

Estimated Reductions in Mortality Rates in Poland if Vitamin D Levels Were Raised to 60+ ng/ml

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Disclosure

- ▶ My non-profit organization, Sunlight, Nutrition and Health Research Center receives funding from Bio-Tech Pharmacal (Fayetteville, AR, USA), a supplier of high-quality vitamin D supplements.



Why Vitamin D?

- ▶ Vitamin D is readily available, safe, and inexpensive.
- ▶ Vitamin D is the most common nutritional deficiency in the world and is one of the most studied molecules in history.
- ▶ It reduces risk of many adverse health conditions and diseases, generally through affecting gene expression.
- ▶ There are over 95,500 publications on vitamin D at pubmed.gov including 4400 from January 1 to early-October 2021.



Mortality Rates for Major Diseases in Germany, Poland, Russia, 2016

Mortality rates (deaths/100,000/yr) in 2016

Outcome	Poland Males	Poland Females	Russia Males	Russia Females	Germany Males	Germany Females
All causes	726	381	1152	549	504	328
CVD	287	167	536	296	160	106
IHD	191	109	319	167	95	54
Stroke	50	34	144	97	24	20
Cancer	207	116	222	114	148	97
Breast	0.2	18	0.4	21	0.2	19
Lung	61	20	58	7	36	17
COPD	32	12	25	5	26	15
Lower respiratory	30	14	28	8	12	7
Diabetes mellitus	13	9	4	4	12	8
Alcohol abuse	13	2	26	5	7	2
Alzheimer's	3	3	23	17	15	16

COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; IHD, ischemic heart disease

Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018.



25(OH)D for the older Polish population <https://is.gd/cMjzLR>

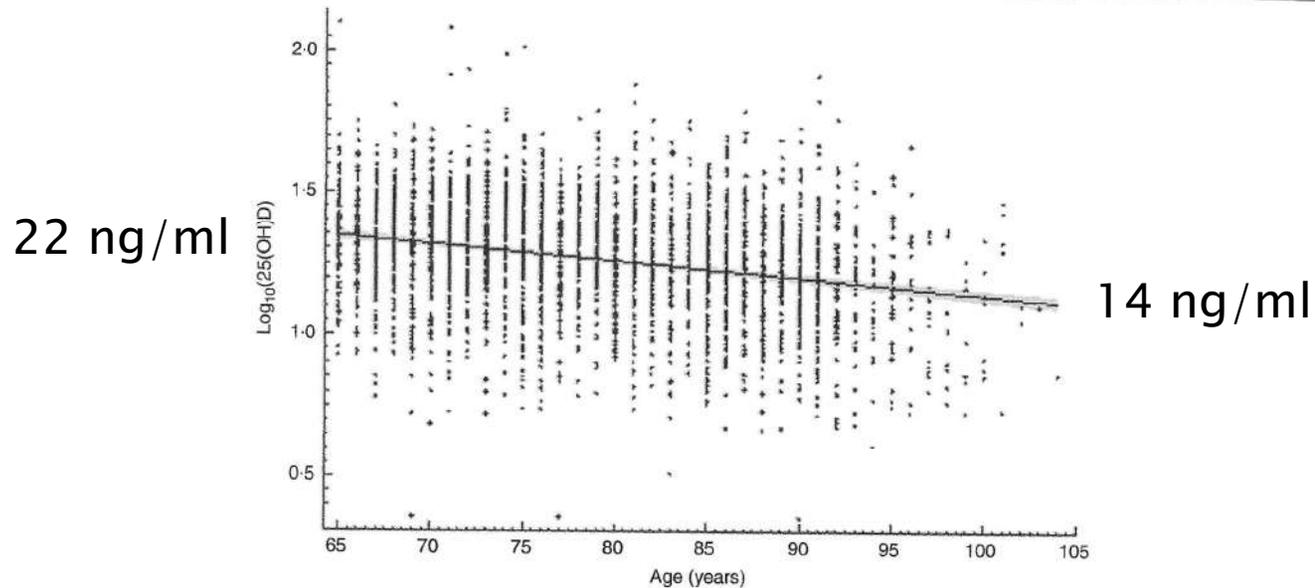
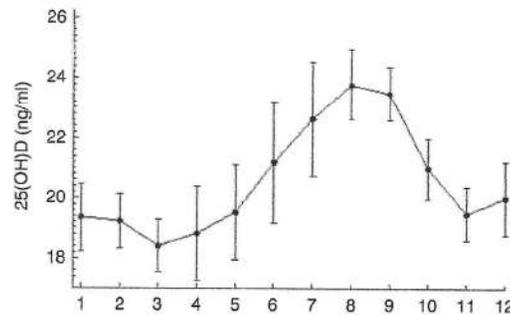


Fig. 1 The relationship between serum vitamin D concentration (measured as 25-hydroxyvitamin D in ng/ml and log-transformed; $\log_{10}(25(OH)D)$) and age among community-dwelling Polish men and women aged 65 years or older (n 3472), PolSenior study, 2007–2011. — is the regression line and the grey zone is the 95% CI for the regression line



**Mean serum 25(OH)D concentrations for those
>49 yrs in Russia, Ukraine, and Belarus**

	Summer (nmol/L)	Autumn (nmol/L)	Winter (nmol/L)
Male	59		33
Female	58	40	30

**Blood Serum 25-Hydroxyvitamin *D* in Various
Populations of Russia, Ukraine, and Belarus: A
Systematic Review with Elements of Meta-analysis A. I.
Kozlov and G. G. Vershubsky. Human Physiology, 2017,
<https://is.gd/HlyxaE>**



Types of Studies

- ▶ Ecological studies, both geographical and temporal, have been important historically.
- ▶ Observational studies have given us a good understanding of health outcomes with respect to serum 25(OH)D concentration.
- ▶ Randomized controlled trials (RCTs) have found few effects of vitamin D due to being based on vitamin D dose rather than serum 25(OH)D and generally enrolling participants with above average 25(OH)D and used low vitamin D doses.
- ▶ Grant et al. Why vitamin D clinical trials should be based on 25-hydroxyvitamin D concentrations.
- ▶ JSBMB 2018 <https://is.gd/A5TROu>

