Nutrition and dementia

A review of available research

Alzheimer's Disease International

The global voice on dementia

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Nutrition and dementia

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Design by Julian Howell

The Global Observatory for Ageing and Dementia Care

The Global Observatory for Ageing and Dementia Care, hosted at the Health Service and Population Research Department, King's College London, was founded in 2013. Supported by Alzheimer's Disease International, and King's College London, the Observatory has a tripartite mission:

1 To build upon ADI's 10/66 Dementia Research Group programme of population-based and intervention research in low and middle income countries, maximising the impact that research findings from our data can have upon policy and practice.

2 To develop, evaluate, and promote primary care and community interventions for people with dementia.

3 To synthesise global evidence for policymakers and public, in particular, continuing and developing our role in the preparation of high impact evidence-based reports for Alzheimer's Disease International (World Alzheimer Reports 2009, 2010, 2011 and 2013), the World Health Organization (Dementia: a public health priority, 2012) and other relevant intergovernmental organisations.

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Introduction

Eating and having a good meal is part of our everyday life and important to everybody, not least to people living with dementia. But it is still an almost totally neglected area of focus in relation to these diseases.

Compass Group and Alzheimer's Disease International (ADI) have come together in commissioning this report to investigate how the right nutrition can help to make life better for people who live with dementia. This is clearly reflected in ADI's mission and vision: 'an improved quality of life for people with dementia and their carers'. Compass Group, as world-leading food and support services organisation, shares this vision in their work to support people who are affected by dementia.

This report was prepared by Professor Martin Prince, Professor Emiliano Albanese, Dr Maëlenn Guerchet and Dr Matthew Prina for the Global Observatory for Ageing and Dementia Care, King's College London. They have reviewed a number of areas in existing research regarding the relevance of nutritional factors to primary and secondary prevention of dementia, undernutrition in dementia and interventions to improve the nutrition of people living with dementia.

The report shows the importance of each of these factors in the everyday nutrition and care of people with dementia. In addition, it identifies how we can start building methods and guidelines that will complement clinical treatment of the diseases. It highlights:

- the link between nutrition and quality of life
- the previous neglect of this important issue, as evidenced by the high prevalence of undernutrition and inadequate food intake among people with dementia
- the untapped potential to improve outcomes for people with dementia, given the evidence for effective interventions
- the need for more research in this area.

A healthy diet and nutrition is fundamental to wellbeing at any stage of life and to helping to combat other life-threatening diseases. We believe it can play as important a role in relation to dementia.

ADI believes that the key to winning the fight against dementia lies in a unique combination of global solutions and local knowledge. As such, it works globally to focus attention on the epidemic of dementia, while also empowering local Alzheimer associations to promote and offer support for people with dementia and their carers.

Compass Group is a company that operates in more than 50,000 client locations in around 50 countries and serves over 4 billion meals per year. By working closely with our care home clients, we can improve the quality of their food and support services allowing them to focus on caring for their residents. People living with dementia are a small but growing constituency of Compass' business.

ADI and Compass Group believe that a focus on diet, nutrition and wellbeing is a positive approach to supporting people with dementia and their carers in dealing with this terrible disease. It is not only a good collaboration but the right thing to do.

Marc Wortmann
Executive Director
Alzheimer's Disease International

Mike Iddon
Group Healthcare Director
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Key messages

1 Undernutrition is common among older people generally, particularly in low and middle income countries. For this age group it is, arguably, a larger public health problem than obesity. The consequences include increased frailty, skin fragility, falls, hospitalisation and mortality.

2 Undernutrition is particularly common among people with dementia in all world regions. It tends to be progressive, with weight loss often preceding the onset of dementia and then increasing in pace across the disease course.

3 Obesity in mid-life may be a risk factor for developing dementia in late-life. If so, this is an important modifiable risk factor, and a matter of concern given rising levels of obesity worldwide. However, careful examination of the existing evidence casts some doubt upon the validity and robustness of this finding, which requires more research.

4 There are many dietary factors that might plausibly increase or decrease risk for the onset of dementia. However, we could find no clear or consistent evidence to support a causal protective role for vitamins B_6, B_{12}, C or E, folate or omega-3 PUFA (polyunsaturated fatty acids). There is quite consistent evidence from epidemiological cohort studies that adherence to a Mediterranean diet (with a high proportionate intake of cereals, fruits, fish and vegetables) may lower the risk of cognitive decline and dementia. However, to date, only one trial has been carried out, with encouraging findings.

5 The mechanisms underlying weight loss and undernutrition in dementia are complex, multifactorial, and only partly understood. Reduced appetite, increased activity, and, in the more advanced stages of the illness, the disruption of eating and feeding behaviours by cognitive and behavioural problems all play a part. For some forms of dementia, it may be that central regulation of appetite and metabolism is disturbed as an inherent feature of the disease.

6 A key finding in this report is that while weight loss is a common problem for people with dementia, undernutrition can and should be avoided. Proof of concept comes from a new review of the use of oral nutritional supplements, indicating that it is possible to stabilise or even increase the weight of people with dementia over relatively long periods. The nutritional benefits of education and training for caregivers was less apparent, although such interventions were popular and there are likely to be other benefits.

7 In care homes, attention to staff training and mealtime environment can lead to significant enhancement in calorie intake among residents. Eating is a social activity, and more thought should be given to how this can be optimised, normalised and made a core aspect of person-centred care. Sensitive and inclusive design of dining rooms, kitchens, furniture and tableware can all make important contributions.

8 There is no current evidence that nutritional supplementation whether with micronutrients, 'medical foods' or macronutrients can modify the course of dementia (cognitive and functional decline). Vitamin E shows some promise, but at doses that may lead to harmful side effects.

9 Much more attention needs to be focused upon the problem of undernutrition in dementia. This has been grossly neglected in research and practice. Studies reviewed in this report indicate that 20-45% of those with dementia in the community experience clinically significant weight loss over one year, and that up to half of people with dementia in care homes have an inadequate food intake.

Recommendations

1 More research needs to be conducted into
   - The possibility that nutritional supplementation of dietary components with high mechanistic plausibility may be effective in reducing the incidence of dementia if targeted upon those with evidence of deficiency (for example vitamin B_{12} and folate).
   - The effective components of a Mediterranean diet with respect to the prevention of dementia and progression of Mild Cognitive Impairment, and the feasibility of sustained implementation of such dietary modification.
   - The possibility that some forms of micronutrient supplementation may yet be effective in altering the course of dementia, if targeted upon those who are deficient.
   - The minimum effective dose of vitamin E as a treatment for clinical progression in dementia, and the balance of associated risks and benefits.
   - The relative efficacy of food fortification and oral nutritional supplementation in maintaining weight among people with dementia at risk for undernutrition.
   - The feasibility and effectiveness of long-term fortification or oral nutritional supplementation strategies, including the wider health and quality of life benefits.
2 It is important that clear, consistent and independent evidence-based advice is provided to support decision-making on nutritional supplements by those at risk of, or already living with, dementia.
3 Nutritional standards of care for people with dementia should be introduced throughout the health and social care sectors, and monitored for compliance.
   - All people with dementia should have their weight monitored and nutritional status assessed regularly.
   - All people with dementia, and their family carers, should receive dietary advice from a dietician as a part of post-diagnostic care, updated, as appropriate, as their condition evolves, particularly with the onset of weight loss, aversive feeding behaviours, and need for feeding assistance.
   - Undernutrition, once established, is a serious health concern requiring medical attention and input from a dietician and occupational therapy as appropriate. Those at risk of undernutrition require a detailed assessment of diet, feeding behaviours and need for feeding assistance. This should inform an immediate and intensive nutritional intervention to restore and maintain normal nutrition.
   - Nutritional advice and natural food fortification should be tried first, but the use of oral nutritional supplements should not be delayed for those with undernutrition and those at risk who fail to respond.
   - All care homes and hospitals that care for people with dementia need to develop and implement plans to optimise and monitor their nutritional status. This should include staff training; attention to the nutritional content and variety of the food provided, and its suitability for people with different eating and feeding difficulties; the way in which food is prepared and delivered; and dining room design and mealtime environment.
   - Staff training in care homes and hospitals should be part of a comprehensive programme of workforce development linking managers, nursing staff, care assistants and caterers all of whom need to understand the challenges involved in maintaining adequate nutrition for people with dementia, and the part that they have to play. This should address gaps in knowledge (the nutritional content of food, the impact of dementia on diet and nutrition) and skills (in monitoring nutritional status, providing feeding assistance, managing aversive feeding behaviours).

Executive summary

1 Background

Dementia: numbers and burden

- The world's population is ageing, as improvements in public health and health care contribute to people living longer and healthier lives. However, this has resulted in a worldwide increase in the number of people living with chronic diseases, including dementia.
- The global epidemic of dementia can no longer be neglected and should be considered a public health priority in all countries.
- Dementia is a syndrome affecting memory, thinking, behaviour and the ability to perform everyday activities, usually chronic or progressive by nature, which is caused by a variety of brain illnesses, of which Alzheimer's disease, vascular dementia, dementia with Lewy bodies, and frontotemporal dementia are the most common. Dementia is not a normal part of ageing.
- It is estimated that 44 million people worldwide live with dementia in 2013, with numbers doubling every 20 years, to reach 135 million by 2050. Most of this increase will occur in low and middle income countries (LMIC); currently 62% of all people with dementia live in such regions, this proportion rising to 66% in 2030 and 71% in 2050.
- It is estimated that there are 7.7 million new cases of dementia each year worldwide, with one new case every four seconds.
- Dementia and cognitive impairment are by far the most important contributors, among chronic diseases, to disability, dependence, and transition into residential and nursing home care. Behavioural and psychological symptoms (BPSD) typically occur later in the course of the disease, have an impact on the quality of life of the old person and increase caregiver strain.
- The total estimated worldwide cost of dementia in 2010 was US$ 604 billion, equivalent to around 1% of global gross domestic product, of which about 70% was incurred in western Europe and North America. Costs of informal care and the direct costs of social care contribute similar proportions of total costs worldwide; while the direct costs of medical care are much lower. However, in low and middle income countries informal care costs predominate, accounting for up to two-thirds of all costs.

Malnutrition, undernutrition, and obesity: worldwide patterns of the 'double burden'

- Diet and nutrition play an important role in maintaining health and wellbeing. Diet can be defined as what we habitually eat and drink and is best conceived as a lifestyle. Nutrition encompasses the processes of ingesting and digesting foods, and absorbing and metabolising their nutrients. Adequate nutrition is essential for healthy living.
- Malnutrition comprises both overnutrition (excess food/calorie intake) and undernutrition, which is the depletion of body energy stores and loss of body mass (mainly lean mass). Malnutrition results mainly from eating an inadequate diet in which either the quantity and/or quality of nutrients does not meet the needs of our body.
- Undernutrition (insufficient calories, protein or other nutrients needed for tissue maintenance and repair) is the most common nutritional problem, affecting up to 10% of older people living at home, 30% of those living in care homes, and 70% of hospitalised older people. The prevalence of undernutrition among older people in LMIC is likely to be even higher, particularly in rural and less developed settings, and increases with age.
- Consequences of undernutrition include frailty, reduced mobility, skin fragility, an increased risk of falls and fractures, exacerbation of health conditions, and increased mortality. Risk factors include the older person's social, economic and environmental situation; problems with mouth, teeth and swallowing; mental, neurological and other chronic physical diseases; and side effects of long-term treatment with certain drugs.
- With progressive globalisation of western dietary habits and lifestyles (e.g., underactivity and increased consumption of saturated fat, animal proteins and refined carbohydrates) obesity is now rising dramatically in low and middle income countries, especially in urban settings. Obesity also has important adverse consequences for health – it is a major risk factor for diabetes, cardiovascular diseases and cancer, and is the fifth leading modifiable risk determinant for global deaths.

2 Nutrition and dementia across the life course

Key life course concepts: sensitive periods and accumulation

- Evidence suggests that the determinants of dementia risk impact across the life course in a manner comparable to several other chronic diseases of late life, sometimes with relatively long latent periods before the onset of clinical dementia syndromes.
- A life course approach to late-onset dementia may improve our understanding of the disease, and provide evidence on potential additive effects of exposures over time ('accumulation'), and on 'sensitive periods' of life during which exposure to a risk factor may be more detrimental for dementia risk.
- It is therefore possible that prevention should begin early in life and be concerned not only with the onset of dementia and its progression, but also with trajectories of cognitive ageing from mid-life, when impairment likely begins.

Nutrition for optimal brain/cognitive development

- Micronutrients and fat stores accumulated during intra-uterine life are important for brain and nervous system maturation and development, which may in turn influence risk of cognitive impairment and dementia in older age.
- Brain reserve (enhanced structural or functional brain capacity) may buffer the effects of dementia-related neuropathology and explain the observed variability in the expression and severity of the dementia syndrome in people with comparable levels of neuropathology. The extent of brain reserve is likely to be influenced by a variety of genetic and environmental factors, including early life nutrition.
- Low birth weight and stunting in early life, indicating inadequate nutrition in utero or early life, are independently associated with lower cognitive abilities in adulthood. These associations may then track across the life course; among older people studied in diverse geographic regions and cultures, longer leg length and larger skull circumference (indicating favourable early development), were associated with lower dementia prevalence.

Role of high adiposity (overweight/obesity)

- While larger birth weight and high (optimal) body size in childhood may be associated with better cognition, overweight and obesity are generally harmful for health, and may contribute to the neurodegenerative and cerebrovascular changes underlying late-life dementia. However, while the relationship between obesity and dementia-related brain damage is biologically plausible, its complexity makes mechanistic evidence hard to reconcile.
- Obesity might, hypothetically, impact upon cognitive development, cognitive ageing, and dementia risk – all of these pathways have been assessed in cohort studies reviewed in detail in Chapter 2.
- Any associations between early life adiposity (childhood overweight and obesity) and cognitive function or impairment in mid-life seem to be accounted for by a strong confounding effect exerted by childhood intelligence and educational achievement.
- Cognitive decline that leads to dementia may begin in mid-life. Furthermore, higher levels of cognitive function in mid-life have been suggested to potentially act as a reserve to ward off the consequences of accumulated brain damage and reduce functional impairment.
- Studies on the relationship between adiposity measured in young adulthood and cognitive function or cognitive decline in mid-life show heterogeneous results but seem to indicate that any potential detrimental effect of adiposity on mid-life cognitive function may be largely confounded. Increasing adiposity (BMI gain) in younger adults is also not related to worse cognitive ageing before older age.
- The existence of a causal association between mid-life adiposity and dementia is quite widely accepted. A recent systematic review of evidence from epidemiological cohort studies estimated a relative risk for Alzheimer's disease (AD) associated with mid-life obesity of 1.60 (95% CI 1.34–1.92).
- There are several plausible underlying mechanisms, including; insulin resistance and hyperinsulineamia caused by high adiposity; metabolic and inflammatory cytokines released by adipose tissue; cardiovascular risk factors e.g. hypertension, linked to obesity; and cerebrovascular disease for which obesity is a prominent risk factor. All of these products or processes have direct effects on brain regions linked to dementia, and may be implicated in AD neuropathologies.

- Metabolic, cognitive and behavioural changes associated with dementia and its long mid- to late-life clinical prodrome can have an impact on risk factor profiles, complicating elucidation of the direction of any causal relationships.
- The evidence, from three systematic reviews, suggests that the picture is complex. Findings for an association with mid-life body mass index (BMI) vary greatly across studies, and pooled estimates are strongly influenced by the positive findings from two large studies that relied largely upon ascertainment of dementia diagnosis by health services. Bias may have occurred since those who are obese are likely to be heavier users of health care, and are hence more likely to have their dementia detected. In one of the two studies, no attempt was made to control for education, a likely confounder associated both with obesity and dementia risk.
- Two more recent cohort studies, not included in these reviews, find no independent association of mid-life obesity with late-life dementia, any observed associations being confounded by sociodemographic factors.
- Given these methodological limitations, overall, the evidence on the association between high adiposity in mid-life and higher dementia risk is weak and remains highly conflicting.
- The association between central obesity, measured by waist circumference, and dementia risk is less studied, but much more consistent. This finding supports the hypothesis of an underlying metabolic mechanism, because central adiposity, measured by waist circumference, is a better indicator than global adiposity, measured by BMI, of obesity associated-metabolic changes (insulin resistance and hyperinsulinaemia).
- Our understanding of the complex relationship between adiposity and dementia could be improved by studies that investigate associations with dementia-related brain damage. However, evidence from longitudinal, prospective, population-based studies on this topic is scanty, and no studies have explored the association of mid-life BMI with brain atrophy and vascular lesions, the structural changes underlying dementia.
- Further research is warranted, because an improved understanding of the critical pathways that may lead from high adiposity to greater dementia risk could have a significant impact on targeting of primary prevention strategies.
- The association between adiposity and dementia may be explained by underlying genetic and environmental factors that may influence lifelong adiposity trajectories, vascular risk profile, and late-life cognitive decline.
- Childhood intelligence may play an important underlying role. Intelligence strongly influences the maintenance of a healthy lifestyle throughout life, and may also confer advantages in brain structure (brain reserve) and function (cognitive reserve), that can buffer the impact of brain damage in late-life and delay the symptomatic onset of dementia.

Conclusion

- The relationship between fats and the brain is extremely complex. Fats may be harmful in mid-life if in excess, but could also be an important energy reserve that could improve resilience to the effects of dementia-related neuropathology and comorbidities in later life. The same factors that influence the accumulation of adiposity across the life course be implicated in the development and decline of cognitive function.
- More research is needed to elucidate the complex relationship between adiposity and cognitive function, cognitive impairment and dementia. The use of a life course approach in future studies is imperative.

3 Nutritional factors and dementia prevention

- Dementia prevention is an urgent priority, both to reduce incidence and slow the progression of the condition. We need to identify important modifiable risk factors, particularly in the absence of any treatments that modify the course of dementia after its onset.
- Epidemiologic evidence can inform dietary recommendations to reduce dementia risk, when associations are consistent and biologically plausible. However, the design and interpretation of such studies is complicated by the impact of dementia on dietary habits (reverse causality) and the link between general good health and healthier diets (confounding). Long-term longitudinal (cohort) studies are required to clarify possible causal links.
- Experimental evidence from randomised controlled trials provides the best basis for guiding treatment and prevention strategies. However, given the long latent period between the beginning of complex pathophysiological mechanisms and the clinical, detectable onset of symptoms, definitive trials may be difficult

to conduct particularly when treatment or prevention may need to be implemented in mid-life to delay or prevent dementia onset in late-life.

B vitamins

- B vitamins, which play key roles in cell metabolism, cannot be synthesised in sufficient quantities and have to be acquired through diet. Vitamins B_6 (pyridoxine), B_9 (folate) and B_{12} (cobalamin) have all been proposed to have protective effects on cognitive ageing.
- When folate or vitamin B_{12} are deficient, homocysteine levels rise, which predisposes to cardiovascular disease, and may contribute to amyloid and tau protein accumulation and neuronal death. Deficiencies in B_{12} and in folate increase with age.
- The association between B vitamins and cognition has been the subject of several recent systematic reviews with further new studies published since then.
- There is insufficient evidence, despite a large number of cohort studies, for an association between vitamin B_6, folate or vitamin B_{12} and cognitive decline or dementia. There is, however, consistent evidence that high levels of homocysteine are associated with cognitive decline.
- Randomised controlled trials targeting elevated homocysteine levels have shown that supplementation with B vitamins (B_6, B_{12} and folate alone or in combination) consistently reduces homocysteine levels, but without any significant effect on cognitive function. There is a suggestion from some studies that those with higher homocysteine levels at baseline, or clear and defined vitamin deficiencies may benefit from supplementation. However, this has not been clearly demonstrated, and more research is required.

Antioxidants

- Neural inflammation and oxidative damage are thought to be key mechanisms in the development of dementia. Oxidative stress directly damages cell components, resulting in damage to synapses and nerve cell death. Antioxidants are thought to act against neurodegeneration by limiting the production of toxic substances and reducing damage by free radicals.
- Nutrients with antioxidant properties include vitamins C and E and flavonoids. Most research has focused on the potential protective effect of vitamin E.
- There is currently insufficient evidence from either longitudinal epidemiological studies or randomised controlled trials to support a role for antioxidants in cognition.
- The only consistent associations were reported in epidemiological cohort studies that have assessed vitamin E status using food frequency questionnaires, rather than biochemical measures. Three randomised controlled trials failed to show any clear or consistent benefit of vitamin E supplementation on cognitive decline or dementia incidence among those with mild cognitive impairment.
- One recent cohort study indicated a possible relationship between flavonoid consumption and cognitive decline, and one randomised controlled trial indicated possible benefits of flavonoid supplementation.
- No clinical trials were specifically limited to people with low levels of vitamin E/C or flavonoids.

Omega-3 polyunsaturated fatty acids (PUFA)

- Omega-3 PUFA (polyunsaturated fatty acids) cannot be synthesised in the human body but are an essential dietary constituent, particularly for the brain. Over 22% of both the cerebral cortex and the white matter are made of phospholipids, and the function of neuronal cell membranes is modulated by their fatty acid composition. Dietary omega-3 PUFA are also implicated in neuronal growth and influence synapse formations. Omega-3 PUFA may be implicated in the vascular, inflammatory and also the amyloid pathways of dementia, and are therefore potentially important in vascular dementia, Alzheimer's disease and mixed forms.
- The main food sources of omega-3 PUFA are 'oily fish' such as salmon, mackerel, herring, sardines, fresh tuna, and swordfish.
- The evidence from epidemiological studies on the beneficial effects of fish consumption to prevent dementia incidence is conflicting, with no clear evidence for a protective effect. Confounding by healthy lifestyles and life circumstances (including socio-economic and educational level) that are associated both with higher fish consumption and lower dementia risk may explain positive results found in some studies.

- Evidence from experimental studies on the beneficial effects of omega-3 PUFA supplementation is insufficient to recommend their use in populations either for the prevention, or treatment of dementia. However, dietary recommendations to increase the amount intake of omega-3 PUFA from foods and the use of supplements in those who are deficient in these fatty acids is indicated for other reasons.
- There are some limitations in experimental studies conducted to date. Longer follow-ups may be needed to observe significant changes in cognitive function in primary prevention trials because changes in cognitive function were small in both the treated and placebo arms of existing trials. Inability to control fish consumption as part of the experimental design may have diminished the difference in total dietary omega-3 PUFA intake between those who were given the supplement and those who receive placebo.

Mediterranean diet

- A Mediterranean diet (with high intake of cereals, fruits, fish, legumes, and vegetables) has been associated in some studies with reduced risk for cardiovascular disease, type 2 diabetes, some forms of cancer and overall mortality.
- Mediterranean diet could reduce the risk of dementia through its effects on the vascular system, reducing cardiovascular disease, by increasing the concentration of plasma neutrophins, which protect neurons against oxidative stress, or by limiting pro-inflammatory cascades.
- Moderate evidence from epidemiological studies suggests an association between adherence to the Mediterranean diet and reduced dementia risk. Not all the studies did, however, report positive findings, in particular regarding cognitive decline.
- Only one study, the PREDIMED-NAVARRA randomised trial has attempted to test this association in an experimental design, by comparing a nutritional Mediterranean diet intervention supplemented with either extra-virgin olive oil (EVOO) or mixed nuts, with a low-fat control diet. The intervention, lasting 6.5 years showed encouraging results; participants that supplemented Mediterranean diet with EVOO but not with mixed nuts, had better cognitive function, and less incident mild cognitive impairment (MCI) than the control group (OR for MCI = 0.34, 95% CI 0.12–0.97).

Conclusion

- Overall, there is currently insufficient evidence to confirm a relationship between the micro- and macronutrients described above (vitamin B_6, vitamin B_{12}, folate, vitamin C, vitamin E, flavonoids, omega-3, Mediterranean diet) and cognitive function. Although some studies have shown positive results, particularly those using cross-sectional designs, the findings have not been consistently supported in prospective cohort studies, and preventive interventions have generally failed the critical test of randomised controlled trials.
- The strongest and most consistent evidence to date is for the potential benefits of adherence to a Mediterranean diet. Implementing such an intervention on a large scale, and in a sustainable way, would be difficult. More intervention studies are needed to further understand the preventive role of the Mediterranean diet, and the active ingredients for improving cognitive function and reducing dementia risk.
- A general limitation is that very few randomised controlled trials to date have targeted supplementation upon those who are deficient in the relevant micronutrient.

4 Undernutrition in dementia

- Undernutrition and underweight are common problems in older people. Weight loss is associated with increased morbidity and mortality, and it also worsens the prognosis for several chronic diseases.

Mechanisms

- Progressive malnutrition and weight loss are observed almost inexorably in dementia patients, resulting from an imbalance between nutrient/energy intake and needs. There are numerous potential mechanisms, divided into those that may cause a reduction in energy intake and those that may cause an increase in energy expenditure, which may act from as early as the pre-clinical and asymptomatic phase of the disease to the most advanced stages.
- Evidence suggests that dementia-related brain atrophy may impact on brain regions implicated in appetite control and energy balance, with metabolism in these regions significantly reduced in dementia.
- Dietary habits are influenced by diverse factors, from food availability and preparation, to appetite, taste and feeding problems.

Brain damage in general, and the cognitive and behavioural symptoms of dementia in particular, influence these factors and hence may impact on dietary habits in different ways at different stages of dementia.

- Aversive feeding behaviours are common, severely disrupting dietary intake, and making assistance at mealtimes indispensible and progressively more problematic. They also are, understandably, a source of considerable anxiety and strain for family caregivers.

Occurrence and dynamic of dementia-related undernutrition

- Numerous studies have investigated the association of dementia, or dementia severity with weight loss.
- Evidence on the association between dementia and weight loss is compelling. Several epidemiological studies have confirmed that people with dementia experience a significantly more marked decline in body weight in older age, across high income countries and LMIC. This weight loss likely starts sometimes in late mid-life, and may even represent an early marker of disease.
- Several mechanisms may be implicated and are not fully understood. It is likely that causal pathways vary from the pre-clinical phase, to the clinical onset and through the severity of dementia.
- Future studies should also investigate whether faster cognitive ageing in mid-life is associated with any weight loss before older age. Monitoring of weight change is highly recommended in people with dementia, and in older people. Further research is needed to determine whether monitoring in mid-life may also be beneficial for prevention.

Consequences of dementia-related undernutrition and weight loss

- The consequences of weight loss and undernutrition in people with dementia are well characterised. Overall weight loss and undernutrition have a significant impact on the course of the disease, on both cognitive and functional symptoms, and on the overall clinical prognosis.
- Weight loss may be part of the clinical expression of dementia, worsens the clinical course of dementia, leads to greater functional impairment and dependence, and increases the risk of morbidity, hospitalisation, institutionalisation, and ultimately mortality.
- Close monitoring of body weight is very important in people with dementia, and should guide strategies to prevent and treat weight loss.

5 Improving nutrition for people with dementia

- In considering strategies to improve the nutrition of people living with dementia it is important to consider care homes and hospitals, as well as the home setting.
- There may be benefits from systems level interventions; for example a hospital or care home introducing staff training or changes to the environment, ambience and context in which food is provided; as well as individual approaches.
- Studies have been conducted to assess the effect of four main types of intervention; training and education programmes for caregivers; mealtime environment or routine modification; nutritional supplements; and provision of feeding assistance.
- A structured assessment of the problem is the first step. Nutritional support (simple dietary advice, with assessment and management of risk factors, and attention to needs for feeding assistance) may suffice. If this fails, or in the case of more severe undernutrition, high-energy and/or high-protein oral nutritional supplements (ONS) may be a quick, reliable and generally well-tolerated way of improving nutritional status.

Nutritional assessment for people with dementia

- The continuous monitoring and surveillance of nutritional status is critical to plan, and evaluate the efficacy of nutritional interventions for people with dementia. The main types of nutritional assessment are: 1) dietary assessment, 2) weight history, 3) physical anthropometry, 4) screening questionnaires for nutritional status, 5) nutritional biomarkers and 6) eating and feeding behaviour. Anthropometric measures and screening questionnaires are most widely used.
- Dietary assessment of food intake can be prospective or retrospective. Commonly used methods include 24-hour dietary recall, food frequency questionnaires and food records. Prospective methods require the diarised recording of foods and fluids consumed over a specified period of time, and can be carried out by a family member or care assistant.

- A detailed weight history should be obtained along with current weight (a history of weight loss, whether intentional or unintentional, and over what period). Weight loss exceeding 5 kg (10lb) over six months is a red flag for further assessment.
- Body weight and height are the essential physical parameters. Body Mass Index (BMI) is the ratio of weight to height-squared (kg/m^2) and is widely used to assess nutritional status. A BMI cut off of <18.5 kg/m^2 defines adult chronic dietary energy deficiency. Overweight is defined as a BMI between 25 and 29.9 kg/m^2 and obesity as BMI ≥30 kg/m^2.
- Other simple physical assessments used to monitor nutritional status include triceps and truncal skinfold thickness, and mid-upper arm or calf muscle circumference.
- Nutritional screening aims to identify those who are malnourished or 'at risk' of malnutrition, and composite screening tools have been developed, e.g. the widely used Malnutrition Universal Screening Tool (MUST) (http://www.health.gov.il/download/ng/N500-19.pdf) and the six item mini nutritional assessment (MNA-SF®) http://www.mna-elderly.com/
- Nutritional biomarkers are part of a comprehensive assessment of nutritional status of frail older persons. An initial screen might comprise haematology (full blood count with differential) and biochemistry (electrolytes, urea and creatinine, fasting glucose, albumin, and ferritin).
- Eating and feeding behaviour assessments are usually observer rated, and assess aversive feeding behaviours and feeding dependency (need for assistance). The most widely used and best validated measure is the 10 item Edinburgh Feeding Evaluation in Dementia Scale (EdFED), developed for those with moderate to late-stage dementia, and brief and simple enough to be used in routine care. It establishes the level and type of feeding disability and can be used to plan effective interventions.
- Measurements of energy expenditure (resting, physical activity and dietary) and body composition (fat and lean body mass) do not form a part of current routine clinical assessment. However, assessments are becoming cheaper and easier to perform, and such evaluations, in research, may help to identify mechanisms explaining weight loss in dementia.

Education and training interventions

- Most caregivers understand that nutrition is an important component of the care that they provide. New skills must be learnt, and roles assumed, particularly for male caregivers who plan meals, shop for food and cook.
- Spouse caregivers gradually assume decision-making responsibility for what to eat, and when to eat it, where this may have previously been a shared activity. This can weigh heavily. Weight loss, and how to prevent or treat it is a preoccupation for many caregivers. As dementia evolves it is increasingly likely that aversive feeding behaviours develop, and that the person with dementia may need feeding assistance. Managing such problems is demanding of caregiver time, and requires patience, empathy and skill.
- People living in care homes are more likely to have advanced dementia, and feeding dependence and aversive feeding behaviours are therefore more prevalent. Residents with dementia take longer to eat, require prompting and encouragement, and may have problems with coordination and swallowing. Mealtimes are a busy time for care assistants. Feeding a person with dementia can take up to 40 minutes per resident.
- In a large US study of care home residents with dementia, 54% had low food intake, and 51% had low fluid intake. In another study in up to a quarter of cases of advanced dementia with feeding difficulties the family was not satisfied with the assistance provided.
- There is no reason to assume that family caregivers, or indeed care assistants in care homes are naturally equipped with the knowledge and skills to assess and manage the often complex nutritional needs of a person with dementia. Education and training interventions targeting caregivers may therefore have an important part to play in decreasing negative outcomes and increasing quality of life.
- There are many excellent practical guides and sources of information for caregivers of people with dementia, one of which is the factsheet prepared by the UK Alzheimer's Society 'Eating and Drinking' (http://www.alzheimers.org.uk/site/scripts/download_info.php?fileID=1799). This explains the importance of a healthy balanced diet, and the risks of weight loss in people with dementia. The contributions of cognitive problems, sensory deficits and aversive feeding behaviours are described, and strategies proposed to address them.

