Identifying the Modifiable Risk Factors for Alzheimer's Disease in Older Adults

A Literature Review

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Research Question: What are the modifiable risk factors that contribute to developing Alzheimer's disease in older adults?

Abstract

Alzheimer's disease is becoming increasingly common worldwide. This disease, which affects cognitive function and progressively worsens over time, currently has no cure. Ongoing research is uncovering various factors that contribute to the development of this disease. This literature review examines information from 10 relevant articles selected from the Web of Science and PubMed databases. Each article focuses on a different modifiable risk factor linked to the development of Alzheimer's disease. The review highlights the potential role of these factors in prevention and early intervention. The identified risk factors discussed within the literature fall into two main categories: lifestyle factors and health factors. Lifestyle factors include a wide range of topics divided into two sections: sleep and mindfulness as well as diet and exercise, and mindfulness practices. Health factors include various medical conditions, such as chronic obstructive pulmonary disease (COPD) that can negatively affect the progression and development of Alzheimer's disease. Additionally, the review discusses biomarkers, a newly researched area that is shown to indicate levels of cognitive function. This review emphasizes the importance of addressing these factors to potentially mitigate the impact of Alzheimer's disease.

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Introduction

According to the World Health Organization, over 55 million people have dementia worldwide and there are 10 million new cases each year (*Dementia*, 2023). Dementia is the seventh leading cause of death and is a major cause of dependency globally (*Dementia*, 2023). Dementia describes the severe loss of cognitive ability that interferes with daily life (*What is dementia?*, 2024). Dementia is not a single disease but is an umbrella term describing the symptoms of many diseases (*What is dementia?*, 2024). Alzheimer's is the most common form of dementia accounting for 60-80% of cases (*Dementia*, 2023). Alzheimer's is a progressive and fatal brain disease that slowly impairs brain function ("2024 Alzheimer's disease facts and figures," 2024). This disease significantly impacts quality of life and places a huge financial burden on individual families and the economy. Despite having financial assistance from Medicare or other insurance, the out-of-pocket costs are high ("2024 Alzheimer's disease facts and figures," 2024). Adults aged 70 to 80 with Alzheimer's spend 40% of their time in the severe stage, most of which is in a nursing home due to their severe dependence and disability ("2024 Alzheimer's disease facts and figures," 2024). It costs an estimated $240,046 to care for a family member with dementia in the last seven years of life ("2024 Alzheimer's disease facts and figures," 2024). This is almost double the cost for those without dementia paying $121,674 ("2024 Alzheimer's disease facts and figures," 2024). Furthermore, total annual healthcare costs in America for those with dementia are expected to reach $360 billion in 2024 and up to $1 trillion in 2050 ("2024 Alzheimer's disease facts and figures," 2024).

Alzheimer's is a leading cause of morbidity among older adults. Determining the exact number of deaths caused by it each year is challenging because cases are severely underreported ("2024 Alzheimer's disease facts and figures," 2024). For a death to be counted by the CDC as

related to Alzheimer's, it must be listed as the underlying cause of death ("2024 Alzheimer's disease facts and figures," 2024). The underlying cause of death is defined as the disease or injury initiating the events leading to death ("2024 Alzheimer's disease facts and figures," 2024). It is reported that 61% of people aged 70 with Alzheimer’s dementia are expected to die before 80 compared to 30% of those without the disease ("2024 Alzheimer's disease facts and figures," 2024).

Severe dementia leads to complications that increase the risk of life-threatening conditions ("2024 Alzheimer's disease facts and figures," 2024). The brain is the body's control center containing different areas that are responsible for various processes and body functions. Cognitive impairment caused by Alzheimer's and other dementia can result in issues such as immobility and swallowing disorders, increasing the risk of developing other serious conditions ("2024 Alzheimer's disease facts and figures," 2024).

