Proceedings of the 4th International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/64/2024.17994

Implications of Modifiable and Non-Modifiable Determinants of Dementia for Public Health Policies and Prevention Strategies

Yifei Xu

Division of Bioscience, University College London, London, United Kingdom

zcbtxul@ucl.ac.uk

Abstract. Dementia, characterized by cognitive decline and memory deterioration, poses a significant and growing global health challenge. Alzheimer's disease (AD) is the most common form, with others including Lewy body dementia (LBD), frontotemporal dementia (FTD), and vascular dementia (VaD). The World Health Organization estimates that 55 million people worldwide are affected, a number projected to triple by 2050. This essay explores both non-modifiable and modifiable determinants of dementia and their implications for public health policies and prevention efforts. Non-modifiable determinants include age, genetics, and sex, all of which significantly influence dementia risk. Ageing is the primary risk factor, with genetic factors such as mutations in APP, PSEN1, and PSEN2, and the APOE ε4 allele increasing susceptibility. Women, due to their longer lifespan and hormonal differences, are at a higher risk compared to men. Modifiable determinants encompass lifestyle factors and medical conditions, notably diet, physical activity, alcohol and tobacco use, hypertension, and diabetes. Effective public health policies, like the WHO's Global Action Plan, emphasize early intervention and lifestyle modifications. Integrating these determinants into policy making requires a balanced approach, considering the dynamic nature of modifiable factors and the specific needs of an aging population. The essay underscores the need for comprehensive public health education, destigmatization of dementia, and an inclusive healthcare infrastructure to enhance dementia prevention and care, ultimately reducing the societal burden of this condition.

Keywords: Dementia, Genetic Risk Factors, Alzheimer's Disease (AD), Public Health Policies.

1. Introduction

Dementia is a broad term used to represent various symptoms of cognitive decline, including deterioration in memory, difficulties with thinking, and problem-solving issues that are severe enough to interfere with daily life. Though there are many other varieties of dementia, each with its own set of causes and symptoms, Alzheimer's disease (AD) is the most frequent type. Lewy body dementia (LBD), frontotemporal diseases (FTD), and vascular dementia (VaD) are examples of other types of dementia. Mixed dementia is a prevalent condition in which two or more kinds of dementia coexist. Dementia's global influence is significant and expanding. The World Health Organisation (WHO) estimates that 55 million people worldwide suffer from dementia; as the population ages, this figure is projected to almost triple by 2050. In addition, dementia has significant expenditures connected with it, including direct medical care, social care, and the loss of income for patients and carers. Individuals and society as a

DOI: 10.54254/2753-8818/64/2024.17994

whole are affected significantly on an emotional, social, and economic level by this syndrome. Therefore, it is imperative for public health to comprehend the factors that contribute to dementia for multiple reasons, and they can be divided into non-modifiable (such as age, genes and sex) and modifiable (such as lifestyle factors and medical conditions).

2. Non-Modifiable Determinants

Non-modifiable determinants are factors that influence an individual's health status but cannot be changed or altered by the individual. These determinants are beyond one's control and for dementia, they can be age, genetics and sex.

2.1. Age

Ageing is considered the primary risk factor for all significant types of dementia and is believed to represent the initial stage of neurodegeneration. People 65 years of age and older make up the majority of AD cases, and dementia risk doubles annually since 65 [1]. It is thought that as people age, previous healthy neurons stop functioning, and lose their connections and become less efficient and ultimately die [2]. Initially, the damage seems to occur in the hippocampus and the entorhinal cortex, critical regions of the brain for learning and memory. These areas are early and significantly impacted by neurofibrillary tangles (NFTs), composed of tau proteins. These proteins form abnormal structures suspected of causing brain cell damage, alongside senile plaques (SPs) primarily made of amyloid β (Aβ). Both are the result of accumulation of atypical proteins [3]. In AD, plaques and tangles can expand into many other regions, playing a complex role in the disease's pathogenesis by disrupting the network of brain cells and interfering with essential cellular processes. This leads to extensive damage and noticeable shrinkage in brain tissues [2]. Additionally, FTD and LBD both exhibit hippocampal disease and degeneration [1].

Furthermore, dementia, particularly VaD, was linked to small-vessel disease, infarcts, and the existence of multiple vascular pathological changes known as vascular ageing [5]. This is because older adults' blood vessels are less flexible and narrower, which contradicts blood flow. Comorbidities are another factor contributing to the higher risk of dementia in the elderly. Diseases include heart disease, diabetes, and hypertension—all of which are established risk factors for dementia.

