



# The future of senior healthcare: nutritional issues and solutions for healthy aging



March 2018

HEALTH • NUTRITION • MATERIALS



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# FOREWORD

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People are living longer than ever before. While this is certainly a positive development, these additional years are not necessarily in good health. The twilight years are often accompanied by a range of non-communicable diseases (NCDs) and other age-related chronic diseases that can significantly affect an individual's quality of life. The so-called Silver Economy, which considers the economic opportunities associated with the growing public and consumer expenditure resulting from an aging population, should be a sign of social and economic progress, but instead it has become a drain on a number of different resources.<sup>1</sup> Not only has an aging population placed a burden on healthcare systems around the world, but it also has an indirect impact on individuals' families and wider society.

Aging, however, has become more complex in recent years, as it is increasingly difficult to define an 'older person'. Some 80-year-olds appear to have the mental and physical capabilities of somebody much younger, while others of the same age are dependent on everyday care. The question of why some people age healthier than others has been the subject of extensive research over the years. Although there are still knowledge gaps among healthcare practitioners and the wider scientific community, extensive studies are highlighting the importance of nutrition as part of a preventative approach to age-related chronic disease risk reduction.

The concept of 'healthy aging' should therefore be a priority for public health agencies, to reduce the risks associated with age-related and

infectious diseases, and help ensure our later years are as healthy as possible. With the number of older people set to grow even more in the next few years, we will face a global health crisis unless action is taken soon. There needs to be increased awareness of the importance of nutrition interventions as a measure of healthcare quality, that can be established before the problem inevitably worsens.

This white paper has been developed by DSM in collaboration with the Sackler Institute for Nutrition Science and the Council for Responsible Nutrition (CRN), and will be distributed in conjunction with the New York Academy of Science's 'Hidden hunger: solutions for America's aging population' event on March 23, 2018 in Washington, DC.

## EXECUTIVE SUMMARY

Although life expectancy has dipped in the last two years, it still remains high.<sup>2</sup> The global population of people over 60 years of age is expected to double by 2050 to more than 2 billion. Not only this, but the number of people over 80 is predicted to be three times higher in 2050 than it was in 2013 (figure 1).<sup>3</sup> As such, the concept of healthy aging is becoming more important than ever.

Functional ability is made up of intrinsic capability, comprising mental and physical

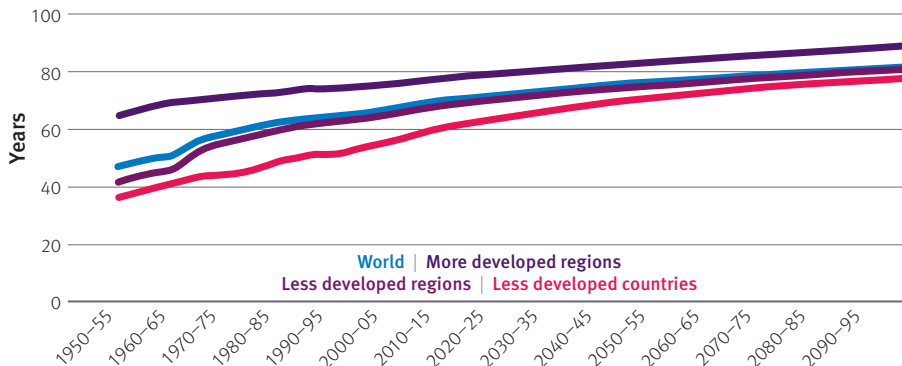
capacities, as well as environmental factors, such as a person's relationship with home, the community and wider society. Although a recent study found that some people have a faster innate aging rate than others, the majority of research on centenarians has focused mainly on genetics as a key factor in longevity.<sup>4</sup> Given the prevalence of chronic and infectious diseases in later years and the disparity between nutrition and health, investigating the role of lifestyle factors could prove beneficial in supporting adults to age in a healthy way.

Maintaining adequate health and nutrition as we age is a critical concern for people across the world. According to a consumer survey, 55% of adults globally find it important to stay 'young' for as long as possible. Although 26% of people currently worry a lot about their health, their future health presents even more of a concern; 35% of adults worldwide are already thinking about their health over the next five years. Among these concerns, mature adults over 51 years worry specifically about protection against disease in later life, as well as bone and joint health.<sup>5</sup>

According to the World Health Organization (WHO), healthy aging is defined as 'the process of developing and maintaining the functional ability that enables wellbeing in older age'.<sup>6</sup> This enables individuals to be and do what they value, including a person's ability to:

- Meet their basic needs
- Learn, grow and make decisions
- Be mobile
- Build and maintain relationships
- Contribute to society

**Figure 1: Global and regional variations in life expectancy at birth from 1950-2050<sup>7</sup>**



## Spotlight on the United States

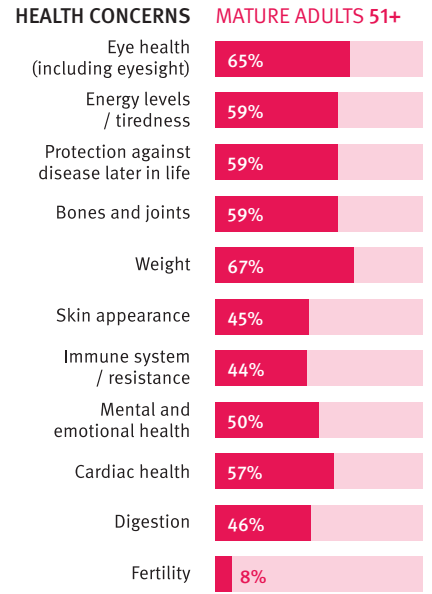
Healthy aging is a particular concern for Americans. A recent consumer survey found that 59% of mature adults in the United States (US) worry about the protection against disease later in life (figure 2). These concerns are heightened with advancing years, with 68% of mature adults over 51 years of age globally having the same worry.<sup>8</sup>



docosahexaenoic acid [DHA]), dietary fiber, magnesium, potassium, zinc and calcium, as well as carotenoids and lutein, have been found to hold great potential in specific health areas that could prove beneficial in the elderly. Improvements have been noted in heart, eye and brain health, as well as bone health and immunity, although national surveys and observational cohort studies have identified that consumption of these nutrients in older adults may be below recommended levels.<sup>9</sup>

This white paper examines the evidence, role and mechanism of these key nutrients, and uses the latest scientific studies to highlight how effective implementation could overcome barriers in improving adequate nutrition in the elderly. While it is important to take a preventative approach to healthy aging across the life course, this white paper will focus on the nutritional strategies for older adults aged over 50 years, as it presents the most urgent challenge.

### Figure 2: Health concerns in mature adults<sup>10</sup>



A significant amount of research shows that nutrition is an important modifiable factor in the risk reduction of age-related chronic and infectious diseases. Micronutrients, including vitamins D and E, B vitamins, omega-3 fatty acids (i.e. eicosapentaenoic acid [EPA] and

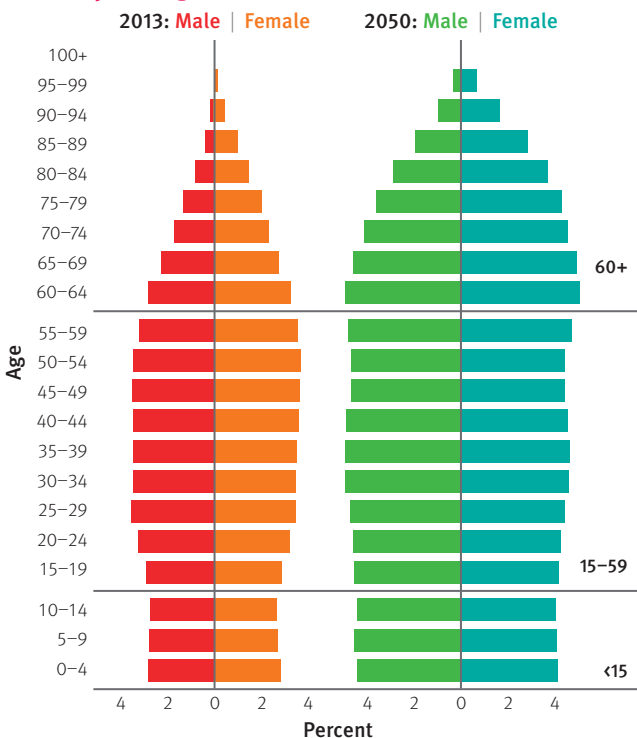
## ADDRESSING THE AGING CHALLENGE

Although life expectancy in the US is projected to decline, due in part to growing obesity levels, the number of older people in the world is rising.<sup>11</sup> This is due to a combination of factors, including reduced childhood and childbirth mortality in