- We identified seven studies of education and training interventions.
- In two Taiwanese studies, training was provided to people with dementia who were resident in care homes in an attempt to modify their feeding behaviours. Montessori-based activities (practicing hand-eye coordination, scooping, pouring, and squeezing, and distinguishing food from non-food items) were associated with a significant reduction in feeding difficulties with some evidence for reduced need for feeding assistance. In neither study was the intervention associated with improvements in weight, BMI or overall nutritional status.
- In two other studies, the intervention comprised education and training of professional caregivers in nursing homes or other long-term care facilities for people with dementia. While improvements were noted in staff knowledge, attitudes and behaviour, there was no increase in food intake in one study, while in the other study an improvement in intake was not associated with improvement in nutritional status of the residents with dementia.
- Education programmes for informal caregivers were evaluated in three studies, two randomised controlled trials, and a controlled non-randomised study. The format of the training programmes was similar, comprising group sessions conducted by a dietician or other health professional. Topics covered included; the importance of a healthy balanced diet; dietary challenges in dementia; monitoring food intake, weight and nutritional status; advice on enriching dietary protein and energy content; and strategies to manage aversive eating behaviours. The largest trial indicated a moderate positive benefit for overall nutritional status, but no change in weight. The other trial did indicate statistically significant weight gain, but with a smaller effect size than for another arm of the same trial that was randomised to oral nutritional supplement.
- There is currently little or no evidence to suggest that training and education interventions, whether for paid care assistants in care homes, or for family caregivers of people with dementia, result in clinically meaningful improvements in the nutritional status of people with dementia. That is not to say that there may not be benefits. Surprisingly little research has been conducted in care homes, and evidence regarding training and education for family caregivers is dominated by one large well-conducted cluster-randomised controlled trial.
- Training and education on diet and nutrition is generally appreciated by caregivers, and there is a clear need for support particularly when aversive feeding behaviours and feeding difficulties occur. It may be that basic information should be provided to all families, while more concentrated training and dietician services should be focused upon those developing feeding difficulties or undernutrition.

Modifications to mealtime environment and routine

- In terms of experimental evidence, according to a recent systematic review applying standard criteria, ‘insufficient evidence’ exists to make clear recommendations regarding mealtime environment and routine modifications given the poor quality and limited quantity of trials (mostly small time-series comparisons).
- While poorly researched, this is currently a fertile area for innovation with successful advocacy driving forward change based to a large extent upon core principles, supported by some evidence and expert opinion.
- The last 30 years have seen a gradual transition to flexible, individualised and person-centred care in care settings that more resemble households or homes. The four core design principles relate to their scale, the nature and use of space, the relationships between living areas, and creation of spaces that support the autonomy and independence of residents. Kitchen and dining areas are an important part of this broader design framework.
- ‘Households’ typically comprise 8–12 residents, and the Life Safety Code Task Force has recommended 24 as the maximum feasible number. Household designs seek to replicate the living areas of houses, comprising resident rooms with bathrooms, a kitchen and dining area, and a living room or activity space.
- Large communal dining areas should be avoided, in particular for residents with dementia. It takes time to assemble residents, meaning that some will be left waiting for long periods for the meal to begin. Large dining spaces can be noisy and confusing, with too much sensory distraction, and do not provide the sensory cues that orientate a person with dementia to mealtime.
- Smaller dining rooms can have a more intimate and familiar ambience, and reduce confusion as to the function of the room. Smaller dining rooms, ‘bright and welcoming’ colours,

and other residential features (sideboards, paintings, objets d'art, use of a bulk re-thermalization system in place of tray service) seem to be associated with increased food intake. Low food intake is less common in smaller assisted living and residential care facilities, in facilities with 'non-institutional' dining rooms, and where residents take their meals in public dining rooms.

- As a design principle for care homes, ideally, each room should have just one activity associated with it. For people with dementia it may be particularly important to have a dedicated dining room, the use of which is limited to meals and food. This should look like a dining room in a home, with recognisable furniture such as dining tables and sideboards.
- The room can be a social hub throughout the day; for having coffee with friends after breakfast, inviting visitors to share food snacks from the kitchen between meals, and having afternoon tea with staff and residents.
- 'Eat-in-kitchens' linked to dining areas help to involve residents in meal preparation. Kitchens evoke feelings of warmth, comfort and security. Linking the eating area with a kitchen stimulates all of the senses with the smell and sound of cooking, cueing that a meal is about to take place. Diffusion of food-preparation smells has been suggested to stimulate the appetite of people with dementia and to remind them of meal times.
- Meals should be relaxed, unhurried and free from distraction. People with dementia find it difficult to concentrate on meals, and are sensitive to excessive noise and stimulation. Staff activities and other intrusions should be kept to a minimum and services areas (for food preparation and plating) should be outside the dining area. On the other hand, staff dining with residents may normalise the activity and foster person-centred care. For those with eating difficulties, quiet spaces free from distracting views can be helpful.
- While distracting noise should be reduced, familiar background music may increase calorie consumption.
- Good quality lighting is essential in dining areas so that older people with visual impairment can identify food and cutlery. In a study conducted in US care homes, increasing the light levels at table level led to an increase in food intake and feeding independence. A lighting intensity of 50 foot candles (540 lux) has been recommended for dining areas. Food consumption also increases when there is high contrast between the plate and table.
- Residents should sit in chairs with arms that slide under the table, so that they can be close enough to focus their attention on eating. Tables should be high and broad enough to allow wheel chairs to be accommodated, and with no central columns or support structures to restrict access.
- The creation of a 'family-style' eating environment with food served at table, more staff involvement and less distraction was associated with impressive improvements in energy intake, body weight, quality of life and physical performance in a large cluster-randomised controlled trial in Dutch nursing home residents without dementia. A much smaller study of a similar intervention in cognitive impairment nursing home units in Canada showed similar results, and the greatest nutritional benefit was gained by the most cognitively impaired residents.

Macronutrient oral nutritional supplementation (ONS)

- Oral protein and energy supplements are widely used in older people with undernutrition, or at risk of undernutrition, among whom their use is associated with significant weight gain, and a reduction in mortality for those who are undernourished.
- The main concerns associated with their use are problems with the willingness and ability of older people to consume them, the potential for gastrointestinal adverse effects, and the risk that the additional calories from the supplement may be more than offset by a compensatory reduction in customary diet.
- We conducted a review of studies identified in three previous systematic reviews, supplemented by a recently completed and unpublished systematic review of nutritional interventions for frail dependent older people (personal communication AT Jotheeswaran). Our objective was to identify all randomised controlled trials and controlled studies of oral nutritional supplements for people with dementia.
- We identified six randomised controlled trials (RCTs) of ONS, one crossover trial, a controlled trial, and an RCT of micronutrient supplementation in which both arms received macronutrient ONS. All of the studies were small ranging from 33 to 99 participants. In all 440 participants with dementia were included in placebo or other controlled comparisons of ONS, and pre-post within group data was available for 246 individuals receiving ONS.

- Six of the studies were conducted in care homes or other long-stay accommodation, and three in the community.
- Oral nutritional supplements provided were between 125 and 680 kcal per day, and were generally offered between meals and mainly in the morning to maximize adherence and reduce substitution. Duration of the intervention varied between three weeks and one year. Total calorie supplementation varied between 5,418 and 91,350 kcal.
- There was strong evidence that ONS was effective in increasing weight (pooled mean difference in % weight gain across five studies = 3.43%, 95% CI 2.08–4.78) and body mass index (pooled mean difference across four studies 1.15 kg/m^2, 95% CI 0.48–1.82).
- The % gain in body weight was proportional both to the daily calorie supplementation, and to the duration of ONS.
- ONS was generally well tolerated, and the calorie value of supplements was not offset by a reduction in the usual diet from regular meals.
- There was insufficient evidence to judge the impact of ONS on mortality among people with dementia (RR 0.69, 95% CI 0.00–1.46). No effect of ONS on cognitive function was observed in three RCTs, while in one non-randomised controlled study cognitive deterioration was more marked in the ONS intervention group. No benefit of ONS on activities of daily living was observed in five studies.

Micronutrient supplementation

- Micronutrient deficiencies are relatively common among older people, due to insufficient dietary intake, inefficient absorption, or both. Low levels of vitamin B_{12} and folate (folic acid) are associated with high blood levels of homocysteine which has been linked with the risk of arterial disease, dementia and Alzheimer's disease (AD). Evidence that free radicals may contribute to the pathological processes of Alzheimer's disease has led to interest in the use of vitamin E, which has antioxidant properties, in its treatment.
- There was no evidence, from several RCTs that supplementation with either folate or vitamin B_{12}, alone or in combination has any beneficial effects on cognitive function in people with dementia. In one trial, those randomised to folate were much more likely to be considered as 'treatment responders' to cholinesterase inhibitors (OR 4.06, 95% CI 1.22–13.53), but this finding requires replication. While the standard recommendation from systematic reviews is that there is insufficient evidence to conclude either way on the possible benefits or harms of supplementation the evidence on cognitive impairment does seem conclusively null.
- Two multi-centre RCTs conducted in the USA indicate some possible benefits of vitamin E supplementation in slowing clinical progression and/or functional decline in Alzheimer's disease of mild to moderate severity. In the most recent trial all-cause mortality and safety analyses did not suggest increased rates of adverse outcomes in the vitamin E group.

Medical foods

- Medical foods are defined as a special category of products that are intended for the dietary management of a disease or condition with distinctive nutritional requirements. Three medical foods have claimed to have benefits for people with dementia and are available in the USA and/or Europe: Axona® (AC-1202, Accera, Inc., CO, USA), Souvenaid® (Danone Research, France) and CerefolinNAC® (LA, USA). Randomised controlled trials of Souvenaid and Axona do not support any consistent or clinically significant cognitive benefit, and no studies have been reported regarding the efficacy of CerefolinNAC.

Conclusion

- There is consistent evidence that macronutrient oral nutritional supplementation (ONS) is effective in maintaining or improving weight among people with dementia. Supplements are well tolerated, with high levels of adherence under controlled clinical trial conditions.
- Nutritional benefit from ONS is proportionate to its intensity and duration, but benefits gained from short term supplementation, over weeks or months, is retained in the short to medium term. Hence brief cycles of ONS may be as effective as long-term supplementation.
- Most trials focused mainly on those who were at risk of undernutrition, or normally nourished. There is therefore an important outstanding question as to the effectiveness of ONS among people with dementia who are already undernourished.
- Given the health hazards of undernutrition, particularly when this involves protein catabolism and loss of lean body mass, one might expect maintenance of nutritional status

with ONS to be associated with wider health benefits than those identified in the studies reviewed. This may be due to the short period of nutritional support and follow-up (disability, mortality), and the failure to assess relevant outcomes (quality of life, depression, physical functioning).

- There is, as yet, no evidence to recommend the use of micronutrient supplementation at any stage of dementia. The possible exception to this advice is that of vitamin E supplementation given two positive trials with respect to cognitive and functional decline outcomes, although the balance of risks and benefits need to be more clearly established.
- There is currently no evidence to support the widespread screening for folate and B_{12} deficiency enshrined in many good-practice post-diagnostic recommendations. Supplementation does not seem to affect cognitive function, and the cost-effectiveness of these non-evidence based recommendations needs to be established in RCTs.
- There is currently insufficient evidence to recommend the use of any medical foods currently marketed for the treatment of Alzheimer's disease, and some evidence to suggest that they do not confer clinically significant cognitive benefit.
- Given the strong theoretical basis for micronutrient supplementation, it is under researched, with relatively few trials, most of which are small and underpowered, do not focus upon those with proven micronutrient deficiency, and have relatively short follow-up periods.

Feeding Assistance – managing aversive feeding behaviours in advanced dementia

- A case study from the Dominican Republic demonstrates the importance, and the feasibility of managing aversive feeding behaviours, through training paid caregivers of people with dementia, whether domestic workers (hired originally to clean the house and prepare food), or care assistants in nursing homes. Neither the behaviours, nor the consequent weight loss were recognised as part of the illness.
- Dr Daisy Acosta obtained consent to videotape several settings; private homes, nursing homes and state nursing homes; identifying the different types of eating behaviours and how the staff reacted and handled them. She then watched the videos with the staff and explained what was happening.
- Dr Acosta provided caregivers with tools to assess cognitive and functional impairment, and identify and classify feeding behaviours and needs for feeding assistance. 'In other words, I went with them, the staff, through a process of informal education about dementia, the course of dementia, and feeding and eating problems through the illness'. In private homes, both the paid caregiver and the main family caregiver were involved in the same education process.
- Dr Acosta then worked with nursing home staff and home caregivers to find approaches to help improve 'eating time' without incurring additional expense. The lessons learnt from this programme were that:
  - The enthusiasm and active involvement of the staff in the process was crucial. They began to give ideas as to how to improve each patient's behaviour and were very creative in their suggestions.
  - Categorising the behaviour was an essential first step in order to plan and implement measures to help it.
  - The measures can be very simple, not costly, and some of them were quite effective (see Chapter 5 for details).
  - The education and the positive attitude of the feeder were crucial in determining the success of the intervention. The education of those involved, about eating and feeding in patients with AD, helped to reduce the neglect of this essential aspect of care.
  - Not all people with dementia would have equal needs for calorie intake - think of hunger as a possible explanation for those residents who screamed or otherwise vocalised distress.
  - As well as calorie intake, staff needed to be taught about the importance of offering liquids often, and to avoid fluid restriction with the intention of avoiding incontinence or frequent diaper changes.

Assistive tableware

- Research by a Royal College of Art design team revealed that assistive tableware was not used as much as it might have been in UK care homes. Some care home managers opted not to use it because of a lack of aesthetic appeal. Since residents had different needs and abilities, and assistive tableware stood out from standard items, users of assistive table settings felt different, and stigmatised.

- The aim of the design team was to create a range of matching tableware that formed a complete set, could be used by people of all abilities, and resembled standard domestic tableware.
- Colour contrasts help to distinguish food from the plate upon which it is placed, and from the table covering. The same approach can be used to highlight the handle of a cup and its rim.
- Special plates with high lips were designed to assist those eating pureed or diced food with just a plate and spoon.
- The 'care cup' is one of the most disliked assistive tableware items, because of its similarity in appearance to a baby product (made from plastic with two handles and a nippled lid). The design team normalised this product by crafting it in ceramic but with a double skin to insulate the heat and prevent burning. The lid minimises the association to the nipple of a baby cup by elongating the form around the rim.
- The tableware includes items designed specifically for use with assisted feeding, including a plate, a bowl and lids for cups. The items are reduced in weight, and designed so that they can be easily and securely grasped by the carer, with one hand. The plate allows the carer to orientate it in an 'offering position' (in the sensory range of the person being fed so that they can see and smell what they are eating).

Managing oropharyngeal dysphagia in advanced dementia through enteral tube feeding

- Problems with swallowing are common in advanced dementia. However, the use of nasogastric or percutaneous endoscopic gastrostomy (PEG) feeding tubes, while widespread, is controversial, and needs to be evaluated carefully with respect to patient and caregiver preferences, and the balance of risks and benefits for individual patients.
- A Cochrane systematic review suggests that tube feeding for people with dementia does not confer any benefit regarding nutritional status, reduction of pressure sores, mortality risk or survival time.
- Families and health professionals often have unrealistic expectations of the outcomes of tube feeding. Potential for harm exists from an increase in urinary and faecal incontinence, leading to pressure sores; from discomfort, and attempts to remove the tubes, which may lead to sedation being given.
- Advanced eating and swallowing problems need to be seen more in the context of holistic palliative end-of-life care. Communication and shared decision-making are key factors, and having trust in doctors and surrounding staff is essential for patients and caregivers. However, many nurses and care home staff do not feel confident with issues related to end-of-life and dying with dementia, and there is a need to improve training.

Summary and conclusion

- Micronutrient and macronutrient (protein and energy) deficiency are common in dementia and Alzheimer's disease, and it is clear that undernutrition has important consequences for health, quality of life and survival. Loss of body weight seems on the one hand to be a natural part of the condition, with complex multifactorial determinants, and yet to be amenable to intervention.
- Standard recommendations for dietary management in dementia emphasise the role of dietary advice including fortification of existing diet to boost the protein and energy content, before resorting to oral nutritional supplements (ONS). Boosting calorie intake should improve nutritional status, and doing this through natural foods is likely to be more appealing than supplements, which can be costly. However, the evidence to support the efficacy, safety and tolerability of ONS is particularly strong, and this may be the most reliable means of restoring nutritional balance.
- Therefore, while dietary advice and food fortification can be tried first, ONS should be implemented without delay if this approach fails to improve nutritional status. This is particularly the case for those with established undernutrition.
- Given the relative lack of large definitive long-term trials in this area, there are still some important questions to be resolved:
  - Should those with undernutrition receive continuous ONS (and is this feasible and acceptable), or is short interval ONS equally effective and more acceptable?
  - Is ONS as effective for those with undernutrition as for those at risk of undernutrition?
  - Is long-term ONS associated with net benefits for cognition, functional status, depression, quality of life, and survival?

- Dietary advice should remain a standard recommendation. There is a clear demand from caregivers for advice and support, particularly with aversive feeding behaviours. There has been remarkably little research into nutritional training and education of care assistants in long-term care facilities, with many anecdotal examples of potential benefit.
- While many people with dementia use micronutrient supplements, there is little or no evidence of any benefit as regards progression of the condition. On the current evidence, the recommendation would be that these supplements should not be used for the treatment of Alzheimer's disease or other forms of dementia. B_{12} or folate deficiency, if identified, should be corrected. However, the overall cost-benefits of screening for these deficiencies in all patients with newly diagnosed dementia are not established, and current recommendations are not based on evidence.
- Very few older people are deficient in vitamin E. However, hypersupplementation of this vitamin (2000 IU total daily) does seem to be associated, in two randomised controlled trials, with slower progression of the cognitive and functional impairment of Alzheimer's disease. However, these doses are 100 times higher than the recommended daily allowance to maintain vitamin E levels and exceed the tolerable upper intake level. Excess intake of vitamin E, particularly over the longer term may be associated with bleeding and haemorrhagic stroke. Therefore the use of this agent cannot be recommended until more data is available on the balance of risks and benefits.
- There is strong evidence, although not from randomised controlled trials, that systems level interventions, for example small scale household level dining, 'family style' eating arrangements, and use of appropriate tableware and lighting levels may be associated with increased calorie consumption and increases in weight. Much more work needs to be carried out into the effectiveness of assistive feeding interventions to address aversive feeding behaviours.
- Although much of the work on nutritional interventions has been carried out in long-term care facilities, many of the findings are generalisable to home care by informal carers. This would include the benefits of ONS (and the relative inefficacy of dietary advice alone), the importance of a home dining environment, and including the person with dementia as part of the family social dining activity. Many informal caregivers struggle with aversive feeding behaviours, and the benefits of focused support and training interventions needs to be evaluated in this group.

Chapter 1 Background

The world's population is ageing. Improvements in health care in the past century have contributed to people living longer and healthier lives. However, this has also resulted in an increase in the number of people with non-communicable diseases, including dementia. There is lack of awareness and understanding of dementia, at some level, in most countries, resulting in stigmatisation, barriers to diagnosis and care. The condition impacts upon caregivers, families and societies physically, psychologically and economically. Dementia can no longer be neglected and should be considered an important part of the public health agenda in all countries.

Dementia: numbers and burden

What are dementia and cognitive impairment?

Dementia is a syndrome affecting memory, thinking, behaviour and the ability to perform everyday activities, usually chronic or progressive by nature, which is caused by a variety of brain illnesses. Cognitive impairment, which includes the more operationalised category of 'Mild Cognitive Impairment' (MCI), describes measurable deficits in one or more cognitive abilities (e.g. memory, planning, language, attention or visuospatial skills) which may be noticeable to the older person or those around them, but do not yet interfere substantially with everyday living. When the impact on everyday abilities is significant, this may suggest dementia.

Whilst dementia mainly affects older people, it is not a normal part of ageing. Although the prevalence is high among the "oldest-old", most do not have dementia. At the same time, there is a growing awareness of 'young onset' cases starting before the age of 60 years.

Dementia is linked to several underlying brain pathologies, of which Alzheimer's disease, vascular dementia, dementia with Lewy-Bodies, and frontotemporal dementia are the most common. The boundaries between the subtypes can be difficult to define, and mixed forms exist. The relation between the pathological lesions present in the brain and the severity or the symptoms of dementia is not clear. The co-existence of other conditions, especially cerebrovascular disease, may be important.

Dementia and cognitive impairment are by far the most important contributors, among chronic diseases, to disability, dependence, and, in high income countries, transition into residential and nursing home care[1]. The behavioural and psychological symptoms (BPSD) linked to dementia, typically occurring later in the course of the disease, also have an impact on the quality of life of the old person and are an important cause of caregiver strain. Dementia is overwhelming not only for the people who have it, but also for their caregivers and families. Around half of all people with dementia need personal care (and the others will develop such needs over time)[1]. Compared with other chronic conditions, the need for care and supervision typically develop early in the course of the condition, and intensify over time, leaving those with more advanced dementia completely reliant on caregivers for their basic needs[1].

Prevalence of dementia

The coming global epidemic of Alzheimer's disease and other types of dementia is recognised by the World Health Organization as a public health priority [2,3]. It is estimated in 2013 that 44.35 million people worldwide live with dementia, with numbers affected doubling

every 20 years, to reach 135.46 million by 2050[4]. Much of the increase is attributable to increases in the number of people with dementia in low and middle income countries (LMIC); currently 62% of all people with dementia live in such regions, this proportion rising to 66% in 2030 and 71% in 2050.

The epidemic is driven mainly by population ageing, given the strong association with older age; consistently across regions, dementia prevalence increases exponentially with age, doubling with every five to six year increment[3].

Incidence of dementia

The latest systematic review on the incidence of dementia included 34 studies, of which 16 had been conducted in Western Europe, five in North America, four in East Asia, six in Latin America and the Caribbean, one in Australasia, one in the Asia-Pacific region and one in West Sub Saharan Africa. Summarising the evidence from all studies, the incidence of dementia increases exponentially with increasing age, from 3.1 per 1000 person years at age 60–64 to 175.0 per 1000 person years at age 95+ [2]. While the incidence appears to be somewhat higher in high income countries than in LMIC this effect is no longer apparent when the 10/66 Dementia Research Group's* cross-culturally validated dementia diagnosis was applied to the studies that the group conducted in LMIC. It is estimated that there will be nearly 7.7 million new cases of dementia each year worldwide, implying one new case every 4 seconds. The majority of new cases will arise in LMIC: 3.6 million (46%) in Asia, 2.3 million (31%) in Europe, 1.2 million (16%) in the Americas, and 0.5 million (7%) in Africa.

Costs of dementia

The total estimated worldwide cost of dementia in 2010 was US$ 604 billion, equivalent to around 1% of global gross domestic product, of which about 70% was incurred in Western Europe and North America[5]. Costs of informal care (unpaid care provided by families and others) and the direct costs of social care (provided by community care professionals and in residential home settings) contribute similar proportions (42%) of total costs worldwide; while the direct costs of medical care are much lower (16%). However, in low and middle income countries where formal care services are not well developed direct social care costs are negligible and informal care costs predominate, accounting for up to two-thirds of all costs.

Malnutrition, undernutrition, and obesity: worldwide patterns of the 'double burden'

Diet and nutrition play an important role in maintaining health and wellbeing. You are, after all, what you eat. Diet can be defined as what we habitually eat and drink. Diet is thus best conceived as a lifestyle and plays a relevant role in both morbidity and mortality. This is because diet is critical for nutrition, although there are non-nutritive compounds in foods, often referred to as phytochemicals, which are likely, beneficial to health too.

Nutrition can be simply defined as the use of foods that humans (and all living organisms) make in order to live and maintain their health. Nutrition encompasses the processes of ingesting and digesting foods, and absorbing and metabolising their nutrients. It is implicated in the provision of water, micronutrients (i.e., vitamins and minerals), macronutrients (i.e., carbohydrates, proteins and lipids), and energy. These components are used by the human body to build and maintain tissues, and to allow its optimal functioning, hence adequate nutrition is essential for healthy living.

Malnutrition comprises both overnutrition (excess food/calorie intake) and undernutrition, which is the depletion of body energy stores and loss of body mass (mainly lean mass). Malnutrition results mainly from eating an inadequate diet in which either or both quantity and/or quality of nutrients do not meet the needs of our body. Health status influences diet, and several diseases may concomitantly lead to excess losses of micronutrients and increased energy expenditure, which can also cause and exacerbate malnutrition.

Undernutrition (insufficient calories, protein or other nutrients needed for tissue maintenance and repair) is the most common nutritional problem, affecting up to 10% of older people living at home, 30% of those living in care homes, and 70% of hospitalised older people. Evidence from studies conducted in low and middle income countries is more limited, but the prevalence of undernutrition in older people is likely to be even higher, probably linked to poverty and food insecurity. In studies conducted in sub-Saharan African countries between 11.5% and 40.0% of 65 years and over had a body mass index (BMI) <18.5, indicating undernutrition[6–9]. In the 10/66 Dementia Research Group studies in Latin America, India, China and Nigeria the prevalence of undernutrition indicated by low arm circumference (≤23.5cms)

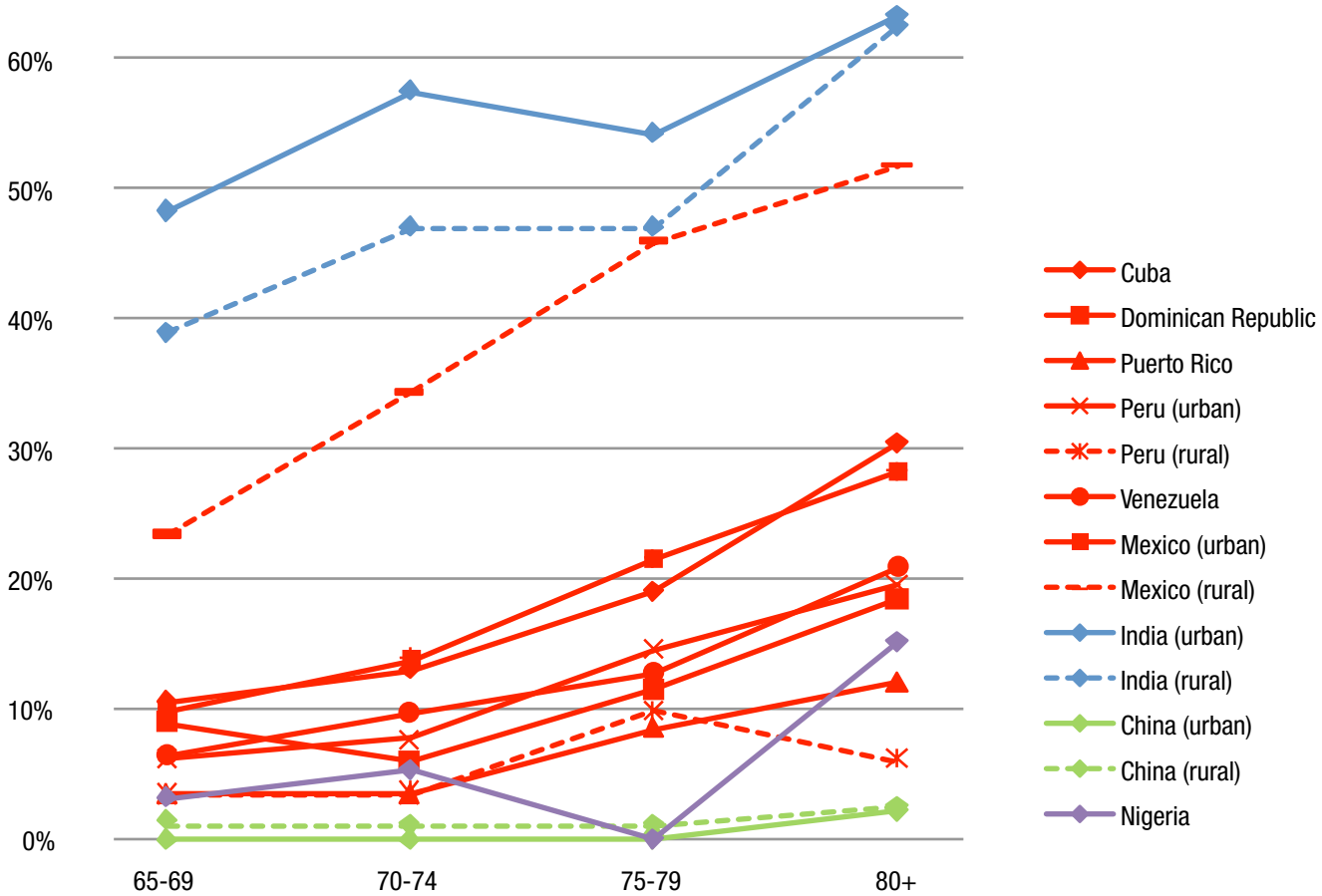
* The 10/66 Dementia Research Group is a collective of researchers carrying out population-based research into dementia, non-communicable diseases and ageing in low and middle income countries. More information on: http://www.alz.co.uk/1066/

ranged from 0.5% in China to 53.9% in rural India. Prevalence was higher in less developed and rural settings, and increased with age (Figure 1.1).

Consequences of undernutrition include frailty, reduced mobility, skin fragility, an increased risk of falls and fractures, exacerbation of health conditions, and increased mortality[10,11]. Risk factors include; the older person's social, economic and environmental situation; problems with mouth, teeth and swallowing; mental, neurological and other chronic physical diseases; and side effects of long-term treatment with certain drugs[12]. Older people are also at risk of micronutrient deficiency (vitamins and minerals, needed in small quantities), often as part of a generally inadequate diet, but also seen in normal weight or obese people due to lack of meat, dairy products, or vegetables in the diet. Calorie requirements decrease with age but nutrient needs either remain the same or even increase in some cases. Thus, meeting the nutritional requirements of older adults is a challenge, even for those that eat what we would consider an adequate diet.

With globalisation and rapid social and economic development, many low and middle income countries are now facing a "double burden" of disease. While they continue to deal with the problems of infectious disease and undernutrition, they are experiencing a rapid upsurge in non-communicable disease risk factors including obesity, particularly in urban settings. Rapid societal and lifestyle changes are progressively modifying indigenous dietary and lifestyle habits, and driving the assimilation of westernised habits (e.g., increased physical inactivity and consumption of saturated fat, animal proteins and refined carbohydrates)[13]. It is not uncommon to find undernutrition and obesity existing side-by-side within the same country, the same community and the same household[14]. Overweight and obesity (abnormal or excessive fat accumulation that presents a risk to health) are major risk factors for several chronic diseases, including diabetes, cardiovascular diseases and cancer, and is the fifth leading modifiable risk determinant for global deaths[14]. The main cause of obesity is an energy imbalance between calories consumed and calories expended. Globally, there has been an increased intake of energy-dense foods that are high in fat and an increase in physical inactivity (increased sedentary nature of many forms of

Figure 1.1
Prevalence of undernutrition (arm circumference ≤23.5cms) in the 10/66 studies, by age group



work, changing modes of transportation, and increasing urbanisation). Obesity in the elderly will be an increasing problem in the coming decades. In Europe, several studies already reported a prevalence ranging from 18% in France[15], 18–20% in the Netherlands[16] and 35% in Spain[17] among the old population (above 60/65 years) while the European Prospective Investigation into Cancer and Nutrition (EPIC), with participants aged 40–65 years in 1996, predicted a prevalence of obesity of about 30% in 2015[18]. In the US, it was estimated that the prevalence of obesity in older Americans aged 60 years and older, would increase from 32.0% in 2000 to 37.4% in 2010[19]. Once considered a problem only in high income countries, overweight and obesity are also now rising dramatically in low and middle income countries, especially in urban settings.

