Faculteit Geneeskunde en Levenswetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Vitamin D supplementation during strength training in healthy adults

Stijn Nullens
Maaike Withofs

Eerste deel van het scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie

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VITAMIN D SUPPLEMENTATION DURING STRENGTH TRAINING IN HEALTHY ADULTS.

OUTLINE

Various types of tissues are responsive to vitamin D. One important tissue, regulated by vitamin D, is the skeletal muscle. Studies have shown a positive correlation between vitamin D concentration and muscle function whereas sufficient serum 25(OH)D will have a positive influence on grip strength, jump performance and overall muscle function towards different populations. On the other hand, low blood values of 25(OH)D negatively affect muscle function and strength. Vitamin D supplementation has a positive effect on skeletal muscles and will reverse vitamin D insufficient to vitamin D sufficient. However, there is strong evidence that exercise has a positive effect on skeletal muscles. Various studies show a positive correlation between exercise and overall muscle function.

The literature search focused on the following research question: "Does vitamin D supplementation, in combination with strength training have an effect on muscle strength, muscle fiber type and the muscle cross sectional area of skeletal muscles within a healthy population?". Twelve studies have been analyzed, with the most important findings being:

- Except for one, all studies investigated the effect of vitamin D supplementation during strength training within an insufficient or deficient population. No consensus was reached on the effect thereof within this population because of the differences in the methods applied. Four studies found an effect of supplementation on muscle strength, while five studies did not find any difference between intervention (IG) and control group (CG). Two studies found a trend for significance between IG and CG. Concerning muscle power, two articles found an effect, while five did not find any difference between IG and CG.
- Only one study included only participants with a sufficient level of 25(OH)D. No significant differences between IG and CG were found in any outcome measurement.
- It is difficult to make a clear conclusion on the effect of vitamin D supplementation during strength training because of the heterogeneity in supplementation, training program and population within all studies.
- Further research is necessary to investigate the effect of vitamin D supplementation, combined with strength training, on skeletal muscles. All studies should use the same training program with the same exercises and training volume, and an identical supplementation protocol (> 5000 IU/day for > 12 weeks) within the same population.

Stijn Nullens & Maaike Withofs

Promotor: dr. Anouk Agten

Co-promotor: Prof. dr. Frank Vandenabeele and Mr. Sjoerd Stevens

CONTEXT OF THE MASTER THESIS

This master thesis fits in the research domain of musculoskeletal rehabilitation. Patients with musculoskeletal pathology, like muscle strains, muscle tears or atrophy, often suffer from different types of impairment, with reduced muscle function being one. This can vary from reduced strength (1RM, isometric/concentric/eccentric contractions, isokinetic strength, hand grip strength) to reduced muscle power (reduced vertical jump), speed and agility. Various types of strengthening exercises can be used for both the rehabilitation of impairments and gaining strength in healthy individuals, but it is suggested that other factors, such as the use of supplements, could have an impact as well. Unfortunately, these two factors are often investigated separately.

Therefore, this literature study has specifically focused on the following research question: "Does vitamin D supplementation, in combination with strength training have an effect on muscle strength, muscle fiber type and the muscle cross sectional area of skeletal muscles within a healthy population?" The effect of vitamin D supplementation, in combination with various types of strength training on several outcome measures (muscle strength as primary outcome measure) was studied through a literature review. Furthermore, a research protocol has been set out in the second part of the thesis. This protocol makes it possible to analyze the possible changes in skeletal muscles due to vitamin D supplementation, combined with various types of strength training within a healthy population.

These days, a lot of people suffer from an insufficient vitamin D concentration caused by the lack of sunlight exposure. This insufficiency can be solved by supplements. Therefore, it is important to know, not only for all health care providers (such as physiotherapists), but also for patients, if a sufficient or even a more than sufficient vitamin D concentration may have beneficial effects on, for example, gaining muscle strength. The physiotherapist, who constructs and guides the individual through the exercise programs, should be aware of the effects thereof in order to optimize muscle strength. Other health care providers, such as doctors and nurses, should be aware of this possible effect as well. Hereby, they could assess an individual's concentration and take steps if needed to optimize its muscle strength. Lastly, the individual himself needs to be aware of the effect of their vitamin D concentration on skeletal muscles. In this way, he will understand if and for which reason supplementation is needed.

This master thesis part one is executed as a part of the first master year at the UHasselt in Diepenbeek. The second part will also be executed in Diepenbeek, more specifically at the rehabilitation research center REVAL of UHasselt. This master thesis is part of a broader research project, about the effects of High Intensity Training on muscle characteristics of back muscles in patients with low back pain, and is performed under the supervision of dr. Anouk Agten, Prof. dr. Frank Vandenabeele and Mr. Sjoerd Stevens, at the rehabilitation research center REVAL of UHasselt in Diepenbeek.
The central format was applied for this master thesis.
As for the literature review, the final research question and search strategy have been determined by both students in November 2017 and January 2018 respectively. Both students first performed the

literature search separately, followed by a common study selection. The formulation of the research question and the search strategy, as well as the analysis of the articles found by this search, was supervised by dr. Anouk Agten.

This thesis was a duo-master thesis.

The students provided a detailed description regarding the protocol and research design of the experimental study that will be implemented at the rehabilitation research center REVAL. Both students will attend baseline and post-measurements and assist other physiotherapists during the training program.

TABLE OF CONTENTS

PART 1: OVERVIEW OF THE LITERATURE

1. Abstract

Background: The skeletal muscle is regulated by vitamin D. Studies show positive correlation between serum 25(OH)D levels and overall muscle function, whereby insufficient values negatively affect muscle function. Vitamin D supplementation will reverse vitamin D insufficiency to sufficiency. Furthermore, there is evidence that exercise has a positive effect on skeletal muscles. This literature study focused on the question: “Does vitamin D supplementation, in combination with strength training have an effect on overall skeletal muscle function within a healthy population?”

Methods: Literature review used databases PubMed and Web Of Knowledge (WOK). Categories ‘Vitamin D supplementation’, ‘Muscle characteristics’ and ‘Exercise type’ were created. Within each category, all terms were combined with ‘OR’. Finally, the categories were combined with ‘AND’. This resulted in 405 articles.

Results: 12 studies were included and analyzed. The articles used differ in supplementation (concentration, frequency and duration of supplementation period), training program (maintaining active daily living or sport activities, implementation of strength training programs) and population.

Discussion and conclusion: It is difficult to make a clear conclusion because of the heterogeneity of the studies.

Operationalization: This master thesis is executed as part of the first master year at the UHasselt in Diepenbeek and is part of a broader research project, about the effects of High Intensity Training on muscle characteristics of back muscles in patients with low back pain. Performed under supervision of dr. Anouk Agten, Prof. dr. Frank Vandenabeele and Mr. Sjoerd Stevens.

Most important key words: vitamin D supplementation, strength training, muscle function, healthy adult

2. Introduction

Vitamin D is a fat soluble vitamin that is biologically inactive and needs conversion to 25-hydroxyvitamin D (25(OH)D) inside the liver. This inactive 25(OH)D is transformed to its biologically active form, 1.25 dihydroxyvitamin D (1,25(OH)2D), in the kidneys. There are two major forms of vitamin D: (i) vitamin D2 (ergocalciferol), which is mostly extracted from nutrition, and (ii) vitamin D3 (cholecalciferol), which is synthesized from exposure to sunlight. Vitamin D3 is the major source of vitamin D for humans and animals. Under the influence of sunlight (UVB light), 7-dehydrocholesterol is converted into cholesterol, which is then converted into an active form of vitamin D3. Both forms undergo two enzymatic hydroxylation reactions in order to be transformed into the active form 1,25(OH)D2.

The serum levels of the inactive form, 25(OH)D, is used to determine the vitamin D concentration in the blood. According to the National Institute of Health, there is discussion on the optimal serum concentration of 25(OH)D, associated with deficiency, adequacy for bone health and optimal overall health. The Institute of Medicine defines an optimal level of serum 25(OH)D at >50nmol/L (>20nl/mL), which is considered adequate for bone and overall health in healthy individuals. Levels of 30 to < 50nmol/L (12 to <20nl/mL) are generally considered inadequate for bone and overall health. Vitamin D deficiency is defined as serum 25(OH)D being lower than 30nmol/L (<12ng/mL).

Various types of tissues are responsive to vitamin D. One important tissue, regulated by vitamin D, is the skeletal muscle. The biological actions of the active vitamin D are initiated through precise changes in gene expression, which are mediated by an intracellular vitamin D receptor (VDR). VDR is a ligand-dependent nuclear transcription factor, which has been identified in skeletal muscles (Ceglia & Harris, 2013). It controls the rate of transcription of genetic information from DNA to mRNA, by binding to a specific DNA sequence (Latchman, 1997). When 1,25(OH)2D binds at the nuclear VDR gene, transcription takes place. This will activate several slow pathways, which mediates the stimulation of muscle growth and differentiation. These complex actions result in changes in mRNA gene transcription and novo protein synthesis (Pike & Meyer, 2010).

Studies have shown a positive correlation between vitamin D concentration and muscle function (Hamilton, 2010), whereby sufficient serum 25(OH)D will have a positive influence on grip strength, jump performance and overall muscle function towards different populations (Hazell, DeGuire, & Weiler, 2012). On the other hand, low blood values of 25(OH)D negatively affect muscle function and strength. There is an impairment in the excitation-contraction coupling in skeletal muscle. This can be explained by: 1. impaired Ca^{2+} transport across the plasma membrane or sarcolemma, 2. a decrease in sarcoplasmic reticulum (SR) volume, which impairs the rate of Ca^{2+} uptake as well as the amount of Ca^{2+} released in response to an action potential, 3. impaired Ca^{2+} transport across the sarcolemma due to a decreasing activity of membranous Ca^{2+}pump (Hazell et al., 2012). These findings emphasize the importance of maintaining a sufficient vitamin D status for optimal muscle function.

Supplementation of vitamin D will increase serum 25(OH)D and will reverse vitamin D insufficiency to vitamin D sufficiency. Furthermore, vitamin D supplementation has a positive effect on skeletal muscles. A low-dose supplementation prevents muscular atrophy in women after stroke (Sato, Iwamoto, Kanoko, & Satoh, 2005), improves neuromuscular function in older people (Dhesi et al., 2004) and demonstrates beneficial effects on strength and balance (Muir & Montero-Odasso, 2011). Possible explanations may be an increased intra myonuclear VRD concentration (Ceglia et al., 2013) or an improvement in Ca^{2+} uptake and Ca^{2+} flux, as mentioned earlier.

There is strong evidence that exercise has a positive effect on skeletal muscles. Training will prevent muscle atrophy by inducing muscle hypertrophy, increasing aerobic capacity, altering mitochondrial function, improving balance, strength, etc. Various studies show a positive correlation between exercise and overall muscle function (McGlory & Phillips, 2015; Nader et al., 2014; Porter, Reidy, Bhattarai, Sidossis, & Rasmussen, 2015; Straight, Lindheimer, Brady, Dishman, & Evans, 2016). There is an interest in combining training with vitamin D supplementation (Chiang, Ismaeel, Griffis, & Weems, 2017). Increasing serum 25(OH)D concentrations could be a complementary approach to improve muscle function.

In this systematic review, the goal is to examine and summarize the results of studies that explored the effect of vitamin D supplementation during strength training on skeletal muscles within a healthy population.

3. Methods

3.1. Research question

A literature search was conducted to examine and summarize the results and to answer the following research question: “Does vitamin D supplementation, in combination with strength training have an effect on muscle strength, muscle fiber type and the muscle cross sectional area of skeletal muscles within a healthy population?” The latter can be summarized as the following PICO:

P: Healthy adults (18-60 years)

I: Vitamin D supplementation and strength training

C: Strength training alone

O: Changes in skeletal muscles (muscle strength, muscle fiber type and the muscle cross sectional area)

3.2. Literature search

Two databases were used for the literature search: PubMed and Web of Knowledge (WOK). Three categories (‘Vitamin D supplementation’, ‘Muscle characteristics’ and ‘Exercise type’) were created, consisting of various Medical Subject Headings (MeSH) terms and keywords. Within each category, all terms were combined with ‘OR’. Finally, the three categories were combined with ‘AND’. The full literature search is shown in table 1. In case there was no MeSH-term available, title/abstract was used on PubMed. On WOK, ‘Topic’ (TS) was used for all terms. The list of all used terms on both PubMed and WOK can be found in table 1. The obtained articles were first screened on title and abstract. The remaining eligible articles were then screened on full text before inclusion.

There were no restrictions on period of publication or language. The final search, used to complete the set of included articles in the master thesis, was conducted on May 2, 2018.

3.3. Selection criteria

To select adequate articles, ‘healthy adults, aged between 18 and 60 years old’ was used as inclusion criterion. Every pathology or disease, systematic review and review was excluded. Two independent assessors conducted the selection of articles. During the selection, both assessors included the same publications.

3.4. Quality assessment

To assess the quality of the included articles, the Physiotherapy Evidence Database (PEDro) checklist was used. This is a checklist, consisting of 11 criteria for the assessment of RCT’s and CCT’s. Each criterion was awarded with a point in case it had been clearly satisfied. If, after a literal reading of the article, a criterion is not satisfied, no point should be awarded. More specifications for each criterion can be found in the appendix. All articles were assessed by two independent researchers, whereby the differences in scoring were resolved through discussion. Furthermore, strengths and limitations of all articles were assessed. This can be found in table 4. The table contains the strengths and limitations stated by the articles themselves, but also of strengths and limitations analyzed by both assessors of the master thesis.

