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e-SPEN guideline

# ESPEN guidelines on nutrition in dementia

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SUMMARY

*Background:* Older people suffering from dementia are at increased risk of malnutrition due to various nutritional problems, and the question arises which interventions are effective in maintaining adequate nutritional intake and nutritional status in the course of the disease. It is of further interest whether supplementation of energy and/or specific nutrients is able to prevent further cognitive decline or even correct cognitive impairment, and in which situations artificial nutritional support is justified.
*Objective:* It is the purpose of these guidelines to cover these issues with evidence-based recommendations.
*Methods:* The guidelines were developed by an international multidisciplinary working group in accordance with officially accepted standards. The GRADE system was used for assigning strength of evidence. Recommendations were discussed, submitted to Delphi rounds and accepted in an online survey among ESPEN members.
*Results:* 26 recommendations for nutritional care of older persons with dementia are given. In every person with dementia, screening for malnutrition and close monitoring of body weight are recommended. In all stages of the disease, oral nutrition may be supported by provision of adequate, attractive food in a pleasant environment, by adequate nursing support and elimination of potential causes of malnutrition. Supplementation of single nutrients is not recommended unless there is a sign of deficiency. Oral nutritional supplements are recommended to improve nutritional status but not to correct cognitive impairment or prevent cognitive decline. Artificial nutrition is suggested in patients with mild or moderate dementia for a limited period of time to overcome a crisis situation with markedly insufficient oral intake, if low nutritional intake is predominantly caused by a potentially reversible condition, but not in patients with severe dementia or in the terminal phase of life.
*Conclusion:* Nutritional care and support should be an integral part of dementia management. In all stages of the disease, the decision for or against nutritional interventions should be made on an individual basis after carefully balancing expected benefit and potential burden, taking the (assumed) patient will and general prognosis into account.


*Abbreviations:* AD, Alzheimer's disease; APOE, apolipoprotein E-e4 allele; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MCI, mild cognitive impairment; MNA, mini nutritional assessment; MNA-SF, mini nutritional assessment short form; MMSE, mini mental state examination; RCT, randomized controlled trial.

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## 1. Development of guidelines on nutrition in dementia

The European Society for Clinical Nutrition and Metabolism (ESPEN) launched a process of developing guidelines on nutrition care for patients with dementia. The group included physicians, nutritionists and dietitians with a background in geriatrics, nutrition and/or ethics, all experienced in treatment and nutritional therapy of persons with dementia, as well as the guidelines coordinator (SMS); all are authors of this guideline document.

The experts followed the GRADE method, which was based on determinations of *grade of evidence* and *strength of recommendation*; the methodology is described elsewhere [1]. A two-day live meeting was organized in Biedenkopf, Germany, in April of 2014, and three phone conferences were held.

Descriptive findings that did not lead to specific recommendations are grouped in a first part (general considerations), whereas all questions that led to comparisons of interventions and to recommendations are grouped in a second part (recommendations).

A systematic literature search was conducted in PubMed and the Cochrane Library. The *grade of evidence* (GOE) was determined by a number of factors, starting with the number and type of research studies [2]. Grading from *High* to *Very Low* was used to rate the quality of the underlying evidence and the level of certainty for effect (Table 1) [3]. Highest quality evidence resulted from consistent results or meta-analysis of multiple randomized controlled trials, with the next highest level defined by at least one well-designed randomized controlled trial. Moderate and low-level evidence came from controlled trials that were not randomized, from cohort- or case-controlled studies, or from multiple time series trials. Very low-level evidence was from expert clinical experience or from descriptive studies. The grade was then decreased if there were limitations to study quality, inconsistencies in findings, imprecise or sparse data, or high likelihood of reporting bias. The grade was increased if there was high consistency of findings or strong evidence of association (Table 1).

The *strength of recommendation* was based on a consensus discussion, which included expression and deliberation of expert opinions, risk-benefit ratio of recommendation, costs, and a review of supportive evidence, followed by Delphi rounds and votes until agreement was reached (Table 2).

Last, a list of all statements was sent to all 2611 ESPEN members with an e-mail address on file to ask for approval/disapproval of every statement, and in the latter case to provide justification. 86 ESPEN members completed the survey, with approval ratings ranging from 70% to 93%. Comments based on the literature were taken into account in the final version of the manuscript.

**Table 1**
Grades of evidence [3].

| Level | Definitions of evidence |
|---|---|
| High | Further research is unlikely to change our confidence in the estimate of effect. |
| Moderate | Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. |
| Low | Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. |
| Very low | Any estimate of effect is very uncertain. |

**Table 2**
Strength of recommendation.

| Strength of recommendation | |
|---|---|
| Strong | We recommend/do not recommend |
| Weak | We suggest/do not suggest |

## 2. General considerations

### 2.1. Definition of dementia

Dementia is on the rise in our aging societies, not only in Europe and North America but worldwide. Dementia becomes more and more common, but it is not normal healthy aging and it is not benign. It is a malignant and devastating condition leading invariably to dependence and finally death [4]. As a clinical syndrome, it is characterized by global cognitive impairment with a decline in memory and at least in one other cognitive domain, such as language, visuospatial, or executive function. It represents a decline from the previous level of cognitive functioning, and is associated with impairment in functional abilities and, in many cases, behavioral and psychiatric disturbances [5,6]. Many diseases can cause a dementia syndrome; Alzheimer's disease and cerebrovascular dementia are the two most common causes, and many cases of dementia involve both these disorders. Lewy body disorders (Parkinson's disease and dementia with Lewy bodies) and frontotemporal dementia are less common but still make up 8% of people referred to a memory clinic [5]. Although some potentially reversible conditions, such as hypothyroidism or vitamin $B_{12}$ deficiency, are often thought to cause dementia, no more than 1.5% of cases of mild to moderate dementia are fully reversible. Age is the best-studied and strongest risk factor for dementia, which explains the increasing burden of cognitive disorders in the years to come [7]. Other risk factors for Alzheimer's disease include genetic risk factors such as having a first-degree relative with a history of Alzheimer's disease, having the apolipoprotein $\varepsilon 4$ genotype or suffering from the Down syndrome. Cardiovascular risk factors such as hypertension are associated with an increased risk for both Alzheimer's disease and vascular dementia. Also lifestyle factors such as low educational level or head trauma may play an important role [7].

Dementia causes a high burden of suffering for patients, their families, and society [8]. For patients, it leads to increased anxiety, depression and dependency and complicates other comorbid conditions. For families, it also leads to anxiety, depression, and increased time spent caring for a loved one. The annual societal cost of dementia is huge, due to health care and related costs as well as lost wages for patients and family caregivers.

As for other chronic conditions and geriatric syndromes the processes underlying the development of a progressive cognitive disorder such as the dementia syndrome spans a far longer period than previously thought. The first changes occur in the brain long before the first memory complaint will be present. Autosomal dominant Alzheimer's disease was associated with a series of pathophysiological changes over decades in cerebral spinal fluid biochemical markers of Alzheimer's disease, brain amyloid deposition, and brain metabolism as well as progressive cognitive impairment [9]. Therefore, minor cognitive disorders, such as Mild Cognitive Impairment (MCI) and even more so major cognitive disorders such as dementia are only a later and terminal stage and clinical expression of the longstanding and progressive changes occurring in the brain.

The changes in cognition will have an impact on the functional status of the individual. The person will pass on from being independent, over becoming frail to finally being disabled and dependent [10]. Indeed, the cognitive changes will render the individual slowly more vulnerable and frail. These functional changes together with the assessment of difficulties in communication and social interaction will determine the severity of the condition. The transition from a normal asymptomatic state over mild cognitive impairment to early, mild to moderate and finally severe dementia

can be rated by the use of classic instruments such as the Clinical Dementia Rating scale [11,12] or the Global Deterioration scale [13]. In general three broad levels of severity can be described: early dementia, when memory loss and disorientation are predominant, mild to moderate dementia with marked loss of function in instrumental activities of daily living and finally the severe stage of dementia with marked communication difficulties and reliance on others for basic activities of daily living. In Table 3 an outline of the different stages and their relation to the rating scales is given.

### 2.2. The nutritional situation in older persons with dementia: weight loss and malnutrition

#### 2.2.1. Weight loss

Weight loss is a prominent clinical feature of dementia [14–17]. Compared to cognitively healthy people, individuals with dementia more often have a history of weight loss. Weight loss is present in the initial stages of the disease, beginning even before diagnosis of the disease, and becoming more common with its progression. Evidence from the international 10/66 study confirms that the association between dementia and weight loss increases through the stages of dementia severity, and that geographical variations across diverse regions of the world are essentially negligible [18].

The mechanisms underlying weight loss in dementia are complex, multifactorial and only partly understood [16,19]. Some studies have highlighted the role of neurodegenerative processes in specific brain regions, genetic factors and inflammatory processes for nutritional changes in Alzheimer's disease. Dementia-related brain atrophy may impact regions of the brain involved in appetite regulation and eating behavior. An atrophy of the mesial temporal cortex has been associated with low BMI, suggesting a connection between limbic system damage and low body weight in Alzheimer's disease [20]. The presence of the apolipoprotein E-e4 allele (APOE), a polymorphism associated with an increased risk of developing Alzheimer's disease, has been related to weight loss and a decrease in BMI in women with Alzheimer's disease [21]. Inflammatory processes in the brain are suggested to be of etiologic importance in Alzheimer's disease [22], and high levels of pro-inflammatory cytokines are found in the plasma or cerebrospinal fluid of patients with Alzheimer's disease [23,24]. This may also account for dementia-related anorexia and weight loss [25].

Furthermore, pathological changes in the olfactory system that may occur years before the onset of cognitive decline in Alzheimer's disease are thought to contribute to decreased nutritional intake and weight loss [26]. Studies supporting these findings suggest that olfactory impairment is a pre-clinical marker for dementia and that olfactory evaluations may become a supplementary tool in early detection of dementia [27]. APOEe4 carriers seem more prone to suffer from impaired olfactory function before the onset of cognitive impairment [28].

#### 2.2.2. Nutritional problems and malnutrition

Based on these pathophysiological changes, various nutritional problems may occur in the course of the disease leading to reduced dietary intake and malnutrition (Table 4).

In the early stages of dementia, individuals may have problems with shopping, storing and preparing food, may forget whether they have already eaten and may lose the cognitive ability to initiate or continue effective eating strategies. Dietary habits may change and result in a reduced variety of diet and unbalanced nutrient intake. As the disease progresses the patients may no longer know what they are supposed to do with the food and/or utensils put in front of them, behavioral problems emerge and eating skills are lost. Agitation and hyperactivity may make mealtimes difficult and increase energy requirements. On the other hand sedative effects of pharmacotherapy may reduce eating drive and dietary intake [29–34].

Finally, dysphagia may develop. It is reported in 13–57% patients with different types and in different stages of dementia and is most common in later stages of fronto-temporal dementia (FTD) and AD [35]. Factors that contribute to oral phase dysphagia in AD include inability to recognize food, oral-tactile agnosia and swallowing and feeding apraxia. Dysphagia of the pharyngeal phase leads to aspiration before, during and after swallowing. Aspiration pneumonia has been reported to be a common cause of death in patients with dementia [36,37].

As progression of dementia is accompanied by a more or less continuous decline of competences, it is only a question of time until nutritional intake becomes insufficient. Abilities to drink, eat and swallow are generally the last functions to be lost in a patient with dementia, and result of which is fatal.

In addition to these dementia-specific nutritional problems, in all stages of the disease, older persons with dementia may be affected by age-related impairments, disabilities and comorbidities (e.g. anorexia of aging, chewing problems, depression) leading to reduced dietary intake and malnutrition [38–40].

### 2.3. The role of nutrition in outcome, disease progression and caregiver burden

#### 2.3.1. The role of nutrition in outcome

Deleterious effects of weight loss and malnutrition in older persons are well known [38,41,42], and there is no reason to assume generally different effects in persons with dementia. Loss of body weight implies loss of muscle mass, accompanied by functional decline and frailty, and is associated with an increased risk of morbidity and mortality [39,40].

The association between *weight loss* and increased mortality risk is also documented in patients with dementia [43,44]. In nursing home residents with advanced dementia, weight loss was found as an independent predictor of death [45].

There is also some evidence that *low BMI* is associated with reduced survival and that older patients with dementia may benefit from higher BMIs [46,47]. Recent data from a Swedish dementia registry-study including 11,398 patients with dementia indicate that higher BMI is associated with a decreased risk of mortality, with all higher BMI categories showing reduced risk relative to patients with BMI 18.5–22.9 kg/m$^2$ and excess risk in those with BMI <18.5 kg/m$^2$ [48].

In nursing homes residents with advanced dementia *eating problems* (which developed in 86% over a period of 18 months) were highly predictive for 6-months mortality [49].

#### 2.3.2. The role of nutrition in disease progression

Energy and several nutrients play important roles for brain integrity and metabolism. Energy is permanently required in relatively large amounts in order for the brain to function properly. Brain tissue is composed of nutrients, and diet provides precursors of neurotransmitters. Vascular damage, oxidative stress and inflammatory processes, which are regarded as important pathophysiological mechanisms in the development of dementia, are modulated by specific nutrients.

It is well known that severe deficiencies in several micronutrients, e.g. thiamine, folic acid and vitamin $B_{12}$, are accompanied by cognitive disorders, and it is assumed that also less pronounced nutrient deficiencies may contribute to impaired cognition and aggravation of existing impairments [50]. Epidemiological evidence suggests that in healthy older people specific dietary patterns may decrease the risk of dementia and cognitive decline and consequently, vice versa, unfavorable dietary patterns are associated

**Table 3**
Stages of cognitive dysfunction and dementia.

| | Normal | MCI | Early dementia | Mild to moderate dementia | Severe dementia |
|---|---|---|---|---|---|
| Memory | No memory loss or slight inconsistent forgetfulness | Consistent slight forgetfulness; partial recollection of events; objective memory deficit when interviewed | Moderate memory loss; more marked for recent events; memory loss interferes with everyday activities | Severe memory loss; only highly learned material retained; new material rapidly lost | Severe memory loss; only fragments remain; finally mute |
| Orientation | Fully oriented | Fully oriented except for slight difficulty with time relationship | Moderate difficulty with time relationship; oriented for place in known environment; may have geographic disorientation elsewhere | Severe difficulty with time relationships; usually disoriented to time often to place | Oriented to person only |
| Judgment & problem solving | Solves everyday problems; handles business and finances well; judgment good in relation to past performance | Slight impairment in solving problems, similarities and differences | Moderate difficulty in handling problems; similarities and differences, social judgment usually maintained | Severely impaired in handling problems, similarities and differences; social judgment usually impaired | Unable to make judgments or solve problems |
| Social activities | Independent function at usual level, shopping, volunteer and social groups | Slight impairment | Unable to function independently at these activities although may still be engaged in some; appears normal to casual inspection | No independent function outside home; well enough to be taken to functions outside family home | No independent function outside home; too ill to be taken to functions outside family home |
| Home and hobbies | Life at home, hobbies and intellectual interests well maintained | Life at home, hobbies, and intellectual interests slightly impaired | Mild but definite impairment of function at home; more difficult chores abandoned; more complicated hobbies and interests abandoned | Only simple chores preserved; very restricted interests, poorly maintained | No significant function in home |
| Personal care | Fully capable of self-care | Fully capable of self-care | Needs prompting | Requires assistance in basic ADL; may become incontinent | Dependency in basic ADL; incontinent |
| Affect | Normal | Some denial as defense; mild anxiety | Denial is dominant; emotional blunting; withdrawal | Delusions; anxiety and agitation; repetitive obsessive behavior | Disturbed diurnal rhythm; delusions |
| CDR scale | 0 | 0–0.5 | 1–2 | 2–3 | 3 |
| GDS-Reisberg stage | 1–2 | 3 | 4 | 5–6 | 6–7 |

CDR = clinical dementia rating (copyrighted instrument of the Alzheimer's Diseases Research Center, Washington University, St. Missouri, USA); GDS = global deterioration scale [13]; ADL = activities of daily living.

**Table 4**
Nutritional problems arising in different disease stages.

| Nutritional problems | Stage of dementia |
|---|---|
| Olfactory and taste dysfunction | Preclinical and early stages |
| Attention deficit | Mild to moderate |
| Executive functions deficit (shopping, preparing food) | Mild to moderate |
| Impaired decision-making ability (slowdown in food choice, reduced intake) | Mild to moderate |
| Dyspraxia[a] | Moderate to severe |
| Agnosia[b] | Moderate to severe |
| Behavioral problems (wandering, agitation, disturbed eating behavior) | Moderate to severe |
| Oropharyngeal dysphagia | Moderate to severe |
| Refusal to eat | Severe |

[a] Coordination disorder, loss of eating skills.
[b] Loss of ability to recognize objects or comprehend the meaning of objects, which means that food may not be distinguished from non-food and that eating utensils are not recognized as what they are.

with increased risk of dementia and cognitive decline [51]. There are, however, no studies available indicating that specific dietary habits or low intake of specific nutrients contribute to disease progression.

Low plasma levels of several nutrients are found in patients with cognitive impairment and dementia [52,53], which however may be caused by the disease as well as being a consequence of the disease. There is also no prospective study available relating nutrient status to disease progression.

