The Effects of Vitamin D Supplementation on Fall Reduction in the Elderly: A Critical Appraisal

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Abstract

BACKGROUND: Falls in the elderly is a significant public health problem due to their high prevalence of 30% in those over 65, many of which result in fractures and soft tissue injuries, longstanding pain, functional impairment, reduced quality of life, and increased mortality. The elderly population is more at risk for vitamin D deficiency, and there is increasing evidence for supplementation and reduction in the rates of falls and fractures. OBJECTIVE: The objective of this paper is to critically appraise five keys articles with the aim to answer the question: 'What are the effects of vitamin D supplementation and fall reduction in the elderly?' METHODS: A literature search of PubMed, EMBASE and CINAHL was conducted and five key articles were selected based on relevance and date of publication. Study findings were also considered when selecting articles so as to provide a complete depiction of the variability of results on this topic. RESULTS: Out of the five key studies, the first showed a positive correlation between vitamin D serum concentrations and fall reduction, as well as increased cognition. The second identified a positive role of vitamin D in balance control, which may be a risk factor for falls in the elderly. A third study showed a positive association between serum 25 hydroxyvitamin D levels and physical performance in the elderly. The fourth study found positive associations between vitamin D insufficiency and impairments in factors which predispose the elderly to fall. Finally, the last study identified the effect of oral and parenteral megadose vitamin D supplementation in the elderly, and showed prevention of falls and improvement of functional mobility. Based on these findings as well as the quality of study designs and methods it would appear as though vitamin D supplementation in the elderly plays an important role in fall prevention.

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Introduction

Role of Vitamin D in Fall Prevention

The purpose of this literature review is to determine the role of vitamin D supplementation in fall prevention in the elderly, and whether or not it is effective. The role of Vitamin D in the regulation of calcium and phosphate metabolism is well known and discussed below, in which bone is the target organ. In this case, vitamin D is thought to increase the life span of osteoblasts using an anti-apoptosis effect. Recent data now suggests that muscles and the nervous system, which are important when considering falls in the elderly, are also target organs of vitamin D (1). The role of vitamin D in muscle tissue was first observed in severe vitamin D deficiency- which was responsible for rickets in children and osteomalacia in adults, with associated severe proximal muscle and lower limb weakness. Skeletal muscle is one of the tissues where the vitamin D receptor is found and, when activated promotes de novo protein synthesis in muscle. These proteins allow for calcium influx and muscle fibre proliferation and differentiation. Type 2 muscle fibres are the first to be recruited when the body attempts to prevent a fall, and vitamin D deficiency has been shown to have a predominant role in atrophy of type 2 muscle fibres. It is known that vitamin D supplementation can reverse the atrophy seen in type 2 fibres, improve proximal muscle weakness, increase muscle strength and balance, reduce and reverse myalgias, as well as decrease muscle protein degradation. (2)

The nervous system is also an important target of vitamin D. Vitamin D Receptors (VDRs) are found in the hippocampus, hypothalamus, limbic system, cortical, subcortical, and spinal motor zones. They are also found on neurons and glial cells. There have been some studies on rats and humans which suggest an association between vitamin D supplementation and global cognitive function, however further investigations and randomized controlled trials are required (1).

Fall Prevalence in the Elderly

The World Health Organization defines a fall as the action of finding oneself involuntarily coming to rest on the ground, floor or other lower level, excluding intentional change in position to rest in furniture, wall or other objects. (3) Falls in the elderly are of high prevalence worldwide, occurring in 28-35% of people aged 65 and older. This increases to 32-42% of people over the age of 70. Falls represent the most common accident of daily living and are the leading cause of accidental death in the elderly. In fact, falls account for more than 50% of injury related hospitalizations in those over 65 years old. These hospital admissions are largely due to fall-related hip fractures, traumatic brain injuries and upper limb injuries. The frequency of falls increases with age and frailty level, and those living in nursing homes fall more often than community dwellers. (3) Fall related fractures are associated with excess morbidity and mortality, as well as significant costs to the healthcare system. Therefore, it is important to delay or prevent the occurrence of falls in order to reduce the impact on individuals as well as public health. (1)

Mechanism of Falls

There are many mechanisms involved in falls in the elderly, which result from a complex interaction of risk factors. According to the WHO, these risk factors can be broken down into four categories: biological, behavioural, environmental, and socioeconomic.(3) The biological factors of falling that will be focused on are those which are associated with age related changes, such as the decline of physical, cognitive and affective capacities. Therefore, it is not only the skeletal system which is involved in falls in the elderly, but also the muscular and central nervous systems. It is the interaction of such biological factors with behavioural and environmental risks which increase the risk of falling. An example of this is loss of muscle strength leads to a loss of function and increased frailty, which intensifies the fall risk.

Vitamin D Guidelines

The US Institute of Medicine (IOM) released a report on the review of the Dietary Reference Intakes for vitamin D and Calcium on Nov. 30, 2010, as seen in **Table 1.**

This paper will focus on the Vitamin D recommendations in the elderly, in particular those prone to falls and fractures. According to the American Geriatrics Society workgroup on Vitamin D Supplementation for Older Adults, clinicians are strongly advised to recommend vitamin D supplementation of at least 1000 IU/d to older adults, in order to achieve a serum 25(OH)D concentration of 30 ng/mL. It is also recommended that an average daily input from all sources of Vitamin D should be 4000 IU for all older adults. This includes dietary, supplementary and sunlight sources. (4). It should be noted that there are two forms of vitamin D supplementation: Vitamin D_2 and Vitamin D_3, which differ slightly in their pharmacokinetic properties. Vitamin D3, also known as cholecalciferol is associated with higher serum concentrations that remain more consistent. Vitamin D2, or ergocalciferol supplementation results in large fluctuations in serum 25(OH)D concentrations. Vitamin D3 is available over the counter in dosages of 400, 800, 1000, 5000 and 10,000 IU. Vitamin D2, however is only available with a prescription and is dosed at 50,000 IU.

