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Review Article

Physical Activity for the Reduction of Alzheimer's Disease Risk in Women: A Scoping Literature Review

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Abstract

Background: Each year, twice as many women than men are diagnosed with Alzheimer's Disease (AD). As there is no known cure for AD, preventing it has become a vital public health issue. One lifestyle intervention that may reduce the risk of AD is physical activity (PA). This scoping review aimed to examine the existing literature on PA and AD risk to identify whether PA has a sex-specific effect on AD risk in women.
Methods: A scoping review was conducted based on PRISMA-ScR guidelines. Cochrane recommended databases, MEDLINE, Embase, and PsycINFO were searched via Ovid between May and June 2022. Articles were screened at the title, abstract, and full-text level for inclusion criteria (female participants, results reported by sex, PA, or exercise reported separately from other variables, and participants with no known cognitive impairment). For each study, sample characteristics, PA and AD measures, follow-up times, and results were summarized.
Results: Ten studies met the inclusion criteria, and their results were assessed for quality using the Cochrane GRADE tool. Most studies (80%) reported significant results for females. When broken down by sex, six studies reported differences in result significance with some studies finding that PA can reduce AD risk in women but not in men. Increased weekly PA sessions, duration, and intensity all significantly reduced AD risk for women.
Conclusion: While there are some limitations, including reliance on self-report, short follow-up times, and variations in AD and PA measures, the results have important implications. Findings may facilitate the development of tailored interventions that target women with unique lifestyle recommendations and inspire future research on the specifics of PA type, timing, and duration.

Keywords: Alzheimer, Physical activity, Women, Exercise, Cognitive decline

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1. Introduction

Twice as many women as men are diagnosed with Alzheimer's Disease (AD) globally each year (1). This disparity is seen worldwide and is often attributed to the fact that women, on average, live longer than men (2). However, emerging evidence suggested that sex-specific clinical, medical, hormonal, and lifestyle factors contribute to this disparity (3, 4). Living with AD has a significant impact on an individual's quality of life and that of their wider community, as the inevitable loss of independence means that most AD patients require full-time care (5). Furthermore, individuals living with AD are more likely to experience burdensome comorbidities such as hypertension, sleep disorders, diabetes, cardiovascular disease, and depression, which are some of the most prevalent and costly public health concerns (6). As a result, AD has a significant economic impact, with the global cost expected to surpass 2 trillion dollars by 2023 (7, 8). With no known cure, preventing AD in high-risk populations, such as women, is an important public health issue (9). One lifestyle intervention that may not only reduce the risk of AD but also alleviate symptoms in those already living with the disease is physical activity (PA) (10-12). To date, most of the research has not been sex-specific, and there have been limited reviews published on the topic (13).

1.1. Existing Evidence Base

A pivotal paper by Barnes and Yaffe, published in 2011, found that half of the world's AD cases could be attributed to seven modifiable lifestyle factors: diabetes, midlife hypertension, midlife

obesity, smoking, depression, cognitive inactivity or low educational attainment, and physical inactivity (14). Using population attributable risk and worldwide prevalence estimates of modifiable risk factors, the study was replicated in 2014, and it was concluded that up to one-third of worldwide AD cases may be linked to these seven risk factors (15). Of these seven factors, physical inactivity was found to be the major contributor to AD cases in Europe, the UK, and the USA.

1.2. Systematic Reviews on PA and AD

The few published reviews on PA and AD have generated mixed results and are limited by underpowered studies, a lack of longitudinal studies, and short follow-up times, which is particularly problematic given AD's long latency period. While some reviews did not report a link between PA and AD risk, two reviews concluded that PA significantly reduced AD risk (13, 16-18). However, the type of PA appeared to be important; with leisure-time PA was found to reduce AD risk, but work-related PA did not have the same effect. Results reported in the existing reviews did not report sex-specific findings.

