COVID-19 mortality increases with urbanization, but social distancing was largely ineffective in reducing deaths in Brazil and most parts of the World

A mortalidade por COVID-19 aumenta com a urbanização, mas o distanciamento social foi amplamente ineficaz na redução de mortes no Brasil e na maior parte do mundo

La mortalidad por COVID-19 aumenta con la urbanización, pero el distanciamiento social fue en gran medida ineficaz para reducir las muertes en Brasil y en la mayor parte del mundo

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Abstract
Our aim is to assess how environmental and social variables are associated with COVID-19 mortality among countries and in the first and second waves among Brazilian states. We show that social isolation was not significantly, or was positively associated with COVID-19 mortality, which probably reflects people staying at home in the high mortality periods. The magnitude of temperature effects in Brazil varied depending on whether or not Index of Human Development was included in the regression analyses, but higher temperatures consistently reduced per capita deaths among countries. Availability of hospital bed capacity or intensive-care units had no detectable effect on mortality among countries, and within Brazil there was a positive relationship with excess deaths and a negative relationship with deaths per case during the second wave. Counterintuitively, mean age was negatively associated with deaths among Brazilian states, but was positively associated with mortality among countries. Mortality tended to be higher in states and countries with greater urbanization. Overall, the relationships of mortality-curve flatness, social isolation, temperature and hospital infrastructure with COVID-19 mortality were much weaker than is often assumed or are opposite in sign to the predictions, indicating that more complex models are needed to confront future epidemics.
Keywords: Pandemic; Hospital bed capacity; Intensive care units; SARS-CoV-2; Temperature.

Resumo
Nosso objetivo é avaliar como variáveis ambientais e sociais estão associadas à mortalidade por COVID-19 entre os países e na primeira e segunda onda entre os estados brasileiros. Mostramos que o isolamento social não foi significativamente ou foi associado positivamente à mortalidade por COVID-19, o que provavelmente reflete as pessoas que ficam em casa nos períodos de alta mortalidade. A magnitude dos efeitos da temperatura no Brasil variou dependendo da inclusão ou não do Índice de Desenvolvimento Humano nas análises de regressão, mas temperaturas mais altas reduziram consistentemente as mortes per capita entre os países. A disponibilidade de capacidade de leitos hospitalares ou unidades de terapia intensiva não teve efeito detectável na mortalidade entre os países, e no Brasil há uma relação positiva com o excesso de óbitos e uma relação negativa com os óbitos por caso durante a segunda onda. Contra intuitivamente, a média de idade foi negativamente associada a óbitos entre os estados brasileiros, mas positivamente associada à mortalidade entre os países. A mortalidade tendeu a ser maior em estados e países com

maior urbanização. No geral, observamos que as relações da planicidade da curva de mortalidade, isolamento social, temperatura e infraestrutura hospitalar com a mortalidade por COVID-19 são muito mais fracas do que muitas vezes se supõe ou são de sinal contrário às previsões, indicando que são necessários modelos mais complexos para enfrentar futuras epidemias.
Palavras-chave: Pandemia; Capacidade de leitos hospitalares; Unidades de terapia intensiva; SARS-CoV-2; Temperatura.

Resumen
Nuestro objetivo es evaluar cómo las variables ambientales y sociales están asociadas con la mortalidad por COVID-19 entre los países y en la primera y segunda ola entre los estados brasileños. Mostramos que el aislamiento social no se asoció significativamente o se asoció positivamente con la mortalidad por COVID-19, lo que probablemente refleja que las personas se quedan en casa en los períodos de alta mortalidad. La magnitud de los efectos de la temperatura en Brasil varió dependiendo de si el Índice de Desarrollo Humano se incluyó o no en los análisis de regresión, pero las temperaturas más altas redujeron consistentemente las muertes per cápita entre los países. La disponibilidad de camas de hospital o unidades de cuidados intensivos no tuvo un efecto detectable sobre la mortalidad entre los países, y dentro de Brasil existe una relación positiva con el exceso de muertes y una relación negativa con las muertes por caso durante la segunda ola. Contrariamente a la intuición, la edad media se asoció negativamente con las muertes entre los estados brasileños, pero se asoció positivamente con la mortalidad entre los países. La mortalidad tendió a ser mayor en los estados y países con mayor urbanización. En general, observamos que las relaciones de la planitud de la curva de mortalidad, el aislamiento social, la temperatura y la infraestructura hospitalaria con la mortalidad por COVID-19 son mucho más débiles de lo que a menudo se supone o tienen un signo opuesto a las predicciones, lo que indica que se necesitan modelos más complejos para enfrentar futuras epidemias.
Palabras clave: Pandemia; Capacidad de camas de hospital; Unidades de cuidados intensivos; SARS-CoV-2; La temperatura.

1. Introduction

The COVID-19 epidemic caused by the SARS-CoV-2 virus caught the World unprepared and different tactics to avoid deaths were integrated into distinct strategies in different countries. With hindsight, it is obvious that the most effective strategy to reduce the number of deaths was to institute surveillance, lockdown areas with contagious individuals and, where necessary, massively bolster the health system (Tangcharoensathien et al., 2021). However, this strategy was most effective in countries with one-party central governments, such as China and Thailand, and islands, such as Australia, New Zealand and Japan (Greer et al., 2021; Tangcharoensathien, 2021). As it is impossible to maintain isolation indefinitely, those countries combined isolation with development or purchase of vaccines.

