Key-Note Speech
9th Vitamin D Congress, Abu Dhabi, UAE
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# Vitamin D and The Immune System: Clinically Relevant Doses and 25(OH)D Levels to Overcome Infections, Including COVID-19

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# Outline — Learning Objectives

01 Key concepts related to vitamin D

02 Biology of vit D—related to immunology

03 Evidence for causality of Vit D to COVID

04 Importance of calcifediol in infections

05 Cost effectiveness of using vitamin D in COVID & sepsis

# Other Micronutrients For Immunity

- Vitamins —$K_2$, A, C, magnesium, zinc, selenium, omega-3 fatty acids, resveratrol, quercetin —are important for a robust immune system.

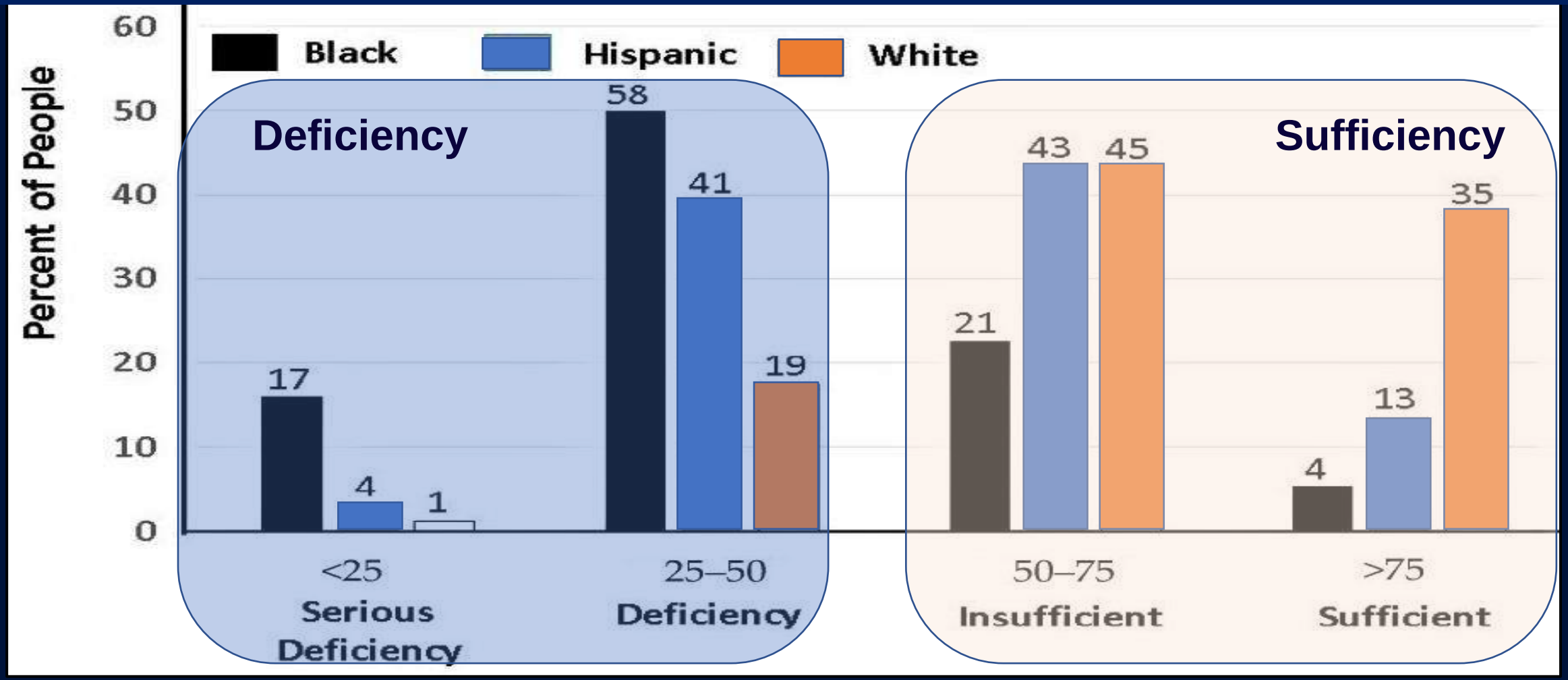
- Supplemental nutrients together with essential fatty acids, dietary iron, iodine ($T_3$), and especially magnesium, enhances the efficacy of vitamin D and VDR system in boosting the immune system.

# Certain Groups Are More Vulnerable?

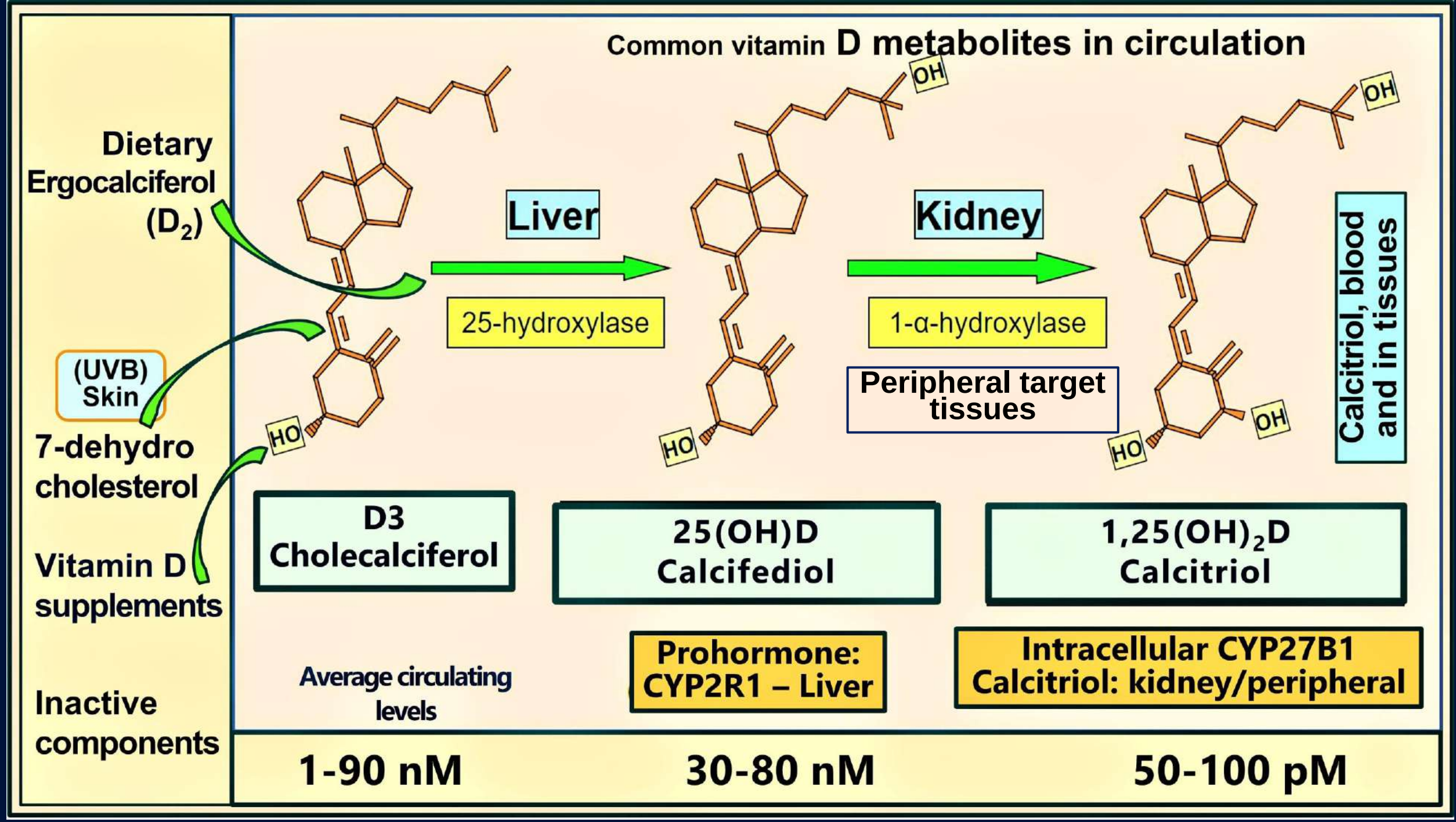
- There is a racial and ethnic disparity of "population" serum 25(OH)D concentrations.
- This is due to several reasons, including related to darkens of the skin colour
- Consequently, the vulnerability to chronic diseases and infections—sepsis, is higher among those groups with a low 25(OH)D

