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## Conference on 'Nutrition and healthy ageing' Symposium 2: Epidemiology of human ageing

## Nutrition and healthy ageing: the key ingredients

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> Healthy longevity is a tangible possibility for many individuals and populations, with nutritional and other lifestyle factors playing a key role in modulating the likelihood of healthy ageing. Nevertheless, studies of effects of nutrients or single foods on ageing often show inconsistent results and ignore the overall framework of dietary habits. Therefore, the use of dietary patterns (e.g. a Mediterranean dietary pattern) and the specific dietary recommendations (e.g. dietary approaches to stop hypertension, Polymeal and the American Healthy Eating Index) are becoming more widespread in promoting lifelong health. A posteriori defined dietary patterns are described frequently in relation to age-related diseases but their generalisability is often a challenge since these are developed specifically for the population under study. Conversely, the dietary guidelines are often developed based on prevention of disease or nutrient deficiency, but often less attention is paid to how well these dietary guidelines promote health outcomes. In the present paper, we provide an overview of the state of the art of dietary patterns and dietary recommendations in relation to life expectancy and the risk of age-related disorders (with emphasis on cardiometabolic diseases and cognitive outcomes). According to both a posteriori and a priori dietary patterns, some key 'ingredients' can be identified that are associated consistently with longevity and better cardiometabolic and cognitive health. These include high intake of fruit, vegetables, fish, (whole) grains and legumes/pulses and potatoes, whereas dietary patterns rich in red meat and sugar-rich foods have been associated with an increased risk of mortality and cardiometabolic outcomes.

> > Overall diet: Dietary pattern: Mortality: Cardiometabolic: Cognition

#### Nutrition and healthy ageing: a matter of reciprocity?

Those over age 65 years constitute the fastest growing segment of populations worldwide. This change in the world's age distribution and consequent demographic shift can be attributed to a large extent to reduced birth rate, greater economic development, more effective medical interventions (hence reductions in mortality), and to improvements in hygiene, nutrition, lifestyle and in general preventive care<sup>(1)</sup>.

Ageing is often defined as a continuous process that includes loss of functional capability and the increase

in risk of morbidity and mortality<sup>(2)</sup>. Although ageing is a risk factor for chronic diseases, ageing is not necessarily defined by the presence of morbidities but is a process that starts early in life and which is modulated by the accumulation of experiences and exposures throughout the life-course<sup>(2)</sup>. As suggested earlier, a 'healthy ageing phenotype' can be defined as 'the condition of being alive, while having highly preserved functioning metabolic, hormonal and neuro-endocrine control systems at the organ, tissue and molecular levels<sup>(2)</sup>. This phenotype represents a state of adequate resilience that minimises the risk of major chronic conditions such as

**Abbreviations:** DASH, dietary approaches to stop hypertension; HDI, healthy diet indicator; HEI, healthy eating index MD, Mediterranean diet; PNNSG, Programme National Nutrition Santé Guideline Score. \*Corresponding author: J. C. Kiefte-de Jong, fax +31 10 7044657, email j.c.kiefte-dejong@erasmusmc.nl



CVD and dementia, but also represents the maintenance of cognitive and physical functioning<sup>(2)</sup>. Although life expectancy has increased in the past decade, following improved care and diagnosis, the years lived with disabilities and diseases are increasing<sup>(1)</sup>, emphasising that the maintenance of a healthy phenotype in later life has become a major public health challenge. Dietary habits are one of the important modifiable factors that can affect the maintenance of a healthy ageing phenotype<sup>(3)</sup>. For example, high intake of both *n*-6 and *n*-3 PUFA have been found to reduce the risk of CHD<sup>(4)</sup>, whereas *trans*-fatty acids intake is considered to increase CVD risk<sup>(4,5)</sup>.