A second strategy was to impose social distancing to spread the epidemic over a longer period, known as flattening the curve, which reduced the chance of health-service collapse, and allowed a longer period for the development of vaccines (Feng et al., 2020; Boumans, 2021). The effect of health-service collapse probably varies among countries. At the peak of the epidemic in Brazil, desperate relatives tried to get beds in intensive-care units (ICU) for their loved ones. However, mortality of patients admitted to ICUs and intubated was over 90% in the northern region of Brazil, and 83% for the whole country (Bastos et al., 2021). This compares with < 30% mortality in intubated COVID-19 patients in Florida (Oliveira et al., 2021). Assumptions of the second strategy were that the main cause of mortality would be lack of access to medical care and that vaccines would be available before the end of the within-country epidemic (Boumans, 2021; Pequeno et al., 2022). These assumptions have not been rigorously evaluated in most countries.

Different tactics were adopted by different Brazilian States, and different tactics were recommended by different Federal authorities, so the collection of tactics could hardly be called a strategy (Castro et al., 2021). The Brazilian President recommended business as usual and assumed that the disease would not be worse than influenza (Chaib, 2020). However, that ignores the fact that influenza can cause >25% mortality in immunologically naïve populations (Mathews et al., 2009; Walker et al., 2015). All States implemented some measures of social distancing and personal protection (washing hands and wearing masks), but the effectiveness of those actions in flattening the mortality curve varied enormously among States (Castro et al., 2021). There were also enormous differences in the availability and quality of health care (Schaefer et al., 2020). In no State was social distancing sufficient to eliminate the virus and the first wave of the epidemic had subsided long before vaccines became available (Pequeno et al., 2022). The different combinations of tactics allowed us to evaluate the effects of several factors on the differences in mortality among Brazilian states in each wave of the pandemic. We then tested whether the major patterns observed in Brazil can be seen in comparisons among countries. Correlative studies may identify spurious relationships (Barceló & Saez, 2021), so we concentrate the discussion on those factors that were consistent temporally and spatially.

The effectiveness of social distancing has often been evaluated from records of where people were in relation to their homes when making internet connections (Kleinschroth & Kowarik, 2020; Mena et al., 2021), and it has been assumed that those records would reflect the degree of flattening of the infection and mortality curves, but this relationship has not been validated for Brazil.

The Brazilian government ignored offers of vaccines in 2020, and only started to acquire vaccines in 2021, after a second wave of deaths that started in late 2020 (Pequeno et al., 2022; Reuters, 2021). As a result, vaccination had little observable effect on the second wave before it reached its peak, and possibly only limited influence on the descending phase of the curve (Pequeno et al., 2022).

Not all subsets of the population are equally vulnerable to COVID-19. Mortality rates are generally low among children, and much higher among the elderly (O'Driscoll et al., 2021). Therefore, analyses of the causes of mortality should take into account the proportion of the population with high risk, which is highly correlated with the proportion of the population that is elderly (O'Driscoll et al., 2021). There is also evidence that mortality is higher among segments of the population with lower socioeconomic status (Barceló & Saez, 2021; Mena et al., 2021). Degree of urbanization may also affect mortality rates, because urban areas tend to have more health-care options (Pinchoff et al., 2020), but also may facilitate transmission because viral loads are probably higher in indoor settings (Morawska et al., 2020).

Most of the predictions and interpretations about COVID-19 death rates were initially based on rates of spread. Pequeno et al. (2020), and Prata et al. (2020) predicted that mortality would be higher in areas with lower temperatures at the peak of the epidemic. Castro et al. (2021) concluded that social distancing was effective in reducing the number of deaths due to COVID-19. However, studies of rates of change of multiple variables are complex and sensitive to the assumptions of the analyses. People in lower socio-economic suburbs may suffer higher mortality from COVID-19 (Mena et al., 2021), and it has been assumed that it is generally true that lower socio-economic status leads to higher mortality due to COVID-19. Therefore, it is important to include socio-economic factors in comparisons among regions (Barceló & Saez, 2021). Despite the clues offered by studies of transmission rates (e.g. Salom et al., 2021), only retrospective analyses can give strong inferences about the correlates of mortality rates.

It is also important to differentiate the effects of variables on transmission and mortality after infection. We, analyzed overall mortality rates attributed to COVID-19, but this statistic involves two components. It is expected to increase with factors that increase transmission (infection rate), and factors that increase the probability of mortality in persons that were infected (lethality). Presumably all deaths reported as due to COVID-19 were included in the computation of number of cases. We believe that the number of registered cases underestimates the total number of cases, but the ratio of deaths due to COVID-19 to the number of cases registered of COVID-19 gives an index that is probably monotonically related to lethality or case fatality. This, within the limits of uncertainty associated with case reporting, is presumably independent of transmission. We used the ratio of COVID deaths to reported COVID-19 cases to distinguish factors that might act through lethality from those that mainly act through their influence on transmission (i.e. those that affect mainly the number of cases).