*Wimalawansa, SJ. 2004*

# Serum 25(OH)D in National Health & Nutrition Examination Survey (NHANES), 2001–10 by race/ethnicity—vit D not supplement gps



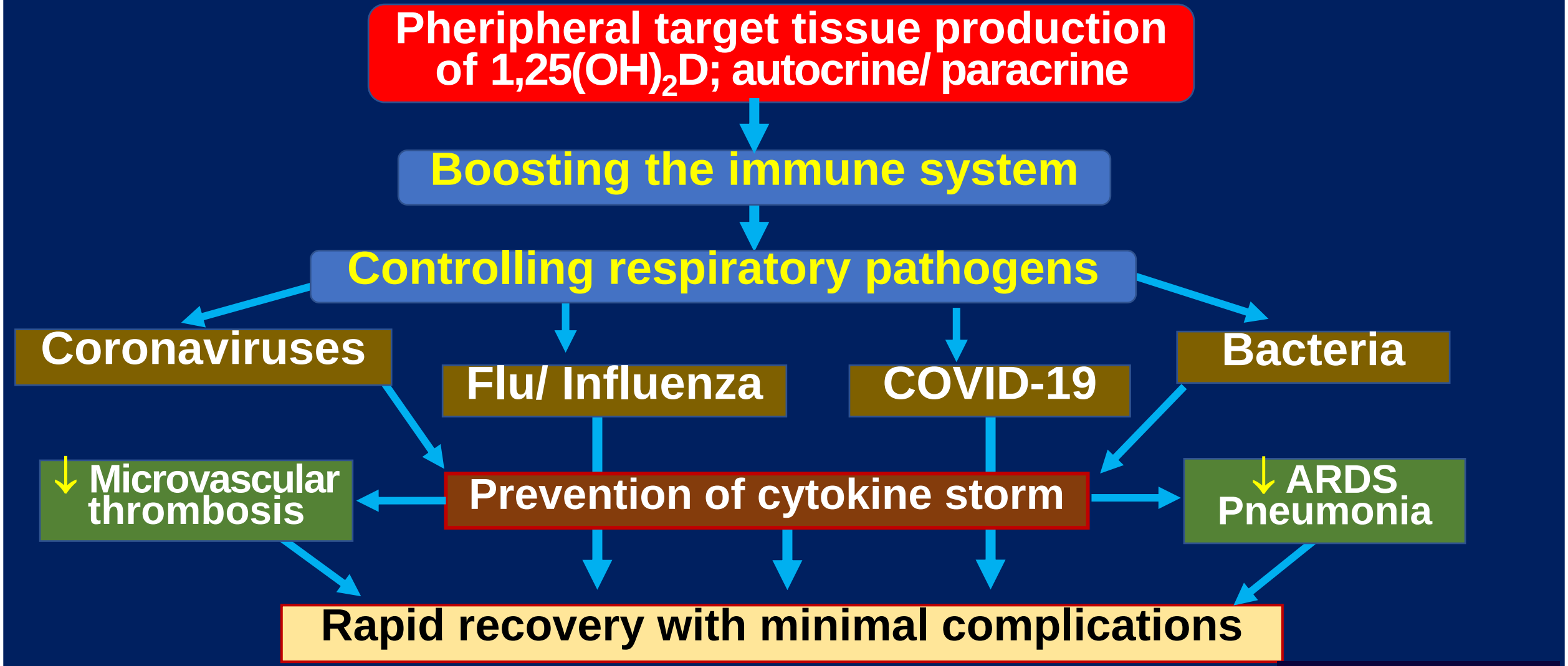

Liu, X.; Baylin, A.; Levy, P.D. Vitamin D deficiency and insufficiency among US adults: Prevalence, predictors and clinical implications. *Br. J. Nutr.* 2018, *119*, 928–936

