The impact of vitamins on physical performance, muscle strength and muscle mass in the elderly.

Systematic review on the effects of vitamins on physical performance, muscle strength and muscle mass in the elderly.
The impact of vitamins on physical performance, muscle strength and muscle mass in the elderly.

Systematic review on the effects of vitamins on physical performance, muscle strength and muscle mass in the elderly.

Bachelor thesis

Name and Student number: Thomas van Geelen (500677468)
Date: 3 June 2016
Period of thesis project: 1 February 2016/30 June 2016
Number of thesis: 2016212
Company: Amsterdam University of Applied Sciences, Lectorate Weight Management
Contact information: Dr. Meurerlaan 8 1067 SM Amsterdam The Netherlands
Supervising Lecturer: Dr. Ir. Michael Tieland
Examiner: Dr. Ir. Marielle Engberink
Version: 1
Semester: 8
Abstract

Background

Nutrition is an important denominator in the treatment and prevention of sarcopenia. To date, few systematic reviews exist with an overview of the RCT's conducted on vitamins and their role in muscle mass, muscle strength and physical performance.

Objective

The goal of this study is to explore current literature on the effect of vitamin B-11, B-12, C, D and E and its effect on muscle mass, muscle strength and physical performance in the elderly aged 60 and older. Studying the collected data might give more insight in the role that these vitamins play in the prevention and treatment of sarcopenia.

Methods

Systematic research was performed in PubMed between March 1st and April 15th. Included studies were randomized control trials (RCT), with a research population above 60 years of age, without a calorie restricted diet or diseases and illnesses that effected metabolism that studied muscle mass, muscle strength or physical performance. All dosing intervals and doses of vitamin supplementation with or without calcium, compared with placebo were included as long as only the effect of the vitamin was part of the intervention. 1324 potential studies were selected of which 6 RCT's got included in this systematic review. The search was performed by one independent reviewer.

Results

In total 6 randomized controlled trials were included in this systematic review in which 4275 individuals were involved, the mean age of the subjects was 76.3 years. One study found significant positive effects of vitamin D supplementation on muscle strength in institutionalized elderly. Three studies found a significant positive effect in secondary analysis on physical performance and muscle strength after vitamin D supplementation in those with low baseline physical performance. Vitamin D supplementation mainly effected time up and go, postural sway, chair stand, hip extensor, hip adductor, knee extension and hip flexion. No improvements in muscle mass were found after vitamin D supplementation. One study examined the effect of a combined intervention with B-11 and B-12, but found no significant results after treatment. No data was found on vitamin C and E.

Conclusion

Vitamins are poorly studied, no data was found concerning vitamin C and E and limited data of B11-12 and more research is needed. However, vitamin D seems to play a role in physical performance and muscle strength in the elderly, especially in those with low baseline performance and low vitamin D status. Despite the difficulty in analyzing the data due to various designs, populations, supplementation dose and variations in baseline vitamin D status, supplementation of 800IU or higher seems useful for most frail elderly in improving muscle function and consequently might increase self-reliance. These doses come with no adverse effects. Vitamin D supplementation might prove valuable in preventing and treating sarcopenia, however, more research is needed to confirm the effectiveness.
Preface

This thesis was written as closure of a 4 year studying period and was needed in order to obtain my bachelor of applied science in nutrition and dietetics. My knowledge obtained over the last couple of years on research and nutrition was applied in writing this systematic review and was a valuable learning experience. Working on this thesis greatly increased my knowledge about clinical nutrition and provided me with the skills for performing a literature search. My study is part of a manuscript on the effects of nutrition and exercise on physical performance, muscle strength and muscle mass in the elderly. This systematic review will focus on vitamin B-11, B-12, C, D and E and might help to better understand the effects of vitamins on these important factors that make up sarcopenia. I thank Michael Tieland and Stefan van Geelen for guidance while writing this thesis. There shared knowledge was of great value, while writing my first systematic review.
## Contents

1 Introduction .............................................................................................................. 6
2 Method ..................................................................................................................... 8
3 Results ..................................................................................................................... 12
   3.1 Physical performance ....................................................................................... 12
   3.2 Muscle strength ............................................................................................... 17
   3.3 Muscle mass ................................................................................................... 21
4 Discussion ............................................................................................................... 22
5 Reference list ......................................................................................................... 26
Appendix .................................................................................................................... 29
1 Introduction

The worldwide population is aging fast. This will have great consequences for healthcare and with that, for politics as well (1). In the Netherlands the aging of the population is also a problem, since 2013 the number of elderly in the Netherlands is growing rapidly (2).

With aging comes decrease in daily functioning. This decline in daily functioning in the elderly is partly the result of a decrease in muscle mass and power due to age, also called sarcopenia. An important factor in the decline of daily functioning and physical performance is greatly influenced by this decrease in muscle mass and power. Other physical problems that are often seen with aging people is a decline in bone density, increased fat mass and a decrease in aerobic activity (3).

The amount of people suffering from sarcopenia is increasing. In men and women between 60 to 95 years of age, 45% of the men and 30% of the women suffer from sarcopenia (4). In the elderly aged 80 years and older 60% is effected by sarcopenia (5). Due to sarcopenia, more and more elderly will need increased outside help to manage their everyday life, for example in the form of informal care or home care (3).

The exact mechanisms behind sarcopenia are not clear, but what is known is that metabolic changes, disease, nutrition and physical activity play an important factor (6). With age, muscle protein synthesis goes down and existing muscle is more easily broken down. A decline in anabolic hormones, like testosterone, growth hormone and insulinlike-growth factor-1, limits the muscle protein synthesis and a rise in interleukin-6 promotes muscle breakdown.. This results in a decrease in muscle fibers, especially type II (7).

Research has shown that resistance training in combination with a nutritional intervention has positive effects in reducing muscle loss. The importance of a good diet with the right balance in macronutrients and micronutrients is a possible weapon in reducing sarcopenia in the elderly (6).

Energy needs reduce with aging. A reason for this, is a lower metabolism and a decrease in physical activity. Although energy needs are reduced, needs for micronutrients don’t change. Research among American elderly above 65 years of age, showed that a substantial part of the researched group had insufficient vitamin A, B11, B12, C, D, E and K intake. These deficiencies can negatively affect daily functioning and general health (8).

For example. vitamin D deficiencies are thought to decrease muscle strength in elderly. Some research shows that improving vitamin D status in elderly with deficiencies and insufficiencies results in increased muscle strength and physical performance (9). Vitamin C and E have shown to reduce exercise induced oxidative stress and with that decrease the chance of muscle injury and a study on B11 and B12 showed that supplementation significantly lowered homocysteine levels (10,11). Elevated homocysteine levels are associated with decreased physical performance in the elderly (12). As such, these vitamins might prove valuable in treating and preventing sarcopenia.

Verlaan et al (13) studied the nutrient intake of a group of sarcopenia patients and a control group without sarcopenic complications. Both groups had equal energy intakes, nutrient intake however was different. The nutrient intake of the intervention group had less protein (-6%), vitamin D (-38%), vitamin B-12 (-22%), magnesium (-6%), phosphorus (-5%) and selenium (-2%). However intake in both groups was different, only B-12 serum concentrations were lower (-15%) in the intervention group (13).
Until now, not much research has been done concerning the role of vitamins in the prevention and treatment of sarcopenia. Also, the existing literature provides equivocal advice on the prevention and treatment of sarcopenia. This systematic review will give more insight on the effect of vitamin B-11, B-12, C, D en E on muscle mass, muscle strength and physical performance in the elderly aged 60 years and older. Improving vitamin status in this group might improve muscle mass, muscle strength and physical performance and with that, lower prevalence and improve treatment of sarcopenia.
2 Method

Research question

The main research question for this systematic review was formulated as followed:

- What is the impact of vitamin B-11, B-12, C, D and E on muscle mass, muscle strength and physical performance on the elderly aged 60 years and older?