2.2. Genetics

Genetics, including specific gene mutations and risk genes, play an important role in defining the risk and course of dementia. At present, researchers have identified over 80 genomic areas linked to AD. Only three causal genes, APP, PSEN1, and PSEN2, have been identified as causing early-onset autosomal dominant familial AD, which accounts for less than 10% of all cases. An individual who inherits a mutation in one of these genes (APP, PSEN1, or PSEN2) is likely to develop AD before the age of 65 or much sooner [6]. However, these three genes in some early AD patients did not mutate. This shows that some early AD is related to other genetic mutations or unknown factors. Other genes may not cause dementia directly but increase the risk of developing it. The most well-known example is the apolipoprotein E (APOE) gene, particularly the APOE ε4 allele [6]. Empirical data indicates that APOE impacts AD mostly through its impact on Aβ metabolism. It may function by modifying the build-up of Aβ plaques in the brain and ε4 carriers tend to have more amyloid deposition at an earlier age. AD is hypothesised to occur as a result of issues with this mechanism [8].

2.3. Sex

Women make up about two thirds of those with dementia diagnosis. Compared to males, females are around twice as likely to suffer from AD. This is mostly due to their longer lifespan and increases the time during which they may develop the disease [9]. Differences in the development of dementia between the sexes can also be explained by genetic factors. For instance, the ApoE4 allele, is a known risk factor for AD. The ApoE4 gene variant is equally common in men and women, but it appears to have a higher impact on dementia risk in women than in men. This could be related to tau pathology

DOI: 10.54254/2753-8818/64/2024.17994

[10]. Moreover, hormonal effects also play a vital role that suggests oestrogen protecting the brain, possibly even preventing some of the negative effects linked to AD. Women may be more susceptible to dementia after menopause due to a drop in sex hormone levels, such as progesterone and oestrogen [11]. There is evidence linking the menopausal transition to a decline in verbal memory, and an elevated risk of dementia has been linked to an early menopause [12]. Because of this, some researchers propose that women who have AD dementia may consider using estrogen-containing hormone therapy to lower the risk [13]. There is still a lot of disagreement, though, and additional study is required.

3. Modifiable Determinants

Modifiable determinants are factors that can be changed or influenced to potentially reduce the risk of developing dementia, which can be understood in 2 aspects: lifestyle factors and medical conditions.

3.1. Lifestyle Factors

Firstly, a healthy diet is linked to brain health and can therefore be a contributing factor to dementia. Recent research has demonstrated a BMI of 30 or higher was associated with a doubling of the risk of any dementia and diets heavy in fat and calories are directly linked to high rates of AD prevalence [14]. Secondly, regular physical activity is one of the most beneficial lifestyle choices for reducing the risk of dementia. Exercise may stimulate the growth of new brain cells and cause the production of a chemical that shields existing ones, according to research. When opposed to a sedentary lifestyle, an active one can virtually halve the risk [14]. Moreover, exercise's effect of increasing blood flow to the brain helps lower cardiovascular risk factors and dementia risk. Thirdly, it has been discovered that dementia development is substantially correlated with alcohol and tobacco use. One of the initial degenerative alterations of the brain in people with AD is oxidative stress, which has been linked to persistent exposure to cigarette smoking [15]. As alcohol is thought to exacerbate neuroinflammation and the neurotoxicity of the ß-amyloid cascade, excessive alcohol consumption raises the risk of dementia [16]. Low alcohol intake, though, might be beneficial [17]. Hence, there is debate on the impact of light to moderate alcohol use on cognitive function and the risk of dementia.

3.2. Medical Conditions

Mounting data indicates that diabetes and hypertension may both markedly raise the risk of various forms of dementia, especially AD and VaD. On the one hand, there is ample research that there is a connection between high blood pressure in middle age and the onset of cognitive decline years later. Hypertension leads to vascular changes that affect blood flow and brain metabolism, potentially causing cognitive disorders. It's associated with focal ischemic lesions like infarction, and chronic white matter ischemia due to small cerebral artery disease, which accelerate the onset of AD [18]. In hypertensive patients, episodes of low blood pressure, perfusion, and oxygen cause neuronal ischemia in sensitive brain regions, which in turn reduces blood flow and exacerbates cognitive deficits in AD [18]. On the other hand, hyperglycemia, a characteristic of diabetes, can lead to cognitive decline through various mechanisms: acute changes in blood glucose affect cerebral blood flow and osmotic balance in brain neurons. Studies in people with type 2 diabetes show that acute hyperglycemia results in decreased working memory, attention, and mood alterations [19]. Additionally, the established link between type 2 diabetes and macro- and microvascular diseases is relevant to dementia pathogenesis. Vascular conditions, particularly embolic strokes, contribute to cognitive impairment in individuals with type 2 diabetes [20].

