant studies, reviews, commentaries, guidelines, case reports, perspectives, meeting abstracts, animal, cellular/molecular studies, and non-English studies. Of the remaining 736 studies, a total of 38 longitudinal studies were included in the meta-analysis after reviewing the full texts.[5-7,15-20,27-e55]

Figure 3 Forest Plot of the Protective Role of Leisure Activities in the Risk of Alzheimer Disease



The results are expressed as RRs and 95% CIs. RR = relative risk.

Characteristics of Eligible Studies

The characteristics of the 38 eligible longitudinal studies (37 cohort studies and 1 nested case-control study) are presented in Table 1.[5-7,15-20,27-e55] These studies had a total of 2,154,818 participants (mean age: 45.00–93.00 years) at baseline, 74,700 ACD cases, 2,848 AD cases, and 1,423 VD cases during follow-up (2.90–44.00 years). Among these studies, 12 were conducted in North America,[5,15,31,33,35,36,44-46,48,50,e53] 22 were conducted in Europe,[6,16-19,27-30,32,37-43,47,49,e51,e52,e55] 3 were conducted in Asia,[20,34,e54] and 1 was conducted in Oceania.[7] According to the NOS (eTable 4, links.lww.com/WNL/C200), 32 studies were of high quality,[5-7,15,16,18-20,28-38,40,42,43,45-e51,e53-e55] and 6 studies were of medium quality.[17,27,39,41,44,e52] The measurement of leisure activities was based on self-report questionnaires in 24 studies[5,6,15,17-20,28,32,34-36,41,43-47,49-e51,e53-e55] and interviews in 14 studies.[7,16,27,29-31,33,37-40,42,48,e52] Detailed information about the methods that were used to reflect features of leisure activities, such as frequency, intensity, or duration, in the original studies is shown in eTable 5. All studies provided RRs (HRs or ORs) and 95% CIs based on adjustment for multiple potential covariates, including age, sex, education, and ApoE (eTable 5).

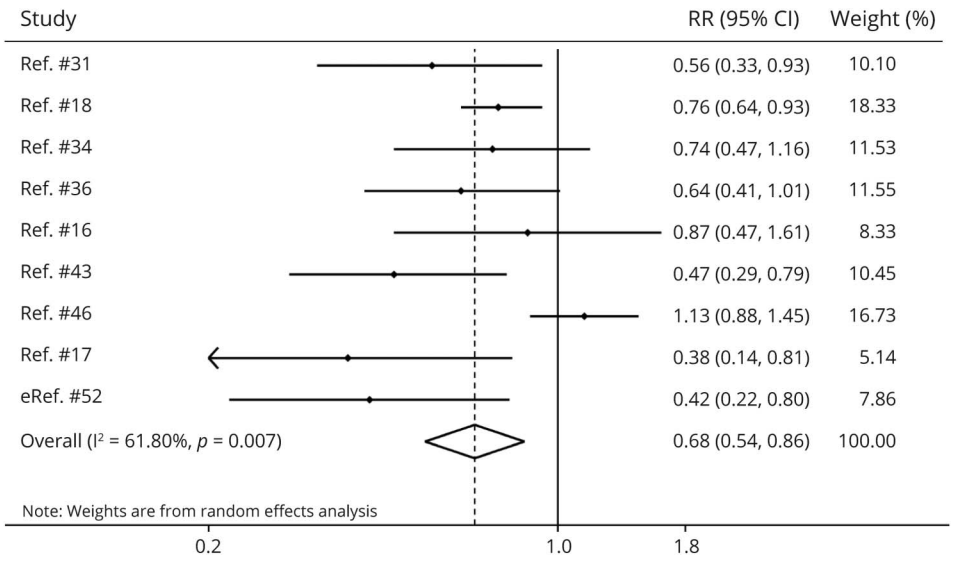
Leisure Activities and ACD

Thirty-six studies investigated the relationship between leisure activities and ACD,[5-7,16-20,27-e52,e54,e55] including 2,152,163 participants (mean age: 45.00–93.00 years) at baseline and 74,700 ACD cases during follow-up (2.90–44.00 years). Five studies of these studies showed only the relationship of leisure activities and incident dementia.[30,40,44,48,49] Others investigated the role of different types of leisure activities, including PA (29 studies), CA (8 studies), and SA (4 studies), in the incidence of ACD. The meta-analysis showed that individuals who engaged in leisure activities were associated with a 0.83-fold lower risk of developing ACD compared with individuals who did not engage in leisure activities (RR 0.83, 95% CI 0.80–0.87, I^2 = 79.9%, p < 0.001; Figure 2). The subgroup analyses showed that PA, CA, and SA were inversely associated with incidence of ACD (PA: RR 0.83, 95% CI 0.78–0.88, I^2 = 73.8%, p < 0.001; CA: RR 0.77, 95% CI 0.68–0.87, I^2 = 83.6%, p < 0.001; SA: RR 0.93, 95% CI 0.87–0.99, I^2 = 12.7%, p = 0.329; Figure 5; eFigure 1, links.lww.com/WNL/C200). The meta-regression showed that types of leisure activities, number of participants, sex, age at baseline, follow-up duration, and WHO regional classification were not significantly associated with development of ACD (eTable 6).