To answer the main research question several sub questions were articulated:

- What is the impact of vitamin B-11, B-12, C, D and E on physical performance on the elderly aged 60 years or older?
- What is the impact of vitamin B-11, B-12, C, D and E on muscle strength on the elderly aged 60 years or older?
- What is the impact of vitamin B-11, B-12, C, D and E on muscle mass on the elderly aged 60 years or older?

Search protocol

For this systematic review PubMed was searched for literature between 1st of March and April 15th. This systematic review will study the existing literature. Research will focus on the effect of vitamin B-11, B-12, C, D and E and its effect on muscle mass, muscle strength and physical performance in the elderly population. A detailed systematic search was performed to identify all studies done between February 2006 and February 2016 using a search string (appendix 1). The PICO process (14) was used to compose a search string, only population, intervention and outcome (appendix 2) were filled in for composing the search. Other studies with comparable populations, interventions and outcomes were checked in advance for additional search terms to add to the search string and inclusion criteria. This search string was entered into PUBMED using MESH-terms. The search gave 1324 hits, the hits were individually assessed based first on title (n=1324), abstract (n=52) and eventually full text (n=12). Citation chaining (15) (n=0) was used to assess reference lists of included studies.

Study selection

One reviewer examined all titles, abstracts and full-text to determine whether the study met the inclusion criteria (table 1). All studies that were not randomized controlled trials, studies that did not have a control group, animal studies and studies that had an intervention of multiple nutritional supplements that did not include the selected vitamins were excluded. Hits were screened by subject, research population, study design and age using the inclusion and exclusion criteria that were made prior to the search.
Assessment of risk bias

One reviewer assessed all articles and tested all included studies using a quality research tool for quantitative studies (16)(appendix 3). This tool screened the studies for possible bias and rating them either strong, moderate or weak. These ratings were used in assessing the value of each study in the discussion. The tool used 6 topics for rating the study.

- Selection bias
- Study design
- Confounders
- Blinding
- Data collection
- Withdrawals and drop-outs

Each topic consists of several questions, after finishing each topic the section gets rated strong, moderate or weak. If no topics get rated weak, the study gets rated strong, if one topic gets rated weak then the study gets moderate quality, if two or more topics are rated weak, the study is also rated weak. All included studies were rated strong.

Eligibility criteria

The study will include randomized controlled trials from February 2006 until February 2016. No minimum was set for the duration of the study. There will be searched for studies that involve at least one of the named vitamins in the intervention. If the intervention involves other macro-or micronutrients or exercise the study will be excluded. The target population are the healthy and frail elderly aged 60 years and older without a calorie restriction or diseases and illnesses that affect metabolism. For all in- and exclusion criteria see table 1.
<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Muscle mass</strong></td>
<td>• Dual-energy X-ray Absorptiometry (DXA)</td>
</tr>
<tr>
<td></td>
<td>• Bioelectrical Impedance analysis (BIA)</td>
</tr>
<tr>
<td></td>
<td>• Dual Photon Absorptiometry (DPA)</td>
</tr>
<tr>
<td></td>
<td>• Computer tomography scan (CT-scan)</td>
</tr>
<tr>
<td></td>
<td>• BODPOD</td>
</tr>
<tr>
<td></td>
<td>• Mid Arm Circumference (MAC)</td>
</tr>
<tr>
<td></td>
<td>• Skinfold measurements</td>
</tr>
<tr>
<td><strong>Muscle Strength</strong></td>
<td>• Handgrip strength</td>
</tr>
<tr>
<td></td>
<td>• Knee extension</td>
</tr>
<tr>
<td></td>
<td>• Knee flexion</td>
</tr>
<tr>
<td></td>
<td>• Leg press</td>
</tr>
<tr>
<td></td>
<td>• Leg extension</td>
</tr>
<tr>
<td></td>
<td>• Hip adduction</td>
</tr>
<tr>
<td></td>
<td>• Hip abduction</td>
</tr>
<tr>
<td></td>
<td>• Hip flexion</td>
</tr>
<tr>
<td></td>
<td>• Hip extension</td>
</tr>
<tr>
<td></td>
<td>• Elastic band</td>
</tr>
<tr>
<td></td>
<td>• Dumbbells</td>
</tr>
<tr>
<td><strong>Physical function</strong></td>
<td>• Walking tests (MWT)</td>
</tr>
<tr>
<td></td>
<td>• Short Physical Performance Battery (SPPB)</td>
</tr>
<tr>
<td></td>
<td>• Time up and go (TUAG)</td>
</tr>
<tr>
<td></td>
<td>• Chair stand test (CST)</td>
</tr>
<tr>
<td></td>
<td>• Gait speed test (GST)</td>
</tr>
<tr>
<td></td>
<td>• 400m walking test</td>
</tr>
<tr>
<td></td>
<td>• Balance tests</td>
</tr>
<tr>
<td></td>
<td>• Postural sway</td>
</tr>
<tr>
<td><strong>Vitamins</strong></td>
<td>• Vitamin B-11</td>
</tr>
<tr>
<td></td>
<td>• Vitamin B-12</td>
</tr>
<tr>
<td></td>
<td>• Vitamin C</td>
</tr>
<tr>
<td></td>
<td>• Vitamin D</td>
</tr>
<tr>
<td></td>
<td>• Vitamin E</td>
</tr>
<tr>
<td><strong>Research population</strong></td>
<td>Healthy and frail elderly aged 60 years or older</td>
</tr>
<tr>
<td><strong>Study design</strong></td>
<td>• Randomized controlled trials</td>
</tr>
<tr>
<td></td>
<td>• The control group must be comparable to treated group with exception of the included vitamins</td>
</tr>
<tr>
<td></td>
<td>• all durations of interventions</td>
</tr>
<tr>
<td></td>
<td>• Research population with negative energy balance or disease effecting metabolism</td>
</tr>
<tr>
<td></td>
<td>• older then February2006</td>
</tr>
<tr>
<td></td>
<td>• Exercise part of the intervention</td>
</tr>
</tbody>
</table>
Data extraction

The data extraction was done by one independent reviewer. The different chapters were defined by the general outcome measures, physical performance, muscle strength and muscle mass. The articles included in this review had the following data extracted; Author, year, study design, sample size (%female), age mean, study duration, researched vitamin, measurements, outcome, effect size and study quality. Studies were included if the right measurements were used. For muscle mass DPA, BIA, BODPOD, DEXA, CT-scan, MRI were included, knee extension, knee flexion, leg extension leg press, hip adduction, hip abduction, hip flexion, hip extension and hand grip strength for muscle strength, for physical performance walking speed tests, time up and go, gait speed, balance tests, postural sway, short physical performance battery and chair stand test were used.
3 Results

Figure 1 shows the flowchart with the articles found in the search on PubMed, with the included and excluded articles. After screening was complete, a total of six studies were included of which all were randomized control trials. In total one article reported on muscle mass, five about muscle strength and five about physical function. Vitamin B-11 and B-12 were researched in one study, vitamin D in five and no data was found on vitamin C and E. In total 4275 individuals were involved in this systematic review. The mean age of the subject in this review was 76.3. Two studies (17,18) only included women, the other studies were mixed groups.

### Figure 1: Flowchart of literature search

#### 3.1 Physical performance

**B-11 and B-12**

One study focused on the combined effect of vitamin B-11 and B-12. Swart et al (19) investigated 2919 subjects on the combined effect of B-11 and B-12 supplementation on physical performance. Both groups declined in physical performance over the 2-year study period. Results did not show any significant differences in physical performance between control and intervention groups.