Regarding general nutritional status, a close relation between weight loss [18,43,54] as well as BMI [55,56] and disease severity is documented in older patients with dementia. There are also several prospective observational studies available which have demonstrated that weight loss [43,57,58] and malnutrition [59,60] are associated with disease progression and cognitive decline. Thus, in a cohort of 414 community-dwelling ambulatory patients with a diagnosis of probable Alzheimer's disease, weight loss of 4% body weight or more during the first year of follow up was independently predictive for rapid cognitive decline (loss of 3 points or more in MMSE over 6 months) during the following 3 years in a multivariate cox-proportional model (HR = 1.5, 95%-CI 1.0–2.2) [58]. In patients with very mild Alzheimer's disease a poorer nutritional status assessed by the Mini Nutritional Assessment was found as predictor of disease progression after 1 year [60].

Thus, general malnutrition may trigger a vicious circle of dementia leading to decreased nutritional intake and deterioration of nutritional status, which itself contributes to acceleration of the disease (Fig. 1).

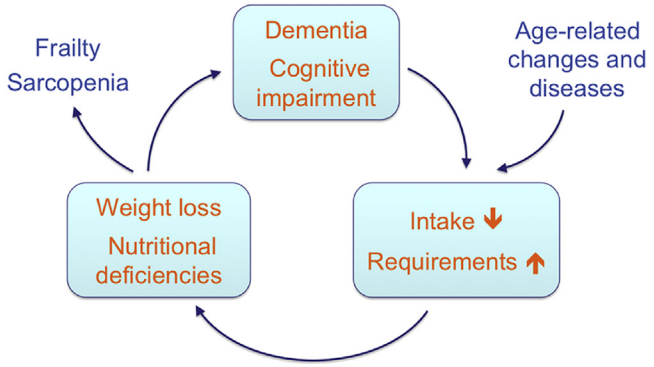


**Fig. 1.** Vicious circle of malnutrition and dementia.

*2.3.3. The role of nutrition in caregiver burden*

The majority of people with dementia live in the community, and care is to a great extent provided by family caregivers, who are often older spousal caregivers affected by multiple chronic diseases and functional disabilities [61].

In general, the loss of a person's mental abilities and everyday skills implies stress and physical, psychological, time und financial consequences for caregivers [62–66].

Nutritional problems occurring in the course of the disease substantially add to this burden. Professionals as well as family caregivers of persons with dementia feel responsible to maintain a good meal ambience and nutritional status of the person with dementia and have many concerns about weight changes, inadequate and unbalanced food intake and understanding nutritional needs [67]. Shopping and preparation of food, preservation of being independent, social interaction, cultural issues and rituals during meals, dealing with adverse eating behavior and ensuring an adequate and balanced diet are experienced as daily recurring problems by caregivers [30,68–70]. Male caregivers have expressed to be more concerned about nutrition than females when adopting a caregiver's role, as they were not familiar with household activities, often have poor cooking skills and poor nutritional knowledge [70–72]. This places female dementia patients at higher risk of weight loss and malnutrition than men. Supervising the nutritional situation and assisting a person in daily routine tasks is an everyday challenge, which is demanding and also emotionally stressful. A particularly serious problem that arises in feeding a person with dementia is the difficulty in interpreting and dealing with refusal-like behavior, the real causes of which often cannot be detected [73].

Thus, on the one hand, nutritional problems are a source of strain and contribute to caregiver burden, on the other hand caregiver stress and burden may aggravate nutritional problems of the person with dementia. It has been shown in longitudinal studies that caregiver burden increases the risk of adverse eating behavior [74] as well as the risk of weight loss [15,75] in patients with Alzheimer's disease.

As a consequence of stress, caregivers themselves are at increased risk of nutritional problems and may develop overweight as well as undernutrition [76–78]. In a small cross-sectional study, the MNA score of 56 community-dwelling older persons with dementia was strongly associated with the MNA score of their family caregivers [79].

Consequently, not only persons with dementia but also their caregivers may need attention and support with respect to adequate nutrition. Decisions regarding nutritional interventions for persons with dementia should also consider potential consequences for their caregivers.

*2.4. The role of nutritional support in dementia therapy – rationale for the guidelines*

In summary, nutritional problems are part of the disease, putting persons with dementia at high risk of developing malnutrition. Malnutrition is clearly associated with poor outcome and contributes to disease progression. It also increases caregiver burden, which in turn may aggravate nutritional problems.

Nutritional interventions generally offer the opportunity to counteract these problems. Disrupting the vicious circle of malnutrition and cognitive decline may support affected persons and decrease the burden of this devastating disease. Regarding the limited effects of present pharmacological interventions for dementia patients, non-pharmacological strategies like nutritional interventions are of particular interest as part of disease management.

Based on the facts described above, nutritional care and support should be an integral part of disease management. In this context, however, the question arises which interventions are indeed effective in maintaining adequate nutritional intake and nutritional status of persons with dementia. Furthermore, it is of interest whether supplementation of energy and/or specific nutrients is able to prevent further cognitive decline or even correct cognitive impairments, and in which situations artificial nutritional support is justified.

It is the purpose of these guidelines to cover these issues with evidence-based recommendations.

## 3. Recommendations

Table 5 lists the statements along with their grade of evidence and strength of recommendation.

### 3.1. Screening & assessment

**1. We recommend screening every person with dementia for malnutrition. In case of positive screening, assessment has to follow. In case of positive assessment, adequate interventions have to follow.** (Grade of evidence: **very low**)

Commentary:

Screening for malnutrition allows early identification of persons with malnutrition or at risk of malnutrition who may benefit from nutritional interventions. Since awareness of malnutrition is generally low and malnutrition and its risk are often overlooked [80–82], it is general consensus among nutrition and geriatric experts that regular screening should be performed in order to recognize persons at risk at an early stage [80,83].

When and how often should screening for malnutrition be performed?

Since malnutrition is widespread and can be successfully addressed, screening should be performed in all health care settings *at the time dementia is diagnosed* – at memory clinics, in hospitals, by primary care physicians and other medical practitioners. This is in line with a consensus rating of a French expert panel, where the statement "For every AD patient, nutritional status must be assessed at the time of diagnosis and/or start of treatment" received strong agreement [14].

As weight loss and nutritional problems may occur more or less through all stages of the disease, may differ from patient to patient and vary across the different dementia diagnoses, *regular* screening is important to identify persons who are not at risk at the time of diagnosis but develop nutritional problems in the course of the disease.

Thus, in all settings, screening should be repeated at regular intervals. There is, however, no consensus on how often this should be performed. In community-dwelling older adults and long-term care residents, screening can be performed every 3–6 months, and additionally if changes in general health, eating ability or eating behavior occur. In case of acute health problems closer supervision of the nutritional situation is necessary.

***Screening tools***: Numerous tools for screening of malnutrition exist, which combine several aspects of the nutritional situation and usually include questions on BMI, weight loss, reduced appetite/dietary intake and disease stress [83–85].

None of these tools have been specifically designed and validated for persons with dementia.

For older persons in general, the MNA-SF has been developed and validated and is widely used in both populations with and without dementia. It consists of 6 questions, that are easy to answer, and is recommended for older persons in all health care settings [84–86]. For screening of persons with dementia it has to be mentioned that the questions should be answered by relatives or professional caregivers in order to receive reliable information and minimize misjudgment [87].

***Assessment***: Screening has to be regarded only as a first step in the process of diagnosing and managing malnutrition. In those people who have been categorized as malnourished or as being at risk of malnutrition, screening must be followed by individual assessment, which should include a more detailed evaluation of nutritional status, search for modifiable causes of malnutrition, monitoring of dietary intake and assessment of specific eating problems and behavioral symptoms.

For the identification of specific eating problems and behavioral symptoms in persons with moderate to severe dementia several specific tools have been developed and may be helpful:

- The Aversive Feeding Behavior Inventory (AFBI) [88], also known as "Blandford Scale" can be of help in evaluating the causality of eating problems particularly in patients in advanced stages of dementia. This tool still needs validation, nevertheless it can be of help in dealing with such problems in the care of patients with dementia.
- The Edinburgh Feeding Evaluation in Dementia Questionnaire (EdFED-Q) [34] is a validated tool that aids in recognizing problems with eating and drinking in patients with dementia. It helps in planning an appropriate multidimensional intervention.
- The Eating Behavior Scale (EBS) [89] measures the ability to eat independently and consequently may enable judgment for the need of care during meals.

Comprehensive nutritional assessment should directly lead to the derivation of adequate interventions, that should be initiated immediately. Whenever nutritional treatment is initiated, the process should be monitored closely by follow-up evaluations and documentation of changes. Where required, interventions should be adapted.

In summary, nutritional screening and assessment have to be an integral part of the comprehensive geriatric assessment in persons with dementia and part of the care process. They are indispensible prerequisite for the implementation of treatment strategies to avoid or delay malnutrition and its serious consequences [16].

Whereas standardized screening and assessment are mandatory in early, mild and moderate stages of the disease, in severe stages of dementia regular formal screening and assessment could create unnecessary pressure to caregivers and do more harm than good. In advanced disease stages the focus should be placed on informal identification of individual needs and problems, with the aim to allow optimal personalized palliative care and to support eating and drinking as long as possible.

**2. We recommend close monitoring and documentation of body weight in every person with dementia**. (Grade of evidence: **very low**)

Commentary:

Since weight loss is the most important sign of malnutrition and occurs in nearly half of the patients with mild to moderate forms of Alzheimer's disease [16], weight should be monitored and recorded regularly.

Prevention of weight loss is crucial for maintenance of general health and requires regular weighing in order to detect body weight changes at an early stage and to enable taking appropriate countermeasures. Thus, monitoring of weight should be part of the regular management of the disease.

**Table 5**
Complete list of statements on nutrition in dementia.

| # | Statement | Grade of evidence | Strength of recommen-dation |
|---|---|---|---|
| 1. | We recommend screening every person with dementia for malnutrition. In case of positive screening, assessment has to follow. In case of positive assessment, adequate interventions have to follow | Very low | Strong |
| 2. | We recommend close monitoring and documentation of body weight in every person with dementia. | Very low | Strong |
| 3. | We recommend provision of meals in a pleasant, homelike atmosphere. | Moderate | Strong |
| 4. | We recommend provision of adequate food according to individual needs with respect to personal preferences. | Very low | Strong |
| 5. | We recommend to encourage adequate food intake and to provide adequate support. | Very low | Strong |
| 6. | We do not recommend the systematic use of appetite stimulants. | Very low | Strong |
| 7. | We recommend educating caregivers to ensure basic knowledge on nutritional problems related to dementia and possible strategies to intervene. | Low | Strong |
| 8. | We recommend elimination of potential causes of malnutrition as far as possible. | Very low | Strong |
| 9. | We recommend avoiding dietary restrictions. | Very low | Strong |
| 10a. | We do not recommend the use of omega-3-fatty acid supplements in persons with dementia for correction of cognitive impairment or prevention of further cognitive decline. | High | Strong |
| 10b. | We do not recommend the use of vitamin B1 supplements in persons with dementia for prevention or correction of cognitive decline when there is no indication of vitamin B1 deficiency. | Very low | Strong |
| 10c. | We do not recommend the use of vitamin B6, vitamin B12 and/or folic acid supplements in persons with dementia for prevention or correction of cognitive decline when there is no indication of vitamin B6, vitamin B12 and/or folic acid deficiency. | Low | Strong |
| 10d. | We do not recommend the use of vitamin E supplements in persons with dementia for prevention or correction of cognitive decline. | Moderate | Strong |
| 10e. | We do not recommend the use of selenium supplements for prevention or correction of cognitive decline. | Very low | Strong |
| 10f. | We do not recommend the use of copper supplements for prevention or correction of cognitive decline. | Very low | Strong |
| 10g. | We do not recommend the use of vitamin D supplements for prevention or correction of cognitive decline. | Very low | Strong |
| 11. | We recommend the use of ONS to improve nutritional status. | High | Strong |
| 12. | We do not recommend the use of ONS in persons with dementia to correct cognitive impairment or prevent further cognitive decline. | Moderate | Strong |
| 13. | We do not recommend the systematic use of special medical foods for persons with dementia to correct cognitive impairment or prevent further cognitive decline. | Low | Strong |
| 14. | We do not recommend any other nutritional product for persons with dementia to correct cognitive impairment or prevent further cognitive decline. | Very low | Strong |
| 15. | We recommend that each decision for or against artificial nutrition and hydration for patients with dementia is made on an individual basis with respect to general prognosis and patients' preferences. | Very low | Strong |
| 16. | We suggest tube feeding for a limited period of time in patients with mild or moderate dementia, to overcome a crisis situation with markedly insufficient oral intake, if low nutritional intake is predominantly caused by a potentially reversible condition. | Very low | Weak |
| 17. | We recommend against the initiation of tube feeding in patients with severe dementia. | High | Strong |
| 18. | We suggest parenteral nutrition as an alternative if there is an indication for artificial nutrition, as described in recommendation 16, but tube feeding is contraindicated or not tolerated. | Very low | Weak |
| 19. | We suggest parenteral fluids for a limited period of time in periods of insufficient fluid intake to overcome a crisis situation. | Very low | Weak |
| 20. | We recommend against the use of artificial nutrition (enteral nutrition, parenteral nutrition and parenteral fluids) in the terminal phase of life. | Very low | Strong |

There is no scientific evidence regarding the frequency of weighing. Depending on general health and nutritional status, time intervals between two weight measurements may vary. We suggest repeated weighing at least every 3 months and at least monthly if nutritional, health or weight problems arise.

Body weight should be measured under the same conditions (time of day, clothing defecation, urination) and using the same scale. When interpreting the results, changes in total body water have to be taken into account. In acute care hospitals, where dehydration as well as water retention are widespread, a closer control of body weight is necessary.

In a consensus process of a French expert panel, the statement that "every AD patient must be weighed when consulting his/her physician or at admission to hospital, and weight loss must be sought in these situations" obtained strong agreement [14].

Whereas regular weighing is imperative in early, mild and moderate stages of the disease, in severe stages assessment and monitoring of weight could create unnecessary pressure to caregivers and do more harm than good. In this situation individual nutritional problems and needs should be closely monitored as basis for individualized palliative care.

### 3.2. Strategies to support oral nutrition

**3. We recommend provision of meals in a pleasant, homelike atmosphere**. (Grade of evidence: **moderate**)

Commentary:

Environmental factors play an important role for the atmosphere during mealtimes, among them eating location, furniture and companions, ambient sounds, odors, temperature and lighting, food accessibility, portion size and presentation of the food [90,91]. These factors are known to be important determinants of food intake and can be modified in order to support adequate dietary intake in persons with eating difficulties.

It is generally known and has been observed in healthy adults that eating in company can increase dietary intake [92].

In nursing home residents without dementia, it has been shown in a randomized controlled trial that changing the ambience during mealtimes to a homelike, family-style one (with tablecloth and napkins, meals served on dishes on the table with individual choice of portion size, staff sitting down at tables and chatting with residents, balanced seating of residents and shared rituals regarding the beginning of the meals) resulted in a significant increase in food intake and prevented a decline in BMI, physical performance and quality of life [93,94].

The question whether specific mealtime interventions are effective in improving the nutritional situation of people with dementia has been addressed in several observational trials which are summarized in two systematic reviews [95,96]. Improvements in behavioral symptoms and increased dietary intake are described as a result of improved lighting, relaxing music and change from meals served on a tray to a more homelike food service [95,96]. In a controlled trial, implementation of a breakfast club resulted in increased communication and independence, interest and involvement [97]. Another controlled study in two special care units for persons with dementia in France reported positive effects on body weight and eating behavior as a consequence of shared mealtimes between residents and caregivers [98].

Moreover, anecdotal evidence exists on positive effects on dietary intake from the implementation of an aquarium in the dining area of specialized dementia units [99] and the use of high-contrast, colored tableware for patients with severe Alzheimer's disease in long-term care [100].

Despite partly conflicting results and limited quality of most of the studies, it seems obvious that dietary intake of persons with dementia can be supported by creating an environment during meals, where residents can be relaxed and feel comfortable, safe and in good hands.

**4. We recommend provision of adequate food according to individual needs with respect to personal preferences**. (Grade of evidence: **very low**)

Commentary:

Regarding energy and nutrient requirements, there are no indications that these are generally different in persons with dementia.

Energy requirements may be decreased in the case of reduced physical activity (e.g. immobility, apathy, somnolence) and may be increased in the case of hyperactivity (e.g. restlessness, constant pacing up and down), and energy intake has to be adapted accordingly.

A diet rich in fruits, vegetables, legumes and unrefined cereals, with moderate amounts of dairy products, low meat but regular fish intake ("Mediterranean-type diet") seems to deliver all nutrients in adequate amounts to support maintenance of cognitive function and reduce the risk of cognitive decline in healthy older persons [51]. As long as no data are available regarding the effects of specific dietary pattern on cognitive function in persons with dementia, food and nutrient intake recommendations for healthy older persons are equally applied to persons with dementia.

