The Role of Social Determinants on the Development of Alzheimer's Disease

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This literature review examines the influence of Social Determinants of Health (SDOHs) on the development of Alzheimer's disease (AD). While the biological mechanisms involving amyloid-beta and tau protein aggregation are the main factors contributing to AD development, SDOHs also play a significant role. This review analyzed 25 studies on how SDOHs affect AD risk and development. SDOHs were categorized into groups by macrosystem, microsystem, mesosystem, and chronosystem and each system was reviewed separately and compared. The findings demonstrate that factors such as socioeconomic status, social network size, built environment, education, occupation, cognitive reserve, physical activity, and mental activity are directly linked to AD incidence. The discussion expands on these connections and suggests directions for future investigations, aiming to enhance understanding of the relationship between SDOHs and AD development.

Introduction

Alzheimer's disease (AD) is a neurodegenerative condition characterized by a progressive decline in cognitive function that primarily affects older adults. In AD, proteins called amyloid-beta and tau misfold and form prions, which clump into neuritic plaques and neurofibrillary tangles. These aggregations of malformed proteins lead to neuronal dysfunction, loss of synaptic plasticity, and eventual cell death, thereby disrupting the transport system of neurotransmitters and messages in the brain[1]. These changes are especially evident in the hippocampi which become physically smaller due to the loss of neuronal mass[2].

Although considerable attention has been given to AD's biological aspects, recent research indicates that social factors also play a crucial role in its development. Specifically, various social determinants of health (SDOHs), the non-medical factors that influence health outcomes, can also influence the risk and course of AD[3]. Across the AD literature, there is general agreement regarding the primary SDOHs. These include race, ethnicity, sex, socioeconomic status, social network size/engagement, built environment, education, occupation, and lifestyle[4,5]. There are many conceptual frameworks to categorize and examine these social factors. However, prior studies suggest utilizing Bronfenbrenner's ecological systems theory[4,6] because it explains how various systems influence AD risk and how these associations can vary at the individual or person level. The four different subsystems based on Bronfenbrenner's theory are as follows.

1. A macrosystem is the outer layer of systems that drive social determinants, such as bias, disparity, and ideologies. These values that are set in place by the macrosystem are reflected in the other systems since the macrosystem influences societal structure that may dictate things like healthcare access, living space, and job opportunities[4]. Some specific SDOHs in a macrosystem are demographic biases such as sex differences or racial bias, socio-economic bias, and class-based bias.

2. A microsystem is the immediate environment or setting that a person is in direct interaction with[4]. Some key SDOHs in a microsystem are social network size, neighborhood and community, educational opportunities, occupation, and lifestyle factors. Each of these factors contributes to the brain's resistance to damage, called cognitive reserve.

3. The connectivity and interdependence of multiple microsystems together make up a mesosystem[4]. For example, the connection between one's job and their living space is a part of the mesosystem, whereas just one's occupation and just their living space are a part of the microsystem.

4. A chronosystem is made up of the exposures to social determinants throughout the life course and through human development[4]. All of the experiences over one's lifetime through microsystems, mesosystems, and macrosystems and their effect on a person make up the chronosystem. For example, events that occurred during one's childhood can have a lasting effect on their life course, which is part of the chronosystem.

5. The final system involves the exosystem. The exosystem is made up of the occurrences and interactions that affect someone indirectly[4]. These factors include but are not limited to climate change, natural disasters, and pollution.