4. Public Health Policies

The WHO's "Global Action Plan on the Public Health Response to Dementia 2017 - 2025" designates dementia as a public health priority, emphasizing the need for early intervention policies and establishing a specific global target for risk reduction. The plan also focuses on public health initiatives which aimed at enhancing people's ability to recognize early signs of dementia and promoting early diagnosis. It underscores the importance of addressing modifiable dementia risk factors from childhood

DOI: 10.54254/2753-8818/64/2024.17994

onwards. Innovative health technologies in prevention, early diagnosis and risk reduction is another demand made in the global action plan [21]. Using the UK as an example, early diagnosis and prevention initiatives are supported by the country's efforts to raise awareness of dementia and lessen its stigma [22].

In terms of modifiable determinants, the emphasis on public awareness and lifestyle interventions aligns with contemporary research suggesting that modifying certain behaviors can contribute to dementia risk reduction. The UK's example of incorporating healthy lifestyle information into the NHS Health Check programme is a positive step. However, the critical analysis should consider the actual impact on behavior change and the long-term sustainability of such initiatives. For non-modifiable determinants, the plan acknowledges the importance of timely diagnosis and continuous care, recognizing the inevitability of aging-related risk. Additionally, the example from the UK highlights efforts in awareness and prevention, but there may be gaps in addressing non-modifiable factors such as genetics, emphasizing the need for ongoing research and personalized approaches.

5. Prevention Efforts & Integrating Determinants in Policy Making

According to an update to The Lancet Commission on dementia prevention, intervention, and care, about 40% of dementia can be prevented or delayed. Therefore, preventing dementia requires a comprehensive approach targeting both modifiable and non-modifiable determinants. Lifestyle interventions play a pivotal role in mitigating dementia risk. For example, to protect the brain against the cell damage caused by AD and provide essential nutrients and antioxidants that protect brain cells and reduce inflammation by preventing beta-amyloid deposits, diets rich in the omega-3 fatty acid DHA (docosahexaenoic acid) and diets rich in fruits, vegetables, whole grains, and lean proteins, have been linked to a lower risk of cognitive decline and dementia [23]. Studies consistently underscore the positive impact of balanced diets rich in antioxidants, regular exercise, and the avoidance of smoking and excessive alcohol consumption.

Reducing vascular pathology's risk factors, such as hypertension and diabetes, may be a key strategy for preventing dementia. According to a recent study, taking antihypertensive drugs may lower the incidence of AD, VaD, and cognitive decline by 19–55% [24]. Research has also looked at the possibility of treating diabetes to prevent dementia. Those who started taking metformin had a markedly lower risk of dementia when compared to those who did not take anti-diabetes medication. However, regardless of the drug employed, this might represent the benefits of glucose lowering on cognition [25].

The endeavour to integrate both modifiable and non-modifiable determinants of dementia in policy making presents a complex challenge. One prominent challenge is the dynamic nature of modifiable determinants, wherein the efficacy of interventions may vary across diverse populations. Crafting policies that effectively promote lifestyle changes requires understanding and adaptation to the cultural, socioeconomic, and educational contexts of individuals. Conversely, non-modifiable determinants introduce inherent differences. Age, a predominant risk factor, demands policies that address the specific needs of an aging population, including comprehensive healthcare and support services. The genetic component brings complexities related to personalized medicine, ethical consideration. The conflict between modifiable and non-modifiable determinants creates a resource allocation dilemma.

To address these challenges, future policies should adopt an integrated and interdisciplinary approach. Firstly, a comprehensive public health education strategy is imperative. Policies should emphasize the importance of lifestyle modifications while promoting awareness of non-modifiable risk factors. Public health campaigns should aim to destigmatize dementia, educate individuals about genetic predispositions, and encourage regular health check-ups, especially for aging populations. Furthermore, policies must prioritize the creation of an inclusive and supportive healthcare infrastructure. This includes accessible healthcare services for individuals with diverse risk profiles. To conclude, the integration of modifiable and non-modifiable determinants in dementia policy making requires a delicate balance between adapting interventions to diverse populations.

