Evidence profile: malnutrition

Scoping question:
Does oral nutritional supplement, dietary advice or mealtime enhancement produce any benefit for older people at risk of undernutrition or who are affected by undernutrition?

The full ICOPE guidelines and complete set of evidence profiles are available at who.int/ageing/publications/guidelines-icope

Painting: “Wet in Wet” by Gusta van der Meer. At 75 years of age, Gusta has an artistic style that is fresh, distinctive and vibrant. A long-time lover of art, she finds that dementia is no barrier to her artistic expression. Appreciated not just for her art but also for the support and encouragement she gives to other artists with dementia, Gusta participates in a weekly art class. Copyright by Gusta van der Meer. All rights reserved.
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ICOPE guidelines – World Health Organization
Background

Undernutrition is common among older people over 60 years of age. The prevalence of undernutrition in older people living in the community ranges between 1.3% and 47.8% (1–5). The reported prevalence is much higher in studies from low- and middle-income countries than high-income countries (6).

Several observational studies have investigated adverse health outcomes in undernourished older people. These have reported strong associations between undernutrition and premature mortality, poor quality of life and reduced functional ability. A recent systematic review of prospective studies from high-income countries reported a strong association between undernutrition and subsequent mortality in older people (7). In another review of longitudinal studies, undernourished older people were found to be twice as likely to experience a poor quality of life than their normally nourished counterparts (8). Other studies have found that older people who report (unintentional) weight loss have a higher risk of developing limitations in basic activities of daily living (ADLs) such as bathing, eating and dressing (9–12). In a three-year longitudinal study, low body mass index (BMI) was a moderate risk factor for the onset of ADL limitations (13).

Despite the high prevalence of undernutrition reported in population studies, nutritional trials targeting community-dwelling older people are limited. Earlier systematic reviews found that nutritional interventions produced some clinical benefits, including weight gain, albeit the data were less conclusive for improvements in functional outcomes (14). Results from a meta-analysis examining the effect of dietary advice in older persons at risk of undernutrition showed a significant increase in energy and protein intake, and body weight, but no significant effect on physical function or mortality. Most studies included in these reviews recruited healthy older people or older people living in long-term care or admitted to hospital. The effects of nutritional interventions in older people living in the community who are undernourished or at risk of undernutrition therefore remain unclear. This current review was undertaken systematically to review and analyse published reviews and randomized controlled trials, and to summarize the evidence for formulating recommendations for the prevention and management of undernutrition among older people in community and primary care settings.
Part 1: Evidence review

Scoping question in PICO format (population, intervention, comparison, outcome)

Populations
- Older people, 60 years of age and over (both male and female) at risk of undernutrition
- Older people, 60 years of age and over (both male and female) affected by undernutrition

Interventions
- Oral nutritional supplement (macro- and/or micronutrients)
- Dietary advice
- Mealtime strategy to improve food intake

Comparisons
- Placebo
- Usual care
- Control group (waiting to receive intervention)

Outcomes
- Critical: Mortality, weight change
- Important: Hand grip strength, activities of daily living (ADLs)

Settings
- Primary health care/community
Search strategy

An independent search for systematic reviews and clinical trials was performed in September 2015 using the Ovid MEDLINE, Embase and PsycINFO electronic databases. The detailed search strategy is listed in Annex 1.

List of systematic reviews and trials identified by the search process

Included reviews in GRADE\(^1\) analysis and considered for recommendations (14–16):


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\(^1\) GRADE: Grading of Recommendations Assessment, Development and Evaluation. More information: http://gradeworkinggroup.org
### PICO table

<table>
<thead>
<tr>
<th>Intervention/comparison</th>
<th>Outcomes</th>
<th>Studies used for GRADE tables</th>
</tr>
</thead>
</table>
| 1 Oral nutritional supplement compared with placebo or usual care controls | • Mortality  
• Weight gain  
• Hand grip strength  
• Activities of daily living (ADLs)  
• Quality of life  
• Adverse effects  
• Compliance | Community settings (n = 12) (17–28)  
Hospital/long-term care settings (n = 43) (29–69) |
| 2 Dietary advice or education compared with no advice, usual care or exercise | • Mortality  
• Weight gain  
• ADLs  
• Quality of life | Community settings (n = 6) (70–75) |
| 3 Mealtime enhancement strategies | • Weight gain  
• ADLs  
• Quality of life | Long-term care settings (n = 2) (76, 77) |
Narrative summary of the reviews included in the analysis

Milne et al. (14) examined trials to evaluate interventions designed to improve the nutritional status of older people and their clinical outcomes; extra protein and energy sources were provided, usually as commercial sip-feeds. Most studies were randomized or quasi-randomized controlled trials of oral protein and energy supplementation in older people, and were included in the review with the exception of groups recovering from cancer treatment or in critical care. Sixty-two trials were included (n = 10,187), of which only 38 involved undernourished older people or frail dependent older people. We included only these studies in our WHO review to summarize the evidence. In 2015, this review was updated by WHO and an additional 29 trials were included in the evidence synthesis.

