

原文: <http://www.doctoryourself.com/omns/v16n33.shtml>

维生素 D 在降低 COVID-19 风险中的作用: 文献综述

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The Chinese translation of this article is made possible by a generous grant from Dr. Bill Grant and from the Cheng Integrative Health.

本文翻译工作得到 Bill Grant 博士资助及上海成氏健康资助。

OMNS June 9, 2020

The Role of Vitamin D in Reducing Risk of COVID-19: A Brief Survey of the Literature

by William B. Grant, PhD

(2020 年 6 月 9 号) 维生素 D 水平升高与 Covid-19 发病率、严重程度和死亡风险降低有因果关系的证据继续增加, 这份简短的报告概述了到 2020 年六月初所了解到的情况, 并提供了一些关键参考资料的链接。

应该注意的是在发表证明维生素 D 补充的随机对照实验显著降低 COVID-19 发病率或死亡率的报道发表之前, 可能无法接受维生素 D 补充的作用, 一些关于维生素 D 补充和 COVID-19 发病率和结果的随机对照试验和观察性研究正在规划阶段或进行中, 需要研究的明显群体是那些风险最高的人群: 生活在高海拔地区的深色皮肤的人, 住在养老院或医疗机构的人、囚犯、工厂工人, 如美国肉类加工厂的工人, 医疗保健工作者。一个主要的

问题是当权者认为维生素 D 对收入和利润是一种威胁，因此他们使用“虚假信息剧本”来压制维生素 D 的正面信息。【1】

在四月初发表的一份综述中，有人评论补充维生素 D 可以降低 Covid-19 的风险，发现了两种机制，1、通过维生素 D 刺激释放的应激诱导的和防御素，减少病毒存活和复制；2、通过减少促炎细胞因子的产生，降低细胞因子风暴的风险。【2】

还提到了随机对照实验证明的补充维生素 D 可降低急性呼吸道感染的风险。【3】建议补充维生素 D 的目的是增加血清 25 羟维生素 D 水平至 40-60ng/毫升（100-150 毫摩尔/升）纳克，每天需要 4,000-5,000 国际单位维生素 D3 的剂量，由于维生素 D 转化为不同的代谢物需要镁的存在，因此也应该补充镁，也许是 400 毫克/天，这一建议是基于观察性研究的结果，如 Grassrootshealth.net 进行的一项关于流感样病例的研究。【4】

最近有人建议，对于那些没有补充维生素 D 的人，他们在一到两周内开始补充大剂量的维生素 D 几十万单位，基本原理是，如果没有推注，身体将需要几个月来达到最佳水平。【5】也有人认为，虽然补充维生素 D 可以阻止 COVID-19 从症状开始发展，它可能在肺和器官发生急性损伤期后，不会有很大作用。最近的概述证据表明，在英格兰的黑人，亚洲和少数民族居民维生素 D 缺乏可以解释更高的事件和死亡率的原因。【6】

References

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3. Martineau AR, Jolliffe DA, Greenberg L, et al. (2017) Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. BMJ. 356:i6583. <https://www.bmj.com/content/356/bmj.i6583>
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5. Grant WB, Baggerly CA, Lahore H. (2020) Response to Comments Regarding "Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths". Nutrients June 1, 2020, 12(6), 1620. <https://www.mdpi.com/2072-6643/12/6/1620>
6. Grant WB, Boucher BJ. (2020) Vitamin D deficiency due to skin pigmentation and diet may explain much of the higher rates of COVID-19 among BAME in England. BMJ comments, June 6, 2020. <https://www.bmj.com/content/369/bmj.m1548/rr-22>

Here are annotated links to related publications and preprints

"Of the 212 cases of COVID-19, majority had ordinary clinical outcome. Mean serum 25(OH)D level was 23.8 ng/ml. Serum 25(OH)D level was lowest in critical cases, but highest in mild cases.

Serum 25(OH)D levels were statistically significant among clinical outcomes."

Alipio, MM. (2020) Vitamin D Supplementation Could Possibly Improve Clinical Outcomes of Patients Infected with Coronavirus-2019 (COVID-2019); April 9,

2020. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3571484

"A lot of COVID-19 infected patients develop acute respiratory distress syndrome (ARDS), which may lead to multiple organ damage. These symptoms are associated with a cytokine storm syndrome.

The aim of this letter is to note the 5 crucial points that vitamin D could have protective and therapeutic effects against COVID-19. For that reason, COVID-19 infection-induced multiple organ damage might be prevented by vitamin D."

Aygun H. (2020) Vitamin D can prevent COVID-19 infection-induced multiple organ damage.

Naunyn Schmiedebergs Arch Pharmacol. 2020 May 25:1-

4. <https://pubmed.ncbi.nlm.nih.gov/32451597>

"Timely implementation of vitamin D supplementation programmes worldwide is critical; initial priority should be given to those who are at the highest risk, including the elderly, immobile, homebound, BAME and healthcare professionals. Population-wide vitamin D sufficiency could prevent seasonal respiratory epidemics, decrease our dependence on pharmaceutical solutions, reduce hospitalisations, and thus greatly lower healthcare costs while significantly increasing quality

of life."

