Meta-analyses

Use of nutritional complete supplements in older adults with dementia: Systematic review and meta-analysis of clinical outcomes

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SUMMARY

Background & aims: Malnutrition is prevalent in people diagnosed with dementia however ensuring adequate oral intake within this group is often problematic. It is important to determine whether providing nutritionally complete oral nutritional supplements (ONS) drinks is an effective way of improving clinical outcomes for older people with dementia. This paper systematically reviewed clinical, wellbeing and nutritional outcomes in people with long-term cognitive impairment.

Methods: The CINAHL, Medline and EMBASE databases were searched from their inception until January 2012. Reference lists of the included papers, foreign language papers and review articles obtained were manually searched.

Results: Twelve articles were included in the review containing 1076 people in the supplement groups (intervention) and 748 people in the control groups. Meta-analysis shows there was a significant improvement in weight (p = <0.0001), Body Mass Index (BMI) (p = <0.0001) and cognition at 6.5 ± 3 month follow-up (p = 0.002) when supplements were given compared to the control group.

Conclusions: Providing ONS drinks has a positive effect on weight gain and cognition at follow-up in older people with dementia. Additional research is required in both comparing nutritional supplements to vitamin/mineral tablets and high protein/calorie shots and clinical outcomes relevant to people with dementia.

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1. Introduction

Malnutrition is a common problem affecting 27%–37% of older adults within nursing homes1,2 and 39% of adults over 65 years admitted to hospital are at risk of malnutrition.1 Additionally, decreasing cognition has been recognised as having a negative impact on nutritional status.3 People with dementia are more likely to be malnourished than age matched individuals who are cognitively intact (approximately 44% vs 25%, p < 0.0001).4,5

It has previously been proposed that weight loss in people with dementia is caused by metabolic alterations within this group. However, this is not substantiated in studies comparing resting energy expenditure using indirect calorimetry6 and doubly labelled water when participant’s fat free mass was considered.7 A longitudinal study of individuals with Alzheimer’s disease did, however, find that weight loss was predicted not only by the severity of the dementia but, also by behavioural problems and burden to caregiver.8 People with dementia often have a decline in ability to feed themselves9 and present with poor eating behaviour. These adverse behaviours which prevent oral intake are usually associated with severe dementia and include disruptive or restrictive behaviour when eating such as refusing to swallow, spitting food out and leaving the mouth open.10 People with dementia who have the most feeding problems are at higher risk of malnutrition.11 Dysphagia and dyspraxia are also common in people in the later stages of dementia which are a concern among their relatives.12 These factors may lead to people with dementia not responding to nutritional interventions as positively as observed within other groups.

There are several consequences of under-nutrition in elderly people. Longitudinal observational studies indicate that being
underweight is a predictor of increased mortality at follow-up and also has negative implications on admissions to hospital or long-term care establishments, mortality rates and weight loss greater than 2.5% at six month follow-up.

Oral nutritional supplement drinks are nutritionally complete drinks containing vitamins/mineral (micro-) and calories/protein (macro-) nutrients where overall intake provides an appropriate and balanced diet. The European Society of Parenteral and Enteral Nutrition recommends the use of oral nutritional supplements to improve nutritional intake in those who are malnourished or at risk of malnourishment. However, compliance with these supplements is recognised to limit their effectiveness.

Poor feeding behaviours are an additional challenge in ensuring adequate consumption of foods and fluids in older adults with cognitive impairment and dementia. This includes factors such as refusing to eat, refusing to open their mouth, turning their head away, leaving the mouth open, refusing to swallow and spitting, as highlighted within the EdFED questionnaire. Challenges in feeding behaviour within individuals with dementia could result in nutritional complete beverages having more positive outcomes within this group compared to other older adult groups due to low macro and micronutrient intake from consumed food. However, poor feeding behaviours may also lead to poorer compliance with these supplements and therefore reduce their benefit.

