# Vitamin D Effects on Health, Body Composition, and Athletic Performance

Updated March 16, 2022, by Mauro Di Pasquale, B.Sc. (Hons), M.D. Copyright 2002-2022

# **Table of Contents**

1troauction	.3
itamin D and the Covid-19 Pandemic	
oem by Mauro	
bstracts of Interest for Vitamin D and Covid-19Vitamin D regulation of the immune system and its implications for COVID-19: A mini review	
Abstract	
	.5
Vitamin D Supplementation to Prevent COVID-19 Infections and Deaths-Accumulating Evidence from Epidemiological and Intervention Studies Calls for Immediate Action	.6
The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality	.6
Early nutritional supplementation in non-critically ill patients hospitalized for the 2019 novel coronavirus disease (COVID-19): Rationale and feasibility of a shared pragmatic protocol	.6
Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths.	.7
Current status of potential therapeutic candidates for the COVID-19 crisis	.8
Optimal Nutritional Status for a Well-Functioning Immune System Is an Important Factor to Protect Against Viral Infections.	.8
A new threat from an old enemy: Re-emergence of coronavirus (Review)(Review)	.9
itamin D is More Than Just for Strong Bones	.9
/hy Most of Us May Be Vitamin D Deficient1	
unburn and Vitamin D1	
itamin D is Vital for Exercise Performance	
ow Much Vitamin D Can We Take?	
ow Much Vitamin D do Athletes Need?1  Vhat Else is Needed for Optimum Effects from Vitamin D	
conclusions and Recommendations1	
lushrooms and Vitamin D	
Ultraviolet Irradiation Increased the Concentration of Vitamin D₂ and Decreased the	
Concentration of Ergosterol in Shiitake Mushroom (Lentinus edodes) and Oyster Mushroom	
(Pleurotus ostreatus) Powder in Ethanol Suspension	17
ome of the best natural sources of vitamin D1	17
itamin D in my MD+ supplements:1	18
nportance of Magnesium1	
ecommended Screening Blood Work1	
sampling of Vitamin D Relevant Citations and Abstracts	
A Review of Mushrooms as a Potential Source of Dietary Vitamin D2	21
Ultraviolet Irradiation Increased the Concentration of Vitamin D <sub>2</sub> and Decreased the Concentration of Ergosterol in Shiitake Mushroom ( <i>Lentinus edodes</i> ) and Oyster Mushroom	21
(Pleurotus ostreatus) Powder in Ethanol Suspension	
Role of Magnesium in Vitamin D Activation and Function	22
Magnesium status and the physical performance of volleyball players: effects of magnesium supplementation	22

Association between erythrocyte concentrations of magnesium and zinc in high- performancehandball players after dietary magnesium supplementation23
Magnesium intake is associated with strength performance in elite basketball, handball and volleyball players23
Magnesium and strength in elite judo athletes according to intracellular water changes2
Effects of magnesium supplementation on testosterone levels of athletes and sedentary subjects at rest and after exhaustion24
Effects of Vitamin D on Skeletal Muscle and Athletic Performance25
Vitamin D and Sport Performance25
Role of Vitamin D in Athletes and Their Performance: Current Concepts and New Trends25
Vitamin D, Skeletal Muscle Function and Athletic Performance in Athletes-A Narrative Review.
Non-musculoskeletal benefits of vitamin D20
Supplemental protein from dairy products increases body weight and vitamin D improves physical performance in older adults: a systematic review and meta-analysis
Vitamin D testing: advantages and limits of the current assays2
Associations between 25-hydroxyvitamin D levels, body composition and metabolic profiles in young women28
Vitamin D Supplementation Improves Quality of Life and Physical Performance in Osteoarthritis Patients28
Vitamin D and muscle trophicity29
Vitamin D modulates adipose tissue biology: possible consequences for obesity?30
Changes in circulating vitamin D levels with loss of adipose tissue30
Vitamin D treatment protects against and reverses oxidative stress induced muscle proteolysis31
Vitamin D: a review on its effects on muscle strength, the risk of fall, and frailty3
Effects of vitamin D in skeletal muscle: falls, strength, athletic performance and insulin sensitivity32
Vitamin D signaling in myogenesis: potential for treatment of sarcopenia32
Vitamin D status and supplementation in elite Irish athletes32
Assessment of vitamin D concentration in non-supplemented professional athletes and healthy adults during the winter months in the UK: implications for skeletal muscle function. 33
Sunlight and Vitamin D: A global perspective for health34
Vitamin D and physical performance34
Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality-a review of recent evidence
Vitamin D status and biomarkers of inflammation in runners
Vitamin D: an overview of its role in skeletal muscle physiology in children and adolescents30
The effects of vitamin D on skeletal muscle function and cellular signaling30
Vitamin D, muscle function, and exercise performance33
Vitamin D and human skeletal muscle37
Vitamin D and its role in skeletal muscle37

The level of vitamin D in the serum correlates with fatty de rotator cuff	_
Vitamin D: what is an adequate vitamin D level and how m	• •
Vitamin D production after UVB exposure depends on bas cholesterolbut not on skin pigmentation	eline vitamin D and total
Is vitamin D the fountain of youth?	40
Vitamin D: current status and perspectives Vitamin D level in summer and winter related to measured	
Vitamin D and skeletal muscle tissue and function	42
Relationship between vitamin D status, body composition girls in Beijing.	
[Stress fracture in female athlete runner carrying weights]	44
The vitamin D deficiency pandemic and consequences for action	
Associations of diet, supplement use, and ultraviolet B rac status in Swedish women during winter	
Estimation of the dietary requirement for vitamin D in heal	thy adults46
Low vitamin D status despite abundant sun exposure	47
Vitamin D physiology	48
Vitamin D and muscle function	49
The vitamin D deficiency pandemic and consequences for action.	
Athletic performance and vitamin D	51
Should we be concerned about the vitamin D status of ath	letes?52
The effect of conventional vitamin D(2) supplementation o weak among peripubertal Finnish girls: a 3-y prospective s	n serum 25(OH)D concentration is study52

# Introduction

Vitamin D is vital for almost all processes in the body including genetic expression, all aspects of metabolism, immune function, decreasing morbidity, and increasing longevity. As well it's important for body composition and physical and mental performance.

The Information below originated as a short article released in 2002. To keep it relevant is maintained in draft form and revised regularly to keep it relevant and up to date.

### Vitamin D and the Covid-19 Pandemic

### **Poem by Mauro**

It's a constant battle And always has been Us against them Forever making a scene

But we'll prevail in the end Always finding a way to mend Even when the odds are against us We'll win because we can

-----

Because of the world-wide Covid-19 pandemic, and the fact that we will face further viral pandemics over the coming years, I've added information on the potential of vitamin D, with a mention of other vitamins, minerals, antioxidants, and anti-inflammatory compounds, in both protecting against and the treatment of viral as well as bacterial and other pathogenic infections.

It is critical that we use all the measures we can to defeat the highly pathogenic coronavirus Covid-19. The use of natural ingredients and foods that show some effectiveness against Covid-19, are low hanging fruits that can be used right now since they are readily available, and taken at the right dosages, universally considered safe.

Vitamin D has significant anti-inflammatory and immunomodulatory effects. Recent evidence has shown that optimizing and even going beyond optimum levels of vitamin D has potential in offering some preventative protection and treatment for the Covid-19 pandemic. 1234 It's also been shown that vitamin D deficiency, which is common world-wide, is associated with an increased risk of infection and morbidity from Covid-19 infections. 56789

In the past year, several papers have been published on the beneficial effects of vitamin D, many advising higher daily doses, on the current Covid-19 pandemic. 1011121314151617181920212223 It also seems that vitamin D3 (used in my nutritional supplement formulations) supplementation is more beneficial than vitamin D2 supplementation. 2425

As well, other ingredients likely have beneficial immune and protective effects including vitamins A, B<sub>6</sub>, B<sub>12</sub>, C, D, E, and folate; trace elements, including zinc,<sup>26</sup> iron, selenium, magnesium, and copper; and the omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid, present in  $\underline{\text{MVM}}$ ,  $\underline{\text{EFA+}}$  and to some extent, all of the other products in my line of supplements.

For example, a recent study found that zinc, selenium, and vitamin D are essential for resistance to not only Covid-19, but for other viral infections, as well as improving immune function, and reducing inflammation.<sup>27</sup> Another recent study concluded that "On balance, given the negligible risk profile of supervised nutritional supplementation, weighed against the known and possible benefits, it appears pertinent to ensure adequate, if not elevated intake of these key vitamins and minerals in people both at risk of, and suffering from COVID-19."<sup>28</sup>

These ingredients have beneficial effects on the immune system, as well as antioxidant and antiinflammatory effects. They provide a protective effect on a variety of stressors such as poor lifestyles, pollution, poor diets, and act as a barrier to infectious agents such as bacterial and viral infections that target us on so many fronts.<sup>29</sup>

Even before any of the research came out citing the advantages of vitamin D, I was already taking at least 5000 units per day starting in early February 2020. My usual intake prior to then was in the 2000 to 4000 IU range. My vitamin D intake comes from food (see list below) and more importantly from my use of MVM, EFA+ and several other supplements in my lineup that contain vitamin D. As an aside, I don't just formulate the products in my nutritional supplement lineup, I use them exclusively every day and have been for decades.

My most recent test for vitamin D shows that my level is at 68 ng/mL, which I consider a high effective range, exactly where I want it to be.

While many sources state that the present RDA for vitamin D is adequate, it isn't.

## **Abstracts of Interest for Vitamin D and Covid-19**

# Vitamin D regulation of the immune system and its implications for COVID-19: A mini review

2021 May 18;9:20503121211014073. doi: 10.1177/20503121211014073. eCollection 2021. Linda Bui <sup>1</sup>, Zahra Zhu <sup>1</sup>, Stephanie Hawkins <sup>1</sup>, Alonso Cortez-Resendiz <sup>2</sup>, Alfredo Bellon <sup>123</sup>

### Abstract

The novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is at the origin of the current pandemic, predominantly manifests with severe respiratory symptoms and a heightened immune response. One characteristic of SARS-CoV-2 is its capacity to induce cytokine storm leading to acute respiratory distress syndrome. Consequently, agents with the ability to regulate the immune response, such as vitamin D, could become tools either for the prevention or the attenuation of the most severe consequences of the coronavirus disease 2019 (COVID-19). Vitamin D has shown antimicrobial as well as anti-inflammatory properties. While SARS-CoV-2 promotes the release of proinflammatory cytokines, vitamin D attenuates the release of at least some of these same molecules. Inflammatory cytokines have been associated with the clinical phenomena of COVID-19 and in particular with its most dangerous complications. Therefore, the goals of this article are as follows: first, present the numerous roles vitamin D plays in modulating the immune response; second, gather data currently available on COVID-19 clinical presentation and its relation to cytokines and similar molecules; third, expose what it is known about how coronaviruses elicit an inflammatory reaction; and fourth, discuss the potential contribution of vitamin D in reducing the risk and severity of COVID-19.

Full paper in PDF format available at <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8135207/pdf/10.1177\_20503121211014073.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8135207/pdf/10.1177\_20503121211014073.pdf</a>.

Nutrients. 2021 Jan 28;13(2):411. Doi: 10.3390/nu13020411.

# Vitamin D Supplementation to Prevent COVID-19 Infections and Deaths-Accumulating Evidence from Epidemiological and Intervention Studies Calls for Immediate Action

Hermann Brenner

Abstract1

The COVID-19 pandemic poses an unprecedented threat to human health, health care systems, public life, and economy around the globe. The repertoire of effective therapies for severe courses of the disease has remained limited. A large proportion of the world population suffers from vitamin D insufficiency or deficiency, with prevalence being particularly high among the COVID-19 high-risk populations. Vitamin D supplementation has been suggested as a potential option to prevent COVID-19 infections, severe courses, and deaths from the disease, but is not widely practiced. This article provides an up-to-date summary of recent epidemiological and intervention studies on a possible role of vitamin D supplementation for preventing severe COVID-19 cases and deaths. **Despite limitations and remaining uncertainties, accumulating evidence strongly supports widespread vitamin D supplementation, in particular of high-risk populations, as well as high-dose supplementation of those infected.** Given the dynamics of the COVID-19 pandemic, the benefit-risk ratio of such supplementation calls for immediate action even before results of ongoing large-scale randomized trials become available.

Aging Clin Exp Res. 2020 Jul;32(7):1195-1198. Doi: 10.1007/s40520-020-01570-8. Epub 2020 May 6.

# The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality.

Ilie PC<sup>1</sup>, Stefanescu S<sup>2</sup>, Smith L<sup>3</sup>.

#### **Abstract**

WHO declared SARS-CoV-2 a global pandemic. The present aim was to propose an hypothesis that there is a potential association between mean levels of vitamin D in various countries with cases and mortality caused by COVID-19. The mean levels of vitamin D for 20 European countries and morbidity and mortality caused by COVID-19 were acquired. Negative correlations between mean levels of vitamin D (average 56 mmol/L, STDEV 10.61) in each country and the number of COVID-19 cases/1 M (mean 295.95, STDEV 298.7, and mortality/1 M (mean 5.96, STDEV 15.13) were observed. Vitamin D levels are severely low in the aging population especially in Spain, Italy and Switzerland. This is also the most vulnerable group of the population in relation to COVID-19. It should be advisable to perform dedicated studies about vitamin D levels in COVID-19 patients with different degrees of disease severity.

Nutrition. 2020 Apr 3:110835. Doi: 10.1016/j.nut.2020.110835. [Epub ahead of print]

Early nutritional supplementation in non-critically ill patients hospitalized for the 2019 novel coronavirus disease (COVID-19): Rationale and feasibility of a shared pragmatic protocol.

<u>Caccialanza R¹</u>, <u>Laviano A²</u>, <u>Lobascio F³</u>, <u>Montagna E³</u>, <u>Bruno R⁴</u>, <u>Ludovisi S⁴</u>, <u>Corsico AG⁵</u>, <u>Di Sabatino A</u>⁶, <u>Belliato M</u>⁵, <u>Calvi M</u>⁶, <u>Iacona I</u>⁶, <u>Grugnetti G</u>⁶, <u>Bonadeo E¹⁰</u>, <u>Muzzi A¹⁰</u>, <u>Cereda E³</u>. <u>Abstract</u>

**OBJECTIVES:** 

Beginning in December 2019, the 2019 novel coronavirus disease (COVID-19) has caused a pneumonia epidemic that began in Wuhan, China, and is rapidly spreading throughout the whole world. Italy is the hardest hit country after China. Considering the deleterious consequences of malnutrition, which certainly can affect patients with COVID-19, the aim of this article is to present a pragmatic protocol for early nutritional supplementation of non-critically ill patients hospitalized for COVID-19 disease. It is based on the observation that most patients present at admission with severe inflammation and anorexia leading to a drastic reduction of food intake, and that a substantial percentage develops respiratory failure requiring non-invasive ventilation or even continuous positive airway pressure.

#### METHODS:

High-calorie dense diets in a variety of different consistencies with highly digestible foods and snacks are available for all patients. Oral supplementation of whey proteins as well as intravenous infusion of multivitamin, multimineral trace elements solutions are implemented at admission. In the presence of 25-hydroxyvitamin D deficit, cholecalciferol is promptly supplied. If nutritional risk is detected, two to three bottles of protein-calorie oral nutritional supplements (ONS) are provided. If <2 bottles/d of ONS are consumed for 2 consecutive days and/or respiratory conditions are worsening, supplemental/total parenteral nutrition is prescribed.

#### CONCLUSION:

We are aware that our straight approach may be debatable. However, to cope with the current emergency crisis, its aim is to promptly and pragmatically implement nutritional care in patients with COVID-19, which might be overlooked despite being potentially beneficial to clinical outcomes and effective in preventing the consequences of malnutrition in this patient population.

Full paper available at: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7194616/pdf/main.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7194616/pdf/main.pdf</a>.

Nutrients. 2020 Apr 2;12(4). Pii: E988. Doi: 10.3390/nu12040988.

# Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths.

Grant WB¹, Lahore H², McDonnell SL³, Baggerly CA³, French CB³, Aliano JL³, Bhattoa HP⁴. Abstract

The world is in the grip of the COVID-19 pandemic. Public health measures that can reduce the risk of infection and death in addition to quarantines are desperately needed. This article reviews the roles of vitamin D in reducing the risk of respiratory tract infections, knowledge about the epidemiology of influenza and COVID-19, and how vitamin D supplementation might be a useful measure to reduce risk. Through several mechanisms, vitamin D can reduce risk of infections. Those mechanisms include inducing cathelicidins and defensins that can lower viral replication rates and reducing concentrations of pro-inflammatory cytokines that produce the inflammation that injures the lining of the lungs, leading to pneumonia, as well as increasing concentrations of anti-inflammatory cytokines. Several observational studies and clinical trials reported that vitamin D supplementation reduced the risk of influenza, whereas others did not. Evidence supporting the role of vitamin D in reducing risk of COVID-19 includes that the outbreak occurred in winter, a time when 25-hydroxyvitamin D (25(OH)D) concentrations are lowest; that the number of cases in the Southern Hemisphere near the end of summer are low; that vitamin D deficiency has been found to contribute to acute respiratory distress syndrome; and that case-fatality rates increase with age and with chronic disease comorbidity, both

of which are associated with lower 25(OH)D concentration. To reduce the risk of infection, it is recommended that people at risk of influenza and/or COVID-19 consider taking 10,000 IU/d of vitamin D<sub>3</sub> for a few weeks to rapidly raise 25(OH)D concentrations, followed by 5000 IU/d. The goal should be to raise 25(OH)D concentrations above 40-60 ng/mL (100-150 nmol/L). For treatment of people who become infected with COVID-19, higher vitamin D<sub>3</sub> doses might be useful. Randomized controlled trials and large population studies should be conducted to evaluate these recommendations.

#### **KEYWORDS:**

COVID-19; UVB; acute respiratory distress syndrome (ARDS); ascorbic acid; cathelicidin; coronavirus; cytokine storm; influenza; observational; pneumonia; prevention; respiratory tract infection; solar radiation; treatment; vitamin C; vitamin D

Full text available at: https://www.mdpi.com/2072-6643/12/4/988/htm.

Brain Behav Immun. 2020 Apr 22. Pii: S0889-1591(20)30589-4. Doi: 10.1016/j.bbi.2020.04.046. [Epub ahead of print] **Current status of potential therapeutic candidates for the COVID-19 crisis.**Zhang J¹, Xie B², Hashimoto K³.

#### **Abstract**

As of April 15, 2020, the ongoing coronavirus disease 2019 (COVID-2019) pandemic has swept through 213 countries and infected more than 1,870,000 individuals, posing an unprecedented threat to international health and the economy. There is currently no specific treatment available for patients with COVID-19 infection. The lessons learned from past management of respiratory viral infections have provided insights into treating COVID-19. Numerous potential therapies, including supportive intervention, immunomodulatory agents, antiviral therapy, and convalescent plasma transfusion, have been tentatively applied in clinical settings. A number of these therapies have provided substantially curative benefits in treating patients with COVID-19 infection. Furthermore, intensive research and clinical trials are underway to assess the efficacy of existing drugs and identify potential therapeutic targets to develop new drugs for treating COVID-19. Herein, we summarize the current potential therapeutic approaches for diseases related to COVID-19 infection and introduce their mechanisms of action, safety, and effectiveness.

Full paper available at: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7175848/pdf/main.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7175848/pdf/main.pdf</a>.

Calder PC, Carr AC, Gombart AF, Eggersdorfer M.

Nutrients. 2020 Apr 23;12(4):1181. Doi: 10.3390/nu12041181

# Optimal Nutritional Status for a Well-Functioning Immune System Is an Important Factor to Protect Against Viral Infections.

Abstract

Public health practices including handwashing and vaccinations help reduce the spread and impact of infections. Nevertheless, the global burden of infection is high, and additional measures are necessary. Acute respiratory tract infections, for example, were responsible for approximately 2.38 million deaths worldwide in 2016. The role nutrition plays in supporting the immune system is well-established. A wealth of mechanistic and clinical data show that vitamins, including vitamins A, B<sub>6</sub>, B<sub>12</sub>, C, D, E, and folate; trace elements, including zinc, iron, selenium, magnesium, and copper; and the omega-3 fatty

acids eicosapentaenoic acid and docosahexaenoic acid play important and complementary roles in supporting the immune system. Inadequate intake and status of these nutrients are widespread, leading to a decrease in resistance to infections and as a consequence an increase in disease burden. Against this background the following conclusions are made: (1) supplementation with the above micronutrients and omega-3 fatty acids is a safe, effective, and low-cost strategy to help support optimal immune function; (2) supplementation above the Recommended Dietary Allowance (RDA), but within recommended upper safety limits, for specific nutrients such as vitamins C and D is warranted; and (3) public health officials are encouraged to include nutritional strategies in their recommendations to improve public health.

