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COVID-19 seasonality in temperate countries

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ABSTRACT

Introduction: While the beneficial effect of vaccination, restrictive measures, and social distancing in reducing mortality due to SARS-CoV-2 is intuitive and taken for granted, seasonality (predictable fluctuation or pattern that recurs or repeats over a one-year period) is still poorly understood and insufficiently taken into consideration. We aimed to examine SARS-CoV-2 seasonality in countries with temperate climate.

Methods: We identified countries with temperate climate and extracted average country temperature data from the National Center for Environmental information and from the Climate Change Knowledge Portal. We obtained mortality and vaccination rates from an open access database. We used the stringency index derived from the Oxford COVID-19 Government Response Tracker to quantify restriction policies. We used Spearman's and rank-correlation non-parametric test coefficients to investigate the association between COVID-19 mortality and temperature values. We employed multivariate regression models to analyze how containment measures, vaccinations, and monthly temperatures affected COVID-19 mortality rates.

Results: The time series for daily deaths per million inhabitants and average monthly temperatures of European countries and US states with a temperate climate had a negative correlation ($p < 0.0001$ for all countries, $0.40 < R < 0.86$). When running multivariate regression models with country fixed effects, we noted that mortality rates were significantly lower when temperature were higher. Interestingly, when adding an interaction term between monthly temperatures and vaccination rates, we found that as monthly temperatures dropped, the effect of the vaccination campaign on mortality was larger than at higher temperatures.

Discussion: Deaths attributed to SARS-CoV-2 decreased during the summer period in temperate countries. We found that the effect of vaccination rates on mortality was stronger when temperatures were lower. Stakeholders should consider seasonality in managing SARS-CoV-2 and future pandemics to minimize mortality, limit the pressure on hospitals and intensive care units while maintaining economic and social activities.

1. Introduction

Novel coronavirus disease (COVID-19) is a newly discovered respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which first broke out in Wuhan, China. The World Health Organization declared COVID-19 a global pandemic on March 11th, 2020 (World Health Organization, 2020). Over this two-year period, healthcare systems worldwide faced an unprecedented challenge (World Health Organization, 2021).

In anticipation of a widely accessible vaccine or an effective cure for COVID-19, governments implemented non-pharmaceutical measures, notably self-isolation and lockdown, to limit virus spreading and the

overall pandemic impact on national healthcare systems. Results suggest that lockdowns were effective in reducing cases and in containing the pandemic (Li et al., 2021). The vaccination campaign is rapidly advancing, especially in developed countries, and is associated with a clear reduction in the number of SARS-CoV-2 infections, attenuation of viral RNA load, symptoms, and illness duration among those with breakthrough infection despite vaccination. (Polack et al., 2020).

However, the pandemic dynamics, even if attenuated by health policies, is still to be comprehensively understood. The seasonal cycle of several respiratory viruses is well-known and studied (Lofgren et al., 2007). For example, the influenza virus affects the human population during the winter season in temperate regions (Moriyama et al., 2020).

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Coronaviruses exhibit winter seasonality but, as far as SARS-CoV-2 is concerned, there is no clear consensus supporting this assumption (Dowell and Ho, 2004). Several factors interfered with the SARS-CoV-2 pandemic course, making it difficult to disentangle the role played by human interventions with respect to its evolution, and thus to estimate the effectiveness of these measures. Understanding whether or not SARS-CoV-2 has seasonal features is essential for directing future health policies and identifying the current state of the pandemic. Countries with extreme or non-temperate climates, such as the majority of the United States of America (US) or Equatorial countries (e.g., Brazil and Indonesia), may not have a sufficient degree of climate variability to display seasonality. In countries with a temperate climate, such as those of the Mediterranean area, the course of the pandemic during the summer months seems to have a concordant mortality rate timeline, regardless of the containment measures adopted and the extent of the vaccination campaign.

The aim of this work is to study whether countries with a temperate climate - such as those of the Mediterranean area - display significant seasonality (i.e., an inverse correlation between temperature and COVID-19 mortality), as well as to correlate the concurrent time series variation in the stringency of containment measures and in the level of the vaccination campaign.