1.3. The Impact of PA on Women's AD Risk

There is extremely limited evidence that isolates PA's impact on women's AD risk. Research that explored this link by sex is imperative not only due to the disparity in diagnosis but also because there is evidence indicated PA may have the ability to slow cognitive decline, often a precursor to AD, at a greater rate in women compared to men (19, 20). There have been only large sample, long-duration studies conducted on women's PA in mid-life and cognition in late life. The first study found, after following 15,000 participants over 25 years, that those with higher levels of PA experienced slower cognitive decline in their 70s (21). The second study followed 18,000 women for 15 years and found a significant association between lower cognitive impairment and greater PA (22). While these studies demonstrated the potential impact PA interventions may have on women's cognition and AD risk, both studies rely heavily on self-report data, include a variety of PA types, and are not specific to the diagnosis of AD.

1.4. Justification for Research

Alzheimer's disease (AD) is the most common form of dementia and the fifth leading cause of death for women globally. The World Health Organization has identified AD as a priority public health issue (23). Although there is no cure for AD, lifestyle interventions such as physical activity (PA) have been shown to reduce the risk or delay the onset of symptoms (10-12). However, most research on PA and AD risk reduction was generalized to entire populations, with results not reported by sex, despite women being more likely to be affected by the disease (13). Based on the literature search, no scoping review has been conducted on PA and AD risk reduction specifically for women, who are the most at-risk population. Therefore, looking at the impact of PA on women's AD risk in isolation is essential, given that sex-based physiological differences can facilitate unique cognitive risks, as well as previously reported sex-unique responses to PA interventions. This study aimed to explore whether PA reduces women's risk of AD and identify whether increased weekly PA sessions, duration, and/or intensity significantly impact AD risk.

2. Methods

To provide the first comprehensive summary of all available literature, a scoping review was conducted following the 2018 *Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist* (24). By conducting a rigorous scoping review, we formed a collection of evidence, identified common limitations among the evidence base, and evaluated and compared findings. The resulting information can be used to inform data-driven and actionable findings that clinicians, policymakers, and other key stakeholders can use to make decisions tailored to the target population.

2.1. Search Terms and Inclusion Criteria

We searched Cochrane recommended databases including MEDLINE, Embase, and PsycINFO via Ovid for English language, peer-reviewed, human, primary research using the logic: "Exercise" OR (Physical Activity OR Physical Fitness) OR "Active" AND "Prevent" OR "Risk" AND "Alzheimer*" AND (Wom*n OR Female) (25). We required all studies to be available in full-text form, have female participants, report results by sex, report PA or exercise separately from other variables, and include participants with no known cognitive

impairment. Given the inconsistencies between PA and exercise definitions, we used the WHO definition of "any bodily movement produced by skeletal muscles that requires energy expenditure" for inclusion (26). To ensure completeness, we manually inspected the Alzheimer's Association websites of USA and UK, as well as Google Scholar and the reference lists of other literature reviews for additional studies.

2.2. Methods of Data Extraction and Review

The search strategy was carried out twice, two weeks apart, on May 25, 2022, and June 8, 2022. The process was documented according to the PRISMA guidelines (Figure 1) (27). After retrieving the search results, duplicates were removed manually and by using Ovid's deduplication tool. Titles were then evaluated, and the abstracts of selected studies were appraised for inclusion criteria. Sample and population characteristics, PA and AD measures, follow-up times, and the results of each study were summarized in tables (Tables 1 and 2). The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) tool, as recommended in the Cochrane guidelines, was used to assess the quality of the findings of each included study (Table 3). GRADE is a systematic approach to rate the certainty of evidence included in reviews (25). There are five GRADE criteria that impact confidence in the effect estimate of a study: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The first criterion risk of bias specifically assesses methodological quality, including study design and methodological quality (25). For each of these criteria, the quality of the evidence is expressed as either high, moderate, low, or very low (25).

