



OPEN

Association of lockdowns with the protective role of ultraviolet-B (UVB) radiation in reducing COVID-19 deaths

Rahul Kalippurayil Moozhipurath[✉] & Lennart Kraft

Nations are imposing unprecedented measures at a large scale to contain the spread of the COVID-19 pandemic. While recent studies show that non-pharmaceutical intervention measures such as lockdowns may have mitigated the spread of COVID-19, those measures also lead to substantial economic and social costs, and might limit exposure to ultraviolet-B radiation (UVB). Emerging observational evidence indicates the protective role of UVB and vitamin D in reducing the severity and mortality of COVID-19 deaths. This observational study empirically outlines the protective roles of lockdown and UVB exposure as measured by the ultraviolet index (UVI). Specifically, we examine whether the severity of lockdown is associated with a reduction in the protective role of UVB exposure. We use a log-linear fixed-effects model on a panel dataset of secondary data of 155 countries from 22 January 2020 until 7 October 2020 ($n = 29,327$). We use the cumulative number of COVID-19 deaths as the dependent variable and isolate the mitigating influence of lockdown severity on the association between UVI and growth rates of COVID-19 deaths from time-constant country-specific and time-varying country-specific potentially confounding factors. After controlling for time-constant and time-varying factors, we find that a unit increase in UVI and lockdown severity are independently associated with -0.85 percentage points (p.p) and -4.7 p.p decline in COVID-19 deaths growth rate, indicating their respective protective roles. The change of UVI over time is typically large (e.g., on average, UVI in New York City increases up to 6 units between January until June), indicating that the protective role of UVI might be substantial. However, the widely utilized and least severe lockdown (governmental recommendation to not leave the house) is associated with the mitigation of the protective role of UVI by 81% (0.76 p.p), which indicates a downside risk associated with its widespread use. We find that lockdown severity and UVI are independently associated with a slowdown in the daily growth rates of cumulative COVID-19 deaths. However, we find evidence that an increase in lockdown severity is associated with significant mitigation in the protective role of UVI in reducing COVID-19 deaths. Our results suggest that lockdowns in conjunction with adequate exposure to UVB radiation might have even reduced the number of COVID-19 deaths more strongly than lockdowns alone. For example, we estimate that there would be 11% fewer deaths on average with sufficient UVB exposure during the period people were recommended not to leave their house. Therefore, our study outlines the importance of considering UVB exposure, especially while implementing lockdowns, and could inspire further clinical studies that may support policy decision-making in countries imposing such measures.

Nations are imposing unprecedented non-pharmaceutical intervention measures at a large scale to contain the extent of COVID-19 pandemic^{1,2}. Recent studies indicate that non-pharmaceutical interventions such as lockdowns, ceasing business operations, and closing schools may have substantially slowed down the growth of COVID-19¹⁻³, indicating their protective role. Emerging observational evidence on the epidemiology of COVID-19 shows that vitamin D deficiency might be a risk factor for COVID-19 incidence, severity, and deaths⁴⁻⁷. They also indicate the protective role of a significant source of vitamin D—ultraviolet-B radiation (UVB)⁸—in mitigating COVID-19 deaths. In addition to substantial economic and social costs, an unintended consequence

Faculty of Economics and Business, Goethe University Frankfurt, Theodor-W.-Adorno-Platz 4, 60629 Frankfurt, Germany. ✉email: rahulkm85@gmail.com

of lockdown is the likelihood of limited exposure to UVB. However, to the best of our knowledge, no empirical study has explored the association between the severity of lockdown, the subsequent reduction in UVB exposure, and the number of deaths attributed to COVID-19 (COVID-19 deaths).

In this observational study of secondary data, we empirically outline the independent protective roles of lockdown and UVB as measured by ultraviolet index (UVI) and subsequently examine whether the severity of lockdown is associated with a reduction in the protective role of UVB. After controlling for time-constant and time-varying factors, we find that a unit increase in UVI and lockdown severity are independently associated with 0.85 percentage points (p.p) and 4.7 p.p decline in the growth rate of COVID-19 deaths. The change of UVI over time is typically large (e.g., Fig. S1 in Supplementary Appendix on an average UVI in New York City increases up to 6 units between January until June), indicating that the protective role of UVI might be substantial. These declines indicate the protective roles of UVI and lockdowns. Surprisingly, the widely utilized lockdown with the least severity (e.g., recommendation to not leave the house) is already associated with almost complete mitigation of the protective role of UVI by 0.76 p.p, which represents a decline of 81%.

Association of lockdown severity and UVB radiation with cumulative COVID-19 deaths

In general, non-pharmaceutical interventions such as the lockdowns aim to reduce the likelihood of transmission of the virus by limiting the movement of people, reducing the contact among individuals via restricting economic activities such as closing restaurants¹. Earlier studies indicate that such large-scale non-pharmaceutical intervention measures might have slowed down COVID-19 spread, indicating their protective role, thereby providing public health benefits^{1,3,9}. However, such policies' unintended health consequences (e.g., reduced exposure to UVB radiation) are largely unknown.

Prior studies indicate that UVB radiation plays a protective role in human health^{10–14}. Humans get vitamin D either via diet (natural food, fortified food, or supplements) or skin synthesis by UVB radiation exposure¹⁵. Likelihood of UVB exposure and subsequent vitamin D synthesis undergo substantial variation according to several time-varying and time-constant factors such as latitude¹⁵, seasons¹⁵, time of the day¹⁵, lifestyle^{16,17}, mobility¹⁸, age¹⁵, skin pigmentation¹⁵, and obesity¹⁹. Prior studies associate vitamin D deficiency with the likelihood of weakened immune response^{20–22}, infectious respiratory diseases^{15,23,24}, and the severity and mortality²⁵.