3.5. Data extraction

The following data were extracted from the included articles and put into tables 5.1. and 5.2.:

a) population of the study (age, group characteristics), b) aim of the study, c) description of the interventions, d) outcome measures (primary and secondary measures), and lastly, e) results (baseline and post-intervention).

4. Results

4.1. Results study selection

The search was performed and resulted in a total of 1061 articles. 405 articles were found on PubMed, 656 on Web of Knowledge. After screening on title and abstract, 143 articles remained. These articles were then screened on full text and excluded for the following reasons:

(1) Is the article some sort of review or news article?
This was the case for 30 articles. 28 articles concerned reviews, two publications were news articles.

(2) Does the article address vitamin D supplementation?
For 50 out of the 143 articles, this was not the case. Quite often, the articles only assessed vitamin D status and did not use vitamin D as an intervention, resulting in exclusion.

(3) Do participants have some kind of disease or pathology?
In nine publications, participants did have a disease or pathology, often being overweight, obesity and sarcopenia. Other pathologies were exercise induced laryngospasm and fontan palliation.

(4) Are participants of correct age?
Based on age, 16 articles were excluded.

(5) Furthermore, some articles did not properly address the topic (n=15). Quite often, articles did use vitamin D supplementation as intervention, but did not combine it with strength training.

(6) Finally, one article did research on animals and one article did not have results available. A list of the excluded articles can be found in table 2.

After removing common search results, eight articles remained on PubMed and two on Web of Knowledge. Reference lists of these ten articles were screened for publications that were not found with the initial literature search, resulting in two extra publications. A more detailed version of the study selection can be found in figure 1.

4.2. Results quality assessment

Out of the 12 included publications, 11 articles were RCT's and one article was a controlled prospective study.

For the quality assessment, the PEDro-checklist was used. This checklist was eligible for all 12 articles. The results of all criteria are shown in table 3.

Six articles met all 11 criteria. Two articles met all but one being the studies of both Wyon et al. (2016) and Close et al. (2013b), having no concealed allocation. The study of Jastrzębska, Kaczmarczyk & Jaztrzębski (2016) received a score of 9/11, reason being not having specified criteria and no randomization of participants at the start of their study. Josse, Tang, Tarnopolsky & Phillips (2010) received the same score as the latter: they did not have blinding of therapists who administered the therapy and all assessors that measured at least one key outcome.

The publication of Owens et al. (2015) did not mention if the participants, therapists or assessors were blinded for intervention/control group, resulting in a score of 8/11.

The study of Wyon, Koutedakis, Wolman, Nevill & Allen (2014) received the lowest score of 5/11. They scored '-' six times for several reasons: they did not specify criteria, participants were not randomized and allocation was not concealed. Furthermore, there was no mention of blinding of subjects, therapists or assessors.

4.3. Results data extraction

Tables 4 and 5 provide a complete overview of the extracted data. The strengths and limitations, the population, the aim of the study and the intervention for each article are shown.

The population of all studies varied: all participants were healthy adults between 18 and 45 years old, but other characteristics differed. Quite often eligible criteria were not specified (Jastrzebska et al., 2016; Wyon et al., 2014), whereas Scholten et al. (2015) used volunteers. Close et al. (2013a) used rugby players from only one Super League team and one soccer team, and Barker et al. (2012) did not stringently examine the level of physical activity. This results in difficulties generalizing findings. Baseline characteristics regarding serum total 25(OH)D however were similar between intervention and control group in a lot of articles. In table 5.3., a detailed presentation of all serum 25(OH)D levels is shown.
In only one study (Scholten, Sergeev, Song, & Birger, 2015), all participants had an optimal serum level (31/35 >50nmol/L and 9/35 >75nmol/L). Josse et al. (2010) only used participants with an inadequate level (Josse et al., 2010), while Gupta et al. (2010) and Wyon et al. (2014) both had inadequate and deficient levels of serum 25(OH)D. Three articles (Agergaard et al., 2015; Jastrzębska et al., 2016; Owens et al., 2015) had participants with both optimal and inadequate levels. Furthermore, four articles (Barker et al., 2012; Barker, Schneider, Dixon, Henriksen, & Weaver, 2013; Close, Leckey, et al., 2013; Close, Russell, et al., 2013) consisted of optimal, inadequate and deficient levels. Close et al. (2013b) even consisted of participants with severely deficient levels of serum 25(OH)D.
Sample size was rather low, ranging between 10 (Close, Russell, et al., 2013) and 40 participants (Gupta et al., 2010). However, there was a high compliance/low drop out in most studies and there were no major adverse side effects, adverse events or injury relating to the study in some studies.

In general, **the aim of each study** was to identify the effect of vitamin D supplementation in combination with training. However, the specific goals of the studies differed, such as identifying the effect on training adaptation, physical fitness/performance and injury parameters, muscular response to resistance training, the effect on cardiorespiratory and muscular fitness, muscle function, Delayed Onset Of Muscle Soreness (DOMS), strength recovery, enhance muscle function, muscle cell regeneration and muscle strength. The included articles were often the first in the literature to investigate that specific topic.

Based on the **interventions**, the studies can be divided into four groups.

- Group one: supplementation period during active daily living
- Group two: supplementation period combined with sport activities
- Group three: supplementation pre-training
- Group four: supplementation post-training

In **the first group,** consisting of three articles, a supplementation period was performed while maintaining active daily living. The activity level consisted of moderate to vigorous physical exercise, three to five days per week for 30 to 90 minutes a day, for each study. Vitamin D3 was supplemented in all three studies, but the amount of supplementation and protocol were different. Scholten et al. (2015) included three intervention protocols, one being supplemented with 4000 IU, another with 1000 mg quercetin and the third combining both. Intake was daily for eight weeks. Gupta et al. (2010) used 60 000 IU, three days per week for eight weeks, followed by one ingestion per month for four months and 1g. elemental calcium daily (Gupta et al., 2010). This ingestion was with milk. The last article of this group, Barker et al. (2012), also used two intervention groups: one with 200 IU and the other with 4000 IU, both daily during a period of 28 days.

The outcome measures of group one are shown in table 5.4.1. (which summarizes information from table 5.4. in the appendix).

All three articles had <u>muscle strength</u> as outcome measure. Scholten et al. (2015) and Barker et al. (2012) did not find significant changes between any of the three groups in pre- and post-supplementation. On the other hand, Gupta et al. (2010) found a significant difference between the intervention- and control group after six months in handgrip- (p=0,001) and Gastro-soleus (p=0,04) strength, whereby the intervention group showed higher values compared to the control group. There was no difference for pinch-grip strength between the two groups (p=0,06).
Concerning <u>muscle power</u>, both Scholten et al. (2015) and Barker et al. (2012) did not find significant changes between any groups pre-post supplementation (p-values from 0,425 to 0,999).

The second group, which consists of six articles, combined a supplementation period with sport activities. Two studies (Close, Russell, et al., 2013; Jastrzębska et al., 2016) focused on soccer players. All the participants continued their training program, which consisted of endurance, speed, strength and agility training. Close et al. (2013a) included rugby players and Wyon et al. (2014) ballet dancers. Both groups continued their training program during the study period. The remaining two articles (Agergaard et al., 2015; Josse et al., 2010) both used progressive resistance training programs, individually composed based on 1RM (one-repetition maximum) measurements.
Five articles of group two used vitamin D3 (cholecalciferol) as supplement, while one used fat free milk (Josse et al., 2010). The studies of Close et al. (2013b) and Jastrzębska et al. (2016) used an amount of 5000 IU per day for eight weeks. Wyon et al. (2014) also had a daily intake but supplemented 2000 IU for four months. One article (Agergaard et al., 2015) combined a daily intake of 4000 IU of vitamin

D3 with 800 mg Calcium for eight weeks. Close et al. (2013a) investigated two doses of vitamin D supplementation, 20 000 IU and 40 000, with one weekly intake for 12 weeks. Josse et al. (2010) used fat free milk supplement, which participants ingested immediately after exercise and one hour post-exercise, five days/week for 12 weeks.

The outcome measures of group two are shown in table 5.4.2. (which summarizes information from table 5.4. in the appendix).
All articles, except for Jastrzębska et al. (2016), had muscle strength as outcome measure. Wyon et al. (2014) found a mean increase of 13% for the intervention group between days one to eight, whereas the control group increased with 3% in quadriceps and hamstrings muscle strength. Main effects for muscle strength (p<0,001), speed (p<0,001) and time (p<0,001) were found. Furthermore, there was a time by treatment interaction: the intervention group had greater improvement of muscle strength compared to the control group over time (p = 0.01) and a muscle by time by treatment interaction: the intervention group also had greater improvement in muscle strength over time and per muscle, compared to the control group (p=0.027). Agergaard et al. (2015) stated a significant increase for both intervention- and control group (p<0,05), but no difference between groups (p=0,71). Close et al. (2013a) did not show significant changes and differences between groups (p=0,17 - 0,90) and Close et al. (2013b) found a trend for time by group interaction (p=0,065). Josse et al. (2010) stated that both intervention- and control group gained strength in all performance tests (p<0,05) and that there was a time by treatment interaction for bench press (p=0,029) and a trend toward significance for chest fly's (p=0,086) for the intervention group, compared with the control group.
Three studies in this group investigated the effect on muscle power. Close et al. (2013b) mentions a time by group interaction for ten meter sprint for intervention group (p=0,008). Furthermore, Jastrzębska et al. (2016) and Close et al. (2013a) found no significant differences between intervention- and control group (p=0,338 and p=0,90), but both studies mentioned an improvement over time (p<0,05).
Secondary, two articles investigated the effect on speed. Jastrzębska et al. (2016) stated a significant improvement for both groups after the training period for 10m. and 20m. running (p<0,001) but no significant difference between intervention- and control group (p=0,505 and p= 0,436). Close et al. (2013b) found a time by group interaction for 10m. sprint for intervention group (p=0,008). No significant difference was found in the control group or between group.

Only one study examined the effect on muscle CSA and fiber type. Agergaard et al. (2015) found significant gains in quadriceps muscle CSA after 12 weeks for both intervention- and control group. But there was no significant difference between both groups (p=0,87). Fiber %type IIa and I increased and % of type IIx decreased significantly (p<0,05). There was more increase in type IIa for intervention group compared to control group, but this was not significant.

The third group consists of one article, Barker et al. (2013). Subjects received a 28 days-during supplementation period of 4000 IU vitamin D3. After that, one exhausting exercise was given for one leg. Barker et al. (2013) found a decrease of muscle strength in the control leg immediately and 48h after the damaging event, but the intervention leg was more severe ($p<0,05$). However, no significant difference between the intervention- and control group was found. For muscle power, the intervention group had a bigger decrease than the control group ($p<0,05$), however no significant difference was found between groups at different time points. Regarding delayed onset muscle soreness (DOMS), There was an increase in DOMS immediately after exercise ($p<0,05$). Furthermore, this persisted for 24 hours to 72 hours. Supplementation had no effect on it.

The outcome measures of the third group are shown in table 5.4.3. (which summarizes information from table 5.4. in the appendix).

The fourth group, consisting of two articles, had a different training protocol compared to the other groups. Participants underwent an exercise protocol and received supplementation afterwards. Participants in the study of Wyon et al. (2016) were professional national level judoka athletes, who underwent three weeks training consisting of two hours strength, one hour conditioning, one hour technical training and three hours randori training, each day. After the eight-weeks during training period they received just one intake of 150 000 IU vitamin D3. In the study of Owens et al. (2015), participants received a daily intake of 4000 IU after a damaging exercise, for six weeks. They had to complete 20x 10 damaging eccentric contractions, to induce muscle damage. Afterwards the supplementation period started.

Regarding muscle strength, Wyon et al. (2016) found significant group by time interaction ($p=0,03$) with small effect ($eta^2 = 0,197$), while Owens et al. (2015) reported a loss of peak torque immediately post-exercise in both the intervention- and control group ($p<0,005$). After supplementation they reported a significant improvement in torque recovery in the intervention group at 48h and seven days post-exercise ($p=0,042$).

Regarding muscle power, Wyon et al. (2016) found a significant group by time interaction ($p=0,004$) with moderate effect size ($eta^2=0,322$).
Owens et al. (2015) also investigated the effect on DOMS. There was no interaction between intervention group and time for muscle soreness at the midpoint of the Quadriceps or 5 cm. above the patella ($p=0,71$ and $p=0,418$), measured with pressure algometry. For recovery, Owens et al. (2015) mentioned that the migration velocity and distance significantly enhanced in intervention group one and two (study part two) ($p<0,0005$). This partly explains the improved functional recovery of skeletal muscle with higher serum 25(OH)D in vivo. It may also point toward a positive role for vitamin D in muscle remodeling given the increases in myotube size and nuclear accretion.

An overview of all the outcome measures and results can be found in table 5.2. in the appendix.
Measures were taken to reduce variability. This varied from measuring samples at the same time (Agergaard et al., 2015) to completing a test-retest reliability study (Close, Leckey, et al., 2013),

performing a quality control test on a daily basis (Josse et al., 2010) or zeroing and load calibrating before every testing session (Barker et al., 2012). Furthermore, quite often measures were also taken to ensure proper blinding and randomization. For example, in the study of Agergaard et al. (2015), calcium was given to both groups, whereas Josse et al. (2010) used vanilla-flavored drinks to ensure identical odor and taste. Barker et al. (2012) used a randomized, double-blind, placebo-controlled design and randomized leg selection for the single-leg peak isometric force measurements.

