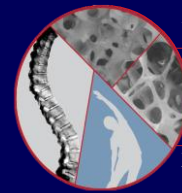


# Vitamin D and COVID-19

NOF ISO, May 2021

Neil Binkley, M.D.

University of Wisconsin School of Medicine and Public Health  
Madison, WI, USA



UNIVERSITY OF WISCONSIN  
Osteoporosis Clinical  
Research Program  
MADISON, WI



# Disclosures

- Consultant: Amgen
- Research Support: Radius, GE Healthcare
- No disclosures relevant to vitamin D

Some of this is my opinion:  
Noted as such by orange text color

*“With my opinion and five dollars  
you can get a cup of coffee.”*



*“For every problem there’s a solution  
that is simple, neat and wrong.”*

H. L. Mencken



# Why Are We Talking About COVID at an Osteoporosis Meeting?

Data as of May 1, 2021

## COVID-19 CORONAVIRUS PANDEMIC

Last updated: April 30, 2021, 13:54 GMT

[Weekly Trends](#) new - [Graphs](#) - [Countries](#) - [News](#)

Coronavirus Cases:

**151,274,224**

[view by country](#)

Deaths:

**3,182,376**

## WORLD / COUNTRIES / UNITED STATES

Last updated: April 30, 2021, 13:54 GMT



United States

Coronavirus Cases:

**33,044,068**

Deaths:

**589,207**



For perspective –  
1918 H1N1 pandemic

- 500 million infected (1/3 of world's population)
- 50 million deaths
- 675,000 in US

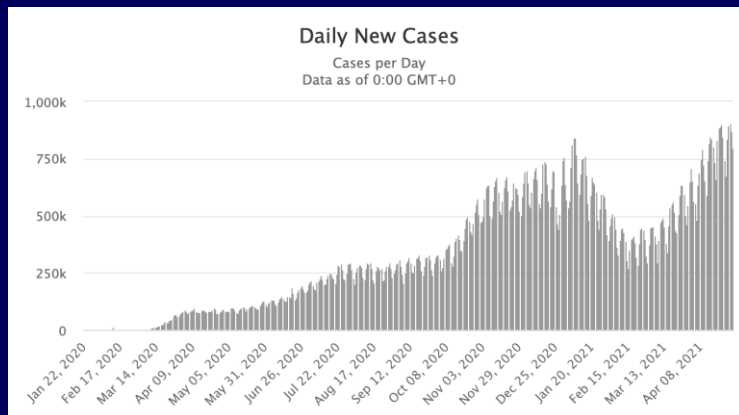


<https://www.worldometers.info/coronavirus>

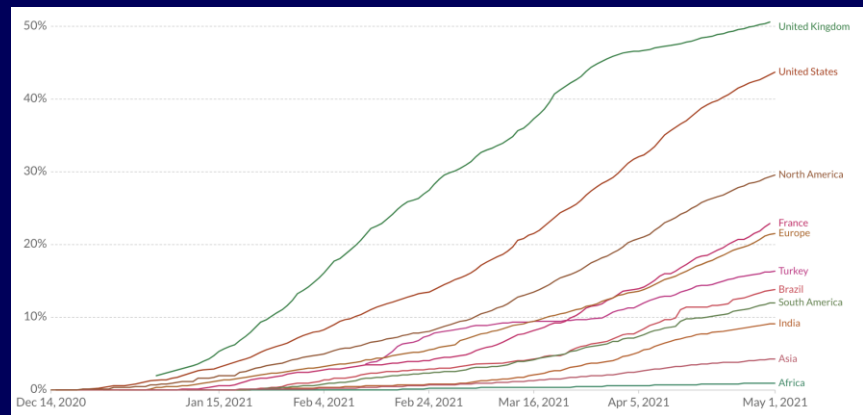
[www.cdc.gov](http://www.cdc.gov)

# Why Are We Talking About COVID and Vitamin D at an Osteoporosis Meeting?

Data as of May 1, New cases and % of population with 1 dose of vaccine



Data as of May 1, [www.worldometers.info/coronavirus](http://www.worldometers.info/coronavirus)



Data as of May 1, [www. https://ourworldindata.org/covid-vaccinations](https://ourworldindata.org/covid-vaccinations)

With almost 1 million new infections daily and <8% of the worlds population vaccinated, this will not be over soon....  
If vitamin D MIGHT be of help, it is worthy of consideration



# Rationale That Vitamin D Might be Important in SARS-COV 2 Infection

## □ Vitamin D:

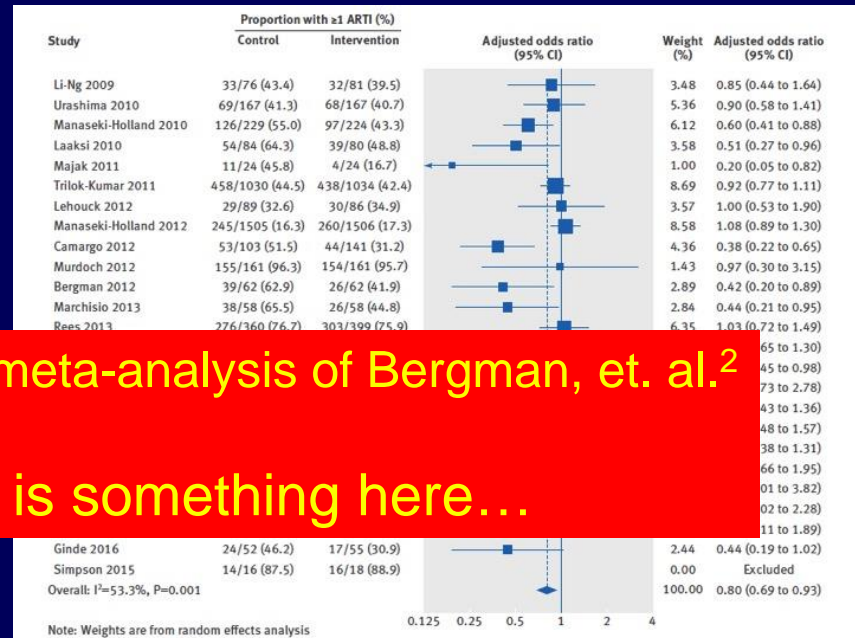
- May have antiviral effects
- Involved in innate immune system regulation
- Might modulate the cytokine storm of SARS-CoV-2
- Potential beneficial cardiovascular effects
- Other?

