Neurocosm International Journal (NIJ)
Vol-2, Issue-2, June 2021

e-ISSN: 2582-7480

The Role of Modern Medicine in Dementia Prevention and Intervention

Bodipudi Sravani [1*], Anitha SP [2]

[1] Department of Biotechnology
[2] Department of Bioengineering, SASTRA University, Tamil Nadu, India
*Corresponding Author Email: bodipudisravani14@gmail.com

Abstract

The study has clearly provided the impact of dementia on the elderly individuals and also its prevention process. Due to biological aging, most of the individuals have suffered from the deterioration of cognitive function among individuals from all over the world. Dementia can impact negatively on the brain as a primary and secondary aspects. Alzheimer's can be considered as one of the most common form of dementia and almost 60% to 70% of individuals are already subjected to the disease dementia. The study help others to put a insight on the disability rate of elders due to dementia and it can be considered as the seventh leading cause for the death of people. Dementia is a wide variety of disease that includes Alzheimer's, Parkinson's disease, depression, anxiety and some other cognitive impairment. There are mainly two types of protein that help in the formation of dementia, those proteins are Tau and amyloid. The improper build-up of proteins within the brain can cause tangles within the brain, which may lead to the formation of abnormalities. Some of the major medicines for dementia are mainly known as Acetylcholinesterase inhibitors. In order to treat Alzheimer's, healthcare practitioners have been suggesting Donepezil and galantamine. Sometimes, individuals can suffer from depression and anxiety, therefore healthcare practitioners provide antidepressants to reduce the impact of those issues. Apart from that, sometimes non pharmacological approaches play an essential role in minimising the effect of dementia.

Keywords

Alzheimer's, Amyloids, communication therapy, Dementia, Donepezil, Tau.

INTRODUCTION

In recent years, most of the elderly individuals have been affected with dementia which may lead to the mortality of those people from all over the world. The term dementia can be explained as a serious mental disorder along with memory loss and incapability of solving problems in day to day lives. Dementia is a wide range of disease that can cover the alternation of brain activities and also Alzheimer's. Individuals may not properly think and accomplish their daily works; hence a decline of cognitive abilities can be observed. Therefore, individuals are required to be educated properly about healthcare and alternation in lifestyles to reduce the risk of dementia. This current study will shed light on the early detection of the disease dementia and its preventive measurements. Different policies are required to be implemented with the help of evidence-based synthesis models, to take care of people who have been experiencing dementia for a long time. These intervention policies should be emphasized on the education of children and also take initiatives to minimise the level of injuries due to dementia. The disease dementia can occur in early life and also at later stages of life. In the case of early stage, the age of individuals should be under 45 years and late life dementia occurs to those individuals after the age 65 years. In this context, it can be observed that, there are near about 50 million individuals who have been suffering from dementia and the number will rapidly enhance up to 152 million by the year 2050. In UK, there are near about 57% more cases regarding dementia were reported by the year 2022 and the healthcare sector of the UK has estimated that more than 1.2 million individuals will be affected by dementia. In that case, those individuals are required to be treated with complex care. As previously stated, dementia is a wide range of diseases, and no specific medication can cure dementia. Henceforth, some symptoms of dementia can be noticed easily and treated with some oral medications. In the case of memory impairment, some types of Cholinesterase inhibitor such as donepezil and galantamine can be used.

LITERATURE REVIEW

Factors that cause the formation of dementia

The disease dementia is associated with the decline of brain's activities, which also includes a variety of brain issues. Abnormalities inside the brain occur due to the different build-up of proteins in that portion. Extreme protein builds up inside the brain can lead to the shrinkage of nerve cells of human beings, that ultimately leads to the death of individuals [1]. The cells present in the brain become affected and damaged due to dementia and brain cells cannot communicate or work properly in that situation. Dementia can occur due to the abnormalities of two major proteins such as tau and amyloid. The activities of neurons at the brain are highly related to "Microtubule associated protein or MAP". These MAP proteins can be further divided into two parts such as MAP1 and MAP2 [2]. In the normal phase, Tau protein contains 2 to 3 moles of phosphatase, however at the

NEUROCOSM
e-ISSN: 2582-7480
Neurocosm International Journal (NIJ)
Vol-2, Issue-2, June 2021

disruptive phase hyperphosphorylation occurs and it ultimately depressed the biological activities. During Alzheimer's disease, the Tau protein normally folded into 3 to 4 parts and also hyperphosphorylated. As a result, the mixture of chemical filaments with the straight filaments are generally formulated along with neurofibrillary tangles inside the brain.

