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Covid-19 in context: comparison with monthly mortality from respiratory causes in each Brazilian state

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Abstract

Critical decisions in the fight against the ongoing COVID-19 pandemic, caused by SARS-CoV-2, have been often made based on data that are still incomplete. While official health authorities do not solve the bottlenecks in the flow of essential health-related information, epidemiologists and other researchers must produce technical evidence for decision-making that bypass these limitations. In the present study, focused on Brazil, we compare data on COVID-19 associated deaths, made available on a daily basis, with time series of mortality from respiratory and other diseases from the years 2014 to 2018 (the last five complete years with available data). Additionally, we analysed the time series of deaths from respiratory diseases to describe the typical annual period of the peak of mortality due to these diseases in each Brazilian state. The reported mortality from SARS-CoV-2 in April is equivalent to 44% of the expected mortality from respiratory causes in the same period in previous years, with wide variation between states (from 310% in Amazonas to 4.5% in Tocantins). We are currently in the typical peak season of mortality from respiratory diseases in much of the North and Northeast (with the exception of Roraima). In the Southeast and South regions, this peak is later (June – August). The evolution of the pandemic in each state will depend, however, on several other factors, such as the pathogen's behavior – not yet sufficiently known. We emphasize the need for actions to increase agility in making data on mortality and morbidity from different causes publicly available in near real time, so that research teams with different analytical approaches can join efforts in combating this global health challenge.

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Resumo

Decisões críticas no combate à pandemia de COVID-19, doença causada pelo SARS-CoV-2, têm sido realizadas frequentemente com dados e informações ainda incompletas. Enquanto as autoridades de saúde não solucionam os gargalos no fluxo de informações de vital importância, epidemiólogos e outros pesquisadores devem produzir subsídios técnicos para o enfrentamento da crise contornando essas limitações. No presente estudo, focado no Brasil, comparamos os óbitos associados à infecção pelo SARS-CoV-2 (disponibilizados diariamente), com os dados de óbitos por doenças respiratórias e outras doenças nos anos de 2014 a 2018 (os últimos cinco anos completos para os quais os dados estão disponíveis). Adicionalmente, extraímos os sinais temporais anuais dos óbitos por doenças respiratórias para que o período típico de pico na mortalidade por essas doenças possa ser considerado em cada estado Brasileiro. A porcentagem de óbitos pelo SARS-CoV-2 em abril equivale a 44% da mortalidade esperada por causas respiratórias no mesmo período, com base em anos anteriores, com grande variação entre os estados (desde o Amazonas, com 310%, até o Tocantins, com 4.5%). Estamos na época típica de pico de mortalidade associada a doenças respiratórias em grande parte do Norte e Nordeste (com exceção de Roraima). Nas regiões Sudeste e Sul, esse pico é mais tardio (junho–agosto). A evolução da pandemia em cada estado dependerá, no entanto, de vários outros fatores, como o comportamento do patógeno – ainda não conhecido suficientemente. Ressaltamos a necessidade de ações para aumento da agilidade na disponibilização dos dados atuais de mortalidade (por diversas causas), para que equipes de pesquisa com diferentes abordagens analíticas possam se somar no combate a este desafio sanitário global.

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Introduction

The Covid-19 pandemic, a disease caused by the new coronavirus SARS-CoV-2, has forced governments worldwide to make swift decisions of enormous social, health and economic impact in an extremely dynamic situation, where empirical data to support the choice of the best courses of action are often not available in real time (1–3). Thus, authorities and populations have found themselves in the difficult task of taking a position on relevant policies based on incomplete information and polarised opinions.