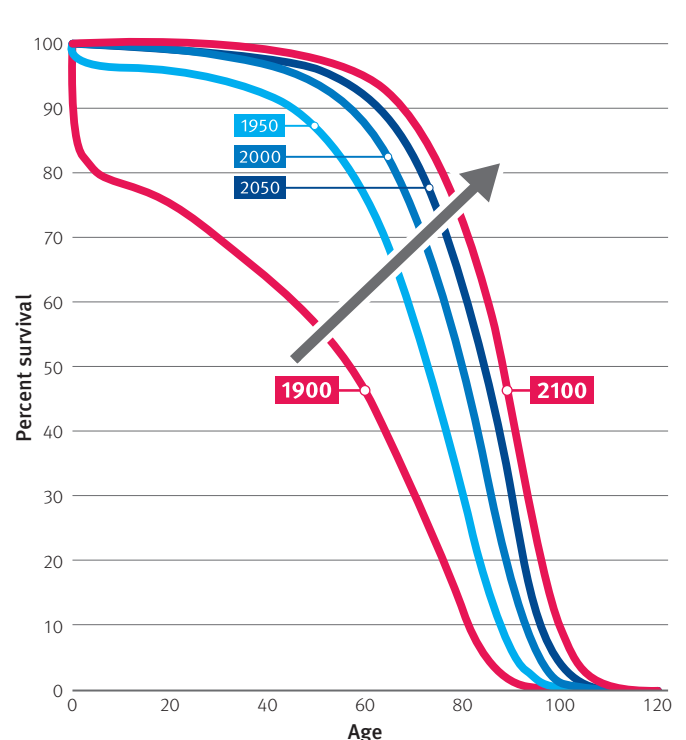
low- and middle-income countries, as well as declining mortality in developed countries. Together with falling fertility rates across the world, it has led to the largest proportion of people aged 60 years and over for the first time

in history.<sup>12</sup> As the global population is predicted to rise even further in the coming years, with survival rates continuing to rise year-on-year, the proportion of older adults is expected to increase (figures 3 and 4).<sup>13</sup>

### Figure 3: Age composition of populations in developed regions in 2013 versus 2050<sup>14</sup>



### Figure 4: Past and projected population survival curves in the US from 1900-2100<sup>15</sup>

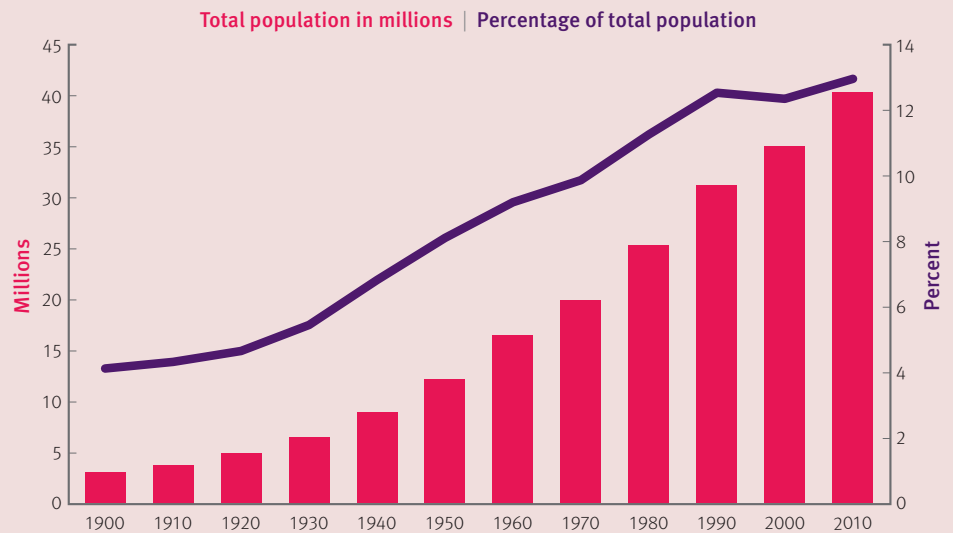


### Spotlight on the United States



The rapidly aging generation is particularly prominent in the US (figure 5), where the proportion of the population over 65 years old is expected to increase from 12.4% in 2000 to 19.6% in 2030.<sup>16</sup> The number of people over 65 years old is also predicted to rise from approximately 35 million in 2000 to an estimated 71 million in 2030. Florida has the largest proportion of older people – 26% of the population will be over 65 years old by 2050 according to recent figures, compared to up to 15% across the rest of the US.

**Figure 5: Proportion of adults aged 65 years and older from 1900-2010<sup>17</sup>**

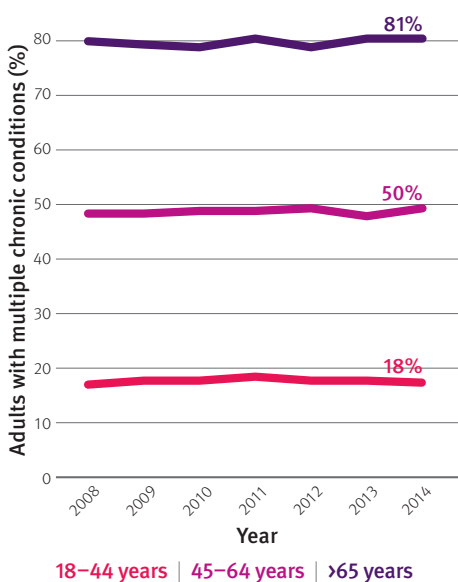


The consequences of an increasingly older population are profound, as an extended lifespan brings a new set of challenges. Although there is no 'typical' older person, most individuals aged over 65 years will inevitably experience various health concerns at some stage.<sup>18</sup> This is largely associated with the rise of NCDs and other age-related chronic diseases, such as osteoporosis, type 2

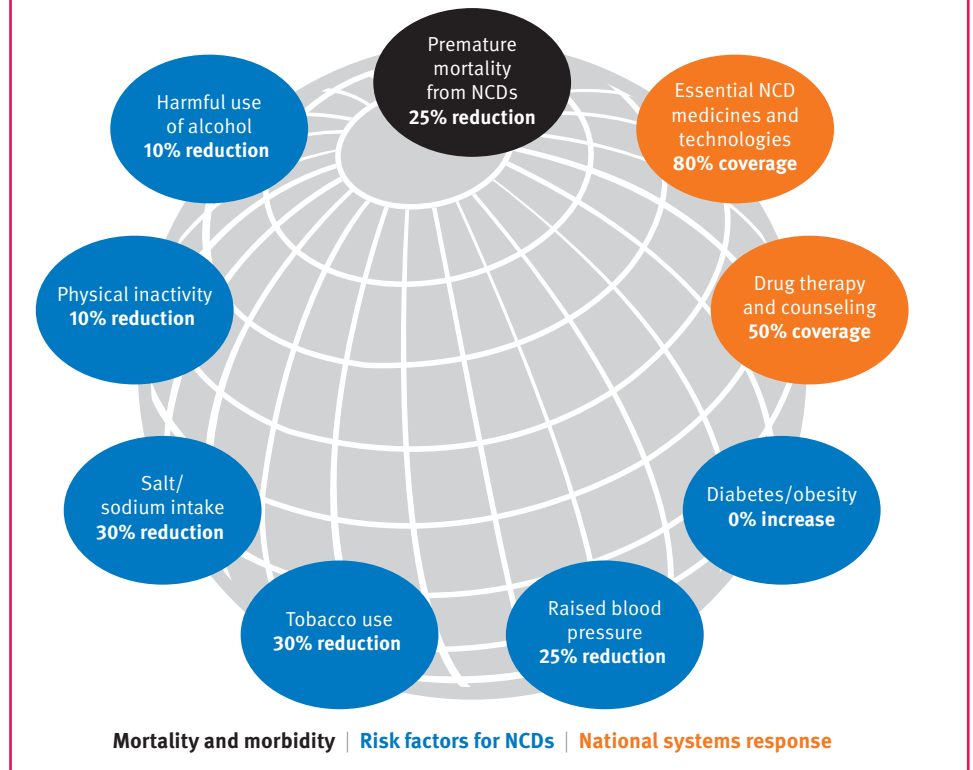
diabetes, cardiovascular disease (CVD) and cancer. In the US, for example, approximately 50% of people aged 45-64 years have multiple chronic conditions, with this figure rising to 81% in people aged over 65 years (figure 6).<sup>19</sup> As the worldwide population increases, the number of people dying from NCDs is estimated to increase from 36 million in 2008 to 52 million in 2030.<sup>20</sup> It is a serious issue; in