Bilezikian, et. al., Eur J Endocrinol, 2020; 183: R133-R147



# Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data

- 25 RCTs of vitamin D supplementation; n = 11321
- Acute respiratory infection risk reduced; OR 0.80
- Replicates smaller 2013 meta-analysis of Bergman, et. al.<sup>2</sup>
- Patients with baseline 25(OH)D < 25 nmol/L



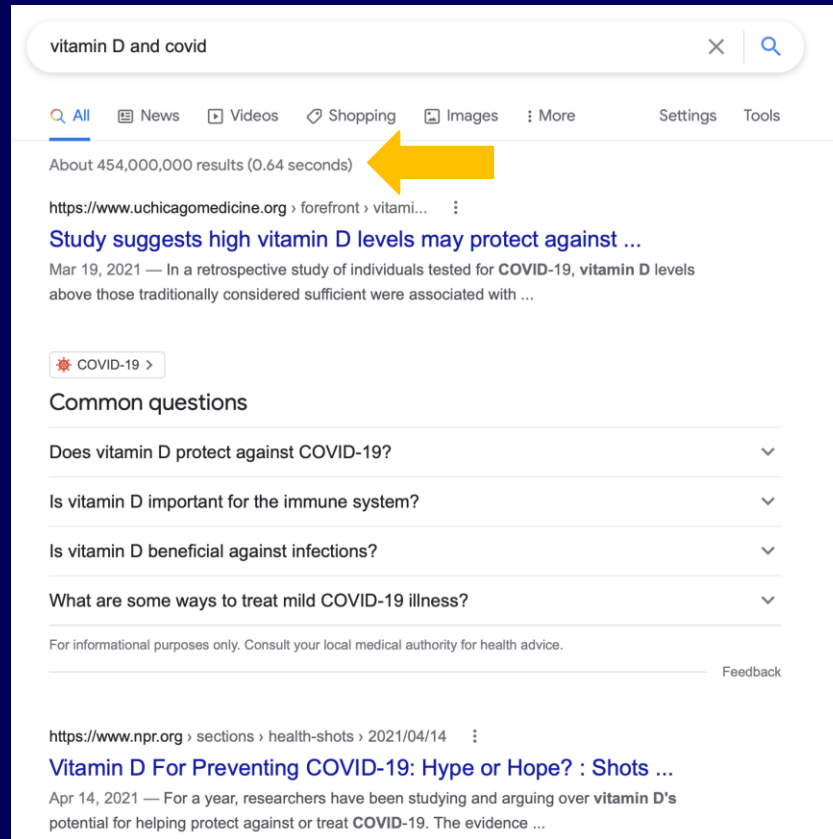
*“Vitamin D supplementation was safe and protected against acute RTI overall. Patients very vitamin D deficient experienced the most benefit.”*



Martineau, et. al., BMJ, 2017; 356:i6583, doi:10.1136/bmj.i6583

<sup>2</sup>Bergman, et. al., PLoS one, 2013; 8; e65835

# Appropriate Huge Interest in Vitamin D and COVID



A screenshot of a Google search interface. The search bar at the top contains the text "vitamin D and covid". Below the search bar, there are tabs for "All", "News", "Videos", "Shopping", "Images", and "More". The "All" tab is selected. Below the tabs, it says "About 454,000,000 results (0.64 seconds)". A yellow arrow points to this text. Below the results count, there is a snippet from a website: "https://www.uchicagomedicine.org › forefront › vitam...". The snippet title is "Study suggests high vitamin D levels may protect against ...". The snippet text is "Mar 19, 2021 — In a retrospective study of individuals tested for COVID-19, vitamin D levels above those traditionally considered sufficient were associated with ...". Below the snippet, there is a "COVID-19" tag. Below the tag, there is a section titled "Common questions". This section contains four questions, each with a dropdown arrow: "Does vitamin D protect against COVID-19?", "Is vitamin D important for the immune system?", "Is vitamin D beneficial against infections?", and "What are some ways to treat mild COVID-19 illness?". Below the questions, there is a disclaimer: "For informational purposes only. Consult your local medical authority for health advice." and a "Feedback" link. Below the disclaimer, there is another snippet from a website: "https://www.npr.org › sections › health-shots › 2021/04/14". The snippet title is "Vitamin D For Preventing COVID-19: Hype or Hope? : Shots ...". The snippet text is "Apr 14, 2021 — For a year, researchers have been studying and arguing over vitamin D's potential for helping protect against or treat COVID-19. The evidence ...".

Selected from a Google search: vitamin D and COVID May 3, 2021





Over 200 Scientists & Doctors Call For Increased Vitamin D  
Use To Combat COVID-19

Scientific evidence indicates vitamin D reduces infections & deaths

## There Has Been a Worldwide Call to Increase Vitamin D

*“To all governments, public health officials, doctors, and  
healthcare workers,*

*Research shows low vitamin D levels almost certainly promote COVID-  
19 infections, hospitalizations, and deaths. Given its safety, we call for  
immediate widespread increased vitamin D intakes.”*

***There is no need to wait for further clinical trials to increase use of  
something so safe, especially when remedying high rates of  
deficiency/insufficiency should already be a priority.”***

<https://vitamind4all.org/letter.pdf>



## This Worldwide Call States: Specifically to:

1. Recommend amounts from all sources sufficient to achieve 25(OH)D serum levels over **30 ng/mL** (75 nmol/L), a widely endorsed minimum with

2. *IT'S BEEN NINE MONTHS. THE EVIDENCE  
WAS UNDENIABLE IN MARCH FOR ANYONE  
WILLING TO LOOK.*

3. *weight, dark skin, or living in care homes may need higher intakes (e.g., 2x). Testing can help to avoid levels too low or high.*
4. Recommend **10,000 IU** (250,000 IU/kg) daily for 8 weeks. *amounts get 30 ng/mL if widely regarded as safe.*
5. Measure 25(OH)D levels of all hospitalized COVID-19 patients & treat w/ calcifediol or D<sub>3</sub>, to at least remedy insufficiency <30 ng/ml (75 nmol/L)..."