Early evidence indicates that lockdown severity² and weather factors such as temperature and humidity may reduce the likelihood of transmission of the SARS-CoV-2 virus (Severe Acute Respiratory Syndrome Coronavirus 2), which causes COVID-19²⁶. Even though UV radiation may help in reducing the likelihood of transmission by inactivating viruses in fomite transmission²⁷, emerging epidemiological evidence related to COVID-19 suggests a protective role of UVB and the plausible role of vitamin D in improving immunity and decreasing the likelihood of COVID-19 severity and mortality^{4–8,28}.

Specifically, emerging COVID-19 studies provide evidence of the protective role of UVB as well as vitamin D^{8,29–31}. Studies indicate that 1,25-dihydroxy vitamin D [1,25 (OH)₂D], one of vitamin D's active forms, modulates innate and adaptive immune systems^{4,32} as well as renin-angiotensin system (RAS)^{32–34}. Further, studies note that it may reduce the risk of cytokine storm^{4,32} by modulating the inflammatory response. Furthermore, studies indicate that it plays a role in stimulating antimicrobial peptides with antiviral properties such as defensins and human cathelicidin^{4,32,35,36}. Emerging COVID-19 studies also provide evidence of the role of vitamin D deficiency in the incidence^{29,30,37,38}, severity^{37,39}, and mortality^{31,40–42} associated with COVID-19⁴³. A quasi-experimental study notes that vitamin D supplementation is associated with a higher chance for survival in elderly hospitalized patients⁴⁴. Further, a recent randomized placebo-controlled study provides early evidence that vitamin D supplementation may help in SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) viral clearance⁴⁵. Furthermore, a pilot randomized clinical study by Castillo et al.⁴¹ notes that Calcifediol, a metabolite of vitamin D, seems to mitigate the severity of COVID-19.

We explain the plausible association between the severity of lockdown and the subsequent reduction in the likelihood of UVB exposure with the COVID-19 deaths in Fig. 1. Figure 1 also summarizes various time-varying (e.g., weather, season, etc.) and time-constant factors (age, skin pigmentation, latitude, etc.) affecting the likelihood of UVB exposure and subsequent vitamin D synthesis. In light of the evidence from the emerging studies regarding the role of vitamin D^{4–8}, we anticipate that an increased UVB radiation might be associated with a reduction in the number of COVID-19 deaths as it might affect the likelihood of vitamin D deficiency⁸ and the transmission of COVID-19. Although lockdowns might help reduce the likelihood of transmission of SARS-CoV-2 virus², they potentially also reduce the likelihood of UVB radiation exposure, increasing the likelihood of vitamin D deficiency, as indicated in Fig. 1⁸. Therefore, we anticipate that the severity of lockdown and UVB radiation are independently associated with a reduction in the number of COVID-19 deaths. However, an increased lockdown severity might also be associated with a reduction in the protective role of UVI in mitigating COVID-19 deaths.

We extend the theoretical and methodological framework of Moozhipurath et al.⁸ by exploring the protective role of lockdown in the context of UVB exposure. Although Moozhipurath et al.⁸ study the protective role of UVB radiation, it is not yet clear from their results whether the severity of lockdown is associated with a reduction in the protective role of UVB due to reduced likelihood of exposure. We also empirically explore in detail the different types of lockdown severities and whether and which lockdown severity mitigates the protective role of UVI. Thus, the results of this study aim to support the policy decision-making related to COVID-19 in countries that are currently implementing lockdowns or are considering them.

Furthermore, Moozhipurath et al.⁸ investigated the protective role of UVB radiation when the Northern Hemisphere transitioned to spring and Southern Hemisphere countries transitioned to their autumn season. During their study period until 8 May 2020, the COVID-19 outbreak was focused mainly on European countries⁸.