Vitamin D metabolism

Vitamin D is a steroid hormone that is vital for the optimal function of numerous physiological systems. The classical function of vitamin D is to help the body use calcium and phosphorous to build and maintain strong bones and teeth. It was originally thought that bone was the main target organ of vitamin D, with its main action being to increase the life span of osteoblasts. However, recent data supports that muscles and the nervous system are also target organs of vitamin D (1). Sources of vitamin D come from sun exposure, dietary supplements, and vitamin D fortification in certain common foods, such as dairy products and fish oils. Vitamin D3 (either obtained from diet or UVB exposure) is stored in the liver and in adipose tissue. It is transported in the blood by the vitamin D binding protein, and must be converted to its active form, $1,25(OH)_2D_3$ in order to affect mineral metabolism and physiologic functions. Therefore, it is first hydroxylated, primarily in the liver, to 25 hydroxyvitamin D, also known as 25(OH)D via one or more cytochrome P450 vitamin D hydroxylases. This is the storage form of vitamin D and the major circulating form, which is useful in measuring a person's serum concentration of the vitamin. It is then transported to the kidneys, and bound to plasma vitamin D binding protein and internalized via endocytosis to the renal proximal tubule. From there, it is hydroxylated through several sequential steps in the kidney, resulting the hormonally active form of vitamin D: 1,25 dihydroxyvitamin D_3. This is primarily accomplished by cytochrome P450 mono-oxygenase 25(OH)D 1α hydroxylase.(5).

Vitamin D increases serum calcium and phosphorus levels required for skeletal mineralization through actions on the intestine, bone and kidney. In the intestine, $1,25(OH)_2D_3$ stimulates the active transport of calcium and phosphate from the lumen to the blood. It uses the VDR in the intestine to regulate calcium absorption via four proposed models: facilitated diffusion, vesicular trafficking, transcaltachia and paracellular transport (5). It also acts on the distal nephron in the presence of parathyroid hormone to improve reabsorption of calcium. Vitamin D3 acts on the bone to increase reabsorption, which provides an additional source of mineral for new bone formation. When dietary calcium and phosphate are low, the kidney and bone retain these minerals. When they are sufficient, vitamin D has a greater effect on the intestine, since parathyroid hormone secretion is suppressed in this case. (6)

Methods

Literature Search

Relevant articles related to vitamin D supplementation and fall reduction in the elderly were sought through PubMed, EMBASE and CINAHL. The initial search was conducted using the keywords "Vitamin D" AND "falls" AND "elderly", which gave 68 results. These articles were then filtered by date of publication within 5 years, human species, and clinical trials, which lead to 15 results. Of these articles, five were chosen based on relevance of this topic as well as quality and appropriateness for a critical appraisal.

Results

Article 1

In 2012, Peterson *et al* developed an observational study to determine the mechanism in by which vitamin D was associated with decreased falls. (8) The study examined the relationship between vitamin D and falls, motor function and cognition in independently living individuals over the age of 70. Participants were a part of the "Intelligent Systems for Assessment of Aging Changes Study", which examines changes in motor and cognitive function. The average age of the subjects was 85 years old, the average education level was high (15 years of total education), and the population was mostly Caucasian females. The mean serum vitamin D level was 37.7nm/mL. The 159 participants were assessed with standardized health and function questionnaires, physical and neurological examinations, and a variety of motor and cognitive function tests. The number of falls each subject reported were calculated for the 3 months before and 3 months after the date of a vitamin D blood collection- which were collected as a non fasting sample; 90% of samples were collected in the autumn months.

Results of this study are described in **Table 2**. The study found that those who suffered falls had a significantly lower serum vitamin D level compared to non-fallers. (32.9ng/mL to 39.2ng/mL respectively, $p=<0.01$). Of the participants, there were 122 non-fallers, 29 single fallers, and 8 multi fallers. The study found no significant correlation between vitamin D and motor measures. There did seem to be a correlation between serum vitamin D levels and MMSE scores- subjects with mild dementia had significantly lower vitamin D concentration as compared to those who were cognitively intact (30.9ng/mL vs 38.8ng/mL, $p<0.1$). There was also a trend correlating global cognition with serum concentration, however the correlation did not meet significance.

The data collected from this study are consistent with other research indicating that higher plasma vitamin D concentrations are associated with reduced falls. This particular study showed that a 5 ng/mL increase in vitamin D decreased odds of falling by 20%. The data collected by Peterson *et al*. is suggestive that the role of cognitive effects of vitamin D on fall prevention may be more important the motor function component. Additional factors regarding fall prevention must also be present, however, because “after correcting for cognitive status the relationship between vitamin D and falls remained.” (7)

Some strengths of this study are that it corrected for age and health status (which did not turn out to modify the correlation), and included both male and female genders. The study however was not able to show a correlation between vitamin D concentration and physical strength, which has been highly suggested in other research. It also did not show a significant correlation of vitamin D concentration with gait or balance measures. A limitation which may account for this is that the measure of muscle function may not have been sensitive enough. Perhaps the difference in blood levels was too small. Perhaps it would have been useful to provide supplementation to subjects as a variable, in order to truly see the effect of supplementation. Other limitations to consider in the study are reverse causation, that those who are less cognitively intact may forget to take their supplements, and those who are more prone to falling may spend more time indoors without much sun exposure.

Overall, the study by Peterson et al provides useful insight towards the literature regarding the role that vitamin D has on fall reduction, and supports that specific intervention studies are warranted in the future.

