

Vitamin D Deficiency and Its Impact On The Immune System

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1. Introduction

It is now widely accepted that Vitamin D deficiency is a global health concern, affecting over a *billion* people worldwide. And, although there's much debate as to what defines sufficient vitamin D levels, most medical experts agree that a "circulating level of 25-hydroxyvitamin D of >75 nmol/L, or 30 ng/mL, is required to maximize the vitamin D beneficial effects for health."¹ As I've noted, the methods for defining adequate Vitamin D levels do differ. For instance, found inside the pages of *Aging and Disease*, a peer reviewed medical journal, a Vitamin D deficiency is suggested "if the level of 25 (OH)D in circulating blood in humans is less than or equal to 20 ng/mL (50 nmol/L)."²

Vitamin D has long been known for its promotion of calcium absorption, and bone health. But along with that, it has also been shown to help reduce inflammation, encourage cell growth, strengthen immune functions, and even *prevent cancers*.³ In this paper we'll discuss some of the unique characteristics that make Vitamin D different than most other Vitamins. We'll also look at Vitamin D deficiency, and some of its causes and symptoms. In recent years, increasing evidence has documented the correlation with the progression of chronic diseases and 25(OH) D deficiency— "Studies suggest vitamin D deficiency may be a contributor to the development of cardiovascular disease potentially through associations with diabetes or hypertension."⁴

My efforts in writing this paper is to shed light on the importance of vitamin D and its role in optimizing a healthy immune system. I'll cover both the **innate** and **adaptive** levels of defense that make up the human immune system. And how this complex system, if properly functioning, can recognize invading pathogens, prevent their spread, and eliminate them from your body. Indeed, Vitamin D plays an important role in supporting this process. Without a healthy immune system, the human body is vulnerable to a variety of infections, diseases, cancers, and ultimately death. We'll also discuss the safety and effectiveness of Vitamin D supplementation. I hope that by the end of this paper, there is a better understanding of the human immune system, as well as a deeper appreciation toward how important a healthy, functioning immune system is. Also, the vital role Vitamin D plays in making sure your immune system is strong, and well nourished—optimizing its defense mechanisms for survival.

2. Vitamin D

Vitamin D is unique from most other vitamins in that it acts like a *steroid hormone*⁵ inside of the body. It's produced from cholesterol when your skin is exposed to the Ultraviolet B rays from sunlight. For that reason, it has also been dubbed the "sunshine vitamin." However, exposure and adequate levels of vitamin D from sunlight can depend on a number of factors : *season, time of day, smog, skin melanin, sunscreen*, and even *age* have the ability to affect UV radiation exposure and the amount of vitamin D synthesized in the body. Vitamin D is a fat-soluble vitamin, which means it dissolves in fats and oils and can store in your body for long periods of time. There are *two dietary forms of vitamin D* ⁶ :

- **Vitamin D3** (cholecalciferol) -- found in oily fish, butter, egg yolk
- **Vitamin D2** (ergocalciferol) -- found in some mushrooms (grown in UV light), fortified foods, dietary supplements

*Both vitamin D2 and D3 are considered biologically inactive*⁷ until two enzymatic chemical processes take place; the first happening in the liver and the second in the kidney. After which *calcitriol is produced*, the active form of the vitamin.⁸ As I reviewed the literature, I've noticed plenty of human trials, meta-analyses, and reviews to date, comparing which form (vitamin

¹ *The American Journal of Clinical Nutrition*, Volume 87, Issue 4, April 2008, Pages 1080S–1086S,

² Wang H, Chen W, Li D, et al. Vitamin D and Chronic Diseases. *Aging Dis*. 2017;8(3):346-353. Published 2017 May 2. doi:10.14336/AD.2016.1021

³ Jenab M, Bueno-de-Mesquita HB, Ferrari P, et al. Association between pre-diagnostic circulating vitamin D concentration and risk of colorectal cancer in European populations: a nested case-control study. *BMJ*. 2010;340:b5500.