A limitation on using data available for COVID-19 mortality, especially for comparisons among countries, is that differences in rates may reflect differences in reporting. Therefore, we also evaluated the effects of the predictor variables on excess mortality, which presumably reflects the combined effects of the disease and the strategies used to contain it. Excess mortality is calculated as the ratio of the number of deaths in periods before the pandemic to the number during the pandemic. Not all of these will be directly related to infection. Social distancing may lead to fewer traffic deaths in some countries (Brodeur et al., 2020; Oguzoglu, 2020; WHO, 2021), and increase deaths due to other causes (Naito et al., 2021), especially when health systems are overloaded (Tangcharoensathien et al., 2021). However, this statistic has the advantage that differences in reporting probably applied before and during the pandemic, so the excess proportion is likely less affected by reporting rates than the registered number of deaths due to COVID-19.

Our initial hypotheses were that the degree of social distancing, the degree of flattening of the mortality curve, warmer temperatures, the availability of health services, the proportion of young people in the population, and the region´s index of human development (IHD) would be negatively associated with mortality due to COVID-19. We also thought that degree of urbanization would reduce mortality due to the generally greater availability of health services in urban areas.

2. Methodology

Our methods for determining magnitudes and significance of relationships largely follow the philosophy of Tukey (1980) and Osenberg et al. (1999) and are detailed in Magnusson et al. (2015).

2.1 Data sources

2.1.1 Brazil

Deaths and cases attributed to COVID-19 for Brazilian states were obtained from the official COVID-19 website of the Brazilian Ministry of Health (2021a). We analyzed the data both for number of deaths per 100.000 individuals in the population, which reflects per capita deaths due to COVID-19, and as deaths per case, which reflects the probability of death among those that were infected. Excess mortality was calculated as the percentage difference between the number of deaths during the pandemic (first wave in 2020 and from the second wave up to the peak in each State in 2021) and the mean number of deaths in the corresponding months of the five years (January 2015 to December 2019) before the pandemic.

To estimate the temperature at which patients who died contracted SARS-CoV-2, we originally used the mean temperature of all recording stations in each State (INMET, 2021) in the month prior to the deaths. The mean temperature weighted by the number of deaths in the following months was used as an index of the temperature at which patients who died in that state contracted the disease. However, that was highly correlated with the yearly mean temperature of the states (Figure S1 - Supplementary Material) and we used the latter statistic because it was also available for comparisons among countries. We carried out the analyses for the whole of the first wave of the epidemic, but only until the peak of the second wave because comparisons among States after the second peak is complicated by the potential effects of vaccination.

To determine the end of the first wave and the onset of the second wave, we looked for the inflection point (place where the derivative shifted from negative to positive in sigmoid curves) in the cumulative death curve from August 2020 onwards, using the Bisection Extremum Surface Estimator. There were differences of up to three months among States in the onset of the second wave (Pequeno et al., 2022), but the combined data indicated that the end of the first wave was on about 11 November 2020 (Figure S2 - Supplementary Material). We analyzed data from the second wave up to the peak in each State, when there had been negligible vaccination coverage. Mortality rates had started to decline in all states before a significant part of the population had been vaccinated (Pequeno et al., 2022).

We used the mean number of intensive-care units per 100,000 people in the population as an index of availability of health care (and probability of overloading the health-care system) for each State. Data were obtained from the website Portal da Saúde maintained by the Brazilian Ministry of Health (2021b).

We used locations of internet connections as an index of social isolation. Various measures based on internet connections have been used successfully to relate epidemiological variables to measures of isolation or its inverse, mobility (Candido et al., 2020; Kleinschroth & Kowarik, 2020; Mena et al., 2021). We used the Residential percent change index from Community Mobility Reports obtained from Google, which is related to the proportion of time spent at home, because it was available for all Brazilian states, all time periods, and for most countries. Time spent at home is probably less affected by social or economic factors than mobility indices based on consumerism, such as time spent near shopping centers and fuel outlets. This index is also epidemiologically informative because it accounts for 85% of the variance in the time from the onset of the epidemic to the start of the second wave in Brazilian states (Pequeno et al., 2022). We also measured the degree of curve flatness, which is considered a measure of the effectiveness of non-pharmacological interventions (NPIs) in reducing viral transmission (Branswell, 2020; Boumans, 2021). As an index of degree of curve flatness, we used one minus the number of deaths on the day with the highest number of deaths during the week with highest number of deaths divided by the total number of deaths during the first or second wave for that State. We used the combination of day and week because some states had anomalous daily peaks due to repressed reporting. Data on deaths were obtained from the official COVID-19 website (Painel Coronavírus, https://covid.saude.gov.br/) of the Brazilian Ministry of Health (2021a).

As this is a correlative study, a lack of relationship between mortality-curve flatness and overall mortality could be due to other confounding factors that are specific to each state, so we tested whether within-state rates of change in curve flatness were related to within-state changes in mortality rates between the first and second waves.

We used mean IHD per state to reflect socio-economic status (Atlas Brasil, 2021).

Degree of urbanization was obtained from the Brazilian Institute of Geography and Statistics (IBGE, 2021) for Brazilian States, and from the website of Our World in Data (2021) for countries.

The proportion of elderly (> 60 years old) in the population was highly correlated with the median age of people in Brazilian states ($r = 0.94$, $DF = 25$, $N = 27$, $p < 0.001$; Figure S4A - Supplementary Material) and we used the latter statistic because it was also available for comparisons among countries.