Article 2

A study by Menant *et al* conducted in 2011 investigated the relationship between serum 25OHD levels and physiological and neuropsychological function in older people and prospective falls. (8) The participants included 463 community dwelling seniors aged 70-90 years, who were independent in activities of daily living (ADLs) and could walk 400m without assistance. Serum 25OHD concentrations were obtained from the participants and described as either insufficient (≤50nmol/L) or sufficient (>50nmol/L). The mean serum level in the study population was 62.2 nmol/L, and was lower in women than in men. A neuropsychological assessment was administered by trained psychologists using various methods to measure cognitive function, attention, processing speed, and executive function. Another set of tests were conducted to assess neuromuscular function and balance, as well as a physical assessment. Fall frequency was determined after 12 months of monitoring monthly falls diaries and follow up telephone calls.

The results of this study showed that participants with vitamin D insufficiency had weaker strength, slow reaction times, poorer leaning balance and slower gait, even after controlling for age and body mass index. They also demonstrated worse performance in executive function tests. In terms of falls, 45.9% of the participants reported one or more falls, with no significant difference between men and women. Interestingly, negative binomial analyses within sexes revealed that vitamin D insufficiency was a significant independent risk factor for falls among the men, but not among the women.

It is surprising that the significant relationship between vitamin D and falls was found in men and not women, since other studies have reported significant associations with women as well. Perhaps this is due to some of the tests used to measure strength did not account for natural gender differences. This study does however demonstrate some significant associations between serum vitamin D concentrations and the cognitive domains of executive function and attention processing speed, all of which are factors playing a role in falls. "Impaired executive function and attention processing speed have previously been linked to falls in older people", and it would make sense to have a mediating role between vitamin D and falls. However, the participants in this study who performed more poorly in physical and cognitive assessments with vitamin D insufficiency, did not actually translate into increased falls. What may account for this is that the sample size of participants with serum 25OHD <25nmol/L was too small to significantly affect the incidence of falls. Perhaps if the study would have broken down the categories of vitamin D status further, other than simply sufficient vs insufficient, a more useful representation would be seen. For example, a person with a serum concentration of 50 is considered “insufficient”, where 51 is “sufficient”.

Other limitations of this study include the high proportion of participants who were relatively healthy, with increased physical activity including outdoor mobility. This would lead to increased exposure to environmental hazards, but also to increased exposure to vitamin D through sunlight. The study also reported a higher proportion of outdoor falls, which may have weakened the association between vitamin D insufficiency and physiological falls. This association may be more evident in a less active, frailer population. Another reason why the population of relatively healthy individuals limits the study is that it is not a good representation of the general community dwelling population. Furthermore, this study did not consider other mechanisms other than serum 25(OH)D as an explanation for these results. In future studies, serum concentrations of calcium and other minerals should be accounted for as well.

Overall, the findings of this particular study do help to clarify some mechanisms by which vitamin D interventions may help to decrease risk factors to reduce falls. There is adequate evidence from the study that there are benefits of vitamin D which extend beyond cognition and the musculoskeletal system, however more investigations are required before concluding that it is solely the vitamin D blood level which accounts for these benefits.

Article 3

In 2013, Boye et al performed a cross sectional study, called the “IMPROveFALL study” to investigate whether serum 25OHD was associated with physical performance in older men and women who visited an emergency department (ED) due to a fall. (9) The study was designed to address the fact that previous studies which investigated similar topics have been done either in female only populations, or if they involved men, they were often younger and highly functional. In addition, most studies including the ones described above screen for healthy, non-symptomatic persons. This study addresses these issues by having the following criteria: age over 65 who visited the ED because of a fall, used one or more fall-risk increasing drugs, had a MMSE score of ≥21/30, able to walk without assistance, and community dwelling. The fall could not be induced by an acute medical condition such as a stroke, and comorbidities were all documented. There were 616 participants who met these requirements and enrolled in the study.

During the baseline assessment, non-fasting blood samples were collected, and serum 25OHD groups were chosen based on the levels of severe deficiency (<25nmol/L), moderate deficiency (25-49 nmol/L), sufficient (50-74.9 nmol/L) and optimal (>75 nmol/L). The mean serum 25OHD concentration was 59=/- 29 nmol/L. The number of participants in each category are described in **Table 3.**

Physical performance was evaluated using handgrip strength measurements, the Timed Up and Go (TUG) test, the Five Time Sit to Stand test (FTSS) and the tandem stand test. Descriptions of these tests can be found elsewhere (9). **Figure 1** shows linear representations of a summary of these tests.