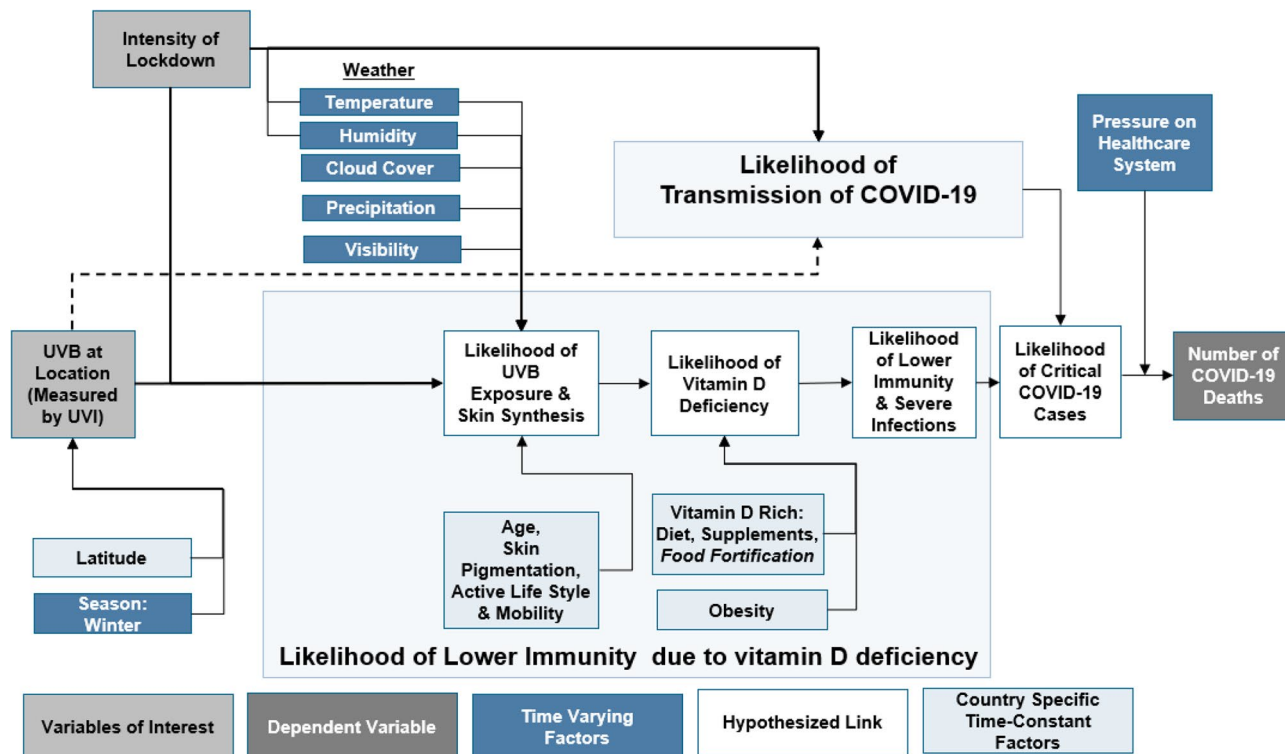


Figure 1. Explanation of the Association of Severity of Lockdown & UVB Radiation with Cumulative COVID-19 Deaths. *Note* We extended the theoretical framework of the protective role of UVB radiation in reducing COVID-19 deaths from Moozhipurath et al.⁸.

Number of countries in the world	195
Number of countries in our dataset	163
... > 0 cumulated COVID-19 deaths before 7 October 2020	155
... > 20 cumulated COVID-19 infections before 7 October 2020	155
Latitude and longitude data source for each state that is used to match weather data	Geocoder (Python)
COVID-19 data source (JHU CSSE COVID-19 Data)	https://github.com/CSSEGISandData/COVID-19 ⁴⁷
Weather data source	https://darksky.net/
Lockdown severity data source	https://www.bsg.ox.ac.uk/research/research-projects/coronavirus-government-response-tracker ^{48,49}
Granularity of data	Daily
Covered time-period	COVID-19 data: 22 January 2020–7 October 2020 (260 days) Weather data: 1 June 2019–7 October 2020 (495 days) Lockdown data: 1 January 2020–7 October 2020 (281 days)

Table 1. Summary of dataset.

Therefore, it is not clear whether their results concerning the protective role of UVB radiation are valid with a longer time horizon in both hemispheres covering different seasons. This study uses secondary data, namely weather data covering 495 days from 1 June 2019 until 7 October 2020, COVID-19 data covering 260 days from 22 January 2020 until 7 October 2020, and lockdown data covering 281 days from 1 January 2020 until 7 October 2020, across 163 countries.

Data and methods

Description of data. To empirically estimate the independent protective roles of lockdown, UVB, and the mitigating influence of lockdown severity on the protective role of UVB in reducing COVID-19 deaths, we use the dataset based on secondary data⁴⁶ as outlined in Table 1⁸. The dataset covers 495 days from 1 June 2019 until 7 October 2020 across 163 countries. Out of these 163 countries, 155 countries reported COVID-19 deaths, starting from 22 January 2020, and 155 reported more than 20 COVID-19 infections before 7 October 2020. To ensure that our results are not biased by countries at a very early stage of COVID-19 outbreak, we focus on the above 155 countries⁸ and drop the first 20 daily observations of every country after reporting the first COVID-19 infection⁸.

Variable	Number of countries	Number of observations	Mean	SD	Min	Max
Cumulated COVID-19 deaths on 7 October	155	155	6789	23,920	1	211,801
Growth rate of cumulative COVID-19 deaths on 7 October	155	155	0.0076	0.016	0	0.13
Daily growth rate of cumulative COVID-19 deaths	155	29,333	0.034	0.13	-1	9
Time-passed by from first reported infection until 7 October	155	155	219	20	148	260
Daily ultraviolet index (UVI)	155	31,044	7.44	2.91	0	15
Daily precipitation index	155	31,044	0.32	0.32	0	1
Daily cloud index	155	31,044	0.49	0.32	0	1
Daily ozone level	155	31,044	289	33	229	481
Daily visibility level	155	31,044	15.5	1.60	0.12	16.1
Daily humidity level	155	31,044	0.66	0.22	0.02	1
Minimum temperature per day within a country	155	31,044	15.75	8.23	-31.85	36.76
Maximum temperature per day within a country	155	31,044	26.73	8.89	-18.17	51.22
Lockdown severity	0	1		2	3	
Description of lockdown severity	No measures	Recommend to not leave the house		Require not to leave the house with exceptions only for daily exercises, grocery shopping, and 'essential' trips	Require not to leave the house with minimal exceptions (e.g., allowed to leave only once every few days, or only one person can leave)	
Number of countries with lockdown severity at the end of observational period	54	56		43	2	

Table 2. Descriptive statistics. We drop the first 20 observations after the first infection in a given country. Therefore, we have 31,044 observations which are less than 76,725 (155 countries \times 495 days).