2013 all 194 member states of the United Nations' WHO agreed on a global strategy to lower the incidence of NCDs. The Global Action Plan for the Prevention and Control of NCDs 2013-2020 aims to reduce the deaths from NCDs by 25% by 2025 through nine voluntary global targets (figure 7).<sup>21</sup>

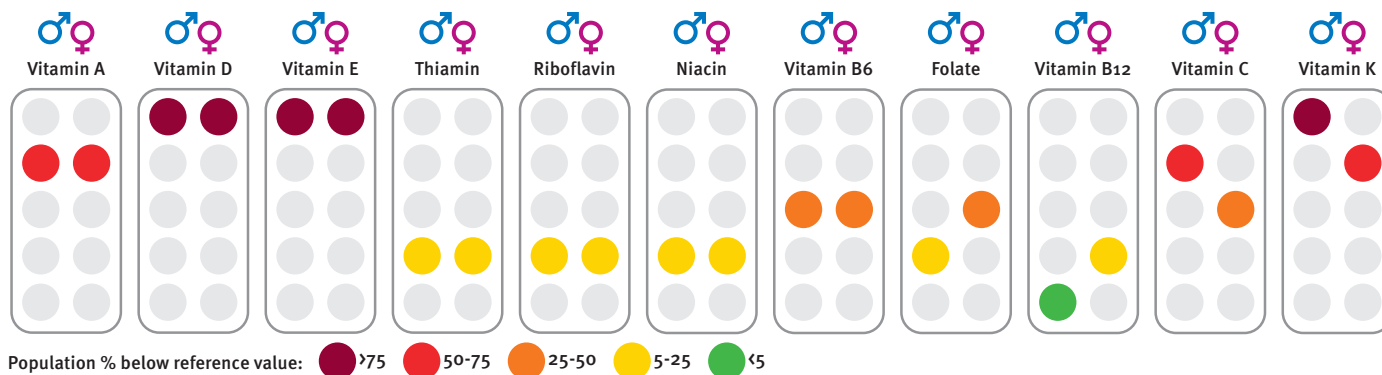
**Figure 6: Prevalence of US adults with multiple chronic conditions from 2008-2014<sup>22</sup>**



**Figure 7: Voluntary global targets set by WHO to support the prevention and control of NCDs by 2025<sup>23</sup>**



**Figure 8: Proportion of the elderly US population with nutrient intakes below the country's recommended reference values<sup>24</sup>**



Older adults are particularly at risk of NCDs, as lifestyle factors, such as nutrition and exercise, play a key role in risk reduction. Low nutritional status is prevalent among the elderly, due to decreased income, lower levels of physical activity, lack of social contact and an increased risk of dementia and other psychological factors. Research has shown that nutritional intake remains below the Estimated Average

Requirement (EAR) for individuals aged over 71 years in the US. For instance, only 50% of elderly Americans currently meet the requirements for vitamin A, 40% for vitamin C and up to 75% for vitamin E (figure 8). Age can also prove a biological barrier for achieving adequate intake; serum vitamin B12 concentrations are not absorbed well due to age-related chronic diseases, such as atrophic gastritis.

Despite widespread low micronutrient levels in the elderly and the associated nutritional frailty, older people can also be obese as the result of longstanding poor diet quality, that is often energy-dense and nutrient-deplete. This can lead to an increased risk of malnutrition – or so-called ‘hidden hunger’ – as older people are often deficient in many essential micronutrients.

## INCREASED REQUIREMENTS FOR CARE MEANS GROWING COSTS

A rapidly aging population is having a significant impact on economies and societies across the world. In general, older age is associated with an increased requirement for care – and therefore, expenditure. However, this varies across the world (figure 9). In the US and Canada, for example, healthcare costs for age-related chronic diseases are much higher than in Sweden and Spain, reflecting the differing approaches to healthy aging globally.<sup>25</sup>

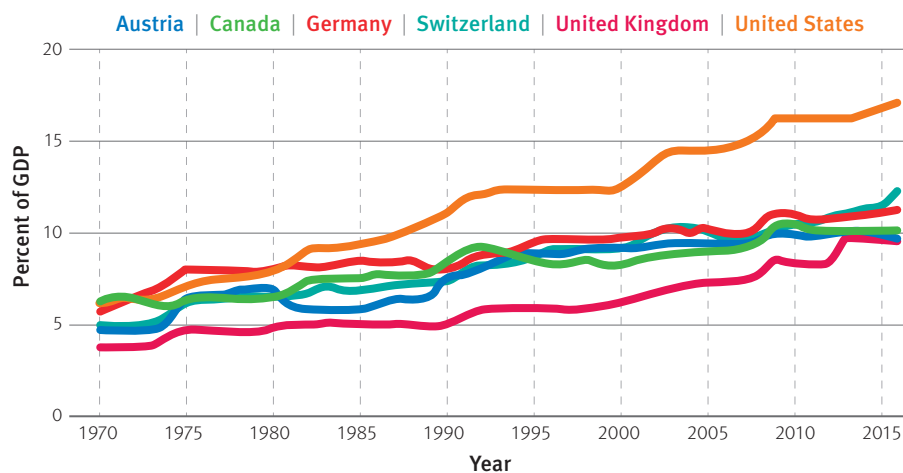
Research shows that wealthy, industrialized countries currently have the highest expenditure – mainly due to high incomes, increased healthcare spending and a rapidly aging population. However, it is estimated that the cost of aging in middle-income countries will also increase in upcoming years, due to the steep rise of NCDs in these areas.<sup>26</sup> The impact of an aging population also has wider socioeconomic consequences. Older people depending on family for care can reduce productivity, as well as overall labor contribution.

Age is a significant risk factor for NCDs, which is why the majority of healthcare costs relate to the high expenditure of treating disease-

related malnutrition. Although improved nutrition may not alter the course or outcome of disease, the associated inflammatory response could soften the effectiveness of subsequent nutritional interventions. In the European Union (EU), approximately 20 million patients are affected by this condition, with estimated costs of \$148 billion annually for EU governments.<sup>27</sup> A report found that the cost of disease-related malnutrition was four times higher for patients over 60 years of age \$1.8

billion than between 18 and 60 years (\$500 million). Unsurprisingly, hospital stays accounted for the highest expenditure (66%, at a cost of \$1.5 billion), with nursing and residential home settings accounting for 10%, at \$228 billion. In addition, mental disorders, CVD and oncology are the age-related chronic diseases that contribute to the highest share of the costs.<sup>28</sup> Given the high costs of treating disease-related malnutrition, there is a viable rationale for improving nutrition in older people.

**Figure 9: Rising healthcare costs in seven countries from 1970-2016<sup>29</sup>**

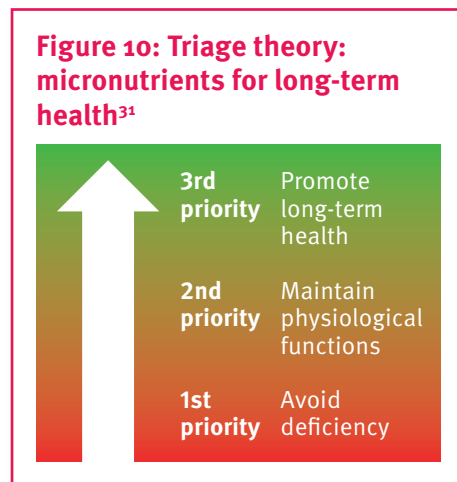


# EVIDENCE: THE IMPORTANCE OF NUTRITION IN AGING

The relationship between nutrition and health is complex. Despite the widespread evidence to suggest that vitamins, minerals and omega-3s are essential in maintaining human health, average intakes remain low worldwide – even in developed countries. Although there has been extensive research on the short-term benefits of essential nutrients on health, emerging studies highlight the potential of micronutrients over the longer term – in particular, in aging.