⁴ Michos ED, Melamed ML. Vitamin D and cardiovascular disease risk. *Curr Opin Clin Nutr Metab Care*. 2008 Jan;11(1):7-12. doi: 10.1097/MCO.0b013e3282f2f4dd. PMID: 18090651.

⁵ Monastra G, De Grazia S, De Luca L, Vittorio S, Unfer V. Vitamin D: a steroid hormone with progesterone-like activity. *Eur Rev Med Pharmacol Sci*. 2018 Apr;22(8):2502-2512. doi: 10.26355/eurrev_201804_14845. PMID: 29762856.

⁶ Tripkovic L, Lambert H, Hart K, et al. Comparison of vitamin D2 and vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and meta-analysis. *Am J Clin Nutr*. 2012;95(6):1357-1364. doi:10.3945/ajcn.111.031070

⁷ Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium; Ross AC, Taylor CL, Yaktine AL, et al., editors. *Dietary Reference Intakes for Calcium and Vitamin D*. Washington (DC): National Academies Press (US); 2011. 3, Overview of Vitamin D. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK56061/>

⁸ Brandi ML. Indications on the use of vitamin D and vitamin D metabolites in clinical phenotypes. *Clin Cases Miner Bone Metab*. 2010;7(3):243-250.

D3 or D2) are most effective for raising serum blood vitamin D levels. One common find that the studies have shown include both vitamin D2 and D3 help with raising serum vitamin D levels. Using meta-regression analysis, a study conducted in 2018, where nine RCTs comparing the results of vitamin D2 and vitamin D3 supplementation with increasing serum 25 (OH) D levels concluded— *“this research shows both vitamin D2 and D3 supplementation can significantly increase serum 25 (OH) D levels. Though the results did not reach statistical significance, there is a consistent trend of vitamin D3 offering additional effectiveness relative to vitamin D2.”*⁹

3. Vitamin D Deficiency : Causes and Symptoms

Vitamin D deficiency has been recognized as a worldwide health concern, affecting over a *billion* people across the globe. There has been debate over what exactly defines adequate Vitamin D levels. With experts using 40 ng/mL as ideal and still others who believe *30 ng/mL to be sufficient levels.*¹⁰ A number of factors can affect an individual's ability to maintain healthy Vitamin D levels— *diet, sun exposure, sedentary lifestyle* and obesity. Inadequate levels of Vitamin D have been linked to a number of diseases : *“metabolic disorders, autoimmune conditions ... psychiatric, respiratory and cardiovascular disorders, cancers, as well as osteoporosis, and osteomalacia.”*¹¹ All of this further emphasizes the important role Vitamin D plays in keeping a population healthy.

3.1. Causes

So many environmental factors contribute to a Vitamin D deficiency. We'll discuss a few common causes of Vitamin D deficiency as well some of its symptoms :

- **Diet** - Because Vitamin D is found in very few foods, there is a large percentage of the population receiving very little Vitamin D through diet. Vitamin D is found *naturally present in fatty foods such as cream, cheese and fish oil (cod liver, halibut liver).*¹² Because of that, vegans and those avoiding animal products for religious or ethical reasons will have to find dietary supplements (certain mushrooms e.g., UV light grown, fortified soy products). We also have to consider those affected by poverty, and living in low-income regions where the quality of food sources may not be as plentiful. A *systematic Vitamin D food fortification from health authorities to improve the Vitamin D status in the general population in countries such as United States, Canada and Finland*¹³ has been introduced. With the fine line between providing adequate amounts of Vitamin D to those deficient and distributing too much, being considered.
- **Sun Exposure** - *“People living in nursing homes, prisons ... house-bound such as the disabled, elderly and sick are at risk of developing a Vitamin D deficiency.”*¹⁴ The amount of UV-B exposure for any individual can vary greatly e.g., skin pigmentation, geographical location, age, sunscreen use, and clothing. For instance, a large percentage of Arab women have been found to be Vitamin D deficient. One small pilot study published in the East Mediterranean Health Journal investigated the effect of sun exposure on 8 healthy Arab women. No changes to their dietary Vitamin D intake were made. They exposed their face, arms and hands for 15 minutes per day, twice a week— *“Although vitamin D levels remained sub-optimal median serum 25(OH) D levels were significantly higher post-intervention (23.0 nmol/L) than pre-intervention (17.6 nmol/L)”*¹⁵ And another study found *“adults older than 70 years need almost 3 times the duration of sun exposure to produce the same amount of vitamin D as a child”*¹⁶
- **Obesity** - *“Lower vitamin D in obese people is a consistent finding across age, ethnicity, and geography.”*¹⁷ Researchers have found a few suggested mechanisms that are commonly cited in medical literature explaining low Vitamin D status in obesity : decreased sun exposure, Vitamin D is trapped inside the *fat tissue*¹⁸, and the volume of Vitamin dosing as supplementation— *“Vitamin D dosing regimen for treatment of vitamin D deficiency in obesity should be based on body weight, i.e. one size does not fit all”*¹⁹ Evidence is showing how body weight can negatively influence 25(OH) D response to supplemental Vitamin D. And it remains unclear whether the same can be said about 'fortified foods'. Taking these studies into consideration, the importance of maintaining a healthy BMI should be encouraged.