The country-level dataset consists of daily observations of cumulative COVID-19 infections and deaths, ultraviolet index (UVI—closely associated with UVB spectrum of solar radiation), and a set of weather factors that we use as control variables—precipitation index, cloud index, ozone level, visibility level, humidity level, as well as minimum and maximum temperature on a daily basis. We merged this dataset with another dataset containing the severity of lockdown enforced by various governments. We describe each dataset in Table 1. We use the interaction of the lockdown severity with UVI to examine whether higher lockdown severity is associated with a reduction in the protective role of UVI in mitigating COVID-19 deaths. Table S3 in the Supplementary Appendix shows the number of observations of countries used in the analysis, whereas Table S4 shows the countries' latitude and longitude information used in the analysis.

In Table 2, we present the descriptive statistics of the dataset. On 7 October 2020, the average growth rate of COVID-19 deaths per country was 0.76%, and there were on average 6789 cumulative COVID-19 deaths across these 155 countries. The daily average COVID-19 deaths growth rate per country was 3.4% across the duration of the study. The corresponding average for UVI was 7.44, indicating a moderate to high risk of harm from sun exposure. We use cumulative COVID-19 deaths as the primary dependent variable to test our hypothesis that lockdowns mitigate the protective role of UVB radiation. Based on the severity of governmental advice and restrictions, there are four different severity levels that could decrease skin exposure to UVB radiation ranging from “no measures” to “requiring the population not to leave the house with minimal exceptions”. On 7 October 2020, 54 countries had not implemented a lockdown, whereas 56 countries recommended their people not to leave the house. 43 countries required people to not leave the house except for daily exercises, grocery shopping, and essential trips, whereas 2 countries implemented a severe lockdown and required their people not to leave the house with minimal exceptions.

Summary of method. We apply a log-linear fixed-effects model to estimate the mitigating influence of lockdown severity on the association between UVI and growth rates of COVID-19 deaths⁸. We describe and discuss the log-linear fixed-effect model and the structural equation, which we estimate, in the Supplementary Appendix Section 1, building upon and extending Moozhipurath et al.⁸ as well as Hsiang et al.¹. We chose this type of model since (i) a log-linear model considers percentage rather than absolute changes, the changes in COVID-19 deaths are more comparable over time across countries⁸, and (ii) the fixed-effect model separates the associations of interest from country-specific time-constant factors that are outlined in Fig. 1⁸. The main model isolates the associations of interest from time-varying linear factors, and we do robustness checks with flexible time-trends as mentioned in the Supplementary Appendix Section 3⁸.

Further, Hsiang et al.¹ use log-linear fixed effects model to analyze the effect of lockdowns on the COVID-19 pandemic, whereas Moozhipurath et al.⁸ and Carleton et al.⁵⁰ follow this approach to investigate the association of UV with the reduction in COVID-19 growth rates⁵⁰. Furthermore, prior epidemiological studies such as Barecca et al. use a fixed-effects approach to study humidity's role in influenza by isolating its effect from other

	Model 1	Model 2	Model 3
	COVID-19 deaths	COVID-19 deaths	COVID-19 deaths
Dependent variables			
UVI	−0.0085*** (14.49)	−0.0094*** (15.53)	−0.0092*** (14.49)
LD	−0.047*** (32.95)		
LD × UVI	0.0037*** (15.00)		
LD severity 1		−0.081*** (25.71)	
LD severity 1 × UVI		0.0076*** (15.04)	
LD severity 2 or 3		−0.027* (4.14)	
LD severity 2 or 3 × UVI		0.0008 (0.24)	
LD severity 1 or 2			−0.09*** (30.15)
LD severity 1 or 2 × UVI			0.0081*** (16.94)
LD severity 3			−0.011 (0.76)
LD severity 3 × UVI			−0.0004 (0.07)
Control variables			
Time trend	Linear	Linear	Linear
Country fixed effects	Yes	Yes	Yes
Precipitation index	Yes	Yes	Yes
Cloud index	Yes	Yes	Yes
Ozone level	Yes	Yes	Yes
Visibility level	Yes	Yes	Yes
Humidity level	Yes	Yes	Yes
Temperature (min and max)	Yes	Yes	Yes
Number of coefficients	61 (+ 155 FE)	73 (+ 155 FE)	73 (+ 155 FE)
Number of observations	29,327	29,327	29,327
Number of countries	155	155	155
R-squared within	17.61%	18.16%	17.92%

Table 3. Results of log-linear fixed-effects model. LD Lockdown severity. +: $p < 0.10$; *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$. F-statistic for long-run coefficients in parentheses.

weather parameters⁵¹. Such models are also used in the emerging literature⁵⁰ to estimate climate change's impact on mortality⁵² and the migration pattern of humans⁵³.

To assess the respective protective roles of lockdown and UVI in mitigating the growth rates of COVID-19 deaths and subsequently determine whether and which lockdown severity mitigates the protective role of UVI, we estimate three versions of the log-linear fixed-effects model. Model 1 outlines whether a unit increase in the lockdown severity mitigates the association between UVI and the growth rates of COVID-19. Model 2 and model 3 outline whether a more severe lockdown measure (e.g., LD severity 2 or 3 and LD severity 3, respectively) mitigates this association more strongly than a less severe lockdown (LD severity 1 and LD severity 1 or 2, respectively).

