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Editorial: low population mortality from COVID-19 in countries south of latitude 35 degrees North supports vitamin D as a factor determining severity

The excellent review by Al-Ani et al reflects a consensus approach to management of inflammatory bowel disease during the SARS-CoV-2 pandemic that has been established remarkably rapidly by very effective international collaboration.[1] Much of the focus has appropriately been on the potential impact of immuno-modulating therapies. We would also like to highlight the potential importance of nutrition and particularly vitamin D as raised by Panarese and Shahini.[2]

There are marked variations in mortality from COVID-19 between different countries. It is becoming clear that countries in the Southern Hemisphere are seeing a relatively low mortality (Figure 1 and Table 1).[2,3] It could be argued that the virus spread later to the Southern Hemisphere and that countries there are simply behind those in the Northern Hemisphere but as time goes by this argument looks increasingly weak. In Australia, 100 cases were reported by 10th March, 1000 by 21st March; in the UK, the first 100 had been reported by 5th March and the first 1000 by 14th March, just 1 week earlier. If one compares the mortality (68 per million) in the UK by 3rd April with the mortality (2 per million) in Australia by 10th April, there is still a huge discrepancy.

When mortality per million is plotted against latitude, it can be seen that all countries that lie below 35 degrees North have relatively low mortality. Thirty-five degrees North also happens to be the latitude above which people do not receive sufficient sunlight to retain adequate vitamin D levels during winter. This suggests a possible role for vitamin D in determining outcomes from COVID-19. There are outliers of course—mortality is relatively low in Nordic countries—but there vitamin D deficiency is relatively uncommon, probably due to widespread use of supplements.[4] Italy and Spain, perhaps surprisingly, have relatively high prevalences of vitamin D deficiency. Vitamin D deficiency has also been shown to correlate with hypertension,[5] diabetes,[6] obesity[7] and ethnicity[8]—all features associated with increased risk of severe COVID-19.

There are considerable experimental data showing that vitamin D is important in regulating and suppressing the inflammatory cytokine response of respiratory epithelial cells and macrophages to various pathogens including respiratory viruses.[9] Evidence that vitamin D might protect against infection is modest but it is important to note that the hypothesis is not that vitamin