In fact, there is a growing body of evidence for Triage Theory, which was developed by Dr. Bruce Ames and states that as the result of recurrent shortages of micronutrients during evolution, natural selection has developed a strategic rationing response (figure 10). This has meant that vitamins and minerals are preferentially retained by proteins for short-term survival and reproduction, but the proteins essential in the protection against aging are starved of micronutrients and are thereby disabled. The theory suggests that in order for vitamins and minerals to ‘trade-off’ between short-term survival and long-term health, it requires different mechanisms for both. According to the mechanistic, genetic and epidemiological evidence on a key study, this metabolic reaction could accelerate age-related chronic diseases, such as CVD, immune dysfunction and cognitive decline.<sup>30</sup>

The Triage Theory is especially noteworthy when looking at the nutritional diets of the



elderly globally. Energy intake and body weight are both critical factors for healthy longevity in old age. Evidence on calorie restriction has so far been unclear, as long-term, randomized studies are generally unfeasible and unethical.

While the benefits of calorie restriction have been recognized in other species, it is thought to have the opposite effect in humans.<sup>32</sup> Instead, regular calorie reduction can bring a state of ‘nutritional frailty’ to vulnerable, older adults. This is often characterized by sudden, significant weight loss and reduced muscle mass and strength. As well as calorie restriction, obesity can also contribute to nutritional frailty, due to longstanding poor, energy-dense and nutrient-deplete diets. It is often difficult for older people to obtain the right amount of nutrients, because many

experience changes in taste and smell, loss of appetite, dental and chewing problems and limitations in mobility, as well as limited access to high quality, fresh food. As such, mature adults routinely fall below recommended nutrient levels, including calcium, vitamins D and E, dietary fiber, magnesium, potassium, zinc, protein and omega-3 fatty acids, among others.

## Spotlight on the United States

A comprehensive report states that Americans do not currently meet federal dietary recommendations. Collating data from over 16,000 people in the US over four years, the study found that the majority of the population did not meet recommendations for all the nutrient-rich food groups, except total grains, meat and beans. However, the consumption of solid fats, added sugars and alcoholic beverages – so-called ‘empty calories’ – was widespread across the sample group. Older adults were found to be particularly vulnerable; 80% of people aged over 71 years had an intake of empty calories that exceeded the discretionary calorie allowances.<sup>33</sup>



# THE ROLE OF MICRONUTRIENTS FOR HEALTHY AGING

Extensive research highlights that diets including low-fat dairy products, fruit, whole grains, poultry, fish and vegetables, with a lower intake of meat, fried foods, sweets, high-energy drinks and added fat have been associated with superior nutritional status, quality of life and survival among older adults.<sup>34</sup> For instance, there is evidence to suggest that dietary fiber may play an important role in preventing colonic cancer and in treating bowel diseases and symptoms.<sup>35</sup> In addition to the benefits of a well-balanced diet, supplements

at higher doses could show promise as part of a preventative approach to healthy aging – magnesium, for example, has been linked to the aging process, with associations found between inadequate magnesium intake and certain neuromuscular and cardiovascular disorders in the elderly.<sup>36</sup> While further studies are needed, there is significant evidence to suggest that micronutrients and omega-3 fatty acids could play a valuable role in supporting specific biological functions in the risk reduction of age-related chronic disease.



## Cardiovascular health



Extensive research on the role of micronutrients indicate positive results in reducing the risks associated with CVD. Hypercholesterolemia is highly prevalent in the elderly population, due to its association with environmental factors and comorbidity.<sup>39</sup> A pivotal clinical trial, the Japan EPA Lipid Intervention Study (JELIS) was the first large-scale, prospective randomized trial on the use of EPA with statins. The results demonstrated that EPA supplementation can extend the benefits of statins in patients with hypercholesterolemia.<sup>40</sup>

As well as the potential heart health benefits of EPA and DHA, there is emerging evidence to suggest that vitamin E may play an important role in reducing oxidative stress and inflammation that is associated with the onset of CVD.<sup>43</sup> As well as protecting cells from

A recent meta-analysis demonstrated that EPA, together with DHA, can significantly reduce the risk of coronary heart disease (CHD) in individuals with elevated triglycerides ( $>150\text{mg/dL}$ ) or LDL cholesterol ( $>130\text{mg/d}$ ).<sup>41</sup> In addition, another recent meta-analysis demonstrated that supplemental EPA and DHA, compared to a placebo, significantly reduces the risk of cardiac death.<sup>42</sup>

damage, the micronutrient may help to limit oxidative damage to fatty acids, including EPA and DHA. This means that more vitamin E could be required in individuals with higher levels of omega-3 intake.<sup>44</sup> Vitamin E also holds

CVD is the leading cause of death in the US among men and women, and continues to be one of the biggest threats to human health.<sup>37</sup> Given the prevalence and severity of the condition, risk reduction has been a key priority in recent public health policies. Age is an important risk factor for CVD, but this can be reduced partly by the modification of traditional coexisting risk factors. This includes a number of modifiable lifestyle behaviors, including:<sup>38</sup>

- Dietary patterns
- Obesity
- Lack of exercise
- Alcohol
- High cholesterol
- Diabetes
- Psychosocial factors
- Smoking

potential in arterial health. In a review of adults with low plasma vitamin E and C levels, vitamin E supplementation resulted in a significant reduction in arterial stiffness.<sup>45</sup>

Studies have also found an important link between higher vitamin C intake and a lower risk of CHD.<sup>46</sup> For example, an instrumental meta-analysis found that high-level vitamin C supplementation (500 mg median dose) over a course of two months helped to reduce blood pressure in adults.<sup>47</sup> Not only this, a bank of evidence indicates that an intake of vitamin C over 500 mg (between 500 and 3,000 mg) may result in improved vasodilation in individuals with CHD.<sup>48</sup>

Vitamin D may also support heart health in older adults. An analysis of over 41,000 medical records found that vitamin D inadequacy, which was the case in 30% of the selected group, was associated with increased prevalence of cardiovascular conditions, including hypertension, coronary artery disease and stroke.<sup>49</sup> This is further substantiated by evidence that shows that suboptimal vitamin D levels have been linked with arterial stiffness, which is one of the main causes of high blood pressure.<sup>50</sup> Hypertension risk reductions of up to 30% have also been observed in people with a sufficient vitamin D blood level, compared to those with an insufficient status.<sup>51</sup>

There are several major ongoing clinical trials on the use of micronutrients and omega-3 fatty acids in the risk reduction of age-related chronic diseases. The results of these studies are to be presented shortly. The VITAL study, for instance, is currently assessing men and women across the US to investigate if a daily dietary supplement of vitamin D and fish oil can help reduce the risk of developing cancer, heart disease and stroke in people who do not have a prior history of these illnesses.<sup>52</sup>

A second, separate clinical trial in Europe is also expected to clarify the role of vitamin D (2,000 IU/d), when used in combination with omega-3 fatty acids (1 g/d) and a home exercise program in the prevention of disease in older age. The results from the DO-HEALTH study are expected to be published in mid-2018, and will examine five primary endpoints: the risk of incident non-vertebral fractures, the risk of functional decline, the risk of blood pressure increase, the risk of cognitive decline and the rate of any infection.<sup>53</sup>

Another pivotal study is Lifelines, which examines the more general mechanisms of aging, and the subsequent development of chronic diseases in the Netherlands. Lifelines collects data and biological samples on a large scale, to create a biobank and databank. This information will then be made available for use in public health policies.<sup>54</sup>



## Brain health



Cognitive health and mental wellbeing, such as depression, is becoming an increasing challenge in the face of an aging population.