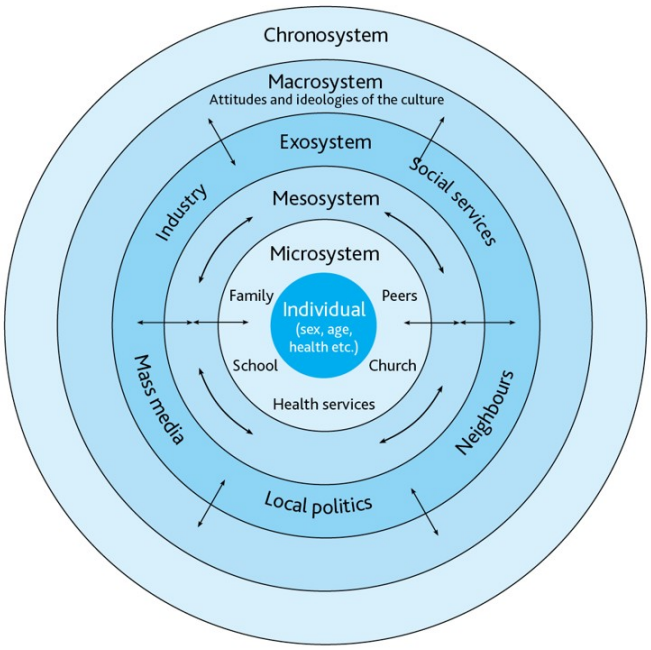

Fig. 1 Adopted from Cambridge International Education Blog, 2021

This literature review aims to shed light on SDOHs that are associated with AD risk that directly impact older adults (i.e., those within macro-, micro-, meso-, and chronosystems) and may be modifiable at the community level. By exploring the impact of cultural, social, and lifestyle dynamics on the development of AD, this paper serves to broaden the understanding of AD and has the potential to inform new preventive measures and interventions that help individuals affected by AD as well as their caregivers.

Methods

A comprehensive search was conducted using Google Scholar database. Search terms included "Alzheimer's disease", "risk", "social", "determinants of health", "impact", "prevention", and "factors". Only papers from 2005 to 2024 were included. The initial search yielded 3,770 studies. After a more comprehensive screening, 25 peer-reviewed studies were selected given their relevance to AD and SDOHs. The most common exclusion criteria were a lack of focus on the relationship between SDOHs and AD risk. The 25 selected studies were further categorized into one of the first four Bronfenbrenner's ecological theory systems (macro-, micro-, meso-, or chrono-) to allow for a more systematic comparison of SDOHs and their link to AD risk. As noted above, this review is focused on factors that have a direct impact on older adult communities. Thus, indirect factors within the exosystem were not reviewed.

Results

This review focuses on the link between SDOHs and AD development. The articles chosen for review and the SDOH subsystems in which they belong are outlined in Table 1 (Macrosystem), Table 2 (Meso and Microsystems), and Table 3 (Chronosystems). Given that microsystems closely interact to form mesosystems, these categories were combined to form Table 2. Following these tables, summary and discussion of themes and system impacts are discussed.

Broadly speaking, certain elements, such as demographic bias, socio-economic/class-based bias, social isolation, disadvantaged neighborhoods, low education level, low income, stress, poor lifestyle, and early adversity may increase the risk of AD. Alternatively, other elements such as social engagement, large family size, better built environment, high education level, education into adulthood, job complexity, high wages, physical activity, healthy diet, and high cognitive reserve may decrease the risk of AD.

Across studies that examined SDOHs at the macrosystem level, several societal biases (i.e., demographic biases and socioeconomic & class biases) emerged as factors that increased the risk of AD. More specifically, studies revealed that the cumulative impact of belonging to a marginalized race and/or ethnic group and lower socioeconomic class was linked to reduced healthcare access and quality and subsequently higher rates of AD development. Increased AD risk was also associated with fthe emale sex due to a higher prevalence of feelings of loneliness. One study revealed that growing up with parents with higher socioeconomic status was associated with lower AD risk.

At the micro- and mesosystem levels, the primary SDOHs that are associated with increased risk of AD include loneliness, reduced social network size, lower levels of social interaction frequency, living in a disadvantaged neighborhood, leaving education early, lower job complexity, poor sleep quality, and alcohol overuse. Conversely, SDOHs that are associated with decreased risk of AD include lower stress levels, regular engagement with enjoyable activities, regular physical activity, larger households, higher wages, education into late life, following good nutritional practices, and specific quantity and type of caffeine consumption.

experiences were linked with increased AD risk, while higher quality and longevity of educational and occupational experiences were associated with decreased AD risk.

Discussion

This review explored key SDOHs and their individual and combined associations with AD risk in older adults. Overall, relevant studies indicate the importance of two key demographic biases (i.e., sex and race) as well as socioeconomic biases that are associated with increased risk of AD. Studies also demon-