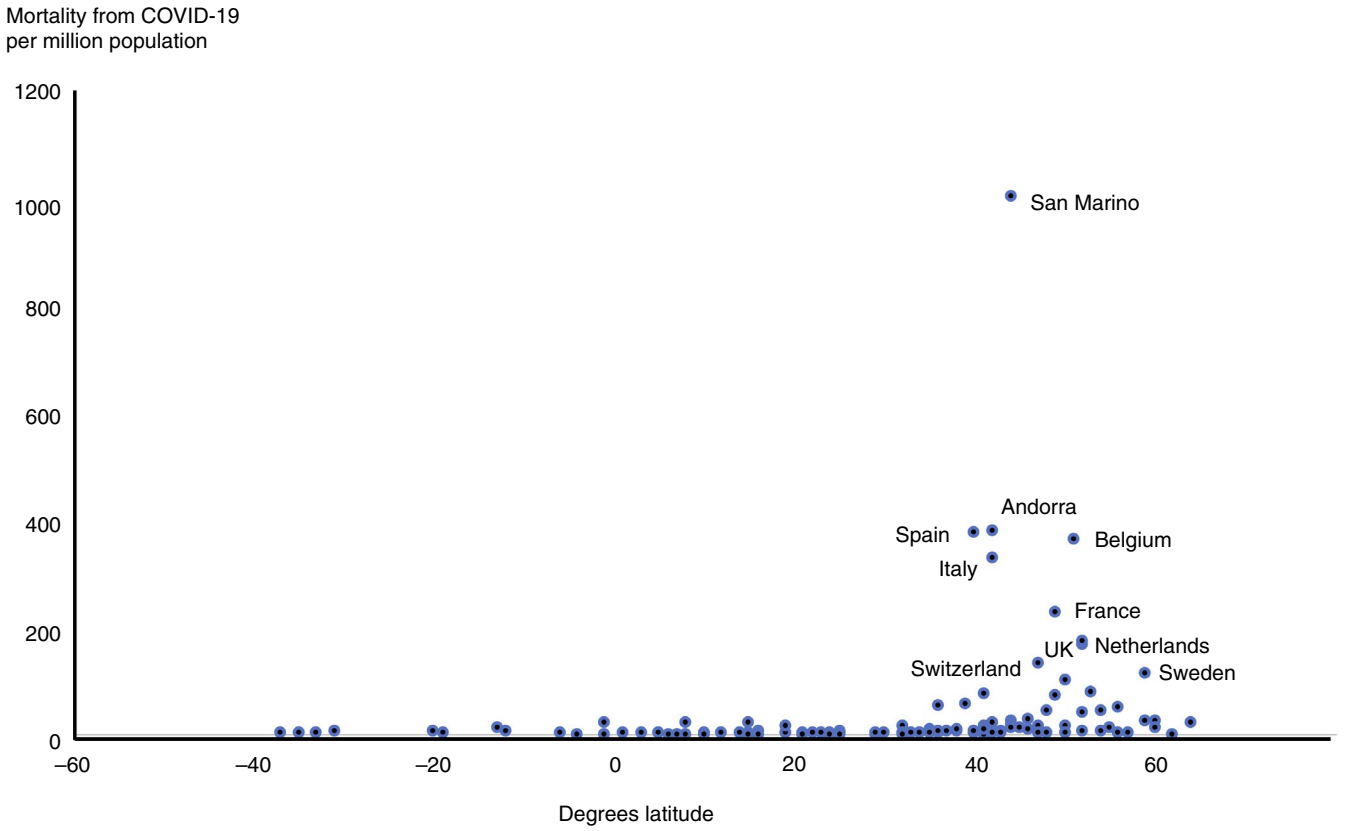

FIGURE 1 Correlation between mortality from COVID-19 per million by country and latitude. All countries with >150 cases included. Data are from https://www.worldometers.info/coronavirus/[3] accessed 15th April 2020. Latitude is for capital city. It can be seen that mortality is relatively low at latitudes less than 35 degrees North, the point below which adequate sunlight is likely to have been received to maintain vitamin D levels during the winter. Correlation between mortality and latitude $r = 0.53$, $P < 0.0001$ by Spearman's rank correlation

D would protect against SARS-CoV-2 infection but that it could be very important in preventing the cytokine storm and subsequent acute respiratory distress syndrome that is commonly the cause of mortality.[10]

Research is urgently needed to assess whether there may be a correlation between vitamin D status and severity of COVID-19 disease. Meanwhile, the evidence supporting a protective effect of vitamin D against severe COVID-19 disease is very suggestive, a substantial proportion of the population in the Northern Hemisphere will currently be vitamin D deficient, and supplements, for example, 1000 international units (25 micrograms) per day are very safe. It is time for governments to strengthen recommendations for vitamin D intake and supplementation, particularly when under lock-down.

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AUTHORSHIP

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LINKED CONTENT

This article is linked to Al-Ani et al and Garg et al papers. To view these articles, visit https://doi.org/10.1111/apt.15779 and https://doi.org/10.1111/apt.15796.

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TABLE 1 Comparison between latitude (of capital city in each country) and mortality from COVID-19 per million population—as per Panarese et al,[2] with further analysis and updated 15th April 2020 from https://www.worldometers.info/coronavirus/[3]