**Vitamin D**

Out of 5 studies (17,18,19,20,21) that focused on vitamins and its effect on physical function, four focused (17,18,20,21) on the effect of either vitamin D2 (17) or D3 (18,20,21). Two studies (20,21) focused on both sexes, two (17,18) on just women investigating 1300 subjects total. None of the studies showed significant
differences between control and intervention groups. Two studies (17,20) showed significant improvements in intervention groups in subgroups.

In the two studies that investigated both sexes, 312 subjects were investigated. One studied the effect of vitamin D supplementation with D3 or placebo and its effect on a population with a deficiency (20). The other study did not look at vitamin D baseline values for inclusion, and looked at the difference between a high and lower dose of vitamin D3 supplementation (2).

Lips et al (20) studied the effect of weekly oral 8400UI cholecalciferol supplementation on physical performance in elderly 70 years and older, who had vitamin D insufficiency. Measurements used for assessing physical function were postural sway and SPPB. All though serum concentrations of vitamin D almost doubled over the 16 weeks, no changes were measured for mediolateral sway, nor in the SPPB. However, in post hoc analysis, patients in the intervention group with high baseline mediolateral sway (≥0.46 and <0.46 cm) improved significantly compared to placebo on the balance test as seen in figure 2. These improvements were not noted in the group with relatively low mediolateral sway.

Lagari et al (21) did not have a control group without vitamin D3 supplementation, instead the control group was given 400UI of vitamin D3 and the intervention group 2000UI daily. After 6 months of supplementation with vitamin D3 with either 400IU or 2000IU no statistically significant changes were noted in physical performance between groups. In the groups with low baseline gait speed there was a significant correlation (P=0,033) between increased serum vitamin D3 levels and improved chair stands. These improvements were not significantly greater in the group treated with 2000IU then 400IU of vitamin D3.
Two studies (17,18) were focused on vitamin D2 and D3 and physical function in 988 women. One group consisting out of postmenopausal women above 70 years old and the effect of D3 supplementation, the other on women with vitamin D2 insufficiency aged 70-90 years old.

Zhu et all (17) studied women with vitamin D insufficiency and the effect of vitamin D2 on physical performance using TUAG, this showed no difference between the control and intervention groups. Both groups were daily given 1000mg calcium and the intervention group was also supplemented with 1000IU Vitamin D2. Both groups showed significant improvements in TUAG, however no changes were found between the groups. When both groups were grouped by tertile and adjusted for baseline age and vitamin D2 serum concentration, the lowest tertile in the intervention group showed significant performance improvements in the TUAG as shown in figure 3.

In Glendennir et al study (18) on postmenopausal women, participants were either given 3 capsules calcium and placebo or calcium and a 150000IU cholecalciferol (D3) every 3 months for a period of 9 months. No changes in TUAG between control and intervention group were noted at any of the 3 monthly intervals.

**Vitamin C and E**

No data was available concerning the effect of vitamin C and E on physical performance in the elderly.

*Figure 3: Intervention and control, grouped by baseline TUAG*
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Type of study</th>
<th>Sample size (% female)</th>
<th>Age mean (SD)</th>
<th>Study duration (months)</th>
<th>Nutrient</th>
<th>Measure -ment</th>
<th>Outcome</th>
<th>Effect size</th>
<th>Study quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lips et al (20)</td>
<td>2010</td>
<td>RCT</td>
<td>226(%)</td>
<td>78,1 (SD 6,4)</td>
<td>4</td>
<td>D3 (oral)</td>
<td>SPPB, Postural sway</td>
<td>SPPB</td>
<td>P= 0,162 / postural sway P= N.A</td>
<td>N.A strong</td>
</tr>
<tr>
<td>Post hoc Lips (20)</td>
<td>2010</td>
<td>C= high body sway / I=high body sway</td>
<td>31</td>
<td>N.A</td>
<td>4</td>
<td>D3 (oral)</td>
<td>Postural sway</td>
<td>P=0.047</td>
<td>N.A</td>
<td></td>
</tr>
<tr>
<td>Zhu et al (17)</td>
<td>2010</td>
<td>RCT</td>
<td>302 (100%)</td>
<td>76,9 (SD 4,5)</td>
<td>12</td>
<td>D2 (oral)</td>
<td>TUAG</td>
<td>P=&gt;0,05</td>
<td>TUAG: 17,5%</td>
<td>strong</td>
</tr>
<tr>
<td>Zhu (17) secondary analysis</td>
<td>2010</td>
<td>C= lowest tertile / I= lowest tertile</td>
<td>N.A</td>
<td>N.A</td>
<td>12</td>
<td>D2 (oral)</td>
<td>TUAG</td>
<td>P= 0,02</td>
<td>TUAG: 17,5%</td>
<td></td>
</tr>
<tr>
<td>Lagari (21)</td>
<td>2013</td>
<td>RCT</td>
<td>86 (83%)</td>
<td>73.4 (SD 6.4)</td>
<td>6</td>
<td>D3 (oral)</td>
<td>4MWT, Single leg balance, CST</td>
<td>P=&gt;0,05</td>
<td>N.A</td>
<td>strong</td>
</tr>
<tr>
<td>Glendenning et al (18)</td>
<td>2012</td>
<td>RCT</td>
<td>686 (100%)</td>
<td>76,7 (SD 4,1)</td>
<td>9</td>
<td>D3 (oral)</td>
<td>TUAG</td>
<td>P=&gt;0,93</td>
<td>N.A</td>
<td>strong</td>
</tr>
<tr>
<td>Swart et al (19)</td>
<td>2015</td>
<td>RCT C= 600IU cholecalciferol + placebo / I= 400ug B-11 + 500ug B-12 + 600IU cholecalciferol</td>
<td>2919 (50,4%)</td>
<td>74,1 (SD 6,5)</td>
<td>24</td>
<td>B-11, B-12 (oral)</td>
<td>6MWT, CST, tandem stand</td>
<td>6MWT P= 0,08/ CST= P= 0,39 /tandem stand P= 0,43</td>
<td>N.A</td>
<td>strong</td>
</tr>
</tbody>
</table>

*SD = standard deviation; NA = not available; C= control group; I = intervention group*
3.2 Muscle strength

B-11 and B-12

One study focused on vitamin B-11 and B-12. Swart et al (19) investigated 2919 subjects on the combined effect of B-11 and B-12 supplementation on muscle strength using handgrip strength to measure changes. Both groups declined in muscle strength over the 2-year study period. Results did not show any significant differences in muscle strength between control and intervention groups.

Vitamin D

Out of 5 studies (17,18,19,21,22) that focused on vitamins and its effect on muscle strength, four focused (18,20,21,22) on the effect of either vitamin D2 (17) or D3 (17,21,22). Two studies (21,22) focused on both sexes, two (17,18) on just women, investigating 1130 subjects total. Moreiro et al (22) showed significant improvements in lower limb muscle strength after either vitamin D3 supplementation, Zhu et al (17) showed significant improvements on secondary analysis.

In the 2 studies that investigated both sexes, 142 subjects were investigated. One studied the effect of vitamin D supplementation with D3 on lower limb muscle strength (22). The other study did not look at vitamin D baseline values for inclusion, and looked at the difference between a high and lower dose of vitamin D3 supplementation on handgrip strength (21).

Moreiro-Pfrimer et al (22) found significant improvements in knee and hip strength after monthly supplementation of 150000UI D3 in the first 2 months and 90000UI in the following 4 months. Lagari et al (21) found no difference in changes in handgrip strength with either 400UI or 2000UI of vitamin D3 supplementation.