### Key statistics for mental health

Depression is a growing concern across the globe and a major contributor to the general burden of disease. 300 million people are currently estimated to be affected by the illness worldwide.<sup>55</sup>



There are 44 million people worldwide living with dementia, with the number set to double by 2030, and more than triple by 2050.



Over the age of 65 years, dementia prevalence doubles with every five-year increment in age.<sup>56</sup>



Alzheimer's disease is the most common cause of dementia and contributes to 60–70% of cases.



Dementia is one of the major causes of disability and dependency among older people worldwide.<sup>57</sup>



Like CVD, in recent years there has been much more focus on treatment rather than preventative approaches to maintaining good brain health, as they are generally less expensive and require shorter term studies. However, research on the use of nutritional

intervention in brain health has been promising. While initial investment in this research is required, the high social and public return-on-investment (ROI) means that nutrition could present a viable option in supporting cognitive health and mental wellbeing, which may decline with aging.

### Mental wellbeing

Promising studies have suggested that omega-3 fatty acids could play an important role in reducing the risk of depression. Although findings have historically been mixed in more serious cases of depression, several more recent clinical trials have been noteworthy. In a meta-analysis of over 6,000 participants with diagnosed depression receiving omega-3s EPA and DHA, the results were positive. EPA-predominate formulations (>50% EPA or 1-2 g EPA range) demonstrated superior antidepressant efficacy compared with a placebo, whereas DHA-predominate formulations showed no benefit.<sup>58</sup> Another key meta-analysis suggested a beneficial overall effect of a high intake of EPA (>60% EPA) in patients with major depressive disorder (MDD) taking antidepressants.<sup>59</sup>

Recent scientific findings from Norway reveal a strong association between low vitamin D levels in the blood and increased adverse psychotic symptoms and depression.<sup>60</sup> This has been further backed up by a meta-analysis that suggests EPA (1-2 g) and vitamin D (>1,500 IU/d) can reduce depressive symptoms beyond the placebo, and could therefore have significance in clinical and public health.<sup>61</sup>

### Cognitive health

There is substantial evidence that supports the use of omega-3s EPA and DHA in protecting brain health in older people. A comprehensive meta-

analysis demonstrated that EPA and DHA supplementation significantly improved episodic memory in healthy adults with mild memory complaints, regardless of initial cognitive status.<sup>62</sup> This is consistent with other findings, that indicate that a diet rich in fish oil for older people has beneficial effects on white matter microstructural integrity and grey matter volume in frontal, temporal, parietal and limbic areas in the left hemisphere.<sup>63</sup>

In addition, the antioxidant properties of vitamin E may help to protect cells from damage associated with oxidative stress caused by free radicals. The mechanisms of coping with oxidative stress are reduced as individuals age, which can result in neurodegeneration. Associations have been found between high plasma vitamin E levels and cognitive performance, which has led to further studies on the ability of the micronutrient to support brain health in mature adults.<sup>64</sup> Additional research indicates that vitamin E may slow the progression of Alzheimer's disease.<sup>65</sup>

A further noteworthy study for older people indicates the potential brain health benefits of B vitamins in the risk reduction of Alzheimer's disease. Brain atrophy is a common observation in mature adults with cognitive decline. B vitamins have been shown to slow the rate of atrophy in brain by up to 30% compared to a placebo.<sup>66</sup> Furthermore, a separate review from the Baltimore Longitudinal Study of Aging found that subjects who received a daily intake of more than 400 mg of folate had a 55% reduction in the risk of developing Alzheimer's disease.<sup>67</sup>

Although more research is needed to establish the long-term effects, emerging research also highlights the potential role that beta-carotene, lutein and vitamin D<sub>3</sub> could play in reducing the risk of age-related cognitive decline. Beta-carotene is a precursor for vitamin A, that so far has been shown to have a promising effect on cognition.<sup>68</sup> As well as the potential benefits of lutein on eye health, it may also support cognition.<sup>69</sup> Furthermore, vitamin D<sub>3</sub> is implicated in neurotransmission, in the coordination of motor function and in mood. As such, the micronutrient has demonstrated a positive influence on cognition, as well as brain energy, depression and mood.<sup>70</sup>

## Eye health

Emerging studies highlight the potential benefits of lutein and omega-3s in maintaining eye health. Particularly given the prevalence of age-related macular degeneration (AMD) and cataracts in older adults, any developments in this area could significantly improve quality of life for this demographic.

AMD is a progressive eye disease and the main cause of blindness in people aged over 50 years. The number of people with AMD is expected to reach 5.44 million by 2050.<sup>71</sup> Cataracts is a growing problem around the world; in the US alone, the number of people living with the condition is expected to rise to 50 million.<sup>72</sup>

The Age-Related Eye Disease Study 2 (AREDS2) is currently the largest human study conducted on nutritional supplements related to eye health.<sup>73</sup> The results found that intake of lutein and zeaxanthin led to an 18% reduction in the risk of progression to advanced AMD over a five-year period, as well as a significant reduction in the progression of cataracts. There was a 36% risk reduction in progression to severe cataracts and a 32% risk reduction to cataracts surgery.

In addition, further research has demonstrated improved visual performance in adults with lutein intake. For example, a meta-analysis found that lutein supplementation helped to increase macular pigment optical density (MPOD) values, while also improving visual acuity and contrast sensitivity in AMD subjects (20 mg/d in first three months, then 10 mg/d in months 4-6).<sup>74</sup> Not only this, but lutein intake is also associated with significant decreases in inflammation activity in the macula in subjects receiving 10 mg/d. This highlights how high lutein intake could control the inflammatory pathway of the innate immune system in patients with AMD.<sup>75</sup>

There have been several studies on how older people can lose macular pigment (MP) with age. Decreased MP levels can lead to a decrease in scotopic and shortwave sensitivity, which can result in loss of visual acuity. A double-blind, placebo controlled study examined the visual effects of 10 mg/d zeaxanthin in 115 young, healthy subjects over a year. It found that MPOD significantly increased with supplementation compared with a placebo. Chromatic and photo stress time also increased, in line with previous studies.<sup>76</sup>

As well as lutein and zeaxanthin, there has been emerging scientific evidence on the benefits of

omega-3 fatty acids in the protection of adult eyes from dry eye syndrome. Another highly prevalent condition in people over 65 years, it is estimated that over 3.23 million North Americans currently suffer from dry eyes, which can severely affect quality of life. Studies also show that consumption of omega-3 fatty acids, like EPA and DHA, could offer an effective therapy in the management and treatment of dry eye syndrome.<sup>77,78</sup>

The potential of micronutrients in the protection of the elderly's eye health is promising. The REACT (Roche European Anti-Cataract Trial) study evaluated whether daily supplementation of an antioxidant micronutrient combination can delay, stop or reverse the progression of AMD. The results indicated a significant reduction in the cataract progression rate in the subjects that received supplementation in vitamins C, E and beta-carotene, although more research is still needed at this stage.<sup>79</sup>

Further positive results have been found with zinc, which is highly concentrated in the eye, primarily in the retina and choroid, the vascular tissue layer under the retina. Zinc levels tend to decline in the eye with advancing age, but there is emerging evidence that suggests high doses could improve eye health. Initial trials showed that 200 mg/d of zinc sulfate could further reduce vision loss in patients with AMD.<sup>80</sup>



## Muscle maintenance and bone health



Malnutrition in older people is strongly associated with frailty and ultimately, primary or secondary sarcopenia. These conditions can lead to disability, including loss of independence, falls, fractures and even death. 92% of people aged over 65 years develop sarcopenia, and 95% after 80 years. In older adults with osteoporosis, the risk of frailty is doubled.<sup>81</sup>

The role of protein in the diets of older people is well established in maintaining muscle mass. There is strong evidence to suggest that adequate protein intake can help limit and treat age-related decline in muscle mass, like

sarcopenia, strength and functional abilities. In combination with exercise, nutrition is considered an important consideration in muscle maintenance. However, nutrition can be a more viable option for much older adults, particularly when used together with increased resistance exercise. For instance, there is emerging evidence to suggest a benefit of omega-3 fatty acids in individuals with aging- or chronic disease-associated sarcopenia, as well as in enhancing anabolic responses to exercise.<sup>82,83</sup> Nutrition is also an important aspect, as it has been suggested that older adults require a higher protein intake than younger people, otherwise muscle proteins can be degraded faster than they are synthesized.<sup>84</sup>