2. Material and methods

We considered the pandemic period from April 1st, 2020, to July 1st, 2021, and limited our analyses to the Northern Hemisphere countries (or states in case of the US). Following the Köppen climate classification (Köppen, 1936), we selected and studied temperate climate countries only, defined as countries whose mean temperature is above -3°C (26.6°F) and below 18°C (64.4°F) in the coldest month. Overall, only 10 European countries (Albania, Belgium, France, Greece, Italy, Netherlands, North Macedonia, Portugal, Spain, United Kingdom), and 6 US states (Alabama, Arkansas, Georgia, Mississippi, South Carolina, Tennessee) fulfilled the inclusion criteria. We excluded states with less than 100 total deaths (San Marino, Vatican) and those in the Southern Hemisphere (Uruguay, New Zealand). No other countries in Asia, Africa, and North and South America were included since they have a temperate climate only in partial areas of their extension and therefore cannot be considered temperate countries (Beck et al., 2020). We obtained temperature data for European countries from the World Bank's Climate Change Knowledge Portal (WORLD BANK GROUP, 2015), and for states in the US from NOAA's National Center for Environmental information (National Centers for, 2021). We extracted mortality and vaccination rates from the public database managed by Johns Hopkins University (Dong et al., 2020). This study did not require ethics committee approval because data were already in the public domain.

We quantified restriction policies by means of the stringency index from the Oxford COVID-19 Government Response Tracker (OxCGRT). This is a composite measure based on nine response indicators including school closure, workplace closure and travel bans, recorded on a scale from 0 to 100, the latter being the most stringent measure (Hale et al., 2021). We compared restriction policies concordance over time among countries. In addition, we compared stringency index time series with daily mortality rate. We then correlated the mortality trends with vaccination rates.

2.1. Statistical analysis

Through a descriptive analysis we provided an overview of COVID-19 mortality and climate temperature during the study period, and we then correlated temperature with daily mortality rate. We also conducted a time series analysis for daily mortality rate and temperature to evaluate concordance.

Data were downloaded from the above described publicly available databases, plotted using Microsoft Excel (Microsoft Corporation, 2018)

and graphically represented. For time series of data, we used a linear regression model to fit the dependent variable COVID-19 mortality with the monthly average meteorological parameter (air temperature expressed in degree Celsius, $^{\circ}\text{C}$) and daily stringency index. The dependence between pairs of time series was quantified in this study by standard tools of statistical analysis, Spearman's and rank-correlation non-parametric test coefficients. The normality of data was evaluated using Kolmogorov-Smirnov Tests for Normality for time series data sets. As the data on daily new COVID-19 deaths showed non-normal distribution, Spearman's rank correlation was selected to investigate the association between COVID-19 mortality and temperature data, using STATA 16 software. The Bonferroni correction was applied for multiple comparison. We used non-parametric statistical tests since they are more suitable than parametric tests for non-normally distributed data, such as the climate variable we employed in our study. The values for levels of correlation are bound in the range $[0, +1]$, with 0 for no association and $+1$ for complete positive association and $[0, -1]$ with -1 as negative correlation. P values < 0.05 were considered statistically significant.

We then run a set of multivariate linear regressions in order to check whether the bivariate correlations between (i) COVID-19 mortality and temperatures, (ii) COVID-19 mortality and vaccinations and (iii) COVID-19 mortality and containment measures were robust to jointly analyzing them and to controlling for other confounding factors. In fact, throughout the multivariate analysis we included country/state fixed effects (i.e., we controlled for time-invariant features of each location that might be correlated with our explanatory variables of interest). Standard errors were robust to heteroscedasticity. We considered again the period from April 2020 to June 2021, and we introduced a 20-days delay when analyzing the correlation between stringency index, number of SARS-CoV-2 positive cases and COVID-19 mortality, and therefore analyses started on April 21st, 2020. We added an interaction term between average monthly temperature and the percentage of fully vaccinated people, per hundred: the purpose of this addition was to investigate whether vaccination rates were differentially effective on COVID-19 mortality as a function of average temperatures. We also added an interaction term between the 20-days lagged number of new COVID-19 cases and the percentage of fully vaccinated people, to check whether the vaccination effort dampened the relationship between new COVID-19 cases and mortality.