2.1.2 Comparisons among countries

Due to the complex patterns involving many different factors, we did not attempt to separate the different waves in each country and analyzed the complete period in each country until 17 June 2021 as a single sampling unit for comparisons among countries. The list of countries for which this data was available is given in Data 2 in the Supplementary Material. We also included the proportion of the population vaccinated because this is probably related to other government measures to contain the outbreak, such as shutdowns. However, it was not significantly related to either cumulative deaths or excess mortality in the period we studied (Table S1 - Supplementary Material).

We obtained data on COVID-19 mortality (until 17 June 2021), index of human development (IHD) before the pandemic, and median age of people in each country ($N = 184$) from the data available in OurWorldInData.org. As median age was highly correlated with the proportion of people >65 years old ($r = 0.91$, $DF = 182$, $N = 184$, $p < 0.001$; Figure S4B – Supplementary Material) and >75 years old ($r = 0.89$, $DF = 182$, $N = 184$, $p < 0.001$; Figure S4C - Supplementary Material), we used median age in analyses, but results were qualitatively similar for the other age variables (Table S2 - Supplementary Material). Mean temperatures for each country were obtained from WorldClim (2021).

We tested for multicollinearity and used only variables with variance inflation factor (VIF) < 5. This meant that we could not include IHD in models, but we also ran the analyses including this variable to determine to what degree it destabilized the results (Table S3 - Supplementary Material).

2.2 Data analysis

In order to obtain an unbiased estimate of the significance of relationships between per capita deaths, excess mortality and deaths per case with many different factors (e.g. proportion of elderly and others) and for comparisons among countries, we first measured the linear correlation to identify the relationship between two variables when this variable carried the same kind of information; for example, proportion of elderly (> 60 years old) and median age of people. In this case, both variables represent age structure in a given country or state, and as they were highly correlated, we could use median age, because this variable was available for all Brazilian states and all countries.

To test whether degree of curve flatness, index of social isolation, temperature, hospital bed capacity or intensive care units, degree of urbanization, and median age could predict the outcome of per capita deaths, excess mortality and deaths per cases; we used multiple linear regressions. Nonlinear relationships were transformed before inclusion in the analyses and predictor variables were only included in the same analysis when the variance inflation factor was < 5. The variance inflation factor measures how much the overall variance explained by the model is inflated by the interaction among independent variables. We checked that the distribution of residuals of all analyses met the assumptions of the test.

3. Results

Table 1 summarizes the results of the regression analyses we tested, indicating whether the variable affected mortality positively or negatively, and the probability of encountering an effect of that magnitude if the null hypothesis (no effect) were correct. We do not imply that decisions should be based only on probabilities, but initial interpretations should be based on effects that have magnitudes greater than expected due to the vagaries of sampling. The full models are given in Full Models and Tables S1-S3 in the Supplementary Material and graphs of the partial effects of each predictor in Figures S9-S17 in the Supplementary Material. We adjusted the results for the total number of tests undertaken with Fisher´s multiple test procedure to obtain a probability value when there were multiple tests of the same hypothesis, and we only discuss those results that are consistent across time and space.

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Table 1. Summary of results of multiple regressions analyzing the effects of degree of curve flatness, isolation index, temperature, intensive-care units in Brazilian states or hospital bed capacity in countries, degree of urbanization and median age on per-capita deaths due to COVID-19, excess mortality and deaths per case. Numbers in parentheses next to the response variables indicates the sample size (i.e number of countries or states) used in each regression analysis (this number depends on the information available). NS = P > 0.1, (+) indicates a positive regression coefficient, (-) indicates a negative regression coefficient. Full details of regressions are given in Full Models in the Supplementary Material.

Variables	Brazil		
	First Wave		
	Per capita deaths (N = 27, DF = 20)	Excess mortality (N = 27, DF = 20)	Deaths per case (N = 27, DF = 22)
Degree of curve flatness	NS	NS	Not analyzed
Index of social isolation	(+) 0.079	NS	Not analyzed
Temperature	(+) 0.056	NS	(+) 0.023
Hospital bed capacity and intensive care units	NS	NS	NS
Degree of urbanization	(+) < 0.001	(+) < 0.001	NS
Median age	(-) 0.051	(-) < 0.001	(+) 0.008
	Second Wave		
	Per capita deaths (N = 27, DF = 20)	Excess mortality (N = 27, DF = 20)	Deaths per case (N = 27, DF = 22)
Degree of curve flatness	NS	NS	Not analyzed
Index of social isolation	NS	NS	Not analyzed
Temperature	NS	NS	(+) 0.046
Hospital bed capacity and intensive care units	NS	(+) 0.038	(-) 0.045
Degree of urbanization	(+) 0.039	(+) 0.079	(+) 0.022
Median age	NS	(-) 0.001	(+) 0.016

Variables	World*		
	Other countries		
	Per capita deaths (N = 107, DF = 101)	Excess mortality (N = 150, DF = 144)	Deaths per case (N = 65, DF = 60)
Degree of curve flatness	Not analyzed	Not analyzed	Not analyzed
Index of social isolation	(+) 0.003	(+) 0.052	Not analyzed
Temperature	(-) < 0.001	NS	(-) 0.077
Hospital bed capacity and intensive care units	NS	NS	NS
Degree of urbanization	(+) 0.019	NS	NS
Median age	(+) 0.083	(-) 0.075	NS

*193 countries according to United Nations. Source: Authors.