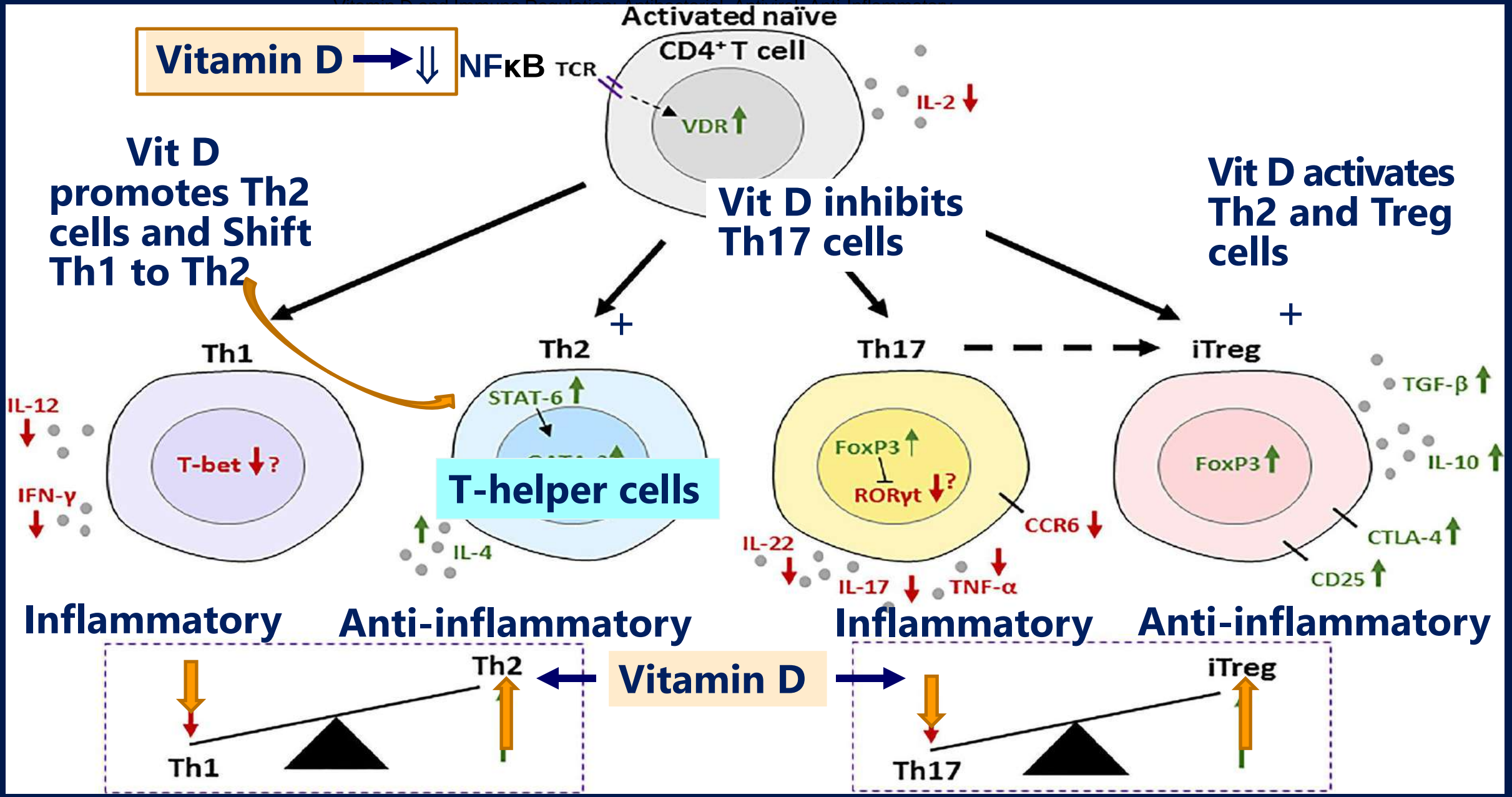

Common vitamin D metabolites in circulation
Dietary Ergocalciferol ($D_2$)
(UVB) Skin
7-dehydro cholesterol
Vitamin D supplements
Inactive components
Liver
25-hydroxylase
Kidney
1-α-hydroxylase
Peripheral target tissues
Calcitriol, blood and in tissues
HO
OH
D3 Cholecalciferol
25(OH)D Calcifediol
$1,25(OH)_2D$ Calcitriol
Prohormone: CYP2R1 – Liver
Intracellular CYP27B1 Calcitriol: kidney/peripheral
Average circulating levels
1-90 nM
30-80 nM
50-100 pM

# Key Benefits of Vitamin D in COVID-19

- Stimulate Innate & Adaptive immunity
- Potent anti-inflammatory and anti-oxidant
- Anti-microbial properties—both viruses & bacteria
- Prevent complications (e.g., cytokine storm)
- Enhance neutralizing antibodies and synthesis of ACE-2 receptors
- Protect all tissues

# $D_3$ & 25(OH)D in blood—Enter into Immune Cells






JBMR Plus, Vol: 5, Issue: 1: 22 August 2020, DOI: (10.1002/jbm4.10405)

# Why the Efficacy of COVID Vaccines is Gradually Failed?

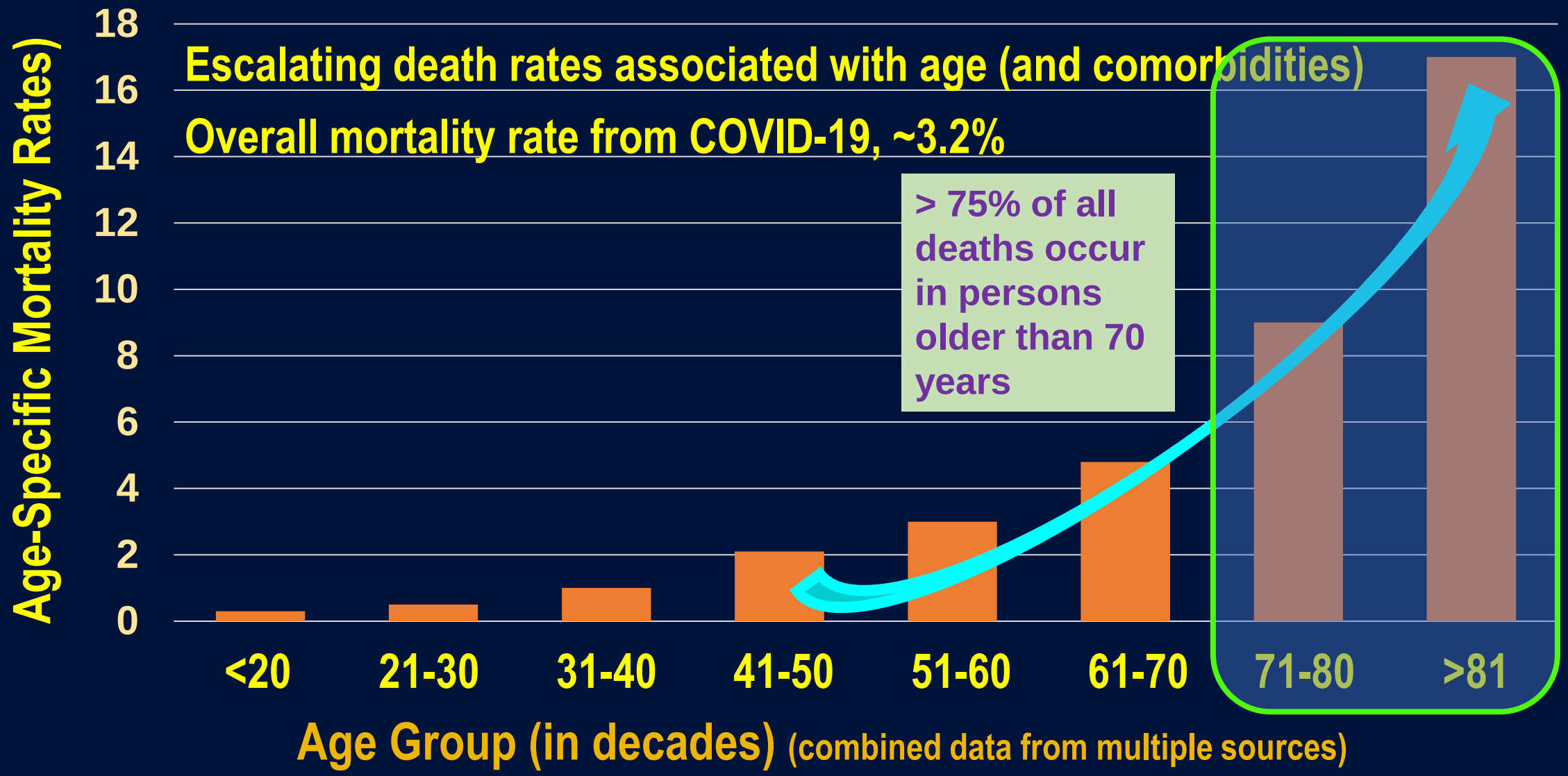
**Vaccine failure is due to a number of reasons:**