3.2 Symptoms

- **Infections (getting sick often)**
- **Weakness in muscles, muscle degeneration**

⁹ Meline Chakalian, Joyce Cao, Jiang Hu, Casey Vanous, Simon Sum, Vitamin D2 and D3 Supplementation Effect on Serum 25(OH)D Levels: A Meta-Analysis, *Current Developments in Nutrition*, Volume 4, Issue Supplement_2, June 2020, Page 1782

¹⁰ Wang H, Chen W, Li D, et al. Vitamin D and Chronic Diseases. *Aging Dis.* 2017;8(3):346-353. Published 2017 May 2. doi:10.14336/AD.2016.1021

¹¹ Straube S, Andrew Moore R, Derry S, McQuay HJ
Pain. 2009 Jan; 141(1-2):10-3.

¹² Course In Naturopathic Nutrition, Module 1, Pg 49, Linda Lazarides

¹³ Pilz, Stefan et al. “Rationale and Plan for Vitamin D Food Fortification: A Review and Guidance Paper.” *Frontiers in endocrinology* vol. 9 373. 17 Jul. 2018, doi:10.3389/fendo.2018.00373

¹⁴ Course In Naturopathic Nutrition, Module 1, Pg 49, Linda Lazarides

¹⁵ Dawodu A, Kochiyil J, Altaye N. Pilot study of sunlight exposure and vitamin D status in Arab women of childbearing age. *East Mediterr Health J.* 2011 Jul;17(7):570-4. PMID: 21972479.

¹⁶ The Journal of the American Osteopathic Association, May 2017, Vol. 117, 301-305.

¹⁷ Walsh JS, Bowles S, Evans AL. Vitamin D in obesity. *Curr Opin Endocrinol Diabetes Obes.* 2017 Dec;24(6):389-394. doi: 10.1097/MED.0000000000000371. PMID: 28915134.

¹⁸ Wortsman, J, Matsuoka, LY, Chen, TC et al. (2000) Decreased bioavailability of vitamin D in obesity. *Am J Clin Nutr* 72, 690–693.

¹⁹ Drincic, AT, Armas, LA, Van Diest, EE et al. (2012) Volumetric dilution, rather than sequestration best explains the low vitamin D status of obesity. *Obesity (Silver Spring)* 20, 1444–1448.

- Pain in lower limbs²⁰
- Multiple Sclerosis, auto-immune diseases²¹
- Rickets (in children)

4. The Immune System: Innate and Adaptive

The purpose of your immune system is to recognize invading pathogens, prevent their spread, and eliminate them from your body. A healthy immune system is able to distinguish potential threats (tumour cells, pathogens) from the body's own healthy cells and tissues. *Detection can be complicated at times*²² as pathogens have the ability to evolve rapidly in order to adapt, stay alive and avoid the immune systems defense. Your immune system provides two levels of defense : **innate** and **adaptive**. Below, we'll look at each of the two parts in more detail.