Baldwin et al. (15) published a Cochrane review that examined the evidence that dietary advice in adults with disease-related malnutrition improves survival, weight and anthropometry; estimated the size of any additional effect of oral nutritional supplement (ONS) combined with dietary advice; and compared the effects of dietary advice with those of ONS administration. Forty-five studies (n = 3,186) met the inclusion criteria. Dietary advice was compared with: no advice (n = 1,053); ONS (n = 332); dietary advice and ONS (n = 731). Dietary advice plus ONS was compared with no additional intervention (n = 1,070). Four studies from this review targeted older people and were included in this WHO review.

Munk et al. (16) undertook a systematic review and meta-analysis to evaluate the evidence for an effect of individualized dietary counselling on physical function, readmissions, mortality, nutritional status, nutritional intake and quality of life in nutritionally at-risk older patients following discharge from hospital. Four randomized controlled trials (n = 729) were included. Overall, the evidence was of moderate quality. Dietitians provided counselling in all studies. Three studies from this review were included in the evidence synthesis.
**GRADE table 1:** Oral nutritional supplement (ONS) with or without dietary advice compared with placebo or usual care for older people at risk of undernutrition or undernourished

**Author:** WHO systematic review team  
**Date:** 5 November 2015 (last updated 20 November 2015)  
**Question:** Does ONS with or without dietary advice compared with usual care or placebo produce any benefit or harm for older people at risk of undernutrition or undernourished?  
**Setting:** Primary care or community  
**Bibliography:** (14) 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):CD003288 – this systematic review was updated by WHO in 2015

<table>
<thead>
<tr>
<th>Quality assessment</th>
<th>Number of patients</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of studies</td>
<td>Study design</td>
<td>Risk of bias</td>
<td>Inconsistency</td>
<td>Indirectness</td>
</tr>
<tr>
<td>Mortality (follow-up ranged from 3 months to 18 months)</td>
<td>10 randomized trials</td>
<td>serious</td>
<td>not serious</td>
<td>not serious</td>
</tr>
<tr>
<td>Mortality – subgroup at risk of undernutrition</td>
<td>5 randomized trials</td>
<td>serious</td>
<td>not serious</td>
<td>not serious</td>
</tr>
</tbody>
</table>

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## Mortality – subgroup with undernutrition

<table>
<thead>
<tr>
<th>5</th>
<th>randomized trials</th>
<th>serious</th>
<th>not serious</th>
<th>not serious</th>
<th>not serious</th>
<th>none</th>
<th>12/202 (5.9%)</th>
<th>10/206 (4.9%)</th>
<th>RR 1.20 (0.58 to 2.50)</th>
<th>10 more per 1000 (from 20 fewer to 73 more)</th>
<th>CRITICAL</th>
</tr>
</thead>
</table>

#### Weight gain (follow-up ranged from 3 months to 18 months; assessed in kilograms, with digital scale \([n = 9]\), self-report \([n = 1]\))

<table>
<thead>
<tr>
<th>10</th>
<th>randomized trials</th>
<th>serious</th>
<th>serious</th>
<th>not serious</th>
<th>not serious</th>
<th>none</th>
<th>295</th>
<th>291</th>
<th>MD 1.14 more (0.59 more to 1.7 more)</th>
<th>CRITICAL</th>
</tr>
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</table>

#### Weight gain – subgroup at risk of undernutrition

<table>
<thead>
<tr>
<th>6</th>
<th>randomized trials</th>
<th>serious</th>
<th>serious</th>
<th>not serious</th>
<th>not serious</th>
<th>none</th>
<th>182</th>
<th>173</th>
<th>MD 0.35 more (0.3 fewer to 1.01 more)</th>
<th>CRITICAL</th>
</tr>
</thead>
</table>

#### Weight gain – subgroup with undernutrition

| 4 | randomized trials | serious | not serious | not serious | not serious | none | 113 | 118 | MD 3.17 more (2.12 more to 4.21 more) | MODERATE | CRITICAL |
|---|------------------|---------|-------------|-------------|-------------|------|-----|-----|-----------------------------------|---------|

#### Hand grip strength (follow-up 3–18 months; assessed with handheld dynamometer; higher score = better performance)

| 6 | randomized trials | serious | not serious | not serious | not serious | none | 181 | 203 | SMD 0.17 fewer (0.37 fewer to 0.03 more) | MODERATE | IMPORTANT |
|---|------------------|---------|-------------|-------------|-------------|------|-----|-----|-----------------------------------|---------|

#### Hand grip – subgroup at risk of undernutrition

| 3 | randomized trials | serious | not serious | not serious | serious | none | 89 | 90 | SMD 0.07 fewer (0.37 fewer to 0.22 more) | LOW | IMPORTANT |
|---|------------------|---------|-------------|-------------|---------|------|-----|-----|-----------------------------------|------|

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Evidence profile: malnutrition

Hand grip – subgroup with undernutrition

<table>
<thead>
<tr>
<th>3 randomized trials</th>
<th>serious (^1)</th>
<th>not serious</th>
<th>not serious</th>
<th>serious (^1)</th>
<th>none</th>
<th>92</th>
<th>113</th>
<th>SMD 0.26 fewer (0.54 fewer to 0.02 more)</th>
<th>LOW</th>
<th>IMPORTANT</th>
</tr>
</thead>
</table>

CI: confidence interval; MD: mean difference; RR: relative risk; SMD: standardized mean difference

