Evidence on Covid19 and micronutrients

Secondary Prevention = prevention of death or bad symptoms
Other 2' prevention: humidity here, 3' prevention (physio) here

1. **THIS DOC IS OUT OF DATE AND NEEDS A CRITICAL REVIEW**

2. **Has anyone got time to assess the evidence on gum (especially for habitual mouthbreathers) for prevention of covid/flu/colds in oral cavity and throat, and whether liquorice adds any benefit (below overdose limit)?**

"**Vitamin D status is strongly associated with COVID-19 mortality outcome of cases."**
https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3585561

"..... Vitamin D stops you getting infected with viruses and, even if you do get infected, it helps to mitigate the worst effects."
Links to many papers: sott.net/article/433544-Focus-on-Vitamin-D-for-COVID-and-much-more

"100% of ICU [covid19] patients less than 75 years old had vitamin D deficiency"
Vitamin D insufficiency is prevalent in severe COVID-19 | medRxiv

"**supplementation with vitamin D may reduce the mortality from this pandemic"**
Does vitamin D status impact mortality from SARS-CoV-2 infection?

"the odds of having a mild clinical outcome rather than a critical outcome were increased approximately 19.61 times," indicating that, in COVID-19 patients, increased [D3] level could improve clinical outcomes,
Alipio, M. (2020). Vitamin D Supplementation Could Possibly Improve Clinical Outcomes of Patients Infected with Coronavirus-2019

We recommend that all ... vulnerable groups ...**be urgently supplemented with 20-50µg/d of vitamin D to enhance their resistance to Covid19**"
http://imj.ie/wp-content/uploads/2020/04/Optimisation-of-Vitamin-D-Status-for-Enhanced-Immuno-protection-Against-Covid-19.pdf

Strategies for India for D3
General prevention info: https://vaidyam.ai/covid/faqs
Humidity: www.facebook.com/andyraytaylor/posts/10159063475053598

NB Studies selected on use-ability for ministries, funders, project proposals, ministries, *not academics/clinical doctors* so will take into account **cost, doability, viability and strength of recommendations,** as well as pure clinical effectiveness.

ie. clear case for real world effectiveness and likely overall cost-benefit more important than biochemical mechanisms/theoretical justifications/multiple confirmations for specific covid19 benefit alone.

We are also biased towards urgent needs of humanitarian missions where distancing is not possible, lower income groups, and bottom billions / BRICs / Global South.

More recent additions:
https://www.sciencedirect.com/science/article/pii/S1871402121000746

Prevalence of vitamin D deficiency is positively correlated with COVID-19 infection and mortality in Asian countries.

Correlation improved after including confounders such as median age, prevalence of obesity and diabetes.

Mean vitamin D level is negatively correlated with COVID-19 infection and mortality when predicting with confounders.

Sections:

I. Studies on prophylaxis (prevention) of respiratory viruses infections

C. Early papers on *covid19 specifically*

F. Fortification and Supplementation

P. WHO and Public health recommendations

T. Therapeutics

G. Global deficiency info

O. Overall health and economic benefits of D fortification / supplementation

D. Dosage papers - most recent are probably most reliable

M. more sources

R. Research proposing papers

B. Biochemical mechanisms

P. Proxy measures: D3 and C-reactive peptides

N. Neonates and women and children

S. South Asia

C. Vitamin D importance in other conditions

I. Studies on prophylaxis of respiratory viruses infections

Harvard recommendations: D3 and zinc

Many refs on selenium and selenium from supplements vs onions

"Vitamin D supplementation was safe and it protected against acute respiratory tract infection overall."
Systematic review by Martineau et al

New Zealand review: vitamin A, D, K, Se, Zinc, NAC

"Vitamin D supplementation ... moderately reduced non-influenza respiratory viral infection." 8 month RCT

"Maintenance of a 25-hydroxyvitamin D serum concentration of 38 ng/ml or higher should significantly **reduce the incidence of acute viral respiratory tract infections** and the burden of illness caused thereby, …"
Yale study: www.ncbi.nlm.nih.gov/pubmed/20559424

"Current **data support vitamin D3 supplementation as risk-modifying intervention** in tuberculosis and viral respiratory tract infection…" www.tandfonline.com/doi/abs/10.3109/1040841X.2011.622716

Systematic review from India:
... D supplementation decreases...respiratory tract infections.

"In short, it seems Vitamin D stops you getting infected with viruses and, even if you do get infected, it **helps to mitigate the worst effects.**"
Links to many papers: sott.net/article/433544-Focus-on-Vitamin-D-for-COVID-and-much-more

Results indicate that **vitamin D has a protective effect against RTI, and dosing once-daily seems most effective.** 2013, Bergman, Sweden

NAC (N-acetyl-cysteine) study

Bayer staff study on C, D3 and Zn:
https://jeffreydachmd.com/wp-content/uploads/2017/11/Vitamins-C-D-Zinc-Synergistic-Immune-Function-Infections-Maggini-Vitam-Miner-2017.pdf

"Results indicate that vitamin D has a **protective effect against RTI,** and dosing once-daily seems most effective."
A Systematic Review and Meta-Analysis of Randomized Controlled Trials.

"Low-dose supplementation of zinc and selenium provides significant improvement in elderly patients by increasing the humoral response after vaccination and could have considerable public health importance by reducing morbidity from respiratory tract infections."

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/484994

Big zinc antiviral immunity review (Australia):
www.researchgate.net/profile/Scott_Read5/publication/334492528_The_Role_of_Zinc_in_Antiviral_Immunity/links/5d34f36d4585153e59166fd5/The-Role-of-Zinc-in-Antiviral-Immunity.pdf

Mannose Binding Lectin, part of innate response:
These results suggest that MBL contributes to the first-line host defense against SARS-CoV and that MBL deficiency is a susceptibility factor for acquisition of SARS
https://academic.oup.com/jid/article/191/10/1697/789682

Sun and vitamin D levels may also predispose higher MBL levels. University of Copenhagen research found in a study of nearly 1,000 children that mannose-binding lectin levels were lower in the wintertime and higher in the summertime.
https://plantmedicines.org/antiviral-plant-lectins-viruses/

See also Cochrane reviews especially on zinc:
https://www.cochrane.org/search/site/micronutrient

Overall, 41% (95% CI 20%-58%) of respiratory disease mortality was statistically attributable to vitamin D insufficiency or deficiency. Vitamin D insufficiency and deficiency are common and account for a large proportion of respiratory disease mortality in older adults
https://www.medrxiv.org/content/10.1101/2020.06.22.20137299v1

C. Early papers on secondary prophylaxis/severity of *covid19 specifically* (NB proof on covid19 prophylaxis with RCTs is difficult as there *simply hasn't been enough time to do them,* so when proposing interventions, we have to go with evidence for (a) overall health benefit, (b) overall cost-benefit (c) best sliver-standard evidence for and against likely fatality reduction.Nevertheless, the following papers are interesting.)

The three clinchers:

1. D3 levels and C-reactive protein (a measure of inflammation) are inversely correlated in human blood.

"Conclusions In patients with COVID-19, admission CRP correlated with disease severity and tended to be a good predictor of adverse outcome."
www.researchgate.net/publication/340106540_Prognostic_value_of_C-reactive_protein_in_patients_with_COVID-19 www.ncbi.nlm.nih.gov/pmc/articles/PMC7146693/ More on CRP here

2. 25-Hydroxyvitamin D Concentrations Are Lower in Patients with Positive PCR for SARS-CoV-2

Department of Laboratory Medicine EOLAB, Ente Ospedaliero Cantonale, 6500 Bellinzona, Switzerland, Renzo.Lucchini@eoc.ch

Nutrients **2020**, *12*(5), 1359; **https://doi.org/10.3390/nu12051359**
https://www.mdpi.com/2072-6643/12/5/1359/htm

3. "vitamin D3 supplementation might make a major contribution to limit the burden of the COVID-19 pandemic, particularly among women"
https://www.medrxiv.org/content/10.1101/2020.06.22.20137299v1

Zinc review:
"Currently, indirect evidence suggests zinc may potentially reduce the risk, duration and severity of SARS-CoV-2 infections, particularly for populations at risk of zinc deficiency including people with chronic disease co-morbidities and older adults."
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7395818/

