



# Strong correlation between prevalence of severe vitamin D deficiency and population mortality rate from COVID-19 in Europe

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## Summary

**Background** Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes a very wide range of disease severity: from completely asymptomatic to fatal, and the reasons for that are not well understood; however, there are some data that show vitamin D may have a protective effect.

**Methods** To retrieve the vitamin D levels data, the authors analyzed the vitamin D European population data compiled by 2019 European Calcified Tissue Society (ECTS) statement on vitamin D status published in the *European Journal of Endocrinology*. For the data set to be used for analysis, only recently published data that included general adult population of both genders aged 40–65 years or wider and must have included the prevalence of vitamin D deficiency.

**Results** There were data sets from 10 countries that fitted the criteria and were analyzed. Severe vitamin D deficiency was defined as 25(OH)D less than 25 nmol/L (10 ng/dL). Pearson correlation analysis between death rate per million of population from coronavirus disease 2019 (COVID-19) and prevalence of severe vitamin D deficiency showed a strong correlation with  $r=0.79$ ,  $p=0.007$ . Over time, correlation strengthened, and  $r$  coefficient asymptotically increased. After adjusting for countries' age structure and per capita health expenditures, multiple linear regression analysis showed that higher prevalence of severe vitamin D deficiency is associated with in-

creased mortality. Each 1% increase in prevalence increased deaths by 55 per million (95% confidence interval, CI 8–102),  $p=0.03$ .

**Conclusion** The authors recommend universal screening for vitamin D deficiency, and further investigation of Vitamin D supplementation in randomized control studies, which may lead to possible treatment or prevention of COVID-19.

**Keywords** Prevention · Protective effect · Death rate · SARS-CoV-2 · Coronavirus

## Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes a very wide range of disease severity: from completely asymptomatic to fatal, and the reasons for that are not well understood; however, there are some data that show vitamin D may have a protective effect [2].

## Methods

The authors analyzed European countries vitamin D data compiled by 2019 ECTS statement on vitamin D Status published in the *European Journal of Endocrinology* [4]. For the data set to be used for analysis, it must have been published in the last 10 years, must have included general adult population of both genders aged 40–65 years or wider, and must have had breakdown on the prevalence of vitamin D deficiency.

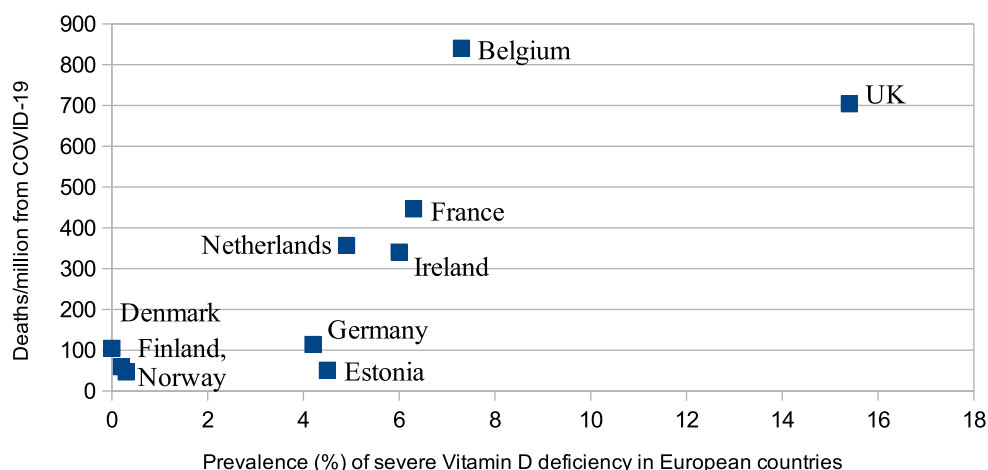
Deaths from coronavirus 2019 (COVID-19) data were retrieved from the John Hopkins University of Medicine Coronavirus Resource Center [4]. Demographics data for 2020 were retrieved from the CIA World Factbook [1]. Healthcare expenditures were retrieved from UN data [6]. Six data retrievals were performed between 11 May 2020 and 4 August 2020.

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**Fig. 1** Prevalence of severe vitamin D deficiency vs COVID-19 deaths/million in Europe



Pearson correlations and multiple linear regression analysis were performed on the data using LibreOffice Calc version 6.3 software (Free Software Foundation Europe [FSFE], Berlin, Germany).