- **Primary failure of vaccines:- Failed to maintain the immune system's alertness (losing efficacy).**
- **Mutants of SARS-CoV-2 developed immune evasion: collectively termed "vaccine resistance."**
- **The terminology *'outbreaks'* that currently used to characterise peaks of COVID-19 is not appropriate.**

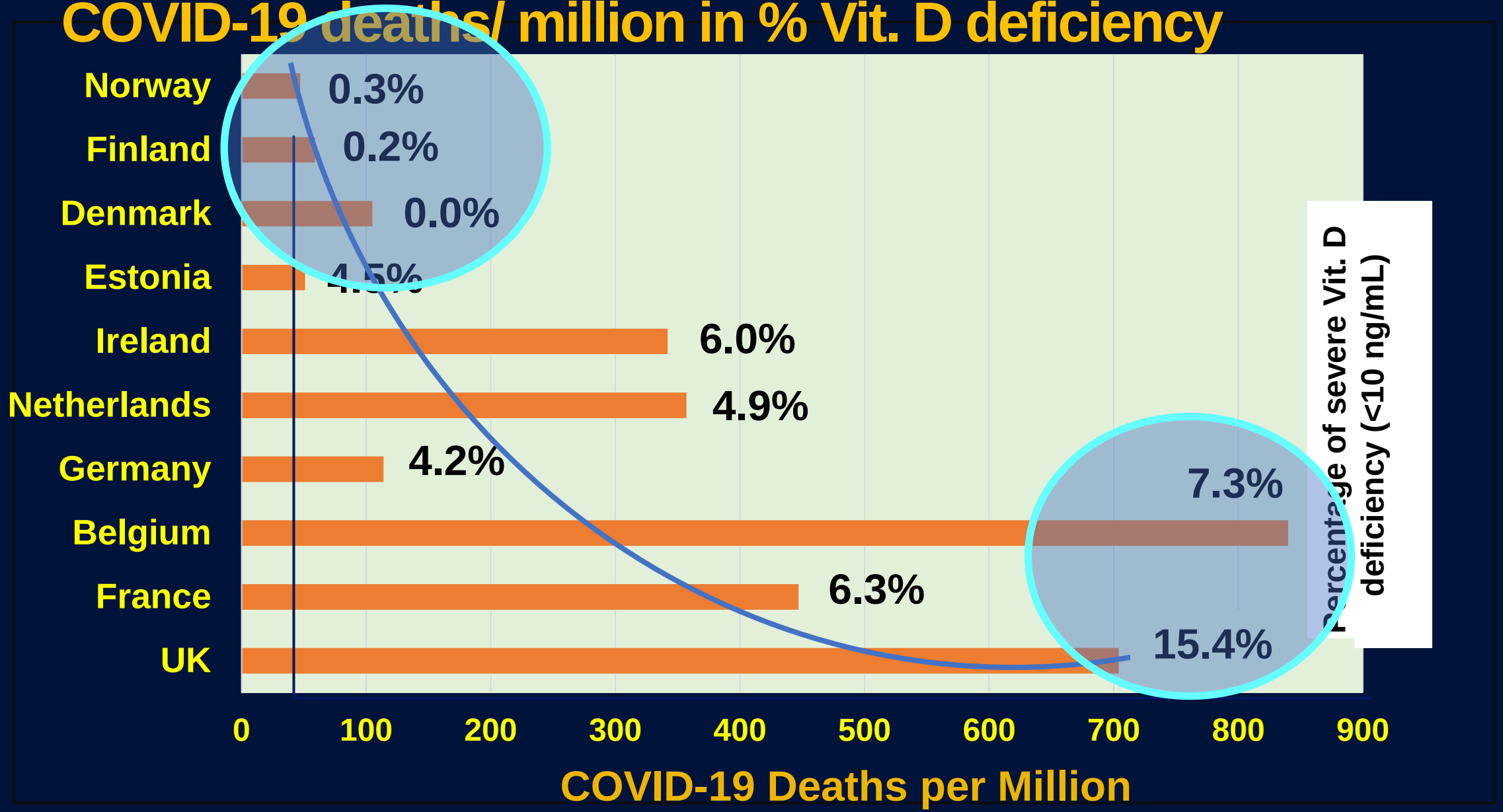
# Vaccine Alone Will Not Control The Pandemic

- Despite over 80% are vaccinated in some states and countries, it failed to control the pandemic: implausible it will be.
- Vaccine alone is not capable of achieving hard immunity
- The world needs affordable alternative strategies and therapies to overcome COVID-19.
- Hindered by gaging data by WHO/CDC and mainstream media that promotes only "patented" medications.

