***Title:*** **Healthy lifestyle to reduce risk of dementia**

*Abstract:*

Dementia is a growing problem worldwide and prevention is currently the only method of treatment. Previous observational studies have suggested that diet can help prevent dementia. Treatment trials have shown contrasting results, however. This chapter reviews the evidence of different studies, and provides a detailed overview of the state of research on micro-nutrients and their impact on preventing cognitive decline and Alzheimer's disease. Physical activity and possibly cognitive activity may be more likely to have lifelong positive preventative effects against cognitive decline and dementia. We will focus on studies investigating diet, nutrition, physical and cognitive activities to both prevent and treat dementia symptoms. These studies suggest that a lifespan approach may be needed as some interventions are more successful in midlife (nutrition/diet, prevention of cardiovascular disease and obesity), while others can still be effective in old age, such as physical and cognitive activities.

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*Introduction:*

Population ageing was identified by the European Commission as the most pressing policy issue in the 21$^{st}$ century. Life expectancy has grown rapidly during the last century due to improved living standards, better healthcare, medical progress and increased awareness of health issues, and this trend is expected to continue. In Europe, the life expectancy is now 83.6 years old for women and 78.1 years old for men (Statistical Office of the European Communities, 2016). By 2050, the number of people over 65 living in the European Union will grow by 70% and the number of people aged over 80 by 170%, with consequent challenges in terms of demand for healthcare, needs of an ageing population and sustainability of workforce (Statistical Office of the European Communities, 2016).

The literature has highlighted that the prolongation of the life span is associated with numerous age-related changes in key physiological processes, such as bone marrow, immune system and cardiovascular functioning (Griffith, 2013; Wong et al., 2016); as well as changes in key psychological, physical and cognitive processes, potentially resulting from changes in gray matter in the hippocampus and functional connectivity between brain regions (Fogel et al., 2017; Geerligs, Renken, Saliasi, Maurits, & Lorist, 2014). Overall these age-related changes, among others, lead to a decrease in general functional capacity. During the normal ageing process, even without the presence of pathology, most physiological systems experience structural and functional deterioration (Marom-Klibansky & Drory, 2002). These age-related physiological changes affect a broad range of functions, such as muscular, cardiovascular, pulmonary, body composition and in general the physical functional capacities, which, cumulatively, could impact the preservation of the activities of daily living and independence in older adults (Brustio, Magistro, Rabaglietti, & Liubicich, 2017; Chodzko-Zajko et al., 2009; Magistro, Candela, Brustio, Liubicich, & Rabaglietti, 2015).

Neuron loss and alterations in synaptic density that increase with age have been shown to contribute to cognitive changes observed with age (Dickstein et al., 2007; Hedden & Gabrieli, 2004; Hof & Morrison, 2004). Although changes are not observed in a uniform manner, many cognitive functions can be affected, including attention and memory (Hedden & Gabrieli, 2004). Long-term memory, the memory system for permanently storing and retrieving information, is frequently affected by the ageing process while other memory functions, such as working memory, short-term memory and semantic memory, remain relatively stable (Kaschel, Kazén, & Kuhl, 2017; Mattay et al., 2006; Ishihara, Gondo, & Poon, 2002; Grady & Craik, 2000). Attentional difficulties have been shown to occur specifically in selective attention, rather than overall attention (Cabeza, Nyberg, Park…et al, 2016; Commodari & Guarnera, 2008; West, 2004). Selective attention consists of the ability to focus on a specific stimulus and the ability to inhibit other stimulus that are occurring simultaneously.

In general, the decline in long-term memory and selective attention is particularly relevant to overall well-being and autonomy of older adults. The maintenance of cognitive performance is associated with the correct execution of daily physical tasks (Chodzko-Zajko et al., 2009; Magistro, Liubicich, Candela, & Ciairano, 2014; Tabbarah, Crimmins, & Seeman, 2002) and activities of daily living (Candela, Zucchetti, & Magistro, 2013; Perrig-Chiello, Perrig, Uebelbacher, & Stähelin, 2006). These include cooking, shopping, housekeeping, and taking care of financial matters. The literature has highlighted numerous consequences of memory and attentional impairments that shape an individuals' ability to conduct activities of daily living. The maintenance of cognitive abilities and the prevention of severe cognitive deterioration therefore represent the most predominant health challenges adults contend with as they age.

To optimize prevention of mild cognitive impairment and the varying subtypes of dementia, considering the complexity and multifactorial nature of the disorders, multi-domain interventions are required to target several risk factors and disease mechanisms simultaneously (Ngandu et al., 2015). Cognitive decline and especially dementia is strongly associated with dependency and disability. This, in turn, impacts individuals, families and society through the associated costs. Currently, the cost of dementia in the U.K. is estimated at £26 billion a year, which works out as an average annual cost of £32,250 per person with dementia (Alzheimer's Association, 2015). Subsequently, dementia has been recognised worldwide as an imminent health priority (World Health Organisation, 2012; World Health Organization, 2002). The increases in life expectancy and consequential increase in number of older adults in society has led to a rapid increase in the prevalence of dementia and cognitive decline, impacting economic and social development worldwide. At present there are roughly 46.8 million people living with dementia worldwide and this number is set to almost double every 20 years (Prince et al., 2015).