In light of the high risk of malnutrition in persons with dementia, particular attention should be paid to providing sufficient amounts of energy and nutrients in an appealing and appetizing way in order to facilitate and encourage intake. Sensory characteristics (e.g. appearance, flavor, taste, colors), texture and variety of food play important roles in this context, and personal likes and dislikes must mandatorily be considered. Meals based on individual needs, desires and resources and including patients in diet-related decisions as far as possible may increase the desire to eat and maintain the pleasure of eating.

Besides regular main meals, snacks should be available as needed and also provided at other times of day if requested, since shifts in diurnal eating patterns may occur [101,102]. In case of weight loss and reduced food intake, meals should be enriched by energy and protein, and high-energy snacks offered, which has been shown to increase intake in mixed samples of nursing home residents with and without dementia [103,104]. Finger food may help to maintain independence in eating even if the ability to use eating utensils has declined, and may also allow for eating while walking for persons with dementia who are constantly on the move [105–107]. Food, where the texture has been modified but is nevertheless appealing may be necessary and may support safe and sufficient intake when chewing and swallowing problems occur [108]. Furthermore, all kinds of diets restricting food selection (restrictive diets), such as low salt, sugar or cholesterol diets, which may reduce dietary intake and the enjoyment of eating, should be avoided as far as possible [109]. (see recommendation 9.)

In few observational studies in long-term care residents with dementia, it has been shown that individualized adaptation of food and meals and use of high-energy/protein foods as part of a comprehensive nutritional care concept has positive effects on dietary intake and body weight [105,110]. Despite very low scientific evidence in total, provision of adequate food according to the individual needs and meeting personal preferences is a basic prerequisite for adequate dietary intake in all stages of the disease, and thus clearly recommended.

**5. We recommend to encourage adequate food intake and to provide adequate support**. (Grade of evidence: **very low**)

Commentary:

Due to physical, mental and behavioral changes in older persons with dementia, food intake is often compromised and insufficient to maintain adequate nutritional status.

As the disease progresses, the need for help with nutritional affairs gradually increases.

In early stages, when the ability to perform complex tasks is declining, difficulties in shopping, preparing meals and eating regularly may arise, especially in persons living alone, which may mark the entry into the vicious circle of malnutrition. Relatives play a central role in recognizing these difficulties and in organizing adequate support to compensate for these problems and to ensure the right conditions for adequate eating, e.g. by assistance with shopping, domestic help, meals on wheels and/or a person present at mealtimes.

With progressing disease and decreasing ability to remember to eat, to recognize food and eat independently, personal support and help during meals becomes necessary. Food intake has then to be supervised, encouraged and supported by adequate nursing actions. These interventions should on the one hand compensate for existing deficits and on the other promote independence as far as possible at the same time. Assistance should be provided according to individual needs and resources in a manner that is safe and preserves the dignity of the affected person. Finally, all actions should be integrated in a comprehensive concept of strategies to support oral nutrition (see recommendations 3–5 and 7–9).

Possible interventions to support adequate food intake are summarized in Table 6.

There are some observational and quasi-experimental studies supporting these recommendations:

In long-term care units caring specifically for patients with dementia, it has been documented that lacking feeding assistance is related to low food intake [111], and that increased time spent by nurses on feeding and increased help during meals may positively affect eating behavior, dietary intake and nutritional status [105,110,112–115]. Studies in nursing home residents with varying dementia prevalence also provide some evidence that simple nursing actions like placing patients or residents at a dining table, providing emotional support, supervision, verbal prompting, encouragement and assistance at mealtimes may promote self-feeding and enhance the feeding process [116–122].

Especially in the advanced stages of the disease, emotional support and specific behavioral and communication strategies become increasingly important. In this regard it has been observed in long-term care institutions that the quality of interaction between the patient and the caregiver during meals influences the amount of food consumed [123]. Positive effects were reported when patients with severe dementia were fed by the same carer compared to various carers [124]. Specific behavioral and communication strategies have been shown to positively affect eating behavior and increase food intake in three case reports [125] and in a small controlled, non-randomized study [126].

RCTs for this topic would be unethical since adequate support cannot be withheld from a person in need of such.

In summary, although scientific evidence is low, based on common sense and fundamental ethical principles, adequate food intake should be encouraged and supported by appropriate measures in all stages of the disease to the extent required in each case.

**Table 6**
Possible interventions to support adequate food intake.

| Disease stage | Problem | Possible support |
|---|---|---|
| Early stages | Difficulties in shopping, preparing meals and/or eating regularly | • Help with shopping<br>• Domestic help<br>• Meals on wheels<br>• Person who is present at mealtimes |
| | Forgetting to eat | • Supervision during meals<br>• Verbal prompting, encouragement |
| | Decreasing ability to remember eating, to recognize food and to eat independently | • Feeding assistance<br>• Increased time spent by nurses during feeding<br>• Energy-dense meals |
| Advanced stages | Behavioral problems, wandering | • Emotional support<br>• Specific behavioral and communication strategies |
| | Dysphagia | • Texture modification |

**6. We do not recommend the systematic use of appetite stimulants**. (Grade of evidence: **very low**)

Commentary:

Drugs that stimulate appetite (orexigenic drugs) might be helpful for patients with persistently reduced or lacking appetite in order to stimulate eating, increase dietary intake and maintain or improve nutritional status. Various agents, mainly cannabinoids (dronabinol) and megestrol acetate, are used in various patient groups suffering from anorexia – including older patients and long-term residents [127,128].

In patients with dementia only one small randomized, placebo-controlled study of 12 patients with Alzheimer's disease is available that found an increase in body weight and triceps skinfold thickness after 6 weeks of *dronabinol* administration despite unchanged caloric intake during the study period [129].

A systematic review on the effects of cannabinoids in the treatment of dementia, published in 2009, did not identify any additional study in the meantime [130].

Only recently, a retrospective chart review of 40 geriatric neuropsychiatric inpatients diagnosed with dementia who received dronabinol for behavior and appetite disturbances reported significant improvement in the percentage of meals consumed during the treatment periods [131].

The effects of *megestrol acetate* were tested in two studies in nursing home residents with weight loss or at risk of weight loss, however only partly affected by dementia (dementia diagnosis in 41% in both studies) [132,133]. Whereas in one of the studies (RCT, $n = 69$) positive effects on appetite and body weight were reported [132], no significant effects on body weight were found in the other (no control group, $n = 17$) [133].

In conclusion, the evidence for the use of appetite stimulants in patients with dementia is very limited. Dronabinol and megestrol acetate were tested only in small trials with weak methodology (and not always focused on dementia patients) and did not achieve a consistent effect on outcomes. The mechanism of action is unknown [129], and various, potentially harmful, side effects must be taken into account [128,129]. Consequently, the systematic use of appetite stimulants cannot be recommended for patients with dementia and reduced appetite. Further research is required.

Though the use of appetite stimulating agents is not generally recommended, in specific clinical situations the choice of medication might be important. If a concomitant depressive syndrome is to be treated pharmacologically, appetite stimulating drugs such as Mirtazapin might be an option. Mirtazapin was associated with weight gain in randomized trials on antidepressant therapy [134].

**7. We recommend educating caregivers to ensure basic knowledge on nutritional problems related to dementia and possible strategies to intervene**. (Grade of evidence: **low**)

Commentary:

Basic knowledge of caregivers on nutrition-related problems in the course of the disease and on adequate intervention and

communication is essential for adequate nutritional care of patients with dementia. This knowledge may help to anticipate difficulties and to address these difficulties adequately if they appear which finally may contribute to improve the patient's nutritional situation on the one hand and reduce stress for the caregiver on the other.

Education and training programmes should ideally be designed for the dyad of patient and caregiver and could provide for example information on weight loss, loss of appetite and loss of eating skills, nutritional needs, interaction and communication strategies during mealtimes and adequate techniques for mealtime tasks. As older male caregivers often are not familiar with household activities, cooking, preparing meals and caring [70,72], there seems to be a need for specific training for this subgroup of caregivers.

In several studies, teaching and training interventions for family caregivers and nursing home staff have been tested (Evidence Table 1).

Two large French studies carried out in the community setting – one non-randomized controlled trial [135] and one cluster-randomized trial of good methodological standards with complex training programmes for patients with Alzheimer dementia and their family caregivers over one year [136] – found some indication of improvements of nutritional status of the patients with dementia. Eating behavior, independence, agitation and cognition, however, remained unchanged.

In the nursing home setting, in a smaller Finish study, education of nursing staff resulted in significant improvements of dietary intake of 21 residents with moderate to severe dementia compared to before the training [137]. A one-week training programme for the staff of a long-term care ward followed by a three-months intervention period with alterations in meal routines, communication and environment resulted in a significantly better development of the residents' body weight compared to the control ward without training [138], and a feeding skills programme for nursing assistants in two long-term care facilities specialized in caring for persons with dementia in North Taiwan improved knowledge, attitudes and behavior of the staff – although food intake and eating behavior of the residents did not change [139].

In conclusion, several studies provide evidence on positive effects of caregiver training and education with respect to knowledge and attitudes of the caregivers and also regarding the nutritional situation of persons with dementia.

Furthermore, two RCTs could demonstrate that specific training for long-term care residents with dementia with respect to specific feeding skills (by Montesori-based activities) may have positive effects on nutritional behavior and eating ability [140,141].

However, research in this area is rather difficult to conduct, and training effects are difficult to verify due to the complexity of influencing factors and very individual resources (of patients as well as of caregivers) and occurring problems. Moreover, training effects depend very much on baseline knowledge and attitudes before the training, which may vary.

**8. We recommend elimination of potential causes of malnutrition as far as possible**. (Grade of evidence: **very low**)

Commentary:

It is a basic principle of clinical nutrition in geriatrics to identify specific causes of malnutrition and eliminate them as far as possible [42,142,143].

Besides nutritional problems related to cognitive decline (→ Table 4), low dietary intake of a person with dementia may also be due to various other causes, e.g. mastication problems, acute disease, side effects of medications, pain or family conflicts.

In the case of reduced oral nutritional intake and weight loss, potential causes must be looked for by systematic assessment. Subsequently, identified potential causes should be eliminated or treated as far as possible in order to create the preconditions for adequate food intake, e.g. by adequate oral care, denture improvement, swallowing training, treatment of underlying diseases (e.g. infection, depression, gastrointestinal disorder), reduction of polypharmacy or replacement of medications with adverse side effects.

Interventions should however only be taken as long as they are clinically appropriate. If an intervention is associated with appreciable burden (e.g. complex dental treatment or surgical intervention in a frail patient with advanced dementia), its risks should be carefully weighed against the potential benefits of improved nutrition.

Other examples for possible causes and reasonable interventions are summarized in Table 7.

**9. We recommend avoiding dietary restrictions**. (Grade of evidence: **very low**)

Commentary:

Dietary restrictions are one potential cause of malnutrition since they may limit food choice and pleasure to eat and thus bear the risk of limiting dietary intake.

In addition, as recently reviewed by Darmon et al. [144], restrictive diets such as low sugar, low salt, or low cholesterol diets for persons with diabetes mellitus, hypertension or hypercholesterolemia, respectively, seem to be less effective with increasing age, albeit data on their effects in older persons in general are rare and are also lacking for persons with dementia. In a position statement, the American Dietetic Association concludes that liberalization of diet prescriptions for older adults in long-term care may enhance nutritional status and quality of life [109]. In individual cases, e.g. patients with severe kidney failure, benefits of a specific diet, have to be weighted against the potential risk of developing malnutrition. Of course, intolerable foods have to be omitted in case of food intolerances, and patient-desired restrictions, e.g. for cultural or religious reasons, must be respected.

Generally, in view of the high risk and prevalence of malnutrition in persons with dementia, and due to the potentially harmful

**Table 7**
Potential causes of malnutrition in older persons with dementia and reasonable interventions.

| Potential causes | Interventions |
|---|---|
| Mastication problems | • Oral care<br>• Dental treatment<br>• Texture modification |
| Swallowing problems | • Swallowing evaluation<br>• Swallowing training<br>• Texture modification |
| Xerostomia | • Check medication for adverse side effects – remove or change medication if possible<br>• Ensure adequate fluid intake<br>• Use mouth rinse and gel |
| Restricted mobility, immobility | • Physiotherapy<br>• Group exercise<br>• Resistance training<br>• Help with shopping and cooking<br>• Meals on wheels |
| Psychiatric disorders (e.g. depressive mood, depression, anxiety) | • Adequate medical treatment<br>• Eating with others/shared meals<br>• Pleasant meal ambience/eating environment<br>• Group activities, occupational therapy |
| Acute disease, (chronic) pain | • Adequate medical treatment |
| Adverse effects of medications (e.g. xerostomia, nausea, apathy) | • Check medications<br>• Reduce/replace medications |
| Social problems (e.g. lacking support, family conflict) | • Help with shopping, cooking and eating<br>• Meals on wheels, shared meals<br>• Resolve conflicts |

effects of dietary restrictions with respect to the development of malnutrition, we recommend avoiding dietary restrictions in older persons with dementia.

### 3.3. Oral supplementation

#### 3.3.1. Nutrient supplementation

Several nutrients play important roles for brain integrity and metabolism. They are essential constituents of brain tissue (e.g. fatty acids in neuronal membranes), precursors of neurotransmitters (e.g. specific amino acids) or act as cofactors for metabolic processes (e.g. B vitamins). Due to their antioxidant properties, some nutrients (e.g. vitamin E, selenium, copper) may protect brain tissue from oxidative damage.

Against this background and based on preclinical and epidemiologic evidence for a protective role of several particular nutrients, intervention trials have been performed to establish the efficacy of nutrient supplementation. For all nutrients so far examined, present evidence from these trials suggests that supplements are unlikely to be effective in the treatment of dementia. We, thus, do not recommend the systematic use of nutrient supplements to prevent or correct cognitive decline in persons with dementia. Existing evidence regarding individual nutrients is summarized below. Existing studies are, however, limited and heterogeneous with regard to type and stage of dementia, supplement dose, duration and size. Baseline nutrient status and dietary intake, two important determinants of the effects of nutrient supplementation, are generally not considered, and there may be circumstances, where supplements are beneficial.

Definitely, in the case of specific nutrient deficiencies, that mainly occur as a consequence of diseases associated with malabsorption, metabolic disorders or increased excretion and may also occur in persons with long-term unbalanced diets, the respective nutrients should be supplemented, preferably in normal doses (not mega-doses). Potentially toxic effects of high doses should be taken into account.

As persons with dementia are at specific risk, the possibility of existing nutrient deficiency should be considered in each individual patient, and suspected cases clarified.

When no deficiency exists, however, specific supplementation does not seem reasonable, and we generally recommend providing adequate amounts of all essential nutrients through a balanced dietary pattern (see recommendation 4).

**10a. We do not recommend the use of omega-3-fatty acid supplements in persons with dementia for correction of cognitive impairment or prevention of further cognitive decline**. (Grade of evidence: **high**)

Commentary:

Omega-3 fatty acids (n3-FA) are important brain constituents, exerting anti-inflammatory effects, and epidemiologic evidence suggests a relation between dietary intake of n3-FA as well as fish and cognitive function [145,146].

The effects of n3-FA supplementation on cognition were examined in a systematic review of sound methodology [147]. Seven RCTs including persons with dementia, MCI or memory complaints were identified. Most studies used a combination of DHA and EPA for supplementation, with a predominance of DHA. Treatment duration spanned from 13 to 81 weeks. A high degree of safety and tolerability was reported. In 3 RCTs with 611 participants with dementia no effect on cognition was found. Side effects did not differ between the groups. In 4 RCTs including 678 persons with MCI or memory complaints, the overall composite memory was unaffected by the intervention, but in two sub-domains, immediate recall and attention and processing speed, a significant difference in favor of the intervention group was observed. A methodological concern is that no adjustment for multiple comparisons was performed. A more recent RCT in 36 older Malaysians of low socio-economic status and with MCI reported positive effects of a 12 month DHA-concentrated fish oil supplementation on memory (short-term, working and immediate verbal) and delayed recall [148].

In summary, available intervention studies show that n3-FA did not improve cognition in people with dementia but might be effective in early stages of cognitive impairment, which however requires confirmation. Based on this evidence we do not recommend the use of omega-3-fatty acid supplements in persons with dementia for correction of cognitive impairment or prevention of further cognitive decline.

**10b. We do not recommend the use of vitamin $B_1$ supplements in persons with dementia for prevention or correction of cognitive decline when there is no indication of vitamin $B_1$ deficiency**. (Grade of evidence: **very low**)

Commentary:

The importance of vitamin $B_1$ (**Thiamine**) in the Wernicke-Korsakoff syndrome cannot be extended to patients with Alzheimer's disease due to the lack of studies with sufficient patients. A Cochrane review that examined this question included 3 RCTs with a total number of 49 participants [149]. No reliable evidence can be drawn from these studies.

See also general comment on nutrient supplementation (at the beginning of chapter 3.3.1).