**Is This True?**  
**Let's Look at the Literature**

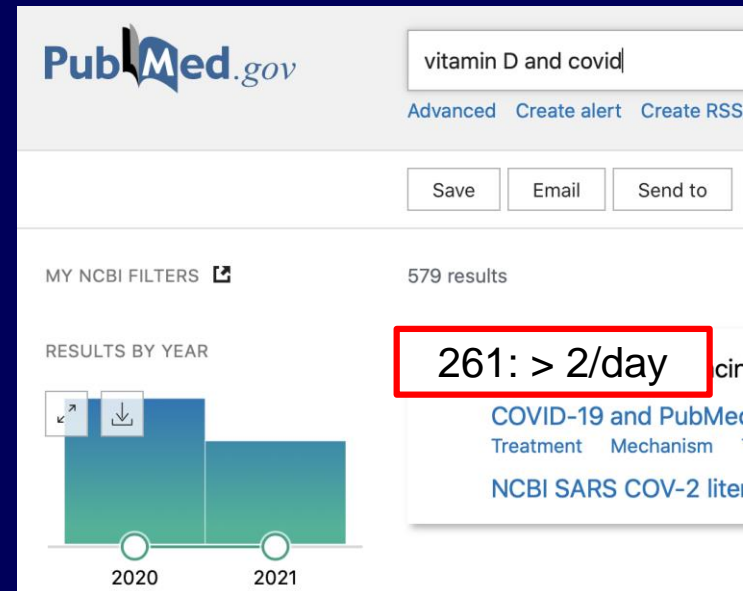


<https://vitamind4all.org/letter.pdf>

# Scientific Literature: HUGE Number of Publications on Vitamin D and COVID

- Vitamin D
  - 2020: 5,432 (~15/day)
  - 2021: 2220 (~18/day)
- COVID
  - 2020: 87,795 (~241/day)
  - **2021: 49,037 (~399/day)**

I have not attempted to review everything and have doubtlessly missed and/or will not comment upon important works



Source: Pubmed (accessed May 3, 2021)



# Many Publications Review the Physiologic Rationale Behind a Vitamin D and COVID Relationship

*“....apply our current understanding of vitamin D as a facilitator of immunocompetence both with regard to innate and adaptive immunity and to consider how this may relate to COVID-19 disease. There are also intriguing potential links to vitamin D as a factor in the cytokine storm...”*

Bilezikian, et. al., Eur J Endocrinol, 2020; 183: R133-R147



# Some Reviews Are Essentially Editorials

*Review*

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

*“To reduce the risk of infection, it is recommended that people at risk of influenza and/ or COVID-19 consider taking 10,000 IU/day of vitamin D<sub>3</sub> for a few weeks to rapidly raise 25(OH)D concentrations, followed by 5000 IU/day. 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.”*

Grant, et. al., Nutrients 2020, 12, 988; doi:10.3390/nu12040988



# A Fair Number Are Commentaries/Editorials

## LETTER TO THE EDITOR

COVID-19 and vitamin D—Is there a link and an opportunity for intervention?

*“Owing to the lack of specific treatment and urgency to act, these findings could be tentatively extrapolated to SARS-CoV-2 infection, justifying the use of vitamin D as a possible adjuvant therapy. From the public health aspect, the recommendation of intensive supplementation as possible prophylaxis also could be considered. Given the good tolerability and safety of even high doses of vitamin D, this approach complies with primum non nocere principle.”*

Jacovac., Am J Physiol Endocrinol Metab 318: E589, 2020;  
doi:10.1152/ajpendo.00138.2020



## Some Editorials Urge Caution

Vitamin D and COVID-19: causal factor or bystander?

*“Given that vitamin D deficiency or insufficiency are highly prevalent globally, there is no harm in recommending optimal sunlight exposure or vitamin D supplementation to the general public....”*

*“However, **it may be premature to make any claims on the indication of vitamin D for COVID-19.** Blind faith in taking vitamin D to prevent COVID-19 may give a **false sense of invulnerability** and increase the risk of infection and delay seeking medical diagnosis and treatment.”*

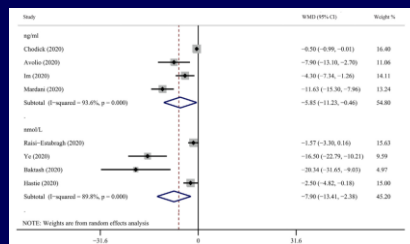
Cheung and Cheung, Postgrad Med J 2021, <http://dx.doi.org/10.1136/postgradmedj-2020-139388>



# Systematic Reviews Have Explored the Relationship of 25(OH)D With COVID

- Systematic review of 9 studies involving over 1 million participants
- “Low vitamin D levels” were correlated with COVID-19 infection, seriousness and mortality
 

Yisak, et. al, Risk Management and Healthcare Policy 2021: 14. 31-38
- Systematic review of 10 studies involving ~360,000 participants
- COVID-19 positive individuals had lower vitamin D levels than negative individuals**



Liu, et. al, Int J Infect Dis 2021:104 58-64

Forrest plot of “serum vitamin D levels”  
in those with or without COVID-19

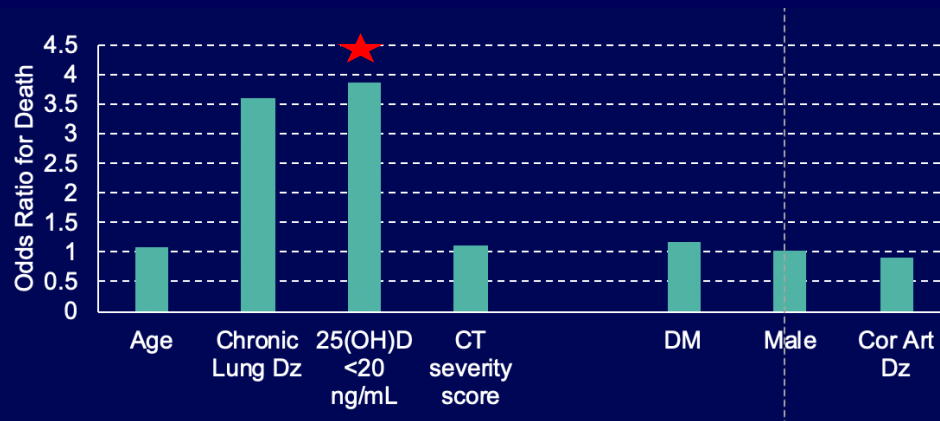




# Low 25(OH)D is Associated With Higher Mortality

**Serum 25(OH)D Level on Hospital Admission Associated With COVID-19 Stage and Mortality**

- Retrospective observational study of 186 patients with severe acute respiratory distress who had chest CT and 25(OH)D
- 59% were D deficient ( based on 25(OH)D <20 ng/mL) on admission
- Vitamin D deficiency was associated with mortality independent of age, chronic lung disease and extent of lung damage on chest CT



*“Our study shows an association between vitamin D deficiency and mortality of COVID-19 pneumonia and makes a call for general avoidance of vitamin D deficiency as a safe and inexpensive possible mitigation of the pandemic.”*