Leisure Activities and AD

Fifteen articles assessed the role of leisure activities in incident AD.[6,15-18,28,31,34-36,38,43,46,50,e53] These studies included a total of 60,666 participants (mean age: 47.20–81.10 years) at baseline and 2,848 AD cases during follow-up (3.90–44.00 years). Compared with participants who did not engage in leisure activities at baseline, participants who engaged in leisure activities were associated with an 18% lower risk of developing AD (RR 0.82, 95% CI 0.74–0.90, I^2 = 72.7%, p < 0.001; Figure 3). The subgroup analysis, including PA (14 studies), CA (4 studies), and SA (1 study), showed that the tendency was the same when examining the roles of PA and CA in the occurrence of AD (PA: RR 0.87, 95% CI 0.78–0.96, I^2 = 64.4%, p < 0.001; CA: RR 0.66, 95% CI 0.52–0.85, I^2 = 70.3%, p = 0.018; Figure 5;

Figure 4 Forest Plot of the Protective Role of Leisure Activities in the Risk of Vascular Dementia



The results are expressed as RRs and 95% CIs. RR = relative risk.

eFigure 2, links.lww.com/WNL/C200). Because of the limited number of studies (n = 1), no significant association was found between SA and the risk of AD (RR 0.89, 95% CI 0.63–1.26; Figure 5; eFigure 2). The meta-regression showed that types of leisure activities, number of participants, sex, age at baseline, follow-up duration, and WHO regional classification were not significantly associated with incidence of AD (eTable 6).

Leisure Activities and VD

The overall weighted RRs for associations between leisure activities and VD are shown in Figure 4. Nine articles that included 40,600 participants (mean age: 47.20–74.80 years) at baseline and 1,423 VD cases during follow-up (3.00–44.00 years) evaluated the role of leisure activities in incident VD.[16-18,31,34,36,43,46,e52] We found that participants who engaged in leisure activities were associated with a 0.68-fold lower risk of VD compared with participants who did not engage in leisure activities (RR 0.68, 95% CI 0.54–0.86, I^2 = 61.8%, p = 0.007; Figure 4). The subgroup analyses of PA (9 studies) showed that participants who engaged in PA were associated with a lower risk of VD compared with participants who did not engage in PA (RR 0.67, 95% CI 0.53–0.85, I^2 = 61.5%, p = 0.008; Figure 5; eFigure 3, links.lww.com/WNL/C200). With regard to the relationship between CA and VD risk, only 1 study found that CA was not significantly associated with development of VD (RR 0.98, 95% CI 0.44–2.18; Figure 5; eFigure 3). No study evaluated the relationship between SA and incident VD. The meta-regression showed that types of leisure activities, number of participants, sex, age at baseline, follow-up duration, and WHO regional classification were not significantly associated with occurrence of VD (eTable 6).

Publication Bias and Sensitivity Analysis

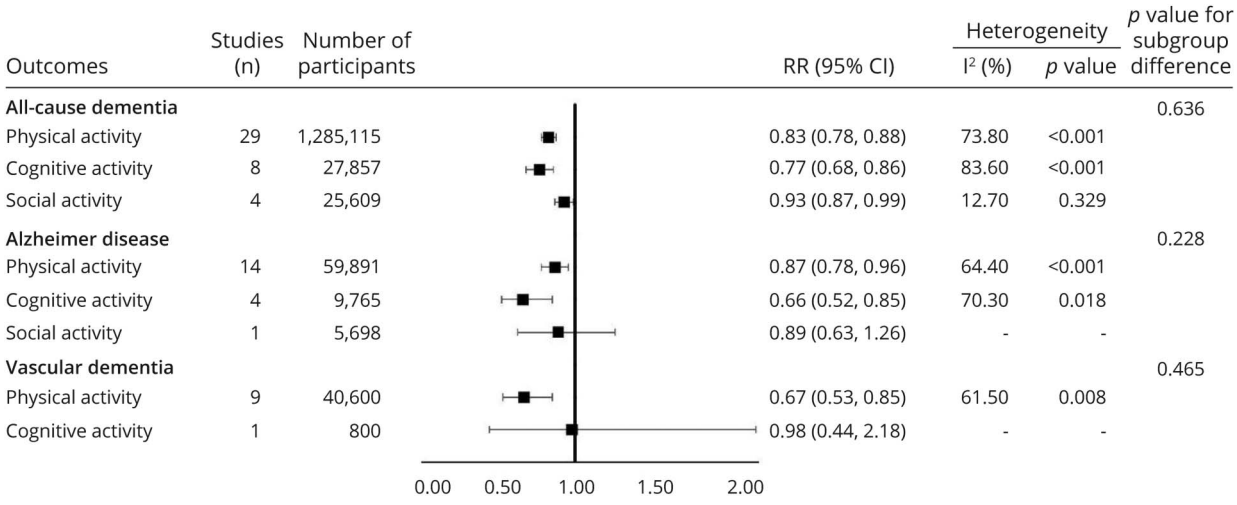
eFigure 4 (links.lww.com/WNL/C200) presented funnel plots of the meta-analyses of the roles of leisure activities in incident ACD, AD, and VD. Publication bias assessed using Egger tests was found when evaluating the relationships between leisure activities and incident ACD and AD, indicating that there was a selective publication, and some negative results might be underreported (eFigure 5). To investigate the effect of any 1 study on the overall results, sensitivity analysis was performed. No change in the direction of the results was found after excluding any single study (eFigures 6 and 7).