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Chapter 2

Nutrition and dementia across the life course

Nutrition can influence our risk of developing dementia, and our chances of 'living well with dementia' if we develop the disease.

- Good nutrition contributes to healthy brain development, which may protect against the onset of dementia in late life.
- Obesity in midlife and diets rich in saturated fat, which predispose to cardiovascular disease, may increase the risk of developing dementia in late life.
- The onset of dementia is associated with a decade-long gradual decline in body mass.
- Maintaining an adequate diet is challenging for people with dementia, leading to a particularly high prevalence of undernutrition.

This chapter explores the latest evidence on the complex relationship between nutrition and dementia across the life course.

Key life course concepts: 'sensitive periods' and 'accumulation'

The study of how risk and protective factors dynamically interact to influence later disease outcomes is referred to as life course epidemiology[1]. Accumulating evidence suggests that dementia has a lifelong trajectory in a manner comparable to several other chronic diseases of late life, with risks clustering around specific developmental epochs and often accumulating in their effects, sometimes with relatively long latent periods before onset of clinical dementia syndromes[2].

For instance, it has been observed that while mid-life vascular risk factors, including high blood pressure and high adiposity may increase the risk of dementia in late life[3], declining values of blood pressure and body weight after midlife are also associated with dementia, possibly in relation to underlying disease processes. Because dementia-related neuropathology likely begins decades prior the symptomatic onset of the disease[4], issues related to directionality are not easily disentangled and the age at which exposure to a putative risk factor is measured is clearly crucial. A life course approach to late-onset dementia may improve our understanding of the disease[5,6], and create evidence on potential additive effects of exposures over time ('accumulation'), and on 'sensitive periods' of life during which exposure to a risk factor may be more detrimental for dementia risk. This could have a considerable impact on prevention. At present there are significant design and analytical challenges that limit the feasibility of life course epidemiological studies of dementia and cognitive decline. Besides, controversial conceptual and methodological issues exist in life course epidemiology relevant to the causal inference debate in epidemiology[7,8]. As far as dementia is concerned, these issues are the contentions that prevention should begin early in life and be concerned not only with the onset of dementia and its progression, but also with trajectories of cognitive ageing from mid-life, when impairment likely begins[9].

Nutrition for optimal brain/ cognitive development

Micronutrients and fat stores accumulated during intra-uterine life, particularly between the 35th and 40th weeks of gestation, are chiefly important for brain and nervous system maturation and development that occur primarily up until age five[10]. In turn brain development may influence risk of cognitive impairment and dementia in older age[11]. Post-mortem studies have shown that people with evidence of the pathological hallmarks of Alzheimer's disease in their brains

(i.e., amyloid plaques and fibrillary tangles) may yet have shown no signs of cognitive impairment or dementia up to the time of death[12]. Hence, brain reserve, the number of neurons and synapses (for which brain size may be a marker), may buffer the effects of dementia-related neuropathology and explain the observed variability in the expression and severity of the dementia syndrome in people with comparable levels of neuropathology. Brain reserve is likely to be influenced by a variety of factors, both genetic and environmental, including early life nutrition.

Evidence suggests that low birth weight, a marker of inadequate nutrition in uterus, may be associated with lower cognitive level in both childhood and adulthood[13]. Persistent insufficient nutrient intake in early infancy slows growth and causes low height for age (stunting) that tracks through young adulthood and results in shorter legs for total height. Therefore having shorter legs relative to total height in adulthood is considered a valid proxy of early life inadequate nutritional level. Evidence from the 1946 British birth cohort study suggests that height in early life is positively associated with cognitive function in adolescence independently of birth weight[14]. These associations may track across the life course and influence risk for dementia onset, as suggested by the finding in the 10/66 study that longer leg length and larger skull circumference were associated with lower dementia prevalence amongst over 15,000 older people studied in diverse geographic regions and cultures in Latin America, China and India[15].

While larger birth weight and high (optimal) body size in childhood may be associated with better cognition, overweight and obesity that result from an excess of nutrient/energy intake and/or reduced physical activity level are notoriously harmful for health. Overweight and obesity are associated with higher mortality risk and reduced life expectancy[16], and may contribute to neurodegenerative and cerebrovascular changes underlying late-life dementia through both vascular and metabolic pathways[17]. These issues are spreading worldwide to epidemic proportions[18], and if their link with dementia should be proved to be causal, the public health impact would be tremendous. Luchsinger and Gustafson have proposed several potential linking mechanisms, emphasising the continuum of high adiposity, hyperinsulinaemia, and non-insulin dependent diabetes (type 2 diabetes)[19] – Box 2.1.

However, although the relationship between obesity and dementia-related brain damage is certainly biologically plausible, its complexity can be problematic, making mechanistic evidence hard to reconcile. For instance, prolonged exposure to high levels of pro-inflammatory molecules (i.e. Tumor Necrosis Factor-α and Intereleukin-6) produced by adipocytes (where body fat is stored) may affect the brain directly. Nevertheless, high levels of leptin, an important cytokine produced in the adipose tissue, seem to enhance cognitive function[20,21] and may have neuroprotective effects[22]. The association between fat cell metabolism and brain damage is complex, and is further complicated by the fact that some neuropathologic changes in the brain that build up several years before the clinical onset of dementia may be associated with weight loss[23].

In the next section of this chapter we focus on high adiposity before older age, and report

Box 2.1

Links between adiposity and cognitive impairment

Mechanisms that may link adiposity to cognitive impairment and dementia, revised by Luchsinger and Gustafson[17]

Hyperinsulineamia – Insulin resistance and hyperinsulineamia are caused by high adiposity. Excess of insulin can have direct effects in the brain, for instance it may interfere with the clearance of amyloid and contribute to brain damage.

Advanced glycosylation end products (AGEs) – AGEs are produced in excess in diabetes and are responsible for the end organ damage. AGEs have been found both in amyloid plaques and in fibrillary tangles; the glycation of amyloid oligomers enhances their aggregation into insoluble plaques seen in Alzheimer's disease, and may facilitate neuronal damage.

Adipokines and cytokines – The adipose tissue produces inflammatory cytokines (which may increase the brain inflammatory state), and acts as an endocrine diffuse organ too. Adipokines (adiponectin, leptin, and resistin) have direct effects on brain regions implicated in dementia (e.g., the hippocampus), and may affect cognitive function.

Vascular risk factors – Obesity is associated with several vascular risk factors including lower physical activity, poorer diet and higher blood pressure. These vascular risk factors are associated with dementia and may thus mediate the effect of adiposity.

Cerebrovascular diseases – Adiposity may increase dementia risk also through cerebrovascular disease (diffuse and focal vascular damage) and stroke, which are strongly associated with dementia.

the main conclusions of available systematic reviews and any new research in which the effect of mid-life adiposity as a potential risk factor for dementia was the question under study. In Chapter 4 we will address this association in the opposite direction, that is dementia-associated undernutrition, particularly weight loss; reviewing and commenting on studies that focused on adiposity in late-life, or investigated the natural history of weight or BMI changes from mid- to late-life as a function of a later dementia diagnosis (or of measures of brain damage).

Role of high adiposity (overweight/obesity)

When energy ingested is greater than energy expended, fat is stored in adipose tissue. The term adiposity is used to indicate the total amount of adipose tissue, and adiposity is considered to be excessive when it adversely affects health. To measure the level of excess adiposity in populations, measures of body weight and height are combined using a simple formula to calculate body mass index (BMI, weight in kilograms divided by height in meters squared, i.e. kg/m^2). Overweight and obesity are commonly used terms to refer to excess of adipose tissue. In adults, a BMI between 25 and 29.9 kg/m^2 indicates overweight, and BMI equal to or greater than 30 kg/m^2, obesity[24]. BMI is widely used as a reliable clinical measure of both global and central adiposity in population as well as in clinical settings[25]. However, BMI cut points for overweight and obesity are less clear in older age due to physiologic changes in body composition with a progressive decrease of lean compared to fat mass[26]. Waist circumference, a measure of central adiposity, is also commonly used to measure adiposity, and is a valid indicator of the associated metabolic changes. Cut-offs of waist circumference of 102 cm for men, and 88 cm for women predict adiposity-associated negative health consequences[27]. Waist circumference measures are more prone to measurement error and cannot be self-reported (whereas height and weight are commonly known). In addition, waist circumference may underestimate the so-called gynoid fat distribution characterised by a preferential accumulation of body fat in the limbs and lower body depots.

The association between adiposity and ensuing dementia is biologically plausible, and of great potential public health relevance. The existence of a causal association is quite widely accepted; for example a recent review of modifiable risk factors for Alzheimer's disease estimated the relative risk associated with mid-life obesity as 1.60 (95% CI 1.34–1.92), and the population attributable fraction (the proportion of incident cases of AD that might be prevented if the risk factor was completely removed from the population) as 2.0%[28]. Nevertheless, the literature is constantly developing, and a critical overview of the evidence accumulated to date is necessary.

A significant number of prospective epidemiological studies have been conducted on the associations between BMI and/or waist circumference in mid-life and dementia. We have identified three reviews published in recent years. These reviews have slightly different main objectives and the included and excluded studies differ. Overall, evidence on the association between high adiposity in mid-life and higher dementia risk is weak and remains highly conflicting.

Gorospe and colleagues[29] included in their review seven studies that were published up until 2007[30-36]. The authors concluded that the evidence that high BMI increases dementia risk is compelling. However, of the seven primary studies included only four found a positive, significant association. In addition, amongst these, issues related to residual confounding may exist in two studies in which adjustment was limited to age and education[31], or did not include education level[34]. BMI was measured in late-life in another of the studies reporting significant associations[30], making this difficult to compare with studies that focused on exposure to high adiposity in mid-life.

Beydoun and colleagues conducted a systematic review and meta-analysis one year later[37] and were able to include three further published studies and one unpublished in addition to those found by Gorospe[38-40]. They concluded that current evidence shows that the association between obesity and the risks of dementia and Alzheimer's disease is moderate. However, the findings from the primary studies were heterogeneous and results from the largest study included in the meta-analysis[35] strongly influenced the combined estimate.

Finally, Anstey et al. (2011) published the most recent available review on the association between adiposity and (any) dementia[41]. Primary studies that used BMI or waist circumference measured either in mid-life or late-life were eligible, and were separately combined. Pooled effects were calculated for the association of overweight or obesity with Alzheimer's disease, vascular dementia, and any dementia. The authors concluded that underweight, overweight and obesity in mid-life all increase dementia risk[41]. The authors' conclusions are based on results of their meta-analysis, in which the primary studies' estimates are pooled. However, they comment on the large heterogeneity across the

primary studies included in their review. The reported pooled relative risks (RR) of dementia (Alzheimer's, vascular dementia or any dementia) for both overweight (see Table 3 in Anstey et al.'s paper[41]) and obesity (see Table 4 in Anstey et al.'s paper[41]) in mid-life compared to normal BMI were, again, all largely driven by results from the Kaiser Permanente study[35], and to a lesser extent by the Primary Prevention Study in Goteborg, Sweden[34]. In the Kaiser Permanente study, generalisability of the finding may be limited by the fact that participants were part of the Kaiser Permanente medical care programme in northern California. In the Goteborg study[34] educational level was not controlled for; residual confounding seems likely, because education is strongly associated with both BMI and dementia risk. Moreover, in both studies, dementia diagnosis was largely or entirely based only upon available medical records, which may have introduced an important ascertainment bias. Since higher BMI predicts morbidity and hospitalisation, those who were leaner in mid-life may have been less likely to be diagnosed with dementia simply because they were not as frequently routinely assessed[35]. In addition to these limitations, Anstey et al. did not include in their review two large and important epidemiological studies, the Finnish Cardiovascular Risk Factors, Aging and Dementia (CAIDE) study[32], and the Prospective Population Study of Women in Sweden (PPSW)[42] although both seem to meet the inclusion criteria. These Scandinavian studies reported no significant associations between overweight and obesity measured in mid-life and dementia in late life, and indicate that the association between mid-life BMI and dementia may be largely explained by confounding by socio-demographic, health and lifestyle characteristics.

It has been recently suggested that the association between adiposity and dementia may be in fact explained by factors (both genetic and environmental) that may influence lifelong adiposity trajectories, vascular risk profile, and late-life cognitive decline too[43]. Waist circumference is less often measured than BMI in prospective, longitudinal epidemiological studies of the association with onset of dementia in late-life. Nevertheless, in contrast with the highly conflicting evidence on BMI, the association between central obesity and dementia risk is more consistent. Results are unequivocal in the Kaiser Permanente study, in which those with highest central obesity in mid-life (as measured with sagittal abdominal diameter, SAD) were almost three times more likely to have been diagnosed with dementia three decades later[44]. A positive, prospective association between a waist-to-hip ratio (WHR) greater than 0.80 and greater dementia risk was found also in the Prospective Population Study of Women in Sweden (PPSW), in which BMI at the same age in mid-life was not associated with dementia (see above)[42]. The fact that in the same cohort (i.e. PPSW) contrasting results emerged using two measures of adiposity is extremely interesting. Because central adiposity captures the associated-metabolic changes better than global adiposity (i.e. BMI), this finding supports the hypothesis that any link between adiposity and dementia may be best understood as a continuum through insulin resistance and type 2 diabetes[17]. Conversely, the production by adipose tissue of substances with metabolic (adipokines) and inflammatory (cytokines) functions may be less important.

Further research is warranted because an improved understanding of the critical pathways that may lead from high adiposity to greater dementia risk could have a significant impact on targeting of primary prevention strategies.

Adiposity and cognitive function in mid-life

Dementia has an insidious onset. The latency period, defined as the time between initiation and detection of the disease, can be as long as 20–30 years. Evidence on changes of cognitive function in adulthood suggests that cognitive impairment may begin in mid-life[9,45]. Modifiable factors across the life course may influence the achievement and maintenance of optimal cognitive function levels in mid-life, and higher levels of cognitive function before older age have been suggested to potentially act as a reserve to ward off the consequences of accumulated brain damage and reduce symptoms[46]. A focus on progressive cognitive ageing from adulthood into older age rather than on dementia diagnosis in late-life seems very promising for prevention[47]. Also, the metabolic changes associated with dementia and its symptoms (both cognitive and behavioural) can have a considerable impact on risk factor profiles, including declining blood pressure and weight loss. This complicates elucidation of the direction of causal relationships, and has led to an increasing interest in studies that track both exposure and outcome measures before older age.

Few studies have investigated the relationship between adiposity measured in young adulthood and cognitive function or cognitive decline in mid-life. Overall results are heterogeneous but seem to indicate that the potential detrimental effect of adiposity on cognitive function may be largely confounded. In the Vieillissement et Santé au Travail (ageing and health at work; VISAT) Study, higher BMI at baseline but no gain

in BMI in adulthood was associated with lower scores in memory and speed/attention tests, independently of relevant covariates and potential confounders[48]. In the Whitehall II study, with the exception of executive function, compared to those who had a normal weight, those who were obese or overweight in young adulthood (mean age 25 years), and early mid-life (mean age 44 years) did not have lower cognitive function levels in late mid-life (mean age 61 years). However, there was a significant cross-sectional association at age 61 years, such that both obese and underweight participants had lower scores, and being obese at all three assessments compared to never having been obese was significantly associated with a 1.6 point (out of 30) lower score on the Mini Mental State Examination in late mid-life[49]. Further analysis showed that obesity was associated with a steeper 10-year cognitive decline in mid-life only in obese participants who were also 'metabolically abnormal' (having two or more of three metabolic syndrome factors; dyslipidaemia, high blood pressure, and diabetes)[50]. In the 1946 British[51] birth cohort study the positive association between gain in BMI from adolescence (15 years) until mid-life (53 years), with mid-life cognitive function and steeper cognitive decline in mid-life (from 43 to 53 years) was largely explained by educational level and childhood intelligence. Moreover, there were no significant associations in this cohort between BMI gain and crystallised intelligence (which captures the slippery concept of cognitive reserve beyond educational level).

Finally, in the Coronary Artery Risk Development in Young Adults (CARDIA) study, Reis et al. investigated the relationship of cardiovascular health (defined according to the American Heart Association (AHA) criteria) in young adulthood and mid-life with cognitive function in mid-life (before age 60)[52]. BMI is one of the seven cardiovascular health components indicated by AHA. Those with higher BMI in both young adulthood (i.e. before 30 years of age) and mid-life (i.e. before 60 years of age) had significant lower scores in tests of executive functions, attention and speed but similar scores on memory tests administered in mid-life. Though statistically significant, differences in cognitive tests scores across BMI levels were very small, and of negligible clinical significance. These tests have been developed to assess cognitive performance in older people. A ceiling effect may exist when they are used in relatively young adults that makes it hard to detect objective cognitive impairment defined for example by a score that is more than 1.5 standard deviations lower than the mean score in the source population.

Taken together, evidence from these studies of younger adults suggests that BMI gain across the life course is not related to worse cognitive ageing before older age, and that childhood intelligence may in fact largely explain any associations between high adiposity and dementia observed in some epidemiologic studies (above). This is plausible, because intelligence strongly influences the maintenance of a healthy lifestyle throughout life, including lower adiposity, and may confer advantages in brain structure (brain reserve) and function (cognitive reserve), that can buffer the impact of brain damage in late-life and delay the symptomatic onset of dementia. A recent hypothesis posited by Corley et al. maintains that the association of adiposity with cognitive impairment is in fact confounded by genotype and life circumstances that may shape lifelong adiposity trajectories, and also cognitive ability and decline[43].

Adiposity and brain measures

A further improvement in our understanding of the complex relationship between adiposity and dementia could come from studies that investigate associations with dementia-related brain damage. However to date evidence from longitudinal, prospective, population-based studies on this topic is scanty, to our knowledge no studies have explored the association of mid-life BMI with brain atrophy and vascular lesions (both focal and diffuse), the structural changes underlying dementia. The only evidence we could find was on BMI and changes in MRI (magnetic resonance imaging) structural measures, both measured in mid-life. Results were not significant after relevant potential confounders were controlled for[53].

Conclusions

In conclusion, the available evidence from epidemiological studies on the association of overweight and obesity in mid-life, clinically measured with BMI, with dementia is still conflicting. Factors that may explain discrepancies across studies are summarised in Box 2.2.

Any associations between early life adiposity and cognitive function or impairment in mid-life seem to be accounted for by a strong confounding effect exerted by childhood intelligence and educational achievement.

Central obesity in mid-life, as measured by waist circumference, waist hip ratio or other anthropometric measures, may be more consistently linked to the development of dementia in older age. This is consistent with the fact that waist circumference seems to capture obesity-related health problems better than BMI[27],

and that central obesity is a strong predictor of insulin resistance and diabetes[54], which in turn may be harmful for the brain and are associated with dementia. However, there are different types of central obesity, and visceral fat rather than subcutaneous fat deposits seem to be most associated with harmful health outcomes[55].

The relationship between fats and the brain is extremely complex. Fats are fundamental for brain and cognitive development, may be harmful (if in excess) in mid-life, and may be an important energy reserve that could improve resilience to the effects of dementia-related neuropathology and comorbidities in later life. The evidence we have presented seems to suggest that the same factors that influence the accumulation of adiposity across the life course may also be implicated in the development and decline of cognitive function. New studies are certainly needed to elucidate the complex relationship between adiposity and cognitive function, cognitive impairment and dementia. The use of a life course approach in future studies is imperative[56].

Box 2.2

Discrepancies in evidence

Reasons that may explain discrepancies across epidemiologic studies on the association between adiposity and dementia

Healthy average adiposity level in mid-life – When average adiposity in mid-life is below or around healthy levels in the cohort under study, detrimental effects cannot be observed simply because too few people are truly 'at risk'. Descriptive data on average BMI in the sample under study should be carefully considered to interpret results.

Age of participants when the adiposity is measured with respect to ascertainment of cognitive status – The life course hypothesis in epidemiology posits that critical periods during which the effect of risk factors may have more impact may exist. Under this assumption, null findings in cohort studies with relatively few repeated observations across the life course may be explained by the lack of data in the supposed time window when high adiposity is truly detrimental. Evidence on the existence of such critical periods is best derived from birth cohort studies, in which participants sampled at birth are followed up and measured several times across the life course.

Reverse causality – Subtle weight loss may precede the symptomatic onset of dementia by several decades. Long follow-up intervals between adiposity measures at baseline and cognitive assessment in late-life reduce this possible nuisance, but it cannot be entirely excluded (see Chapter 4).

Variation of the validity of adiposity measures with age, and across populations – Age, gender and ethnicity influence the validity of the standard cut-points of BMI used to define overweight and obesity. Relationship of dementia to continuous BMI should be always explored before categorising BMI using thresholds for overweight and obesity.

Dementia diagnosis, cognitive assessments – It is very likely that dementia diagnosis and cognitive assessments vary significantly across epidemiologic studies. This clearly limits the appropriateness of direct comparisons. The 10/66 study is an example of how pre-validated diagnostic procedures and the use of standard study protocols in diverse world regions allow for comparison and contrasting of results in different cohorts.

Survival bias and competing risks – A true association between high adiposity and dementia may be difficult to observe because those who are obese in mid-life are less likely to survive to older age than those who are lean. This means that 'mortality and dementia' compete in people exposed to high adiposity. Indeed, very few studies have considered survival across levels of BMI in mid-life.

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Chapter 3

Nutritional factors and dementia prevention

With an estimated 7.7 million new cases each year[1], dementia prevention is an urgent priority, both to reduce incidence and slow the progression of the condition. We need to identify important risk factors, particularly those that can be modified. Nutrition, brain development and adult brain health are linked together by complex pathways across the life course, suggesting multiple opportunities for prevention. This is important as a cure for dementia is still lacking.

Mechanistic evidence and animal models suggest that nutrients can be directly implicated in modifying brain damage. Micro- (vitamins) and macronutrients (fatty acids) are natural antioxidants that can reduce oxidative stress levels in the brain. Moreover, some micronutrients and fatty acids modulate the production and activity of neurotrophins (proteins implicated in the development, function, and survival of neurons), have vasoprotective effects, and favour the clearance of β amyloid. Sufficient intake of nutrients is also important to avoid micronutrient deficiencies that are potentially harmful to the brain. Therefore evidence on the association between nutrients and cognitive impairment spans treatment and prevention of micronutrient deficiencies, to investigations of the potential beneficial effects of healthy dietary patterns (e.g. the so-called Mediterranean diet) or supplements.

The association of diet and nutrients with cognitive function, impairment and dementia has received much attention in past decades. Evidence from cross-sectional studies showed that compared to adults with dementia, healthy older people tend to have a healthier diet, richer in fruits and vegetables, rather than meat, processed carbohydrates and fats. Because dementia alters dietary habits, these initial studies have been useful in generating hypotheses but could not prove any causal link. Prospective cohort studies with long follow-up intervals are needed to clarify the direction of the association under study. When associations are biologically plausible, reported consistently across numerous studies, and independent of potential confounding factors, epidemiologic evidence can inform dietary recommendations to reduce risk of dementia in populations.

Experimental evidence from randomised controlled trials always provides the best basis for guiding treatment and prevention strategies. However, dementia is a multifactorial chronic disease, with a long latent period between the beginning of complex pathophysiological mechanisms and the clinical, detectable onset of symptoms. Definitive trials may therefore be difficult to conduct, particularly when treatment or prevention may need to be implemented in mid-life to delay or prevent dementia onset in late-life, and their feasibility to test the effect of diet on dementia risk may be limited.

In this chapter we will summarise and review the expanding epidemiological and clinical trial evidence assessing the relevance of nutrition to cognitive impairment and dementia. Nutrient deficiencies and their associations with cognitive decline will be described from cohort studies, and the evidence surrounding the benefits of nutrient supplementation will be derived from randomised controlled trials. Searches were carried out on Pubmed/Medline and the Cochrane Library using the search strategies included in Appendix 1. Reference lists to identify further studies were also hand-searched.

B vitamins

Introduction

Researchers have had a long interest in the link between neurological disorders and vitamin B complex, with first reports of a relationship between vitamin B_{12} and 'subacute combined degeneration of the cord' dating back to 1849[2]. B vitamins are organic, water-soluble, chemical compounds that cannot be synthesised in sufficient quantities by an organism and have to be acquired through diet. B vitamins play key roles in cell metabolisms. There are eight different chemically distinct types of vitamin B, with B_6, B_9 and B_{12} all being linked with protective roles in cognition (see Box 3.1).

Folate (vitamin B_9) and vitamin B_{12} have related roles in the metabolism of DNA and protein synthesis. They are both essential for the remethylation of homocysteine to methionine by using 5-methyltetrahydrofolate (THF) as a methyl donor. When folate or vitamin B_{12} are deficient, homocysteine levels rise, which may contribute to amyloid and tau protein accumulation and neuronal death. Homocysteine stimulates apoptosis and neurotoxicity (leading to nerve cell death), and platelet activation (contributing to white matter lesions, vascular injury and ischaemic strokes[3]).

Deficiencies in B_{12} and in folate increase with age. In a UK study the prevalence of B_{12} deficiency was 5% in people aged 65–74, doubling to 10% in people aged 75 and over, with similar trends reported for folate deficiency[4].

Box 3.1

B vitamins

Vitamin B_6, also known as pyridoxine, is involved in the synthesis of haemoglobin, neurotransmitters, and the production of Vitamin B_3. Pyridoxine is also involved in the metabolism of lipids and amino acids.
Sources: bread, eggs, fish, milk, peanuts, potatoes, pork, poultry, soya beans, vegetables
Guideline intake*: 1.7 mg a day for men, 1.5 mg a day for women

Vitamin B_9, also known as folate, is involved in the production of red blood cells, in the metabolism of amino acids and nucleic acids and in aiding normal cell division during pregnancy.
Sources: asparagus, broccoli, brown rice, brussels sprouts, chickpeas, liver, peas, spinach
Guideline intake*: 0.4 mg a day

Vitamin B_{12}, also known as cobalamin, is essential in the production of red blood cells (together with folic acid) and nerve sheaths, and in the metabolism of carbohydrates, lipids and proteins.
Sources: cheese, cod, eggs, meat, milk, salmon
Guideline intake*: 0.0024 mg a day

*Guideline intakes are for adults aged 50 and over and are based on dietary reference intakes (DRI) issued by the Food and Nutrition Board of the Institute of Medicine.

Evidence from the latest reviews

The association between B vitamins and cognition has been the subject of several recent systematic reviews.

O'Leary and colleagues identified 35 cohort studies (with a total population of 14,235 participants and a mean sample size of 409 subjects) that assessed the relationship between serum vitamin B_{12} or B_{12} biomarkers and dementia[5]. Only 21 studies were deemed to be of good quality, and among those only seven studies reported significant associations between B_{12} status and AD, dementia or cognitive decline, the conclusion being that there was insufficient evidence to reach a final verdict on this relationship. However, the subgroup of studies that assessed B_{12} status using a marker with greater specificity (e.g. methylmalonic acid (MMA), holotranscobalamin (holoTC)), reported consistent associations with cognition.

There is also insufficient evidence to support an association between either folate or B_6 deficiency and cognitive impairment or dementia with mixed findings reported in reviews of prospective studies[6-8]. An added problem, which may partially explain the heterogeneity of results, is the fact that few studies consider the underlying nutrient status of the populations studied; this issue is particularly important in the case of folate, because folic acid fortification in certain countries has led to an almost complete eradication of folate deficiency[9].

As mentioned in the introduction, deficiencies in B_{12} and folate can lead to an abnormal elevation of homocysteine (Hcy) blood levels, called hyperhomocysteinaemia (HHcy). Homocysteine levels have also been identified as a potential modifiable risk factor for dementia, and there seems to be more consistent evidence regarding the association between Hcy and dementia. One systematic review identified 12 retrospective studies assessing this relationship, and found that all studies apart from two found a significant relationship between Hcy levels and cognitive decline[10]. The consistent associations from

Table 3.1
Characteristics of included studies

APSYMAD (Asymptomatic and partially symptomatic Alzheimer's disease). tHcy (total homocysteine), holoTC (holotranscobalin). a) population of people with previous stroke or transient ischaemic attack b) population of community-dwelling older people with depressive symptoms c) participants with MCI. $ participants with low B vitamin levels were selected/analysed

Study/ location/ reference	Population (sample size and baseline mean age)	Follow-up (years)	Exposure/ Intervention measure	Control group	Outcome measure	Effect
Longitudinal/cohort studies						
Morris et al. 2012 Framingham, USA	n=549 74.8	8	Vitamin B_{12}, folate		Cognitive decline	Protective
Hooshmand et al. 2011 Kuopio, Finland	n=274 70.1	7.4	tHcy, holoTC, folate		Cognitive decline	Direct effect between tHCy and some cognitive domains, mainly non-statistical associations between holoTC, folate and cognitive functions
Ford et al. 2012 Perth, Australia	n=4,227 77.9	5.8	tHcy		Dementia risk	direct
Zylberstein 2011, Gothenburg, Sweden	n=1,368 46.8	35	tHcy		Dementia risk, AD risk	direct
Randomised controlled trials						
Hankey et al. 2013 20 countries	n=8,164[a] 63.5	2.8	B vitamin treatment (folic acid 2 mg, vitamin B_6 25 mg, vitamin B_{12} 0.5 mg)	placebo	tHcy, cognitive decline, cognitive impairment	No effect on cognitive impairment or decline but lowering of tHcy
Douaud et al. 2013 Oxford, UK	n=156 76.5$	2	B vitamin treatment (folic acid 0.8 mg, vitamin B_6 20 mg, vitamin B_{12} 0.5 mg)	placebo	Cerebral atrophy in grey matter regions	Grey matter regions athropy slowed down in individuals with high homocysteine levels
Walker et al. 2013 3 cities, Australia	n=900[b] 65.9	2	B vitamin treatment (folic acid 0.4 mg, vitamin B_{12} 0.1 mg)	placebo	Cognitive function	Improvement in cognitive function (in particular in immediate and delayed memory performance), but not in other domains
De Jager et al. 2011 Oxford, UK	n=226[c] 76.7$	2	B vitamin treatment (folic acid 0.8 mg, vitamin B_6 20 mg, vitamin B_{12} 0.5 mg)	placebo (vitamin-free tablets)	Cognitive decline	Lowering of tHcy. Improvement in global cognition, episodic memory and semantic memory but only in participants with baseline homocysteine levels above the median
Kwok et al. 2011 Hong Kong	n=140 78.15$	2	Folic acid 5 mg, methylcobalamin 1 mg	placebo (capsules containing starch)	tHcy, cognitive decline	Lowering of tHcy. No effect on cognitive decline, with the exception of the group with elevated plasma tHcy

these epidemiological studies have led to an increase in trials of interventions targeting homocysteine levels and their consequent effect on cognitive function. Nineteen English language trials of B vitamin supplementation targeting lowering of elevated homocysteine levels have been synthesised and meta-analysed[11]. The dosage and composition of the supplementation varied across studies, but mainly consisted of vitamin B_6, vitamin B_{12} and folic acid alone or in any combination. Dosage of vitamin B_{12} ranged between 0.05–1 mg, vitamin B_6 between 3–50 mg and folic acid 0.75–15 mg. B vitamins supplementation, in any form, was found to be effective in reducing total homocysteine (tHcy) levels in older people with or without significant cognitive impairment. However, the pooled estimates of the meta-analyses suggested that

supplementation with B vitamins did not improve cognitive function either in cognitively impaired or healthy individuals, irrespective of study size, study duration and whether the countries from which participants were recruited had instituted folate fortification procedures.

