



ELSEVIER

Contents lists available at ScienceDirect

Geriatric Nursing

journal homepage: www.gnjournal.com

Effects of oral nutrition supplements in persons with dementia: A systematic review

Randi J. Tangvik, RD, PhD^{a,*}, Frøydis K. Bruvik, RN, PhD^{b,1}, Jorunn Drageset, RN Prof^{b,c}, Kristin Kyte, RN, MSc^d, Irene Hunskår, MSc^d

^a Mohn Nutrition Research Laboratory, Centre for Nutrition, Department of Clinical Medicine, University of Bergen, Postboks 7804, 5020 Bergen

^b Faculty of Health and Social Sciences, Western Norway University of Applied Sciences, Inndalsveien, 28, 5063 Bergen, Norway

^c Department of Global Health and Primary Care, University of Bergen, Bergen, Norway

^d Faculty of Health Studies, VID Specialized University Norway



ARTICLE INFO

Article history:

Received 5 August 2020

Received in revised form 30 November 2020

Accepted 2 December 2020

Available online xxx

Keywords:

Nutrition supplement

Nutrition intervention

Dementia

ABSTRACT

Objective: Persons with dementia are at risk of malnutrition, evidenced by low dietary intake, which has consequences for nutritional status, activity of daily living and disease progression. The effects of oral nutrition supplements (ONS) on nutritional intake, nutritional status, and cognitive and physical outcomes in older persons with dementia were evaluated.

Methods: PubMed, Medline, Embase, CINAHL and the Cochrane Central Register of Controlled Trials were searched in December 2017, and this was repeated in May 2019. The Preferred Reporting Items for Systematic Reviews and Analysis (PRISMA) checklist was used. Papers were considered if they presented experimental clinical trials using oral nutritional supplements to persons diagnosed with dementia, including Alzheimer's disease and mild cognitive impairment, and conducted in hospitals, nursing homes or homes.

Results: We included ten articles reporting nine clinical trials. A total of 407 persons with dementia were included, of whom 228 used ONS for 7 to 180 days. Nutritional intake improved by 201 to 600 kcal/day. Energy intake from ordinary foods was not affected, thus ONS improved the persons daily intake of energy and protein. Body weight, muscle mass, and nutritional biomarkers in blood improved in the intervention groups compared with the control groups. No effects on cognition or physical outcomes were observed.

Conclusion: ONS increases the intake of energy and protein and improves nutritional status in persons with dementia; however, RCTs with longer intervention periods are needed to investigate the impact on cognitive and functional outcomes.

© 2020 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)

Introduction

Dementia is a chronic condition characterised as a decline in cognitive functioning that leads to dependence in the performance of daily activities, including nutritional sufficiency.¹ More than 46 million people in the world have dementia, and the number is projected to increase to 152 million by 2050.² The incidence of dementia increases progressively with age.³

Abbreviations: ONS, Oral nutrition supplements; DXA, dual X-ray absorptiometry; TSF, triceps skinfold; MUAMC, mid-upper-arm muscle circumference; MUAC, mid-upper-arm circumference; BW, body weight; RDA, recommended daily allowance; RCT, randomized controlled trial; CT, control trial; MNA, mini nutritional assessment; NuSc, nutrition score index; ADL, Activity of daily living; MMSE, Mini Mental Status Examination

Sources of Support: This research received no external funding.

*Corresponding author.

E-mail address: randi.tangvik@uib.no (R.J. Tangvik).

¹ Equal contributors.

People with dementia often experience several problems related to nutrition. In the early stages, issues with memory and thoughts may affect planning, shopping, and preparation of food. As the disease progresses, eating and drinking may become more difficult. Dysphagia has been reported in 13 to 57% of persons with dementia.⁴ Sensory failure, loss of appetite, and eating skills are other common symptoms.^{4,5} Difficulties in communicating discomfort due to, e.g., hunger, pain, tiredness, medication, and constipation can also negatively affect the intake of food and fluid.^{4,5} Confusion about where they are and who they are with may cause agitation and increased energy needs.^{4,5} Consequently, people with dementia lose weight and increase the risk of malnutrition as the condition progresses.⁴

Malnutrition is a state resulting from a lack of intake or uptake of nutrition that leads to altered body composition and body cell mass and, subsequently, diminished physical and mental function and impaired clinical outcomes.⁶ The presence of malnutrition may accelerate the progression of dementia, as a lack of energy and micronutrients,

<https://doi.org/10.1016/j.gerinurse.2020.12.005>

0197-4572/\$ – see front matter © 2020 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)

such as vitamin B12, folic acid, thiamine, and others, contributes to impaired cognition and aggravation of existing impairments.⁷ Muscle waste leads to functional decline and frailty, which are in turn associated with a loss of independence, increased risk of morbidity and mortality.^{4,8,9}

Oral nutrition supplements (ONS), classified as food for special medical purposes to manage disease-related malnutrition, is one out of several ways to aid the person in reaching their nutritional goals. The goal of ONS is to enrich the person's dietary intake without suppressing it or replacing feeding assistants or meal provisions. ONS have been shown to improve nutritional intake and nutritional status in persons with insufficient dietary intake and reduce complications such as pressure sores, infection, venous thrombosis, pulmonary embolism and confusion;^{10,11} however, studies regarding the effect of ONS on persons with dementia are lacking.