Lastly, limitations concerning time were detected in the articles. Interventions were too short (Agergaard et al., 2015; Barker et al., 2012), data collection was limited to weekly blood draws, while evidence suggests that the cytokine modulating property of vitamin D could be time sensitive (Barker et al., 2012). Finally, Gupta et al. (2010) assessed muscle strength and energy parameters after six months of dual supplementation, while serum 25(OH)D levels were significantly higher at two months. This makes it possible that subjects in the supplementation group could have shown a higher degree of improvement at two months.

5. Discussion

5.1. Reflection on the quality of the included studies

Based on the PEDRO-checklist, the quality of the included articles is rather good. Criteria eight to eleven were met in all articles, whereas no blinding was the most frequent reason of lower scores, even though the design of all interventions allowed for proper blinding of both patients, therapists and assessors. Only one article, Wyon et al. (2014), is of bad quality due to not having specified criteria, no randomization and no blinding of subjects, therapists and assessors. This was the result of having a small sample size and volunteers as control group.

5.2. Reflection on the findings in function of the research questions

Only four studies observed beneficial effects of vitamin D supplementation during training on muscle strength and two found a trend towards significance, while only two studies found a beneficial effect on muscle power. These studies included a population with insufficient or deficient serum vitamin D concentrations at baseline. This confirms the previously mentioned statement that studies have shown a positive correlation between vitamin D concentration and muscle function (Hamilton, 2010).

On the other hand, five studies did not found an additional effect of vitamin D supplementation during training on muscle strength or muscle power.

Research on other effects such as the improvement in speed, muscle cross-sectional area (CSA), muscle fiber type and/or Delayed Onset of Muscle Soreness (DOMS) is scarce. Vitamin D supplementation had no additional effects on these muscle characteristics in the present thesis. All these results were found if vitamin D was added into a normal active daily living pattern, if it was combined with sport and if combined with strengthening exercises.

Important to mention is that the articles did not investigate every effect: some articles investigated a possible change in muscle strength and muscle power, other articles analyzed cross-sectional area, muscle fiber type and/or DOMS. Furthermore, a wide variety in the supplements' concentration was used: some articles supplemented high concentrations, other used lower ones. Lastly, the frequency of supplementation differed: some articles supplemented daily, some weekly. These differences in the intervention of the included articles may be the cause of the variety in findings.

5.3. Reflections on the strengths and weaknesses of the literature study

An overview of the strengths and weaknesses of the included articles can be found in table 4.

Because baseline characteristics concerning serum total 25(OH)D were similar between intervention and control groups, a proper investigation on the possible effect of vitamin D supplementation could be executed. Furthermore, measures that were taken to ensure proper blinding, randomization and to reduce variability, increased the reliability of results. With no major side effects, a high compliance and a low dropout rate regarding the intervention, conclusions can be drawn that the interventions are easy executable and well tolerated.

However, because the included articles consisted of a small sample size and a heterogeneous population between the articles (volunteers, sedentary men/women, professional/ club athletes, rugby, soccer players, ballet dancers/ judokas), it makes it difficult to generalize the results. Conclusions about a long term effect cannot be drawn, because of the short intervention periods.

At last, the literature search conducted for the master thesis also has some strengths and weaknesses. The main strength is the inclusion of a sufficient amount of articles of high quality. Also, the inclusion and exclusion criteria allowed for the examination of a specific population concerning vitamin D concentration and age within articles, without making it too narrow. The main weakness of the literature search is the fact that a consensus about the appropriate concentration for vitamin D supplementation has not been found, because results differ. Furthermore, a conclusion about the ideal exercise protocol cannot be made, reason being the fact that all articles used another exercise program.

5.4. Recommendations for further research

In order to improve research on the effect of vitamin D supplementation, combined with strength training on skeletal muscles, several recommendations can be made.

5.4.1. Optimize supplementation

The included articles all vary in different aspects. One being the differences in concentration of the supplement, another being differences in the frequency and duration of supplementation. This makes it hard to draw clear conclusions. For example, a concentration of 2000 IU/day for four months while maintaining regular sport activities results in significant better muscle power in the intervention group, compared to the control group, whereas a concentration of 4000 IU/day, combined with or without quercetin or 800 mg Calcium is not significant better for the intervention group while maintaining active daily living or regular sport activities. This concentration of vitamin D is only significantly more effective in the intervention group, compared to the control group for an improvement in torque recovery at 48h and seven days post-exercise and the migration velocity and distance, when supplemented after a damaging event for six weeks.

Supplementing 5000 IU/day for eight weeks has mixed results: one article shows no significant difference between groups, another one found a trend for strength and a significant difference for power and the 10 meter sprint. Results regarding one supplement/week were clear: both concentrations of 20.000 or 40.000 IU for 12 weeks were not significant better compared to the control group. However, supplementing 60.000 IU, three times/week for 8 weeks, combined with a follow-up supplementation of one/month for four months while maintaining active daily living, resulted in significantly higher handgrip and gastro-soleus strength improvements in the intervention group, compared to the control group. Lastly, supplementing 150.000 IU once after a training period of eight weeks, resulted in significant higher strength measurements in the intervention group, compared to the control group.

Although serum total 25(OH)D increased significantly in each study, additional effects of vitamin D supplementation on muscle function was scarce. A clear conclusion about which total serum level 25(OH)D should be obtained in order to induce a physiological response in the skeletal muscles cannot be drawn. One article states a concentration of more than 100 nmol/L, another more than 127,2 nmol/L (40ng/mL). Since not all populations in the articles achieved these quantities, it can be assumed that higher supplementation concentrations (> 5000 IU) are necessary to achieve these serum levels for a

longer period (> 12 weeks). Furthermore, it can be suggested that a daily dose may be superior in raising 25(OH)D levels when compared to a weekly dose (40,000IU/week).
Finally, it is important to know that the baseline serum 25(OH)D concentration determines the level of response, meaning there is a need for an individualized approach towards supplementation. With these concepts in mind, further research should investigate the effect of vitamin D supplementation, combined with strength training.

5.4.2. Nature of training program

Not only the supplementation, but also the training program differs between articles. Both maintaining active daily living, maintaining sport activities and the implementation of strength training programs are analyzed in the articles. Even within these groups, activity levels widely differ: the effect of supplementation while maintaining sport activities is analyzed on different sports such as soccer, rugby or ballet, but training in these sports differ. Although both articles in group four used strengthening exercises, the programs itself had a lot of differences regarding exercises and training volume. Hereby, future research should try to investigate effects of vitamin D supplementation, in combination with a strengthening program that has the same exercises and same training volume in each study. In this way, the intervention is standardized, which makes it easier to draw possible conclusions.

5.4.3. Length of the training program and follow-up

Some training programs in the included articles were rather short and follow up was mostly not added. Several studies with longer duration and a follow-up period should be executed in order to determine the optimal length of training programs. The addition of different follow-up periods allows for the assessment if possible effects can be preserved.

5.4.4. Patient population: larger number of people with more homogeneity within the population

The number of participants in most studies was rather low. Furthermore, comparing studies is difficult because the heterogeneity of the population. Both amateur and professional athletes were analyzed, but also sedentary young men, active male adults, and sufficient, insufficient and even deficient adults. Only one study investigated a population of adults with a sufficient serum vitamin D concentration. This is something that needs to be examined more in the future. It is also required that larger, homogeneous populations are analyzed to draw conclusions about a possible effect.

6. Conclusion

According to the literature review it is difficult to make a clear conclusion because of the heterogeneity in supplementation, training program and population. Further research is necessary to investigate the effect of vitamin D supplementation on overall muscle function.

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8. Appendix- overview of the literature

Table 1: Overview of number of hits for different combinations of search terms

Term	Hits (30/01)	Hits (2/05)
1. "Vitamin D" [MeSH]	52276	53014
2. Vitamin d	75007	76131
3. Vitamin d supplement	6109	6296
4. Vitamin d supplement*	5907	6100
5. Vitamin d supplements	6614	6811
6. Vitamin d supplementation	8599	8857
7. Vitamin d intake	6789	6912
8. Supplemental vitamin d	716	739
9. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8*	73589	74707
10. Muscle	1014394	1023660
11. "Muscle strength"[MeSH]	26230	27006
12. Muscle strength	56059	57311
13. "Muscle, skeletal"[MeSH]	240323	242948
14. ‘'Muscle Fibers, Skeletal"[MeSH]	40238	40478
15. Skeletal muscle	298472	301674
16. Muscle fiber typing	181	181
17. Muscle fibre typing	91	92
18. Muscle cross sectional area	9625	9849
19. Muscle csa	2447	2492
20. 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19*	696903	704389
21. "Exercise"[MeSH]	160178	164245
22. Exercise	363126	370118
23. Training	1464412	1495169
24. Exercise training	363126	370118
25. Resistance training	17774	18359
26. Strengthening training	6670	6860
27. Strengthening program	3806	3909
28. Endurance training	15149	15408

29. “Sports”[MeSH]	159026	161811
30. 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29*	655855	668283
31. 9 AND 19 AND 30 *	398	405

Full literature search:

((((((((("Vitamin D"[MeSH]) OR vitamin d[Title/Abstract]) OR vitamin d supplement[Title/Abstract]) OR vitamin d supplement*[Title/Abstract]) OR vitamin d supplements[Title/Abstract]) OR vitamin d supplementation[Title/Abstract]) OR vitamin d intake[Title/Abstract]) OR supplemental vitamin d[Title/Abstract])) AND ((((((((((muscle[Title/Abstract]) OR "Muscle Strength"[MeSH]) OR muscle strength[Title/Abstract]) OR "Muscle, Skeletal"[MeSH]) OR "Muscle Fibers, Skeletal"[MeSH]) OR skeletal muscle[Title/Abstract]) OR muscle fiber typing[Title/Abstract]) OR muscle fibre typing[Title/Abstract]) OR muscle cross sectional area[Title/Abstract]) OR muscle csa[Title/Abstract])) AND (((((((("Exercise"[MeSH]) OR exercise[Title/Abstract]) OR training[Title/Abstract]) OR exercise training[Title/Abstract]) OR resistance training[Title/Abstract]) OR strengthening training[Title/Abstract]) OR strengthening program[Title/Abstract]) OR endurance training[Title/Abstract]) OR "Sports"[MeSH])