New studies

Since the latest reviews, a number of new studies have been published (Table 3.1). The role of B vitamins/homocysteine in cognitive decline has been explored in four cohort studies. In the Framingham study, participants with plasma vitamin B_{12} concentrations of 257 pmol/L or less had a significantly faster cognitive decline than individuals with higher concentrations, and the cognitive disadvantages linked to low vitamin B_{12} were increased at high folate levels[9], suggesting that there may be an interaction between vitamin B_{12} and folate on cognition status. The other three cohort studies investigated the relationship between homocysteine and cognitive decline or dementia risk[12-14]. All the studies identified a direct relationship between high homocysteine levels and poor cognitive function, strengthening the findings from previous studies. The Australian "Health in Men Study" reported that tHcy was related with an increased risk of dementia and cognitive impairment after a follow up of almost 6 years. Similar findings were also reported by two Scandinavian cohorts[12,14], backing up the evidence of the systematic review.

Several new randomised controlled trials have also been published in the past couple of years with mixed results (Table 3.1). One of the largest studies was carried out across 20 countries in 8,164 people who previously had a stroke or a transient ischaemic attack[15]. Although mean tHcy levels were reduced after B vitamins supplementation, there was no significant effect on cognitive decline. Lowering of tHcy levels was also seen in two other trials, neither of which reported a significant effect of homocysteine lowering treatment on the reduction of cognitive decline[16,17]. However, clinical benefits in cognition were seen in the groups that already had elevated homocysteine levels. In a similar fashion, a UK study[18] identified that B-vitamin supplementation was associated with a decline of cerebral atrophy in the grey matter regions of the brain that are vulnerable to Alzheimer's disease, but that this beneficial effect was limited to participants with high homocysteine levels (above 11µmol/L). No studies specifically recruited only those participants who were B_{12}/folate deficient or who had hyperhomocysteinemia, however some studies, as described above, considered baseline levels in their analyses. These studies are identified with a small $ sign in the table.

Conclusions

So far, cohort studies have produced inconclusive evidence on the association between vitamin-B deficiency and cognitive decline, but have seemed to confirm that high levels of homocysteine are associated with poorer cognition.

Randomised controlled trials have shown that supplementation with B vitamins can consistently reduce levels of homocysteine, but that this does not necessarily translate into slower cognitive decline, improvement in cognitive function or reduction in dementia incidence. It is important to note that more encouraging findings have been reported in individuals with higher homocysteine levels at baseline, suggesting that those with clear and defined deficiencies may be the ones who could actually benefit from vitamin supplementation.

Antioxidants

Introduction

Neural inflammation and oxidative damage are thought to be key mechanisms in the development of dementia, and in particular of Alzheimer's disease (AD) and Dementia with Lewy bodies (DLB). Oxidative stress directly damages cell components, resulting in damage to synapses and nerve cell death. Antioxidants (Box 3.2) are thought to act against neurodegeneration by limiting the production of toxic substances and by reducing damage by free radicals[19]. There are relatively fewer antioxidant enzymes specifically focused on neuronal protection, suggesting that antioxidant nutrients may have a more prominent role in older and ageing brains than in other organ systems[20].

Evidence from the latest reviews

Most of the research that has investigated the relationship between antioxidants and cognitive function has focused on vitamin E. Most of the longitudinal studies that have investigated this relationship using a food frequency questionnaire have reported an inverse association between vitamin E levels and the incidence of cognitive decline or dementia[21]. The evidence is not as conclusive and consistent in the studies that have assessed vitamin E status using biochemical levels (concentrations of individual tocopherols). It has been suggested that this may be due to the fact that total tocopherols levels, rather than the individual components, may be more important for neuroprotection[21]. This seems to be supported by studies that have reported a significant relationship between low levels of total tocopherols, cognitive decline and incident dementia[22,23].

The role of flavonoids and vitamin C has also been scrutinised[21,24,25], but the evidence from cohort studies is once again very mixed and inconclusive, with highly heterogeneous studies (e.g. deficiency definition, populations, follow-up time, investigated outcomes, etc.) showing inconsistent results for both types of antioxidants.

A recent Cochrane systematic review did not find any supportive evidence that vitamin E supplementation is beneficial to cognition[26]. This review identified three randomised controlled trials. Only one study found vitamin E to have some beneficial effects[27], with the two other studies showing no significant changes in cognitive decline and no slower conversion from mild cognitive impairment to Alzheimer's disease[28,29]. Further details are given in Chapter 5. Similar inconsistent results have been reported by Mecocci and colleagues who have reviewed clinical trials of antioxidants, not focusing solely on vitamin-E but also considering other nutrients with antioxidant properties[30]. One of the potential explanations to support the lack of positive findings is the low permeability of the blood brain barrier to the type of antioxidants that are currently used, which suggests the need to identify new delivery systems.

New studies

The Nurses' Health study, which followed up 16,010 older participants for an average 6.4 years, has recently published on the association between antioxidants and cognition (Table 3.2). Vitamin C and E were assessed using a semi-quantitative food frequency questionnaire, but no consistent associations between vitamin C and E intake and cognitive decline were identified[31]. In the same study, with regard to flavonoids (berries in particular), a higher intake of strawberries and blueberries was associated with slower cognitive decline at follow up[32].

There are four recently published trials of antioxidant supplementation (Table 3.2), not included in recent reviews. Using a double-blinded, parallel arm study, an Italian group randomised 90 adults with mild cognitive impairment to consume a drink containing either 900 mg (high), 520 mg (intermediate) or 45 mg (low) levels of flavanols for 8 weeks[33]. Participants consuming drinks with high levels or intermediate levels of flavanols had better scores in some cognitive domains at the end of the trial, compared to the control group, but there were no overall differences in general cognition. Two studies, one in Washington State (USA) and one in France, assessed the effect of a daily dose of 120 mg of a ginkgo biloba extract, a potent antioxidant, on cognition, both reporting negative findings. The American study did not report any significant improvement in cognitive performance in people with multiple sclerosis, after the 12 week intervention[34]. Similarly, the 5 year ginkgo biloba intervention on a group of 2,854 French participants did not slow down conversion to Alzheimer's disease[35]. Finally, one of the largest and longest multivitamin trials did not report any differences in mean cognitive change between the intervention and the control

Box 3.2

Antioxidants

Antioxidants include several different nutrients, such as vitamin C, vitamin E and flavonoids.

Vitamin E belongs to a group of eight fat-soluble complexes, which include tocopherols and tocotrienols. Vitamin E has important antioxidant functions, but it is also involved in gene expression and cell signalling, enzymatic activities and neurological functions.
Sources: nuts and seeds, plant oils (corn, olive and soya oil), wheat germ
Guideline intake*: 15 mg a day

Vitamin C also known as ascorbic acid or ascorbate, is a water-soluble vitamin, which cannot be stored in the body, and is a co-factor for several enzymatic reactions. Vitamin C is essential for connective tissue maintenance, helps protect cells and has important roles in wound healing. Vitamin C also has antioxidant properties.
Sources: blackcurrants, broccoli, brussel sprouts, oranges and orange juice, red and green peppers, potatoes, and strawberries
Guideline intake*: 90 mg a day for men, 75 mg a day for women.

Flavonoids are a class of plant secondary metabolites, responsible for many plant colours. The term "flavonoids" include several different chemical structures, including flavanones, flavanonols, flavans, anthocyanidins and anthoxanthins. Flavonoids have antioxidant properties, but also support vitamin C, help with inflammation control, and in some cases have antibiotic properties.
Sources: dark chocolate, dry beans, fruit (citrus, grapes, apples, berries), grains, herbs (thyme, parsley, celery, hot peppers), soy foods, tea, vegetables (broccoli, kale, onions, scallions [spring onions]) and wine.
Guideline intake: no current guidelines

*Guideline intakes are for adults aged 50 and over and are based on dietary reference intakes (DRI) issued by the Food and Nutrition Board of the Institute of Medicine

Table 3.2
Characteristics of included studies investigating antioxidants and cognition

a) participants with mild cognitive impairment b) participants with multiple sclerosis

Study/ location/ reference	Population (sample size and baseline mean age)	Follow-up (years)	Exposure/ Intervention measure	Control	Outcome measure	Effect
Longitudinal/cohort studies						
Devore et al. 2012/2013 United States	n=16,101 74.2	6.4	Vitamin C (diary) Vitamin E (diary) Flavonoids (diary)		Cognitive decline	Vitamin C and E were not consistently related to cognition. Higher intake of flavonoids reduced rates of cognitive decline
Randomised controlled trials						
Desideri et al. 2012 Italy	n=90[a] 71.1	8 weeks	Cocoa Flavanols drink (990 mg high/520 mg intermediate)	Cocoa Low flavanol drink (45 mg low)	Cognitive function	Improvement in some cognitive domains (verbal fluency, visual attention/task switching) but not in overall cognition
Grodstein et al. 2013 Unites States	n=5947 71.6	12 years	Supplementation of β-carotene(lurotin, 50 mg), vitamin E (α-tocopherol, 400IU), ascorbic acid (500 mg) and multivitamin (centrum silver)	Placebo	Cognitive function	No difference in mean cognitive function changes between intervention and placebo group
Lovera et al. 2012 United States	n=120[b] 52.1	12 weeks	Ginkgo biloba supplement (120- mg)	Placebo	Cognitive function	No improvement in cognitive function in the intervention group
Vellas et al. 2012 France	n=2854 76.3	5 years	Ginkgo biloba supplement (120- mg)	Placebo (containing quinine hydrochloride)	AD risk	No reduction of AD risk in the intervention group

group[36]. This study was once again not limited to undernourished or vitamin deficient individuals, and the vitamin dosage may have been too low to have an effect on this population, potentially explaining the negative findings. No clinical trials were specifically limited to people with low levels of vitamin E/C or flavonoids.

Conclusions

There is currently insufficient evidence from either longitudinal studies or randomised controlled trials to support a role for antioxidants in cognition. The only consistent associations were reported in studies that have assessed vitamin E status using food frequency questionnaires, rather than biochemical measures, suggesting that more work is needed to better understand these nutrients and their relationship with dementia.

Omega-3

Introduction

Alpha linolenic acid (ALA), eicosapentanoic acid (EPA), and docosahexanoic acid (DHA) are omega-3 polyunsaturated fatty acids (PUFA), which means that in the long carbon chain of which they are made, there is a double bond at the third carbon atom from the end (or w-3).

Omega-3 PUFA cannot be synthesised in the human body but are very important, particularly for the brain – therefore they are an essential dietary constituent. Brain tissue is made primarily by lipids and DHA is the most abundant structural omega-3 PUFA in the brain. Over 22% of both the cerebral cortex and the white matter are made of phospholipids, and their fatty acids composition is heavily influenced by diet, which affects in particular cell membranes. The function of cell membranes is modulated by their fatty acid composition. Dietary omega-3 PUFA are

also implicated in neuronal growth and influence synapse formations, thus impacting also on the interaction between neurons. Dietary omega-3 PUFA are important throughout life, from before birth (particularly during the third trimester of pregnancy), to older age when diets poor in omega-3 PUFA accelerate the physiological reduction of their concentration in cell membranes in the nervous system.

The main food sources of omega-3 PUFA are 'oily fish' such as salmon, mackerel, herring, sardines, fresh tuna, and swordfish. Eggs and meat may contain DHA and EPA if animals are fed with diet rich in ALA. In humans the conversion of ALA in DHA and EPA is not efficient, thus foods rich in ALA, like soybean, black currant, and nuts are minor sources of omega-3 PUFA.

There are several potential mechanisms for a protective effect of dietary omega-3 PUFA in dementia (Box 3.3). Omega-3 PUFA may be implicated in the vascular, inflammatory and also the amyloid pathways of dementia, and are therefore potentially important in vascular dementia, Alzheimer's disease and mixed forms.

Evidence from latest reviews

The relationship of omega-3 PUFA with cognitive impairment and dementia has been investigated in cross-sectional and cohort studies, and in randomised controlled trials.

Cross-sectional studies have shown that older people with dementia consume significantly less fish and more meat than those without dementia[37], and that people who consume more fish have better cognitive function in mid-life[38]. However, evidence from longitudinal studies is conflicting. In a recent meta-analysis, Lin et al. have demonstrated that the concentration of omega-3 PUFA (EPA, DHA) is significantly reduced in older people with dementia compared to those without the disease. Whether this reduction is a consequence of the disease and particularly of brain damage is unknown[39].

There was a lower risk of incident dementia in the Rotterdam study in the short-term[40] but not in the long-term follow-up[41]. Risk of dementia was reduced also in the Three-City cohort study in France[42], and in older people in the Chicago Health and Aging Project (CHAP)[43] amongst those who consumed more fish and whose diets were richer in omega-3 PUFA content compared to their counterparts. However, the association between higher fish consumption and lower dementia risk was apparently confounded by educational level and healthy lifestyle in another French PAQUID cohort study[44]. Furthermore, serial cognitive testing over 4 years was not related with dietary consumption of omega-3 PUFA in the Women's Health Study[45].

Negative results have been reported in studies that used the plasma concentration of omega-3 PUFA as exposure rather than dietary consumption of fats in relation to subsequent dementia risk. In the Canadian Study of Health and Aging, higher plasma concentration of omega-3 PUFA at baseline were found in those who developed dementia at the 5-year follow-up compared to those who did not[46]. In the Uppsala Longitudinal Study of Adult Men, after more than 30 years follow-up dementia incidence did not vary by baseline measurements of plasma concentration of omega-3 PUFA[47]. However, lower DHA concentration in red blood cells was

Box 3.3

Omega-3 PUFA

Postulated mechanisms for the protective role of omega-3 PUFA in dementia.

1 Cardiovascular and cerebrovascular protection – omega-3 PUFA have antiarrhythmic and antithrombotic effects that reduce the risk of both stroke and diffuse microinfarcts. Omega-3 PUFA also have antiatherogenic effects, and may improve endothelial function benefiting the integrity and health of arteries. Moreover, omega-3 PUFA lower blood pressure levels and improve serum lipid profiles, both of which are implicated in dementia risk.

2 Omega-3 PUFA directly reduce the synthesis of cytokines that have pro-inflammatory functions (like interleukin 1 and 6), which in turn can reduce the brain inflammation that accompanies brain damage.

3 Omega-3 PUFA, particularly DHA, are key components of the phospholipids that form cell membranes and preserve the integrity and the function of neuronal membranes.

4 Omega-3 PUFA modulate the metabolism of the amyloid precursor protein and may reduce the formation and favour the clearance of β amyloid, the main component of the extracellular plaques deposited in Alzheimer's disease.

Guideline intake*: 1.6g a day per men, and 1.1g a day per women

*Guideline intakes are for adults aged 50 and over and are based on dietary reference intakes (DRI) issued by the Food and Nutrition Board of the Institute of Medicine.

Table 3.3
Characteristics of included studies

PUFA (total polyunsaturated), DHA (docosahexaenoic acid), EPA (eicosapentaenoic acid), MNA (Mini Nutritional Assessment).
a) participants with MCI. $ participants were excluded if they ate fish more than once per month and if they had taken fish oil supplements in the previous 3 months

Study/ location/ reference	Population (sample size and baseline mean age)	Follow-up (years)	Exposure/ Intervention measure	Control	Outcome measure	Effect
Randomised controlled trials						
Stough et al. 2012 Australia	n=50 71.1	3 months	HiDHA® (1000 mg of tuna oil comprising of 252 mg DHA, 60 mg EPA, 10 mg vitamin E).	1000 mg of tuna oil	Cognitive function	No significant effect of DHA on cognitive functioning
Sinn et al. 2012 Australia	n=78[a] 74.1[$]	6 months	Either EPA-rich fish oil (1670 mg EPA +160 mg DHA) or DHA-rich fish oil (1550 mg DHA +400 mg EPA)	Safflower oil (containing 2.2.g of n-6 PUFA linoleic acid)	Cognitive function	No significant effect of supplementation and cognitive domains. Reduction in depressive symptoms in treatment groups
Rondanelli et al. 2012 Italy	n=25[a] 85.7	12 weeks	Oily emulsion (DHA 720 mg, EPA 280 mg, vitamin E 16 mg, soy phospholipids 160 mg, tryptophan 95 mg, melatonin 5 mg)	Non-fish oil placebo	Cognitive function	Improvement in cognitive function, and also improvement in MNA scores

cross-sectionally associated with smaller brain volume and worse cognitive performance in the Framingham study[48].

Evidence on the potential enhancing effect of omega-3 PUFA on cognitive function from childhood to older age has been recently reviewed[49]. Luchtman and colleagues concluded that there is strong evidence of a beneficial effect of omega-3 PUFA to improve cognitive impairment in those who have an insufficient intake, particularly of DHA through diet. However, epidemiologic and experimental evidence on the potential protective effect of omega-3 PUFA to prevent dementia or slow cognitive decline was considered to be weak.

Similar conclusions were reached in a recent Cochrane systematic review of randomised controlled trials that tested the efficacy of omega-3 PUFA supplementation to prevent cognitive impairment in cognitive healthy people. Though only three studies could be included in the meta-analysis[50,51,52], their results consistently showed no beneficial effects of omega-3 PUFA supplementation for the prevention of cognitive decline[53]. In a further review that included additional trials on the effect of omega-3 PUFA supplementation also in participants with cognitive impairment or dementia, Dangour et al. similarly concluded that the use of omega-3 PUFA supplements for prevention or treatment of cognitive impairment in older age cannot be recommended on the basis of the available experimental evidence, regardless of level of cognitive function when supplementation starts[54].

New studies

Three new randomised controlled trials have recently been published testing the effect of omega-3 supplementation on cognitive decline (Table 3.3). Cognitive function was tested after a 90-day supplementation with the Omega-3 essential fatty acid docosahexaenoic acid (DHA) in a group of 74 healthy participants[55]. No significant effects of the intervention on cognitive function were reported. Similar non-significant results were reported by an Australian group, who carried out a 6-month double-blind trial of n-3 PUFA, DHA and EPA in a group of people with mild cognitive impairment. Cognitive functions did not improve in the intervention groups compared to the control group, with the exception of verbal fluency in the DHA group. However, depressive symptoms scores were reduced in both groups that received supplementation (DHA or EPA) compared with the control group[56]. Participants with mild cognitive impairment were also the subject of another intervention trial that was conducted in a small group of 25 adults[57].

The intervention, lasting for 12 weeks, was a supplementation with an oily emulsion of DHA. Several domains of cognitive function were reported to be improved in the intervention group, compared to placebo, including overall cognitive function, measured using the Mini-Mental State Examination (MMSE). These results should however be interpreted with caution because of the small sample size. Moreover the results were not adjusted for multiple comparisons and MMSE

was one of several endpoints, suggesting that these findings may be explained by chance.

Conclusions

The evidence on the beneficial effects of fish consumption to prevent dementia incidence is overall conflicting, but a protective role does not seem to exist. Healthy lifestyles and life circumstances (including socio-economic and educational level) that are associated both to higher fish consumption and lower dementia risk may explain the positive results found by some studies.

Evidence from experimental studies on the beneficial effects of omega-3 PUFA supplementation is insufficient to recommend their use in populations either for the prevention, or treatment or amelioration of dementia. But dietary recommendations to increase the amount of the intake of omega-3 PUFA from foods and the use of supplements in those who be deficient in these fatty acids, particularly of DHA, seems indicated for other reasons.

Some issues related to experimental studies may exist that could explain the weak results reported so far. Longer follow-ups may be needed to observe significant changes in cognitive function in primary prevention trials because changes in cognitive function were somewhat minimal in both the treated and placebo arms of existing trials. An additional concern exists regarding the experimental integrity of these trials, because the absence of limitations in fish consumption may have diminished the difference in total dietary omega-3 PUFA intake between those who were given the supplement and those who receive placebo.

Mediterranean diet

Introduction

Several studies have reported that a Mediterranean diet (Box 4) is associated with reduced risk for a number of outcomes, including cardiovascular disease, type 2 diabetes, some forms of cancer and overall mortality[58]. More recently, there has been an increased interest in understanding the potential protective role of such diet against dementia risk and cognitive decline.

Three main biological mechanisms, relating to impact on the vascular system, oxidative stress and attenuation of the inflammatory pathway, have been proposed to support these associations. The Mediterranean diet could reduce the risk of dementia by affecting the vascular system, reducing cardiovascular disease, which in itself is a risk factor for dementia. However, this hypothesis does not seem to be supported by Scarmeas and colleagues[59] who have shown that the association between Alzheimer's disease and the Mediterranean diet is not mediated by vascular co-morbidity.

Oxidative stress has also been suggested as a potential mechanism to explain an association between the Mediterranean diet and dementia. Cognitively impaired brains show evidence of injury mediated by highly unstable reactive oxygen and nitrogen species. Some of the components of the Mediterranean diet (e.g. vegetables, olive oil, wine and fruits) are rich in antioxidants. Neutrophins, which are basic proteins, usually protect neurons against oxidative stress, and some have proposed that the Mediterranean diet could increase the concentration of plasma neutrophins[60].

Finally, the Mediterranean diet could reduce the risk of dementia by limiting pro-inflammatory cascades, reducing C-reactive protein levels and inflammatory cytokines such as IL-6[61,62]

What is the evidence?

The effect of the Mediterranean diet on cognitive decline and dementia risk has been assessed in nine longitudinal studies (Table 3.4). Six were conducted in the United States, one in Australia, one in France and one in Greece. Five studies investigated cognitive decline, four dementia risk (three specifically risk of AD), and three Mild Cognitive Impairment (MCI) risk. The average sample size was 1,715 individuals (SD=888). The follow-up period ranged between 2.2 and 8 years. Non adherence to a Mediterranean diet was associated with cognitive decline in three studies [63] [64,65], but no significant associations were reported by Psaltopoulou[66] and by Cherbuin[67]. Higher Mediterranean dietary pattern scores using the MedDiet assessment were related to slower rates of cognitive decline after adjustment for age, sex, education, race, energy, and participation in cognitive activities in a study in the Chicago Health and Aging Project (CHAP)[64]. Similar findings were reported in the Washington Heights Inwood and Columbia Aging Project (WHICAP)[65] and the French "Three-City Cohort"[68]. In the latter, higher adherence to a Mediterranean diet was associated with slower cognitive decline, measured using the Mini Mental State Examination (MMSE), but was not associated with a lowered risk of incident dementia. Two other cohort studies [65,69,70] investigated the association between Mediterranean diet and incident Alzheimer's disease, both reporting lower risks for AD among people who had better adherence to Mediterranean diet. The WHICAP study also reported that higher adherence to this diet was linked to a reduced risk of converting from Mild Cognitive Impairment to Alzheimer's

disease (HR 0.55, 95% CI 0.34–0.90)[71], but with no reduced risk of developing MCI (HR 0.72, 95% CI 0.62–1.12). MCI a finding (i.e. no reduced risk of MCI) shared by Cherbuin and colleagues[67]. A recent meta-analysis of four longitudinal cohort studies reported that people who had a high adherence to the Mediterranean diet had a 40% reduced risk of incident cognitive impairment (RR 0.72, 95% CI 0.58-0.88).

To date, only one study, the PREDIMED-NAVARRA randomised trial[72] has attempted to test this association in an experimental design, by comparing a nutritional Mediterranean diet intervention supplemented with either extra-virgin olive oil (EVOO) or mixed nuts, with a low-fat control diet. The intervention that lasted 6.5 years showed encouraging results, where participants that supplemented Mediterranean diet with EVOO

Box 3.4

What constitutes a Mediterranean diet?

A diet with a high intake of cereals, fruits, fish, legumes, and vegetables. This diet is often rich in unsaturated fatty acids, its main source being olive oil, and low intake of meat, poultry and saturated fatty acids. Dairy products intake, especially yogurt and cheese, tend to be low to moderate and meals are often accompanied by a moderate amount of alcohol (particularly wine). This type of diet is particular common across Greece, Southern Italy, Spain and Morocco.

Table 3.4
Characteristics of included studies

FFQ (Food Frequency Questionnaire), SFFQ (Semi-quantitative Food Frequency Questionnaire), CDR (Clinical Dementia Rating), MCD (Mild Cognitive Disorder), MCI (Mild Cognitive Impairment), AD (Alzheimer's disease). a) median age

Study/ location/ reference	Population (sample size and baseline mean age)	Follow-up (years)	Exposure/ Intervention measure	Outcome measure	Effect
Longitudinal/cohort studies					
Cherbuin et al. 2012 Canberra, Australia	n=1,528 62.5	4	FFQ/MeDi score	Cognitive decline, MCD risk	Non-significant
Tagney et al. 2012 Chicago, USA	n=3,790 75.4	7.6	FFQ/MedDiet score	Cognitive decline	Protective
Roberts et al., 2010 Minnesota, USA	n=1,233 79.6[a]	2.2	FFQ/MeDi score	MCI risk	Protective
Gu et al. 2010 New York, USA	n=1,219 76.7	3.8	SFFQ/MeDi score	AD risk	Protective
Scarmeas et al. 2009b New York, USA	n=1,393 76.9	4.5	SFFQ/MeDi score	MCI risk, conversion to AD	Protective
Scarmeas et al. 2009a New York, USA	n=1,880 77.2	5.4	SFFQ/MeDi score	AD risk	Protective
Feart et al. 2009 Bordeaux, France	n=1,410 75.9	5	FFQ/MeDi score	Cognitive decline, dementia risk	Protective for cognitive decline, but non-significant for dementia risk
Psaltopoulou, 2008 Athens, Greece	n=732 60+	8	FFQ/MeDi score	Cognitive decline	Non-significant
Scarmeas et al. 2006 New York, USA	n=2,258 77.2	4	SFFQ/MeDi	Cognitive decline, AD risk	Protective
Randomised controlled trials					
Martinez et al. 2013 Navarra, Spain	n=285 74.1	6.5	MedDiet intervention	Cognitive decline, MCI risk, dementia risk	Protective

but not with mixed nuts, had better cognitive function, and significantly less incident MCI than the control group (OR for MCI = 0.34, 95% CI 0.12–0.97).

Conclusions

There is currently moderate evidence suggesting a positive link between adherence to the Mediterranean diet and dementia risk. Not all the studies did, however, report positive findings, in particular regarding cognitive decline. Unfortunately, there is very little evidence from clinical trials, with only one study that has used the Mediterranean diet as an intervention. This is potentially due to intrinsic difficulties of implementing such an intervention on a large scale, and in a sustainable way. More intervention studies are needed to further understand the preventive role of the Mediterranean diet, and the active ingredients for improving cognitive function and reducing dementia risk.

Overall conclusions

There is currently insufficient evidence to confirm a relationship between the micro- and macronutrients described above (vitamin B_6, vitamin B_{12}, folate, vitamin C, vitamin E, flavonoids, omega-3, Mediterranean diet) and cognitive function. Although some studies have shown positive results, particularly those using cross-sectional designs, the findings have not been consistently supported in prospective cohort studies, and preventive interventions have generally failed the critical test of randomised controlled trials (Table 5).

A review conducted for the 2011 World Alzheimer Report looking at treatment of established dementia concluded 'There is, as yet, no evidence to recommend the use of (micro) nutritional supplementation at any stage of dementia', and we believe that the statement is also currently applicable for prevention. Yet, supplementation for cognitive problems is a large market, with a recent survey of adults in the United States, reporting that 15 million Americans specifically consumed supplements to "prevent" or "treat" cognitive problems[73], with little empirical evidence.

In this chapter we have shown that there is, however, a strong theoretical basis for implicating deficiencies in these micronutrients in the known mechanisms of neurodegeneration, and that the negative results may be the result of methodological issues with current study designs, rather than with a lack of relationship per se. The main limitation is that trials have been few in number, and often small and underpowered. The duration of supplementation may have been too short to demonstrate an effect. It has also been suggested that simultaneous supplementation with multiple micronutrients (fatty acids, phospholipids, vitamins E, C, B_6 and B_{12}, and folic acid) might be required synergistically to increase brain levels of molecules that are essential building blocks of brain synapses. However, results from RCTs of such 'medical foods' are mixed, with preliminary data showing some improvement in specific cognitive tasks but not in overall cognition, clinical status, or functioning[74]. Moreover the majority of the studies have not focused on those with deficiencies of the supplemented micronutrient. It has been postulated that vitamin supplementation may

Table 3.5
Summary of evidence for each nutrient

↓ signifies decreased risk with higher levels of nutrient ↑ signifies increased risk

Nutrient	Type of association	Evidence for Cohort Studies	Evidence from Randomised Controlled Trials
Vitamin B_6, B_{12}, folate	↓	Insufficient conflicting evidence	Insufficient evidence (but encouraging for participants with high homocysteine levels)
Homocysteine levels	↑	Good evidence	
Vitamin C	↓	Conflicting, insufficient evidence	Insufficient evidence
Vitamin E	↓	Conflicting evidence (good evidence using frequency questionnaire, but not with biochemical levels)	Insufficient evidence
Flavonoids	↓	Insufficient evidence	Insufficient evidence
Omega-3	↓	Insufficient evidence	Insufficient evidence
Mediterranean diet	↓	Moderate evidence	Insufficient evidence

not be effective because the levels of nutrition in the researched populations are already at optimal level, and that most nutrients have an inverted U-shaped, non-linear, association with physiological functions[75]. This seems to be confirmed by the few more promising studies that specifically stated in their inclusion criteria that participants should be micronutrient deficient (see sections above). We therefore share the conclusion and recommendation of Morris and Tangney that

> "Clinical trials are both costly and important for substantiation of nutrient effects on health. The public health may be better served by initially conducting trails in individuals with insufficient nutriture and, if effective, further testing the effectiveness in those with adequate nutrient levels."[75]

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Chapter 4 Undernutrition in dementia

Undernutrition and underweight are common problems in older people. Weight loss is associated with increased morbidity and mortality, and it also worsens the prognosis for several chronic diseases[1,2]. Maintaining body mass seems to have a greater protective effect on health with increasing age[3], probably because the health risks associated with excess body weight (and fat) seem to be reduced in older people. A moderate excess of body fat may provide a '*reserve to the individual in times of stress, such as illness*'[3]. In older people weight loss is considered to be clinically significant or potentially harmful, when it amounts to 5% of total body weight or more over one year. A weight loss of 10 lb (4.5 kg) or more over few months is easily detected because of loose-fitting clothes or other obvious changes.

Weight loss occurs in part as a result of the ageing process itself, but underlying diseases often contribute[4], of which dementia, along with cancer and cardiovascular disease, is a well-recognised cause. In 1906 Alois Alzheimer recorded Ms August D's progressive weight loss in his celebrated case report[5]. This observation remained long neglected in research, and relatively few clinical studies followed[6]. However, nearly half of all patients with dementia experience clinically significant weight loss[7], and weight loss is now considered a characteristic feature of Alzheimer's disease[8].