Two studies (17,18) were focused on vitamin D2 and D3 and physical function in 988 women. One group consisting out of postmenopausal women above 70 years old and the effect of D3 supplementation, the other on women with vitamin D2 insufficiency aged 70-90 years old.

Zhu et al (17) concentrated on women with vitamin D2 insufficiency and the effect of supplementation on muscle strength. No differences were noted between the placebo and intervention group. Both groups were daily given 1000mg calcium and the intervention group was also supplemented with 1000IU Vitamin D2. Both groups improved significant in lower body muscle strength, however no changes were found between the groups. When both groups were grouped by tertile and adjusted for baseline age and vitamin D2 serum concentration, the lowest tertile in the intervention group showed significant improvements in hip adduction and hip extension strength as shown in figure 4.
Glendennir et al (18) study on postmenopausal women, participants were either given 3 capsules calcium and placebo or calcium and a 15000IU cholecalciferol (D3) every 3 months for a period of 9 months. No changes in handgrip strength were noted after the 9 month intervention period.

**Vitamin C and E**

The search for this review found no data on the relation between C and E on muscle strength in the elderly.

---

**Table:**

<table>
<thead>
<tr>
<th>Tertile of Strength (kg)</th>
<th>Vitamin D</th>
<th>Placebo</th>
<th>% Difference in Change (Vitamin D–Placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hip extensor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowest (≤ 11)</td>
<td>5.2 (0.7)</td>
<td>3.1 (0.6)</td>
<td>22.6 (3.5)*</td>
</tr>
<tr>
<td>Middle (12–15)</td>
<td>3.5 (0.6)</td>
<td>4.3 (0.7)</td>
<td>–38 (5.0)</td>
</tr>
<tr>
<td>Highest (≥ 16)</td>
<td>0.1 (0.7)</td>
<td>0.7 (0.8)</td>
<td>–11 (5.1)</td>
</tr>
<tr>
<td><strong>Hip adductor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowest (≤ 12)</td>
<td>3.4 (0.5)</td>
<td>2.1 (0.6)</td>
<td>13.5 (6.7)*</td>
</tr>
<tr>
<td>Middle (13–15)</td>
<td>2.2 (0.5)</td>
<td>3.2 (0.5)</td>
<td>–58 (4.5)</td>
</tr>
<tr>
<td>Highest (≥ 17)</td>
<td>–0.4 (0.6)</td>
<td>–0.3 (0.6)</td>
<td>–92 (4.2)</td>
</tr>
</tbody>
</table>

*The increase in strength was significantly greater in the vitamin D group than in the placebo group in the same tertile, P<.05.*

*Figure 4: Intervention and control, grouped by baseline hip strength.*
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Type of study</th>
<th>Sample size (% female)</th>
<th>Age mean (SD)</th>
<th>Study duration (months)</th>
<th>Nutrient</th>
<th>Measurement</th>
<th>Outcome</th>
<th>Effect size</th>
<th>Study quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhu et al (17)</td>
<td>2010</td>
<td>RCT</td>
<td>302 (100%)</td>
<td>76.9 (SD 4.5)</td>
<td>12</td>
<td>D2 (oral)</td>
<td>Hip extensor, hip Abductor</td>
<td>P =&gt;0.05</td>
<td>N.A</td>
<td>strong</td>
</tr>
<tr>
<td>Zhu (17) secondary analysis</td>
<td>2010</td>
<td>C= lowest tertile I= lowest tertile</td>
<td>N.A</td>
<td>N.A</td>
<td>12</td>
<td>D2</td>
<td>Hip extensor, Hip Abductor</td>
<td>Hip extensor: P=0.05 Hip adductor: 0.048</td>
<td>N.A</td>
<td>strong</td>
</tr>
<tr>
<td>Lagari et al (21)</td>
<td>2013</td>
<td>RCT</td>
<td>86 (83%)</td>
<td>73.4 (SD 6.4)</td>
<td>6</td>
<td>D3 (oral)</td>
<td>HGS</td>
<td>P =&gt;0.05</td>
<td>N.A</td>
<td>strong</td>
</tr>
<tr>
<td>Glendenning et al (18)</td>
<td>2012</td>
<td>RCT</td>
<td>686 (100%)</td>
<td>76.7 (SD 4.1)</td>
<td>9</td>
<td>D3 (oral)</td>
<td>HGS</td>
<td>P =&gt;0.93</td>
<td>N.A</td>
<td>strong</td>
</tr>
<tr>
<td>Study (Ref)</td>
<td>Year</td>
<td>Design</td>
<td>C Group</td>
<td>I Group</td>
<td>Duration</td>
<td>n</td>
<td>Treatment</td>
<td>Outcome Measure</td>
<td>p Value</td>
<td>Effect Size</td>
</tr>
<tr>
<td>------------</td>
<td>------</td>
<td>--------</td>
<td>---------</td>
<td>---------</td>
<td>----------</td>
<td>---</td>
<td>-----------</td>
<td>-----------------</td>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>Moreiro-Phrimer et al (22)</td>
<td>2009</td>
<td>RCT</td>
<td>C=1000mg Ca + placebo / I=1000mg Ca + cholecalciferol (15000IU for 2 months, then 9000IU for 4 months (every month))</td>
<td>56 (79%)</td>
<td>6</td>
<td>D3 (oral)</td>
<td>Knee extension, hip flexion</td>
<td>&lt;0.001 / Hip flexion</td>
<td>&lt;0.0007</td>
<td>strong</td>
</tr>
<tr>
<td>Swart et al (19)</td>
<td>2015</td>
<td>RCT</td>
<td>C=600IU cholecalciferol + placebo / I=400ug B-11 + 500ug B-12 + 600IU cholecalciferol</td>
<td>2919 (50,4%)</td>
<td>24</td>
<td>B-11, B-12 (oral)</td>
<td>HGS</td>
<td>&gt;0.71</td>
<td>N.A</td>
<td>strong</td>
</tr>
</tbody>
</table>

SD = standard deviation; NA = not available; C = control group; I = intervention group
3.3 Muscle mass

Vitamin D

Lagari et al (21) reported on the effect of cholecalciferol (D3) and its effect on muscle mass. The study investigated 86 individuals on the effect of vitamin D3 and its role in physical performance in the elderly. A DXA scan was used to measure changes in total lean body mass, skeletal muscle mass, legs and arms. No significant changes in muscle mass were observed before and after treating the groups with either 400UI or 2000UI of vitamin D3.

B-11, B-12, Vitamin C and E

The search for this review found no data on the relation between folate, B-12, C or E on muscle mass in the elderly.

Table 4: Characteristics of studies on muscle mass

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Type of study</th>
<th>Sample size (% female)</th>
<th>Age mean (SD)</th>
<th>Study duration (months)</th>
<th>Nutrient</th>
<th>Measurement</th>
<th>Outcome</th>
<th>Effect size</th>
<th>Study quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lagari et al (21)</td>
<td>2013</td>
<td>RCT C=400UI cholecalciferol/ I=2000UI cholecalciferol</td>
<td>86 (83%)</td>
<td>73.4 (SD 6.4)</td>
<td>6</td>
<td>D3 (oral)</td>
<td>DXA</td>
<td>P=&gt;0.05</td>
<td>N.A</td>
<td>strong</td>
</tr>
</tbody>
</table>

SD = standard deviation; NA = not available; C= control group; I = intervention group
4 Discussion

For this review 6 randomized controlled trials (RCT) were included on the effect of vitamin B-11, B-12 and D on physical performance, muscle strength and muscle mass in the elderly aged 60 years and older. Five of these studied the effect of vitamin D and one studied the effect of vitamin B-11 and B-12, no studies were found on the effect of vitamin C or E. The study (19) that reported on vitamin B-11 and B-12 supplementation found no significant improvements after supplementation. Divergent results were observed in the RCT’s on vitamin D included in this study. Although, the findings of these studies suggest a possible effect of vitamin D on physical performance and muscle strength, only one study (22) reported significant improvements after primary analyses – i.e. in knee extension and hip flexion after vitamin D supplementation.