# Age-Related Mortality Rate From COVID-19



# Correlations:
# COVID-19 deaths/ million in % Vit. D deficiency

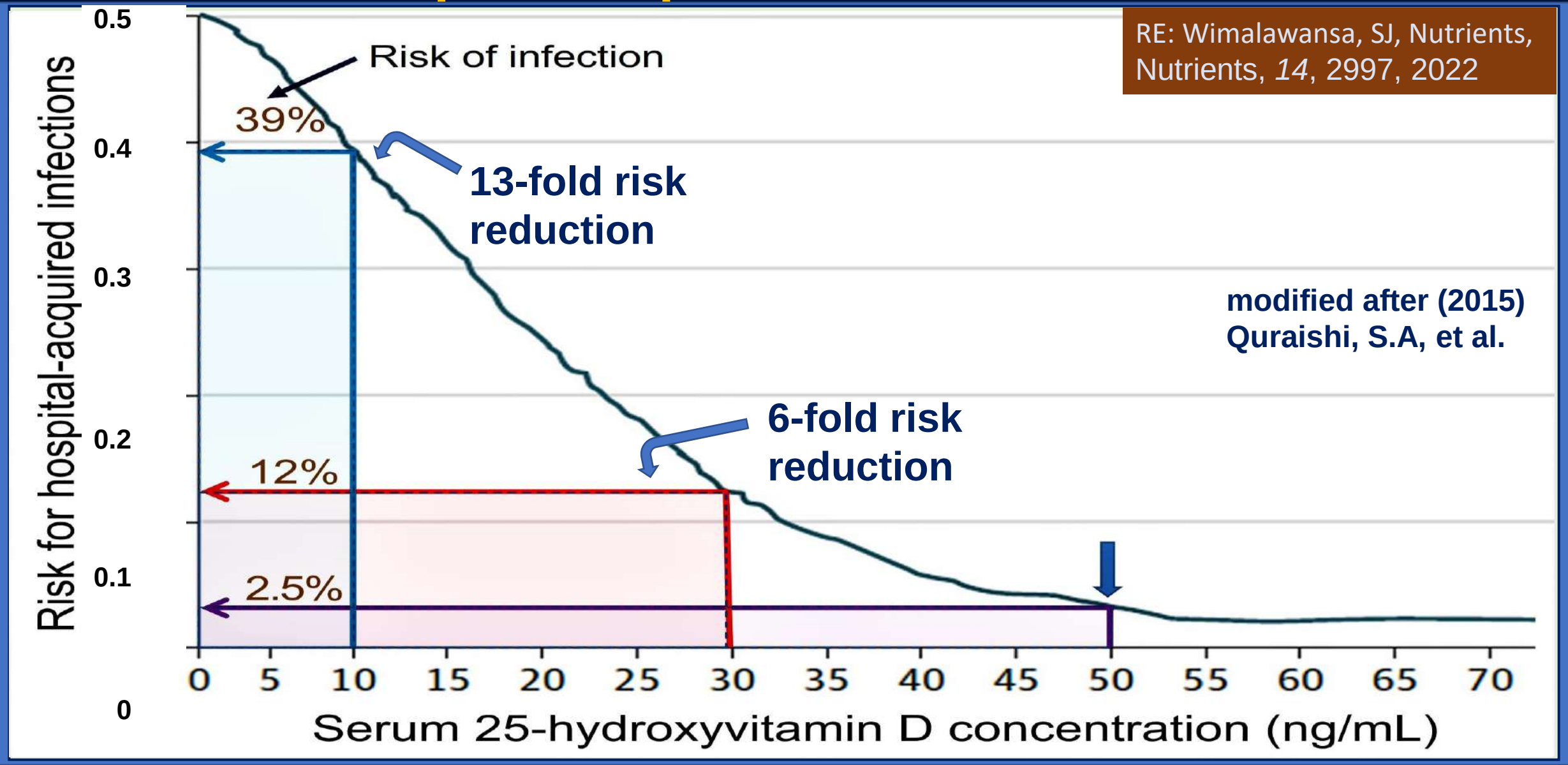


# COVID-19 Mortality Risk—Inversely Correlates With Vitamin D Status

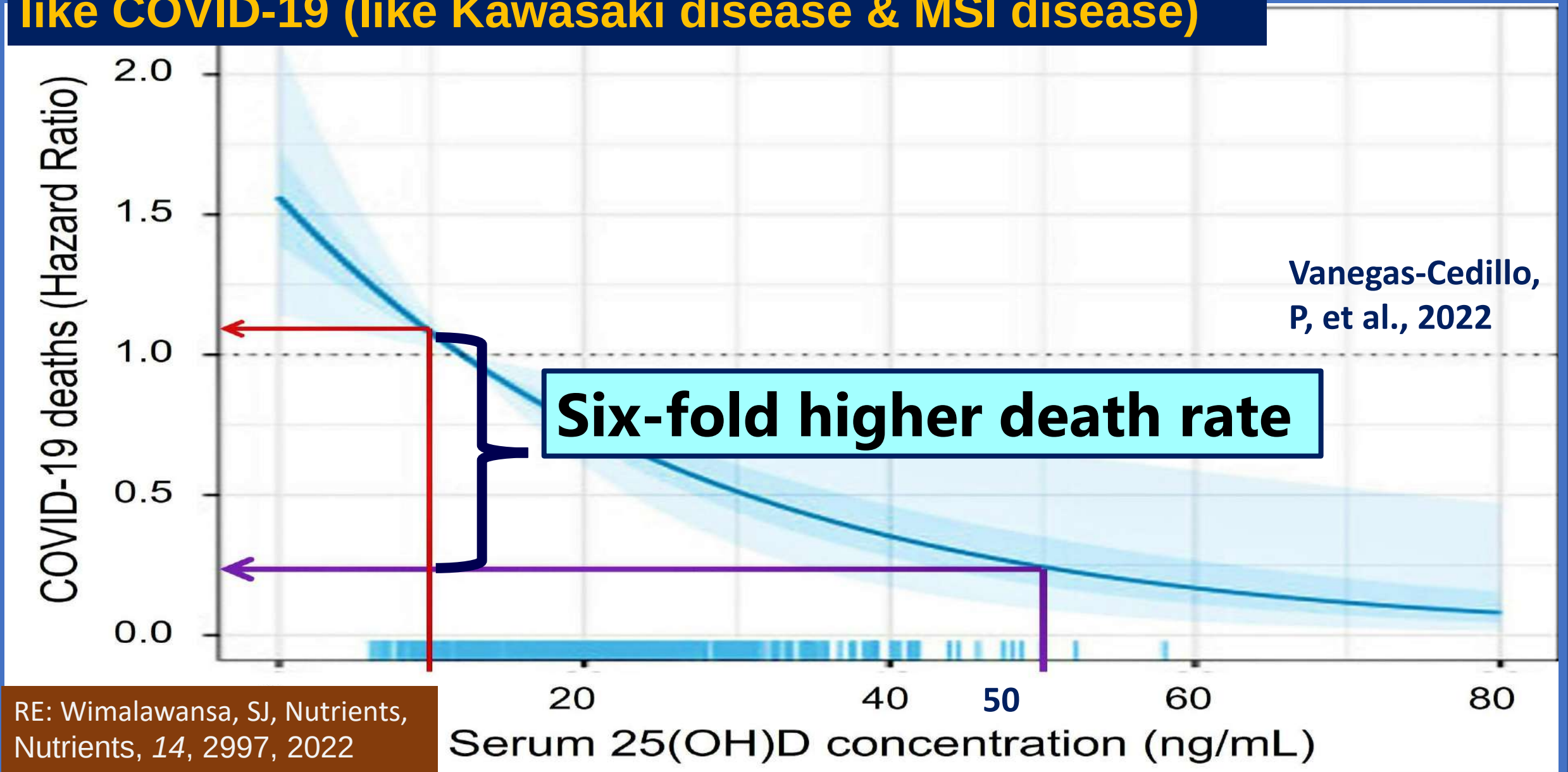
- The correlation between low Vitamin D blood levels, and severity and mortality of Covid-19 is Causal.
- Vitamin D concentrations above 50 ng/mL needed to protect from SARS-CoV-2 complications and deaths.
- The current recommendations of health organisations (e.g., WHO) for Vitamin D blood levels (20 to 30 ng/mL) and the recommended daily Vitamin D supplementation are much too low to fight against COVID-19.