Therefore, an integrated approach, that applies methodological, geographical, multi-disciplinary expertise and considers the abundance of co-morbidity, acute and chronic diseases, is necessary for tackling the physical and psychological health conditions of an expanding population of older adults. This integrated approach should hence aim to reduce the costs of cognitive decline to both the individual and society; and to improve quality of life for older adults. This is consistent with worldwide health priorities set out to promote healthy and active ageing.

Dementia, as defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) (4th ed., text rev.; DSM–IV–TR; American Psychiatric Association, 2000) is characterised by organic and acquired disturbances of intellectual functions, most notably memory impairments and at least one other cognitive function without disturbance in consciousness and to a degree that significantly interferes with interpersonal and working relationships. Dementia is the largest predictor of disability and dependence in older adults over the age of 65 (World Health Organisation, 2012; Burns & Iliffe, 2009). The global burden incurred as a result of dementia has shown a one hundred percent increase over the past 20 years, through mortality and disability measures (i.e, Disability Adjusted Life Year, DALYs) (Troeger et al., 2017). Dementia prevalence across the literature is estimated at 6.4% for adults over 65 years old (Lobo et al., 2000) and doubles every five years, increasing prevalence to 40% for older adults over 85 years old (Alzheimer's Association, 2015). Alzheimer disease (AD) is the most common form of dementia, encompassing between 50 and 70% of total people with dementia (Alzheimer's Association, 2015).

In the last decade, dementia research has significantly developed. First, several experimental and clinical studies have demonstrated that dementia and related disorders are characterized by a long preclinical period. Changes in brain structure and functioning caused by the disease may begin years, or even decades, before clinical symptoms are detected. Preclinical brain changes engender mild changes in memory and cognition that are not severe enough to disrupt everyday life, but progress gradually. In the context of dementia, mild cognitive impairment (MCI) may represent this stage (Petersen et al., 1999). A significant risk factor for the development of MCI (with a probability of conversion to dementia) has been shown as 10-15% per year compared to 1%-2% of healthy controls. MCI refers to a clinical condition in which objective evidence of cognitive impairment in one or more cognitive domains is present, such as a slight decrease in memory, verbal skills or orientation, but without a profound negative impact on daily activity, functioning and personal independence (Gauthier et al., 2006; Petersen et al., 1999). Although the cognitive impairments associated with MCI do not preclude independent functioning, research suggests that individuals with MCI experience changes in their psychological and daily functioning, as well as quality of life (QoL) (Teng, Tassniyom, & Lu, 2012). A recent review article noted that neuropsychiatric symptoms are very common in individuals with MCI, with prevalence rates of at least one neuropsychiatric symptom ranging from 35-85% (Monastero, Mangialasche, Camarda, Ercolani, & Camarda, 2009). The most common neuropsychiatric issues associated with MCI include depression, anxiety, irritability, agitation, apathy, euphoria, disinhibition, delusions, hallucinations, and sleep disorders (Monastero et al., 2009). Moreover, the hypothesis that MCI is a transitional stage between normal ageing and dementia implies that individuals with MCI are at risk for an eventual inability to live independently, further decreasing QoL (Petersen et al., 1999).

MCI consequently has been viewed as an intermediate stage between normal ageing and dementia(Gauthier et al., 2006; Petersen et al., 1999), or as a risk factor for dementia. More specifically, subjects with amnestic MCI constitute subtypes that are most likely to progress to AD, while non-amnestic single- or multiple-domain MCI have a higher chance of developing an alternative type of dementia, such as, vascular dementia, dementia with Lewy bodies or frontotemporal dementia (Tabert et al., 2006). Early identification and treatment of people with MCI may help delay or slow the progression to various types of dementia. Indeed, a recent study (Chen et al., 2016) demonstrated that, using multimodal biomarkers measured by neuroimaging, biological fluid, and cognitive assessments, is possible to determine the progressive development of AD. Moreover, has been shown the link between symptomatic onset of cognitive decline and preclinical AD status (Chen et al., 2016).

Currently, the only available medications for dementia and AD are symptomatic drugs. However, these drugs have a limited efficacy, for a relatively short period of time of up to 6 months, and are only effective for up to 30% of individuals being prescribed the drug (Birks, 2006; McShane, Areosa Sastre, & Minakaran, 2006). In addition, behavioural and psychological symptoms of dementia, which strongly predict loss of autonomy, institutionalization, caregiver strain, and impact on patients' prognosis, are difficult to treat pharmacologically. Furthermore, people with dementia often present other comorbidities, for example, type 2 diabetes and hypertension (Schubert et al., 2006), which can affect cognitive function and dependency.

The connection between ageing and cognitive decline is well established, with different studies showing that advancing age is predictive of lower performance on certain cognitive process. However, some longitudinal researchers have highlighted that age-related cognitive decline does not occur equally (Albert et al., 1995; Marden, Tchetgen, Kawachi, & Glymour, 2017), with many older adults still ageing successfully and maintaining both good general and cognitive health (Kok, Aartsen, Deeg, & Huisman, 2017; Rowe & Kahn, 1997). Hence, cognitive decline can not only be attributed to age. It is possible to identify different lifestyle factors that can constitute health status as we age.

In general, an older age is related to the onset of different non-communicable diseases (NCDs), also known as infectious or chronic diseases too. These tend to have a long duration and are the result of a combination of different factors: genetic, physiological, environmental and behaviours (Forouzanfar et al., 2015). They are the leading causes of morbidity, disability, and mortality. Essentially, they are diseases that relate to the ageing process and later life functioning. NCDs negatively affect quality of life, and bear a high economic burden to individuals, families, and society (World Health Organization, 2002). By midlife, 45/50 years old, and in the later years, NCDs are responsible for the vast majority of diagnoses and deaths. The associated risk of developing NCDs increases as individuals age (Forouzanfar et al., 2015).