**10c. We do not recommend the use of vitamin $B_6$, vitamin $B_{12}$ and/or folic acid supplements in persons with dementia for prevention or correction of cognitive decline when there is no indication of vitamin $B_6$, vitamin $B_{12}$ and/or folic acid deficiency**. (Grade of evidence: **low**)

Commentary:

**Vitamin $B_6$** is required for the regulation of mental function and mood. It is also an essential homocysteine re-methylation cofactor, and deficiency is associated with an increase in blood homocysteine levels. Hyperhomocysteinaemia has been suggested as a cause or mechanism in the development of Alzheimer's disease and other forms of dementia [150]. Supplementation with B vitamins including vitamin B6 has been shown to reduce blood homocysteine levels. No RCTs testing vitamin $B_6$ in patients with dementia are available [151].

Regarding **vitamin $B_{12}$**, a Cochrane systematic review of sound methodology included 3 RCTs examining the efficacy of treating people with dementia and low serum levels of vitamin $B_{12}$ (total number of patients 183) with this vitamin [152]. No benefit on cognition was found. Given the strong biological plausibility of effect, the short follow-up between 1 and 5 months and the wide confidence intervals around the point estimates, the data are not conclusive.

Another Cochrane review examined the question, whether **folic acid** (with or without the addition of $B_{12}$) can improve cognition in people with dementia [153]. Although in one RCT including only persons with high homocysteine levels functional capacity was improved in the intervention group during the 3 years of the study duration, in the 4 other RCTs that addressed people with dementia, no effect on outcomes was observed.

In a RCT of excellent methodology [154] supplementation of vitamins $B_6$, $B_{12}$ and folic acid vs placebo was effective in reducing homocysteine levels, but did not slow cognitive decline in patients with mild to moderate Alzheimer's disease. Another RCT with multivitamin supplementation containing vitamins $B_6$, and $B_{12}$ and folic acid as adjunctive treatment with a cholinesterase inhibitor in

patients with Alzheimer's disease also did not identify significant effects [155].

A systematic review of RCTs on folic acid, vitamin $B_{12}$ and combined vitamin B supplementation concluded that there was no evidence that supplementation improves dementia or slows cognitive decline in subjects without vitamin deficiency, even though it might normalize homocysteine levels [156].

In summary, based on the available evidence, we do not recommend supplementation of B vitamins and/or folic acid for prevention or correction of cognitive decline in patients with dementia when there is no indication of deficiency.

See also general comment on nutrient supplementation (at the beginning of chapter 3.3.1).

**10d. We do not recommend the use of vitamin E supplements in persons with dementia for prevention or correction of cognitive decline**. (Grade of evidence: **moderate**)

Commentary:

The efficacy of Vitamin E in the treatment of Alzheimer's disease and prevention of progression of MCI to dementia was examined in a recent meta-analysis by Farina et al. [157]. Two studies in patients with Alzheimer's disease (800 and 2000 IU/d) and one study in persons with MCI (2000 IU/d) met the methodological criteria, but were not able to show a positive effect of vitamin E supplementation [157]. A subsequent RCT in 613 patients with mild to moderate Alzheimer's disease taking an acetylcholine esterase inhibitor showed that 2000 IU/d of alpha-tocopherol compared with placebo resulted in slower functional decline, however no significant effects on cognition (secondary outcome) were observed [158].

Thus, based on the available evidence, we do not recommend vitamin E supplementation for prevention or correction of cognitive decline in patients with dementia.

**10e. We do not recommend the use of selenium supplements for prevention or correction of cognitive decline**. (Grade of evidence: **very low**)

Commentary:

A systematic review [159] of very low quality found one RCT with 31 patients with Alzheimer's disease in which supplementation with selenium was compared to placebo. No conclusions can be drawn from these data. Thus, there is insufficient evidence to suggest selenium supplementation for prevention or correction of cognitive decline.

**10f. We do not recommend the use of copper supplements for prevention or correction of cognitive decline**. (Grade of evidence: **very low**)

Commentary:

In a RCT of low methodological rigor [160] 68 people with dementia were randomized to receive copper or placebo. During the 12 month follow-up the worsening in cognitive function was similar in the intervention and placebo group. A subsequent systematic review from the year 2012 did not identify any further study [159]. Thus, there is insufficient evidence to recommend copper supplementation for prevention or correction of cognitive decline.

**10g. We do not recommend the use of vitamin D supplements for prevention or correction of cognitive decline**. (Grade of evidence: **very low**)

Commentary:

Neuroprotective functions have also been assigned to **vitamin D** [161–163], but up to now no clinical trials are available on the effects of vitamin D supplementation on cognitive performance, neither in patients with nor without vitamin D deficiency. Regardless of the presence of dementia, an existing deficiency of vitamin D should be corrected by adequate supplementation. Dementia per se is no indication for vitamin D supplementation. See also general comment on nutrient supplementation (at the beginning of chapter 3.3.1).

### 3.3.2. Oral nutritional supplements (ONS)

Oral nutritional supplements (ONS) are multi-nutrient products containing macronutrients (protein, carbohydrates, fat) and micronutrients (vitamins, minerals) in a balanced composition. They are available in a wide range of flavors, mostly in liquid form but also as powder, dessert-style or bars.

ONS are intended for the dietary management of patients who cannot meet their nutritional requirements by usual food alone, in order to improve intake of energy and nutrients.

Standard products vary mainly in energy and protein content, and have not been specifically developed with the intention to improve cognitive functioning. If nutritionally complete, they can be used as sole source of nutrition, in most cases ONS are however used as a supplement to the usual diet.

Legally, ONS are “food for special medical purposes” (FSMP), which should be used under medical supervision [164].

Presently, eleven trials studying the effects of ONS compared to usual care or placebo in persons with dementia are available (Evidence Table 2): ten randomized [165–174] and one non-randomized controlled trial [175]. Several recent reviews tried to summarize existing evidence [95,176–179], unfortunately all except one [177] were of poor quality, e.g. including inappropriate studies (participants only partly with dementia, other interventions than ONS) and are thus not further considered.

**11. We recommend the use of ONS to improve nutritional status**. (Grade of evidence: **high**)

Commentary

All above mentioned available trials included body weight and/or BMI as outcome parameter and all except one [169] report significant improvements. Most of the studies were small in size ranging from 30 to 100 participants. The majority were conducted in nursing homes or in psychiatric/geriatric hospital units. Stage of dementia varied from mild to severe but was not specified in all studies. Mean BMI ranged between 20 and 25 $kg/m^2$ and only one study was restricted to malnourished patients (BMI < 20 $kg/m^2$; [165]). ONS provided between 125 and 680 kcal per day and were generally offered between meals, mainly in the morning. The intervention time varied between three weeks and one year. In general, ONS seemed to be well tolerated with high levels of adherence.

A recent report by Alzheimer's Disease International (ADI) [177] included 8 of the above mentioned 11 studies and performed two meta-analyses, one on the effect of ONS on percentage body weight change and one regarding BMI. Fixed effects pooled mean difference in % weight gain across 5 studies was 3.43% (95% CI 2.08–4.78), random effects pooled mean difference across 4 studies in BMI 1.15 $kg/m^2$ (95% CI 0.48–1.82). Effect size varied considerably across studies, e.g. for % weight gain, mean differences between intervention and control groups ranged from 1.92% to 6.61%. The % gain in body weight was greater for studies with a higher daily energy supplementation [177].

In addition to body weight/BMI, three of the studies used the *Mini Nutritional Assessment* (MNA) to assess nutritional status. All of them noted significant improvements associated with ONS [166–168]. One trial showed a statistically significant within group increase in *fat-free mass* measured using dual-energy x-ray absorptiometry (DEXA) scan [168].

In summary, there is strong evidence that ONS have positive effects on body weight/BMI. Consequently, ONS are recommended

for persons with dementia and insufficient oral nutritional intake from normal food in order to improve nutritional status.

Since ONS can certainly only be effective if they are actually consumed, it is important to mention that intake has to be ensured by close supervision and help as required.

Furthermore, ONS should always be regarded as only one tool in the nutritional management of persons with dementia and insufficient dietary intake (see recommendations 3–9), and their use should always be tailored to the patient.

See also general comment on ONS (at the beginning of chapter 3.3.2).

**12. We do not recommend the use of ONS in persons with dementia to correct cognitive impairment or prevent further cognitive decline**. (Grade of evidence: **moderate**)

Commentary:

**Cognitive function**: The effects of ONS on cognitive function of persons with dementia were evaluated in only four trials comparing ONS to usual care or placebo, all using the Mini Mental State Examination (MMSE): three RCTs [166,168,169] and one non-randomized controlled trial [175] (Evidence Table 2). These trials yielded inconsistent results.

Positive effects in terms of a significantly smaller MMSE decline after one year in the intervention group are reported in one study including 100 institutionalized patients with Alzheimer's disease (stage not given) who were randomized to receive ONS or continue usual nutrition. Unfortunately exact figures are not given, neither for the difference between the two groups nor regarding MMSE values at baseline and after 1 year [169].

In contrast, no significant differences between intervention and control groups [166,168] or even worse development in the intervention group [175] were found in the other studies. Gil Gregorio et al. [167] mentioned “no cognitive changes” in the discussion of their publication, however figures are also not given.

**Physical function**: Five trials documented the effects of ONS on functional status (physical function), measured as ability to perform basic activities of daily living (ADL), scored either with Katz [168,175], Barthel [166,173] or Zorg Index [172]. In all studies, no statistically significant difference between control and intervention groups was observed.

In summary, the available evidence regarding the effects of ONS on cognitive and physical function is very limited: Only a few small studies of generally poor quality and with great heterogeneity regarding duration, amount of ONS, type and degree of dementia are available. These trials in general do not reveal beneficial effects.

It can be assumed that by improving nutritional status general condition and function will also improve, this is however not confirmed by the existing studies. A number of factors – also including duration of the intervention, type and stage of dementia, nutritional status and amount and combination of nutrients provided – may explain the lack of benefits. Future studies have to further clarify the functional effects of ONS.

Based on the presently available evidence, ONS cannot be recommended for prevention or correction of cognitive or functional decline in persons with dementia.

See also general comment on ONS (at the beginning of chapter 3.3.2).

**13. We do not recommend the systematic use of special medical foods for persons with dementia to correct cognitive impairment or prevent further cognitive decline**. (Grade of evidence: **low**)

Commentary:

Based on the assumption that certain nutrients and nutritional compounds have specific functions for brain integrity and metabolism, several specific medical food products have been developed with the aim to prevent, delay or even correct cognitive decline in persons with cognitive impairment or dementia.

One of these products is *Souvenaid* (Nutricia, Groupe Danone, Amsterdam NL), an oral liquid nutritional supplement, which was designed to support synapse formation and function in patients with mild Alzheimer's disease [180]. It contains a specific combination of nutritional compounds (Fortasyn® Connect: omega-3 polyunsaturated fatty acids, uridine monophosphate, choline, phospholipids, vitamins E, C, $B_6$, $B_{12}$, folic acid, selenium), which are thought to be beneficial in this regard, added to a standard ONS. The product composition is based on thorough and comprehensive exploration of related preclinical evidence from basic science and animal studies and on a well-founded pathophysiologic concept [180]. Up to now, its efficacy compared to an equivalent oral liquid supplement without Fortasyn® Connect has been studied in three double-blind RCTs of high quality [181–183]. Whereas some improvements in specific cognitive domains were observed in two trials in patients with mild Alzheimer's disease who were untreated with acetylcholinesterase inhibitors and/or memantine [181,182], no benefit could be documented in patients with mild-to-moderate Alzheimer's disease taking medications [183]. No general cognitive improvement could be achieved, also regarding activities of daily living and quality of life no significant effects were observed [181,184]. The treatment was however well tolerated with a favorable safety profile and high intake adherence [185]. Further trials are ongoing and planned to evaluate the potential wider benefits of Souvenaid [186].

Another ONS product enriched with micronutrients (vitamins E, C, $B_{12}$, folate, zinc, copper, manganese and arginine) was tested in an earlier small study with the aim to slow the progression of mild Alzheimer's disease [187]. 43 patients were randomized to receive standard or enriched ONS for 6 months. Biochemical changes reflecting an increased bioavailability of the added nutrients are reported, but no significant differences in cognitive function (measured by MMSE), verbal fluency and memory were observed between the groups.

In a Spanish randomized-controlled trial, a nutritionally complete formula diet based on lyophilized foods (Vegenat®-med) (Vegenat S.A., Madrid, Spain) was studied in patients with advanced Alzheimer's disease in need of semi-solid or liquid diets. An increase in body weight compared to a control group receiving dietary advice was reported, but no effects on mental function (cognition, depression) and adverse events (hospitalization, death) were observed [188].

A nutraceutical formulation (“NF”) consisting of folic acid, vitamin $B_{12}$, vitamin E, S-adenosyl-methionine, N-acetyl cysteine, acetyl-L-carnitine (Nutricap Labs, Farmingdale, New York, USA) was developed with the aim to achieve neuroprotective effects by correcting folate deficiency, lowering homocysteine and reducing oxidative stress [189]. In an uncontrolled trial with 14 community-dwelling individuals with early stage Alzheimer's disease [189], a RCT with 12 institutionalized persons with moderate to late stage Alzheimer's disease [190] and a recent RCT with 106 individuals diagnosed with AD (disease stage not given) [191] uniformly a significant delay in decline in the Dementia Rating Scale and clock-drawing test but no change in ADL after 3 months are reported. Results of these studies are remarkably similar and of questionable trustworthiness.

A specific approach was taken by Henderson et al. [192–194] based on the observation of reduced brain glucose metabolism in the early stages of dementia, which led to the hypothesis that alternate energy sources aimed at increasing neuronal metabolism may protect neurons. Medium-chain triglycerides (MCTs) are metabolized to ketone bodies that serve as an alternative source of energy for neurons. Some data from clinical trials suggest that a

proprietary formulation of capriylic acid (*Axona*® AC-1202, Accera, Inc. CO, USA) improved cognition in patients with mild to moderate dementia in APO-E4 negative subjects. Adverse events observed were marginal and included gastrointestinal problems such as diarrhea, dyspepsia, and flatulence [193,194]. Since genomic profiles are not routinely analyzed in patients with dementia, the role of MCTs in clinical practice presently seems to be not relevant.

In summary, several specific medical food products are presently available, which are at least partly based on sound nutritional principles and pathophysiologic concepts. They have the potential to affect cognitive function and might be effective under certain conditions, e.g. in specific disease stages or possibly long-term. Presently available evidence is, however, too weak to recommend their general use, and further research is mandatory to fully establish their efficacy.

Regarding minimal risk of adverse effects, these products may provide an option to individual patients after careful discussion of burden and benefits with a specialized physician.

**14. We do not recommend any other nutritional product for persons with dementia to correct cognitive impairment or prevent further cognitive decline**. (Grade of evidence: **very low**)

Commentary:

Based on pathophysiologic considerations, preclinical studies or epidemiologic observations a wide variety of food components (besides micronutrients) and nutrient-derived compounds have been suggested to have beneficial effects on cognitive function of persons with dementia.

Among them, phytochemicals like polyphenols, flavonoids or carotenoids are discussed to have strong potential for neuroprotective action [195]. For example, curcumin, a natural phenolic compound derived from the perennial herb Curcuma longa, is well known to exhibit anti-inflammatory and antioxidant activities, and has been claimed to improve cognition. In a recent systematic review, two small RCTs were identified, that did not observe any effect on cognition [196].

Other substances have received attention and occasionally been studied, e.g. alpha lipoic acid [197], N-acetyl-cysteine [198] or phosphatidylserine [199,200] without significant results.

More research is available on acetyl-L-carnitine. In a systematic (Cochrane) review 16 trials were identified, all including patients with mild-moderate dementia or cognitive decline. No evidence of benefit regarding severity of dementia or functional ability was found [201].

Not all substances are of natural origin, and there is an also dose-dependent fluent transition between nutritional compounds and drug substances.

Overall, there is a substantial lack of high-level evidence studies and no clear evidence to recommend the use of any nutritional product presently available for prevention or correction of cognitive decline in patients with dementia.

### 3.4. Artificial nutrition and hydration

Enteral tube feeding and parenteral nutrition allow the provision of energy and nutrients to patients who are unable to consume adequate amounts orally. These modes of feeding, however, in particular via PEG, are invasive interventions implying potential complications that are not negligible [56] and have to be weighed against the potential benefits of improved nutrition.

For ethical reasons, randomized controlled trials studying the effects of artificial nutrition compared to no intervention are not available.

Existing observational studies on the effects of tube feeding in patients with dementia are generally of poor quality. In most studies the control group is not adequate, the population is not well defined and the stage of dementia remains unclear. Studies on the effects of parenteral nutrition are completely lacking. Therefore, existing scientific evidence is inconclusive, and recommendations have to include expert consensus.

**15. We recommend that each decision for or against artificial nutrition and hydration for patients with dementia is made on an individual basis with respect to general prognosis and patients' preferences**. (Grade of evidence: **very low**)

Commentary:

Since artificial nutrition and hydration (ANH) constitutes a medical treatment, necessitating an invasive procedure, decision making on initiating and also terminating ANH must be carried out on the basis of a medical indication [202]. Only if there is an indication for a therapeutic procedure that can realistically meet therapeutic goals – like prolonging life without prolonging suffering and discomfort at the end of life, or maintaining independence and physical function – weighing of probable benefits and burdens of the therapy can be considered. This is in line with the ethical concepts of beneficence and non-maleficence [203]. After achieving informed consent it is the individual patient's decision to accept the therapy, thus respecting the ethical principle of patient's autonomy [203].