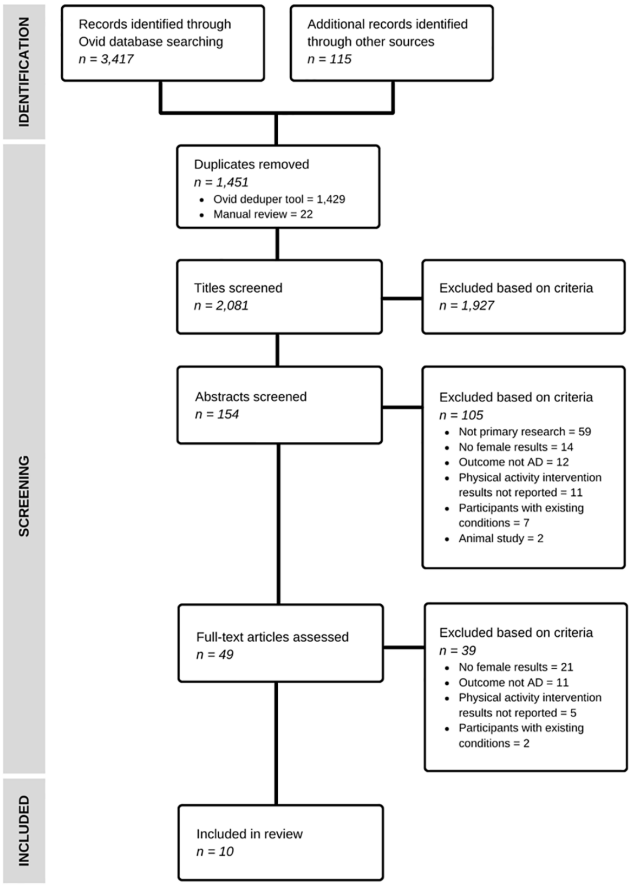

Figure 1: The figure shows the PRISMA flow diagram outlining the literature search.

3. Results

The initial search returned 3,532 results. Titles and abstracts were screened, with 49 articles being examined in full. Ten studies were included in the review. Participants in all studies were recruited from North America and Europe, with sample sizes ranging from 86 to 37,524, and follow-up times from 1.8 to 44 years. The findings of six studies were determined to be of moderate quality based on the GRADE criteria (Table 3). As there is no single conclusive test for AD, as seen in other AD-related reviews, measures varied, with a combination of biomarkers or standardized tests to be used (28). Three studies used the National Institute of Neurologic and Communicative Disorders and Stroke, and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria. Others used doctor diagnosis or AD biomarkers, including hippocampal volume and grey matter. PA was also measured in a variety of ways, including self-report questionnaires, professionally-administered exercise tests, and daily steps. The type of PA varied between studies and was often not explicitly reported; hence it could not be compared. Results of included studies are shown in Table 3, with eight studies (80%) reporting significant results for female participants. Most commonly, the impact of PA on AD risk was reported using Odds or Hazard Ratios. Three core themes emerged from the results including sex disparities in result significance, PA intensity and duration, and the number of PA sessions per week.

3.1. Result Significance by Sex

Six studies reported differences in result significance by sex. Dougherty and colleagues