Adding to the lack of studies and data, there has been great confusion with the use of appropriate terminology both by the press and health authorities. For example, the term "lethality" of the disease has been widely used to designate the ratio of deaths to reported cases (the subgroup of cases clinically and / or serologically confirmed and reported). This use of the term has had catastrophic effects for the understanding and communication of the severity of the pandemic, since the proper denominator to determine its lethality is the total number of infected people, whether they have been tested and reported or not (this is equivalent to the prevalence of infection, which can be punctual or periodic (4), with the number of deaths adjusted accordingly to the period considered). An emblematic example of this problem is the online platform developed by the Brazilian Ministry of Health to disclose information on Covid-19 (https://covid.saude.gov.br/), which on the last day of April (April 30) informs that the lethality of Covid-19 is 6.9%, a result obtained by simply dividing the number of deaths (5,901) by the number of confirmed cases (85,380). Obviously, such a figure is overestimated – at least by an order of magnitude – since the vast majority of infected people (especially those who had no symptoms or mild manifestations of the disease) are not tested (5–7). In fact, preliminary results indicate that, in Brazil, only 8% of Covid-19 cases are reported (8). If this is indeed the case, and the number of deaths is not underestimated, the lethality of Covid-19 in Brazil (the percentage of infected people who died) would be approximately 0.55%. This figure is similar to estimates based on the number of unreported cases in other countries. In China, for example, such estimates indicate that Covid-19's lethality rate was 0.66% (9).

If, on the one hand, the number of deaths associated with Covid-19 can be more accurately obtained, particularly in a context of intense public and medical attention to the pandemic, estimates of the actual number of cases require conducting serological testing in representative samples of the population. And again, given the high transmissibility of Covid-19, the estimate (even if correctly inferred) would quickly lose its value as an auxiliary tool for decision-making, especially when the proportion of susceptible (not yet infected) people is still high.

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An alternative way to estimate the severity of an epidemic is to calculate the "excess" number of deaths relative to what would be expected, based on the mortality rates observed in previous years. This is the approach, for example, of the EuroMOMO initiative (European Monitoring of Excess Mortality for Action in Public Health; https://www.euromomo.eu/ - see also (10)). Unfortunately, it is not yet possible to conduct this type of analysis in Brazil, since mortality data are published on the Ministry of Health's website only in the following year, thus preventing the analysis of any ongoing epidemic.

In a situation where critical decisions must be made swiftly, it is essential to use alternative means to assess the severity of Covid-19. Within this context, we present the results of a series of analyses on typical mortality rates due to respiratory diseases in each Brazilian state and age group, month by month, during the last five years for which the data are available (2014 to 2018). By decomposing the seasonal signal of the mortality time series , the analyses also show the months of greatest risk of death from respiratory causes in each Brazilian state. The results can be used as a reference against which the number of deaths caused by the current pandemic can be compared, as well as for tailoring action plans to each region of the country.

Methodology

Data

Mortality data were obtained from the Mortality Information System of the Brazilian Ministry of Health (http://www2.datasus.gov.br/DATASUS/index.php?area=0205). These data are collected uniformly and systematically throughout the year and cover approximately 96.3% of deaths in Brazil. In 2013, regional differences in coverage ranged from 89.3% in the North to 100% in the South (11). Because mortality data for the year 2019 is not yet complete, we used the previous five years (2014–2018) for the analyses.

Data on mortality due to Covid-19 were obtained from the Coronavirus Panel (https://covid.saude.gov.br/), made available by the Ministry of Health of Brazil (12), on May 01, 2020.

Analysis

Death records were filtered using ICD-10 codes J00-J99 (Chapter X, Respiratory System Diseases) (13), comprising those (anonymized) records where the primary cause of death was respiratory. These records were then grouped by temporal resolution (month), geography (27