It is of primary necessity that after evaluating the medical indication and weighing the clinical benefits and burdens of ANH, the individual patient's wishes, his or her values and goals of care have to be respected and incorporated in an open discussion with the patient, his or her family and next of kin and in the multidisciplinary team taking care of him or her [204,205].

ANH can have a symbolic importance apart from measurable benefits for the patient. Such views, often expressed by family members, should be understood and respected in keeping with the patient and family values, religious beliefs and culture. Communication is essential in this situation, explaining the patient's condition and prognosis, that the inability to eat and drink can be a natural part of dying and that it does not mean suffering. Optimal palliative care is indicated, including provision of careful “hand feeding”. In situations when there is uncertainty whether a patient will benefit from ANH, a time-limited trial of ANH may be useful [204,205].

Patients in advanced stages of dementia lack decisional capacity, they are incapable of understanding their prognosis and the treatment choices, and informed consent is not possible. In this situation advance directives stating the patient's preferences and/or formally designated surrogate decision makers determine the decision. It is encouraged to obtain advance directives early in the course of the disease.

Competent palliative care counsel or the possibility of discussing individual problematic cases with a clinical ethics committee should be available [206].

**16. We suggest tube feeding for a limited period of time in patients with mild or moderate dementia, to overcome a crisis situation with markedly insufficient oral intake, if low nutritional intake is predominantly caused by a potentially reversible condition**. (Grade of evidence: **very low**)

Commentary:

If there is a valid medical indication, and it is in accordance with the patient's will, tube feeding should be initiated irrespective of the presence of early, mild or moderate dementia. In this situation, tube feeding should be performed to overcome a crisis situation with markedly insufficient oral intake, if no other means are able to cover the nutritional needs of the patient. This may be the case e.g. when anorexia is a major concomitant symptom during an infectious period, in case of dysphagia due to acute stroke or in case of

delirium with markedly reduced fluid and food intake in a patient with mild dementia.

There is no data to what extent of insufficient intake tube feeding may enhance the clinical situation and prognosis and what could be a beneficial time frame for tube feeding. From the experts' point of view, an intake below ca. 50% of energy requirements expected for more than 10 days in spite of adequate support and oral supplements would be a reasonable indication for nasogastric feeding. If the period of markedly low intake is expected to last longer than 4 weeks or if nasogastric feeding is not tolerated or accepted, a PEG should be inserted. If tube feeding is performed in such a situation, the indication should be reassessed every week during the first month and monthly thereafter. If nutritional demands are again partly covered orally, an attempt without tube feeding might be useful for further judgment.

**17. We recommend against the initiation of tube feeding in patients with severe dementia**. (Grade of evidence: **high**)

Commentary:

There is no conclusive evidence supporting the use of artificial nutrition (tube feeding and parenteral nutrition) in patients with severe dementia. In fact, due to ethical reasons, there is not a single prospective randomized controlled trial evaluating a potential benefit.

There is some evidence available from retrospective and prospective observational trials on tube feeding and mortality in patients with severe dementia [207–216]. In controlled studies available no significant difference between mortality rates of patients with advanced dementia receiving tube feeding and those without tube feeding has been found.

A Cochrane review, summarizing all relevant previous studies, identified 6 controlled trials assessing mortality and found no evidence of increased survival in patients with advanced dementia receiving enteral tube feeding [206].

A recent large prospective database analysis from Teno and colleagues [217] added valuable evidence confirming this statement. They evaluated minimal data set (MDS) information of 36,492 US nursing home residents with advanced dementia and newly developed eating problems. The study compared 1956 residents who underwent PEG insertion with 34,536 residents who were fed orally and found no significant difference of survival.

No evidence is available for the effectiveness of tube feeding for older people with advanced dementia regarding quality of life, pressure ulcers, physical and mental function, behavioral and psychiatric symptoms of dementia.

Thus, considering the available evidence and clinical experience of experts in the field, there may rarely be an individual situation where tube feeding might look advantageous. The initiation of tube feeding in the advanced stage of dementia should be a very rare exception. Before initiation of tube feeding in this situation, it is recommended to make use of ethical counseling. In case of a treatment trial, it should be regularly controlled, if the expected benefits of tube feeding will occur. From the medical perspective, tube feeding can be discontinued like any other medical procedure, if a beneficial effect is not observed or no longer expected. In some cultures the initiation or maintenance of artificial feeding is regarded as a basic human right and not a medical procedure. In this circumstance it may be considered inacceptable to discontinue even artificial feeding out of fear of potentially accelerating the dying process. Thus, with the evidence that tube feeding does not prolong survival in the end stage of dementia, this argument should no longer be brought into discussion.

In the vast majority of cases, careful hand-feeding according to individual needs and capacity (comfort-feeding) is the best alternative.

**18. We suggest parenteral nutrition as an alternative if there is an indication for artificial nutrition, as described in recommendation 16, but tube feeding is contraindicated or not tolerated**. (Grade of evidence: **very low**)

Commentary:

There are no data available regarding the effects of parenteral nutrition in patients with dementia.

As in patients without dementia, artificial nutrition should be predominantly performed via the enteral route whenever possible. In case of contraindications for enteral nutrition, parenteral nutrition may be a substitute. If additional nutritional support is necessary for a period shorter than 10 days or if nasogastric feeding is not accepted, peripheral parenteral nutrition might help to overcome a crisis situation of low intake. The same is true if a central venous line is already in place for other reasons, i.e. in the perioperative period.

In any case a medical indication is required, the individual patient's will has to be considered, and potential risks have to be weighed against the potential benefits of improved nutrition (see also recommendation 15).

Thus, parenteral nutrition will be reserved to justified individual cases of mild to moderate dementia. In the vast majority of cases, careful hand-feeding according to individual needs and capacity (comfort-feeding) is the best alternative.

**19. We suggest parenteral fluids for a limited period of time in periods of insufficient fluid intake to overcome a crisis situation**. (Grade of evidence: **very low**)

Commentary:

Generally, the oral route is the preferred route for fluid administration. There are, however, clinical circumstances (i.e. febrile states, diarrhea) when patients with dementia may require parenteral administration of fluids because – due to dysphagia or perturbed perception of thirst accompanying advanced states of dementia – oral intake is not sufficient to meet the requirements [218–221].

Intravenous (i.v.) fluid supplementation is standard for patients who need an i.v. cannula for other reasons. If the patient's compliance is reduced, if the peripheral venous route is too burdensome for the patient or impossible, and the central venous route is not practicable, or if the patient is treated at home or in a nursing home, a subcutaneous (s.c.) access is an advantageous alternative.

The infusion of fluids into the subcutaneous tissue – hypodermoclysis – is an easy, effective and safe hydration technique in mild to moderate dehydration, particularly in cognitively impaired patients [219,220,222,223]. There is little discomfort inserting and maintaining the s.c. infusion, and patients are less likely to interfere with s.c. infusions than with i.v. lines [220]. There is evidence that hypodermoclysis is as effective as i.v. hydration [221,222]. The infused electrolyte solutions should be isotonic, it is recommended that the infused volume should not exceed 3000 mL per day (max. 1.500 mL per infusion site), however in the majority of the reported cases, the infused daily volumes do not exceed 1000 mL [218,220,222,223]. The s.c.

application is not suitable for patients needing larger volumes, hypertonic or electrolyte-free solutions. Coagulation disorders, dermatological problems on the infusion site, lack of subcutaneous tissue in severely malnourished patients are further limitations [221,222]. There are no studies about hypodermoclysis including only patients with dementia, they all consider the general patient population including geriatric patients with various stages of cognitive impairment.

**20. We recommend against the use of artificial nutrition (enteral nutrition, parenteral nutrition and parenteral fluids) in the terminal phase of life**. (Grade of evidence: **very low**)

Commentary:

Artificial nutrition and hydration (ANH) is associated with uncertain benefits and substantial risks in patients in the terminal phase of life, including patients with advanced dementia [205,224,225]. When ANH is administered via a gastrostomy tube, physical restraints and their inherent risks are being applied more frequently. There is also a higher risk of aspiration pneumonia, diarrhea, gastrointestinal discomfort and pressure ulcers [206,217,226].

ANH should not be started or continued if it is associated with complications and additional symptom burden for the dying patient with or without dementia. In the dying patient ANH can cause discomfort due to increased oral and pulmonary secretions and dyspnea due to pulmonary edema [224].

The sensation of hunger is not generally apparent in dying patients; when offered they will take very little nourishment. The major discomfort is thirst, which can be satisfactorily managed by sips of fluids, ice cubes, hard candy or good oral care moistening the oral cavity [224,227,228]. There is little correlation between the sensation of thirst in patients in the terminal stages of their lives and their actual intake of fluids, even when administered intravenously [205,224,228,229].

Observational studies indicate that forgoing ANH in patients with insufficient intake and severe dementia who have attained the terminal phase of their life, marked by severe disability and complications like recurrent infections, is in general not associated with high levels of discomfort if optimal palliative care is provided [230,231]. Further studies are needed on this topic, though they are difficult to conceive and to conduct due to ethical conside rations [232].

## Conflict of interest

None declared.


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## Appendix

**Evidence Table 1**
Nutrition education and training programs for caregivers and patients.

| | Study design | Intervention | | | Setting | Patients | | | Results | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Kind of training | Amount | Duration | | n | Age [y.]* | Kind/stage of dementia | Characteristics | Intake | Nutritional status | Other |
| **… for private caregivers** | | | | | | | | | | | | |
| Riviere et al. (2001) [135] | CT | Nutritional sessions for caregivers | 9 sessions, 1 h each | 1 year | Community | IG 151, CG 74 | IG 77.3, CG:75.4 | Alzheimer dementia, diagnosis according to NINCDS-ADRDA, GDS 2–6 | IG: MNA 22.9, MMSE 15.4, ADL 4.4; CG: MNA 24.3, MMSE 15.4, ADL 4.7 | n.i. | Body weight↑ (ns), MNA↑ (ns) | MMSE↑, ADL=, IADL=, EBS=, CMAI=, mood/ depression = |
| Salva et al. (2011) [136] | RCT (cluster) | Teaching and training intervention - health and nutrition promotion program for physicians, caregivers and patients (NutriAlz) | 4 booklets, 4 sessions, | 12 months | Community (11 AD outpatient and day care centers) | IG 448, CG 498 | IG 79.4, CG:78.6 | Alzheimer dementia diagnosed according to DSM IV, MMSE ≤ 26 | IG: MNA 22.3, MMSE 14.7, ADL 3.75, CG: MNA 24.0, MMSE 16.0, ADL 4.2 | n.i. | MNA↑, BMI=, weight= | ADL/IADL=, MMSE=, CDR=, NPI-Q=, EBS=, caregiver burden= |
| Pivi et al. (2011) [171] | RCT | Nutritional education for caregivers and | 10 classes with nutritional topics | 6 months | Clinic of behavioral neurology | IG 25, CG 27 | >65, mean 75 | Probable Alzheimer | MMSE 13; 40% dependent during meals | n.i. | BMI=, weight=, AC=, AMC=, total protein=, | n.i. |

(*continued on next page*)

**Evidence Table 1** (*continued*)

| | Study design | Intervention | | | Setting | Patients | | | | Results | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Kind of training | Amount | Duration | | n | Age [y.]* | Kind/stage of dementia | Characteristics | Intake | Nutritional status | Other |
| | | patients vs control | | | | | | | | | total lymphocyte count= | |
| **… for long term care staff** | | | | | | | | | | | | |
| Mamhidir et al. (2007) [138] | CT | Integrity-promoting care training programme for the staff | 1 week training consisting of 20 h lectures and 18 h group discussions | 3 months | 2 long term care wards | IG 18, CG 15 | IG: 82.4 CG:82 | Alzheimer diagnosis according to NINCDS-ADRDA, DSM-III; MMSE | Severely disabled in ADL functions | n.i. | Body weight↑ | n.i. |
| Suominen et al. (2007) [137] | Pre-post | Education for nursing staff (lectures, group discussion, homework tasks, personal feedback) | 6 sessions, 2–3 h each | 6 months | Nursing home dementia ward | 28 professionals from 5 NHs, 21 patients in 1 ward | 85 (62–95) | Moderate to severe dementia | 43% energy intake <1200 kcal, 11% malnourished according to MNA | Energy↑, protein↑, calcium↑, folate↑ | MNA↑ (ns), BMI=, | n.i. |
| Chang & Lin (2005) [139] | CT | Feeding skills training programm for nursing assistants (NAs) | 3 h classes, 1 h hands-on training | n.i. | Dementia-specialized LTCF | 67 NAs (IG 31, CG 36); 20 patients and NAs | IG:84.2, CG: 72.0 | Patients diagnosed with dementia | n.i. | Food intake= | n.i. | Total eating time↑, EdFED↓; NAs: more knowledge, more positive attitutde, better behaviors |
| **… for patients** | | | | | | | | | | | | |
| Lin et al. (2010) [140] | RCT | Residents: training of eating skills by spaced retrieval (IG1) or Montessori-based activities (IG2) | Three 35–40 min sessions per week | 8 weeks | Long term care dementia special care units | 85 | 81.2 (66–96) | Diagnosed with dementia | EdFED ≥ 2, MMSE CG: 10.5, IG2 10.8, IG1 13.6, ADL CG: 55.8, IG2 48.3, IG1: 69.5 | Eating amount: IG1=, IG2↓ | MNA: IG1↑, IG2↓, BMI=, weight= | EdFED↑, assisted feeding↑, self-eating time↑ |
| Lin et al. (2011) [141] | RCT | Residents: training of eating skills by Montessori methods | Three 30 min sessions per week for 8 weeks | 22 weeks, 16 weeks intervention | Long term care dementia special care units | 29 | 82.9 (68–95) | Diagnosed with dementia | EdFED ≥ 2, MMSE 11.2, BMI 21.4, | n.i. | BMI=, MNA= | EdFED↑, self-feeding time↑, eating beahviour scale↑, self-feeding frequency↑, verbal and physical assistance=, assisted feeding=, eating time= |

AC = arm circumference; AD = Alzheimer's disease; ADL = activity of daily living; ALF = assisted living facility; AMC = upper-arm muscle circumference; CDR = clinial dementia rating scale; CG = control group; CMAI = Cohen Mansfield Agitation Inventory; CRP = C-reaktives protein; CT = controlled trial; DSM = diagnostic and statistical manual of mental disorders; EBS = eating behavior scale (Blandford, Tully); EdFED = Edinburgh feeding evaluation in dementia questionnaire; FAST= functional assessment staging test; GDS = global deterioration scale; IADL = instrumental activities of daily living; IG = intervention group; LEI = level of eating independance; LTCF = long term care facility; MMSE = mini-mental state examination; MNA = mini nutrial assessment; NA = nursing assistant; NINCDS-ARDRA = National Institute of Neurological and Communicative Disorders and Stroke and the Alzeheimer's Disease and Related Disorders Association criteria; ONS = oral nutritional supplements; RCT = randomized controlled trial. n.i. = no information. ns = not significant.

* Means or median (range).

↑ Improvement through intervention (intervention vs. control, or pre-post).

↓ Deterioration through intervention (intervention vs. control, or pre-post).

= No changes.