"Our results show **an association between the reported cure rates for COVID-19 and selenium status**. These data are consistent with the evidence of the antiviral effects of selenium from previous studies."
https://academic.oup.com/ajcn/advance-article/doi/10.1093/ajcn/nqaa095/5826147 [refs: www.ncbi.nlm.nih.gov/pubmed/25593145
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7197590/

A good summary:
https://journals.sagepub.com/doi/full/10.1177/1060028020928052
supports **D3 up to 4000iu and zinc gluconate up to 40mg**

"100% of ICU [covid19] patients less than 75 years old had vitamin D deficiency"
https://www.medrxiv.org/content/10.1101/2020.04.24.20075838v1

"We see a possible role of Vit D in reducing complications attributed to unregulated inflammation and cytokine storm."
https://www.medrxiv.org/content/10.1101/2020.04.08.20058578v4

Enhancing immunity in viral infections, with special emphasis on COVID-19: A review

RanilJayawardena[ab]

"Among vitamins, A and D showed a potential benefit, especially in deficient populations. Among trace elements, selenium and zinc have also shown favourable immune-modulatory effects in viral respiratory infections. Several nutraceuticals and probiotics may also have some role in enhancing immune functions. Micronutrients may be beneficial in nutritionally depleted elderly population."
https://www.sciencedirect.com/science/article/pii/S1871402120300801

"Our findings suggest that vitamin D deficiency may partly explain the geographic variations in the reported case fatality rate of COVID-19, implying that **supplementation with vitamin D may reduce the mortality from this pandemic.**
Marik et al 2020 Apr 29
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7189189/

Our results show an association between the reported cure rates for COVID-19 and selenium status. These data are consistent with the evidence of the antiviral effects of selenium from previous studies .... Indeed, multiple cellular and viral mechanisms involving selenium and selenoproteins could influence viral pathogenicity, including virally encoded selenium-dependent glutathione peroxidases [reviewed in (14, 15)]. Such viral mechanisms could contribute to the well-documented oxidative stress associated with many RNA virus infections (2, 5, 6, 14, 15); increased viral replication (hence increased mutation rate); and observed **higher pathogenicity or mortality under selenium deficiency**, as reported here for SARS-CoV-2.
https://academic.oup.com/ajcn/advance-article/doi/10.1093/ajcn/nqaa095/5826147

"Vitamin D status is significantly associated with clinical outcomes ($p<0.001$). For each standard deviation increase in serum 25(OH)D, the odds of having a mild clinical outcome rather than a severe outcome were increased approximately 7.94 times; the odds of having a mild clinical outcome rather than a critical outcome were increased approximately 19.61 times," indicating that, in COVID-19 patients, increased serum 25(OH)D level could improve clinical outcomes, and/or mitigate the worst (severe to critical) outcomes. *NB this is a very high figure, and remains to be proved in a prospective trial. However, dear reader, if you're not getting the RDA of D3, why not?!*
Alipio, M. (2020). Vitamin D Supplementation Could Possibly Improve Clinical Outcomes of Patients Infected with Coronavirus-2019

(COVID-2019). http://dx.doi.org/10.2139/ssrn.3571484 https://ssrn.com/abstract=3571484 examines vitamin D status, and hospitalization outcomes in 212 COVID-19 patients …

"Vitamin D deficiency is common and may contribute to increased risk of respiratory infection including Covid. We recommend that all older adults, hospital inpatients, nursing home residents and other vulnerable groups (e.g. those with diabetes mellitus or compromised immune function, those with darker skin, vegetarians and vegans, those who are overweight or obese, smokers and healthcare workers) **be urgently supplemented with 20-50µg/d of vitamin D to enhance their resistance to Covid19**, and that this advice be quickly extended to the general adult population."
Recommendation for vulnerable and whole nation D3 supplementation (Ireland) D.M. McCartney , D.G. Byrne
http://imj.ie/wp-content/uploads/2020/04/Optimisation-of-Vitamin-D-Status-for-Enhanced-Immuno-protection-Against-Covid-19.pdf

"Targeting the unbalanced RAS with **vitamin D supplementation in SARS-CoV-2 infection may be an approach with excellent cost and benefit ratio**"
A R Garamani: https://www.bmj.com/content/368/bmj.m810/rr-24

"When controlling for age, sex, and comorbidity, **Vitamin D status is strongly associated with COVID-19 mortality outcome of cases."**
30 Apr 2020 Prabowo Raharusun Indonesia
https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3585561

"After excluding duplicates and articles that did not meet the inclusion criteria, 43 studies were obtained … Among **vitamins, A and D showed a potential benefit,** especially in deficient populations. Among trace elements, **selenium and zinc have also shown favourable immune-modulatory effects in viral respiratory infections**. Several nutraceuticals and probiotics may have some role in enhancing immune functions. Micronutrients may be beneficial in nutritionally depleted elderly population."
Jaywardena systematic review, **April 2020:** ncbi.nlm.nih.gov/pmc/articles/PMC7161532/

F. Fortification and Supplementation

Comprehensive paper on strategies for D3 fortification in India, mostly via flour; *also personal supplementation tactics.*

Meta analysis and review of fortification, supplementation and blood levels

Rationale and Plan for Vitamin D Food Fortification: A Review and Guidance Paper
2018 Jul 17;9:373. doi: 10.3389/fendo.2018.00373.

[Fortification] significantly reduced the risk of ARIs in winter among Mongolian children with vitamin D deficiency.
https://pediatrics.aappublications.org/content/130/3/e561.short

Europe, Afghanistan, Pakistan, India, Tunisia and Mongolia most of Middle East, China, Africa, USA are confirmed *low D3* but in interestingly, studies in East Africa reported vitamin D levels in non-westernised groups (Av: Masai 119nmol/L; Hadzabe 109nmol/L)

Strategies for India for D3 Strategies for Europe Fortification of flour

Commercial supplementation can be increased by private companies such as BASF, GSK

Calcifediol fortification works better than D3 supplementation. Zinc is a necessary cofactor of D3; Magnesium too. I'm trying to locate research on B3/NAD+/niacin.

Fortification issues in Germany, 2013

UN Guidelines for fortification at scale:

UNICEF has people who can advise:

P. Public health recommendations:

Public health England: why UK population should consider D supplements
www.standard.co.uk/lifestyle/wellness/vitamin-d-supplement-benefits-a4421901.html

Public health case for vitamin D supplementation for infants and children (Ireland)
imj.ie/wp-content/uploads/2020/04/Vitamin-D-Covid-19-and-Children.pdf
and adults:
http://imj.ie/vitamin-d-and-inflammation-potential-implications-for-severity-of-covid-19/

Oxford recommendations: May 1 2020
cebm.net/covid-19/vitamin-d-a-rapid-review-of-the-evidence-for-treatment-or-prevention-in-covid-19
"The current advice is that the **whole population of the UK should take vitamin D supplements** to prevent vitamin D deficiency. This advice applies irrespective of any possible link with respiratory infection. Clinicians should treat patients with vitamin D deficiency irrespective of any link with respiratory infection. Policymakers should attend to public health measures to ensure the population has adequate vitamin D intake."

"A wealth of mechanistic and clinical data show that vitamins, including vitamins A, B6, B12, C, D, E, and folate; trace elements, including zinc, iron, selenium, magnesium, and copper; and the omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid play important and complementary roles in supporting the immune system"
www.mdpi.com/2072-6643/12/4/1181

WHO: Implementation in settings with limited resources

Vitamin D supplementation for preventing respiratory tract infection is not routinely done. For this intervention to be effective, it should be done continuously, before the respiratory tract infection starts. This could be a major challenge in many under-resourced settings, as programme managers and policy-makers will have to plan for procurement of the preparation, storage, distribution, quality-control, and compliance assurance of vitamin D supplements for children on a routine basis. Failures in implementation of this intervention have been attributed in many instances to inadequate infrastructure and poor compliance, particularly in developing countries. Intermittent vitamin D supplementation would reduce some of these challenges, although results from these trials show that bolus doses are not effective. Future studies could evaluate the effectiveness of different dosing schemes on respiratory tract infections, such as once a week, which may be easier to implement.
www.who.int/elena/titles/commentary/vitamind_pneumonia_children/en

The data on a benefit for mortality and prevention of infections, at least in severely deficient individuals, appear convincing. Vitamin D is clearly not a panacea, and is most likely efficient only in deficiency. Given its rare side effects and its relatively wide safety margin, it may be an **important, inexpensive, and safe adjuvant therapy for many diseases**, but future large and well-designed studies should evaluate this further. A worldwide public health intervention that includes vitamin D supplementation in certain risk groups, and systematic vitamin D food fortification to avoid severe vitamin D deficiency, would appear to be important. In this narrative review, the current international literature on vitamin D deficiency, its relevance, and therapeutic options is discussed.
Eur J Clin Nutr. 2020 Jan 20;1-16. doi: 10.1038/s41430-020-0558-y.