Full text available at: https://www.mdpi.com/2072-6643/12/4/1181/htm.

### A new threat from an old enemy: Re-emergence of coronavirus (Review).

Docea AO, Tsatsakis A, Albulescu D, Cristea O, Zlatian O, Vinceti M, Moschos SA, Tsoukalas D, Goumenou M, Drakoulis N, Dumanov JM, Tutelyan VA, Onischenko GG, Aschner M, Spandidos DA, Calina D. A new threat from an old enemy: Re-emergence of coronavirus (Review). Int J Mol Med. 2020 Jun;45(6):1631-1643. Doi: 10.3892/ijmm.2020.4555. Epub 2020 Mar 27. PMID: 32236624; PMCID: PMC7169834.

#### Abstract

The new outbreak of coronavirus from December 2019 has brought attention to an old viral enemy and has raised concerns as to the ability of current protection measures and the healthcare system to handle such a threat. It has been known since the 1960s that coronaviruses can cause respiratory infections in humans; however, their epidemic potential was understood only during the past two decades. In the present review, we address current knowledge on coronaviruses from a short history to epidemiology, pathogenesis, clinical manifestation of the disease, as well as treatment and prevention strategies. Although a great amount of research and efforts have been made worldwide to prevent further outbreaks of coronavirus-associated disease, the spread and lethality of the 2019 outbreak (COVID-19) is proving to be higher than previous epidemics on account of international travel density and immune naivety of the population. Only strong, joint and coordinated efforts of worldwide healthcare systems, researchers, and pharmaceutical companies and receptive national leaders will succeed in suppressing an outbreak of this scale.

This comprehensive paper is a must read for an overall picture of the Covid-19 pandemic. There is a mentions of the use of vitamin D as one of the modalities available to us in prevention and treatment of coronavirus infections, and specifically Covid-19.

Full text available at: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7169834/pdf/ijmm-45-06-1631.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7169834/pdf/ijmm-45-06-1631.pdf</a>

# **Vitamin D is More Than Just for Strong Bones**

Up to a few decades ago vitamin D wasn't generally considered all that vital beyond helping calcium challenged people, especially women who were or had a tendency toward osteoporosis, and of course to prevent rickets, something rarely seen in industrialize countries since even minimal amounts of

vitamin D prevents severe deficiency. As well much of the research up to the mid 1990s was about the potential adverse effects of vitamin D especially.

As such, when most people heard about vitamin D they thought of sunshine and bones and most still do. That's because it's common knowledge that exposure to the sun results in the formation of vitamin D and that vitamin D is important, along with calcium, magnesium, and associated hormones and signalling pathways, for strong bones.

While that aspect of vitamin D is important, there's a lot more to the vitamin D story as shown by an exponential increase in studies over the past decade that concentrated more on the many beneficial effects of vitamin D beyond its effects on bone physiology and pathology.

As well, many studies in the last decade pointed out the existence of widespread vitamin D deficiency in the general population including athletes (**see multiple abstracts below**). There is still controversy at arriving at a consensus of what levels are optimal and what can be done to optimize vitamin D levels, considering genetic, epigenetic, and other factors that affect how much vitamin D is needed to optimize any one individual's endogenous vitamin D levels.

Taking the many factors involved in the amount of vitamin D needed by any one individual person will take more research to arrive at more robust consensus on just how much vitamin D is optimal not only for the individual but also what levels may be necessary for specific beneficial effects.

Vitamin D is a group of fat-soluble prohormones called secosteroids. Thus, unlike most other vitamins, **vitamin D is really a steroid hormone** that the body uses to manufacture 1,25(OH)2D3, which is the active form of vitamin D in our bodies.

The two major forms of the vitamin obtained from sun exposure, food, and supplements are vitamin D2 (or ergocalciferol) and vitamin D3 (or cholecalciferol). Cholecalciferol is the vitamin D produced in humans by exposure to the sun and is felt to be more effective than ergocalciferol for enhancing 1,25(OH)2D3 levels in our bodies.

Because it can be confusing this is the sequence of vitamin D metabolism from vitamin D2 (from food and some supplements) to vitamin D3 (formed by exposure to sunlight and present in some supplements) to the final active form of vitamin D in the body.

The process of vitamin D formation is Vitamin D2/ergocalciferol, (food and supplements) to vitamin D3/cholecalciferol (sun and supplements) to 25(OH)D/calcifediol (liver) to 1,25(OH)<sub>2</sub>D3/calcitriol (kidney). The 1,25(OH)<sub>2</sub>D3/calcitriol is the active form of vitamin D in the body.

Recent research shows that vitamin D is crucial for many functions in the body, and has widespread detrimental effects if deficient, and beneficial effects even in cases where vitamin D levels are considered normal.

Vitamin D is crucial for musculoskeletal functioning, athletic performance, body composition and many internal cellular processes including hormonal and immune system regulation.

However, adequate levels of vitamin D, besides improving body composition and performance, are also important for decreasing the rate of infection and treatment of Covid-19 (see above).<sup>30</sup>

A recent study found that vitamin D supplementation had a beneficial effect on body composition in elite male college athletes.<sup>31</sup> The study found that vitamin D supplementation was effective in maintaining athletes' body fat percentage, which normally would increase under circumstances where sports activity has decreased.

It has been shown to have beneficial physical and psychological effects, including heart disease, pregnancy problems, birth defects, skin and other cancers, inflammation in the body from various sources, and aging and longevity in both those with normal levels of vitamin D and especially in those with low serum vitamin D levels, which was especially associated with an increase in all-cause mortality, cancer, and cardiovascular disease mortality. 3233343536373839404142

As a measure of just how important vitamin D is for all of us including athletes, it's felt that possibly up to several thousand genes and even more pathways are affected by vitamin D.<sup>4344</sup>

### Why Most of Us May Be Vitamin D Deficient

Vitamin D deficiency is increasingly being recognized as a worldwide epidemic and occurs even in Africa. According to various reports experts believe that 2 and up to 3 out of every four adolescents and adults are vitamin D deficient, which is generally defined as having blood levels of less than 30 ng/mL

For your skin to make enough, you would need direct midday summer sunlight on a large portion of your body for around 15 minutes a day. If you live north of Atlanta, it's impossible to get enough D from sunlight between October and March, no matter how exposed you are. And it's tougher for people of color to make vitamin D — the melanin in dark skin decreases vitamin D production by up to 90 percent.

Although it seems logical to assume that people in high altitudes would not be deficient in vitamin D given that the ultraviolet light intensity is higher at high altitudes resulting in a greater vitamin D3 synthetic rate, the opposite is case. The reason for this is likely that at higher altitudes the cooler weather involves using more clothing and less sunbathing.

Declines in vitamin D occur over the winter, with the level of decline, without conscious efforts to expose yourself to adequate sunshine or tanning UVB rays and without supplementation, is dependant on the level of vitamin D at the beginning of winter. So, the more you're able to maximize your vitamin D storage levels, the more you'll be left with by the end of winter. However, if you rely on your summer acquired stores of vitamin D, and because winter can last several months, somewhere along the line you'll develop vitamin D deficiency.

Much of the decline during winter months, and for those who don't get a lot of sunlight during the summer, is due to the lack of vitamin D in the food we eat. Only certain kinds of fish and some fortified foods such as dairy and orange juice have significant amounts of vitamin D (**see list below**), and it would be hard to consume enough of these every day to get 1,000-plus IU.

And it's possible that even those who seem to get lots of sun, because of variable responsiveness to UVB radiation may be vitamin D deficient (see full paper and abstract below - Low vitamin D status despite abundant sun exposure).

There's one myth about vitamin D from sunlight that you should ignore. You can shower after sun exposure without affecting the amount of vitamin D that's produced. That's because the sebum and some of the top dead layers of the skin that can be washed off when you shower with soap, are not involved with vitamin D synthesis from the sun.

During exposure to sunlight solar radiation with wavelengths of 290–315 nm penetrate into the skin and are absorbed by proteins, DNA and RNA as well as 7-dehydrocholesterol. Most of this UVB radiation is absorbed in the epidermis and as a result when exposed to sunlight most of the vitamin D3 that is produced in the skin is made in the living cells in the epidermis. This is the reason why after exposure to sunlight vitamin D3 remains in the skin even when the skin is washed with soap and water immediately after the exposure to sunlight.<sup>47</sup>

#### Sunburn and Vitamin D

Even with the liberal use of sunscreen, and other methods, getting a sunburn is almost inevitable with prolonged exposure to full sunlight.<sup>48495051</sup>

There are no valid studies showing any protective effects of adequate levels of vitamin D at the time you're getting a sunburn. I personally believe that having high normal values of vitamin D does have a protective effect on developing sunburn, up to a point.

However, it's possible that excessive sun exposure may damage the keratocytes and dermal layers of the skin resulting in a disruption of vitamin D synthesis and therefore less protection from sunburn.

On the other hand, and this may be because of my theory on the effects of sunburn on endogenous vitamin D production, there is some evidence that an oral vitamin D bolus may decrease the toxic effects of sunburn.<sup>52</sup> In this study no participant was taking supplemental vitamin D3 before study initiation. As such, no determination could be made to see if prior use of oral vitamin D had a beneficial effect on sunburn toxicity.

A more recent study in mice also found that vitamin D given after UV radiation had protective effects of skin from UV damage.<sup>53</sup>

There are also other nutrients that can mitigate the damaging effects of sun exposure and that are valuable for skin health. For example, studies have found photoprotective effects in several ingredients including vitamins A, C, D3, E, selenium, lycopene, lutein, astaxanthin, green tea, and grape extracts. All of these are in MVM and other products in my line of nutritional supplements.

#### Vitamin D is Vital for Exercise Performance

The effects of vitamin D on performance have been known for several decades. Back in the 1950s several German studies alluded to the beneficial effects of vitamin D on athletic performance.<sup>56</sup> As well, it's well known that physical and athletic performance is seasonal in that it follows levels of vitamin D, peaking when it peaked and declining as vitamin D levels declined.

Since then, several studies, including many done in the past few years, have shown the importance of vitamin D in improving skeletal muscle function and athletic/sports performance as well as improving recovery after exercise and attenuating skeletal muscle atrophy. 57585960616263

Vitamin D also increases the size and number of Type II (fast twitch) muscle fibers. Most cross-sectional studies show that 25(OH)D levels are directly associated with musculoskeletal and physical performance in older individuals.

But its not just the performance of older people that are affected by vitamin D deficiency. One review concluded that "Accumulating evidence supports the existence of a functional role for vitamin D in skeletal muscle with potentially significant impacts on both the performance

and injury profiles of young, otherwise healthy athletes."64 Other studies have shown that low vitamin D is a contributory factor in stress fractures and bone injuries in athletes.65

Another review<sup>66</sup> (concluded "Most cross-sectional studies show that 25(OH)D levels are directly associated with musculoskeletal performance in older individuals. Most randomized controlled trials, again mostly in older individuals, show that vitamin D improves physical performance. CONCLUSIONS: Vitamin D may improve athletic performance in vitamin D-deficient athletes. Peak athletic performance may occur when 25(OH)D levels approach those obtained by natural, full-body, summer sun exposure, which is at least 50 ng x mL (-1). Such 25(OH)D levels may also protect the athlete from several acute and chronic medical conditions."

A recent study found that vitamin D supplementation had a beneficial effect on body composition in elite male college athletes.<sup>67</sup> The study found that vitamin D supplementation was effective in maintaining athletes' body fat percentage, which normally would increase under circumstances where sports activity has decreased.

Several other studies have shown the benefits of adequate levels of vitamin D for health, body composition, physical and mental performance, and in alleviating various diseases (see several of the citations and abstracts below).

#### **How Much Vitamin D Can We Take?**

Vitamin D is fat-soluble, which means it stays in the body for longer periods of time as opposed to the water-soluble vitamins such as vitamin C.

This is good because it takes a longer period to become deficient if you start off with healthy levels in your body. For example, if you build up vitamin D over the summer then there's less chance you'll be come deficient over the winter as long as you take in some vitamin D by eating foods high in vitamin D, take vitamin D supplements or expose your skin to artificial ultraviolet light.

It's also bad in that if you take way too much it can accumulate in the body and can cause toxicity. However, this aspect of vitamin D has been overemphasized in the past as it was thought that vitamin D accumulated and stayed in the body much more than it does. And it's been shown that high dosages exceeding 10,000 units a day for months rarely causes any problems and may in fact be beneficial in many ways.

The general consensus that vitamin D accumulates to dangerous levels over time is a fallacy unless mega doses are consumed all at once or over a long period of time.

That's because vitamin D doesn't stay in the body forever as it is broken down continually by the body and disposed of. Vitamin D stored in the body has a half life of only three or four weeks, and this half life shortens with higher vitamin D levels. Exposure of skin to direct sunlight can produce up to 25,000 IU of vitamin D. However, when vitamin D is produced by sunlight, and to a certain extent even vitamin D taken exogenously unless mega doses are used, gets to a certain level, after that any further vitamin D that is produced is degraded.

That means that the body can degrade and lower vitamin D levels in the body if it must and thus can handle a lot more vitamin D than was previously thought. That doesn't mean that our bodies can handle a lot more than previously understood, and that you can't overdose on exogenous vitamin D and develop some counter productive and health damaging toxicity.

However, in my opinion it would take at least 10,000 IU per day of supplementation, and likely even double that amount, for several months before you would overwhelm the body's ability to degrade excess vitamin D and produce more than high optimal levels.

#### **How Much Vitamin D do Athletes Need?**

With sun exposure, the pre-vitamin D2 (found in food and in supplements, although for purposes of supplementation vitamin D3 is a superior form to the use of vitamin D2) is rapidly converted in the dermis to vitamin D3 (cholecalciferol), before its subsequent conversion to calcifediol (25-hydroxycholecalciferol, or 25-hydroxyvitamin D [25(OH)D]) in the liver. Further hydroxylation of 25(OH)D to its active form, calcitriol (1,25 hydroxy vitamin D [abbreviated to 1,25(OH)2D3]), occurs in the kidney. 1,25-(OH)2D3, a secosteroid hormone, is the active form of vitamin D.

Supplementing with vitamin D3 skips the preliminary step of converting vitamin D2 to vitamin D3 and is a more direct and effective form of vitamin D in nutritional supplements.

However, while the active form of vitamin D may be normal in the blood, the lack of reserves in the form of 25(OH)D is the actual measure of vitamin D reserves in the body and is used as a measure of vitamin D deficiency. Besides being a better marker of overall D status, it is the marker that translates best with the overall beneficial effects of vitamin D.

The basis for figuring out how much vitamin D that any one individual needs can be casually stated (such as a suggested range of vitamin D intake) or can be more precise depending on the tools we use. For precise determinations we need to know just what the present state of any individual is by getting a serum 25(OH)D level. From this level we can figure out just how much vitamin D is needed daily to achieve a desired vitamin D level in the body.

Further testing in some may be needed in some individuals by getting a serum 1,25(OH)2D3 to see if the conversion in the kidneys by the enzyme 25(OH)D-1a-hydroxylase into 1,25-(OH)2D3.

Keep in mind that there is still controversy about the accuracy and usefulness of current testing. 6869 However, for our uses, we can still use the results of the current testing to evaluate our vitamin D status since I believe that while not perfect, the results will give us a reasonable ballpark idea of where we stand.

For example, if your 25(OH)D level is OK, and for optimal levels it should be between 50 and 70 ng/mL (for nnmol/L multiply by 2.5 – so 50 ng/mL would be 125 nmol/L – see <a href="http://www.globalrph.com/conv\_si.htm#top">http://www.globalrph.com/conv\_si.htm#top</a>), then you're in the right range and to stay there you should get between 1,000 and 5,000 IU of vitamin D per day depending on your responses to varying daily dosages.

If you're below 50 ng/mL then you need to top up first and that might require 5,000 to 10,000 IU for several weeks depending on how low your levels are. If for example they're below 20 ng/mL then I would suggest you take 10,000 IU for at least a few months and then your levels checked again to see if you should continue at that level or go to maintenance levels of between 1,000 to 5,000 IU per day.

In some cases of severe deficiency up to 100,000 units is injected as a bolus. Studies have shown however that using daily vitamin D3 supplements is superior to using periodic boluses as there is a more consistent level of vitamin D in the body, which in turn optimizes the benefits of vitamin D.

As a guide, I've put my recommendations for maximum health, body composition and performance in the following table.

25(OH)D level in ng/mL	Amount of Daily Vitamin D to take	Length of Time
Less than 20	10,000 IU per day	For at least 8 weeks
Between 20-30	10,000 IU per day	For at least 4 weeks
Between 30-40	5,000 IU per day	For at least 4 weeks
Between 40-50	5,000 IU per day	For at least 2 weeks
Above 50	1,000 to 3,000 IU	Daily

### International Units of Vitamin D

The vitamin-D content of a food is sometimes cited in micrograms of 25(OH)D, while at other times it is reported in International Units.

There is an exact relationship between the two: one IU is equal to 0.025 micrograms of cholecalciferol. Hence:

To convert IUs of vitamin D into micrograms: multiply the number of IUs by 0.025. The result is the number of micrograms in the food.

To convert micrograms to IUs: multiply the number of micrograms by 40. The result is the number of IUs in the food.

How you get the required amounts of vitamin D is up to the individual and his or her circumstances. For those with access to full UV-B sunshine, a half hour a day of near full body exposure (be careful to build up slowly and not get sunburned) will go a long way to giving you the necessary amount of vitamin D. And again, showering after sun tanning will not affect the amount of vitamin D that ends up in your body.

As well, eating food high in vitamin D is also an option although to get enough (unless you're unbelievably fond of fatty fish and liver oils, and even if you are fond of cod and other fish liver oil you have to make sure you don't overdo the vitamin A that these oils also contain), you will likely have to combine the dietary intake with sun exposure and/or vitamin D supplements.

If you feel that you can't meet your requirements through a combination of sun exposure and food, then the use of vitamin D in the form of supplements, ideally as cholecalciferol or vitamin D3, is the easiest, cheapest, and safest way to make sure you're covered.

To make sure that they stay in the optimal vitamin D zone I recommend that athletes take in between 1,500 IU up to 5,000 IU, a day in the form of supplements, depending on how their vitamin D levels respond to specific daily dosages. Once you find out the amount that will insure that your vitamin D levels stay where you want them to be and insure that you don't run into any toxicity, no matter how long you take that level of vitamin D.

## What Else is Needed for Optimum Effects from Vitamin D

Other nutrients are needed for enhanced effects from the benefits of vitamin D. Besides having adequate amounts of the usual beneficial effects of a proper array of vitamins and minerals, one vitamin stands out. Vitamin K

**Vitamin K1 (as phytonadione) and K2 (as MK-4 and MK-7)** have been shown to maintain normal blood coagulation, decrease bone loss, improve musculoskeletal and cardiovascular health, and supplement certain cancer treatments.<sup>7071727374757677</sup> It may also have roles in mitochondrial electron transport, protein synthesis, neuroprotection and immunity.<sup>7879</sup>

A recent study found that combination of low vitamin D and K status was associated with increased blood pressure and a trend for greater hypertension risk.<sup>80</sup> Another recent study found that insufficient K and D vitamin status increased aortic stiffness, a measure of cardiovascular disease.<sup>81</sup>

A similar study concluded that "Vitamins A, B12, C, D, E, and K status (is important in evaluating cardiovascular risk, and vitamin supplementation may be an effective, individualized, and inexpensive destiffening therapy."82 All of the above are in MVM.

Magnesium is also important (and present in MVM and several other products in my line of nutritional supplements.

### **Conclusions and Recommendations**

First, it's important to get your 25(OH)D blood level measured to see just where you are as far as your long-term vitamin D intake. Once you have the initial measurement and make any changes that need to be made as far as daily vitamin D intake, you should have your 25(OH)D level check as needed until you're above 50 ng/mL, and then once it's relatively stabilized get it done at least once a year just to make sure you're not developing a deficiency.

Although this process takes some effort it's important for all athletes who want to maximize natural performance. At the same time other blood tests can be done that will point out other problems and deficiencies. I've copied below the screening protocol I suggest athletes have done. If money is tight then the bolded tests are the ones that are necessary, while the others can be done as finances permit.

Don't hesitate to get some full sun exposure every day. The sensationalistic naysayers and purveyors of skin cancer with any amount of sun exposure should be ignored. Reasonable, and controlled levels of daily sun exposure to your body is not something to avoid but something to be sought as it has significant health benefits if sunburn is avoided and there are no medical contraindications such as the presence or predisposition to skin cancer and interactions with some medications.

Regardless of sun exposure and foods eaten, you'll likely still need to take between 1,000 and 5,000 IU of supplemental vitamin D every day. If your vitamin D levels are low then take more until you're at a level that you feel comfortable with, at least above 50 ng/mL, and then maintain by talking supplemental vitamin D as above.

The bottom line is that regardless of whom you are or what sport you're into, without enough vitamin D, you're not reaching your health, body composition, and performance potential.