Table 1: Population characteristics and measures of included studies

ID	Study title (author, year)	Population and sample size	Follow up	Physical Activity measures	Alzheimer's Disease measures
1	Associations between vigorous physical activity and chronic diseases in older adults: a study in 13 European countries	37,524 individuals over the age of 50 from 13 Scandinavian and Mediterranean countries (43.2% male, 56.8% female)	2 years	Self-reported vigorous physical activity (VPA) frequency (more than once week, once a week, up to 3 times a month, hardly ever or never)	Doctor diagnosis of AD
2	Physical activity and risk of cognitive impairment and dementia in elderly persons	4,615 individuals 65 and older from the Canadian Study of Health and Aging (39.6% male, 60.4% female)	5 years	Self-report risk factor questionnaire about lifestyle factors including PA	AD according to NINCDS-ADRDA criteria
3	Relationships between cardiorespiratory fitness, hippocampal volume, and episodic memory in a population at risk for Alzheimer's disease	86 American enrolees from the Wisconsin Registry for Alzheimer's Prevention (38.4% male, 61.6% female)	N/A	Exercise tests conducted by a certified exercise physiologist and trained exercise specialist measured with an ECG assessment	Hippocampal volume derived from an MRI and the Rey Auditory Verbal Learning Test
4	Physical Activity, Including Walking, and Cognitive Function in Older Women	18,766 American females aged 70 to 81 years from the Nurses' Health Study	Mean 1.8 years (SD 0.4)	Self-reported time spent per week during the past year doing various leisure-time physical activities	Combined immediate and delayed recalls of the EBMT and TICS 10-word list via telephone interviews
5	Cognitive and physical activity and dementia: A 44-year longitudinal population study of women	800 Swedish females aged 38 – 54 years at the beginning of the study	44 years	Saltin-Grimby Physical Activity Level Scale	AD according to NINCDS-ADRDA criteria
6	Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease	1,449 Finnish individuals aged 65 – 79 years (44.3% male, 55.7% female)	Mean 21 years (SD 4.9)	Self-reported frequency of leisure-time physical activity lasting 20-30 mins causing breathlessness and sweating	AD according to NINCDS-ADRDA criteria
7	Leisure-time physical activity from mid- to late life, body mass index, and risk of dementia	3,559 Finnish individuals aged 65 – 79 at time of follow up (45.2% male, 54.8% female)	28 years	Self-reported time spent per week during the past year doing various physical activities	Special Reimbursement Register for all Finnish residents to verify an AD diagnosis or AD medication prescription
8	Fitness, independent of physical activity is associated with cerebral blood flow in adults at risk for Alzheimer's disease	100 American participants from the Wisconsin Registry for Alzheimer's Prevention (37% male, 83% female)	N/A	Maximal exercise test and steps monitored by an accelerometer worn during all waking hours for one week	Cerebral blood flow (CBF) measured via an MRI
9	Impact of cardiovascular risk factors on cognitive function: The Tromsø study	5,033 stroke free Norwegians aged 55 – 74 (44.2% male, 55.8% female)	7 years	Self-reported hours of light and hard physical activity performed during the week	Three standardized tests, Twelve Word Memory Test, Digital-Symbol Coding Test, and Tapping Test
10	Low-intensity daily walking activity is associated with hippocampal volume in older adults	92 Americans over the age of 60 recruited from the Brain Health Study (36% male, 64% female)	N/A	Daily steps measured using an accelerometer worn for three to seven days	Hippocampal atrophy as determined by an MRI

AD: Alzheimer's Disease

reported non-significant results overall; however, when stratified by sex, cerebral blood flow (CBF) was significantly associated with hippocampal volume for women (P=0.02) but not men (P=0.94) (29). A 2020 study, also by Dougherty and colleagues, found that fitness was significantly associated with greater CBF for women (P=0.01) but not men (30). Consistent results were seen for other AD and PA measures. A 2011 study by Arntzen and co-workers found that PA was significantly associated with verbal memory (P=0.01) and improved performance on a coding test (P=0.05) for women, but results were not significant on either test for men (31). Laurin and colleagues found that self-reported PA was significantly