R. Covid/D3 research proposing papers:

Papers in other sections also recommend population level and RCT studies

Standardisation recommendations:

Importantly, retrospective standardisation can be accomplished relatively inexpensively as shown in the re-analyses of the Canadian Health Measures and HunMen study data(12,94). Such approaches could be utilised in virtually all vitamin D research. Journal editors are encouraged to require either‘prospectively’standardised or‘retrospectively’standardised 25(OH)D data as a condition for publication
www.ncbi.nlm.nih.gov/pmc/articles/PMC7167380/pdf/S1368980019005251a.pdf

WHO study recommending study of weekly D3 supplementation:
www.who.int/elena/titles/commentary/vitamind_pneumonia_children/en/

WHO on Further research:
Additional trials testing different dosing regimen (level of dose and intervals) are needed before implementing this at a population level. Also, trials should follow up participants long enough to understand if vitamin D is still effective once vitamin D status is optimal, as once vitamin D deficiency is corrected, giving more vitamin D supplementation may not provide additional benefits. Currently, there are other randomized controlled trials testing the effects of vitamin D on risk of acute respiratory tract infection, which could help elucidate some of these issues. In addition, future studies need to report adherence to the intervention to better understand if inclusion of non-adherent participants would bias the results reported so far. who.int/elena/titles/commentary/vitamind_pneumonia_children/en

Systematic review from India: … D supplementation decreases… respiratory tract infections. There is **need of more well conducted clinical trials to reach to a certain conclusion.**
www.ncbi.nlm.nih.gov/pmc/articles/PMC3543548/

Role of B-glycans review:
www.ncbi.nlm.nih.gov/pmc/articles/PMC5537893/#sec4-nutrients-09-00779title

How to avoid confounding variable in future D3 studies:

https://ccforum.biomedcentral.com/articles/10.1186/s13054-019-2472-z#Sec12
"The increase in vitamin D level on day 3 was associated with a survival benefit in patients with baseline deficiency. In anticipation of more evidence from bench research about the pathophysiology of vitamin D and biomarkers of its late effects in acute severe illness, the two unpublished large RCTs (VITDALIZE, NCT03188796 and VIOLET, NCT03096314) will further elucidate the potential role of vitamin D supplementation in improving clinical outcomes in critical illness."

Switzerland: 25-Hydroxyvitamin D Concentrations Are Lower in Patients with Positive PCR for SARS-CoV-2
"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); this was also confirmed by stratifying patients according to age >70 years. On the basis of this preliminary observation, **vitamin D supplementation might be a useful measure to reduce the risk of infection**. Randomized controlled trials and large population studies should be conducted to evaluate these recommendations and to confirm our preliminary observation." www.mdpi.com/2072-6643/12/5/1359?type=check_update&version=1

"Randomized controlled trials are warranted to investigate the role of vitamin D supplementation on COVID-19 outcomes and to establish the underlying mechanisms." 30 Apr 2020 https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3585561

Vitamin K:

https://www.preprints.org/manuscript/202004.0457/v2

Trials proposed/underway:

Updating list:
https://vitamindwiki.com/COVID-19+treated+by+Vitamin+D+-+studies%2C+reports%2C+videos

Mahir Ozmen, a professor of surgery at the Istinye University, School of Medicine in Istanbul, Turkey, says he thinks the best way to use

chloroquine is in combination with zinc and vitamins A and D. He is running a clinical trial, testing to see whether this combination protects health care workers and their immediate families — including his own. Ozmen, who is collaborating with a chest medicine specialist, an intensive care physician, and two infectious disease experts, says he intended to include only 80 participants, but 98 quickly volunteered. He began providing prophylactic therapy 2 weeks ago, and expects to complete the trial by July.

2. https://www.clinicaltrials.gov/ct2/show/NCT04386044

3. https://www.clinicaltrials.gov/ct2/show/NCT04407572

4. https://www.clinicaltrials.gov/ct2/show/NCT04394390?sfpd_s=05%2F17%2F2020&sfpd_d=14

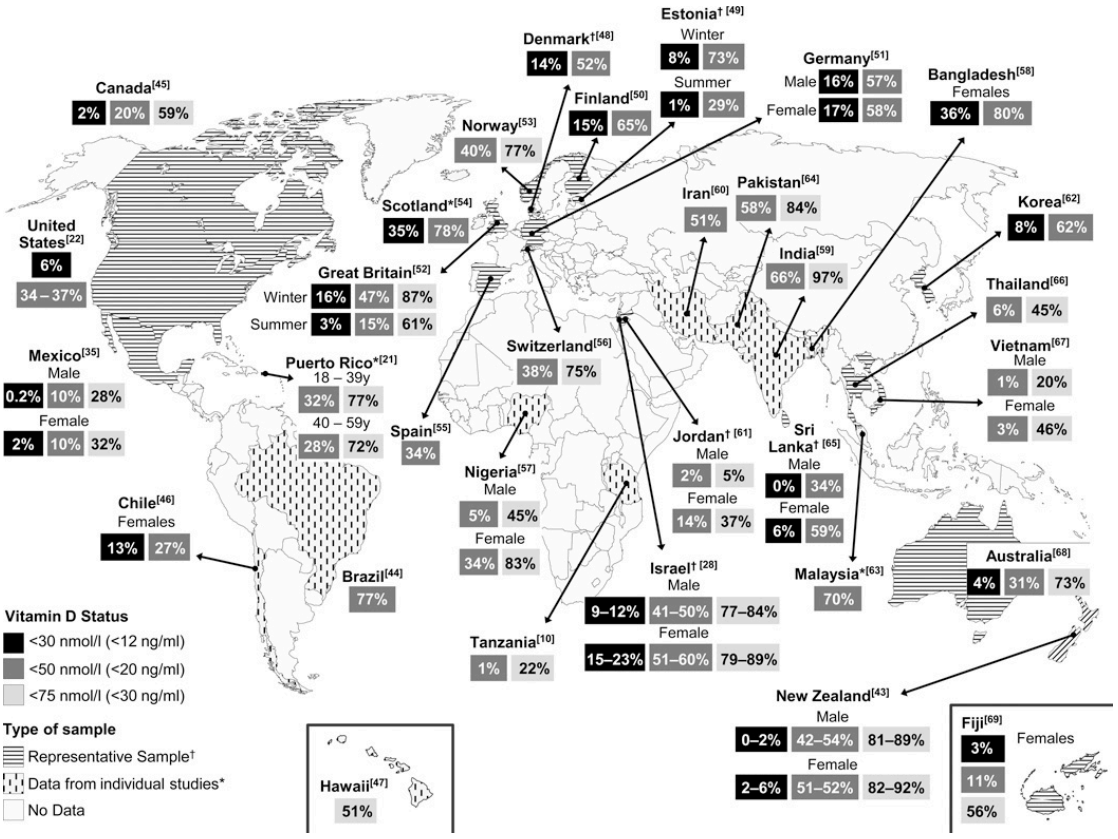
5. https://www.clinicaltrials.gov/ct2/show/NCT04403932

- Clinical trial observing Vitamin D levels of 500 people in Spain at entry into ICU and recording outcomes analysis to be completed July 2020
- Clinical trial to observe vitamin D levels of 100 COVID-19 Turks in hospital to be completed July 2020
    - Bursa City Hospital, NCT04394390
- **WHO** 3 RCT for Vitamin D and COVID-19 as of May 27 (WHO not responding when asked for details)
    - NCT04386044 Investigating the Role of Vitamin D in the Morbidity of COVID-19 Patients 10/05/2020
    - NCT04334005 Vitamin D on Prevention and Treatment of COVID-19 29/03/2020
    - ChiCTR2000029732 Impact of vitamin D deficiency on prognosis of patients with novel coronavirus pneumonia (COVID-19) 2020-02-10

G. Global deficiency info

Europe and USA D3 deficiency data showing correlation with covid mortality mostly from here: https://eje.bioscientifica.com/view/journals/eje/180/4/EJE-18-0736.xml

Here is very interesting data on global D deficiency, with India and Germany's **elder men especially shocking.** Source: www.ncbi.nlm.nih.gov/pmc/articles/PMC4018438
And here is the image for adults overall:



India:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4852574/

Semi-arid regions especially vulnerable, e.g. Saudi Arabia in this study:
https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-27302006000400009

More detailed data on Europe especially Ireland:
http://imj.ie/vitamin-d-and-inflammation-potential-implications-for-severity-of-covid-19/

Overview of vitamin D deficiency in regions highly affected by COVID-19.
https://www.nature.com/articles/s41430-020-0661-0/tables/1

More at vitaminDwiki

Africa review: The prevalence of vitamin D deficiency is high in African populations. Public health strategies in Africa should include efforts to prevent, detect, and treat vitamin D deficiency, especially in newborn babies, women, and urban populations.