3. Results

We identified 16 countries (10 countries in Europe and 6 states in the US) located in the Northern Hemisphere with a temperate climate and with more than 100 COVID-19 deaths in the studied period (April 1st, 2020 to July 1st, 2021).

Average monthly temperatures (supplemental Table 1 and supplemental Figure 1) were similar among the included countries, and new daily confirmed deaths per million people (supplemental Figure 2; supplemental Figure 3; supplemental Figure 7) were low in all countries during late spring and summer months.

In Europe, new daily confirmed deaths per million people time series and mean average monthly temperatures time series appeared to have an opposite trend over time (supplemental Figure 3): the lower the temperature, the higher the number of deaths. The mortality peaks occurred in the coldest months, and gradually approached zero in warm months. This feature occurred in all ten European countries over the studied sixteen-months period. The number of deaths showed a first peak between March and April 2020, followed by a significant reduction in cases in the summer months. The mortality trend increased again in winter and throughout early 2021 (with a reduction reported in January), to decrease once more in summer 2021. Table 1 demonstrates the negative correlation between temperature and COVID-19 deaths per million in European countries, with $p < 0.0001$ for all countries and $0.40 < R < 0.86$.

Restrictive policies among European countries varied in intensity

Table 1

Spearman's rank coefficient of correlation between new COVID-19 deaths and temperature in degree Celsius, and between new COVID-19 deaths and Stringency Index for each temperate country.

	Correlation between death and temperature		Correlation between death and Stringency Index	
	Spearman's rank	p value	Spearman's rank	p value
Europe				
Albania	-0.62	<0.0001	0.05	0.8
Belgium	-0.74	<0.0001	0.68	<0.0001
France	-0.78	<0.0001	0.66	<0.0001
Greece	-0.63	<0.0001	0.54	<0.0001
Italy	-0.86	<0.0001	0.81	<0.0001
Netherlands	-0.83	<0.0001	0.74	<0.0001
North Macedonia	-0.50	<0.0001	NR	NR
Portugal	-0.73	<0.0001	0.48	<0.0001
Spain	-0.40	<0.0001	0.45	<0.0001
United Kingdom	-0.68	<0.0001	0.72	<0.0001
United States of America				
Alabama	-0.20	<0.0001	0.13	0.02
Arkansas	-0.48	<0.0001	-0.06	0.6
Georgia	-0.25	<0.0001	-0.02	0.9
Mississippi	-0.16	0.002	0.33	<0.0001
South Carolina	-0.21	<0.0001	0.09	0.2
Tennessee	-0.40	<0.0001	0.05	0.9

Abbreviations: NR, not reported.

and over time. In the bi-variate analysis we did not find a negative correlation between stringency index and COVID-19 deaths per million in European countries (Table 1, supplemental Figure 4); the restrictive policies were presumably introduced when COVID-19 mortality was high, but their effects took time to manifest.

Vaccination levels were different among European countries (supplemental Figure 5). The magnitude of the drop in COVID-19 mortality observed in late spring 2021 (supplemental Figure 2) was similar in countries with the lowest vaccination rate (<20% in Albania and Macedonia on June 1st, 2021) and in countries with the highest vaccination rate (>35% in Spain and UK).

When analyzing US temperate states, we found similar seasonal trends (supplemental Table 1; supplemental Figure 7) which were more considerable starting from winter 2020. We confirmed the negative correlation between temperature and mortality through multivariate regression analyses including all the sixteen countries involved in the study (supplemental Table 2). In particular, an increment of 1 °C above the average temperature was associated with a reduction of about 61 COVID-19 deaths per million on a yearly basis (supplemental Table 2).

We also confirmed the negative correlation between vaccination rate and COVID-19 daily death per million: again, on a yearly basis, one percent increase of fully vaccinated individuals was associated with a reduction of about 27 COVID-19 deaths per million (supplemental Table 2).

Moreover, we calculated the implied effect of the vaccination rate on mortality at average temperature (14.9 °C), at high temperatures (average temperature plus one standard deviation above, i.e., at 14.91 + 6.69 = 21.6 °C), and at low temperatures (average temperature minus one standard deviation, i.e., at 14.91 - 6.69 = 8.22 °C). On a yearly basis, the estimated reduction on COVID-19 deaths per million for an additional one percent of fully vaccinated citizens was 22 deaths less at high temperatures and 46 deaths less at low temperatures.