#### One for all and all for one

Although nutrition has long been among the main areas of interest for scientists trying to identify the lifestyle factors that exacerbate or reduce the risk of age-related disorders, studies of the specific nutrients, single foods or food groups have multiple challenges<sup>(6)</sup>. A major difficulty in interpreting the outcomes of such studies in relation to health and disease is the high degree of correlation among dietary components. Moreover, the assumption that single foods or nutrients have isolated effects may not be valid when it comes to maintaining a healthy ageing phenotype since this may cover a combination of different pathways. In addition, foods and nutrients interact, or act in synergy, when influencing numerous metabolic processes. As a result, the focus of nutritional research in the last two decades has shifted to the analyses of whole diets or dietary patterns<sup>(6)</sup>. A dietary pattern approach could better capture the totality of diet, and may be a more appropriate approach for investigating diet-disease associations than focusing on single foods or nutrients<sup>(6–8)</sup>.

A posteriori approaches to dietary pattern analysis are driven by the dietary data per se of the population under study and patterns are derived on the basis of correlations or clustering of various dietary factors (e.g. using principal component analysis or k-means clustering) $^{(9)}$ . Conversely, in a priori approaches, researchers define scores or indices of the overall dietary quality on the basis of foods or diets associated with health or according to the specific dietary guidelines<sup>(9)</sup>. While such dietary guidelines can play important roles in health promotion policies and in individual dietary counselling, they are often based on evidence of decreased risk of chronic diseases and/or prevention of nutrient deficiencies<sup>(9)</sup> and their utility in promoting healthy ageing is uncertain. In several countries, adherence of these dietary guidelines is monitored regularly through national food surveys, but less is known about how well adherence to these dietary guidelines predicts health and development of age-related diseases. In recent years, several indices have been developed to assess adherence to these specific dietary guidelines in relation to health outcomes<sup>(9)</sup>. In this review, we describe the existing evidence of several dietary patterns and dietary guidelines in relation to aspects of healthy ageing and we attempt to identify the key characteristics, which they have in common. Emphasis has been placed on life expectancy, cardiometabolic diseases and cognitive outcomes, but not on cancer because of its heterogeneity in the relationship between diet and different cancer sites.

#### A Posteriori defined regional dietary patterns

A posteriori defined dietary patterns have frequently been used in epidemiological studies. One advantage of this approach is that it is data-driven, and, thus, independent of previous hypotheses and not limited by the current knowledge in nutrition<sup>(9)</sup>. However, due to the different populations that are studied, the specific dietary patterns that are associated with health outcomes can be cultural-specific<sup>(10)</sup> and thus difficult to translate to other settings.

Earlier regional dietary patterns have already been described to explain some of the cross-cultural variation in the prevalence of age-related chronic diseases. For example, the original Eskimo diet and Japanese diet are both characterised by relatively high intakes of fish, which is thought to explain the low rate of CHD in these populations<sup>(11,12)</sup>. Later cross-cultural studies, such as the Seven Countries Study initiated in the late 1950s, suggested that fish intake per se may not be that important (fish consumption was not consistently associated with mortality patterns across countries), whereas low intakes of saturated fats may explain reduced mortality risk<sup>(13)</sup>. The Mediterranean diet (MD), which can be characterised by high intake of vegetables, fruit, grains, fish and olive oil (14), has received most attention in relation to mortality because of intriguing differences in chronic disease prevalence and mortality statistics in Mediterranean populations relative to other parts of the world<sup>(15)</sup>, and its potential health effects have been acknowledged since Renaissance<sup>(14)</sup>.

More recently, the importance of diet has been further recognised in other parts of the world where populations exhibit greater healthy ageing, i.e. living longer without disabilities and being more physically active even when aged over 90 years. Population groups in Sardinia (Italy), Nicoya Peninsula (Costa Rica), Loma Linda (California) and Okinawa (Japan), have reputedly longer life expectancy and lower rates of age-related diseases (including CVD and dementia) compared with other countries (16). These areas have been designated as the 'Blue Zones' and are part of a large research project to discover lifestyle factors that explain healthy longevity<sup>(16)</sup>. Despite their different ethnic and socioeconomic backgrounds, those living in these 'Blue Zones' share some common lifestyle characteristics including diets rich in plant-based foods (notably vegetables, beans, soyabean and lentils) and low in meat<sup>(16)</sup>. These findings are consistent with most of the studies using the a posteriori dietary patterns approach within populations where lower risks of mortality and also of cardiometabolic disease and of poor cognitive outcomes are associated with higher intakes of plant-based foods and relatively low meat consumption<sup>(17–22)</sup>.