A study found that for more than half of individuals with Alzheimer’s dementia, respiratory system diseases were their immediate cause of death ("2024 Alzheimer's disease facts and figures," 2024). Death certificates for those with Alzheimer’s often list other conditions as the primary cause of death ("2024 Alzheimer's disease facts and figures," 2024). As a result, it is hard to rely on death certificates alone to determine the rate of mortality for the disease. This issue is referred to as the blurred distinction between death with dementia and death from dementia” ("2024 Alzheimer's disease facts and figures," 2024). From 2000 to 2021, deaths from Alzheimer’s more than doubled, increasing by 141% ("2024 Alzheimer's disease facts and figures," 2024). The number one cause of death, heart disease, simultaneously decreased by 2.1% ("2024 Alzheimer's disease facts and figures," 2024).

Preventing this disease is important as it currently has no cure and is fatal. Although there is no proven way to prevent the disease, it is important to look at risk factors. Risk factors are characteristics that may worsen disease outcomes. Knowing these factors and making the adjustments through healthcare interventions could be the difference between life and death for many. Alzheimer’s disease is the fifth leading cause of death for adults 65 and older ("2024 Alzheimer's disease facts and figures," 2024). America's population is also currently aging, with the number of adults 65 and older expected to go from 58 to 82 million by 2050 ("2024 Alzheimer's disease facts and figures," 2024). This leaves much uncertainty about what care will look like, not only for Alzheimer’s but other chronic diseases. An older population indicates that there will likely be fewer people to provide care but more patients ("2024 Alzheimer's disease facts and figures," 2024). Older individuals tend to be at higher risk for many diseases which is why age tends to play a role in disease development ("2024 Alzheimer's disease facts and figures," 2024).

Research on Alzheimer’s disease is still ongoing, so the literature reflects current knowledge on identified risk factors. Most research is very specific to dementia or focuses on specific aspects of one risk factor at a time. Few studies focus on modifiable risk factors and their impact on disease onset. The author presents a literature review of journal articles from the databases PubMed and Web of Science. The study aims to identify the modifiable risk factors that contribute to Alzheimer’s disease development in older adults.

Methods

The ten articles used in this Literature review were gathered from PubMed and Web of Science. PubMed is a database created by the National Library of Medicine. It contains millions of peer reviewed biomedical and life science literature sources. The literature ranges from clinical studies to randomized controlled trials and it allows you to refine your search as needed. Web of Science is a database containing thousands of scientific and academic research journals on a range of different topics. Like PubMed, Web of Science also allows users to refine the search using various criteria. These databases were selected as they contained many research articles surrounding Alzheimer's and its risk factors which align with my research question. The selection process for the articles in this literature review is shown in *Figure 1*.

For PubMed, the first search term entered was "alzheimers disease" which produced 222,147 results. This search provided a wide range of articles on the broad topic and provided background information for the review. The second set of search terms entered were "alzheimers disease AND modifiable risk factors" which produced 2,168 results. This next search narrowed down the topic even further to the risk factors which are the focus of this review. The final set of search terms used were "alzheimers disease AND modifiable risk factors AND older adults" which produced 1,173 results. Six out of the 10 final articles used in this literature review were selected from the PubMed database.