4.1. Immune System : Innate

This is considered your first line of defense against infections. Providing a rapid response (few hours to days) and fight against invading pathogens. Unlike your adaptive immune response, innate immune responses are general and not specific to a particular pathogen. It includes *physical barriers*.²³ Such as your skin, the cells lining your gut and blood vessels, and *chemical barriers*; saliva and stomach acid. These barriers block out entry of organisms that cause diseases into your body.

Innate Immunity Response :

- **Neutrophils** - Usually the first cells to arrive at the scene of infection. *They can clear microbes*²⁴, bacteria through a process called *phagocytosis* (digesting them inside your white blood cells).
- **Dendritic Cells** - Stimulate the activation of T-lymphocytes and B-lymphocytes, combining innate and adaptive immunity. They are the strongest antigen-presenting cells. *"Located mainly in the skin, nose, lungs stomach and intestines."*²⁵
- **Macrophages** - Another type of white blood cell, which is very versatile. They reside within tissues, producing a variety of chemicals - *enzymes, complete proteins, and cytokines*. Macrophages also act as scavengers. And as most white cells do, they are important in engulfing bacteria plus ridding the body of worn-out cells.

4.2. Immune System : Adaptive

Primarily composed of your T and B lymphocytes. Compared with your innate immunity, your adaptive immune response is slower to start (days to weeks). But it has the ability to generate a long-lasting immune memory — *"It is required to specifically fight against pathogens, and activated by exposure to pathogens, unlike the innate immune system it is able to learn about the pathogen and enhance the immune response accordingly."*²⁶ Thus producing the antibodies that can protect you from future infections. Providing a long lasting immunity.

Adaptive Immunity Response :

- **T cells, CD4+T cells, and CD8+T cells** - These cells play an antiviral role. By balancing the fight against pathogens and the harmful risk of developing autoimmunity or *inflammation*.²⁷
- **CD8+T cells** - Are both toxic to pathogens and can kill viral infected cells
- **Killer T Cells** - Kill cells that are infected with viruses or are damaged and dysfunctional. They are activated when their receptor binds to a specific antigen.
- **Helper T Cells** - *"Help determine which types of immune responses the body will make to a particular pathogen"*²⁸ They're directors, controlling the immune response by making sure other cells perform their task.

5. Vitamin D and Its Support For the Immune System

The affects Vitamin D has on the immune system has been recognized for quite some time. There's increasing data linking the prevalence of immune disorders with Vitamin D deficiency. This awareness of low levels of 25(OH) D in populations all over the world, *"has prompted investigations of health problems which may be associated with Vitamin D insufficiency."*²⁹ One of the

²⁰ Masood H, Narang AP, Bhat IA, Shah GN. Persistent limb pain and raised serum alkaline phosphatase the earliest markers of subclinical hypovitaminosis D in Kashmir. Indian J Physiol Pharmacol. 1989 Oct-Dec;33(4):259-61. PMID: 2620972.

²¹ Course In Naturopathic Nutrition, Module 1, Pg 49, Linda Lazarides

²² Course In Naturopathic Nutrition, Module 4, Pg 39, Linda Lazarides

²³ Sassi F, Tamone C, D'Amelio P. Vitamin D: Nutrient, Hormone, and Immunomodulator. *Nutrients*. 2018;10(11):1656. Published 2018 Nov 3. doi:10.3390/nu10111656

²⁴ Vanherwegen AS, Gysemans C, Mathieu C. Regulation of Immune Function by Vitamin D and Its Use in Diseases of Immunity. *Endocrinol Metab Clin North Am*. 2017 Dec;46(4):1061-1094. doi: 10.1016/j.ecl.2017.07.010. Epub 2017 Oct 6. PMID: 29080635.

²⁵ Course In Naturopathic Nutrition, Module 4, Pg 41, Linda Lazarides

²⁶ Sassi, Francesca et al. "Vitamin D: Nutrient, Hormone, and Immunomodulator." *Nutrients* vol. 10,11 1656. 3 Nov. 2018, doi:10.3390/nu10111656

²⁷ Veiga-Parga T, Sehrawat S, Rouse BT. Role of regulatory T cells during virus infection. *Immunol Rev*. 2013 Sep;255(1):182-96. doi: 10.1111/imr.12085. PMID: 23947355; PMCID: PMC3748387.