Table 1 Macrosystem

Article	Effect on AD risk	Varying SDOH	Main findings
Ren et al. (2023) The impact of loneliness and social isolation on the development of cognitive decline and Alzheimer's Disease	Increased risk	Demographic bias: sex differences	• Pronounced effects of loneliness in women. • Loneliness negatively impacts various cognitive domains, notably memory. • Increased loneliness leads to decreased cognitive performance, leading to greater risk of AD.
Ciciora et al. (2024) Social and Behavior Factors of Alzheimer's Disease and Related Dementias: A National Study in the U.S. - American Journal of Preventive Medicine	Increased risk	Demographic bias: racial bias	• Black and Hispanic Americans are more likely to have AD compared to non-Hispanic White Americans. • Non-White participants had a higher prevalence of poor or fair health status, lack of health insurance, and no usual source of care compared to White participants.
Adkins-Jackson et al. (2023) The structural and social determinants of Alzheimer's disease related dementias	Increased risk	Demographic bias: sex differences, racial bias; Socioeconomic & class-based bias	• In 2020, AD prevalence was approximately 2x higher among those racialized as African American compared to White. • In 2020, AD prevalence was 1.6x higher among women than men. • Persons racialized as White receive more opportunities and resources than persons of color. • Living in areas where a majority of residents are persons of color is associated with increased dementia risk. • Residential segregation reduces access to good quality SDOHs like healthcare, nutrient-rich foods, and jobs. • The link between socioeconomic position and AD exists because the health benefits of money and class are inaccessible to marginalized groups.
Majoka & Schimming (2021) Effect of Social Determinants of Health on Cognition and Risk of Alzheimer Disease and Related Dementias	Increased risk	Socioeconomic & class-based bias	• Lower socioeconomic status is associated with a higher incidence of AD. • Communities with low socioeconomic status are associated with local deprivation, poor cognitive function, cognitive decline, and higher risk of cognitive impairment.
Alzheimer's Association (n.d.) Lower Socioeconomic Status Linked to Dementia	Decreased risk	Socioeconomic & class-based bias	• Individuals who grew up with parents with high socioeconomic status are more resilient to the impact of the AD marker ptau-181 on memory, language, and executive function.

strate there are several factors related to early, middle, and late life experiences that can influence the likelihood of developing AD. Together, these associations highlight that there are several societal inequalities and individual differences that negatively influence the prevalence of the disease among certain older adult communities.

Table 2 Microsystem and Mesosystem

Article	Effect on AD risk	Varying SDOH	Main findings
Ren et al. (2023) The impact of loneliness and social isolation on the development of cognitive decline and Alzheimer's Disease	Increased risk	Social network size: loneliness	• Increased loneliness decreases cognitive performance, strengthening future loneliness.
Röhr et al. (2020) Changes in Social Network Size Are Associated With Cognitive Changes in the Oldest-Old	Increased risk	Social network size: small network & changes over time	• Smaller social networks are linked to significantly lower cognitive function. • Cognitive changes are associated with changes in social network size over time. • Worsened cognitive function linked to shrinking social networks.
Pillai & Verghese (2009) Social networks and their role in preventing dementia	Decreased risk	Social network size: social engagement, family	• Being married positively affects AD risk. • High levels of social engagement and leisure activity reduce dementia risk.
Takahashi et al. (2023) The Role of Oxytocin in Alzheimer's Disease and Its Relationship with Social Interaction	Decreased risk	Social network size: social engagement, family	• Large households are linked to lower dementia mortality. • Oxytocin reverses amyloid-beta-induced cognitive impairment, rescuing memory.
Takahashi et al. (2023) The Role of Oxytocin in Alzheimer's Disease and Its Relationship with Social Interaction	Increased risk	Social network size: social isolation	• Social isolation increases expression of hyperphosphorylated tau, leading to AD pathology.
Qiu et al. (2022) Epidemiology of Alzheimer's disease: occurrence, determinants, and strategies toward intervention	Decreased risk	Social network size: social engagement Education Lifestyle factors: diet, habitual factors	• Rich social networks reduce AD risk. • High education in early life reduces AD risk. • Mediterranean diet decreases AD risk. • Avoiding tobacco and alcohol prevents AD risk.
Drinkwater, Davies, & Spires-Jones (2021) Potential neurobiological links between social isolation and Alzheimer's disease risk	Increased risk	Social network size: loneliness	• Loneliness doubles the likelihood of developing AD-like dementia. • Loneliness linked to increased amyloid-beta protein concentration.
Drinkwater, Davies, & Spires-Jones (2021) Potential neurobiological links between social isolation and Alzheimer's disease risk	Decreased risk	Social network size: social engagement	• Frequent social contact lowers dementia risk. • Large social networks lead to better late-life cognitive function.