DOI: 10.54254/2753-8818/64/2024.17994

6. Conclusion

In conclusion, this essay delves into the multifaceted landscape of dementia, scrutinizing both its non-modifiable and modifiable determinants in the context of public health initiatives and preventive programs. A healthy diet, regular exercise, and the avoidance of smoking and excessive alcohol consumption are linked to a lower risk of cognitive decline and dementia. Additionally, medical conditions like diabetes and hypertension are intricately connected to dementia risk, emphasizing the importance of managing these conditions to prevent cognitive impairment. Public health policies, exemplified by the WHO's Global Action Plan, play a crucial role in addressing dementia as a priority. Early intervention, awareness campaigns, and the emphasis on modifiable risk factors from childhood underscore the proactive stance. However, integrating both modifiable and non-modifiable determinants in policy making necessitates a delicate balance. With future policies requiring a comprehensive public health education strategy, destigmatization of dementia, and the creation of inclusive healthcare infrastructure.

References

[1] Jun Yup Lee, Harney, D., Teo, J.D., Kwok, J.B., Sutherland, G.T., Larance, M. and Don, A.S. (2023). The major TMEM106B dementia risk allele affects TMEM106B protein levels, fibril formation, and myelin lipid homeostasis in the ageing human hippocampus. *Molecular Neurodegeneration*, 18(1). doi:https://doi.org/10.1186/s13024-023-00650-3.

[2] National Institute on Aging (2023a). *Alzheimer's Disease Fact Sheet*. [online] National Institute on Aging. Available at: https://www.nia.nih.gov/health/alzheimers-and-dementia/alzheimers-disease-fact-sheet.

[3] Uddin, M.S. and Ashraf, G.M. (2018). *Introductory Chapter: Alzheimer's Disease—The Most Common Cause of Dementia*. [online] www.intechopen.com. Available at: https://www.intechopen.com/chapters/64605#B6 [Accessed 24 Dec. 2023].

[4] Wilkins, H.M. and Swerdlow, R.H. (2021). Mitochondrial links between brain aging and Alzheimer's disease. *Translational Neurodegeneration*, 10(1). doi:https://doi.org/10.1186/s40035-021-00261-2.

[5] Savva, G.M., Wharton, S.B., Ince, P.G., Forster, G., Matthews, F.E. and Brayne, C. (2009). Age, Neuropathology, and Dementia. *New England Journal of Medicine*, 360(22), pp.2302–2309. doi:https://doi.org/10.1056/nejmoa0806142.

[6] National Institute on Aging. (2023b). *Alzheimer's Disease Genetics Fact Sheet*. [online] Available at: https://www.nia.nih.gov/health/genetics-and-family-history/alzheimers-disease-genetics-fact-sheet.

[7] Mayo Clinic. (2023). *Alzheimer's disease: does it exist in your gene?* [online] Available at: https://www.mayoclinic.org/zh-hans/diseases-conditions/alzheimers-disease/in-depth/alzheimers-genes/art-20046552 [Accessed 25 Dec. 2023].

[8] Holtzman, D.M., Herz, J. and Bu, G. (2012). Apolipoprotein E and Apolipoprotein E Receptors: Normal Biology and Roles in Alzheimer Disease. *Cold Spring Harbor Perspectives in Medicine*, 2(3), pp.a006312–a006312. doi:https://doi.org/10.1101/cshperspect.a006312.

[9] Beam, C.R., Kaneshiro, C., Jang, J.Y., Reynolds, C.A., Pedersen, N.L. and Gatz, M. (2018). Differences Between Women and Men in Incidence Rates of Dementia and Alzheimer's Disease. *Journal of Alzheimer's Disease*, [online] 64(4), pp.1077–1083. doi:https://doi.org/10.3233/jad-180141.

[10] Altmann, A., Tian, L., Henderson, V.W. and Greicius, M.D. (2014). Sex modifies theAPOE-related risk of developing Alzheimer disease. *Annals of Neurology*, 75(4), pp.563–573. doi:https://doi.org/10.1002/ana.24135.

[11] Kiely, A. (2018). *Why is dementia different for women?* [online] Alzheimer's Society. Available at: https://www.alzheimers.org.uk/blog/why-dementia-different-women.