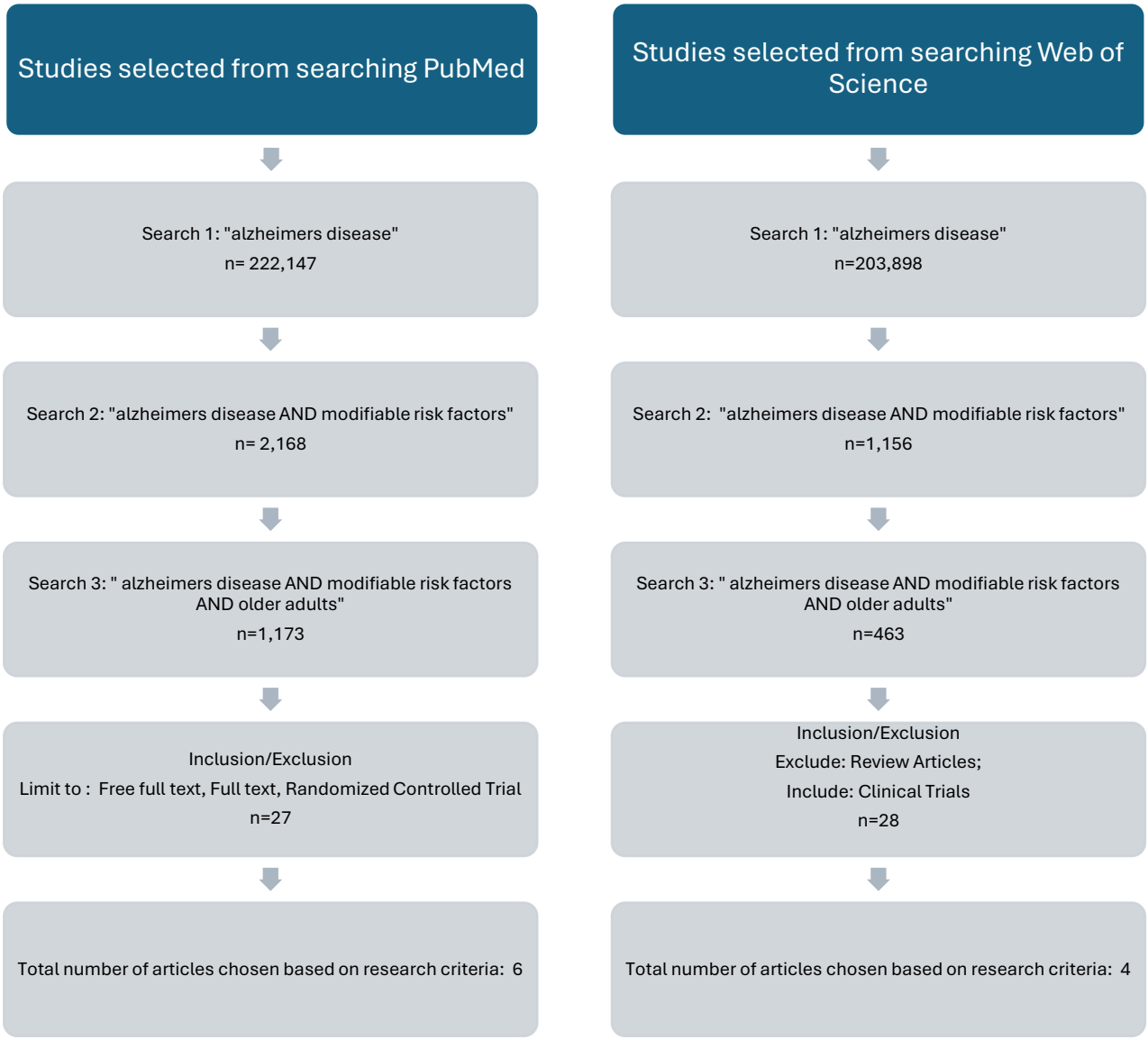
For Web of Science, the first search term was "alzheimers disease" which produced 203,898 results. The second set of search terms were "alzheimers disease AND modifiable risk factors" which produced 1,156 results. The final set of search terms used were "alzheimers disease AND modifiable risk factors AND older adults" and produced 463 results. This search provided me with research articles each focusing on a different modifiable risk factor. Four out

of the ten final articles used in this literature review were selected from the Web of Science database.

Inclusion/Exclusion Criteria

Alzheimer's is a broad topic with many different areas of research. The search terms included "alzheimers disease," "modifiable risk factors," and "older adults" for both databases to limit my results to articles on the modifiable risk factors particularly in older adults. For the PubMed database, the search was limited to including Free full texts and Randomized Controlled Trials producing 27 results. For the Web of Science database, the search was refined to include clinical trials and exclude review articles producing 28 results. It was important to include these two trial types to further narrow down to the relevant research articles. This review was intended to be on original research, so it was necessary to filter out articles reviewing various research sources.

Figure 1: Literature Review Article Selection Process



Results

Alzheimer's cases are currently on the rise, and there are many unanswered questions about the disease. It is important to better understand factors putting people at risk. Modifiable risk factors, which are habits or conditions that can be changed, are particularly important. The ten selected articles for this literature review provide information on specific modifiable risk factors and their impact on Alzheimer's in older adults. The identified risk factors are categorized into two main groups: lifestyle factors and health factors. Lifestyle factors cover a broad range of topics and are further divided into two sections: sleep and mindfulness, as well as diet and exercise. Health factors include preexisting conditions and medications which may also play a role in disease onset and progression. *Table 1* provides a more detailed summary of the ten articles reviewed.