Lancet Glob Health 2019 Published Online November 27, 2019 https://doi.org/10.1016/S2214-109X(19)30457-7

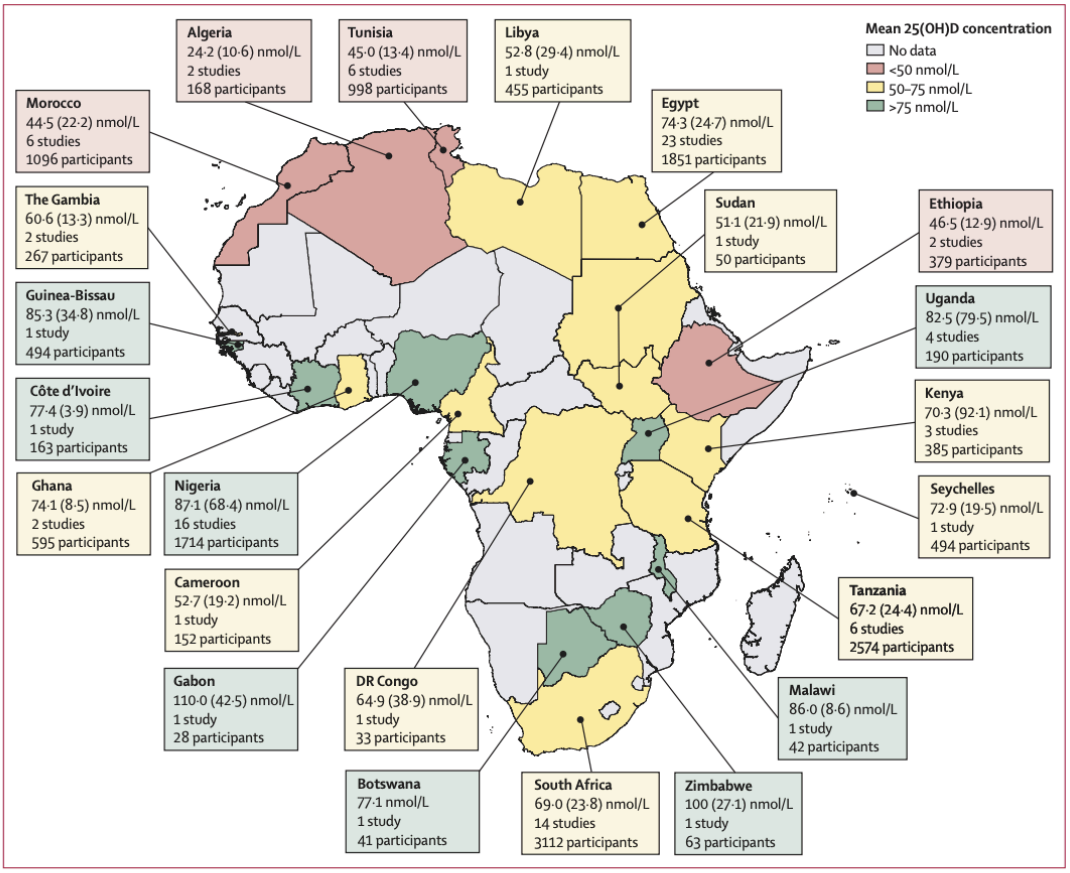


Figure 2: **Mean 25(OH)D concentrations in African countries**
Data are the mean (SD) 25(OH)D concentrations reported in studies done in each country. Pooled means were calculated if the country had more than one study, and were computed only from studies that stated mean (SD) 25(OH)D concentrations. Studies that reported only median concentrations are not included in this map, with the exception of Botswana, which had a single study that reported only median levels. 25(OH)D=25-hydroxyvitamin D.

T. Therapeutics / treatment

1. RCT:

Administration of calcifediol or 25-hydroxyvitamin D to hospitalized COVID-19 patients significantly reduced their need for Intensive Care United admission. Calcifediol seems to be able to reduce severity of the disease. sciencedirect.com/science/article/pii/S0960076020302764?via%3Dihub

2. Patients were administered oral vitamin D3 1000 IU OD, magnesium 150mg OD and vitamin B12 500mcg OD (DMB) upon admission if they did not require oxygen therapy….DMB combination in older COVID-19 patients was associated with a significant reduction in proportion of patients with clinical deterioration requiring oxygen support and/or intensive care support. This study supports further larger randomized control trials to ascertain the full benefit of DMB in ameliorating COVID-19 severity.
https://www.medrxiv.org/content/10.1101/2020.06.01.20112334v1

Atlanta: High dose vitamin D administration in ventilated intensive care unit patients: a pilot double blind randomized controlled trial

"High-dose vitamin D3 safely increased plasma 25(OH)D concentrations into the sufficient range and was associated with **decreased hospital length of stay without altering other clinical outcomes**."

"Health authorities concerning the reimbursability of vitamin D ... we think reasonable a message reinforcing the importance of maintaining vitamin D treatment in those already diagnosed with hypovitaminosis D and **considering the supplementation with vitamin D** of elderly comorbid persons at home confinement (15)."
Prof Andrea Justina, Italy: www.bmj.com/content/368/bmj.m810/rr-36

"…. based on the latest analysis,3 it would seem eminently sensible for clinicians to ensure that **those infected with COVID-19 have adequate vitamin D levels** because this may lessen the effects of the virus and possibly save more lives."
https://hospitalhealthcare.com/covid-19/is-vitamin-d-an-important-biomarker-for-symptom-severity-in-covid-19/ April 22, 2020 Rod Tucker PhD

Marik et al 2020 Apr 29 www.ncbi.nlm.nih.gov/pmc/articles/PMC7189189/
"Our findings suggest that vitamin D deficiency may partly explain the geographic variations in the reported case fatality rate of COVID-19, implying that supplementation with vitamin D may reduce the mortality from this pandemic. However, as commonly suggested in the lay press, high-dose vitamin D appears to have a limited role in the treatment of patients with severe COVID-19 disease."

Vitamin D reducing risk of cytokine storm:

- www.medrxiv.org/content/10.1101/2020.04.08.20058578v4
- www.sciencedaily.com/releases/2020/05/200507121353.htm
- https://journals.lww.com/pidj/fulltext/2010/10000/vitamin_d_supplementation_could_reduce_the_risk_of.30.aspx
- https://www.medrxiv.org/content/10.1101/2020.04.08.20058578v4

O. Overall health and economic benefits of D fortification / supplementation

See also fortification section, especially for India papers

I think it is for several important reasons:

- it's a no-lose intervention

- correcting D3 deficiency has multiple benefits and is economically justified already, even without covid, in many countries

- there are now many countries with pervasive low D3, including Germany, India, Tunisia, USA etc probably made worse by lockdown (less sun exposure, maybe less fish?!)

- if it works, or if it works with Zn, Se, B3, NAD in vulnerable groups *even slightly better than all the really expensive but ineffective treatments,* that would be huge, and would probably reduce flu deaths also

- as a prevention, the medium and long term benefit may be better than lockdown and PPE, and much cheaper, especially in red zone countries

- PPE is a sunk cost and lockdown is extremely expensive, whereas D3 is cheap and has lasting benefit; if supplementation proves successful, fortification and sunshine can be even cheaper; zinc can be fortified indirectly through fertiliser

- we're talking about secondary prophylaxis which has 2 big and linked advantages: you walk away with immunity, and so you don't have to keep doing it (unlike PPE)

- it could be really important for doctors, humanitarian workers, police, journalists

- studies should be done before any Challenge Trials for vaccines (because you wouldn't want to do challenge trials without knowing all the best ways to protect your volunteers)

German language comments: Europa erkennt den tödlichen Vitamin-D-Mangel: 26000 Studien-Teilnehmer
www.vitamindservice.de/node/1285
Vitamin D and mortality: Individual participant data meta-analysis of standardized 25-hydroxyvitamin D in 26916 individuals from a European consortium.