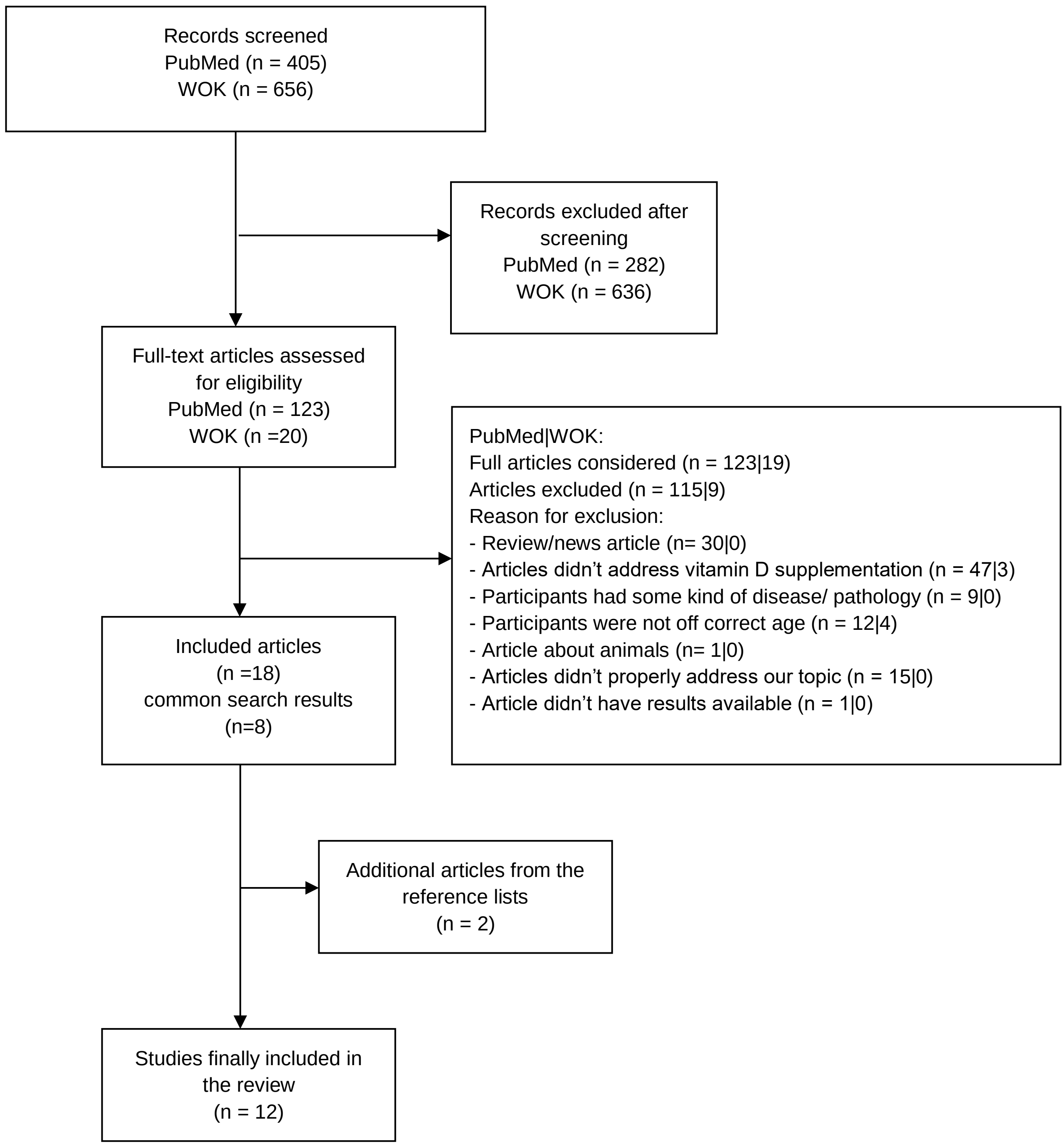

Figure 1: Flow chart in- and excluded articles PubMed + WOK search

Table 2: Overview of the excluded articles + reason for exclusion

Table 2.1: Review/ news article

Author	Title	Source
Review/ news article		
(Abboud et al., 2014)	Uptake of 25-hydroxyvitamin D by muscle and fat cells.	PubMed
(Angeline, Gee, Shindle, Warren, & Rodeo, 2013)	The effects of vitamin D deficiency in athletes.	PubMed
(Bartoszewska, Kamboj, & Patel, 2010)	Vitamin D, muscle function, and exercise performance.	PubMed
(Hamilton, 2011)	Vitamin d and athletic performance: the potential role of muscle	PubMed
(Cannell, Hollis, Sorenson, Taft, & Anderson, 2009)	Athletic performance and vitamin D.	PubMed
(Ceglia & Harris, 2013)	Vitamin D and its role in skeletal muscle.	PubMed
(Dahlquist, Dieter, & Koehle, 2015)	Plausible ergogenic effects of vitamin D on athletic performance and recovery	PubMed
(Daly, 2010)	Independent and combined effects of exercise and vitamin D on muscle morphology, function and falls in the elderly.	PubMed
(Daly, Duckham, & Gianoudis, 2014)	Evidence for an interaction between exercise and nutrition for improving bone and muscle health.	PubMed
(Ogan & Pritchett, 2013)	Vitamin D and the athlete: risks, recommendations, and benefits.	PubMed
(Deane et al., 2017)	"Nutraceuticals" in relation to human skeletal muscle and exercise.	PubMed
(Eskici, 2015)	The Importance of Vitamins for Soccer Players.	PubMed
(Shuler, Wingate, Moore, & Giangarra, 2012)	Sports health benefits of vitamin d.	PubMed
(Close, Hamilton, Philp, Burke, & Morton, 2016)	New strategies in sport nutrition to increase exercise performance.	PubMed
(Girgis, Clifton-Bligh, Turner, Lau, & Gunton, 2014)	Effects of vitamin D in skeletal muscle: falls, strength, athletic performance and insulin sensitivity.	PubMed
(Gross, 2007)	[With guided training and adequate vitamin intake muscle atrophy in the elderly can be prevented].	PubMed
(Hamilton, 2010)	Vitamin D and human skeletal muscle.	PubMed
(Aumiller, 2010)	Sports, healthy nutrition and vitamin D stop dangerous muscle loss. Sarcopenia as age related risk].	PubMed
(Koundourakis, Avgoustinaki, Malliaraki, & Margioris, 2016)	Muscular Effects of Vitamin D In Young Athletes and Non-Athletes and in the Elderly	PubMed
(Larson-Meyer & Willis, 2010)	Vitamin D and athletes.	PubMed

Author	Title	Source
Review/ news article		
(Owens, Allison, & Close, 2018)	Vitamin D and the Athlete: Current Perspectives and New Challenges	PubMed
(Powers, Nelson, & Larson-Meyer, 2011)	Antioxidant and Vitamin D supplements for athletes: sense or nonsense?	PubMed
(Rawson, Miles, & Larson-Meyer, 2018)	Dietary Supplements for Health, Adaptation, and Recovery in Athletes	PubMed
(Rivlin, 2007)	Keeping the young-elderly healthy: is it too late to improve our health through nutrition?	PubMed
(Todd, Pourshahidi, McSorley, Madigan, & Magee, 2015)	Vitamin D: recent advances and implications for athletes.	PubMed
(von Hurst & Beck, 2014)	Vitamin D and skeletal muscle function in athletes	PubMed
(Williams, 1989)	Vitamin supplementation and athletic performance.	PubMed
(Willis, Peterson, & Larson-Meyer, 2008)	Should we be concerned about the vitamin D status of athletes?	PubMed

Table 2.2: No vitamin D supplementation

Author	Title	Source
No vitamin D supplementation		
(Abboud, Rybchyn, Rizk, Fraser, & Mason, 2017)	Sunlight exposure is just one of the factors which influence vitamin D status	PubMed
(Al-Eisa, Alghadir, & Gabr, 2016)	Correlation between vitamin D levels and muscle fatigue risk factors based on physical activity in healthy older adults.	PubMed
(Ardestani et al., 2011)	Relation of vitamin D level to maximal oxygen uptake in adults.	PubMed
(Barker et al., 2013)	Higher serum 25-hydroxyvitamin D concentrations associate with a faster recovery of skeletal muscle strength after muscular injury.	PubMed
(Barker et al., 2014)	Vitamin D sufficiency associates with an increase in anti-inflammatory cytokines after intense exercise in humans.	PubMed
(Bell, Godsen, Henry, Shary, & Epstein, 1988)	The effects of muscle-building exercise on vitamin D and mineral metabolism.	PubMed
(Bezrati et al., 2016)	Association of plasma 25-hydroxyvitamin D with physical performance in physically active children.	PubMed
(Bischoff-Ferrari et al., 2004)	Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged > or =60 y.	PubMed
(Brännström et al., 2017)	Vitamin D in relation to bone health and muscle function in young female soccer players	PubMed

Author	Title	Source
No vitamin D supplementation		
(Carson et al., 2015)	Vitamin D, Muscle Function, and Cardiorespiratory Fitness in Adolescents From the Young Hearts Study.	PubMed
(Chuang et al., 2016)	Circulating 25-hydroxyvitamin D and physical performance in older adults: a nationwide study in Taiwan.	PubMed
(Conrad & Glueck, 2013)	Does low serum 25 OH vitamin D interact with very strenuous physical activity, facilitating development of rhabdomyolysis?	PubMed
(Dubnov-Raz et al., 2014)	Vitamin D concentrations and physical performance in competitive adolescent swimmers.	PubMed
(Ducher et al., 2011)	Vitamin D status and musculoskeletal health in adolescent male ballet dancers a pilot study.	PubMed
(Dupuy et al., 2013)	Dietary vitamin D intake and muscle mass in older women. Results from a cross-sectional analysis of the EPIDOS study.	PubMed
(Forney et al., 2014)	Vitamin D status, body composition, and fitness measures in college-aged students.	PubMed
(Fuller et al., 2011)	Vitamin D status affects strength gains in older adults supplemented with a combination of β-hydroxy-β-methylbutyrate, arginine, and lysine: a cohort study.	PubMed
(Geiker et al., 2017)	Vitamin D status and Muscle Function Among Adolescent and Young Swimmers	PubMed + WOK
(Hildebrand, Miller, Warren, Hildebrand, & Smith, 2016)	Compromised Vitamin D Status Negatively Affects Muscular Strength and Power of Collegiate Athletes.	PubMed
(R., M., S., J., & D., 2010)	Relationship between vitamin D intake and sunshine exposure on the parameters of muscle strength and function in trained rugby players	WOK
(Houston et al., 2007)	Association between vitamin D status and physical performance: the InCHIANTI study.	PubMed
(Houston et al., 2011)	Serum 25-hydroxyvitamin D and physical function in older adults: the Cardiovascular Health Study All Stars.	PubMed
(Iolascon et al., 2015)	Hypovitaminosis D is associated with a reduction in upper and lower limb muscle strength and physical performance in post-menopausal women: a retrospective study.	PubMed
(Jerome et al., 2017)	25(OH)D Levels in Trained versus Sedentary University Students at 64° North	PubMed
(Justice, Pierpoint, Mani, Schwartz, & Enoka, 2014)	Motor function is associated with 1,25(OH)(2)D and indices of insulin-glucose dynamics in non-diabetic older adults	PubMed
(Kobza et al., 2013)	Vitamin D status and resistance exercise training independently affect glucose tolerance in older adults.	PubMed + WOK
(Koundourakis, Androulakis, Malliaraki, & Margioris, 2014)	Vitamin D and exercise performance in professional soccer players.	PubMed
(Lämmle, Bergmann, Bös, & Koletzko, 2013)	Predictors of differences in vitamin D levels in children and adolescents and their relation to endurance performance.	PubMed
(Mastaglia et al., 2011)	Effect of vitamin D nutritional status on muscle function and strength in healthy women aged over sixty-five years.	PubMed
(Mehran, Schulz, Neri, Robertson, & Limpisvasti, 2016)	Prevalence of Vitamin D Insufficiency in Professional Hockey Players.	PubMed
(Morton et al., 2012)	Seasonal variation in vitamin D status in professional soccer players of the English Premier League.	PubMed

Author	Title	Source
No vitamin D supplementation		
(Moschonis et al., 2009)	Association between serum 25-hydroxyvitamin D levels and body composition in postmenopausal women: the postmenopausal Health Study.	PubMed
(Murakami et al., 2009)	Effects of vitamin D receptor gene polymorphisms on low-resistance training using exercise machines: the 'Power Rehabilitation' program.	PubMed
(Nascimento et al., 2016)	Relation among 25(OH)D, Aquatic Exercises, and Multifunctional Fitness on Functional Performance of Elderly Women from the Community.	PubMed
(Ojah & Welch, 2012)	Vitamin D and musculoskeletal status in Nova Scotian women who wear concealing clothing.	PubMed
(Pilch, Tyka, Cebula, Śliwicka, & Pilaczyńska-Szcześniak, 2017)	Effects of a 6-week Nordic walking training on changes in 25(OH)D blood concentration in women aged over 55.	PubMed
(Ring, Dannecker, & Peterson, 2010)	Vitamin d status is not associated with outcomes of experimentally-induced muscle weakness and pain in young, healthy volunteers.	PubMed
(Rizzoli et al., 2014)	The role of dietary protein and vitamin D in maintaining musculoskeletal health in postmenopausal women: a consensus statement from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO).	PubMed
(Salminen et al., 2015)	Vitamin D status and physical function in older Finnish people: A one-year follow-up study.	PubMed
(Scott et al., 2016)	Associations of Vitamin D with Inter- and Intra-Muscular Adipose Tissue and Insulin Resistance in Women with and without Polycystic Ovary Syndrome.	PubMed
(Solarz et al., 2014)	An evaluation of the levels of 25-hydroxyvitamin D3 and bone turnover markers in professional football players and in physically inactive men.	PubMed
(Stewart et al., 2009)	Serum 25-hydroxyvitamin D is related to indicators of overall physical fitness in healthy postmenopausal women.	PubMed
(Toffanello et al., 2012)	Vitamin D and physical performance in elderly subjects: the Pro.V.A study.	PubMed
(Udowenko & Trojian, 2010)	Vitamin D: extent of deficiency, effect on muscle function, bone health, performance, and injury prevention.	PubMed
(Valtueña et al., 2013)	Cardiorespiratory fitness in males, and upper limbs muscular strength in females, are positively related with 25-hydroxyvitamin D plasma concentrations in European adolescents: the HELENA study.	PubMed
(Valtueña, Dominguez, Til, González-Gross, & Drobnic, 2014)	High prevalence of vitamin D insufficiency among elite Spanish athletes the importance of outdoor training adaptation.	PubMed
(van Schoor et al., 2012)	Peak expiratory flow rate shows a gender-specific association with vitamin D deficiency.	PubMed
(Ward et al., 2009)	Vitamin D status and muscle function in post-menarchal adolescent girls.	PubMed

Table 2.3: Disease/ pathology

Author	Title	Source
Disease/ pathology		
(Avitabile et al., 2014)	Lean mass deficits, vitamin D status and exercise capacity in children and young adults after Fontan palliation.	PubMed
(Bauer et al., 2015)	Effects of a vitamin D and leucine-enriched whey protein nutritional supplement on measures of sarcopenia in older adults, the PROVIDE study: a randomized, double-blind, placebo-controlled trial.	PubMed
(Carrillo et al., 2013)	Impact of vitamin D supplementation during a resistance training intervention on body composition, muscle function, and glucose tolerance in overweight and obese adults.	PubMed
(Heffler et al., 2016)	Vitamin D deficiency and exercise-induced laryngospasm in young competitive rowers.	PubMed
(C. Mason et al., 2016)	Effects of Vitamin D3 Supplementation on Lean Mass, Muscle Strength, and Bone Mineral Density During Weight Loss: A Double-Blind Randomized Controlled Tria	PubMed
(Singla et al., 2017)	Vitamin D Supplementation Improves Simvastatin-Mediated decline in exercise Performance: A Randomized Double-Blind Placebo-Controlled Study	PubMed
(Sinha, Hollingsworth, Ball, & Cheetham, 2013)	Improving the vitamin D status of vitamin D deficient adults is associated with improved mitochondrial oxidative function in skeletal muscle	PubMed
(Verreijen et al., 2015)	A high whey protein-, leucine-, and vitamin D-enriched supplement preserves muscle mass during intentional weight loss in obese older adults: a double-blind randomized controlled trial.	PubMed
(Yamada et al., 2012)	Nutritional Supplementation during Resistance Training Improved Skeletal Muscle Mass in Community-Dwelling Frail Older Adults.	PubMed