At any stage of life, including older age, the adoption of health promoting behaviours and actively engaging in healthy lifestyle choices can help to prevent these chronic disease, functional decline, extend longevity and enhance quality of life (Troeger et al., 2017; Forouzanfar et al., 2015). There is accumulating evidence from experimental studies on modifiable risk and protective factors that may relate to cognitive impairment, the pathological phases of AD, the inflammatory and vascular components of all types of dementia and to functional reserve in the brain. Psychosocial factors, such as high educational achievements, mentally-stimulating activity, social engagement, and physical exercise, may delay the onset, development, and clinical manifestations of dementia. Additionally, vascular risk factors, such as high blood pressure, cholesterol, diabetes and high body mass index, have consistently been shown to increase the risk of late-onset dementia (Troeger et al., 2017; World Health Organization, 2002). Results from observational studies have also supported the relationship between lifestyle and vascular related risk factors and risk of late-life MCI and dementia (Ngandu et al., 2015; World Health Organisation, 2012).

Approximately a third of all AD cases worldwide are estimated to be attributable to seven modifiable lifestyle factors. These are physical inactivity, midlife hypertension, midlife obesity, diabetes, low education, smoking and depression (Norton, Matthews, Barnes, Yaffe, & Brayne, 2014). Randomised controlled trials are yet to confirm these associations; however, studies thus far suggest a need for preventative health behaviours to be implemented to potentially reduce dementia risk. This chapter will explore three of the most prominently discussed modifiable lifestyle factors associated with dementia risk reduction; physical activity, cognitive activity and diet and nutrition. This chapter will further discuss the feasibility of making changes to lifestyle behaviours in each of these three categories and the benefits that changes can incur.

*Physical Activity:*

One of the main lifestyle factors that has received intensive experimental attention is the physical activity and it's relation to physical functioning. Physical activity is fundamental in reducing the risk of various diseases, such as heart disease, stroke, osteoporosis, cancers and NCDs. These diseases have also been associated with compromised cognitive health and consequently reduced quality of life (Prakash, Voss, Erickson, & Kramer, 2015). Epidemiological studies have identified physical activity as having a critical role in the prediction of cognitive decline (Middleton, Barnes, Lui, & Yaffe, 2010; Yaffe et al., 2009); and its development into a disease, such as dementia (Hamer & Chida, 2009). Moreover, higher levels of physical activity have been found to have a reduced risk of all causes of mortality, with studies highlighting a relative reduction of risk from 20% to 30% (Chodzko-Zajko et al., 2009; Kampert, Blair, Barlow, & Kohl, 1996; Katzmarzyk, Janssen, & Ardern, 2003).

Longitudinal cohort studies have highlighted the potential of physical functioning to prevent or delay late-life cognitive decline. These studies have consistently shown physical activity in individuals between 55 to 65 years old, to predict performance on assessments of general cognition in later-life (Almeida, Norman, Hankey, Jamrozik, & Flicker, 2006; Etgen et al., 2010; Yaffe et al., 2009), episodic memory (Sabia et al., 2009; Stewart, Prince, & Mann, 2003; Richards, Hardy, & Wadsworth, 2003), processing speed (Chang et al., 2010; Stewart et al., 2003) and executive control (Chang et al., 2010; Sabia et al., 2009). Meta-analysis demonstrated a reduction in risk of cognitive decline by 38% in healthy older adults with high levels of physical activity, and 35% in older adults with low to moderate levels of physical activity (Sofi et al., 2011). These results highlight that engagement in physical activity is associated, not only with lower mortality rate, but also with increased quality of life and helping to preserve cognitive functioning through later life (Prakash et al., 2015).

Moreover, other longitudinal cohort studies have highlighted physical activity as effective in reducing cognitive decline in older people with MCI (Lytle, Vander Bilt, Pandav, Dodge, & Ganguli, 2004; Scherder et al., 2005). Therefore, delaying the risk of developing dementia, by three to six years (Abbott et al., 2004; Karp et al., 2006; Larson et al., 2006; Laurin, Verreault, Lindsay, MacPherson, & Rockwood, 2001). Moreover, the majority of these studies on older adults without dementia have demonstrated that higher levels of physical activity are associated with a reduced risk of cognitive decline and dementia of 30 to 50% (Barnes 2007).

Physical activity intervention studies with older adults have found multiple positive effects, including improved cognition (Angevaren, Aufdemkampe, Verhaar, Aleman, & Vanhees, 2008; Barnes, Whitmer, & Yaffe, 2007; Candela, Zucchetti, Magistro, & Rabaglietti, 2015; Weuve et al., 2004; Yaffe, Barnes, Nevitt, Lui, & Covinsky, 2001), functional ability (Chodzko-Zajko et al., 2009; Magistro et al., 2014), and mental health (Penninx, Deeg, van Eijk, Beekman, & Guralnik, 2000; Penninx et al., 2002; Taylor et al., 2004).