²⁸ Course In Naturopathic Nutrition, Module 4, Pg 41, Linda Lazarides

²⁹ Hewison M. Vitamin D and immune function: an overview. *Proc Nutr Soc*. 2012 Feb;71(1):50-61. doi: 10.1017/S0029665111001650. Epub 2011 Aug 18. PMID: 21849106.

benefits of Vitamin D on protective immunity is in part due to its effect on the *innate immune system*.³⁰ Vitamin D also has numerous effects on cells within the immune system :

Antimicrobial Peptides

Vitamin D receptors have been identified in nearly all of your immune cells :

Monocytes, B and T Lymphocytes, white blood cells, macrophages and dendritic cells.

The reason this is important is because with sufficient Vitamin D circulating in your blood, it can activate these cells to create *antimicrobial peptides*.³¹ Antimicrobial peptides are part of your *innate immune response* and include molecules known as cathelicidins and defensins. They have antiviral effects, shown to *inactivate the influenza virus*³² and respiratory tract infections. The exact mechanisms of “how” are not yet fully understood, but researchers believe it may be “*linked to vitamin D's ability to up-regulate the anti-microbial peptides LL-37 and human beta defensin.*”³³

Vitamin D not only supports the *innate* but *adaptive* immune response in your immune system. Treatment of T Cells with calcitriol (active form of Vitamin D) inhibits the secretion of pro-inflammatory Th1 ... Th22 cytokines, but promotes the *production of more anti-inflammatory cytokines*.³⁴ Cytokines are small proteins secreted by your cells innate and adaptive immune systems. They locate and target immune cells, and interact with receptors on the target immune cells by binding to them. That interaction triggers or stimulates specific responses by target cells. A long period of uncontrolled pro-inflammatory cytokines is known as the “*cytokine storm.*” There is compelling research demonstrating the role of Vitamin D in modulating your T helper cell and cytokine production. Also with promoting T regulatory cells (anti-infectious actions), *suppressing immune responses and limiting inflammatory processes*.³⁵ And there is extensive research showing how chronic inflammation can be extremely harmful to the body, leading to a host of *chronic diseases*³⁶.

6. Vitamin D Supplementation : Safety and Effectiveness

The two primary concerns many experts have with using Vitamin D as a supplement to help improve a healthy, functioning immune system are : **Is it safe** and **does it work?** For example, CNN, a U.S. based media outlet in May of 2020 in their health section published an article mentioned “*too much vitamin D can lead to a toxic buildup of calcium in your blood, causing confusion, disorientation and problems with heart rhythm bone pain, kidney damage and kidney stones.*” They referenced the dietary requirements reported by the IOM (Institute of Medicine) for calcium and Vitamin D—RDAs (Recommended Dietary Allowance) of 600 IU/day for people younger than 70 years of age, and 800 IU/day for those 70 years and older, *with levels around the world-country specific, depending on dietary and environmental requirements, but typically ranged between 400 and 800 IU/day*.³⁷ There are two things worth mentioning about the IOMs dietary recommendations. 1. The date of the report. It was published in 2011, over 10 years ago, making it extremely outdated. 2. And the report found no studies with adverse effects of supplementation with less than 10,000 IU/day of Vitamin D, yet they still set their upper recommendation level at 4,000 IU/D.