**Results**

Table 1 shows vitamin D, demographic, health expenditures, COVID-19 death data and corresponding Pearson correlation statistics for the 10 European countries. Figure 1 graphically displays the relationship between deaths/million from COVID-19 and the prevalence of severe vitamin D deficiency.

Correlation analysis showed that countries' prevalence of severe vitamin D deficiency (serum vitamin 25(OH) D less than 25 nmol/L) is strongly and significantly correlated with COVID-19 deaths per million of the population with  $r=0.79$ ,  $p=0.007$ . Correlation coefficient asymptotically increased from 11 May

2020 to 4 August 2020:  $0.70 \rightarrow 0.72 \rightarrow 0.75 \rightarrow 0.76 \rightarrow 0.78 \rightarrow 0.79$ .

After adjusting for countries' age structure and per capita health expenditures, multiple linear regression analysis showed that higher prevalence of severe vitamin D deficiency is associated with increased mortality. Each 1% increase in prevalence increased deaths by 55 per million (95% confidence interval, CI 8–102,  $p=0.03$ ).

**Discussion**

Data collected shows a strong and significant correlation between prevalence of severe Vitamin D deficiency and COVID-19 deaths per million in European countries. The correlation is asymptotically getting stronger over time, making it even less likely to be caused by a random chance. This is consistent with US and UK trends that show the mortality rate from COVID-19 is higher in dark-skinned and obese indi-

**Table 1** European countries vitamin D, demographic, healthcare expenditures, COVID-19 death data and the correlation with COVID-19 deaths/million [1, 4, 6]

Country	Prevalence (%) of Vit. D <25 nmol/L	Prevalence (%) of Vit. D <50 nmol/L	Mean (nmol/L) Vitamin D	Median Age	Over age 65 (%)	Health spending per capita in US\$	COVID-19 deaths/million
UK	15.4	56.4	47.4	40.6	18.5	\$3648	704
France	6.3	34.6	60	41.7	20.5	\$4690	447
Belgium	7.3	51.1	49.3	41.6	19.2	\$4711	840
Germany	4.2	54.5	50.1	47.8	23.0	\$4683	114
Netherlands	4.9	33.6	59.5	42.8	19.8	\$5737	357
Ireland	6	45	56.4	37.8	13.8	\$3709	341
Denmark	0	23.6	65	42	19.9	\$6304	105
Finland	0.2	6.6	67.7	42.8	22.3	\$4232	59
Norway	0.3	18.6	65	39.5	17.4	\$9055	47
Estonia	4.5	51	51.6	43.7	21.0	\$1010	51
<i>N= 10</i>							
Correlation coefficient	0.79	0.53	-0.58	-0.29	-0.28	-0.15	-
T-statistics	3.63	1.75	-2.03	-0.87	-0.83	-0.42	-
P-value	0.007	0.12	0.08	0.41	0.43	0.68	-
Data retrieved 4 August 2020							

viduals than in general population, as these individuals are at higher risk for vitamin D deficiency.

Since the correlation coefficient  $r=0.79$ , it means that about 62% ( $r^2$ ) of deaths from COVID-19 can be explained by prevalence of severe vitamin D deficiency. This finding by itself does not necessarily mean causality, or that correcting deficiency would decrease the mortality, because another variable could cause both high prevalence of vitamin D deficiency and increased deaths from COVID-19. Examples of such variable could be prevalence of unknown genetic variation or certain healthcare system variations.

However, since there are data that show vitamin D deficiency is associated with greater risk of various infections [3] and that vitamin D supplementation could reduce risk of COVID-19 infections [2], it is very likely that vitamin D supplements have a large role in prevention and possibly treatment of COVID-19. Supporting this theory, Nordic countries' population have low prevalence of vitamin D deficiency as a result of recent campaigns for common use of supplements, cod-liver oil and vitamin D fortification [5], which may also explain low COVID-19 death rate (Sweden is a notable exception due to completely different infection control approach).

## Conclusion

There is a strong correlation between prevalence of severe vitamin D deficiency and the mortality rate

per million from COVID-19 in the European countries. The authors recommend for physicians to universally screen for vitamin D deficiency, and recommend further investigation of vitamin D supplementation in randomized control studies, which may lead to possible treatment or prevention of COVID-19.

**Conflict of interest** I. Z. Pugach and S. Pugach declare that they have no competing interests.

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