#### Mortality and life expectancy

Several independent studies have shown that a dietary pattern rich in plant-based foods, fish and olive oil, but low in whole-fat dairy products was associated with a lower cardiovascular or all-cause mortality in Italy<sup>(23)</sup>, Spain<sup>(24,25)</sup>, UK<sup>(26)</sup>, Japan<sup>(27)</sup> and USA<sup>(28)</sup>. Results from the European Prospective Investigation into Cancer and Nutrition suggested that the relationship between a plant-based diet and mortality in those aged 60+ years may be country-specific since there were relatively strong associations in Greece, Spain, Denmark and the Netherlands, but no associations in the UK and Germany<sup>(29)</sup>. The consequences of dietary patterns rich in dairy products for mortality seem to be inconsistent. Studies from Japan and the Netherlands found that a dietary pattern rich in dairy products was associated with decreased risk of mortality (27,30), whereas a study in USA found that a pattern characterised by intake of particularly high-fat dairy products was associated with higher all-cause mortality in middle-aged and older people<sup>(25)</sup>. In addition, studies have linked dietary patterns characterised by high intakes of meat and sugar-containing foods to increased risk of overall mortality in several countries including Germany<sup>(31)</sup>, USA<sup>(28)</sup>, Canada<sup>(32)</sup> and Spain<sup>(25)</sup>. Nevertheless, most of these studies have been conducted in adult populations below age 75 years and evidence of the dietary patterns associated with healthy ageing among those aged >75 years is scarce. To our knowledge, there is only one such study, which found no link between mortality risk and any of three dietary patterns namely those rich in dairy and sweets, a health-conscious pattern, and a Western dietary pattern, which suggests that the effects of dietary patterns may differ between age-groups(33).

#### Cardiometabolic disorders

Several dietary patterns have been found to be associated with cardiometabolic disorders. For example, a 'prudent diet' characterised by high intake of vegetables, fruit, legumes, whole grains, fish and poultry, has been associated with almost 30% decrease in the risk of CVD among men and women in the USA, Germany, Spain and the Netherlands<sup>(18–21,24,34)</sup>. In contrast, a 'Western' dietary pattern characterised by high intake of red meat, processed meat, refined grains and sweets was associated with increased risk of CHD in the USA and Sweden<sup>(18–20,35)</sup>, but this relationship was not observed in Spain<sup>(24)</sup>. An Italian study found that a dietary pattern featuring high consumption of bread, cereals (pasta), potatoes, vegetables, fish and oil and low consumption of milk, sugar, fruit and alcoholic beverages was associated with a reduced risk of CHD (23), whereas in Chinese adults, a pattern characterised by refined cereals, salted vegetables and potatoes was associated with an increased risk of stroke<sup>(36)</sup>. In addition, several studies confirmed an association between dietary patterns and the risk of type 2 diabetes mellitus. For example, both a 'Western' dietary pattern during both adolescence and adulthood was found to be associated with an increased risk

of type 2 diabetes in US middle-aged and older people<sup>(17,37,38)</sup> as well as in Chinese men and women<sup>(39)</sup>.

#### Cognitive function and dementia

In contrast to the relative wealth of studies of cardiometabolic outcomes and mortality, less attention has been paid to the relationship between a posteriori defined dietary patterns and cognitive outcomes in middle-aged and older people. The Supplémentation en Vitamines et Minéraux Antioxydant study studied the association between a posteriori dietary patterns in relation to cognitive performance among French participants aged 45 years and older. Adherence to a 'prudent' dietary pattern (characterised by high intake of fruit, whole grains, dairy, vegetable fat, nuts and fish) was associated with better global cognitive function and verbal memory whereas no association with cognitive outcomes was found for adherence to a pattern characterised by intake of vegetable fat, meat and poultry<sup>(40)</sup>. Conversely, in a study group of 249 people aged 65-90 years with mild cognitive impairment, there was no association between a 'prudent' diet and cognitive function but participants adhering to a dietary pattern characterised by high intake of potatoes, fried foods, confectionery, red meat and sugar-containing beverages, were more likely to have poor executive functioning<sup>(41)</sup>. Gu *et al.* found that a dietary pattern characterised by high intake of nuts, tomatoes, poultry, vegetables, fruit, and a low intake of high-fat dairy, red meat, organ meat and butter was associated with lower risk of dementia<sup>(42)</sup>. Also, in the Hisayama study of Japanese people, adherence to a dietary pattern characterised by a high intake of soyabeans and soyabean products, vegetables and dairy products was associated with a reduced risk of dementia<sup>(22)</sup>.