This systematic review has several strengths and limitations. An important limitation of this study is the lack of a peer reviewer, giving a second opinion. Even though a systematic search method was used this increases the chance of bias by reducing objectivity and accuracy. Another limitation of this study is the low number of studies included, with only one reporting on muscle mass. This might be due to not including enough significant measurements that are used to assess muscle mass. However, the included measurements were chosen because they give the most accurate results and with that give high quality data. Also for vitamin C and E no data was found. As the decision was made to only include RCT’s that were no older than 10 years, this limited the amount of studies applicable and might explain the lack of studies on vitamin C and E. The reason for initially choosing RCT’s is the high evidence value of these studies. Other elements that should be taken into account when reading, is that a large part of the study population consists of women and vitamin D dosing is done at different time intervals (e.g. daily, weekly, monthly), divergent baseline serum vitamin D, and disparate outcome measures. Moreover, only one of the included studies used vitamin D2 for supplementation. However, a recent study (23) showed that vitamin D2 supplementation is as effective at raising serum 25(OH)D concentration, which suggests, that making comparisons between vitamin D2 and D3 supplementation is possible. Although limited data was collected on the elderly due to the strict inclusion criteria, this age group represents the population that is most effected by sarcopenia. It is in this population in which sarcopenia related complications start to get more severe. Furthermore, to limit confounders, studies with a negative energy intake and diseases that effected metabolic rate were excluded, because of their possible effect of muscle metabolism. This will make the data more applicable to the healthy and frail elderly. Also, the healthy elderly are more likely to experience sarcopenia related problems, due to reaching higher age without the adverse effect of other diseases.

Based on the limited amount of included studies on vitamin D and the mixed results, it is hard to make any conclusions on the overall effectivity of vitamin D supplementation. However, some suggestions can be made. While, only one study found significant results between control and intervention group, three of the other studies (17,20,21) found significant improvements in subgroups on physical performance and muscle strength in secondary analysis. Zhu et al (17) suggests a correlation between baseline muscle strength and performance in the effectiveness of D2 supplementation. When the control and intervention group were compared in the lowest tertile of either TUAG, knee extension and hip adduction, significant improvements were found in the intervention group. Lagari et al (21) noted that in the tertile with the lowest baseline gait speed, a significant correlation between increased serum vitamin D3 levels and improved chair stands was observed. Lips et al (20) found that when control and intervention groups were divided by high and low mediolateral sway, the intervention group improved significantly in the group with high mediolateral sway. These findings all suggest that vitamin D supplementation has greater effect on individuals with low baseline strength and/or physical performance.
This might explain why Moreiro-Phrimer (22) was the only one getting significant results in the primary analysis between control and intervention group - and other studies (17,20,21) only in those with low physical performance - since this study is the only one studying institutionalized elderly. Research (24) shows that institutionalized elderly, compared to those living at home, have significantly lower mobility, balance and physical performance. So possibly, the elderly studied by Moreiro-Phrimer fell in the category with relatively low physical performance and strength and therefore were more likely to get significant improvements in the intervention.

Another point to consider is that serum 25(OH)D concentration before and after intervention diverges between studies. Tieland et al (25) found that low vitamin D status is associated with reduced muscle mass and impaired physical performance in the frail elderly. The WHO defines vitamin D serum concentration lower then 50nmol/l as deficient and a concentration lower then 75nmol/l insufficient. This value is based on the finding that serum parathyroid hormone (PTH), which is inversely related to serum 25(OH)D, increases as serum 25(OH)D increases and reaches a plateau at a serum 25(OH)D of approximately 30ng/ml (75 nmol/l) (26). Values above 75nmol/l minimize the negative effect of PTH on muscle mass, strength and bone loss (32, 33). Serum 25(OH)D rise was greatest in Moreiro-Phrimer (22) and rose from being deficient to within the normal range. Two of the studies (17,20) that also had significant improvements in secondary analysis also improved there serum 25(OH)D from being deficient to insufficient. Lagari et al (21) found that in those with low baseline gate speed, the increase in chair stand was correlated to the increase in serum 25(OH)D. In this study 37% of the participants were also deficient at baseline, while in Glendennin et al (18) study 94% of the population had a 25(OH)D concentration of 50nmol/l or higher. It’s possible that the groups in the study population (17,20,21,22) that were deficient or insufficient at baseline benefited more from both the rise in serum 25(OH)D (25) and the reduction of PTH (32), then those with high baseline values. Jansen et al (29) found that vitamin D supplementation in the vitamin D deficient improved muscle strength, walking distance and functional ability and resulted in a reduction of falls. On the contrary, in the healthy elderly strength declined with age and was not prevented by vitamin D supplementation (29).

Also, Lagari et al (21) and Glendinnin et al (18) had the highest baseline serum 25(OH)D and were respectively considerate within normal range and insufficient. The rise in serum 25(OH)D was lowest in these studies even though dosing was higher than in Zhu et al (17) and Lips et al (20) studies. For example, Zhu et al (17) intervention group went from 45nmol/l to 60nmol with a dose of 1000UI vitamin D daily, Lagari et al (21) intervention group went from 85nmol to 97.5 at a dose of 2000UI daily. This might indicate that increasing serum 25(OH)D needs higher vitamin D supplementation to attain improvements when serum values get higher.

It has been suggested that vitamin D influences muscle strength, but also other muscle functions such as muscle power and muscle contraction speed, that influence physical performance. Aside from these muscle functions, vitamin D also affects neuromuscular control and neural coordination and there is growing evidence to support that vitamin D also has a neurotrophic effect (30). For example, vitamin D deficiency has been associated with reduction of nerve conduction. With vitamin D acting as a neurosteroid, possible improvements in nerve conduction and with that, in balance could be achieved through supplementation (31).

Supplementation of vitamin D is effective at raising 25(OH)D status (26). Although this study found mixed results on vitamin D supplementation and its effect on physical performance and muscle strength in the elderly, other non-RCT studies found a positive correlation between these factors (25). Since 25(OH)D status is low in the frail and elderly population supplementation might help improve muscle strength and physical performance (25). Vitamin D serum concentration lower than 50nmol/l are considered deficient and a concentration lower then 75nmol/l insufficient. The International Osteoporosis Foundation recently gave recommendations on vitamin D supplementation to reach these serum concentration of 75nmol/l, these varied greatly from 800UI up
to 2000UI (32). Intake was adjusted upwards in individuals with limited sun exposure, obesity, osteoporosis, malabsorption and non-European populations with high risk of vitamin D deficiency living in Europe (32).

While most recommendations for serum 25(OH)D concentrations are based on the plateau of PTH at 75nmol/l, a recent study suggests that this recommendation might be too low (33). This study on 25(OH)D serum concentrations in the elderly suggests that this cut off point is not fixed, but increases with age. They found that PTH went up in concentration lower then 36,7ng/ml (92nmol/l) in men, but failed to reach plateau for women. Also PTH was consistently higher in the older individuals partaking in the study. This suggests that vitamin D requirements go up with age as PTH increases, with a higher intake in women needed to minimize the effect of PTH (33). Elderly with low serum 25(OH)D and high concentration of PTH are more likely to experience sarcopenia related problems (27).