- **Risk of bias:** downgraded once as information on blinding procedure was unclear in four included trials and information on incomplete data was not described in three trials.
- **Risk of bias:** downgraded once as information on allocation concealment method was unclear in two trials and information on incomplete data was unclear in two trials.
- **Risk of bias:** downgraded once as information on allocation concealment method was unclear in three trials and information on incomplete data was unclear for two included trials.
- **Risk of bias:** downgraded once as information on allocation concealment method was unclear in seven trials and analysis was not performed on an intention-to-treat principle in two trials.
- **Inconsistency:** downgraded once as substantial heterogeneity was observed in the meta-analysis: Tau\(^2\) = 4.66; Chi\(^2\) = 42.20, df = 9 (P < 0.00001). No subgroup analysis was performed and we were not able to explain the heterogeneity.
- **Risk of bias:** downgraded once as information on allocation concealment was unclear in four trials and information on incomplete data was unclear in two trials.
- **Inconsistency:** downgraded once as moderate heterogeneity was observed in the meta-analysis: Chi\(^2\) = 15.39, df = 5 (P = 0.009); I\(^2\) = 68%. No subgroup analysis was performed and we were not able to explain the heterogeneity.
- **Risk of bias:** downgraded once as allocation concealment was unclear in three trials and information on incomplete data management was unclear in two trials.
- **Inconsistency:** moderate heterogeneity: Chi\(^2\) = 6.89, df = 3 (P = 0.08); I\(^2\) = 56%; however, P value was not less than 0.05.
- **Risk of bias:** downgraded once as allocation concealment was unclear in three trials and outcome assessor was not masked in three trials.
- **Risk of bias:** downgraded once as allocation concealment was unclear in one trial and outcome assessor was not masked in another trial.
- **Imprecision:** downgraded once as small sample size was smaller than 200.
- **Risk of bias:** downgraded once as allocation concealment was unclear in two trials and outcome assessor was not masked in two trials. In on trial, analysis was not based on intention-to-treat principle.
- **Imprecision:** downgraded once as sample size was small.
GRADE table 2: Oral nutritional supplement (ONS) with or without dietary advice compared with placebo or usual care controls for older people at risk and/or undernourished (setting: hospital or long-term care)

Author: WHO systematic review team
Date: 5 November 2015 (last updated 20 November 2015)
Question: Does ONS compared with placebo, usual care or no supplement produce any benefit or harm for older people with or at risk of undernourishment?
Setting: Hospital/long-term care (n = 43)
Bibliography: (14) 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):CD003288 – this systematic review was updated by WHO in 2015

<table>
<thead>
<tr>
<th>Quality assessment</th>
<th>Number of patients</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of studies</td>
<td>Study design</td>
<td>Risk of bias</td>
<td>Inconsistency</td>
<td>Indirectness</td>
</tr>
<tr>
<td>Mortality (follow-up 10 weeks to 3 years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>43</td>
<td>randomized trials</td>
<td>serious *</td>
<td>not serious</td>
<td>not serious</td>
</tr>
</tbody>
</table>

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### ICOPE guidelines – World Health Organization

### Mortality – subgroup at risk of undernutrition

<table>
<thead>
<tr>
<th></th>
<th>randomized trials</th>
<th>serious</th>
<th>not serious</th>
<th>not serious</th>
<th>not serious</th>
<th>none</th>
<th>40/656 (6.1%)</th>
<th>39/674 (5.8%)</th>
<th>RR 1.08 (0.71 to 1.63)</th>
<th>5 more per 1000 (from 17 fewer to 36 more)</th>
<th>CRITICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MODERATE</td>
</tr>
</tbody>
</table>

### Mortality – subgroup with undernutrition

<table>
<thead>
<tr>
<th></th>
<th>randomized trials</th>
<th>serious</th>
<th>not serious</th>
<th>not serious</th>
<th>not serious</th>
<th>none</th>
<th>186/1430 (13.0%)</th>
<th>223/1436 (15.5%)</th>
<th>RR 0.84 (0.72 to 0.99)</th>
<th>25 fewer per 1000 (from 2 fewer to 43 fewer)</th>
<th>CRITICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>MODERATE</td>
</tr>
</tbody>
</table>

### Weight change (follow-up 10 days to 6 months; assessed with digital scale [kg]; self-report [n = 2], GP report [n = 1], unclear [n = 11])

<table>
<thead>
<tr>
<th></th>
<th>randomized trials</th>
<th>serious</th>
<th>not serious</th>
<th>not serious</th>
<th>not serious</th>
<th>none</th>
<th>1253</th>
<th>1248</th>
<th>—</th>
<th>MD 2.35 more (1.59 more to 3.11 more)</th>
<th>CRITICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>42</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>LOW</td>
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</table>

### Weight gain – subgroup at risk of undernutrition

<table>
<thead>
<tr>
<th></th>
<th>randomized trials</th>
<th>serious</th>
<th>not serious</th>
<th>not serious</th>
<th>not serious</th>
<th>none</th>
<th>376</th>
<th>379</th>
<th>—</th>
<th>MD 0.26 more (0.1 more to 0.41 more)</th>
<th>CRITICAL</th>
</tr>
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<tbody>
<tr>
<td>15</td>
<td></td>
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<td></td>
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<td>LOW</td>
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### Weight gain – subgroup with undernutrition