### **Mushrooms and Vitamin D**

A common misconception is that mushrooms are a good source of vitamin D. However, the issue with mushrooms is convoluted. Firstly, the usual mushrooms, whether in nature or cultivated, contain minimal amounts of vitamin D. They do contain ergosterol, provitamin D2, which can be converted to vitamin D2

by subjecting the mushrooms to UV irradiation. Irradiated mushrooms, which are commonly available, can be a good source of vitamin D2, especially for vegetarians where mushrooms are the only natural source of vitamin D.<sup>8384</sup>

ACS Omega. 2020 Mar 23;5(13):7361-7368. doi: 10.1021/acsomega.9b04321. eCollection 2020 Apr 7.

Ultraviolet Irradiation Increased the Concentration of Vitamin D<sub>2</sub> and Decreased the Concentration of Ergosterol in Shiitake Mushroom (*Lentinus edodes*) and Oyster Mushroom (*Pleurotus ostreatus*) Powder in Ethanol Suspension.

<u>Hu D</u><sup>1,2,3</sup>, <u>Chen W</u><sup>1</sup>, <u>Li X</u><sup>3</sup>, <u>Yue T</u><sup>2</sup>, <u>Zhang Z</u><sup>3</sup>, <u>Feng Z</u><sup>1</sup>, <u>Li C</u><sup>1</sup>, <u>Bu X</u><sup>1</sup>, <u>Li QX</u><sup>4</sup>, <u>Hu CY</u><sup>3</sup>, <u>Li L</u><sup>1</sup>. **Abstract** 

Vitamin D deficiency is a serious global health problem. Edible mushrooms are a good source of vitamin D for human health. The objective of this experiment was to investigate the efficiency of converting its precursor ergosterol to vitamin D<sub>2</sub> in shiitake mushroom (Lentinus edodes) and oyster mushroom (Pleurotus ostreatus) powder in ethanol suspension under ultraviolet (UV) irradiation. UV irradiation conditions were optimized for several parameters, such as material form, wavelength, wavelength combination, and exposure time. Under the optimal conditions, UV irradiation increased the concentrations of vitamin D<sub>2</sub> from undetectable to 40.59 ± 1.16 µg/g (dw) in dry shiitake mushroom powder and to 677.28 ± 40.42 µg/g (dw) (an approximately 16.69-fold increase) in ethanol suspension. The concentration of vitamin D<sub>2</sub> increased from undetectable to 23.71 ± 5.72 μg/g (dw) in the dry oyster mushroom powder upon UV irradiation, whereas UV irradiation increased the concentration to 275.32 ± 48.45 µg/g (dw) (an approximately 11.61-fold increase) in the ethanol suspension. Comparing the effects of varying combinations of wavelengths showed that irradiation with UV-A, UV-C, or a combination of both is more effective than UV-B irradiation. In addition, the increase in vitamin D<sub>2</sub> in shiitake mushrooms irradiated by UV-C was time-dependent, that is, dose-dependent. Nevertheless, the increase rates decreased with time. The concentration of ergosterol decreased with the increase in vitamin D<sub>2</sub>, but ergosterol was only partially converted to vitamin D<sub>2</sub>, whereas most of the ergosterol was probably UV-degraded. Exposure to ultraviolet light in ethanol suspension offers an effective way to increase the concentration of vitamin D<sub>2</sub> and thus improve the nutritional value of edible mushrooms, as well as make them more functional as a source of vitamin D to improve the consumer health.

The full paper in PDF format is available at:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7144143/pdf/ao9b04321.pdf.

## Some of the best natural sources of vitamin D

**Fish Liver Oil** – amount depends on the fish.

Cod liver oil 1 tablespoon 1383 IU

#### Fish

Herring 3 oz 1383 IU Sardines 3.5 oz 500 IU

Salmon 3.5 oz 360 IU

Mackerel 3.5 oz 345 IU

Tuna 3 oz 200 IU

Eel 3.5 oz 200 IU

#### Other Foods

Orange Juice 1 cup 100 IU

Milk 1 cup 98 IU

Margarine, 1 tbsp 60 IU

Whole Egg 1 medium 20 IU

Beef Liver3 oz1 5 IU

# Vitamin D in my MD+ supplements:

When buying supplements or fortified foods, make sure the label reads vitamin D3 (cholecalciferol). This is the more biologically active form of vitamin D and is what I use in all my supplements.

For more information on the supplements listed below, as well as the rest of nutritional supplement line up go to the shop at <a href="https://www.MetabolicDiet.com">www.MetabolicDiet.com</a>.

By clicking on the Product PDF button under each of the supplements you can view the complete information piece on that supplement.

Supplement	Amount of vitamin D3
MVM	1200 IU
Resolve	1000 IU
GHboost	600 IU
EFA+	400 IU
TestoBoost	400 IU
LipoFlush	400 IU

Joint Support	400 IU
Metabolic	400 IU
MRP LoCarb	200 IU
Amino	200 IU

Total vitamin D intake if all these supplements were used daily, which isn't likely although many elite athletes do especially when training for competition, there would be an intake of over 5,000 IU a day.

MVM along with EFA+, part of my Foundation supplements along with Antiox, meant to provide an optimal foundation for maximizing body composition and performance, contain a daily amount of 1600 IU units of vitamin D3.

Amino and MRP LoCarb, which make up two of the three supplements that I recommend all athletes use after training and competition, provide an additional 400 IU. And if any of the other supplements are used, as they are by many of my athlete, and are often included in their nutritional supplement regimens, there is an additional 200 to 400 IU per day.

Overall, it's easy to fall within my suggested 2,000 to 5,000 IU of vitamin D daily with just the use of my supplements.

# Importance of Magnesium

It's important to realize that vitamin D is only a small part of my multi-ingredient, targeted formulations and that my supplements, used in concert, cover all the nutritional bases for optimizing body composition and athletic performance.

As well, for vitamin D to be optimally utilized it's necessary for other ingredients to be present. For example, a recent study found that optimum levels of magnesium are needed to properly use vitamin D. Without enough magnesium vitamin D isn't fully metabolized to the active form in the body.<sup>85</sup>

Magnesium deficiency is common in the US and it's estimated that half the population is magnesium deficient as the average diet contains only half of the daily requirement. Magnesium deficiency is not a problem if you use one or more products in my supplement line since several contain magnesium in forms that are most bioavailable.

Magnesium has a multitude of other benefits on health, testosterone levels, body composition, strength, physical and mental performance, and as a preventative and treatment for various disorders. As such, it's important to have adequate amounts of magnesium in your diet and in many cases, especially for athletes, by the use of nutritional supplements.

Magnesium seems especially useful if used prior to exercise and/or competition. Resolve, the best pre-training/pre-competition supplement on the market by far contains 1000 IU of vitamin D and 250 mg of magnesium, both of which have many beneficial effects both in the short and long term. Other products in my nutritional supplement lineup contain magnesium together with vitamin D3.

I include magnesium in the lab work done on athletes that I work with. I've included the screening panel below with the more important tests in bold.

# **Recommended Screening Blood Work**

Samples should normally be obtained in the morning, prior to coffee, breakfast or exercise

Avoid high intensity exercise for 24 hourss prior to sample collection

Blood work should be done at least two times in the yearly training plan to ensure optimal health status during training and leading into key competitions.

Tests can also be ordered after an athlete presents with symptoms and requires subsequent treatment.

Any abnormalities would trigger additional tests and possible follow up testing.

- ACTH
- Albumin
- Apolipoprotein (b) and (a)
- Blood group and Rh Factor
- Complete Blood Count
- Cortisol serum AM and PM
- C-reactive Protein
- Creatine Kinase
- DHEA and DHEAS
- Electrolytes/minerals etc. Calcium, CO2, Chloride, Magnesium, Phosphorus, Potassium, Sodium, Zinc.
- Erythrocyte Sedimentation Rate (ESR)
- Estradiol
- Fibrinogen
- Free, bioavailable, and Total Testosterone
- Glucose Fasting
- Glycosylated Hemoglobin (HB A1C)
- HDL/LDL, Total Cholesterol
- Heavy Metal Profile (mercury, nickel, lead, arsenic and cadmium)
- Homocysteine
- Insulin-like growth factor-I (IGF-I)
- Lipoprotein (a)
- Liver Function Tests (serum total bilirubin, alkaline phosphatase, aminotransferase (AST and ALT)), GGT.
- Luteinizing Hormone (LH)
- Melatonin
- Prolactin
- RBC Folate
- Renal Function Tests Creatinine, Bun, Bun/Creatinine Ratio
- Serum Hormone Binding Protein (SHBG)
- Serum Iron Status Iron, Ferritin, Transferrin, Percentage Transferrin Saturation
- Thyroid Profile TSH, T4, T3, rT3
- Serum Protein Total Protein, Albumin, Globulin Albumin/Globulin Ratio.
- Triglycerides
- Uric Acid
- Vitamin B12
- Vitamin D 25-hydroxy vitamin D [25(OH)D]

A complete urinalysis is also a good idea as some kidney dysfunction indices may show up in the urine but not in the blood work.

I'll be covering magnesium and other minerals in upcoming newsletters but for now I've copied below some relevant citations and abstracts on magnesium and after that some on vitamin D.

\_\_\_\_\_

# A sampling of Vitamin D Relevant Citations and Abstracts

Nutrients. 2018 Oct 13;10(10). pii: E1498. doi: 10.3390/nu10101498.

A Review of Mushrooms as a Potential Source of Dietary Vitamin D.

Cardwell G<sup>1</sup>, Bornman JF<sup>2,3</sup>, James AP<sup>4</sup>, Black LJ<sup>5</sup>.

**Abstract** 

When commonly consumed mushroom species are exposed to a source of ultraviolet (UV) radiation, such as sunlight or a UV lamp, they can generate nutritionally relevant amounts of vitamin D. The most common form of vitamin D in mushrooms is  $D_2$ , with lesser amounts of vitamins  $D_3$  and  $D_4$ , while vitamin  $D_3$  is the most common form in animal foods. Although the levels of vitamin  $D_2$  in UV-exposed mushrooms may decrease with storage and cooking, if they are consumed before the 'best-before' date, vitamin  $D_2$  level is likely to remain above  $10 \mu g/100 g$  fresh weight, which is higher than the level in most vitamin D-containing foods and similar to the daily requirement of vitamin D recommended internationally. Worldwide mushroom consumption has increased markedly in the past four decades, and mushrooms have the potential to be the only non-animal, unfortified food source of vitamin D that can provide a substantial amount of vitamin  $D_2$  in a single serve. This review examines the current information on the role of UV radiation in enhancing the concentration of vitamin  $D_2$  in mushrooms, the effects of storage and cooking on vitamin  $D_2$  content, and the bioavailability of vitamin  $D_2$  from mushrooms.

The full paper in PDF format is available at:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6213178/pdf/nutrients-10-01498.pdf

-----

ACS Omega. 2020 Mar 23;5(13):7361-7368. doi: 10.1021/acsomega.9b04321. eCollection 2020 Apr 7.

Ultraviolet Irradiation Increased the Concentration of Vitamin D<sub>2</sub> and Decreased the Concentration of Ergosterol in Shiitake Mushroom (*Lentinus edodes*) and Oyster Mushroom (*Pleurotus ostreatus*) Powder in Ethanol Suspension.

<u>Hu D</u><sup>1,2,3</sup>, <u>Chen W</u><sup>1</sup>, <u>Li X</u><sup>3</sup>, <u>Yue T</u><sup>2</sup>, <u>Zhang Z</u><sup>3</sup>, <u>Feng Z</u><sup>1</sup>, <u>Li C</u><sup>1</sup>, <u>Bu X</u><sup>1</sup>, <u>Li QX</u><sup>4</sup>, <u>Hu CY</u><sup>3</sup>, <u>Li L</u><sup>1</sup>. Abstract

Vitamin D deficiency is a serious global health problem. Edible mushrooms are a good source of vitamin D for human health. The objective of this experiment was to investigate the efficiency of converting its precursor ergosterol to vitamin  $D_2$  in shiitake mushroom (*Lentinus edodes*) and oyster mushroom (*Pleurotus ostreatus*) powder in ethanol suspension under ultraviolet (UV) irradiation. UV irradiation conditions were optimized for several parameters, such as material form, wavelength, wavelength combination, and exposure time. Under the optimal conditions, UV irradiation increased the concentrations of vitamin  $D_2$  from undetectable to  $40.59 \pm 1.16 \,\mu\text{g/g}$  (dw) in dry shiitake mushroom powder and to  $677.28 \pm 40.42 \,\mu\text{g/g}$  (dw) (an approximately 16.69-fold increase) in ethanol suspension. The concentration of vitamin  $D_2$  increased from undetectable to  $23.71 \pm 5.72 \,\mu\text{g/g}$  (dw) in the dry oyster mushroom powder upon UV irradiation, whereas UV irradiation increased the concentration to  $275.32 \pm 48.45 \,\mu\text{g/g}$  (dw) (an approximately 11.61-fold increase) in the ethanol suspension. Comparing the effects of varying combinations of wavelengths showed that irradiation with UV-A, UV-C, or a combination of both is more effective than UV-B irradiation. In addition, the increase in vitamin  $D_2$  in shiitake mushrooms irradiated by UV-C was time-dependent, that is, dose-dependent.

Nevertheless, the increase rates decreased with time. The concentration of ergosterol decreased with the increase in vitamin  $D_2$ , but ergosterol was only partially converted to vitamin  $D_2$ , whereas most of the ergosterol was probably UV-degraded. Exposure to ultraviolet light in ethanol suspension offers an effective way to increase the concentration of vitamin  $D_2$  and thus improve the nutritional value of edible mushrooms, as well as make them more functional as a source of vitamin D to improve the consumer health.

-----

J Am Osteopath Assoc. 2018 Mar 1;118(3):181-189.

### Role of Magnesium in Vitamin D Activation and Function.

Uwitonze AM, Razzaque MS.

**Abstract** 

Nutrients usually act in a coordinated manner in the body. Intestinal absorption and subsequent metabolism of a particular nutrient, to a certain extent, is dependent on the availability of other nutrients. Magnesium and vitamin D are 2 essential nutrients that are necessary for the physiologic functions of various organs. Magnesium assists in the activation of vitamin D, which helps regulate calcium and phosphate homeostasis to influence the growth and maintenance of bones. All of the enzymes that metabolize vitamin D seem to require magnesium, which acts as a cofactor in the enzymatic reactions in the liver and kidneys. Deficiency in either of these nutrients is reported to be associated with various disorders, such as skeletal deformities, cardiovascular diseases, and metabolic syndrome. It is therefore essential to ensure that the recommended amount of magnesium is consumed to obtain the optimal benefits of vitamin D.

Full text of this paper is available at <a href="http://jaoa.org/article.aspx?articleid=2673882">http://jaoa.org/article.aspx?articleid=2673882</a>.

-----

J Sports Sci. 2014;32(5):438-45.

# Magnesium status and the physical performance of volleyball players: effects of magnesium supplementation.

<u>Setaro L</u><sup>1</sup>, <u>Santos-Silva PR</u>, <u>Nakano EY</u>, <u>Sales CH</u>, <u>Nunes N</u>, <u>Greve JM</u>, <u>Colli C</u>. <u>Abstract</u>

The aim of this study was to test the hypothesis that magnesium supplementation influences the physical performance of volleyball players, as the efficacy of this approach remains questionable. Twenty-five professional male volleyball players were assigned randomly to experimental (350 mg Mg · d(-1), 4 weeks) and control groups (500 mg maltodextrin · d(-1), 4 weeks) maintaining inter-group homogeneity of urinary magnesium. Erythrocyte, plasma and urinary magnesium levels, plasma creatine kinase activity, lactate production, maximal oxygen uptake (VO2 max) and plyometric (squat jump, countermovement jump, countermovement jump with arm swing) and isokinetic (peak torque, potency and total work) performances were evaluated before (T0) and after (T1) supplementation. Levels of erythrocyte and urinary magnesium and creatine kinase activity and VO2 max remained within normal ranges in both groups. Plasma magnesium decreased significantly only within the experimental group. Significant decreases in lactate production and significant increases (of up to 3 cm) in countermovement jump and countermovement jump with arm swing values were detected in the experimental group following magnesium supplementation, but not in the control

group at T1. It is concluded that magnesium supplementation improved alactic anaerobic metabolism, even though the players were not magnesium-deficient.

-----

Magnes Res. 2012 Jul;25(2):79-88. doi: 10.1684/mrh.2012.0311.

# Association between erythrocyte concentrations of magnesium and zinc in highperformancehandball players after dietary magnesium supplementation.

Molina-López J¹, Molina JM, Chirosa LJ, Florea D, Sáez L, Millán E, Planells E.

#### **Abstract**

Currently, research on athletes focuses on optimizing the nutritional status in order to adjust their minerals requirements. This study was designed to evaluate baseline nutritional status and the effect of a nutritional intervention based on magnesium (Mg) supplementation, on plasma and erythrocyte concentrations of Mg and zinc (Zn), and their relationship with training load. We analyzed training load by recording the training volume, intensity and rating of perceived exertion (RPE) during a four-month period, in 14 high-performance handball players. Intensity was studied in different levels of residual heart rate (RHR). We analyzed nutrient intake and plasma and erythrocyte concentrations of Mg and Zn by FAAS. All biomarkers were measured at baseline, after two months of dietary supplementation with Mg, and after two months without supplementation. RPE was associated with training volume at different intensities of RHR. Mg supplementation significantly increased plasma Mg levels during the supplemented period and preserved for subsequent changes in the non-supplemented period. Erythrocyte concentrations of Mg and Zn show associations between baseline and Mg supplementation. Mg levels were associated with training volume at different intensities after supplementation. In conclusion, our findings in high-performance handball players show that during competition, there is a relationship between erythrocyte Zn and Mg levels, regardless of Mg supplementation or Zn intake. Mg dietary supplementation tended to preserve changes in mineral levels during training and competition.

-----

Magnes Res. 2011 Dec;24(4):215-9. doi: 10.1684/mrh.2011.0290.

# Magnesium intake is associated with strength performance in elite basketball, handball and volleyball players.

Santos DA<sup>1</sup>, Matias CN, Monteiro CP, Silva AM, Rocha PM, Minderico CS, Bettencourt Sardinha L, Laires MJ. Abstract

Magnesium plays significant roles in promoting strength. Surveys of athletes reveal that intake of magnesium is often below recommended levels. We aimed to understand the impact of magnesium intake on strength in elite male basketball, handball, and volleyball players. Energy and nutrient intake were assessed from seven-day diet record. Strength tests included maximal isometric trunk flexion, extension, and rotation, handgrip, squat and countermovement Abalakov jump, and maximal isokinetic knee extension and flexion peak torques. Linear regression models were performed with significance at p<0.1. Mean magnesium intake was significantly lower than the recommended daily allowance. Regression analysis indicated that magnesium was directly associated with maximal isometric trunk flexion, rotation, and handgrip, with jumping performance tests, and with all isokinetic strength variables, independent of total energy intake. The observed associations between magnesium intake and muscle strength performance may result

from the important role of magnesium in energetic metabolism,	, transmembrane transport and muscle of	ontraction and
relaxation.		

-----

Magnes Res. 2010 Sep;23(3):138-41. doi: 10.1684/mrh.2010.0217. Epub 2010 Sep 22.

# Magnesium and strength in elite judo athletes according to intracellular water changes.

Matias CN<sup>1</sup>, Santos DA, Monteiro CP, Silva AM, Raposo Mde F, Martins F, Sardinha LB, Bicho M, Laires MJ. Abstract

Magnesium (Mg) deficiency strongly affects muscle performance. In judo, many athletes often undergo impressive weight changes associated with severe dehydration. Common practices used by athletes to achieve a target weight can lead to Mg deficit. This study aimed to understand the impact of Mg changes on strength from periods of weight stability to prior to competition in a sample of elite judo athletes who differentially changed their intracellular water (ICW). The sample consisted of 20 elite male judo athletes. Subjects were divided according to ICW changes: losses below 2% and losses equal to or above 2%. Mg was measured in serum, red blood cells and urine by atomic absorption spectrophotometry. ICW was calculated as the difference between total-body water and extracellular water using dilution techniques. Maximal handgrip strength was evaluated using Jamar Hydraulic Hand Dynamometer. Upper-body power was determined in a bench press. Higher ICW decreases were associated with higher strength reductions, though our results suggest that an increase in red blood cell Mg might attenuate those strength reductions in athletes who decrease the ICW compartment. As Mg losses can be considerable and intake is frequently insufficient, athletes should consider supplementation, especially during periods of weight reduction.

-----

Biol Trace Elem Res. 2011 Apr;140(1):18-23. doi: 10.1007/s12011-010-8676-3. Epub 2010 Mar 30.

# Effects of magnesium supplementation on testosterone levels of athletes and sedentary subjects at rest and after exhaustion.