Countries	Latitude degrees	Total cases (N)	Total deaths (N)	Deaths/ Million population
Iceland	64	1720	8	23
Faeroe	62	184	0	0
Norway	60	6740	145	27
Finland	60	3237	64	12
Sweden	59	11 927	1203	119
Estonia	59	1400	35	26
Latvia	57	666	5	3
Russia	56	24 490	198	1
Denmark	56	6681	309	53
Lithuania	55	1091	29	11
Belarus	54	3728	36	4
Isle of Man	54	256	4	47
Ireland	53	11 479	406	82
Germany	52	132 321	3502	42
UK	52	93 873	12 107	178
Netherlands	52	28 153	3134	183
Poland	52	7408	268	7
Belgium	51	33 573	4440	383
Czechia	50	6151	163	15
Luxembourg	50	3307	67	107
Ukraine	50	3764	108	2
France	49	143 303	15 729	241
Channel Islands	49	445	13	75
Austria	48	14 321	393	44
Slovakia	48	863	6	1
Switzerland	47	26 336	1221	141
Moldova	47	1934	43	11
Hungary	47	1579	134	14
Kazakhstan	47	1290	16	0.9
Croatia	46	1741	34	8
Slovenia	46	1248	61	29
Serbia	45	4873	99	11
Canada	44	27 063	903	24
Romania	44	7216	362	19
Bosnia and Herzegovina	44	1110	41	12
San Marino	44	372	36	1061
Bulgaria	43	735	36	5
Kyrgyzstan	43	449	5	0.8
Italy	42	162 488	21 067	348
North Macedonia	42	974	45	22
Andorra	42	659	31	401
Montenegro	42	288	4	6
Georgia	42	306	3	0.8
USA	41	614 246	26 064	79
Turkey	41	65 111	1403	17
Uzbekistan	41	1275	4	0.1
Albania	41	494	25	9
Spain	40	177 633	18 579	397
China	40	82 295	3342	2
Azerbaijan	40	1253	13	1
Armenia	40	1111	17	6
Portugal	39	18 091	599	59
S. Korea	38	10 591	225	4
Greece	38	2170	101	10
Algeria	37	2070	326	7
Iran	36	76 389	4777	57
Japan	36	8100	146	1
Malta	36	399	3	7
Cyprus	35	695	12	10
Afghanistan	35	784	25	0.6
Pakistan	34	5988	107	0.5
Tunisia	34	747	34	3
Lebanon	34	658	21	3
Iraq	33	1400	78	2
Israel	32	12 200	126	15
Morocco	32	1988	127	3
Jordan	32	397	7	0.7
Palestine	32	308	2	0.4
Egypt	30	2350	178	2
India	29	11 555	396	0.3
Kuwait	29	1405	3	0.7
Saudi Arabia	25	5862	79	2
Qatar	25	3711	7	2
Bahrain	25	1671	7	4
Taiwan	25	395	6	0.3
UAE	24	4933	28	3
Bangladesh	24	1231	50	0.3
Cuba	23	766	21	2
Hong Kong	22	1017	4	0.5
Oman	21	910	4	0.8
Reunion	21	391	0	0
Vietnam	21	297	0	0
Mexico	19	5399	406	3

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TABLE 1 (Continued)

Countries	Latitude degrees	Total cases (N)	Total deaths (N)	Deaths/ Million population
Dominican Republic	19	3286	183	17
Brazil	16	25 758	1557	7
Guatemala	16	180	5	0.3
Philippines	15	5453	349	3
Senegal	15	314	2	0.1
Martinique	15	158	8	21
Thailand	14	2643	43	0.6
Niger	14	570	14	0.6
Honduras	14	419	31	3
Burkina Faso	12	528	30	1
Djibouti	12	363	2	2
Costa Rica	10	618	3	0.6
Guinea	10	404	1	0.1
Venezuela	10	197	9	0.3
Panama	8	3574	95	22
Ivory Coast	8	638	6	0.2
Nigeria	7	373	11	0.05
Sri Lanka	7	235	7	0.3
Ghana	6	636	8	0.3
Colombia	5	2979	127	2
Cameroon	5	848	17	0.6
Malaysia	3	5072	83	3
Singapore	1	3252	10	2
Ecuador	−1	7603	369	21
Kenya	−1	225	10	0.2
DRC	−4	241	20	0.2
Indonesia	−6	5136	469	2
Peru	−12	10 303	230	7
Mayotte	−13	217	3	11
Bolivia	−19	397	28	2
Mauritius	−20	324	9	7
Chile	−31	7917	92	5
South Africa	−33	2415	27	0.5
Australia	−35	6447	63	2
Argentina	−35	2443	108	2
Uruguay	−35	492	8	2
New Zealand	−37	1386	9	2

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