Exploring the Interplay of UV Index, Population Density, and SARS-CoV-2 Clades on COVID-19 Propagation: A Comprehensive Analysis of the Pandemic Dynamics

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A B S T R A C T

Background: Despite the passage of more than two years since the coronavirus disease 2019 (COVID-19) pandemic, the persistence of the coronavirus and its circulation at varying levels globally necessitates a deeper understanding of the factors influencing its transmission and impact. This study aimed to investigate the relationship between environmental factors, population density, and genetic variations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with a specific focus on elucidating their implications for public health measures and vaccine development.

Materials & Methods: This observational analysis was conducted utilizing daily reported SARS-CoV-2 cases in various countries. Additionally, monthly changes in ultraviolet (UV) radiation index, population density per km[2], and viral genetic variations were assessed. Comparative analysis was performed to examine correlations between these variables. Data analysis was conducted using SAS 9.3 software with a generalized linear model (GLM) approach.

Findings: This study revealed significant correlations between UV index and key epidemiological parameters, including mortality rate, average case number, and transmission rate. Population density per square kilometer did not exhibit any substantial relationship with these variables. Analysis of viral clades suggests potential immunological insights, indicating varying degrees of immunity conferred by certain genetic variants.

Conclusion: These findings underscore the importance of environmental and genetic factors in shaping the trajectory of the COVID-19 pandemic. By elucidating the role of UV radiation and viral genetic diversity, this study informs public health strategies and underscores the necessity of ongoing surveillance and vaccine development efforts tailored to the evolving SARS-CoV-2 landscape.

CITATION LINKS

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel beta coronavirus with a 30-kb genome. It is the causative agent of COVID-19 (coronavirus disease 2019), which was initially reported in December 2019 in Wuhan, Hubei, China [1-4] and later declared as a pandemic in March 2020 by the World Health Organization (WHO) [5], with Europe being the "epicenter" of this global infectious pathogen [6, 7].

SARS-CoV-2 demonstrates different spread rates across different countries [8]. The half-life of the virus plays a crucial role in its transmissibility [9, 10]. Country-to-country variations in the spread rate of the virus may be associated with differences in meteorological conditions [11]. While factors such as humidity and temperature could impact virus survival, ultraviolet radiation in sunlight is recognized as the primary virucidal agent in the environment [12]. Even after more than two years of the COVID-19 pandemic, researchers continue to study the virus and its behavior in different environments. A comprehensive understanding of the genomic epidemiology of SARS-CoV-2 is essential for a deeper exploration of its characteristics.

The global solar ultraviolet index (UVI) stands out as a highly effective tool in combating the skin cancer epidemic. Developed collaboratively by renowned organizations like WHO, WMO (World Meteorological Organization), UNEP (United Nations Environment Programme), ICNIRP (International Commission on Non-Ionizing Radiation Protection), and their partner centers, the primary objective of UVI is to standardize UV radiation reporting on a global scale. It serves as a comprehensive indicator and describes the level of solar ultraviolet radiation (UVR) at the Earth's surface, starting at zero and gradually increasing, providing vital information for various countries [13]. The virus exhibits swift mutations, giving rise to significant clades of sequence variants that demonstrate diverse outcomes in infected patients [14].

This study aimed to identify significant differences in mortality rate, average case number, and propagation frequency between the first and second fortnights of each month and to compare the impact of different viral clades on the mortality rate and the number of new cases, highlighting the dynamic nature of the pandemic and the critical importance of timely interventions. Specifically, this study aimed to determine if exposure to one clade could confer strong immunity against other clades.

Objectives: This study also aimed to investigate the potential association between changes in the UV index and the spread of SARS-CoV-2 infection in countries with varying population densities across different continents. By understanding the dynamics of these factors over time, the findings could inform policy makers on implementing targeted interventions to effectively mitigate the risk of health crises.

Materials and Methods

Study design: An observational analysis was performed on daily reported SARS-CoV-2 cases and monthly changes in UV index in five European countries including Italy, Spain, France, Germany, and United Kingdom; four Middle Eastern countries including Qatar, Kuwait, United Arab Emirates, and Saudi Arabia: and Australia. In addition, the impact of population density per km² and the types of clades found in each of these countries was evaluated on the propagation frequency of the virus (Figure 1). Figure 1 represents the study design organizational diagram.