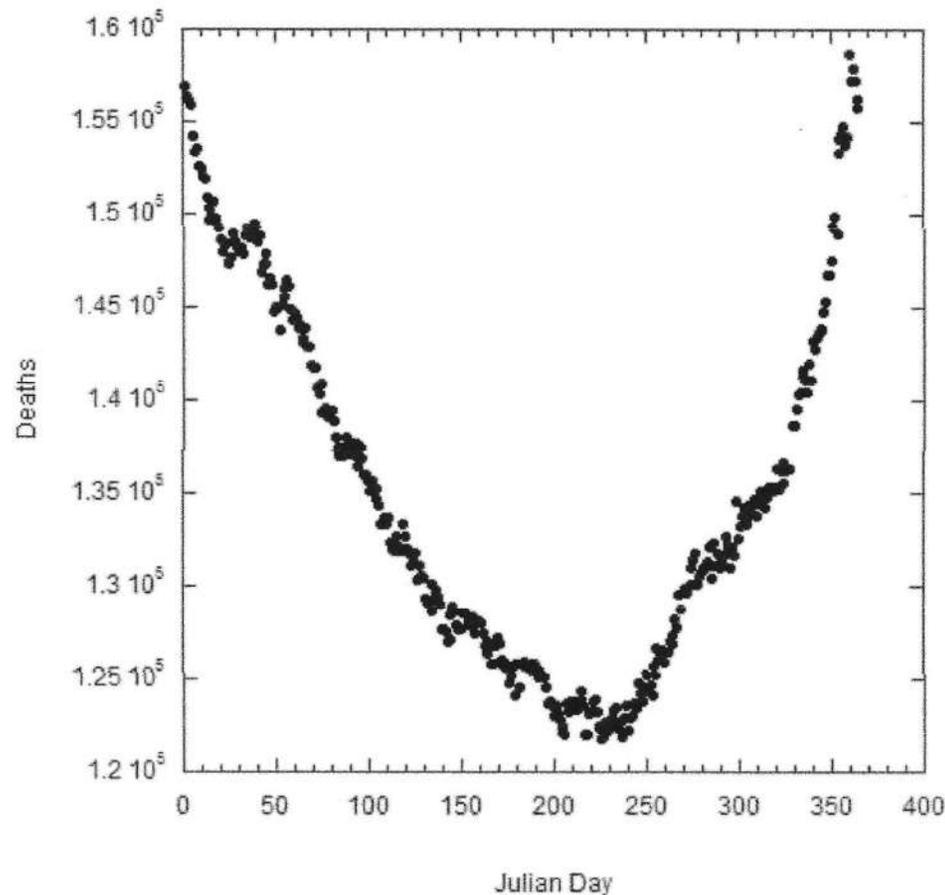


Cardiovascular Disease (CVD)

- ▶ CVD rates are much higher in winter (~25%) than in summer.
- ▶ Observational studies have long found that low vitamin D levels are associated with increased risk of CVD and that
- ▶ Several mechanisms have been proposed for how vitamin D can reduce risk of CVD.



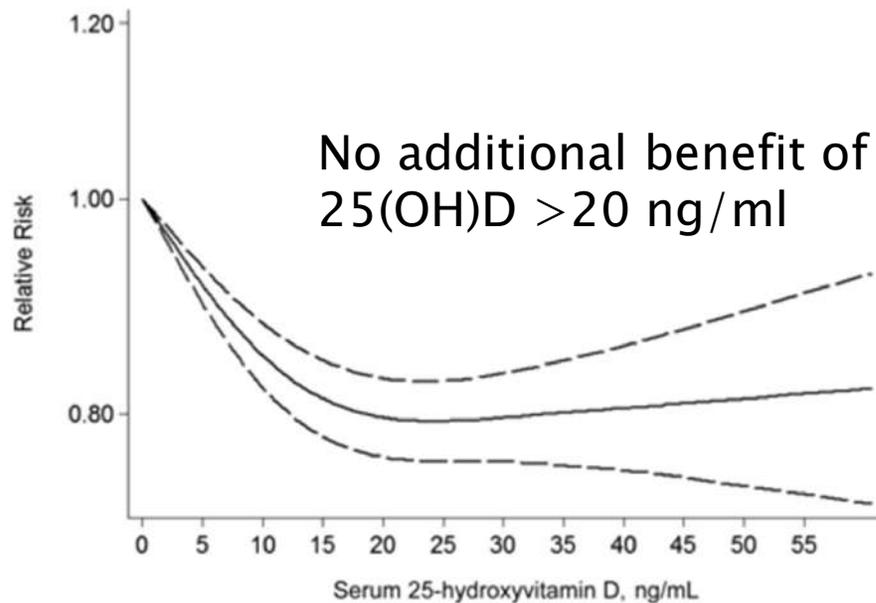
Seasonal variations of mortality rates in the US [tps://is.gd/TjgKCC](https://is.gd/TjgKCC)



23% lower
Death rates
in summer;
CVD and
infectious
diseases are
the largest
contributors.

Figure 1. Deaths per day of the year, according to all official U.S. death certificates for 1979–2004 from Phillips et al., 2010.

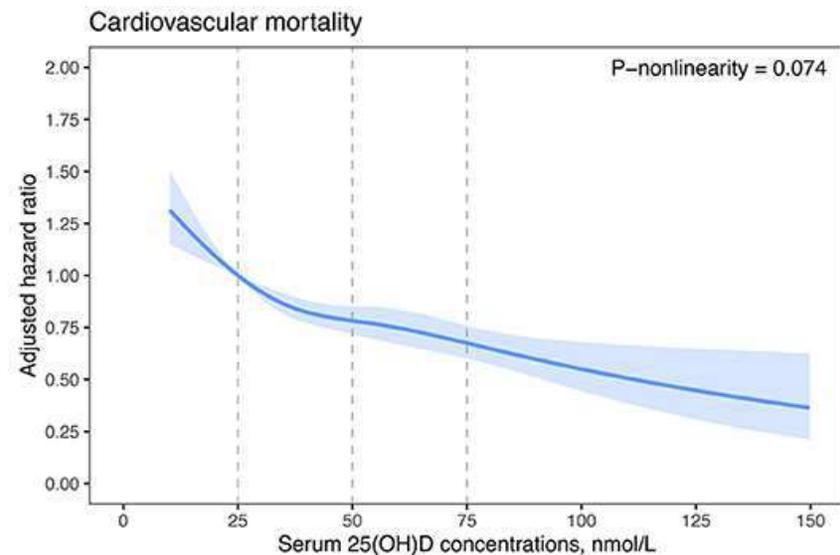
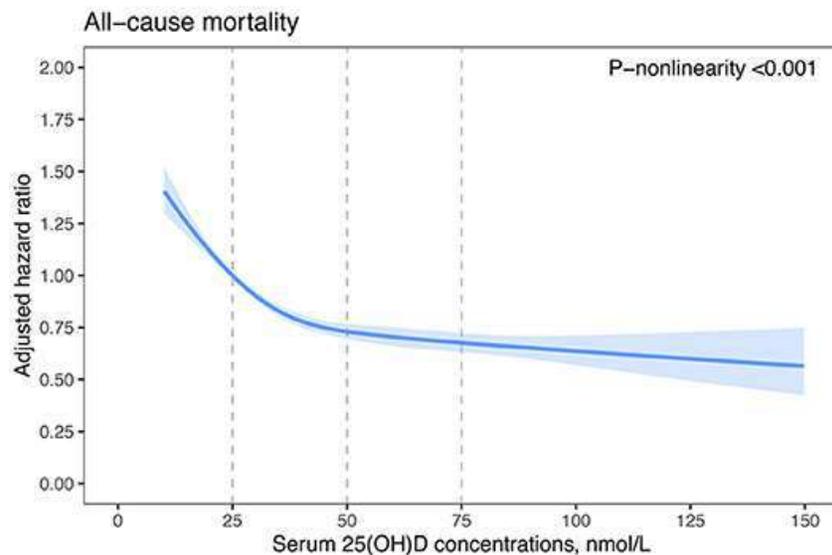
Dose-response analysis between serum 25(OH)D and the relative risk of total cardiovascular events: incidence.