Similarly, bone health can have a severe impact on the mobility of the elderly. It is estimated that nearly 200 million people currently suffer from osteoporosis, of which it is increasingly prevalent in individuals aged over 50 years old.<sup>85</sup> Nearly 75% of hip, spine and distal forearm fractures occur among patients aged over 65 years old, underlining the importance of bone health in the elderly.<sup>86</sup> There is evidence that vitamin D and calcium supplementation could help in risk reduction for osteoporosis,

which could result in improved quality of life. Vitamin D deficiency has been associated with a greater incidence of hip fractures in many populations, including post-menopausal women.<sup>87</sup> Furthermore, a study found 50% of women hospitalized due to hip fractures had signs of vitamin D deficiency.<sup>88</sup>

Consistent with these learnings, further research indicates that vitamin D supplementation is more beneficial when taken together with calcium. One study showed that this was the case with elderly women who have suffered hip fractures – thereby reducing the incidence of secondary falls. This is particularly noteworthy as survivors of hip fractures are at a five- to ten-fold increased risk of a second hip fracture.<sup>89</sup>

Intake of vitamin D above recommended levels (between 700 and 800 IU per day) could reduce the risk of hip and nonvertebral fractures in ambulatory or institutionalized elderly people, while additional calcium supplementation could provide further benefits.<sup>90</sup>

## Immunity

Immune function declines with age, leading older adults to become more susceptible to infections. Low T-cell mediated activity has been shown to increase morbidity and mortality from infectious disease and cancer in the elderly.<sup>91</sup> Although the process of aging accumulates cellular, molecular and organ level damage, research highlights the promise of nutrition in improving immune function in the elderly.

Vitamin E is considered one of the more effective nutrients in enhancing immune function. Several studies show that vitamin E deficiency impairs humoral and cell-mediated immune functions. Further to this, vitamin E levels above those recommended in the older generation have been associated with increased resistance against a number of pathogens. Although vitamin E supplementation has resulted in improved cell-mediated immune

function in the elderly, responses are varied depending on baseline levels of response and genetic factors.<sup>94</sup>

There have also been several studies on zinc's effect on infection in the elderly. In a controlled clinical trial, institutionalized elderly people over the age of 65 years had a significant decrease in the mean number of respiratory infections over a two-year period of zinc supplementation.<sup>95</sup> Zinc deficiency is widespread worldwide, but more research is needed to determine optimal zinc intake in the elderly.

Recent studies have indicated that 30% of elderly nursing home residents in the US have low serum zinc levels, which was associated with an increased incidence and duration of pneumonia.<sup>96</sup> Furthermore, zinc supplementation in elderly adults with low serum zinc levels has been shown to improve their zinc status and T cell mediated function.<sup>97</sup> It has been noted, however, that although zinc shows promise in improving immune function, high levels in older adults with adequate zinc status might not be beneficial,

and instead could cause harm. It is therefore key that when considering nutritional intervention, healthcare providers should take a more tailored approach, rather than a one-size-fits-all methodology. Further studies are also needed to establish the effects of these micronutrients on targeted populations.



# ASSESSING PROMISING NUTRITIONAL SOLUTIONS FOR HEALTHY AGING

Despite the knowledge gaps that exist in healthy aging research, there is still a substantial body of evidence to suggest that incorporating nutritional evaluations and services into preventative care for aging adults could prove beneficial in avoiding and minimizing the effects of age-related chronic diseases. This could be achieved by optimizing nutrition screenings and dietary assessments, as well as re-evaluating how current body mass index (BMI) guidelines are calculated in mature adults. One study found that in patients over the age of 65 years, physicians need to be ‘aggressive’ in instituting preventative measures for those at risk of malnutrition. By providing clinicians with the tools and education to complete successful assessments of patients, the nutritional status of the elderly could be greatly improved.<sup>98</sup>

Given that there is no ‘typical’ older person, a more targeted approach to nutrition could offer an effective strategy in the risk reduction of age-related chronic diseases. By assessing patients on biological age, rather than chronological age, there is an opportunity for preventative measures to form the basis of primary health care. For instance, a pivotal review found that with regular screenings as part of a wider healthcare strategy, a solid foundation could be formed in health modulation in later years.

This theory has been supported by a wide range of studies, including a pivotal call-to-action review from the interdisciplinary Alliance to Advance Patient Nutrition, which highlights the critical role of nutrition in clinical care. According to the paper, preventing and treating hospital malnutrition offers an opportunity to optimize patient care, improve clinical outcomes and reduce costs. However, further work needs to be done to raise awareness of malnutrition and the importance of nutrition.<sup>99</sup>

As well as the inferred health benefits for older people, a preventative nutritional strategy presents a cost-effective option for healthcare providers. A recent market research report found that targeted dietary supplementation could help to reduce expenditure associated with aging. For example, the use of omega-3 supplements (1,000 mg/d) in adults over 55 years in the US could potentially save as much as \$2.06 billion on average per year in hospital utilization costs for CVD, with a cumulative saving of \$16.46 billion from 2013 to 2020.<sup>100</sup> Similarly, the use of folic acid (>1.7 mg), and vitamins B6 (<29 mg) and B12 (<0.5 mg) in the target population at a preventative level could save on average \$1.52 billion per year in CVD-related hospital costs.



## Case study: Finland

Relatively small changes in lifestyle can lead to significant outcomes. Historically, Finland had one of the highest incidences of heart disease in the developed world. As part of a government policy targeting diet and lifestyle, new initiatives were implemented, including nationwide salt reductions and better product labeling. As a result of these primary health care measures, there were substantial improvements in the care of patients with myocardial infarctions. This led to the number of cases of CVD and other heart diseases falling dramatically – CVD mortality in men has reduced by up to 65%.<sup>101</sup>

## Recommended doses for older adults

Given the difficulties for some older adults in consuming enough micronutrients in their diets, there is evidence to suggest that supplementation could be complementary to a healthy, balanced diet – although it remains a controversial topic. In light of the extensive research in the area, a report has outlined recommended doses for a range of key micronutrients:<sup>102</sup>

- Vitamin B12: 2.4 µg/d for adults over 50 years
- Vitamin D: 600 IU/d up to 70 years, 800 IU/d 70 years and above
- Calcium: 1,000 mg/d for men aged 51 to 70 years, 1,200 mg for women aged 51 to 70 years and for all adults aged over 70 years

# CONCLUSION

Through a combination of good lifestyle choices, including a nutritious diet and physical exercise, healthy aging is a realistic objective. By improving quality of life in older people and enabling them to have a better relationship with their local community, these additional years can be enjoyed as much as possible. Allowing elderly people to care for themselves not only helps improve state of mind, but also lightens the burden for families and wider society.

While a healthy, nutrient-rich diet appears to be a broad, all-encompassing solution, the specific health benefits of the varied micronutrients and omega-3 fatty acids within it could prove highly beneficial in older people. Particularly given widespread nutrient deficiencies in mature adults across the globe, nutrition presents an affordable and safe strategy. As the range of studies reviewed in this paper has shown, a long-term preventative model based on improved nutrition could be a viable option for

the risk reduction of age-related chronic diseases, especially compared to more expensive treatment alternatives.

Although further research is needed to learn how dietary requirements change during the aging process, implementing a framework of action for intervention strategies could prove beneficial across a range of sectors. As such, fortified food and supplementation could help to increase overall nutrient levels, allowing people to enjoy healthy years later in life.