Borsche L, et a,, Nutrients 2021, 13, 3596. https://doi.org/10.3390/nu13103596

# Relationship Between Vitamin D and Risk of Hospital-Acquired Infections

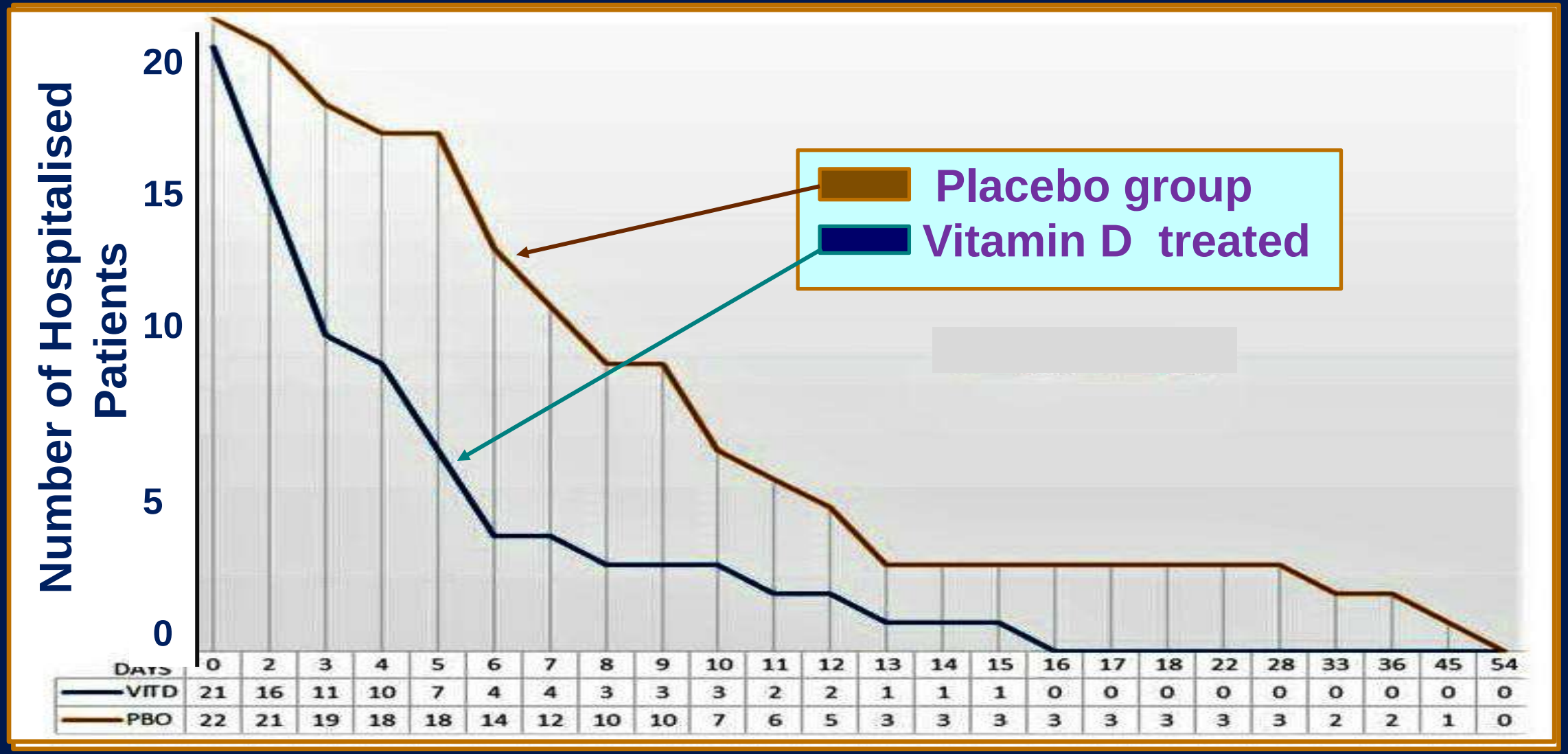


# Low Vitamin D Drives Complications From infections like COVID-19 (like Kawasaki disease & MSI disease)



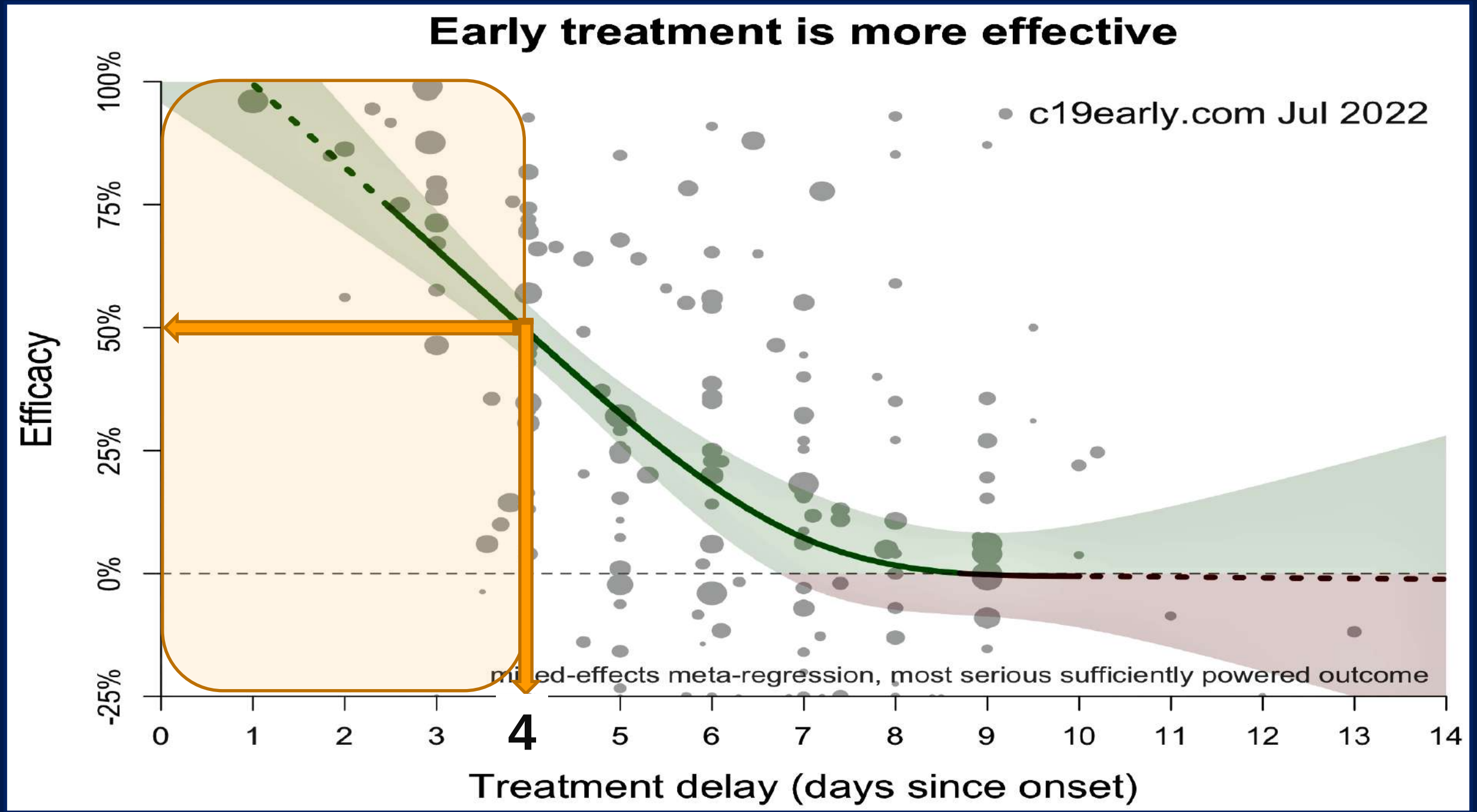

RE: Wimalawansa, SJ, Nutrients, Nutrients, *14*, 2997, 2022

# Hospital Length of Stay—RCT-Vit D vs Placebo




| Days | 0 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 22 | 28 | 33 | 36 | 45 | 54 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VitD | 21 | 16 | 11 | 10 | 7 | 4 | 4 | 3 | 3 | 3 | 2 | 2 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PBO | 22 | 21 | 19 | 18 | 18 | 14 | 12 | 10 | 10 | 7 | 6 | 5 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 1 | 0 |