**Evidence Table 2**
Oral nutritional supplements in older persons with dementia.

| | Study design | Intervention | | | Setting | Patients | | | | Results | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Kind of ONS | Amount/day | Duration | | n | Age [y.] | Kind and stage of dementia | Characteristics | Intake | Nutritional status | Other |
| Carver et al. (1995) [165] | RCT | Fortisip (Cow&Gate) | 2*200 mL, 600 kcal | 12 weeks | Psychatric teaching hospital | 45 | 60–90 | Different degrees of dementia | BMI 15–20 | *n.i.* | Body weight↑, MAMC, TST↑ | *n.i.* |
| de Sousa et al. (2012) [166] | RCT | High-protein, energy dense liquid ONS | 200 mL, 400 kcal, 18 g protein | 3 weeks | Geriatric unit of psychiatric hospital | 37 | >60 | Probable mild Alzheimer | Weight loss >5% in last year, MNA<17 | *n.i.* | Body weight↑, BMI↑, MNA↑. AMC, TST↑, albumin↑, protein↑ | MMSE=, ADL= |
| Faxén-Irving et al. (2002) [175] | Controlled, non-randomized | Balanced liquid ONS (Semper Komplett Näring) and juicy supplement (Addera) | 400 mL, 410 kcal, 18 g protein | 6 months | Group-living for demented elderly people, 2 units | 33 | 75–90 | Different degrees of dementia | All ambulatory, 14% independent in ADL, BMI 23 ± 4; 19% BMI<20; | *n.i.* | Body weight↑, albumin, CRP, hemoglobin, vitamin B12, IGF-I= | CDR=, MMSE↓; ADL= |
| Gil Gregorio et al. (2003) [167] | RCT | Nutrison (Nutricia) | *n.i.* | 12 months | 8 nursing homes | 99 (25 in IG) | 86.5 | Alzheimer (moderate) | FAST 5–6, BMI 24 ± 3.4 | Protein↑ | BMI↑, MNA↑, TST↑, albumin, prealbumin, iron, zinc, β-carotin↑ | Infections↓, days in bed↓, cognition=, function= |
| Lauque et al. (2004) [168] | RCT | Clinutren – soup, dessert or drink (Nestle) | 300–500 kcal, 10–20 g protein | 3 months | Geriatric wards and day care centers | 91 | >65 | Alzheimer | At risk of malnutrition, MNA<23, BMI 22 ± 3 | Energy↑ protein↑ | Body weight↑, FFM↑ MNA↑ albumin= | MMSE=, ADL= |
| Navratilova et al. (2007) [169] | RCT | Nutridrink mutifibre (Nutricia) | 600 kcal, 24 g protein | 12 months | 7 institutions | 100 | *not given* | Alzheimer | *n.i.* | Energy↑ protein↑ | Body weight, BMI= (no figures given) | MMSE↑, mortality= |
| Parrott et al. (2006) [170] | RCT, cross-over | | 250–258 kcal | 3 weeks | Nursing home | 30 | 88.1 (±4.1) | Probable Alzheimer | Independent eating, stable weight | Energy↑ | BMI↑ | *n.i.* |
| Pivi et al. (2011) [171] | RCT | Ensure with FOS (Abott) | 680 kcal, 25.6 g protein | 6 months | Clinic of behavioral neurology | 53 | >65, median 76 y. | Probable Alzheimer | 49% dependent during meals | *n.i.* | Body weight, BMI↑, AC, AMC↑, protein, TLC↑, TST, albumin= | *n.i.* |
| Wouters-Wesseling et al. (2002) [173] | RCT (placebo, double-blind) | *Not specified* | 2× daily 250 kcal, 8.5 g protein | 7 months | 2 psycho-geriatric nursing homes | 35 | ≥60 | *n.i.* | BMI<23 (m), <25 (w), no acute illness | *n.i.* | Body weight↑, albumin, CRP=; homocysteine, vitamins↑; | ADL=; diarrhea, GI-complaints= |
| Wouters-Wesseling et al. (2006) [172] | RCT | *Not specified* | 200 mL, 309 kcal, 11.2 g protein | 5 weeks | Psycho-geriatric nursing homes | 34 | >65 | Alzheimer | BMI 24.5 ± 4.2, different infections | Energy= | Body weight↑, TST, MAMC, CC= | Dependency (ZIG score)= |
| Young et al. (2004) [174] | RCT, cross-over | *Not specified* | 250–258 kcal, 9.1–10.4 g protein | 3 weeks | Nursing home | 34 | 88.2 (±3.9) | Alzheimer | Ability to self-feed or to require only minimal levels of assistance | Energy↑ protein↑ | Body weight↑ | *n.i.* |

AC = arm circumference; ADL = activity of daily living; AMC = arm muscle circumference; CC = calf circumference; CDR = clinical dementia rating scale; CRP = C-reactive protein; FAST = functional assessment staging test; FFM = fat-free mass; GDS = global deterioration scale; GI = gastrointestinal; IGF-I = insulin-like growth factor I; MAC = mid arm circumference; MAMC = mid-arm muscle circumference; MMSE = mini-mental state examination; MNA = mini nutrial assessment; ONS = oral nutritional supplement; TLC = total lymphocyte count; TST = triceps skinfold thickness; ZIG = Zorg index geriatrie. n.i. = no information.
↑ Improvement through intervention (intervention vs. control, or pre-post).
↓ Deterioration through intervention (intervention vs. control, or pre-post).
= No changes.

## References


[1] Preiser JC, Schneider SM. ESPEN disease-specific guideline framework. Clin Nutr 2011;30:549–52.
[2] Goisser S, Schrader E, Singler K, Bertsch T, Gefeller O, Biber R, et al. Low postoperative dietary intake is associated with worse functional course in geriatric patients up to 6 months after hip fracture. Br J Nutr 2015:1–11.
[3] Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. BMJ 2004;328:1490.
[4] Weuve J, Hebert LE, Scherr PA, Evans DA. Deaths in the United States among persons with Alzheimer's disease (2010–2050). Alzheimers Dement 2014;10:e40–6.
[5] Feldman HH, Jacova C, Robillard A, Garcia A, Chow T, Borrie M, et al. Diagnosis and treatment of dementia: 2. Diagnosis. CMAJ 2008;178:825–36.
[6] McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack Jr CR, Kawas CH, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011;7:263–9.
[7] Patterson C, Feightner JW, Garcia A, Hsiung GY, MacKnight C, Sadovnick AD. Diagnosis and treatment of dementia: 1. Risk assessment and primary prevention of Alzheimer disease. CMAJ 2008;178:548–56.
[8] van der Lee J, Bakker TJ, Duivenvoorden HJ, Droes RM. Multivariate models of subjective caregiver burden in dementia: a systematic review. Ageing Res Rev 2014;15C:76–93.
[9] Bateman RJ, Xiong C, Benzinger TL, Fagan AM, Goate A, Fox NC, et al. Clinical and biomarker changes in dominantly inherited Alzheimer's disease. N Engl J Med 2012;367:795–804.
[10] Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, et al. Frailty consensus: a call to action. J Am Med Dir Assoc 2013;14:392–7.
[11] Vitaliano PP, Breen AR, Russo J, Albert M, Vitiello MV, Prinz PN. The clinical utility of the dementia rating scale for assessing Alzheimer patients. J Chronic Dis 1984;37:743–53.
[12] Moelter ST, Glenn MA, Xie SX, Chittams J, Clark CM, Watson M, et al. The dementia severity rating scale predicts clinical dementia rating sum of boxes scores. Alzheimer Dis Assoc Disord 2015;29:158–60.
[13] Reisberg B, Ferris SH, de Leon MJ, Crook T. The global deterioration scale for assessment of primary degenerative dementia. Am J Psychiatry 1982;139:1136–9.
[14] Belmin J. Practical guidelines for the diagnosis and management of weight loss in Alzheimer's disease: a consensus from appropriateness ratings of a large expert panel. J Nutr Health Aging 2007;11:33–7.
[15] Gillette-Guyonnet S, Nourhashemi F, Andrieu S, de Glisezinski I, Ousset PJ, Riviere D, et al. Weight loss in Alzheimer disease. Am J Clin Nutr 2000;71:637S–42S.
[16] Gillette Guyonnet S, Abellan Van Kan G, Alix E, Andrieu S, Belmin J, Berrut G, et al. IANA (International Academy on Nutrition and Aging) Expert Group: weight loss and Alzheimer's disease. J Nutr Health Aging 2007;11:38–48.
[17] White H, Pieper C, Schmader K, Fillenbaum G. Weight change in Alzheimer's disease. J Am Geriatr Soc 1996;44:265–72.
[18] Albanese E, Taylor C, Siervo M, Stewart R, Prince MJ, Acosta D. Dementia severity and weight loss: a comparison across eight cohorts. The 10/66 study. Alzheimers Dement 2013;9:649–56.
[19] Smith KL, Greenwood CE. Weight loss and nutritional considerations in Alzheimer disease. J Nutr Elder 2008;27:381–403.
[20] Grundman M, Corey-Bloom J, Jernigan T, Archibald S, Thal LJ. Low body weight in Alzheimer's disease is associated with mesial temporal cortex atrophy. Neurology 1996;46:1585–91.
[21] Vanhanen M, Kivipelto M, Koivisto K, Kuusisto J, Mykkanen L, Helkala EL, et al. APOE- 4 is associated with weight loss in women with AD: a population-based study. Neurology 2001;56:655–9.
[22] Engelhart MJ, Geerlings MI, Meijer J, Kiliaan A, Ruitenberg A, van Swieten JC, et al. Inflammatory proteins in plasma and the risk of dementia: the rotterdam study. Arch Neurol 2004;61:668–72.
[23] Fillit H, Ding WH, Buee L, Kalman J, Altstiel L, Lawlor B, et al. Elevated circulating tumor necrosis factor levels in Alzheimer's disease. Neurosci Lett 1991;129:318–20.
[24] Tarkowski E, Blennow K, Wallin A, Tarkowski A. Intracerebral production of tumor necrosis factor-alpha, a local neuroprotective agent, in Alzheimer disease and vascular dementia. J Clin Immunol 1999;19:223–30.
[25] Zuliani G, Ranzini M, Guerra G, Rossi L, Munari MR, Zurlo A, et al. Plasma cytokines profile in older subjects with late onset Alzheimer's disease or vascular dementia. J Psychiatr Res 2007;41:686–93.
[26] Braak E, Griffing K, Arai K, Bohl J, Bratzke H, Braak H. Neuropathology of Alzheimer's disease: what is new since A. Alzheimer? Eur Arch Psychiatry Clin Neurosci 1999;249(Suppl. 3):14–22.
[27] Stanciu I, Larsson M, Nordin S, Adolfsson R, Nilsson LG, Olofsson JK. Olfactory impairment and subjective olfactory complaints independently predict conversion to dementia: a longitudinal, population-based study. J Int Neuropsychol Soc 2014;20:209–17.
[28] Olofsson JK, Nordin S, Wiens S, Hedner M, Nilsson LG, Larsson M. Odor identification impairment in carriers of ApoE-varepsilon4 is independent of clinical dementia. Neurobiol Aging 2010;31:567–77.
[29] Lechowski L, de Stampa M, Denis B, Tortrat D, Chassagne P, Robert P, et al. Patterns of loss of abilities in instrumental activities of daily living in Alzheimer's disease: the REAL cohort study. Dement Geriatr Cogn Disord 2008;25:46–53.
[30] Silva P, Kergoat MJ, Shatenstein B. Challenges in managing the diet of older adults with early-stage Alzheimer dementia: a caregiver perspective. J Nutr Health Aging 2013;17:142–7.
[31] Chang CC, Roberts BL. Feeding difficulty in older adults with dementia. J Clin Nurs 2008;17:2266–74.
[32] Keller HH, Edward HG, Cook C. Mealtime experiences of families with dementia. Am J Alzheimers Dis Other Demen 2006;21:431–8.
[33] Aselage MB, Amella EJ. An evolutionary analysis of mealtime difficulties in older adults with dementia. J Clin Nurs 2010;19:33–41.
[34] Watson R, Deary IJ. Measuring feeding difficulty in patients with dementia: multivariate analysis of feeding problems, nursing intervention and indicators of feeding difficulty. J Adv Nurs 1994;20:283–7.
[35] Alagiakrishnan K, Bhanji RA, Kurian M. Evaluation and management of oropharyngeal dysphagia in different types of dementia: a systematic review. Arch Gerontol Geriatr 2013;56:1–9.
[36] Chouinard J, Lavigne E, Villeneuve C. Weight loss, dysphhagia, and outcome in advanced dementia. Dysphagia 1998;13:151–5.
[37] Langmore SE, Skarupski KA, Park PS, Fries BE. Predictors of aspiration pneumonia in nursing home residents. Dysphagia 2002;17:298–307.
[38] Miller SL, Wolfe RR. The danger of weight loss in the elderly. J Nutr Health Aging 2008;12:487–91.
[39] Chapman IM. Weight loss in older persons. Med Clin North Am 2011;95:579–93. xi.
[40] Agarwal E, Miller M, Yaxley A, Isenring E. Malnutrition in the elderly: a narrative review. Maturitas 2013;76:296–302.
[41] Newman AB, Yanez D, Harris T, Duxbury A, Enright PL, Fried LP. Weight change in old age and its association with mortality. J Am Geriatr Soc 2001;49:1309–18.
[42] McMinn J, Steel C, Bowman A. Investigation and management of unintentional weight loss in older adults. BMJ 2011;342:d1732.
[43] White H, Pieper C, Schmader K. The association of weight change in Alzheimer's disease with severity of disease and mortality: a longitudinal analysis. J Am Geriatr Soc 1998;46:1223–7.
[44] Guerin O, Andrieu S, Schneider SM, Cortes F, Cantet C, Gillette-Guyonnet S, et al. Characteristics of Alzheimer's disease patients with a rapid weight loss during a six-year follow-up. Clin Nutr 2009;28:141–6.
[45] Hanson LC, Ersek M, Lin FC, Carey TS. Outcomes of feeding problems in advanced dementia in a nursing home population. J Am Geriatr Soc 2013;61:1692–7.
[46] Faxen-Irving G, Basun H, Cederholm T. Nutritional and cognitive relationships and long-term mortality in patients with various dementia disorders. Age Ageing 2005;34:136–41.
[47] Gambassi G, Landi F, Lapane KL, Sgadari A, Mor V, Bernabei R. Predictors of mortality in patients with Alzheimer's disease living in nursing homes. J Neurol Neurosurg Psychiatry 1999;67:59–65.
[48] Garcia-Ptacek S, Kareholt I, Farahmand B, Cuadrado ML, Religa D, Eriksdotter M. Body-mass index and mortality in incident dementia: a Cohort Study on 11,398 patients from SveDem, the Swedish Dementia Registry. J Am Med Dir Assoc 2014;15.
[49] Mitchell SL, Teno JM, Kiely DK, Shaffer ML, Jones RN, Prigerson HG, et al. The clinical course of advanced dementia. N Engl J Med 2009;361:1529–38.
[50] Morley JE. Nutrition and the brain. Clin Geriatr Med 2010;26:89–98.
[51] Lourida I, Soni M, Thompson-Coon J, Purandare N, Lang IA, Ukoumunne OC, et al. Mediterranean diet, cognitive function, and dementia: a systematic review. Epidemiology 2013;24:479–89.
[52] Lopes da Silva S, Vellas B, Elemans S, Luchsinger J, Kamphuis P, Yaffe K, et al. Plasma nutrient status of patients with Alzheimer's disease: systematic review and meta-analysis. Alzheimers Dement 2014;10:485–502.
[53] Kamphuis PJ, Scheltens P. Can nutrients prevent or delay onset of Alzheimer's disease? J Alzheimers Dis 2010;20:765–75.
[54] Orsitto G, Fulvio F, Tria D, Turi V, Venezia A, Manca C. Nutritional status in hospitalized elderly patients with mild cognitive impairment. Clin Nutr 2009;28:100–2.
[55] Coin A, Veronese N, De Rui M, Mosele M, Bolzetta F, Girardi A, et al. Nutritional predictors of cognitive impairment severity in demented elderly patients: the key role of BMI. J Nutr Health Aging 2012;16:553–6.
[56] Wirth R, Voss C, Smoliner C, Sieber CC, Bauer JM, Volkert D. Complications and mortality after percutaneous endoscopic gastrostomy in geriatrics: a prospective multicenter observational trial. J Am Med Dir Assoc 2012;13:228–33.
[57] White HK, McConnell ES, Bales CW, Kuchibhatla M. A 6-month observational study of the relationship between weight loss and behavioral symptoms in institutionalized Alzheimer's disease subjects. J Am Med Dir Assoc 2004;5:89–97.
[58] Soto ME, Secher M, Gillette-Guyonnet S, Abellan van Kan G, Andrieu S, Nourhashemi F, et al. Weight loss and rapid cognitive decline in community-dwelling patients with Alzheimer's disease. J Alzheimers Dis 2012;28:647–54.
[59] Guerin O, Andrieu S, Schneider SM, Milano M, Boulahssass R, Brocker P, et al. Different modes of weight loss in Alzheimer disease: a prospective study of 395 patients. Am J Clin Nutr 2005;82:435–41.