Table 2.4: age

Author	Title	Source
Age		
(Bunout et al., 2006)	Effects of vitamin D supplementation and exercise training on physical performance in Chilean vitamin D deficient elderly subjects.	PubMed
(Dubnov-Raz, Livne, Raz, Cohen, & Constantini, 2015)	Vitamin D supplementation and physical performance in adolescent swimmers.	PubMed
(El-Hajj Fuleihan et al., 2006)	Effect of vitamin D replacement on musculoskeletal parameters in school children: a randomized controlled trial.	PubMed
(Gmiat et al., 2017)	Changes in Pro-Inflammatory Markers and Leucine Concentrations in Response to Nordic Walking training Combined with Vitamin D Supplementation in Elderly Women.	PubMed
(Kukuljan, Nowson, Sanders, & Daly, 2009)	Effects of resistance exercise and fortified milk on skeletal muscle mass, muscle size, and functional performance in middle-aged and older men: an 18-mo randomized controlled trial.	PubMed + WOK
(Kukuljan, Nowson, Bass, et al., 2009)	Effects of a multi-component exercise program and calcium-vitamin-D3-fortified milk on bone mineral density in older men: a randomised controlled trial.	PubMed
(C. Mason et al., 2016)	Effects of Vitamin D-3 Supplementation on Lean Mass, Muscle Strength, and Bone Mineral Density During Weight Loss: A Double-Blind Randomized Controlled Trial	WOK

Author	Title	Source
Age		
(Oesen et al., 2015)	Effects of elastic band resistance training and nutritional supplementation on physical performance of institutionalised elderly--A randomized controlled trial.	PubMed
(Peake, Kukuljan, Nowson, Sanders, & Daly, 2011)	Inflammatory cytokine responses to progressive resistance training and supplementation with fortified milk in men aged 50+ years: an 18-month randomized controlled trial.	PubMed + WOK
(Povoroznyuk, Dzerovych, & Povorznyuk, 2017)	The role of vitamin D and exercises in correction of age-related skeletal muscle changes in postmenopausal women	WOK
(Shanely et al., 2014)	Influence of vitamin D mushroom powder supplementation on exercise-induced muscle damage in vitamin D insufficient high school athletes	PubMed
(Uusi-Rasi et al., 2015)	Exercise and vitamin D in fall prevention among older women: a randomized clinical trial.	PubMed
(Uusi-Rasi et al., 2017)	A 2-Year Follow-Up After a 2-Year RCT with Vitamin D and Exercise: Effects on Falls, Injurious Falls and Physical Functioning Among Older Women	PubMed
(Verschueren et al., 2011)	The effects of whole-body vibration training and vitamin D supplementation on muscle strength, muscle mass, and bone density in institutionalized elderly women: a 6-month randomized, controlled trial.	PubMed

Table 2.5: animals

Author	Title	Source
Animals		
(Ke et al., 2016)	Vitamin D3 Reduces Tissue Damage and Oxidative Stress Caused by Exhaustive Exercise.	PubMed

Table 2.6: Didn’t properly address topic

Author	Title	Source
Didn't properly address topic		
(Brock, Cant, Clemson, Mason, & Fraser, 2007)	Effects of diet and exercise on plasma vitamin D (25(OH)D) levels in Vietnamese immigrant elderly in Sydney, Australia.	PubMed
(Darr et al., 2016)	Vitamin D supplementation affects the IGF system in men after acute exercise	PubMed
(Hansen et al., 2015)	Treatment of Vitamin D Insufficiency in Postmenopausal Women: A Randomized Clinical Trial.	PubMed
(Iolascon, Moretti, de Sire, Calafiore, & Gimigliano, 2017)	Effectiveness of Calcifediol in Improving Muscle Function in Post-Menopausal Women: A Prospective Cohort Study.	PubMed
(Kenny, Biskup, Robbins, Marcella, & Burleson, 2003)	Effects of vitamin D supplementation on strength, physical function, and health perception in older, community-dwelling men.	PubMed
(Lagari, Gómez-Marín, & Levis, 2013)	The role of vitamin D in improving physical performance in the elderly.	PubMed

Author	Title	Source
Didn't properly address topic		
(Moreira-Pfrimer, Pedrosa, Teixeira, & Lazaretti-Castro, 2009)	Treatment of vitamin D deficiency increases lower limb muscle strength in institutionalized older people independently of regular physical activity: a randomized double-blind controlled trial.	PubMed
(Nieman et al., 2013)	Vitamin D2 supplementation amplifies eccentric exercise-induced muscle damage in NASCAR pit crew athletes.	PubMed
(Okuno et al., 2011)	[Examination of effects of alfacalcidol vitamin D supplement and renal function on improvement in the physical fitness of pre-frail elderly persons attending a nursing care prevention class].	PubMed
(Park et al., 2013)	Concomitant increase in muscle strength and bone mineral density with decreasing IL-6 levels after combination therapy with alendronate and calcitriol in postmenopausal women.	PubMed
(Sheedy et al., 2014)	(1)H-NMR analysis of the human urinary metabolome in response to an 18-month multi-component exercise program and calcium-vitamin-D3 supplementation in older men.	PubMed
(Tellioglu, Basaran, Guzel, & Seydaoglu, 2012)	Efficacy and safety of high dose intramuscular or oral cholecalciferol in vitamin D deficient/insufficient elderly.	PubMed
(Verhaar et al., 2000)	Muscle strength, functional mobility and vitamin D in older women.	PubMed
(Wijnen, Salemink, Roovers, Taekema, & de Boer, 2015)	Vitamin D supplementation in nursing home patients: randomized controlled trial of standard daily dose versus individualized loading dose regimen.	PubMed
(Xue et al., 2017)	Effects of Enhanced Exercise and Combined Vitamin D and Calcium Supplementation on Muscle Strength and Fracture Risk in Postmenopausal Chinese Women	PubMed

Table 2.7: No results available

Author	Title	Source
No results available		
(Uusi-Rasi et al., 2012)	Study protocol for prevention of falls: a randomized controlled trial of effects of vitamin D and exercise on falls prevention.	PubMed

Table 3: PEDRO-checklist for RCT's and CCT's

Table: quality assessment													
Author	**Criteria**	**1. Specified criteria?**	**2. Randomization?**	**3. Concealed allocation?**	**4. Baseline characteristics?**	**5. Blinding of subjects?**	**6. Blinding of therapists?**	**7. Blinding of assessors?**	**8. Loss to follow up?**	**9. Intention to treat?**	**10. Between-group comparison?**	**11. Point measure?**	**total score (%)**
Agergaard et al. (2015)		+	+	+	+	+	+	+	+	+	+	+	11/11 (100%)
Barker et al. (2012)		+	+	+	+	+	+	+	+	+	+	+	11/11 (100%)
Barker et al. (2013)		+	+	+	+	+	+	+	+	+	+	+	11/11 (100%)
Close et al. (2013)		+	+	+	+	+	+	+	+	+	+	+	11/11 (100%)
Close et al. (2013)		+	+	+	-	+	+	+	+	+	+	+	10/11 (91%)
Gupta et al. (2010)		+	+	+	+	+	+	+	+	+	+	+	11/11 (100%)
Jastrzębska et al. (2016)		-	-	+	+	+	+	+	+	+	+	+	9/11 (91%)
Josse et al. (2010)		+	+	+	+	+	-	-	+	+	+	+	9/11 (91%)
Owens et al. (2015)		+	+	+	+	?	?	?	+	+	+	+	8/11 (73%)
Scholten et al. (2015)		+	+	+	+	+	+	+	+	+	+	+	11/11 (100%)
Wyon et al. (2014)		-	-	-	+	-	-	-	+	+	+	+	5/11 (45%)
Wyon et al. (2016)		+	+	+	-	+	+	+	+	+	+	+	10/11 (91%)

+: met criterium; - : did not meet criterium; ?: not mentioned

Criteria:

1. Eligibility criteria were specified
2. subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received).
3. Allocation was concealed.
4. The groups were similar at baseline regarding the most important prognostic indicators.
5. There was blinding of all subjects.
6. There was blinding of all therapists who administered the therapy.
7. There was blinding of all assessors who measured at least one key outcome.
8. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups.
9. All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by "intention to treat".
10. The results of between-group statistical comparisons are reported for at least one key outcome.
11. The study provides both point measures and measures of variability for at least one key outcome.

Table 4: Strengths and weaknesses of the included articles

Article	Strengths	Limitations
Agergaard et al. (2015)	- There were no serious injuries or adverse events associated with the exercise program - calcium was given to both groups (plays role in skeletal muscle outcome) - All 25(OH)D samples were measured at the same time with the ELISAkit. - CSA of the quadriceps muscle was measured in the middle third of the thigh, as the greatest increase is known to occur in this location.	- The present study was too short for the elderly.
Barker et al. (2012)	- the experimental design (randomized, double-blind, placebo-controlled) and the examination of two different doses of supplemental vitamin D are strengths of this investigation. - Before every testing session, the mounted force plate was zeroed and load calibrated. - For the single-leg peak isometric force measurements, leg selection was randomized. - Subject characteristics were similar between groups (Table 1): <6% difference in body mass, <1% difference in BMI between vitamin D groups	- A rather short-intervention phase. - the level of physical activity was not stringently examined. - The study consisted of thirty subjects. - Data collection was limited to weekly blood draws and emerging evidence is suggesting that the cytokine modulating property of vitamin D could be time sensitive. - There was variability across time in the cytokine data. - Serum 25(OH)D, inflammatory cytokines and muscular strength might respond differently in diverse populations or conditions → extrapolating findings to other populations is not recommended.
Barker et al. (2013)	- Prior to supplementation, subject characteristics and serum 25(OH)D concentrations were similar between the groups	- Some subjects performed exercise protocol until volitional exhaustion, while others completed the protocol → differences in exercise volume. - VitD group tended to display greater decreases in peak isometric forces and peak power outputs at Post→ could suggest greater fatigue after exercise protocol and greater capacity for faster recovery. - It does not identify if supplemental vitamin D is modulating fatigue- or damage related mechanisms, or both. - Muscle biopsies were obtained to ascertain microscopic alternations in skeletal muscle indicative or damage - subjects were block randomized according to vitamin D status prior to supplementation.
Close et al. (2013)	- All participants initially completed a test–retest reliability study - There was no significant difference in serum total 25[OH]D concentration between groups at baseline.	/
Close et al. (2013)	- The median vitamin D concentration of the healthy controls was almost identical to the median vitamin D concentration of the pooled athletes (with a wide range)	- All the rugby players were taken from one Super League team. - A caveat of the preliminary experiment was that all tests were performed on only one professional soccer team with a low sample size.

Article	Strengths	Limitations
Gupta et al. (2010)	- This study provides useful information on the efficacy of 60 000 IU of cholecalciferol per month in maintaining serum 25(OH)D levels. - Male to female ratio, mean age, BMI, serum total calcium, 25(OH)D, iPTH, parameters of muscle strength and ratio of various metabolites on MRS were comparable in the two groups.	- Muscle strength and energy parameters were assessed after 6 months of dual supplementation. However, serum 25(OH)D levels were significantly higher at 2 months → possible that subjects in the supplementation arm could have shown higher degree of improvement in the muscle strength and energy parameters at 2 months. - The study could not separate the individual effects of cholecalciferol and calcium on muscle strength. - Although none of the subjects returned any sachet or tablets, two of them had distributed their sachets and tablets to their children, assuming the intervention to be a strength-giving measure.
Jastrzebska et al. (2016)	- The pre-supplementation plasma concentration of 25(OH)D did not differ between supplemented and placebo groups - Participation in training sessions of the analyzed players reached 95%.	- no specified eligibility criteria - No randomization of group allocation - there is no consensus on optimal serum 25(OH)D level. The optimal level might have been obtained too late during the study. - no formal dietary assessment of the participants intake of vitamin D before study has been undertaken.
Josse et al. (2010)	- The drinks were flavored with vanilla to ensure identical odor and taste. - Training was monitored daily one on one by personal trainers or trained study personnel to ensure proper exercise technique was used to avoid injury and to adjust the weight lifted accordingly as subjects became stronger. - The DXA machine underwent quality control testing daily to ensure no significant deviations existed in the day-to-day variability. - Subject compliance with the daily drinks and exercise training was excellent with all subjects in both MILK and CON, consuming almost all their assigned drinks in the appropriate manner and completing 92% of their scheduled exercise sessions. - Both the drinks and the exercise protocol were well tolerated, with no major adverse side effects of increased dairy consumption or adverse events relating to exercise.	- Some subjects reported mild cases of upper-body (n = 3 in MILK and n = 2 in CON) and lower-body (n = 1 in MILK) tendonitis
Owens et al. (2015)	- This study is the first to identify a novel role for vitamin D in human skeletal muscle regeneration. - No significant differences were detected between experimental groups for total serum 25(OH)D at baseline.	- the sample size of the RCT is small. - the chosen model of exercise is highly specific, with movements performed at two fixed velocities (not common in everyday life). - Blinding of subjects, therapists and assessors not mentioned.
Scholten et al. (2015)	- The “plotblockrand” function in 3.0.2 was used to create the randomization cards used when assigning participants to the groups.	- Participants were volunteers.

Article	Strengths	Limitations
Wyon et al. (2014)	/	- No specified eligibility criteria - Relatively low number of participants - Lack of proper randomization into groups - Control group were volunteers → no blinding of subjects, therapists and assessors - Control group: 5 participants with 1 injury, 1 with 2 injuries - Intervention group: 5 participants with 1 injury
Wyon et al. (2016)	- For the period of the study and for 3 weeks previously, all participants engaged in the same training schedule to reduce potential confounding factors. - first known study to examine the acute effects of vitamin D3 supplementation.	- Lower serum 25(OH)D3 levels at baseline in intervention group due to seasonality - Single 150 000 IU dose of vitamin D3: appropriate dose?