Results

We present our results in Table 3. After controlling for all time-constant and various time-varying factors⁸, we find that unit increases in UVI and lockdown severity are independently associated with 0.85 percentage points (p.p) and 4.7 p.p decline in COVID-19 deaths growth rate, indicating their respective protective roles. However, we find a significant mitigating influence of lockdown severity on the protective role of UVI in reducing the growth rates of COVID-19 deaths. A unit increase of the lockdown severity weakens the association of UVI in reducing the growth rates of COVID-19 deaths by −44% (= 0.0037/−0.0085). This decrease represents the average mitigation of a unit increase of the lockdown severity from 0 to 1, 1 to 2, and 2 to 3.

Surprisingly, Model 2 and Model 3 outline that the mitigation effect is mostly associated with lockdown severity of level 1 rather than level 2 or level 3 (stricter lockdowns) as the interaction of lockdown severity of level 2 or 3 with UVI is insignificant. Besides, the lockdown severity of level 1 mitigates the association of UVI and growth rates of COVID-19 deaths by −81% (0.0076/−0.0094) and, thus, almost completely mitigates the association. Finally, all models outline the significant negative association of lockdown severity and UVI with growth rates of COVID-19 deaths, indicating their protective roles.

To assess the robustness of our results of the primary model—Model 1—we isolate the mitigating influence of lockdown severity on the association of UVI and growth rates of COVID-19 deaths from time trends in flexible ways. Models 4–9 in Tables S1 and S2 in the Supplementary Appendix isolate our findings from linear, square and exponential time trends, which may be similar across countries or even country-specific. Overall, we find consistent results across different model specifications.

Next, we compare two scenarios to illustrate the mitigated protective role of a unit increase of UVI on the cumulative COVID-19 deaths. In scenario 1, UVI's protective role is not mitigated by lockdown, whereas in

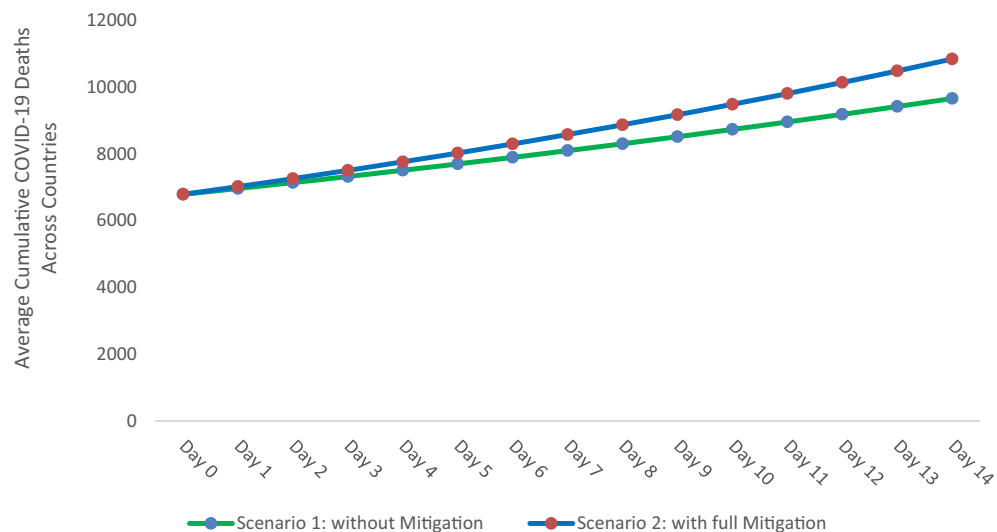


Figure 2. Comparison of “no mitigation of UVI’s protective role by lockdown” versus “full mitigation of UVI’s protective role by lockdown” on cumulative COVID-19 deaths averaged across countries.

scenario 2, UVI’s protective role is fully mitigated. To relate the mitigated protective role with COVID-19 deaths, we take the average number of COVID-19 deaths at the end of the observational period, i.e., 6,789, as cumulative COVID-19 deaths at day 0 shown in Fig. 2. In the full mitigation scenario (Scenario 2), we use the growth rate of COVID-19 deaths in our sample, i.e., 3.4%. Scenario 1, where UVI’s role is not mitigated, uses an average growth rate of 2.55% (i.e., 3.4%—0.85 p.p). Figure 2 outlines that this mitigating influence of lockdown on the protective role of UVI translates into 1,183 or 11% fewer COVID-19 deaths after 14 days.

Discussion

Our empirical results indicate that large-scale lockdowns are associated with a substantial slowdown in the daily growth rates of COVID-19 deaths consistent with prior studies¹. However, such measures also significantly reduce the protective role of UVB in COVID-19 deaths.

Specifically, we find that unit increases in UVI and lockdown severity are independently associated with a decline in the growth rate of COVID-19 deaths, indicating their respective protective roles. However, the lowest lockdown severity (recommendation not to leave the house) is already associated with almost complete mitigation of the protective role of UVI in reducing the growth rate of COVID-19 deaths via a reduction of 0.76 percentage points or -81% ($p < 0.001$). Our results are consistent across different model specifications.

Our results suggest that lockdowns in conjunction with adequate exposure to UVB radiation might have provided even more substantial health benefits than lockdowns alone. For example, we estimate that there would be 11% fewer deaths on average with more UVB exposure while people were recommended not to leave their houses.