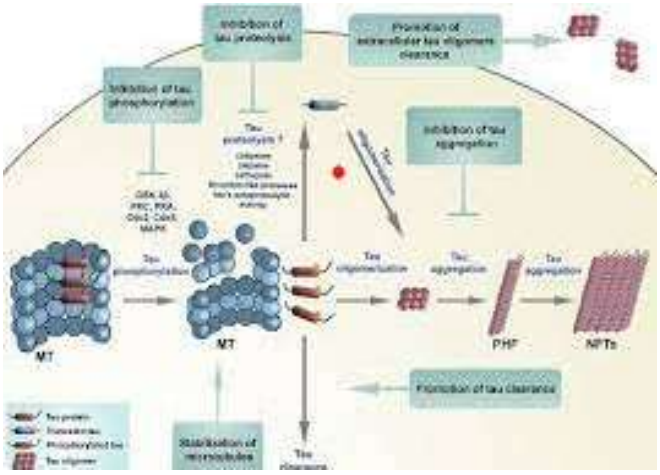

Figure 1. Impact of Tau protein
Source: [2]

On the other hand, amyloid proteins are taken as one of the identical factors that can generate enough space within the nerve cells of the individuals and amyloid plaques occurs with some misfolded proteins. After sequencing of proteins into many pieces can form beta amyloid aggregates. According to some other research, the long chain of amyloid proteins become fragmented into small parts and also release some free radicals [3]. Those free radicals can further attack neurons of the brain which can leads to the dysfunction of the brain and form dementia. Sometimes, it can be observed that beta amyloids have the capability to form a tiny hole at the membrane that can cause a neural influx of calcium ions that ultimately cause the death of nerve cells.

Process of early intervention of dementia

Dementia can be diagnosed with the help of two essential processes such as primary and secondary care approaches. Patients with dementia are generally contacted primarily with the healthcare practitioners. Dementia can occur due to the disturbance of thyroid, depression or the deficiency of vitamin B12. Patients who have developed psychological or neurological alteration should contact primary caregivers [4]. Therefore, primary caregivers are required to go through a complete physical examination, along with neurological signs and symptoms. In the case of further intervention process, a blood test is necessary to be accomplished. During blood test, the rate of sedimentation, b12 proportion and function of thyroid should be measured. Apart from that, radiography and electrocardiography can be clinically appropriate for this study. Caregivers are generally utilised the “mini mental state examination” and it can be considered as one of the major assessment tools.

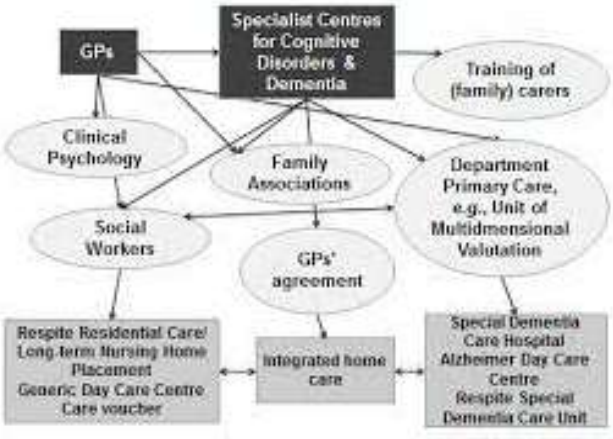

Figure 2. early intervention of dementia
Source: [5]