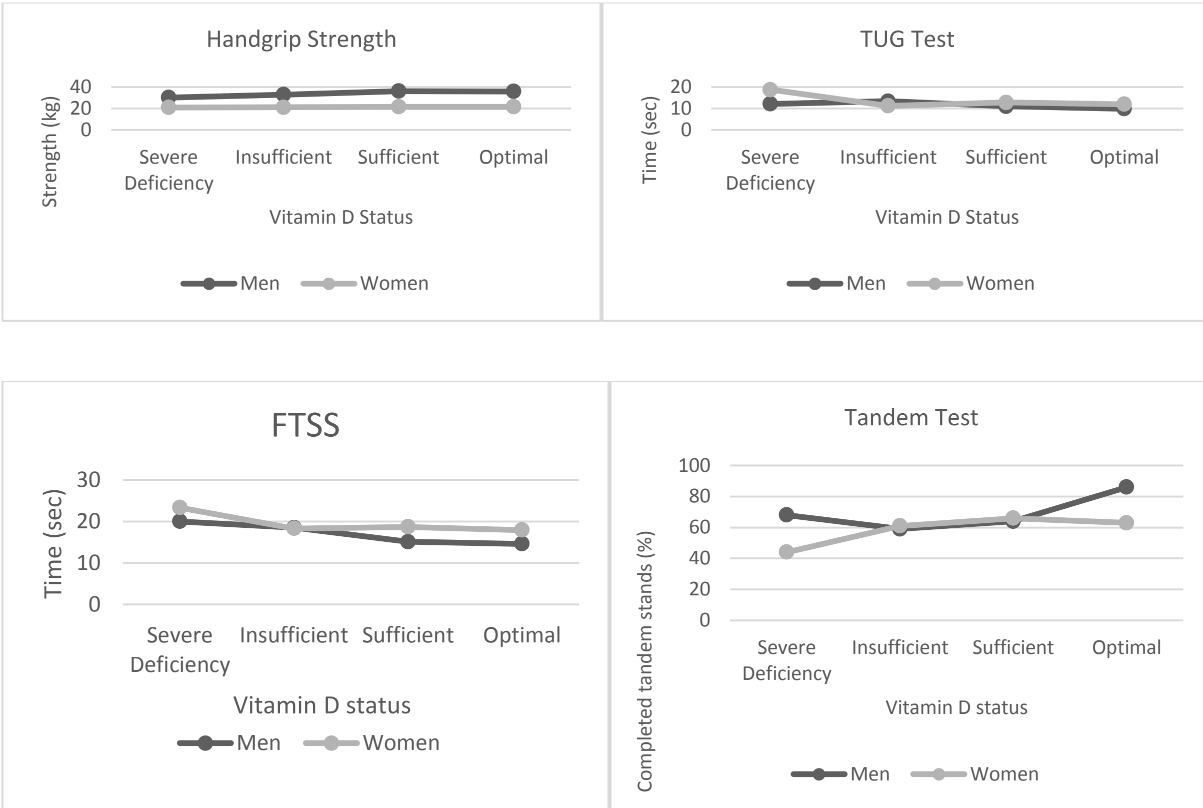

Figure 1. Linear representation of strength and physical performance results according to serum vitamin D group and sex. Adjusted for age, number of comorbidities, smoking, degree of urbanization, BMI, MMSE score. Adapted from Boye *et al*, (10)

According to this study, serum 25(OH)D levels were significantly associated with the physical performance of adults over the age of 65, with some variances between gender. In men, there was an association between vitamin D levels and handgrip strength, TUG time and FTSS time, whereas in woman there was only a significant correlation with TUG time. The researchers offer a hypothesis to the discrepancy between genders, that being the fact that sex hormones are known to modulate the vitamin D endocrine system and calcium homeostasis. An example of this is that estrogen stimulates vitamin D receptor expression as well as 1α hydroxylase activity, while testosterone stimulates intestinal calcium channel expression. (10)

Due to the fact that this study incorporated participants who had already fallen, participants may have a possible neuromuscular dysfunction, which sets this study apart from other similar research.

There are many strengths of this study design, including the large population size with a good proportion of both men and women, and the wide range of serum vitamin D concentrations. A major strength is the substantial proportion of vitamin D deficient participants included which is not seen in most similar studies. This enabled physical performance to be analyzed accurately in the most extremes of populations. There are limitations of this study which must be taken into account, the first being that the cross-sectional set up cannot determine a causal relationship between serum 25(OH)D concentration and physical performance, and similar to the previous study does not exclude the possible reverse causality. Another limitation is the criteria of an MMSE score above 21 may have excluded the frailest "fallers" which could possibly skew the results.

Overall, this study is a valid contribution to the conclusion that higher serum 25(OH)D concentration is associated with better strength and physical performance in older male and female fallers.

Article 4

In 2012, Boersma *et al* conducted a cross-sectional study investigating the impact of vitamin D deficiency on postural instability in 145 adults over 65 years who have had at least one fall episode within 6 months prior to the study. (11) A previous study by Bischoff-Ferrari et al found that fall prevention by vitamin D could be mediated by a change in postural and dynamic balance. (12) They concluded that of the 60% fall reduction rate, 22% of the treatment effect was explained by a change in postural balance and 14% by dynamic balance, suggesting that low vitamin D levels may be associated with impaired postural control.(12) Postural instability, according to Horlings et al is a common risk factor to falls in the elderly, and is challenging to assess for and treat. (13) It occurs as a consequence of degenerations in visual and vestibular sensory systems, proprioception and impairments in central processing, and combinations of these.(13) This information led to the current study, which used a more precise method for balance assessment. This new method of testing postural instability was used to investigate the impact of vitamin D deficiency on postural instability indicators in community dwelling older subjects.

The participants of this study were selected via a convenience sample attending the Falls and Fractures Clinic in Australia. The subjects were selected in a way to mimic the participants' of the previous study, as well as to choose subjects who had a higher risk of future falls, who would then have a higher likelihood of identifying postural instability. The postural assessment was performed using the Medicaa Balance Rehabilitation Unit, which studied the postural control responses to different types of visual and visual-vestibular stimulation. Details of the methods and exclusion criteria of this study can be found elsewhere.(12). Subjects were categorized into three groups based on their serum 25(OH)D concentration, those being deficient (<30nmol/L), insufficient (30-50nmol/L) and normal (>50nmol/L). Amongst the 145 participants aged 73-88 years old, 21% were deficient, 19% insufficient and 40% normal. There was a significant difference in the number of falls between these categories: 7+/-2, 2+/-1 and 3+/-1 respectively, p=0.01. Other characteristics of the study participants are found in **Table 4.**

The study found that deficient subjects have significantly lower limits of stability (LOS) and higher sway in the "eyes closed on foam" (ECF). Deficient participants also show slower gait velocity (GV), however there was no difference in the centre of pressure (COP) for visual vestibular conditions. Results of these tests are represented in **Figure 2** below.