Data sources: During the period of January 1 to March 31, 2020, data on the number of new SARS-CoV-2 cases reported daily in each country were sourced from the European
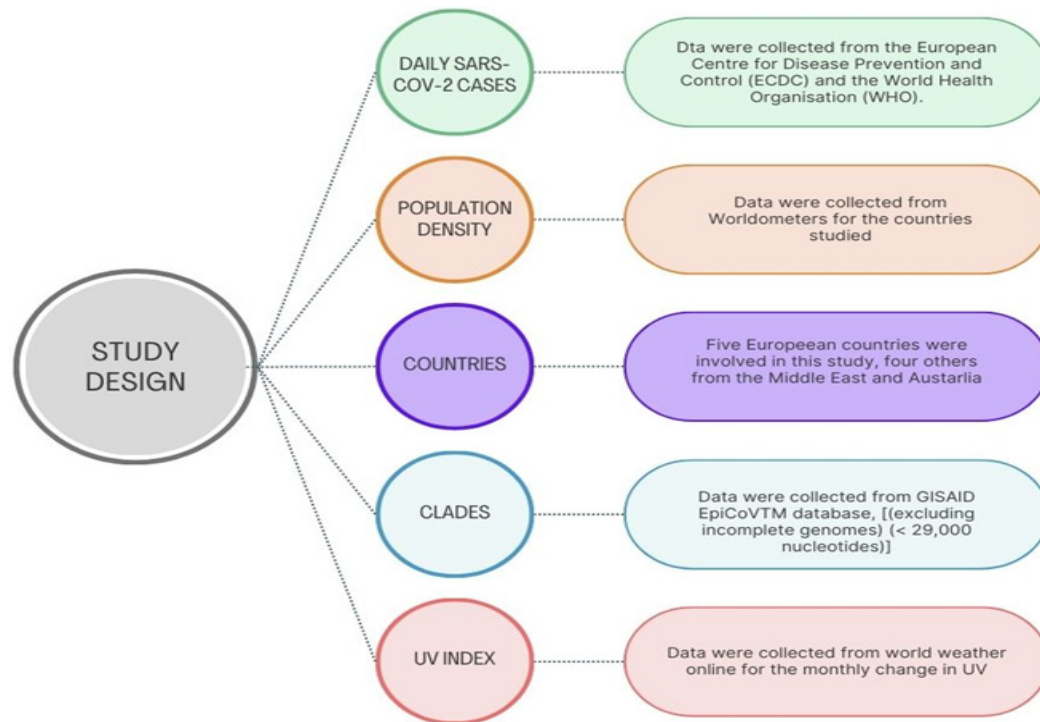
Figure 1) Study design organizational diagram

Centre for Disease Prevention and Control (ECDC) (https://www.ecdc.europa.eu/en/covid-19/data).

To provide context for the analysis, population density per square kilometer was also determined for each country. This information was obtained from worldometers utilizing the latest estimates provided by the United Nations Population Division (https://www.worldometers.info/world-population/population-by-country/). By accessing these datasets, the relationship between SARS-CoV-2 cases and population density as well as their potential implications during the specified timeframe were explored.

UV index values for the months of December, January, and February were collected from the world weather online website (https://www.worldweatheronline.com/). In order to capture the variability of UV index values within each country, the UV index was recorded for 15 cities per country. Specifically, cities significantly impacted by the pandemic with higher population density were selected. In cases where the UV index values varied between cities within a country, the range of values was recorded as an interval.

To complement the analysis, SARS-CoV-2 genomic sequences were downloaded from the GISAID EpiCoVTM database for the countries under study. Sequences were selected based on their collection dates, and incomplete genomes with less than 29,000 nucleotides were excluded. As of June 14, 2020, a total of 10,029 SARS-CoV-2 genomic sequences were retrieved for our analysis. These data collection processes were an integral part of the present investigation, as they allowed us to explore the relationship between UV index values, viral genomic sequences, and epidemiological dynamics of SARS-CoV-2 over the specified timeframe.