Davies G, Garami AR, Byers J. (2020) Evidence Supports a Causal Model for Vitamin D in

COVID-19 Outcomes. 1 May, updated 3 June,

2020. <https://www.medrxiv.org/content/10.1101/2020.05.01.20087965v2.full.pdf>

"We retrospectively investigated the 25-hydroxyvitamin D (25(OH)D) concentrations in plasma obtained from a cohort of patients from Switzerland. In this cohort, significantly lower 25(OH)D levels ($p = 0.004$) were found in PCR-positive for SARS-CoV-2 (median value 11.1 ng/mL) patients compared with negative patients (24.6 ng/mL)."

D'Avolio A, Avataneo V, Manca A, et al. (2020) 25-Hydroxyvitamin D Concentrations Are Lower in

Patients with Positive PCR for SARS-CoV-2. *Nutrients*. 2020 May

9;12(5):E1359. <https://pubmed.ncbi.nlm.nih.gov/32397511>

"COVID-19 patients showed lower median 25(OH)D (18.6 ng/mL, IQR 12.6-25.3, versus 21.5 ng/mL, IQR 13.9-30.8; $P=0.0016$) and higher vitamin D deficiency rates (58.6% versus 45.2%, $P=0.0005$). Surprisingly, this difference was restricted to male COVID-19 patients who had markedly higher deficiency rates than male controls (67.0% versus 49.2%, $P=0.0006$) that increased with advancing radiological stage and were not confounded vitamin D-impacted comorbidities."

De Smet D, De Smet K, Herroelen P, et al. (2020) (2020) Vitamin D deficiency as risk factor for

severe COVID-19: a convergence of two pandemics, May 5,

2020. <https://www.medrxiv.org/content/10.1101/2020.05.01.20079376v2>

"The RAS, which includes ACE and ACE2, is a complex network that has a major role in various biological functions 31. Chronic vitamin D deficiency may induce RAS activation lung fibrosis through activation of the RAS 35; therefore, increasing evidence indicates that 1,25(OH)₂D₃ may also be a negative endocrine regulator of the RAS. Inducing the expression of renin, ACE, Ang II and AT1R, and inhibiting ACE2 expression could result in acute lung injury. Vitamin D inhibits renin, ACE and Ang II expression, and induces ACE2 levels in ALI."

Ghavideldarestani M, Honardoost M, Khamseh ME. (2020) Role of Vitamin D in Pathogenesis and Severity of COVID-19 Infection <https://www.preprints.org/manuscript/202004.0355/v1>

"We performed a retrospective study in two tertiary medical centers in South Asia. The medical records of COVID19 patients were reviewed and a total of 176 subjects included were the elderly whose age is at least 60 years, We reported that majority of the subjects had 25(OH)D level below 30 ng/ml, most of them were male, had diabetes, and were classified as severe. Most of the male and female subjects had 25(OH)D level below 30 ng/ml."

Glicio, EJ.(2020) Vitamin D Level of Mild and Severe Elderly Cases of COVID-19: A Preliminary Report (May 5, 2020). SSRN: <https://ssrn.com/abstract=3593258>

Several recent publications and preprints report multi-country studies based of COVID-19 case or death rates with respect to country mean 25(OH)D concentration. One concern regarding such studies is that the 25(OH)D concentrations used are probably not related to those most likely to develop COVID-19 at the time of incidence. However, a more serious problem is that life expectancy has a

much stronger correlation (direct) than does 25(OH)D as discussed in this preprint. I have confirmed their findings using more recent COVID-19 case and death rate data.

Kumar V, Srivastaa A. (2020) Spurious Correlation? A review of the relationship between Vitamin D and Covid-19 infection and mortality. <https://www.medrxiv.org/content/10.1101/2020.05.25.20110338v1.full.pdf>

This article presents retrospective results for 780 patients in Indonesia. Compared to 25(OH)D >30 ng/ml, 25(OH)D between 20 and 30 ng/ml had an odds ratio for death of 7.6 (P<0.001), while 25(OH)D <20 ng/ml had an odds ratio for death of 10.1 (P<0.001).

Raharusun, P, Priambada S, Budiart C, Agung E, Budi C. (2020) Patterns of COVID-19 Mortality and Vitamin D: An Indonesian Study (April 26, revised 6 May, 2020). SSRN. <https://ssrn.com/abstract=3585561>

JoAnn E. Manson, MD, DrPH, (2020) Does Vitamin D Protect Against COVID-19? MEDSCAPE, May 11, 2020

The recommended dietary allowance of vitamin D is 600-800 IU/daily, but during this period, a multivitamin or supplement containing 1000-2000 IU/daily of vitamin D would be reasonable. <https://www.medscape.com/viewarticle/930152>

Other resources on vitamin D and COVID-19

<https://www.grassrootshealth.net/>

<https://vitamindwiki.com/>

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