## A priori defined dietary patterns: dietary guidelines and dietary scores

A priori defined dietary patterns are generally based on evidence showing that the dietary patterns are important to health. In practical terms, diets are assessed for the presence or absence of a certain amount of foods or nutrients and the resulting score is then operationalised as a dietary index. Generally, three groups of a priori defined dietary patterns can be distinguished: (a) dietary scores based on the national or international dietary guidelines, (b) scores derived from assessment of concordance with nutrients or foods associated with the specific health outcomes and (c) scores based on characteristics of regional diets, e.g. an MD pattern (Table 1)<sup>(9)</sup>.

#### Mortality and life expectancy

The American Healthy Eating Index (HEI) is a measure of diet quality based on the Dietary Guidelines for Americans. The original HEI was developed in 1995<sup>(43)</sup> and was revised in 2005<sup>(44)</sup> to include whole grains, beans and oils (Table 1). Subsequently, in 2010 the HEI-2005 was updated according to the revised Dietary





**Table 1.** Examples of a priori developed dietary patterns

Authors (year)	Dietary pattern/dietary index	Food components	Associated outcomes*
Guenther <i>et al.</i> (2013) <sup>(93)</sup>	American HEI-2010	Dietary patterns according to the dietary guidelines  Adequacy: total and whole fruit, vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant protein, and fatty acids (PUFA, MUFA, SFA)	
Guenther et al. (2008) <sup>(44)</sup>	American HEI-2005	Moderation: Refined grains, sodium, 'empty calories'  Adequacy: total and whole fruit, vegetables, dark green and orange vegetables and legumes, total grains, whole grains, milk, meat and beans and oils  Moderation: saturated fat, sodium, calories from solid fats, alcoholic	All-cause and cause-specific mortality, cardiometabolic disease, cognitive outcomes
Kennedy <i>et al.</i> (1995) <sup>(43)</sup>	American HEI-1995	beverages and added sugars  Adequacy: grains, vegetables, fruit, milk and meat  Moderation: total fat, saturated fat, cholesterol and sodium	All-cause and cause-specific mortality, cardiometabolic disease, cognitive outcomes
McCullough et al. (2002) <sup>(94)</sup>	Alternate HEI (adapted from HEI)	Adequacy: fruit, vegetables, nuts, seeds, cereals, fish/poultry to red meat ratio, PUFA/SFA ratio and multivitamin supplementation Moderation: alcohol	All-cause and cause-specific mortality, cardiometabolic disease
van der Lee <i>et al</i> . (2012) <sup>(95)</sup>	Dutch Healthy Diet Index	Adequacy: vegetables, fruit and fruit juice, fibre and fish Moderation: saturated fat, trans fatty acids, acidic drinks, sodium and alcohol Other: physical activity	
Kant et al. (2000) <sup>(50)</sup>	Recommended Food Score	Adequacy: fruits, vegetables, whole grains, lean meats or meat alternates and low-fat dairy	All-cause and cause-specific mortality, cardiometabolic disease, cognitive outcomes
Knudsen et al. (2012) <sup>(96)</sup>	Danish Diet quality Index	Adequacy: potatoes, rice or pasta and whole meal bread, fruits and vegetables, fish and fish products  Moderation: total fat and saturated fat and sugar	Myocardial infarction
Estaquio <i>et al</i> . (2009) <sup>(97)</sup>	Programme National Nutrition Santé Guideline Score	Adequacy: fruits and vegetables, bread, cereals, potatoes, legumes, whole-grain food, milk and dairy products, meat and poultry, seafood, and eggs, vegetable fats and water  Moderation: added fats, sweetened foods and beverages, alcohol and salt  Other: physical activity	Cognitive outcomes
McNaughton et al. (2008) <sup>(52)</sup>	Australian Dietary Guideline Index	Adequacy: fruit, vegetables, cereals, whole grain cereals, lean meat/fish/poultry, dairy, low-fat dairy and water  Moderation: saturated fat, salt, alcohol, added sugar, extra foods	All-cause mortality, cardiometabolic outcomes
Huijbregts <i>et al</i> . (1997) <sup>(58)</sup>	HDI (WHO)	Adequacy: polyunsaturated fat, protein, complex carbohydrates, dietary fibre, fruit/vegetables, pulses, nuts and seeds  Moderation: saturated fat, mono- and disaccharide, cholesterol	All-cause mortality, cognitive outcomes