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federal units: 26 states and the Federal District) and age (age groups classified according to the color code shown in Figure 1). Based on these time series, the average and 95% confidence interval for the monthly number of deaths from respiratory causes was then determined for each age group and federal unit. For comparative purposes, the average number of deaths from all causes was also calculated for the period from 2014 to 2018, and grouped into the following categories: infectious and parasitic diseases (A00-99, B00-99), neoplasms (C00-99, D00 -48), diabetes (E10-14), diseases of the nervous system (F00-99, G00-99), circulatory diseases (I00-99), diseases of the digestive system (K00-99), genitourinary (N00-99), transport accidents (V00-99), suicides (intentional self-harm: X60-84), interpersonal violence (aggression, X85-Y09), other external causes (W00-99, X0-59, Y10-99, S00- 99, T00-99) and remaining death codes (others). Given the fluidity of the situation, we added in Supplemental Material 3 a dynamic dashboard with the average number of deaths from all causes as calculated above, along with the daily update of the number of Covid-19 deaths, provided by the Coronavirus Panel.

The period of peak mortality from respiratory causes in each state was also analysed. This analysis is based on the detection of the periodic annual function of the time series of deaths by a method (Fourier analysis) that removes interannual variations (trends and anomalies), and preserves the seasonal signal of the series (14). The month corresponding to the peak of mortality in each state is then plotted against the state's latitude. The analysis of latitudinal gradients was pioneered in Brazil (15), and later applied to the study of the seasonality of various diseases in several countries (16–21). All analyses and charts were produced with the software Epipoi (14) (written in Matlab R2007, MathWorks©, Natick, WA), freely available at http://www.epipoi.info.

Results

Data on mortality from respiratory causes in Brazil for the years 2014–2018, by month and age group, are shown in Figure 1. The same data are also available for each Brazilian state in Supplementary Figure 1 (mortality incidences, by 100,000 population, are shown for each state in the Supplementary Material 2). Only records containing data for all variables were considered (0.1% of death records were incomplete and therefore excluded from the analysis). To provide all possible comparisons against which to analyse the severity of this pandemic, Supplementary Material 2 also illustrates the monthly mortality burden of several disease groups typically observed throughout the year in Brazil.

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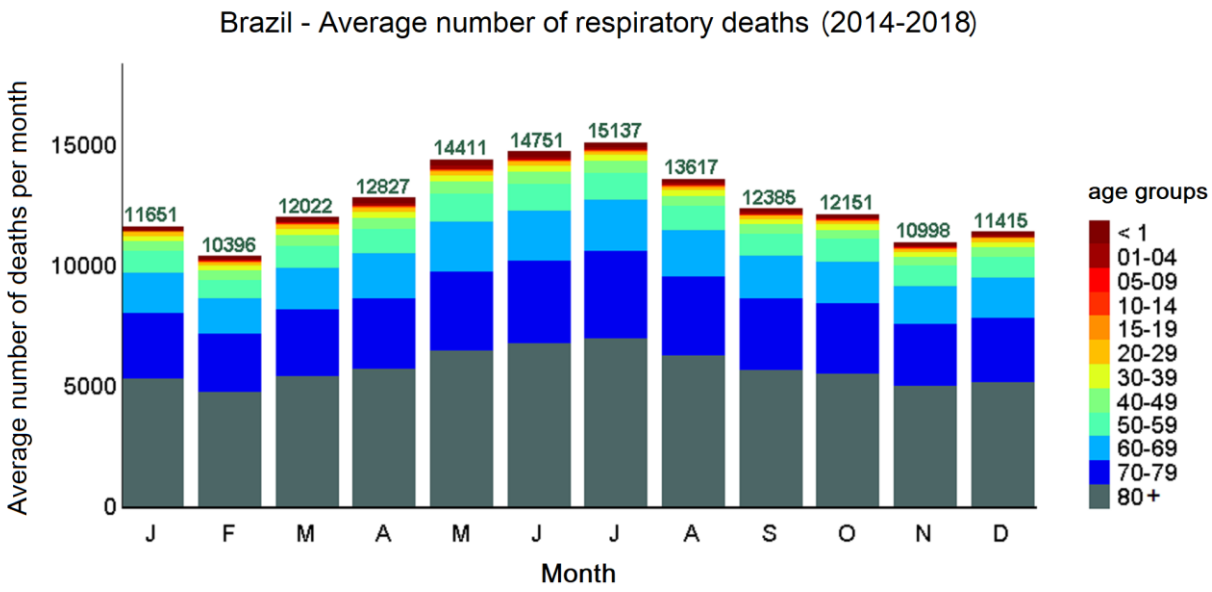

Figure 1. Average (number above the bars) number of deaths attributed to respiratory causes in Brazil, per month, from 2014 to 2018. Bar colors correspond to the age groups (in years). Data source: DATASUS (11).