De Smet, et. al., Am J Clin Pathol, 2020, XX: 1-8; doi:10.1093/ajcp/aqaa252



## Be Cautious With Sensational Headlines

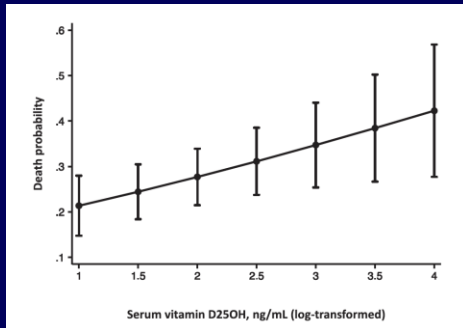
*“What is not clear is whether vitamin D levels are acting as an acute-phase reactant, dropping because of the infection with larger drops indicating more severe disease, or whether vitamin D deficiency is causing worse outcomes.”*

Clinical Endocrinology News, V 16, #1, Jan 2021

Vitamin D 25OH deficiency in COVID-19 patients admitted to a tertiary referral hospital

## Low 25(OH)D is Associated With LOWER Mortality

- 129 consecutive COVID-19 patients admitted to an Italian hospital
- 25(OH)D measured within 48 hours of admission
  - Normal  $\geq 30$ , insufficient 20-30, moderately deficient 10-20, severely deficient  $< 10$  ng/mL: 90%  $< 30$  ng/mL
- Outcomes: severe pneumonia, admission to ICU, mortality and markers of disease severity, e.g., CRP
- 26% mortality; 25(OH)D not associated with clinical outcomes



*“Unexpectedly, after adjusting for major confounders (age, sex, CRP, heart disease and severe pneumonia), a significant positive association between increasing 25(OH)D levels and in-hospital mortality was observed.”*



Cereda, et. al., Clin Nutr, 2020; S0261-5614(20)30601-4. doi: 10.1016/j.clnu.2020.10.055

## Adding 25(OH)D to “Best Available Treatment”

“Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study”

- 76 consecutive patients hospitalized at a Univ Hosp in Spain with COVID-19 pneumonia on x-ray and positive SARS-CoV-2 PCR
- All received hydroxychloroquine and azithromycin
- Eligible patients calcifediol or not; 2:1 on day of admission
- Oral calcifediol 0.532 mg on admission; 0.266 mg on day 3 and 7 then weekly vs. nothing until discharge or ICU admission
- Outcomes: rate of ICU admission and death
- **50 treated with calcifediol, 1 (2%) admitted to ICU and no deaths vs. 13/26 (50%) untreated and 2 deaths**
- Limitations: not double blind or placebo controlled, small number
- *“....calcifediol administration may **improve clinical outcome** of subjects requiring hospitalization for COVID-19.”*

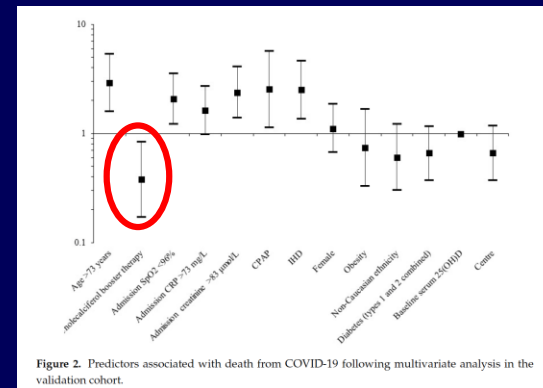
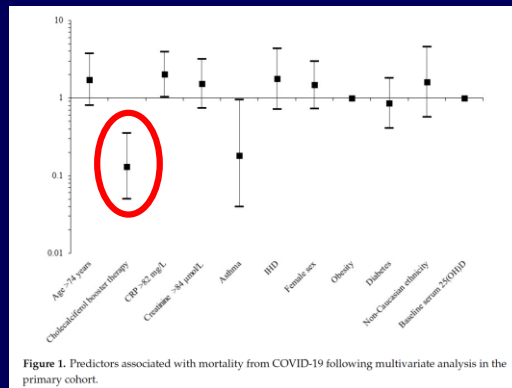


Castillo, et. al., J Steroid Biochem Mol Biol, 2020, 203: 105751

# Vitamin D Reduced Inpatient Mortality

High-Dose Cholecalciferol Booster Therapy is Associated with a Reduced Risk of Mortality in Patients with COVID-19: A Cross-Sectional Multi-Centre Observational Study

- Observational study: UK COVID inpatients; 444 initial 541 validation
- Received various cholecalciferol regimens: generally 4000-5000 IU daily or 20,000-50,000 weekly**
- Primary outcome measure = COVID-19 mortality



*“...cholecalciferol booster therapy, regardless of baseline 25(OH)D, appears to be associated with a reduced risk of mortality in inpatients with COVID-19.”*



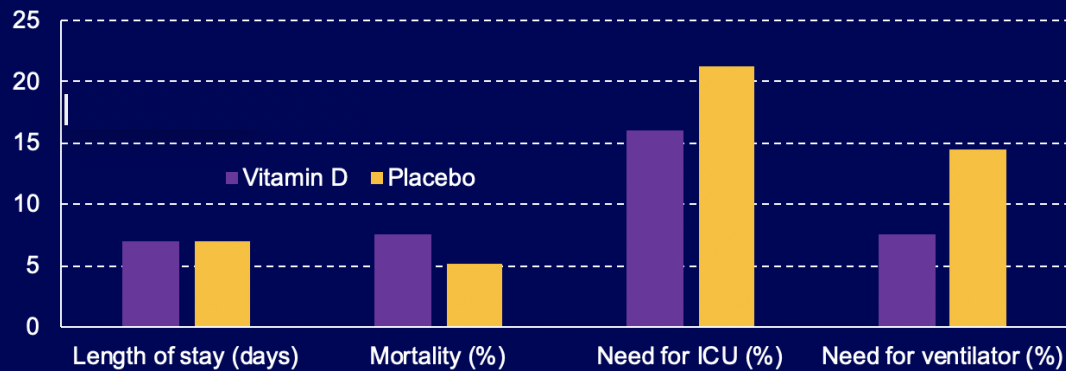
Ling, et. al., Nutrients, 2020, 12, 3799; doi:10.3390/nu12123799

# Vitamin D Had No Effect in Hospitalized Patients

JAMA | Original Investigation

Effect of a Single High Dose of Vitamin D<sub>3</sub> on Hospital Length of Stay in Patients With Moderate to Severe COVID-19  
A Randomized Clinical Trial

- Two site, double blind RCT in Brazil: 240 hospitalized with moderate to severe COVID
- Received **cholecalciferol 200,000 IU orally once or placebo**
- Primary outcome measure = Hospital length of stay



