Low Vitamin D Worsens COVID-19 Risk: Evidence & Imperatives

June 5, 2020 (updated Sept 20)   Karl Pfleger, Independent Researcher (I declare no conflicts.)

There's no reason not to fix low vitamin D & overwhelming evidence it could help against COVID-19.

Facts & Evidence

1. It's widely agreed that low vitamin D (<30ng/ml) results in worse health & more deaths. [1,2,3,4]
2. Causal evidence shows D protects against respiratory infections (40 RCTs, n=30k) & lung injury.
3. Low D is prevalent worldwide. USA: 40% D<20ng/ml, 64% healthy D<30. 96% nursing home D<30.
4. D's RDA was set 10x too low by mistake! 6200IU needed. Experts say raise RDA. Fauci takes 6000.
5. D is safe: Toxicity unlikely <80ng/ml. 15+ orgs say 4000IU (0.1mg)/day safe, Many say 10,000IU.
6. Many biological mechanisms argue D is especially important for COVID-19. [1,2,3,4,5 ,6,7,8,review]
7. Calcitriol (active form vitD) has direct inhibitory effect on SARS-CoV-2 in human epithelial cells. [1]
8. CV19 infection risk & severity correlate strongly w/ low D. [1(n=191,779),2(n=7807),3,4,5,6,7,8,9,10]
9. Causal Inference Modeling & Mendelian Randomization show D's effect on COVID-19 to be causal.
10. 1st controlled trial: 1000 IU/d D +Mg&B12 group needed oxygen 6.5x less, adj. f/ age, sex, comorb.
11. 1st RCT: 13/26 hospitalized no-D needed ICU (2 died) vs 1/50 w/D (0 died). Multivar. ICU OR=0.03.

Imperatives

1. Drs. should test D levels of all COVID-19 patients. Aggregated outcome data should be published.
2. COVID-19 standard-of-care should include quickly raising D levels to 30+ ng/ml.
3. Health insurers should try to proactively increase D levels in their insured patients.
4. Governments should message eradicating low D as a top priority alongside distancing & masks.
   Fauci admitted D affects COVID-19 risk in an obscure interview---it should be official messaging.
5. NAM, FDA, etc. should raise RDA, DV, etc. recs to 2000-4000IU (0.05-0.1mg) until end of crisis.
6. The FDA should require all COVID19 clinical trials to test D levels of all subjects.

Objections Dismissed

1. Correlation isn't causation: Facts 2,6,7, & 9-11 are causal evidence very consistent w/ the other data.
2. More RCTs needed / caution urged: Caution applies to mega-doses not remedying deficiency or using safe doses (fact 5). No one advocates keeping D too low. Failure of RCTs that don't test D or use 1 bolus dose wouldn't imply fixing low D is unhelpful. First pilot RCT shows huge benefit, & is peer reviewed. Its small n is countered by effect size: CI upper bound OR=0.25: 75% reduction in ICU odds. Compare vs ~⅓ reduction in deaths from steroids, now advocated by WHO but less safe & can't be prophylactics. RCTs withholding D from controls w/ low D or COVID-19 are now unethical.
3. Preprints might be flawed: True, but when so much evidence is consistent, removing a few pieces won't change much. Authors of facts 7-11 preprints were vetted. Facts 1-5 plus any few of the 20+ new papers would be convincing. Fact 8's 2 big studies & fact 11's RCT peer reviewed & published.
4. Some pre-COVID-19 D supplement trials show no benefit: Most such trials have subjects with already sufficient D, use monthly mega-doses, use D2, or use doses too low to achieve sufficiency (see fact 4). Also, evidence suggests a stronger D link to COVID-19 than other diseases.
5. Studies show D level not related to CV19 infection rate [1,2]: The studies used 10yr-old D tests & are contradicted by better studies [3,4,5,6]. [3,4] big & published. [3] should be considered definitive.

See figures on reverse side. To follow links, find this doc at http://agingbiotech.info/vitamindcovid19facts
See also: My full review w/ discussion. Linda Benskin's published literature review (current to mid-June).
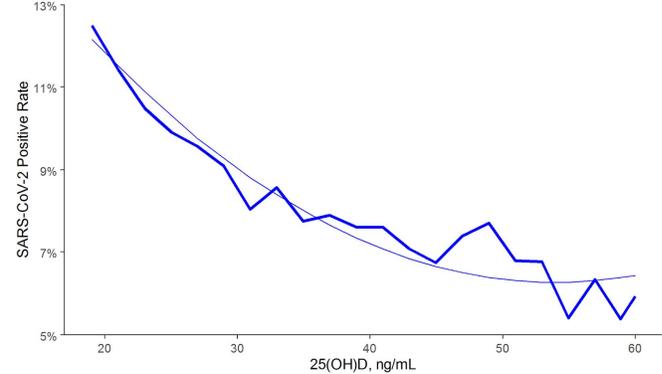
All figures & tables on this page come from peer reviewed, published papers.