The first case of Covid-19 in Brazil was reported in the state of São Paulo, on February 26, followed by a new case on February 29 (total of 2 cases in the country in February). Table 1 shows deaths by Covid-19 in March and April 2020 for each Brazilian state, as well as the average monthly number of deaths from respiratory causes in the years 2014-2018 (which we refer to as typical respiratory mortality hereafter). The last two columns on the right indicate the proportion of deaths by Covid-19 relative to the average number of respiratory deaths in the same months in previous years.

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Table 1. Number of deaths by Covid-19, average number of deaths from respiratory causes (ICD-10 J00-99) and ratio between Covid-19 deaths and the average number of respiratory deaths from 2014–2018 in the same months (stronger colors: higher proportions); 95% CI: 95% confidence interval.

	Covid-19 deaths, 2020		Mean number of respiratory deaths, 2014–2018 (±95%CI)		Deaths (Covid-19) / Typical respiratory deaths	
	March	April	March	April	March	April
Acre	0	19	43 ± 10	41 ± 11	0.00%	46.34%
Alagoas	1	46	155 ± 22	150 ± 31	0.65%	30.67%
Amazonas	3	422	135 ± 15	136 ± 11	2.22%	310.29%
Amapá	0	34	25 ± 8	26 ± 5	0.00%	130.77%
Bahia	2	102	579 ± 49	582 ± 40	0.35%	17.53%
Ceará	7	475	663 ± 191	739 ± 160	1.06%	64.28%
Distrito Federal	3	27	85 ± 9	99 ± 14	3.53%	27.27%
Espírito Santo	0	83	179 ± 12	192 ± 26	0.00%	43.23%
Goiás	1	28	398 ± 39	474 ± 45	0.25%	5.91%
Maranhão	1	183	303 ± 56	314 ± 38	0.33%	58.28%
Minas Gerais	2	80	1211 ± 96	1311 ± 145	0.17%	6.10%
M. Grosso Sul	1	8	157 ± 28	160 ± 28	0.64%	5.00%
Mato Grosso	0	11	163 ± 21	169 ± 36	0.00%	6.51%
Pará	0	208	384 ± 69	425 ± 50	0.00%	48.94%
Paraíba	0	62	260 ± 62	282 ± 44	0.00%	21.99%
Pernambuco	6	559	698 ± 148	688 ± 87	0.86%	81.25%
Piauí	4	20	168 ± 26	217 ± 33	2.38%	9.22%
Paraná	3	80	592 ± 40	646 ± 79	0.51%	12.38%
Rio de Janeiro	23	831	1247 ± 103	1332 ± 142	1.84%	62.39%
Rio G. Norte	1	55	214 ± 54	212 ± 32	0.47%	25.94%
Rondônia	1	15	72 ± 14	85 ± 10	1.39%	17.65%
Roraima	0	7	15 ± 3	13 ± 4	0.00%	53.85%
Rio G. Sul	4	47	701 ± 34	742 ± 94	0.57%	6.33%

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Santa Catarina	2	44	324 ± 13	336 ± 30	0.62%	13.10%
Sergipe	0	12	98 ± 21	95 ± 19	0.00%	12.63%
São Paulo	136	2239	3078 ± 248	3278 ± 415	4.42%	68.30%
Tocantins	0	3	54 ± 9	67 ± 10	0.00%	4.48%
Brasil	**201**	**5700**	**11918±929**	**12811 ± 1230**	**1.69%**	**44.49%**