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Maynard <i>et al.</i> (2005) <sup>(98)</sup>	Modified healthy diet score (Modified for the British population from the HDI)	Adequacy: polyunsaturated fat, protein, total carbohydrates, dietary fibre, fruits, vegetables, pulses, nuts, fish and calcium <i>Moderation</i> : non-milk extrinsic sugars, saturated fat, mono- and disaccharide, cholesterol, red meat and meat products	
Trichopoulou <i>et al.</i> (1995) <sup>(60)</sup> , Trichopoulou <i>et al.</i> (2003) <sup>(61)</sup>	MD (Greek)	Dietary patterns on the basis of a MD  Adequacy: mono-unsaturated: saturated fat ratio, legumes, cereals and potatoes, fruits, vegetables, fish (later included)  Moderation: alcohol	All-cause and cause-specific mortality, cardiometabolic outcomes
Agnoli et al. (2011) <sup>(47)</sup>	Italian Mediterranean Index	Low: meat and meat products, milk and dairy products  Adequacy: pasta, vegetables, potatoes, fruit, legumes and fish  Moderation: alcohol  Low: butter, soft drinks	Cardiometabolic outcomes
Fung <i>et al</i> . (2005) <sup>(99)</sup>	Alternate MD (adapted from Trichopoulou et al.)	Adequacy: vegetables (excluding potatoes), fruits, nuts, whole grains, legumes, fish, ratio of monounsaturated to saturated fat <i>Moderation</i> : alcohol	All-cause mortality, cardiometabolic outcomes
Willet et al. (1995) <sup>(100)</sup>	MD Pyramid	Low: red and processed meat  Adequacy: grains, potatoes, fruit, vegetables, beans, nuts, legumes and olive oil  Moderation: cheese, yoghurt, fish, poultry, eggs  Low: sweets, red meat	All-cause mortality, cardiometabolic outcomes
Alberti <i>et al</i> . (2009) <sup>(101)</sup> , Alberti-Fidanza <i>et al</i> . (2004) <sup>(102)</sup>	Mediterranean Adequacy Index (Italian)	Adequacy: cereals, legumes, potatoes, vegetables, fruit, fish, wine and virgin olive oil  Moderation: milk, cheese, meat, eggs, animal fats and margarines, sweet beverages, cakes, pies and cookies	Cardiometabolic outcomes
Lee et al. (2007) <sup>(103)</sup>	Die Heart Disease Prevention Eating Index	stary patterns developed for specific health outcomes  Adequacy: fruits, vegetables, whole grains  Moderation: Saturated fat, trans-fat, salt and alcohol  Other: matching energy to overall energy needs, substitution of grains and unsaturated fatty acids from fish, vegetables, legumes, and nuts, maintaining a dietary pattern that emphasises fruits, vegetables and low-fat dairy products, and is reduced in fat	
Appel <i>et al.</i> (1997) <sup>(104)</sup> , Fung <i>et al.</i> (2008) <sup>(105)</sup>	Dietary Approaches to Stop Hypertension	Adequacy: fruits, vegetables, nuts, low-fat dairy products and whole grains	All-cause and cause-specific mortality, cardiometabolic outcomes
Franco <i>et al.</i> (2004) <sup>(75)</sup>	Polymeal	Moderation: sodium, sweetened beverages, red and processed meats Adequacy: wine, fish, dark chocolate, fruits, vegetables, garlic and almonds	CVD

HEI, healthy eating index; MD, Mediterranean diet; HDI, healthy diet indicator. \* With emphasis on mortality, cardiometabolic disease and cognitive outcomes.