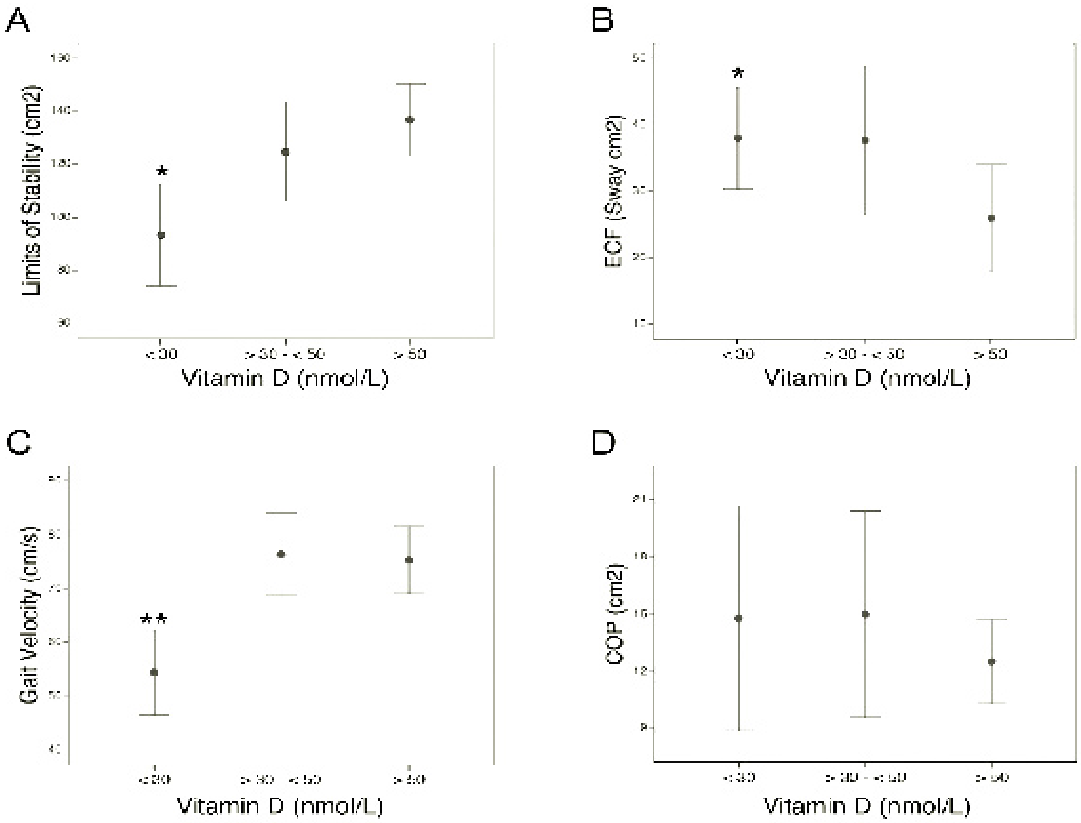

Figure 2. Summary of parameters for balance and gait parameters according to vitamin D status. A) Limits of stability, B) Eyes closed on foam condition, C) Gait Velocity, and D) Centre of Pressure for visual vestibular conditions. Adapted from Boersma et al. (12)

This study determined that postural instability is associated with low vitamin D concentrations in community dwelling older fallers, independently of nutritional and functional status. A major strength of this study was the use of an accurate and reliable method to perform a postural assessment. Also, the study included a wide range of demographic characteristics, and the homogeneousity amongst the 3 categories is another strength of this study. A limitation is that self-report was used to calculate the number of falls, so recall bias must be taken into account. In addition, the study did not include institutionalized subjects or those who are cognitively impaired, which are as mentioned above two higher risk populations.

This particular study provides a better understanding on the role of vitamin D and postural instability, where the association has remained only partially assessed. The reliable techniques and methods of this study are an excellent contribution towards the research of various mechanisms of falls and the role of vitamin D.

Article 5

In 2011, Sakalli et al performed a prospective, double-blinded, randomized study in order to determine the effect of oral and parenteral vitamin D supplementation in the elderly. (14) The basis of this study is the theory that vitamin D deficiency may result as osteoporosis, osteomalacia and impaired neuromuscular functions in the elderly, which may result in falls. This study acknowledges that vitamin D replacement reduces falls and fractures in the elderly, and its aim is to determine the benefits of a single megadose of 300 000 IU.

The population of this study were 120 men and women over the age of 65 years who attended a rheumatology outpatient clinic. Subjects were randomly assigned to 4 groups with 30 subjects per group: Group 1 took intramuscular (I.M.) vitamin D, group 2 took I.M. placebo, group 3 took per os (po) vitamin D and group 4 took po placebo. Serum vitamin D levels, creatinine, calcium, phosphorous, ALT, ALP, PTH, 24 h calcium excretion, as well as visual analog scale (VAS) for pain assessment, timed up and go test (TUG) and a short form questionnaire (SF-36) for quality of life were all assessed in each subject before and after treatment. The SF-36 consists of the physical component scale (PCS), physical functioning (PF), role physical (RP), bodily pain (BP) and general health (GH). There is also a mental component scale (MCS), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH). A summary and results of these tests are found in **Tables 5 and 6**.

Based on these results, this study shows an improvement in the four parameters of physical health and two parameters in mental health in the intramuscular vitamin D group. The per os vitamin D group showed improvement in the VAS test and two parameters of physical health. The study therefore concluded even a single megadose of vitamin D is effective enough to increase quality of life, decrease nonspecific musculoskeletal pain, and to prevent falls via improving functional mobility in the elderly.

Limitations of this study include the fact that IM vitamin D may have a stronger placebo effect than oral, which may account for the increased effects of IM. An explanation as to why 300 000IU of vitamin D was chosen as a megadose is not available in the study, and it is also not clarified if vitamin D2 or vitamin D3 supplementation was given. Another limitation is that the serum vitamin D levels were difficult to standardize, and the study was also conducted in a sunny city in Turkey. Participants were all patients in a rheumatology clinic, which may also skew the results based on co-morbidities. This study is unique because there are no other studies available which assess the effect of single and megadose vitamin D on functional status, pain, quality of life and correlations between these parameters. It is also the first study to evaluate the quality of life using the SF-36 measurement. The effect on vitamin D on the many various parameters, as well as comparing po vs IM vs placebo also make this study one of a kind.