Positive effects of physical activity training on cognitive functioning of older adults have been widely supported (e.g. Colcombe & Kramer, 2003). Sedentary older adults who start an aerobic exercise program for at least 6 months have shown improvements in attention, memory, executive functioning and speed of cognitive processing (Kramer, Erickson, & Colcombe, 2006; Colcombe & Kramer, 2003; Candela et al., 2015); as well as on general cognitive ability, speed of reasoning and memory (World Health Organization, 2002). Further review (Angevaren et al., 2008) on randomized controlled trials of aerobic physical activity training for healthy older adults highlighted the largest effects on delayed memory functions, cognitive speed, auditory and visual attention. Meta-analysis has also emphasised positive effects of physical activity on psychological wellbeing (Netz, Wu, Becker, & Tenenbaum, 2005). A recent longitudinal study has suggested that a multidomain intervention can improve or maintain cognitive functioning in at-risk older adults that are otherwise healthy (Ngandu et al., 2015). Overall, these results have been confirmed by numerous reviews and meta-analyses summarizing research into this topic (Angevaren et al., 2008; Heyn, Abreu, & Ottenbacher, 2004; Kramer & Erickson, 2007; Van Uffelen, Hopman-Rock, Paw, & van Mechelen, 2005). Memory and attention especially can be improved through participation in physical activity. In fact, studies have shown that older adults that have been involved in physical activity programs have improved their long-term memory (Candela et al., 2015; Ruscheweyh et al., 2011) and selective attention (Owsley & McGwin, 2004; Roth, Goode, Clay, & Ball, 2003).

Generally, the literature is pointing out the potential ability of physical activity to protect and maintain cognition and functioning. Practical conclusions that could be extracted from this research area are suggesting that older adults who have followed and maintained an active lifestyle participating in regular physical activity show better cognitive function than that of their sedentary counterparts and maintain their cognitive function at a good level with advancing age. Although, in later years, research has made evident progress in understanding the ability of physical activity to delay cognitive impairment in older adults, as well as to delay the onset of neurodegenerative diseases, there is a need for more specific studies on how physical activity could affect brain structure and functioning and enhance cognitive function across the life span and specifically in older age. Indeed, it is not clear yet which type of exercise should be performed, at what intensity, for how many days per week and for how many weeks. Thus, an obvious but fundamental recommendation is that older adults should engage with an active life style as much as they can and being physically active could prolong protection of their cognitive function and abilities.

*Cognitive Activity:*

Successful ageing is concerned with the maintenance and possible improvement of cognitive functioning. This, however, is a major challenge that in recent years, has resulted in an increased focus on cognitive interventions and training to maintain and improve brain functioning. This is observable in the growth of the global computerized brain health software market (Fernandez, 2010). Specific cognitive interventions and training for older adults have shown evidence of neural plasticity, a resultant brain response to increasing cognitive activity (Johansson, 2004; Pascual-Leone, Amedi, Fregni, & Merabet, 2005). Plasticity is the brain's fundamental lifelong ability to adapt to physical and functional changes in response to sensing, perceiving, and learning process (Merzenich & Jenkins, 1999; 1993). Cognitive reserve is the ability of the brain to compensate and respond against brain degeneration and cognitive decline (Shah, Weinborn, Verdile, Sohrabi, & Martins, 2017). Older adults that are showing high cognitive reserve demonstrate more tolerance to AD (Stern, 2006, 2012) supported by a 50% reduction in dementia cases (Valenzuela & Sachdev, 2006). The study of Stern and colleagues (2012) demonstrated that engaging in cognitive activities may stimulate plasticity and thereby increase cognitive reserve. In fact, observational studies have shown that high levels of cognitive activity could be beneficial in preserving cognitive functioning and reducing cognitive decline and risk of dementia in older adults (Verghese et al., 2003).