"There is a **strong economic case** for fortifying wheat flour with Vitamin D, alone or in combination with targeted vitamin D3 supplementation." August 2019
Economic case for Vitamin D fortification
www.nature.com/articles/s41430-019-0486-x

"High prevalence of vitamin D deficiency and insufficiency worldwide have proven ill-effects on health. Governmental efforts to improve population repletion by recommending minimal daily intakes does benefit some but is not effective at the population-level. However, food fortification with vitamin D3, already implemented in some countries, **can solve this highly avoidable problem cost-effectively** …"
https://www.tandfonline.com/doi/abs/10.1080/17446651.2018.1533401 2018

"Vitamin D supplementation conferred substantial survival benefit (odds ratio for death 0.39, 95% confidence interval 0.277 to 0.534, p <0.0001)."
Vitamin D Deficiency and Supplementation and Relation to Cardiovascular Health

"Since the dietary sources of Vitamin D are scarce, especially in **India and Brazil,** recommendations for a healthy and safe sunlight exposure (more than 90% of Vitamin D is obtained by skin synthesis trough sunlight), associated with Vitamin D food enrichment (most food contains very little Vitamin D naturally), could be sufficient to control the epidemic of hypovitaminosis D and its negative health effects, in addition of reducing the medicalization of a easily preventable problem. **Until these objectives are met, Vitamin D supplementation should be indicated** to meet the minimum requirements."
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5434715/ May 2017

Is there a need of Vitamin D supplementation programme in India?
www.ncbi.nlm.nih.gov/pmc/articles/PMC5883901

People supplemented with Vitamin D had 13 percent fewer Cancer deaths – Meta-analysis of RCT June 2019 Many more here

M More sources (which get updated)

Impact studies: https://developmentevidence.3ieimpact.org/

Funding and volunteer researchers here and here and here

D. Dosage papers - most recent are probably most reliable

1000iu per day may be optimum for general population:
meta-analysis of vitamin D RCTs to reduce risk of acute respiratory infection to include data from an additional ~20k participants in 14 RCTs. The pre-print is here: https://www.medrxiv.org/content/10.1101/2020.07.14.20152728v1 .

serum level of 75-80nmol/l could be ideal for covid
(that's 30-35mg/l)
https://chrismasterjohnphd.com/covid-19/the-second-study-on-vitamin-d-and-covid-19-is-now-out?fbclid=IwAR0Lds3at5parDJJ9pToHUe3dB1UrqYo3DE0U6S6hBqNDWbD9dujW6IacWA

but 50nmol/l is sufficient:
We found that 25(OH)D at a level ≥21 ng/ml is associated with an increase in serum CRP. It is possible that the role of vitamin D supplementation to reduce inflammation is beneficial only among those with a lower serum 25(OH)D.
www.researchgate.net/publication/51717805_Relation_Between_Serum_25-Hydroxyvitamin_D_and_C-Reactive_Protein_in_Asymptomatic_Adults_From_the_Continuous_National_Health_and_Nutrition_Examination_Survey_2001_to_2006

https://www.nature.com/articles/s41430-020-0661-0

Selenium recommendations:
https://ods.od.nih.gov/factsheets/Selenium-HealthProfessional/

Vitamin D3 75 vs 100nmol

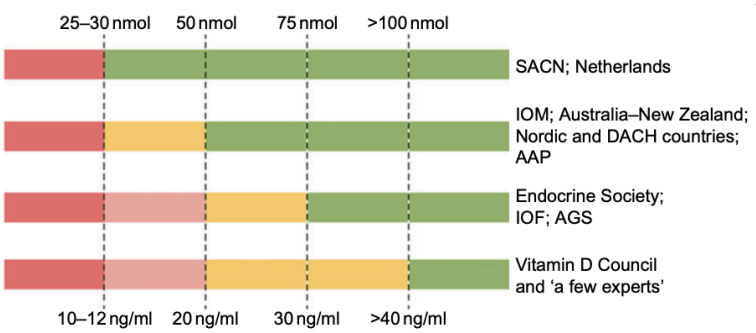


Fig. 1 Recommendations for interpreting serum levels of 25-hydroxyvitamin D. 'A schematic representation of how different agencies and countries interpret serum levels of 25-hydroxyvitamin D is shown. Colour code: red denotes a state of severe deficiency (danger) that has to be corrected without exception; orange denotes a state of mild deficiency (modest concern), in which intervention is desirable; green denotes a state of sufficient supply that does not benefit from additional supplementation. AAP, American Academy of Pediatrics; AGS, American Geriatrics Society; DACH, Deutschland (Germany, Austria and Confoederatio Helvetica (Switzerland); IOF, International Osteoporosis Foundation; IOM, Institute of Medicine; SACN, Scientific Advisory Committee on Nutrition.' Source: Bouillon[1]

www.ncbi.nlm.nih.gov/pmc/articles/PMC7167380/pdf/S1368980019005251a.pdf

Consensus guidelines on supplement dosage?
www.sciencedirect.com/science/article/abs/pii/S0960076017300316

Study with great list of references, which recommends 2,000IU daily supplement dose
https://link.springer.com/article/10.1007/s00198-009-1119-3

250 microgram / 10,000 IU daily dose recommended:
https://academic.oup.com/ajcn/article/69/5/842/4714819

maternal supplementation in pregancy:
https://pubmed.ncbi.nlm.nih.gov/29021285/

D dosage and role of intra-cellular Magnesium:
www.sott.net/article/286503-low-vitamin-d-levels-correlated-with-magnesium-deficiency

D3 overdosing:
https://pubmed.ncbi.nlm.nih.gov/25636720/

X - Studies which we liked but which may be over-confident:

Biggest systematic review:
https://www.sciencedirect.com/science/article/pii/S1871402120300801#bib57

Glycans:
www.geneticlifehacks.com/genetics-and-mannose-binding-lectin/

COVID-19: Melatonin as a potential adjuvant treatment

https://doi.org/10.1016/j.lfs.2020.117583Get rights and content

Abstract

This article summarizes the likely benefits of melatonin in the attenuation of COVID-19 based on its putative pathogenesis. The recent outbreak of COVID-19 has become a pandemic with tens of thousands of infected patients. Based on clinical features, pathology, the pathogenesis of acute respiratory disorder induced by either highly homogenous coronaviruses or other pathogens, the evidence suggests that excessive inflammation, oxidation, and an exaggerated immune response very likely contribute to COVID-19 pathology. This leads to a cytokine storm and subsequent progression to acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) and often death. Melatonin, a well-known anti-inflammatory and anti-oxidative molecule, is protective against ALI/ARDS caused by viral and other pathogens. Melatonin is effective in critical care patients by reducing vessel permeability, anxiety, sedation use, and improving sleeping quality, which might also be beneficial for better clinical outcomes for COVID-19 patients. Notably, melatonin has a high safety profile. There

is significant data showing that melatonin limits virus-related diseases and would also likely be beneficial in COVID-19 patients. Additional experiments and clinical studies are required to confirm this speculation.