Our contributions are three-fold. First, to the best of our knowledge, this study is one of the first ones that outlines the association between the severity of lockdown, the subsequent reduction in UVB exposure, and COVID-19 deaths. Second, our study outlines the need for further large-scale clinical studies exploring the role of vitamin D in mitigating the pandemic. Third, even though emerging studies suggest the need for continued large-scale interventions^{1,2}, in addition to substantial economic and social costs, the findings of our study indicate that an unintended consequence is the limited UVB exposure, which plausibly increases the risk of COVID-19 deaths. The results of our study can therefore inspire observational or experimental clinical studies that can further support COVID-19 related policy decision-making in countries that are currently implementing lockdowns or are considering them in the future to slow down COVID-19 growth. Specifically, such clinical studies may investigate if sensible sunlight exposure in conjunction with lockdown or with proper social distancing can mitigate COVID-19 deaths. Sensible UVB exposure is possible during lockdown by spending time outside in a garden, on balconies, or by exposing to sunlight through open windows. Further, the results of large scale clinical studies could help guide nations to create awareness regarding the importance of sensible sunlight exposure and also to assist vulnerable populations at a higher risk of vitamin D deficiency—e.g., darker-skinned people living in high latitudes, people with limited mobility or indoor lifestyle (nursing home residents), and vegetarians⁸.

Limitations

We follow a macro-level statistical backward-looking approach that captures real-life behavior without making any specific assumptions regarding epidemiological parameters¹. Although this macro-level approach is a crucial strength of the study, the results cannot be interpreted as health guidance, which often comes from clinical studies¹. Therefore, further clinical studies are needed to establish a causal relationship between UVB-induced vitamin D and COVID-19 deaths.

We use a fixed-effects model that isolates the effect of relevant weather parameters from country-specific time-constant factors⁸. Such country-specific time-constant factors consist of various economic, social, and health factors that are likely to remain relatively stable over the period of our study⁸. The time constant factors include the location (e.g., latitude and longitude), demographics, age composition, gender, genetics, and culture at a country level⁸. More importantly, such time-constant factors include factors that are closely associated with the severity of COVID-19, such as age, gender, mobility, lifestyle of the population, the prevalence of co-morbidities (e.g., obesity, hypertension, etc.), and skin pigmentation⁸. Fixed-effects also may capture factors associated with regular habits such as regular dietary patterns, the proportion of vegetarians in the population, regular dietary supplement consumption, and food fortification that may affect COVID-19 severity⁸.

Our methodology also flexibly controls for various time-varying factors⁸. First, our methods control for relevant confounding time-varying weather factors, including air pollution. Second, we control for various remaining time-varying factors by incorporating linear, quadratic, and exponential time-trends at a country level⁸ in the robustness checks of the Supplementary Appendix. These flexible time-trends control for time-varying factors such as pressure on the health care system and exponential-shaped or s-shaped trends associated with the COVID-19 growth rate.

Although our methodology controls for all time-constant and various time-varying confounding factors, we acknowledge that our method has limitations. First, our method may be limited in capturing some of the time-varying confounding factors that may confound the results. For instance, our methodology may not capture behavioral changes of the people that are likely to be associated with seasonal changes (UVB variation), vitamin D levels, and COVID-19 deaths. For example, such time-varying behaviors include seasonal travel patterns, seasonal nutritional supplement intake, and seasonal dietary habits⁸. Second, although we use governmental measures, we do not have granular data on whether people comply with these measures. Therefore, we have limited information about whether people followed governmental instructions and stayed indoors during the lockdown. Third, we do not have data on the vitamin D level at a population level across these countries corresponding to the UVB radiation that prevents us from directly analyzing the association between COVID-19 deaths and vitamin D levels. Finally, our study is an ecological study based on country-level data and therefore has inherent limitations that are commonly associated with such ecological studies.

Even though we anticipate that reduced likelihood of skin synthesis due to lockdown plausibly explain these associations, we may not be able to rule out the possibility of other UVB-induced mediators—such as nitric oxide^{8,10,54}. While we acknowledge there may be confounding factors posing challenges to our analysis, we used statistical methods to account for all time-constant and various time-varying factors as much as possible. We also acknowledge that UVB exposure may not substantially increase the vitamin D synthesis of specific categories of people, such as those wearing cultural protective clothing due to lower exposure to sunlight¹⁵ and those who are elderly due to less efficient skin synthesis⁵⁵. Although we do not model these factors explicitly, our fixed-effects model accounts for most of these time-constant confounding factors.

Data availability

The data used in the study are from publicly available sources. Data regarding COVID-19 are obtained on 9 October 2020 from *COVID-19 Data Repository* by the *Center for Systems Science and Engineering (CSSE)* at *Johns Hopkins University* and can be accessed at <https://github.com/CSSEGISandData/COVID-19>. Data regarding weather is obtained from *Dark Sky* on the 9 October 2020 and can be accessed at <https://darksky.net/>. Data regarding lockdown severity is obtained from <https://www.bsg.ox.ac.uk/research/research-projects/coronavirus-government-response-tracker>. We will make specific dataset used in this study available for any future research. Interested researchers can contact one of the authors via email to get access to the data.