With regard to cognitive training, various studies have confirmed the effectiveness of this type of activity (Ball et al., 2002; Candela et al., 2015; Nouchi et al., 2012; Wolinsky et al., 2006). Moreover, studies on cognitive training involving both paper/pencil and computer methodology have been found to improve targeted cognitive domains of processing speed, memory, and reasoning in both healthy older adults and those reporting memory problems (Ball et al., 2002; Engvig et al., 2010; Mahncke et al., 2006; Nouchi et al., 2012). Some studies sustain that computerized cognitive training could be beneficial to cognitively healthy older adults, and at the same time to those with MCI or AD (Galante, Venturini, & Fiaccadori, 2007; Günther, Schäfer, Holzner, & Kemmler, 2003; Tárraga et al., 2006). Previous studies have also shown that playing a video game could lead to improvements in some cognitive functions for healthy older adults (Basak, Boot, Voss, & Kramer, 2008; Goldstein et al., 1997). Cognitive training seems to be effective for specific cognitive functions, such as memory and attention, which included long-term memory and attention (Candela et al., 2015; Mozolic, Long, Morgan, Rawley-Payne, & Laurienti, 2011; Shah et al., 2017). This could be related to the fact that, usually, cognitive training, cognitive stimulation and cognitive rehabilitative activity are involving structured, repeated, and frequent engagement in standardized protocols of specific cognitive tasks, focused on specific cognitive domains such as memory, working memory, attention, and problem-solving (Bahar-Fuchs, Clare, & Woods, 2013; Gates, Sachdev, Singh, & Valenzuela, 2011; Nouchi et al., 2012). Domain-specific analyses underline the efficacy of the training for nonverbal memory, processing speed, working memory, and visuospatial outcomes, but not for attention and executive functions (Lampit, Hallock, & Valenzuela, 2014). Computerized cognitive training is therefore improving cognitive performance in healthy older adults, but efficacy is varied across the different cognitive domains and is strictly related to the design choices (Lampit et al., 2014) considering that training usually involves structured practice on standardized cognitive and challenging tasks (Clare, Woods, Moniz Cook, Orrell, & Spector, 2003). Cognitive training protocols stimulate and increase the neuro-cognitive ability by improving performance on tasks of daily life in patients with dementia (Clare et al., 2003; García-Casal et al., 2017). More specifically, cognitive training aims to directly stimulate the mnemonic capacities of attention and planning, which can be seriously compromised by dementia and related pathology. It is assumed that cognitive stimulation can modulate synaptic activity and the brain plasticity, changing the process of beta-amyloid production (Kamenetz et al., 2003; Lazarov et al., 2005). While, cognitive training can maintain and promote neuroplasticity (Mowszowski, Batchelor, & Naismith, 2010). It might also provide method of preventing and slowing the progression of cognitive decline (Gates et al., 2011), even if it does not necessarily reverse the disease trajectory (Shah et al., 2017). Meta-analysis has highlighted an important issue of whether the training is conducted at home or in a (Lampit et al, 2014), Home-based cognitive training is easier to administer, customize and adapt to individuals' needs, with potential for lower implementation cost (Kueider, Parisi, Gross, & Rebok, 2012) and in many cases could facilitate the participation of frail and disabled older adults. Alternatively, group-based training that includes supervision from a trainer, requires a suitable environment for delivery and is less personalized. However, during group training it is possible to ensure protocol compliance, adherence, provision of motivational support and encouragement to master new abilities and tasks; also emphasising the importance of social interaction. Thus cognitive training conducted as a group could be more beneficial than individual home based training (Lampit et al., 2014; Verhaeghen, Marcoen, & Goossens, 1992).

*Diet and nutrition:*

The protective and deleterious effects of different dietary choices on risk for dementia development have been increasingly acknowledged throughout the literature. As a result recommendations and guidelines for the prevention of dementia through diet have been widely discussed. Firstly, recommendations have stipulated minimising intake of saturated and trans fats (Barnard et al, 2014). Earlier research showed little effect. For instance, the Rotterdam study of 5395 healthy older adults found no association between high intake of total saturated fats, trans fats and cholesterol, alongside low intake of alternative forms of fatty acid and risk of dementia (Engelhart et al, 2002). More recent findings, however, have strongly indicated that saturated fats increase the risk of developing dementia (e.g: Morris, 2016; Morris and Tangney, 2014; Amadieu et al, 2017). Alternative forms of fatty acids have been suggested to act as a protective factor against dementia development. For instance, high intake of n-3 PUFA, may protect against age related cognitive decline, but research is inconsistent and therefore cannot strongly assert a protective effect here (e.g. van de Rest, Geleynse, Kok, et al, 2008).

In conjunction with fats, sugary foods, including fruit juices, fruit drinks and sodas should be considered. Extensive research has associated sugary foods and drinks with an increased risk of heart disease, obesity and diabetes. Hence, dementia researchers have used data from the Framington Heart study (Gordon, Castelli, Hjortland, Kannel & Dawber, 1977) containing 1484 adults aged 60 and over, to assess the relation with dementia directly. Daily consumption of diet soda indicated an almost threefold increased risk of developing dementia. Interestingly, sugary soda, rather than sugar from diet, did not increase dementia risk (Owens, 2017).

Recommendations have also suggested that vegetables, legumes, fruits and whole grains should replace meats and dairy products as primary staples of diet (Barnard et al, 2014). The evidence supporting these foods to play a role in prevention is in abundance. Most recently, a meta-analysis has shown that an increased consumption of fruit and vegetables was associated with a significant reduction in the risk of cognitive impairment and dementia (Jiang, Huang, Song, Deng, Wey & Zhang, 2017). Plant-based foods, such as those advocated here are rich in several B vitamins. Vitamin B6, B12 and folate. These are specifically noteworthy due to their role in the methylation of homocysteine. If this process is not successfully carried out homocysteine levels can elevate. The literature has subsequently underlined increased plasma homocysteine as a strong, independent risk factor for the development of dementia (e.g. Seshadri et al, 2002). The numerous neurotoxic effects of homocysteine can be blocked by folate, glutamate receptor antagonists or various antioxidants (Obeid & Herrmann, 2006). Therefore, homocysteine levels can be reduced through intake of B vitamins and folate found in leafy green vegetables, such as broccoli, kale and spinach, as well as in beans, peas, citrus fruits and cantaloupe and melons. Lafevre-Arbogast, Feart, Dartigues, Helmer, Letenneur & Samieri (2016) further supported the benefit of folate in a French cohort with a relatively low baseline folate status. After giving folate those with higher folate intake were associated with a decreased risk of dementia.

Another key biological mechanisms implicated in the development of dementia is oxidative stress (e.g. Bennett, Grant & Adred, 2009). The literature has therefore discussed higher intake of vitamin E, an antioxidant, to potentially reduce oxidative stress and thus risk for dementia (Barnard et al, 2014). vitamin E occurs naturally in the form of tocopherols and tocotrienols and is found in many foods including mangoes, papaya, avocadoes, tomatoes, red bell peppers, spinach, nuts, seeds and oils. Literature is conflicted on the success of Vitamin E to reduce risk of dementia. In supplement form vitamin E has been repeatedly shown to be ineffective for dementia prevention (e.g. Kryscio, Abner & Holt. 2017). Therefore, opposing studies have suggested benefitting from whole food Vitamin E, however, systematic review findings do not support the association between vitamin E intake and increased cognitive performance or reduced risk for dementia consistently (Crichton, Bryan & Murphy, 2013). Vitamin E, alongside corresponding antioxidants, such as vitamin C and A constitute total dietary antioxidant capacity, which has not been associated with a risk of developing dementia or MCI (Engelhart et al, 2002).