Apart from that, for older individuals’ behaviour therapy intervention can be considered as one of the essential approaches for the disease. According to the previously conducted studies, behaviour therapy is the primarily reported non pharmacological intervention. Behaviour therapy can aid the elderly individuals who have suffered from depression, mood disturbance and dementia [5]. In this case, caregivers are mainly taking the assistance of communication therapies for reducing depression and improving activities of patients with family members. Caregivers are also responsible for giving essential strength to those patients with dementia through helping them doing proper exercise. It can be taken as a long-term planning for providing them mobility and strength, henceforth an exercise program should be arranged [6]. A total 12-week exercise program should be assigned for those patients and after that a minimum 6 month follow up is required. Early intervention process of dementia also includes the rehabilitation process, it may help those individuals to maintain cognitive functioning. Patients with dementia disease should provide some dietary measurements by healthcare givers. Those patients should take more fish, vegetables and vegetables to obtain “omega 3 fatty acid” and antioxidants. Allele can be considered as one of the major risk factors for dementia, hence a daily intake of fish and fruits can provide essential vitamins to those patients. As a result, it may lower the rate of being affected by the disease dementia. Patients with dementia should be trained with cognitive skills that may help those patients to recall their memories.

Influence of modern medicines to prevent dementia

The disease dementia also includes bipolar disorders and the utilisation of lithium can be considered as one of the essential precautions for the disease. Further inhibition capacity of Lithium can be detected in case of tau protein and beta amyloid phosphorylation. There were near about 30% individuals with dementia depicted positive result after using lithium and the process of using lithium is not generally dose dependent [7]. In this context, it can be observed that, the disease dementia does not start immediately, a certain

transitional stage can be observed from a mild cognitive disorder to the extreme level. In that case, Donepezil and vitamin E can be taken as essential drugs to treat cognitive impairment. According to previous studies, Donepezil generally acts as a cholinesterase inhibitor, which has already proved as an effective medicine for dementia. Patients with dementia can intake donepezil at the rate of 10 mg per day after consulting with their healthcare practitioners [8]. Apart from that Vitamin E contains the properties of antioxidants that can act as neurodegeneration, as a result, it may slow down the further progress of dementia disease. On the other hand, individuals who have developed the symptoms of Alzheimer's, can be treated with PBT2.

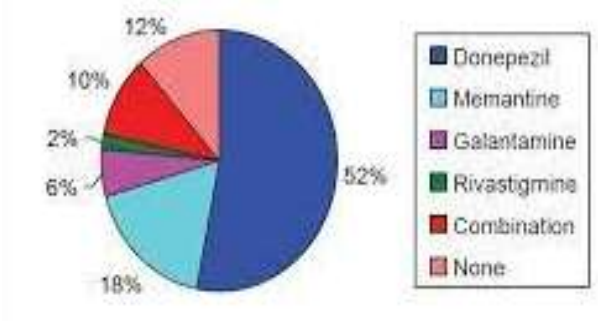

Figure3: Drugs used for Dementia
Source: [8]

The compound PBT2 can be known as a metal protein substance that can effectively eliminate the compounds such as copper and zinc toxicity of amyloid beta chain. The dosage of PBT2 for this disease is 250 mg/day. Another drug, named Memantine can be used to control the different activities of the brain and also maintain the release of chemicals within the brain of dementia patients. In case of a more severe case of dementia, sometimes medical practitioners provide the combination of Donepezil and Memantine to the patients [9]. Sometimes patients have mood swings and low mood activities in the initial phase of dementia disease, henceforth, doctors can recommend antidepressants for selective cases. Anxiety can be denoted as another part of the disease dementia; therefore, Anxiolytics drugs can be taken as beneficial for treating early phases of dementia. In case of behavioural changes like aggression, hallucination and agitation, those patients are recommended to consume some Antipsychotic medicines such as haloperidol and risperidone that can be effective for the treatment of dementia.