Table 5: Overview of the included articles:

Table 5.1: Population, aims, interventions:

Article	Population	Aims Study	Intervention
Agergaard et al. (2015) *Nutrition & Metabolism*	20 Healthy untrained/sedentary young men **CG** (n=10): mean age 22,4 yrs **IG** (n=10): mean age 23,3 yrs	Whether vitamin-D intake can improve the muscular response to resistance training in healthy young individuals.	**CG:** 800mg Ca **IG:** Vitamin D3, 1920IU + 800 mg Ca **Protocol:** daily intake, 16 weeks **Training:** progressive resistance training of lower extremities 4w supplement – 12 w suppl + strength training LE 3x/week
Barker et al. (2012) *Nutrition & Metabolism*	30 healthy, vitamin D sufficient men and women. **CG** (n=10):5M/5F,mean age 30,2 yrs **IG1**(n=10):4M/6F,mean age 26,6 yrs **IG2** (n=10): 6M/4F, mean age 29 yrs	Identify the influence of different doses of supplemental vitamin D on inflammatory cytokines and muscular strength in young adults.	**CG**: placebo **IG1**: Vitamin D3, 200 IU **IG2:** Vitamin D3, 4000 IU **Protocol:** daily intake, 28 days **Training:** continued level of physical activity during study period: minimum 30min continuous exercise, 3x/w for 1yr. Pre-test – start supplementation and training - , 7-, 14, 21- and 28 days after supplementation measures.
Barker et al. (2013) *Nutrition & Metabolism*	28 deficient (3), insufficient (10) and sufficient (15) healthy and modestly active men. **CG** (n=13): mean age 31 yrs **IG** (n=15): mean age 30 yrs	Identify the influence of supplemental vitamin D on strength recovery following intense exercise, that induces a persistent deficit in peak isometric force.	**CG**: Placebo **IG**: Vitamin D3, 4000IU **Protocol:** daily intake, 35-days **Training:** 10x10 reps ecc-conc contractions 75% body mass (one leg only) 28 days supplementation – 1 leg exercise protocol – posttest. Part 2: 90 min ecc-based exercise – test 1h, 24h, 48h, 72h, 168h
Close et al. (2013) *British Journal of Sports Medicine*	25 healthy club-level athletes **CG** (n=10): mean age 21 yrs **IG1** (n=10): mean age 22 yrs **IG2** (n=10): mean age 21 yrs	investigate two doses of vitamin D supplementation (20 000 vs 40 000 IU/week vs placebo) on serum 25[OH]D concentration in club-level male athletes over 6 and 12 weeks and (2) to assess if there was any effect of changes in serum 25[OH]D on physical performance.	**CG**: 100mg maltodextrin (placebo) **IG1**: Vitamin D3, 20 000 IU **IG 2:** Vitamin D3, 40 000 IU **Protocol:** 1 intake per week, 12 weeks **Training:** continued to perform their own training plans (no major change in level of physical activity). Pre-test – supplementation + training – post-test (6 and 12 weeks)
Close et al. (2013) *Journal of Sports Sciences*	10 male soccer athletes **CG** (n=5): mean age 18 yrs **IG** (n=5): mean age 18 yrs	To examine the effects of 5000IU.day vitamin D3 supplementation for 8-weeks on musculoskeletal performance.	**CG**: Cellulose **IG**: Vitamin D3, 5000 IU **Protocol:** daily intake, 8 weeks **Training:** continued soccer training Pretest – supplementation + training period – post test (8weeks)

Article	**Population**	**Aims Study**	**Intervention**
Gupta et al. (2010) *Clinical Endocrinology*	40 healthy volunteers (20-40y) with hypovitaminosis D **CG** (n=20): mean age 30,2 yrs **IG** (n=20): mean age 32,9 yrs	Study the effect of cholecalciferol and calcium supplementation on muscle strength and energy metabolism in young individuals.	**CG**: Lactose granules **IG**: Vitamin D3, 60 000IU **Protocol:** 3d/w, 8 weeks, followed by 1x/month for 4 months + 1g elemental calcium daily. Ingestion with milk **Training:** maintain usual physical activity Pre-test – start supplementation + training – post-test
Jastrzebska et al. (2016) *Journal of Strength and Conditioning Research*	36 well-trained football players > 17-19 years > high sport level **CG** (n=16) **IG** (n= 20)	Identify the effect of vitamin D supplementation on training adaptation in well-trained football players.	**CG**: Sunflower oil (placebo) **IG**: Vitamin D3, 5000IU **Protocol**: daily intake, 8 weeks **Training**: HIIT(AnT, but not >90%Hrmax) > endurance, speed, strength training > 7days/week – 8 weeks Supplementation- and training periods are similar
Josse et al. (2010) *American college of Sports Medicine*	20 young healthy women **CG** (n=10): mean age 23y **IG**(n=10): mean age 24y	Determine whether women consuming fat-free milk vs isoenergetic carbohydrate after resistance exercise, would augmented gains in lean mass and reduction in fat mass	**CG**: Isoenergetic carbohydrate **IG**: Fat-free milk **Protocol:** 2x500mL intake, 5d/week, 12 weeks **Training**: 5d/w pushing-, pulling- and leg exercise 80-90%1RM, 2 sets, 10-12 reps -> 4 sets, 4-6 reps. Supplementation immediately after exercise + 1h post
Owens et al. (2015) *Journal Physiol Endocrinol Metab*	**Part one:** 20 healthy males with insufficient (<75 nmol/l) concentrations of serum 25(OH)D. Mean age 18-30 yrs **Part two:** 14 volunteers with low serum 25(OH)D. Mean age 25yrs	**1.** to investigate the effect of low serum 25(OH)D on functional recovery from eccentric exercise **2**. to identify aspects of muscle cell regeneration that are responsive to supplemental vitamin D	**1. CG**: Cellulose, 50mg **IG**: Vitamin D3, 4000IU **Protocol:** daily intake, 6 weeks **Training:** 20x10 damaging eccentric contractions + MVC Pretest - training – supplementation period starts – post-test. **2. CG:** 10nmol **IG:** 100nmol **'Training':** damage to cells 48h later: biopsy – training –supplementation. Measure 7 days.
Scholten et al. (2015) *Journal of Sports Medicine*	40 physically active males **CG** (n=12): mean age 29,9 yrs **IG1**(n=11): mean age 32,8 yrs **IG2** (n=6): mean age 30,3 yrs **IG3** (n=6): mean age 32,2 yrs	Determine the effects of vitamin D and quercetin supplementation on the cardiorespiratory and muscular fitness outcomes and determine the possible mechanisms of these effects, converging on the steroid hormone regulators of muscle function and linked to maintaining antioxidant status.	**CG**: Placebo **IG1:** Vitamin D3, 4000IU **IG2:** 1000mg quercetin **IG3:** Vitamin D3, 4000 IU + 1000mg quercetin **Protocol:** daily intake, 8 weeks **Training:** activity level maintained during study. Moderate to vigorous physical exercise 3-5d/week, 30-90min/day. 4 pre-test visits – 8 weeks supplementation + training – posttest.

Article	Population	Aims Study	Intervention
Wyon et al. (2014) *Journal of Science and Medicine in Sport*	24 elite ballet dancers **CG** (n=7): 2M/5F, mean age 27,5 yrs **IG** (n=17): 9M/8F, mean age 28,5 yrs	Assess the effects of oral vitamin D3 supplementation on selected physical fitness and injury parameters in elite ballet dancers.	**CG**: No supplementation **IG**: Vitamin D3, 2000IU **Protocol:** daily intake, 4 months **Training:** 532h of dance 6-8h dancing, 38h/week (no direct strength or power training). Supplementation- and training periods are similar
Wyon et al. (2016) *Clin Journal Sport Medicine*	22 adult male white professional national level judoka athletes. **CG** (n=11): mean age 26 yrs **IG** (n= 11): mean age 29 yrs	Examine the acute effects of vitamin D supplementation on selected muscle function parameters.	**CG**: placebo **IG**: Vitamin D3, 150 000 IU **Protocol:** 1 intake **Training:** 2h strength,1h conditioning, 1h technical, 2h randori training. 3 weeks training - +8 days (start study) –supplementation

Table 5.2: Outcome measures, results

Article	Outcome measures	Results
Agergaard et al. (2015) *Nutrition & Metabolism*	**Serum 25(OH)D:** fasting blood sample **Muscle strength:** isometric knee extension – custom-made rigid chair **CSA:** quadriceps **Fiber type:** cross sections	**Serum 25(OH)D:** significant increase at time-point 0, 2, 6 and 12 weeks compared with week -4. Time point 6 and 12 weeks IG > CG (p<0,05) **Muscle strength:** significant increase for CG (8,9%) and IG (6,3%) but no significant difference between CG and IG. (p=0,71) **CSA:** significant gains in quadriceps muscle CSA after 12 weeks (IG 11,3% and CG 7,7%) but no significant difference between CG and IG. (p=0,87) **Fiber type:** %type IIa + I increased and % of type Iix decreased significantly. Increase in IIa IG > CG, but not significant.
Barker et al. (2012) *Nutrition & Metabolism*	**Serum 25(OH)D:** fasting blood sample **Muscle power:** plyo-press **Muscle strength:** plyo-press – repetitive single-leg jumps	**Serum 25(OH)D:** before supplementation n=4 deficient, n=7 insufficient and n=19 sufficient. Serum increased significantly in IG2 compared to IG1 and CG. After 7 days no difference between IG 1 and CG. At 21-and 28 days increase in IG1 significantly higher than CG. (p<0,05) **Muscle power:** after 28 days: no difference between IG's and CG. Significant main effect of time on peak and average power output (p<0,05), indicating learning effect. **Muscle strength:** after 28 days: no difference between IG's and CG.
Barker et al. (2013) *Nutrition & Metabolism*	**Serum 25(OH)D:** fasting blood sample **Muscle power:** single-leg jumps, repetitive maximal effort on force platform **Muscle strength:** isometric contraction with plyo-press hip & knee extension **DOMS:** squat position against wall for 5sec. VAS	**Serum 25(OH)D:** average concentration 30,8 ng/mL. Concentration similar between groups. CG: n=1 deficient, n=5 insufficient, n=7 sufficient. IG: n=2 deficient, n=5 insufficient, n=8 sufficient. After 35days supplementation: no changes in CG, significant increase 47,9 ng.mL. (p<0,05) **Muscle power:** SSC (43% post, 12% 24-h, 12% 48-h) more decrease than CON (4 and 5% post + 24-h). no significant difference between IG and CG. (p<0,05) **Muscle strength:** decreased (6%) in CON immediately and 48h after damaging event. But SSC more severe (32% post, 17% 24-h, 21% 48h, 14% 72h) (p<0,05). No significant difference between IG and CG. **DOMS:** increased immediately after and persisted for 24-h to 72-h. (p<0,05) Vitamin D had no effect.
Close et al. (2013) *British Journal of Sports Medicine*	**Serum 25(OH)D:** fasting blood sample **Muscle power:** vertical jump height **Muscle strength:** 1RM bench press, 1RM leg press	**Serum 25(OH)D:** before supplementation CG 52nmol/l, IG 1 53nmol/l, IG 2 51nmol/l, no significant difference between groups. (p<0,05) Mean values slightly > 50nmol/l being classed as deficient or severely deficient. After supplementation IG2 significant greater values than IG1. (p=0,0016) At 6 weeks. But at 12 weeks no significant difference. CG had a significant decline in serum. (p=0,006) **Muscle power:** no significant changes and differences between groups over 12-week period. CG: pre 46,5cm, 6w: 47,5cm, 12w: 47,7cm. IG1: pre 49,1cm, 6w 49,9cm, 12w 49,2cm. IG2: pre 47,1cm, 6w 49,5cm, 12w 48,3cm. (p=0,90) **Muscle strength:** no significant changes and differences between groups over 12-week period. > 1RM bench press: CG pre 79kg, 6w 82kg, 12w 79kg. IG 1 pre 90kg, 6w 90kg, 12w 92kg. IG 2 pre 91kg, 6w 94kg, 12w 90kg. (p=0,17) 1RM leg press: CG pre 187kg, 6w 182kg, 12w 181kg. IG 1 pre 195kg, 6w 200kg, 12w 198kg. IG 2 pre 204kg, 6w 206kg, 12w 198 kg. (p=0,17)