Lifestyle factors: Sleep and Mindfulness

Most of the articles in this review conclude that making lifestyle changes is a way to reduce Alzheimer's severity. A person's diet, level of exercise, and even sleep patterns can be altered under proper guidance. Early intervention in these areas is most important as it is shown to likely delay the onset of Alzheimer's (Kilpatrick et al., 2023)**.** Yoga is one of the many physical activities that can easily be added to a daily routine. Yoga has been shown to benefit cardiorespiratory fitness and even blood pressure (Dougherty et al., 2017; Kilpatrick et al., 2023). Studies show that yoga can help improve cognitive functioning in older adults including those with dementia in the earlier stages (Kilpatrick et al., 2023). Regular yoga training is also shown to positively influence hippocampal volume, a brain area responsible for memory (Dougherty et al., 2017; Kilpatrick et al., 2023). Preserving hippocampal volume may be a

critical component of maintaining cognitive health and delaying the onset of Alzheimer's (Dougherty et al., 2017). Higher levels of general physical activity were also linked to larger volumes in the brain regions that process memory (Aslanyan et al., 2023). Loss of memory is a major Alzheimer's symptom that presents itself early on in disease development.

Sleep is another important factor shown to benefit individuals in earlier Alzheimer's stages (Aslanyan et al., 2023). Sleeping habits are important for maintaining health, as the lack of proper sleep negatively influences brain function ("2024 Alzheimer's disease facts and figures," 2024). Sleep studies have shown that those with sleep disturbances and disorders performed poorly on cognitive assessments and were at higher risk for Alzheimer's (Aslanyan et al., 2023). This study examined the effect of sleep duration and found it was associated with Amyloid Beta deposits (Aslanyan et al., 2023). Amyloid beta is part of the plaque that accumulates in the brains of individuals with Alzheimer's (Aslanyan et al., 2023). Therefore, improved sleep duration early on would reduce the deposition of Amyloid beta in the brain (Aslanyan et al., 2023). Longer sleep duration was also found to be associated with improved cognitive performance and larger brain regional volume (Aslanyan et al., 2023).

Lifestyle factors: Diet and Exercise

Another aspect of lifestyle includes a person's diet. A study examining the impact of multi-nutrients concluded that proper nutrient intake slows cognitive decline (Soininen et al., 2021). Participants in early Alzheimer's development were given a list of nutrients over the trial period and reportedly had a decline in the atrophy of the hippocampus (Soininen et al., 2021). The results of this intervention were improved with long-term use (Soininen et al., 2021). The more time an individual has spent receiving proper nutrition slows disease progression (Soininen et al., 2021).

Exercise is an important aspect of a healthy lifestyle (Arab et al., 2021). Research has shown that it can help protect against cognitive decline associated with aging (Arab et al., 2021). Exercise increases heart rate and enhances cardiovascular health which positively impacts cognition (Reynolds et al., 2023). Dementia typically begins to affect adults around the age of 80 (Arab et al., 2021). With the aging global population, maintaining cognitive health for this at-risk population is increasingly important. A study found that moderate-intensity physical activity leads to improved long-term cognitive outcomes (Arab et al., 2021). Older adults who participated in the study showed improvement in their baseline memory scores after the intervention (Arab et al., 2021). They engaged in physical activities such as gardening and walking three times a week over four years (Arab et al., 2021).

Studies indicate certain genotypes can impact an individual's susceptibility to Alzheimer's (Solomon et al., 2018). The apolipoprotein E(APOE) ε4 allele is the strongest known Alzheimer's disease risk factor (Solomon et al., 2018). It has also been linked to cognitive decline in individuals without dementia (Solomon et al., 2018). A multidomain intervention was conducted as part of a Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (Solomon et al., 2018). The intervention involved modifying diet and exercise alongside cognitive training (Solomon et al., 2018). The study concluded that healthy lifestyle changes are beneficial to reducing the onset of Alzheimer's (Solomon et al., 2018). This is also true for those with the APOE ε4 gene (Solomon et al., 2018).