After effect of medicines on dementia patients

The study also includes the area of using medications or drugs for treating the disease dementia and its positive aspects. There were lots of uncertainties regarding the implementation of appropriate drugs for dementia. A proper observation can be helpful for detecting the exact cognitive impairment for any individual. In the case of healthy loving and improvement of the patient's condition, medications play an important role. Untreated cases of dementia may demonstrate a serious alternation of behaviour, which can cause communication difficulties [10]. Non-medical approaches can be considered as the primary approaches for dementia patients, in that case healthcare practitioners are generally communicate with dementia patients to improve their mental health. Treatment or dosage should be started at the low rate as per the patient's condition, then it can be gradually enhanced at the higher dose rate. In this phase, healthcare practitioners are naturally focussed on the avoiding such medication which can develop cognitive issues. Anxiety can be treated with Benzodiazepine drugs and also observation should be done at least up to for 3 months after the usage [11]. Some issues or side effects may occur for some patients; therefore, relation techniques can be combinedly used for the treatment process. Apart from that deep breathing, communication strategies and detailed interaction with patients can be used to reduce anxiety. After observing the depression related issues of individuals, sometimes healthcare practitioners take some non-drug strategies to avoid the side effects. Long term usage of cholinergic drugs can affect the memories and thinking of individuals. Healthcare practitioners then prefer to use counselling therapy and perfect diet to those dementia patients. Those patients are suggested to consume foods which contain more vitamins on a daily basis and a daily exercise can further improve the condition of patients. Long term use of Antipsychotic medicines is able to block the effect of dopamine, as a result it may increase hallucination. Patients with dementia should be treated with a proper environment along with physical and medical therapy.

METHODOLOGY

This research paper is based on dementia prevention and intervention through modern medicine. In order to get the data on this subject matter was not easy and that is why a secondary qualitative process has been selected to provide authentic data on the relevant subject matter. In this case, an internet resource is the largest way of getting the relevant data on the topic. accordingly, it can be said that this method has various kinds of opportunities to provide knowledge and information on the topic that helps to identify the important data for the project. This method also helps to get the raw information for the research and also provides the chance to get the opportunities to see the difference between the information. Apart from this, the secondary qualitative process is much easy and quick than other research methods. In this context, the data analysis process is also quite easy and it also helps to provide accurate outcomes from the research process [12]. The secondary qualitative process provides a large amount and different kinds of data sets on the particular topic and also supports the entire research work. This study has chosen secondary qualitative due to expanding the value of the research work and it makes a positive impact on the research study.

Nowadays, the elderly population has been enhancing a lot and aging can be taken as one of the common reasons for developing dementia disease. In that case, multiple new cases

emerge after the alternation of brain function and death of the brain cells. Therefore, collection of secondary data is beneficial for conducting the research in the near future. A wide variety of dementia cases from the different parts of the country can be beneficial for collecting data. That information should also cover the early intervention for the dementia, henceforth individuals should understand different types of prevention along with medication, primary and secondary care approaches [13]. Secondary data should be collected from the scholarly journals, books and articles. Apart from that, some previously conducted research on the topic of dementia and its intervention should also be added. In that case, the authentication of the study is required to be maintained, hence the study has some inclusion and exclusion criteria as well. Secondary data can be easily obtained through the internet and it can be cost effective also.

Current research is also dependent on pharmacological approaches and its advancement on dementia prevention. In that case, data should be taken from some authentic medical journals, websites or sources. PubMed can be considered as one of the most accepted websites or online libraries to gather a huge number of medical data [19]. Additionally, PubMed is a free source or site for gathering health related information. Databases used in PubMed, can effectively help individuals in improving the personal and global health. Journals or articles available at PubMed are generally properly structured along with Publication date, Journal name, Language, authors name and publication library name. Methodology part of the study also have some inclusion and exclusion criteria. Inclusion criteria includes, a proper journal with authors name and date, henceforth, selected journals should not be older than the year 2018. One of the major exclusion criteria of this research is, all articles should be selected from scholarly journals.

DISCUSSION

Ageing can be considered as one of the major reasons for developing dementia and most of the individuals have been suffering from this severe disease. Disabilities with aging is one of the major concerns for healthcare givers, hence they have aimed to promote healthy aging and a proper mental health for elders with dementia disease. Further projection of disabled individuals is 101 million throughout the world and the number will enhance up to 277 million by the year 2050 [14]. From the above-mentioned literature, it can be observed that fundamental reasons for disabilities for older individuals are dementia and cognitive impairment. Dementia can be occurred due to multiple factors such as genetic issues and environmental factors. As per the previously conducted research, it can be estimated that, almost 40% of cases occur due to the following factors such as, depression, brain disease, Trauma, lack of physical activities, and consumption of alcohols [15]. Healthcare authorities have targeted to take preventive measurement of Dementia to reduce the number of affected individuals from all over the world. In this context, it can be observed that Alzheimer's is one of the most common Dementia that can be easily noticed. With the help of the neuroimaging tools, have successfully evaluated that dementia includes vascular disease and also the characteristics of neurodegenerative disease Therefore, the treatment process of dementia also focuses on the mild characteristics of AD and also patients' behavioural symptoms should be recorded at the preclinical phase.