As shown in Table 1, deaths by Covid-19 in March represented 1.69% of the average number of respiratory deaths in Brazil in the same month in previous years. In April, this proportion rises to 44%. Amazonas is the state of greatest pandemic severity relative to the typical respiratory mortality in past years, where the number of reported deaths by Covid-19 (422) greatly exceeded the average respiratory mortality expected for this month (136). The second highest proportion of deaths by Covid-19 relative to the typical number of respiratory deaths was observed in Amapá (130.8%), followed by Pernambuco (81.3%), São Paulo (68.3%), Ceará (64.3%), Rio de Janeiro (62.4%), Maranhão (58.3%) and Roraima (53.9%). In the other states, this proportion is lower than 50%.

Figure 2 shows a clear seasonal pattern in the number of deaths from respiratory causes in Brazil from 2014 to 2018, with higher mortality during autumn and winter. In July, over fifteen thousand respiratory deaths are observed on average in Brazil, with this number falling to approximately 10,400 deaths in February. At any time, most respiratory deaths occur in the elderly population, with those aged over 70 years accounting for more than half of all respiratory deaths. However, the seasonal pattern of respiratory mortality differs across the several Brazilian states and regions. In Supplementary Figure 1, which shows the mortality for each state (organized from north to south), it is possible to observe how the northern states have a concentration of deaths earlier in the year than the Southern states. In Figure 2 this information is synthesised, illustrating the temporal shift in the peak of respiratory mortality from north to south of the country, by latitude.

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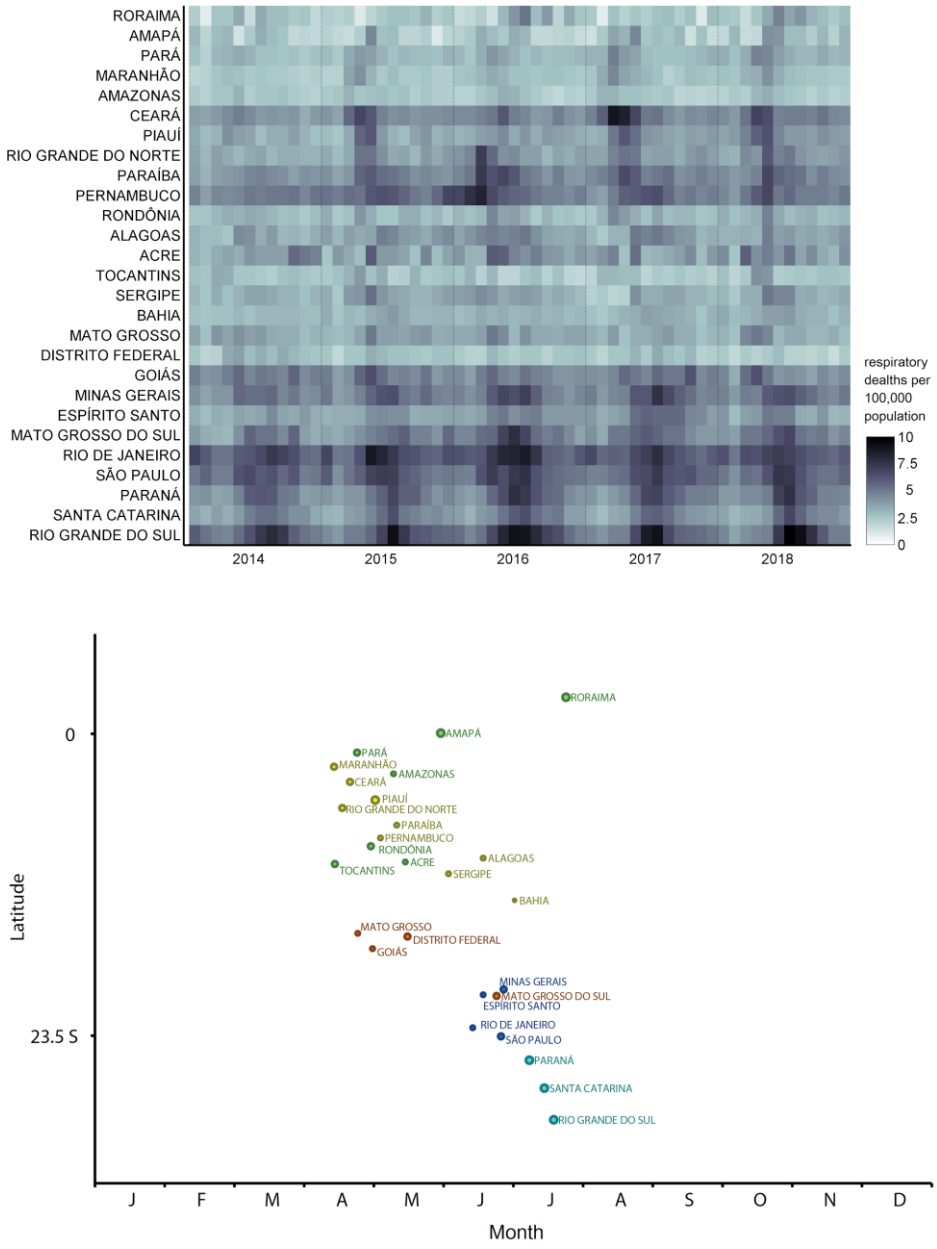