Statistical analysis: The fixed factors investigated in this research included UV index, country, month, population density per km^2, and clades. Data analysis was conducted using SAS 9.3 software (SAS Institute, Cary, North Carolina, USA) (Figure 2). A generalized linear model (GLM) was

employed to examine the effects of various fixed factors on the number of cases, the number of deaths, and the frequency of propagation, which were considered as variable factors. All statistical analyses were performed with a significance level of 95%. To compare the mean values of the number of cases, the number of deaths, and the frequency of propagation between the first and second fortnights, the MEANS procedure was utilized, and the Duncan-Waller test was employed to analyze the grouping of homogeneous fixed factors.

To explore the correlations between the variable factors, the SAS 9 CORR procedure was employed. Finally, to analyze the effects of different relationships between the fixed factors on the variable factors, the FREQ procedure was utilized.

Figure 2 represents SAS software different procedures applied.

Findings

Comparison between the number of cases and deaths: A comparison between the number of cases and deaths in each situation was made over a period of 15 days in accordance with what has been published about the virus incubation rate,

and the results were considered statistically significant when $p \leq .05$ (Table 1).

According to the Wilcoxon statistical test, comparing averages per 15 days showed significant differences in the frequency of propagation (162917), number of active cases (equal to 172513.50), and number of deaths (equal to 173522.50) between the first and second fortnights of each month. Table 1 compares cases, deaths, and propagation frequency of SARS-CoV-2. **Generalized linear model (GLM) procedure**: Table 2 shows the values of mortality, average number of active cases per 15 days, and frequency of propagation per 15 day according to the GLM procedure. **Grouping of homogeneous subsets:** Grouping of homogeneous clades and UV indices according to mortality, average number of cases per 15 days, and frequency of propagation according to the Waller-Duncan test showed that clades G, G&S, and G&V&O&S and UV indices 3-4, 3-5, and 5-6 were statistically different.

Propagation frequency: An analysis was performed to examine the variations in propagation frequency considering UV indices, different combinations of clades, time periods (months), and regions

Table 1) Comparing cases, deaths, and propagation frequency of SARS-CoV-2

Comparison	Test Used	Wilcoxon Statistic	Normal Approximation (*P*-Value)	t Approximation (*P*-Value)	Significance Level
The average number of cases per day	Wilcoxon	172513.50	<.0001	<.0001	.05
The average number of deaths per day	Wilcoxon	173522.50	<.0001	<.0001	.05
The average of the frequency of propagation per 15 days	Wilcoxon	162917	<.0001	<.0001	.05

Table 2) GLM values for mortality, average number of active cases per 15 days, frequency of propagation per 15 days

| Variable	R2	UV Index (ddl/*F*-Value/ *P*-Value)	Clades (ddl/*F*-Value/ *P*-Value)	Months (ddl/*F*-Value/ *P*-Value)	Countries (ddl/*F*-Value/ *P*-Value)	Density (ddl/*F*-Value/ *P*-Value)
Mortality	47.48%	12/23.86/< .0001	14/17.43/< .0001	2/3.07/ .047	No significant difference was found	No significant difference was found
Average number of active cases	61.51%	12/43.82/<.0001	14/25.73/< .0001	2/22.28/< .0001	9/3.78/ .0022	No significant difference was found
Frequency of propagation	58.70%	12/35.35/<.0001	14/29.58/< .0001	No significant difference was found	No significant difference was found	No significant difference was found
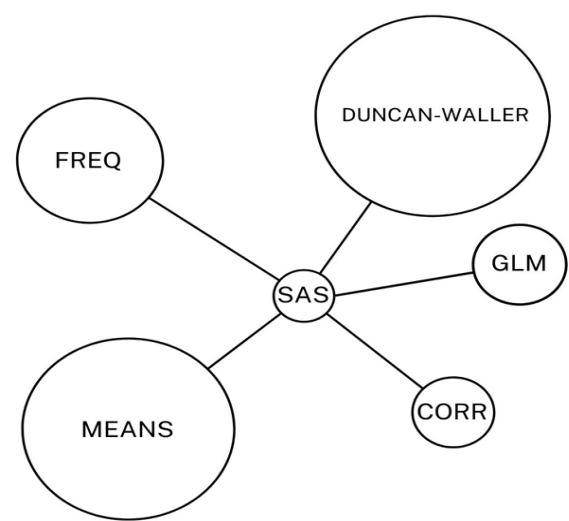
Figure 2) Representation of SAS software different procedures applied

(countries) from the highest to the lowest frequency.