The process of treating dementia starts from evaluating the pathological situation of the disease, hence the process also includes the rehabilitation approaches for multiple factors. The study has provided a clear concept of developing dementia within male and female both individuals. In that case, the Apolipoprotein E allele can be taken as the responsible allele for developing dementia [16]. Apart from that, some other observational studies help others to evaluate that a lack of physical activities may develop the decline of cognitive activities, which can cause the formation of Alzheimer and Dementia. In that case, healthcare practitioners are generally responsible for helping those dementia patients to conduct aerobic exercise on a regular basis. These types of intervention policies also required long term planning and a continuous observation of those dementia patients. In order to cope up with the mobility related risk factors, it is required to follow a proper walking planning to enhance the flexibility of those patients. On the other hand, lower education can also help in developing dementia, because people with less education may not know about the adverse effect of improper lifestyles [22]. In that case, the frontline helpers have taken initiatives to provide sufficient education to the families of those dementia patients. Therefore, "cognitive stimulation therapy" and "cognitive training" can be taken as non-pharmacological intervention for the treatment of dementia. Stress and depression are the two major factors for the cognitive decline and patients can be more introverted during this phase. In this context, the social participation of those patients is required to make the feel prioritised.

The aforementioned studies help individuals to understand the impact of dementia, which can further include lots of brain diseases. Dementia also includes abnormalities in the brain due to the rapid build-up of proteins inside the brain. The participation of two essential proteins can be observed such as MAP1 and MAP2. Apart from that, the role of Tau protein is also significant and due to the hyperphosphorylation the depression of biological activities within the brain occurs [17]. On the other hand, Beta Amyloid protein is mainly responsible for the generation of space inside the nerve cells. As a result, plaque occurs inside the brain after folding of some proteins, so it may cause sequencing of proteins. From the previously mentioned study, it can be observed that treating dementia depends on some pharmacological and non-pharmacological approaches as well. Untreated cases of dementia can be more stressful and severe; therefore, it may generate more chances to be affected by it. Non pharmacological approaches include a rapid participation of healthcare practitioners in treating

dementia patients with a rapid communication therapy. Benzodiazepine drugs have been suggested to use anxiety at least for 3 months. Apart from that another drug named PBT2 can be used to treat dementia. It is a protein substance made up of metals and doctors should start from a low dosage, as per the patient's condition. Behavioural changes can be noticed within the patients of dementia, in that case practitioners can also recommend to use Donepezil and Vitamin E for treatment purposes [18]. The dosage of Donepezil drugs is a minimum 10 mg/day, and patients should consult with their healthcare practitioners before taking any medications. Sometimes, doctors suggest to provide proper counselling therapy to that dementia affected patients for the wellbeing of their health.

The discussion part of the study also includes a lack of participation of family members and healthcare givers. As a result, patients cannot get proper treatment or care for treating dementia. The drug therapy for the dementia treatment also includes some psychological and physiological intervention processes [20]. The process of early intervention includes a proper participation of caregivers for improving the depressive stage of individuals lives. Before suggesting any medications to the dementia patients, healthcare practitioners are preferring to conduct some ability tests such as problem solving, balancing, movement, language, skills and attention. Patterns of memory loss in the case of dementia patients generally differ from each other. It can be considered as one of the major issues that healthcare practitioners may get confused due to the variation of issues. Doctors also prefer to conduct health check-up to those individuals and diagnosis should be done after testing. Scanning of brain tissues to those patients are required for the early detection. In that case, CT scan or MRI and PET scan plays an essential role in detecting the alternation of activities within the brains of those patients [21]. A proper care planning is one of the essential approaches for treating dementia, and the process also fosters the homecare environment. Local governments also promote the community care approach and person-centred care approach for dementia patients. On the other hand, the role of registered nurses in treating and physiotherapist are also significant in assisting dementia patients at least for 24 hours.