<table>
<thead>
<tr>
<th></th>
<th>randomized trials</th>
<th>serious</th>
<th>not serious</th>
<th>not serious</th>
<th>not serious</th>
<th>none</th>
<th>877</th>
<th>869</th>
<th>—</th>
<th>MD 1.8 more (1.42 more to 2.17 more)</th>
<th>CRITICAL</th>
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<tbody>
<tr>
<td>27</td>
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<td></td>
<td></td>
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</table>

### Hand grip strength (follow-up 3–6 months; assessed with handheld dynamometer; higher score = better performance)

<table>
<thead>
<tr>
<th></th>
<th>randomized trials</th>
<th>serious</th>
<th>not serious</th>
<th>not serious</th>
<th>not serious</th>
<th>none</th>
<th>445</th>
<th>485</th>
<th>—</th>
<th>SMD 0.09 more (0.08 fewer to 0.27 more)</th>
<th>IMPORTANT</th>
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</thead>
<tbody>
<tr>
<td>13</td>
<td></td>
<td></td>
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</table>

continued next page
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### Hand grip strength – subgroup at risk of undernutrition

<table>
<thead>
<tr>
<th>Trials</th>
<th>Serious trials</th>
<th>Not serious trials</th>
<th>Not serious trials</th>
<th>Not serious trials</th>
<th>None</th>
<th>246</th>
<th>264</th>
<th>SMD 0.18 more (0 to 0.35 more)</th>
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<th>IMPORTANT</th>
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<tbody>
<tr>
<td>7</td>
<td>Serious</td>
<td>Not serious</td>
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<td>Not serious</td>
<td>None</td>
<td>246</td>
<td>264</td>
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### Hand grip strength – subgroup with undernutrition

<table>
<thead>
<tr>
<th>Trials</th>
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<th>Not serious trials</th>
<th>Not serious trials</th>
<th>Not serious trials</th>
<th>None</th>
<th>199</th>
<th>221</th>
<th>SMD 0.1 (0.19 fewer to 0.2 more)</th>
<th>MODERATE</th>
<th>IMPORTANT</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>199</td>
<td>221</td>
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</table>

### Activities of daily living (ADLs) (follow-up 4–6 months; assessed with Barthel Index (higher score = better performance))

<table>
<thead>
<tr>
<th>Trials</th>
<th>Serious trials</th>
<th>Not serious trials</th>
<th>Not serious trials</th>
<th>Not serious trials</th>
<th>None</th>
<th>197</th>
<th>200</th>
<th>MD 0.09 more (0.7 fewer to 0.87 more)</th>
<th>MODERATE</th>
<th>IMPORTANT</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>197</td>
<td>200</td>
<td></td>
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</tbody>
</table>

### ADLs – subgroup at risk of undernutrition

<table>
<thead>
<tr>
<th>Trials</th>
<th>Serious trials</th>
<th>Not serious trials</th>
<th>Not serious trials</th>
<th>Not serious trials</th>
<th>None</th>
<th>115</th>
<th>128</th>
<th>MD 0.07 more (0.73 fewer to 0.87 more)</th>
<th>LOW</th>
<th>IMPORTANT</th>
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<tbody>
<tr>
<td>2</td>
<td>Serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Serious</td>
<td>None</td>
<td>115</td>
<td>128</td>
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<table>
<thead>
<tr>
<th>ADLs – subgroup with undernutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 randomized trials</td>
</tr>
</tbody>
</table>

CI: confidence interval; MD: mean difference; RR: relative risk; SMD: standardized mean difference

Full details of the trials cited in the footnotes below that were included for further analysis (17–69, 78–80) are listed sequentially on pages 25–28, References; details of the studies that were not included are listed alphabetically – references i–iv on pages 28–30.