<u>Cinar V</u><sup>1</sup>, <u>Polat Y</u>, <u>Baltaci AK</u>, <u>Mogulkoc R</u>. <u>Abstract</u>

This study was performed to assess how 4 weeks of magnesium supplementation and exercise affect the free and total plasma testosterone levels of sportsmen practicing tae kwon do and sedentary controls at rest and after exhaustion. The testosterone levels were determined at four different periods: resting before supplementation, exhaustion before supplementation, resting after supplementation, and exhaustion after supplementation in three study groups, which are as follows: Group 1-sedentary controls supplemented with 10 mg magnesium per kilogram body weight. Group 2-tae kwon do athletes practicing 90-120 min/day supplemented with 10 mg magnesium per kilogram bodyweight. Group 3-tae kwon do athletes practicing 90-120 min/day receiving no magnesium supplements. The free plasma testosterone levels increased at exhaustion before and after supplementation compared to resting levels. Exercise also increased testosterone levels relative to sedentary subjects. Similar increases were observed for total testosterone. Our results show that supplementation with magnesium increases free and total testosterone values in sedentary and in athletes. The increases are higher in those who exercise than in sedentary individuals.

J Am Acad Orthop Surg. 2018 Apr 15;26(8):278-285. doi: 10.5435/JAAOS-D-16-00464.

### Effects of Vitamin D on Skeletal Muscle and Athletic Performance.

Abrams GD<sup>1</sup>, Feldman D, Safran MR.

Abstract

Vitamin D is known to be important for calcium homeostasis and bone metabolism. It also has important direct effects on skeletal muscle. Unlike authentic vitamins, which cannot be synthesized in the body, vitamin D is produced in the skin using sunlight. Through its nuclear receptor (ie, vitamin D receptor) located throughout the body, including skeletal muscle, vitamin D initiates genomic and nongenomic pathways regulating multiple actions, including myocyte proliferation and growth. In some studies, vitamin D supplementation has been shown to increase muscle strength, particularly in people who are vitamin D deficient. Higher serum levels of vitamin D are associated with reduced injury rates and improved sports performance. In a subset of the population, vitamin D appears to play a role in muscle strength, injury prevention, and sports performance.

Nutrients. 2020 Mar 21;12(3). pii: E841. doi: 10.3390/nu12030841.

Vitamin D and Sport Performance.

Knechtle B<sup>1,2</sup>, Nikolaidis PT<sup>3,4</sup>.

Abstract

Vitamin D seems to be very important for general health but also for athletic performance [...].

Full PDF paper available at <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146184/pdf/nutrients-12-00841.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146184/pdf/nutrients-12-00841.pdf</a>.

Nutrients. 2020 Feb 23;12(2). pii: E579. doi: 10.3390/nu12020579.

# Role of Vitamin D in Athletes and Their Performance: Current Concepts and New Trends.

<u>de la Puente Yagüe M</u><sup>1</sup>, <u>Collado Yurrita L</u><sup>2</sup>, <u>Ciudad Cabañas MJ</u><sup>2</sup>, <u>Cuadrado Cenzual MA</u><sup>2</sup>. <u>Abstract</u>

We are currently experiencing a vitamin D (VITD) deficiency pandemic across the world. Athletes have the same predisposition to low levels of vitamin D, the majority of its concentrations being below 20 ng/mL in a wide range of sports, especially in the winter months. Vitamin D is important in bone health, but recent research also points out its essential role in extraskeletal functions, including skeletal muscle growth, immune and cardiopulmonary functions and inflammatory modulation, which influence athletic performance. Vitamin D can also interact with extraskeletal tissues to modulate injury recovery and also influence the risk of infection. The data presented in this paper has triggered investigations in relation to the importance of maintaining adequate levels of vitamin D and to the possible positive influence supplementation has on immune and musculoskeletal functions in athletes, benefiting their performance and preventing future injuries. The objective of this review is to describe the latest research conducted on the epidemiology of vitamin D deficiency and its effects on sports performance and musculoskeletal health.

Full paper in PDF format available at:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7071499/pdf/nutrients-12-00579.pdf.

Nutrients. 2019 Aug 4;11(8). pii: E1800. doi: 10.3390/nu11081800.

# Vitamin D, Skeletal Muscle Function and Athletic Performance in Athletes-A Narrative Review.

Książek A¹, Zagrodna A², Słowińska-Lisowska M². Abstract

The active form of vitamin D (calcitriol) exerts its biological effects by binding to nuclear vitamin D receptors (VDRs), which are found in most human extraskeletal cells, including skeletal muscles. Vitamin D deficiency may cause deficits in strength, and lead to fatty degeneration of type II muscle fibers, which has been found to negatively correlate with physical performance. Vitamin D supplementation has been shown to improve vitamin D status and can positively affect skeletal muscles. The purpose of this study is to summarize the current evidence of the relationship between vitamin D, skeletal muscle function and physical performance in athletes. Additionally, we will discuss the effect of vitamin D supplementation on athletic performance in players. Further studies are necessary to fully characterize the underlying mechanisms of calcitriol action in the human skeletal muscle tissue, and to understand how these actions impact the athletic performance in athletes.

Full paper in PDF format available at:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6722905/pdf/nutrients-11-01800.pdf.

J Steroid Biochem Mol Biol. 2018 Jan;175:60-81.

#### Non-musculoskeletal benefits of vitamin D.

Wimalawansa SJ<sup>1</sup>.

Abstract

The aim of this study is to determine and critically evaluate the plausible relationships of vitamin D with extra-skeletal tissues in humans. Severe vitamin D deficiency results in rickets in children and osteomalacia in adults; these beneficial effects in the musculoskeletal system and certain physiological functions are well understood. Nevertheless, mounting reports support additional beneficial effects of vitamin D, outside the musculoskeletal system. This review explores the recent advances in knowledge about the non-skeletal effects of vitamin D. Peer-reviewed papers were extracted from research databases using key words, to assess correlations between vitamin D and extra-skeletal diseases and conditions. As per the guidelines of the Preferred Reporting Items for Systematic Reviews (PRISMA); general interpretations of results are included; taking into consideration the broader evidence and implications. This review summarizes current knowledge of the effects of vitamin D status on extra-skeletal tissues with special attention given to relationships between vitamin D status and various diseases commonly affecting adults; the effects of intervention with vitamin D and exposure to sunlight. Evidence suggests that vitamin D facilitates the regulation of blood pressure; and cardiac; endothelial; and smooth muscle cell functions; playing an important role in cardiovascular protection. In addition; 1,25(OH)<sub>2</sub>D improves immunity; subdues inflammation; and reduces the incidence and severity of common cancers; autoimmune diseases and infectious diseases. Almost all adequately powered; epidemiological and biological studies that use; adequate doses of vitamin D supplementation in D-deficient populations have reported favorable outcomes. These studies have concluded that optimizing 25(OH)D status improves the functionality of bodily systems; reduces comorbidities; improves the quality of life; and increases survival. Although accumulating evidence supports biological associations of vitamin D sufficiency with improved physical and mental functions; no definitive evidence exists from well-designed; statistically powered; randomized controlled clinical trials. Nevertheless, most studies point to significant protective effects of vitamin D in humans when the minimum 25(OH)D serum level exceeds 30ng/mL and is maintained throughout the year.

-----

Nutr Res. 2018 Jan;49:1-22.

# Supplemental protein from dairy products increases body weight and vitamin D improves physical performance in older adults: a systematic review and meta-analysis.

<u>Dewansingh P</u>¹, <u>Melse-Boonstra A</u>², <u>Krijnen WP</u>³, <u>van der Schans CP</u>⁴, <u>Jager-Wittenaar H</u>⁵, <u>van den Heuvel</u> EGHM<sup>6</sup>.

Abstract

The purpose of these systematic review and meta-analysis was to assess the effectiveness of dairy components on nutritional status and physical fitness in older adults, as evidence for efficacy of the supplementation of these components is inconclusive. Scopus and MEDLINE were searched. Main inclusion criteria for articles were as follows: double-blind, randomized, placebo-controlled trials including participants aged ≥55 years who received dairy components or a placebo. Outcome measures were nutrient status (body weight and body mass index) and physical fitness (body composition, muscle strength, and physical performance). Thirty-six trials with 4947participants were included. Most trials investigated protein and vitamin D supplementation and showed no effect on the outcomes. Metaanalysis on the effect of protein on body weight showed a significant increase in mean difference of 1.13 kg (95% confidence interval, 0.59-1.67). This effect increased by selecting trials with study a duration of 6 months in which less nourished and physically fit participants were included. Trials where the participants were (pre-)frail, inactive older adults or when supplementing ≥20 g of protein per day tended to increase lean body mass. Only small significant effects of vitamin D supplementation on Timed Up and Go (mean difference -0.75 seconds; 95% confidence interval -1.44 to -0.07) were determined. This effect increased when vitamin D doses ranged between 400 and 1000 IU. Additional large randomized controlled trials of ≥6 months are needed regarding the effect of dairy components containing an adequate amount of vitamin D (400-1000 IU) and/or protein (≥20 g) on nutritional status and physical fitness in malnourished or frail older adults.

-----

Eur J Clin Nutr. 2020 Feb;74(2):231-247. doi: 10.1038/s41430-019-0553-3. Epub 2020 Jan 6.

Vitamin D testing: advantages and limits of the current assays.

Altieri B<sup>1,2</sup>, Cavalier E<sup>3</sup>, Bhattoa HP<sup>4</sup>, Pérez-López FR<sup>5,6</sup>, López-Baena MT<sup>5</sup>, Pérez-Roncero GR<sup>5</sup>, Chedraui P<sup>7,8</sup>, Annweiler C<sup>9,10</sup>, Della Casa S<sup>11</sup>, Zelzer S<sup>12</sup>, Herrmann M<sup>12</sup>, Faggiano A<sup>13</sup>, Colao A<sup>14</sup>, Holick MF<sup>15</sup>.

Abstract

Vitamin D deficiency and insufficiency has become a pandemic health problem with a consequent increase of requests for determining circulating levels of 25-hydroxyvitamin D [25(OH)D]. However, the analytical performance of these immunoassays, including radioimmunoassay and ELISA, is highly variable, and even mass spectrometric methods, which nowadays serves as the gold standard for the quantitatively determination of 25(OH)D, do not necessarily produce comparable results, creating limitations for the definition of normal vitamin D status ranges. To solve this problem, great efforts have been made to promote standardization of laboratory assays, which is important to achieve comparable results across different methods and manufacturers. In this review, we performed a systematic analysis evaluating critically the advantages and limits of the current assays available for the measure of vitamin D status, i.e., circulating 25(OH)D and its metabolites, making suggestions that could be used in the clinical practice. Moreover, we

also suggest the use of alternatives to blood test, including standardized surveys that may be of value in alerting health-care professionals about the vitamin D status of their patients.

-----

Eur J Clin Nutr. 2018 Jan 24.

# Associations between 25-hydroxyvitamin D levels, body composition and metabolic profiles in young women.

Tabesh M, Callegari ET, Gorelik A, Garland SM, Nankervis A, Subasinghe AK, Wark JD; YFHI and Safe-D study groups.

Abstract

BACKGROUND/OBJECTIVES:

Cardiovascular disease (CVD) is a major cause of mortality and morbidity globally. Results from previous studies are inconsistent and it remains unclear whether low-serum 25 OHD levels are associated with an increased risk of CVD. These associations have been little studied in young women. The aim of this study was to assess the relationship between serum 25 OHD and obesity, body composition, metabolic profiles and blood pressure in young women. SUBJECTS/METHODS:

Women aged 16-25 years living in Victoria, Australia, were recruited through Facebook advertising in this cross-sectional study. Participants completed an online survey and attended a site visit in a fasted state, where parameters, including blood pressure, anthropometry, metabolic profiles, serum 25 OHD levels and body composition (using dual energy X-ray absorptiometry) were measured.

#### **RESULTS:**

A total of 557 participants were recruited into this study. Multiple linear regression analysis showed that after adjusting for visceral fat, season, smoking, physical activity, age, alcohol intake, oral contraceptive use, country of birth, taking multivitamins and taking vitamin D supplement, a 10 nmol/L increase in 25 OHD levels was associated with 0.65% greater HDL levels (p = 0.016) and 0.92% greater triglyceride levels (p = 0.003). It was also associated with 0.48% lower BMI (p < 0.001), 0.50% lower total fat percentage (p < 0.001), 0.09% lower visceral fat percentage (p < 0.001), 0.14% lower visceral fat to total fat ratio (p < 0.001) and 0.36% lower trunk fat to total fat ratio (p < 0.001), after adjustment for season, smoking, physical activity, age, alcohol intake, oral contraceptive use, country of birth, taking multivitamins and taking vitamin D supplements. Although these associations were statistically significant, they were very small in magnitude and of uncertain clinical significance.

#### CONCLUSIONS:

These findings may help to explain an association between 25 OHD levels and CVD risk factors through associations with HDL, BMI, total body and visceral fat mass. Possible underlying mechanisms warrant further investigation.

-----

Nutrients. 2017 Jul 26;9(8). pii: E799.

# Vitamin D Supplementation Improves Quality of Life and Physical Performance in Osteoarthritis Patients.

Manoy P<sup>1</sup>, Yuktanandana P<sup>2</sup>, Tanavalee A<sup>3</sup>, Anomasiri W<sup>4</sup>, Ngarmukos S<sup>5</sup>, Tanpowpong T<sup>6</sup>, Honsawek S<sup>7,8</sup>. Abstract

(1) Background: Lower levels of serum 25-hydroxyvitamin D (25(OH)D) are common in osteoarthritis (OA) patients. However, the effect of vitamin D supplementation on muscle strength and physical performance remains unclear. This study will investigate the effects of vitamin D<sub>2</sub> supplementation on muscle strength and physical performance in knee OA patients; (2) Methods: One hundred and seventy-five primary knee OA patients with low levels of serum 25(OH)D (<30 ng/mL) received 40,000 IU vitamin D<sub>2</sub> (ergocalciferol) per week for six months. Body composition, muscle strength, physical performance, serum 25(OH)D level, leptin, interlukin-6 (IL-6), parathyroid hormone (PTH), protein carbonyl, and metabolic profile were analyzed; (3) Results: Baseline mean serum 25(OH)D levels in knee OA patients was 20.73 ng/mL. Regarding baseline vitamin D status, 58.90% of patients had vitamin D insufficiency, and 41.10% had vitamin D deficiency. After vitamin D<sub>2</sub> supplementation for six months, mean serum 25(OH)D level was 32.14 ng/mL. For post-supplementation vitamin D status, 57.10% of patients had vitamin D sufficiency and 42.90% had vitamin D insufficiency. From baseline to six months, there was a significant increase in mean serum 25(OH)D level (p. < 0.001), while mean LDL cholesterol (p = 0.001), protein carbonyl (p = 0.04), and PTH (p = 0.005) all significantly decreased. Patient quality of life (SF-12) and pain (visual analog scale, VAS) both improved significantly from baseline to the six-month time point (p = 0.005 and p = 0.002, respectively). Knee OA patients demonstrated significant improvement grip strength and physical performance measurements after vitamin  $D_2$  supplementation (p < 0.05); (4) Conclusions: Vitamin D<sub>2</sub> supplementation for six months reduced oxidative protein damage, decreased pain (VAS), improved quality of life, and improved grip strength and physical performance in osteoarthritis patients.

-----

Curr Opin Clin Nutr Metab Care. 2017 May;20(3):169-174.

## Vitamin D and muscle trophicity.

Domingues-Faria C1, Boirie Y, Walrand S.

**Abstract** 

PURPOSE OF REVIEW:

We review recent findings on the involvement of vitamin D in skeletal muscle trophicity.

#### RECENT FINDINGS:

Vitamin D deficiencies are associated with reduced muscle mass and strength, and its supplementation seems effective to improve these parameters in vitamin D-deficient study participants. Latest investigations have also evidenced that vitamin D is essential in muscle development and repair. In particular, it modulates skeletal muscle cell proliferation and differentiation. However, discrepancies still exist about an enhancement or a decrease of muscle proliferation and differentiation by the vitamin D. Recently, it has been demonstrated that vitamin D influences skeletal muscle cell metabolism as it seems to regulate protein synthesis and mitochondrial function. Finally, apart from its genomic and nongenomic effects, recent investigations have demonstrated a genetic contribution of vitamin D to muscle functioning.

#### SUMMARY:

Recent studies support the importance of vitamin D in muscle health, and the impact of its deficiency in regard to muscle mass and function. These 'trophic' properties are of particular importance for some specific populations such as elderly persons and athletes, and in situations of loss of muscle mass or function, particularly in the context of chronic diseases.

-----

Proc Nutr Soc. 2016 Feb;75(1):38-46.

Vitamin D modulates adipose tissue biology: possible consequences for obesity? <u>Landrier JF</u><sup>1</sup>, <u>Karkeni E</u><sup>1</sup>, <u>Marcotorchino J</u><sup>1</sup>, <u>Bonnet L</u><sup>1</sup>, <u>Tourniaire F</u><sup>1</sup>.

Abstract

Cross-sectional studies depict an inverse relationship between vitamin D (VD) status reflected by plasma 25-hydroxy-vitamin D and obesity. Furthermore, recent studies in vitro and in animal models tend to demonstrate an impact of VD and VD receptor on adipose tissue and adipocyte biology, pointing to at least a part-causal role of VD insufficiency in obesity and associated physiopathological disorders such as adipose tissue inflammation and subsequent insulin resistance. However, clinical and genetic studies are far less convincing, with highly contrasted results ruling out solid conclusions for the moment. Nevertheless, prospective studies provide interesting data supporting the hypothesis of a preventive role of VD in onset of obesity. The aim of this review is to summarise the available data on relationships between VD, adipose tissue/adipocyte physiology, and obesity in order to reveal the next key points that need to be addressed before we can gain deeper insight into the controversial VD-obesity relationship.

-----

Curr Opin Clin Nutr Metab Care. 2016 Nov;19(6):464-470.

### Changes in circulating vitamin D levels with loss of adipose tissue.

Gangloff A<sup>1</sup>, Bergeron J, Lemieux I, Després JP.

**Abstract** 

PURPOSE OF REVIEW:

Low vitamin D levels have been extensively reported in obesity. Thus, the pandemic of obesity has been paralleled by a high prevalence of low vitamin D status. Given the well documented associations linking poor vitamin D status to adverse health outcomes (diabetes, cardiovascular disease, cancers, all-cause mortality), a proper understanding of the mechanisms linking excess adiposity to low vitamin D status is key to identify and implement effective interventions to replenish vitamin D levels in obese individuals. In this review, we will discuss recent literature investigating the effects of adipose tissue volume loss through energy restriction and/or physical activity on circulating 25-hydroxyvitamin D [25(OH)D] levels.

**RECENT FINDINGS:** 

Improvements of circulating 25(OH)D levels with adiposity loss through lifestyle interventions without supplementation is being reported by a growing number of studies, including recent randomized controlled trials.

SUMMARY:

Low 25(OH)D is one of the metabolic disturbances associated with excess adiposity, particularly visceral adiposity. Recommendations for the treatment of obesity-related vitamin D deficiency should emphasize the role of visceral adiposity loss through healthy lifestyle habits, in conjunction with weight-adjusted vitamin D supplementation, not only to replenish 25(OH)D levels but also to address other visceral adiposity-related disturbances, such as insulin resistance, inflammation, hypertension, and dyslipidemia.

.....

J Steroid Biochem Mol Biol. 2015 Aug;152:171-9.

# Vitamin D treatment protects against and reverses oxidative stress induced muscle proteolysis.

Bhat M<sup>1</sup>, Ismail A<sup>2</sup>.

Abstract

Vitamin D is known to have a biological role in many extra skeletal tissues in the body including muscle. Vitamin D deficiency has been associated with preferential atrophy of type II fibres in human muscle. Vitamin D at physiological concentrations is known to protect cells against oxidative damage. In this study we examined whether vitamin D deficiency induces muscle oxidative stress in a rat model and further if pre or post treatment of C2C12 muscle cells with vitamin D offers protection against oxidative stress induced muscle proteolysis. Protein carbonylation as a marker of protein oxidation was increased in both the deficient muscle and vehicle-treated C2C12 cells. Vitamin D deficiency led to an increase in activities of the glutathione-dependent enzymes and decrease in SOD and catalase enzymes in the rat muscle. Higher nitrate levels indicative of nitrosative stress were observed in the deficient muscle compared to control muscle. Rehabilitation with vitamin D could reverse the alterations in oxidative and nitrosative stress parameters. Increase in total protein degradation, 20S proteasomal enzyme activity, muscle atrophy gene markers and expression of proteasome subunit genes induced by oxidative stress were corrected both by pre/post treatment of C2C12 muscle cells with vitamin D. Increase in SOD activity in the presence of vitamin D indicates antioxidant potential of vitamin D in the muscle. The data presented indicates that vitamin D deficiency leads to mild oxidative stress in the muscle which may act as a trigger for increased proteolysis in the vitamin D deficient muscle.