Discussion

Summary of Main findings:

The purpose of this literature review was to determine the effects of vitamin D on fall reduction in the elderly. The five studies analyzed for this review assessed various mechanisms of falls in the elderly, and the role in which vitamin D supplementation may or may not have. Each of the articles did show a significant positive correlation between serum vitamin D concentration and fall reduction, or in risk factor reduction. The first study, by Peterson *et al* assessed found a positive correlation between vitamin D and fall reduction, as well as cognitive function effects. However no significant relationship between vitamin D and motor measures was found. The study by Menant et al (9) demonstrates a relationship between risk factors for falls and serum 25(OH)D levels, including cognitive domains of executive function and attention processing speed, as well as fall reduction in men but not women. Similarly, the IMPROVeFall Study also showed sex discrepancy, however serum 25(OH)D levels were significantly associated with physical performance, inferring the association with fall reduction. Boersma et al (12) found a significant correlation between vitamin D and postural instability, which is suggested to be a risk factor for falls in the elderly. Finally, the study by Sakalli et al (15) concludes that even a single megadose of vitamin D was effective in fall prevention.

Inconsistencies between Studies

Although the studies analyzed above were all strong and of good quality and design, there were certainly inconsistencies amongst them. One of these inconsistencies is the discrepancies between which 25OHD concentrations classify as "deficient, insufficient, sufficient" and "optimal". The studies were also all carried out in different locations in the world and different times of year, so vitamin D levels due to sun exposure must be taken into account. Each study was also quite different in the parameters they assessed. Since the mechanism for falls in the elderly is so broad, each of the above studies assesses different parameters which the authors consider to be risk factors for falls. The fifth study was the only relevant study in terms of providing a supplementation intervention. Articles 1-4 measured serum concentration only, which does not provide insight in terms of how much supplementation is required to achieve those concentrations. Therefore, further supplementation intervention studies are warranted.

Implications for Professional Practice

There is existing evidence that decreased serum vitamin D levels play a significant role in increased incidences of falls in the elderly, as well as increased risk factors for potential falls. The implications in professional practice are therefore substantial. The articles above reinforce the theory that hypovitaminosis D is a biological characteristic of elderly fallers, so it can be inferred that older adults should routinely receive vitamin D supplementation to prevent both bone and non-bone adverse events. (15) In regards to the last article described by (15)**,** further studies should be carried out to verify the increased effects of single megadosing of vitamin D and IM vs PO effectiveness. From a clinical perspective, the research which has been done to date on this topic aids in providing effective guidelines on the proper use of vitamin D supplements for fall prevention in the elderly.

Conclusion

The purpose of this paper was to answer the question "What are the effects of vitamin D supplementation on fall reduction in the elderly?" Five studies were critically appraised in order to help answer this question, all of which show positive effects on either vitamin D supplementation and/or increased serum 25(OH)D levels in fall reduction. Each study also recognizes the issue of vitamin D deficiency in the elderly and comments on the detrimental effects of low serum 25(OH)D concentration. Further simple studies are required associating vitamin D supplementation at various doses with fall reduction. The variety of mechanisms by which vitamin D improves falls in the elderly are broad and not yet fully understood. It is therefore important that such research continues, so that the standardized guidelines for vitamin D supplementation may be optimized.

List of Tables

Table 1. Dietary Reference Intakes for Calcium and Vitamin D.

Age group	Recommended Dietary Allowance (RDA) per day	Tolerable Upper Intake Level (UL) per day
Infants 0-6 months	400 IU (10 mcg)*	1000 IU (25 mcg)
Infants 7-12 months	400 IU (10 mcg) *	1500 IU (38 mcg)
Children 1-3 years	600 IU (15 mcg)	2500 IU (63 mcg)
Children 4-8 years	600 IU (15 mcg)	3000 IU (75 mcg)
Children and Adults 9-70 years	600 IU (15 mcg)	4000 IU (100 mcg)
Adults > 70 years	800 IU (20 mcg)	4000 IU (100 mcg)
Pregnancy & Lactation	600 IU (15 mcg)	4000 IU (100 mcg)

Adapted from The Institute of Medicine, 2010 (16).