Article	Outcome measures	Results
Close et al. (2013) *Journal of Sports Sciences*	**Serum 25(OH)D:** fasting blood sample **Muscle power:** vertical jump height **Muscle strength:** 1RM bench press, back squat **Speed:** 10- and 30m sprints **Agility:** Illinois agility test	**Serum 25(OH)D:** before supplementation, insufficient n=7 (<50nmol.l-1), deficient n=2. No one had optimal concentration (>100nmol.l-1). After supplementation period total serum significantly increased in IG. (p=0,0029) No change in CG. (p=0,12) **Muscle power:** time by group interaction for 10-metre print for IG (p=0,008). No significant difference in CG. **Muscle strength:** trend for time-by-group interaction. Mean increase bench press 6,5kg for IG, 2,5kg for CG (p=0,065). Mean increase in squat 9kg for IG and 3kg for CG. (p=0,094) **Speed:** time by group interaction for 10-metre sprint for IG (p=0,008). No significant difference in CG. (p<0,05) **Agility:** no significant type-by-group interaction. (p=0,431)
Gupta et al. (2010) *Clinical Endocrinology*	**Serum 25(OH)D:** fasting blood sample **Muscle strength:** handgrip dynamometer, gastro-soleus dynamometer, pinch-grip	**Serum 25(OH)D:** at baseline all subjects were vitamin D deficient, mean values of 25,4 nM (IG) and 21,1 nM (CG) (p=0,17). Serum increased in IG to 94,5 at 2months, 56nM at 6months. No change in CG. (p<0,01) **Muscle Strength:** > Handgrip: IG significantly higher values than CG after 6 months (2,4kg difference) (p=0,001) > Gastro-soleus: IG significantly higher values than CG after 6 months. (p=0,04) > Pinch-grip: no difference between IG and CG. (p=0,06)
Jastrzebska et al. (2016) *Journal of Strength and Conditioning Research*	**Serum 25(OH)D:** fasting blood sample **Muscle power:** squat jump test, Wingate test, vertical jumps **Speed:** 10,20,30m running speed	**Serum 25(OH)D:** before supplementation IG=CG - (IG (n=12), CG (n=10) <50nmol.L-1), (IG (n=9) > 100nmol.L-1). After supplementation period (week 8): IG mean change 57,8nmol.L-1 – CG mean change -4nmol.L-1. (p<0,0001) **Muscle power:** no significant differences between IG and CG at baseline. After training period (week 8): significant improvement for squat jump, Wingate and vertical jumps. No significant differences between IG and CG. (p=0,338) **Speed:** no significant differences between IG and CG at baseline. After training period (week8): significant improvement for 10m + 20m running (p<0,001). Not for 30m. (p=0,153) No significant differences between IG and CG.
Josse et al. (2010) *American college of Sports Medicine*	**Serum 25(OH)D:** fasting blood sample. **Muscle strength:** 1RM shoulder press, bench press, triceps push down, chest fly's, lat pull down, biceps curl, leg press, hamstrings curl, knee extension	**Serum 25(OH)D:** during 12w serum increased significantly in IG (58,4 to 64,8 nM) and in CG (53,7 to 56,5 nM). (p<0,05) **Muscle strength:** Both IG and CG strength gains in all the performance tests. (p<0,05). Time x treatment interaction for bench press (p=0,029) and trend toward significance for chest fly's (p=0,89) where IG greater increase in post-test compared with CG. (p<0,05)

Article	Outcome measures	Results
Owens et al. (2015) *Journal Physiol Endocrinol Metab*	**Serum 25(OH)D:** fasting blood sample **Muscle strength:** MVC with isokinetic dynamometer, quadriceps **DOMS:** algometer **Recovery:** biopsy	**Serum 25(OH)D:** before supplementation no significant differences between IG (45nmol/l) and CG (45nmol/l). IG significant increase after supplementation period (6weeks) (115nmol/l) (p<0,005) and significant different with CG. (p<0,005) **Muscle strength:** los of peak torque immediately post exercise in IG and CG. (p<0,005) Significant improvement in torque recovery IG at 48h and 7days post (improved functional recovery). (p=0,042) **DOMS:** no interaction between IG and time mid quadriceps or 5-cm patella (p=0,71 and p=0,418) **Recovery:** migration velocity and distance significantly enhanced with IG1 and IG2 (study part two). So improved functional recovery with higher serum in vivo (increase in myotube size and nuclear accretion)
Scholten et al. (2015) *Journal of Sports Medicine*	**Serum 25(OH)D:** fasting blood sample **Muscle power:** vertical jump **Muscle strength:** hand grip strength, isokinetic leg strength	**Serum 25(OH)D:** before supplementation IG=CG - 88,6% > 50nmol/L, 25,7% > 100nmol/L. After supplementation period (week 8) serum increased: IG1 58,7nmol/L, IG3 31nmol/L. (p<0,05) **Muscle power:** no significant changes between any groups pre-post supplementation IG1: 52,76cm to 54,38cm (p=0,631) , IG 2: 56,52cm to 56,52 cm (p=0,999), IG 3: 67,31cm to 72,14cm, CG: 54,29cm to 56,09cm (p=0,581). CG no change (p=0,668) **Muscle strength:** no significant changes between any groups pre-post supplementation (p-values ranged from 0,425 to 0,999)
Wyon et al. (2014) *Journal of Science and Medicine in Sport*	**Serum 25(OH)D:** fasting blood sample **Muscle strength:** concentric hamstrings and quadriceps by isokinetic dynamometer	**Serum 25(OH)D:** IG had significant lower serum at baseline. After supplementation IG increase (still insufficient 10-30ng/mL). CG remained constant. Treatment by time interaction (p>0,001). Participants with lowest serum pre-test had greatest increase. **Muscle strength:** mean increase 13% in IG, 3% CG. Main effects for muscle, speed and time. (p<0,001) Time by treatment interaction (p=0,01) and muscle by time by treatment interaction (p=0,027)
Wyon et al. (2016) *Clin Journal Sport Medicine*	**Muscle power:** vertical jump **Muscle strength:** 5-s isometric quadriceps contraction in custom-made isometric strength chair **Injury:** reporting	**Muscle power:** significant main effects due to 'gender' (p<0,001), 'time' (p=0,010) a group-by-time interaction (p=0,004)with moderate effect size (eta^2=0,322). CG pre-post difference: 0,714 cm (95% CI was -0,93 to 2,36) IG pre-post difference: -3,05 cm (95% CI was -4,05 to -2,06) **Muscle strength:** significant main effects due to 'gender', 'time' a group-by-time interaction (p=0,030) but small effect (eta^2=0,197). CG pre-post difference: 1,79N (95% CI was -143,98 to 140,39) IG pre-post difference: -190,32N (95% CI was -276,61 to -104,02) **Injury:** CG reported 1 injury (n=5), 2 injury (n=1). IG1 injury (n=5)

Table 5.3: Serum concentration

Article	Baseline serum 25(OH)D	Post-supplement
Agergaard et al. (2015)	**IG** average of <50nmol/L **CG** average of >50nmol/L	**IG** average of 60-70nmol/l **CG** average of 50nmol/l
Barker et al. (2012)	Mean serum 32,3 ng/ml. 4p. deficient (<20ng/ml) 7p. insufficient (21-29 ng/ml) 19p. sufficient (>30ng/ml)	**IG2** significant increase compared to IG1 and CG. **IG1** increase = **CG** increase (p<0,05)
Barker et al. (2013)	3 p. deficient (<20ng/mL) 10 p. insufficient (20-29ng/mL) 15 p. sufficient (>30ng/mL)	**IG** significant increase (47,9 ng/mL) **Cg** no change in serum
Close et al. (2013)	**IG1** average of 53 nmol/l **IG2** average of 51nmol/l **CG** average of 52 nmol/l *But 17 p. <50nmol/l, 6p. deficient or severely deficient.*	Significant increase in **IG1** and **IG2** but IG2>IG1 (p=0,016) **CG**: progressive decline (p=0,006)
Close et al. (2013)	18% severely deficient (<12,5nmol.l^{-1}) 18% deficient (12,5-30nmol.l^{-1}) 18% inadequate (30-50nmol.l^{-1}) 45% adequate (50-100nmol.l^{-1})	**IG** significant increase (p=0,0029) > 60% > 100nmol.l^{-1} **CG** no change in serum (p=0,12)
Gupta et al. (2010)	All p. deficient with level <50nM. (mean values of IG 25,4 and CG 21,1 nM, p=0,17)	**IG** mean serum of 94,5 (2m) and 56 (6m) nM (p<0,01) **CG** 32,8 (2m) and 29,7 (6m) (p<0,01) Significant difference between IG and CG at 6m (p<0,01)
Jastrzebska et al. (2016)	22 p. : <50nmol/l^{-1} 14 p. : sufficient levels No difference between groups	**IG** 57,8 nmol.L^{-1}. > 9 p. > 100 nmol.L^{-1} **CG** -4 nmol.L^{-1} (p<0,0001)
Josse et al. (2010)	**IC** serum range from 43,5 to 71,2nM **CG** serum range from 39,8 to 83,1 nM All p. (except one) insufficient (<80nM)	**IG** and **CG** significant increase compared with baseline (+6,5, +2,5 nM, P<0,05) → IG range from 48,2 to 79,2, CG range from 43,8 to 77,6nM. All p. (except one) insufficient (<80nM)
Owens et al. (2015)	**IG** mean serum 45nmol/l **CG** mean serum 45nmol/l	**IG** significant increase compared with baseline and **CG**. (45 → 115nmol/l., p<0,005) **CG** significant decline (45 → 33 nmol/l, p=0,013)
Scholten et al. (2015)	31 p. >50nmol/L 9 p. > 75nmol/L	**IG** increased by 58,7 nmol/L **IG2** increased by 31 nmol/L **CG** no change in serum
Wyon et al. (2014)	Insufficient (10-30ng/ml) or deficient (<10ng/ml)	Not mentioned
Wyon et al. (2016)	**IG** serum **<** **CG** serum (p<0,05)	**IG** 34% increase in serum level **CG** no change in serum

Table 5.4.: Outcome parameters

Article	**Outcome parameters**						
	muscle power	Muscle strength	Speed	CSA	Fiber type	DOMS	Recovery
Agergaard et al. (2015)		X		X	X		
Barker et al. (2012)	X	X					
Barker et al. (2013)	X	X				X	X
Close et al. (2013)	X	X	X				
Close et al. (2013)	X	X					
Gupta et al. (2010)		X					
Jastrzebska et al. (2016)	X		X				
Josse et al. (2010)		X					
Owens et al. (2015)		X		X		X	X
Scholten et al. (2015)	X	X					
Wyon et al. (2014)		X					
Wyon et al. (2016)	X	X					

Table 5.4.1.: Group 1

Article	**Outcome parameters**						
	muscle power	Muscle strength	Speed	CSA	Fiber type	DOMS	Recovery
Barker et al. (2012)	X	X					
Gupta et al. (2010)		X					
Scholten et al. (2015)	X	X					

Table 5.4.2.: Group 2

Article	Outcome parameters						
	muscle power	Muscle strength	Speed	CSA	Fiber type	DOMS	Recovery
Agergaard et al. (2015)		X		X	X		
Close et al. (2013)	X	X	X				
Close et al. (2013)	X	X					
Jastrzebska et al. (2016)	X		X				
Josse et al. (2010)		X					
Wyon et al. (2014)		X					

Table 5.4.3.: Group 3

Article	Outcome parameters						
	muscle power	Muscle strength	Speed	CSA	Fiber type	DOMS	Recovery
Barker et al. (2013)	X	X				X	X

Table 5.4.4.: Group 4

Article	Outcome parameters						
	muscle power	Muscle strength	Speed	CSA	Fiber type	DOMS	Recovery
Owens et al. (2015)		X		X		X	X
Wyon et al. (2016)	X	X					

Progression form master thesis part 1

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UHASSELT KNOWLEDGE IN ACTION

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
27/10	Bespreking onderwerpen Opzet PICO	Promotor: Copromotor: Student(e): Student(e):
29/11	Overlopen PICO · In- & exclusie criteria · Zoekstrategie	Promotor: Copromotor: Student(e): Student(e):
22/1	Presentatie zoekstrategie	Promotor: Copromotor: Student(e): Student(e):
26/1	Bespreking / aanpassing zoekstrategie	Promotor: Copromotor: Student(e): Student(e):
12/3	Presentatie	Promotor: Copromotor: Student(e): Student(e):
2/5	Bespreking strategie data-extractie	Promotor: Copromotor: Student(e): Student(e):
		Promotor: Copromotor: Student(e): Student(e):
		Promotor: Copromotor: Student(e): Student(e):
		Promotor: Copromotor: Student(e): Student(e):
		Promotor: Copromotor: Student(e): Student(e):

Self-reflection master thesis part 1

BEOORDELING VAN DE WETENSCHAPPELIJKE STAGE-DEEL 1

Wetenschappelijke stage deel 1 (Masterproef deel 1- MP1) van de Master of Science in de revalidatiewetenschappen en de kinesitherapie bestaat uit **twee delen**:

1) De literatuurstudie volgens een welomschreven methodiek.
2) Het opstellen van het onderzoeksprotocol ter voorbereiding van masterproef deel 2.

Omschrijving van de **evaluatie**:

1) 80% van het eindcijfer wordt door de promotor in samenspraak met de copromotor gegeven op grond het product en van het proces dat de student doorliep om de MP1 te realiseren, met name het zelfstandig uitvoeren van de literatuurstudie en het zelfstandig opstellen van het onderzoeksprotocol, alsook de kwaliteit van academisch schrijven.
2) 20% van het eindcijfer wordt door de interne jury gegeven op grond van het ingeleverde product en de mondelinge presentatie waarin de student zijn/haar proces toelicht.

In de beoordeling dient onderscheid gemaakt te worden tussen studenten die, in samenspraak met de promotor, een nieuw onderzoek uitwerkten en studenten die instapten in een lopend onderzoek of zich baseren op voorgaande masterproeven of onderzoeksprojecten. Van deze laatste worden bijkomende inspanningen verwacht zoals bv. het bijsturen van de eerder geformuleerde onderzoeksvraag, de kritische reflectie over het onderzoeksdesign, het uitvoeren van een pilotexperiment.