Discussion

The present meta-analysis comprehensively and quantitatively assessed the association between different types of leisure activities and the risk of ACD and its 2 major subtypes, AD and VD, based on studies with large sample sizes. We found that leisure activities were significantly associated with a lower risk of incident ACD, AD, and VD, even after adjusting for confounding factors. PA was inversely associated with a risk of ACD, AD, and VD. CA was in relation with a reduced risk of ACD and AD. SA was associated with a reduced incidence of ACD. These findings indicate the potential relationship between various types of leisure activities and different subtypes of dementia risk, with implications for future strategies that seek to prevent the incident dementia.

After pooling 2,154,818 participants at baseline and 74,700 ACD cases during follow-up from 38 articles, we found that participants who engaged in leisure activities were associated with a 0.83-fold lower risk of incident ACD. Leisure activities were in relation with a decreased risk of AD and VD. Leisure activities are generally modifiable factors. Based on the

Figure 5 Subgroup Analysis of the Protective Role of Different Types of Leisure Activities in the Risk of All-Cause Dementia, Alzheimer Disease, and Vascular Dementia



RR = relative risk.

findings, some measures may be considered to decrease the incident dementia. Our results are consistent with previous meta-analyses,[41,e56,e57] but these previous studies did not consider the relationship between different types of leisure activities and dementia risk. Because different types of leisure activities may have distinct influences, we classify leisure activities into PA, CA, and SA and discussed the unique possible influence of each activity on dementia. Furthermore, we focus on the 2 most prevalent dementia subtypes to determine the associations between different types of leisure activities and AD and VD. This study provides a comprehensive synthesis of 3 types of leisure activities and ACD and its 2 subtypes, AD and VD, for the development of early and effective management strategies and policies for the prevention of dementia. In addition, this study not only provides an update to previous meta-analyses in this field but also uses a unified selection criteria and quality assessment for different types of leisure activities to reduce heterogeneity and ensure the robustness of epidemiologic evidence and quantitative estimation.

Many studies have assessed the association between PA and the risk of developing dementia. Our results are consistent with previous studies and provide further evidence of the correlation between PA and incident ACD and its 2 subtypes, AD and VD.[7,15,17,18,20,27,29,31,34-38,42,43,45,e51,e52,e54] Fibronectin type III domain-containing protein 5 (FNDC5)/irisin was found to be reduced in AD patients and in AD experimental models, and PA might rescue synaptic plasticity and memory deficits, important factors in the dementia process, by the mediation of FNDC5/irisin.[e58] A previous meta-analysis showed that PA was associated with a lower risk of AD compared with ACD and VD.[e57] Evidence from animal and human studies suggests that PA is related to lower levels of brain β-amyloid plaques and tau proteins, which have been implicated in the progression of AD.[e59-e62] PA is also beneficial for attenuating β-amyloid–related gray matter volume loss in the brain, ameliorating impairments in hippocampal neurogenesis and plasticity, and lowering oxidative stress.[e63-e67] Long-term PA was reported to be associated with improvement on cognitive function with increased hippocampal brain-derived neurotrophic factor (BDNF) and synaptophysin.[e63] With regard to VD, the association between PA and the lower risk of VD is consistent with previous studies.[17,31,e52] A meta-analysis showed that the increased risk of dementia was related to physically inactive individuals with cardiometabolic disease.[14] Moreover, previous studies found that PA decreased the risk of vascular and metabolic adverse events, enhanced insulin sensitivity, increased BDNF levels, and increased hippocampus volume.[e68-e71] A recent study showed that PA benefited the brain by increasing clusterin and decreasing neuroinflammation in patients with cognitive impairment.[e72] However, detailed relationships between PA and the incidence of AD and VD and the associated mechanisms need further exploration.