Guidelines for Americans, which resulted in the inclusion of seafood in the current index. In several studies, adherence to the HEI has been associated with lower chronic disease risk<sup>(45–47)</sup>, and whereas adherence to the HEI-1995 was associated with a 30% reduction in mortality risk in males, this relationship was not apparent in females<sup>(48)</sup>. For those aged 65+ years, a higher HEI-1995 score was associated with lower overall and cardiovascular mortality irrespective of gender<sup>(49)</sup>.

The Recommended Food Score developed by Kant et al. (50) is a composite measure based on the sum of the number of foods recommended by the current dietary guidelines (fruit, vegetables, whole grains, low-fat dairy and lean meats and poultry) that were reported to be consumed at least once weekly and higher scores were associated with lower risk of all-cause mortality (28 and 18% lower risk in men and women, respectively) (50,51).

Adherence to a modified version of the HEI-1995 for an Australian population (Australian dietary guidelines index)<sup>(52)</sup> was associated with a 21% reduction in all-cause mortality<sup>(53)</sup>. The HEI-1995 was further adapted by McCullough *et al.*<sup>(54)</sup> by adding fish/poultry to red meat ratio as a component and excluding milk. Adherence to this alternative HEI was associated with a reduced risk of mortality and of cause-specific mortality (CVD, cancer and inflammatory-related diseases) in the Iowa Women's Health Study<sup>(55)</sup> and in the Whitehall II cohort study<sup>(56)</sup>.

The healthy diet indicator (HDI) was developed according to the dietary recommendations of the WHO and includes components of saturated fat, mono- and disaccharides as well as fruit and vegetables, and pulses, nuts and seeds (Table 1)<sup>(57)</sup>. The main focus of the HDI has been the prevention of chronic diseases (i.e. obesity, diabetes mellitus and CVD), but higher HDI scores have been associated with decreased mortality risk in Finland, the Netherlands and Italy<sup>(58)</sup> but not in older Swedish men<sup>(59)</sup>.

Several indices the based on MDbeen developed (Table 1). The original MD score developed by Trichopoulou *et al.* (60) was further adapted by including fish as component of the score since this food was consumed widely in the Mediterranean countries<sup>(61)</sup>. Even though questions have been raised about the generalisability of MD scores to non-Mediterranean countries, adherence to the original MD score has been associated with survival not only in Greece<sup>(61)</sup> but also in Northern Europe<sup>(62)</sup>, Australia<sup>(63)</sup>, Spain<sup>(64)</sup> and the USA<sup>(65,66)</sup>. When adapted for the European Prospective Investigation into Cancer and Nutrition study, which studied the mortality across several European countries (including Denmark, France, Germany, Greece, Italy, the Netherlands, Spain, Sweden and UK), higher scores in this MD were associated with an overall 8% reduction in mortality risk per 2 point change in score (10 point scale). There was no evidence of statistically significant heterogeneity among countries although the association was less evident in the Netherlands and Germany<sup>(67)</sup>.

#### Cardiometabolic disease

The dietary approaches to stop hypertension (DASH) diet (rich in fruits, vegetables, low-fat dairy products, grains, poultry, fish and nuts, and low in saturated fat, red meat, sweets and sugar-containing beverages) was originally designed to decrease hypertension<sup>(68)</sup>. Later it was shown that adherence to the DASH dietary pattern may also be successful in decreasing the risk of CVD, CHD, stroke and heart failure in several studies among middle-aged and older people<sup>(69)</sup>.

Earlier studies using the HEI-1995 found that a high score was associated with moderately reduced risk of CVD in men but not in women<sup>(70,71)</sup>. Also, adherence to HEI-2005, DASH and the Greek and Italian Mediterranean Index was linked with a lower risk of stroke in an Italian population aged 35–74 years<sup>(47)</sup>. Even in secondary prevention cohorts, there were protective relations between adherence to the alternative HEI and secondary CVD events<sup>(72)</sup>. Adherence to the HEI-2005, the alternative HEI, the Recommended Food score, the alternative MD score, and the DASH diet has been associated with lower risk of type 2 diabetes mellitus in both men and women<sup>(73)</sup>.