It is also known clinically that people with dementia are more likely to have dysphagia and are at increased risk of aspiration compared to people with no cognitive deficit. This is supported by a study evaluating the swallowing response in patients given a 1 ml bolus of distilled water. People with dementia took approximately four times longer to swallow than those without cognitive problems (5.2 ± 0.6 s vs 1.2 ± 0.1). In one study, 15% of 91 participants with dementia had problems swallowing food and 8% had problems swallowing fluids. This higher incidence of dysphagia with food may suggest that people with dementia may be able to consume a higher proportion of their nutritional requirements from supplement drinks compared to their usual diet. However, this questionnaire based study may underestimate the true prevalence of dysphagia in people with dementia. A study of people with Alzheimer’s type dementia using video fluoroscopy found only 4 (16%) had normal swallowing function and the severity of the swallow abnormality correlated with the severity of dementia. This high risk of dysphagia and aspiration among people with dementia may therefore make them less able to consume sufficient nutritional supplement drinks for a clinical benefit to occur thus reducing their usefulness.

This systematic review recognises these additional challenges that older adults with cognitive impairment have during oral intake compared to other older adult groups and therefore, evaluates the effectiveness of these supplements independent to other population groups. This systematic review and meta-analysis aims to identify the effects of oral nutritional supplements on health, nutrition and wellbeing outcomes in people with dementia.

2. Materials and methods

Relevant articles were searched for using Medline, CINHAL & EMBASE databases up to January 2012, using the search terms described in Fig. 1 and articles had to fulfil the three criteria outlined to be included. Searches were not restricted to merely randomised control trials and quasi randomised trials. Although systematic reviews often restrict searches to these types of studies, there were insufficient studies of this rigour within this population group. Therefore, papers using all research methodologies were included.

In addition to searches of computerised databases, hand searches of reference lists were undertaken of all relevant articles obtained for review, relevant articles not in English and any relevant review articles obtained in the search. The review process used is based on the PRISMA guidelines; identification, screening, eligibility and inclusion.

All abstracts were read for relevance and inappropriate articles were excluded. Full texts of the remaining abstracts were obtained to review.

Information extracted from the reviewed articles encompassed; population size, population demographics, location of participants, duration of supplementation, whether participants were randomised to treatment group and details of study controls. From the papers any change in outcome variable was calculated. This data was agreed by two reviewers. Meta-analysis was carried out on the data extracted from articles which provided sufficient data to be included comparing two groups, either; ONS drink and control or ONS drink and baseline. This was undertaken using Comprehensive Meta-analysis software (version 2, Biostat, New Jersey, USA).

Downs and Black scores were undertaken to assess study quality. This asks questions on reporting (maximum mark = 11), external validity (maximum mark = 3), internal validity: bias (maximum mark = 7), internal validity: confounding (maximum mark = 6) and power (maximum mark = 5). Two independent reviewers undertook screening and methodological quality assessment, using the Downs and Black scoring system.

3. Results

3.1. Studies identified

The initial search identified 248 articles. However, after abstracts were screened for eligibility and repeated results removed, sixteen full text articles were obtained. On reading the full text articles eight articles were excluded; one French, five literature reviews and two that did not compare ONS drinks against a control group or time-period. After hand searching relevant reference lists four articles were added to the review (Fig. 1).

A total of twelve studies were included in the review. These twelve studies contained a total of 1076 participants in their ONS groups (intervention) and 748 in their control groups.

The intervention periods studied ranged from 3 weeks to 1 year (mean 22.1 ± 17.5 weeks). Most studies compared the impact of ONS drinks against a normal diet and care (66%). However, one study gave participants a placebo drink (low Kcal, no micronutrients), two studies gave a drink with similar Kcal and protein content but no micronutrients and one study gave a micronutrient tablet to the control group.

Participants with dementia in these studies were mainly residing in long-term care establishments (75%). However, three studies also included participants from the wider community and day centres. Most of the studies included participants who were at risk of malnutrition. However, two studies excluded people already on ONS drinks and therefore the group at most risk of malnutrition.