CA is different from PA, although it was still shown to be related to decreased incidence of ACD and AD. CA helps maintain and improve cognitive skills, such as memory, processing speed, thinking, and reasoning skills. Many studies have confirmed the beneficial role of CA in preventing dementia, even after controlling for vascular risk factors, depressive symptoms, and physical functioning.[5,6,20,e53] A large-sample cohort study that included 15,582 participants (aged 71–77 years) and a 5.0-year median follow-up time showed that CA was linked to a 29% lower risk of dementia.[20] CA has been found to modulate disease progression and increase hippocampal neurogenesis by upregulating neurotrophins

and BDNF in mutant mice with AD-like pathology.[e73] A systematic review of diffusion tensor imaging in middle-aged adults showed that cognitive training was effective against age-related frontal and medial white matter microstructural decline.[e74] Moreover, previous studies have shown that CA is more related to mental stimulation than PA and SA and may enhance the survival of hippocampal neurons and lead to better cognitive performance.[e75-e77] However, because of the limited number of studies that were included in the present meta-analysis, we cannot exclude the possible role of CA in the development of VD. Furthermore, watching television was defined as a CA in 3 of 9 studies that investigated the correlation between CA and dementia included in this meta-analysis.[6,20,48] This broad definition may contribute to a bias because watching television may be insufficiently stimulating to promote cognitive performance,[e78] and the effect of watching television needs to be further investigated by strictly designed large-scale clinical trials. A more stringent definition needs to be used in further studies when investigating the association between CA and dementia.

SA was also associated with a decreased incidence of ACD, although this finding was based on only 4 studies. However, this finding was inconsistent with the results of 2 cohort studies.[6,20] This discrepancy may be attributable to the relatively low number of studies. The protective effect of SA on cognitive function may be associated with the enhancement of social contact and emotional support and reduction of depression and stress.[e76,e79] However, socially active people tend to engage in more CA and PA, which are associated with a lower risk of ACD. Because the intercorrelation and complexity among different types of leisure activities were not clearly reported in most studies, we were unable to investigate the extent to which people engage in all 3 activities. Thus, ascertaining the real effect of SA on ACD may be difficult. Future studies should determine whether specifically SA plays a role in preventing ACD. Moreover, the association between SA and incident AD and VD is still unclear. Only one such study was included in the present meta-analysis, and no significant relationship was found between SA and AD.[6] The finding of the effect of SA on dementia prompts the importance of implementation of SA for public health of the elderly especially in the context of coronavirus disease 2019 pandemic and quarantine strategy. Further studies should investigate the relationship between SA, especially social communication, and the development of AD and VD.

The present meta-analysis benefited from a large sample size and comprehensive examinations of the correlation between 3 types of leisure activities and ACD and its subtypes. However, our study has several limitations. First, self-reports via questionnaires and interviews were mostly used to assess leisure activities, which may lead to misestimation of the effects of leisure activities on dementia. Second, we did not analyze the effects of different levels (strenuous or frequent) of leisure activities on the risk of dementia because of the limited number of studies that met the selection criteria. Specifically defining different levels of PA, CA, and SA using uniform standards is difficult because the methods used to assess leisure activities were quite different among the original studies. Third, publication bias exists when evaluating the relationship between leisure activities and incident ACD and AD. This article was limited to longitudinal studies that were published in English, and research in other languages and gray literature were not captured, which may result in publication bias, meaning that the correlative inference is limited. Fourth, as over a third of the included studies had a follow-up of less than 6 years, many of the participants with dementia were likely to have undiagnosed early stage disease at the time of enrollmentin this study. Therefore, a longer follow-up period is needed to confirm the correlation between leisure activities and dementia in the future. Finally, leisure activities were divided into 3 different categories including PA, CA, and SA, and each of which also included different kinds of activities. Our analysis did not provide evidence of the association between each specific activity and dementia because of the limited number of studies.

In conclusion, the present meta-analysis found that leisure activities were significantly associated with a lower risk of incident dementia. Physical, cognitive, and social activities were inversely associated with incidence of ACD. The lower incidence of AD was significantly related to PA and CA, and individuals who engaged in PA were correlated to a relatively low risk of VD. Future studies should include large sample sizes and long follow-up time to objectively assess leisure activities based on standard methods to reveal further associations between leisure activities and incident dementia.

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Continued

Appendix *(continued)*

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Additional references e51–e79 available at Appendix (links.lww.com/WNL/C200)