Figure 2. Deaths attributed to respiratory causes (2014–2018) in each Brazilian state. Upper panel: incidence of monthly deaths in each state (sorted by the latitude of their capitals). Lower panel: Primary peak of deaths, plotted against the latitude of their respective capitals. Colors are used to

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distinguish the 5 regions of Brazil (light blue: South; dark blue: Southeast, red: Mid-West, green: Northeast, dark yellow: North). Analytical software: Epipoi (14). Data source: DATASUS (11).

Discussion

In the absence of representative and sensitive testing of the population, the most accurate way to estimate the mortality burden of an epidemic (namely the number of deaths that would not have occurred in its absence) is to compare the historical time series of deaths with the total number of deaths, during the pandemic period, (a) by all causes (ideally with information on the causes of death) and (b) by the subgroup of causes potentially associated with or aggravated by the epidemic. In this way, it is possible to determine the "excess" number of deaths in the epidemic period relative to the number expected for each geographic unit and age group. Unfortunately, the data needed for this type of analysis has not yet been made available. Thus, it is not possible to establish how many deaths reported as associated with SARS-CoV-2 infection represent deaths in addition to those typically expected, and how many are from individuals who would die from other respiratory infections or causes, but who were infected with the SARS-CoV-2 virus and died instead from Covid-19.

This study was developed in light of this limitation (which we encourage to be overcome as soon as possible by the personnel in charge of the mortality information services[1]). In this context, the analyses provide relevant data to assess the severity of the current health crisis and determine those states where it is plausible to expect an increase in the number of cases and deaths in the coming weeks, which would occur if three conditions are met: (i) the seasonality of SARS-CoV-2 is similar to the seasonality of other respiratory infections in the country, such as those caused by influenza, respiratory syncytial virus and other coronaviruses (15,22,23), (ii) there is a large proportion of the population that is still susceptible, and (iii) there are no hospital capacities (e.g. enough ventilators and ICU beds (2)) and pharmacological solutions available and implemented at the scale needed.