*“The findings do not support the use of a high dose of vitamin D<sub>3</sub> for treatment of moderate to severe COVID-19.”*



Murai, et. al., JAMA, 2021, 325:1053-1060; doi:10.1001/jama.2020.26848

## Potential Conclusions

- ❑ Vitamin D deficiency/insufficiency is common worldwide
- ❑ 25(OH)D is often low in people infected with SARS-CoV2
- ❑ Vitamin D deficiency might be related to the pathophysiology of COVID
- ❑ Some reports that D administration improves outcomes
- ❑ We don't have great drugs to cure COVID
- ❑ This is a pandemic like none of us have ever seen
- ❑ ***Give everybody vitamin D***



# **Be Cautious When Drawing Conclusions About Measured “Low” 25(OH)D Levels in COVID Patients**

Personal opinion

**There is a Lot to Think About Regarding the  
Relationship of Vitamin D With COVID (AND with  
Osteoporosis/Fractures)**

**I Don't Know the “Right” Answer  
Things to Consider.....**





# Challenges That Have Plagued the Vitamin D Field Remain in Effect for COVID

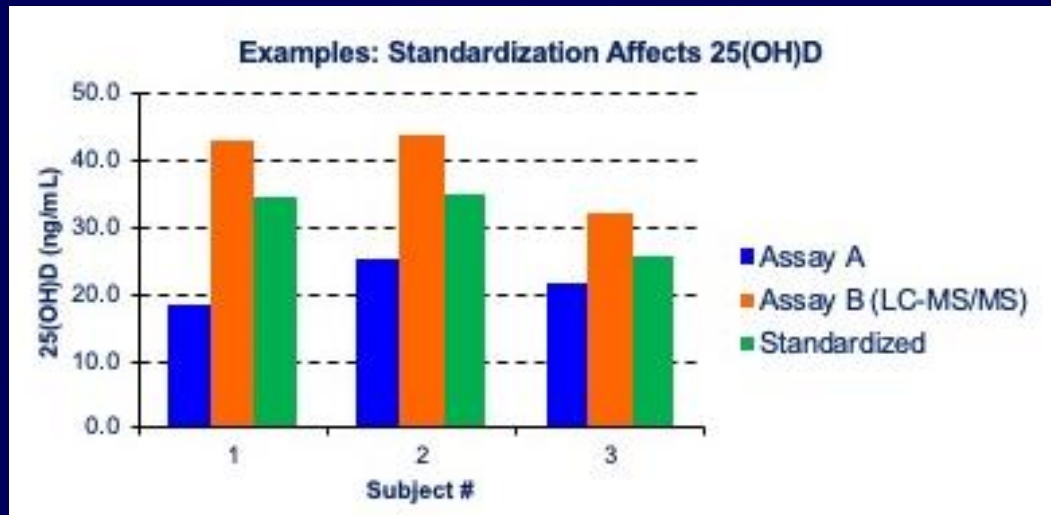
Personal opinion

- ❑ Association does not prove causation
- ❑ How to define “low?”
  - Acute illness/surgery/Inflammation lowers 25(OH)D
- ❑ If 25(OH)D is indeed the correct test to define “low vitamin D status, it is necessary to report standardized data
- ❑ Vitamin D is likely a nutrient, not a drug; more is unlikely to be better and supplementing/treating vitamin D replete subjects may well have no effect



# We Need to be Reporting Standardized 25(OH)D Results

“25(OH)D”  $\neq$  “25(OH)D”



Unpublished data; manuscript submitted

Various studies reporting “25(OH)D” will include those  
with different vitamin D status based upon assay used



**Even if All Studies Immediately  
Started Reporting Standardized  
25(OH)D Values in COVID Patients...**



**Do We Know What  
a “Low” 25(OH)D  
Means??**



# Low 25(OH)D May be DUE TO Inflammation

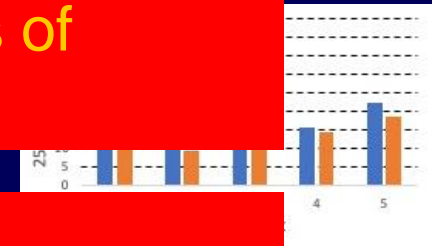
Does serum 25-hydroxyvitamin D decrease during acute-phase response? A systematic review

Mariana Costa Silva<sup>a</sup>, Tania Weber Furlanetto<sup>a, b, \*</sup>

- • Mechanism(s) unclear
- Essential to consider in all studies of acutely ill patients with COVID

□ • Mean decrease = 28%

- Worthy of consideration....
- Is this only an assay effect OR are these people truly vitamin D deficient?
- Said another way; are low measured 25(OH)D levels truly indicative of tissue/cellular level vitamin D inadequacy?



“The  
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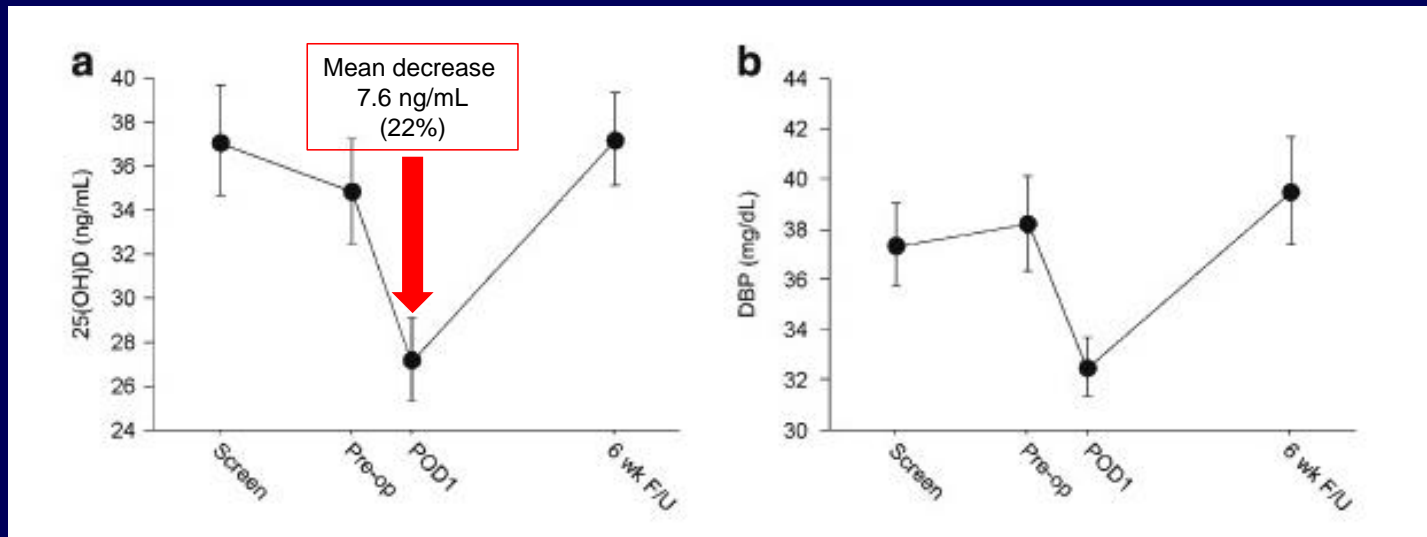
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Silva and Furlanetto, Nutr Rev, 2015; 35: 91-96