Health Factors

Some articles reviewed showed how preexisting health conditions could impact cognitive function. One of which is Chronic Obstructive Pulmonary Disease or COPD, a progressive but treatable disease of the lungs that limits airflow (Singh et al., 2014). This disease has been shown

to predispose patients to the risk of cognitive impairment (Singh et al., 2014). Individuals with a COPD duration longer than 5 years were at greater risk of impaired brain function due to the lack of oxygen to the brain (Singh et al., 2014). COPD is also associated with an increased heart disease risk, which is a risk factor for mild cognitive impairment (Singh et al., 2014). Patients with the disease also possessed inflammatory markers believed to be associated with brain function (Bettermann et al., 2012). Despite this, there are medications for preexisting conditions that have been shown to slow Alzheimer's progression. Lipid-lowering medication (LLM) especially statin drugs have been shown to delay cognitive decline (Bettermann et al., 2012). Statins lower amyloid beta levels which is a plaque that covers the brain of individuals with Alzheimer's (Bettermann et al., 2012).

Though biomarkers for the disease are still being studied, the research conducted demonstrated how interventions not only impacted these biomarkers but also the cognition of the individuals. The repressor element 1-silencing transcription (REST) factor regulates the brain stress response as it ages (Ashton et al., 2017). Researchers found the REST factor to be a promising biomarker for Alzheimer's disease (Ashton et al., 2017). When an individual is under stress or has Alzheimer's disease, REST levels are reduced in the brain (Ashton et al., 2017). REST levels were also found to be associated with reduced hippocampal volume and cognitive impairment (Ashton et al., 2017). REST levels can be modified through various stress reduction interventions (Ashton et al., 2017).

Table 1: Detailed Summary of Articles Reviewed

	Author	Year	Article Title and Journal	Purpose	Sample	Study Type	Findings	Limitations
1	Kilpatrick, L. A., Siddarth, P., Krause-Sorio, B., Milillo, M. M., Aguilar-Faustino, Y., Ercoli, L., Narr, K. L., Khalsa, D. S., Lavretsky, H.	2023	Impact of Yoga Versus Memory Enhancement Training on Hippocampal Connectivity in Older Women at Risk for Alzheimer's Disease. *Journal of Alzheimer's Disease*	To examine the effects of Kundalini yoga compared to memory enhancement training on the brain's hippocampus regions.	Women with subjective memory decline and cardiovascular risk factors; 63 participants	Randomized Controlled Trial	The study found that although both interventions showed major improvements, yoga has additional benefits for overall brain health.	This study was only conducted on women with memory decline and cardiovascular risk factors.
2	Aslanyan, V., Ortega, N., Fenton, L., Harrison, T. M., Raman, R., Mack, W. J., Pa, J.	2023	Protective effects of sleep duration and physical activity on cognitive performance are influenced by β-amyloid and brain volume but not tau burden among cognitively unimpaired older adults.	The study examined how sleep duration and physical activity affected cognition and if it can be explained by brain volume and amyloid-β burden.	4322 participants (1208 with MRI, 59% female, 29% amyloid positive)	Cross-sectional study	The study found that increased sleep and physical activity improve cognitive outcomes.	Some of the data is self-reported which could lead to inaccurate conclusions.

			Neuroimage: Clinical					
3	Soininen, H., Solomon, A., Visser, P. J., Hendrix, S. B., Blennow, K., Kivipelto, M., Hartmann, T..	2021	36-month LipiDiDiet multinutrient clinical trial in prodromal Alzheimer's disease *Alzheimer's & Dementia*	The study investigates the effects of specific nutrients on cognitive function and the progression of Alzheimer's.	311 participants Aged 55-85 with prodromal (early onset) Alzheimer's Disease	Randomized, double-blind, placebo-controlled trial	The study showed that the Mult nutrient intake with long-term use slows Alzheimer's Disease progression.	The study's main focus was the multinutrient intake but there could be other confounding variables such as lifestyle factors possibly influencing the outcome.
4	Ashton, N. J., Hye, A., Leckey, C. A., Jones, A. R., Gardner, A., Elliott, C., Wetherell, J. L., Lenze, E. J., Killick, R., Marchant, N. L.	2017	Plasma REST: a novel candidate biomarker of Alzheimer's disease is modified by psychological intervention in an at-risk population. *Translational psychiatry*	The study examines the impact of psychological intervention on the levels of the REST biomarker in blood plasma. REST is an Alzheimer's disease biomarker.	103 participants Aged 65+	Clinical trial	The study shows that REST biomarkers are modified by psychological interventions. The study also highlights the importance of mental health interventions and other changes to lifestyle factors on Alzheimer's progression.	The study had a smaller sample size which could mean the results don't accurately represent the entire population.