We expected reporting-rate bias to be less in Brazil than among countries, but some factors that were significant for COVID per-capita mortality were not significant for excess mortality, and vice versa. Nevertheless, most results were consistent for per-capita deaths and excess deaths, so differences in reporting rates among states and countries had little impact on our overall conclusions.

3.1 Flatness of the mortality curve

We were only able to obtain realistic estimates of curve flatness for the first and second waves separately in Brazil. There was little relationship between the isolation index based on internet connections and the degree of curve flatness during the first (r = 0,26, N = 27, P = 0.18; Figure S5A – Supplementary Material) or second waves (r = -0,17, DF = 25, N = 27, P = 0.36; Figure S5B - Supplementary Material) and the combined results using Fisher´s test were not significant (P = 0.24). Also, differences in degree of social distancing among states in the first wave only explained about 25% of the variance in social distancing in the second wave ($r^2 = 0.25$, DF = 25, N = 27, P < 0.001; Figure S6 - Supplementary Material).

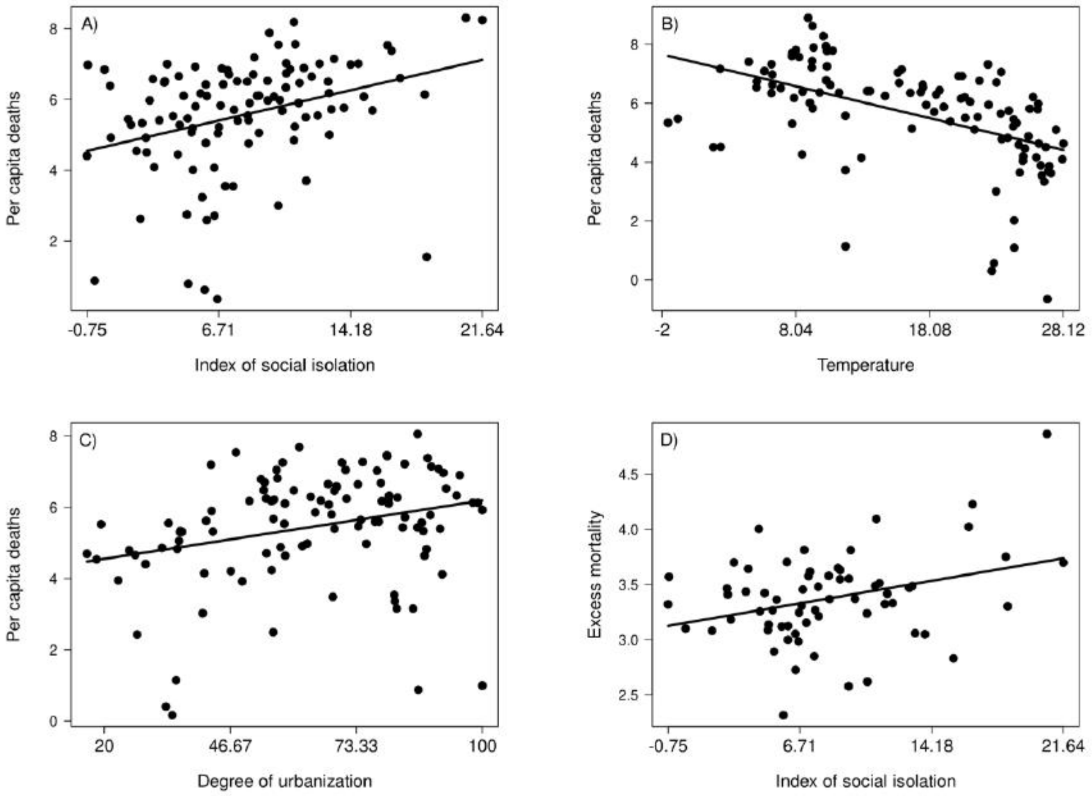
Mortality in Brazil during the second wave (total deaths: 340,056 up to the second peak in each state) was much higher than mortality during the first wave (total deaths: 163,373), even though the second wave was ongoing, but the degree of flattening of the mortality curves was not highly correlated between first and second waves (r = 0.28, DF = 25, N = 27, P = 0.28; Figure S7 - Supplementary Material). There was no statistically significant relationship between degree of curve flatness and per capita deaths attributed to COVID-19 or excess mortality during either wave (Table 1).

To take into account potential differences in states independent of mortality-curve flattening, we tested whether within-state rates of change in curve flatness were related to changes in within-state mortality rates between the first and second waves. There was little relationship for states between the degree of curve flatness in the first and second waves (r = 0.28, DF = 25, N = 27, P = 0.15; Figure S3 - Supplementary Material), and changes in the degree of curve flattening within states had no statistically significant effect on the within-state changes in mortality rates between the first and second waves (r = 0.03, DF = 25, N = 27, P = 0.86; Figure S8 - Supplementary Material).