Table 2: Significance of findings from included studies

ID	Significant for entire sample	Significant for female participants	Difference in significance between sexes	Findings summary
1	Yes	Yes	No	Vigorous physical activity (VPA) significantly reduced the risk of AD in both men and women in cross sectional and prospective analyses. VPA had a similar effect for men and women when done once a week but had a greater effect for women when done more than once a week (OR=0.25, 95% CI 0.12-0.52).
2	Yes	Yes	Yes	PA was significantly protective for women (P=0.05) but not men (P=0.62). More PA sessions (3 or more exercise sessions per week at a greater intensity than walking) was most effective for reducing AD risk for women (OR=0.27, 95% CI 0.08-0.90).
3	No	Yes	Yes	Across the full sample, PA was not significantly associated with hippocampal volume (P=0.25). However, when stratified by sex, CBF was significantly associated for women (P=0.02) but not men (P=0.94). The inverse was found for memory scores, the relationship was significant for men (0.05) but not women (P=>0.05).
4	N/A	Yes	N/A	Significant association between higher scores on cognitive measures and higher levels of long-term PA (P<0.001), women in the highest quintile of PA had 20% lower odds than women in 5th lowest quintile (OR=0.8, 95% CI 06.67-0.95). Excluding women who also participated in VPA, those who walked more had significantly higher scores on 4/5 cognitive tests the more hours they walked per week.
5	N/A	No	N/A	Midlife PA was not significantly associated with risk reduction of later life AD (HR: 0.97, 95% CI 0.55-1.70).
6	Yes	Yes	No	PA had a significant effect for both men (OR: 0.32, 95% CI 0.09-1.12) and women (OR: 0.43, 95% CI 0.14-1.28).
7	Yes	No	Yes	Leisure-time PA during midlife was not significantly associated with AD in women (HR: 1.00, 95% CI 0.73-1.36), however it was in men (HR: 1.76, 95% CI 1.12-2.78).
8	Yes	Yes	Yes	Results are sex dependent, fitness is significantly associated with greater CBF for women (P=0.01), however, PA was not significant (P=0.57). Neither fitness nor PA were significant for men.
9	N/A	Yes	Yes	PA was significantly associated with verbal memory (P=0.01) and improved performance on a coding test (P=0.05) for women, but the results were not significant for men. Results were not significant for either sex on the tapping test.
10	N/A	Yes	Yes	Greater walking levels had a significantly protective effect on hippocampal volume for women (P=between<0.01 and 0.02), however, walking did not have significant effect for men. An additional 1000 low-intensity steps/day or 10 minutes of walking were both significantly associated with larger hippocampal volume for women.

AD: Alzheimer's Disease; PA: Physical Activity; CBF: Cerebral Blood Flow; OR: Odds Ratio; HR: Hazard Ratio

Table 3: GRADE quality assessment of findings of included studies

ID	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall GRADE level of certainty*
1	High [ac]	Low	Low	High [ac]	Low	Moderate
2	High [ac]	Low	Low	High [ac]	Low	Moderate
3	High [bde]	Moderate [f]	High [de]	Moderate [b]	Low	Low
4	High [abe]	Low	Moderate [e]	Moderate [a]	Low	Low
5	Low	High [g]	Low	Low	Moderate [h]	Moderate
6	Moderate [a]	Low	Low	Moderate [a]	Moderate [h]	Moderate
7	Moderate [a]	High [g]	Low	Moderate [a]	Low	Moderate
8	High [bde]	Low	High [de]	Moderate [b]	Moderate [h]	Low
9	High [ace]	Low	Moderate [e]	Moderate [a]	Low	Moderate
10	High [bde]	Low	High [de]	Moderate [b]	Low	Low

GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; *GRADE four levels of certainty: very low, low, moderate, and high (Higgins et al., 2022); [a]Self-reported data; [b]Small sample size; [c]Short follow up time; [d]Fitness, not PA measured; [e]AD indicated by biomarkers or standardized tests rather than NINCDS-ADRDA criteria or doctor diagnosis; [f]Non-significant result overall; [g]Non-significant result for female participants; [h]Limited reporting of findings

protective for women (P=0.05) but not men (P=0.62) according to AD diagnosis based on the NINCDS-ADRDA criteria (32). Varma and colleagues measured PA by monitoring daily steps and found that daily walking was significantly protective for women across all models (P=between<0.01 and 0.02) based on MRI-measured hippocampal volume; however, results were not significant for men (33). Two studies reported contrasting results, with self-reported leisure-time PA significantly associated with reducing the risk of AD in men but not women (34, 35). Two studies did not report any significant difference between sexes (36, 37).