5	Solomon, A., Turunen, H., Ngandu, T., Peltonen, M., Levälahti, 'E., Helisalmi, S., Antikainen, R., Bäckman, L., Hänninen, T., Jula, A., Laatikainen, T., Lehtisalo, J., Lindström, J., Paajanen, T., Pajala, S., Stigsdotter-Neely, A., Strandberg, T., Tuomilehto, J., Soininen, H., Kivipelto, M.	2018	Effect of the Apolipoprotein E Genotype on Cognitive Change During a Multidomain Lifestyle Intervention: A Subgroup Analysis of a Randomized Clinical Trial *JAMA neurology*	The study investigates the changes in cognition based on multidomain lifestyle changes for patients at risk for Dementia.	1109 total participants 514 females 595 males 60-77 years	Randomized Clinical Trial	The study showed that healthy lifestyle changes may improve cognition in older at-risk individuals including those susceptible to dementia. The study also highlighted the importance of early prevention.	The study mainly focused on at-risk individuals with a particular genotype, meaning the results may not apply to the broader population.
6	Arab, A., Christie, G. J., Mansouri, M., Ahmadzadeh, M.,	2021	Moderate-Intensity Physical Activity, Music and Art Activities	The study examined the impact of moderate physical activity, art, and music on	Data from the English Longitudinal Study of Aging:	Clinical trial	The study concluded that increased moderate physical activity and learning	The study was done on self-reported data which could introduce reporter bias

	Sixsmith, A., Ester, M., & Moreno, S.		Preserved Cognitive Health in Older Adults: An Argument for Social Prescribing Solution *Frontiers in Aging Neuroscience*	the cognitive health of older adults.	Community-dwelling people aged 50 and older; participants		activities positively impact the cognitive function of older adults.	from the participants and skew the findings.
7	Bettermann, K., Arnold, A. M., Williamson, J., Rapp, S., Sink, K., Toole, J. F., Carlson, M. C., Yasar, S., Dekosky, S., & Burke, G. L.	2012	Statins, Risk of Dementia, and Cognitive Function: Secondary Analysis of the Ginkgo Evaluation of Memory Study *Journal of Stroke and Cerebrovascular Diseases*	This study investigates the relationship between statin use and the risk of developing dementia.	3069 cognitively healthy patients 75 years of age and older enrolled in the Ginkgo Evaluation of Memory Study	Longitudinal Observational Study	The study concluded that statins may slow the rate of cognitive decline in healthy older adults and delay the onset of Alzheimer's Disease.	The study is observational meaning it can only establish associations and likely needs further study to solidify the findings.
8	Dougherty, R. J., Schultz, S. A., Boots, E. A., Ellingson, L. D., Meyer, J.	2017	Relationships between cardiorespiratory fitness, hippocampal volume, and episodic	To determine the relationship between cardiorespiratory fitness and changes in cognition in older	86 participants	Randomized Controlled Trial	The study concluded that the relationship between cardiorespiratory fitness, memory, and	The study was conducted on a smaller population sample, meaning these findings may

	D., Van Riper, S., Stegner, A. J., Edwards, D. F., Oh, J. M., Einerson, J., Korcarz, C. E., Koscik, R. L., Dowling, M. N., Gallagher, C. L., Carlsson, C. M., Rowley, H. A., Bendlin, B. B., Asthana, S., Hermann, B. P., Cook, D. B.		memory in a population at risk for Alzheimer's disease *Brain and Behavior*	adults at risk for Alzheimer's disease.			hippocampal volume is not clear and might be gender dependent.	not apply to the general population.
9	Aslanyan, V., Ortega, N., Fenton, L., Harrison, T. M., Raman, R., Mack, W. J., & Pa, J.	2023	Protective effects of sleep duration and physical activity on cognitive performance are influenced by β-amyloid and brain volume but not tau	This study determined the association between sleep duration and physical activity on cognition and whether they can be explained by Amyloid Beta	4322 participants; cognitively unimpaired aged 65 to 85	Cross-sectional study	The study concluded that adequate sleep and physical activity may reduce dementia risk as they are associated with improved cognition. Sleep	The study was conducted on self-reported data from questionnaires on lifestyle habits and sleep which could introduce bias