Pre-2020, low D has high risk & high D low risk
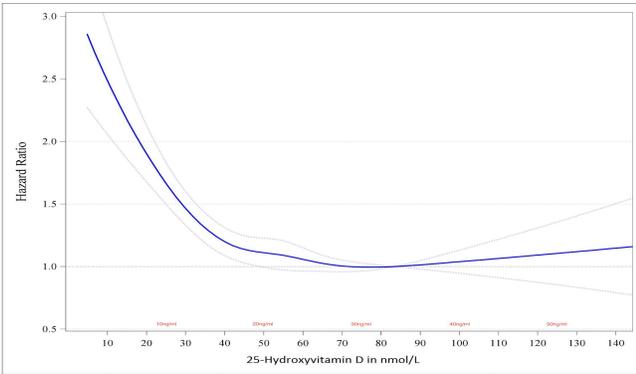
All cause mortality hazard ratio vs 25(OH)D level. From Gaksch et al, "Vitamin D and mortality…" PLOS ONE, 2017 based on 26,916 people tracked for median 10.5 years.

Low D raises risk of COVID-19 infection

COVID-19 infection rate vs 25(OH)D level. From Kaufman et al, "SARS-CoV-2 positivity rates…" PLOS One, 2020 based on 191,779 people. More D decreases risk until ~55ng/ml.

D after hospitalization almost eliminates ICU need

Table 3. Requirements for admission to the Intensive Care Unit, in patients hospitalized with COVID-19 (treated or not with calcifediol).

	Without Calcifediol Treatment (n = 26)	With Calcifediol Treatment (n = 50)	p value (1d712;2) Fischer Test
Need for ICU			<0.001
Not requiring ICU, n (%)	13 (50)	49 (98)	
Requiring ICU, n (%)	13 (50)	1 (2)	

* Univariate Risk Estimate Odds Ratio for ICU in patients with Calcifediol treatment vs Without Calcifediol treatment: 0.02 (95 %CI 0.002–0.17).

** Multivariate Risk Estimate Odds Ratio for ICU in patients with Calcifediol treatment vs Without Calcifediol treatment ICU (adjusting by Hypertension and T2DM): 0.03 (95 %CI: 0.003–0.25).

From Castillo et al, ""Effect of Calcifediol Treatment …: A Pilot Randomized Clinical study", J Ster Biochem & MolBio, 2020 based on 76 people hospitalized w/ COVID-19. Even the top of the 95% CI (which takes the small n into account) shows 75% lower odds of ICU, a huge effect. Best current other treatments (steroids) reduce deaths by only ~⅓.

Fewer people with high D levels die from CV19
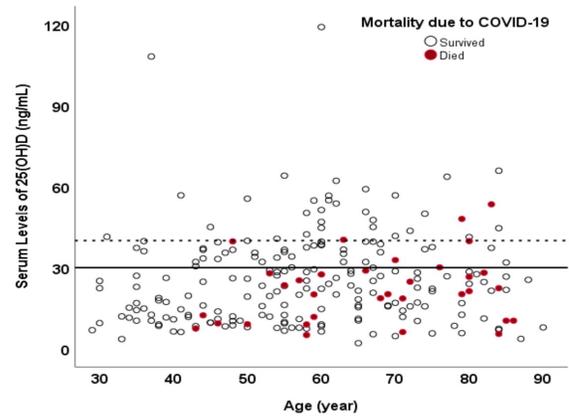
Mortality vs D level & age. From Maghbooli et al, "Vitamin D sufficiency … reduced risk for adverse clinical outcomes..." PLOS ONE, 2002 based on 235 people hospitalized w/ COVID-19. 6.3% with D>40 ng/ml died vs. 9.7% with D=30-40 vs 20% with D<30.

Low D is common across the world, with more than half the world having levels that increase risk
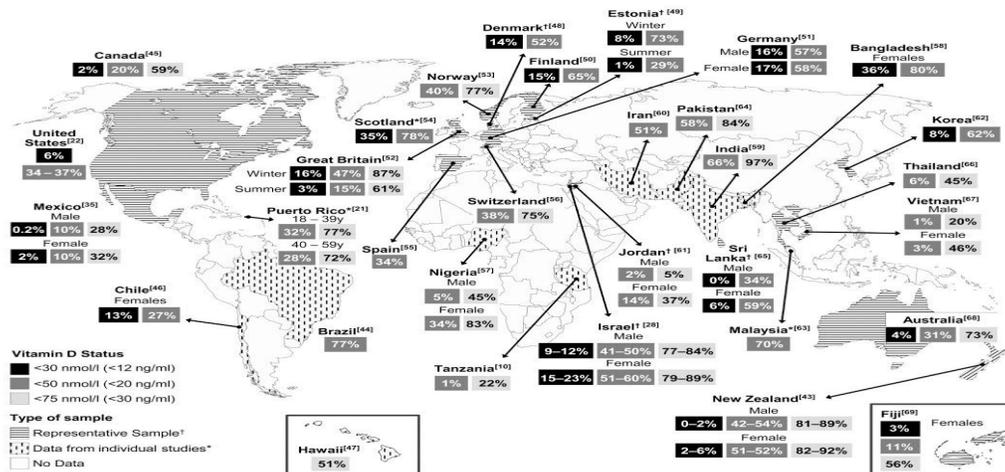
Figure 4.
Prevalence of low vitamin D status in adults worldwide.

From Palacios et al, "Is Vitamin D deficiency a major global public health problem?", J Ster Biochem MolBio, 2014. Worldwide 40% of people have D <20ng/ml, 60% <30n, from Charoenngam et al, "Immunologic effects of vitamin D…", Nutrients, 2020.