Aim

The overall aim was to investigate the effects of ONS on nutritional intake and clinical outcomes in older persons with dementia. A systematic review was conducted, and the following research questions (RQs) were addressed: What effects do ONS have on total dietary intake and consumption of voluntary food intake (RQ1)? What effects do ONS have on nutritional status (RQ2)? What effects do ONS have on cognitive or functional outcomes (RQ3)?

Methods

The study protocol for this review was registered on PROSPERO, registration number CRD42019082493. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement were used to identify, screen, evaluate, and include papers for this review.^{12,13} Inclusion and exclusion criteria are presented in Table 1, and Fig. 1 shows the inclusion process.

The identification process included search strategies inspired by the article of Droogsmá¹⁴ and developed after preliminary searches discussed by the authors. See Appendix 1 for the entire search strategy. The literature searches were conducted in PubMed, Medline, Embase, CINAHL and the Cochrane Central Register of Controlled Trials in December 2017 and May 2019. The MeSH terms "Alzheimer's Disease" or "Dementia" were combined with ("Malnutrition" or "Body Weight" or "Weight Loss" or "Thinness" or "Body Weight Changes") and ("Diet Therapy" or "Dietary Supplements" or "Nutritional Support" or "Food, fortified" or "Eating"). No year or language limitation was placed on the search, and only publications such as conference abstracts, editorials, and letters were excluded during the identification process. The search results were collected in Endnote, and duplicates were removed using both automatic and manual procedures.

Table 1
Inclusion and exclusion criteria

Criteria	Inclusion criteria	Exclusion criteria
Population	Persons with dementia, Alzheimer's disease or impaired cognitive function, 18 years or older	Animal study Low income countries Patients with end-stage diseases such as cancer, chronic obstructive pulmonary disease (COPD), and other
Intervention	ONS	ONS without micronutrients, ONS with only one macronutrient, or not using ONS
Comparators	Placebo or treatment as usual	
Outcome	Objective and measurable effect on dietary intake, nutrition status, cognitive and/or functional outcomes	
Timing	Any duration of the intervention	
Setting	Hospitalised, living in nursing homes or home dwelling	
Study design	Experimental clinical trials, including RCTs and cross-over study designs	Qualitative study design or case report
Other	English or Scandinavian language	Abstract only or conference proceedings

ONS, oral nutrition supplements

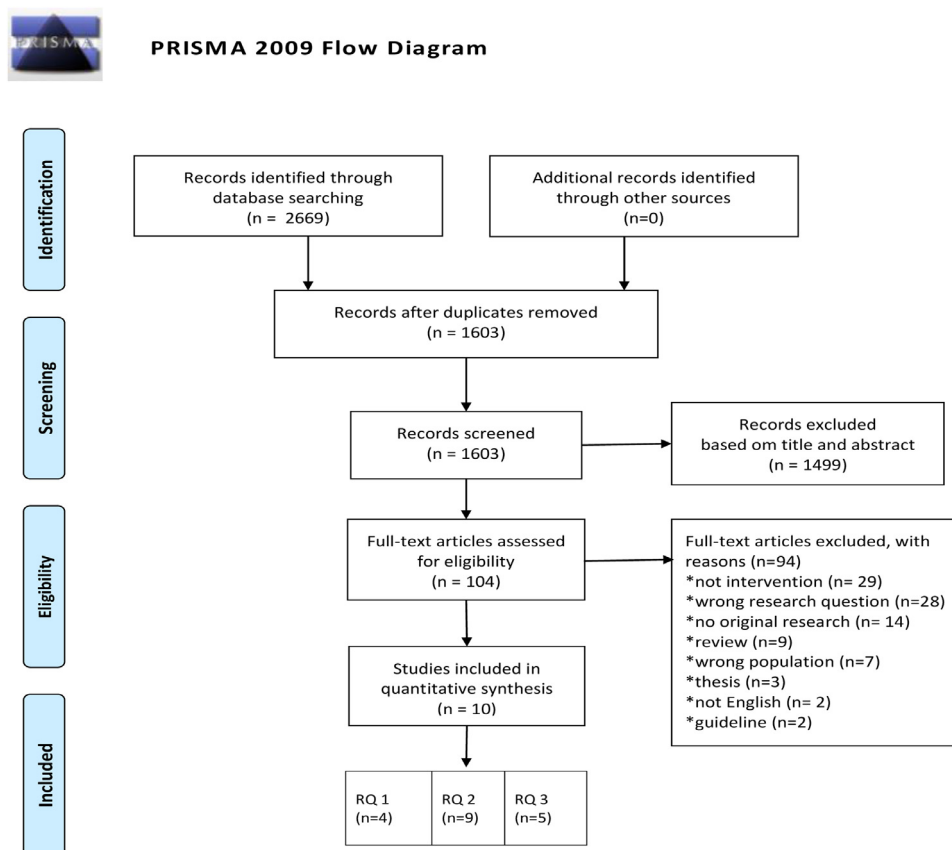
During the screening step, conducted by Rayyan,¹⁵ title and abstracts were read for relevance, and inappropriate articles were excluded due to the criteria (Table 1). Two pairs of reviewers (RT and FB; JD and KK) performed the screening, which was completed independently (blinded). Disagreements within the pairs of reviewers were resolved through discussion, and a third reviewer was available when needed. The articles' eligibility was assessed by the same pairs of reviewers who read them in full text (Table 1).