Received: 17 January 2021; Accepted: 1 November 2021

Published online: 24 November 2021

References

- Hsiang, S. *et al.* The effect of large-scale anti-contagion policies on the COVID-19 pandemic. *Nature* **584**, 262–267 (2020).
- Flaxman, S. *et al.* Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. *Nature* **584**, 257–261 (2020).
- Chinazzi, M. *et al.* The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. *Science* **368**, 395–400 (2020).
- Grant, W. B. *et al.* Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients* **12**, 988 (2020).
- Watkins, J. Preventing a COVID-19 pandemic. *Br. Med. J.* <https://doi.org/10.1136/bmj.m810> (2020).
- Panarese, A. & Shahini, E. Letter: COVID-19, and vitamin D. *Aliment. Pharmacol. Ther.* **51**, 993–995 (2020).
- Lanham-New, S. A. *et al.* Vitamin D and SARS-CoV-2 virus/COVID-19 disease. *Br. Med. J. Nutr. Prev. Health.* <https://doi.org/10.1136/bmjnp-2020-000089> (2020).
- Moozhipurath, R. K., Kraft, L. & Skiera, B. Evidence of protective role of ultraviolet-B (UVB) radiation in reducing COVID-19 deaths. *Sci. Rep.* **10**, 17705 (2020).
- Kraemer, M. U. G. *et al.* The effect of human mobility and control measures on the COVID-19 epidemic in China. *Science* **368**, 493–497 (2020).
- Hart, P. H., Gorman, S. & Finlay-Jones, J. J. Modulation of the immune system by UV radiation: More than just the effects of vitamin D?. *Nat. Rev. Immunol.* **11**, 584–596 (2011).
- Bodiwala, D. *et al.* Prostate cancer risk and exposure to ultraviolet radiation: further support for the protective effect of sunlight. *Cancer Lett.* **192**, 145–149 (2003).
- Grant, W. B. An estimate of premature cancer mortality in the US due to inadequate doses of solar ultraviolet-B radiation. *Cancer* **94**, 1867–1875 (2002).
- Grant, W. B. An ecologic study of the role of solar UV-B radiation in reducing the risk of cancer using cancer mortality data, dietary supply data, and latitude for European countries. In *Biologic Effects of Light 2001* (ed. Holick, M. F.) 267–276 (Springer, 2002).

14. Rostand, S. G. Ultraviolet light may contribute to geographic and racial blood pressure differences. *Hypertension* **30**, 150–156 (1997).
15. Holick, M. F. Vitamin D deficiency. *N. Engl. J. Med.* **357**, 266–281 (2007).
16. Zittermann, A. Vitamin D in preventive medicine: Are we ignoring the evidence?. *Br. J. Nutr.* **89**, 552–572 (2003).
17. Tangpricha, V., Pearce, E. N., Chen, T. C. & Holick, M. F. Vitamin D insufficiency among free-living healthy young adults. *Am. J. Med.* **112**, 659–662 (2002).
18. Semba, R. D., Garrett, E., Johnson, B. A., Guralnik, J. M. & Fried, L. P. Vitamin D deficiency among older women with and without disability. *Am. J. Clin. Nutr.* **72**, 1529–1534 (2000).
19. Wortsman, J., Matsuoka, L. Y., Chen, T. C., Lu, Z. & Holick, M. F. Decreased bioavailability of vitamin D in obesity. *Am. J. Clin. Nutr.* **72**, 690–693 (2000).
20. Bouillon, R. *et al.* Skeletal and extraskeletal actions of vitamin D: Current evidence and outstanding questions. *Endocr. Rev.* **40**, 1109–1151 (2019).
21. White, J. H. Vitamin D signaling, infectious diseases, and regulation of innate immunity. *Infect. Immun.* **76**, 3837–3843 (2008).
22. Liu, P. T. *et al.* Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response. *Science* **311**, 1770–1773 (2006).
23. Martineau, A. R. *et al.* Vitamin D supplementation to prevent acute respiratory tract infections: Systematic review and meta-analysis of individual participant data. *Br. Med. J.* **356**, i6583 (2017).
24. Martineau, A. R. *et al.* High-dose vitamin D3 during intensive-phase antimicrobial treatment of pulmonary tuberculosis: A double-blind randomised controlled trial. *Lancet* **377**, 242–250 (2011).
25. Perron, R. M. & Lee, P. Efficacy of high-dose vitamin D supplementation in the critically ill patients. *Inflamm. Allergy-Drug Targets* **12**, 273–281 (2013).
26. Wang, J., Tang, K., Feng, K. & Lv, W. High temperature and high humidity reduce the transmission of COVID-19. Preprint at <https://doi.org/10.2139/ssrn.3551767> (2020).
27. Sagripanti, J.-L. & Lytle, C. D. Inactivation of influenza virus by solar radiation. *Photochem. Photobiol.* **83**, 1278–1282 (2007).
28. Skutsch, M. *et al.* The association of UV with rates of COVID-19 transmission and deaths in Mexico: The possible mediating role of vitamin D. Preprint at <https://doi.org/10.1101/2020.05.25.20112805> (2020).
29. D'Avolio, A. *et al.* 25-Hydroxyvitamin D concentrations are lower in patients with positive PCR for SARS-CoV-2. *Nutrients* **12**, 1359 (2020).
30. Meltzer, D. O. *et al.* Association of vitamin D status and other clinical characteristics with COVID-19 test results. *JAMA Netw. Open* **3**, e2019722 (2020).
31. Maghbooli, Z. *et al.* Vitamin D sufficiency, a serum 25-hydroxyvitamin D at least 30 ng/mL reduced risk for adverse clinical outcomes in patients with COVID-19 infection. *PLoS ONE* **15**, e0239799 (2020).
32. Charoengam, N. & Holick, M. F. Immunologic effects of vitamin D on human health and disease. *Nutrients* **12**, 2097 (2020).
33. Cui, C. *et al.* Vitamin D receptor activation regulates microglia polarization and oxidative stress in spontaneously hypertensive rats and angiotensin II-exposed microglial cells: Role of renin-angiotensin system. *Redox Biol.* **26**, 101295 (2019).
34. Xu, J. *et al.* Vitamin D alleviates lipopolysaccharide-induced acute lung injury via regulation of the renin-angiotensin system. *Mol. Med. Rep.* **16**, 7432–7438 (2017).
35. Adams, J. S. *et al.* Vitamin D-directed rheostatic regulation of monocyte antibacterial responses. *J. Immunol.* **182**, 4289–4295 (2009).
36. Herr, C., Shaykhiyev, R. & Bals, R. The role of cathelicidin and defensins in pulmonary inflammatory diseases. *Expert Opin. Biol. Ther.* **7**, 1449–1461 (2007).
37. Merzon, E. *et al.* Low plasma 25 (OH) vitamin D level is associated with increased risk of COVID-19 infection: an Israeli population-based study. *FEBS J.* **287**, 3693–3702 (2020).
38. Kaufman, H. W., Niles, J. K., Kroll, M. H., Bi, C. & Holick, M. F. SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels. *PLoS ONE* **15**, e0239252 (2020).
39. Honardoost, M., Ghavideldarestani, M. & Khamseh, M. E. Role of vitamin D in pathogenesis and severity of COVID-19 infection. *Arch. Physiol. Biochem.* 1–7 (2020).
40. Ilie, P. C., Stefanescu, S. & Smith, L. The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. *Aging Clin. Exp. Res.* **32**, 1195–1198 (2020).
41. Castillo, M. E. *et al.* 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. *J. Steroid Biochem. Mol. Biol.* **203**, 105751 (2020).
42. Jain, A. *et al.* Analysis of vitamin D level among asymptomatic and critically ill COVID-19 patients and its correlation with inflammatory markers. *Sci. Rep.* **10**, 1–8 (2020).
43. Benskin, L. L. A basic review of the preliminary evidence that COVID-19 risk and severity is increased in vitamin D deficiency. *Front. Public Health* **8**, 513 (2020).
44. Annweiler, G. *et al.* Vitamin D supplementation associated to better survival in hospitalized frail elderly COVID-19 patients: The GERIA-COVID quasi-experimental study. *Nutrients* **12**, 3377 (2020).
45. Rastogi, A. *et al.* Short term, high-dose vitamin D supplementation for COVID-19 disease: A randomised, placebo-controlled, study (SHADE study). *Postgrad. Med. J.* (2020).
46. Swart, E. & Schmitt, J. STandardized Reporting Of Secondary data Analyses (STROSA)—Vorschlag für ein Berichtsformat für Sekundärdatenanalysen. *Z. Evid. Fortbild. Qual. Gesundheitswes.* **108**, 511–516 (2014).
47. Dong, E., Du, H. & Gardner, L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet. Infect. Dis* **20**, 533–534 (2020).
48. Hale, T., Petherick, A., Phillips, T. & Webster, S. Variation in government responses to COVID-19. Blavatnik School of Government Working Paper 31, (2020).
49. Hale, T. *et al.* A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker). *Nat. Hum. Behav* **5**, 529–538 (2021).
50. Carleton, T., Cornet, J., Huybers, P., Meng, K. C. & Proctor, J. Global evidence for ultraviolet radiation decreasing COVID-19 growth rates. *PNAS* **118**, e2012370118 (2021).
51. Barreca, A. I. & Shimshack, J. P. Absolute humidity, temperature, and influenza mortality: 30 years of county-level evidence from the United States. *Am. J. Epidemiol.* **176**, S114–S122 (2012).
52. Deschênes, O. & Greenstone, M. Climate change, mortality, and adaptation: Evidence from annual fluctuations in weather in the US. *Am. Econ. J. Appl. Econ.* **3**, 152–185 (2011).
53. Missirian, A. & Schlenker, W. Asylum applications respond to temperature fluctuations. *Science* **358**, 1610–1614 (2017).
54. Deliconstantinos, G., Villiotou, V. & Stravrides, J. C. Release by ultraviolet B (uvB) radiation of nitric oxide (NO) from human keratinocytes: A potential role for nitric oxide in erythema production. *Br. J. Pharmacol.* **114**, 1257–1265 (1995).
55. MacLaughlin, J. & Holick, M. F. Aging decreases the capacity of human skin to produce vitamin D3. *J. Clin. Invest.* **76**, 1536–1538 (1985).