a. Risk of bias: downgraded once as allocation was not concealed in four trials, outcome assessor was not masked in three trials and unclear in others. Further analysis was based on intention-to-treat principle in five trials.
b. Twenty-two trials that recruited older persons at risk of undernutrition were included in GRADE table 2 (17, 21, 23, 26, 28–30, 33, 39, 43, 44, 45, 54, 55, 59–63, 64, 65, 67, 79), of which five were conducted in a community setting (17, 21, 23, 26, 28).
c. Risk of bias: downgraded once as allocation concealment method was unclear in four trials, outcome assessor was not masked in three trials and unclear in others. Further analysis was based on intention-to-treat principle in five trials.
d. Thirty-four trials included undernourished older persons (18, 19, 22, 24, 25, 27, 31, 32, 34–38, 40–43, 45–53, 56–58, 64–67, 80), of which seven were conducted in a community setting (18–20, 22, 24, 25, 27).
e. Risk of bias: downgraded once as allocation was not concealed in three trials and unclear in another 13 trials. Further, outcome assessors were not masked in nine trials and procedure was unclear in other 13 trials. Only six trials adequately provided information on incomplete data.
f. Risk of bias: downgraded once as allocation concealment was unclear in 23 trials and allocation was not concealed in four trials. In 25 trials, the procedure of masking outcome assessor was unclear. Further information on incomplete data was adequately described in only 11 trials.
g. Inconsistency: downgraded once as substantial heterogeneity was observed: Tau² = 3.11; Chi² = 292.00, df = 41 (P < 0.00001); I² = 86%. Heterogeneity may be considerable due to the large I² (> 75%). No subgroup analysis was conducted to explore the heterogeneity, and we were not able to explain the heterogeneity.
h. Risk of bias: downgraded once as outcome assessor was not masked in three trials and procedure was unclear in another nine trials. Further, information on incomplete data was not described adequately in five trials, and inclusion of incomplete data in the analysis was unclear in three trials.
i. Inconsistency: downgraded once as considerable heterogeneity was observed: Chi² = 173.55, df = 14 (P < 0.00001); I² = 92%. No further subgroup analysis was conducted to explore the heterogeneity, and we were not able to explain the heterogeneity.
j. Risk of bias: downgraded once as allocation concealment was unclear in 13 trials and not concealed in another three trials. Information on incomplete data was not adequately presented in seven trials, and only one trial masked assessors in the outcome assessment.
k. Inconsistency: downgraded once as moderate heterogeneity was observed: Chi² = 63.12, df = 26 (P < 0.0001); I² = 59%. No further subgroup analysis was conducted to explore the heterogeneity, and we were not able to explain the heterogeneity.
l. Risk of bias: downgraded once as allocation concealment was unclear in six trials and the procedure for masking outcome assessor was unclear in three trials.
m. Risk of bias: downgraded once as allocation concealment was unclear in three trials, and outcome assessors were not masked in two trials. Information on incomplete outcome data or intention-to-treat was not adequately described in three trials.

Risk of bias: downgraded once as allocation concealment was unclear in three trials, and outcome assessors were not masked in three trials. In one trial, information on incomplete data was not adequately described, and in another trial, the analysis was not based on intention-to-treat principle.
o. Risk of bias: downgraded once as allocation concealment was unclear in two trials and outcome assessors were not masked in another two trials. Four trials reported incomplete data and did not perform the final analysis in intention-to-treat principle.
p. Risk of bias: downgraded once as allocation concealment was unclear and the outcome assessor was not masked in one trial.
q. Imprecision: downgraded once as the sample size was small.
r. Risk of bias: downgraded once as allocation concealment was unclear in one trial, and outcome assessors were not masked in two trials.
s. Imprecision: downgraded once as the sample size was smaller than 200 participants.
### GRADE table 3: Dietary advice compared with no advice or exercise or usual care for older people at risk of undernutrition and/or undernourished

**Author:** WHO systematic review team  
**Date:** 19 October 2015 (last updated 20 November 2015)  
**Question:** Does dietary advice compared with no advice or exercise or usual care produce any benefit or harm for older people at risk of undernutrition and/or undernourished?  
**Setting:** Primary care or community  
**Bibliography:**  

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Dietary advice</th>
<th>No advice or exercise or usual care</th>
<th>Relative (95% CI)</th>
<th>Absolute (95% CI)</th>
<th>Quality</th>
<th>Importance</th>
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<td>Mortality (follow-up 3–12 months)</td>
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<td>not serious</td>
<td>serious *</td>
<td>serious b</td>
<td>none</td>
<td>51/618 (8.3%)</td>
<td>37/674 (5.5%)</td>
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<td>Mortality – subgroup at risk of undernutrition</td>
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<tr>
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<td>not serious</td>
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<td>serious b</td>
<td>none</td>
<td>47/521 (9.0%)</td>
<td>36/577 (6.2%)</td>
<td>RR 1.45 (0.95 to 2.20)</td>
<td>28 more per 1000 (from 3 fewer to 75 more)</td>
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</table>

续表...
### Evidence profile: malnutrition

#### ICOPE guidelines – World Health Organization

### Mortality – subgroup with undernutrition

<table>
<thead>
<tr>
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<th>Randomized trials</th>
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<th>Serious a</th>
<th>None</th>
<th>4/97 (4.1%)</th>
<th>1/97 (1.0%)</th>
<th>RR 2.94 (0.48 to 17.85)</th>
<th>20 more per 1000 (from 5 fewer to 174 more)</th>
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### Weight change (follow-up 3–12 months; assessed with digital scale [kg])

<table>
<thead>
<tr>
<th>N</th>
<th>Randomized trials</th>
<th>Serious a</th>
<th>Not Serious</th>
<th>Serious a</th>
<th>Not Serious</th>
<th>None</th>
<th>662</th>
<th>705</th>
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### Weight change – subgroup at risk of undernutrition

<table>
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<th>625</th>
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### Weight change – subgroup with undernutrition

<table>
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<th>Serious h</th>
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</tbody>
</table>

CI: confidence interval; MD: mean difference; RR: relative risk.