COVID-19 deaths per million were positively and significantly correlated with the 20-days lagged number of new COVID-19 cases: quantitatively, one hundred additional new cases was associated with 1.1 additional COVID-19 deaths per million (supplemental Table 2). The estimated coefficient on the interaction term of 20-days lagged new COVID-19 cases with the percentage of fully vaccinated people is significantly negative (i.e., vaccination rates appeared to dampen the

relationship between new COVID-19 cases and COVID-19 mortality, supplemental Table 2). Finally, the negative correlation between the stringency index and COVID-19 mortality was confirmed only by the more parsimonious specification of the multivariate analysis that did not control for the number of new COVID-19 cases (supplemental Table 2).

4. Discussion

The most remarkable result of our study is to document that COVID-19-attributed deaths are closely related to temperature variations in temperate countries: as temperatures increase in late spring, the number of COVID-19 deaths dramatically decreases. These findings were more statistically robust in the case of European countries than in the case of US states.

The COVID-19 daily deaths per million remained low in the 16 temperate countries/states during summer 2020 and summer 2021, while there was an important increase in mortality in autumn 2020. We demonstrated that for each degree Celsius increase in temperature, a decrease of 61 COVID-19 yearly deaths per million occurred.

Within our multivariate regression analysis, we found a reduction of COVID-19 deaths with restrictive policies only when *not* controlling for the number of new COVID cases. This might suggest that stringency measures mainly worked through (negative) changes in the number of new COVID-19 cases.

We also found that the decrease in mortality observed in late spring 2021 was not only related to the progression of the vaccination campaign in these countries, but also to the therein climatic conditions. We demonstrated that each percentage point of vaccinated people corresponds to a reduction of 27 COVID-19 yearly deaths per million. The summer decrease in COVID-19 mortality was concordant in all countries, regardless of the different vaccination rates. Macedonia and Albania, whose rate of people that received complete vaccination did not exceed 20%, presented a summer decrease in mortality similar to that of the other temperate climate countries. Moreover, we demonstrated that vaccinations have larger impact on mortality at low temperatures, while at higher temperatures their impact on mortality decreased. This suggests that temperatures were pivotal for the striking mortality drop during the summer months.

Our work can be compared to other previously published studies on seasonality and COVID-19, among which those focused on non-temperate areas failed to show an association with temperature changes (Kumar, 2020; Xiao et al., 2021; Byun et al., 2021). Bukhari et al. demonstrated that 90% of SARS-CoV-2 infections during the early months of the pandemic occurred at relatively cold temperatures, between 5 and 10 °C (Bukhari and Jameel, 2020). Other studies confirmed the seasonal trend of COVID-19 mortality, but none of them focused on temperate climate countries only. Some of them analyzed individual countries or cities (Zoran et al., 2021; Hoogeveen and Hoogeveen, 2021; Choi et al., 2021; Danon et al., 2021), while others arbitrarily selected sets of states around the world with significant climate differences (Smith et al., 2021; Rouen et al., 2020). In addition, most papers focused on incidence rates, which may be biased by the testing capacity of individual countries (Zoran et al., 2021; Hoogeveen and Hoogeveen, 2021; Choi et al., 2021; Danon et al., 2021; Smith et al., 2021; Rouen et al., 2020; Lagacé-Wiens et al., 2021; Christophi et al., 2021).

Respiratory viral infections generally show seasonality (Moriyama et al., 2020), as revealed by previous pandemics that displayed significant correlations with climate conditions. Conventionally, the surveillance period for seasonal influenza runs from the 42nd week of the year until the 17th week of the following one (World Health Organization, 1999). This climate-related seasonality happens in both hemispheres (World Health Organization report, 2006). In history, several viral pandemics affected humans. The H1N1 virus caused the Spanish flu in 1918-1919, causing almost 50 million deaths worldwide. This pandemic was characterized by three waves, since it displayed a significant decrease in the number of cases during the summer 1918 to end