3.2. Compliance with supplement drinks

Nine studies reported compliance with the intervention. This was reported to be good to high within most (88.9%) studies, with one study stating that approximately 90% of ONS provided was consumed. However, in two studies, participants with poor compliance (two or three individuals) with the intervention were withdrawn. One study reported consumption much lower at 8.5% of supplements given. This study lasted 1 year, which was one of the longest studies.
3.3. Impact on calorie and protein intake

Five studies reported the impact of ONS on either overall or habitual intake of energy and proteins. Overall energy increased within the three studies reporting this. The overall difference in energy intake between the days when ONS were supplied and baseline was an improvement of 392.3, SE 39.5 Kcal/day ($p < 0.0001$). Total protein intake with ONS supplementation increased from between 16 g/day to 32 g/day. Although none of the studies reported whether participants received sufficient energy or protein for their requirements either with or without ONS supplementation.

There are conflicting results on the influence that ONS drinks have on habitual intake of energy in the three studies that analysed this. One study found habitual intake improved with ONS consumption over a 1 year study period, another found no significant change and one found a small but significant decrease in habitual intake of energy ($56 \pm 81.3$ Kcal, $p = 0.006$). Meta-analysis of these three studies indicates that overall there were no significant differences in consumption at mealtimes between supplement and
control groups (−0.024 ± 0.095 Kcal, p = 0.8). The disparity between the different studies may have arisen from differences in consumption volume of the ONS drinks provided. One of the studies, supports this, reporting intake of meals (%) was less when a typical 200 mL ONS supplement drink was provided between meals compared to when dense protein/calorie shots (120 Kcal, 5 g protein in 60 cc) were provided four times a day (−7.3 ± 13.4%, p < 0.005).26

3.4. Impact on mortality

A comparison of mortality rate between ONS support and control was analysed in six studies.24,28,30,33–35 A meta-analysis considering these found mortality rates tended to be higher in those who were in the control group, although it was not statistically significant (p = 0.309).

3.5. Impact on anthropometric measurements

Ten studies analysed the influence of ONS support on participant weight over the study.24,26,27,29–35 A meta-analysis of these studies found ONS drinks had a significant positive benefit on weight. A fixed effects model demonstrated that the mean difference in participant weight gain between control and ONS drink intervention was 3.54 kg (SE 0.10) which was statistically significant (p < 0.0001). The study by Planas failed to show a positive effect of ONS drinks on weight.25 However, this study did not compare the use of ONS drinks to ‘normal practice’. This study compared the provision of a nutritionally complete beverage to protein and energy dense nutritional shots which were not fortified with micronutrients.

Seven studies analysed the effect of ONS on body mass index (BMI).24,25,27,28,30,33,34 When analysing these seven studies, ONS were shown to significantly impact on BMI (p < 0.0001). A fixed effects model demonstrated that the mean difference in participant BMI gain between control and ONS drink intervention was 0.92 kg/m² (SE 0.16). However, one of these studies found that BMI increased more in the control than in the ONS intervention group.25 This study used energy (Kcal) and protein dense drink without micronutrients as the control and both the ONS drink and control drink resulted in an increased BMI over the 6-month study period. The majority of these studies also reported weight, as previously discussed. However, analysis of BMI allowed the inclusion of two additional studies25,28 in the meta-analysis. Meta-analysis of all studies analysing both weight and BMI with supplement use involved a total of 349 participants in the intervention groups and 399 participants in the control groups. Meta-analysis of these studies showed an increase over time in weight/BMI with the provision of ONS compared to the control group (p < 0.0001) (Fig. 2). However, studies analysing the impact of nutritional supplement consumption on skin fold thickness (SFT)25,27,28,32–34 and mid arm muscle circumference (MAMC)27,32–34 found that there was no overall statistically significant difference between ONS and control groups.

3.6. Impact on cognitive ability

Four studies evaluated the influence of ONS drinks on cognitive performance, as measured by the mini-mental state examination (MMSE).25,29,30,33 These studies lasted 6.5 ± 3.9 months until follow-up. A meta-analysis considering these four found that ONS drinks had a positive benefit on MMSE in this population group, p = 0.002 (Fig. 3). A fixed effects model demonstrated that the mean difference on the MMSE examination test scores between the control and ONS drinks was 1.6 (SE 0.3). However, caution should be applied to this finding due to the small number of studies that evaluate this outcome. There were in total only 141 people in the intervention groups and 130 in the control groups.