Zhang, Am J Clin Nutr 2017.
<https://is.gd/ObwHrg>



Association of Serum 25(OH)D Concentrations With All-Cause and Cause-Specific Mortality Among Adult Patients With Existing CVD



Dai et al. Frontiers in Nutrition. 23 Sept. 2021. <https://is.gd/TMJiPR>

The Effects of Vitamin D Supplementation and 25(OH)D Levels on the Risk of Myocardial Infarction and All-cause Mortality – 1

- ▶ This was a retrospective, observational, nested case-control study of 20,000 patients with low baseline 25(OH)D (<20 ng/ml) who received care at the U.S. Veterans Health Administration from 1999 to 2018. Patients were divided into 3 groups:
- ▶ Group A (untreated, ≤ 20 ng/ml),
- ▶ Group B (treated, 21–29 ng/ml), and
- ▶ Group C (treated, ≥ 30 ng/ml).
- ▶ Acharya P, et al. J Endocr Soc. 2021 Jul 15;5(10):bvab124
- ▶ <https://is.gd/2R3Juw>



The Effects of Vitamin D Supplementation and 25(OH)D Levels on the Risk of Myocardial Infarction and All-cause Mortality – 2

- ▶ MI survival was higher by 30% for 25(OH)D >30 ng/ml than for 20–29 and <20 ng/ml.
- ▶ All-cause mortality rate was lower by 40% for 25(OH)D >30 ng/ml than for 20–29 and <20 ng/ml.
- ▶ Acharya P, et al. J Endocr Soc. 2021; 5(10):bvab124
- ▶ <https://is.gd/acharya2021>



The U.S. Veterans Administration Hospitals Treat Many Patients with 25(OH)D <20 ng/ml with Vitamin D to Save Money

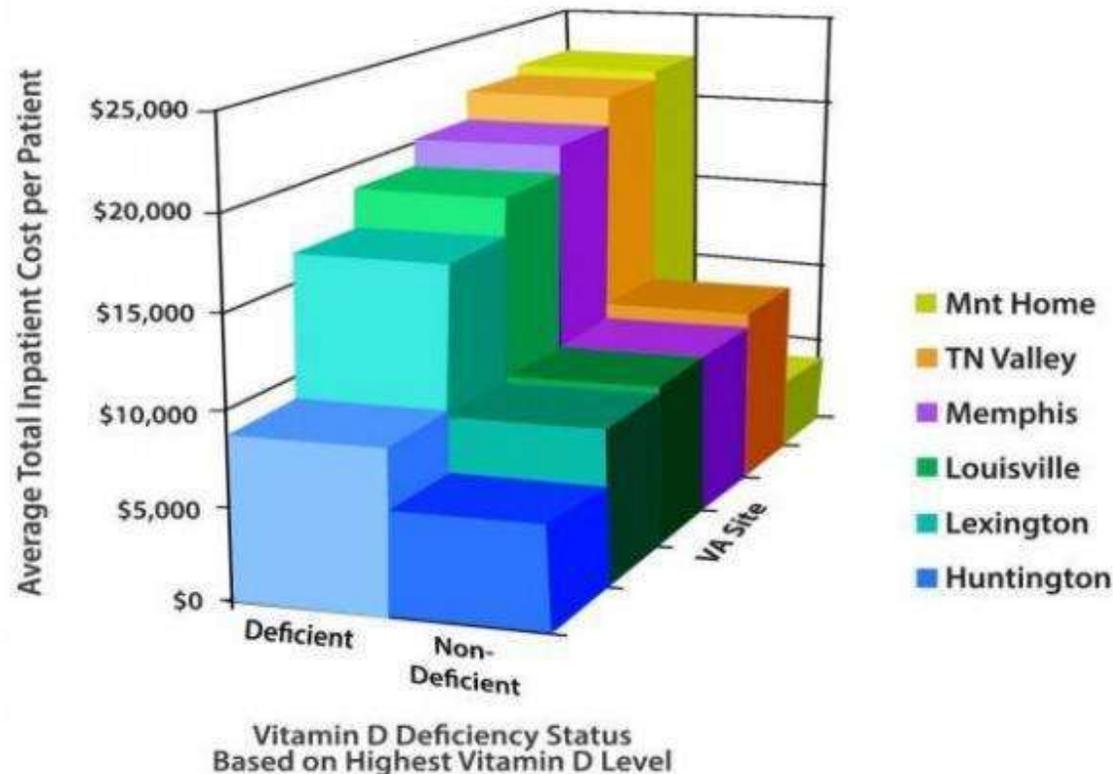


Figure 11: Total inpatient costs by VA site and vitamin D deficiency status

(Bailey, Manning & Peiris, 2012, p. 74).