3.2 Social isolation

The effect of social isolation (average time spent at home) was not analyzed for deaths per case because presumably isolation does not affect survival after the person becomes symptomatic. Among Brazilian states, the effect of isolation on both per capita deaths and excess mortality was not statistically significant, except for a possible positive effect on deaths per capita during the first wave (P = 0.07, Figure S9B - Supplementary Material). Per capita deaths among countries increased with social isolation (P < 0.001, Fig.1A) and there was evidence also for an increase in excess mortality (P = 0.052, Fig.1D). In no case was social isolation negatively associated with overall mortality (Table 1). The results for social isolation were qualitatively similar (p = 0.08) when IHD was included in the analysis (Table S3 - Supplementary Material).

Figure 1. Among-country analysis of relationships of per capita deaths until 17 June 2021 with A) Index of social isolation, B) Temperature, C) Degree of urbanization; and Excess mortality with D) Index of social isolation. Each dot represents a country. Only significant predictors (p ≤ 0.05) are shown. Predictors that exhibited non-significant effects are shown in Full Models in the Supplementary Material.

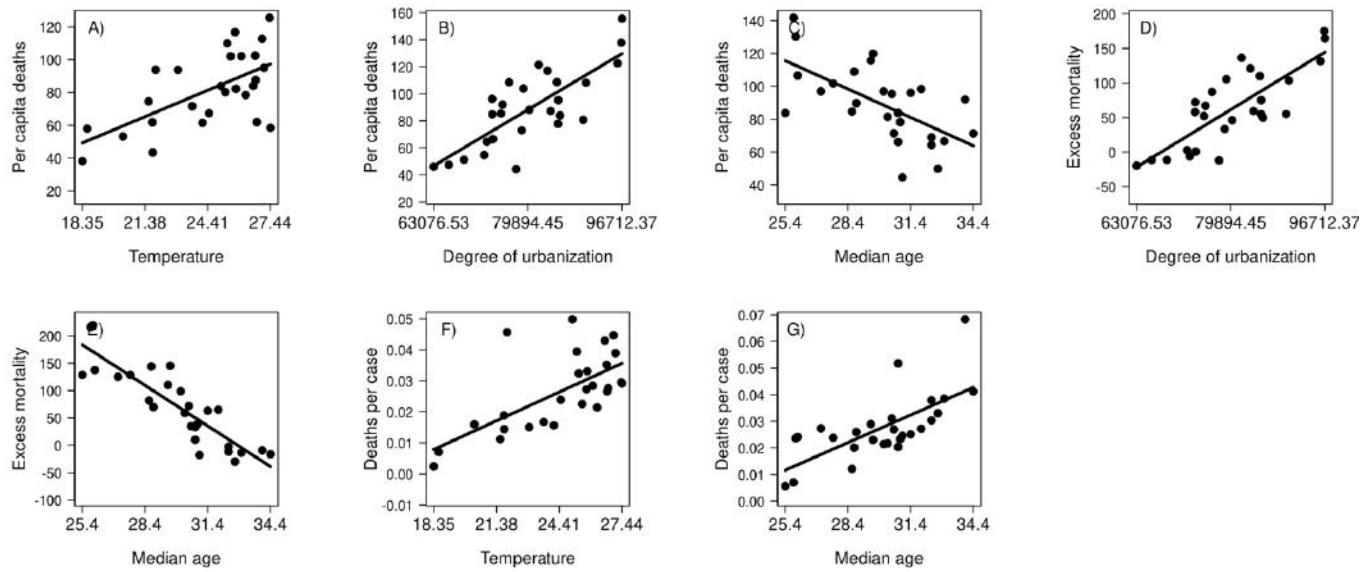


Source: Authors.

3.3 Temperature

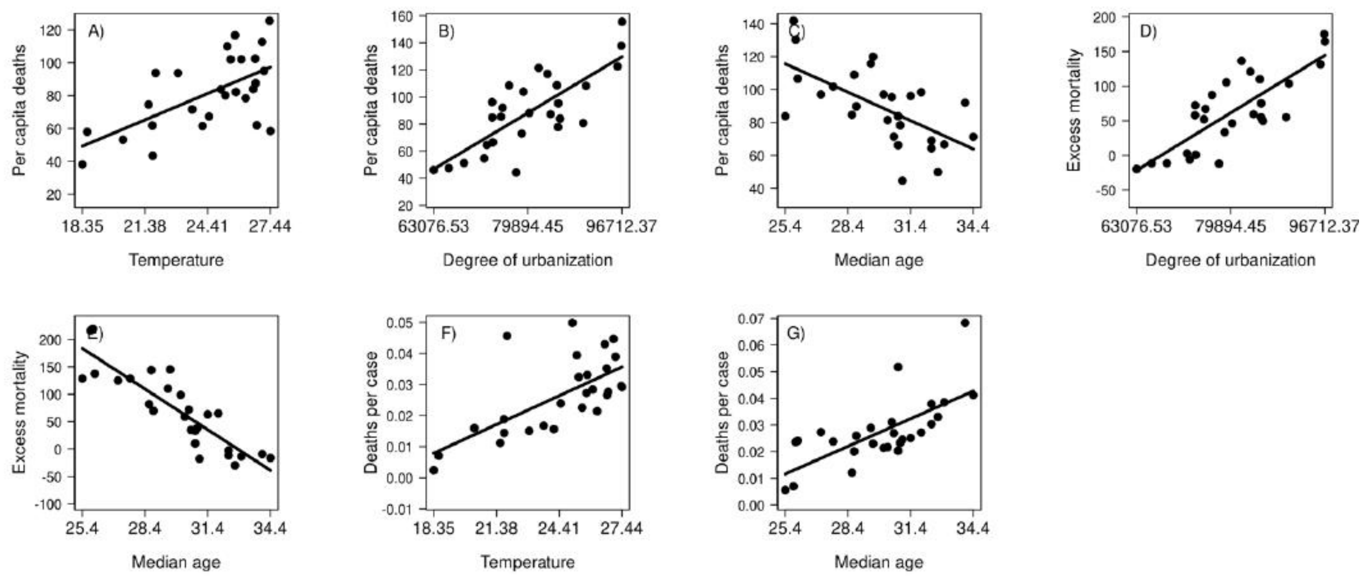
Among Brazilian states, temperature was not significantly associated with per capita deaths or excess deaths during either wave, with weak evidence of a positive effect of temperature on per capita deaths during the first wave (P = 0.05, Fig.2A); however, strong evidence of a positive effect on deaths per case was detected (P = 0.02 and P = 0.04; first and second wave, respectively; Fig.2F and Fig.3D; P = 0.006 for the combined probabilities with Fisher´s test). Temperature was negatively associated with per capita deaths (P < 0.001, Fig.1B), but not significantly associated with deaths per case or excess mortality among countries (Table 1). However, the positive effects of temperature on deaths per case among Brazilian states were not apparent in the first or second waves when IHD was included in the analysis (Table S3), and the effects of temperature on per-capita deaths and excess mortality became significantly positive during the first wave (Table S3), indicating that the model was unstable and temperature may have been acting as a surrogate for some other socio-economic factor. The negative relationship between temperature and per capita deaths and temperature and deaths per case for comparisons among countries remained after inclusion of IHD (Table S3 - Supplementary Material).