3.7. Impact on functional ability and behaviour

Two studies analysed a participant’s ability to undertake activities of daily living over time using the Katz assessment30,33 and one used the Barthel index.24 In these three studies there was no statistically significant difference in scores between the control groups and the intervention (ONS) groups.24,30,33

Two studies analysed the impact of ONS support on feeding behaviours25,30 and neither found a statistically significant difference between the ONS and control groups.

4. Discussion

Results from the literature review indicate that skin fold thickness (SFT) and arm muscle circumference are not affected by supplement use. However, these anthropometric measurements have a low level of reproducibility with the same observer at different time points. Therefore, more reliable and reproducible measurements include BMI and weight.

Fig. 2. Meta-analysis for weight and BMI from 12 studies of older adults with dementia, where the intervention of nutritional supplement was compared to a control.
times,36,37 in different positions37 and between observers.36,37 Skin fold thickness measurements are, therefore, an inaccurate method for obtaining evidence of changes in body composition. Mid arm muscle circumference (MAMC) is calculated from SFT measurements.38 Therefore, it is also unlikely to detect small changes in body composition.

BMI is recognised as being less accurate in older populations when determining fat mass and subsequent nutritional status.39,40 Many authors attribute these inaccuracies to height loss41 or more commonly the redistribution of fat mass with aging.40,42,43 However, the duration of the studies analysing weight or BMI changes in this review was one year or less (22.1 ± 17.5 weeks). It is unlikely that age related changes in height or body composition will occur over this time. Therefore, BMI and weight measurements would be appropriate to detect the influence of ONS.

Findings demonstrate that oral nutritional supplement drinks have positive effects on weight gain and BMI in older adults with dementia. This increase in weight and BMI is likely to be the result of ingesting an increased amount of energy (kcal) and protein supplied by these drinks as overall energy and protein intake was demonstrated to improve with ONS provision in studies that reported this. However, effectiveness of ONS drinks is often limited by poor compliance,16 which is an additional challenge in older adults with dementia.

Overall the consumption of nutritional supplement drinks was fairly good. However, consumption of nutritional drinks was lowest in one of the longest studies.29 This may indicate that during shorter studies staff behaviour is different, such as increased staff vigilance and verbal prompting which is known to improve the consumption of ONS drinks.44,45 However, these positive staff behaviours may return to normal practice as the duration of interventions increase.

Two studies compared the provision of a nutritionally complete beverage to protein and energy dense nutritional drinks (with no micronutrients).25,26 One of these studies analysed a protein and energy dense 60 ml shot (120 calories, 5 g protein) supplied several times throughout the day with nutritionally complete supplement drinks (approximately 237 ml, 240 calories, 10 g protein).26 The proportion of the supplement shot consumed was significantly greater than the nutritionally complete beverages26 which results in higher macro nutrient consumption. It is already known that poor compliance impacts on the effectiveness of nutritional supplements.45 Therefore a protein and an energy dense nutritional shot that is more readily consumed may result in better clinical outcomes. This is supported when comparing the nutritionally complete beverage (intervention) to protein and energy dense shots, where weight and BMI improved more in the cohort receiving protein and energy dense shots.26 However, another study compared two 250 ml energy dense and protein-rich supplements (250 kcal with 30% of energy from protein) with and without micronutrients. Weight also improved more in the cohort consuming 250 ml energy dense and protein-rich supplements compared to a 250 ml nutritionally complete beverage25 indicating that factors beyond volume may impact on consumption of nutritional drinks and subsequent health outcomes.