-----

Biomed Res Int. 2015;2015:953241...

Vitamin D: a review on its effects on muscle strength, the risk of fall, and frailty. Halfon  $M^1$ , Phan  $O^1$ , Teta  $D^1$ .

Abstract

Vitamin D is the main hormone of bone metabolism. However, the ubiquitary nature of vitamin D receptor (VDR) suggests potential for widespread effects, which has led to new research exploring the effects of vitamin D on a variety of tissues, especially in the skeletal muscle. In vitro studies have shown that the active form of vitamin D, calcitriol, acts in myocytes through genomic effects involving VDR activation in the cell nucleus to drive cellular differentiation and proliferation. A putative transmembrane receptor may be responsible for nongenomic effects leading to rapid influx of calcium within muscle cells. Hypovitaminosis D is consistently associated with decrease in muscle function and performance and increase in disability. On the contrary, vitamin D supplementation has been shown to improve muscle strength and gait in different settings, especially in elderly patients. Despite some controversies in the interpretation of meta-analysis, a reduced risk of falls has been attributed to vitamin D supplementation due to direct effects on muscle cells. Finally, a low vitamin D status is consistently associated with the frail phenotype. This is why many authorities recommend vitamin D supplementation in the frail patient.

-----

# Effects of vitamin D in skeletal muscle: falls, strength, athletic performance and insulin sensitivity.

Girgis CM<sup>1</sup>, Clifton-Bligh RJ, Turner N, Lau SL, Gunton JE. Abstract

Accompanying the high rates of vitamin D deficiency observed in many countries, there is increasing interest in the physiological functions of vitamin D. Vitamin D is recognized to exert extra-skeletal actions in addition to its classic roles in bone and mineral homeostasis. Here, we review the evidence for vitamin D's actions in muscle on the basis of observational studies, clinical trials and basic research. Numerous observational studies link vitamin D deficiency with muscle weakness and sarcopaenia. Randomized trials predominantly support an effect of vitamin D supplementation and the prevention of falls in older or institutionalized patients. Studies have also examined the effect of vitamin Din athletic performance, both inferentially by UV radiation and directly by vitamin D supplementation. Effects of vitamin D in muscle metabolic function, specifically insulin sensitivity, are also addressed in this review. At a mechanistic level, animal studies have evaluated the roles of vitamin D and associated minerals, calcium and phosphate, in muscle function. In vitro studies have identified molecular pathways by which vitamin D regulates muscle cell signaling and gene expression. This review evaluates evidence for the various roles of vitamin D in skeletal muscle and discusses controversies that have made this a dynamic field of research.

-----

Biomed Res Int. 2014;2014:121254.

# Vitamin D signaling in myogenesis: potential for treatment of sarcopenia.

Wagatsuma A1, Sakuma K2.

Abstract

Muscle mass and strength progressively decrease with age, which results in a condition known as sarcopenia. Sarcopenia would lead to physical disability, poor quality of life, and death. Therefore, much is expected of an effective intervention for sarcopenia. Epidemiologic, clinical, and laboratory evidence suggest an effect of vitamin D on muscle function. However, the precise molecular and cellular mechanisms remain to be elucidated. Recent studies suggest that vitamin D receptor (VDR) might be expressed in muscle fibers and vitamin D signaling via VDR plays a role in the regulation of myoblast proliferation and differentiation. Understanding how vitamin D signaling contributes to myogenesis will provide a valuable insight into an effective nutritional strategy to moderate sarcopenia. Here we will summarize the current knowledge about the effect of vitamin D on skeletal muscle and myogenic cells and discuss the potential for treatment of sarcopenia.

-----

Int J Sport Nutr Exerc Metab. 2013 Oct;23(5):441-8.

## Vitamin D status and supplementation in elite Irish athletes.

Magee PJ1, Pourshahidi LK, Wallace JM, Cleary J, Conway J, Harney E, Madigan SM.

**Abstract** 

BACKGROUND:

A high prevalence of vitamin D insufficiency/deficiency, which may impact on health and training ability, is evident among athletes worldwide. This observational study investigated the vitamin D status of elite Irish athletes and determined the effect of wintertime supplementation on status.

#### METHODS:

Serum 25-hydroxyvitamin D [25(OH)D], calcium, and plasma parathyroid hormone were analyzed in elite athletes in November 2010 (17 boxers, 33 paralympians) or March 2011 (34 Gaelic Athletic Association [GAA] players). A subset of boxers and paralympians (n = 27) were supplemented during the winter months with either 5,000 IU vitamin D3/d for 10-12 weeks or 50,000 IU on one or two occasions. Biochemical analysis was repeated following supplementation. RESULTS:

Median 25(OH)D of all athletes at baseline was 48.4 nmol/L. Vitamin D insufficiency/deficiency (serum 25(OH)D <50 nmol/L) was particularly evident among GAA players (94%) due to month of sampling. Wintertime supplementation (all doses) significantly increased 25(OH)D (median 62.8 nmol/L at baseline vs. 71.1 nmol/L in April or May; p = .001) and corrected any insufficiencies/deficiencies in this subset of athletes. In contrast, 25(OH)D significantly decreased in those that did not receive a vitamin D supplement, with 74% of athletes classed as vitamin D insufficient/deficient after winter, compared with only 35% at baseline.

#### CONCLUSIONS:

This study has highlighted a high prevalence of vitamin D insufficiency/ deficiency among elite Irish athletes and demonstrated that wintertime vitamin D3 supplementation is an appropriate regimen to ensure vitamin D sufficiency in athletes during winter and early spring.

-----

J Sports Sci. 2013;31(4):344-53.

# Assessment of vitamin D concentration in non-supplemented professional athletes and healthy adults during the winter months in the UK: implications for skeletal muscle function.

Close GL¹, Russell J, Cobley JN, Owens DJ, Wilson G, Gregson W, Fraser WD, Morton JP. Abstract

The current study implemented a two-part design to (1) assess the vitamin D concentration of a large cohort of non-vitamin D supplemented UK-based athletes and 30 age-matched healthy non-athletes and (2) to examine the effects of 5000 IU  $\cdot$  day(-1) vitamin D(3) supplementation for 8-weeks on musculoskeletal performance in a placebo controlled trial. Vitamin D concentration was determined as severely deficient if serum 25(OH)D < 12.5 nmol  $\cdot$  I(-1), deficient 12.5-30 nmol  $\cdot$  I(-1) and inadequate 30-50 nmol  $\cdot$  I(-1). We demonstrate that 62% of the athletes (38/61) and 73% of the controls (22/30) exhibited serum total 25(OH)D < 50 nmol  $\cdot$  I(-1). Additionally, vitamin D supplementation increased serum total 25(OH)D from baseline (mean  $\pm$  SD = 29  $\pm$  25 to 103  $\pm$  25 nmol  $\cdot$  I(-1), P = 0.0028), whereas the placebo showed no significant change (53  $\pm$  29 to 74  $\pm$  24 nmol  $\cdot$  I(-1), P = 0.12). There was a significant increase in 10 m sprint times (P = 0.008) and vertical-jump (P = 0.008) in the vitamin D group whereas the placebo showed no change (P = 0.587 and P = 0.204 respectively). The current data supports previous findings that athletes living at Northerly latitudes (UK = 53° N) exhibit inadequate vitamin D concentrations (<50 nmol  $\cdot$  I(-1)). Additionally the data suggests that inadequate vitamin D concentration is detrimental to musculoskeletal performance in athletes. Future studies using larger athletic groups are now warranted.

### Sunlight and Vitamin D: A global perspective for health.

Wacker M1, Holick MF1.

Abstract

Vitamin D is the sunshine vitamin that has been produced on this earth for more than 500 million years. During exposure to sunlight 7-dehydrocholesterol in the skin absorbs UV B radiation and is converted to previtamin D3 which in turn isomerizes into vitamin D3. Previtamin D3 and vitamin D3 also absorb UV B radiation and are converted into a variety of photoproducts some of which have unique biologic properties. Sun induced vitamin D synthesis is greatly influenced by season, time of day, latitude, altitude, air pollution, skin pigmentation, sunscreen use, passing through glass and plastic, and aging. Vitamin D is metabolized sequentially in the liver and kidneys into 25-hydroxyvitamin D which is a major circulating form and 1,25-dihydroxyvitamin D which is the biologically active form respectively. 1,25dihydroxyvitamin D plays an important role in regulating calcium and phosphate metabolism for maintenance of metabolic functions and for skeletal health. Most cells and organs in the body have a vitamin D receptor and many cells and organs are able to produce 1,25-dihydroxyvitamin D. As a result 1,25-dihydroxyvitamin D influences a large number of biologic pathways which may help explain association studies relating vitamin D deficiency and living at higher latitudes with increased risk for many chronic diseases including autoimmune diseases, some cancers, cardiovascular disease, infectious disease, schizophrenia and type 2 diabetes. A three-part strategy of increasing food fortification programs with vitamin D, sensible sun exposure recommendations and encouraging ingestion of a vitamin D supplement when needed should be implemented to prevent global vitamin D deficiency and its negative health consequences.

Full PDF version of this paper is available at: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3897598/pdf/de-5-51.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3897598/pdf/de-5-51.pdf</a>

-----

Sports Med. 2013 Jul;43(7):601-11...

# Vitamin D and physical performance.

Moran DS<sup>1</sup>, McClung JP, Kohen T, Lieberman HR. Abstract

Vitamin D is an essential nutrient obtained from the diet and exposure to sunlight. Roles for vitamin D have been established in the function of the cardiovascular, immune, and musculoskeletal systems. An electronic database search was conducted using EMBASE (1967 to August 2012), MEDLINE (1966 to August 2012), SPORTDiscus™ (1975 to August 2012), and the Scientific Electronic Library Online (SciELO) (1998 to August 2012) with no limits of language of publication. Articles that described vitamin D and performance were considered eligible for this review. Recent studies suggest that vitamin D maintains physical performance in athletes and other active populations, e.g., maximal oxygen consumption may be related to vitamin D status. Poor vitamin D status affects muscle strength, and vitamin D may participate in protein synthesis through the actions of the vitamin D receptor in muscle tissue. Vitamin D may protect against overuse injuries, such as stress fracture, through its well-documented role in calcium metabolism. The objective of this manuscript is to review recent evidence regarding the importance of vitamin D for maintaining physical performance, and includes specific examples of how vitamin D supports the cardiovascular, immune, and musculoskeletal systems.

-----

Autoimmun Rev. 2013 Aug;12(10):976-89. doi: 10.1016/j.autrev.2013.02.004.

# Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality-a review of recent evidence.

<u>Pludowski P</u>1, <u>Holick MF</u>, <u>Pilz S</u>, <u>Wagner CL</u>, <u>Hollis BW</u>, <u>Grant WB</u>, <u>Shoenfeld Y</u>, <u>Lerchbaum E</u>, <u>Llewellyn DJ</u>, <u>Kienreich K</u>, <u>Soni M</u>.

**Abstract** 

BACKGROUND:

Optimal vitamin D intake and its status are important not only for bone and calcium-phosphate metabolism, but also for overall health and well-being. Vitamin D deficiency and insufficiency as a global health problem are likely to be a risk for wide spectrum of acute and chronic illnesses.

METHODS:

A review of randomized controlled trials, meta-analyses, and other evidence of vitamin D action on various health outcomes.

**RESULTS:** 

Adequate vitamin D status seems to be protective against musculoskeletal disorders (muscle weakness, falls, fractures), infectious diseases, autoimmune diseases, cardiovascular disease, type 1 and type 2 diabetes mellitus, several types of cancer, neurocognitive dysfunction and mental illness, and other diseases, as well as infertility and adverse pregnancy and birth outcomes. Vitamin D deficiency/insufficiency is associated with all-cause mortality. CONCLUSIONS:

Adequate vitamin D supplementation and sensible sunlight exposure to reach optimal vitamin D status are among the front line factors of prophylaxis for the spectrum of disorders. Supplementation guidance and population strategies for the eradication of vitamin D deficiency must be included in the priorities of physicians, medical professionals and healthcare policy-makers.

-----

Open Access J Sports Med. 2012 Apr 27;3:35-42. doi: 10.2147/OAJSM.S31022. eCollection 2012.

### Vitamin D status and biomarkers of inflammation in runners.

Willis KS1, Smith DT, Broughton KS, Larson-Meyer DE.

Abstract

BACKGROUND AND PURPOSE:

The extra-skeletal functions of vitamin D - including its role in inflammatory modulation - are now well recognized but have not yet been investigated in an athletic population. Thus, the purpose of this study was to investigate the relationship between vitamin D status and pro- and anti-inflammatory cytokines (as markers of inflammation and immune system function) in endurance athletes.

#### PATIENTS AND METHODS:

We analyzed fasting blood samples from 19 healthy, endurance-trained male and female runners (following a standardized diet and exercise regimen) for vitamin D status (serum 25-hydroxyvitamin D [25(OH)D)] and specific plasma cytokine concentrations (tumor necrosis factor alpha [TNF-α], interferon-gamma [IFN-γ], interleukin [IL]-4, and IL-10). Serum/plasma concentrations were log-transformed and simple regression analysis was used to determine significant associations between 25(OH)D and cytokine concentrations.

RESULTS:

Forty-two percent of participants had insufficient vitamin D status [25(OH)D< 32 ng/mL], whereas 11% were deficient [25(OH)D < 20 ng/mL]. TNF- $\alpha$  and IL-4 were variable, ranging from 2.9 to 36.4 pg/mL and 0 to 252.1 pg/mL, respectively. Concentrations of IFN- $\gamma$  and IL-10 were minimal, with means of 6.7 ± 7.0 pg/mL and 4.8 ± 5.1 pg/mL, respectively. Regression analysis revealed a significant inverse association between 25(OH)D and TNF- $\alpha$  concentrations (R(2) = 56.5, P < 0.001) but not between 25(OH)D and the remaining cytokines, IFN- $\gamma$ , IL-4, and IL-10 (P = 0.477, 0.694, and 0.673, respectively).

CONCLUSION:

These results call further attention to the epidemic of vitamin D insufficiency, even in outdoor athletes, and support a possible link between decreased vitamin D status and one particular marker of inflammation. Future investigations are necessary to determine whether increased inflammation in athletes with reduced vitamin D status could increase risk for inflammation-related injury.

-----

Nutr Rev. 2012 Sep;70(9):520-33.

# Vitamin D: an overview of its role in skeletal muscle physiology in children and adolescents.

Hazell TJ<sup>1</sup>, DeGuire JR, Weiler HA.

Many children may have insufficient serum concentrations of vitamin D, which could prevent optimal muscle development and function. Vitamin D deficiency in animal models results in negative effects on muscle fiber structure and calcium/phosphorus handling, suggesting an integral role of vitamin D in skeletal muscle function. While there is a dearth of data in humans, the available evidence demonstrates a positive association between vitamin D status and muscle function. This review focuses on the important role of vitamin D in muscle function in children and adolescents who live in North American regions where exposure to ultraviolet B radiation is limited and who are thus at increased risk for vitamin D insufficiency. The effects of vitamin D on muscle cell proliferation and differentiation, muscle fiber structure, and calcium and phosphorus handling are discussed. Moreover, the roles of vitamin D and the vitamin D receptor and their genomic and nongenomic actions in muscle function are explored in depth. Future research should aim to establish a vitamin D status consistent with optimal musculoskeletal development and function in young children.

-----

J Steroid Biochem Mol Biol. 2011 Jul;125(3-5):159-68.

# The effects of vitamin D on skeletal muscle function and cellular signaling. Dirks-Naylor AJ1, Lennon-Edwards S.

Abstract

It is thought that every cell in the body expresses the vitamin D receptor, and therefore vitamin D may play a role in health and homeostasis of every organ system, including skeletal muscle. Human, animal, and cell culture studies have collectively shown that vitamin D affects muscle strength and function. Vitamin D functions in a plethora of cellular processes in skeletal muscle including calcium homeostasis, cell proliferation, cell differentiation, fiber size, prevention of fatty degeneration, protection against insulin resistance and arachidonic acid mobilization. These processes appear

to be mediated by several signaling pathways affected by vitamin D. This review aims to explore the effects of vitamin D on skeletal muscle in each model system and to delineate potential cell signaling pathways affected by vitamin D.

-----

Pediatr Clin North Am. 2010 Jun;57(3):849-61.

# Vitamin D, muscle function, and exercise performance.

Bartoszewska M1, Kamboj M, Patel DR.

Abstract

Vitamin D has an important role in skeletal muscles. Previously recognized for its effects on bone, it is now known that vitamin D has a much wider spectrum of usefulness for muscle. Studies indicate that vitamin D deficiency is pandemic. Those affected include the young and otherwise healthy members of the population, including athletes. Controversy exists regarding the amount of supplementation required to reverse deficiency and the relative effect of such a reversal on overall health. This article reviews current data on the role of vitamin D on muscle function, and explores the potential implications of its deficiency and supplementation on physical fitness and athletic performance.

-----

Scand J Med Sci Sports. 2010 Apr;20(2):182-90...

# Vitamin D and human skeletal muscle.

Hamilton B1.

**Abstract** 

Vitamin D deficiency is an increasingly described phenomenon worldwide, with well-known impacts on calcium metabolism and bone health. Vitamin D has also been associated with chronic health problems such as bowel and colonic cancer, arthritis, diabetes and cardiovascular disease. In recent decades, there has been increased awareness of the impact of vitamin D on muscle morphology and function, but this is not well recognized in the Sports Medicine literature. In the early 20th century, athletes and coaches felt that ultraviolet rays had a positive impact on athletic performance, and increasingly, evidence is accumulating to support this view. Both cross-sectional and longitudinal studies allude to a functional role for vitamin D in muscle and more recently the discovery of the vitamin D receptor in muscle tissue provides a mechanistic understanding of the function of vitamin D within muscle. The identification of broad genomic and non-genomic roles for vitamin D within skeletal muscle has highlighted the potential impact vitamin D deficiency may have on both under-performance and the risk of injury in athletes. This review describes the current understanding of the role vitamin D plays within skeletal muscle tissue.

-----

Curr Opin Clin Nutr Metab Care. 2009 Nov;12(6):628-33.

Vitamin D and its role in skeletal muscle.

Ceglia L.

Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, 711 Washington Street, Boston, MA 02111, USA. lisa.ceglia@tufts.edu

PURPOSE OF REVIEW: Vitamin D is best known for its role in regulating calcium homeostasis and in strengthening bone. However, it has become increasingly clear that it also has important beneficial effects beyond the skeleton, including muscle. This review summarizes current knowledge about the role of vitamin D in skeletal muscle tissue and physical performance. RECENT FINDINGS: Molecular mechanisms of vitamin D action in muscle tissue include genomic and nongenomic effects via a receptor present in muscle cells. Knockout mouse models of the vitamin D receptor provide insight into understanding the direct effects of vitamin D on muscle tissue. Vitamin D status is positively associated with physical performance and inversely associated with risk of falling. Vitamin D supplementation has been shown to improve tests of muscle performance, reduce falls, and possibly impact on muscle fiber composition and morphology in vitamin D deficient older adults. SUMMARY: Further studies are needed to fully characterize the underlying mechanisms of vitamin D action in human muscle tissue, to understand how these actions translate into changes in muscle cell morphology and improvements in physical performance, and to define the 25-hydroxyvitamin D level at which to achieve these beneficial effects in muscle.

-----

J Bone Joint Surg Br. 2009 Dec;91(12):1587-93.

The level of vitamin D in the serum correlates with fatty degeneration of the muscles of the rotator cuff.

Oh JH, Kim SH, Kim JH, Shin YH, Yoon JP, Oh CH.

Department of Orthopaedic Surgery, Seoul National University, College of Medicine, Seoul National University Bundang Hospital, Bundang-gu, Seongnam, Korea.

This study examined the role of vitamin D as a factor accounting for fatty degeneration and muscle function in the rotator cuff. There were 366 patients with disorders of the shoulder. A total of 228 patients had a full-thickness tear (group 1) and 138 patients had no tear (group 2). All underwent magnetic resonance arthrography and an isokinetic muscle performance test. The serum concentrations of vitamin D (25(OH)D(3)) were measured. In general, a lower serum level of vitamin D was related to higher fatty degeneration in the muscles of the cuff. Spearman's correlation coefficients were 0.173 (p = 0.001), -0.181 (p = 0.001), and -0.117 (p = 0.026) for supraspinatus, infraspinatus and subscapularis,

respectively. In group 1, multivariate linear regression analysis revealed that the serum level of vitamin D was an independent variable for fatty degeneration of the supraspinatus and infraspinatus. The serum vitamin D level has a significant negative correlation with the fatty degeneration of the cuff muscle and a positive correlation with isokinetic muscle torque.

-----

Best Pract Res Clin Rheumatol. 2009 Dec;23(6):789-95.