<https://is.gd/WxVVGH>

Vitamin D Deficiency among Polish Patients with Coronary Heart Disease

- ▶ The study group consisted of 1043 Caucasian patients (64% males and 36% females) who underwent cardiac catheterization between the years of 2013 and 2017.
- ▶ Vitamin D deficiency was found in 94% of residents of central Poland with angiographically confirmed coronary artery disease. 22% of patients had a severe vitamin D deficiency. Due to the documented effects of vitamin D on the cardiovascular system and the fact that CVD (including coronary artery disease) is still the most common cause of death in developed countries, prophylactic and therapeutic strategies should be considered to combat 25(OH)D deficiency in this group of Polish patients.
- ▶ Dzedzic et al., Pol Med J, 2021; <https://is.gd/SVZzwW>



Severity of Vitamin D Deficiency (VDD) Predicts Mortality in Polish Ischemic Stroke Patients

- ▶ 240 stroke patients in Rybnik, Poland, 480 matched controls.
- ▶ 25(OH)D at admission: patients 10 ± 7 ng/ml; controls 21 ± 9 ng/ml
- ▶ **VitD and Survival.** The period of the follow-up was up to 48 months (mean 25 months). The primary outcome, death, was noted in 79 (32.9%) subjects during the period of follow-up. Median survival time and extended mean survival time were 45 and 65 months, respectively. The mortality rates (per year) were 4.8 and 1.9 in groups with and without severe VDD, respectively, with an incident rate ratio equal to 2.2; (95% CI: 1.4–4.7). We estimated that 60% (95% CI: 31%–77%) of deaths could be assigned to VDD. Therefore, we estimated it would be necessary to treat 5 (95% CI: 3–8) subjects with severe VDD to prevent one death.
- ▶ Wajda et al. *Disease Markers*, 2019 <https://is.gd/lbQRqy>



Blood Pressure Reduced with 4000 IU/d Vitamin D₃

- ▶ A Canadian study gave a moderate dose of vitamin D (~4,000 IU daily) seeking 25(OH)D levels >100 nmol/L. Of the patients with hypertension at the start, 71% were no longer hypertensive 9 to 15 months later, having lowered blood pressure by 12–18 mmHg.
- ▶ Mirhosseini N, Vatanparast H, Kimball SM.
- ▶ Nutrients. 2017;9(11):1244.
- ▶ <https://is.gd/OxJnsZ>



Magnesium Can Also Reduce Risk of CVD

- ▶ Magnesium for the prevention and treatment of cardiovascular disease. DiNicolantonio JJ, Liu J, O'Keefe JH. Open Heart. 2018 Jul 1;5(2):e000775
- ▶ Subclinical magnesium deficiency: a principal driver of cardiovascular disease and a public health crisis. DiNicolantonio JJ, O'Keefe JH, Wilson W. Open Heart. 2018 Jan 13;5(1):e000668.
- ▶ Decreased magnesium status may mediate the increased cardiovascular risk associated with calcium supplementation. DiNicolantonio JJ, McCarty MF, O'Keefe JH. Open Heart. 2017 May 22;4(1):e000617.

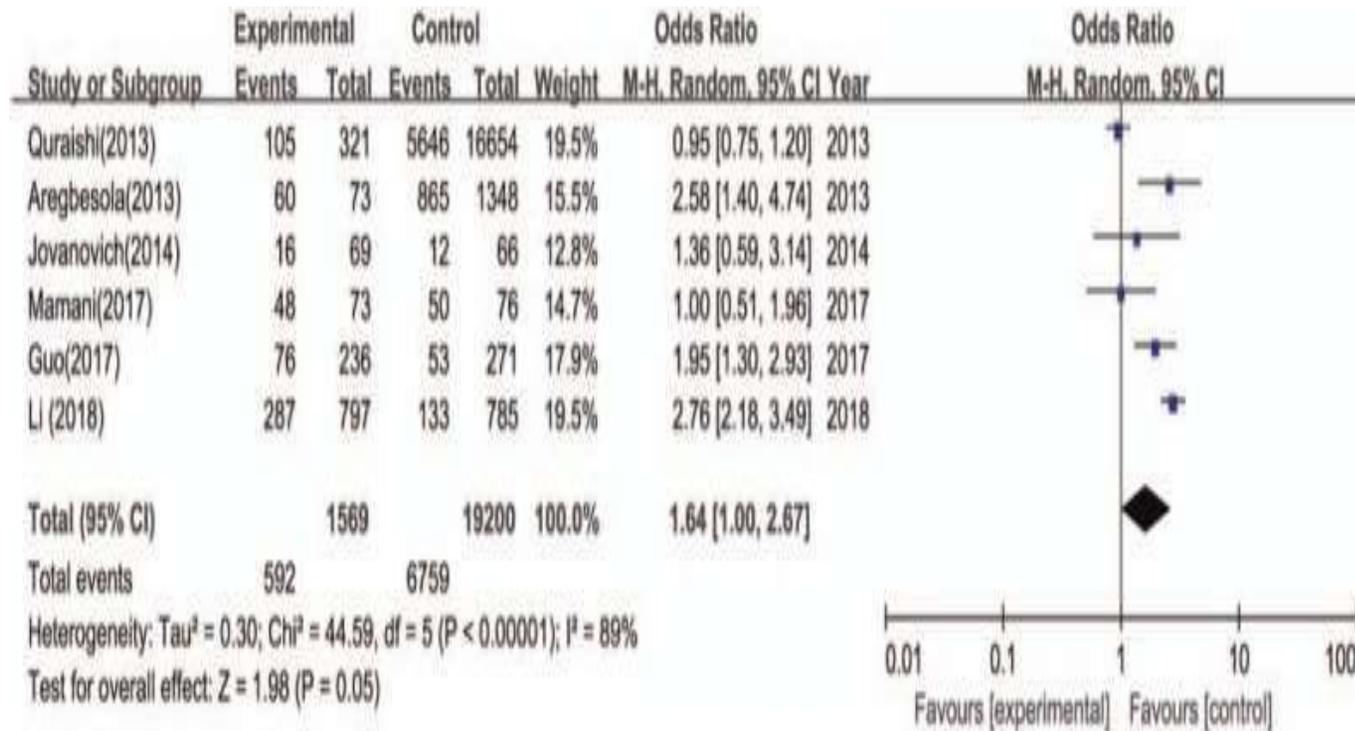


<https://is.gd/npmStW>

- ▶ A total of 21 studies, including 4,818 COPD patients and 7,175 controls, were included. Meta-analysis showed that lower serum vitamin D levels were found in COPD patients than in controls [standardized mean difference (SMD): -0.7 (95% CI: $-1.0, -0.4$)], especially in severe COPD (SMD: -0.9 ($-1.5, -0.2$)) and COPD exacerbation [SMD: -0.4 ($-0.7, -0.2$)]. Vitamin D deficiency was associated with increased risk of COPD [OR: 1.8 ($1.2, 2.6$)] and with COPD severity [OR: 2.8 ($2.0, 4.0$)].
- ▶ Zhu et al. Internat J COPD, 2016
- ▶ <https://is.gd/eNFMis>



Risk of Community Acquired Pneumonia : 25(OH)D <20 ng/ml gives OR= 1.6 (95% CI, 1.0 to 2.7)