De Niet et al, Positive Effects of Vitamin D supplementation in patients hospitalized for COVID-19: A randomized, double-blind, placebo-controlled trial. *Nutrients.* 2022, *14*, 3048. https://doi.org/10.3390/nu14153048


Early treatment is more effective
c19early.com Jul 2022
Efficacy
100%
75%
50%
25%
0%
-25%
ed-effects meta-regression, most serious sufficiently powered outcome
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Treatment delay (days since onset)

# Risk estimates of mortality for low vs high vitamin D levels

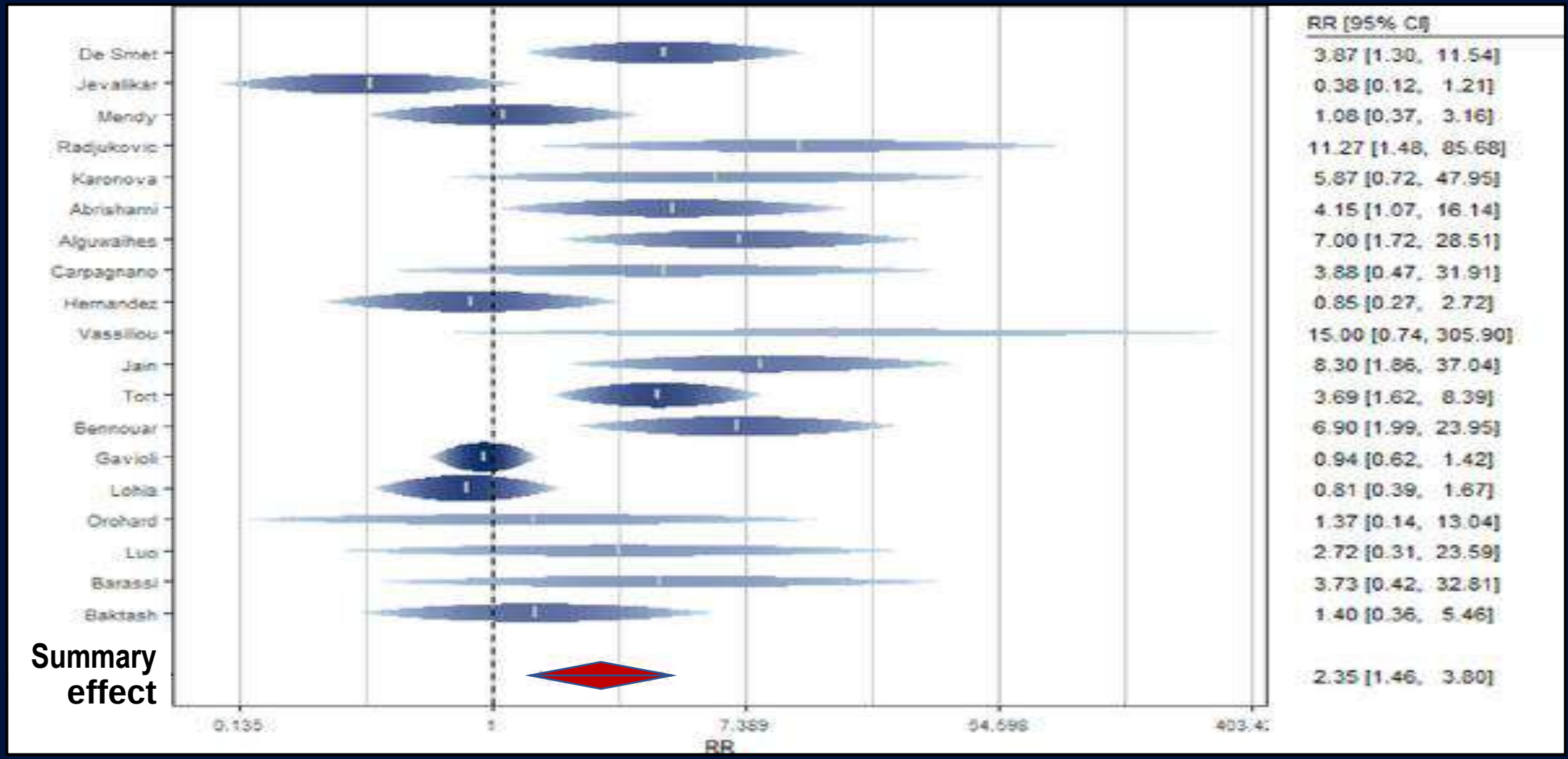
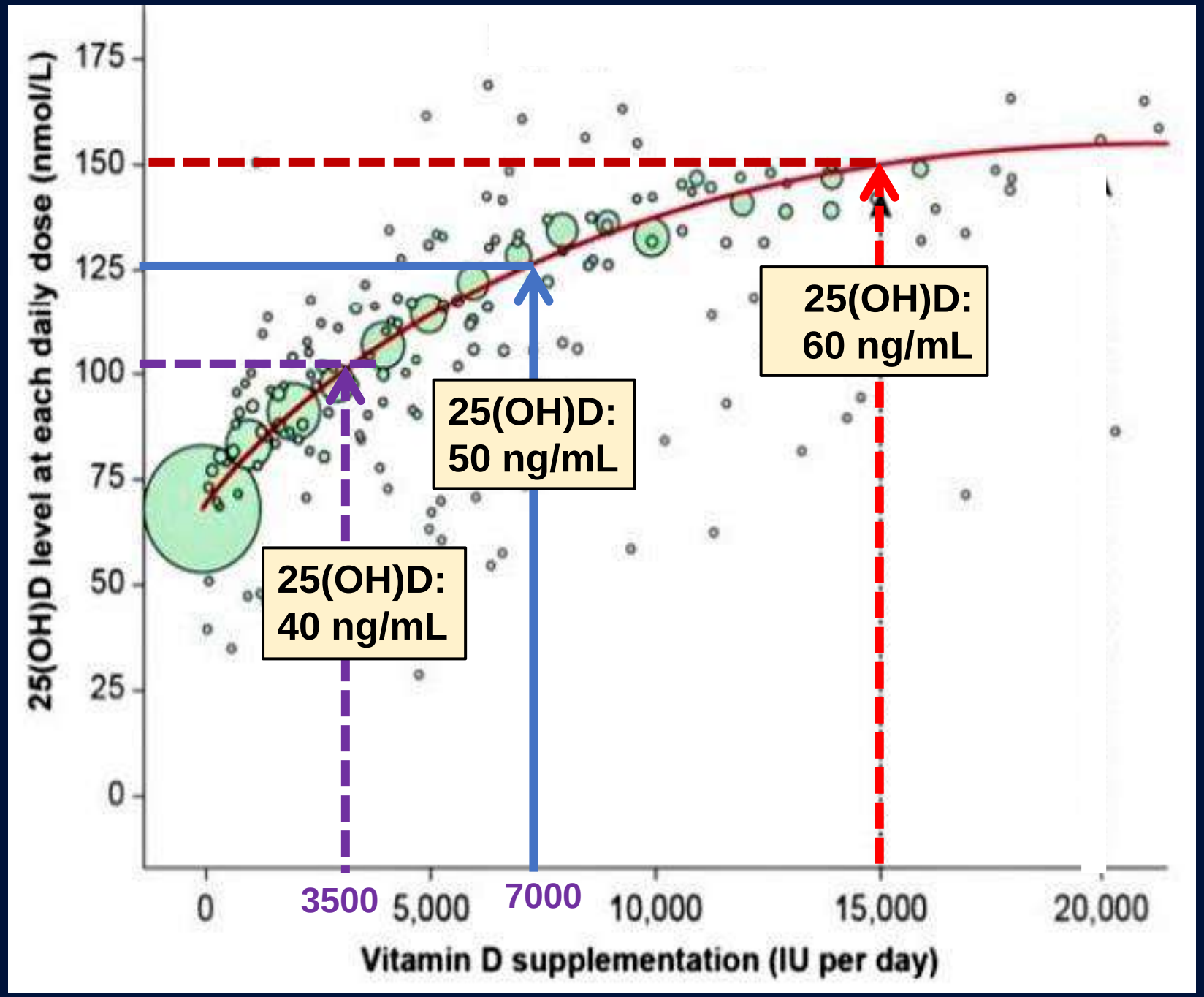