# Acute Illness Lowers 25(OH)D and DBP

Surgery acutely lowers 25(OH)D; Total hip arthroplasty (n = 40)

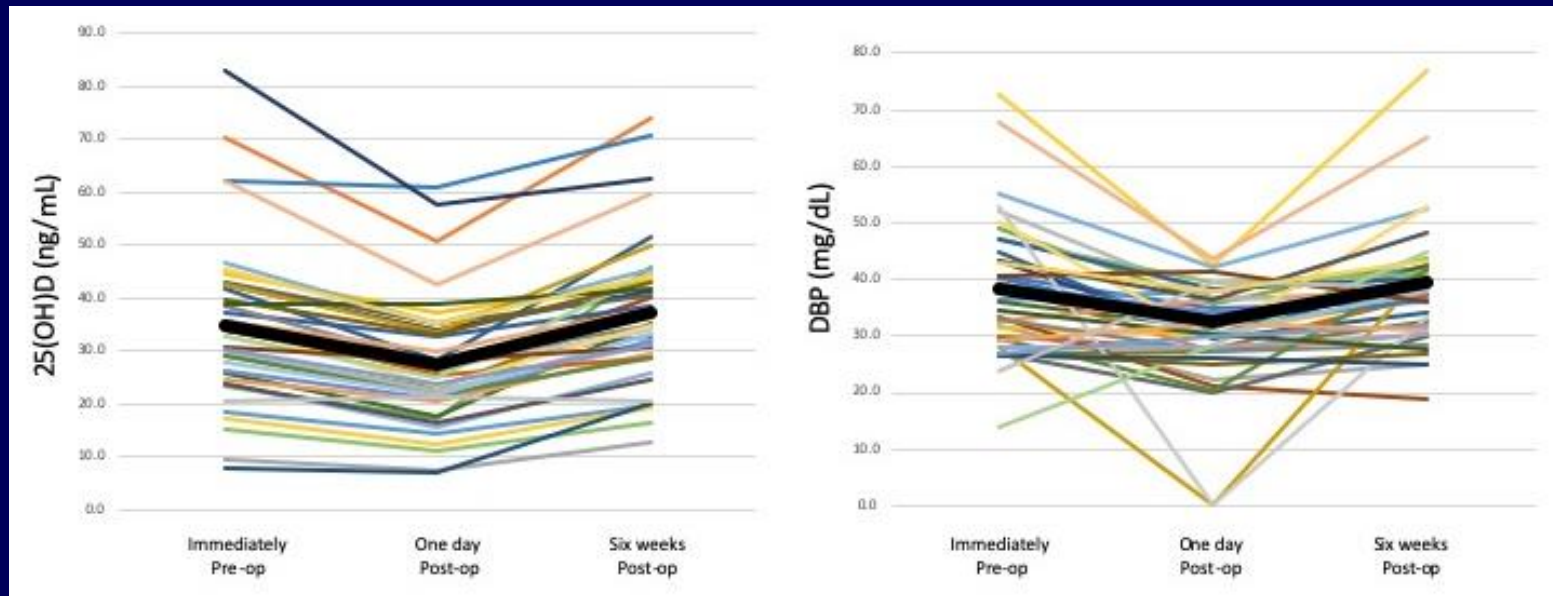


Does this occur in just a few patients, thus affecting the mean?



Binkley, et al., Osteoporos Int, 2017; 28: 1013-1020

# 25(OH)D and DBP Decline In Virtually All Patients with Total Hip Arthroplasty



Binkley, et al., Osteoporos Int, 2017; 28: 1013-1020. Individual data unpublished



## Acute Inflammation Lowers 25(OH)D

*“Our data reveal that systemic inflammation lowers circulating 25(OH)D levels in humans. This mechanism may contribute to the low circulating 25(OH)D concentrations observed in patients suffering from infectious diseases, including COVID-19. In virtually all of these patients, onset of disease precedes hospital admission by at least several days. Our results show that 25(OH)D levels decrease within hours of initiation of a systemic inflammatory response. As such, the developing inflammatory response in COVID-19 patients may have decreased 25(OH)D before in-hospital measurements were performed.”*



Smolders, et. al., Metabolism, 2021; 115:154434. doi: 10.1016/j.metabol.2020.154434

# This Confounds ALL Reports of Low 25(OH) in COVID Patients

Personal opinion



*“These folks are amazingly sick (as sick as I have ever seen)....”*

D. Coursin, M.D.





**Additionally, We Should Ask:  
Is “Vitamin D” a Nutrient or a Drug?**

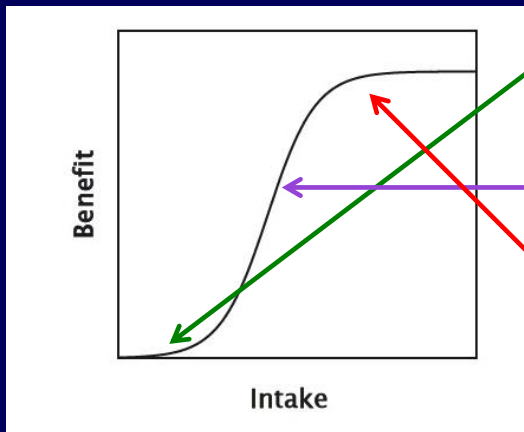
**I'd be OK Using it as a Drug, But We  
Need to Recognize that is What We  
are Doing.....**

Personal opinion





## IF Vitamin D is a Nutrient, We Should Listen to Heaney's Advice....



- "...If the basal status is deficient, then an increase in intake will usually produce a measurable benefit.
- If the nutritional status is replete, an increase in intake will usually produce a null effect,
- and if the nutritional status is high, an increase in intake might be expected to increase risk of toxicity."