Findings demonstrate that oral nutritional supplement drinks have positive benefits on cognition, with MMSE examination test scores improving with the provision of ONS drinks. MMSE scores are positively correlated to quality of life in people with Alzheimer’s disease46 indicating the positive benefits an improving MMSE may have on general wellbeing in people with dementia. Additionally, health related quality of life improves if short term delirium is treated and does not deteriorate as much as an untreated group47 further supporting the importance of improving cognitive ability on wellbeing outcomes.

One study found a non-significant change in MMSE in the control group and the intervention group had a decrease in MMSE scores over the 6-month study.31 At baseline the groups were well matched with no difference in dementia diagnosis, Clinical Dementia Rating (CDR) classification or MMSE scores. However, participants in the intervention and control groups lived in different nursing homes. Environmental stimulation and care practices may have contributed to the difference in MMSE scores over the study period. Activities that stimulate mental or psycho-social functioning prevent elderly community dwelling individuals from developing dementia over a 5 year follow-up periods.48 Therefore, a positive and stimulating environment is also likely to be beneficial in slowing down the progression of cognitive decline in people with diagnosed dementia.

Duration of intervention is likely to impact on the results obtained. Clinical outcomes may also be dependent on the duration of interventions. A three-month intervention study showed no significant difference between the MMSE in the intervention and control groups.30 Therefore, the intervention period may need to be longer to impact on MMSE. In contrast, the positive benefits of supplement use on weight were observed in studies that were as short as three weeks,31 indicating weight gain occurs much earlier with supplement use compared to changes in cognitive ability.

A study of 44 participants illustrated the greatest difference between control and intervention groups. This study provided protein and energy dense shots to the control group, which may indicate that micronutrient components of the supplements that impact MMSE scores.25 However, other studies do not investigate

<table>
<thead>
<tr>
<th>Statistics for each study</th>
<th>Std diff in means and 95% CI</th>
<th>Relative weight</th>
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<tr>
<td>Planas</td>
<td>2.060 0.373 0.139 1.329 2.792 5.520 0.000</td>
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<tr>
<td>Laxque</td>
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<td></td>
<td>0.388 0.127 0.016 0.140 0.637 3.061 0.002</td>
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Fig. 3. Meta-analysis plot for cognitive performance (as measured by mini-mental state examination, MMSE) from four studies of older adults with dementia, where the intervention of nutritional supplement was compared to a control.
this therefore further research comparing micronutrient tablets with nutritionally complete drinks is required.

Studies included in this review had Downs and Black scores of 19.9 ± 2.15 indicating that the general quality of most studies was good. Randomisation of participants into control and intervention groups occurred in the majority of studies (66.7%). However, 75% of studies did not attempt to blind either the participant or the researcher to the intervention that participants were receiving. This may have resulted in bias although, blinding would have been difficult to achieve. The majority of participants with dementia in this review were residing in long-term care establishments (75%). This may represent a large number of patients with cognitive impairment across the United Kingdom as 70% of all nursing home populations cognitive impairment. However, the use of oral nutritional supplements are recommended for elderly patients at risk of malnutrition which is more likely to occur within the hospitalised population who have increased energy and protein requirements due to an acute injury or illness. The outcomes found as part of this review focus on long-term outcomes, with quickest response to the provision of nutritional supplement drinks being weight after a three week intervention. Therefore, it is unclear whether post-operative complications and length of hospital stay in people with dementia will be effected with nutritional supplement drink provision over a short hospital stay.

The provision of supplement drinks may not be the only factor that improves nutritional status and outcomes within this group. A recent review highlights that improving assistance and support with feeding also improved weight within people with dementia. Changing the environment to provide a more pleasant atmosphere such as the addition of music also leads to a reduction in aggressive behaviours among people with dementia which is likely to have a positive impact on improving feeding behaviours and thus reducing the risk of malnutrition.

Findings indicate that the provision of adequately consumed oral nutritional supplement drinks cause a small impact on weight gain and may also have a positive impact on cognitive ability (demonstrated by the MMSE) in older adults with cognitive impairment compared to those receiving no supplement. However, short term outcomes have not been evaluated within the papers reviewed in this study. This is likely to be because of the challenges in recruiting participants with cognitive impairment within hospitals or because findings were not positive.