in May 1919. Interestingly, the three Spanish flu waves featured similar trends compared to COVID-19, with the same decrease in the number of cases observed in January and in the summer (Jordan, 1927). H1N1 caused a second pandemic in 2009 and by May 2010 the number of cases was in steep decline (Taubenberger and Morens, 2006). H3N2 generated two pandemic waves, one in the winter 1968–69, followed by a halt in summer 1969, and the second in the winter 1969–70, which resolved in summer 1970 (Pandemic (H1N1) 2009 – u, 2010). H2N2 had three winter waves, from 1957 to 1963 (Dunn, 1958; Serfling et al., 1967). The Asian H2N2 influenza virus is thought to have first emerged in China in February or March 1957. It reached the United States in early summer, where it caused sporadic outbreaks, but a measurable impact on mortality did not occur until October (Miller et al., 1971).

Coronaviruses are positive single-stranded RNA viruses belonging to the Coronaviridae family, Class IV of the Baltimore classification, which are known to cause several respiratory infections. Of the many viruses belonging to this family, only few affect humans. The most common and most studied human coronaviruses are 229E, HKU1, NL63, and OC43. Their incidence increases during the winter seasons, between December and April, and wanes during the summer months (Gaunt et al., 2010; Friedman et al., 2018). SARS-CoV-1 epidemic started in November 2002 and ended in June 2003 (Pearson et al., 2003).

Our findings have clinical, epidemiological, and social impact. First, policy makers should beware of the influence of climate temperature on the pandemics when estimating the effectiveness and planning of restrictive measures. When acknowledging this interference, we might assume that early autumn increase in mortality is not to be related to human behavior during the summer season but represents the normal progression of a seasonal pandemic trend, and that the decrease in mortality during late spring is not only an effect of restrictions. Secondly, since restrictive measures are intuitively effective in reducing cases and containing pandemic mortality, it would be possible to reinforce or ease them weeks or months in advance. As we are able to predict the progression of the curve, it is feasible to form longer-term plans, with the aim to minimize economic loss and social impact. Third, if a direct effect of temperature on the virus will be demonstrated, this could open new areas of research on low-cost therapeutic strategies.

Further studies could be conducted to understand how climate affects the virus. By graphically evaluating mortality time series in temperate countries, we observed a decrease in January, the month when temperatures are the lowest. It would be important to understand whether the relationship between environmental temperatures and mortality is linear or SARS-CoV-2 manifests its effects in a specific range of temperatures. Furthermore, the reasons behind this phenomenon are unknown and have been topic of scientific discussion for centuries. The main suggested explanations are the following: (i) the different human behaviors during the cold and hot seasons that expose differently to virus transmission (i.e., closed working environments with less air circulation, opening schools and work); (ii) the different human response to virus for endocrine-immunological factors or physical barriers (i.e., Vitamin D, adaptive immunity to viruses, mucosal integrity, mucus production); or (iii) even the instability of the virus (i.e., UV exposure, direct effect of temperature) (Christophi et al., 2021). Moreover, possible therapeutic implications and the applicability to other viruses - to prevent a possible future pandemic - have never been studied so far.

4.1. Strengths and limitations

While the mortality rates can be influenced by testing capacity, classification of COVID-19-related deaths, health system capacity, nutritional habits, pollution, and population density, the trend of mortality over time, especially if concordant across countries, is an objective parameter. Nonetheless, we acknowledge some limitations. First, the epidemic has been ongoing for only two years, so the analysis is limited in time. Second, we do not know whether our findings apply to countries with non-temperate climates. Third, we did not analyze the delay

between temperature changes and variations in mortality. Fourth, we were not able to consider the effect of change in medical treatments for COVID-19 that improved outcome and decreased mortality over time (Ciceri et al., 2020) which, however, implausibly influenced the same summer mortality reduction in two different pandemic years that we found. Lastly, we do not know if temperature influences disease transmission, therefore decreasing infection rate and mortality, or the viral load, affecting disease severity.

5. Conclusions

We showed COVID-19 pandemic seasonality in temperate countries. Policy makers of temperate countries should consider SARS-CoV-2 seasonality when deciding the timing of vaccine booster doses and of restrictive measures, with the purpose of better preventing the progression of the pandemic.

Authors' contributions

All the authors have substantially contributed to the conception of the work, and to the drafting or revision; all the authors have approved the final version and agree to be accountable for all the aspects of the work.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envres.2021.112614>.

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