Figure 2. Relationships between Per capita deaths (A-C), Excess mortality (D-E) and Deaths per case (F-G) in the first wave among Brazilian states with Temperature (A and F), Degree of urbanization (B and D), Median age (C, E and G). Only significant predictors (p ≤ 0.05) are shown. Predictors that exhibited non-significant effects are shown in Full Models in the Supplementary Material.



Source: Authors.

Figure 3. Relationships between Per capita deaths (A), Excess mortality (B-C) and Deaths per case (D-G) in the second wave among Brazilian states with Degree of urbanization (A and F), Mean number of intensive-care units (B and E), Median age (C and G), and Temperature (D). Only significant predictors (p ≤ 0.05) are shown. Predictors that exhibited non-significant effects are shown in Full Models in the Supplementary Material.



Source: Authors.

3.4 Hospital bed capacity and intensive-care units

Among Brazilian states, there was a positive relationship between availability of intensive-care units and excess mortality (P = 0.03, Fig.3B) and an indication of a negative relationship between availability of intensive-care units and deaths per case (P = 0.04, Fig.3E) during the second wave, but neither of these relationships had statistical support when the probabilities for the first and second waves were combined with Fisher´s test. Both these relationships were weakened with inclusion of IHD in the analysis (Table S3) and, overall, availability of hospital bed capacity or intensive-care units had little consistent effect on mortality among Brazilian states or among countries (Table 1).

3.5 Degree of urbanization

The proportion of the population living in urban areas was positively associated with per capita deaths (P = 0.0007 and P = 0.03; first and second wave, respectively; Fig.2B and Fig.3A; combined probability P = 0.0002) and excess mortality (P = 0.0003 and P = 0.07; first and second wave, respectively; Fig.2D and Figure S10 (Supplementary Material); combined probability P = 0.0002) in Brazil during the first and second waves, and with deaths per case during the second wave (Fig.3F; the combined probability for the first (P = 0.20) and second waves (P = 0.02) together was P = 0.026). Among countries, urbanization was positively associated with per capita deaths (P = 0.01, Fig.1C), but not with excess mortality or deaths per case. Inclusion of IHD in the models (Table S3) changed many of the results from positive to not significant, or from not significant to positive, indicating that degree of urbanization may have been representing other socio-economic variables, but there remained strong evidence that urbanization was positively associated with mortality.

3.6 Age structure

Mean age tended to be negatively associated with per capita deaths and/or excess mortality during the first and second waves in Brazil (Table 1), with some evidence (P = 0.07, Figure S11-E - Supplementary Material) of a negative effect on excess mortality among countries. However, it was positively associated with deaths per case in Brazil during both the first and second waves (P = 0.008 and P = 0.01, respectively; Fig.2G and Fig.3G; combined probability P = 0.0008), and there was evidence (P = 0.08, Figure S12-E - Supplementary Material) of a positive effect on per capita deaths among countries. Inclusion of IHD in the model reinforced these conclusions (Table S3).

4. Discussion

Strong social distancing has been shown to reduce mortality rates due to COVID-19, keeping them well below those due to influenza in countries such as China and New Zealand. However, the relationship between mortality reduction and degree of social distancing is not necessarily linear. Some levels of social distancing reduce mortality, but others have no detectable effect. For example, in the USA, differences in within-family rates of transmission of COVID-19 can be related to the presence of children in schools, but only when the schools use a limited number of non-pharmacological interventions (NPIs) (Lessler et al., 2021). The effectiveness of NPIs probably depends on the transmissibility of the virus. There is strong evidence that NPIs used to counteract COVID-19 reduced the transmission of other respiratory diseases (Gomez et al., 2021), but it is not clear how effective they were in reducing mortality rates due to COVID-19 in countries, such as Brazil, where social distancing was carried out at levels far below those recommended by the WHO.