Adkins-Jackson et al. (2023) The structural and social determinants of Alzheimer's disease related dementias	Increased risk	Neighborhood/community	• Participants in disadvantaged neighborhoods had 4.1% lower hippocampal volumes compared to those in non-deprived communities.
Powell et al. (2020) Association of Neighborhood-Level Disadvantage With Alzheimer Disease Neuropathology	Increased risk	Neighborhood/community	• Poor housing quality/disadvantaged neighborhoods are associated with protein malformation. • 8.1% higher chance of developing AD neuropathology.
Majoka & Schimming (2021) Effect of Social Determinants of Health on Cognition and Risk of Alzheimer Disease and Related Dementias	Increased risk	Neighborhood/community	• Local deprivation and poor infrastructure link to poor cognitive function and decline.
Alzheimer's Society (2021) Risk factors for dementia	Increased risk	Education Occupation: job complexity Cognitive reserve	• Leaving education early results in smaller cognitive reserve. • Low job complexity contributes to reduced cognitive reserve. • Lower cognitive reserve makes individuals more prone to dementia.
Zhang et al. (2021) The Epidemiology of Alzheimer's Disease Modifiable Risk Factors and Prevention	Decreased risk	Education Lifestyle factors: diet, habitual factors	• High education levels delay AD onset. • Non-smokers have 18% less AD risk than smokers. • Mediterranean diet and similar eating habits lower AD risk.
Deckers et al. (2019) Modifiable Risk Factors Explain Socioeconomic Inequalities in Dementia Risk	Decreased risk	Education Occupation: wage	• High education and continued learning reduce dementia risk. • Higher wages correlate with slower memory decline.
Hsiao, Chang, & Gean (2018) Impact of social relationships on Alzheimer's memory impairment	Decreased risk	Lifestyle factors: exercise and diet	• Regular exercise and healthy diet slow cognitive decline.
de la Rosa et al. (2020) Physical exercise in the prevention and treatment of Alzheimer's disease	Decreased risk	Lifestyle factors: exercise	• Exercise maintains cognition, reduces amyloid beta, and decreases AD biomarkers.
Harvard Health Publishing (2023) What is cognitive reserve?	Decreased risk	Cognitive reserve	• Cognitive reserve enhances brain function, resilience, and adaptability. • Built through mental stimulation, good diet, exercise, and stress management.

Table 3 Chronosystem

Article	Effect on AD risk	Varying SDOH	Main findings
Corney et al. (2022) The Relationship Between Adverse Childhood Experiences and Alzheimer's Disease: A Systematic Review	Increased risk	Early adversity	• Only three eligible articles for study. • All reviewed studies found adverse childhood experiences were associated with an increased risk of AD.
Qiu, Kivipelto, & von Strauss (2022) Epidemiology of Alzheimer's disease: occurrence, determinants, and strategies toward intervention	Decreased risk	Childhood education & continued education through life	• Good education as a child can have lasting beneficial effects on cognitive function. • Continuing high levels of education, work, and mental stimulation throughout life reduces the risk of AD and dementia.

1.1 — Macrosystem: Demographic Bias

Two types of demographic bias were found to most affect the type of healthcare received and interactions in healthcare to play a role in AD. The first is sex differences and gender-based bias that make women more prone to loneliness and social isolation. This may lead to cognitive decline and higher incidence of AD in women[7]. Racial bias is also a factor that contributes significantly to AD incidence due to it affecting a person's ability to receive appropriate healthcare. Specifically, counties with a majority of residents specified as people of color were associated with increased dementia risk[4,8], while areas with more people specified as "white" were seen to have more access to resources, opportunities, healthcare, housing, and many other factors[4]. This is often due to minority groups and people of color having higher rates of unemployment as well as a lack of representation in jobs that pay well or include health insurance[9]. Naturally, this means that these groups would face the same economic challenges as those in lower classes and would not have easy access to healthcare that is covered by insurance. Additional research looking into the intersection between sex and racial biases can provide more insights into the disadvantages and risk of AD faced by minority women. It is necessary to understand these biases and understand how these societal values alter one's access to resources to help identify how to better ensure equal access to healthcare, thus reducing disparity in the frequency of AD in certain groups. Policies that advocate for equal access already exist, and thus must be reevaluated within each community to improve health outcomes for everyone, and not just those that are male or white.

1.2 — Macrosystem: Socio-economic & Class-based Bias

Socio-economic status and class-based biases were also found to impact the incidence of AD mainly due to their linkage to poor educational and economic opportunities. Lower classes and many marginalized people with a lower socioeconomic position also do not have the health benefits that those with high-class status and wealth have[4]. Those with more wealth and status often have better health insurance, readily available healthcare, access to more public services, safer living areas, and above-average education. Lower socioeconomic wealth as well as local deprivation are linked to the cognitive decline present in AD[10]. Local deprivation refers to poor housing conditions, lack of easily accessible public services such as transportation and recreational buildings, and low safety levels. A high socio-economic status of one's parents, however, was shown to also provide the children with resilience to the negative effects of AD, likely due to better healthcare opportunities, education, and built environments as a child[11]. Analyzing the influence of socioeconomic and class-based biases on AD outcomes provides insight into the factors perpetuating the link between economic status/class and health. This necessitates increased access to healthcare services for economically disadvantaged people as well as others. Considering the long-term perspective of high-quality education lowering AD risk, enhanced childhood education even to those that cannot afford it, as well as offering jobs equally to everyone can also build resilience against AD. Furthermore, those of higher class generally have more access to preventive care and diagnoses, but access to these should also be prioritized for lower classes.