3.2. Physical Activity Intensity

Two studies have examined the impact of physical activity (PA) intensity on the risk of developing Alzheimer's disease (AD). Laurin and co-workers reported that engaging in "high physical activity" (three or more exercise sessions per week at a greater intensity than walking) was the most effective at reducing the risk of AD for women (OR=0.27, 95% CI 0.08 - 0.90) (32). Weuve and colleagues found that higher levels of PA intensity significantly reduced the risk of AD for women (P<0.001) (22). Women who engaged in the highest level of PA intensity had 20% lower odds of developing AD compared to women with the lowest level (OR=0.8, 95% CI 0.67-0.95).

3.3. Physical Activity Duration

Four studies have reported the effect of PA duration on AD risk. Arntzen and colleagues found a similar protective effect for PA resulting in sweating and being out of breath for one hour per week as PA without sweating or being out of breath for three hours a week (31). Weuve and co-workers also found that those who walked for longer durations scored significantly higher on four out of five cognitive tests (22). Comparable results were reported by Varma and colleagues, with an additional 10 minutes per day of walking significantly associated with a 0.02 cm3 increase in hippocampal volume (F (9, 52)=5.57; R2=0.49; t=2.44; P=0.02) (33). Only one study by Tolppanen and co-workers found that PA duration did not impact AD risk in women (34).

3.4. Number of Physical Activity Sessions per Week

Two studies have investigated the relationship between AD risk and the number of discrete PA sessions per week. Marques and colleagues identified a significant effect of PA on AD risk for both male and female participants who participated in one PA session per week (36). However, participation in more than one session per week was only significant for women, not men, in both cross-sectional (OR=0.25, 95% CI 0.12 - 0.52) and prospective analyses (OR=0.43, 95% CI 0.27 - 0.69). Varma and colleagues also found an association between increased walking sessions per week and AD risk, with one additional 10-minute session significantly increasing hippocampal volume by 0.04 cm3 (F (9, 52)=5.54; R2=0.49; t=2.50; P=0.02) (33).

4. Discussion

The primary aim of this study was to conduct the first scoping review exploring the impact of physical activity (PA) on Alzheimer's disease (AD) risk in women. The review found that, in most studies (80%), PA had a significant impact on AD risk reduction for women, even when there was no significant result reported for male participants or the study overall (29-33). The secondary aim of the study was to identify if increased weekly sessions, duration, and/or intensity of PA significantly influenced the effect size of PA on AD risk. All were found to have a significant impact for women, with greater sessions, duration, and intensity further reducing AD risk. Furthermore, in some studies, findings were only significant for female, but not male participants. Significant findings were found on a variety of AD measures and for different forms of PA, both self-reported and professionally observed.

These results mirror the findings of multiple existing studies, which found that PA reduced women's AD risk (19-22). However, as was the case in previous reviews on PA and AD, there were some mixed results, and two of the studies included in the review did not report a significant effect for PA on AD risk for women (34, 35). Additionally, as was commonly omitted in a majority of the existing literature, the results of this review were not able to provide substantial insight into how specific types of PA and their timing may impact AD risk (13, 16). Moreover, most included studies did not stipulate which form of PA participants took part in and did not report results broken down by PA type. However, one distinct parallel between the existing literature and this study's findings was

that leisure-time, but not work-related, physical activity appears to reduce AD risk (13, 16, 34). Furthermore, the findings of the current study suggested that PA may have a unique protective effect on women, justifying the need to look at the impact of AD protective factors by sex to better understand how to mitigate risk and reduce the burden of the disease. This is particularly prudent given the diagnosis disparity between sexes. This sex-specific response to PA interventions was seen in previous literature and provides a promising area for future research (19, 20).

The main strength of the review was its focus on data specifically examining the effect of physical activity (PA) on Alzheimer's disease (AD) risk for female participants, a relationship that has historically been neglected. The review was conducted based on the PRISMA guidelines, which are evidence-based minimum standards; most studies (60%) were of moderate quality, as determined by the GRADE tool (25, 27). Additionally, despite there is no a universal diagnosis measure for AD or PA, all studies used well-justified, evidence-based, valid, and reliable measures.