- **a.** Indirectness: downgraded once as comparison groups were not identical.
- **b.** Imprecision: downgraded once as confidence interval for treatment effect was wide.
- **c.** Risk of bias: downgraded once as allocation concealment and the procedure for masking the outcome assessor were unclear in one trial and the outcome assessor was not masked in another trial.
- **d.** Imprecision: downgraded once as sample size of the trial was small (fewer than 200 participants).
- **e.** Risk of bias: downgraded once as allocation was not concealed in one trial and was unclear in another two trials. Information on the procedure for masking the outcome assessor was not adequately described in two trials, and information on incomplete data was unclear in three trials.
- **f.** Risk of bias: downgraded once as allocation was not concealed in two trials and was unclear in another two trials. Outcome assessors were not masked in two trials.
- **g.** Inconsistency: not downgraded as P value was not significant for Chi² test for heterogeneity: Chi² = 2.59, df = 1 (P = 0.11); I² = 61%.
- **h.** Imprecision: downgraded once as small size was small (fewer than 200 participants).
**GRADE table 4:** Mealtime interventions compared with usual care for older people with or at risk undernutrition

**Authors:** WHO systematic review team  
**Date:** October 2015 (last updated 20 November 2015)  
**Question:** Do mealtime interventions compared with dietary advice or usual care produce any benefit or harm for older persons with or at risk of undernutrition?  
**Setting:** Long-term care  
**Bibliography:**

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<tr>
<th>Number of studies</th>
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<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Number of patients</th>
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<td>118</td>
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CI: confidence interval; MD: mean difference  
a. Risk of bias: downgraded once as allocation concealment and the procedure for masking the outcome assessor were unclear in both trials.  
b. Indirectness: downgraded once as trials were conducted in distinct long-term care settings and feasibility of delivering these interventions in other settings was unclear.
Part 2: From evidence to recommendations

Summary of evidence

<table>
<thead>
<tr>
<th>Settings</th>
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<tbody>
<tr>
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<td>Oral nutrition supplement combined with dietary advice or alone</td>
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(continued next page)
### Evidence profile: malnutrition

#### ICOPE guidelines – World Health Organization

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(continued next page)
## Evidence profile: malnutrition

### Weight gain

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<th>Favours experiment MD 1.61 more (1.49 more to 1.73 more), ( P &lt; 0.01 ) MODERATE QUALITY GRADE table 4</th>
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### Older people at risk of undernutrition

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### Undernourished older people

|                      | Favours experiment RR 0.84 (0.72 to 0.99), \( P = 0.03 \) MODERATE QUALITY GRADE table 2 | No data available | No data available                                                                                 |

(continued next page)
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MD: mean difference; RR: relative risk; SMD: standardized mean difference
## Evidence-to-recommendations table

<table>
<thead>
<tr>
<th>Problem</th>
<th>Explanation</th>
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<tr>
<td>Is the problem a priority?</td>
<td>Undernutrition is a preventable and reversal condition in older people. The prevalence of undernutrition in older people living in the community ranges between 1.3% and 47.8%; it is much higher in low- and middle-income countries than in high-income countries.</td>
</tr>
<tr>
<td>Yes     Yes  No  Uncertain</td>
<td></td>
</tr>
<tr>
<td>Benefits and harms</td>
<td></td>
</tr>
<tr>
<td>Do the desirable effects outweigh the undesirable effects?</td>
<td>There is adequate, moderate-quality evidence to suggest that oral nutritional supplement (ONS) with or without dietary advice improves the nutritional status of undernourished older people. Four trials examined the benefit of ONS for undernourished older people in community settings. Data on weight gain reported as an outcome was pooled in the meta-analysis. Overall, the pooled treatment effect was in favour of the ONS group (mean difference 3.17 [2.12 to 4.21], ( P &lt; 0.01 )). In addition, 14 trials from hospital or long-term care settings that examined the benefit of ONS reported significant reductions in mortality and increased weight gain in the intervention groups compared with usual care or placebo. There is adequate, low-quality evidence to suggest that ONS with or without dietary advice may improve the nutritional status of older people at risk of undernutrition. Fifteen trials that investigated the benefit of ONS in hospital or long-term care settings reported significant improvements in body weight. A further seven trials showed a significant improvement in hand grip strength. However, trials from community settings showed no benefit of ONS for older people at risk of undernutrition in either improving body weight or reducing mortality. Outcomes related to functional status were reported in many trials. Improvements in activities of daily living were assessed in 12 studies; however, the results in only three trials achieved statistical significance. Health-related quality of life was measured in 17 studies. There was a statistically significant benefit in favour of the ONS intervention group in only two of these.</td>
</tr>
<tr>
<td>Yes     Yes  No  Uncertain</td>
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</table>
### Evidence profile: malnutrition

<table>
<thead>
<tr>
<th>Values and preferences/acceptability</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Is there important uncertainty or variability about how much people value the options?</strong></td>
<td>Undernutrition is strongly associated with multimorbidity, premature mortality, lower quality of life, increased need for institutionalization and increased health care. Older people at risk of undernutrition experience significant weight loss, which is directly linked to mortality and functional decline. Therefore, reversing weight loss through nutritional interventions has important clinical significance for health-care providers. Weight gain and improvement in functional ability are valuable clinical outcomes for older people. Reversing weight loss through nutritional interventions is pivotal to improving an older person's health.</td>
</tr>
<tr>
<td>Major variability</td>
<td>Minor variability</td>
</tr>
<tr>
<td>✓</td>
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</tr>
</tbody>
</table>

| Is the option acceptable to key stakeholders? | Adherence to ONS may be challenging: a small number of trials have reported a dislike of the taste of ONS as the main reason for participants dropping out of the studies. Nutrition experts in the GDG panel pointed out that Asians or vegetarians may not be willing to take ONS for cultural reasons. However, some older people might be willing to take the supplements in view of supply of all of their nutritional requirements. |
| Major variability | Minor variability | Uncertain |
|✓ |