NPIs are used to reduce the risk of transmission, which would have the effect of flattening the mortality curve. It is assumed that flattening the mortality curve will avoid overtaxing health services and reduce overall mortality, but if the effect is only to prolong the epidemic, and health services have little effect on mortality, then this strategy may be ineffective. There was little evidence that curve flatness or the availability of ICUs in Brazil, or differences among countries in hospital bed capacity per capita, affected mortality rates. Being admitted to an ICU and intubated was practically a death sentence in the northern region of Brazil, where ICU mortality rates of intubated patients were over 90% (Bastos et al., 2021). Overall, both in Brazil and the countries for which data are available, it seems that overtaxing the health systems had only a negligible effect on overall mortality rates.

The objective of social isolation is to reduce overall mortality, whether part of that mortality is due to overtaxing the health system or not. However, we could not detect effects of flattening the mortality curve on differences in overall mortality among Brazilian states. Differences in mortality-curve flatness among states may have been due to social isolation that was not captured by the internet index, or they may have been due to factors not related to NPIs. In any case, within-state changes in mortality-curve flatness between the first and second waves had no detectable effect on within-state changes in mortality. In general, overall mortality in states was independent of mortality-curve flatness.

Social isolation is expected to reduce mortality due to COVID-19, but social isolation, as measured by the time internet users remain near home, was not significantly, or was positively associated with our measures of mortality due to COVID-19. We are unable to explain why there were more covid deaths in states and countries with more isolation based on internet indications of remaining at home, but it may be that we are confusing cause and effect. Perhaps more people stay at home when there are reports of high mortality. A positive association between staying at home and COVID-19 mortality has already been reported for Brazil (de Souza & de Souza, 2021). In any case, neither staying at home as indexed by internet connections, nor flattening of the curve, noticeably reduced COVID-19 mortality rates. Obviously, much more needs to be known about epidemiological and clinical behavior of SARS-CoV-2 to predict the most effective strategies when stringent isolation is not an option. The evidence to date indicates that the level of social distancing practiced in most Brazilian states, and in most countries, was too little, or too late, to detectably reduce mortality due to COVID-19.

Lack of effective reduction in infection rates could have been beneficial if it resulted in a large part of the population being vaccinated naturally (herd immunity). However, there was no relationship between mortality rates during the first wave and mortality rates during the second wave in Brazil, so even states with the least flattened curves must have retained a large part of the population that was susceptible to the more infectious variants that circulated in 2021.

We cannot explain why mortality due to COVID-19 was higher in Brazilian states with warmer temperatures, and that effect was not seen in comparisons among countries. The coefficient of regression associated with temperature was negative, as we had expected, for comparisons among countries, and this is what had been predicted by Pequeno et al. (2020), and Prata et al. (2020). However, when IHD was included in the models, most of the positive relationships with temperature were lost, so it is likely that differences among Brazilian states in mean temperature reflect other socio-economic factors that we did not measure. More studies will be necessary before it can be assumed that higher temperatures cause higher mortality in Brazil, but the evidence is strong that they reduce mortality in comparisons among countries.

Death rates were higher in countries with greater urbanization, and this was independent of hospital bed capacity and the proportion of the population vaccinated to date. Knowing that mortality increases with urbanization might not be very useful for individual countries. National governments will not impose measures that would decrease urbanization to combat COVID-19. However, this information may be relevant in relation to some general strategies. It has been suggested that the COVID-19 epidemic illustrates the need to suppress traditional hunting and culinary practices (McNamara et al., 2020). This perspective basically says that the risk of an epidemic can be lowered by reducing the contact that people have with natural systems. This puts the burden on people in rural settings because they are usually in much closer contact with wild animals and naturally occurring landscapes. However, the people in rural areas may have another perspective. They may say the problem is that urban people have too little contact with natural systems! Exposure to viruses during childhood can lead to acquired immunity to novel strains (Yang et al., 2021). It is important to determine whether urban environments increase mortality because of increased transmission and viral loads, or whether urban dwellers are more susceptible to new viruses. There was evidence that urbanization increased deaths per case in Brazil, but only during the second wave and other socio-economic factors associated with urbanization may be important. The subject obviously warrants further research.

5. Conclusion

Environmental and social factors related to COVID-19 mortality rates are much more complex than previously assumed. Even factors such as urbanization and social isolation can have effects opposite to those expected, especially when other variables are considered, such as temperature, mean age and hospital bed capacity.

In general, we need to consider much more complex models to deal with future pandemics, especially given the new variants of COVID-19 that circulated in the period posterior to our analyses. For that, the first step is the creation and maintenance of globally standardized databases with variables of interest in pandemics, which need to be minimally validated by its curators and collaborators. Although much social, environmental and COVID-19 data are available, to deal with the complexity imposed by COVID-19 (and other future pandemics) it is increasingly necessary a global effort to improve and facilitated access to the data. With robust and updated data, the next steps can be done, with tests of other environmental and social variables that can be included in pandemic-prediction models.

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