2.1 — Microsystem and Mesosystem: Social Network Size

An individual's social network size contributes to their risk of developing AD, as feelings of belonging, family size, and social engagement all play roles in maintaining cognitive function. Loneliness negatively impacts various cognitive functions, such as memory, which is a key function that deteriorates in AD7. The effects of social isolation and loneliness can be modified over time as a shrinking/growing social network size can lead to either a shrinking or growing cognitive reserve[12].

Family size, as expected, is also a major determinant of AD

development, as the size of one's family directly influences the size of their social network. Being married and having a large household overall was linked to a lower risk of AD, whereas being single or living alone was associated with an increased risk of dementia[13,14]. However, simply having a large social network size will not reduce the risk of AD, as social engagement is crucial in reducing AD incidence as well. The higher the frequency of contact and the more fulfilling a contact was associated with reduced risk of dementia, even as one gets older[13,15,16]. This highlights the importance of making meaningful connections with people to better encourage frequent and beneficial social interaction throughout one's lifetime. Enhancing the amount of social interaction for the elderly through programs that increase interaction with them can also be beneficial in reducing the strain placed on caregivers in two ways. It could lessen the amount of time a caregiver must spend with an elderly patient already diagnosed with Alzheimer's, and it can also possibly delay further development of AD.

2.2 — Microsystem and Mesosytem: Neighborhood/Community

The neighborhood and community that one grows up in are linked to their socioeconomic status and is also associated with AD risk. Many who live in the least advanced areas have lower brain volume in the hippocampus and increased odds of developing AD pathology[4,17]. Individuals experiencing local deprivation and living in areas with poorly built neighborhood infrastructure demonstrated poorer cognitive function compared to those in more advantaged environments[10]. This could be due directly to poorer healthcare or lack of public space for social interaction, unsafe outdoor areas for physical activity, or lack of proper nutrients in food. Living in a disadvantaged neighborhood most likely causes an increased risk of AD due to poor quality housing, low access to green spaces/parks, and little to no community centers, all of which can lead to low social interaction and a less active lifestyle, two factors linked with increased AD risk. Therefore, an improvement in neighborhood infrastructure can play an immense role in decreasing the incidence of AD.

2.3 — Microsystem and Mesosytem: Education

Many education-related factors influence the development and incidence of AD as well. Leaving education early, such as not completing high school can lead to a smaller cognitive reserve due to a lack of education in the brain's critical stages of development18. This smaller cognitive reserve can make an individual more prone to dementia. However, high educational attainment helps engage the brain in mental activity and cognitive stimulation, both of which benefit intellectual capacity and delay the onset of AD[16,18,19]. Education that is attained at this high level in early life and then continued into adulthood is linked to a lower risk of AD[20]. As long as high educational opportunities are provided in early life, one can build their cognitive reserve and continue their education as an adult, which can significantly reduce the incidence of AD.

2.4 — Microsystem and Mesosytem: Occupation

One's occupation is also a major factor in determining their risk of developing AD as it determines the mental stimulation one engages in as well as their socio-economic status, which in turn affects their built environment and possibly education. Similar to education, having a higher job complexity aids regular mental activity which maintains a high cognitive reserve that shows resilience toward AD[18]. Those who were paid lower wages and made a lower regular income experienced faster memory decline in their old age and a high risk of AD[11,20]. Since job complexity also plays a major role in preventing AD, jobs that are not extensively skill-based would benefit from having mental stimulation somewhere in the work environment.