(continued next page)
### Evidence profile: malnutrition

**Feasibility/resource use**

<table>
<thead>
<tr>
<th>How large are the resource requirements?</th>
<th>Explanation</th>
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<tr>
<td><strong>Major</strong></td>
<td>The majority of available studies were carried out in high-income countries. Moreover, there were few available trials (n = 10) focusing specifically on older people living in the community. This may account for the relatively modest effect sizes attained. More research is required to explore the effects of nutritional interventions other than supplementation for this specific group. In many low- and middle-income countries, however, nutritional interventions are delivered by non-specialist health-care workers for undernourished children and pregnant mothers. Based on existing practice, suitably trained non-specialist health-care workers can effectively deliver nutritional interventions to older people at risk of undernutrition or undernourished. Promoting nutritional interventions for older people will increase equity.</td>
</tr>
<tr>
<td><strong>Minor</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Uncertain</strong></td>
<td></td>
</tr>
<tr>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

**Is the option feasible to implement?**

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Uncertain</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Equity

<table>
<thead>
<tr>
<th>Would the option improve equity in health?</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Yes</strong></td>
<td>The GDG strongly believes that this recommendation will increase equity in health.</td>
</tr>
<tr>
<td><strong>No</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Uncertain</strong></td>
<td></td>
</tr>
<tr>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>
Guideline development group recommendation and remarks

<table>
<thead>
<tr>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral supplemental nutrition with dietary advice should be recommended for older people affected by undernutrition.</td>
</tr>
<tr>
<td>Quality of the evidence: Moderate</td>
</tr>
<tr>
<td>Strength of the recommendation: Strong</td>
</tr>
<tr>
<td>(No recommendation: Dietary advice [as stand-alone intervention] received no recommendation because there was limited evidence on its effectiveness among older people at risk of undernutrition or undernourished.)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The policy priority to support nutritional outcomes among older people must focus on food quality and diversity, and nutrition security.</td>
</tr>
<tr>
<td>• The nutrition supplement administered aimed to provide between an additional 97 kcal per day and a maximum additional 1200 kcal per day. There was a wide range of types of oral nutritional supplement tested in the included trials (milk, juice, yoghurt, savoury) in different formats (liquid, powder, pudding, pre-thickened) and in combination.</td>
</tr>
<tr>
<td>• The majority of trials administered nutritional supplement with 20 g protein or more per day. Many of these trials mentioned that micronutrients were included in the supplement.</td>
</tr>
<tr>
<td>• The duration of the nutritional intervention ranged from 10 days to 6 months in trials recruiting</td>
</tr>
</tbody>
</table>

(continued next page)
participants in hospital and long-term care settings. Among trials performed in community settings, duration ranged from 3 months to 18 months.

- Specially formulated supplementary foods – in ready-to-eat or in milled forms that are modified in their energy density, protein, fat or micronutrient composition to help meet the nutritional requirements of older people – should be encouraged.
- Physical, functional, psychological and social factors that predispose older people to undernutrition should be identified and remedied.
- Careful assessment of undernutrition – including functional, anthropometric, biochemical and clinical assessments – should be considered by trained health-care professionals for older people at risk from or suspected of undernutrition.
- Nutrition assessment should be an integral part of primary care for older people.
- A social environment that promotes increased food intake for older people with or at risk of undernutrition could be encouraged.
- Encouraging all older people at risk of undernutrition to consume oral nutritional supplement (particularly in liquid or powder form) may be unacceptable in some communities. Other strategies such as dietary advice or a nutritional-education programme could be considered.
- Although there is no direct evidence for the benefit of dietary advice, guidance on measures to supplement the calorific content in a normal diet should be encouraged when possible.
- The older person’s tastes and preferences should be considered when administering oral nutritional supplements to improve adherence.
- Greater research and clarity is required for the best quality and quantity of oral nutritional supplementation.
- The limited number of studies from low- and middle-income countries mean generalizability warrants consideration.
- The GDG decided not to issue a stand-alone recommendation for mealtime interventions (including family-style meals and social dining) due to the generic nature of the intervention.
References


32. Cameron ID, Kurrle SE, Uy C, Lockwood KA, Au L, Schaafsmam FG. Effectiveness of oral nutritional supplementation for older women after a fracture: rationale, design and study of the feasibility of a randomized controlled study. BMC Geriatrics. 2011;11:32.


Evidence profile: malnutrition

- World Health Organization

 ICOPE guidelines – World Health Organization

(continued next page)


59. Rabadi MH, Coar PL, Lukin, M, Lesser M, Blass JP. Intensive nutritional supplements can improve outcomes in stroke

(continued next page)
79. Weekes CE, Emery PW, Elia M. Dietary counselling and food (continued next page)
The following studies Abbott et al. to Wouters-Wesseling et al. (i–xli) were not included for further analysis.


xv 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.