In summary, supplement use is significantly associated with an improvement in overall energy intake. The provision of oral nutritional supplements also resulted in a small but statistically significant change in weight and BMI. The majority of studies (87.5%) comparing supplement use to normal diet and care or placebo found a significant improvement in these outcomes. However, where the

<table>
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<th>Author reference</th>
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<th>Control (n)</th>
<th>Intervention (n)</th>
<th>Control</th>
<th>Intervention (duration)</th>
<th>Mortality Weight/ BMI</th>
<th>Cognition Functional ability</th>
<th>Feeding behaviour</th>
<th>Downs and Black Score</th>
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<td>Carver &amp; Dobson</td>
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<td>23</td>
<td>23</td>
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<td>–</td>
<td>–</td>
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<td>Faxon Irving</td>
<td>Dementia care sheltered housing</td>
<td>14</td>
<td>22</td>
<td>Normal diet and care</td>
<td>5 Months</td>
<td>NS</td>
<td>↑</td>
<td>↓</td>
<td>NS</td>
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<td>Nursing homes range of BMI/MNA but mainly mild risk</td>
<td>74</td>
<td>25</td>
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<td>1 Year</td>
<td>NS</td>
<td>↑</td>
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<td>↑</td>
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<td>Geriatric wards &amp; day centres MNA&lt;23.5</td>
<td>45</td>
<td>46</td>
<td>Normal diet and care</td>
<td>3 Months</td>
<td>–</td>
<td>↑</td>
<td>NS</td>
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<td>1 Year</td>
<td>NS</td>
<td>↑</td>
<td>–</td>
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<td>Alzheimer’s disease community (Brazil)</td>
<td>27</td>
<td>26</td>
<td>Normal diet and care</td>
<td>6 Months</td>
<td>NS</td>
<td>↑</td>
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<td>21</td>
<td>23</td>
<td>High protein/ calorie drink (no micronutrients)</td>
<td>6 Months</td>
<td>NS</td>
<td>↑</td>
<td>–</td>
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<td>30</td>
<td>30</td>
<td>High protein/ calorie shot (no micronutrients)</td>
<td>4 Weeks</td>
<td>–</td>
<td>↓</td>
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<td>Psycho-geriatric nursing home (BMI &lt; 23 in men &amp; &lt; 25 in women)</td>
<td>16</td>
<td>19</td>
<td>Placebo (no micro- or macro- nutrients)</td>
<td>12 Weeks</td>
<td>NS</td>
<td>↑</td>
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<td>5 Weeks</td>
<td>–</td>
<td>↑</td>
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<td>34</td>
<td>34</td>
<td>Normal diet and care</td>
<td>21 Days</td>
<td>–</td>
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NS = No significant difference between supplement group and control, ↑ – significant improvement in outcome of supplement drink compared to control, ↓ – significant decrease in outcome of supplement drink compared to control, – – not assessed as an outcome measure in study.
control was a macro or micronutrient supplement findings were less positive (see Table 1). This may indicate that the comparison of nutritionally complete supplement drinks to both vitamin/mineral tablets and high protein/calorie shots requires further investigation. Cognitive ability, functional abilities and feeding behaviours have been studied within a small number of papers (Table 1) indicating that further research evaluating these outcomes may be required. However, the four studies that analysed cognitive ability in this population group demonstrated a significant improvement in MMSE at follow-up with supplement use compared to the control thus highlighting the need to investigate some of these outcomes further. Outcomes that may be more relevant to acutely ill patients also need to be evaluated as these have not been evaluated within the literature in people with dementia.

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Statement of authorship
VA undertook systematic searches and carried out the meta-analysis, MG and VA extracted data from articles, rated methodological rigour (Downs and Black scoring) and drafted the manuscript. LM contributed to the manuscript and provided critical logical rigour (Downs and Black scoring) and drafted the manuscript. MG and VA extracted data from articles, rated methodological rigour and provided critical logical rigour (Downs and Black scoring).

Conflict of interest
The authors disclose no conflicts of interest.

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