Fig 5: D'Ecclesiis O, et al. (2022) Vitamin D and SARS-CoV2 infection, severity and mortality: A systematic review and meta-analysis. PLOS ONE 17(7): e0268396. https://doi.org/10.1371/journal.pone.0268396 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0268396

# Dose-response relationships between oral vitamin D and serum 25(OH)D concentrations are NOT linear: healthy volunteers (n=22,215)




Ekwaru JP, et al. The importance of body weight for the dose response relationship of oral vitamin D supplementation and serum 25-hydroxyvitamin D in healthy volunteers. PLoS One. 2014;9(11):e111265

# Recommendations for Those Who are Exposed, PCR Positive or Symptomatic

- **Doses between 100,000 & 400,000 IU – Administration of vitamin $D_3$ earliest possible to rapidly raise 25(OH)D concentration to boost the immune system.**
- **This should be followed by 5000 IU/day OR 50,000 IU/ week OR *(Repeaat the above in every 8 to 16 weeks intervals, as appropriate).***
- **No adverse effects reported using the mentioned doses of vitamin D regimens, including for COVID-19.**

**[https://pubmed.ncbi.nlm.nih.gov; VitaminDWiki.com]**

# An Example of Cost–Effectiveness

- **Molnupiravir (Merck) and Paxlovid (Pfizer):**
  - **Cost of treatment per patient ~$700 (USD)**
  - **Effectiveness: preventing 50% hospitalisation**
- **Vitamin D or ivermectin:**
  - **Cost for per patient = one dollar**
  - **Effectiveness: ~75% preventing hospitalisation**

# T-2: Vit D, Dose Calculation Based On Body weight, When 25(OH)D is Unknown—to maintain serum >50 ng/mL

## In Children & Adults

RE: Wimalawansa, SJ, Nutrients, *14*, 2997, 2022

| Bodyweight Category | | Dose kg/Day (IU) | Dose (IU) (Daily or Weekly) * | |
|---|---|---|---|---|
| (Age) or Using BMI (for age > 18) (kg/Ht. $M^2$) | Average Body Weight (kg) | | Daily Dose (IU) | Once a Week (IU) |
| (Age 1–5) | 5–13 | 70 | 350–900 | 3000–5000 |
| (Age 6–12) | 14–40 | 70 | 1000–2800 | 7000–28,000 |
| (Age 13–18) | 40–50 | 70 | 2800–3500 | 20,000–25,000 |
| BMI ≤ 19 | 50–60 (under-weight adult) | 60 to 80 | 3500–5000 | 25,000–35,000 |
| **BMI 20–29** | **70–90 kg** | **70–90 IU** | **5000–7000 IU** | **35K –50K** |
| BMI 30–39 | 90–120 (obese persons) # | 90 to 130 | 8000–15,000 | 50,000–100,000 |
| BMI ≥ 40 $ | 130–170 (morbidly obese) $ | 140 to 180 | 18,000–30,000 | 125,000–200,000 |

# T-3: Body weight-Base Calcifediol Dose —to Rapidly Raise 25(OH)D Levels (0.014 mg/kg body weight )

## In Children & Adults

| Weight (lbs) | Weight (kg) | Calcifediol ~ (mg) # | If Calcifediol Is Not Available: Bolus/Loading Dose of Vitamin $D_3$ ## |
|---|---|---|---|
| 8–14 | 4–6 | 0.05 | 20,000 |
| 15–21 | 7–10 | 0.1 | 40,000 |
| 22–30 | 10–14 | 0.15 | 60,000 |
| 31–40 | 15–18 | 0.2 | 80,000 |
| 41–50 | 19–23 | 0.3 | 100,000 |
| 51–60 | 24–27 | 0.4 | 150,000 |
| 61–70 | 28–32 | 0.5 | 200,000 |
| **60-70 lbs** | **28–32 kg** | **0.5 mg** | **200,000 IU vit $D_3$** |
| 86–100 | 40–45 | 0.7 | 280,000 |
| 101–150 | 46–68 | 0.8 | 320,000 |
| **150-200 lbs** | **60 – 90 kg** | **1.0 mg** | **400,000 IU vit $D_3$** |
| 201–300 | 91–136 | 1.5 | 600,000 |
| >300 | >137 | 2.0 | 800,000 |

RE: Wimalawansa, SJ, Nutrients, *14*, 2997, 2022

# Summary

- A strong, inverse association of serum 25(OH)D concentrations with COVID-19 severity.
- Better the vitamin D status, lower the risks of complications from COVID-19.
- Taking 5,000 IU/day will maintain a healthy levels of serum 25(OH)D to maintain the immune system
- In emergencies, a loading dose between 100,000 and 400,000 IU needed to rapidly boost immunity.

# Summary

- Vitamin D deficiency must be corrected earliest possible, especially in the elderly.
- Administer between 100 to 200 K IU, Vit D to those who are deficient >3 days prior to vaccination.
- Alternatively, 0.5 or 1.0 mg of oral Calcifediol should be administered at the time of vaccination.
- These strategies will save lives and the economy.