~~Broad range of micronutrients advocated:~~
~~Southampton, UK 23 April 2020:~~
~~www.mdpi.com/2072-6643/12/4/1181~~
~~" A wealth of … data show that vitamins, including vitamins A, B_6, B_{12}, C, D, E, and folate; trace elements, including zinc, iron, selenium, magnesium, and copper; and the omega-3 fatty acids … play important … roles in supporting the immune system. Inadequate intake and status of these nutrients are widespread, leading to a decrease in resistance to infections and as a consequence an increase in disease burden. Against this background the following conclusions are made: …. supplementation with the above micronutrients and omega-3 fatty acids is a safe, effective, and low-cost strategy to help support optimal immune function."~~

~~GARLIC~~
~~Two innate lymphocytes, γδ T and natural killer (NK) cells, appear to be susceptible to diet modification. The purpose of this review was to~~ summarize the influence of aged garlic extract (AGE) on the immune system….AGE supplementation may enhance immune cell function and may be partly responsible for the reduced severity [in respiratory virus infection] https://academic.oup.com/jn/article/146/2/433S/4584824
However a Cochrane review was much less positive

" We believe, that we can **advise Vitamin D supplementation to protect against SARS-CoV2** infection." 3 UK university authors, preprint: www.researchsquare.com/article/rs-21211/v1

Vitamin D deficiency that is not sufficiently treated is associated with COVID-19 risk. Testing and treatment for vitamin D deficiency to address COVID-19 warrant aggressive pursuit and study.
https://www.medrxiv.org/content/10.1101/2020.05.08.20095893v1

Multiple micronutrients review + SIRT-1 pathway:
https://www.researchgate.net/publication/341160062_SARS-CoV-2_Micronutrient_Optimization_in_Supporting_Host_Immunocompetence

Prevention: In addition to the precautions given to us by the medical and government authorities as to wash our hands, use masks, alcohol and sanitizers... what else can we do? Prepare the immune system to work the fastest and most effective! a. Food: 1- Diet low in sugar and simple and refined carbohydrates. 2- Limit processed meals 3- Eat more vegetables,

fruits and nuts. 4- Hydrate well with water! (Your weight in lb. divided by 16 gives you the 8onz cups daily intake) 5- Sleep 8 hours b. Suggested supplementation: 1- Multivitamin and minerals one daily 2- Vitamin C 1000 mg three times daily 3- Vitamin D 10000 IU daily 4- Zinc 25 mg daily 5- Magnesium 500 mg daily 6- Melatonin 3 – 10 mg SL – daily (at bedtime) 7- Selenium 200 mcg daily 8- DHEA 25mg daily 9- NAC 60 mg, twice daily c. Other: Quercetin, probiotics, echinacea, astragalus, rhodiola, maitake, shitake, ginger, garlic, elderberry, vitamin A, DoTERRA Essential Oils (OnGuard - Breathe – Oregano). Optimal hormonal optimization, with testosterone.

www.vascularnutritionpr.com/uploads/7/0/5/2/7052470/covid-19drjvt.pdf

Quercetin, Allicin:https://pharmascope.org/ijrps/article/view/1738

Quercetin: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7202514/

Quercetin: https://www.mdpi.com/1999-4915/8/1/6

Quercetin post exercise: journals.physiology.org/doi/full/10.1152/ajpregu.90319.2008

Foods rich in isoquercitrin include leafy vegetables, broccoli, red onions, peppers, apples, grapes, black tea, green tea, red wine, and some fruit juices. The amount of quercetin received from food is primarily dependent on an individual's dietary habits. Research has found a typical Western Diet provides approximately 0 to 30 mg of quercetin per day, but a diet rich in fruits and vegetables was estimated to provide more.1 It is also important to note, that the food content of quercetin reflects variations in soil quality, time of harvest, and storage conditions. https://www.integrativepro.com/Resources/Integrative-Blog/2017/Quercetin-Food-Compared-Supplementation

On its own, quercetin has a low bioavailability, which means your body absorbs it poorly (41Trusted Source, 42Trusted Source). That's why the supplements may include other compounds, such as vitamin C or digestive enzymes like bromelain, as they may increase absorption (43, 44). Additionally, some research indicates that quercetin has a synergistic effect when combined with other flavonoid supplements, such as resveratrol, genistein, and catechins (45Trusted Source, 46Trusted Source, 47Trusted Source). Quercetin appears to be generally safe with little to no side effects. However, it may interact with various medications and may be unsuitable for pregnant and breastfeeding women, so speak with your healthcare provider before using it.

https://www.healthline.com/nutrition/quercetin#bottom-line

Quercetin immunology/biochemistry: https://www.integrativepro.com/Resources/Integrative-Blog/2017/Quercetin-Food-Compared-Supplementation

NAC and others, detailed pathophysiology: https://www.sciencedirect.com/science/article/pii/S0033062020300372

Nutraceuticals have potential for boosting the type 1 interferon response to RNA viruses including influenza and coronavirus

www.sciencedirect.com/science/article/pii/S0033062020300372

Ferulic acid	**500-1,000 mg**
Lipoic acid	**1,200-1,800 mg (in place of ferulic acid)**
Spirulina	**15 g (or 100 mg PCB)**
N-Acetylcysteine	**1,200–1,800 mg**
Selenium	**50-100 mcg**
Glucosamine	**3,000 mg or more**
Zinc	**30-50 mg**
Yeast Beta-Glucan	**250-500 mg**
Elderberry	**600–1,500 mg**

Zinc, and herbals review:

https://journals.sagepub.com/doi/full/10.1177/2156587216641831

[PDF] plos.org

[PDF] Effect of broccoli sprouts and live attenuated influenza virus on peripheral blood natural killer cells: A randomized, double-blind study

L Müller, M Meyer, RN Bauer, H Zhou, H Zhang… - PloS one, 2016 - journals.plos.org

Enhancing antiviral host defense responses through nutritional supplementation would be an attractive strategy in the fight against influenza. Using inoculation with live attenuated influenza virus (LAIV) as an infection model, we have recently shown that ingestion of sulforaphane-containing broccoli sprout homogenates (BSH) reduces markers of viral load in the nose. To investigate the systemic effects of short-term BSH supplementation in the context of LAIV-inoculation, we examined peripheral blood immune cell populations in non

Hesperidin

Review of Evidence Available on Hesperidin-Rich Products as Potential Tools against COVID-19 and Hydrodynamic Cavitation-Based Extraction as a Method of Increasing Their Production Francesco Meneguzzo 1,* 1 Institute for Bioeconomy, National Research Council, 10 Via Madonna del Piano, I-50019 Sesto Fiorentino, Italy; Correspondence: francesco.meneguzzo@cnr.it; Tel.: +39-392-985-0002 Received: 9 April 2020; Accepted: 5 May 2020; Published: 8 May 2020

Abstract: Based on recent computational and experimental studies, hesperidin, a bioactive flavonoid abundant in citrus peel, stands out for its high binding affinity to the main cellular receptors of SARS-CoV-2, outperforming drugs already recommended for clinical trials. Thus, it is very promising for prophylaxis and treatment of COVID-19, along with other coexistent flavonoids such as naringin, which could help restraining the proinflammatory overreaction of the immune system. Controlled hydrodynamic cavitation processes showed the highest speed, effectiveness and efficiency in the integral and green aqueous extraction of flavonoids, essential oils and pectin from citrus peel waste. After freeze-drying, the extracted pectin showed high quality and excellent antioxidant and antibacterial activities, attributed to flavonoids and essential oils adsorbed and concentrated on its surface. This study reviews the recent evidence about hesperidin as a promising molecule, and proposes a feasible and affordable process based on hydrodynamic cavitation for the integral aqueous extraction of citrus peel waste resulting in hesperidin-rich products, either aqueous extracts or pectin tablets. The uptake of this process on a relevant scale is urged, in order to achieve large-scale production and distribution of hesperidin-rich products. Meanwhile, experimental and clinical studies could determine the effective doses either for therapeutic and preventive purposes.

https://www.sciencedirect.com/science/article/pii/S030698772031358X

Is hesperidin essential for prophylaxis and treatment of COVID-19 Infection?