Quality assessment was performed by using the Critical Appraisal Skills Program (CASP) checklists for randomised control trials (RCT), cross-over trials and case-control studies.¹⁶ These checklists include quality assessment components regarding aims, participants, clinical outcomes and methodological issues, and relevance of results. For each article, two reviewers independently assessed quality by answering 10 subcategories with "yes," "can't tell," or "no." Any discrepancies in component ratings were resolved through discussion between reviewers and then the expert opinion of the group, if required. The quality rating for the studies in this review was overall high, and no articles were excluded after quality assessment.

Data extraction

Information extracted from the articles encompassed study design, setting, population size, participants' demographic data, and details of the intervention as presented in Table 2. Table 3 presents the mean daily consumption of energy and protein from the ONS intervention and changes in the mean outcome's variables. The effects of ONS on nutritional intake was reported by mean intake of energy and protein at baseline compared with intake at the end of intervention. Intake of energy and protein at the end of the follow-up period were investigated in cases where this was reported. The effects of ONS on nutritional status was described by changes in the results of the mini nutritional assessment (MNA), nutrition score index (NuSc), body weight, body mass index (BMI), muscle mass (MUAMC), body fat (TSF) and nutritional biomarkers in blood. The MNA is specifically developed to be used in frail older adults. Based on the scores, persons are classified as malnourished (<17 points), at risk of malnutrition (17 to 23.5 points), or well-nourished (34 to 30 points).¹⁷ The NuSc is calculated by giving one score to each variable (body mass index (BMI), triceps skinfold (TSF), arm muscle circumference (AMC), albumin, transferrin, and IGF-I) below the reference range. A NuSc of 0 indicates a well-nourished state, while a NuSc of 1 or 2 indicates a risk of malnutrition and a NuSc ≥ 3 denotes malnutrition.¹⁸ Muscle mass (mid-upper-arm muscle circumference (MUAMC)) is calculated by mid-upper-arm circumference (MUAC) and TSF: $MUAMC = MUAC \text{ (cm)} - 0.3142 \times TSF \text{ (mm)}$.

Several screening tools were used to report the effects of ONS on cognitive or functional outcomes. The Mini-Mental State Examination (MMSE) tool assesses orientation, memory, and other cognitive skills



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org

Fig. 1. Flow-chart of study identification and inclusion.

to classify the severity of cognitive deficit and evaluate the progression of the disease.¹⁹ MMSE scores range from 0 to 30. A score of <20 points is usually considered to be indicative of clinically significant cognitive impairment.¹⁸ Functional status and the level of independence was reported by the Barthel index (BI). The scores indicated independence (100 points), slight dependence (≥ 65 points) and moderate (45 to 60 points), severe (20 to 45 points) and total dependence (<20 points).

Data management

The nutritional value of the ONS intervention presented in Table 3 is based on information from the nutritional prescription and compliance listed in Table 2. The study's results from ONS intervention are presented in Table 3. Changes in outcome measurements were the difference between baseline values and the values at the end of the intervention in both the intervention group and the control group. Thus, the effect of ONS are expressed both within and between the groups.

Results

Out of 2669 eligible articles, 104 articles were read in full (Fig. 1). Finally, ten publications were included in the review reporting on nine experimental clinical studies: six RCTs and three non-RCTs.^{18–27}

One study reported peri- and post-intervention effects in two separate articles.^{19,27}

Description of the included studies

The study participants were either living at home,^{19,23,24,27} in nursing homes,^{18,20,26} or in geriatric hospitals.^{19–22,25,27} The reported outcomes were dietary intake,^{19,20,24,27} nutritional status^{18,21–27} and cognitive or functional status.^{18,22–24,26,27} The publication years ranged from 1995 until 2017, with seven European, two Canadian and one Brazilian article(s). All included studies were approved by the Committee of The Ethics of Medical Research, and all except one reported that all subjects and/or their representatives had signed an informed consent form.

Table 2 summarizes the characteristics of the included articles. A total of 407 persons, 60 years or older and 75% female, participated in the nine clinical trials: 171 in the intervention groups, 179 in the control groups, and 57 who were their own control in the two cross-over studies. Nutritional status was reported according to MNA,^{22–24} low BMI,^{21,26} NuSc¹⁸ or not reported.^{19,20,25,27} ONS provided 250 to 850 kcal and 9 to 42 g of protein per day for 7 to 180 days. Compliance with the prescription was 98 to 100% in five RCTs,^{21–24,26} 70 to 89% in four non-RCTs^{18–20,27} and unreported in one study.²⁵ In addition to reporting the effects of ONS post supplementation, the effects of ONS after a one-week follow-up¹⁹ and three-month follow-up²⁴

Table 2
Characteristics of the included studies.