Weight loss seems to precede the symptomatic onset of dementia by several decades[9–11], and accrues as the disease progresses[9,12]. Evidence from the 10/66 study confirms that the association between dementia and weight loss strengthens through the stages of dementia severity, and that geographical variations across diverse world regions are essentially negligible[13]. This may support a causal role of dementia on weight loss, with diverse underpinning mechanisms acting during the course of the disease.

In this chapter we aim to:

1 Provide an overview of the mechanisms that may underline dementia-related undernutrition / weight loss.
2 Systematically review the evidence on dementia-related undernutrition / weight loss.
3 Revise the evidence on the consequences of undernutrition in people with dementia.

We used PubMed and the Cochrane Library to retrieve publications of observational studies on dementia, dementia severity, dementia-related neuropathology and measures of undernutrition (i.e., low body weight, weight loss, changes in body composition). We further hand-searched references lists of relevant studies. We focused on existing reviews, which were integrated with new evidence when available.

Mechanisms

Introduction

Undernutrition results from an imbalance between nutrient/energy intake and needs. This is usually due to an inadequate diet, but can also be the result of altered digestion, absorption and metabolism of nutrients and energy from foods. Complex endocrine, nervous, cognitive and sensory signals and information are processed in the central nervous system in order to regulate energy homeostasis, mainly through modulation of food intake. Both pathways are likely to be implicated in dementia-related weight loss. Evidence suggests that dementia-related brain atrophy may impact on brain regions implicated in appetite control and energy balance including the mesial temporal cortex[14], the hypothalamus[15], and the cingulate gyrus[16], with metabolism in these

regions (a marker of brain activity) significantly reduced in dementia[17,18]. The existence of a hypermetabolic state has been demonstrated in animal models of AD, in mice that overexpress amyloid-precursor protein, but not as yet in humans[19].

Dietary habits are influenced by diverse factors, from food availability and preparation, to appetite, taste and feeding problems. Brain damage in general, and the cognitive and behavioural symptoms of dementia in particular influence these factors and hence may impact on dietary habits in different ways at different stages of dementia; in the pre-clinical phase, as neuropathology subtly builds up; in the early stages of dementia, when mild cognitive and psychological symptoms progressively appear along with impairments in complex activities of daily living; and finally in advanced dementia, when the impact of neurological and behavioural impairments are most evident. Feeding problems are extremely common in advanced dementia. Some degree of feeding supervision or assistance is almost always required. Aversive feeding behaviours are common, swallowing is slow and poorly coordinated, and oropharyngeal dysphagia (distinct from the laryngeal or oesophageal forms that are more usually encountered) can cause choking and food avoidance. The multifactorial and stage-specific nature of weight loss in dementia is corroborated by evidence on the natural history; weight loss starts decades before symptomatic onset and then accrues progressively from mild, to moderate and severe dementia[9–11,13].

Evidence from latest reviews

The various mechanisms that may explain weight loss in people with dementia have been comprehensively reviewed[20]. Mechanisms are illustrated in Table 4.1, along with examples of how the different pathologies and symptoms of dementia may interfere with dietary habit, and energy balance. Mechanisms can be broadly divided into those that may cause a reduction in energy intake, and those that may cause an increase in energy expenditure. The proposed mechanisms may act at different stages of the development of dementia syndrome (Table 4.1). Some may interfere with nutrition during the asymptomatic phase, as brain damage slowly progresses. Others are more prominent through the early (mild to moderate) stages of dementia (characterised by impairment of memory, changes in personality, and psychological symptoms including apathy, irritability and depression), which, along with the related difficulties in carrying out complex, instrumental activities of daily living (like shopping, and preparing meals) alter dietary habits more broadly.

Finally, aversive feeding behaviours and loss of interest in eating develop progressively in the advanced stages of the disease. A classification of these behaviours has been proposed by Blandford et al.[21] as summarised in Table 4.2. The underlying mechanisms are largely neurological, resulting from advanced cortical brain damage. Agnosia (loss of ability to recognise or comprehend the meaning of objects even with intact sensation), means that food may not be distinguished from non-food, and that feeding utensils are not recognised for what they are. Dyspraxia (loss of higher order control of complex motor functions) can lead to loss of feeding skills, for example normal use of plates, cups and cutlery. Oropharyngeal dysphagia is a prominent end stage feature of both AD and frontotemporal dementia, and can result from cortical (premotor, primary motor, primary somatosensory, insula) or sub-cortical neurodegeneration. Aversive feeding behaviours are, understandably, a source of considerable anxiety and strain for family caregivers – there is also evidence from one longitudinal study that such behaviours are more likely to present when caregivers have high baseline levels of strain[22].

Conclusions

Progressive undernutrition and weight loss are observed almost inexorably in dementia patients (see also below). There are numerous potential mechanisms, which may act from as early as the pre-clinical and asymptomatic phase of the disease to the most advanced stages, when aversive feeding behaviours are common, severely disrupting dietary intake, and making assistance at mealtimes indispensible and progressively more problematic.

Occurrence and dynamic of dementia-related undernutrition

Introduction

Numerous studies have investigated the association of dementia, or dementia severity with weight loss. Dementia-related weight loss can be conceived as the study of the natural history of body weight in those with dementia.

Evidence from latest reviews

A comprehensive review on weight loss and Alzheimer's disease, focussing upon prospective studies, was carried out in 2007 under the auspices of the International Academy of Nutrition and Aging (IANA)[21]. The first epidemiologic studies on the topic were carried out in the mid-nineties[32].

Table 4.1
Possible mechanisms of undernutrition (i.e. weight loss) in dementia from pre-clinical to advanced stages of the disease

Reduced energy intake	Example	Stage of the natural history of dementia when the mechanism is more relevant
Brain damage	Damage of brain regions implicated in appetite control and food intake (i.e. the hypothalamus, and mesial temporal cortex) causes anorexia	From the pre-clinical phase of the disease onwards
Cognitive impairment	Forgetfulness may lead to skipping meals Apraxia and impaired executive function may reduce the ability to use utensils and to prepare meals Aphasia and communication problems affect the ability to ask for food and communicate hunger Impaired decision-making ability may slow food choice and reduce intake	May prevail in the early stages of the disease, when severity is mild to moderate
Psychological symptoms	Apathy is associated with decreased interest in food Sadness, depressive symptoms are associated with anorexia	Mild to moderate stages of disease progression
Behavioural symptoms	Agitation/aggression/hostility lead to aversive feeding behaviours and interfere with family members and carers who may not be able or willing to provide meals or food	More likely when the disease is severe
	Personality changes can alter attitude towards food and change dietary preferences in ways that may be difficult to understand and meet	Personality changes may occur very early in the course of the disease, even before the clinical diagnosis
Sensory functions	Olfactory dysfunction (reduced sense of small), common in AD, affects taste and can reduce appetite	Progressive sensory dysfunction (loss of taste and smell) is part of normal ageing, but loss of smell is more marked in AD and may be present already in the pre-clinical stage and worsen with disease severity
Oral and dental health (see also Box 4.1 for more details on bidirectional associations with cognition)	Tooth loss, dental or gum disease, ill-fitting dentures, ulcers and infections impact on chewing and may cause pain that interferes with eating	These issues are a normal part of ageing, and may worsen when dental care is compromised as dementia symptoms progress
Motor disturbances	Wandering may lead to skipped or interrupted meals and may significantly reduce eating time	Moderate to severe stages of dementia
Social factors	In most cultures, eating is a social activity, from which people with dementia may be excluded, particularly when they develop feeding dependence (needing to be fed) Isolation, poverty and low socio-economic circumstances impact on food availability and on its nutritional quality	Depending on the social context, social factors can be prominent at any stage of the disease, including the pre-clinical phase when subtle personality changes may alter social relationships and mild cognitive impairment may impact on the socio-economic circumstances
Increased energy expenditure (EE)	**Example**	**Stage when more relevant**
Increased resting metabolic rate (RMR) (the energy required for basic metabolic functions at rest)		
Central hypermetabolism	Pathology of the hypothalamus and mesial temporal cortex can re-set RMR higher	All phases of dementia natural history, starting already at the pre-clinical phase
Inflammation	Increased systemic levels of pro-inflammatory molecules (interleukin 1, and 6, TNF-alpha) promote a catabolic state leading to loss of muscle mass	Pre-clinical phase, getting worse with the accruing of the inflammatory response in damaged brain regions
Physical activity EE	**Example**	**Stage when more relevant**
Motor disturbances	Wandering increases the average physical activity level	Severe stage
Sleep disturbance	Increase in waking hours means less resting time and higher EE	Mild to moderate, and exacerbates in the severe stage
Behavioural symptoms	Overexcitement / over activity may increase EE through increased body movements	From mild to severe stage

Table 4.2
Aversive feeding behaviours (adapted from Gillette-Guyonette et al.[21])

Dyspraxia/agnosia	Resistance	Oral neuromuscular incoordination (oropharyngeal dysphagia)	Selective feeding behaviours
Cannot use utensils properly Does not recognise food or eats non edible items present on the table Requires coaxing Wanders away from the table during meals	Turns head away from food or pushes food away Holds hands in front of mouth/ clenches teeth and lips Grabs, hits or bites feeding assistant Spits or throws food	Problems with mouth and tongue control e.g. does not open mouth; chews without swallowing; cannot form food bolus Problems passing bolus from mouth to pharynx	Change in preference for quality (e.g. taste or texture) or quantity of food Requests specific foods, which will complain about and refuse to eat

Box 4.1
Oral health and cognition

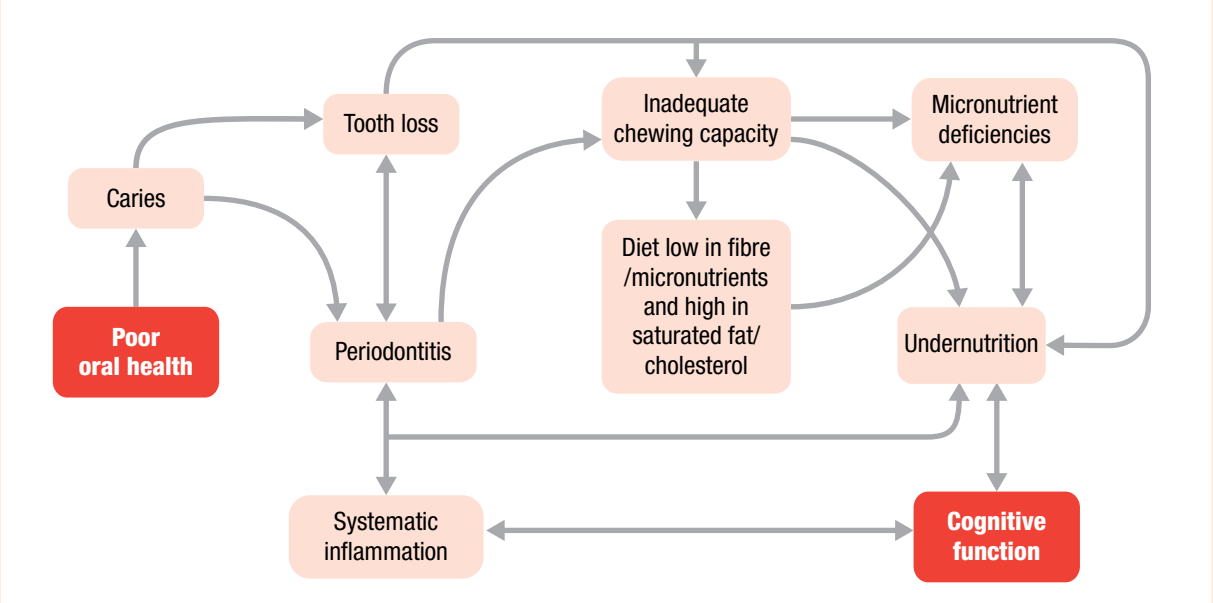
Oral health has an important but complex relationship with cognition (Figure 4.1). Poor oral health is most often thought of as an outcome driven by lack of access to routine oral care and inattention to oral hygiene among people with dementia. However, it may also be an underlying risk factor for cognitive impairment.

A recent review indicates relationships between poor oral hygiene, caries and dementia[23]. For example, a study conducted in Finland identified that people with AD had poorer oral hygiene (OR 12.2: 95% CI 1.9–77.0) and worse denture hygiene (OR 2.9, 95% CI 1.1–7.8), than people without AD[24]. This relationship has been reported to worsen with time; in a one year prospective study oral health deteriorated faster in people with dementia, including worsening caries[25].

Caries and poor oral hygiene can lead to periodontitis (a chronic infection affecting the tissues surrounding the teeth), which has been associated with tooth loss and also with poor cognitive performance in older people[23,26]. Several prospective studies have found a relationship between tooth loss and cognitive decline[27] or incident dementia[28].

Tooth loss leads to inadequate chewing capacity. This, in turn, can force people to adopt a diet low in fibres and micronutrients[29], and high in saturated fats and cholesterol, often easier to chew than foods rich in fibres[30], which, in the long term, can lead to micronutrient deficiencies (B_{12} and thiamine), undernutrition[31] and exacerbation of cognitive impairment.

Figure 4.1
The complex and multi-directional relationship between oral health and cognitive function, with potential mediators and confounders



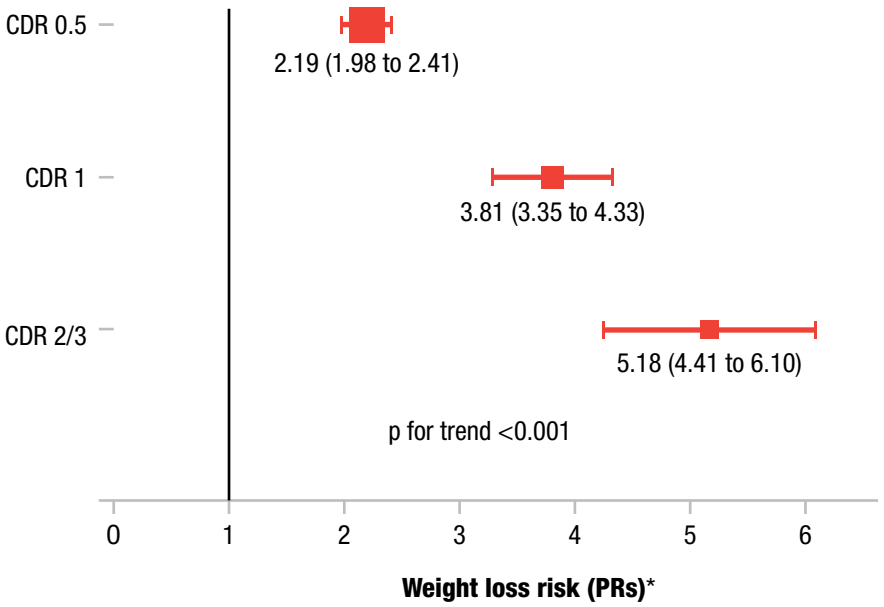
Since then consistent evidence has accumulated on the association of dementia, dementia severity and subsequent weight loss[12,33]. In a two year prospective study comparing those with mild to moderate dementia with controls, dementia was the sole factor independently associated with clinically significant weight loss of 5% of body mass or greater (OR 2.54, 95% CI 1.76–3.78). In another five year prospective study, controlling for age and gender, those with AD lost an average of 0.52 kg/m² compared with 0.14 in healthy controls[12,33]. In three French cohorts of those with mild to moderate Alzheimer's disease, clinically significant weight loss (4% or more of body mass over one year) was observed in 45% of patients (cohort size, n=76)[34], 33.4% (n=395)[35], and 20% (n=486)[36]. In a large north American cohort study, 666 patients with dementia were followed up for up to six years, allowing the natural course of disease progression and weight loss to be monitored beyond the mild to moderate stages observed in other studies[12]. The loss of weight tended to increase with the severity and progression of the disease; each one stage progression in Clinical Dementia Rating severity (from mild to moderate to severe) was associated with a loss of approximately one kilogram in weight.

The 10/66 study of dementia and ageing is the largest cross-sectional survey to date on dementia severity, quantified with the Clinical Dementia Rating scale, and reported weight loss[13]. We enquired about any weight loss of 4.5 kg or more experienced in the three months preceding the interview. This information was recalled by participants and was corroborated by an informant in all dubious cases. There was a strong, linear association between dementia and reported weight loss, resistant to adjustment for a variety of socio-demographic, lifestyle and health characteristics. Compared to older people who were cognitively healthy, those with dementia were two, four and five times more likely to have lost weight in the previous 3 months, if the severity of the disease was mild (CDR=0.5), moderate (CDR=1), or severe (CDR=2/3), respectively. This is illustrated in Figure 4.2.

The observed associations were very similar across eight very diverse low and middle-income countries in Latin America and Asia. The validated and highly standardised procedures applied in the 10/66 study allowed to directly compare the significance and magnitude of the association between dementia severity and weight loss in very diverse settings. Because these differences encompass lifestyle, culture, social structure and a number of other circumstances, the fact that weight loss was a consistent feature amongst patients with dementia, and that the likelihood of its occurrence increased linearly with the severity of the disease, supports the hypothesis that dementia causes weight loss.

The association between dementia and weight loss is indirectly supported by studies that found, contrary to prior hypotheses, that higher BMI in older age seems to protect against the onset of

Figure 4.2
Increase in weight loss risk by dementia severity calculated combining country-specific estimates
From Albanese et al. 2013[13]



*Meta-analytic prevalence ratios from Poisson models: CDR = Clinical Dementia Rating scale

cognitive decline and dementia[37–40]. Weight loss in those with incipient dementia likely explains the apparent paradox of a beneficial effect for dementia risk of higher adiposity in older age, since when trajectories of body weight or BMI from mid- to late-life in those with and without dementia in late-life are compared, those who had gone on to develop dementia had tended to lose weight more rapidly from mid-life onwards, a trend that may begin up to two decades prior the clinical diagnosis[9–11].

Weight loss in the pre-clinical phase of the disease is certainly not explained by the symptoms of dementia (either cognitive or behavioural), nor by impaired instrumental activities of daily living including shopping and cooking. During the pre-clinical phase of dementia, which may last decades, neuropathology is thought to build up progressively and slowly. Brain damage may therefore cause a decrease in appetite and may impair the central regulation of energy. This hypothesised mechanism is in line with research that shows that Alzheimer's disease neuropathology is associated with a steeper decline in BMI prior to death also amongst those that were not diagnosed with dementia before death[41].

Conclusions

Evidence on the association between dementia and weight loss is compelling. Several epidemiological studies have confirmed that people with dementia experience a significantly more marked decline in body weight in older age. This weight loss likely starts sometimes in late mid-life already, and may even represent an early marker of disease. Future studies should also investigate whether faster cognitive ageing in mid-life is associated with any weight loss before older age. Monitoring of weight change is highly recommended in people with dementia, and in older people. Further research is needed to determine whether monitoring in mid-life may also be beneficial for prevention.

Consequences of dementia-related undernutrition and weight loss

Introduction

The consequences of weight loss and undernutrition in people with dementia are well characterised. Overall weight loss and undernutrition have a significant impact on the course of the disease, on both cognitive and functional symptoms. Moreover, the overall clinical prognosis is profoundly worsened by the loss of lean body mass, increasing risk of falls (and therefore fractures), pressure sores and infection. An increase in disability and needs for care is therefore explained both by worsening of physical health and functioning, as well as by the more rapid progression of dementia itself. Undernourished people with dementia may need earlier institutionalisation, and longer and more frequent periods of hospitalisation. Ultimately, survival is significantly shorter in people with dementia who experience marked weight loss and who are severely malnourished.

Evidence

Available studies in this field typically follow-up clinical samples of patients with dementia to allow close monitoring of weight change and assessment of its impact on dementia severity and other clinical outcomes. Evidence from epidemiologic studies on the consequences of weight loss in dementia patients is limited. According to a recent review conducted by members of the International Academy on Nutrition and Aging (IANA), the evidence of the detrimental effects of weight loss and undernutrition in clinical samples is compelling. Weight loss was strongly associated with dementia severity, more rapid progression of cognitive impairment[12], and with subsequent mortality[12,42]. Undernutrition is also prospectively associated with the clinical progression of dementia and with institutionalisation[43,44]. Weight loss and feeding difficulties are also strongly predictive of mortality in advanced dementia; in a cohort of nursing home residents the combination of advanced dementia and feeding difficulties was associated with a 27% nine month mortality, and weight loss at baseline was the only significant predictor of mortality[45].

Such findings are certainly not unique to dementia. In population-based studies of older people in general, weight loss increases risk of mortality[46–49], and is associated with a steeper decline in activities of daily living or physical function[50,51]. The association with mortality is particularly marked among frail older people[52]. Underweight, rather than obesity is associated with increased cardiovascular and all cause mortality among those with coronary artery disease[1]. There is some evidence that improvement of nutritional status through, for example, the use of oral nutritional supplements for older people may be associated with a reduction in subsequent mortality (RR 0.79; 95% CI 0.64–0.97) at least among those that are frankly undernourished[53]. However, evidence for improvement in functional status or other relevant health outcomes is lacking.

Whether weight loss and undernutrition among people with dementia causes more rapid disease progression, disability, institutionalization and death, or is merely a marker of underlying disease processes is uncertain. This question is best settled through observing the effects of nutritional interventions in people with dementia, ideally in randomised controlled trials. The first question is whether it is possible to modify trajectories of weight loss hence stabilizing or improving nutritional status, and the second is whether, by so doing, relevant health outcomes improve. Mortality is greatly increased among people with dementia[54,55], and it may be that some part of this increased risk is mediated through dementia-related undernutrition. However, the most helpful benefits potentially associated with nutritional intervention would be those that help to slow down disease progression, and improve quality of life.

Conclusions

Weight loss accompanies dementia almost invariably, and may indeed precede the symptomatic onset of the disease. Several mechanisms may be implicated and are not fully understood. It is likely that causal pathways vary from the pre-clinical phase, to the clinical onset and through the severity of dementia. Weight loss may be part of the clinical expression of dementia, worsens the clinical course of dementia, leads to greater functional impairment and dependence, and increases the risk of morbidity, hospitalisation, institutionalisation, and ultimately mortality. Close monitoring of body weight is very important in people with dementia, and should guide strategies to prevent and treat weight loss, which will be reviewed in the next and final chapter of this report.

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Chapter 5

Improving nutrition for people with dementia

In this chapter, we review strategies to improve the nutrition of people living with dementia, with a particular focus on evidence to support their effectiveness. It is important to consider the special contexts of care homes and hospitals, as well as the prevention and management of undernutrition in the home setting. As well as individual approaches, we highlight case studies of systems level interventions, where for example a hospital or care home seeks to change the way that staff are trained, clients with dementia are assessed, and the environment, ambience and context in which food is provided.

Studies have been conducted to assess the effect of four main types of intervention:

1 Training and education programmes for caregivers

2 Mealtime environment or routine modification

3 Nutritional supplements

4 Provision of feeding assistance

A simple structured assessment of the problem should always be the first step. This should include the degree of undernutrition, dietary intake and habits, risk factors and potential causes, aversive feeding behaviours, and needs for assistance with feeding. Suitable assessments and scales are highlighted, with evidence for their validity.

Nutritional support (simple dietary advice, coupled with assessment and management of risk factors, and attention to needs for feeding assistance) may be enough to address the problem. Current guidelines for older people suggest two to three servings a day of protein (meat, fish or eggs), three or four servings a day of milk and dairy products, and at least five portions of fruit and vegetable per day. If this fails, or in the case of more severe undernutrition, high-energy and/or high-protein oral nutritional supplements (ONS), usually provided in liquid form, may be a quick, reliable and generally well-tolerated way of improving nutritional status.

Nutritional assessment for people with dementia

Introduction

The continuous monitoring and surveillance of nutritional status during lifestyle is critical to plan, and evaluate the efficacy of nutritional interventions for people with dementia. A number of anthropometric and body composition, biochemical, haematological, and dietary indicators are commonly used in the assessment of nutrition status[1]. Nutritional assessment in older people with dementia is similar to the generic approach used for frail older people[2]. Here, we focus specifically of the use of physical and biochemical indicators of nutritional status to provide a systematic and evidence-based approach for the assessment of nutritional status in older people with dementia. The main areas of nutritional assessment are: 1) dietary assessment, 2) weight history, 3) physical anthropometry, 4) screening questionnaires for nutritional status, 5) nutritional biomarkers and 6) eating and feeding behaviour. In the context of dementia-related malnutrition, anthropometric techniques and screening questionnaires are by and large the preferred approach both in epidemiologic studies and in clinical settings. Assessment of energy expenditure and body composition do not yet have a part to play in routine clinical assessment, but are important for research to gain further understanding of the origins of weight loss in

dementia, and may have clinical applications as assessments become simpler and cheaper to perform.

Dietary assessment

Dietary assessment only measures intake and is not a measure of 'status', which ultimately depends on the balance between absorption and losses of nutrients[1]. Assessment of food intake can be prospective or retrospective. Commonly used methods include 24-hour dietary recall, food frequency questionnaires and food records. The element that is common to all dietary methods is that they all rely on the respondent remembering and recalling information regarding their diet.

Retrospective methods (food frequency questionnaire (FFQ) and 24-hour dietary recall)

Retrospective methods are based on the recollection of food and drinks eaten in the past over a certain period of time. For the FFQ, this period is usually extended since the main aim is to capture typical dietary habits. Respondents are usually prompted in the questionnaire with pictures representing different food types and average portion sizes. The 24-hour dietary recall involves the recollection of all foods and fluids consumed the day prior the interview[1]. Multiple-pass dietary recall, with repeated re-assessments of dietary intake in the previous 24 hours may help to improve accuracy of assessment of habitual intake over FFQ[3]. For people with dementia, such questionnaires would typically be administered to family carers or care home staff. The validity of the FFQ and 24-hour dietary recall has not been assessed under these circumstances and the adoption of one method over the other cannot be scientifically justified. The choice of the most appropriate dietary method depends on clinical and cognitive factors as well as on the information that is required for scientific and/or clinical purposes. The development of portable technologies (online platforms, tablets) have increased the reliability of these methods as well as decreasing errors relating to dietary coding and extraction of dietary information[4].

Prospective methods (food records)

Prospective methods require the recording by each participant of foods and fluids consumed over a specified period of time; this usually varies from four days to one week and includes at least one weekend day[1]. This method is considered the gold-standard method for dietary assessment but there has been debate around the intrusiveness of the method, its complexity in dietary coding and the possibility of influencing eating behaviour during the recording period day[1]. This method can be applied to those with cognitive impairment as dietary records could to be completed by carers at home or in residential care homes[2]. A high compliance is needed to record all consumed food items and their weight (or approximate portion size). Technological advancement can again enhance compliance and improve accuracy of the dietary estimates[4].

Weight history

A detailed weight history should be obtained along with current weight. Detailed history should include a history of weight loss, whether the weight loss was intentional or unintentional, and during what period. A considerable and unexplained weight loss (>5 kg) during a 6-month period, whether intentional or unintentional, is a critical indicator for further assessment.

Physical anthropometry

Body weight and height are essential physical parameters for the evaluation of nutritional status in older people. Body Mass Index (BMI) is calculated as the ratio of weight to height-squared (kg/m^2) and is a widely used tool to assess nutritional status. A BMI cut off of <18.5 kg/m^2 has been recommended to define adult chronic dietary energy deficiency. Overweight is defined as a BMI between 25 and 29.9 kg/m^2 and obesity as BMI ≥30 kg/m^2. The validity of BMI as a measure of excess fat may decline in older people because of height loss[5] and increases in fat mass[6] occurring with age even in the absence of weight gain. Waist circumference is a better predictor than BMI of cardio-metabolic risk[7]. Other simple physical assessments can be used to monitor nutritional status. These include triceps and truncal skinfold thickness, and mid-upper arm or calf muscle circumference. The former is a rough indicator of fat and the latter two indicators of lean body mass. These measurements can be easily performed using standardised protocols and they do not require costly and specialised equipment.

Screening tools for nutritional status

Nutritional screening aims to identify those who are malnourished or 'at risk' of malnutrition. There is a wide variety of signs and symptoms associated with nutritional problems. Body measurements and biochemical tests may be used but they could be difficult or expensive to measure in bed-bound or disabled people. To address this problem composite screening tools have been developed. Two have been most commonly applied in older people with and without dementia and a brief description of their characteristics is provided below.

Mini Nutritional Assessment (MNA®)[8] *

The MNA test is composed of simple measurements and brief questions in four sections that can be completed in less than 10 minutes:

1 Anthropometric measurements (weight, height, and weight loss)

2 Global assessment (six questions related to lifestyle, medication, and mobility)

3 Dietary questionnaire (eight questions, related to number of meals, food and fluid intake, and autonomy of feeding)

4 Subjective assessment (self-perception of health and nutrition)

The maximum score is 30 points. The MNA classifies respondents as well-nourished (a score of 24–30), at risk for malnutrition (a score of 17–23.5), or malnourished (a score of <17). Sensitivity is 74 % and specificity is 95% in a community population against a gold-standard based on clinical assessment.[8]

The Mini Nutritional Assessment short-form (MNA-SF®) is a short version of the original 18 item MNA full version, comprising six items that best discriminated between malnourished, at risk, and normal older people[9]; decline in food intake; weight loss in the last three months; mobility limitation; psychological stress or acute diseases in the past three months; neurological problems (dementia and depression); and body mass index (BMI). BMI, requiring accurate assessment of height and weight, is time-consuming and difficult to measure in the community, particularly in bed or chair-bound older people. In the revised MNA, calf-circumference was substituted for BMI, with good criterion[10] and predictive validity[11]. The MNA short form has a maximum score of 14 points, with risk of malnutrition increasing with lower scores. Respondents are classified as well-nourished (a score of 12–14), at-risk for malnutrition (8–11), or malnourished (0–7).

Malnutrition Universal Screening Tool (MUST)[12] †

The MUST is a five-step screening tool to identify adults at risk of malnutrition (undernutrition). It also includes management guidelines, which can be used to develop a care plan. It is for use in hospitals, community and other care settings and can be used by all care workers.

Step 1. Measure height and weight to get a BMI score using chart provided. If unable to obtain height and weight, use the alternative procedures shown in the guide.

Step 2. Note percentage unplanned weight loss and score using tables provided.

Step 3. Establish acute disease effect and score.

Step 4. Add scores from steps 1, 2 and 3 together to obtain overall risk of malnutrition.

Step 5. Use management guidelines and/or local policy to develop a care plan.

Nutritional biomarkers

Nutritional biomarkers are essential for a comprehensive assessment of nutritional status of frail older persons, and is included in most good practice guidelines for dementia care. An initial screen might comprise haematology (full blood count with differential) and biochemistry (electrolytes, urea and creatinine, fasting glucose, albumin, and ferritin). Full blood count may indicate possible B_{12}, folate or iron deficiency, or systemic inflammation (raised WBC count or C reactive protein). Serum albumin is not considered to be a sensitive enough biomarker to predict declining nutritional status, undernourishment, protein malnutrition or improved nutrient stores following nutrition interventions. Low serum albumin most likely reflects the presence of inflammatory stress. Individuals with marasmus-type malnutrition experience weight loss as the result of decreasing fat and muscle mass while maintaining a normal serum albumin. The need for assessment of vitamin status should be guided by the clinical picture; assessment of folate, B_6 and B_{12} is often performed, and any deficiency should be corrected, not least to moderate the increased cardiovascular risk from hyperhomocysteinaemia (see Chapter 3).