Vitamin D: what is an adequate vitamin D level and how much supplementation is necessary?

#### Bischoff-Ferrari H.

Centre on Aging and Mobility, University of Zurich, Department of Rheumatology and Institute of Physical Medicine, Zurich, Switzerland. heike.bischoff@usz.ch

Strong evidence indicates that many or most adults in the United States and Europe would benefit from vitamin D supplements with respect to fracture and fall prevention, and possibly other public health targets, such as cardiovascular health, diabetes and cancer. This review discusses the amount of vitamin D supplementation needed and a desirable 25-hydroxyvitamin D level to be achieved for optimal musculoskeletal health. Vitamin D modulates fracture risk in two ways: by decreasing falls and increasing bone density. Two most recent meta-analyses of double-blind randomised controlled trials came to the conclusion that vitamin D reduces the risk of falls by 19%, the risk of hip fracture by 18% and the risk of any non-vertebral fracture by 20%; however, this benefit was dose dependent. Fall prevention was only observed in a trial of at least 700 IU vitamin D per day, and fracture prevention required a received dose (treatment dose\*adherence) of more than 400 IU vitamin D per day. Anti-fall efficacy started with achieved 25-hydroxyvitamin D levels of at least 60 nmol I(-1) (24 ng mI(-1)) and anti-fracture efficacy started with achieved 25-hydroxyvitamin D levels of at least 75 nmol I(-1) (30 ng ml(-1)) and both endpoints improved further with higher achieved 25-hydroxyvitamin D levels. Founded on these evidence-based data derived from the general older population, vitamin D supplementation should be at least 700-1000 IU per day and taken with good adherence to cover the needs for both fall and fracture prevention. Ideally, the target range for 25-hydroxyvitamin D should be at least 75 nmol I(-1), which may need more than 700-1000 IU vitamin D in individuals with severe vitamin D deficiency or those overweight.

-----

J Invest Dermatol. 2010 Feb;130(2):546-53.

# Vitamin D production after UVB exposure depends on baseline vitamin D and total cholesterolbut not on skin pigmentation.

Bogh MK<sup>1</sup>, Schmedes AV, Philipsen PA, Thieden E, Wulf HC. Abstract

UVB radiation increases serum vitamin D level expressed as 25-hydroxyvitamin-D(3) (25(OH)D), but the influence of skin pigmentation, baseline 25(OH)D level, and total cholesterol has not been well characterized. To determine the importance of skin pigmentation, baseline25(OH)D level, and total cholesterol on 25(OH)D production after UVB exposure, 182 persons were screened for 25(OH)D level. A total of 50 participants with a wide range in baseline 25(OH)D levels were selected to define the importance of baseline 25(OH)D level. Of these, 28 non-sun worshippers with limited past sun exposure were used to investigate the influence of skin pigmentation and baseline totalcholesterol. The participants had 24% of their skin exposed to UVB (3 standard erythema doses) four times every second or third day. Skinpigmentation and 25(OH)D levels were measured before and after the irradiations. Total cholesterol was measured at baseline. The increase in 25(OH)D level after UVB exposure was negatively correlated with baseline 25(OH)D level (P<0.001) and positively correlated with baselinetotal cholesterol level (P=0.005), but no significant correlations were found with constitutive or facultative skin pigmentation. In addition, we paired a dark-skinned group with a fair-skinned group according to baseline 25(OH)D levels and found no differences in 25(OH)D increase after identical UVB exposure.

-----

Endocr Pract. 2009 Sep-Oct;15(6):590-6.

Is vitamin D the fountain of youth?

#### Binkley N.

University of Wisconsin Osteoporosis Research, 2870 University Avenue, Suite 100, Madison, WI 53705, USA. nbinkley@wisc.edu

OBJECTIVE: To review the role of vitamin D deficiency for both classic and "nonclassic" effects and raise the caution that association does not prove causation. METHODS: The pertinent literature regarding vitamin D and its effects on bone, muscle function, immune function, glucose tolerance, cancer risk, and development of cardiovascular disease and other conditions is reviewed. In addition, the limitations of observational studies are discussed. RESULTS: Vitamin D inadequacy is common worldwide and classically causes osteomalacia and rickets. More recently, the contribution of low vitamin D status to increased falls and fracture risk has become appreciated. Additionally, nonclassic effects of vitamin D inadequacy are being recognized, and low vitamin D status is being potentially associated with a multitude of conditions (including Alzheimer disease, osteoarthritis, multiple sclerosis,

and hypertension) and higher overall mortality. It is important to recognize that associations in observational studies can be due to chance, bias, or confounders or may be indicative of causality. CONCLUSION: Because vitamin D deficiency has been established to have adverse musculoskeletal consequences, optimization of vitamin D status, for both the individual patient and the overall population, is indicated.

-----

Clin Chem Lab Med. 2009;47(2):120-7.

Vitamin D: current status and perspectives.

Cavalier E, Delanaye P, Chapelle JP, Souberbielle JC.

Department of Clinical Chemistry, University Hospital of Liege, University of Liege, Belgium. Etienne.cavalier@chu.ulg.ac.be

The role of vitamin D in maintaining bone health has been known for decades. Recently, however, the discovery that many tissues expressed the vitamin D receptor and were able to transform the 25-OH vitamin D into its most active metabolite, 1,25-(OH)(2) vitamin D, has led to a very promising future for this "old" molecule. Indeed, observational studies, and more and more interventional studies, are raising the importance of a significant vitamin D supplementation for not-only skeletal benefits. Among them, 25-OH vitamin D has been found to play an important role in prevention of cancers, auto-immune diseases, cardiovascular diseases, diabetes, and infections. Vitamin D deficiency, defined as serum 25-OH vitamin D levels <30 ng/mL, is very common in our population. The cost/benefit ratio and some recently published studies are clearly now in favor of a controlled and efficient vitamin D supplementation in these patients presenting a 25-OH vitamin D level <30 ng/mL. More attention should also be focused on pregnant and lactating women, as well as children and adolescents.

-----

Photochem Photobiol. 2009 Nov-Dec;85(6):1480-4.

Vitamin D level in summer and winter related to measured UVR exposure and behavior.

Thieden E, Philipsen PA, Heydenreich J, Wulf HC.

Department of Dermatology, Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark. et01@bbh.regionh.dk

The influence of the summer UVR exposure on serum-25-hydroxyvitamin D (25(OH)D) in late summer and winter was investigated in an open study on 25 healthy, adult volunteers. The UVR exposure dose in standard erythema dose (SED) was monitored continuously during a summer season with personal, electronic wristwatch UVR dosimeters and sun exposure diaries. Constitutive and facultative skin pigmentation was measured in September. 25(OH)D was measured in September and February and was in mean 82 nmol/L +/- 25 (mean +/- SD) in September and 56 nmol/L +/- 19 (mean +/- SD) in February. The received cumulative UVR dose measured during a mean of 121 days was 156 SED +/- 159 (mean +/- SD). The following UVR exposure parameters correlated with 25(OH)D in September and February, respectively: (1) The cumulative UVR dose (r = 0.53; P < 0.01) and (r = 0.43; P = 0.03); (2) Mean daily hours with UVR measurements monitored by the dosimeter (r = 0.64, P = 0.001) and (r = 0.53; P = 0.007); (3) Days "with sun-exposed upper body" (r = 0.58, P = 0.003) and (r = 0.50; P = 0.01); (4) Facultative pigmentation (r = 0.47; P < 0.02) and (r = 0.7; P < 0.001); (5) Constitutive pigmentation (r = 0.06, r = 0.08). Neither days "sunbathing" nor days with "sunscreen applied" correlated with 25(OH)D. The fall in 25(OH)D during winter was dependent on the entry value.

-----

Mol Aspects Med. 2008 Dec;29(6):407-14.

Vitamin D and skeletal muscle tissue and function.

#### Ceglia L.

Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Bone Metabolism Laboratory, 711 Washington Street, Boston, MA 02111, USA. lisa.ceglia@tufts.edu

This review aims to summarize current knowledge on the role of vitamin D in skeletal muscle tissue and function. Vitamin D deficiency can cause a myopathy of varying severity. Clinical studies have indicated that vitamin D status is positively associated with muscle strength and physical performance and inversely associated with risk of falling. Vitamin D supplementation has shown to improve tests of muscle function, reduce falls, and possibly impact on muscle fiber composition and morphology in vitamin D deficient older adults. Molecular mechanisms of vitamin D action on muscle tissue include genomic and non-genomic effects via a receptor present in muscle cells. Genomic effects are initiated

by binding of 1,25-dihydroxyvitamin D [1,25(OH)(2)D] to its nuclear receptor, which results in changes in gene transcription of mRNA and subsequent protein synthesis. Non-genomic effects of vitamin D are rapid and mediated through a cell surface receptor. Knockout mouse models of the vitamin D receptor provide insight into understanding the direct effects of vitamin D on muscle tissue. Recently, VDR polymorphisms have been described to affect muscle function. Parathyroid hormone which is strongly linked with vitamin D status also may play a role in muscle function; however, distinguishing its role from that of vitamin D has yet to be fully clarified. Despite the enormous advances in recent decades, further research is needed to fully characterize the exact underlying mechanisms of vitamin D action on muscle tissue and to understand how these cellular changes translate into clinical improvements in physical performance.

-----

Osteoporos Int. 2009 Mar;20(3):417-25.

Relationship between vitamin D status, body composition and physical exercise of adolescent girls in Beijing.

Foo LH, Zhang Q, Zhu K, Ma G, Trube A, Greenfield H, Fraser DR.

Faculty of Veterinary Science, University of Sydney, Sydney, NSW, Australia. lhfoo@kb.usm.my

Little is known about the prevalence of actual vitamin D deficiency in healthy school-aged adolescents, particularly in China. The aim of this study was to examine the prevalence of hypovitaminosis D and to identify whether there was any association between vitamin D status, body composition and physical exercise in 323 Chinese adolescent girls in Beijing, China (40 degrees N). INTRODUCTION: It is well recognized that persistent severe vitamin D deficiency is associated with the bone abnormalities of rickets and osteomalacia. However, there is now evidence suggesting that low vitamin D status, not previously considered to be a state of deficiency is associated with secondary hyperparathyroidism, increased bone remodelling and other clinical signs thought only to be found in severe vitamin D deficiency. Hypovitaminosis D in healthy children and adolescents has been reported frequently in many countries, especially in winter. METHODS: We performed a cross-sectional analysis of 323 Chinese adolescent girls in Beijing in winter. Mean age of the subjects was 15.0 (+/-0.4) years. About 32.8%, 68.4% and 89.2% of the subjects were at risk of vitamin D deficiency when defined as plasma concentrations of 25OHD of 25, 37.5 or 50 nmol/L, respectively. RESULTS: This cross-sectional analysis of 323 Chinese adolescent girls in Beijing in winter showed that hypovitaminosis D was

common in these subjects. In addition, body mass index, milk intake, participation in organized sports and total physical activity were all significant independent determinants of vitamin D status. An inverse association was found between plasma 25OHD and intact-parathyroid hormone (iPTH) concentration. Body mass index (BMI), milk intake, participation in organized sports and total physical activity all emerged as major independent determinants of vitamin D status as assessed by plasma 25OHD concentration. Vitamin D status was positively associated with lean body mass (LBM), but there was no association with the degree of body adiposity. Regardless of the concentration of 25OHD in blood used to define vitamin D deficiency, hypovitaminosis D was common in these subjects. CONCLUSION: It is recommended that policies be developed to prevent vitamin D deficiency in adolescent girls. Further studies are needed to identify the mechanisms whereby vitamin D status is related to exercise and to body composition during growth.

-----

Ugeskr Laeger. 2008 Sep 29;170(40):3138-9.

[Stress fracture in female athlete runner carrying weights]

Olesen UK, Lauritzen JB.

Ortopaedkirurgisk Afdeling M, Bispebjerg Hospital, DK-2400 København NV. ulrik@instruksen.dk

Comment in:

Ugeskr Laeger. 2008 Oct 20;170(43):3447; author reply 3448.

A 32-year old female athlete was referred with a femoral neck fracture. She practiced intensive cycling and running while carrying weights. The fracture had been overlooked on multiple occasions. She suffered from underweight, Vitamin D deficiency, ammenorhea and osteopenia.

-----

Mol Aspects Med. 2008 Dec;29(6):361-8.

The vitamin D deficiency pandemic and consequences for nonskeletal health: mechanisms of action.

Holick MF.

Department of Medicine, Section of Endocrinology, Nutrition, and Diabetes, Vitamin D, Skin and Bone Research Laboratory, Boston University Medical Center, Boston, MA, USA. mfholick@bu.edu

Vitamin D, the sunshine vitamin, is important for childhood bone health. Over the past two decades, it is now recognized that vitamin D not only is important for calcium metabolism and maintenance of bone health throughout life, but also plays an important role in reducing risk of many chronic diseases including type I diabetes, multiple sclerosis, rheumatoid arthritis, deadly cancers, heart disease and infectious diseases. How vitamin D is able to play such an important role in health is based on observation that all tissues and cells in the body have a vitamin D receptor, and, thus, respond to its active form 1,25-dihydroxyvitamin D. However, this did not explain how living at higher latitudes and being at risk of vitamin D deficiency increased risk of these deadly diseases since it was also known that the 1,25-dihydroxyvitamin D levels are normal or even elevated when a person is vitamin D insufficient. Moreover, increased intake of vitamin D or exposure to more sunlight will not induce the kidneys to produce more 1,25-dihydroxyvitamin D. The revelation that the colon, breast, prostate, macrophages and skin among other organs have the enzymatic machinery to produce 1,25-dihydroxyvitamin D provides further insight as to how vitamin D plays such an essential role for overall health and well being. This review will put into perspective many of the new biologic actions of vitamin D and on how 1,25-dihydroxyvitamin D is able to regulate directly or indirectly more than 200 different genes that are responsible for a wide variety of biologic processes.

-----

Am J Clin Nutr. 2007 Nov;86(5):1399-404.

Associations of diet, supplement use, and ultraviolet B radiation exposure with vitamin D status in Swedish women during winter.

Burgaz A, Akesson A, Oster A, Michaëlsson K, Wolk A.

Division of Nutritional Epidemiology, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden.

BACKGROUND: Vitamin D is produced endogenously after sun exposure but can also be obtained from natural food sources, food fortification, and dietary supplements. OBJECTIVE: We aimed to determine the vitamin D status of women (61-86 y old) living in central Sweden (latitude 60 degrees ) during winter and its relation with vitamin D intake and exposure to ultraviolet B radiation. DESIGN: In a cross-sectional study, we assessed the vitamin D status (serum 25-hydroxyvitamin D [25(OH)D]) of 116

women by using an enzyme immunoassay. The women completed questionnaires covering food habits, use of dietary supplements, and sun-related behavior. RESULTS: In a multiple linear regression model, the main determinants of serum 25(OH)D concentrations (x +/- SD: 69 +/- 23 mmol/L) were dietary vitamin D (6.0 +/- 1.8 mug/d), travel to a sunny location during winter within the previous 6 mo (26%), and the use of dietary supplements (16%). There was no association between serum 25(OH)D status during the winter and age, time spent outdoors, the use of sunscreen, or skin type. Serum 25(OH)D concentrations increased by 25.5 nmol/L with 2-3 servings (130 g/wk) fatty fish/wk, by 6.2 nmol/L with the daily intake of 300 g vitamin D-fortified reduced-fat dairy products, by 11.0 nmol/L with regular use of vitamin D supplements, and by 14.5 nmol/L with a sun vacation during winter. Among nonsupplement users without a wintertime sun vacation, 2-3 servings fatty fish/wk increased serum vitamin D concentrations by 45%. CONCLUSION: Fatty fish, vitamin D-fortified reduced-fat dairy products, regular supplement use, and taking a sun vacation are important predictors for serum concentrations of 25(OH)D during winter at a latitude of 60 degrees.

-----

Am J Clin Nutr. 2008 Dec;88(6):1535-42.

Estimation of the dietary requirement for vitamin D in healthy adults.

Cashman KD, Hill TR, Lucey AJ, Taylor N, Seamans KM, Muldowney S, Fitzgerald AP, Flynn A, Barnes MS, Horigan G, Bonham MP, Duffy EM, Strain JJ, Wallace JM, Kiely M.

Department of Food and Nutritional Sciences, University College, Cork, Ireland. k.cashman@ucc.ie

Comment in:

Am J Clin Nutr. 2009 Oct;90(4):1114-5; author reply 1115-6.

BACKGROUND: Knowledge gaps have contributed to considerable variation among international dietary recommendations for vitamin D. OBJECTIVE: We aimed to establish the distribution of dietary vitamin D required to maintain serum 25-hydroxyvitamin D [25(OH)D] concentrations above several proposed cutoffs (ie, 25, 37.5, 50, and 80 nmol/L) during wintertime after adjustment for the effect of summer sunshine exposure and diet. DESIGN: A randomized, placebo-controlled, double-blind 22-wk intervention study was conducted in men and women aged 20-40 y (n = 238) by using different supplemental doses (0, 5, 10, and 15 microg/d) of vitamin D(3) throughout the winter. Serum 25(OH)D concentrations were measured by using enzyme-linked immunoassay at baseline (October 2006) and

endpoint (March 2007). RESULTS: There were clear dose-related increments (P < 0.0001) in serum 25(OH)D with increasing supplemental vitamin D(3). The slope of the relation between vitamin D intake and serum 25(OH)D was 1.96 nmol x L(-1) x microg(-1) intake. The vitamin D intake that maintained serum 25(OH)D concentrations of >25 nmol/L in 97.5% of the sample was 8.7 microg/d. This intake ranged from 7.2 microg/d in those who enjoyed sunshine exposure, 8.8 microg/d in those who sometimes had sun exposure, and 12.3 microg/d in those who avoided sunshine. Vitamin D intakes required to maintain serum 25(OH)D concentrations of >37.5, >50, and >80 nmol/L in 97.5% of the sample were 19.9, 28.0, and 41.1 microg/d, respectively. CONCLUSION: The range of vitamin D intakes required to ensure maintenance of wintertime vitamin D status [as defined by incremental cutoffs of serum 25(OH)D] in the vast majority (>97.5%) of 20-40-y-old adults, considering a variety of sun exposure preferences, is between 7.2 and 41.1 microg/d.

-----

J Clin Endocrinol Metab. 2007 Jun;92(6):2130-5.

Low vitamin D status despite abundant sun exposure.

Binkley N, Novotny R, Krueger D, Kawahara T, Daida YG, Lensmeyer G, Hollis BW, Drezner MK.

University of Wisconsin Osteoporosis Research Program, Madison, WI 53705, USA. nbinkley@wisc.edu

CONTEXT: Lack of sun exposure is widely accepted as the primary cause of epidemic low vitamin D status worldwide. However, some individuals with seemingly adequate UV exposure have been reported to have low serum 25-hydroxyvitamin D [25(OH)D] concentration, results that might have been confounded by imprecision of the assays used. OBJECTIVE: The aim was to document the 25(OH)D status of healthy individuals with habitually high sun exposure. SETTING: This study was conducted in a convenience sample of adults in Honolulu, Hawaii (latitude 21 degrees). PARTICIPANTS: The study population consisted of 93 adults (30 women and 63 men) with a mean (sem) age and body mass index of 24.0 yr (0.7) and 23.6 kg/m(2) (0.4), respectively. Their self-reported sun exposure was 28.9 (1.5) h/wk, yielding a calculated sun exposure index of 11.1 (0.7). MAIN OUTCOME MEASURES: Serum 25(OH)D concentration was measured using a precise HPLC assay. Low vitamin D status was defined as a circulating 25(OH)D concentration less than 30 ng/ml. RESULTS: Mean serum 25(OH)D concentration was 31.6 ng/ml. Using a cutpoint of 30 ng/ml, 51% of this population had low vitamin D status. The highest 25(OH)D concentration was 62 ng/ml. CONCLUSIONS: These data suggest that variable responsiveness to UVB radiation is evident among individuals, causing some to have low

vitamin D status despite abundant sun exposure. In addition, because the maximal 25(OH)D concentration produced by natural UV exposure appears to be approximately 60 ng/ml, it seems prudent to use this value as an upper limit when prescribing vitamin D supplementation.

-----

Prog Biophys Mol Biol. 2006 Sep;92(1):4-8.

Vitamin D physiology.