Table 2. Correlations between clinical variables and vitamin D concentration

<table>
<tr><th colspan="2">Motor Measure</th><th colspan="2">Correlation</th><th colspan="2">P value</th></tr>
<tr><td colspan="2">Stopwatch Walk</td><td colspan="2">-0.08</td><td colspan="2">0.33</td></tr>
<tr><td colspan="2">Tinetti gait</td><td colspan="2">0.1</td><td colspan="2">0.21</td></tr>
<tr><td colspan="2">Tinetti Balance</td><td colspan="2">0.02</td><td colspan="2">0.89</td></tr>
<tr><td colspan="2">UPDRS *</td><td colspan="2">-0.01</td><td colspan="2">0.88</td></tr>
<tr><td colspan="2">Grip Strength</td><td colspan="2">-0.14</td><td colspan="2">0.09</td></tr>
<tr><td colspan="2">Chair Stands (n=120)</td><td colspan="2">0.04</td><td colspan="2">0.7</td></tr>
<tr><td>Cognitive Measure</td><td>Correlation</td><td>p-value</td><td>`Regression coefficient</td><td>95% confidence interval</td><td>p value</td></tr>
<tr><td>Global Score</td><td>0.14</td><td>0.07</td><td>3.30</td><td>-0.5, 7.10</td><td>0.09</td></tr>
<tr><td>Attention</td><td>0.15</td><td>0.06</td><td>2.68</td><td>-0.68, 6.04</td><td>0.12</td></tr>
<tr><td>Executive Function</td><td>0.10</td><td>0.21</td><td>1.73</td><td>-1.35, 4.80</td><td>0.27</td></tr>
<tr><td>Memory</td><td>0.12</td><td>0.13</td><td>1.35</td><td>-0.90, 3.60</td><td>0.24</td></tr>
<tr><td>Working Memory</td><td>0.14</td><td>0.08</td><td>2.30</td><td>-0.44, 5.04</td><td>0.10</td></tr>
<tr><td>Visuospatial</td><td>0.08</td><td>0.35</td><td>1.63</td><td>-1.18, 4.44</td><td>0.25</td></tr>
<tr><td>MMSE</td><td>0.24</td><td><0.01</td><td>1.50</td><td>-0.01, 3.01</td><td>0.05</td></tr>
<tr><td colspan="2">Cognitive Status</td><td colspan="2">Mean Vit. D concentration</td><td colspan="2">P value</td></tr>
<tr><td colspan="2">CDR=0.5</td><td colspan="2">30.9ng/ml</td><td colspan="2" rowspan="2">0.02</td></tr>
<tr><td colspan="2">CDR=0</td><td colspan="2">38.8 ng/ml</td></tr>
</table>

*****Unified Parkinson's disease rating scale
Adapted from Peterson *et al* (8).

Table 3. Serum 25(OH)D concentration in the IMPROveFALL Study.

Serum 25(OH)D (nmol/L)	**Number of Participants**
<25	55
25-49.9	209
50-74.9	172
≥75	164

Adapted from Boye *et al*, (10).

Table 4. Characteristics of the study participants in the Boersa *et al* study by vitamin D Status.

Variables	**Vitamin D < 30 nmol/L (n=38)**	**Vitamin D ≥ 30nmol/L (n=28)**	**Control Group >50 nmol/L, (n=79)**	**p-value ***
Age (years)	**79.7 ± 7**	**78.5 ± 7**	**79.2 ± 9**	NS
Gender (%women)	57	57	64	NS
BMI (kg/m2)	**30 ± 5**	**29 ± 7**	**26 ± 4**	NS
Mini nutrition assessment (score)	**15 ± 4**	**14 ± 4**	**16 ± 4**	NS
Albumin (g/L)	**41.8 ± 2**	**41.8 ± 4**	**42.3 ± 2**	NS
Vitamin D (nmol/L)	**22 ± 5**	**41± 5**	**81 ± 22**	a, b
Parathyroid hormone (pmol/L)	**7.5 ± 2.7**	**6 ± 3.5**	**6 ± 5.2**	NS
Corrected Calcium (mmol/L)	**2.3 ± 0.1**	**2.4 ± 0.1**	**2.3 ± 0.1**	NS
Falls (last 6 months)	**7 ± 2**	**2 ± 1**	**3 ± 1**	B
Grip strength (kg)	17	20	15	NS
Global Development Score (/15)	6	5	5	NS

Figures are means ± SD; * independent sample t test. a P<0.05 for deficient vs. insufficient group; b P<0.05 for insufficient vs normal group. Adapted from Boersa *et al*, (12).

Table 5. The biochemical parameters of each group before and after medication was given (mean+/- standard deviation).

	Group 1 (I.M.. VD)		**Group 2 (I.M. placebo)**		**Group 3 (P.O. VD)**		**Group 4 (P.O. placebo)**	
Calcium (mg/dl)	***Before***	***After***	***Before***	***After***	***Before***	***After***	***Before***	***After***
Phosphor (mg.dl)	9.1 +/- 0.4	9.2+/-0.4	9.2+/-0.3	9.3+/-.04	9.4+/-0.3	9.5+/-0.4	9.2+/-0.4	9.3+/-0.4
24 h urine calcium (g/day)	3.5+/-0.5	3.6+/-0.6	3.6+/-0.5	3.6+/-0.5	3.6+/-0.6	3.7+/-0.5	3.6+/-0.6	3.5+/-0.5
ALP (IU/L)	81.1+/- 56.8	86.1+/- 61.8	73.5+/- 23.6	72.7+/- 22.5	76.6+/- 22.7	77.0+/- 24.6	78.1+/- 14.9	71.8+/- 20.1
PTH (pg/mL)	98.1+/- 61.0	69.3+/- 323.0***	73.0+/- 42.7	74.1+/- 110.4	82.7+/- 32.5	50.8+/- 23.4***	68.4+/- 22.7	65.6+/- 27.2
VD (ng/mL)	21.0+/-9.9	26.4+/- 12.9***	20.7+/-8.7	21.0+/-7.4	20.9+/-9.5	27.0+/- 12.0***	21.2+/-7.4	21.0+/-5.5

*P<0.05, **P<0.01, ***P<0.001
Adapted from: Sakalli *et al.* (15)

Table 6. The functional status, pain, and quality of life parameters before and after medication (mean +/- standard deviation).