[60] Ousset PJ, Nourhashemi F, Reynish E, Vellas B. Nutritional status is associated with disease progression in very mild Alzheimer disease. Alzheimer Dis Assoc Disord 2008;22:66–71.
[61] Raivio M, Eloniemi-Sulkava U, Laakkonen ML, Saarenheimo M, Pietila M, Tilvis R, et al. How do officially organized services meet the needs of elderly caregivers and their spouses with Alzheimer's disease? Am J Alzheimers Dis Other Demen 2007;22:360–8.
[62] Grafström M, Fratiglioni L, Sandman PO, Winblad B. Health and social consequences for relatives of demented and non-demented elderly. A population-based study. J Clin Epidemiol 1992;45:861–70.
[63] Gustavsson A, Svensson M, Jacobi F, Allgulander C, Alonso J, Beghi E, et al. Cost of disorders of the brain in Europe 2010. Eur Neuropsychopharmacol 2011;21:718–79.
[64] Pinquart M, Sorensen S. Differences between caregivers and noncaregivers in psychological health and physical health: a meta-analysis. Psychol Aging 2003;18:250–67.
[65] Wimo A, Prince M. World Alzheimer report – the global economic impact of dementia. 2010. p. 1–56.
[66] Wimo A, von Strauss E, Nordberg G, Sassi F, Johansson L. Time spent on informal and formal care giving for persons with dementia in Sweden. Health Policy 2002;61:255–68.
[67] Keller HH, Smith D, Kasdorf C, Dupuis S, Schindel Martin L, Edward G, et al. Nutrition education needs and resources for dementia care in the community. Am J Alzheimers Dis Other Demen 2008;23:13–22.
[68] Amella EJ. Feeding and hydration issues for older adults with dementia. Nurs Clin North Am 2004;39:607–23.
[69] Amella EJ, Grant AP, Mulloy C. Eating behavior in persons with moderate to late-stage dementia: assessment and interventions. J Am Psychiatr Nurses Assoc 2008;13:360–7.
[70] Fjellstrom C, Starkenberg A, Wesslen A, Licentiate MS, Tysen Backstrom AC, Faxen-Irving G, et al. To be a good food provider: an exploratory study among spouses of persons with Alzheimer's disease. Am J Alzheimers Dis Other Demen 2010;25:521–6.
[71] Hughes G, Bennett KM, Hetherington MM. Old and alone: barriers to healthy eating in older men living on their own. Appetite 2004;43:269–76.
[72] Puranen TM, Pietila SE, Pitkala KH, Kautiainen H, Raivio M, Eloniemi-Sulkava U, et al. Caregivers' male gender is associated with poor nutrient Intake in AD families (NuAD-Trial). J Nutr Health Aging 2014;18:672–6.
[73] Pasman HR, The BA, Onwuteaka-Philipsen BD, van der Wal G, Ribbe MW. Feeding nursing home patients with severe dementia: a qualitative study. J Adv Nurs 2003;42:304–11.
[74] Riviere S, Gillette-Guyonnet S, Andrieu S, Nourhashemi F, Lauque S, Cantet C, et al. Cognitive function and caregiver burden: predictive factors for eating behaviour disorders in Alzheimer's disease. Int J Geriatr Psychiatry 2002;17:950–5.
[75] Bilotta C, Bergamaschini L, Arienti R, Spreafico S, Vergani C. Caregiver burden as a short-term predictor of weight loss in older outpatients suffering from mild to moderate Alzheimer's disease: a three months follow-up study. Aging Ment Health 2010;14:481–8.
[76] Johansson L, Sidenvall B, Malmberg B, Christensson L. Who will become malnourished? A prospective study of factors associated with malnutrition in older persons living at home. J Nutr Health Aging 2009;13:855–61.
[77] Torres SJ, McCabe M, Nowson CA. Depression, nutritional risk and eating behaviour in older caregivers. J Nutr Health Aging 2010;14:442–8.
[78] Rullier L, Lagarde A, Bouisson J, Bergua V, Torres M, Barberger-Gateau P. Psychosocial correlates of nutritional status of family caregivers of persons with dementia. Int Psychogeriatr 2014;26:105–13.
[79] Rullier L, Lagarde A, Bouisson J, Bergua V, Barberger-Gateau P. Nutritional status of community-dwelling older people with dementia: associations with individual and family caregivers' characteristics. Int J Geriatr Psychiatry 2013;28:580–8.
[80] Arvanitakis M, Beck A, Coppens P, De Man F, Elia M, Hebuterne X, et al. Nutrition in care homes and home care: how to implement adequate strategies (report of the Brussels Forum (22–23 November 2007)). Clin Nutr 2008;27:481–8.
[81] Suominen MH, Sandelin E, Soini H, Pitkala KH. How well do nurses recognize malnutrition in elderly patients? Eur J Clin Nutr 2009;63:292–6.
[82] Volkert D, Saeglitz C, Gueldenzoph H, Sieber CC, Stehle P. Undiagnosed malnutrition and nutrition-related problems in geriatric patients. J Nutr Health Aging 2010;14:387–92.
[83] Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. ESPEN guidelines for nutrition screening 2002. Clin Nutr 2003;22:415–21.
[84] Phillips MB, Foley AL, Barnard R, Isenring EA, Miller MD. Nutritional screening in community-dwelling older adults: a systematic literature review. Asia Pac J Clin Nutr 2010;19:440–9.
[85] van Bokhorst-de van der Schueren MAE, Guaitoli PR, Jansma EP, de Vet HCW. Nutrition screening tools: does one size fit all? A systematic review of screening tools for the hospital setting. Clin Nutr 33:39–58.
[86] Vandewoude M, Van Gossum A. Nutritional screening strategy in nonagenarians: the value of the MNA-SF (mini nutritional assessment short form) in NutriAction. J Nutr Health Aging 2013;17:310–4.
[87] Kaiser R, Winning K, Uter W, Lesser S, Stehle P, Sieber CC, et al. Comparison of two different approaches for the application of the mini nutritional assessment in nursing homes: resident interviews versus assessment by nursing staff. J Nutr Health Aging 2009;13:863–9.
[88] Blandford G, Watkins L, Mulvilhill MN, Taylor B. Assessing abnormal feeding behavior in dementia: a taxonomy and initial findings. In: Vellas B, Riviere S, Fitten J, editors. Weight loss & eating behaviour in Alheimer's patients. Toulouse; Los Angeles: Serdi; 1998. p. 47–64.
[89] Tully MW, Lambros Matrakas K, Musallam K. The eating behavior scale: a simple method of assessing functional ability in patients with Alzheimer's disease. J Nutr Health Aging 1998;2:119–21.
[90] Stroebele N, De Castro JM. Effect of ambience on food intake and food choice. Nutrition 2004;20:821–38.
[91] Nieuwenhuizen WF, Weenen H, Rigby P, Hetherington MM. Older adults and patients in need of nutritional support: review of current treatment options and factors influencing nutritional intake. Clin Nutr 2010;29:160–9.
[92] de Castro JM, Brewer EM. The amount eaten in meals by humans is a power function of the number of people present. Physiol Behav 1992;51:121–5.
[93] Nijs KA, de Graaf C, Siebelink E, Blauw YH, Vanneste V, Kok FJ, et al. Effect of family-style meals on energy intake and risk of malnutrition in dutch nursing home residents: a randomized controlled trial. J Gerontol A Biol Sci Med Sci 2006;61:935–42.
[94] Nijs KA, de Graaf C, Kok FJ, van Staveren WA. Effect of family style mealtimes on quality of life, physical performance, and body weight of nursing home residents: cluster randomised controlled trial. BMJ 2006;332:1180–4.
[95] Liu W, Cheon J, Thomas SA. Interventions on mealtime difficulties in older adults with dementia: a systematic review. Int J Nurs Stud 2013.
[96] Whear R, Abbott R, Thompson-Coon J, Bethel A, Rogers M, Hemsley A, et al. Effectiveness of mealtime interventions on behavior symptoms of people with dementia living in care homes: a systematic review. J Am Med Dir Assoc 2014;15:185–93.
[97] Santo P MJ, Boczko F. The Breakfast Club: results of a study examining the effectiveness of a multi-modality group communication treatment. Am J Alzheimer's Dis 1998;13:146–58.
[98] Charras K, Fremontier M. Sharing meals with institutionalized people with dementia: a natural experiment. J Gerontol Soc Work 2010;53:436–48.
[99] Edwards NE, Beck AM. The influence of aquariums on weight in individuals with dementia. Alzheimer Dis Assoc Disord 2013;27:379–83.
[100] Dunne TE, Neargarder SA, Cipolloni PB, Cronin-Golomb A. Visual contrast enhances food and liquid intake in advanced Alzheimer's disease. Clin Nutr 2004;23:533–8.
[101] Young KWH, Greenwood CE. Shift in diurnal feeding patterns in nursing home residents with Alzheimer's disease. J Gerontol A Biol Sci Med Sci 2001;56:M700–6.
[102] Young KW, Binns MA, Greenwood CE. Meal delivery practices do not meet needs of Alzheimer patients with increased cognitive and behavioral difficulties in a long-term care facility. J Gerontol A Biol Sci Med Sci 2001;56:M656–61.
[103] Odlund Olin A, Armyr I, Soop M, Jerstrom S, Classon I, Cederholm T, et al. Energy-dense meals improve energy intake in elderly residents in a nursing home. Clin Nutr 2003;22:125–31.
[104] Smoliner C, Norman K, Scheufele R, Hartig W, Pirlich M, Lochs H. Effects of food fortification on nutritional and functional status in frail elderly nursing home residents at risk of malnutrition. Nutrition 2008;24:1139–44.
[105] Biernacki C, Barratt J. Improving the nutritional status of people with dementia. Br J Nurs 2001;10:1104–14.
[106] Soltesz KS, Dayton JH. Finger foods help those with Alzheimer's maintain weight. J Am Diet Assoc 1993;93:1106–8.
[107] Soltesz KS, Dayton JH. The effects of menu modification to increase dietary intake and maintain the weight of Alzheimer residents. Am J Alzheimers Dis Other Demen 1995;10:20–3.
[108] Boylston E, Ryan C, Brown C, Westfall B. Preventing precipitous weight loss in demented patients by altering food texture. J Nutr Elder 1996;15:43–8.
[109] Niedert KC. Position of the American Dietetic Association: liberalization of the diet prescription improves quality of life for older adults in long-term care. J Am Diet Assoc 2005;105:1955–65.
[110] Keller HH, Gibbs AJ, Boudreau LD, Goy RE, Pattillo MS, Brown HM. Prevention of weight loss in dementia with comprehensive nutritional treatment. J Am Geriatr Soc 2003;51:945–52.
[111] Lin LC, Watson R, Wu SC. What is associated with low food intake in older people with dementia? J Clin Nurs 2010;19:53–9.
[112] Wong A, Burford S, Wyles CL, Mundy H, Sainsbury R. Evaluation of strategies to improve nutrition in people with dementia in an assessment unit. J Nutr Health Aging 2008;12:309–12.
[113] Kayser-Jones J. Mealtime in nursing homes: the importance of individualized care. J Geront Nurs 1996;22:26–31.
[114] Kayser-Jones J, Schell E. The mealtime experience of a cognitively impaired elder: ineffective and effective strategies. J Gerontol Nurs 1997;23:33–9.
[115] Boffelli S, Rozzini R, Trabucchi M. Nutritional intervention in special care units for dementia. J Am Geriatr Soc 2004;52:1216–7.
[116] Manning AM, Means JG. A self-feeding program for geriatric patients in a skilled nursing facility. J Am Geriatr Soc 1975;75:275–6.
[117] Lange-Alberts ME, Shott S. Nutritional intake. Use of touch and verbal cuing. J Gerontol Nurs 1994;20:36–40.
[118] Van Ort S, Phillips LR. Nursing intervention to promote functional feeding. J Gerontol Nurs 1995;21:6–14.
[119] Simmons SF, Osterweil D, Schnelle JF. Improving food intake in nursing home residents with feeding assistance: a staffing analysis. J Gerontol A Biol Sci Med Sci 2001;56:M790–4.

[120] Simmons SF, Schnelle JF. Individualized feeding assistance care for nursing home residents: staffing requirements to implement two interventions. J Gerontol A Biol Sci Med Sci 2004;59:M966–73.
[121] Simmons SF, Keeler E, Zhuo X, Hickey KA, Sato HW, Schnelle JF. Prevention of unintentional weight loss in nursing home residents: a controlled trial of feeding assistance. J Am Geriatr Soc 2008;56:1466–73.
[122] Altus DE, Engelman KK, Mathews RM. Using family-style meals to increase participation and communication in persons with dementia. J Gerontol Nurs 2002;28:47–53.
[123] Amella EJ. Factors influencing the proportion of food consumed by nursing home residents with dementia. J Am Geriatr Soc 1999;47:879–85.
[124] Athlin E, N A. Interaction between patients with severe dementia and their caregivers during feeding in a task-assignment versus a patient-assignment care system. Eur Nurse 1998;3:215–27.
[125] Beattie ER, Algase DL, Song J. Keeping wandering nursing home residents at the table: improving food intake using a behavioral communication intervention. Aging Ment Health 2004;8:109–16.
[126] Coyne ML, Hoskins L. Improving eating behaviors in dementia using behavioral strategies. Clin Nurs Res 1997;6:275–90.
[127] Ruiz Garcia V, Lopez-Briz E, Carbonell Sanchis R, Gonzalvez Perales JL, Bort-Marti S. Megestrol acetate for treatment of anorexia-cachexia syndrome. Cochrane Database Syst Rev 2013;3. CD004310.
[128] Thomas DR. Guidelines for the use of orexigenic drugs in long-term care. Nutr Clin Pract 2006;21:82–7.
[129] Volicer L, Stelly M, Morris J, McLaughlin J, Volicer BJ. Effects of dronabinol on anorexia and disturbed behavior in patients with Alzheimer's disease. Int J Geriatr Psychiatry 1997;12:913–9.
[130] Krishnan S, Cairns R, Howard R. Cannabinoids for the treatment of dementia. Cochrane Database Syst Rev 2009. CD007204.
[131] Woodward MR, Harper DG, Stolyar A, Forester BP, Ellison JM. Dronabinol for the treatment of agitation and aggressive behavior in acutely hospitalized severely demented patients with noncognitive behavioral symptoms. Am J Geriatr Psychiatry 2014;22:415–9.
[132] Yeh SS, Wu SY, Lee TP, Olson JS, Stevens MR, Dixon T, et al. Improvement in quality-of-life measures and stimulation of weight gain after treatment with megestrol acetate oral suspension in geriatric cachexia: results of a double-blind, placebo-controlled study. J Am Geriatr Soc 2000;48:485–92.
[133] Simmons SF, Walker KA, Osterweil D. The effect of megestrol acetate on oral food and fluid intake in nursing home residents: a pilot study. J Am Med Dir Assoc 2005;6:S5–11.
[134] Domecq JP, Prutsky G, Leppin A, Sonbol MB, Altayar O, Undavalli C, et al. Clinical review: drugs commonly associated with weight change: a systematic review and meta-analysis. J Clin Endocrinol Metab 2015;100:363–70.
[135] Riviere S, Gillette-Guyonnet S, Voisin T, Reynish E, Andrieu S, Lauque S, et al. A nutritional education program could prevent weight loss and slow cognitive decline in Alzheimer's disease. J Nutr Health Aging 2001;5:295–9.
[136] Salva A, Andrieu S, Fernandez E, Schiffrin EJ, Moulin J, Decarli B, et al. Health and nutrition promotion program for patients with dementia (NutriAlz): cluster randomized trial. J Nutr Health Aging 2011;15:822–30.
[137] Suominen MH, Kivisto SM, Pitkala KH. The effects of nutrition education on professionals' practice and on the nutrition of aged residents in dementia wards. Eur J Clin Nutr 2007;61:1226–32.
[138] Mamhidir AG, Karlsson I, Norberg A, Mona K. Weight increase in patients with dementia, and alteration in meal routines and meal environment after integrity promoting care. J Clin Nurs 2007;16:987–96.
[139] Chang CC, Lin LC. Effects of a feeding skills training programme on nursing assistants and dementia patients. J Clin Nurs 2005;14:1185–92.
[140] Lin LC, Huang YJ, Su SG, Watson R, Tsai BW, Wu SC. Using spaced retrieval and Montessori-based activities in improving eating ability for residents with dementia. Int J Geriatr Psychiatry 2010;25:953–9.
[141] Lin LC, Huang YJ, Watson R, Wu SC, Lee YC. Using a Montessori method to increase eating ability for institutionalised residents with dementia: a crossover design. J Clin Nurs 2011;20:3092–101.
[142] Alibhai SM, Greenwood C, Payette H. An approach to the management of unintentional weight loss in elderly people. CMAJ 2005;172:773–80.
[143] Morley JE. Undernutrition in older adults. Fam Pract 2012;29(Suppl. 1):i89–93.
[144] Darmon P, Kaiser MJ, Bauer JM, Sieber CC, Pichard C. Restrictive diets in the elderly: never say never again? Clin Nutr 2010;29:170–4.
[145] Cederholm T, Palmblad J. Are omega-3 fatty acids options for prevention and treatment of cognitive decline and dementia? Curr Opin Clin Nutr Metab Care 2010;13:150–5.
[146] Cederholm T, Salem Jr N, Palmblad J. omega-3 fatty acids in the prevention of cognitive decline in humans. Adv Nutr 2013;4:672–6.
[147] Mazereeuw G, Lanctot KL, Chau SA, Swardfager W, Herrmann N. Effects of omega-3 fatty acids on cognitive performance: a meta-analysis. Neurobiol Aging 2012;33. 1482 e17-29.
[148] Lee LK, Shahar S, Chin AV, Yusoff NA. Docosahexaenoic acid-concentrated fish oil supplementation in subjects with mild cognitive impairment (MCI): a 12-month randomised, double-blind, placebo-controlled trial. Psychopharmacol Berl 2013;225:605–12.
[149] Rodriguez-Martin JL, Qizilbash N, Lopez-Arrieta JM. Thiamine for Alzheimer's disease. Cochrane Database Syst Rev 2001. Cd001498.
[150] Oulhaj A, Refsum H, Beaumont H, Williams J, King E, Jacoby R, et al. Homocysteine as a predictor of cognitive decline in Alzheimer's disease. Int J Geriatr Psychiatry 2010;25:82–90.
[151] Malouf R, Grimley Evans J. The effect of vitamin B6 on cognition. Cochrane Database Syst Rev 2003. CD004393.
[152] Malouf R, Areosa Sastre A. Vitamin B12 for cognition. Cochrane Database Syst Rev 2003. Update: 2009: CD004326.
[153] Malouf R, Grimley Evans J. Folic acid with or without vitamin B12 for the prevention and treatment of healthy elderly and demented people. Cochrane Database Syst Rev 2008. CD004514.
[154] Aisen PS, Schneider LS, Sano M, Diaz-Arrastia R, van Dyck CH, Weiner MF, et al. High-dose B vitamin supplementation and cognitive decline in Alzheimer disease: a randomized controlled trial. JAMA 2008;300:1774–83.
[155] Sun Y, Lu CJ, Chien KL, Chen ST, Chen RC. Efficacy of multivitamin supplementation containing vitamins B6 and B12 and folic acid as adjunctive treatment with a cholinesterase inhibitor in Alzheimer's disease: a 26-week, randomized, double-blind, placebo-controlled study in Taiwanese patients. Clin Ther 2007;29:2204–14.
[156] Vogel T, Dali-Youcef N, Kaltenbach G, Andres E. Homocysteine, vitamin B12, folate and cognitive functions: a systematic and critical review of the literature. Int J Clin Pract 2009;63:1061–7.
[157] Farina N, Isaac MG, Clark AR, Rusted J, Tabet N. Vitamin E for Alzheimer's dementia and mild cognitive impairment. Cochrane Database Syst Rev 2012;11. CD002854.
[158] Dysken MW, Sano M, Asthana S, Vertrees JE, Pallaki M, Llorente M, et al. Effect of vitamin E and memantine on functional decline in Alzheimer disease: the TEAM-AD VA cooperative randomized trial. JAMA 2014;311:33–44.
[159] Loef M, Schrauzer GN, Walach H. Selenium and Alzheimer's disease: a systematic review. J Alzheimers Dis 2011;26:81–104.
[160] Kessler H, Bayer TA, Bach D, Schneider-Axmann T, Supprian T, Herrmann W, et al. Intake of copper has no effect on cognition in patients with mild Alzheimer's disease: a pilot phase 2 clinical trial. J Neural Transm 2008;115:1181–7.
[161] Schlogl M, Holick MF. Vitamin D and neurocognitive function. Clin Interv Aging 2014;9:559–68.
[162] Anastasiou CA, Yannakoulia M, Scarmeas N. Vitamin D and cognition: an update of the current evidence. J Alzheimers Dis 2014;42(Suppl. 3):S71–80.
[163] Annweiler C, Dursun E, Feron F, Gezen-Ak D, Kalueff AV, Littlejohns T, et al. 'Vitamin D and cognition in older adults': updated international recommendations. J Intern Med 2015;277:45–57.
[164] Lochs H, Allison SP, Meier R, Pirlich M, Kondrup J, Schneider S, et al. Introductory to the ESPEN guidelines on enteral nutrition: terminology, definitions and general topics. Clin Nutr 2006;25:180–6.
[165] Carver AD, Dobson AM. Effects of dietary supplementation of elderly demented hospital residents. J Hum Nutr Diet 1995;8:389–94.
[166] de Sousa OL, Amaral TF. Three-week nutritional supplementation effect on long-term nutritional status of patients with mild Alzheimer disease. Alzheimer Dis Assoc Disord 2012;26:119–23.
[167] Gil Gregorio P, Ramirez Diaz SP, Ribera Casado JM. Dementia and Nutrition. Intervention study in institutionalized patients with Alzheimer disease. J Nutr Health Aging 2003;7:304–8.
[168] Lauque S, Arnaud-Battandier F, Gillette S, Plaze JM, Andrieu S, Cantet C, et al. Improvement of weight and fat-free mass with oral nutritional supplementation in patients with Alzheimer's disease at risk of malnutrition: a prospective randomized study. J Am Geriatr Soc 2004;52:1702–7.
[169] Navrátilová M, Jarkovsky J, Ceßková E, Leonard B, Sobotka L. Alzheimer disease: malnutrition and nutritional support. Clin Exp Pharmacol Physiol 2007;34:11–3.
[170] Parrott MD, Young KW, Greenwood CE. Energy-containing nutritional supplements can affect usual energy intake postsupplementation in institutionalized seniors with probable Alzheimer's disease. J Am Geriatr Soc 2006;54:1382–7.
[171] Pivi GA, da Silva RV, Juliano Y, Novo NF, Okamoto IH, Brant CQ, et al. A prospective study of nutrition education and oral nutritional supplementation in patients with Alzheimer's disease. Nutr J 2011;10:98.
[172] Wouters-Wesseling W, Slump E, Kleijer CN, de Groot LC, van Staveren WA. Early nutritional supplementation immediately after diagnosis of infectious disease improves body weight in psychogeriatric nursing home residents. Aging Clin Exp Res 2006;18:70–4.
[173] Wouters-Wesseling W, Rozendaal M, Snijder M, Graus Y, Rimmelzwaan G, de Groot L, et al. Effect of a complete nutritional supplement on antibody response to influenza vaccine in elderly people. J Gerontol A Biol Sci Med Sci 2002;57:563–6.
[174] Young KW, Greenwood CE, van Reekum R, Binns MA. Providing nutrition supplements to institutionalized seniors with probable Alzheimer's disease is least beneficial to those with low body weight status. J Am Geriatr Soc 2004;52:1305–12.
[175] Faxen-Irving G, Andren-Olsson B, af Geijerstam A, Basun H, Cederholm T. The effect of nutritional intervention in elderly subjects residing in group-living for the demented. Eur J Clin Nutr 2002;56:221–7.
[176] Allen VJ, Methven L, Gosney MA. Use of nutritional complete supplements in older adults with dementia: systematic review and meta-analysis of clinical outcomes. Clin Nutr 2013;32:950–7.