Eating and feeding behaviour

Semi-structured assessment tools of problematic eating and feeding behaviours are mainly observational and semi-structured in nature. Existing measures were recently systematically reviewed for content, validity and clinical relevance[13]. The work of Blandford was formative and influential, in developing a taxonomy of 24 adversive feeding behaviours (AFB) in four domains; oropharyngeal dysphagia (seven items), selective feeding behaviours (six items), resistive behaviours (five items) and dyspraxia/agnosia (six items)[14]. Blandford also proposed a four level 'feeding dependency scale'; normal feeder (self feeds with no AFB); aversive self-feeder (exhibits at least one AFB but self feeds); intermittently dependent (needs to be fed intermittently); and dependent (eats only when fed). Inter-rater reliability was demonstrated, and a two factor solution (active and passive aversive behaviours) identified on exploratory factor analysis. The most widely used and best validated measure is the

* http://www.mna-elderly.com/

† http://www.health.gov.il/download/ng/N500-19.pdf

Edinburgh Feeding Evaluation in Dementia Scale (EdFED), developed for those with moderate to late-stage dementia[15]. The EdFED assesses 10 items: is the person with dementia refusing to eat, refusing to swallow, refusing to open their mouth, turning their head away, spitting food, or leaving mouth open; and does the person require supervision, physical help with feeding, leaving food on the plate at the end of the meal, and is there spillage while feeding? The items are scored with 0 (never), 1 (sometimes) or 2 (often) based on the frequency of the problem behaviour. An 11th item scores the person's level of assistance: 'supportive-educative, partly compensatory or wholly compensatory'. The EdFED has been subject to extensive psychometric testing demonstrating internal consistency, hierarchical scaling properties (items 5–10), confirmatory factor analysis, construct, convergent and discriminant validity, inter-rater and test-retest reliability[13]. The EdFED is brief and simple enough to be used in routine clinical practice in care homes and hospitals, and might in principle be used to interview caregiver informants in the community. It establishes the level and type of disability and can be used to plan effective interventions.

Energy expenditure

The prevention of weight loss is critical for people with dementia, and matching energy intake to expenditure can help to achieve this. Total energy expenditure can be divided into three main components: 1) resting energy expenditure, 2) physical activity energy expenditure and 3) energy expenditure induced by diet. All three components contribute to the progressive decline in total energy expenditure with ageing, which is predominantly a function of reduced physical activity and muscle mass[16]. There appears to be no difference in total energy expenditure in older people with and without dementia[17]. The component of total energy expenditure that may specifically contribute to unintentional weight loss in people with dementia is currently an under-explored area of research. Better understanding may help to tailor nutritional and lifestyle treatments. Several methods can be used to measure total energy consumption and its components. In clinical practice, simple methods such as portable calorimeters (i.e., MedGem) or prediction equations (i.e., Harris Benedict, Fredrix, Mifflin-St Jeor) can be used to calculate resting energy expenditure; total energy expenditure can then be obtained by applying specific coefficients to an estimated physical activity level (low, moderate, high)[18].

Body composition

The human body can be considered to comprise fat mass (FM) and lean body mass (LBM – muscle, bone). Ageing is associated with progressive changes in body composition including reciprocal changes in fat mass and lean body mass, influenced by gender, degree of adiposity and age-related hormonal changes[6]. Muscle mass declines by 1% per year from the third decade of life, and older people, even those with stable normal weight or overweight have difficulties in maintaining muscle mass; an accelerated decline in LBM may have important clinical consequences[19]. Several models have been proposed for measuring body composition varying from two compartment models (fat mass, fat free mass) to more complex models sub-dividing the body into mineral mass, total body water, fat mass, and protein and carbohydrate mass[20]. These assessments require relatively complex techniques such as whole body scanning with Dual X Ray Absorptiometry (DXA), or Air Displacement Phlethysmography (ADP). Bioelectrical impedance is a non-invasive, user-friendly, portable technique which could be more routinely applied in research and clinical practice for people with dementia. A careful monitoring of muscle mass may be particularly important for people with dementia, and nutritional interventions that succeed in maintaining or improving lean muscle mass (as opposed to adiposity) may have more beneficial impact on physical and overall functioning.

Education and training interventions

Background and rationale

Most caregivers understand that maintaining the nutrition of the cared for person with dementia is an important component of the care that they provide, even seeing this as part of the treatment for the condition. From the early stages of dementia, new skills must be learnt, and new roles assumed[21;22]. This is particularly the case for male caregivers who may not previously have been much involved in meal planning, food shopping or cooking[21]. All spouse caregivers must gradually assume decision-making responsibility for what to eat, and when to eat it, where this may have previously been a shared activity. This responsibility can weigh heavily, occasioning anxiety as to whether the ambiguous food preferences of the person with dementia are being correctly interpreted, and whether their diet is adequate[21–23]. Weight loss, and how to prevent or treat it is a preoccupation for many caregivers. In a study in Sweden, for example,

carers worried about the health risks of increasing the amount of fat in their partner's diet in an effort to achieve weight gain[21]. As dementia evolves it is increasingly likely that aversive feeding behaviours develop, and that the person with dementia may need some feeding assistance. In a French study conducted among 224 home-dwelling people with dementia (mean MMSE score 15), 3.6% would only eat when fed, and 23.7% needed to be fed intermittently[24]. A further 31.8% had at least one aversive feeding behaviour, but fed themselves. Thus only 40% were completely free of feeding difficulties. Managing such problems is demanding of caregiver time, and requires patience, empathy and skill. While one might imagine that the emergence of feeding problems might cause caregiver strain, evidence is stronger for an effect in the opposite direction – that is that feeding problems are more likely to arise when the caregiver experiences strain[24]. There is also evidence that caregiver strain is an independent predictor for weight loss in patients with Alzheimer's disease[25].

People living in care homes are more likely to have advanced dementia, and feeding dependence and aversive feeding behaviours are therefore more prevalent. Residents with dementia take longer to eat, require prompting and encouragement, and may have problems with coordination and swallowing. Some residents are bed-bound and need food to be brought to them. Therefore, mealtimes are a busy time for care assistants. Feeding a person with dementia can take up to 40 minutes per resident to ensure that the experience is a calm and enjoyable one. A detailed observational study suggests that the quality of the interaction between the nurse providing feeding assistance and the patient with dementia is positively associated with the quantity of food consumed[26]. However, as staff-to-resident ratios are low in many homes, care workers report that meal times can be one of the most stressful parts of their day[27]. In a large US study of 407 residents with dementia in 45 assisted living facilities and nursing homes, overall, 54% of residents had low food intake, and 51% had low fluid intake[28]. In another study in 24 US nursing homes, in up to a quarter of cases of advanced dementia with feeding difficulties the family was not satisfied with the assistance provided for the person with dementia[29].

There is no reason to assume that family caregivers, or indeed care assistants in care homes are naturally equipped with the knowledge and skills to assess and manage the often complex nutritional needs of a person with dementia. Undernutrition, and mealtime difficulties can have physical, cognitive, behavioural, social, environmental and cultural determinants[30].

Early intervention to improve awareness of the importance of a balanced diet, strategies to boost protein and energy content of the diet, and advice and support with managing aversive feeding behaviours may help to prevent or delay the complications of long-term inadequate food intake. Education and training interventions on mealtime difficulties in older adults with dementia targeting caregivers (e.g., family members, nursing staff) may therefore have an important part to play in decreasing negative outcomes and increasing quality of life.

There are many excellent practical guides and sources of information for caregivers of people with dementia, one of which is the factsheet prepared by the UK Alzheimer's Society 'Eating and Drinking'.*

This explains very clearly the importance of a healthy balanced diet, and the risks of weight loss in people with dementia. The contributions of cognitive problems, sensory deficits and aversive feeding behaviours are described, and strategies proposed to address them. Key points are that:

- Poor appetite may arise from depression, intercurrent physical illness, difficulty in communicating their needs, lack of activity, pain, oral or dental problems, side effects of medication, or constipation. Medical assessment may be required to identify and treat these problems, particularly if weight loss is recent and marked.
- Appetite may be stimulated by
  - Regular snacks and small meals
  - Experimentation – try food they like, food they have not tried before, stronger flavours, different times of day
  - Naturally soft food
  - Keeping food hot
  - A relaxed atmosphere
  - Eat with the person with dementia, using it as an opportunity for activity and social stimulation
  - Getting them to help with meal preparation
- It is important not to assume that a person who does not eat, does not want to eat. They may not recognize food (agnosia) or not be able to feed themselves independently (apraxia)
- Do not assume that a person has finished if they stop eating. They may find it difficult to concentrate on the task. Gentle encouragement and persistence may allow them to finish the meal

* http://www.alzheimers.org.uk/site/scripts/download_info.php?fileID=1799

- Problems with coordination, and difficulty using cutlery can be managed by
  - Chopping up the food, so that they can use a spoon
  - Providing nutritious 'finger food' – for example sandwiches, fruit, slices of quiche
- In advanced dementia, loss of feeding skills, and aversive feeding behaviours can mean that the person with dementia needs to be fed by the caregiver. Caregivers are reminded
  - Aversive feeding behaviours are not a deliberate attempt to be 'difficult', or a personal attack.
  - Try not to rush the person with dementia, and help them maintain as much independence as possible.
  - Look for non-verbal clues such as body language and eye contact as a means of communication.
  - If a person is agitated or distressed, do not put pressure on them to eat or drink. Wait until the person is calm and less anxious before offering food and drink.
  - Difficulties in swallowing (oropharyngeal dysphagia) can lead to risk of aspiration. It is important that the person with dementia is alert, comfortable, and sitting up in a good position before feeding is attempted. The advice of an appropriate specialist (speech and language therapist, occupational or physiotherapist) may be needed.

The evidence

In a recent systematic review, there was considered to be moderate evidence for efficacy of education and training interventions in reducing feeding difficulty and increasing eating time of older people with dementia[30]. However, just five studies were identified, and these tested quite different types of intervention, applied in different contexts.

Training people with dementia

In two Taiwanese studies, training was provided to people with dementia who were resident in long-term care settings in an attempt to modify their feeding behaviours[31;32]. While described as randomised controlled trials, the unit of randomisation was the long-term care facility; in one study (n=85 participants) three facilities were randomised to spaced retrieval, Montessori-based activities or usual care[32], and in the other study (n=29 participants) two facilities were randomised to receive Montessori-based activities in the first or second phase of a crossover trial[31]. These are therefore quasi-experimental studies, lacking the usual benefits associated with randomization.

The Montessori approach uses rehabilitation principles including guided repetition and task breakdown, progressing from simple to complex tasks. Activities practiced were hand-eye coordination, scooping, pouring, and squeezing, and distinguishing food from non-food items. Spaced retrieval training focused upon eating procedures and behaviours with progressively lengthening intervals for repetition of the learnt material (from one to 32 minutes). In both studies, the Montessori-based activity intervention was associated with a significant net reduction in feeding difficulties with some evidence for reduced need for feeding assistance. In neither study was the intervention associated with improvements in weight, BMI or overall nutritional status.

Training care assistants in care homes

In two studies, the intervention comprised education and training of professional caregivers in nursing homes or other long-term care facilities for people with dementia[33;34]. In a study conducted in Taiwanese nursing homes[33], two facilities were allocated either to feeding skills training programme including three hours of in-service classes (31 nursing assistants) and one hour of hands-on training, or a control group with no training (36 nursing assistants). Knowledge, attitudes and observed behaviours were more positive among the trained nursing assistants. However, there was no significant difference in food intake between the two groups, and feeding difficulties worsened in the intervention group. In a Finnish study[34] 28 nurses and food service attendants attended six half-day training sessions delivered by a dietician with the aim of assessing and monitoring nutritional status of residents using the Mini Nutritional Assessment and detailed food diaries, and then implementing planned adjustments to their diet. Pre- and post-intervention assessments were made of energy and nutrient intake (21 residents) and nutritional status (19 residents). After one year, residents' mean daily energy intake had increased by 21% from 1230 to 1487 kcal, but there was no significant change in residents' nutritional status according to the MNA.

Training family caregivers

Education programmes for informal caregivers were evaluated in three studies, two randomised controlled trials, and a controlled non-randomised study[35–37]. The format of the training programmes was similar in each of the studies, comprising group sessions conducted by a dietician or other health professional. Topics covered included; the importance of a healthy balanced diet; dietary challenges in dementia; techniques to monitor food intake, weight and nutritional

status; advice on enriching dietary protein and energy content; and strategies to manage aversive eating behaviours. The largest study by far was the Spanish, multi-centre cluster-randomised controlled trial of the NutriAlz health and nutrition promotion programme[35]. Eleven outpatient clinics or day centres (n=946 home-dwelling people with mild to moderate dementia and their caregivers) were randomised to an education and training intervention, or usual care. Over a third of participants did not complete outcome assessments at one year. No effect of the intervention was noted upon ADL (activities of daily living) score (the main outcome), weight, BMI, MMSE, dementia severity or behavioural symptoms. Nutritional status improved in the intervention group, but deteriorated in the control group, with a mean difference in MNA score of +1.12, 95% CI +0.65 to +1.59. This converts to a standardised mean difference of +0.33 (95% CI +0.19 to +0.47), hence suggesting a small to moderate effect size of doubtful clinical significance. There was also no effect of the intervention on caregiver burden. The other randomised controlled trial, conducted in Brazil, included 90 people with AD randomised to oral nutritional supplementation, a nutritional education group, or treatment as usual control. After six months of follow-up weight increased in the education group and declined in the control group, with a MD for % weight change of 5.65% (+0.22 to +11.08) SE 2.77. However, weight gain was much greater in the oral nutritional supplementation group than in the education group (6.7 kg vs 1.2 kg). The non-randomised study was conducted in three European cities, in which 151 people with Alzheimer's disease and their main informal caregiver were recruited from day centres or Alzheimer associations into an educational programme, while 74 patient/caregiver dyads recruited from the same facilities and receiving normal clinical care acted as a control group. The mean difference for percentage weight change over one year was +1.93% (95% CI -0.34 to +4.20 SE 1.16) after adjusting for baseline covariates. There was no difference in overall nutritional status (MNA score mean difference = +0.60, 95% CI -0.11 to +1.31). Cognition declined in both groups, but to a greater extent in the control group MD = +1.1 (0.0 to +2.2). Combining the results across the three community-based studies suggests no effect of nutritional education interventions on weight (pooled MD for % weight gain +1.14%, 95% CI -0.22% to 2.50%).

Conclusion

There is currently little or no evidence to suggest that training and education interventions, whether for paid care assistants in care homes, or for family caregivers of people with dementia, result in clinically meaningful improvements in the nutritional status of people with dementia. That is not to say that there may not be benefits associated with such interventions. Surprisingly little research has been conducted in care home settings. The evidence base regarding training and education for family caregivers is dominated by one large well conducted cluster-randomised controlled trial[35]. However, fewer training sessions (four) were provided for family caregivers in this trial than in two other smaller studies that did show positive benefits[36;37]. Training and education on diet and nutrition is generally appreciated by caregivers[35], and there is a clear need for support particularly when aversive feeding behaviours and feeding difficulties occur (see case study on page 73). It may be that while basic information should be provided to all families, more concentrated training and dietician services should be focused upon those developing feeding difficulties or undernutrition[35].

Modifications to mealtime environment and routine

Background and rationale

In terms of experimental evidence, according to a recent systematic review applying standard criteria, 'insufficient evidence' exists to make clear recommendations regarding mealtime environment and routine modifications given the poor quality and limited quantity of trials (mostly small time-series comparisons)[30]. This may therefore be a case of 'absence of evidence' rather than 'evidence of absence' of effective interventions. Indeed, while poorly researched, this is currently a fertile area for innovation with successful advocacy driving forward change based to a large extent upon core principles, supported by some evidence and expert opinion. Available evidence on the effect of design innovation on dementia care has been helpfully collated at the Dementia Design Info website maintained by the University of Wisconsin Institute of Aging and Environment, I.D.E.A.S inc, and the Polisher Research Institute.*

The last 30 years has seen a gradual transition away from institutional models of long-term care for older people. Typically, these prioritize efficiencies of scale and the convenience of staff, over the rights of residents to flexible, individualised and person-centred care in settings that more resemble households or homes. This 'household' philosophy has been strongly advocated by the Culture Change movement,

* https://www4.uwm.edu/dementiadesigninfo/

whose work has been influential in the USA and internationally[38]. Design has an important part to play. The aim is to create layouts and facilities that support residents' residual abilities and limit the impact of their disabilities, while improving working conditions and providing a better care culture for staff, residents and visitors[39]. The four core design principles that distinguish the newer household and neighbourhood care settings relate to their scale, the nature and use of space, the relationships between living areas, and creation of spaces that support the autonomy and independence of residents[40]. Kitchen and dining areas form an important part of this broader design framework[39].

The evidence

Downscaling

There is no clear threshold of size or scale that distinguishes a home from an institution, but clearly it would be very difficult for a single building with 60 residents or more to be 'homelike'. 'Households' typically comprise 8–12 residents, and the Life Safety Code Task Force has recommended 24 as the maximum feasible number. Smaller, low-density homes facilitate social interactions among residents and with staff members, and reduce environmental over-stimulation. There is evidence that moving from high-density to low-density care settings is associated with a reduction in disruptive behaviours[41]. However, it is important to note that there is no simple relationship between the size of a home and the quality or outcomes of the care provided[42]. Household designs seek to replicate the living areas of houses, comprising resident rooms with bathrooms, a kitchen and dining area, and a living room or activity space. Care provider organisations can still achieve economies of scale by clustering households into 'neighbourhoods' of 30 to 50 residents with shared group leisure and social activities, and opportunities for staff training and support. These shared areas should, ideally, be separate from where residents live, respecting the normal distinction between home and community space. Large communal dining areas should be avoided, in particular for residents with dementia. It takes time to assemble residents in a central facility, meaning that some will be left waiting for long periods for the meal to begin. Large dining spaces can be noisy and confusing, with too much sensory distraction. Furthermore, such anonymous spaces fail to provide the sensory cues that orientate a person with dementia to mealtime. Smaller dining rooms can have a more intimate and familiar ambience, and reduce confusion as to the function of the room. The effect of reduced size dining rooms, 'bright and welcoming' colours, and other residential features (sideboards, paintings, objets d'art, use of a bulk re-thermalization system in place of tray service) has been evaluated[43]. Food intake significantly increased with the environmental changes alone, and increased again (but not significantly) when combined with staff training. In a large US study of predictors of low food and fluid intake in care homes, such problems were less common in smaller assisted living and residential care facilities, in facilities with 'non-institutional' dining rooms, and where residents took their meals in public dining rooms as opposed to in their bedrooms[28].

Dining rooms for dining

Disorientation in people with dementia, arising from problems with memory and gnosis, can be reduced by providing clear visual and other sensory cues as to the function of spaces. In this way, information is embedded in the design environment, rather than having to be remembered[39]. Generic multi-purpose living spaces where food is provided on trays to residents in the chairs where they sit for much of the day are a feature of many institutionalised care settings – there is a burden on residents to interact with each other, and studies suggest that this both leads to withdrawal and increases the likelihood of conflict. As a design principle for care homes, ideally, each room should have just one activity associated with it. For people with dementia it may be particularly important to have a dedicated dining room, the use of which is limited to meals and food. Hence, a dining room should look, as far as possible, like a dining room in a home, with recognisable furniture such as dining tables and sideboards. Thus, residents can develop a familiarity with its purpose over time, evoking positive and useful associations and cueing appropriate eating behaviours[39]. As with a dining room or kitchen in a home, the room can be a social hub throughout the day; for having coffee with friends after breakfast, inviting visitors to share food snacks from the kitchen between meals, and having afternoon tea with staff and residents. In non purpose-built care homes it may be difficult to reserve a room for dining times only. In such instances it is important to provide clear cues for when dining and non-dining activities are taking place, for example by changing the layout of the room, and involving the residents in preparatory activities such as laying the tables. Noise levels and visual stimuli cannot be controlled.

Kitchens next to dining areas

In homes, kitchens are generally next to dining rooms, or one room serves both functions. Across cultures, in the rituals surrounding food, there is a strong link between its preparation

and consumption, and a prominent social component to these activities as evidenced by the importance of food to family and community celebrations. However, as highlighted in a recent collaborative research project between the Helen Hamlyn Centre at the Royal College of Art and Bupa, in many care homes design features and food management procedures make it difficult or impossible for residents to participate in these processes[39]. This is particularly the case when food is prepared in a central kitchen apart from the residential area, and then delivered either already plated on trays or from a heated trolley. Food service areas only include basic amenities for washing and serving and residents are not allowed into these areas for reasons of health and safety. One of the key recommendations of the research project was for 'eat-in-kitchens' to be included in the design of dining environments in care homes[39]. This could be achieved by splitting the kitchen into two sections; one equipped with everything necessary for the operation of a large-scale catering system, and the other a therapeutic 'activity kitchen' for residents in which everything is geared towards orientation, engagement and safety. The kitchen is homely in appearance, has a large cooker with unobtrusive safety features, and appliances that trigger memories of cooking activities. Residents can congregate at a large family-style table for leisure and supervised group activities including baking and other food preparation. Kitchen spaces evoke ideas and feelings of warmth, comfort and security. Associating the eating area with a space that looks and feels like a kitchen stimulates all of the senses with the smell and sound of cooking, evoking positive memories and cueing that a meal is about to take place in a much more direct and powerful way than words, signs or instructions could do. The diffusion of food-preparation smells has been suggested to stimulate the appetite of older people with dementia and to remind them of meal times. Suggestions include the ambient smell of fresh baked bread during meal times (i.e. the use of bread machine)[44], and a Design Council technical innovation called ODE (www.myode.org), a small device releasing up to three food-fragrances per day just before meal-times to stimulate appetite. ODE has been piloted tested in some care homes, with suggestions of increased interest in eating, requests for extra food, and weight gain among people with dementia. However, no formal experimental evaluations have been carried out to date.

Dining environment – family-style eating

Having dedicated dining areas allows layouts and decor to be customised to reflect the specific function of the room. Dining areas should have a comfortable and appealing atmosphere avoiding elements that detract from a resident's residual abilities or make the environment feel institutional. Three key design issues to be addressed are controlling distracting stimuli, making tables accessible and safe, and deploying good quality lighting[39].

Meals should be relaxed, unhurried and free from distraction. People with dementia find it difficult to concentrate on meals, and are sensitive to excessive noise and stimulation. Extraneous background noise should be reduced, for example by removing television sets. Large dining areas with many residents are intrinsically noisy and distracting; spaces can be broken up using moveable dividers and curtains and other soft materials can also reduce noise in the dining area[39]. Staff activities and other intrusions should be kept to a minimum, for example the circulation of a medication trolley during mealtimes should be avoided. On the other hand, staff dining with residents may normalise the activity and foster person-centred care. For those with prominent eating difficulties, quiet spaces free from distracting views can be helpful. As a design feature, moving services areas (for food preparation and plating) outside of the dining area may again help residents to focus on their eating. In the prototype design from the Royal College of Art project, the service hatch opens into the corridor to avoid staff having to distribute food from the dining area where residents are concentrating on their meals. While distracting noise should be reduced, another approach that has been trialled is to play music during mealtime. In the USA, an intervention study, investigating the effect of music during lunchtime on the caloric consumption of residents of nursing homes with middle-stage AD, showed a 20% increase in calories consumption when familiar background music was played[45]. Weekly average caloric consumption increased each week that music was played.

Good quality lighting is essential in dining areas so that older people with visual impairment can identify food and cutlery. In a study conducted in US care homes increasing the light levels at table level led to an increase in food intake and independent feeding among residents[46]. Due to age-related changes to the pupil, lens and retina, older people may need as much as three times as much light as younger persons, and a lighting intensity of 50 foot candles (540 lux) has been recommended for dining areas[46]. The Royal College of Art design team proposed overhanging lights for each table that could be individually adjusted, from 400 to 1200 lux, to the needs of the people sitting at it[39]. Decreased pupil reaction time and lens elasticity limits ability to adapt quickly to changes in lighting level, leading

to sensitivity to glare. This can be managed by combining direct and indirect light sources to provide even lighting throughout the room. All light sources should be shaded with diffusers, including semi-sheer curtains for windows on bright days. Lights that cast shadows should be avoided because people with dementia may have trouble interpreting them. The place setting should contrast in colour with the table top to improve visibility. Food consumption increases when there is high contrast between the plate and table[46]. The table surface can also be contrasted at its edges to help those with low vision.

Square tables seating up to four residents may be optimal for communication and interaction among diners[47], although for safety reasons corners should be curved to avoid sharp edges. Such tables can be grouped together for larger group activities or special occasions. Residents should sit in chairs with arms which need to slide under the table, so that the resident can be close enough to focus their attention on eating. Tables should also be high enough (74 cms, or 19 inches) and broad enough (107 cms or 42 inches) to allow wheel chairs to be accommodated, and with no central columns or support structures to prevent chair arms from clearing the underside of the table. The seat height of the chair should be 43 to 48 cms (17 to 19 inches) enabling residents to sit with their feet firmly on the floor.

The various elements described above constitute a 'complex' (multicomponent) intervention, which has been described as the creation of a 'family-style' eating environment. This does away with the practice of pre-plated meal delivery on trays and replaced it with a more informal 'family style' eating environment with bulk delivery of food to be served individually at the table. Staff are more involved in the process, but distractions are kept to a minimum. In a large and well conducted cluster randomised controlled trial in five nursing homes in the Netherlands, for 178 residents without dementia, the introduction of family-style eating was associated with impressive improvements in energy intake, body weight, quality of life and physical performance[48;49]. A much smaller quasi-experimental study of a similar intervention (changes to foodservice and physical environment from institutional to more home-like environment in cognitive impairment nursing home units in Canada) has shown similar results[50]. Increases in energy, carbohydrate, and protein intake, but not fat intake were noted. Importantly, the greatest nutritional benefit seemed to be gained by the most cognitively impaired residents, and among those with lower body mass indexes (BMIs)[50].

Oral nutritional supplementation for people with dementia

Background – macronutrient supplementation

Oral protein and energy supplements are widely used in older people, for undernutrition is more common than overnutrition, particularly in the context of chronic illness and hospitalisation. The supplements, usually in the form of commercially available liquid sip feeds, are safer and easier to administer than nasogastric feeds. The main concerns associated with their use are problems with the willingness and ability of older people to consume them, the potential for gastrointestinal adverse effects, and the risk that the additional calories from the supplement may be more than offset by a compensatory reduction in customary diet[51]. A Cochrane review of 62 trials of protein and energy supplementation in older people at risk from malnutrition indicated that their use was associated with a significant increase in weight (Mean difference +2.2%, 95% CI +1.8% to +2.5%) and a significant reduction in mortality risk among those who were undernourished (Relative Risk 0.79, 95% CI 0.64 to 0.97)[51]. We identified two further relevant systematic reviews, one of oral feeding options for people with dementia[52], one of interventions on mealtime difficulties in older adults with dementia[30]. Evidence from these reviews were cross-referenced with those from a recently completed systematic review of nutritional interventions for frail dependent older people (personal communication AT Jotheeswaran). None of the reviews was completely satisfactory for our purposes. The review of oral feeding options for people with dementia[52] included five trials which either focused upon cognitive impairment, or included frail or dependent older people not all of whom were affected by dementia. Some details of trial design and results seemed to have been incorrectly transcribed. No quantitative meta-analysis was attempted. The review of mealtime interventions[30] did focus upon studies recruiting people with dementia, and included seven trials, two of which were of micronutrient rather than protein/energy macronutrient supplementation, and one of which was a trial of whole formula diet replacement for normal dietary intake, rather than supplementation. Again details of trial design were incorrectly described. No quantitative data was presented, and no meta-analysis attempted. The Cochrane review[51] included 62 randomised and quasi-experimental controlled trials, of which just five recruited only people with dementia; one of these was the trial of whole formula diet replacement. Quantitative meta-analysis was

carried out but with no sub-group analysis for trials of ONS among people with dementia.

The evidence – macronutrient supplementation

Description of the trials

From the systematic reviews, we identified five parallel group randomised controlled trials of ONS with placebo or treatment as usual control groups[53–57], one crossover trial[58], and a parallel group RCT of micronutrient supplementation in which both arms received macronutrient ONS[59]. From our more recent review we identified a further parallel group RCT[37] and a non-randomised controlled trial[60]. All of the studies were small in size ranging from 33 to 99 participants. In all 440 participants with dementia were included in placebo or other controlled comparisons of ONS, and pre-post within group data was available for 246 individuals receiving ONS. One each of the studies was conducted in the UK, France, Sweden, Canada and Brazil, two in Spain and two in the Netherlands. Six of the studies were conducted in care homes or other long-stay accommodation[53;54;56–58;60], and three in the community[37;55;59]. Oral nutritional supplements provided between 125 and 680 kcal per day, and were generally offered between meals and mainly in the morning to maximize adherence and reduce substitution. Duration of the intervention varied between three weeks and one year. Total calorie supplementation varied between 5,418 and 91,350 kcal.

Change in weight was studied as an outcome in seven studies, in six as a controlled comparison[37;53;55–57;60], and in one other only as a within group change from baseline[58]. Change in body mass index was studied as an outcome in six studies, in five as a controlled comparison[37;54–56;60], and in one other only as a within group change from baseline[59]. Mortality was reported in six trials[37;53–57]. Other outcomes studied included nutritional status (energy consumption, Mini Nutritional Assessment score (MNA), mid upper arm muscle circumference, triceps skinfold thickness, vitamins D, B_1, B_6, B_{12}, homocysteine and folate, magnesium, zinc and selenium); cognitive function; disability; and complications (infections, days in bed, fractures, pressure sores, hospitalisation).

The quality of the studies was generally poor (Table 5.1). Most of the trials gave no information regarding randomisation procedures, it was unclear whether efforts had been made to conceal allocation, or to blind outcome assessors. Intention to treat analyses were infrequently conducted. Notable exceptions were Young et al[58] and Lauque et al[55]. There were also problems with analysis and reporting of findings, which, other than the same two higher quality studies, did not include effect sizes (mean differences) with standard errors or confidence intervals. One of the trials (Pivi et al[37]) could not be included in the meta-analysis because of lack of clarity of the reported effect sizes, and inconsistencies between effect sizes for weight and BMI (Table 3 in the published paper). We have not yet been able to clarify these in correspondence with the authors of the report, but hope to update future published versions of this review.

Data synthesis

Given the small size of the studies, we attempted to calculate or estimate between group mean differences based upon change scores from baseline. Percentage weight gain was estimated as the change in weight divided by the baseline weight expressed as a percentage. Where baseline weight was not given this was estimated, conservatively, as 60 kg[51]. Where standard deviations of change scores were not provided these were imputed from baseline and follow-up SD, applying a between time point correlation derived from Laque et al[55]. If insufficient data was provided, then SD of change in % weight was imputed, conservatively, as 10% and SD of change in BMI was imputed as 1.5 kg/m^2 (higher than those observed in any other study).