Figure 3 shows the bar charts of propagation frequency based on (A) UV index variations, (B) clade variations, (C) monthly variations, and (D) country variations.

Figure 4 shows area charts representing clades-UV index relationship with (A) mortality frequency, (B) case frequency per 15 days, and (C) propagation frequency.

Effect of UV index on mortality frequency:
The findings showed a significant association between UV index intervals and mortality rates, with higher UV index values corresponding to higher mortality rates. However, it is important to note that the specific values mentioned are a function of the dataset used for analysis.

Effect of clades on mortality frequency:
The results emphasized the correlation between different mortality levels and different clades. The clade G demonstrated the highest mortality rate, while the combinations involving clades G&O, G&V, O&S, and O had notably lower mortality rates.

Effect of month on mortality frequency:
The findings indicated significant differences in mortality rates between different months and countries. March showed the highest mortality rate, while January and February had minimal mortalities. Italy had the highest mortality frequency, followed by Spain, France, and Brittany. On the other hand, Saudi Arabia, Australia, Emirates, and Qatar recorded the lowest mortality frequencies.

Linear discriminant function of Mortality per clade and UV index: Based on linear regression analysis, the impact of different combinations of clades on mortality by country was found to be significant. Among
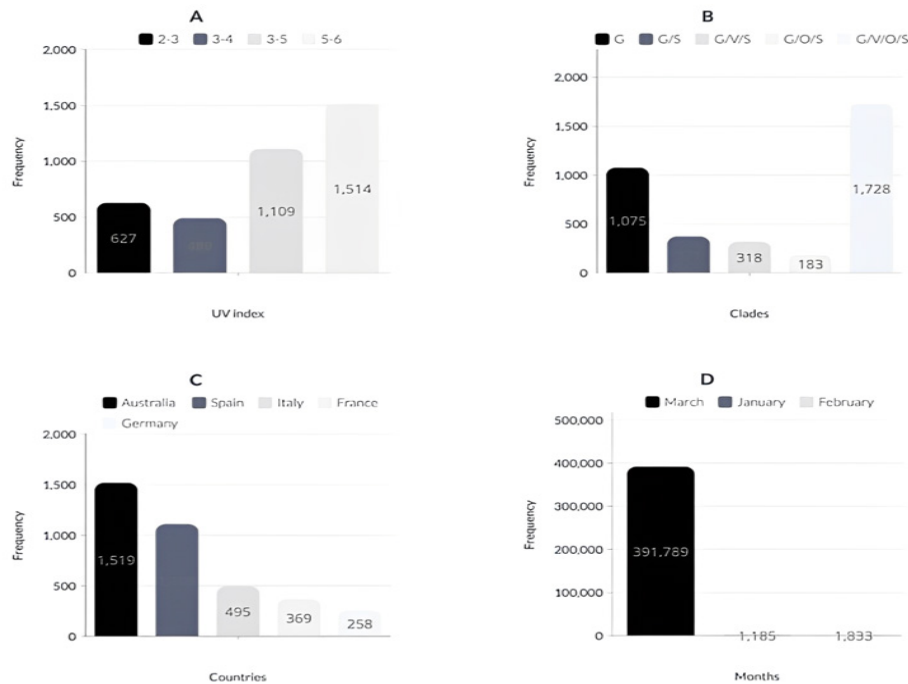
Figure 3) Bar charts of propagation frequency by (A) UV index variations, (B) clade variations, (C) monthly variations, and (D) country variations
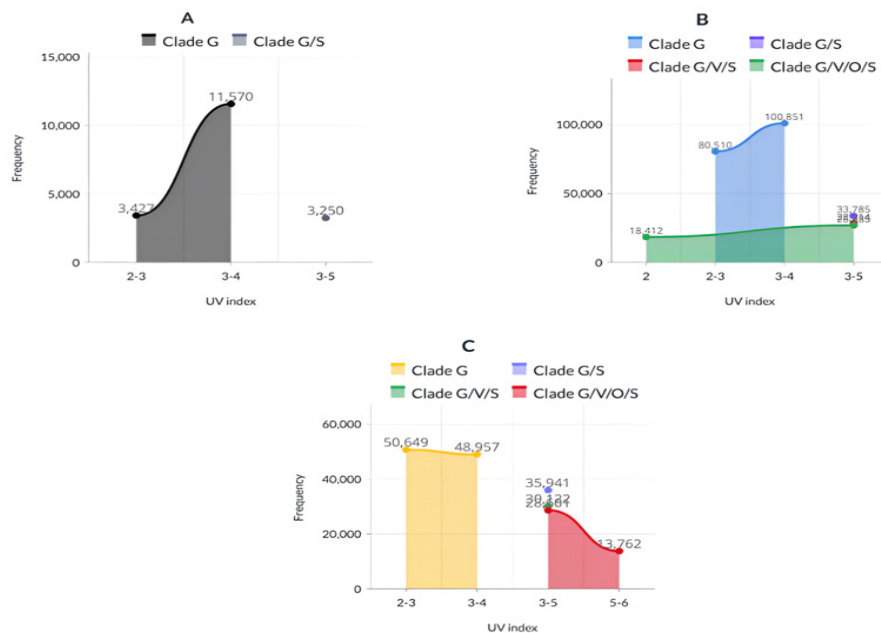