# Lips P.

Department of Endocrinology, VU University Medical Center, P.O. Box 7057, 1007 MB Amsterdam, Netherlands. p.lips@vumc.nl

Vitamin D3 is synthesized in the skin during summer under the influence of ultraviolet light of the sun, or it is obtained from food, especially fatty fish. After hydroxylation in the liver into 25-hydroxyvitamin D (25(OH)D) and kidney into 1,25-dihydroxyvitamin D (1,25(OH)2D), the active metabolite can enter the cell, bind to the vitamin D-receptor and subsequently to a responsive gene such as that of calcium binding protein. After transcription and translation the protein is formed, e.g. osteocalcin or calcium binding protein. The calcium binding protein mediates calcium absorption from the gut. The production of 1,25(OH)2D is stimulated by parathyroid hormone (PTH) and decreased by calcium. Risk factors for vitamin D deficiency are premature birth, skin pigmentation, low sunshine exposure, obesity, malabsorption and advanced age. Risk groups are immigrants and the elderly. Vitamin D status is dependent upon sunshine exposure but within Europe, serum 25(OH)D levels are higher in Northern than in Southern European countries. Severe vitamin D deficiency causes rickets or osteomalacia, where the new bone, the osteoid, is not mineralized. Less severe vitamin D deficiency causes an increase of serum PTH leading to bone resorption, osteoporosis and fractures. A negative relationship exists between serum 25(OH)D and serum PTH. The threshold of serum 25(OH)D, where serum PTH starts to rise is about 75nmol/l according to most surveys. Vitamin D supplementation to vitamin Ddeficient elderly suppresses serum PTH, increases bone mineral density and may decrease fracture incidence especially in nursing home residents. The effects of 1,25(OH)2D and the vitamin D receptor have been investigated in patients with genetic defects of vitamin D metabolism and in knock-out mouse models. These experiments have demonstrated that for active calcium absorption, longitudinal bone growth and the activity of osteoblasts and osteoclasts both 1,25(OH)2D and the vitamin D receptor are essential. On the other side, bone mineralization can occur by high ambient calcium concentration, so

by high doses of oral calcium or calcium infusion. The active metabolite 1,25(OH)2D has its effects through the vitamin D receptor leading to gene expression, e.g. the calcium binding protein or osteocalcin or through a plasma membrane receptor and second messengers such as cyclic AMP. The latter responses are very rapid and include the effects on the pancreas, vascular smooth muscle and monocytes. Muscle cells contain vitamin D receptor and several studies have demonstrated that serum 25(OH)D is related to physical performance. The active metabolite 1,25(OH)2D has an antiproliferative effect and downregulates inflammatory markers. Extrarenal synthesis of 1,25(OH)2D occurs under the influence of cytokines and is important for the paracrine regulation of cell differentiation and function. This may explain that vitamin D deficiency can play a role in the pathogenesis of auto-immune diseases such as multiple sclerosis and diabetes type 1, and cancer. In conclusion, the active metabolite 1,25(OH)2D has pleiotropic effects through the vitamin D receptor and vitamin D responsive elements of many genes and on the other side rapid non-genomic effects through a membrane receptor and second messengers. Active calcium absorption from the gut depends on adequate formation of 1,25(OH)2D and an intact vitamin D receptor. Bone mineralization mainly depends on ambient calcium concentration. Vitamin D metabolites may play a role in the prevention of auto-immune disease and cancer.

-----

Osteoporos Int. 2002 Mar;13(3):187-94.

Vitamin D and muscle function.

Pfeifer M, Begerow B, Minne HW.

Institute of Clinical Osteology Gustav Pommer and Clinic Der Füirstenhof, Bad Pyrmont, Germany. iko\_pyrmont@t-online.de

The aim of this review is to summarize current knowledge on the relation between vitamin D and muscle function. Molecular mechanisms of vitamin D action on muscle tissue have been known for many years and include genomic and non-genomic effects. Genomic effects are initiated by binding of 1,25-dihydroxyvitamin D3 (1,25(OH)2D) to its nuclear receptor, which results in changes in gene transcription of messenger RNA and subsequent protein synthesis. Non-genomic effects of vitamin D are rapid and mediated through a membrane-bound vitamin D receptor (VDR). Genetic variations in the VDR and the importance of VDR polymorphisms in the development of osteoporosis are still a matter of controversy and debate. Most recently, VDR polymorphisms have been described to affect muscle function. The skin has an enormous capacity for vitamin D production and supplies the body with 80-100% of its

requirements of vitamin D. Age, latitude, time of day, season of the year and pigmentation can dramatically affect the production of vitamin D in the skin. Hypovitaminosis D is a common feature in elderly people living in northern latitudes and skin coverage has been established as an important factor leading to vitamin D deficiency. A serum 25-hydroxyvitamin D level below 50 nmol/l has been associated with increased body sway and a level below 30 nmol/l with decreased muscle strength. Changes in gait, difficulties in rising from a chair, inability to ascend stairs and diffuse muscle pain are the main clinical symptoms in osteomalacic myopathy. Calcium and vitamin D supplements together might improve neuromuscular function in elderly persons who are deficient in calcium and vitamin D. Thus 800 IU of cholecalciferol in combination with mg of elemental calcium reduces hip fractures and other nonvertebral fractures and should generally be recommended in individuals who are deficient in calcium and vitamin D. Given the strong interdependency of vitamin D deficiency, low serum calcium and high levels of parathyroid hormone, however, it is difficult to identify exact mechanisms of action.

-----

Mol Aspects Med. 2008 Dec;29(6):361-8.

The vitamin D deficiency pandemic and consequences for nonskeletal health: mechanisms of action.

## Holick MF.

Department of Medicine, Section of Endocrinology, Nutrition, and Diabetes, Vitamin D, Skin and Bone Research Laboratory, Boston University Medical Center, Boston, MA, USA. mfholick@bu.edu

Vitamin D, the sunshine vitamin, is important for childhood bone health. Over the past two decades, it is now recognized that vitamin D not only is important for calcium metabolism and maintenance of bone health throughout life, but also plays an important role in reducing risk of many chronic diseases including type I diabetes, multiple sclerosis, rheumatoid arthritis, deadly cancers, heart disease and infectious diseases. How vitamin D is able to play such an important role in health is based on observation that all tissues and cells in the body have a vitamin D receptor, and, thus, respond to its active form 1,25-dihydroxyvitamin D. However, this did not explain how living at higher latitudes and being at risk of vitamin D deficiency increased risk of these deadly diseases since it was also known that the 1,25-dihydroxyvitamin D levels are normal or even elevated when a person is vitamin D insufficient. Moreover, increased intake of vitamin D or exposure to more sunlight will not induce the kidneys to produce more 1,25-dihydroxyvitamin D. The revelation that the colon, breast, prostate, macrophages

and skin among other organs have the enzymatic machinery to produce 1,25-dihydroxyvitamin D provides further insight as to how vitamin D plays such an essential role for overall health and well being. This review will put into perspective many of the new biologic actions of vitamin D and on how 1,25-dihydroxyvitamin D is able to regulate directly or indirectly more than 200 different genes that are responsible for a wide variety of biologic processes.

-----

Med Sci Sports Exerc. 2009 May;41(5):1102-10.

Athletic performance and vitamin D.

Cannell JJ, Hollis BW, Sorenson MB, Taft TN, Anderson JJ.

Atascadero State Hospital, Atascadero, CA 93422, USA. jcannell@dmhash.state.ca.us

PURPOSE: Activated vitamin D (calcitriol) is a pluripotent pleiotropic secosteroid hormone. As a steroid hormone, which regulates more than 1000 vitamin D-responsive human genes, calcitriol may influence athletic performance. Recent research indicates that intracellular calcitriol levels in numerous human tissues, including nerve and muscle tissue, are increased when inputs of its substrate, the prehormone vitamin D, are increased. METHODS: We reviewed the world's literature for evidence that vitamin D affects physical and athletic performance. RESULTS: Numerous studies, particularly in the German literature in the 1950s, show vitamin D-producing ultraviolet light improves athletic performance. Furthermore, a consistent literature indicates physical and athletic performance is seasonal; it peaks when 25-hydroxy-vitamin D [25(OH)D] levels peak, declines as they decline, and reaches its nadir when 25(OH)D levels are at their lowest. Vitamin D also increases the size and number of Type II (fast twitch) muscle fibers. Most cross-sectional studies show that 25(OH)D levels are directly associated with musculoskeletal performance in older individuals. Most randomized controlled trials, again mostly in older individuals, show that vitamin D improves physical performance. CONCLUSIONS: Vitamin D may improve athletic performance in vitamin D-deficient athletes. Peak athletic performance may occur when 25(OH)D levels approach those obtained by natural, full-body, summer sun exposure, which is at least 50 ng x mL(-1). Such 25(OH)D levels may also protect the athlete from several acute and chronic medical conditions.

-----

#### Should we be concerned about the vitamin D status of athletes?

## Willis KS, Peterson NJ, Larson-Meyer DE.

Department of Family and Consumer Sciences, University of Wyoming, Laramie, WY 82071, USA.

A surprisingly high prevalence of vitamin D insufficiency and deficiency has recently been reported worldwide. Although very little is known about vitamin D status among athletes, a few studies suggest that poor vitamin D status is also a problem in athletic populations. It is well recognized that vitamin D is necessary for optimal bone health, but emerging evidence is finding that vitamin D deficiency increases the risk of autoimmune diseases and nonskeletal chronic diseases and can also have a profound effect on human immunity, inflammation, and muscle function (in the elderly). Thus, it is likely that compromised vitamin D status can affect an athlete's overall health and ability to train (i.e., by affecting bone health, innate immunity, and exercise-related immunity and inflammation). Although further research in this area is needed, it is important that sports nutritionists assess vitamin D (as well as calcium) intake and make appropriate recommendations that will help athletes achieve adequate vitamin D status: serum 25(OH)D of at least 75 or 80 nmol/L. These recommendations can include regular safe sun exposure (twice a week between the hours of 10 a.m. and 3 p.m. on the arms and legs for 5-30 min, depending on season, latitude, and skin pigmentation) or dietary supplementation with 1,000-2,000 IU vitamin D3 per day. Although this is significantly higher than what is currently considered the adequate intake, recent research demonstrates these levels to be safe and possibly necessary to maintain adequate 25(OH)D concentrations.

-----

Eur J Clin Nutr. 2002 May;56(5):431-7.

The effect of conventional vitamin D(2) supplementation on serum 25(OH)D concentration is weak among peripubertal Finnish girls: a 3-y prospective study.

Lehtonen-Veromaa M, Möttönen T, Nuotio I, Irjala K, Viikari J.

Paavo Nurmi Centre, Sport and Exercise Medicine Unit, Department of Physiology, University of Turku, Turku, Finland.

OBJECTIVES: To study the effect of vitamin D supplementation and the impact of summer season on serum 25-hydroxyvitamin D (S-25(OH)D) in Finnish 9-15-y-old girls. DESIGN: Three-year follow-up study with vitamin D(2) supplementation using D(2) 10 microg daily from October to January for the first

and from October to February for the second winter as well as 20 microg daily from October to March for the third winter. SETTING: Paavo Nurmi Centre, University of Turku, Turku, Finland. SUBJECTS: A total of 171 female volunteers aged 9-15 y. METHODS: Vitamin D and calcium intakes were estimated by a semi-quantitative food frequency questionnaire (FFQ). S-25(OH)D was measured by radioimmunoassay. RESULTS: The median daily dietary intakes of vitamin D and calcium were 3.8 microg (interguartile range (IQR) 2.7-5.0) and 1451 mg (IQR 1196-1812), respectively, over 3 y. The prevalence of severe hypovitaminosis D (S-25(OH)D<20 nmol/l) was 14% and of moderate hypovitaminosis D (20 nmol/l < or = S-25(OH)D < or = 37.5 nmol/l) 75% at baseline in winter. None of the participants had severe hypovitaminosis D in summer. The effect of 10 microg of D(2) daily was insufficient to raise S-25(OH)D from baseline. The daily supplementation of 20 microg of D(2) increased S-25(OH)D significantly in wintertime compared with the non-supplement users (to 45.5 vs 31.8 nmol/l; P<0.001). None of the subjects with vitamin D(2) supplementation approximately 20 microg daily had severe hypovitaminosis D; however, 38% of those participants had moderate hypovitaminosis D at 36 months. Sun exposure in summer raised mean S-25(OH)D to 62.0 nmol/l. Both the daily supplementation of approximately 20 microg of D(2) and summer sunlight exposure had more effect on those who had severe hypovitaminosis than those who had a normal vitamin D status (increase of 24.2 vs 0.9 nmol/l (P<0.001), and 38.8 vs 18.2 nmol/l (P<0.001), respectively). CONCLUSION: Vitamin D supplementation daily with 20 microg is needed to prevent hypovitaminosis D in peripubertal Finnish girls in winter. Sunlight exposure in summer is more effective than approximately 20 microg of D(2) supplementation daily in winter to raise S-25(OH)D. Both the daily supplementation with 20 microg of D(2) and summertime sunlight exposure had more effect on those who had severe hypovitaminosis D than those who had a normal vitamin D status. SPONSORSHIP: Supported by the Yrjö Jahnsson Foundation and the Medical Research Foundation of the Turku University Central Hospital.

Note: 20 microg equals 800 IU. This is less than the 1200 IU of vitamin D in MVM, and MVM contains the more effective vitamin D3. See full information on MVM.

------

# References:

\_\_\_\_\_

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7447609/pdf/12967\_2020\_Article\_2488.pdf.

- <sup>2</sup> Kaufman HW, Niles JK, Kroll MH, Bi C, Holick MF. SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels. PLoS One. 2020 Sep 17;15(9):e0239252. doi: 10.1371/journal.pone.0239252. eCollection 2020. PMID: 32941512. Full paper in PDF format available at:
- https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0239252&type=printable.
- <sup>3</sup> Radujkovic A, Hippchen T, Tiwari-Heckler S, Dreher S, Boxberger M, Merle U. Vitamin D Deficiency and Outcome of COVID-19 Patients. Nutrients. 2020 Sep 10;12(9):E2757. doi: 10.3390/nu12092757. PMID: 32927735. Full paper available at: <a href="https://www.mdpi.com/2072-6643/12/9/2757/htm">https://www.mdpi.com/2072-6643/12/9/2757/htm</a>.
- <sup>4</sup> Meltzer DO, Best TJ, Zhang H, Vokes T, Arora V, Solway J. Association of Vitamin D Deficiency and Treatment with COVID-19 Incidence. medRxiv [Preprint]. 2020 May 13:2020.05.08.20095893. doi: 10.1101/2020.05.08.20095893. PMID: 32511549; PMCID: PMC7274230. Full paper in printer friendly format is available at: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7489852/?report=printable">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7489852/?report=printable</a>.
- <sup>5</sup> Demir M, Demir F, Aygun H. Vitamin D deficiency is associated with COVID-19 positivity and the severity of the disease. J Med Virol. 2021 Jan 29. doi: 10.1002/jmv.26832. Epub ahead of print. PMID: 33512007.
- <sup>6</sup> Meltzer DO, Best TJ, Zhang H, Vokes T, Arora V, Solway J. Association of Vitamin D Status and Other Clinical Characteristics With COVID-19 Test Results. JAMA Netw Open. 2020 Sep 1;3(9):e2019722. doi: 10.1001/jamanetworkopen.2020.19722. PMID: 32880651; PMCID: PMC7489852.
- <sup>7</sup> Benskin LL. A Basic Review of the Preliminary Evidence That COVID-19 Risk and Severity Is Increased in Vitamin D Deficiency. Front Public Health. 2020 Sep 10;8:513. doi: 10.3389/fpubh.2020.00513. PMID: 33014983; PMCID: PMC7513835. Full paper available at: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7513835/pdf/fpubh-08-00513.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7513835/pdf/fpubh-08-00513.pdf</a>.
- <sup>8</sup> Despland C, Gilliand M, Schaub C. Carence en vitamine D et immunité sous-optimale : un défi en période de Covid [Vitamin D deficiency and suboptimal immunity : A challenge during Covid pandemia]. Rev Med Suisse. 2021 Oct 6;17(753):1711-1716. French. PMID: 34614313.
- <sup>9</sup> Dror AA, Morozov N, Daoud A, Namir Y, Yakir O, Shachar Y, Lifshitz M, Segal E, Fisher L, Mizrachi M, Eisenbach N, Rayan D, Gruber M, Bashkin A, Kaykov E, Barhoum M, Edelstein M, Sela E. Pre-infection 25-hydroxyvitamin D3 levels and association with severity of COVID-19 illness. PLoS One. 2022 Feb 3;17(2):e0263069. doi: 10.1371/journal.pone.0263069. PMID: 35113901; PMCID: PMC8812897.
- <sup>10</sup> Grant WB, Lahore H, McDonnell SL, Baggerly CA, French CB, Aliano JL, Bhattoa HP. Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths. Nutrients. 2020 Apr 2;12(4). pii: E988. doi: 10.3390/nu12040988. Full paper in PDF format available at: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7231123/pdf/nutrients-12-00988.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7231123/pdf/nutrients-12-00988.pdf</a>.
- <sup>11</sup> McCartney DM, Byrne DG. Optimisation of Vitamin D Status for Enhanced Immuno-protection Against Covid-19. Ir Med J. 2020 Apr 3;113(4):58.
- <sup>12</sup> Caccialanza R, Laviano A, Lobascio F, Montagna E, Bruno R, Ludovisi S, Corsico AG, Di Sabatino A, Belliato M, Calvi M, Iacona I, Grugnetti G, Bonadeo E, Muzzi A, Cereda E. Early nutritional supplementation in non-critically ill patients hospitalized for the 2019 novel coronavirus disease (COVID-19): Rationale and feasibility of a shared pragmatic protocol. Nutrition. 2020 Apr 3:110835. doi: 10.1016/j.nut.2020.110835. [Epub ahead of print]
- <sup>13</sup> Panarese A, Shahini E. Letter: Covid-19, and vitamin D. Aliment Pharmacol Ther. 2020 May;51(10):993-995. doi: 10.1111/apt.15752. Epub 2020 Apr 12.

<sup>&</sup>lt;sup>1</sup> Xu Y, Baylink DJ, Chen CS, Reeves ME, Xiao J, Lacy C, Lau E, Cao H. The importance of vitamin d metabolism as a potential prophylactic, immunoregulatory and neuroprotective treatment for COVID-19. J Transl Med. 2020 Aug 26;18(1):322. doi: 10.1186/s12967-020-02488-5. PMID: 32847594. Full paper in PDF format available at:

- <sup>14</sup> Jakovac H. COVID-19 and vitamin D-Is there a link and an opportunity for intervention? Am J Physiol Endocrinol Metab. 2020 May 1;318(5):E589. doi: 10.1152/ajpendo.00138.2020.
- <sup>15</sup> Zhang J, Xie B, Hashimoto K. Current status of potential therapeutic candidates for the COVID-19 crisis. Brain Behav Immun. 2020 Apr 22. pii: S0889-1591(20)30589-4. doi: 10.1016/j.bbi.2020.04.046. [Epub ahead of print]
- <sup>16</sup> Ilie PC, Stefanescu S, Smith L. The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. Aging Clin Exp Res. 2020 May 6. doi: 10.1007/s40520-020-01570-8. [Epub ahead of print]
- <sup>17</sup> Calder PC, Carr AC, Gombart AF, Eggersdorfer M. Optimal Nutritional Status for a Well-Functioning Immune System Is an Important Factor to Protect against Viral Infections. Nutrients. 2020 Apr 23;12(4):E1181. doi: 10.3390/nu12041181.
- <sup>18</sup> Meltzer DO, Best TJ, Zhang H, Vokes T, Arora V, Solway J. Association of Vitamin D Status and Other Clinical Characteristics With COVID-19 Test Results. JAMA Netw Open. 2020;3(9):e2019722. doi:10.1001/jamanetworkopen.2020.19722. Full paper available at: <a href="https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770157">https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770157</a>.
- <sup>19</sup> Brenner H. Vitamin D Supplementation to Prevent COVID-19 Infections and Deaths-Accumulating Evidence from Epidemiological and Intervention Studies Calls for Immediate Action. Nutrients. 2021 Jan 28;13(2):411. doi: 10.3390/nu13020411. PMID: 33525447.
- <sup>20</sup> Dos Santos RN, Maeda SS, Jardim JR, Lazaretti-Castro M. Reasons to avoid vitamin D deficiency during COVID-19 pandemic. Arch Endocrinol Metab. 2021 May 18;64(5):498-506. doi: 10.20945/2359-399700000291. PMID: 34033288.
- <sup>21</sup> Sánchez-Zuno GA, González-Estevez G, Matuz-Flores MG, Macedo-Ojeda G, Hernández-Bello J, Mora-Mora JC, Pérez-Guerrero EE, García-Chagollán M, Vega-Magaña N, Turrubiates-Hernández FJ, Machado-Sulbaran AC, Muñoz-Valle JF. Vitamin D Levels in COVID-19 Outpatients from Western Mexico: Clinical Correlation and Effect of Its Supplementation. J Clin Med. 2021 May 28;10(11):2378. doi: 10.3390/jcm10112378. PMID: 34071293.
- Peng MY, Liu WC, Zheng JQ, Lu CL, Hou YC, Zheng CM, Song JY, Lu KC, Chao YC. Immunological Aspects of SARS-CoV-2 Infection and the Putative Beneficial Role of Vitamin-D. Int J Mol Sci. 2021 May 16;22(10):5251. doi: 10.3390/ijms22105251. PMID: 34065735.
- <sup>23</sup> Bui L, Zhu Z, Hawkins S, Cortez-Resendiz A, Bellon A. Vitamin D regulation of the immune system and its implications for COVID-19: A mini review. SAGE Open Med. 2021 May 18; 9:20503121211014073. doi: 10.1177/20503121211014073. PMID: 34046177; PMCID: PMC8135207.
- <sup>24</sup> Mengozzi M, Hesketh A, Bucca G, Ghezzi P, Smith CP. Vitamins D3 and D2 have marked but different global effects on gene expression in a rat oligodendrocyte precursor cell line. Mol Med. 2020 Apr 9;26(1):32. doi: 10.1186/s10020-020-00153-7. PMID: 32272884; PMCID: PMC7146914.
- Louise R. Durrant, Giselda Bucca, Andrew Hesketh, Carla Möller-Levet, Laura Tripkovic, Huihai Wu, Kathryn H. Hart, John C. Mathers, Ruan M. Elliott, Susan A. Lanham-New, Colin P. Smith. Vitamins D2 and D3 Have Overlapping But Different Effects on the Human Immune System Revealed Through Analysis of the Blood Transcriptome. Frontiers in Immunology, 2022; 13 DOI: 10.3389/fimmu.2022.790444
- Wessels I, Rolles B, Rink L. The Potential Impact of Zinc Supplementation on COVID-19 Pathogenesis. Front Immunol. 2020 Jul 10;11:1712. doi: 10.3389/fimmu.2020.01712. eCollection 2020. PMID: 32754164,
- <sup>27</sup> Alexander J, Tinkov A, Strand TA, Alehagen U, Skalny A, Aaseth J.Early Nutritional Interventions with Zinc, Selenium and Vitamin D for Raising Anti-Viral Resistance Against Progressive COVID-19. Nutrients. 2020 Aug 7;12(8):E2358. doi: 10.3390/nu12082358. PMID: 32784601.
- Shakoor H, Feehan J, Al Dhaheri AS, Ali HI, Platat C, Ismail LC, Apostolopoulos V, Stojanovska L. Immune-boosting role of vitamins D, C, E, zinc, selenium and omega-3 fatty acids: Could they help against COVID-19? Maturitas. 2021 Jan;143:1–9. doi: 10.1016/j.maturitas.2020.08.003. Epub 2020 Aug 9. PMCID: PMC7415215. Full paper in PDF format available at: <a href="https://www.maturitas.org/action/showPdf?pii=S0378-5122%2820%2930346-7">https://www.maturitas.org/action/showPdf?pii=S0378-5122%2820%2930346-7</a>.