Results

Effect of ONS on weight / body mass

There was strong evidence that oral nutritional supplementation was effective in increasing weight (Figure 5.1: fixed effects pooled mean difference in % weight gain across five studies = 3.43%, 95% CI 2.08–4.78, random effects pooled within intervention group weight gain across six studies = 3.61%, 95% CI 1.89–5.33) and body mass index (Figure 5.2: random effects pooled mean difference across four studies 1.15 kg/m^2, 95% CI 0.48–1.82; pooled within intervention group BMI gain across seven studies 1.09 kg/m^2, 95% CI 0.72–1.46). There was, however, considerable variation in the size of the effect across studies (Table 5.1 and Figure 5.1). For % weight gain, mean differences between intervention and control groups ranged from 1.92% to 6.61% (Higgins' I2 heterogeneity between studies = 11.1%), and within intervention group from 1.30% to 9.87% (I2=85.8%). Mean differences for BMI gain ranged from 0.70 to 1.90 kg/m^2 (I2=82.5%), and within intervention group from 0.50 to 1.60 (I2=71.9%). Sources of heterogeneity were explored using meta-regression of within intervention group effect sizes for % change in body weight. The % gain in body weight was greater for studies with a

Table 5.1
Description of included trials and studies

Trial authors	Design	Setting	Inclusion	Intervention	Control	Duration	Quality
Carver & Dobson, 1995[53]	Parallel group randomised controlled trial	Older long stay patients in psychiatric care of the elderly facility, Scotland, UK	Underweight (BMI15.1-19.9) Mean 19.9 'Senile dementia' diagnosis, any severity	Fortisip 200ml ONS BD, 600 kcal R=23 A=20	Acaloric vitamin placebo R=23 A=20 'Normal encouragement' for maintenance of diet given to both groups	12 weeks	Concealment –No Blinding – yes for anthropometry outcomes No ITT
Gil Gregorio 2003[54]	Parallel group randomised controlled trial	Nursing home residents Spain	Moderate to severe AD (MMSE 12.7 FAST 5-6) Malnourished MNA 20.1 16.5% BMI ≤21 55.7% > 23 Assume median 23.5	Nutrison ONS 125 kcal R=25 A=21?	Not specified R=74 A=57?	12 months	Randomisation not described Concealment not described Blinding not described No information on loss to follow-up, other than mortality
Lauque et al 2004[55]	Parallel group randomised controlled trial	Geriatric wards and day centres Toulouse France	AD (MMSE 15 (sd 8) – moderate dementia and risk of malnutrition (MNA <23.5). BMI 22.4 (3.1)	Clinutren ONS (soup, dessert or liquid supplement). 300-500 kcal, mean 368 kcal: Dietician home visits R=46 A=37	Usual care R=45 A=43	3 months (used for outcome) intervention. FU to 6 months Nutritional benefit maintained at 6 months	Concealment unclear Blinding yes ITT no
Wouters-Wesseling 2002[56]	Parallel group randomised controlled trial	Psychogeriatric Nursing home residents. Netherlands	Dementia syndrome diagnosis and low BMI body mass index (BMI) <23 kg/m^2 for men or <25 kg/m^2 for women BMI 20.65	Micronutrient enriched ONS 125 ml BD. 270 kcal R=21 A=19	Placebo controlled R=21 A=16	12 weeks	Concealment not clear ITT not done Double blind
Wouters-Wesseling 2006[57]	Parallel group randomised controlled trial	Residents of psychogeriatric unit in NH Netherlands		Early liquid supplement OD after onset of acute infection 309 kcal R=20 A=18	Standard treatment Dietician referral R=19 A=16	5 weeks	Concealment and blinding not clear ITT mentioned but no results
Young et al 2004[58]	Crossover randomised controlled trial	Geriatric care center Alzheimer's unit residents. Canada	Mod to severe dementia Mean BMI 23.8	¾ of a nutrient supplement bar and juice between meals 258 kcal R=15 A=15 (Phase 2)	Crossover with washout period R=19 A=19	21 days (then washout and another 21 days in other condition)	Concealment yes Blinding – for some outcomes ITT - yes

Pivi et al 2011[37]*	Parallel group randomised controlled trial	Behavioural neurology OPD, Brazil	Probable AD, CDR 1+ No information on nutritional status at baseline	Ensure ONS BD. 680 kcal R=30 A=26	TAU R=30 A=27	6 months	No information on randomization, concealment or blinding ITT not carried out Change scores reported without SD
Faxen-Irving et al[60]	Controlled but not randomised trial	Group living facilities for older people with dementia, Sweden	All participants had dementia. 43% of IG and 18% of CG had severe dementia. Body mass index (BMI) < or =20 was found in 19% of the participants and 44% had BMI< or =23 BMI mean 22.2 IG	ONS (410 kcal/day) and staff nutritional education A=21	TAU A=12	5 months intervention with 6 months FU assessment	No randomization No blinding
Planas, 2004[59]	Parallel group randomised controlled trial, but both arms received protein/energy ONS	44 Alzheimer's disease day centre participants in Spain	Mild dementia and feeding problems Mean BMI 25.4/24.4	Oral liquid supplements 500 kcal/d with micronutrient enhancement R=23 A=22	Oral liquid supplements 500 kcal/d without micronutrient enhancement R=21 A=18	Trial of micronutrient only (everyone had macronutrient)	No information on randomization, concealment or blinding ITT not carried out

R = Number randomised A = Number assessed ITT = Intention to treat analysis * The trial by Pivi et al could not be included in the meta-analysis, due to lack of clarity regarding the reported effect sizes (Table 3 in the published paper)

higher daily calorie supplementation (Figure 5.3: 2.28%, 95% CI 1.00–3.57 higher gain per 100 kcal increment), and for those with a higher total calorie supplementation (Figure 5.4: 0.89%, 95% CI 0.31–1.46 per 10,000 kcal increment). Controlling for the duration of supplementation reduced variation due to heterogeneity from 82.5% to 66.1%, controlling for daily calories to 17.1%, and for total calories to 37.1%.

Other nutritional outcomes

Other data from these trials supported the broader nutritional benefits of ONS for people with dementia. Only two studies used the Mini Nutritional Assessment to assess overall nutritional status, both noting significant benefits associated with ONS[54;55]. ONS was associated with increases in upper arm circumference or arm muscle circumference (reflecting lean mass)[37;53;59], and triceps skin fold thickness (reflecting fat deposition)[54;59;60] in some but not all studies. Therefore the finding from one study that ONS was associated with selective benefits for lean body mass[37] was not clearly replicated. More direct evidence comes from one trial of ONS among people with dementia, showing a statistically significant within group increase in fat-free mass measured using dual-energy x-ray absorptiometry (DEXA) scan[55].

Issues in the administration and use of ONS

The main concerns regarding ONS are that older people do not like to take it; that it is associated with gastrointestinal side effects, including bloating, nausea and diarrhoea; and that the calorie value of supplements is offset by a reduction in the usual diet from regular meals. However, where reported, ONS was considered to be well tolerated, with typically high levels of adherence[54–56], specified in three studies as 95%[53], 78.8%[58] and 76%[60]. In only one study were adverse effects specifically examined, with no difference in the incidence of diarrhoea between ONS and placebo[56]. The trials that assessed overall energy consumption reported a net increase among those randomised to ONS[55;58;59], suggesting that those taking supplementation did not compensate by reducing their customary dietary intake. In one crossover trial that addressed this directly, mean compensation levels were 25.8% in those receiving ONS in the first phase and 27.6% for those receiving ONS in the second phase[58]; however, compensation was greater for those with lower BMIs, worse cognitive functioning and worse aberrant motor behaviours, suggesting that these at risk groups might receive least benefit from ONS. In a further analysis of data from the same study, those who responded successfully to ONS with increases in

Table 5.2
Results

Trial authors	% Weight change MD	Weight change in ONS	BMI change MD	BMI change in ONS	Mortality	Other sig findings	Non sig findings
Carver & Dobson, 1995[53]	IG +7.50 (3.86) CG +1.32 (3.75) MD = +6.18 (-0.02-+12.38) SE = 3.16 (From Milne) MD = +6.18 (3.82-8.54) SE = 1.20 (recalc from paper)	7.50 (5.81-9.19) SE=0.86	IG +1.3 (1.5*) CG +0.2 (1.5*) MD = +1.5		No deaths in either group	MUAC + TSF +	
Gil Gregorio 2003[54]			IG +1.6 (0.96) CG -0.3 (1.08) MD = 1.90 (1.41-2.39) SE=0.25	1.60 (1.19-2.01) SE= 0.21	Mortality 16% 4/25 vs 22.7% 17/74	Infection - Days in bed - 0.05 MNA + -0.2 vs -3.2 P=0.05 TSF +0.01	Cognitive Functional 'conduct' variables
Lauque, 2004[55]	IG +3.46 (4.24) CG +0.69 (4.15) MD=+2.77 (0.93-4.61) SE=0.94	3.46 (2.09-4.83) SE = 0.70	IG 0.80 (0.98) CG 0.16 (0.90) MD=0.64 (0.23-1.05) SE = 0.21	0.80 (0.48-1.12) SE=0.16	Deaths 2/46 treatment 0/45 control	MNA+ Calorie intake+	Fractures Pressure ulcers Hospitalization Cognition ADL
Wouters-Wesseling 2002[56]	IG +2.71 (4.65) CG -1.50 (5.62) MD = +4.21 (0.75-7.67) SE= From Milne	+2.71 (0.62-4.80) SE=1.06	IG +0.5 (0.91) CG -0.2 (0.95) MD = 0.70 (0.07-1.33) SE=0.32	0.50 (0.09-0.91)	Deaths 1/21 in ONS and 2/32 in placebo	Homocysteine, vitamin B_1 vitamin B_6 vitamin B_{12} folate and vitamin D	Barthel index (ADL) Diarrhoea
Wouters-Wesseling 2006[57]	IG +1.30 (3.69) CG -0.62 (6.00) MD=+1.92 (-1.48 to +5.32) (from Milne)	+1.30 (-0.40 to +3.00) SE=1.70			no deaths		Dietary energy intake mid-upper arm muscle circumference triceps skin fold thickness calf circumference ZIG score

Young et al 2004[58]	Baseline weight not reported hence assumed to be 60 kg	MD=1.55 (1.01-2.09) SE=0.27			No deaths	24h energy protein and carb intake +	Cog function, behavioural disturbance and behavioural function
Pivi et al 2011[37]	Assume baseline wt 60 kg and SD 10% IG +11.1[10] CG -3.7[10] MD = +14.7 (9.31-20.09) SE=2.75	11.1 (7.26-14.94) SE=1.96	No SD given Assume 1.5 IG 6.55 (1.5) CG -2.21 (1.5) MD=8.76 (8.16-9.56) SE=0.41 Within grp	6.55 (5.97-7.13) SE=0.29	3 deaths in IG 30, 1 in CG 30	MUAC+ AMC+	Triceps skin foldthickness
Faxen-Irving et al[60]	CG -0.48% (5.88) IG +6.13% (5.70) MD = 6.61 (2.49-10.73) SE=2.10	6.13 (3.69-8.57) SE=1.24	CG -0.10 (1.38) IG +1.30 (1.24) MD = 1.40 (0.58-2.22) SE=0.42	1.30 (0.71-1.89) SE=0.30		MMSE worsened in those in IG (p=0.01)	Katz ADL
Planas, 2004[59]			Grp A + micronutrient N=23 1.1 (1.26) 1.1 (0.59-1.61) SE = 0.26 GrpB - micronutrient N=21 1.6 (1.24) 1.6 (1.07-2.13) SE=0.27			energy consumption triceps skin fold thickness mid-upper-arm circumference serum magnesium zinc selenium	No difference in feeding behaviour or cognitive function.

IG= Intervention Group CG = Control Group MD = Mean Difference SE = Standard Error MNA = Mini Nutritional Assessment MUAC = Mid-upper arm circumference
TSF = Triceps skinfold thickness ADL = activities of daily living

Figure 5.1
Random effects meta-analysis forest-plot

Mean differences for the effect of oral nutritional supplementation on % change in body weight

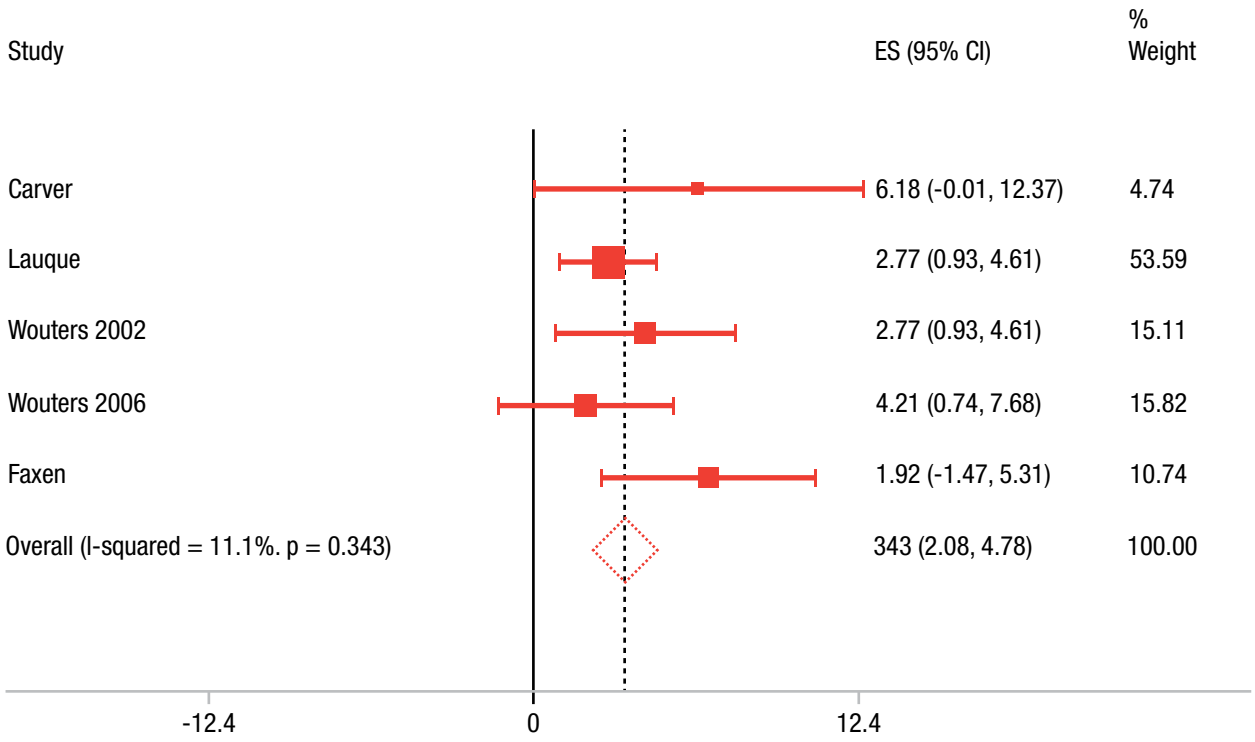


Figure 5.2
Random effects meta-analysis forest-plot

Mean differences for the effect of oral nutritional supplementation on Body Mass Index

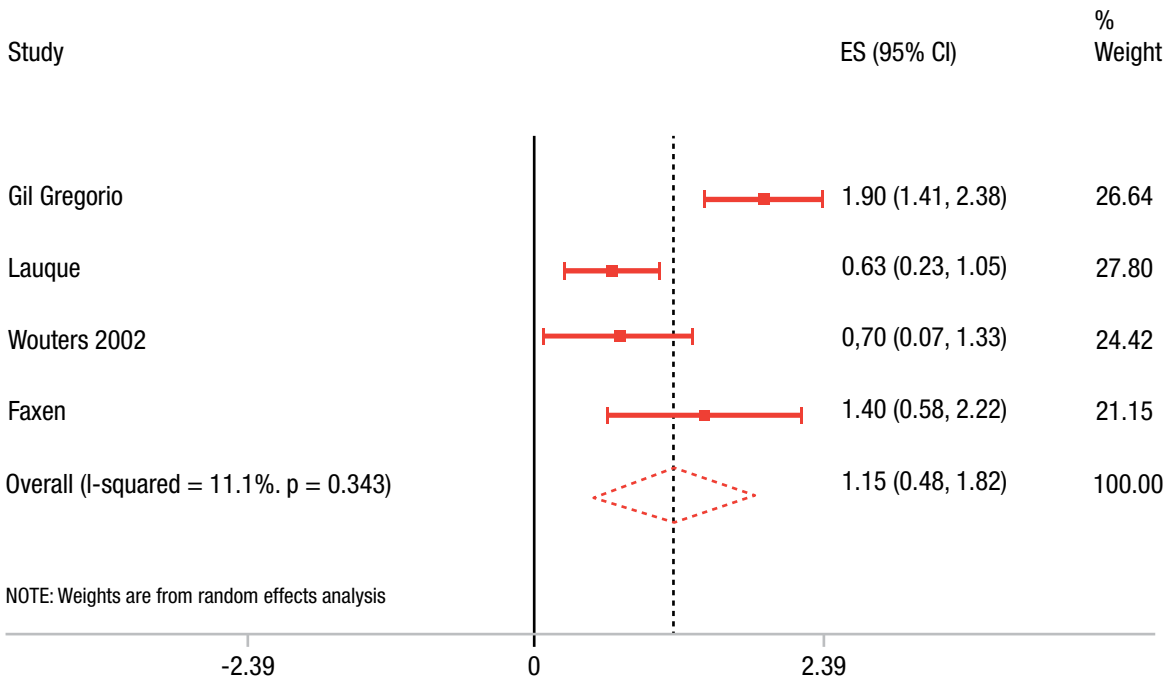


Figure 5.3
Metaregression indicating the effect of daily supplementation

Kilocalories upon % weight gain

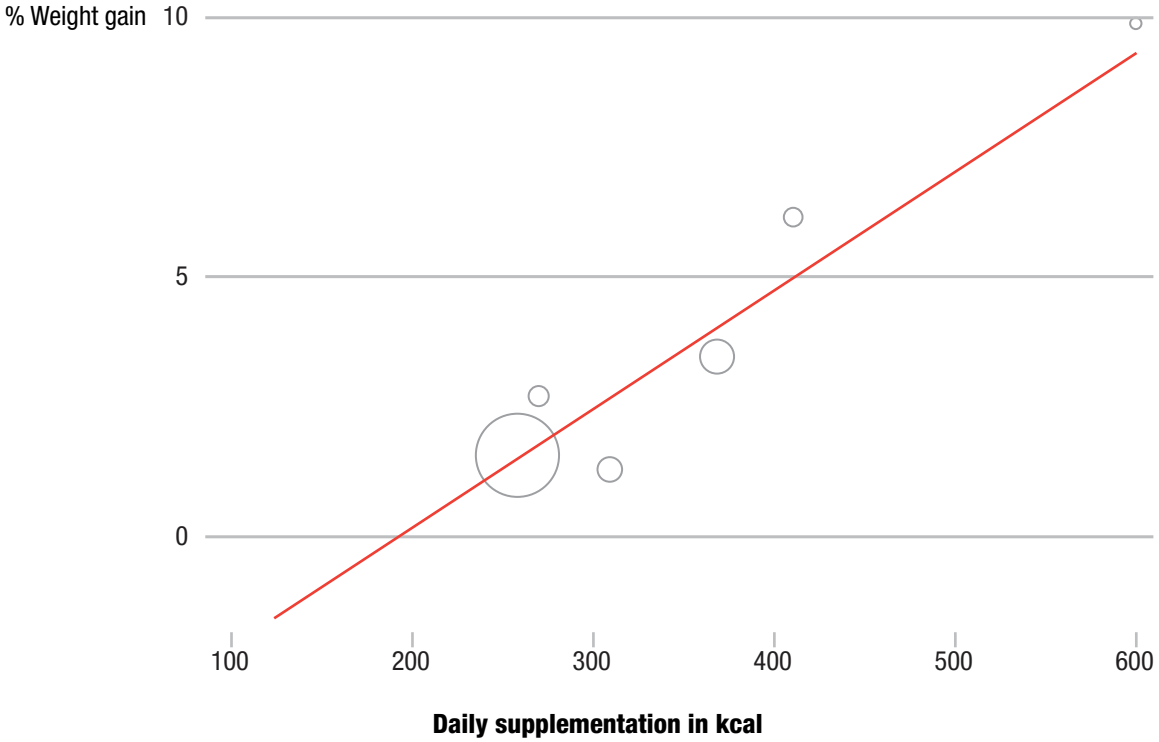
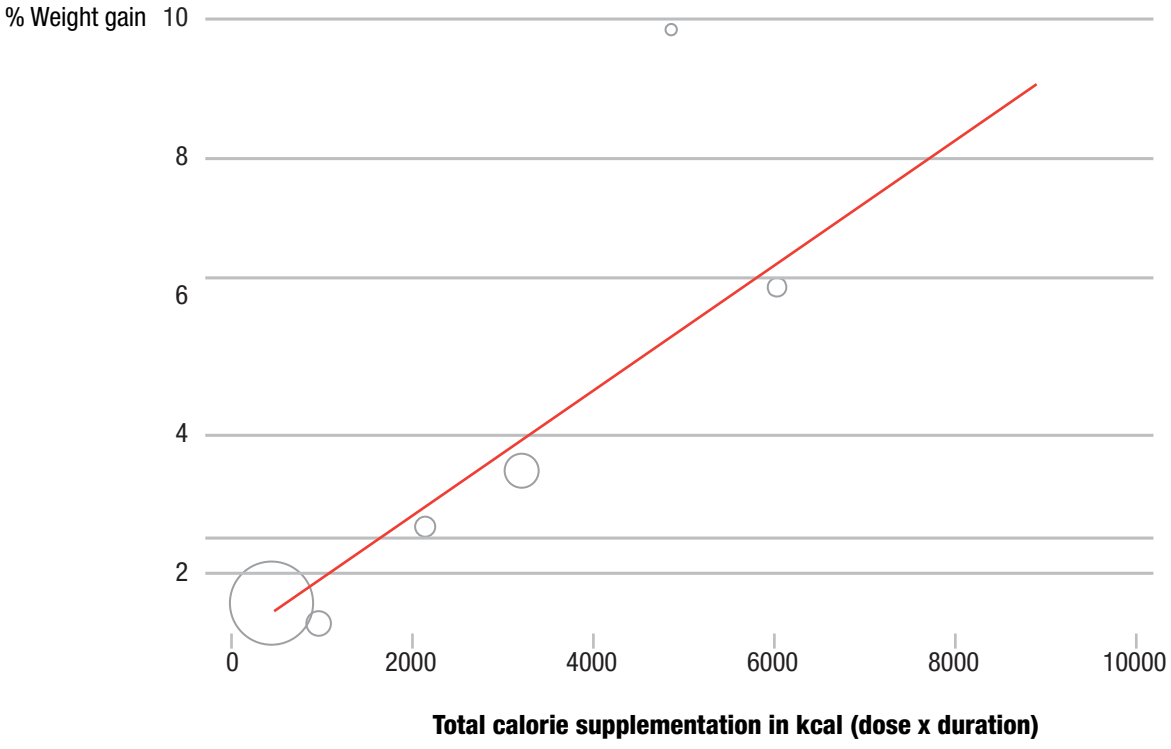


Figure 5.4
Metaregression indicating the effect of total calorie supplementation

Kilocalories upon % weight gain



daily energy intake maintained on average 58.8% of that increase post-supplementation, although stopping the supplement was associated with decreased habitual energy intake in low-BMI individuals who reduced their daily intakes during supplementation in response to the extra calories. For most of the trials, ONS was continued up to the final outcome assessment. However, in one other study, ONS were withdrawn after three months and outcomes reassessed at 6 months – significant increments in weight, BMI and fat-free body mass were retained in the intervention group, and significant weight loss (>4% of body weight) was reported to have occurred less often than in the control group[55].

Effect of ONS on other outcomes

There was insufficient evidence to judge the impact of ONS on mortality among people with dementia. Three trials reported no deaths[53;57;58], and 21 of the 35 deaths were observed in one trial with a relatively long (one year) follow-up[54]. The meta-analysed effect across four trials was RR 0.69, 95% CI 0.00–1.46.

No effect of ONS on cognitive function was observed in three trials[54;55;58] and one within group evaluation[59], while in one non-randomised controlled study cognitive deterioration was more marked in the ONS intervention group[60]. No benefit of ONS on activities of daily living was observed in five trials[54–56;58;60]. Such data as were provided for these outcomes did not permit meta-analysis.

Micronutrient supplementation

Background

Micronutrient deficiencies are relatively common among older people, due to insufficient dietary intake, inefficient absorption, or both. Low levels of vitamin B_{12} and folate (folic acid) are associated with high blood levels of the amino acid homocysteine which has been linked with the risk of arterial disease, dementia and Alzheimer's disease. Vitamin E is another dietary compound, with antioxidant properties. Evidence that free radicals may contribute to the pathological processes of Alzheimer's disease (AD) has led to interest in the use of vitamin E in its prevention and treatment. Here, we specifically report studies and reviews that have focused on micronutrient supplementation for the treatment of dementia.

Results

We identified three relevant reviews each covering the treatment of dementia as well as the use of these compounds in healthy older people; on folate with or without B_{12}[61] published in 2009 and with review content assessed as up-to-date on 21 July 2008; on B_{12}[62] published in 2009 with review content assessed as up-to-date on 23 January 2006; and on vitamin E[63] published in 2008 with review content assessed as up-to-date on 15 January 2007.

Vitamin B_{12}

Three trials were identified. Two trials included those with dementia and low B_{12} blood levels[64;65]. One evaluated oral supplementation with one month follow-up (n=31)[64], the other used B_{12} injections with 5 months of follow up (n=11)[65]. One much larger trial (n=140) recruited those aged 75 and over with B_{12} deficiency regardless of cognitive function[66]; at baseline 40 participants had a MMSE score below 25, and the mean MMSE was 26.5 points. There was no evidence from any of the trials of any benefits of treatment on cognitive function. However, the two treatment trials of those with dementia were underpowered to detect anything other than very large effects[64;65]. For the third trial[66] results were not presented for the subgroup of participants with cognitive impairment. The authors of the review considered the evidence to be 'insufficient' meaning that efficacy was neither demonstrated, nor excluded. A subsequent controlled study[67] of B_{12} intramuscular supplementation of those with deficiency in nursing homes (n=28) versus a non-deficient comparison group (n=28) failed to identify any cognitive benefit of supplementation. A more recent systematic review, noting 2.9 million B_{12} tests in Ontario in 2010 at a cost of $40 million concluded that 'moderate quality of evidence indicates treatment with vitamin B_{12} does not improve brain function'[68].

Folate

Two trials were identified that recruited patients with dementia, 41 patients with AD from Scotland[69], and 11 patients with varying subtypes of dementia and MMSE scores between 16 and 27[70]. A further UK trial included 149 participants; 95 had dementia (AD or mixed AD/VaD) and the remainder cognitive impairment no dementia[71]. Combined treatment with 2 mg folate and B_{12} had a significant effect on reducing serum homocysteine levels[71]. However, no such effect was seen with 1 mg daily folate supplementation alone[69]. In the Clarke trial there was no effect of folate 2 mg combined with B_{12} on MMSE (MD 0.39, 95% CI -0.43 to 1.21) or ADAS-Cog (change from baseline at 12 weeks MD 0.41, 95% CI -1.25 to 2.07). The only outcome for which pooling was possible, across two trials, was the effect of folate with or without B_{12} on MMSE for cognitive impairment and dementia (pooled MD 0.30, 95% CI -0.45 to 1.05). In the Connelly trial, while there was no effect of folate 1 mg on MMSE -0.13 (-1.96, 1.70) there was a significant net benefit on

Instrumental Activities of Daily Living 2.67 (0.25, 5.09), but not social behaviour. Those randomised to folate were much more likely to be considered as 'treatment responders' to cholinesterase inhibitors (OR 4.06, 95% CI 1.22–13.53).

The authors of the review conclude that there is insufficient evidence to conclude either way on the possible benefits or harms of folic acid. This is probably justified, although the evidence on cognitive impairment does seem conclusively negative. The findings of a possible positive interaction with acetylcholinesterase inhibitor medication requires replication[69]. For healthy older people, in the same review, possible cognitive benefits were identified in just one trial of those with elevated homocysteine levels; it may be that people with dementia with raised homocysteine may also be more likely to benefit.

Vitamin E

One trial was identified that recruited people with dementia[72], 341 patients with a diagnosis of probable AD of moderate severity (CDR of two), from 23 centres in the USA. The trial had a factorial design trial in which patients were randomised to vitamin E (2000 IU total daily) only, selegeline only, the two drugs combined, or placebo. The primary outcome was the survival time to any one of four endpoints, death, institutionalisation, progression to CDR severe (3.0) or change in loss of activities of daily living. Secondary outcomes were change in ADAS-Cog and MMSE, but since these were assessed on the basis of change between baseline and last follow-up with no fixed endpoint, these were not assessed in the Cochrane review. The Cochrane reviewers only compared the vitamin E and placebo groups, to avoid confounding. In so doing they confirmed the findings from the original analysis of a statistically significant reduction in the main endpoint (progression) with an OR of 0.49, 95% CI 0.25 to 0.96, but a statistically significant increase in falls OR 3.09, 95% CI 1.07 to 8.62. (RR 0.70, P=0.08). The effect size for the main endpoint was similar to the survival analysis conducted by the trial investigators once baseline differences in MMSE scores had been accounted for (HR 0.47, p=0.001)[72]. The authors of the Cochrane review conclude that there is no evidence of efficacy of vitamin E in the treatment of people with AD, but that more research is needed to identify its role of vitamin E, if any, in the management of cognitive impairment.

A recent trial assessed a 16-week multi-vitamin supplementation programme, comprising 800 IU/d of vitamin E, 500 mg/d of vitamin C and 900 mg/d of α-lipoic acid[73]. This intervention did not influence cerebrospinal fluid Alzheimer's disease biomarkers, but the group that received this supplementation experienced accelerated cognitive decline, compared to controls, raising potential safety concerns.

In 2014 results were published of the TEAM-AD VA collaborative double-blind, placebo-controlled, parallel-group, randomised clinical trial involving 613 patients with mild to moderate AD, comparing either 2000 IU/d of alpha tocopherol (vitamin E, n=152), 20 mg/d of memantine (n=155), the combination (n=154), or placebo (n=152)[74]. Over the mean follow-up of 2.3 years, ADCS-ADL Inventory scores declined by 3.15 units (95% CI 0.92–5.39) less in the vitamin E group compared with the placebo group. This change in the vitamin E group translates into a delay in clinical progression of 19% per year compared with placebo or a delay of approximately 6.2 months over the follow-up period. Caregiver time increased least in the vitamin E group. All-cause mortality and safety analyses did not suggest increased rates of adverse outcomes in the vitamin E group. These findings suggest benefit of vitamin E in mild to moderate AD by slowing functional decline and decreasing caregiver burden.

Medical food interventions

Medical foods are defined as a special category of products that are intended for the specific dietary management of a disease or condition that has distinctive nutritional requirements. There are three medical foods that claim to have benefits for use in dementia patients and are available in the USA and/or Europe: Axona® (AC-1202, Accera, Inc., CO, USA), Souvenaid® (Danone Research, France) and CerefolinNAC® (LA, USA)[75].