Figure 4) Area charts representing the clades-UV index relation with (A) mortality frequency, (B) case frequency per 15 days, and (C) propagation frequency

various combinations, the combination of clades G&S (0.01838) demonstrated the highest association with mortality, followed by clade G (0.00863). However, when clade O or V was combined with clade G, the mortality rate decreased, as observed in the combinations G&O (0.0000958) and G&V (0.0000951). Furthermore, the analysis of mortality in relation to different UV indices revealed noteworthy observations. Mortality

was found to be substantial within the UV index interval 3-5, with a value of 0.02127. As the UV index increased, mortality gradually decreased within the intervals 6-7 and 5-6, with respective values of 0.0000276. However, UV indices 4-5, 6-8, 7-8, and 1-2 showed no significant association with mortality, as evidenced by values close to zero.

Number of cases per 15 days per UV index, clades and their associations: Based on the analysis of the highest number of cases per 15 days, it was observed that the combination of clades G&S (0.00211) had the highest frequency, followed by clade G (0.00113).

In contrast, when clade O or V was combined with other clades, the frequency of cases decreased significantly. The combination of clades G&O (0.0001586), G&O&V (0.0001751), and G&O&S (0.0000897) and clade O (0.0000154) all exhibited low frequencies. Similar to the mortality findings, the analysis of the UV index revealed similar patterns in terms of the frequency of cases. The interval 3-5 showed the highest frequency of cases, which was equal to 0.00353. This was followed by the interval 3-4, which had a frequency of 0.00116. Moderate frequencies were observed in UV indices 3 and 4-5, with values equal to 0.0000207 and 0.0000122, respectively.

Propagation frequency according to UV index, clades and clades associations: According to the findings, the combination of four clades G&V&O&S exhibited the highest propagation frequency of 0.15953, which was followed by the combination of G&S clades with a frequency of 0.14929. The frequency was moderate for the following combinations: G (0.04178), G&V&S (0.0361), and V (0.01103). However, the frequency tended to decrease or be negligible for the combination of clades O&S (0.00192), G&O (0.00511), and V&O&S (0.000333).

Regarding the impact of the UV index on propagation frequency, the analysis revealed that the interval 3-5 was the most favorable, exhibiting a frequency of 0.19325.

Correlation models between all variable factors: An analysis was performed to examine the correlation between the following variables: number of deaths, population density per km^2, average number of cases per 15 days, and frequency of propagation per 15 days. The analysis was performed using the CORR procedure in SAS 9 software. The results clearly indicated the following relationships:

There was a strong relationship between mortality and the average number of cases per 15 days ($p < .001$, correlation coefficient = .809). The frequency of propagation was correlated with the average number of cases per 15 days ($p < .0001$, correlation coefficient = .568). The frequency of propagation was also correlated with the number of deaths ($p < .0001$, correlation coefficient = .438). There was no relationship between population density per km^2 and mortality ($p = .4503$, correlation coefficient = .02). Likewise, there was no relationship between population density per km^2 and the average number of cases per 15 days ($p = .2756$, correlation coefficient = .03). These findings indicated significant correlations between mortality, average number of cases, and frequency of propagation, while population density per km^2 did not show any significant relationship with these variables.