Author Year	Design	Setting	Intervention N (% female)	Control N (% female)	Age, mean years \pm SD	Nutrition status at baseline	Intervention with ONS		
							Prescription energy/protein	Duration no. days	Compliance %
Allen 2013	Cross-over trial	Geriatric hospital Nursing home	26 (69%)	23 (78% female in total population)	84 \pm 8	n.r.	850 kcal/42 g	7	70
Carver 1995	Randomised control trial	Geriatric hospital	23 (78% female in total population)	23 (78% female in total population)	M: 69 \pm 9 F: 80 \pm 10	Low BMI < 20 kg/m ² : 100%	600 kcal/20 g	90	100
Faxen-Irving 2002 Lauque 2004	Control trial Randomised control trial	Nursing home Home	21 (81%) 37 (n.r.)	12 (100%) 43 (n.r.)	84 \pm 4 I: 80 \pm 6 C: 78 \pm 5	At nutritional risk (NuSc): 69% At nutritional risk (MNA): 100%	410 kcal/18 g 3–500 kcal/n.r.	150 90	89 100
Pivi 2011 de Sousa 2012	Randomised control trial Randomised control trial	Geriatric hospital Geriatric hospital	26 (62%) 20 (75%)	27 (74%) 15 (64%)	75 \pm n.r. I: 79 \pm 7 C: 78 \pm 5	n.r. At nutritional risk (MNA): 100%	680 kcal/26 g 400 kcal/18 g	180 21	n.r. 100
de Sousa 2017	Randomised control trial	Home	25 (60%)	43 (65%)	I: 78 \pm 7 C: 78 \pm 6	At nutritional risk (MNA): 100%	300 kcal/12 g	21	100
Wouters-Wesseling 2002	Randomised, double-blinded placebo-controlled trial	Nursing home	19 (89%)	16 (88%)	I: 85 \pm 8 C: 79 \pm 9	Low BMI < 25 kg/m ² (W) and BMI < 23 kg/m ² (M): 100%	273 kcal/9 g	90	98
Young 2004 Parrott 2006	Cross-over trial	Geriatric hospital/Home	31 (83%) 30 (87%)	31 (83%) 30 (87%)	88 \pm 4 88 \pm 4	Stable weight	255 kcal/11 g 250–8 kcal/n.r.	21	79

Abbreviations: N=number, SD=standard deviation, M=male, F=female, I= intervention group, C=control group, MNA=mini nutritional assessment, NuSc=nutritional score index, n.r.=not reported

were reported. Four studies used multiple interventions that included staff education^{18,24,25} or psycho-motor rehabilitation.²³

Effects of ONS on dietary intake

Three studies revealed an improved intake of energy and protein due to the intervention with ONS.^{20,24,27} In the study by Allen and co-workers,²⁰ the energy intake was 1238 (\pm 512) kcal/d on control days and 1755 (\pm 644) kcal/d on intervention days. The intake of protein was 47.5 (\pm 20.4) g/d and 73.4 (\pm 29.5) g/d on control days and intervention days, respectively. Thus, during consumption of ONS, 56% of the persons met the recommended daily allowance for energy, with 74% acquiring the necessary protein, compared to 17% and 34% during the control period.²⁰ Lauque reported energy intake to be 1476 (\pm 380) kcal/d at baseline and 291 (\pm 481) kcal more per day at the end of the intervention. Three months post intervention, daily energy intake was close to the baseline at 1547 (\pm 42.5) kcal/d. The participants' intake of energy was 28 kcal/kg body weight (BW) at baseline and 33 kcal/kg BW during the intervention.²⁴ Two studies^{19,24} reported a minor improvement in dietary intake of 22.7 (\pm 108.7) kcal/d for seven days post supplementation and 87 (\pm 419) kcal/d for three months post supplementation. In two cross-over studies, the intake of ordinary food was slightly reduced during the intervention period compared to the control period.^{20,27} Participants with the lowest BMIs were more likely to reduce their food intake when using ONS.²⁷

Effects of ONS on nutritional status

Eight studies found significant improvements in nutritional status due to ONS. Individual nutrition risk status improved,^{22,23} although the prevalence of malnutrition risk was not affected.^{18,23} Even the categorisation of malnutrition was not affected, and the MNA-scores improved in the intervention group compared with the control group: 1.4 (\pm 0.8) score vs. 0 (\pm 0.1) score,²² and 0.4 (\pm 0.8) vs. -0.1 (\pm 1.1) score, both respectively.²³

Mean body weight (BW) improved, with a range of 0.3 to 6.7 kg from baseline to end of the intervention, compared with a range of -2.2 to 0.97 kg in the control groups.^{18,21,22,24–27} In other words, the prescription of 680 kcal/d for 180 days resulted in a mean weight gain of 6.7 kg in the intervention group compared with -2.2 kg in the control group.²⁵

Muscle mass improved in three out of six studies investigating this.^{18,21–25} The MUAMC changed by 0.2 (\pm 0.4) cm from baseline to post intervention in the intervention group and -0.2 cm (\pm 0.8) in the control group after 3 weeks with ONS.²² After ONS for six months, muscle mass improved by 3.43 cm in the intervention group compared to -0.19 cm in the control group. Otherwise, no muscle gain was reported; however, Faxen-Irving reported that female controls lost more muscle mass than females on ONS.¹⁸ Also, body fat (TSF) improved by 2.5 mm among female participants in the intervention group and declined by 0.6 mm among the female controls.¹⁸ After ONS for three weeks, TSF changed by 0.4 (\pm 0.5) mm in the intervention group and 0.0 (\pm 0.1) mm in the control group, de Sousa reported.²² The remaining studies reported no changes in body fat.^{21,23,25}