The 'Polymeal', a collection of food ingredients, was developed as a natural alternative to the 'Polypill', a multi-pharmaceutical approach intended to reduce CVD risk<sup>(74)</sup>. Components of the 'Polymeal' include wine, fish, dark chocolate, fruit and vegetables, almonds and garlic<sup>(75)</sup>. Using life tables based on information from the Framingham Heart Study, it was estimated that the combined effects of these dietary components might increase life expectancy free from CVD by 9 years for men and 8 years for women among populations over age 50 years<sup>(75)</sup>. However, this theoretical concept has yet to be tested in population and intervention studies.

#### Cognitive function and dementia

Adherence to some *a priori* defined dietary patterns has been linked with prevention of some adverse cognitive outcomes. The MD score, the French National Nutrition and Health Programme (Programme National Nutrition Santé) Guideline Score (PNNSG), the Recommended Food Score and the DASH diet have all been associated with lower risks of cognitive impairment, and dementia or Alzheimer's disease<sup>(76)</sup>. In addition, adherence to the HEI, HDI and to the MD have been associated with better cognitive function in middle-aged and older adults<sup>(45,77–79)</sup>.

#### From observation to intervention?

Although, several indices of MD patterns as well as adherence to the DASH diet and other healthy diet scores are associated with a lower risk of stroke, CHD and CVD in numerous prospective cohort studies in different populations<sup>(69,80–84)</sup>, residual confounding by other lifestyle and socioeconomic factors remains a major challenge in determining causality. While a trial of the



DASH diet has demonstrated that adherence to DASH can reduce numerous cardiovascular risk factors<sup>(85)</sup> the causal effects on mortality and on other age-related end points are unknown.

The benefit of adherence to an MD pattern on primary prevention of cardiovascular endpoints was confirmed recently in a randomised controlled trial (PREDIMED) conducted in Spain. In this study, an MD supplemented with either extra-virgin olive oil or nuts reduced the risk of major cardiovascular events by almost 30%<sup>(86)</sup>. Also, results from the PREDIMED trial showed that this intervention improved cognition (0.6 points increase in score on the Mini-Mental State Examination and Clock Drawing Tests) in participants aged 75+ years with high vascular risk<sup>(87)</sup>. Although whether the PREDIMED trial is a test of an MD per se or of the effects of supplemental extra-virgin olive oil or nuts can be debated, the study provides strong evidence that greater adherence to this dietary pattern can have substantial beneficial effects on health in the older people and reduces the risk of common age-related diseases (86,87). However, before such findings can be translated to public health-level interventions regionally or nationally, more evidence is needed about the most effective intervention modalities for achieving the necessary changes in eating behaviour and to sustain those behavioural changes in the long term<sup>(88)</sup>. In addition, there is a need for an objective panel of outcome measures, which can be used to ascertain whether the interventions have been successful in enhancing healthy ageing. Recently, a preliminary panel of such measures (based on the healthy ageing phenotype concept<sup>(2)</sup>) which is designed to assess the efficacy of lifestyle-based interventions in promoting healthy ageing in community settings has been proposed<sup>(89)</sup>.

# Nutrition and healthy ageing: agreement on the key ingredients

Dietary patterns define relevant and modifiable risk factors for deviations from a healthy ageing phenotype. Using both *a posteriori* and *a priori* dietary patterns, some key 'ingredients' (food groups) can be identified that are associated consistently with longevity and with better cardiometabolic and cognitive health. These include: high intakes of fruits, vegetables, fish, (whole) grains and legumes/pulses and potatoes (Fig. 1).

Fruit, vegetables and (whole) grains are components included in the HEI-2005, HEI-1995, Recommended Food score and the WHO HDI, but are also found in indices of the MD (Table 1). All of these indices and also *a posteriori* defined dietary patterns that include these food groups have been associated with lower risk of mortality, cardiometabolic disease and adverse cognitive outcomes in middle-aged and older people.