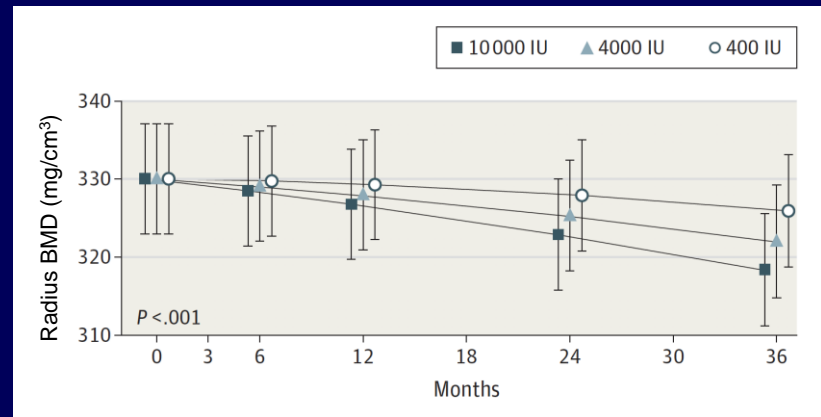
*"This point is so obvious from simple inspection of the curve that one should have thought it would go without saying."*

Heaney RP, Nutr Reviews 2013, 72:48-54



## Effect of High-Dose Vitamin D Supplementation on Volumetric Bone Density and Bone Strength A Randomized Clinical Trial

- 3 year RCT
- 311 community dwelling adults
- Daily vitamin D<sub>3</sub>; 400, 4000 or 10000 IU
- Baseline 25(OH)D respectively: 31.4, 32.5, 30.7 ng/mL



*“At trial end, radial vBMD was lower for the 4,000 and 10,000 IU dose group....”*

Burt, et. al., JAMA, 2019, 322: 736-745

*“... if the nutritional status is high, an increase in intake might be expected to increase risk of toxicity.”*

Heaney RP, Nutr Reviews 2013, 72:48-54



## Adding 25(OH)D to “Best Available Treatment”

“Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study”

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- Limitations: not double blind or placebo controlled, small number
- *“....calcifediol administration may **improve clinical outcome** of subjects requiring hospitalization for COVID-19.”*



Castillo, et. al., J Steroid Biochem Mol Biol, 2020, 203: 105751

# Even IF Vitamin D Has an Immunomodulatory Effect in COVID Infection, Could Any Such Effect be Observed Given That:

1. Patients are REALLY sick by the time they get to the hospital

Has the horse left the barn?



2. Dexamethasone is standard treatment

Can anything produce a more profound anti-inflammatory effect?



# **Does an Illness/Inflammation Induced Drop in Circulating 25(OH)D Translate to Tissue/Cellular Level Vitamin D Deficiency?**

**Well Designed and Thoughtful RCTs Are  
Needed to Clarify What Role, If Any,  
Vitamin D Deficiency Plays in COVID  
Infection and Outcomes**



# Many Clinical Trials are Ongoing

ClinicalTrials.gov: COVID19 & vitamin D yielded 93 studies on May 3, 2021

Showing: 1-93 of 93 studies 100 studies per page Show/Hide Columns

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input type="checkbox"/>	Completed	<a href="#">Impact of Vitamin D Level and Supplement on SLE Patients During COVID-19 Pandemic</a>	• Covid19	• Drug: <b>Vitamin D</b> • Diagnostic Test: ELISA	• Mansoura University Hospital Mansoura, DK, Egypt
2	<input type="checkbox"/>	Recruiting	<a href="#">N-terminal Pro B-type Natriuretic Peptide and Vitamin D Levels as Prognostic Markers in COVID-19 Pneumonia</a>	• COVID19 Pneumonia	• Other: Pro BNP , <b>Vitamin D</b>	• Kasr Alainy Cairo University Cairo, Giza, Egypt
3	<input type="checkbox"/>	Recruiting	<a href="#">Vitamin D and COVID-19 Trial</a>	• COVID-19	• Dietary Supplement: <b>vitamin D</b> • Dietary Supplement: Placebo	• Brigham and Women's Hospital Boston, Massachusetts,

Huge dose range and varying dosing schedules  
From 400 IU daily, through a bolus of 50,000 or 100,000 IU followed by weekly or daily to as high as 500,000 IU once

7	<input type="checkbox"/>	Recruiting	<a href="#">Prevention of COVID-19 With Oral Vitamin D Supplemental Therapy in Essential healthCare Teams</a>	• COVID-19	• Dietary Supplement: Placebo • Dietary Supplement: <b>Vitamin D</b>	• CHUM Montreal, Quebec, Canada • CHU Sainte-Justine (CHUSJ) Montreal, Quebec, Canada
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Clinicaltrials.gov; accessed May 3, 2021

# Is “Vitamin D” a Nutrient or a Drug?

Recognize that some studies (two selected examples) are using non-physiologic, i.e., pharmacologic doses

- “CARED-Trial” protocol; RCT in Argentina of hospitalized SARS-CoV-2 patients with  $O_2$  sat  $\geq 90\%$
- Intervention one dose of vitamin  $D_3$ , **500,000 IU** or placebo
- Primary outcome is change in respiratory sepsis-related organ failure assessment score

Mariani, et. al., Trials, 2021; 22: 111

- 91 consecutive patients admitted with COVID
- “Supplemented” with **400,000 IU  $D_3$**  based on physician decision
- Composite outcome of death or ICU transfer reduced by 43%
  - OR 0.57 (0.214-1.34);  $p = 0.20$

Giannini, et. al., Nutrients, 2021; 13: 219. doi.org/10.3390/nu13010219





# The Human Clinical Trials Are Going to be a Mixture of Supplementation and Massive Pharmacological Doses

Personal opinion

Additionally, a “COVID patient” Can Have Radically Differing Degrees of Illness from Asymptomatic to Lethal



# Perhaps Animal Studies Could Provide Rigorously Controlled Data Assessing the Potential Importance, or Lack Thereof, for COVID Patients

Review

Animal models for influenza virus pathogenesis, transmission, and immunology

Rajagowthamee R. Thangavel<sup>a</sup>, Nicole M. Bouvier<sup>a,b,\*</sup>

*“Animal models are used in influenza research not only to elucidate the viral and host factors that affect influenza disease outcomes in and spread among susceptible hosts, but also to evaluate interventions designed to prevent or reduce influenza morbidity and mortality in man.”*



Thangavel and Bouvier, J Immunol Methods, 2014, 410: 60-79

## Current global vaccine and drug efforts against COVID-19: Pros and cons of bypassing animal trials

BIJAYEETA DEB<sup>†</sup>, HEMAL SHAH<sup>†</sup> and SUCHI GOEL\*

*“For an animal to be a model for a disease, the pathogen should be able to infect the animal using the same receptor on cell used in humans and then multiply inside the host successfully. Additionally, it should provide similar clinical symptoms as humans....”*