			burden among cognitively unimpaired older adults. *Neuroimage: Clinical*	burden and brain volume.			was found to be associated with Amyloid beta and physical activity with brain volume.	and error into the conclusion. Further research would help solidify the findings.
10	Singh, B., Mielke, M. M., Parsaik, A. K., Cha, R. H., Roberts, R. O., Scanlon, P. D., Geda, Y. E., Christianson, T. J., Pankratz, V. S., Petersen, R. C.	2014	A Prospective Study of Chronic Obstructive Pulmonary Disease and the Risk for Mild Cognitive Impairment *JAMA Neurology*	To investigate the association between Chronic Obstructive Pulmonary Disease (COPD) and the development of mild cognitive impairment.	1425 cognitively normal individuals aged 70 to 89 years with COPD	Prospective Cohort Study	The study concluded that individuals with a longer duration of COPD have the greatest risk of developing MCI.	The study was conducted on a primarily European population which is not representative of the general population. This means these findings could differ for non-European individuals with COPD.

Discussion

Alzheimer's is a deadly disease with no current cure. When studying this disease, it's important to identify the risk factors that may help reduce the likelihood of its development. While these factors are not cures, they provide methods of intervention for those in the earlier stages. This literature review aims to identify the modifiable risk factors of Alzheimer's development in older adults. Within this review, two main categories of modifiable risk factors were discussed: lifestyle and health factors. The lifestyle category was further separated into sections: sleep and mindfulness, as well as diet and exercise. Intervention that targets an individual's lifestyle may include changes to diet, sleep patterns, and exercise routines. It might also include managing pre-existing conditions and prioritizing well-being. Improvement in these areas has been shown to positively impact cognitive function and may help slow the progression of Alzheimer's disease.

Implications

This review demonstrates the need for increased research on risk factors associated with Alzheimer's disease. More studies are necessary to deepen our understanding of the disease and find a possible cure. Longitudinal studies that follow individuals through the progression of the disease are necessary to determine the impact of the modifiable risk factors. It is also important to research more diverse populations as this disease may affect various ethnic and socioeconomic groups differently. It is also important to study the interactions between the different risk factors and their impact on disease progression. Many claim that more rest will improve cognition and base their studies on this idea. However, there are many other factors that when coupled with sleep, diet, and exercise could influence the observed improvement. It is also important to consider socioeconomic status in research as a person's environment, age, income, and other

factors significantly impact outcomes. Programs and interventions should be developed, aimed at encouraging healthy lifestyle practices in older adults. The articles reviewed have shown that maintaining good health can reduce the risk of disease development. An active and healthy lifestyle can help reduce the risk of disease in older adults and would help them remain independent for as long as possible ("2024 Alzheimer's disease facts and figures," 2024).

Limitations

This literature review was conducted using ten peer-reviewed articles from the sources PubMed and Web of Science. The limited number of articles means this review is unable to cover the topic in its entirety. Many risk factors of the disease cannot be addressed in this review. Research on Alzheimer's disease is ongoing, and many aspects remain unknown. As more information becomes available, this topic will expand further. More research is necessary, particularly focusing on Alzheimer's and the risk factors that may help slow disease progression.

Conclusion

Alzheimer's cases are alarmingly increasing worldwide. This disease with no cure continues to impact many families and the economy. The situation is expected to worsen in the coming years due to our aging population, as the disease primarily affects older individuals. This review examined the modifiable risk factors of Alzheimer's development in older adults and categorized them. Targeting these risk factors through early intervention and care for individuals with early-onset Alzheimer's may help reduce the prevalence of the disease. Slowing its progression could reduce the years of suffering for those affected. This paper emphasizes the need for further research to better understand Alzheimer's risk factors and improve disease interventions.

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