## Key take-away messages

- Life expectancy has increased substantially in recent years, bringing a wide range of NCDs and other age-related chronic diseases that affect the heart, brain, eye, bone and muscle health, as well as immunity
- The aging population is having a severe socioeconomic impact across the world, as older people in poor health become more dependent on others in everyday life
- Healthy aging has become a key priority in global healthcare policies, but more awareness is needed to ensure quality of life is improved
- Malnutrition is prevalent in the elderly, due to poor, energy-dense nutrient deplete diets and lack of essential micronutrients in their diets – leading to a state of ‘hidden hunger’
- Extensive scientific evidence indicates the potential positive health benefits of micronutrients, including vitamins D, E, B vitamins, calcium, omega-3 fatty acids
- EPA and DHA, lutein and zinc in reducing the risks of age-related chronic diseases
- By improving adequate nutrition in older people as part of a preventative approach, there could be significant cost savings
- More evidence is needed to ascertain the long-term effects of nutritional strategies in this life stage, but studies so far have been promising. Cross-sector working could also prove important in furthering research in this area



## References

- European Commission, 'Growing the European Silver Economy', [report], 2015.
- National Center for Health Statistics, Data Brief, 'Mortality in the United States', [report], 2017.
- UN Department of Economic and Social Affairs, Population Division, 'World population ageing 2013', [report], 2013.
- B. Chen et al., 'DNA methylation-based measures of biological age: meta-analysis predicting time to death', *Aging*, vol. 8, no. 9, 2017, p. 1844-1865.
- DSM, 'Global health concerns', [report], 2017.
- WHO, 'Ageing and life course', [website], 2018, <http://www.who.int/ageing/healthy-ageing/en/>, (accessed 17 January 2018).
- UN Department of Economic and Social Affairs, Population Division, 'World population ageing 2013', [report], 2013.
- DSM, 'Global health concerns', [report], 2017.
- J. Shlisky et al., 'Nutritional considerations for healthy aging and reduction in age-related chronic disease', *Advances in Nutrition*, vol. 8, 2017, p. 17-26.
- DSM, 'Global health concerns', [report], 2017.
- J. Olshansky et al., 'A potential decline in life expectancy in the United States in the 21st Century', *N Engl J Med.*, vol. 352, 2005, p. 1138-1145.
- WHO, 'World report on ageing and health', [report], 2015.
- Social Security Administration, 'Life tables for the United States Social Security Area 1900-2100: Actuarial Study No. 116', [report], 2002.
- Op. cit. (UN Department of Economic and Social Affairs).
- Op. cit. (Social Security Administration).
- US Census Bureau, 'The older population: 2010', [report], 2011.
- Ibid.
- Op. cit. (WHO, 2015).
- RAND Corporation, 'Multiple chronic conditions in the United States', [report], 2017.
- WHO, 'WHO global status report on noncommunicable diseases 2010', [report], 2010.
- WHO, 'Global action plan for the prevention and control of NCDs 2013-2020', [report], 2013.
- Op. cit. (RAND Corporation).
- WHO, 'Global monitoring framework', [website], [www.who.int/nmh/global\\_monitoring\\_framework/en/](http://www.who.int/nmh/global_monitoring_framework/en/), (accessed 19 February 2018).
- M. Eggersdorfer and M. McBurney, 'NHANES data indicates that adequate vitamin intake remains a challenge for a large part of the elderly even in affluent societies', *International Journal of Food and Nutritional Science*, vol. 3, no. 1, 2016, p. 1-6.
- Op. cit. (WHO, 2015).
- Op. cit. (J. Shlisky et al.).
- K. Freijer et al., 'The economic cost of disease related malnutrition', *Clinical Nutrition*, vol. 32, 2013, p. 136-141.
- Ibid.
- OECD, 'Health expenditure and financing: health expenditure indicators', *OECD Health Statistics (database)*, [website], <http://stats.oecd.org/Index.aspx?DataSetCode=SHA>, (accessed 19 February 2018).
- B. Ames, 'Vitamin and mineral inadequacy accelerates aging-associated disease', *University of California*, [presentation], 2014.
- Ibid.
- Op. cit. (J. Shlisky et al.).
- S. Krebs-Smith et al., 'Americans do not meet federal dietary recommendations', *The Journal of Nutrition*, vol. 140, no. 10, 2010, p. 1832-1838.
- A. Anderson et al., 'Dietary patterns and survival of older adults', *J Am Diet Assoc.*, vol. 111, no. 1, 2011, p. 84-91.
- L.M. Donini et al., 'Nutrition in the elderly: the role of fiber', *Archives of Gerontology and Geriatrics*, vol. 49, 2009, p. 61-69.
- R. B. Costello and P.B. Moser-Veillon, 'A review of magnesium intake in the elderly. A cause for concern?', *Magnes Res*, vol. 5, no. 1, 1992, p. 61-67.
- NCHS, National Vital Statistics System, Mortality, [website], 2015, [www.cdc.gov/nchs/data/databriefs/db267\\_table.pdf#3](http://www.cdc.gov/nchs/data/databriefs/db267_table.pdf#3), (accessed 24 January 2018).
- R. Dhingra and R. Vasan, 'Age as a cardiovascular risk factor', *Med Clin North Am.*, vol. 96, no. 1, 2012, p. 87-91.
- F. Felix-Redondo et al., 'Cholesterol and cardiovascular disease in the elderly. Facts and gaps', *Aging Dis.*, vol. 4, no. 3, 2013, p. 154-169.
- M. Yokoyama et al., 'Effects of eicosapentaenoic acid (EPA) on major cardiovascular events in hypercholesterolemic patients: the Japan EPA Lipid Intervention Study (JELIS): a randomised open-label, blinded endpoint analysis', *Lancet*, vol. 369, no. 9567, 2007, p. 1090-1098.
- D. Alexander et al., 'A meta-analysis of randomized controlled trials and prospective cohort studies of eicosapentaenoic and docosahexaenoic longchain omega-3 fatty acids and coronary heart disease risk', *Mayo Clinic Proceedings*, 2017.
- K. C. Maki et al., 'Use of supplemental long-chain omega-3 fatty acids and risk for cardiac death: An updated meta-analysis and review of research gaps', *J Clin Lipidol*, vol. 11, no. 5, 2017, p. 1152-1160.
- E. Rimm and M. Stampfer, 'Antioxidants for vascular disease', *Med Clin North Am*, vol. 84, no. 1, 2000, p. 239-49.
- D. Raederstorff et al., 'Vitamin E function and requirements in relation to PUFA', *Br J of Nutrition*, vol. 114, no. 8, 2015, p. 1113-1122.
- A. Ashor et al., 'Antioxidant vitamin supplementation reduces arterial stiffness in adults: a systematic review and metaanalysis of randomized controlled trials', *J Nutr.*, vol. 144, no. 10, 2014, p. 1594-1602.
- P. Knekt et al., 'Antioxidant vitamins and coronary heart disease risk: a pooled analysis of 9 cohorts', *Am J Clin Nutr.*, vol. 80, no. 6, 2004, p. 1508-20.
- S. Juraschek et al., 'Effects of vitamin C supplementation on blood pressure: a meta-analysis of randomized controlled trials', *Am J Clin Nutr.*, vol. 95, no. 5, 2012, p. 1079-88.
- A. Carr et al., 'Toward a new recommended dietary allowance for vitamin C based on antioxidant and health effects in humans', *Am J of Clin Nutr.*, vol. 69, no. 6, 1999, p. 1086-107.
- J. Anderson et al., 'Relation of vitamin D deficiency to cardiovascular risk factors, disease status, and incident events in a general healthcare population', *Am J Cardiol.*, vol. 106, no. 7, 2010, p. 963-8.
- I. Mheid et al., 'Vitamin D status is associated with arterial stiffness and vascular dysfunction in healthy humans', *J Am Coll Cardiol.*, vol. 58, no. 2, 2011, p. 186-92.
- S. Kunutsor et al., 'Vitamin D and risk of future hypertension: meta-analysis of 283,537 participants', *Eur J Epidemiol.*, vol. 28, no. 3, 2013, p. 205-21.
- VITAL, 'Welcome to the VITAL study', [website], <https://www.vitalstudy.org/>, (accessed 23 January 2018).
- DO-HEALTH, 'What is DO-HEALTH?', [website], <http://do-health.eu/wordpress/>, (accessed 23 January 2018).
- Lifelines, 'About Lifelines', [website], <https://www.lifelines.nl/>, (accessed 23 January 2018).
- WHO, 'Depression', [website], 2017, <http://www.who.int/mediacentre/factsheets/fs369/en/>, (accessed 7 February 2018).
- Alzheimer's Disease International, World Alzheimer Report 2014, 'Dementia and risk reduction: an analysis of protective and modifiable factors', [report], 2014.
- Ibid.
- B. Hallahan et al., 'Efficacy of omega-3 highly unsaturated fatty acids in the treatment of depression', *B J Psych*, vol. 209, no. 3, 2016, 192-201.
- R. Mocking et al., 'Meta-analysis and meta-regression of omega-3 polyunsaturated fatty acid supplementation for major depressive disorder', *Transl Psychiatry*, vol. 15, no. 6, 2016, p. 756.
- M. Nerhus et al., 'Low vitamin D is associated with negative and depressive symptoms in psychotic disorders', *Schizophr Res.*, vol. 178, no. 1-3, 2016, p. 44-49.
- J. Sarris et al., 'Adjunctive nutraceuticals for depression: a systematic review and meta-analyses', *Am J Psychiatry*, vol. 173, no. 6, 2016, p. 575-87.
- K. Yurko-Mauro, D. Alexander and M. van Elswyk, 'Docosahexaenoic acid and adult memory: a systematic review and meta-analysis', *PLoS One*, vol. 10, no. 3, 2015.
- A. Witte et al., 'Long-chain omega-3 fatty acids improve brain function and structure in older adults', *Cereb Cortex.*, vol. 24, no. 11, 2014, p. 3059-68.
- G. La Fata, P. Weber and M. Mohajeri, 'Effects of vitamin E on cognitive performance during aging and in Alzheimer's disease', *Nutrients*, vol. 6, no. 12, 2014, p. 5453-72.
- H. Mohajeri, B. Troesch and P. Weber, 'Inadequate supply of vitamins and DHA in the elderly: implications for brain aging and Alzheimer-type dementia', *Nutrition*, vol. 31, no. 2, 2015, p. 261-275.
- A. Smith, 'Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in mild cognitive impairment: a randomized controlled trial', *PLoS One*, vol. 5, no. 9, 2010.
- Op. cit. (H. Mohajeri et al.).
- F. Grodstein et al., 'A randomized trial of beta carotene supplementation and cognitive function in men: the Physicians' Health Study II', *Arch Intern Med*, vol. 167, no. 20, 2007, p. 2184-90.
- A. Walk et al., 'The role of carotenoids and age on neuroelectric indices of attentional control among early to middle-aged adults', *Frontiers in Aging Neuroscience*, vol. 9, 2017, p. 183.
- D. Gezen-Ak et al., 'Why vitamin D in Alzheimer's disease? The hypothesis', *J Alzheimers Dis*, vol. 40, no. 2, 2014, p. 257-269.
- National Eye Institute, 'Age-related macular degeneration (AMD)', [website], <https://nei.nih.gov/health/maculardegen>, (accessed 23 January 2018).
- NEI, 'Cataracts' [website], <https://nei.nih.gov/health/ataract>, (accessed 23 January 2018).
- E. Chew et al., 'The age-related disease study 2 (AREDS2): study design and baseline characteristics (AREDS2) report number 1', *Ophthalmology*, vol. 119, no. 11, 2012, p. 2282-2289.
- G. Weigert et al., 'Effects of lutein supplementation on macular pigment optical density and visual acuity in patients with age-related macular degeneration', *Invest Ophthalmol Vis Sci.*, vol. 52, no. 11, 2011, p. 8174-8178.
- A. Kijlstra et al., 'Lutein: More than just a filter for blue light', *Prog Retin Eye Res*, vol. 31, no. 4, 2012, p. 303-315.
- B. R. Hammond et al., 'A double-blind, placebo-controlled study on the effects of lutein and zeaxanthin on photostress recovery, glare disability, and chromatic contrast', *Invest Ophthalmol Vis Sci*, vol. 55, 2014, p. 8583-8589.
- A. Liu and J. Ji, 'Omega-3 essential fatty acids therapy for dry eye syndrome: a meta-analysis of randomized controlled studies', *Med Sci Monit*, vol. 20, no. 6, 2014, p. 1583-9.
- H. Kangari, 'Short-term consumption of oral omega-3 and dry eye syndrome', *Ophthalmology*, vol. 120, issue 11, 2013, p. 2191-2196.
- L. Chylack et al., 'The Roche European American Cataract Trial (REACT): a randomized clinical trial to investigate the efficacy of an oral antioxidant micronutrient mixture to slow progression of age-related cataract', *Ophthalmic Epidemiol*, vol. 9, no. 1, 2002, p. 49-80.