Nutritional biomarkers were investigated in five studies.^{18,22,24–26} The changes in the albumin levels were inconsistent; however, three studies reported that the albumin improved by a range of 0.34 to 1.3 g/L during intervention.^{22,24,25} Faxen-Irving reported an overall reduction in nutritional biomarkers, which was most pronounced in the control group.¹⁸ In addition, Wouters-Wesseling reported improved levels of homocysteine, thiamine diphosphate, vitamin B6, vitamin B12, folic acid, and vitamin D in the intervention group compared with the control group.²⁶

Table 3
Results

Author Year	Intervention	Results			
		Nutritional intake (RQ1) (ΔI vs. ΔC)	Nutritional status (RQ2) (ΔI vs. ΔC)	Nutritional biomarkers (RQ2) (ΔI vs. ΔC)	Cognitive and physical function (RQ3) (ΔI vs. ΔC)
Allen 2013	595 kcal/29 g	E: 517 kcal/d* P: 2 g/d*	n.r.	n.r.	n.r.
Carver 1995	600 kcal/20 g	n.r.	BW: 3.5* vs. 0.6 kg MUAMC: 0.5 vs. 0 cm TSF: 1.5 vs. 0.5 mm	n.r.	n.r.
Faxèn-Irving 2002	361 kcal/16 g	n.r.	BW: 3.4 vs. -0.3 kg** TSF-W: 2.6 vs. -0.7 mm** TSF-M: 1.0 vs. n.r. MUAMC-W: -0.1 vs. -0.5 cm MUAMC-M: -0.6 vs. n.r. cm	S-albumin: -2 vs. -2.6 g/l** S-transferrin: -0.1 vs. 0 g/l S-Hb: -1 vs. -4 g/l** Vit B12: 37 vs. 0 pmol/l IGF-1: -5 vs. -4 μ g/l	ADL: E to F vs. D to E MMSE: -2.5 vs. 0.5**
Lauque 2004	368 kcal/n.r.	E: 291 vs. -1 kcal/d** P: 16 vs. -3 g/d** E2: 87 vs. 178 kcal/d* P2: 17 vs. 1 g/d	BW: 1.9 vs. 0.4 kg** FFM: 0.8 vs. 0.2 kg MNA: 3.4 vs. 1.9 scores**	S-albumin: 0.34 vs. -0.21 g/l	MMSE: 0.3 vs. -0.4 ADL: -0.2 vs. -0.3
Pivi 2011	n.r.	n.r.	BW: 6.7 vs. -2.2 kg** MUAMC: 3.4 vs. -0.2 cm** TSF: 1.4 vs. 2.2 mm	S-protein: 4.3 vs. 0.1 μ g/dl** S-albumin: 0.7 vs. -1.2 g/l	n.r.
de Sousa 2012	400 kcal/18 g	n.r.	BW: 2.1 vs. 0 kg** TSF: 0.4 vs. 0 mm** MUAMC: 0.2 vs. -0.2 cm** MNA: 1.4 vs. 0 scores**	S-albumin: 1.1 vs. -0.7 % g/l** S-protein: 0.2 vs. 0 g/dL** Vit B12: 233 vs. 221 ng/ml Folic acid: 2.7 vs. 4.0 ng/ml	MMSE: 0 vs. 0 ADL(v/BI): 0 vs. -0.7
de Sousa 2017	300 kcal/12 g	n.r.	BW: 0.3 vs. 0.1 kg** MNA: 0.4 vs. -0.1 scores** TSF: 0 vs. 0.7 mm MUAMC: 0 vs. -0.3 cm FFM: -0.3 vs. -0.1 kg BW: 1.4 vs. -0.8 kg**	Vit B1: 0.5 vs. -0.1 nmol/ Vit B6: 114 vs. 8.3** nmol/l Vit B12: 129.5 vs. -1** pmol/l Folic acid: 23.4 vs. 0.3** nmol/l Vit D: 29.4 vs. 13.4** nmol/l S-albumin: 1.3 vs. 1.4 g/l	L(v/BI): 0 vs. -0.3 MMSE: -0.2 vs. 0
Wouters-Wesseling 2002	268 kcal/8 g	n.r.	FFM: -0.3 vs. -0.1 kg BW: 1.4 vs. -0.8 kg**	Vit B1: 0.5 vs. -0.1 nmol/ Vit B6: 114 vs. 8.3** nmol/l Vit B12: 129.5 vs. -1** pmol/l Folic acid: 23.4 vs. 0.3** nmol/l Vit D: 29.4 vs. 13.4** nmol/l S-albumin: 1.3 vs. 1.4 g/l	ADL(v/BI): 0 vs. -0.5
Young 2004	201 kcal/9 g	E: 154 kcal/d* P: 7 g/d	BW: 0.97 kg*	n.r.	n.r.
Parrott 2006	201 kcal/n.r.	E3: 23 kcal/d*	BMI: 23.7 vs. 24.3 kg/m ² *	n.r.	n.r.

Δ The difference from baseline to end of the intervention period. Cross-over studies reported from the intervention period only. *statistic within-significance, **statistic between-significance.