Author links open overlay panelYusuf A.Haggaga1Nahla E.El-AshmawybKamal M.Okashac

Show more

https://doi.org/10.1016/j.mehy.2020.109957Get rights and content

Abstract

SARS-CoV-2 or COVID-19 is representing the major global burden that implicated more than 4.7 million infected cases and 310 thousand deaths worldwide in less than 6 months. The prevalence of this pandemic disease is expected to rise every day. The challenge is to control its rapid spread meanwhile looking for a specific treatment to improve patient outcomes. Hesperidin is a classical herbal medicine used worldwide for a long time

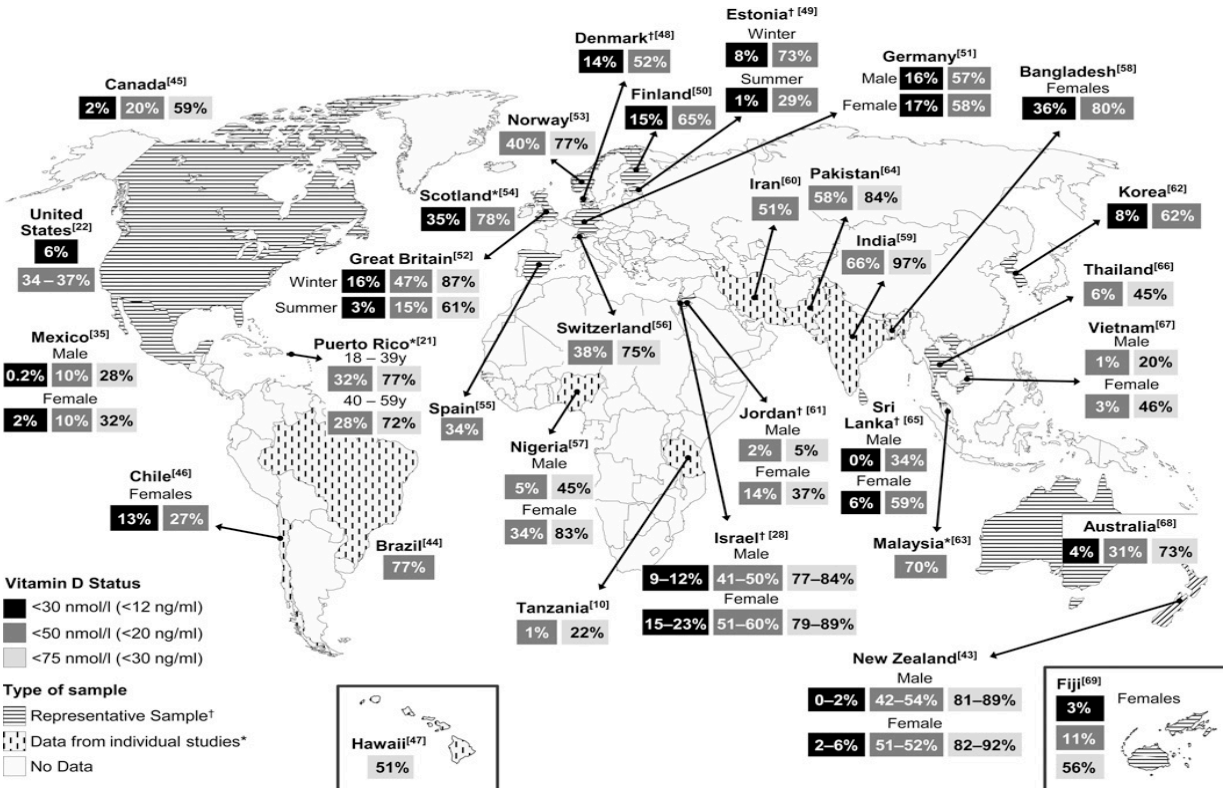
with an excellent safety profile. Hesperidin is a well-known herbal medication used as an antioxidant and anti-inflammatory agent. Available shreds of evidence support the promising use of hesperidin in prophylaxis and treatment of COVID 19. Herein, we discuss the possible prophylactic and treatment mechanisms of hesperidin based on previous and recent findings. Hesperidin can block coronavirus from entering host cells through ACE2 receptors which can prevent the infection. Anti-viral activity of hesperidin might constitute a treatment option for COVID-19 through improving host cellular immunity against infection and its good anti-inflammatory activity may help in controlling cytokine storm. Hesperidin mixture with diosmin co-administrated with heparin protect against venous thromboembolism which may prevent disease progression. Based on that, hesperidin might be used as a meaningful prophylactic agent and a promising adjuvant treatment option against SARS-CoV-2 infection.

Identification of potent COVID-19 main protease (Mpro) inhibitors from natural polyphenols: An in silico strategy unveils a hope against CORONA

Sevki Adem1 , Volkan Eyupoglu1 , Iqra Sarfraz2 , Azhar Rasul2*
Muhammad Ali3 1 Department of Chemistry, Faculty of Science, Cankiri Karatekin University, 18100 Cankırı, Turkey

Global distribution of D3 deficiency - maps

Here is very interesting data on global D deficiency, with Germany's **elder men especially shocking.** (I know there's a fortification issue in Germany - is it the same in neighbouring countries with similar culture/diet/weather?) Sourcencbi.nlm.nih.gov/pmc/articles/PMC4018438
And here is the image for adults overall:



B. Biochemical mechanisms

Interestingly, Jacobson's team also suggests vitamin D as a potentially useful Covid-19 drug. The vitamin is involved in the RAS system and could prove helpful by reducing levels of another compound, known as REN. Again, this could stop potentially deadly bradykinin storms from forming. The researchers note that vitamin D has already been shown to help those with Covid-19. The vitamin is readily available over the counter, and around 20% of the population is deficient. If indeed the vitamin proves effective at reducing the severity of bradykinin storms, it could be an easy, relatively safe way to reduce the severity of the virus.

https://elemental.medium.com/a-supercomputer-analyzed-covid-19-and-an-interesting-new-theory-has-emerged-31cb8eba9d63

15 genes were identified as major mediators of the action of vitamin D in innate and adaptive immunity and their individual functions are explained based on different gene regulatory scenarios.

https://pubmed.ncbi.nlm.nih.gov/32325790/

"The finding that D3 and its metabolites **modulate endothelial stability** may help explain the clinical correlations between low serum vitamin D levels and the many human diseases with well-described vascular dysfunction phenotypes."
https://pubmed.ncbi.nlm.nih.gov/26469335/?from_term=Gibson+2015+vitamin+d&from_pos=3
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0140370

NF-KB and SiRT-1 pathways:

COVID-19: NAD+ deficiency may predispose the aged, obese and type2 diabetics to mortality through its effect on SIRT1 activity R.Miller A.R.Wentzela G.Richards
www.sciencedirect.com/science/article/pii/S0306987720314742?fbclid=IwAR1SIRaCckeJnOs8qfOv3mZVmDmgIg9eF02oXL2I-xjOe3oq-d2XC2UugoY

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4041949/
"NF-κB is a transcription factor that integrates pro-inflammatory and pro-survival responses in diverse cell types."

"De-acetylation at this site is performed by sirtuin 1(SIRT1) and possibly other sirtuins in an NAD+ dependent manner, such that SIRT1 inhibition promotes NF-κB transcriptional activity."

https://pubmed.ncbi.nlm.nih.gov/26469335/?from_term=Gibson+2015+vitamin+d&from_pos=3

"We estimated a link between Vit D status and high CRP in healthy subjects (CRP greater than or equal to 0.2 mg/dL) with an adjustment for age and income to explore the possible role of Vit D in reducing complications attributed to unregulated inflammation and cytokine production"
www.medrxiv.org/content/10.1101/2020.04.08.20058578v4

Vitamin D has a critical role in the innate immune system through the production of antimicrobial peptides – particularly cathelicidin.
www.tandfonline.com/doi/abs/10.1586/eri.10.102

Selenium status may affect the function of cells of both adaptive and innate immunity. Supranutritional selenium promotes proliferation and favors differentiation of naive CD4-positive T lymphocytes toward T helper 1 cells, thus supporting the acute cellular immune response, whereas excessive activation of the immune system and ensuing host tissue damage are counteracted through directing macrophages toward the M2 phenotype. https://academic.oup.com/advances/article/6/1/73/4558052

The Essential Role of Vitamin D in the Biosynthesis of Endogenous Antimicrobial Peptides May Explain Why Deficiency Increases Mortality Risk in COVID-19 Infections McCullough *
https://www.preprints.org/manuscript/202005.0265/v1

Thrombosis

https://pubmed.ncbi.nlm.nih.gov/31653092/

P. Proxy measures: D3 and C-reactive peptides

in babies: https://www.nature.com/articles/pr20179
adults (up to 50nmol/l): https://pubmed.ncbi.nlm.nih.gov/21996139

N. Neonates and women

Among 9 pregnant women with severe COVID-19 disease, at the time of reporting 7 of 9 died, 1 of 9 remains critically ill and ventilator-dependent, and 1 of 9 recovered after prolonged hospitalization. We obtained self-verified familial/household cohort data in all 9 cases, and in each and every instance the maternal outcomes were more severe when compared to other high and low-risk familial/household members (n=33 members for comparison).
www.sciencedirect.com/science/article/pii/S0002937820305160

For babies, we need an urgent proposal team:

because this:

https://www.moneycontrol.com/news/trends/expert-columns-2/covid-19-pandemic-india-battles-to-save-its-newborns-in-titanic-struggle-against-coronavirus-5283551.html

I found some age vs deaths data for covid in India with shockingly high baby deaths, but didn't take it seriously enough, and now I can't recover it. Probably a small sample.