[177] Alzheimer's Disease International (ADI). Nutrition and dementia. A review of available research, 2014 (accessed 14.10.15 at: http://www.alz.co.uk/sites/default/files/pdfs/nutrition-and-dementia.pdf).
[178] Hanson LC, Ersek M, Gilliam R, Carey TS. Oral feeding options for people with dementia: a systematic review. J Am Geriatr Soc 2011;59:463–72.
[179] Hines S, Wilson J, McCrow J, Abbey J, Sacre S. Oral liquid nutritional supplements for people with dementia in residential aged care facilities. Int J Evid Based Healthc 2010;8:248–51.
[180] van Wijk N, Broersen LM, de Wilde MC, Hageman RJ, Groenendijk M, Sijben JW, et al. Targeting synaptic dysfunction in Alzheimer's disease by administering a specific nutrient combination. J Alzheimers Dis 2014;38:459–79.
[181] Scheltens P, Kamphuis PJ, Verhey FR, Olde Rikkert MG, Wurtman RJ, Wilkinson D, et al. Efficacy of a medical food in mild Alzheimer's disease: a randomized, controlled trial. Alzheimers Dement 2010;6. 1-10 e1.
[182] Scheltens P, Twisk JW, Blesa R, Scarpini E, von Arnim CA, Bongers A, et al. Efficacy of Souvenaid in mild Alzheimer's disease: results from a randomized, controlled trial. J Alzheimers Dis 2012;31:225–36.
[183] Shah RC, Kamphuis PJ, Leurgans S, Swinkels SH, Sadowsky CH, Bongers A, et al. The S-Connect study: results from a randomized, controlled trial of Souvenaid in mild-to-moderate Alzheimer's disease. Alzheimers Res Ther 2013;5:59.
[184] Kamphuis PJ, Verhey FR, Olde Rikkert MG, Twisk JW, Swinkels SH, Scheltens P. Effect of a medical food on body mass index and activities of daily living in patients with Alzheimer's disease: secondary analyses from a randomized, controlled trial. J Nutr Health Aging 2011;15:672–6.
[185] Olde Rikkert MG, Verhey FR, Blesa R, von Arnim CA, Bongers A, Harrison J, et al. Tolerability and safety of Souvenaid in patients with mild Alzheimer's disease: results of multi-center, 24-week, open-label extension study. J Alzheimers Dis 2015;44:471–80.
[186] Mi W, van Wijk N, Cansev M, Sijben JW, Kamphuis PJ. Nutritional approaches in the risk reduction and management of Alzheimer's disease. Nutrition 2013;29:1080–9.
[187] Planas M, Conde M, Audivert S, Perez-Portabella C, Burgos R, Chacon P, et al. Micronutrient supplementation in mild Alzheimer disease patients. Clin Nutr 2004;23:265–72.
[188] Salas-Salvado J, Torres M, Planas M, Altimir S, Pagan C, Gonzalez ME, et al. Effect of oral administration of a whole formula diet on nutritional and cognitive status in patients with Alzheimer's disease. Clin Nutr 2005;24:390–7.
[189] Chan A, Paskavitz J, Remington R, Rasmussen S, Shea TB. Efficacy of a vitamin/nutriceutical formulation for early-stage Alzheimer's disease: a 1-year, open-label pilot study with an 16-month caregiver extension. Am J Alzheimers Dis Other Demen 2008;23:571–85.
[190] Remington R, Chan A, Paskavitz J, Shea TB. Efficacy of a vitamin/nutriceutical formulation for moderate-stage to later-stage Alzheimer's disease: a placebo-controlled pilot study. Am J Alzheimers Dis Other Demen 2009;24:27–33.
[191] Remington R, Bechtel C, Larsen D, Samar A, Doshanjh L, Fishman P, et al. A phase II randomized clinical trial of a nutritional formulation for cognition and mood in Alzheimer's disease. J Alzheimers Dis 2015;45:395–405.
[192] Henderson ST. Ketone bodies as a therapeutic for Alzheimer's disease. Neurotherapeutics 2008;5:470–80.
[193] Henderson ST, Vogel JL, Barr LJ, Garvin F, Jones JJ, Costantini LC. Study of the ketogenic agent AC-1202 in mild to moderate Alzheimer's disease: a randomized, double-blind, placebo-controlled, multicenter trial. Nutr Metab (Lond) 2009;6:31.
[194] Henderson ST, Poirier J. Pharmacogenetic analysis of the effects of polymorphisms in APOE, IDE and IL1B on a ketone body based therapeutic on cognition in mild to moderate Alzheimer's disease; a randomized, double-blind, placebo-controlled study. BMC Med Genet 2011;12:137.
[195] Mecocci P, Tinarelli C, Schulz RJ, Polidori MC. Nutraceuticals in cognitive impairment and Alzheimer's disease. Front Pharmacol 2014;5:147.
[196] Brondino N, Re S, Boldrini A, Cuccomarino A, Lanati N, Barale F, et al. Curcumin as a therapeutic agent in dementia: a mini systematic review of human studies. ScientificWorldJournal 2014;2014:174282.
[197] Sauer J, Tabet N, Howard R. Alpha lipoic acid for dementia. Cochrane Database Syst Rev 2004. CD004244.
[198] Adair JC, Knoefel JE, Morgan N. Controlled trial of N-acetylcysteine for patients with probable Alzheimer's disease. Neurology 2001;57:1515–7.
[199] More MI, Freitas U, Rutenberg D. Positive effects of soy lecithin-derived phosphatidylserine plus phosphatidic acid on memory, cognition, daily functioning, and mood in elderly patients with Alzheimer's disease and dementia. Adv Ther 2014;31:1247–62.
[200] Kato-Kataoka A, Sakai M, Ebina R, Nonaka C, Asano T, Miyamori T. Soybean-derived phosphatidylserine improves memory function of the elderly Japanese subjects with memory complaints. J Clin Biochem Nutr 2010;47:246–55.
[201] Hudson S, Tabet N. Acetyl-L-carnitine for dementia. Cochrane Database Syst Rev 2003. CD003158.
[202] Marckmann G, Sandberger G, Wiesing U. Limiting life-prolonging treatments: a practical guidance reflecting the current legislation in Germany. Dtsch Med Wochenschr 2010;135:570–4.
[203] Beauchamp TL, Childress JF. Principles of biomedical ethics. 5th ed. New York: Oxford University Press, Inc.; 2001.
[204] American Academy of Hospice and Palliative Medicine (AAHPM). Statement on artifical nutrition and hydration near the end of life, 2013. (accessed 14.10.15 at: http://aahpm.org/positions/anh).
[205] Ganzini L. Artificial nutrition and hydration at the end of life: ethics and evidence. Palliat Support Care 2006;4:135–43.
[206] Sampson EL, Candy B, Jones L. Enteral tube feeding for older people with advanced dementia. Cochrane Database Syst Rev 2009:1–25.
[207] Murphy LM, Lipman TO. Percutaneous endoscopic gastrostomy does not prolong survival in patients with dementia. Arch Intern Med 2003;163:1351–3.
[208] Callahan CM, Haag KM, Weinberger M, Tierney WM, Buchanan NN, Stump TE, et al. Outcomes of percutaneous endoscopic gastrostomy among older adults in a community setting. J Am Geriatr Soc 2000;48:1048–54.
[209] Sanders DS, Carter MJ, D'Silva J, James G, Bolton RP, Bardhan KD. Survival analysis in percutaneous endoscopic gastrostomy feeding: a worse outcome in patients with dementia. Am J Gastroenterol 2000;95:1472–5.
[210] Abuksis G, Mor M, Segal N, Shemesh I, Plout S, Sulkes J, et al. Percutaneous endoscopic gastrostomy: high mortality rates in hospitalized patients. Am J Gastroenterol 2000;95:128–32.
[211] Mitchell SL, Kiely DK, Lipsitz LA. The risk factors and impact on survival of feeding tube placement in nursing home residents with severe cognitive impairment. Arch Intern Med 1997;157:327–32.
[212] Meier DE, Ahronheim JC, Morris J, Baskin-Lyons S, Morrison RS. High short-term mortality in hospitalized patients with advanced dementia: lack of benefit of tube feeding. Arch Intern Med 2001;161:594–9.
[213] Nair S, Hertan H, Pitchumoni CG. Hypoalbuminemia is a poor predictor of survival after percutaneous endoscopic gastrostomy in elderly patients with dementia. Am J Gastroenterol 2000;95:133–6.
[214] Alvarez-Fernandez B, Garcia-Ordonez MA, Martinez-Manzanares C, Gomez-Huelgas R. Survival of a cohort of elderly patients with advanced dementia: nasogastric tube feeding as a risk factor for mortality. Int J Geriatr Psychiatry 2005;20:363–70.
[215] Jaul E, Singer P, Calderon-Margalit R. Tube feeding in the demented elderly with severe disabilities. Isr Med Assoc J 2006;8:870–4.
[216] Peck A, Cohen CE, Mulvihill MN. Long-term enteral feeding of aged demented nursing home patients. J Am Geriatr Soc 1990;38:1195–8.
[217] Teno JM, Gozalo PL, Mitchell SL, Kuo S, Rhodes RL, Bynum JP, et al. Does feeding tube insertion and its timing improve survival? J Am Geriatr Soc 2012;60:1918–21.
[218] Dasgupta M, Binns MA, Rochon PA. Subcutaneous fluid infusion in a long-term care setting. J Am Geriatr Soc 2000;48:795–9.
[219] Frisoli Junior A, de Paula AP, Feldman D, Nasri F. Subcutaneous hydration by hypodermoclysis. A practical and low cost treatment for elderly patients. Drugs Aging 2000;16:313–9.
[220] Turner T, Cassano AM. Subcutaneous dextrose for rehydration of elderly patients–an evidence-based review. BMC Geriatr 2004;4:2.
[221] Faes M, Spigt M, Olde Rikkert MGM. Dehydration in geriatrics. Geriatr Aging 2007;10:590–6.
[222] Sasson M, Shvartzman P. Hypodermoclysis: an alternative infusion technique. Am Fam Physician 2001;64:1575–8.
[223] Slesak G, Schnurle JW, Kinzel E, Jakob J, Dietz PK. Comparison of subcutaneous and intravenous rehydration in geriatric patients: a randomized trial. J Am Geriatr Soc 2003;51:155–60.
[224] Bruera E, Hui D, Dalal S, Torres-Vigil I, Trumble J, Roosth J, et al. Parenteral hydration in patients with advanced cancer: a multicenter, double-blind, placebo-controlled randomized trial. J Clin Oncol 2013;31:111–8.
[225] Finucane TE, Christmas C, Travis K. Tube feeding in patients with advanced dementia. J Am Geriatr Soc 1999;282:1365–70.
[226] Pasman HR, Onwuteaka-Philipsen BD, Kriegsman D, Ooms ME, Ribbe MW, van der Wal G. Discomfort in nursing home patients with severe dementia in whom artificial nutrition and hydration is forgone. Arch Intern Med 2005;165:1729–35.
[227] McCann RM, Hall WJ, Groth-Juncker A. Comfort care for terminally ill patients: the appropriate use of nutrition and hydration. J Am Geriatr Soc 1994;272:1263–6.
[228] Musgrave CF, Bartal N, Opstad J. The sensation of thirst in dying patients receiving i.v. hydration. J Palliat Care 1995;11:17–21.
[229] Casarett D, Kapo J, Caplan A. Appropriate use of artificial nutrition and hydration–fundamental principles and recommendations. N Engl J Med 2005;353:2607–12.
[230] Mitchell SL. A 93-year-old man with advanced dementia and eating problems. JAMA 2007;298:2527–36.
[231] Palecek EJ, Teno JM, Casarett DJ, Hanson LC, Rhodes RL, Mitchell SL. Comfort feeding only: a proposal to bring clarity to decision-making regarding difficulty with eating for persons with advanced dementia. J Am Geriatr Soc 2010;58:580–4.
[232] Geppert CM, Andrews MR, Druyan ME. Ethical issues in artificial nutrition and hydration: a review. JPEN J Parenter Enteral Nutr 2010;34:79–88.