However, the review was limited by multiple factors, including the reliance on self-report data, short follow-up times, a lack of information about the type and timing of PA, and limited inclusion of anatomical structures that play a role in memory. Four of the included studies were deemed to be of low quality based on the GRADE tool assessment (27). Furthermore, study participants were not representative of the global population, with all participants of included studies coming from North America and Europe. This is the case for much of the existing research on this topic, with limited research including participants from other parts of the world. Moreover, the review only included studies where diagnosed AD, or an AD measure was used as the outcome. There was a huge amount of identified research that could have been added to the depth of this review if mild cognitive impairment (MCI) (often the precursor to AD) or dementia (the umbrella term under which AD falls) were also included as outcome measures (they were omitted as this review only included studies where AD was the outcome variable).

Another key limitation is the limited acknowledgement of the varied anatomical structures of the brain that play a role in memory. The hippocampus was the only structure included in any of the studies; therefore, the only structure that can be compared between sexes. Key structures that play a role in memory, including the amygdala, cerebellum, nucleus of Meynert, Papez Circuit, and the Fornix, were notably absent from the literature. Further research that includes the diverse brain structures involved in memory is needed.

The implications of this study are varied. It is the first known review to suggest that physical activity (PA) may have sex-based differences in its ability to reduce the risk of Alzheimer's disease (AD). This research may facilitate the development of interventions that specifically target women with unique lifestyle recommendations to reduce their risk of AD and policies that facilitate PA. These interventions and policies may lead to significant public health implications as well as an increased quality of life for those who are at risk of or live with an AD diagnosis. One successful intervention that was used to promote PA specifically to women was the 2010 National Physical Activity Plan which utilized social media marketing to promote the benefits of PA (38). Furthermore, policies including provision for physical activity counseling in healthcare settings and transportation policies that allow safe and affordable active transportation for women have proven effective in promoting PA (39). Such policies and interventions have been successfully adopted in a number of countries, including USA, Australia, and the UK (40, 41).

Reducing the incidence of AD also has economic and social benefits, a particularly important point given the increasing pressures on society due to the aging population. In terms of future research, considering the significant findings for sessions per week, intensity, and duration, this study may also encourage future research into how women can tailor their participation in PA throughout their lives to reduce the risk of AD. As already mentioned, this review highlights the need for specific research into the type and timing of PA as this is unclear in the current literature. The study could also lay the foundation for future sex-specific studies into other lifestyle factors that may reduce the risk of AD. Diet, social interaction, and education may all have potentially unique outcomes for women.

Overall, this study provides important insights into the potential sex-based differences in the

relationship between PA and AD risk reduction. By developing targeted interventions and policies, we may be able to reduce the burden of AD on individuals and society as a whole.

5. Conclusion

Physical activity (PA) may have a unique and significant impact on reducing the risk of Alzheimer's disease (AD) in women. Given that two-thirds of those diagnosed with AD are women, this is valuable information that could have economic and social impacts, as well as the potential to improve the quality of life for countless women. While the current research has limitations, including reliance on self-report data, short follow-up times, and limited information about the type and timing of exercise, as a first-of-its-kind review, the implications of the largely significant findings are widespread. The results may inspire the development of interventions that specifically target women with unique lifestyle recommendations to reduce their risk of AD. Ultimately, it is recommended that this review be used as a starting point to facilitate focused research on the type and timing of PA, as well as follow-up studies that expand on the female-specific data included.

Ethical Approval

In line with scoping review best practices, prior to the commencement of the review, the method was carefully reviewed for any selection bias, and all inclusivity criteria were transparently outlined for reference throughout the process additionally, papers were reviewed with the limitations of comparable scoping reviews in mind, including short follow-up times, small sample sizes, difficulty retaining participants, and variations regarding the definition of PA. Further, any identified bias and ethical insufficiencies in the studies were considered to ensure that compromised results were not republished.

Conflict of Interest: None declared.

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