80. D. Newsome, 'Oral zinc in macular degeneration', *Arch Ophthalmol*, vol. 106, no. 2, 1988, p. 192-8.
81. N. Deutz et al., 'Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group', *Clin Nutr.*, vol. 33, no. 6, 2014, p. 926-936.
82. A. Buoite Stella et al., 'Update on the impact of omega-3 fatty acids on inflammation, insulin resistance and sarcopenia: a review', *Int J Mol Sci.*, vol. 19, no. 1, 2018.
83. A. Z. Lalia et al., 'Influence of omega-3 fatty acids on skeletal muscle protein metabolism and mitochondrial bioenergetics in older adults', *Aging*, vol. 9, no. 1, 2017, p. 1096-1129
84. Op. cit. (N. Deutz et al.).
85. T. Sozen et al., 'An overview and management of osteoporosis', *Eur J Rheumatol.*, vol. 4, no. 1, 2017, p. 46-56.
86. L. Melton et al., 'Fracture incidence in Olmsted County, Minnesota: comparison of urban with rural rates and changes in urban rates over time', *Osteoporos Int.*, vol. 9, no. 1, 1999, p. 9-29.
87. M. Chapuy et al., 'Vitamin D<sub>3</sub> and calcium to prevent hip fractures in elderly women', *N Engl J Med.*, vol. 327, no. 23, 1992, p. 1637-42.
88. M. LeBoff et al., 'Occult vitamin D deficiency in postmenopausal US women with acute hip fractures', *JAMA*, vol. 281, no. 16, 1999, p. 1505-11.
89. R. Harwood et al., 'A randomised, controlled comparison of different calcium and vitamin D supplementation regimens in elderly women after hip fracture: The Nottingham Neck of Femur (NONOF) Study', *Age Ageing*, vol. 33, no. 1, 2004, p. 45-51.
90. J. Sunyecz, 'The use of calcium and vitamin D in the management of osteoporosis', *Ther Clin Risk Manag.*, vol. 4, no. 4, 2008, p. 827-836.
91. M. Pae et al., 'The role of nutrition in enhancing immunity in aging', *Aging Dis.*, vol. 3, no. 1, 2012, p. 91-129.
92. A. Molfino et al., 'The role of dietary omega-3 fatty acids supplementation in older adults', *Nutrients*, vol. 6, no. 10, 2014, p. 4058-4072.
93. Op. cit. (M. Pae et al.).
94. Ibid.
95. F. Girodon, 'Impact of trace elements and vitamin supplementation on immunity and infections in institutionalized elderly patients: a randomized controlled trial', *Arch Intern Med.*, vol. 159, no. 7, 1999 p. 748-54.
96. S. N. Meydani et al., 'Serum zinc and pneumonia in nursing home elderly', *American Journal of Nutrition*, vol. 86, no. 4, 2007, p. 1167-1173.
97. J. B. Barnett et al., 'Effect of zinc supplementation on serum zinc concentration and T cell proliferation in nursing home elderly: a randomized, double-blind placebo-controlled trial', *American Journal of Nutrition*, vol. 103, no. 3, 2016, p. 942-951.
98. J. Wells and A. Dumbrell, 'Nutrition and aging: assessment and treatment of compromised nutritional status in frail elderly patients', *Clin Interv Aging*, vol. 1, no. 1, 2006, p. 67-79.
99. K. Tappenden et al., 'Critical role of nutrition in improving quality of care: an interdisciplinary call to action to address adult hospital malnutrition', *Journal of the Academy of Nutrition and Dietetics*, vol. 113, no. 9, 2013, p. 1219-1237.
100. C. Shanahan and R. de Lorimier, 'Smart prevention – health care cost savings resulting from the targeted use of dietary supplements', *Frost & Sullivan*, [report], 2013.
101. European Heart Health Initiative, 'The European Heart Health Initiative: final report', [report], 2000.
102. J. Manson and S. Bassuk, 'Vitamin and mineral supplements: what clinicians need to know', *JAMA*, 2018.

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