Annex 1: Search terms

1. (food* or meal* or snack* or drink* or feed*).ab,ti.
2. (nutri* or diet*).ab,ti.
3. "dining".ab,ti.
4. (screening or monitoring).ab,ti.
5. (documentation or communication).ab,ti.
6. (time* or timing or pattern or style or arrangement* or environment).ab,ti.
7. (staff* or train*).ab,ti.
8. "nurs**.ab,ti.
9. (healthcare or health care).ab,ti.
10. "cater**.ab,ti.
11. (flavo?r* or taste).ab,ti.
12. (content or composition or density).ab,ti.
13. (appear* or presentation).ab,ti.
14. (size or portion or amount).ab,ti.
15. "protected meal**.ab,ti.
16. "red tray**.ab,ti.
17. "fortif**.ab,ti.
18. "supplement**.ab,ti.
19. ((supportive or nutrition* or diet*) adj3 intervention).ab,ti.
20. (assist* or help* or support*).ab,ti.
21. (add* or extra).ab,ti.
22. (alter* or chang* or new or enhance* or modif* or increas* or decreas* or improv* or reduc* or target*).ab,ti.
23. (((food* or meal* or snack* or drink* or feed*) adj3 (time* or timing or pattern or style or arrangement* or environment or (flavo?r* or taste) or (content or composition or density) or (appear* or presentation) or (size or portion or amount) or "fortif** or "supplement** or (assist* or help* or support*) or (add* or extra) or (alter* or chang* or new or enhance* or modif* or increas* or decreas* or improv* or reduc* or target*))).ab,ti.
24. ((nutri* or diet*) adj4 (content or composition or density or "fortif** or "supplement** or (add* or extra) or (alter* or chang* or new or enhance* or modif* or increas* or decreas* or improv* or reduc* or target*)))ab,ti.
25. ("dining** adj4 (time* or timing or pattern or style or arrangement* or environment or (alter* or chang* or new or enhance* or modif* or increas* or decreas* or improv* or reduc* or target*)).ab,ti.
26. ((screening or monitoring) adj4 (nutri* or diet* or (add* or extra) or (alter* or chang* or new or enhance* or modif* or increas* or decreas* or improv* or reduc* or target*)).ab,ti.
27. (document* or communication) adj4 (alter* or chang* or new or enhance* or modif* or increas* or decreas* or improv* or reduc* or target*).ab,ti.
28. ("nurs** or (healthcare or health care) or "cater** or (assist* or help* or support*) or (add* or extra) or (alter* or chang* or new or enhance* or modif* or increas* or decreas* or improv* or reduc* or target*)).ab,ti.
29. ("supplement** adj5 (add* or extra)).ab,ti.
30. ((assist* or help* or support*).ab,ti.
31. 15 or 16 or 19
32. 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
33. (low bmi or low body mass index).ab,ti.
34. (low weight or underweight or under-weight).ab,ti.
35. "maln**.ab,ti.
36. (nutritional risk or (risk adj4 maln*)).ab,ti.
37. (poor nutri* or undernourish* or under-nourish*).ab,ti.
38. (poor or inadequate or suboptimal) adj5 intake*).ab,ti.
39. exp Nutritional Status/
40. exp Nutrition Disorders/dh, th [Diet Therapy, Therapy]
41. nutrition assessment.sh.
42. nutritional support.sh.
43. nutrition policy.sh.

(continued next page)
Evidence profile: malnutrition

44. exp Malnutrition/dh, th [Diet Therapy, Therapy]
45. *diet/
46. *dietetics/
47. *food service, hospital/
48. *energy intake/
49. *food, fortified/
50. 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49
51. elderly.ab,ti.
52. exp Aged/
53. (homebound or home-bound or housebound or house-bound).ab,ti.
54. ((extended or longterm or long-term or community) adj1 care).ab,ti.
55. ((nursing or care or residential) adj1 home).ab,ti.
56. (inpatient* or hospitali?* or hospital patient*).ab,ti.
57. 51 or 52 or 53 or 54 or 55 or 56
58. randomized controlled trial.pt.
59. controlled clinical trial.pt.
60. randomi?ed.ab.
61. placebo.ab.
62. clinical trials as topic.sh.
63. randomly.ab.
64. trial.ti.
65. 58 or 59 or 60 or 61 or 62 or 63 or 64
Annex 2: PRISMA² flow diagram for systematic reviews of reviews

Records (reviews) identified through database searches of Ovid MEDLINE, EMBASE and Cochrane (n = 983) after duplicates removed

Records after duplicates removed (n = 1069)

Records screened against title and abstract (n = 983 reviews, 86 trials)

Full-text articles assessed for eligibility (n = 12 reviews, n = 29 trials)

Trials included in quantitative synthesis (meta-analysis) (n = 67)

Additional trials identified through update in 2015 (n = 86)

Records excluded, with reasons:
- reviews involved unselected or healthy older persons (n = 637)
- majority of the trials involved a younger population (under 60 years of age) (n = 123)
- conference proceedings (n = 12)

Full-text articles excluded, with reasons:
- methodological quality assessment was not performed or reported adequately (n = 7)
- included trials were cited in recent reviews (n = 2)
- trials involved older persons not at risk of malnutrition (n = 57)

² Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). For more information: http://www.prisma-statement.org

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