Further to the discussion of supplements there is a substantial body of literature discussing the difference in benefits between whole food and supplements. The synergy of nutrients and related substances available in foods is yet to be replicated by a pill (Hale, Cadenhead & Hinchliffe, 2016). Sufficient evidence indicates that dementia can be delayed by adequate intake of specific nutrients, but these could be most beneficial through whole foods rather than dietary supplements. Moreover, supplements often contain iron and copper which, if taken in excess, have been found to contribute to cognitive problems (e.g. Squitti et al, 2014). Alongside the discussion of iron and copper is the ongoing debate of the role of aluminium in dementia development. Aluminium, found in pots, pans and cooking equipment, has been weakly associated with dementia, however as research has previously been limited and often less relevant evidence has not corroborated the advice to avoid aluminium. However, novel measurements of aluminium from the brain tissue of participants with Alzheimer's disease found extremely high concentrations of aluminium (Mirza, King, Troakes & Exley, 2017). This research is yet to be replicated and the mechanisms under which this association has occurred are yet to be explained. This indicates the initiation of a line of evidence that could substantiate the advice to avoid aluminium intake to reduce risk of dementia, which has been tentatively issued in earlier guidelines (e.g. Rogers & Simon, 1999; Barnard et al, 2014).

Studies have presented numerous arguments around individual nutrients and specific foods that have been briefly discussed here. However, the recent literature has shifted to analyse dietary patterns as a whole in an attempt to provide a more holistic picture of dementia risk reduction through diet (e.g. van der Rest, 2015). The most widely examined dietary pattern is the Mediterranean diet, essential components of which include monounsaturated fatty acids, derived from the plethora of olive oil, cereals and wine (Panza et al, 2004). Systematic review has associated greater adherence to the Mediterranean diet with slower cognitive decline and lower risk of developing Alzheimer's disease (Lourida et al, 2013). Components of the Mediterranean diet and other suggested dietary patterns, however, do not contain all components that are specifically related to cognitive outcomes. Indexes described by van de Rest and colleagues (2015) in review are mainly based on improving overall health status or blood pressure, which illicit a secondary benefit to cognition rather than targeting cognitive health. However, investigating whole diet approaches is an attractive strategy due to the potential for combined effects to yield more substantial outcomes than single nutrients alone.

When considering nutritional interventions for reducing the risk of an individual developing dementia, whether the aim is to increase folate, B12 and B6, decrease saturated and trans fat or adhere to the whole Mediterranean diet, the literature has suggested that dietary interventions are best placed in midlife due to their potential to protect against dementia pathology for longer (e.g. van de Rest et al, 2015; Hogervorst, 2017).

*Feasibility of risk reduction:*

The focus of dementia research has shifted from identification of potential risk factors to using this information to develop interventions to prevent or delay the onset of dementia (Imtiaz, Tolppanen, Kivipelto & Soininen, 2014). Therefore information presented throughout this chapter should be utilised to inform interventions aimed at reducing the risk of dementia through lifestyle factors. Lifestyle changes can offer additional benefits to those for cognition, particularly for body weight, cardiovascular health and diabetes risk, and essentially render no risk of harm (Barnard et al, 2014). Risk and protective factors can vary with age but the maintenance of healthy lifestyle presents the best option with regard to the prevention of dementia (Peters, 2009). However, an individuals' attitude concerning dementia risk may affect motivation to change health behaviours and lifestyle (Kim, Sargent-Cox, Cherbuin & Anstey, 2014). Thus, numerous barriers that have been highlighted throughout that literature can often develop and inhibit individuals from following healthful lifestyle guidelines. The feasibility of lifestyle interventions can frequently be influenced by perceived barriers. This feasibility could be instrumental in determining an interventions capability to reduce dementia risk. Several barriers that have been discussed have been specific to a particular lifestyle changes, but more often than not barriers can be observed across lifestyle factors.

The most predominant barriers to lifestyle changes were discussed by Kelly and colleagues (2016) in their review of reviews. This included an examination of 28 qualitative studies, 11 longitudinal cohort studies and 46 systematic reviews, specifically looking at the uptake and maintenance of healthy lifestyles during midlife and the factors that influence this. Authors did note that most of the evidence reviewed pertained to developed countries owing to a disproportion between published studies from developed countries and developing countries. Lifestyle changes that were appraised included physical activity, eating behaviours and other health related topics such as alcohol consumption and smoking habits. The review established six themes that encompassed all factors that influenced uptake and maintenance of health behaviours, so both barriers and health promoters, or facilitators as they are often called. These were, health and quality of life, sociocultural factors, the physical environment, access to psychological factors and evidence relating to health inequalities. Throughout this chapter the importance of these themes shall become evident, as they include almost all barriers and facilitators.