Abbreviations: RQ=research questions, I=intervention group, C=control group, BW=body weight, BMI=body mass index, E=energy, P=protein, E2=energy three months after the end of the intervention, P2=protein three months after the end of the intervention, E3=energy seven days after the end of the intervention, TSF=triceps skinfold, TSF-W=triceps skinfold women, TSF-M=triceps skinfold men, MUAMC=mid-upper-arm muscle circumference, MUAMC-W=mid-upper-arm muscle circumference women, MUAMC-M=mid-upper-arm muscle circumference men, MUAC=mid-upper-arm circumference, IGF-1=insulin-like growth factor-1, FFM=fat-free mass. Tests: MMSE=mini mental state examination, BI=Barthel index, ADL=activities of daily living level of dependence, EBS=eating behaviour scale, NuSc=nutritional score index, MNA=mini nutritional assessment, n.r.=not reported.

Effects of ONS on cognitive and functional status

The effects of ONS on cognitive function were inconsistent in the four studies that investigated this. Faxen-Irving reported a decline in the MMSE scores in the intervention group compared to the control group (-2.5 scored vs. 0.5 scores, respectively),¹⁸ and Lauque reported improved MMSE scores (0.33 (\pm 2.88)) in the intervention group and decreased scores (-0.41 (\pm 2.56)) in the control group.²⁴ No significant effects of nutritional treatment on functional status were reported in the five articles,^{18,22-24,26} see Table 3.

Discussion

The findings of this systematic review focus on persons with dementia, of whom most were undernourished. It shows that ONS improved daily intake of energy and protein, compliance was high, and more persons met the recommended nutrition intake. Overall, intervention with ONS improved nutritional status; however, no effects on cognitive or functional outcomes were reported.

Compliance with the intervention was generally high. Considering the multiple factors contributing to limit dietary intake in these patients, compliance with nutrition intervention is important. We did not find a lower consumption of ONS in long lasting studies, as

reported by Allen.²⁸ Hence giving ONS might have been implemented in daily routines in the studies included in this review. However, study design might influence the results, as the RCT-studies reported 98–100% compliance compared to 70–89% in the non-RCTs. It might be a dilemma that persons with higher BMI, fewer motor problems, fewer mental disorders, and increased attention consumed more ONS than subjects with more pronounced needs, such as persons with lower BMI and reduced physical and mental function.²⁷ The most frail persons are in greater need of a proper follow-up regarding nutrition. In addition, Hubbard reported the following instructions to be of importance for compliance among older persons: “take in small doses, take ad libitum, take at set times and as part of medicine rounds”. Additionally, offering a variety of flavours was reported to positively correlate with compliance.²⁹ The studies included in the present review used the following precautions to improve compliance to intervention: 1) giving ONS after/between ordinary meals,^{18,22,26,27} 2) dispersing ONS throughout the day,^{22,26} and 3) removing ONS one hour before the next meal.²⁰ We assumed that not using ONS before ordinary meals have been a success factor for these studies.

The major finding that ONS improved dietary intake without suppressing the intake of ordinary food has high relevance, as the dietary intake of energy and protein was worryingly low in this population,

and solutions to improve intake are valued. This finding is in line with the results of two earlier systematic reviews^{10,30} reporting ONS to increase the intake of energy and protein without noteworthy suppression of the intake of ordinary food. However, and in contrast to people with high BMI (BMI >25 kg/m²), persons with low and even normal BMI (BMI <25 kg/m²) were more likely to reduce dietary intake when using ONS.²⁷ Still, and in line with nutrition guidelines,⁴ we suggest ONS contributes to enriched mealtimes, modified mealtime environment, eating assistance to improve nutrition intake in malnourished patients and even more prevent malnutrition in at-risk patients.

The finding of ONS's contribution to maintain and even increase BW and muscle mass in persons with dementia is also highly relevant. Weight loss in older people is often an indication of muscle waste and is associated with an increased risk of institutionalisation, morbidity, mortality,^{31,32} falls, disabilities, and fractures.³³ Weight loss is common in people with dementia, as they experience several challenges with dietary intakes, such as loss of eating skills, difficulties in communicating, constipation, aspiration due to dysphagia, and increased needs due to restlessness.^{4,18,23} Therefore, an effort to maintain body weight and muscle mass is given priority in ESPEN guidelines on nutrition in persons with dementia,⁴ and we suggest ONS to be beneficial for this purpose.

The results regarding the effect of ONS on cognition were inconsistent in the present review. Available evidence regarding the effects of ONS on cognitive function is very limited. However, studies have reported an association between malnutrition and cognitive decline in persons with dementia,^{34–36} and supplementation of specific nutrients is shown to delay this process.³⁷ Thus, we cannot exclude the possibility that ONS over a longer period would have given other results. Our suggestion is to perform studies using sensitive scales for cognitive function to study the effects of long-lasting individualised nutritional therapy.

After a femoral neck fracture in lean older women, the activity of daily living (ADL) declined less in the intervention group treated with ONS for 6 months than in the control group.³⁸ It can be assumed that by improving nutritional status in patients with dementia, general condition and function will also improve. This is, however, not confirmed by this review. A number of factors such as amount, composition and duration of the intervention; patients nutritional status; and type and stage of dementia may explain the lack of benefits. Nutritional intake and status are essential to preserve a person's independence for as long as possible, and more studies should investigate the effects of ONS on functional outcomes in persons with dementia.