"In mothers infected with coronavirus infections, including COVID-19, >90% of whom also had pneumonia, PTB is the most common adverse pregnancy outcome. Miscarriage, preeclampsia, cesarean, and perinatal death (7-11%) were also more common than in the general population. "
https://pubmed.ncbi.nlm.nih.gov/32292902/

However other studies haven't found that so I suspect it's only in a malnourished subgroup that mothers and babies are dying.

china deaths of babies:
https://www.researchsquare.com/article/rs-25861/v1

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6076921/
The prevalence of vitamin D deficiency in neonates was observed to be very high and needs more attention.

https://pubmed.ncbi.nlm.nih.gov/32056191
Neonates with vitamin D deficiency/insufficiency are at higher risk for developing sepsis than those with sufficient vitamin D levels. Lower vitamin D levels in mothers is also associated with increased risk of sepsis in the neonates.

https://www.bettersafercare.vic.gov.au/resources/clinical-guidance/maternity-and-newborn-clinical-network/vitamin-d-deficiency-in-neonates
Risk factors for maternal vitamin D deficiency include:

- dark-skinned women, including Asian women
- women who spend a lot of time indoors and who 'cover up'
- limited sunlight exposure: cold climate, short winter days, indoor occupation, need for protective clothing.

Vitamin D deficiency, including severe deficiency, was common among breastfed infants in Iowa who did not receive preformed vitamin D. Deficiency occurred mostly during winter but was not completely absent during summer. It affected infants with light as well as dark skin pigmentation. Consumption of preformed vitamin D from vitamin supplements or formula is effective in preventing vitamin D deficiency. Vitamin D supplementation should be provided to all breastfed infants.
https://pubmed.ncbi.nlm.nih.gov/16882813/

Vitamin-D Deficiency Predicts Infections in Young North Indian Children
https://pubmed.ncbi.nlm.nih.gov/28273084/

(Maybe controversial?) archived article on non-covid secondary deaths in India caused by lockdown complications. It shows how a Mumbai hospital reduced these deaths:

"A very large number of people in India continue to die due to preventable causes. The extended lockdown with restricted access and scaled-down health services will lead to a huge increase in deaths due to many of these causes. Managing the Covid-19 epidemic does not mean that we need to restrict access to other services.
The Tata Memorial Cancer Hospital in Mumbai, for instance, has shown how the two objectives can be met simultaneously with understanding, courage and leadership. The hospital set up a core Covid-19 team to plan and coordinate the response, set up screening camps outside the hospital, instituted stan…Pavitra Mohan, a paediatrician and public health physician, is the co-founder of Basic Health Care Services. He leads health services at Aajeevika Bureau. Raj Gautam Mitra is a statistician who earlier served as Inter-regional Advisor to the UN Statistics Division at New York. Arpita Amin is Executive Research at Basic Health Care Services.

South Asia

"We performed a retrospective study in two tertiary medical centers in South Asia. The medical records of COVID-19 patients were reviewed and a total of 176 subjects included were the elderly whose age is at least 60 years, with information in age, body mass index (BMI), sex, comorbidities, pre-hospital 25(OH)D level, and clinical characteristics. 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. Also, most of the subjects with pre-existing condition had 25(OH)D level below 30 ng/ml. Majority of subjects classified as severe had 25(OH)D level below 30 ng/ml. Age and 25(OH)D level were negatively related. Although clinical trials could provide more meaningful findings as to the causation of 25(OH)D levels and COVID-19 severity, basic healthy solutions such as Vitamin D supplementation could be raised even in the community level and awareness on Vitamin D benefits in fighting infections, such as COVID-19, should be

disseminated especially to the vulnerable elderly population."
https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3593258

More on Indians, Delhi and vitamin D3:

www.youtube.com/watch?v=2V21MLAGaB0
Vitamin D Update

The Kerala/Germany study shows a direct link to UVB, with other variables removed:

https://bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-14-510

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3586555

https://www.mdpi.com/2072-6643/6/2/729

Ethnicity:
https://www.bmj.com/content/369/bmj.m1548/rapid-responses

C. Vitamin D importance in other conditions

Association of C-reactive protein and vitamin D deficiency with cardiovascular disease www.ncbi.nlm.nih.gov/pmc/articles/PMC6605633/

Another person's summary here:
http://agingbiotech.info/vitamindcovid19facts/1pager.pdf

Recent paper with good list of references:

https://www.sciencedirect.com/science/article/pii/S2352364620300067?via%3Dihub

Recent papers:

Prospective cohort study:
https://pmj.bmj.com/content/early/2020/09/15/postgradmedj-2020-138712?fbclid=IwAR3Bnv8MBiO16wq3HUM2n4yrwljutyFSo-NeWEAs7Vk7ImmN8Ns-lEoZRL4

Calcifediol
https://medium.com/microbial-instincts/the-first-clinical-trial-to-support-vitamin-d-therapy-for-covid-19-906a9d907468

A Basic Review of the Preliminary Evidence That COVID-19 Risk and Severity Is Increased in Vitamin D Deficiency

Linda L. Benskin1,2*

1Independent Researcher for Improving Health in Rural Areas of Tropical Developing Countries, Austin, TX, United States
2Ferris Mfg. Corp., Makers of PolyMem® Multifunctional Dressings, Ft. Worth, TX, United States

As the world's attention has been riveted upon the growing COVID-19 pandemic, many researchers have written brief reports supporting the hypothesis that vitamin D deficiency is related to the incidence and severity of COVID-19. The clear common thread among the top risk groups—vitamin D deficiency—may be being overlooked because of previous overstated claims of vitamin D benefits. However, the need to decrease COVID-19 fatalities among high-risk populations is urgent. Early researchers reported three striking patterns. Firstly, the innate immune system is impaired by vitamin D deficiency, which would predispose sufferers to viral infections such as COVID-19. Vitamin D deficiency also increases the activity of the X-chromosome-linked “Renin-Angiotensin” System, making vitamin D deficient individuals (especially men) more susceptible to COVID-19's deadly “cytokine storm” (dramatic immune system overreaction). Secondly, the groups who are at highest risk for severe COVID-19 match those who are at highest risk for severe vitamin D deficiency. This includes the elderly, men, ethnic groups whose skin is naturally rich in melanin (if living outside the tropics), those who avoid sun exposure for cultural and health reasons, those who live in institutions, the obese, and/or those who suffer with hypertension, cardiovascular disease, or diabetes. And thirdly, the pattern of geographical spread of COVID-19 reflects higher population vitamin D deficiency. Both within the USA and throughout the world, COVID-19 fatality rates parallel vitamin D deficiency rates. A literature search was performed on PubMed, Google Scholar, and RSMLDS, with targeted Google searches providing additional sources. Although randomized controlled trial results may be available eventually, the correlational and causal study evidence supporting a link between vitamin D deficiency and COVID-19 risks is already so strong that it supports action. The 141 author groups writing primarily about biological plausibility detailed how vitamin D deficiency can explain every risk factor and every complication of COVID-19, but agreed that other factors are undoubtedly at work. COVID-19 was compared with dengue fever, for which oral vitamin D supplements of 4,000 IU for 10 days were significantly more effective than 1,000 IU in reducing virus replication and controlling the

“cytokine storm” (dramatic immune system over-reaction) responsible for fatalities. Among the 47 original research studies summarized here, chart reviews found that serum vitamin D levels predicted COVID-19 mortality rates (16 studies) and linearly predicted COVID-19 illness severity (8 studies). Two causal modeling studies and several analyses of variance strongly supported the hypothesis that vitamin D deficiency is a causal, rather than a bystander, factor in COVID-19 outcomes. Three of the four studies whose findings opposed the hypothesis relied upon disproven assumptions. The literature review also found that prophylactically correcting possible vitamin D deficiency during the COVID-19 pandemic is extremely safe. Widely recommending 2,000 IU of vitamin D daily for all populations with limited ability to manufacture vitamin D from the sun has virtually no potential for harm and is reasonably likely to save many lives.

I like this, a Bradford Hill analysis on vitamin D which doesn't make too outrageous claims:

https://www.sciencedirect.com/science/article/pii/S0378512220302929

More recent (oct 2020) refs here:

https://www.youtube.com/watch?v=HxtddpoPMKo