The rationale for the use of Souvenaid is that a combination of nutrients (eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), phospholipids, choline, uridine monophosphate, vitamins E, C, B_6 and B_{12}, selenium and folic acid) might be required synergistically to increase brain levels of phosphatide molecules that comprise the bulk of brain synaptic membranes. The efficacy of Souvenaid has been tested in a pilot randomised controlled trial in 225 drug-naïve patients with mild AD[76], and two subsequent definitive trials of 259[77], and 527[78] patients with mild to moderate AD. In the pilot trial, at 12 weeks, significant improvement was noted in the delayed verbal recall task in the treatment group compared with control (p = 0.02). However, there was no change and no significant difference in other relevant outcomes; ADAS-Cog, Clinician Interview Based Impression of Change, activities of daily living, or quality of life. The subsequent Souvenir II study was a 24-week, randomised, controlled, double-blind, parallel-group, multi-country trial to confirm and extend previous findings in drug-naive

patients with mild AD. 259 patients, recruited from 27 AD centres in Netherlands, Germany, Belgium, Spain, Italy and France, were randomised 1:1 to receive Souvenaid or an iso-caloric control product once daily for 24 weeks. The primary outcome was the memory function domain Z-score of the Neuropsychological Test Battery (NTB). Electroencephalography (EEG) measures served as secondary outcomes as marker for synaptic connectivity. The NTB memory domain Z-score was reported as being statistically significant in the active versus the control group over the 24-week intervention period (p = 0.023). However, the reported confidence intervals (Cohen's d 0.21, 95% CI -0.06 to +0.49) do not support statistical significance, a likely explanation being that one-tailed rather than two-tailed p-values were calculated although this is not specified. This approach, which assumes that the treatment can only improve and not worsen the outcome is unconventional. No significant effect was observed for the NTB total composite z-score (p = 0.053). EEG measures of functional connectivity in the delta band were significantly different between study groups during 24 weeks in favour of the active group. The definitive trial conducted in the USA with 579 patients with mild to moderate AD failed to show any beneficial effect of Souvenaid upon cognitive outcomes (ADAS-COG mean difference =+0.37 points, 95% -0.75 to +1.49)[78]. Compliance was very high across all three studies (86–97%) with no indication of excess adverse events. The trials were sponsored by Danone Research–Centre for Specialised Nutrition (part of Groupe Danone – the manufacturers of Souvenaid), who were involved in study design, data collection and analysis. Alpha-Plus Medical Communications Limited were involved in drafting and editing the manuscript for the pilot trial.

Two other 'medical foods' have been introduced to the market and are available by prescription in the USA. Axona is a medium-chain triglyceride product combining glycerine and caprylic acid, providing ketone bodies to the brain, as an alternative energy source to glucose. So far there has only been one Phase II randomised clinical trial in patients with mild to moderate AD. Cognitive function, measured by the Assessment Scale-cognitive subscale (ADAS-cog) were slightly improved at day 45 in those taking Axona, but these differences were not significant at day 90, apart from in a subset of ApoE ε4-negative participants[75]. The duration of this trial was very short, and a Phase III trial is needed to confirm any finding. Discontinuation due to adverse events in the treatment group was also relatively high (23%), compared to the placebo group (6%). CerofolinNAC, which consists of 2 mg of vitamin B_{12}, 5.6 mg of L-methylfolate and 600 mg of N-acetylcysteine has also been approved by the FSA for the prevention and treatment of vitamin deficiencies associated with memory loss. One possible advantage of using CerefolinNAC over other B vitamin supplements is that it contains formulations of folic acid and vitamin B_{12}, which are 'active', hence ready to use by the body without the need for conversion. However, no randomised clinical trials of this supplement have ever been carried out, and none are currently taking place. This means that there is no specific evidence on the effectiveness of CerofolinNAC for treatment of cognitive decline.

Conclusion

There is fairly consistent evidence from several randomised controlled trials that macronutrient ONS is effective in maintaining or improving weight among people with dementia. Supplements seem to be relatively well tolerated, with high levels of adherence at least under controlled clinical trial conditions. The nutritional benefit gained from supplementation seems to be proportionate to its intensity and duration. However, benefits gained (improved nutritional status and calorie intake) from short term supplementation, over weeks or months, does seem to be retained in the short to medium term[55;79], raising the possibility that brief cycles of ONS may be as effective as long-term supplementation[79]. While one of the trials[53] included only those who were markedly undernourished, most others focused mainly on those who were at risk of undernutrition, or normally nourished. There is therefore an important outstanding question as to the effectiveness of ONS among people with dementia who are already undernourished[58].

Given the health hazards of undernutrition, particularly when this involves protein catabolism and loss of lean body mass, one might expect that maintenance of nutritional status might be associated with wider health benefits than those identified in the studies reviewed. That this was not the case may be explained by the implausibility of direct benefits (cognition and behavioural disturbance), the need for a longer period of nutritional support and a longer follow-up period (disability, mortality)[51], and the lack of assessment of relevant outcomes (quality of life, depression, physical functioning).

Several of the studies included an element of nutritional education provided to caregivers (usually professionals in care homes)[55;60]. As such, the relative benefits of ONS and nutritional education may be difficult to disentangle. However, equivalent weight gain was observed when ONS was provided without nutritional

education[37;53]. Given the timing of interventions and effects, indirect evidence from one study where both interventions were provided suggested a greater impact of ONS than nutritional education to staff[60]. In one trial in which a randomised comparison was made of ONS and a 10 session nutritional education programme for family caregivers, the ONS intervention was superior for almost all outcomes[37].

There is, as yet, no evidence to recommend the use of micronutrient supplementation at any stage of dementia. The possible exception to this advice is that of vitamin E supplementation in the light of two positive trials with respect to cognitive and functional decline outcomes, although the balance of risks and benefits need to be more securely established. There is, currently no evidence to support the widespread screening for folate and B_{12} deficiency enshrined in many good practice post-diagnostic recommendations. Supplementation does not seem to affect cognitive function, and the cost-effectiveness of these non-evidence based recommendations needs to be established in randomised controlled trials. Despite the strong theoretical basis for micronutrient supplementation (see Chapter 4), there is not yet enough evidence to recommend the use of any medical foods for the treatment of Alzheimer's disease. There have been few trials, most of which are small and underpowered, do not focus upon those with proven micronutrient deficiency, and have relatively short follow-up periods. We do recommend further research in this area.

Feeding assistance – managing aversive feeding behaviours in advanced dementia

A case study from the Dominican Republic

Background

Dr Daisy Acosta is an old age psychiatrist specializing in dementia care, with a large practice in the Dominican Republic. She had noted that during the long course of Alzheimer's disease, aversive behaviours develop related to food selection and intake that have direct consequences on the nutritional status and the physical health of these patients. In the Dominican Republic, food and eating are central to most activities, to the point that eating well is taken as an essential parameter of good health. In the same way, a well fed patient that is gaining or not losing weight is taken as evidence of good care. 'She takes good care of him; look at his red cheeks' or 'She is good with him/her, see how chubby he/she is'. Family care for people with dementia is supplemented by paid workers whether domestic workers (hired originally to clean the house and prepare food), or care assistants in nursing homes. Domestic care workers are employed sometimes just during the daytime, or to sleep over from Monday till Saturday. They usually have very low education; some are illiterate and they tend to be underpaid. Dr Acosta notes:

> These are the people that for the most part we use as caregivers, in the private or public sector, in the patient's residence or in nursing homes. I came to realize that one important reason for the high turnover of paid caregivers had to do with food and feeding; the patient's decreased appetite, selective eating behaviours, weight loss, and feeding difficulties. These symptoms were not well known, or understood by the caregiver or the family member as an aspect of the illness. The family member would often accuse the caregiver of not taking good care of the patient, or of stealing the food to feed others in their own families. I also work in nursing homes in the Dominican Republic and realised that the same thing was happening there. I visited the homes at lunch time, when my practice was quieter and began to notice the chaos and desperation of the staff; residents refusing to eat, spitting rice all over the place. It was then that I started to analyse what was happening and was determined to do something to help.

The method I used

I started by reviewing the literature that I found on this subject. To have a clearer picture, I obtained consent to videotape several settings: private homes, nursing homes and state nursing homes identifying the different types of eating behaviours that the residents presented and how the staff reacted and handled them. I then watched the videos with the staff and explained what was happening. I demonstrated to them the use of the Mini Mental State Examination (MMSE) to assess cognitive impairment, and we administered this to each resident to assess the severity of dementia. We used the FAST scale to teach them to assess the stage of the dementia, and to understand how not only cognition but also functioning was affected in a more or less predictable manner with the progression of the illness. We worked together to assess the probable type of dementia that the each patient had, reviewing their case history. We then categorised the eating and feeding behaviours, using the Adversive Feeding Behaviour Inventory and the Feeding Dependency Scale[14], so that they had a better idea of the needs of each individual resident. In other words, I went with them, the staff, through

Box 5.1

Behaviours observed

Linked to the taxonomy proposed in the Aversive Feeding Behaviours Inventory[14]

- Oropharyngeal dysphagia
  - Accepts food, then fails to swallow
  - Closes the lips
  - Accepts food into mouth, then spits it out
  - Food drools from mouth
  - Close mouth tight, or bites the spoon impairing food entry
  - Continuous mouth movements hinder or prevent food entry
- Selective feeding behaviours
  - Accept only liquids
  - Prefers liquids
- Resistive behaviours
  - Covers mouth with hands
  - Pushes the food away
  - Throws food
- Dyspraxia/agnosia
  - Plays with food
  - Constant vocalization interfering with feeding
  - Goes away from the table, pacing around throughout the eating time
  - Uses fingers instead of utensils
  - Eats non-edible materials
- Not classified in AFBI
  - Sucking fingers, preventing food from entering the mouth (sucking reflex)
  - Choking (indicative of oropharyngeal dysphagia)

a process of informal education about dementia, the course of dementia, and feeding and eating problems through the illness. In private homes, both the paid caregiver and the main family caregiver were involved in the same education process.

I then worked with nursing home staff and home caregivers to find ways, devices, and measures, to help improve 'eating time' without incurring any additional expenses.

In all, we worked with 65 people with dementia, 22 men and 43 women. All had advanced dementia, with MMSE scores ranging from 0–5, and most with FAST grade 7 (severe dementia). Forty of them lived in state institutions, 15 were residents in two private nursing homes, and 10 lived in their own homes. All patients were weighed at the beginning of the programme, and then every month for 8 months. A wide range of aversive feeding behaviours were identified, including most of the 23 categories included in the Aversive Feeding Behaviour Inventory[14] (Box 5.1). Many patients exhibited more than one of the behaviours, with some exhibiting as many as five. Two of the observed behaviours were not included in the AFBI, choking (a likely consequence of oropharyngeal dysphagia), and sucking on fingers interfering with eating (probably a primitive 'release' reflex).

Lessons learnt from the programme

The enthusiasm and active involvement of the staff in the process was crucial. They began to give ideas as to how to improve each patient's behaviour and were very creative in their suggestions. Categorizing the behaviour was an essential first step in order to plan and implement measures to help it. These measures can be very simple, not costly, and some of them were quite effective (see Table 5.3). The education and the positive attitude of the feeder were crucial in determining the success of the intervention. The education of those involved, about eating and feeding in patients with AD, helped to reduce the neglect of this essential aspect of care. Another important lesson learnt was not to imagine that all people with dementia would have equal needs for caloric intake, and to think of hunger as a possible explanation for those residents who screamed or otherwise vocalised distress, being unable more clearly to articulate their needs. As well as calorie intake, staff needed to be taught about the importance of offering liquids often, and to avoid fluid restriction with the intention of avoiding incontinence or frequent diaper changes.

Four years after the introduction of the programme, all of the patients with severe dementia involved in the study have since died. However, most of the staff involved in the project are still working in the same care settings, and continuing to use what they had learnt. Some of the home care workers, equipped now with some special knowledge and skills regarding dementia care, are still working with other patients.

Assistive tableware

Research by the Royal College of Art design team revealed that assistive tableware was not used as much as it might have been in UK care homes[39]. Some care home managers opted not to use them, because of a lack of aesthetic

Table 5.3
Some solutions generated for managing common aversive feeding behaviours

For those who paced constantly	High chairs, with trays prevented the patients from wandering, and allowed them to focus on their meals, with excellent results, most becoming independent eaters. This was the single measure that resulted in the most weight gain with one patient gaining 10 pounds in the first month.
For those with sucking reflexes, sucking their fingers, preventing the food from entering the mouth	Keeping the hands busy, holding a book or a soft toy, prevented the behaviour, facilitating eating time.
For those who wouldn't open their mouth	A touch on the cheek with an ice cold spoon helped to open the mouth, providing a brief opportunity to place food in the mouth.
For those who chewed continuously and then spat, rather than swallowed	A change from solids to semi-liquids solved most of this behaviour.
There were three patients who used to scream all the time and did not sleep well	After a doubling of the food ration, they stopped screaming and began to sleep better.
For those patients shaking their heads in a negative manner at the sight of food	Feeders were advised to ignore the negative behaviour, avoiding direct conflict, but gently encouraging the person to eat all of the food in the portion.
For those choking on food	The feeder was educated about oropharyngeal dysphagia, and the dangerous consequences of aspiration. They were instructed to put the patient in the right position, to feed slowly with small amounts and to use thickener in the liquids.

appeal. Since residents had different needs and abilities, and assistive tableware stood out from standard items, users of assistive table settings felt different, and stigmatised. The aim of the design team was to create a range of matching tableware that formed a complete set, could be used by people of all abilities, and resembled standard domestic tableware (Figure 5.5). Colour contrasts feature prominently – for example royal blue plates provide a contrast both with a white table covering and food on a plate. The same approach could be used with cups; royal blue and white are used to help those with low visual acuity or agnosia locate the handle and rim. The sides are angled to reduce the need to tip the cup, the handle is large and easily gripped, and the top is wide enough to allow a person's nose to fit inside the cup when tipped.

A common strategy as dementia advances and feeding difficulties develop is to simplify the amount of utensils by providing just a plate and spoon with pureed or diced food that can be eaten without needing to be cut up by the resident. However, residents can push the food off the side of the plate when they are trying to pick it up. To address this, the plate contains a high lip in its profile that helps to push the food onto the spoon as a person tries to scoop it up.

The 'care cup' is one of the most disliked assistive tableware items, because of its similarity in appearance to a baby product (made from plastic with two handles and a nippled lid). The purpose of this item is that residents with reduced dexterity can grip both sides of the cup without spilling the liquid, or burning their hands as they might with a ceramic mug. The design team proposed an alternative approach, made from

Fig 5.5
Examples of assistive tableware

Images courtesy of Helen Hamlyn Center, Royal College of Art

Colour contrast for visual impairment

Plate with a high lip helps to push food onto a spoon

Double sided ceramic cup for easy grip

Ceramic cup with lid to avoid spillage

Assistive plate with divide to ensure separation of soft foods and easy grip with lip underneath

ceramic but from a mould with a double skin and an air-filled cavity between the inside and outside surfaces. With this insulation, the liquid is kept warm while the outside of the cup remains cool and can be gripped without risk of burning. The lid minimises the association to the nipple of a baby cup by elongating the form around the rim.

Feeding a person with dementia is one of the most challenging and time-consuming tasks in a caregiver's day. The tableware includes items designed specifically for use with assisted feeding, including a plate, a bowl and lids for cups. The items are reduced in weight, and designed so that they can be easily and securely grasped by the carer, with one hand. The plate allows the carer to orientate it in an 'offering position' (in the sensory range of the person being fed so that they can see and smell what they are eating) and draw it under the person's chin to minimise the risk of spilling. A version of the plate with a central divide is also available for people who require a soft food diet. This ensures that different food groups stay separated and that people can still enjoy the uniqueness of each flavour.

Managing oropharyngeal dysphagia in advanced dementia through enteral tube feeding

Problems with swallowing are common in advanced dementia. However, the use of nasogastic or of percutaneous endoscopic gastrostomy (PEG) feeding tubes, while quite widespread, is controversial, and needs to be evaluated carefully with respect to patient and caregiver preferences, and the balance of risks and benefits for individual patients. A nasogastric tube is passed through the nose and into the stomach, while a PEG tube is inserted into the stomach via a permanent incision in the abdominal wall requiring a surgical procedure and anaesthetic. A Cochrane systematic review suggests that tube feeding for people with dementia does not confer any benefit regarding nutritional status, reduction of pressure sores, mortality risk or survival time[80]. Families and health professionals often have unrealistic expectations of the outcomes of tube feeding. Potential for harm exists from an increase in urinary and faecal incontinence, leading to pressure sores; from discomfort, and attempts to remove the tubes, which may lead to sedation being given; and from an increase in pulmonary secretions[80].

Advanced eating and swallowing problems need to be seen more in the context of holistic palliative end-of-life care. In addition to eating and swallowing problems, symptom burden at the end-of–life for people with dementia arises from pain[81], pressure sores[82;83], shortness of breath[84], infections (particularly pneumonia[85]), and agitation and other psychological symptoms[86]. These are all conditions that can cause much discomfort and distress, but which can be alleviated through effective palliative care. Communication and shared decision-making are key factors in end-of-life care. Having trust in doctors and surrounding staff is an essential factor for patients and caregivers[87]. However, many nurses and care home staff do not feel well prepared to deal with issues related to end-of-life and dying with dementia, and there is a need to improve training for nursing home and specialist palliative care staff to deal with advanced dementia, and to achieve best practice for people with dementia at the end-of-life[88].

Summary and conclusion

Micronutrient and macronutrient (protein and energy) deficiency are common in dementia and Alzheimer's disease, and it is clear that undernutrition has important consequences for health, quality of life and survival. Loss of body weight seems on the one hand to be a natural part of the condition, with complex multifactorial determinants, and yet to be amenable to intervention.

Standard recommendations for dietary management in dementia emphasise the role of dietary advice including fortification of existing diet to boost the protein and energy content, before resorting to oral nutritional supplements (ONS). This approach could be characterised as 'food first', and is grounded in common sense. Boosting calorie intake should improve nutritional status, and doing this through natural foods is likely to be more appealing than supplements, which can be costly. However, the evidence indicates that dietary advice alone is not effective in maintaining or increasing weight among people with dementia, whereas oral nutritional supplementation is highly effective with weight gain directly proportionate to the dose and duration of the supplementation. Therefore, there is a strong case for being more proactive in the use of oral nutritional supplements, which are probably underutilised, well tolerated and associated with few if any adverse effects. Supplements need not be costly – for example, a current feasibility trial in India is evaluating the acceptability and feasibility for frail dependent older people of a locally developed protein and energy rich product comprising ragi, green gram, roasted Bengal gram, roasted groundnut, and soya flour prepared as a powder that can be consumed as a soup or sprinkled on food, and provides 1854 kcal per daily 500g bag (personal

communication AT Jotheeswaran). The cost is substantially less than one US dollar per day.

Certainly ONS should be used in all those people with dementia found to be undernourished[89]. For those at risk of undernutrition, if nutritional status is not improved with dietary advice, then ONS should be implemented without delay[89]. Given the relative lack of large definitive long-term trials in this area, there are still some important questions to be resolved:

- Should those with undernutrition receive continuous ONS (and is this feasible and acceptable), or is short interval ONS equally effective and more acceptable?
- Is ONS as effective for those with undernutrition as for those at risk of undernutrition?
- Is long-term ONS associated with net benefits for cognition, functional status, depression, quality of life, and survival?

Dietary advice should remain a standard recommendation, not least because of the need to ensure that ONS is used appropriately, and that use of ONS does not lead to substitution (a compensatory reduction of the customary diet). There is a clear demand from caregivers for advice and support, particularly with aversive feeding behaviours. There has been remarkably little research into nutritional training and education of care assistants in long-term care facilities, with many anecdotal examples of the potential benefits of this approach.

While many people with dementia use micronutrient supplements, usually at their own cost, there is little or no evidence of any benefit as regards progression of the condition. On the current evidence, the recommendation would be that these supplements should neither be marketed nor used for the treatment of Alzheimer's disease or other forms of dementia. B_{12} or folate deficiency, if identified, should be corrected. However, the overall cost-benefits of screening for these deficiencies in all patients with newly diagnosed dementia are not established, and current recommendations are not based on evidence. Very few older people are deficient in vitamin E. However, hypersupplementation of this vitamin (2000 IU total daily) does seem to be associated, in two randomised controlled trials, with slower progression of the cognitive and functional impairment of Alzheimer's disease. However, these hypersupplementation levels are 100 times higher than the recommended daily allowance to maintain vitamin E levels (22 IU) and exceed the tolerable upper intake levels of 1500 IU daily. Excess intake of vitamin E, particularly over the longer term may be associated with risk of bleeding and haemorrhagic stroke. Therefore the use of this agent cannot be recommended unequivocally until more data is available on the balance of risks and benefits.

Likewise, there is strong evidence, although not from randomised controlled trials, that systems level interventions, for example small scale household level dining, 'family style' eating arrangements, and use of appropriate tableware and lighting levels may be associated with increased calorie consumption and increases in weight. Much more work needs to be carried out into the effectiveness of assistive feeding interventions to address aversive feeding behaviours.

Although much of the work on nutritional interventions has been carried out in long-term care facilities, many of the findings are generalisable to home care by informal carers. This would include the benefits of ONS (and the relative inefficacy of dietary advice alone), the importance of a home dining environment, and including the person with dementia as part of the family social dining activity. Many informal caregivers struggle with aversive feeding behaviours, and the benefits of focused support and training interventions needs to be evaluated in this group.

Examples of dementia care best practice

Northeast Health (NEH), New York

Submitted by Carole DeBonte

Northeast Health has two assisted living dementia dedicated communities. The communities serve meals in country kitchen style dining venues. Food is provided to the units and placed in the kitchen steam tables. Nursing staff serve the meals to the residents in the dining rooms (3 at each community) in a home like atmosphere.

Residents are offered a variety of seating options including tables in front of the "kitchens" as in your home. Dining is also offered in a "dining room" adjacent to the kitchen area, or in quiet locations. Menus are offered to the residents to view in menu jackets. Residents enjoy stopping by the kitchen island and viewing the menu during the day. Snacks and sandwiches are available in the kitchens throughout the day and night. High calorie and protein snacks are planned in place of supplements whenever possible. Dishware is selected based on the resident needs, for example a large mug like bowl is used for soups offering the residents the opportunity to feed themselves and enjoy a home like soup service. Different color dishware is used based on the resident's cognitive needs.

Menu planning is community process. The nursing staff are very involved in evaluating foods that are well accepted. We start with the main menu and modify for appropriate sides and condiments. We typically offer one hot entrée and sides and an alternative menu is offered based on the always available menu choices. This has minimized difficulty with menu choice concerns at the meals.

Sample entrée plates are presented at each kitchen area to aid the nursing staff in dishing up the food in a pleasing manner, and in the correct portions. The food is delivered to the kitchens, then one nursing staff is in the kitchen and the other aides bring the food to the residents. Food is served based on the resident's dining preference.

Success is measured by the residents' enjoyment at meals and successful nutrition outcomes. The dining process is a continual work in progress noting that residents with dementia may change stages and their needs are evolving. Good team work by the nursing staff, activities, dietitian and food and nutrition services staff are recipe for successful dining services!

Fellowship Senior Living, New Jersey

Submitted by Brian Lawrence

Fellowship Senior Living is just about ready to start a three-year development project that includes new memory care households following the person centered care philosophy. There will be two new households which will house between 16 – 20 residents each. Each household will be on the first floor and will have a 4 seasons porch (sunroom), a covered outside porch and a private courtyard. They will also have their own hair salon, art studio, living room, dining room, kitchen and den plus a private dining room for entertaining guests. Each bedroom will be private with at least two windows to allow for an abundance of natural light. The household will be set up to look like a real house, with a front door and doorbell, common living areas in the front and bedrooms in the back. Aside from the front door, exits will be tucked in corners or out of site to avoid tempting the residents.

Meals will be made by the homemakers; menus planned with the resident's help. Homemakers will serve food much the same as you'd do in your home. Resident's will be able to participate in multiple activities involving food preparation. Breakfast will be made to order as the residents awaken and wander down to the kitchen on their own time schedule; pajamas welcome!

Holly Creek – Christian Living Communities, Colorado

Submitted by Kara Emig

Our memory care is assisted living but we focus on resident-led food activities. Every afternoon they bake/make something to enjoy. Yesterday it was mini corndogs made from scratch. Sometimes it's cookies or just cutting up the apples for a pie. Anything to bring back the memories. It is a small community of 12 residents with very involved staff, so it's a family-type setting.

Aldersgate Village, Mississippi

Submitted by Lindsey Bevans

At Aldersgate Village we have expanded our breakfast always available menu in our dementia neighborhoods with items that nursing staff can prepare during non-traditional meal times when there is not a dining services aide to assist. The Breakfast Always Available Menu contains new items such as homemade biscuits and gravy, fresh muffins, fresh pastries (ex: cinnamon rolls and Danishes), waffles, pancakes, a variety of seasonal fresh fruit and more. The dietitians trained the nursing staff on how to correctly prepare and serve these items to ensure the residents receive appropriate diet (type and texture) and that it is completed in a safe way. Nursing staff were also educated about the different diet textures and shown how they can use the diet manual as a reference any time they have questions pertaining to diets. There have been many benefits observed from these changes. The residents are now able to receive food at their desired time and I have heard multiple comments from residents (and family members) reporting that they like the new menu and being able to eat when they want. Nursing staff have gained knowledge regarding differences in diets and now feel more comfortable dealing with the different diet types. And from a nutritional point of view, I have seen a decrease in weight loss in the dementia neighborhoods.

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Appendix 1

Literature searches for nutrients on Medline

Vitamins B

((“homocysteine”[MeSH Terms] OR “homocysteine”[All Fields]) OR (“homocysteine”[MeSH Terms] OR “homocysteine”[All Fields]) OR (“hyperhomocysteinemia”[MeSH Terms] OR “hyperhomocysteinemia”[All Fields]) OR (“hyperhomocysteinemia”[MeSH Terms] OR “hyperhomocysteinemia”[All Fields] OR “hyperhomocysteinaemia”[All Fields]) OR (“vitamin b complex”[MeSH Terms] OR “vitamin b complex”[All Fields] OR “b vitamins”[All Fields] OR “vitamin b complex”[Pharmacological Action]) OR (“vitamin b 12”[MeSH Terms] OR “vitamin b 12”[All Fields] OR (“vitamin”[All Fields] AND “b12”[All Fields]) OR “vitamin b12”[All Fields]) OR (“vitamin b 12”[MeSH Terms] OR “vitamin b 12”[All Fields]) OR (“vitamin b 12”[MeSH Terms] OR “vitamin b 12”[All Fields] OR “cobalamin”[All Fields]) OR (“vitamin b 12”[MeSH Terms] OR “vitamin b 12”[All Fields] OR “cyanocobalamin”[All Fields]) OR (“vitamin b 6”[MeSH Terms] OR “vitamin b 6”[All Fields] OR (“vitamin”[All Fields] AND “b6”[All Fields]) OR “vitamin b6”[All Fields]) OR (“vitamin b 6”[MeSH Terms] OR “vitamin b 6”[All Fields]) OR (“pyridoxine”[MeSH Terms] OR “pyridoxine”[All Fields]) OR (“folic acid”[MeSH Terms] OR (“folic”[All Fields] AND “acid”[All Fields]) OR “folic acid”[All Fields] OR “folate”[All Fields]) OR (“folic acid”[MeSH Terms] OR (“folic”[All Fields] AND “acid”[All Fields]) OR “folic acid”[All Fields]) OR (“folic acid”[MeSH Terms] OR (“folic”[All Fields] AND “acid”[All Fields]) OR “folic acid”[All Fields] OR (“vitamin”[All Fields] AND “b9”[All Fields]) OR “vitamin b9”[All Fields]) OR ((“vitamins”[MeSH Terms] OR “vitamins”[All Fields] OR “vitamin”[All Fields] OR “vitamins”[Pharmacological Action]) AND B-9[All Fields])) AND ((“memory”[MeSH Terms] OR “memory”[All Fields]) OR (“cognition”[MeSH Terms] OR “cognition”[All Fields]) OR cognitive[All Fields] OR (“alzheimer disease”[MeSH Terms] OR (“alzheimer”[All Fields] AND “disease”[All Fields]) OR “alzheimer disease”[All Fields] OR “alzheimer”[All Fields]) OR (“dementia”[MeSH Terms] OR “dementia”[All Fields])) AND “humans”[MeSH Terms])

Antioxidants

((“vitamin E”[MeSH Terms] OR “vitamin E”[All Fields] OR “tocopherol”[All Fields] OR “tocopherols” [MeSH Terms] “tocotrienol”[All Fields] OR “tocotrienols”[MeSH Terms]) OR (“vitamin C”[All Fields] OR (“ascorbic”[All Fields] AND “acid”[All Fields]) OR “ascorbic acid”[MeSH Terms]) OR “tocopherols” [MeSH Terms] “tocotrienol”[All Fields] OR “tocotrienols”[MeSH Terms]) OR (“beta Carotene”[MeSH Terms] OR (“beta”[All Fields] AND “carotene”[All Fields]) OR “betacarotene”[All Fields]) OR (“carotene”[All Fields] OR “Carotenoids”[MeSH Terms] OR “carotenoids”[All Fields] OR “vitamin A”[MeSH Terms] OR “vitamin A”[All Fields]) OR (“flavonoids”[MeSH Terms] OR “flavonoids”[All Fields]) OR (“antioxidants”[MeSH Terms] OR “antioxidants”[All Fields] OR “anti-oxidants”[All Fields]) OR (“Ginkgo biloba”[MeSH Terms] OR “Ginkgo biloba”[All Fields])) AND ((“memory”[MeSH Terms] OR “memory”[All Fields]) OR (“cognition”[MeSH Terms] OR “cognition”[All Fields]) OR cognitive[All Fields] OR (“alzheimer disease”[MeSH Terms] OR (“alzheimer”[All Fields] AND “disease”[All Fields]) OR “alzheimer disease”[All Fields] OR “alzheimer”[All Fields]) OR (“dementia”[MeSH Terms] OR “dementia”[All Fields])) AND “humans”[MeSH Terms])

Fatty acids

((“Fatty Acids, Omega-3”[MeSH Terms] OR “omega-3”[All Fields] OR (“fatty”[All Fields] AND “acid”[All Fields]) OR “n-3 PUFA”[All Fields] OR “n-3 polyunsaturated fatty acid”[All Fields] OR “PUFA”[All Fields] OR (“unsaturated fatty acid”[All Fields] OR “essential fatty acid”[All Fields]) OR “EFA”[All Fields] OR “eicosapentaenoic acid”[All Fields]) OR (“Docosahexaenoic acid”[All Fields] OR (“docosapentanoic acid “[All Fields] OR “DPA”[All Fields]) OR (“ethyl-eicosapentaenoic acid”[All Fields] OR EPA “E-EPA”[All Fields]) OR (“alpha-linolenic acid”[All Fields] OR “ALA”[All Fields]) OR (“fish oil”[All Fields] OR “n-3 fatty acid”[All Fields] OR “long chain fatty acids”[All Fields]) OR (“primrose oil”[All Fields] OR “linseed oil”[All Fields] OR “oily fish”[All Fields] OR “flaxseed oil”[All Fields])) AND ((“memory”[MeSH Terms] OR “memory”[All Fields]) OR (“cognition”[MeSH Terms] OR “cognition”[All Fields]) OR cognitive[All Fields] OR (“alzheimer disease”[MeSH Terms] OR (“alzheimer”[All Fields] AND “disease”[All Fields]) OR “alzheimer disease”[All Fields] OR “alzheimer”[All Fields]) OR (“dementia”[MeSH Terms] OR “dementia”[All Fields])) AND “humans”[MeSH Terms])

Mediterranean diet

(“Diet, Mediterranean”[Mesh] OR “Mediterranean diet” OR (“Mediterranean” AND “Diet”)) AND ((“alzheimer disease”[MeSH Terms] OR “alzheimer”[All Fields] AND “disease”[All Fields]) OR (“alzheimer disease”[All Fields] OR “alzheimer”[All Fields]) OR (“dementia”[MeSH Terms] OR “dementia”[All Fields]))

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