Below we'll look at both concerns many experts share regarding Vitamin D supplementation. Whether or not it's *safe* and *is it effective?*

6.1. Vitamin D Supplementation : Is It Safe?

As mentioned, the RDA according to the International of Medicine for adults 70 years or younger suggest 600 IU/day. And 800 IU/day for those older than 70 years. Also, supplementation which increases serum 25(OH) D levels past 125-150 nmol/L has been discouraged. Because its potential adverse effects e.g., kidney stone, and hypercalcemia. Since the publishing of their report in 2011, there's been a growing number of RCT (randomized control trials) investigating the health benefits of Vitamin D supplementation. One such study, published in The American Journal of Clinical Nutrition, June of 2019 — The ViDA Study, reported after a bolus (large doses) of “*100,000 IU Vitamin D3 per month for a median period of 3.3 y, and up to a maximum of 4.2 y, did not increase the incidence of kidney stones in adults aged 50–84 y. Nor did it result in any cases of hypercalcemia among those with follow-up serum calcium measurements.*”³⁸ Interestingly, the only case of *hypercalcemia* was detected in the placebo group. In May of 2019, found in The Journal of Biochemistry and Molecular Biology, a study was submitted by a psychiatric hospital in Cincinnati, Ohio. All patients who checked into their hospital since 2011 were offered supplementation of 5,000 or 10,000 IU/day of Vitamin D3. Due to disease concerns, a few patients even agreed to more, ranging from 20,00 - 50,000 IU/day,

³⁰ Aranow C. Vitamin D and the immune system. *J Investig Med*. 2011;59(6):881-886. doi:10.2310/JIM.0b013e31821b8755

³¹ Biophysics Research Division and Department of Chemistry, 930 N. University Avenue, University of Michigan, Ann Arbor, MI 48109-1055, USA

³² Cannell JJ, Vieth R, Umhau JC, Holick MF, Grant WB, Madronich S, Garland CF, Giovannucci E. Epidemic influenza and vitamin D. *Epidemiol Infect*. 2006 Dec;134(6):1129-40. doi: 10.1017/S0950268806007175. Epub 2006 Sep 7. PMID: 16959053; PMCID: PMC2870528.

³³ W. S. Middleton Memorial Veterans Administration Hospital, 53705, USA

³⁴ Cantorna MT. Mechanisms underlying the effect of vitamin D on the immune system. *Proc Nutr Soc*. 2010 Aug;69(3):286-9. doi: 10.1017/S0029665110001722. Epub 2010 Jun 2. PMID: 20515520; PMCID: PMC3138329.

³⁵ Bruce D, Ooi JH, Yu S, Cantorna MT. Vitamin D and host resistance to infection? Putting the cart in front of the horse. *Exp Biol Med (Maywood)*. 2010 Aug;235(8):921-7. doi: 10.1258/ebm.2010.010061. PMID: 20660091; PMCID: PMC3138330.

³⁶ Martens CR, Bansal SS, Accornero F. Cardiovascular inflammation: RNA takes the lead. *J Mol Cell Cardiol*. 2019 Apr;129:247-256. doi: 10.1016/j.yjmcc.2019.03.012. Epub 2019 Mar 14. PMID: 30880251; PMCID: PMC6641543.

³⁷ Ross, A Catharine et al. “The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know.” *The Journal of clinical endocrinology and metabolism* vol. 96,1 (2011): 53-8. doi:10.1210/jc.2010-2704

³⁸ Zarintaj Malihi, Carlene M M Lawes, Zhenqiang Wu, Ying Huang, Debbie Waayer, Les Toop, Kay-Tee Khaw, Carlos A Camargo, Jr, Robert Scragg, Monthly high-dose vitamin D supplementation does not increase kidney stone risk or serum calcium: results from a randomized controlled trial, *The American Journal of Clinical Nutrition*, Volume 109, Issue 6, June 2019, Pages 1578–1587,

the conclusion of their study—“*There have been no cases of vitamin D3 induced hypercalcemia or any adverse events attributable to vitamin D3 supplementation in any patient*”³⁹

6.2 Vitamin D Supplementation : Is It Effective?

While researching, I’ve found that the information on the effectiveness of Vitamin D supplementation can be a bit confusing. Two common factors where Vitamin D supplementation fail to show any benefits are :

1. Doses are specific, using a ‘one size fits all’ approach. Rather than adjusting the dose to achieve optimal vitamin D levels.
2. They are designed like pharmaceutical trials. Participants are randomized to a placebo, and all start with a baseline of zero. Usually with Vitamin D studies, participants start at different Vitamin D levels and their doses vary according to their blood level.