Barriers that have been most consistently highlighted throughout the literature are a lack of time, (this could be due to family, household or occupational responsibilities); access the transport, facilities or resources; financial costs; entrenched attitudes and behaviours; restrictions that stem from the physical environment, being of a low socioeconomic status and a lack of knowledge about health (Kelly et al, 2016). Additionally, specific demographic factors, such as age and family history, were shown throughout a multi-ethnic cohort to significantly determine an individual's willingness to engage with risk reduction (Seifan et al, 2017). It is also apparent that there are differences between genders in the perception of barriers to lifestyle changes. For women, self-esteem has been shown to be the most important barrier, and is significantly higher than for men. Women also perceived money, knowledge, skills and stress as potential barriers to risk reduction behaviours, whereas men did not. Therefore differences between genders should be considered when assessing feasibility of lifestyle interventions (Mosca, McGillen & Rubenfire, 1998).

Further barriers that have been noted in physical activity specific literature include overall health, specific symptoms related to depression and pain, the general environment, neighbourhood crime rate, a lack of physician advice, knowledge, childhood experiences with physical activity and marital hardships (Schutzer & Graves, 2004; Schoeny, Fogg, Buchholz, Miller & Wilbur, 2017). Barriers have also been discussed explicitly in the diet and nutrition literature. Similarly to general barriers and physical activity concerns, time was cited as a key barrier to healthful eating, adjacent to concerns for cost of more nutritious choices (Eikenberry & Smith, 2004) and implications of neighbourhood and surrounding environment have also been discussed in this literature (e.g. Pitts et al, 2017). Dietary studies have also hinted at larger barriers presented as a result of strong intrinsic Western socio-cultural values, norms and traditions that could substantially impede on the feasibility of making lifestyle alterations (Knight, Bryan & Murphy, 2016).

Notwithstanding the barriers to risk reduction behaviours, various mechanisms for facilitating positive health behaviours have been proposed, with many scientists theorizing how to better help people in midlife and older adults to initiate and maintain positive lifestyle and risk reduction behaviours. Most recently, the upward spiral theory of lifestyle changes has sought to explain how positive affect can facilitate long-term adherence to positive health behaviours through processes known as the inner and outer loop. The inner loop supposes that positive affect experienced when engaging with positive health behaviours increases the salience of the unconscious incentive to repeat that behaviour. The outer loop then further works to build up a suite of internal resources which amplify the positive affect experienced during positive health behaviours and therefore strengthen uncounscious motives (Van Cappellen, Rice, Catalino & Fredrickson, 2017).

If the upward spiral theory suggests, facilitators of positive health behaviours are further increased by the positive affect felt when engaging with those health behaviours. This seeks to increase engagement with that positive health behavior and maintain a healthy lifestyle in the longer term. In order for this theory to take effect then health behaviours need to be engaged with in the first instance. Reasons that individuals might engage with lifestyle changes include being aware of the benefits of healthy ageing, a focus on the enjoyment, social support and most crucially family support, clear messages and integration of behaviours into pre-existing lifestyle (Kelly et al, 2016; Eikenberry & Smith, 2004).

Literature has identified education as an integral part of engagement with dementia risk reduction behaviours. Explaining the benefits of healthy lifestyle behaviours has been shown to improve health and discourage behaviours that can lead to poor health (Lafortune, Martin & Kelly, 2017). Additionally, willingness to engage with lifestyle changes and risk reduction behaviours has been shown to increase as education increases (Seifen et al, 2017). Tailoring interventions to include education has been found to incur substantial benefits to intervention success. In the case of physical activity interventions a multimodal intervention was shown to influence decisions to start and maintain physical activity, but was less effective than extensive supervised exercise sessions. Furthermore, interventions that include support, self-monitoring, rewards, personal goal setting and/ or provision of information about local opportunities are more likely to be successful at instigating lifestyle change. In the case of dietary interventions, improvements were noted when printed dietary advice was given (Lafortune, Martin & Kelly, 2017). Moreover, supplementing interventions with between session personal and or automated phone calls may be an effective way to strengthen intervention effects. (Schoeny, Fogg, Buchholz, Miller & Wilbur, 2017) and should therefore be applied where possible to risk reduction interventions and strategies.

Throughout the literature facilitating this reduction in dementia risk has often been discussed in parallel to visiting a physician or general practitioner (e.g. Seifen et al, 2017). Both males and females rated physicians as the most important source of support in changing lifestyle behaviours (Mosca, McGillen & Rubenfire, 1998); despite other sources of support being available in the form of dieticians, exercise physiologists, nurses, counsellors, family members and social or religious groups. However, physicians are suitably positioned to communicate advice regarding lifestyle changes and could act as a catalyst for health behaviour changes. Although evidence regarding health behaviour change resulting from physician advice remains inconclusive (Eden, Orleans, Mulrow, Pender & Teutsch, 2002), several studies have highlighted some success. For instance, Kreuter, Chheda and Bull

(2000), found that individuals who received physician advice to quit smoking, eat less fat or to engage with more physical activity prior to receiving intervention materials on the same topic were far more likely to perceive the materials as pertinent to their health, remember the materials and share them with others. Following this they were also more likely to report making changes or trying to make changes to health behaviours.