Acknowledgements

We would like to acknowledge Bernd Skiera for his immense contribution to this paper and for providing inputs to this paper. We would like to acknowledge Sharath Mandya Krishna, and Rukhshan Ur Rehman for their immense contribution to this paper—for providing inputs and assisting with data collection, data transformation, and data engineering. We thank Matthew Little for his inputs and his assistance in the review. We would also like to acknowledge Magdalena Ceklarcz for her valuable contributions to our paper and the discussions about COVID-19.

Author contributions

R.K.M. conceptualized the research idea, conducted literature research and designed theoretical framework. R.K.M. and L.K. collected the data. L.K. designed empirical methods and analyzed the data. R.K.M. and L.K. interpreted the results and wrote the article. R.K.M. and L.K. reviewed and revised the article.

Funding

Open Access funding enabled and organized by Projekt DEAL. This study is not sponsored by any organization. The corresponding author had full access to all the data and had final responsibility for the submission decision.

Competing interests

RKM was a PhD researcher at Goethe University, Frankfurt, at the time of first submission, when majority of the work was carried out. RKM is an employee of a multinational chemical company involved in vitamin D business and holds the shares of the company. This study is intended to contribute to the ongoing COVID-19 crisis and is not sponsored by his company. LK declares no competing interests. The views expressed in the paper are those of the authors and do not represent that of any organization. No other relationships or activities could appear to have influenced the submitted work.

Additional information

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1038/s41598-021-01908-w>.

Correspondence and requests for materials should be addressed to R.K.M.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2021