This is important to keep in mind when confronted with studies which show Vitamin D supplementation ineffective. And with a better understanding of some of the methods used in said studies e.g., omission of co-factors, ‘one size fits all’ approach, we’re better able at making informed decisions as to what our own personal nutritional needs require. As mentioned earlier in this paper— *Causes of Vitamin D deficiency* — the effectiveness of Vitamin D supplementation will depend on a few factors : *demographics* and *biological*. Another thing to strongly consider is several drugs can interfere with Vitamin D metabolism and function. Drugs (that activate the pregnane X receptor) e.g., antiepileptics, antineoplastics, antibiotics, anti-inflammatories, antihypertensives, antiretrovirals and endocrine drugs, and even some herbal medicines *can decrease Vitamin D levels*.⁴⁰

7. Conclusion

Vitamin D undoubtedly plays an important role in calcium absorption and bone health. It’s a unique vitamin, being that it can be made inside of your skin. The two dietary forms of Vitamin D : ergocalciferol and cholecalciferol can be found in limited foods, making it hard for some people to maintain sufficient Vitamin D levels through diet alone. For that reason, certain countries such as the United States, Canada and Finland have fortified specific foods in order to improve the Vitamin D status within their countries. Between both Vitamin D2 and D3, it seems to be suggested that Vitamin D3 (cholecalciferol) is more *biologically active*.⁴¹ However, Vitamin D2 and D3, have both been found in various studies to increase the serum 25(OH) D levels of individuals.

One of the major causes of Vitamin D deficiency is the lack of sun exposure. Sun exposure is *the major source of Vitamin D*⁴² for most people. Along with a lack of sun exposure, we’ve also learned *diet, weight, and age* can be important contributing factors for Vitamin D deficiency. Vitamin D deficiency has been linked to a wide array of diseases. And this can have a negative impact on our quality of life. With this in mind, many experts have emphasized the value Vitamin D has in strengthening, supporting and maintaining a healthy-functioning immune system. Studies have shown the benefits Vitamin D has for the *innate* and *adaptive* immune responses. I’ve outlined how each play significant parts within the immune system in providing two lines of defense against pathogens, bacteria, and viruses. And this is of utmost importance for overall human health.

Finally, with the growing concern of Vitamin D deficiency all over the world. The various causes, and long list of symptoms and diseases that come with it. Plus the increasing evidence showing the benefits of Vitamin D on the immune system. Should we supplement (if and when necessary) and if so, is it effective and safe? Though it seems certain mainstream media outlets discourage Vitamin D supplementation, largely in part due to its danger of dosing “too much.” I’ve found numerous studies, and medical papers published, whose sources I’ve referenced throughout this paper, suggesting Vitamin D supplementation is in fact *safe*, and very *effective*. This is crucial, especially considering the negative impact Vitamin D deficiency has on the healthcare systems, its cost, and entire population . By properly informing, and educating others on the importance of nutrition, and a healthy lifestyle, we can help encourage others to make healthier choices. That in return can positively cause a ripple effect impacting the world we live in, one person at a time.

³⁹ Department of Psychiatry, Wright State University School of Medicine, Dayton, OH, 45435, United States

⁴⁰ Gröber U, Kisters K. Influence of drugs on vitamin D and calcium metabolism. *Dermatoendocrinol.* 2012;4(2):158-166. doi:10.4161/derm.20731

⁴¹ Lehmann U, Hirche F, Stangl GI, Hinz K, Westphal S, Dierkes J. Bioavailability of vitamin D(2) and D(3) in healthy volunteers, a randomized placebo-controlled trial. *J Clin Endocrinol Metab.* 2013 Nov;98(11):4339-45. doi: 10.1210/jc.2012-4287. Epub 2013 Sep 3. PMID: 24001747.

⁴² Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *Am J Clin Nutr.* 2008 Apr;87(4):1080S-6S. doi: 10.1093/ajcn/87.4.1080S. PMID: 18400738.

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