No apparent effect of vitamin B-11 and B-12 supplementation on physical performance, muscle strength and muscle mass was found in this large RCT (5). The study included elderly with raised homocysteine levels, because elevated homocysteine levels are associated with decline in physical performance in the elderly and is often seen in those with B-6, B-11 and B-12 deficiency (12,19). Therefore one could hypothesize that treatment would be most effective in this population. No results were found after 2 years of supplementation, but in the group of elderly aged 80 years and older, there was a close to significant delay in decline in physical performance in the intervention group (19). Leverin et al (12) found the same results on physical performance after 4 months of supplementation of vitamin B-6, B-11 and B-12. They did find a correlation between increased levels of homocysteine and decreased physical performance (12). These RCT’s (12,19) studied a large population (n=3125) and found no improvements in strength and physical performance. Therefore based on this evidence there is little reason to suspect improvements in physical performance, muscle strength and muscle mass with B-11 and B-12 supplementation in the elderly. More research could be done on the effect of vitamin B-11 and B-12 in the elderly aged above 80.

No RCT’s were found on vitamin C and E, though some research points towards a possible positive effects of supplementation. A study by Richard et al (34) suggests that there is possible benefit in acute ascorbic acid supplementation in the elderly. In this study ascorbic acid increased hand grip strength significantly by increasing muscle blood flow and VO2 during exercise by local vasodilation. Saito et al also found significant correlation between serum Vitamin C and performance on handgrip strength, standing on one leg with eyes open and on walking speed in elderly women (35). On the effect of supplementation of vitamin E and physical performance, muscle strength and muscle mass in the elderly no data was found after manual search. Some research was found on physical performance and vitamin E supplementation. Takanami et al (36) studied the effect of vitamin E supplementation on endurance exercise. They hypothesized that vitamin E during exercise prevents oxidative damage and therefor contributes to preventing exercise-induced peroxidation. Exercise promotes the production of oxidized low density lipoproteins (LDL) which plays and important role in the initiation and progress of atherosclerosis. Although the quality of these studies is low it might point towards possible benefits of vitamin C supplementation on physical performance and muscle strength in the elderly, but quality studies should be performed before these assumptions are transformed into recommendations. For vitamin E more research with an elderly population is needed before any suggestions towards benefits on physical performance, muscle strength and muscle mass can be made.
In future research, some suggestions can be made to get a better idea of the actual effectivity of vitamin D. More high quality clinical trials in men and women would make a great contribution to the knowledge about the effect of vitamin D supplementation. This differentiation seems important because supplementation doses seem to differ for both sexes. Research on vitamin D and its effect on physical performance, muscle strength and muscle mass in those with low baseline physical performance and muscle strength would also be interesting, since most studies found the highest effect in this population (9,17,20,21). Most studies that research subgroups focus on vitamin D deficient elderly, while some evidence (9,17,20,21) suggest that baseline physical performance seems a better indication whether vitamin D supplementation will work. In addition further research on the effect of dosing intervals would give more insight in the best way of supplementing vitamin D to raise serum 25(OH)D. For example, giving the same respective dose with different time intervals (daily, weekly, monthly). Lastly the effect of PTH suppression with vitamin D supplementation by age groups should be studied, since it seems that more vitamin D is needed to suppress PTH as age increases (33).

Based on the studies included in this research a better vitamin D status might improve physical performance and muscle strength in the frail elderly and with that increase quality of life, due to improved self-reliance. For vitamins B-11 and B-12 there was no evidence to support the positive effect of supplementation on physical performance, muscle strength and muscle mass in the elderly, for vitamin C and E no RCT’s were found. More research is needed to confirm whether supplementation with these vitamins could delay loss of physical performance, muscle strength and muscle mass, and with that, delay sarcopenia.

**Recommendations**

In this systematic review the lack of consistent outcomes and many variables affecting intake make it hard to combine the data and draw conclusions and with that give a specific evidence-based recommendations for clinical practice. All studies were rated strong which makes it hard to differentiate on that subject. Although there isn’t enough consistent proof for any specific numbers towards vitamin D supplementation, toxicity of vitamin D only occurs in very high serum concentrations. A first sign of vitamin D toxicity is hypercalcemia, but this is only seen at serum 25(OH)D concentrations of 220nmol/l or higher. Doses up to at least 10000UI daily can be taken without any adverse effects (37). This suggests that vitamin D supplementation is very safe in the doses needed to reach suggested levels. While there is no definite consensus on the effect of vitamin D supplementation on muscle strength and performance in the elderly, vitamin D has little adverse effects.

Dieticians working with elderly suffering from sarcopenia should take some points into consideration when advising about supplementations of vitamins. The Dutch Health Council recommends minimum serum vitamin D concentrations of 50nmol/l for the elderly (38). The WHO however considers concentrations of 50nmol/l to be insufficient and sees concentrations higher then 75nmol/l to be in the sufficient range (24). This is also supported by the International Osteoporosis Foundation (32). The Dutch Health Council recommends a supplementation dose of 800IU for those 70 years and older (38). This might be too low for some individuals to reach optimal values higher then 75nmol/l. When recommending vitamin D supplementation for the elderly the dietician might want to adjust the dose upwards of 800IU in clients with limited sun exposure, obesity, osteoporosis, malabsorption and for non-European clients with high risk of vitamin D deficiency living in Europe. The International Osteoporosis Foundation suggest doses upwards to 2000IU depending on these factors (32). Because adjusting doses for these factors might be hard and subjective, the dietician could choose to supplement 2000IU in all elderly clients to have the highest chance of reaching ideal serum concentrations, since no adverse effects are associated with these doses. For the other studied vitamins, insufficient data was found to make any recommendations for supplementation in the prevention and treatment of sarcopenia.
Reference list.

19. Swart K, Ham A, Wijngaarden J.P, Enkeman A et al. A Randomized Controlled Trial to Examine the Effect of Z-Year Vitamin B12 and Folic Acid Supplementation on Physical Performance, Strength, and


Appendix

Appendix 1: Search string

(Elderly OR older people OR senior OR frail OR age related OR older people) AND (vitamins OR vitamin supplement) AND (vitamin B-11 OR vitamin B-11 supplement OR vitamin B-12 OR vitamin B-12 supplement OR vitamin C OR vitamin C supplement OR vitamin D OR vitamin D supplement OR vitamin E OR vitamin E supplement) AND (muscle mass OR muscles OR muscle density OR muscle development OR lean muscle mass OR fat free mass OR skeletal muscle mass OR hypertrophy OR muscle synthesis OR muscle strength OR muscle power OR physical performance OR physical function OR motor development daily life activity OR daily life OR physical function)

Appendix 2: PIO

<table>
<thead>
<tr>
<th>Population (P)</th>
<th>Elderly, older people, senior, frail, age related, older people</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention (I)</td>
<td>- vitamin B-11, vitamin B-11 supplement,</td>
</tr>
<tr>
<td></td>
<td>- vitamin B-12, vitamin B-12 supplement,</td>
</tr>
<tr>
<td></td>
<td>- vitamin C, vitamin C supplement,</td>
</tr>
<tr>
<td></td>
<td>- vitamin D, vitamin D supplement,</td>
</tr>
<tr>
<td></td>
<td>- vitamin E, vitamin E supplement.</td>
</tr>
<tr>
<td>Outcome (O)</td>
<td>Muscle mass: Muscle mass, muscles, muscle density, muscle development, lean muscle mass, fat free mass, skeletal muscle, hypertrophy, muscle synthesis.</td>
</tr>
<tr>
<td></td>
<td>Muscle strength: Muscle strength, muscle power.</td>
</tr>
<tr>
<td></td>
<td>Physical performance: physical performance, physical function, motor development, daily life activity, daily life, physical function.</td>
</tr>
</tbody>
</table>
Appendix 3

Quality assessment tool for quantitative research.