	Group 1 (I.M.. VD)		**Group 2 (I.M. placebo)**		**Group 3 (P.O. VD)**		**Group 4 (P.O. placebo)**	
	Before	***After***	***Before***	***After***	***Before***	***After***	***Before***	***After***
TUG (s)	11.1 +/- 2.7	8.4+/- 2.2***	10.3+/-2.6	10.1+/-2.6	11.0+/-2.2	10.0+/- 2.0***	10.4+/-2.5	10.2+/-2.9
VAS (cm)	6.8+/-2.6	5.4+/- 2.2***	5.5+/-3.2	4.2+/- 3.1**	5.9+/-2.4	5.1+/- 2.3**	5.9+/-2.7	5.5+/- 2.8**
PF	50+/-20.7	56.8+/- 19.7***	48.3+/- 23.9	50.5+/- 23.1	49.3+/- 21.4	53.7+/- 20.3***	57.0+/- 24.2	54.8+/- 14.8
RP	42.5+/- 22.9	65.8+/- 24.1**	39.8+/- 21.1	42.5+/- 24.7**	38.3+/- 25.2	43.3+/- 27.8**	50.0+/- 33.5	54.0+/- 42.4
BP	40.9+/- 20.8	53.5+/- 21.0***	46.1+/- 31.6	47.3+/- 31.6	39.6+/- 19.4	46.1+/- 21.0	48.5+/- 24.4	53.3+/- 38.7
GH	46.1+/- 15.5	48.2+/- 16.4**	44.6+/- 21.0	44.8+/- 21.3	42.0+/- 19.8	44.1+/- 20.8	45.7+/- 21.4	56.5+/- 72.8
VT	50.2+/- 17.6	51.2+/- 17.6	50.4+/- 20.9	50.5+/- 20.6	50.7+/- 21.7	50.3+/- 21.3	51.3+/- 23.3	50.9+/- 68.6
SF	65.0+/- 24.9	68.8+/- 23.2*	54.2+/- 28.3	57.1+/- 26.8	54.2+/- 28.5	56.8+/- 26.1	63.3+/- 28.8	65.8+/- 48.3
RE	46.8+/- 22.6	52.5+/- 21.1	53.3+/- 24.1	55.8+/- 22.6*	46.2+/- 27.8	51.9+/- 25.3	45.9+/- 35.1	60.5+/- 22.3
MH	58.1+/- 16.3	61.1+/- 13.7*	64.4+/- 13.4	63.6+/- 13.4	57.2+/- 13.8	57.8+/- 13.4	55.9+/- 19.1	71.0+/- 72.2

Adapted from: Sakalli et al. (15)
*P<0.05, **P<0.01, ***P<0.001

References

1. Annweiler C, Montero-odasso M, Schott AM, Berrut G, Fantino B, Beauchet O. Fall prevention and vitamin D in the elderly : an overview of the key role of the non-bone effects. 2010;1–13.

2. Shuler F, Schilierf T, Wingate M. Preventing Falls with Vitamin D: West Virginia Medical Journal. 2014:110; 10-12.

3. Department of Ageing and Life Course. WHO Global Report on Falls Prevention in Older Age. Geneva, CHE: World Health Organization, 2007. ProQuest ebrary. Web. 7 April 2015. Copyright © 2007. World Health Organization. All rights reserved. 2015;(April).

4. American Geriatrics Society Workgroup. Recommendations abstracted from the American Geriatrics Society Consensus Statement on vitamin D for Prevention of Falls and Their Consequences. J Am Geriatr Soc [Internet]. 2014 Jan [cited 2015 Jan 28];62(1):147–52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24350602

5. Christakos S, Ajibade D V, Dhawan P, Fechner AJ, Mady LJ. Vitamin D : Metabolism. 2012;38:1–11.

6. Plum LA, Deluca HF. Vitamin D [Internet]. 2010. Available from: http://link.springer.com/10.1007/978-1-60327-303-9

7. Peterson A, Mattek N, Clemons A, Bowman GL, Buracchio T, Kaye J, et al. SERUM VITAMIN D CONCENTRATIONS ARE ASSOCIATED. 2012;16(10).

8. Menant JC, Close JCT, Delbaere K, Sturnieks DL, Trollor J, Sachdev PS, et al. Relationships between serum vitamin D levels, neuromuscular and neuropsychological function and falls in older men and women. Osteoporos Int [Internet]. 2012 Mar [cited 2015 Mar 9];23(3):981–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21523392

9. Boyé ND a, Oudshoorn C, van der Velde N, van Lieshout EMM, de Vries OJ, Lips P, et al. Vitamin D and physical performance in older men and women visiting the emergency department because of a fall: data from the improving medication prescribing to reduce risk of falls (IMPROveFALL) study. J Am Geriatr Soc [Internet]. 2013 Nov [cited 2015 Feb 27];61(11):1948–52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24116657

10. Oudshoorn C, van der Cammen TJM, McMurdo MET, van Leeuwen JPTM, Colin EM. Ageing and vitamin D deficiency: effects on calcium homeostasis and considerations for vitamin D supplementation. Br J Nutr. 2009;101(11):1597–606.

11. Boersma D, Demontiero O, Amiri ZM, Hassan S, Suarez H, Geisinger D, et al. Vitamin D status in relation to postural stability. J Nutr. 2012;16(3):1–6.

12. Bischoff-Ferrari H a., Conzelmann M, Stähelin HB, Dick W, Carpenter MG, Adkin a. L, et al. Is fall prevention by vitamin D mediated by a change in postural or dynamic balance? Osteoporos Int. 2006;17(5):656–63.

13. Horlings CGC, van Engelen BGM, Allum JHJ, Bloem BR. A weak balance: the contribution of muscle weakness to postural instability and falls. Nat Clin Pract Neurol. 2008;4(9):504–15.

14. Sakalli H, Arslan D, Yucel AE. The effect of oral and parenteral vitamin D supplementation in the elderly: a prospective, double-blinded, randomized, placebo-controlled study. Rheumatol Int [Internet]. 2012 Aug [cited 2015 Mar 2];32(8):2279–83. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21556746

15. Annweiler C, Beauchet O. Questioning vitamin D status of elderly fallers and nonfallers: a meta-analysis to address a "forgotten step". J Intern Med [Internet]. 2015 Jan [cited 2015 Mar 9];277(1):16–44. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24697944

16. Christine Taylor, Ann Yaktine, Heather Delvalle, Heather Breiner, Anton Bandy GK. Dietary reference intakes for calcium and vitamin d. Pediatrics. 2012;130(November):e1424.