Strength and limitations

The major strength of this review is the high compliance with the intervention and high proportion of included studies using the RCT design. In one study, a double-blinded study design was used to reduce intervention bias.²⁶ The limitation of this review was the relatively small sample size in the included studies, the variation in the nutritional content of ONS, the intervention duration, and the insufficient report of the participants' nutritional risk status. Moreover, the included studies were relatively old. Despite a new search performed in 2019, no new studies were found. The variation in the presentation of outcome measurements precluded a meta-analysis of the included studies.

Clinical implications

A growing body of evidence provides support for lifestyle modifications such as social interactions, mental and physical exercise, and nutritional supplements in delaying cognitive decline.³⁷ This review

reveals that persons with dementia will profit from ONS as nutritional intake, body weight, and muscle mass improved; nevertheless, individual nutritional needs were often still not met. To ensure every individual's nutritional needs are fulfilled, we therefore suggest the following routines: 1) nutritional risk screening and assessment to make individual nutrition care plans for persons with such needs; 2) initiation of nutritional treatment such as enriched mealtimes, modified mealtime environment, eating assistant and ONS; 3) systematic monitoring and communication of nutritional issues; and 4) nutrition educated staff to handle this important part of patient treatment. Such routines have been found to have a significant effect on hospitalised patients³⁹ and should be a part of dementia care as well.

Conclusion

Intervention with ONS increased energy and protein intake in persons with dementia. Nevertheless, not all persons met their individual needs. The nutritional status improved, although no effects on functional or cognitive outcomes were observed. A more comprehensive intervention plan for people with cognitive impairments should address the individual nutritional challenges to systematically meet nutritional needs. This should be tested in high-quality RCTs to investigate the impact on functional and clinical outcomes.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:[10.1016/j.gerinurse.2020.12.005](https://doi.org/10.1016/j.gerinurse.2020.12.005).

References

1. WHO. ICD-11: International Classification of Diseases. Dementia. <https://icd.who.int/browse11/l-m/en#/http://id.who.int/icd/entity/546689346>; 2019. Accessed 18 May 2020.
2. WHO. 10 facts on dementia 2019. <https://www.who.int/features/factfiles/dementia/en/>. Accessed 18 May 2020.
3. Abdelhamid A, Bunn D, Copley M, et al. Effectiveness of interventions to directly support food and drink intake in people with dementia: systematic review and meta-analysis. *BMC Geriatrics*. 2016;16(1):26. <https://doi.org/10.1186/s12877-016-0196-3>.
4. Volkert D, Chourdakis M, Faxen-Irving G, et al. ESPEN guidelines on nutrition in dementia. *Clin Nutr*. 2015;34(6):1052–1073. <https://doi.org/10.1016/j.clnu.2015.09.004>.
5. Alzheimer's Society. Eating and common behaviour challenges. <https://www.alzheimers.org.uk/get-support/daily-living/eating-behaviour-challenges#content-start>; 2020. Accessed 18 May 2020.
6. Cederholm T, Barazzoni R, Austin P, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr*. 2017;36(1):49–64. <https://doi.org/10.1016/j.clnu.2016.09.004>.
7. Morley JE. Nutrition and the brain. *Clin Geriatr Med*. 2010;26(1):89–98. <https://doi.org/10.1016/j.cger.2009.11.005>.
8. Agarwal E, Miller M, Yaxley A, Isenring E. Malnutrition in the elderly: a narrative review. *Maturitas*. 2013;76(4):296–302. <https://doi.org/10.1016/j.maturitas.2013.07.013>.
9. Chapman IM. Weight loss in older persons. *Med Clin North Am*. 2011;95(3):579–593. <https://doi.org/10.1016/j.mcna.2011.02.004>.
10. Milne AC, Potter J, Vivanti A, Avenell A. Protein and energy supplementation in elderly people at risk from malnutrition. *Cochrane Database Syst Rev*. 2009(2). <https://doi.org/10.1002/14651858.CD003288.pub3>.
11. Ten Cate D, Ettema RG, Huisman-de Waal G, et al. Interventions to prevent and treat malnutrition in older adults to be carried out by nurses: a systematic review. *J Clin Nurs*. 2020;29(11–12):1883–1902. <https://doi.org/10.1111/jocn.15153>.
12. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med*. 2009;6(7):e1000100. <https://doi.org/10.1371/journal.pmed.1000100>.
13. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*. 2015;4(1):1. <https://doi.org/10.1186/2046-4053-4-1>.
14. Droogsma E, van Asselt D, van Steijn J, Veeger N, van Dusseldorp I, De Deyn PP. Nutritional interventions in community-dwelling Alzheimer patients with (risk of) undernutrition: a systematic review. *Int Psychogeriatr*. 2014;26(9):1445–1453. <https://doi.org/10.1017/S1041610214000817>.
15. Ouzzani M HH, Fedorowicz Z, Elmagarmid A, Rayyan—a web and mobile app for systematic reviews. *Syst Rev*. 2016;5(1):210. <https://doi.org/10.1186/s13643-016-0384-4>.