COMPONENT RATINGS

A) SELECTION BIAS

(Q1) Are the individuals selected to participate in the study likely to be representative of the target population?
1. Very likely
2. Somewhat likely
3. Not likely
4. Can’t tell

(Q2) What percentage of selected individuals agreed to participate?
1. 80 - 100% agreement
2. 60 - 80% agreement
3. Less than 60% agreement
4. Not applicable
5. Can’t tell

<table>
<thead>
<tr>
<th>RATE THIS SECTION</th>
<th>STRONG</th>
<th>MODERATE</th>
<th>WEAK</th>
</tr>
</thead>
<tbody>
<tr>
<td>See dictionary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

B) STUDY DESIGN

Indicate the study design
1. Randomized controlled trial
2. Controlled clinical trial
3. Cohort analytic (two group pre + post)
4. Case-control
5. Cohort (one group pre + post, before and after)
6. Interrupted time series
7. Other specify
8. Can’t tell

Was the study described as randomized? If NO, go to Component C.
No
Yes

If Yes, was the method of randomization described? (See dictionary)
No
Yes

If Yes, was the method appropriate? (See dictionary)
No
Yes

<table>
<thead>
<tr>
<th>RATE THIS SECTION</th>
<th>STRONG</th>
<th>MODERATE</th>
<th>WEAK</th>
</tr>
</thead>
<tbody>
<tr>
<td>See dictionary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
C) CONFOUNDERS

(Q1) Were there important differences between groups prior to the intervention?

1. Yes
2. No
3. Can’t tell

The following are examples of confounders:
1. Race
2. Sex
3. Marital status/family
4. Age
5. SES (income or class)
6. Education
7. Health status
8. Pre-intervention score or outcome measure

(Q2) If yes, indicate the percentage of relevant confounders that were controlled (either in the design (e.g. stratification, matching) or analysis)?

1. 80 – 100% (most)
2. 60 – 79% (some)
3. Less than 60% (few or none)
4. Can’t Tell

RATE THIS SECTION  STRONG   MODERATE   WEAK
See dictionary 1  2  3

D) BLINDING

(Q1) Was (were) the outcome assessor(s) aware of the intervention or exposure status of participants?

1. Yes
2. No
3. Can’t tell

(Q2) Were the study participants aware of the research question?

1. Yes
2. No
3. Can’t tell

RATE THIS SECTION  STRONG   MODERATE   WEAK
See dictionary 1  2  3

E) DATA COLLECTION METHODS

(Q1) Were data collection tools shown to be valid?

1. Yes
2. No
3. Can’t tell

(Q2) Were data collection tools shown to be reliable?

1. Yes
2. No
3. Can’t tell

RATE THIS SECTION  STRONG   MODERATE   WEAK
See dictionary 1  2  3
F) WITHDRAWALS AND DROP-OUTS

(G1) Were withdrawals and drop-outs reported in terms of numbers and/or reasons per group?
1. Yes
2. No
3. Can't tell
4. Not Applicable (i.e. one time surveys or interviews)

(G2) Indicate the percentage of participants completing the study. (If the percentage differs by groups, record the lowest):
1. 80-100%
2. 60-79%
3. less than 60%
4. Can't tell
5. Not Applicable (i.e. Retrospective case-control)

<table>
<thead>
<tr>
<th>RATE THIS SECTION</th>
<th>STRONG</th>
<th>MODERATE</th>
<th>WEAK</th>
<th>Not Applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>See dictionary</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

G) INTERVENTION INTEGRITY

(G1) What percentage of participants received the allocated intervention or exposure of interest?
1. 80-100%
2. 60-79%
3. less than 60%
4. Can't tell

(G2) Was the consistency of the intervention measured?
1. Yes
2. No
3. Can't tell

(G3) Is it likely that subjects received an unintended intervention (contamination or co-intervention) that may influence the results?
4. Yes
5. No
6. Can't tell

H) ANALYSES

(G1) Indicate the unit of allocation (circle one)
- community
- organization/institution
- practice/office
- individual

(G2) Indicate the unit of analysis (circle one)
- community
- organization/institution
- practice/office
- individual

(G3) Are the statistical methods appropriate for the study design?
1. Yes
2. No
3. Can't tell

(G4) Is the analysis performed by intervention allocation status (i.e. intention to treat) rather than the actual intervention received?
1. Yes
2. No
3. Can't tell
GLOBAL RATING

COMPONENT RATINGS
Please transcribe the information from the grey boxes on pages 1-4 onto this page. See dictionary on how to rate this section.

<table>
<thead>
<tr>
<th></th>
<th>SELECTION BIAS</th>
<th>STRONG</th>
<th>MODERATE</th>
<th>WEAK</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>B</td>
<td>STUDY DESIGN</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>C</td>
<td>CONFOUNDERS</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>D</td>
<td>BLINDING</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>E</td>
<td>DATA COLLECTION METHOD</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>F</td>
<td>WITHDRAWALS AND DROPOUTS</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

GLOBAL RATING FOR THIS PAPER (circle one):

1  STRONG  (no WEAK ratings)
2  MODERATE (one WEAK rating)
3  WEAK  (two or more WEAK ratings)

With both reviewers discussing the ratings:

Is there a discrepancy between the two reviewers with respect to the component (A-F) ratings?

No  Yes

If yes, indicate the reason for the discrepancy:

1  Oversight
2  Differences in interpretation of criteria
3  Differences in interpretation of study

Final decision of both reviewers (circle one):

1  STRONG
2  MODERATE
3  WEAK
### Beoordelingsformulier: scriptie afstudeerproject (AP) Voeding & Diëtetiek, Hogeschool van Amsterdam

<table>
<thead>
<tr>
<th>Criterium</th>
<th>B</th>
<th>H</th>
<th>onvoldoende</th>
<th>voldoende</th>
<th>goed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randvoorwaardelijke eisen (weging 0%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zie ook Taal-en schrijfwijzer (OLWO) en Handleiding Afstudeerproject</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naam student:</td>
<td>Thomas van Geelen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Titel en nummer AO</td>
<td>2016212</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opdrachtgever</td>
<td>VITAMINE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naam examinator:</td>
<td>Dr. Ir. Engberink</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naam docentbegeleider:</td>
<td>Dr. Ir. Tieland</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Datum:</td>
<td>03-06-2016</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Op tijd ingeleverd

**Leesbaarheid**
De afstudeeropdracht is vlot leesbaar en in correct Nederlands of Engels geschreven. De formulering is bondig, concreet en efficiënt. De rode draad in het verhaal is duidelijk.

**Structuur**
De indeling in hoofdstukken, paragrafen en alinea's is logisch afgeleid van de probleemstelling en duidelijk. De titels van de afstudeeropdracht, de hoofdstukken en paragrafen zijn kernachtig geformuleerd en representatief voor de inhoud.

**Lay-out**
De lay-out is functioneel en professioneel. Gebruik van beelden, tabellen en figuren is functioneel en bijlagen worden benut waar nodig.

**Omvang**
De omvang is maximaal 500 woorden. De samenvatting leest vlot en is in correct Nederlands of Engels geschreven.

**Bronverwijzing**
De verwijzing naar alle bronnen zijn correct volgens richtlijnen uit de Taal-en schrijfwijzer (afgeleid van Vancouver) uitgevoerd.

---

### Niet op tijd ingeleverd

**Leesbaarheid**
De afstudeeropdracht is een aaneenschakeling van stukken tekst, het geheel loopt niet. Een eigen schrijfstijl is niet herkenbaar. Er zijn veel grammaticale en spellingfouten. De formulering is persoonlijk, subjectief, vaag en wijdlopig.

**Structuur**
De indeling in hoofdstukken, paragrafen en alinea's is niet duidelijk van de probleemstelling afgeleid. De titel van de afstudeeropdracht dekt de lading niet en/of de kopjes van de paragrafen dekken de inhoud van de paragraaf niet.