Inconsistencies in success rates of physician advice could be due to variations between individuals in adherence to health advice (van der Pol, Hennessy & Manns, 2017). Physicians have also been shown to target specific groups of individuals with health advice rather than delivering consistent health advice. Groups that have been found to be more frequently targeted are obese, inactive individuals with poor to fair health and populations that are traditionally not encouraged to be more physically active (Forjuoh, Lee, Won, Towne, Wang… 2017). This could be a result of barriers the physician may have to delivering health advice. Most notably, physicians have been reported to have issues with financial remuneration (e.g: Travers, Martin-Khan & Lie, 2009), time constraints, which lead to health advice coming secondary to heavier work commitments and limited knowledge or experience with the health behaviour being discussed (e.g: Abramson, Stein, Schaufele, Frates & Rogan, 2000). Thus physicians who are more familiar with that health behaviour are more likely to counsel their patients to engage with that health behaviour. This has been most consistently shown with physicians level of engagement with physical activity and their willingness to encourage physical activity as a result (e.g: Abramson, Stein, Schaufele, Frates & Rogan, 2000). It has hence been proposed that medical schools should work to increase the proportion of students adopting and maintaining regular physical activity and healthful dietary habits to increase future likelihood and rates of counselling regarding health behaviours from physicians (Lobelo, Duperly & Frank, 2009).

Further facilitators of physician advice have been suggested to overcome barriers. These have included the integration of interventions into existing activities, the specification of a clear funded role for practice nurses and support for the general practitioners networks that are in place. Incorporating more health promotion into physicians' workload and primary care expectations should consider these factors (Travers, Martin-Khan & Lie, 2009).

*Conclusion:*

Dementia is a mounting concern worldwide (e.g. World Health Organisation, 2012). However, extensive findings on modifiable lifestyle factors using a lifespan approach have shown that it is possible to reduce the risk of developing dementia. The modifiable risk factors discussed were physical activity, cognitive training and diet and nutrition. All highlighted benefits for both healthy older adults and those with MCI, suggesting the potential for lifestyle factors to be beneficial in risk reduction regardless of current cognitive status.

More specifically, research has consistently demonstrated the importance of physical activity in dementia risk reduction, as well as overall health. Engagement in higher levels of physical activity affords a 20% to 30% reduction in risk of all causes of mortality (Chodzko-Zajko et al., 2009; Kampert, Blair, Barlow, & Kohl, 1996; Katzmarzyk, Janssen, & Ardern, 2003). Among other factors, physical activity has been shown to positively influence quality of life, psychological wellbeing and physical health; but most crucially it hosts benefits to overall cognition as well as specific functions, such as attention, memory, executive functioning, speed of cognitive processing and speed of reasoning and memory. Evidence so far thus substantiates the claim that physical activity is a powerful tool in preventing dementia and increases in physical activity should be sought after throughout the lifespan.

Growth of the global computerised brain health software market (Fernandez, 2010) in recent years has highlighted the increase in the popularity of cognitive training. Although cognitive training research is still developing, evidence for increased neuroplasticity (Johansson, 2004) resulting in potential increases in cognitive reserve (Stern et al, 2012) suggests potential for cognitive training to play an equally important role in dementia risk reduction (e.g. Verghese et al, 2003). Specific cognitive domains targeted by training has been shown to yield specific improvements, such as in nonverbal memory, processing speed, working memory, and visuospatial outcomes (Lampit, Hallock, & Valenzuela, 2014). The literature has further suggested that cognitive training could be more suitably administered in a group, although more practically challenging in finding appropriate environments, time and resources, could incur numerous benefits far beyond individual home based training.

Moreover, Diet and nutrition literature indicated interventions to be most effectively positioned in midlife (e.g. van de Rest et al, 2015). Saturated and trans fats have been persistently shown to have negative effects on cognition and therefore should be reduced to reduce risk of developing dementia. Vegetables, legumes, fruits and whole grains have been found to benefit cognition and are suggested as an alternative to meats and dairy products as much as possible. A particular focus on consumption of plant based foods that are high in B vitamins and folate was underlined due to the biological role these vitamins play in metabolising neurotoxic homocysteine, but also having direct protective effects. Studies examining the role of vitamin E, C and A as an anti-oxidants present inconsistent results.

When consumed, however, for maximum benefit whole foods should be sought rather than supplements, as these have been shown to be ineffective. Discussions of whole dietary changes, rather than focus on individual nutrients have been increasingly advocated throughout the literature due to the potential to combine effects of nutrients and yield more substantive outcomes. Positive indications stemming from the success of the Mediterranean diet have been highlighted thus far but further randomised controlled trials are required to establish whether cultural factors are influencing dietary benefits or if the diet alone is of significant benefit enough to warrant use as an intervention.

Considering the difficulties of implementing lifestyle changes is paramount to intervention success. Therefore, lifestyle and behaviour changes cannot be implemented without consideration for the feasibility of the changes, the barriers that could inhibit change and the facilitators and motivators that could increase the likelihood of taking up and maintaining healthy lifestyle changes. Most consistent barriers emphasised for all lifestyle changes were health, time, cost and environment. Physicians are positioned best to advocate beneficial lifestyle changes and their role is far reaching. The most integral factor to help facilitate healthy lifestyle changes was education; with further intervention benefits shown with a focus on enjoyment and support included in the intervention.

Implications for practice are substantial. The role of the physician in instigating lifestyle changes should be harnessed with direct advice pertaining to increases in physical activity and nutritional advice, particularly advocating increases in B vitamins, folate and minimising saturated and trans fat, throughout the lifespan. If interventions are adapted to aim to initiate and sustain healthy lifestyle choices, the risk of developing dementia can be drastically reduced and further health benefits could follow.

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