CONCLUSION

The study clearly provided the reason for mortality of elderly individuals due to dementia. Still now, individuals did not understand the severity of the disease dementia, and it can be considered as one of the major barriers of care planning for dementia patients. The disease dementia can be explained as the formation of mental issues and loss of memory as well. People affected by dementia also lose their capability to talk with family members, communicate and solve their day-to-day activities. The study also provides an insight that dementia can occur at the early stage of life's and also the later phase of life. Most of the cases, aging can be considered as one of the primary risk factors for the disease dementia. The study also represents the current state of UK healthcare system and dementia, and there are near about 57% more cases regarding dementia reported by the year 2022.

The continuous deterioration of the brain's activities can be observed during the affected phase of dementia. Individuals' brains may be affected due to the rapid protein build up in the brain and it may lead to the shrinkage of nerve cells. As a result, it may impact on the different parts of the brain and people also forget to think, learn and communicate. There are mainly two proteins that can be found, those are responsible for the formation of dementia. The care approach of dementia also includes some pharmacological and non-pharmacological approaches. Behaviour therapy can aid the elderly individuals who have suffered from depression, mood disturbance and dementia. Non pharmacological approaches also include a daily exercise to those disabled dementia patients at least for 15 minutes on a daily basis. Donepezil can be considered as one of the major cholinesterase inhibitors that can reduce the impact of dementia. In case of a more severe case of dementia, sometimes medical practitioners provide the combination of Donepezil and Memantine to the patients. Anxiety can be treated with Benzodiazepine drugs and also observation should be done at least up to for 3 months after the usage.

REFERENCE

[1] Ano, Y. and Nakayama, H., 2018. Preventive effects of dairy products on dementia and the underlying mechanisms. *International journal of molecular sciences*, *19*(7), p.1927.

[2] Anstey, K.J., Peters, R., Zheng, L., Barnes, D.E., Brayne, C., Brodaty, H., Chalmers, J., Clare, L., Dixon, R.A., Dodge, H. and Lautenschlager, N.T., 2020. Future directions for dementia risk reduction and prevention research: An International Research Network on Dementia Prevention consensus. *Journal of Alzheimer's Disease*, *78*(1), pp.3-12.

[3] Bali, P., Kaur, N., Tiwari, A., Bammidi, S., Podder, V., Devi, C., Kumar, S., Sivapuram, M.S., Ghani, A., Modgil, S. and Malik, N., 2020. Effectiveness of yoga as the public health intervention module in the management of diabetes and diabetes associated dementia in South East Asia: A narrative review. *Neuroepidemiology*, *54*(4), pp.287-303.

[4] Brayne, C.E., Barnes, L.E., Breteler, M.M., Brooks, R.L., Dufouil, C., Fox, C., Fratiglioni, L., Ikram, M.A., Kenny, R.A., Kivipelto, M. and Lobo, A., 2020. Dementia research fit for the planet: reflections on population studies of dementia for researchers and policy makers alike. *Neuroepidemiology*, *54*(2), pp.157-170.

[5] Frisoni, G.B., Molinuevo, J.L., Altomare, D., Carrera, E., Barkhof, F., Berkhof, J., Delrieu, J., Dubois, B., Kivipelto, M., Nordberg, A. and Schott, J.M., 2020. Precision prevention of Alzheimer's and other dementias: Anticipating future needs in the control of risk factors and implementation of disease-modifying therapies. *Alzheimer's & Dementia*, *16*(10), pp.1457-1468.

[6] [6] Godfrey, A., Brodie, M., van Schooten, K.S., Nouredanesh, M., Stuart, S. and Robinson, L., 2019. Inertial wearables as pragmatic tools in dementia. *Maturitas*, *127*, pp.12-17.

[7] Guzman-Martinez, L., Calfío, C., Farias, G.A., Vilches, C.,

e-ISSN: 2582-7480

Prieto, R. and Maccioni, R.B., 2021. New frontiers in the prevention, diagnosis, and treatment of Alzheimer's disease. *Journal of Alzheimer's Disease*, *82*(s1), pp.S51-S63.