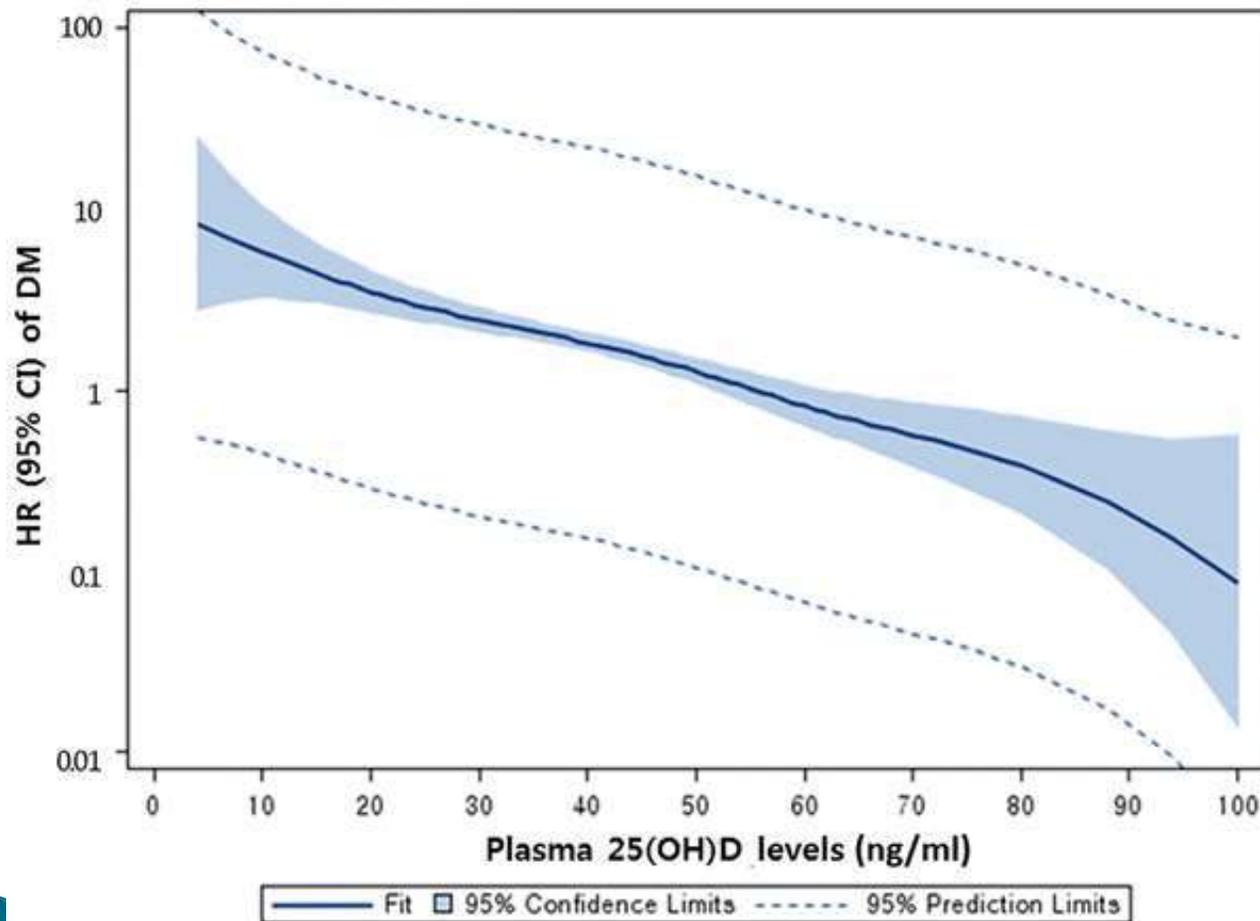
Zhou et al., Medicine (Baltimore) 2019 <https://is.gd/npmStW>

Diabetes Mellitus Type 2

- ▶ Diabetes mellitus type 2 is generally considered a chronic disease caused by a bad diet.
- ▶ However, there is now evidence from both observational studies and an RCT that higher vitamin D levels can greatly reduce risk.



Risk of type 2 diabetes incidence was reduced by 80% for 25(OH)D of <30 to >50 ng/ml



This was a 12-Year follow-up Study in sunny southern California (33° N)

Park, Garland et al.

PLoS One.

2018

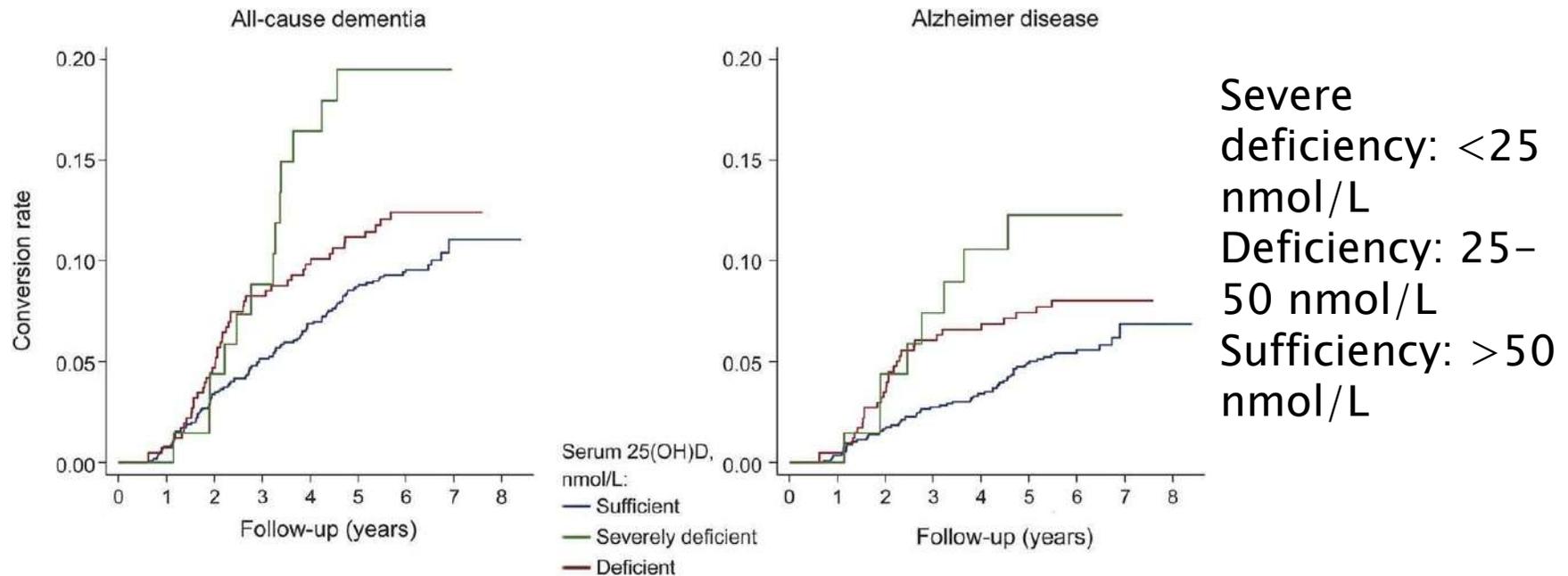
<https://is.gd/qm61Sp>

Intratrial Exposure to Vitamin D and New-Onset Diabetes Among Adults With Prediabetes