**Lay-out**
De lay-out is rommelig. Beelden, tabellen en figuren ondersteunen de tekst en argumenten niet. Omvang
De omvang is te ruim, er zijn herhalingen en niet relevante onderdelen opgenomen. De omvang overschrijdt de 35 pagina's, excl bijlagen en literatuurlijst.

**Samenvatting**
De samenvatting geeft niet duidelijk en bondig de inhoud van de scriptie weer. Bepaalde relevante onderdelen zijn niet opgenomen. De omvang overschrijdt de 500 woorden.

**Bronverwijzing**
De verwijzing naar bronnen is een aantal keren niet goed toegepast. Er staan bronnen in de literatuurlijst die niet in de tekst terug te vinden zijn. Elektronische bronnen zijn verkeerd verwezen en geciteerd.

---

### Op tijd ingeleverd

**Leesbaarheid**
De afstudeeropdracht leest redelijk vlot, er zijn weinig grammaticale en spellingfouten. De formulering is bondig, hier en daar wat algemeen en niet overal even formeel. Het verhaal is een lopend geheel.

**Structuur**
De hoofdstukindeling is logisch afgeleid van de probleemstelling, maar de onderverdeling op lager niveau is voor verbetering vatbaar. De titels van de afstudeeropdracht, de hoofdstukken en paragrafen zijn niet altijd kernachtig geformuleerd en representatief voor de inhoud.

**Lay-out**
Er zijn kleine fouten in de lay-out, maar die beïnvloeden de leesbaarheid niet. Er zijn kleine fouten in de lay-out, maar die beïnvloeden de leesbaarheid niet. Een enkele keer is het gebruik van beelden, tabellen en figuren niet functioneel.

**Omvang**
De omvang is passend en ligt rond de 30 pagina's, exclusief bijlagen en literatuurlijst.

**Samenvatting**
De samenvatting is over het algemeen bondig geformuleerd en passend bij de inhoud.

**Bronverwijzing**
De verwijzing naar alle bronnen zijn correct volgens richtlijnen uit de Taal-en schrijfwijzer (afgeleid van Vancouver) uitgevoerd.
<table>
<thead>
<tr>
<th>Criterium</th>
<th>B</th>
<th>H</th>
<th>Cijfer 1,0- 5,0</th>
<th>Cijfer 5,5-7,5</th>
<th>Cijfer 8-10</th>
<th>Cijfer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. correcte definiëring en consistente uitwerking probleemstelling</td>
<td>1</td>
<td>3</td>
<td>I</td>
<td>Als niet aan de criteria voor 5,5-7,5 is voldaan.</td>
<td>De probleemstelling (en deelvragen) worden systematisch uitgewerkt in 55-75% van de scriptie</td>
<td>De probleemstelling (en deelvragen) worden systematisch uitgewerkt in 80-100% van de scriptie.</td>
</tr>
<tr>
<td>2. verantwoording (onderzoeks)methode</td>
<td>1</td>
<td>3</td>
<td>II</td>
<td>Als niet aan de criteria voor 5,5-7,5 is voldaan.</td>
<td>De gekozen methode sluit aan bij de probleemstelling en wordt inzichtelijk beargumenteerd. (De methode staat zodanig beschreven dat het onderzoek herhaalbaar is)</td>
<td>+ De gekozen methode is informatiever beschreven en wetenschappelijk onderbouwd.</td>
</tr>
<tr>
<td>3. juiste weergave resultaten</td>
<td>1</td>
<td>3</td>
<td>I</td>
<td>Als niet aan de criteria voor 5,5-7,5 is voldaan.</td>
<td>De analyse van gegevens is correct uitgevoerd De resultaten staan objectief, correct en overzichtelijk beschreven/gepresenteerd (resultaten komen voort uit het onderzoek). Tabellen en figuren zijn conform regels.</td>
<td>+ De belangrijkste resultaten worden gescheiden van de minder belangrijke (bv in bijlage) in relatie tot de probleemstelling.</td>
</tr>
<tr>
<td>4. juistheid, opbouw en niveau van discussie en conclusie</td>
<td>1</td>
<td>3</td>
<td>I</td>
<td>Als niet aan de criteria voor 5,5-7,5 is voldaan.</td>
<td>De resultaten worden correct geïnterpreteerd en vergeleken met de literatuur Conclusie geeft antwoord op de probleemstelling. Sterke en zwakke punt worden correct benoemd.</td>
<td>+ De helicopterview wordt toegepast, waarbij relevante ontwikkelingen in de beroepspraktijk en aanverwante domeinen zijn beschreven.</td>
</tr>
<tr>
<td>5. concrete aanbevelingen die voortkomen uit het onderzoek/opdracht (indien eindproduct in bijlage zit wel meerekenen)</td>
<td>4</td>
<td>5</td>
<td>III</td>
<td>Als niet aan de criteria voor 5,5-7,5 is voldaan.</td>
<td>Aanbevelingen vloeien logisch voort uit de discussie en conclusie.</td>
<td>+ De aanbevelingen zijn bruikbaar voor de organisatie en voor het gehele werkveld + De aanbevelingen zijn creatief en innovatief + Er wordt een transfer gemaakt naar</td>
</tr>
<tr>
<td>Criterium</td>
<td>B</td>
<td>H</td>
<td>Cijfer 1-5,5</td>
<td>Cijfer 5,5-7,5</td>
<td>Cijfer 8-10</td>
<td>Cijfer</td>
</tr>
<tr>
<td>-----------</td>
<td>---</td>
<td>---</td>
<td>-------------</td>
<td>--------------</td>
<td>-------------</td>
<td>--------</td>
</tr>
<tr>
<td>6. niveau en actualiteit (Engelstalige) literatuur</td>
<td>7</td>
<td>I II</td>
<td>Als niet aan de criteria voor 5,5-7,5 is voldaan</td>
<td>De student gebruikt wetenschappelijke literatuur die ingaat op recente ontwikkelingen en geeft dit in scriptie voldoende weer.</td>
<td>+ De student laat zien literatuur op een hoger niveau te integreren in de scriptie</td>
<td></td>
</tr>
</tbody>
</table>

Toelichting

Eindcijfer 1+2+3+4+5+6/6 =

Naam en handtekening Examinator/docentbegeleider *:

NB* = weghalen wat niet van toepassing is.

B= Beroepscompetenties Opleiding Voeding & Diëtiek:

1. Advisering: Analyseren van problemen vragen en behoeften op het gebied van voeding, doelen stellen gebaseerd op wetenschappelijke inzichten en afstemming met stakeholders en daarover adviseren, rekening houdend met relevante randvoorwaarden.
2. Begeleiding: Begeleiden van de uitvoering van adviezen gericht op problemen, vragen of behoeften op het gebied van voeding.
3. Rapportage: Registreren, evalueren en rapporteren van resultaten en procedures of richtlijnen ontwikkelen ter optimalisering van effecten van voeding.
5. Management: Coördineren en aansturen van bedrijfsprocessen, gebaseerd op de strategie van de onderneming/organisatie/afdeling. Vaststellen strategie, beleid en planning van een organisatie.
6. Onderzoek: Opzetten en uitvoeren van voeding gerelateerd praktijkgericht onderzoek, verwerken van gegevens en rapporteren van resultaten.
7. Professionalisering: Integreren nieuwe inzichten, werkwijzen, producten en diensten in de eigen werkzaamheden en communiceert hierover.

H= hbo-standaard
I Een gedegen theoretische basis
II Het onderzoekend vermogen
III Professioneel vakmanschap
IV Beroepsethiek en maatschappelijke oriëntatie