Discussion

The propagation behavior analysis of SARS-CoV-2 virus has garnered significant interest, and numerous studies have been conducted to understand its transmission and spread dynamics. This study contributes to this analysis by examining various factors influencing viral dissemination patterns, including weather conditions, particularly the UV index, classifying SARS-

CoV-2 into major clades reported in GISAID, and examining their impact on the three variables investigated in this study, including mortality, the number of cases per 15 days, and the frequency of propagation, based on data collected from multiple countries during the period from December 2019 to March 2020. Moreover, the analysis revealed associations between UV index intervals, clades, and various epidemiological parameters such as mortality rate and case frequency, suggesting the relevance of environmental factors and viral genetic variations with the spread and impact of COVID-19. Additionally, correlation models demonstrated strong relationships between mortality, average number of cases, and frequency of propagation, providing insights into the interconnected nature of these variables and their implications for public health strategies.

In this study, no notable relationship was found between urban density and the three variables investigated. This finding aligns with the findings of a study conducted in the United States, where high population density was not correlated with the number of confirmed cases, explaining that although it seems logical that places with more individuals have larger number of cases, but this issue could not be a significant factor in an outbreak [15]. This suggests that the spread of the virus depends more on contact between people rather than population density alone. Although some studies have shown a moderate association between Covid-19 spread and population density, density is considered as a contributing factor [15, 16]. The obtained results also showed a significant association between UV index and propagation frequency, where high UV ranges resulted in higher propagation frequency and also higher mortality rates. Conversely, one study found an association between higher temperatures and reduced

transmission rates [17], and another study indicated that cold, dry weather and low levels of UV radiation were moderately associated with increased SARS-CoV-2 transmissibility [18].

What stands out in this study is the significant influence of UV indices and types of clades on the three variable parameters. Our analysis reveals that the genetic characteristics of SARS-CoV-2 and its clades could explain the severity of symptoms and provide insights into the propagation frequency of the virus, where clade G was found to be predominant in the majority of countries studied and associated with high mortality rates, particularly in the UVI interval 3-4. However, the presence of other clades (S, O, V) mitigated the risk of high mortality. Our findings suggest that these clades may exhibit lower virulence compared to clade G, with clade O showing almost negligible mortality, as observed in the early stages of the pandemic in Qatar.

This implies that the presence of these clades within a population may confer certain levels of immunity. These findings also have implications for vaccine design, as they offer insights into minimizing adverse disease effects by considering clade O as a reference virus.

Regarding the analysis of propagation frequency, our study highlighted the interplay between UV index and viral clades. A UVI interval between 2 and 5 appeared to be more favorable for the spread of SARS-CoV-2. Considering the genotype of the virus, clade G exhibited a considerable propagation frequency at UV indices 2-3, whereas for UV indices 3-5, the propagation frequency was moderate and potentially favorable for the other clades. Notably, a significant propagation frequency was recorded for the combination of G&V&O&S clades at UVI interval 5-6, which could be influenced by factors such as Australia's low urban density.

Conclusion

In conclusion, this study sheds light on the complex dynamics of SARS-CoV-2 propagation, revealing nuanced factors influencing transmission patterns. While population density is traditionally considered as a key determinant of virus spread, the findings suggest that other variables, particularly weather conditions such as UV index and viral clades, play significant roles. Contrary to conventional wisdom, population density was found to have the least impact on virus transmission compared to environmental and genetic factors. Specifically, higher UV indices were associated with increased virus propagation and mortality rates, highlighting the importance of considering weather conditions in public health interventions. Additionally, the analysis of viral clades revealed distinct patterns of virulence, with clade G exhibiting higher mortality rates and clades S, O, and V showing lower virulence. These findings provide new insights for public health measures and vaccine development strategies and have important immunological implications. By recognizing the potential variations in immunity conferred by different viral clades, the findings could guide more targeted vaccine designs and strategies to mitigate viral spread and minimize adverse outcomes. This study limitations include a restricted timeframe, spanning from January 1 to March 31, 2020, which may not comprehensively reflect the pandemic's evolving dynamics beyond this duration. Furthermore, the analysis was confined to specific European, Middle Eastern, and Australian countries, potentially constraining the applicability of the findings to broader geographical contexts. Additionally, while the study examined the influence of various clades on SARS-CoV-2 dynamics, the variability in clade classification and distribution across different regions and periods could impact the interpretation of results.

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