- ▶ The D2d study compared the effect of vitamin D₃ versus placebo on new-onset diabetes in 2423 adults with prediabetes.
- ▶ Every 10 ng/ml increase in 25(OH)D between 20–30 ng/ml to >50 ng/ml among those given 4000 IU/d vitamin D reduced incidence of type 2 diabetes by 25%.
- ▶ Dawson-Hughes B,Pittas AG; D2d Research Group. Diabetes Care. 2020;43(12):2916–2922. <https://is.gd/k6vesK>

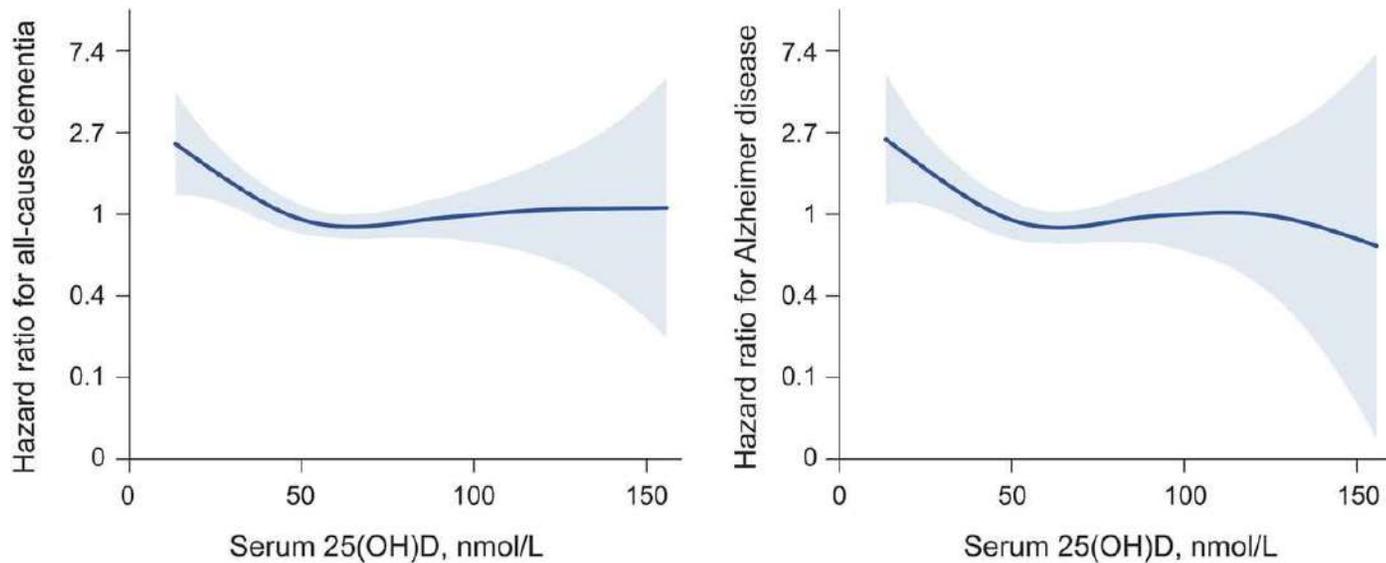


Figure 1 Kaplan-Meier curves for unadjusted rates of all-cause dementia and Alzheimer disease by serum 25(OH)D



Vitamin D and the risk of dementia and Alzheimer disease.
Littlejohns TJ, ... Llewellyn DJ. *Neurology*. 2014;83(10):920–8.
<https://is.gd/0SFOAi>

Figure 2 Multivariate adjusted smoothing spline plots showing the hazard ratios for dementia and Alzheimer disease by serum 25(OH)D concentrations Models adjusted



Dementia

Alzheimer's disease

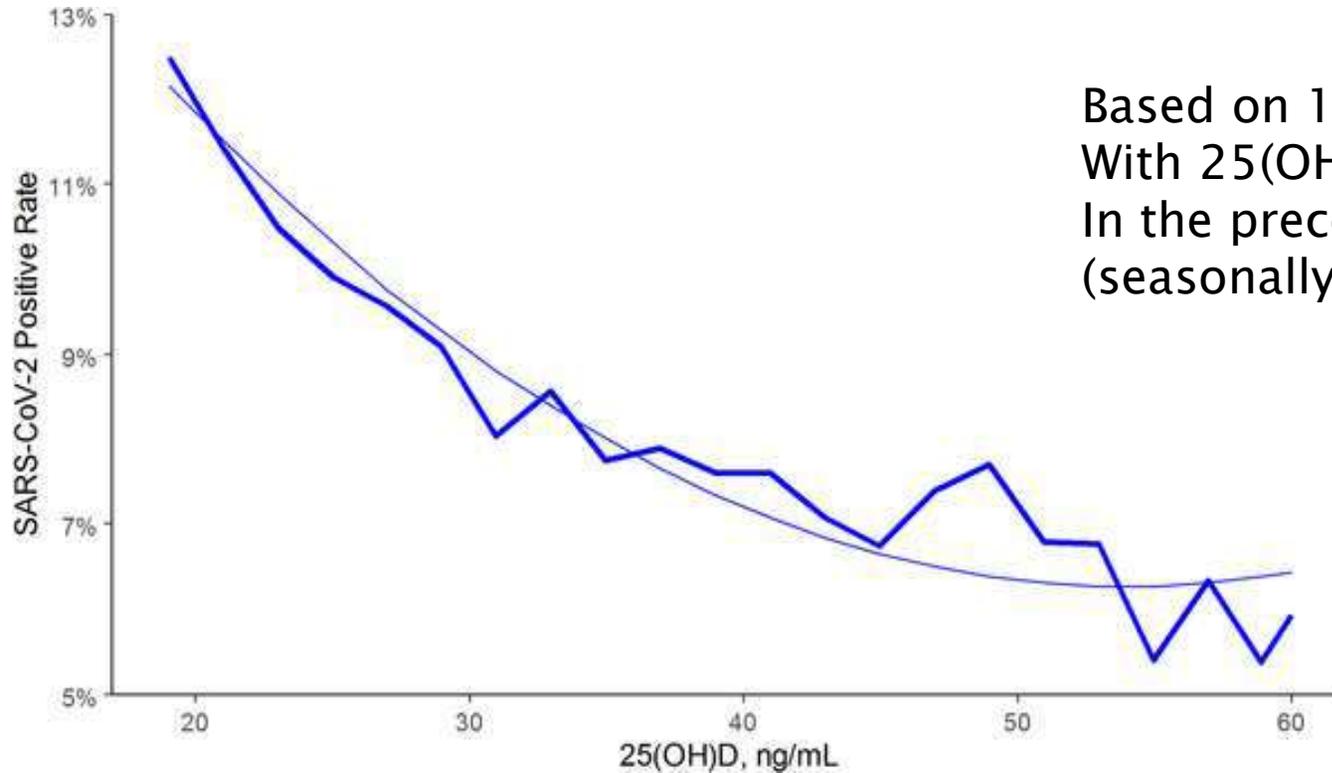
Vitamin D and the risk of dementia and Alzheimer disease.
Littlejohns TJ, ... Llewellyn DJ. *Neurology*. 2014;83(10):920–8.
<https://is.gd/0SFOAi>