16. Critical Appraisal Skills Programme. CASP Randomised Controlled Trial Checklist. <https://casp-uk.net/wp-content/uploads/2018/01/CASP-Randomised-Controlled-Trial-Checklist-2018.pdf>; 2018. Accessed 18 May 2020.
17. Vellas B GY, Garry PJ, Nourhashemi F, Bennahum D, Lauque S, et al. The mini nutritional assessment (MNA) and its use in grading the nutritional state of older patients. *Nutrition*. 1999;15(2):116–122. [https://doi.org/10.1016/S0899-9007\(98\)00171-3](https://doi.org/10.1016/S0899-9007(98)00171-3).
18. 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(3):221–227. <https://doi.org/10.1038/sj.ejcn.1601304>.
19. 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(9):1382–1387. <https://doi.org/10.1111/j.1532-5415.2006.00844.x>.
20. Allen V, Methven L, Gosney M. The influence of nutritional supplement drinks on providing adequate calorie and protein intake in older adults with dementia. *J Nutr Health Aging*. 2013;17(9):752–755. <https://doi.org/10.1007/s12603-013-0364-5>.
21. Carver AD, Dobson AM. Effects of dietary supplementation of elderly demented hospital residents. *J Hum Nutr Diet*. 1995;8(6):389–394.
22. de Sousa OLV, Amaral TF. Three-week nutritional supplementation effect on long-term nutritional status of patients with mild Alzheimer disease. *Alzheimer Dis Assoc Disord*. 2012;26(2):119–123. <https://doi.org/10.1097/WAD.0b013e31822c5bb3>.
23. de Sousa OV, Soares Guerra R, Sousa AS, Pais Henriques B, Pereira Monteiro A, Amaral TF. Impact of nutritional supplementation and a psychomotor program on patients with Alzheimer's disease. *Am J Alzheimer's Dis Other Dementias*. 2017;32(6):329–341. <https://doi.org/10.1177/1533317517705221>.
24. Lauque S, Arnaud-Battandier F, Gillette S, 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(10):1702–1707. <https://doi.org/10.1111/j.1532-5415.2004.52464.x>.
25. Pivi GA, da Silva RV, Juliano Y, et al. A prospective study of nutrition education and oral nutritional supplementation in patients with Alzheimer's disease. *Nutrition J*. 2011;10:98. <https://doi.org/10.1186/1475-2891-10-98>.
26. Wouters-Wesseling W, Wouters AE, Kleijer CN, Bindels JG, de Groot CP, van Staveren WA. Study of the effect of a liquid nutrition supplement on the nutritional status of psycho-geriatric nursing home patients. *Eur J Clin Nutr*. 2002;56(3):245–251. <https://doi.org/10.1038/sj.ejcn.1601319>.
27. 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(8):1305–1312. <https://doi.org/10.1111/j.1532-5415.2004.52360.x>.
28. 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(6):950–957. <https://doi.org/10.1016/j.clnu.2013.03.015>.
29. Hubbard GP, Elia M, Holdoway A, Stratton RJ. A systematic review of compliance to oral nutritional supplements. *Clin Nutr*. 2012;31(3):293–312. <https://doi.org/10.1016/j.clnu.2011.11.020>.
30. Cawood A EM, Stratton R. Systematic review and meta-analysis of the effects of high protein oral nutritional supplements. *Ageing Res Rev*. 2012;11(2):278–296. <https://doi.org/10.1016/j.arr.2011.12.008>.
31. Haugsgjerd TR DJ, Vollset S, Vinknes K, Nygård O, Seifert R, et al. Association between weight change and mortality in community living older people followed for up to 14 years. The Hordaland Health Study (HUSK). *J Nutr Health Aging*. 2017;21(8):909–917. <https://doi.org/10.1007/s12603-016-0866-z>.
32. Tangvik RJ TG, Eisman JA, Guttormsen AB, Henriksen A, Nilsen RM, et al. The nutritional strategy: four questions predict morbidity, mortality and health care costs. *Clin Nutr*. 2014;33(4):634–641. <https://doi.org/10.1016/j.clnu.2013.09.008>.
33. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet (London, England)*. 2013;381(9868):752–762. [https://doi.org/10.1016/s0140-6736\(12\)62167-9](https://doi.org/10.1016/s0140-6736(12)62167-9).
34. Gomez-Gomez ME, Zapico SC. Frailty, cognitive decline, neurodegenerative diseases and nutrition interventions. *Int J Mol Sci*. 2019;20(11). <https://doi.org/10.3390/ijms20112842>.
35. Soto ME, Secher M, Gillette-Guyonnet S, et al. Weight loss and rapid cognitive decline in community-dwelling patients with Alzheimer's disease. *J Alzheimer's Dis*. 2012;28(3):647–654. <https://doi.org/10.3233/jad-2011-110713>.
36. 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(2):89–97. <https://doi.org/10.1097/01.jam.0000110646.48753.ef>.
37. Shea TB, Remington R. Nutritional supplementation for Alzheimer's disease? *Curr Opinion Psychiatry*. 2015;28(2):141–147.
38. Tidermark J PS, Carlsson P, Söderqvist A, Brismar K, Tengstrand B, et al. Effects of protein-rich supplementation and nandrolone in lean older women with femoral neck fractures. *Clin Nutr*. 2004;23(4):587–596. <https://doi.org/10.1016/j.clnu.2003.10.006>.
39. Schuetz P, Fehr R, Baechli V, et al. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. *Lancet (London, England)*. 2019;393(10188):2312–2321. [https://doi.org/10.1016/s0140-6736\(18\)32776-4](https://doi.org/10.1016/s0140-6736(18)32776-4).