[12] Rocca, W.A., Grossardt, B.R. and Shuster, L.T. (2011). Oophorectomy, menopause, estrogen treatment, and cognitive aging: clinical evidence for a window of opportunity. *Brain Research*, [online] 1379, pp.188–198. doi:https://doi.org/10.1016/j.brainres.2010.10.031.

[13] Mielke, M.M. (2018). Sex and Gender Differences in Alzheimer's Disease Dementia. *The Psychiatric times*, [online] 35(11), pp.14–17. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6390276/.

[14] Thoenen, E., Health Statistics Center Statistical Staff, Doria, J., King, F., Leonard, T., Light, T. and Simmons, P. (2005). *Dementia: the Growing Crisis in West Virginia*. [online] www.wvdhhr.org. Available at: http://www.wvdhhr.org/bph/oehp/hsc/dementia/prevent.htm [Accessed 3 Jan. 2024].

[15] Custodio, N., Montesinos, R., Lira, D., Herrera-Pérez, E., Bardales, Y. and Valeriano-Lorenzo, L. (2017). Mixed dementia: A review of the evidence. *Dementia & Neuropsychologia*, [online] 11(4), pp.364–370. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5769994/.

[16] Wiegmann, C., Mick, I., Brandl, E.J., Heinz, A. and Gutwinski, S. (2020). Alcohol and Dementia – What is the Link? A Systematic Review. *Neuropsychiatric Disease and Treatment*, [online] 16, pp.87–99. doi:https://doi.org/10.2147/NDT.S198772.

[17] Chen, J.-H., Lin, K.-P. and Chen, Y.-C. (2009). Risk Factors for Dementia. *Journal of the Formosan Medical Association*, [online] 108(10), pp.754–764. doi:https://doi.org/10.1016/s0929-6646(09)60402-2.

[18] Duron, E. and Hanon, O. (2008). Hypertension, cognitive decline and dementia. *Archives of Cardiovascular Diseases*, 101(3), pp.181–189. doi:https://doi.org/10.1016/s1875-2136(08)71801-1.

[19] Sommerfield, A.J., Deary, I.J. and Frier, B.M. (2004). Acute Hyperglycemia Alters Mood State and Impairs Cognitive Performance in People With Type 2 Diabetes. *Diabetes Care*, [online] 27(10), pp.2335–2340. doi:https://doi.org/10.2337/diacare.27.10.2335.

[20] Tiehuis, A.M., van der Graaf, Y., Visseren, F.L., Vincken, K.L., Biessels, G.J., Appelman, A.P. A., Kappelle, L.J. and Mali, W.P.T.M. (2008). Diabetes Increases Atrophy and Vascular Lesions on Brain MRI in Patients With Symptomatic Arterial Disease. *Stroke*, 39(5), pp.1600–1603. doi:https://doi.org/10.1161/strokeaha.107.506089.

[21] World Health Organization (2017). *Global action plan on the public health response to dementia: 2017-2025*. [online] Available at: https://iris.who.int/bitstream/handle/10665/259615/?sequence=1.

[22] Hampel, H., Vergallo, A., Iwatsubo, T., Cho, M., Kurokawa, K., Wang, H., Kurzman, H.R. and Chen, C. (2022). Evaluation of major national dementia policies and health-care system preparedness for early medical action and implementation. *Alzheimer's & Dementia*, 18(10). doi:https://doi.org/10.1002/alz.12655.

[23] National Institute on Aging. (2023c). *What Do We Know About Diet and Prevention of Alzheimer's Disease?* [online] Available at: https://www.nia.nih.gov/health/alzheimers-and-dementia/what-do-we-know-about-diet-and-prevention-alzheimers-disease.

[24] Rakesh, G., Szabo, S.T., Alexopoulos, G.S. and Zannas, A.S. (2017). Strategies for dementia prevention: latest evidence and implications. *Therapeutic Advances in Chronic Disease*, [online] 8(8-9), pp.121–136. doi:https://doi.org/10.1177/2040622317712442.

[25] Zheng, B., Su, B., Ahmadi-Abhari, S., Dimitrios Kapogiannis, Ioanna Tzoulaki, Elio Riboli and Middleton, L. (2023). Dementia risk in patients with type 2 diabetes: Comparing metformin with no pharmacological treatment. *Alzheimer's & Dementia*, 19(12), pp.5681–5689. doi:https://doi.org/10.1002/alz.13349.