COVID-19

- ▶ We are in the midst of the COVID-19 pandemic.
- ▶ Those at greatest risk include the elderly, those with chronic diseases, and those with low vitamin D levels.
- ▶ Vitamin D supports the immune system. The most important roles vis a vis COVID-19 appear to be reducing the viability and replication of SARS-CoV-2, reducing risk of the cytokine storm, and maintaining the integrity of the epithelial layers of various organs.
- ▶ It is important to raise 25(OH)D at the first symptoms of COVID-19.



SARS-CoV-2 positivity rates associated with circulating 25(OH)D levels

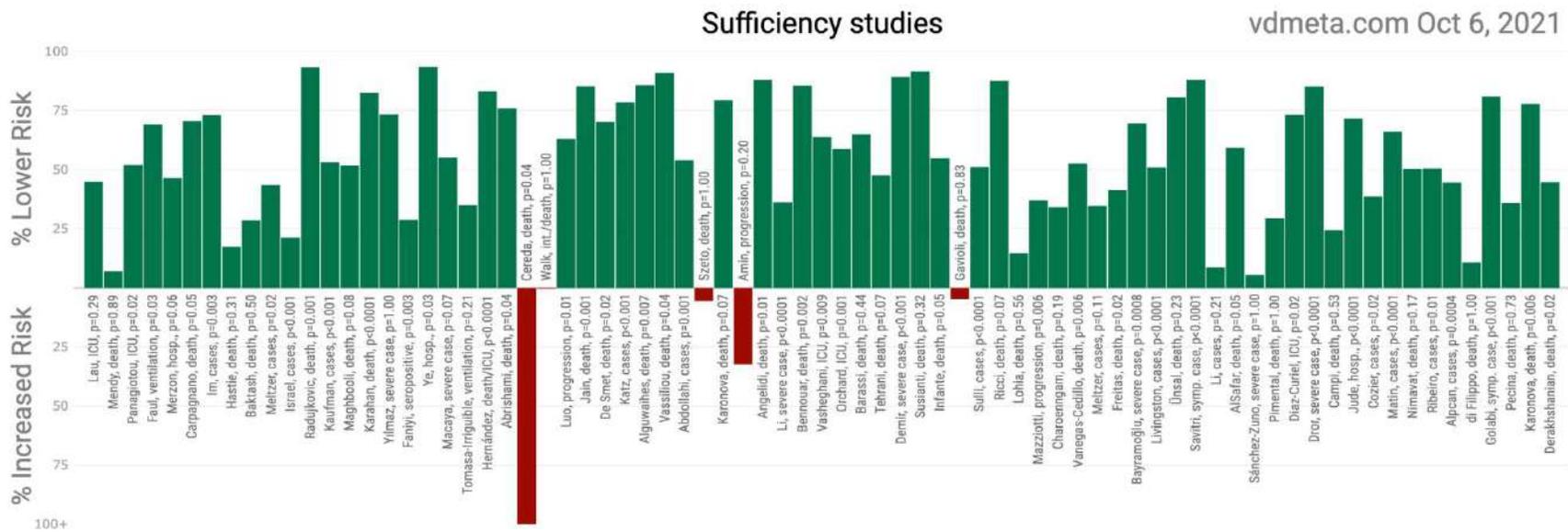


Based on 191,779 patients
With 25(OH)D measurements
In the preceding 12 months
(seasonally adjusted)

Kaufman, .. Holick, PLoS One. 2020 Sep 17;15(9):e0239252
or <https://is.gd/holick920>

COVID-19 Incidence vs. Vitamin D Level <https://vdmeta.com/>

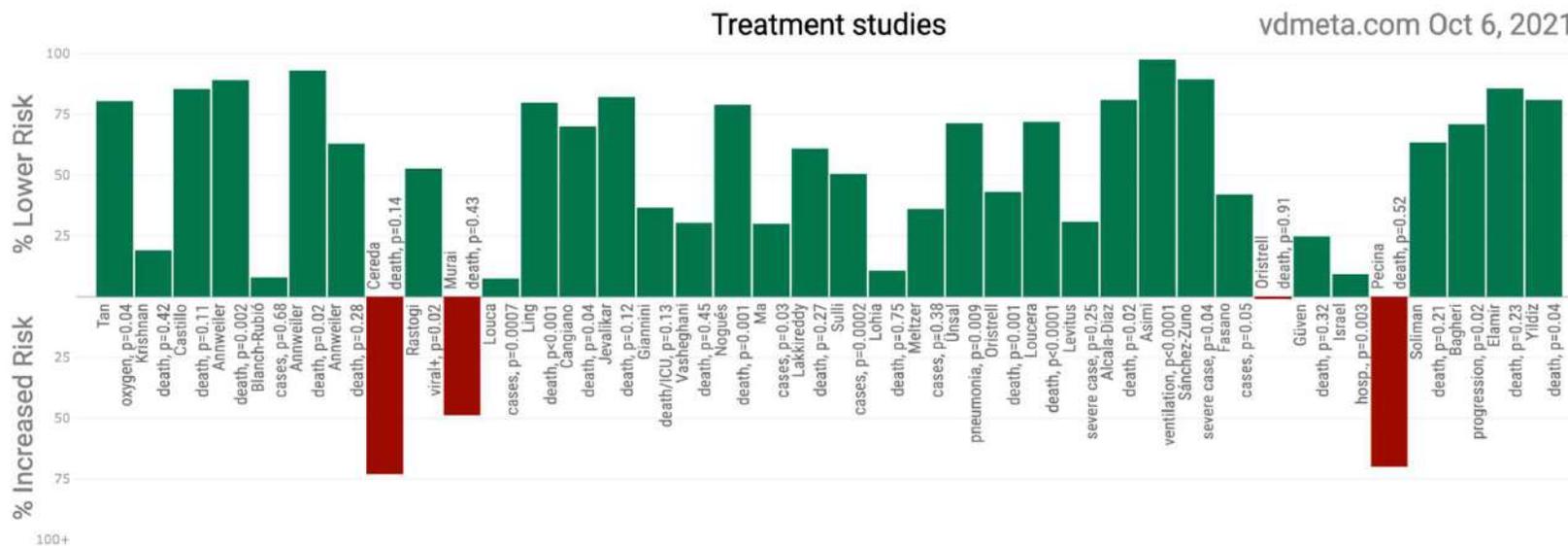
Observational studies



Each bar represents the results from one study regarding incidence for sufficient vs. insufficient vitamin D level. Green indicates lower risk.