[8] Isaacson, R.S. and Saif, N., 2020. A missed opportunity for dementia prevention? Current challenges for early detection and modern-day solutions. *The Journal of Prevention of Alzheimer's Disease*, *7*(4), pp.291-293.

[9] Lisko, I., Kulmala, J., Annetorp, M., Ngandu, T., Mangialasche, F. and Kivipelto, M., 2021. How can dementia and disability be prevented in older adults: where are we today and where are we going?. *Journal of internal medicine*, *289*(6), pp.807-830.

[10] Lisko, I., Kulmala, J., Annetorp, M., Ngandu, T., Mangialasche, F. and Kivipelto, M., 2021. How can dementia and disability be prevented in older adults: where are we today and where are we going?. *Journal of internal medicine*, *289*(6), pp.807-830.

[11] Mart, M.F., Pun, B.T., Pandharipande, P., Jackson, J.C. and Ely, E.W., 2021. ICU Survivorship–The Relationship of Delirium, Sedation, Dementia, and Acquired Weakness. *Critical care medicine*, *49*(8), p.1227.

[12] Perneczky, R., 2022. Dementia prevention and reserve against neurodegenerative disease. *Dialogues in Clinical Neuroscience*.

[13] Shanahan, D.F., Astell–Burt, T., Barber, E.A., Brymer, E., Cox, D.T., Dean, J., Depledge, M., [12] Fuller, R.A., Hartig, T., Irvine, K.N. and Jones, A., 2019. Nature–based interventions for improving health and wellbeing: The purpose, the people and the outcomes. *Sports*, *7*(6), p.141.

[14] Watson, J., Saunders, S., Muniz Terrera, G., Ritchie, C., Evans, A., Luz, S. and Clarke, C., 2019. What matters to people with memory problems, healthy volunteers and health and social care professionals in the context of developing treatment to prevent Alzheimer's dementia? A qualitative study. *Health Expectations*, *22*(3), pp.504-517.

[15] Walton, C.C., Lampit, A., Boulamatsis, C., Hallock, H., Barr, P., Ginige, J.A., Brodaty, H., Chau, T., Heffernan, M., Sachdev, P.S. and Singh, M.A.F., 2019. Design and development of the brain training system for the digital "maintain your brain" dementia prevention trial. *JMIR aging*, *2*(1), p.e13135.

[16] Visontay, R., Rao, R.T. and Mewton, L., 2021. Alcohol use and dementia: new research directions. *Current opinion in psychiatry*, *34*(2), pp.165-170.

[17] Cena, H. and Calder, P.C., 2020. Defining a healthy diet: evidence for the role of contemporary dietary patterns in health and disease. *Nutrients*, *12*(2), p.334.

[18] Dafsari, F.S. and Jessen, F., 2020. Depression—an underrecognized target for prevention of dementia in Alzheimer's disease. *Translational Psychiatry*, *10*(1), pp.1-13.

[19] Stephan, B.C., Siervo, M. and Brayne, C., 2020. How can population-based studies best be utilized to reduce the global impact of dementia? Recommendations for researchers, funders, and policymakers. *Alzheimer's & Dementia*, *16*(10), pp.1448-1456.

[20] Cho, H.K., 2018. The effects of music therapy-singing group on quality of life and affect of persons with dementia: a randomized controlled trial. *Frontiers in medicine*, *5*, p.279.

[21] Zhang, X., Wen, J. and Zhang, Z., 2018. Statins use and risk of dementia: a dose–response meta analysis. *Medicine*, *97*(30).

[22] Müllers, P., Taubert, M. and Müller, N.G., 2019. Physical exercise as personalized medicine for dementia prevention?. *Frontiers in Physiology*, *10*, p.672.

[23] Jennings, L.A., Laffan, A.M., Schlissel, A.C., Colligan, E., Tan, Z., Wenger, N.S. and Reuben, D.B., 2019. Health care utilization and cost outcomes of a comprehensive dementia care program for Medicare beneficiaries. *JAMA Internal Medicine*, *179*(2), pp.161-166.