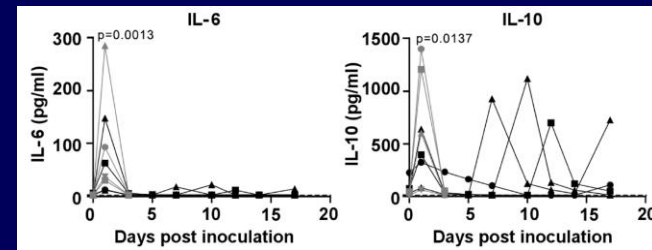
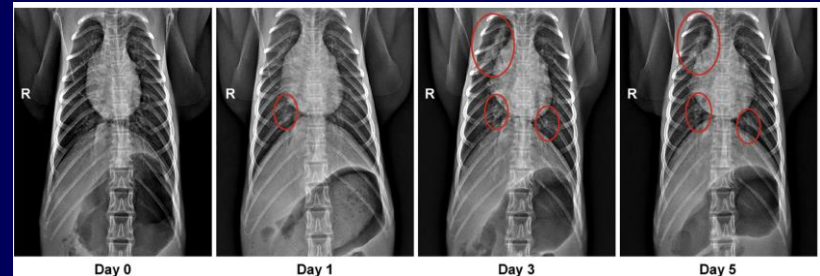
- Ferrets; increase body temperature but not other symptoms
- Mice; not infected due to differing ACE2 receptor
- Syrian hamster; weight loss and high viral load in respiratory tract
- Rhesus macaques



Deb, et. al, J Biosci, 2020, 45: 82. DOI: 10.1007/s12038-020-00053-2

## Respiratory disease in rhesus macaques inoculated with SARS-CoV-2

- Inoculated 8 adult rhesus monkeys with SARS-CoV-2
- Day 1; decreased appetite, fever, cough, tachypnea
- All recovered in 9-17 days
- Pulmonary infiltrates in all
- High viral load in lungs in all



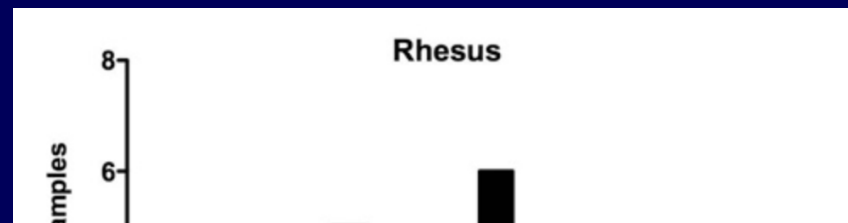
*“Together, our rhesus-macaque model recapitulates COVID-19 in humans with regard to virus replication and shedding, the presence of pulmonary infiltrates, histological lesions and seroconversion.”*



Munster, et. al, Nature, 2020, 585: 268-272

# Not Sure That this is Important, But..... Rhesus Monkeys Have HIGH 25(OH)D Levels

- 25 adult rhesus laboratory raised animals



Not easy, not quick, not cheap, but.....  
Perhaps non-human primates could be the ideal  
animal model to study vitamin D and  
other interventions for COVID

COVID disease??

40

ng/mL

88



Ziegler, et. al, Am. J Primatol, 2015, 77: 801-810



# Could a Monkey Study Provide The Answers??

- Three groups
  - Vitamin D more than sufficient (usual diet)
  - Vitamin D deficient (this would take a while)
  - Pharmacologic dose daily
- Multiple outcomes could be measured
  - Cytokines
  - Radiographs
  - Viral load
  - Etc, etc

Personal opinion



# **Is There An Answer to the Question: Is Vitamin D Deficiency Important in SARS-CoV-2 Infection?**

**I'm Not Sure...**

**But I Suspect That Low 25(OH)D  
Values In Hospitalized COVID Patients  
Identify People With Severe Disease**

Personal opinion



# This Letter to the Editor Was Very Well Done

Vitamin D and SARS-CoV-2 infection—evolution of evidence  
supporting clinical practice and policy development

A position statement from the Covid-D Consortium

Personal opinion

Dr. Michael Ryan, WHO Executive Director: *“Be fast, have no regrets. The virus will always get you if you don’t move quickly; if you need to be right before you move, you will never win.” “Perfection is the enemy of the good when it comes to emergency management. The problem in society we have at the moment is that everyone is afraid of making a mistake. But the greatest error is not to move. The greatest error is to be paralysed by the fear of failure.”*

- Vitamin D deficiency is common across all age groups
- We recommend daily supplementation with 800-1000 IU D<sub>3</sub> for most of the adult population in Ireland for duration of the pandemic
- For vulnerable groups (obese, dark skin, older, NH residents) higher doses will likely be required to achieve > 50 nmol/L
  - This should be prescribed and monitored under medical supervision

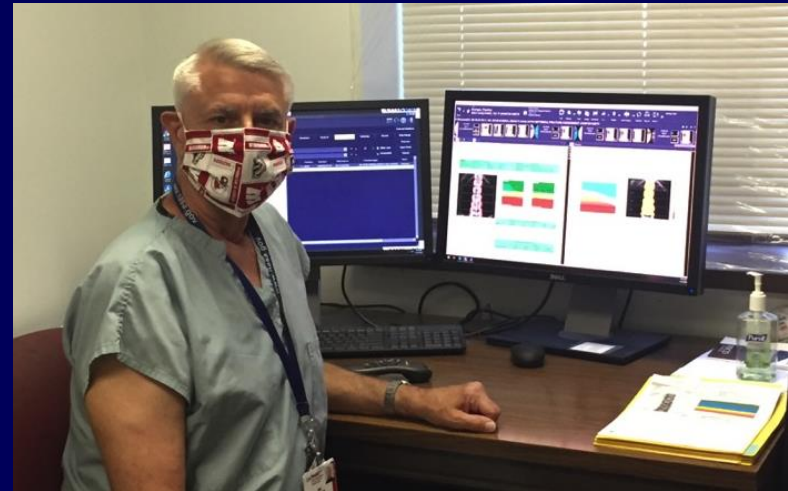


McCartney, et. al., Ir J Med Sci. 2020, 1971; doi.org/10.1007/s11845-020-02427-9



I see no  
downside to  
daily vitamin D  
supplementation  
(800-2,000 IU) to  
maintain a  
25(OH)D level of  
30-40 ng/mL,  
BUT.....

Personal opinion



Doing so does not replace  
social distancing, masking,  
hand washing and vaccination



**Thank You**