- <sup>29</sup> Calder PC, Carr AC, Gombart AF, Eggersdorfer M. Optimal Nutritional Status for a Well-Functioning Immune System Is an Important Factor to Protect against Viral Infections. Nutrients. 2020 Apr 23;12(4):E1181. doi: 10.3390/nu12041181.
- <sup>30</sup> Grant WB, Lahore H, Rockwell MS. The Benefits of Vitamin D Supplementation for Athletes: Better Performance and Reduced Risk of COVID-19. Nutrients. 2020 Dec 4;12(12):3741. doi: 10.3390/nu12123741. PMID: 33291720; PMCID: PMC7761895.
- <sup>31</sup> Kawashima I, Tsukahara T, Kawai R, Mizuno T, Ishizuka S, Hiraiwa H, Imagama S. The impact of vitamin D supplementation on body fat mass in elite male collegiate athletes. Nutr Metab (Lond). 2021 May 21;18(1):51. doi: 10.1186/s12986-021-00578-9. PMID: 34020679; PMCID: PMC8138511.
- <sup>32</sup> Moukayed M, Grant WB. Linking the metabolic syndrome and obesity with vitamin D status: risks and opportunities for improving cardiometabolic health and well-being. Diabetes Metab Syndr Obes. 2019 Aug 16;12:1437-1447. doi: 10.2147/DMSO.S176933. PMID: 31496777; PMCID: PMC6701609.
- <sup>33</sup> Dibaba DT. Effect of vitamin D supplementation on serum lipid profiles: a systematic review and metaanalysis. Nutr Rev. 2019 Dec 1;77(12):890-902. doi: 10.1093/nutrit/nuz037. PMID: 31407792.
- <sup>34</sup> Fan X, Wang J, Song M, Giovannucci EL, Ma H, Jin G, Hu Z, Shen H, Hang D. Vitamin D Status and Risk of All-Cause and Cause-Specific Mortality in a Large Cohort: Results From the UK Biobank. J Clin Endocrinol Metab. 2020 Oct 1;105(10):dgaa432. doi: 10.1210/clinem/dgaa432. PMID: 32620963.
- <sup>35</sup> Ellison DL, Moran HR. Vitamin D: Vitamin or Hormone? Nurs Clin North Am. 2021 Mar;56(1):47-57. doi: 10.1016/j.cnur.2020.10.004. Epub 2020 Dec 28. PMID: 33549285.
- <sup>36</sup> Kusunose K, Okushi Y, Okayama Y, Zheng R, Abe M, Nakai M, Sumita Y, Ise T, Tobiume T, Yamaguchi K, Yagi S, Fukuda D, Yamada H, Soeki T, Wakatsuki T, Sata M. Association between Vitamin D and Heart Failure Mortality in 10,974 Hospitalized Individuals. Nutrients. 2021 Jan 23;13(2):335. doi: 10.3390/nu13020335. PMID: 33498709; PMCID: PMC7911510.
- <sup>37</sup> Boughanem H, Toledo E, Sorlí JV, Estruch R, Castañer O, Lapetra J, Alonso-Gómez AM, Gutiérrez-Bedmar M, Fiol M, Serra-Majem L, Pintó X, Ros E, Fernandez-Lazaro CI, Ramirez-Sabio JB, Fitó M, Portu-Zapirain J, Macias-González M, Babio N, Salas-Salvadó J. Dietary vitamin D intake and colorectal cancer risk: a longitudinal approach within the PREDIMED study. Eur J Nutr. 2021 May 28. doi: 10.1007/s00394-021-02585-1. Epub ahead of print. PMID: 34050394.
- <sup>38</sup> Sizar O, Khare S, Goyal A, Bansal P, Givler A. Vitamin D Deficiency. 2021 Jul 21. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan—. PMID: 30335299.
- <sup>39</sup> Lu Q, Wan Z, Guo J, Liu L, Pan A, Liu G. Association Between Serum 25-hydroxyvitamin D Concentrations and Mortality Among Adults With Prediabetes. J Clin Endocrinol Metab. 2021 Sep 27;106(10):e4039-e4048. doi: 10.1210/clinem/dgab402. PMID: 34089603.
- <sup>40</sup> Ganmaa D, Enkhmaa D, Nasantogtokh E, Sukhbaatar S, Tumur-Ochir KE, Manson JE. Vitamin D, respiratory infections, and chronic disease: Review of meta-analyses and randomized clinical trials. J Intern Med. 2021 Sep 19. doi: 10.1111/joim.13399. Epub ahead of print. PMID: 34537990.
- <sup>41</sup> Dai L, Liu M, Chen L. Association of Serum 25-Hydroxyvitamin D Concentrations With All-Cause and Cause-Specific Mortality Among Adult Patients With Existing Cardiovascular Disease. Front Nutr. 2021 Sep 23;8:740855. doi: 10.3389/fnut.2021.740855. PMID: 34631770; PMCID: PMC8496747.
- <sup>42</sup> Cosentino N, Campodonico J, Milazzo V, De Metrio M, Brambilla M, Camera M, Marenzi G. Vitamin D and Cardiovascular Disease: Current Evidence and Future Perspectives. Nutrients. 2021 Oct 14;13(10):3603. doi: 10.3390/nu13103603. PMID: 34684604; PMCID: PMC8541123.
- <sup>43</sup> Dimitrov V, Barbier C, Ismailova A, Wang Y, Dmowski K, Salehi-Tabar R, Memari B, Groulx-Boivin E, White JH. Vitamin D-regulated Gene Expression Profiles: Species-specificity and Cell-specific Effects on Metabolism and Immunity. Endocrinology. 2021 Feb 1;162(2):bqaa218. doi: 10.1210/endocr/bqaa218. PMID: 33249469; PMCID: PMC7751191.
- <sup>44</sup> Ribbans WJ, Aujla R, Dalton S, Nunley JA. Vitamin D and the athlete-patient: state of the art. J ISAKOS. 2021 Jan;6(1):46-60. doi: 10.1136/jisakos-2020-000435. Epub 2020 Nov 13. PMID: 33833045.
- <sup>45</sup> Lips P. Worldwide status of vitamin D nutrition. J Steroid Biochem Mol Biol. 2010;121:297–300.
- <sup>46</sup> Menon AS, Kapoor R, Anayath S, Garg MK. Vitamin D, body mass composition and metabolic risk factors in healthy young Indians. Med J Armed Forces India. 2021 Oct;77(4):485-489. doi: 10.1016/j.mjafi.2020.05.011. Epub 2020 Jul 31. PMID: 34594080; PMCID: PMC8459086.

- <sup>47</sup> Wacker M, Holick MF. Sunlight and Vitamin D: A global perspective for health. Dermatoendocrinol. 2013 Jan 1;5(1):51-108.
- <sup>48</sup> Holman DM, Ding H, Guy GP Jr, Watson M, Hartman AM, Perna FM. Prevalence of Sun Protection Use and Sunburn and Association of Demographic and Behaviorial Characteristics With Sunburn Among US Adults. JAMA Dermatol. 2018 May 1;154(5):561-568.Full paper available at: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5876912/?report=printable.">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5876912/?report=printable.</a>
- <sup>49</sup> de Troya-Martín M, de Gálvez-Aranda MV, Rivas-Ruiz F, Blázquez-Sánchez N, Fernández-Morano MT, Padilla-España L, Herrera-Ceballos E. Prevalence and predictors of sunburn among beachgoers. Photodermatol Photoimmunol Photomed. 2018 Mar;34(2):122-129.
- <sup>50</sup> Patel AR, Zaslow TL, Wren TAL, Daoud AK, Campbell K, Nagle K, Coel RA. A characterization of sun protection attitudes and behaviors among children and adolescents in the United States. Prev Med Rep. 2019 Sep 9;16:100988. doi: 10.1016/j.pmedr.2019.100988. eCollection 2019 Dec. Full paper available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6807366/pdf/main.pdf.
- <sup>51</sup> DeFlorio-Barker S, Holman D, Landolfi R, Arnold BF, Colford JM Jr, Weisberg SB, Schiff KC, Sams EA, Wade TJ. Incidence and public health burden of sunburn among beachgoers in the United States. Prev Med. 2020 May;134:106047. doi: 10.1016/j.ypmed.2020.106047.
- <sup>52</sup> Scott JF, Lu KQ. Vitamin D as a Therapeutic Option for Sunburn: Clinical and Biologic Implications. DNA Cell Biol. 2017 Nov;36(11):879-882. Full paper in PDF format available at: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5684656/pdf/dna.2017.3978.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5684656/pdf/dna.2017.3978.pdf</a>.
- Lopa M. Das, Amy M. Binko, Zachary P. Traylor, Han Peng, Kurt Q. Lu. Vitamin D improves sunburns by increasing autophagy in M2 macrophages. Autophagy. 2019; 15(5): 813–826. Full paper in PDF format available at: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6526871/pdf/kaup-15-05-1569298.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6526871/pdf/kaup-15-05-1569298.pdf</a>.
- <sup>54</sup> Granger C, Aladren S, Delgado J, Garre A, Trullas C, Gilaberte Y. Prospective Evaluation of the Efficacy of a Food Supplement in Increasing Photoprotection and Improving Selective Markers Related to Skin Photo-Ageing. Dermatol Ther (Heidelb). 2020 Feb;10(1):163-178. Full paper in PDF format available at:
  - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6994571/pdf/13555 2019 Article 345.pdf.
- <sup>55</sup> Ng QX, De Deyn MLZQ, Loke W, Foo NX, Chan HW, Yeo WS. Effects of Astaxanthin Supplementation on Skin Health: A Systematic Review of Clinical Studies. J Diet Suppl. 2020 Mar 23:1-14.
- <sup>56</sup> Seidll E, Hettinger T. Influence of vitamin D3 on strength and efficiency of healthy adults. Int Z Angew Physiol. 1957;16(5):365-72.
- <sup>57</sup> Abrams GD, Feldman D, Safran MR. Effects of Vitamin D on Skeletal Muscle and Athletic Performance. J Am Acad Orthop Surg. 2018 Apr 15;26(8):278-285.
- <sup>58</sup> Ksiazek A, Zagrodna A, Slowinska-Lisowska M. Vitamin D, Skeletal Muscle Function and Athletic Performance in Athletes-A Narrative Review. Nutrients. 2019 Aug 4;11(8). pii: E1800. doi: 10.3390/nu11081800.
- <sup>59</sup> de la Puente Yagüe M, Collado Yurrita L, Ciudad Cabañas MJ, Cuadrado Cenzual MA. Role of Vitamin D in Athletes and Their Performance: Current Concepts and New Trends. Nutrients. 2020 Feb 23;12(2). pii: E579. doi: 10.3390/nu12020579.
- <sup>60</sup> Knechtle B, Nikolaidis PT. Vitamin D and Sport Performance. Nutrients. 2020 Mar 21;12(3). pii: E841. doi: 10.3390/nu12030841.
- <sup>61</sup> Li WX, Qin XH, Poon CC, Wong MS, Feng R, Wang J, Lin FH, Sun YL, Liu SF, Wang YJ, Zhang Y. Vitamin D/Vitamin D Receptor Signaling Attenuates Skeletal Muscle Atrophy by Suppressing Renin-Angiotensin System. J Bone Miner Res. 2021 Sep 7. doi: 10.1002/jbmr.4441. Epub ahead of print. PMID: 34490953.
- <sup>62</sup> Şenişik S, Köyağasıoğlu O, Denerel N. Vitamin D levels on sports injuries in outdoor and indoor athletes: a cross-sectional study. Phys Sportsmed. 2021 Aug 23:1-7. doi: 10.1080/00913847.2021.1969217. Epub ahead of print. PMID: 34402729.
- <sup>63</sup> Caballero-García A, Córdova-Martínez A, Vicente-Salar N, Roche E, Pérez-Valdecantos D. Vitamin D, Its Role in Recovery after Muscular Damage Following Exercise. Nutrients. 2021 Jul 8;13(7):2336. doi: 10.3390/nu13072336. PMID: 34371846; PMCID: PMC8308579.

- <sup>64</sup> Hamilton B. Vitamin D and human skeletal muscle. Scand J Med Sci Sports. 2010 Apr;20(2):182-90. doi: 10.1111/j.1600-0838.2009.01016.x. Epub 2009 Oct 5. PMID: 19807897; PMCID: PMC2860762.
- <sup>65</sup> Şenişik S, Köyağasıoğlu O, Denerel N. Vitamin D levels on sports injuries in outdoor and indoor athletes: a cross-sectional study. Phys Sportsmed. 2021 Aug 23:1-7. doi: 10.1080/00913847.2021.1969217. Epub ahead of print. PMID: 34402729.
- <sup>66</sup> Cannell JJ, Hollis BW, Sorenson MB, Taft TN, Anderson JJ. Athletic performance and vitamin D. Med Sci Sports Exerc. 2009 May;41(5):1102-10. doi: 10.1249/MSS.0b013e3181930c2b. PMID: 19346976.
- <sup>67</sup> Kawashima I, Tsukahara T, Kawai R, Mizuno T, Ishizuka S, Hiraiwa H, Imagama S. The impact of vitamin D supplementation on body fat mass in elite male collegiate athletes. Nutr Metab (Lond). 2021 May 21;18(1):51. doi: 10.1186/s12986-021-00578-9. PMID: 34020679; PMCID: PMC8138511.
- <sup>68</sup> Bjerg LN, Halgreen JR, Hansen SH, Morris HA, Jørgensen NR. An evaluation of total 25hydroxyvitamin D assay standardization: Where are we today? J Steroid Biochem Mol Biol. 2019 Jun;190:224-233.
- <sup>69</sup> Altieri B, Cavalier E, Bhattoa HP, Pérez-López FR, López-Baena MT, Pérez-Roncero GR, Chedraui P, Annweiler C, Della Casa S, Zelzer S, Herrmann M, Faggiano A, Colao A, Holick MF. Vitamin D testing: advantages and limits of the current assays. Eur J Clin Nutr. 2020 Feb;74(2):231-247.
- Vermeer C, Shearer MJ, Zittermann A, Bolton-Smith C, Szulc P, Hodges S, Walter P, Rambeck W, Stöcklin E, Weber P. Beyond deficiency: potential benefits of increased intakes of vitamin K for bone and vascular health. Eur J Nutr. 2004 Dec;43(6):325-35.
- <sup>71</sup> Cranenburg EC, Schurgers LJ, Vermeer C. Vitamin K: the coagulation vitamin that became omnipotent. Thromb Haemost. 2007 Jul;98(1):120-5.
- <sup>72</sup> Hamidi MS, Cheung AM. Vitamin K and musculoskeletal health in postmenopausal women. Mol Nutr Food Res. 2014 Aug;58(8):1647-57.
- <sup>73</sup> Hamidi MS, Gajic-Veljanoski O, Cheung AM. Vitamin K and bone health. J Clin Densitom. 2013 Oct-Dec;16(4):409-13.
- <sup>74</sup> Campbell AW. Vitamin K2 in the Prevention of Cardiovascular Diseases and Diabetes. Altern Ther Health Med. 2017 Mar;23(2):8-10.
- <sup>75</sup> Halder M, Petsophonsakul P, Akbulut AC, Pavlic A, Bohan F, Anderson E, Maresz K, Kramann R, Schurgers L. Vitamin K: Double Bonds beyond Coagulation Insights into Differences between Vitamin K1 and K2 in Health and Disease. Int J Mol Sci. 2019 Feb 19;20(4).
- <sup>76</sup> Xv F, Chen J, Duan L, Li S. Research progress on the anticancer effects of vitamin K2. Oncol Lett. 2018 Jun;15(6):8926-8934.
- <sup>77</sup> Kuang X, Liu C, Guo X, Li K, Deng Q, Li D. The combination effect of vitamin K and vitamin D on human bone quality: a meta-analysis of randomized controlled trials. Food Funct. 2020 Apr 30;11(4):3280-3297.
- <sup>78</sup> Vos M, Esposito G, Edirisinghe JN, Vilain S, Haddad DM, Slabbaert JR, Van Meensel S, Schaap O, De Strooper B, Meganathan R, Morais VA, Verstreken P. Vitamin K2 is a mitochondrial electron carrier that rescues pink1 deficiency. Science. 2012 Jun 8;336(6086):1306-10.
- <sup>79</sup> Myneni VD, Mezey E. Immunomodulatory effect of vitamin K2: Implications for bone health. Oral Dis. 2018 Mar;24(1-2):67-71.
- <sup>80</sup> van Ballegooijen AJ, Cepelis A, Visser M, Brouwer IA, van Schoor NM, Beulens JW. Joint Association of Low Vitamin D and Vitamin K Status With Blood Pressure and Hypertension. Hypertension. 2017 Jun;69(6):1165-1172.
- <sup>81</sup> Mayer O Jr, Seidlerová J, Wohlfahrt P, Filipovský J, Cífková R, Cerná V, Kucerová A, Pešta M, Fuchsová R, Topolcan O, Jardon KMC, Drummen NEA, Vermeer C. Synergistic effect of low K and D vitamin status on arterial stiffness in a general population. J Nutr Biochem. 2017 Apr 22;46:83-89.
- <sup>82</sup> Mozos I, Stoian D, Luca CT. Crosstalk between Vitamins A, B12, D, K, C, and E Status and Arterial Stiffness. Dis Markers. 2017; 8784971. Epub 2017 Jan 12.
- <sup>83</sup> Cardwell G, Bornman JF, James AP, Black LJ. A Review of Mushrooms as a Potential Source of Dietary Vitamin D. Nutrients. 2018 Oct 13;10(10). pii: E1498. doi: 10.3390/nu10101498.
- <sup>84</sup> Hu D, Chen W, Li X, Yue T, Zhang Z, Feng Z, Li C, Bu X, Li QX, Hu CY, Li L. Ultraviolet Irradiation Increased the Concentration of Vitamin D2 and Decreased the Concentration of Ergosterol in Shiitake

Mushroom (Lentinus edodes) and Oyster Mushroom (Pleurotus ostreatus) Powder in Ethanol Suspension. ACS Omega. 2020 Mar 23;5(13):7361-7368.

<sup>85</sup> Uwitonze AM, Razzaque MS. Role of Magnesium in Vitamin D Activation and Function. J Am Osteopath Assoc. 2018 Mar 1;118(3):181-189.