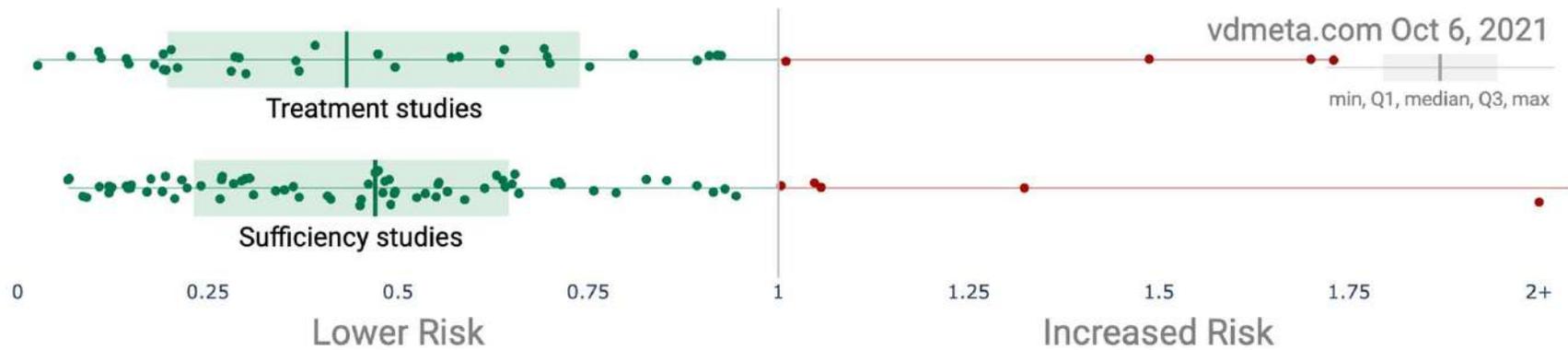
Treatment Studies of COVID-19 by Vitamin D

<https://vdm-meta.com/>



Each bar represents the results from one study regarding Treatment by vitamin D. Green indicates better outcomes

Treatment and Sufficiency Studies of COVID-19 by Vitamin D <https://vdmeta.com/>



The prognostic significance of vitamin D deficiency in patients with COVID-19 pneumonia

- ▶ **Materials and methods:** 207 COVID-19 patients were included in the study. Patients with vitamin D levels <20 ng/ml or 21 to 30 ng received a single 300,000 IU dose of vitamin D.
- ▶ **Results:** Of 207 patients, 37 received vitamin D, while 170 did not. Demographic, radiologic and mean laboratory values were similar between the groups. The mean plasma vitamin D level without vitamin D support (n=170) was 17 ± 6 ng/ml vs. 51 ± 16 ng/ml in the vitamin D group. The most remarkable finding were the mortality rates; while only 1 patient (3 %) died in the vitamin D group, 24 patients (14 %) died in no vitamin D supplementation group (p=0.04).
- ▶ Yildiz et al. Bratisl Lek Listy . 2021;122(10):744–747. <https://is.gd/4Hv0Tc>



Intervention Studies with High-dose Vitamin D₃ with Good Results

- Cluster headache, Crohn's disease,
 - Cystic fibrosis death, Epilepsy,
 - Hemorrhagic stroke, Influenza,
 - Migraine headache, Multiple sclerosis,
 - Periodontal disease, Psoriasis,
 - Rickets, Sepsis, Sleep disturbance
-
- For more information go to VitaminDWiki.com
 - Or Scholar.google.com



History of Serum 25(OH)D Concentration Recommendations

- ▶ Institute of Medicine USA [Ross, 2011], recommended 50 nmol/L for bone health.
<https://is.gd/qaDooj>
- ▶ Endocrine Society, USA, [Holick, 2011] recommended 75 nmol/L for treatment of vitamin D deficiency osteomalacia based on plateauing of PTH levels and the Priemel bone study. <https://is.gd/sgFMAq>
- ▶ GrassrootsHealth.net, recommended 100–150 nmol/L for optimal health in 2017.



Published Vitamin D Recommendation for Poland

- ▶ Vitamin D Supplementation Guidelines for General Population and Groups at Risk of Vitamin D Deficiency in Poland—Recommendations of the Polish Society of Pediatric Endocrinology and Diabetes and the Expert Panel With Participation of National Specialist Consultants and Representatives of Scientific Societies—2018 Update,
- ▶ Pludowski et al. Front. Endocrinol., 31 May 2018
- ▶ <https://is.gd/xN1hri>
- ▶ Optimal Concentration >30–50 ng/ml



Estimated Reductions in Adverse Health Outcomes in the Poland and Russia for 25(OH)D = 35, 50, and 70 ng/ml

Estimated Reductions in Mortality Rates in Poland and Russia by Raising Mean Serum 25(OH)D Concentrations from 18 to 20 ng/ml to 30, 50, or 70 ng/ml

Outcome	30 ng/ml (%)	50 ng/ml (%)	70 ng/ml (%)
Cardiovascular disease mortality	30	35	40
All-cancer incidence (mortality?)	25	45	65
Chronic obstructive pulmonary disease	20	30	40
Lower respiratory infection	20	30	40
SARS-CoV-2 seropositivity	30	40	50
Diabetes mellitus incidence	30	40	50
Alzheimer's disease incidence	10	10	10
All-cause mortality	25	35	45

RCTs vs. Open-label Observational Studies

- ▶ It is very difficult and expensive to conduct vitamin D RCTs.
- ▶ Therefore, do not wait for them to confirm the results presented here.
- ▶ Instead, consider the GrassrootsHealth.net approach of enrolling participants in open-label vitamin D supplementation studies, having them take the dose of their choice after counseling, then measure 25(OH)D every 6 months, as well as report health status at that time.



For Further Information:

- ▶ <https://vitamindwiki.com/>
- ▶ <https://scholar.google.com/>
- ▶ <https://pubmed.ncbi.nlm.nih.gov/>
- ▶ <https://www.grassrootshealth.net/>



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