Beoordelingskader:

Beoordelingskader: criteria op 20	
18-20	Excellente modelmasterproef
16-17	Uitmuntende masterproef
14-15	Zeer goede masterproef die zich onderscheidt van de andere masterproeven
12-13	Goede masterproef
10-11	Voldoende masterproef die op een aantal vlakken zwak scoort
8-9	Onvoldoende masterproef die niet aan de minimumnormen voldoet
6-7	Ernstig onvoldoende masterproef of een masterproef die slechts één van beide bevat
≤ 5	Ernstig onvoldoende en onvolledige masterproef

ZELFEVALUATIERAPPORT

Onderstaand zelfevaluatierapport is een hulpmiddel om je wetenschappelijke stage -deel 1 zelfstandig te organiseren. Bepaal zelf je deadlines, evalueer en reflecteer over je werkwijze en over de diepgang van je werk. Check de deadlines regelmatig. Toets ze eventueel af bij je (co)promotor. Succes!

Prof. M. Vanvuchelen, coördinerende verantwoordelijke wetenschappelijke stages

Naam & Voornaam STUDENT: Stijn Nullens en Maaike Withofs

Naam & Voornaam (CO)PROMOTOR & PROMOTOR: dr. Anouk Agten, Prof. dr. Frank Vandenabeele and Mr. Sjoerd Stevens

TITEL masterproef (Nederlandstalig of Engels): Vitamin D supplementation during strength training in healthy adults

LITERATUURSTUDIE	Gestelde deadline	Behaald op	Reflectie
De belangrijkste concepten en conceptuele kaders van het onderzoekdomein uitdiepen en verwerken	10/11/2017	06/11/2017	
De belangrijkste informatie opzoeken als inleiding op de onderzoeksvraag van de literatuurstudie	10/11/2017	06/11/2017	
De opzoekbare onderzoeksvraag identificeren en helder formuleren in functie van de literatuurstudie	10/11/2017	06/11/2017	
De zoekstrategie op systematische wijze uitvoeren in relevante databanken	22/01/2018	26/01/2018	Moeizame start
De kwaliteitsbeoordeling van de artikels diepgaand uitvoeren	12/03/2018	10/03/2018	
De data-extractie grondig uitvoeren	12/03/2018	19/03/2018	26/4 nog aanpassingen gebeurd
De bevindingen ïntegreren tot een synthese	03/05/2018	07/05/2018	19/5 nog aanpassingen gebeurd

ONDERZOEKSPROTOCOL	Gestelde deadline	Behaald op	Reflectie
De onderzoeksvraag in functie van het onderzoeksprotocol identificeren	18/05/2018	16/05/2018	
Het onderzoeksdesign bepalen en/of kritisch reflecteren over bestaande onderzoeksdesign	18/05/2018	19/05/2018	
De methodesectie (participanten, interventie, uitkomstmaten, data-analyse) uitwerken	18/05/2018	19/05/2018	

ACADEMISCHE SCHRIJVEN	Gestelde deadline	Behaald op	Reflectie
Het abstract tot he point schrijven	21/05/2018	18/05/2018	

De inleiding van de literatuurstudie logisch opbouwen	14/03/2018	02/05/2018	1ste versie helemaal aangepast
De methodesectie van de literatuurstudie transparant weergegeven	18/05/2018	19/05/2018	Samen uitgevoerd met uitwerking
De resultatensectie afstemmen op de onderzoeksvragen	21/05/2018	20/05/2018	
In de discussiesectie de bekomen resultaten in een wetenschappelijke tekst integreren en synthetiseren	21/05/2018	20/05/2018	
Het onderzoeksprotocol deskundig technisch uitschrijven	18/05/2018	19/05/2018	
Referenties correct en volledig weergeven	21/05/2018	19/05/2018	

ZELFSTUREND EN WETENSCHAPPELIJK DENLEN EN HANDELEN	**Aanvangsfase**	**Tussentijdse fase**	**Eindfase**
Een realistische planning opmaken, deadlines stellen en opvolgen	29/11/2017	17/03/2018	30/04/2018
Initiatief en verantwoordelijkheid opnemen ten aanzien van de realisatie van de wetenschappelijke stage	29/11/2017	Gehele traject MP	26/06/2018
Kritisch wetenschappelijk denken	10/11/2017	12/03/2018	20/05/2018
De contacten met de promotor voorbereiden en efficiënt benutten	27/10/2017	Zie voortangsformulier	04/06/2018
De richtlijnen van de wetenschappelijke stage autonoom opvolgen en toepassen	29/11/2017	12/03/2018	20/05/2018
De communicatie met de medestudent helder en transparant voeren	27/10/2017	Gehele traject MP	26/06/2018
De communicatie met de promotor/copromotor helder en transparant voeren	27/10/2017	Gehele traject MP	04/06/2018
Andere verdiensten:			

PART 2: RESEARCH PROTOCOL

1. Introduction

Vitamin D is fat soluble vitamin which is biologically inactive and needs conversion to 25-hydroxyvitamin D (25(OH)D) in the liver. This inactive 25(OH)D is transformed to its biologically active form, 1.25 dihydroxyvitamin D (1,25(OH)2D), in the kidneys. There are two major forms of vitamin D: vitamin D2 (ergocalciferol), mostly extracted from nutrition, and second being vitamin D3 (cholecalciferol) which is synthesized from exposure to sunlight. According to the National Institute of health, there is discussion on the optimal serum concentration of 25(OH)D, associated with deficiency, adequacy for bone health, and optimal overall health. The Institute of Medicine defines an optimal level of serum 25(OH)D at >50 nmol/L (>20nl/mL), considered adequate for bone and overall health in healthy individuals. Levels of 30 to < 50 nmol/L (12 to <20nl/mL), generally considered inadequate for bone and overall health. Vitamin D deficiency is defined when serum 25(OH)D is lower than 30 nmol/L (<12 ng/mL).

These days, a lot of people have an insufficient vitamin D concentration due to lacking sunlight exposure. This insufficiency can be solved by supplements. Therefore, it is important to know, not only for all health care providers (such as physiotherapists), but also for patients, if a sufficient or even a more than sufficient vitamin D concentration may have beneficial effects in for example gaining muscle strength. The physiotherapist, who constructs and guides the individual through the exercise programs, should be aware of the effects to optimize muscle strength. Other health care providers, such as doctors and nurses, should be aware of this possible effect as well. Hereby, they could assess an individuals' concentration and take steps if needed to optimize it. Finally, the individual itself need to be aware of the effect of their vitamin D concentration on skeletal muscles. In this way, they understand if and why supplementation is needed.

Previous research had shown that there is still no consensus about the effect of vitamin D during strength training on the skeletal muscles. Studies who investigated the effect vary in different aspects like differences in concentration of the supplement, another being differences in the frequency and duration of supplementation. Not only the supplementation was different, also serum 25(OH)D concentration in subjects, training intervention and length of training program and follow up varied. This makes it hard to draw clear conclusions.

There are limited studies that investigated the effect of vitamin D supplementation during strength training in a population that only consist of vitamin D insufficient and deficient persons. The aim of this present study is to investigated this effect.

2. Aim of study

This master thesis is executed as a part of the second master year at the UHasselt in Diepenbeek. This will also be executed in Diepenbeek, more specifically at the rehabilitation research center REVAL of UHasselt. This master thesis is part of a broader research project, about the effects of High Intensity Training on muscle characteristics of back muscles in patients with low back pain, performed under the supervision of dr. Anouk Agten, Prof. dr. Frank Vandenabeele and Mr. Sjoerd Stevens. The purpose of this pilot study is to determine if vitamin D supplementation has an effect on skeletal muscles in healthy, insufficient and deficient adults.

2.1. Research question related to master thesis

The overall aim of this master thesis is to answer the question if vitamin D supplementation, in combination with strength training, has an effect on skeletal muscles within a healthy population with an insufficient and deficient vitamin D serum. To answer this question, it will be divided into two smaller research questions:

- Does vitamin D supplementation, in combination with strength training have an effect on **muscle strength and muscle power** of skeletal muscles within a healthy population with an insufficient and deficient vitamin D serum?
- Does vitamin D supplementation, in combination with strength training enhance **skeletal muscle CSA** within a healthy population with an insufficient and deficient vitamin D serum?

2.2. Hypotheses

Based on the aforementioned research questions, following hypotheses are formulated.

- Eight weeks of progressive strength training combined with vitamin D supplementation (4000IU/day), is hypothesized to improve muscle strength and muscle power in a healthy population with an insufficient and deficient vitamin D serum.
- Eight weeks of progressive strength training combined with vitamin D supplementation (4000IU/day), is hypothesized to enhance skeletal muscle CSA in a healthy population with an insufficient and deficient vitamin D serum.

3. Methods

3.1. Research design

A pilot study will be conducted. Participants will be randomized into an intervention (IG) or placebo group (CG) in which all participants execute the same training program (see further). Group allocation will be based on a 1:1 ratio by using sealed opaque envelopes. Both participants and outcome assessors will be blinded. Fig. 1. gives an overview of the study design.

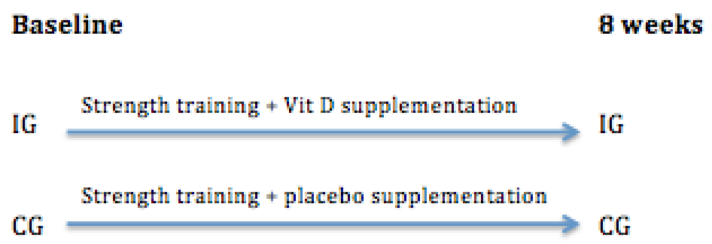

Fig. 1. Study design.

Before the start of the study, all parameters are measured in both intervention- and control group. During these tests, the single-repetition maximum (1RM) is assessed for each exercise and muscle biopsy from m. Vastus Lateralis (MVL) is taken. Blood samples are taken to examine serum 25(OH)D concentrations.
Eight weeks later, all tests are repeated for all participants (both IG and CG) to assess possible changes.

3.2. Participants

The participants in this study will consist of healthy male and female participants with the age ranging from 18 to 60 years.

3.2.1. Inclusion criteria

Subjects that participate in the study should satisfy following criteria:

- Healthy adults
- Insufficient or deficient levels of serum 25(OH)D
- 18-60 years old

3.2.2. Exclusion criteria

- Any sort of pathology or disease
- Sedentary lifestyle
- Participating in another study regarding strength training
- Intake of some kind of vitamin D supplement in the last six months

3.2.3. Participants recruitment

The aim is to recruit 30 participants to join the study after screening and explanation of all procedures. Participants are mainly recruited via social media and e-mail.

3.3. Medical ethics

Approval for the study needs to be requested by the local ethics committee.

3.4. Intervention

The intervention is conducted over an eight week time span, consisting of a progressive strength training program for two days per week, combined with vitamin D supplementation, every day. The strength training program takes place at the rehabilitation research center REVAL in Diepenbeek, were all trainings will be supervised by physiotherapists and two Master students physiotherapy to ensure compliance with good lifting form. The training will start with a five minute warming-up on a treadmill, followed by exercises of the lower extremity consisting of pull- (two-leg knee extension, two-leg hamstrings curl) and press (leg press, squat, calf raises) exercises. Based on the pre-measurements of the single repetition maximum (1RM) at baseline, subjects receive a personalized training schedule every two weeks. All exercises will be performed on guided motion machines at 80% of the subjects' voluntary 1RM strength, were sets and repetitions differ between weeks. The first two weeks subjects complete two sets of 10 to 12 repetitions for each exercise, with a one minute rest interval between sets. From week three to five they complete two sets of 15 to 20 repetitions, weeks six to seven they complete three sets for 10-12 repetitions and week eight to ten it consists of three sets at 15-20 repetitions per set. Week 11-13 subjects complete four sets of 10-12 repetitions and the final stages, week 14-20 subjects complete four sets at 15-20 repetitions per set. All training volumes can be found in figure 2.

Week	Sets	Repetitions	Rest interval between sets
1-2	2	10-12	1 minute
3-5	2	15-20	1 minute
6-7	3	10-12	1 minute
8-10	3	15-20	1 minute
11-13	4	10-12	1 minute
14-20	4	15-20	1 minute

Fig. 2. Training volumes per week.

Besides the training program, participants will document their sport activity during the study period. In this way, activities outside of the training can be registered and differences between activity level can be taken into account.

Participants will be randomly assigned in a double-blind manner to the vitamin D (4000 IU) or a visual identical placebo group (lactose granules). Every day before breakfast, subjects ingest the capsule with water.

3.5. Outcome

3.5.1. Primary outcome measures

The primary outcome measures that will be analyzed are:

- Concentric, eccentric and isometric muscle strength of m. Quadriceps. Using the golden standard Biodex System Isokinetic Dynamometer. Prior to testing procedures, subjects complete a warm-up of five minutes of submaximal cycling. The subject is placed in a comfortable upright position on the Biodex with 85° hip flexion and is stabilized with shoulder and abdominal straps. Anatomical axis of rotation is aligned to the dynamometer axis using manual palpation. Subjects perform eight maximal contractions, each separated by 15 seconds rest. This will be repeated three times, at least three minutes rest separates each test (Harbo et al.). Concentric, eccentric and isometric muscle strength was measured for extension at the knee. Gravity correction will be used.
- Maximum lower limb power. This will be measured with vertical jumps using an electronic jump mat. Participants were given three attempts to reach their maximum height (cm.). The highest of the three trials was recorded.

3.5.2. Secondary outcome measures

The secondary outcome measures will be analyzed are:

- Muscle fiber CSA: muscle biopsy will be taken from the m. Vastus Lateralis.

3.6. Data analysis

Statistical analysis were performed using JMP Pro 12. Differences in primary and secondary outcomes between groups after eight weeks of progressive strength training and supplementation will be compared after adjusting for age, gender and respective baseline parameters. All p-values calculated were two tailed, and values less than 0.05 were considered significant.

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