2.5 — Microsystem and Mesosytem: Lifestyle Factors

Many different lifestyle factors, such as physical activity, exercise, and nutrient intake/diet can also act as preventative measures to stop cognitive decline. Regular exercise as well as regularly eating a healthy diet is shown to be a preventative measure to stop cognitive decline[21]. Poor diets are linked to high cholesterol levels, which increase blood pressure and are linked to the prevalence of AD pathology. Exercise, specifically, is shown to maintain cognition due to its role in regulating amyloid-beta protein folding, inflammation, and synthesis, all of which lead to lower prion formation and fewer amyloid-beta clumps[22]. Many specific diets, such as the Mediterranean diet, DASH (dietary approaches to stop hypertension), and the MIND diet (Mediterranean-DASH intervention for neurodegenerative delay), are also associated with a lower risk of AD[16,19]. Many other habitual lifestyle factors such as a poor sleep schedule, smoking, and alcohol consumption are linked to a higher risk of AD, whereas green tea and coffee are linked to protective effects of cognition on men and women, respectively[19]. Examining these lifestyle factors offers insights into daily habits that can be modified to significantly improve cognitive health and reduce AD incidence. Encouraging healthy lifestyle choices early on in life and even in adulthood as well as making physical activity and proper nutrition more accessible can greatly benefit cognition.

2.6 — Microsystem and Mesosytem: Cognitive Reserve

While cognitive reserve is not itself a social determinant of health, a high cognitive reserve significantly prevents AD and can be enhanced through various other SDOHs. Cognitive reserve is the brain's agility and adaptability in the face of problems, which leads to better function and resilience against neurodegenerative diseases, stress, trauma, and injury[23]. It can be built through mental stimulation, such as high education, job complexity, and social interactions, but also requires certain lifestyle factors to maintain it, such as a nutritional diet, regular physical activity, a sufficient sleep schedule, and low levels of stress[18,23]. If the cognitive reserve is not built up and maintained, cognitive impairment may occur, which will lead to a higher

risk of AD. This concept of cognitive reserve exemplifies the importance of looking at brain health from multiple angles, a technique that can be used to understand approaches taken by caregivers to approach multiple aspects of someone's life in order to slow the development of AD.

3 — Chronosystem

A chronosystem, made up of exposures to social determinants throughout one's lifetime[4], can include social determinants/factors like childhood events. One such factor is early adversity, such as trauma or severe stress under the age of 18, which is shown to increase the risk of AD throughout the lifespan[24]. Research has shown that one brain area affected during heavy stress is the hippocampus, which is a brain region crucial to AD and is shown to be affected more during the younger stages of life[25]. Early interventions to this such as therapy can greatly alter the path of cognitive health for a child and reduce the risk of AD by reducing stress. Therefore, addressing childhood adversity, making mental healthcare available, and ensuring there are supportive environments for a child are essential to understanding how to prevent AD from early on. Additionally, high educational attainment as a child can also have a lasting effect of decreased risk of AD due to early building of a strong cognitive reserve[16]. Furthermore, being in a consistently high-quality educational environment allows a child to interact with like-minded peers, who they will likely know for many years later; this increases the amount of long-term social interaction throughout a child's life. Thus, high educational attainment should be made more accessible to children to reduce the negative impacts low-quality education may have in their lives in the future.

4 — Limitations and Future Direction

While this literature review demonstrates how SDOHs play a role in increasing AD development, there are some limitations to consider. For instance, many of the studies discussed were observational or cross-sectional, which limits assumptions about causality between the two. In addition, the studies primarily focused on a sample within Western or US regions, therefore the findings may differ globally and the link between SDOHs and AD may reflect differently in other parts of the world. Furthermore, this review does not explore how various social/cultural norms or personality traits might influence SDOHs and impact AD risk. The link between AD pathology and SDOHs was also not examined in this review due to its sole focus on SDOHs, however, future studies would benefit from exploring this connection. Lastly, only a few studies regarding chronosystems and adverse childhood experiences in AD risk exist, which are not enough to make a substantial claim, and thus more research should be done on the link between early adversity and AD risk. These limitations suggest that more diverse and long-term studies are needed to better understand the role of SDOHs in AD risk and development.

Conclusion

This literature review emphasizes the significant link between SDOHs and the development of AD. While the biological mechanisms involving amyloid-beta and tau protein aggregation are well-known factors that contribute to AD, this review demonstrates that social factors also play a crucial role in shaping AD risk and pathology. The review categorizes social determinants into macrosystems, microsystems, mesosystems, and chronosystems, and identifies various factors such as socioeconomic status, social network size, built environment, education, occupation, cognitive reserve, physical activity, and mental activity that significantly impact AD incidence. Researchers are encouraged to build upon these findings and continue exploring the impact of cultural, social, and lifestyle dynamics on the development of AD. This will help broaden the understanding of AD risk and potentially inform new preventive measures and interventions that help patients and their caregivers.

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