Although fish has been included recently in the HEI-2010, we are not aware that this new index has yet been studied in relation to healthy ageing outcomes. However, fish is a component in most Mediterranean

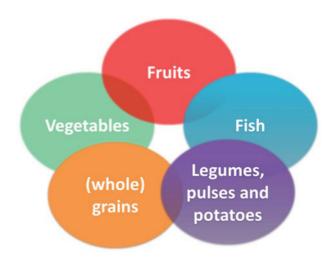


Fig. 1. (colour online) Nutrition and healthy ageing: the key ingredients.

diets and has been included in other indices such the DASH diet, the PNNSG score and the Polymeal as well as in *a posteriori* defined dietary patterns that have been linked with healthy ageing outcomes.

Finally, legumes/pulses and potatoes are not included in all *a priori* defined dietary patterns but those, which included one or more of these components (e.g. HEI-2005, PNNSG, HDI and MD scores) have found that they are associated with lower mortality rates and decreased risk of cardiometabolic diseases and of poor cognitive outcomes.

In contrast, dietary patterns rich in red meat and sugar-rich foods have been associated with an increased risk of mortality, type 2 diabetes mellitus and CHD in studies that defined these patterns a posteriori<sup>(17–20,25,28,31,32,35,37–39)</sup>. There is a general agreement on the potential deleterious effect of higher intakes of these two food items and most of the dietary guidelines and scores designate these foods as unfavourable components (Table 1). However, not all a priori defined dietary patterns include these components (e.g. they are not included in the Recommended Food Score, the Danish Diet quality Index, the PNNSG score and WHO HDI). It can be argued that these guidelines might be improved (made more sensitive) by adding specific recommendations on the intake of red meat and of sugar-rich foods and that such modified guidelines may be better at identifying those with eating behaviours more likely to lead to a healthy ageing phenotype.

Other food groups/items are the subject of controversy. For example, the role of dairy products in healthy ageing remains unclear. Although, some *a priori* dietary patterns (e.g. HEI-1995, -2005, -2010, Recommended Food Score, PNNSG and DASH) have included dairy foods as a beneficial component, none of the MD scores includes dairy products as a beneficial component. In addition, *a posteriori* derived dietary patterns do not show consistent relationships between patterns rich in dairy and beneficial health outcomes<sup>(25,27,30,90)</sup>.



It could be argued that the relationship between dairy-rich dietary patterns and health outcomes are culturally specific and are influenced by the habitual dairy consumption of the population under study and the type of dairy products consumed. For example, the Netherlands and USA are countries with the highest milk consumption worldwide<sup>(91)</sup>, but increased mortality risk was associated with dietary patterns characterised particularly by fat-rich dairy products<sup>(25)</sup>. Future studies in this field need to address the effects of dairyrich dietary patterns on health outcomes in specific subpopulations.

The totality of available evidence suggests that dietary patterns rich in fruit, vegetables, fish, whole grains and starchy low-fat staple foods are likely to play a key role in promoting aspects of healthy ageing including life expectancy and lower risk of cardiometabolic diseases and adverse cognitive outcomes. However, the current evidence is derived mainly from observational studies and more evidence from intervention studies on the effect of whole diets and on how to achieve the necessary sustained dietary behaviour changes is needed to support the development of soundly based public health interventions to promote healthy ageing at the population level. Furthermore, although regional diets such as the MD may be beneficial in other geographical locations, interventions promoting their use may be influenced by local availability, population-specific effects and by culture-specific acceptability of particular foods and food groups. A more tailored approach is needed.

#### Personalised nutrition: the next frontier?

Most of the current dietary guidelines adopt a 'one size fits all' approach and this needs to change since not all individuals within populations will share the same dietary risks and there is considerable heterogeneity in food preferences. Indeed, a more personalised approach to dietary interventions may be both more acceptable and more efficacious.

Future nutritional research should recognise this challenge and aim to disentangle the complex interactions among genotype, diet, lifestyle and environmental factors to understand the basis for varying vulnerabilities and the different responses to dietary patterns<sup>(92)</sup>. Addressing these interactions may provide the basis for a more personalised approach to nutritional recommendations and to nutritional counselling to improve eating patterns and to promote healthy ageing.

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#### **Authorship**

J. C. K. d. J. and O. H. F. conducted the literature search. J. C. K. d. J. and O. H. F. drafted the manuscript. J. C. M. provided critical comments during writing of the manuscript.

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