The pattern of mortality from respiratory causes in the years 2014–2018 (Figure 2) reveals a latitudinal gradient in the country, with peaks of deaths occurring in April in most states in the North and Northeast (coinciding with the rainy season in these regions (15)), and

[1] It would also be recommended that the datasets made available for the analysis of Covid-19 in Brazil (https://covid.saude.gov.br) include more fields, such as municipality of residence, sex and age (which is absolutely critical since over 90% of deaths are among individuals aged 65 years or more (3)) of the patient, and ideally comorbidities, date of onset of symptoms and profession, so that all interested parties (e.g. epidemiologists) can carry out more detailed analyzes, providing more technical subsidies for the development of action plans to mitigate the effects of the pandemic. Note that in no way would such information violate the privacy of patients, as records remain anonymous.

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gradually later in the southernmost states, with mortality peaks in June and July (cold season) in the Southeast and South regions, respectively. This seasonal pattern is similar to that described for the incidence of viral respiratory infections, mainly by influenza viruses (15,24,25) – such as the pandemic influenza H1N1pdm09 (26) – and for the mortality attributed to epidemic influenza and pneumonia. This "traveling wave" of deaths from the Amazon to the south of the country (15) also has implications for the definition of the flu vaccine calendar in Brazil (25) and other equatorial regions of the globe (17).

Thus, the observation of a higher proportion of deaths by Covid-19 (Table 1) in the state of Amazonas (27) coincides with the expectation of higher mortality in the month of April. It is still early, however, to determine whether this will be the case in Amapá and Roraima, states with a relatively high proportion of deaths by Covid-19 relative to typical respiratory mortality, but where the peak in annual respiratory mortality occurs later in the year (May, July; Figure 2). If the conditions that favour an increase in respiratory mortality in the winter months in the South and Southeast – mainly the lower temperature, which tends to aggravate respiratory disease symptoms (28–31) – also favour the transmission and severity of infection by SARS-CoV-2, there may be an aggravation of the epidemiological situation in the coming months in these regions if the proportion of the population susceptible to the Covid-19 virus is still high. Again, these projections depend on the three conditions outlined in a previous paragraph, such as the availability of treatment, equipment and ICU beds. Interestingly, in the state of Amazonas, there are almost no private ICU beds (2,32).

In Brazil, the H1N1pdm09 influenza pandemic caused an excess of 2,787 respiratory deaths in 2009, of which more than 90% occurred in May (beginning of the pandemic), June, July and August (26,33). It is worth mentioning that, at the time, there was great reluctance to recommend the use of antiviral drugs, a reluctance that resulted in an important increase in the number of preventable deaths (34,35). In comparison, the number of deaths from Covid-19 in Brazil from the beginning of the pandemic until the end of April was 5,901. On the one hand, it is not possible to rule out the existence of underreporting of deaths by Covid-19 (for example, due to its attribution to other causes, the absence or failure of tests, and the occurrence of deaths outside the hospital context). On the other hand, it is worth mentioning again that it is not yet possible to distinguish between those deaths caused by Covid-19 in people who would not otherwise die (excess mortality) and those occurring simultaneously (or accelerated) by the virus in a fraction of the population that, in the absence of the pandemic, would also succumb to other diseases and infections. For example, among Brazilian patients who died from Covid-19, most had pre-existing diseases, many of which are also predisposing factors for severity in influenza and other respiratory infections (36). In addition, a positive test for a virus does not necessarily mean that infection by the virus is always the primary cause of death (37).

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While each death by Covid-19 is a tragedy that should not be minimised, it is also important to analyse these numbers in context. In April, there were 5,700 reported deaths by Covid-19 (see Supplementary Figure 3 for a daily update on the number of notified deaths). As a reference, the average number of deaths in recent years in the same month (Supplementary Material 3) are as follows: infectious and parasitic diseases (4,674), neoplasms (17,999), diabetes (5,032), diseases of the nervous system (4,022), circulatory (28,746), respiratory (12,803), digestive tract (5,532), genito-urinary (3,137), transport accidents (3,105), suicides (961), violent deaths from aggression (4,874), other external causes, such as suffocation, others accidents and complications due to the use of drugs (3,862) and other causes (11,565), totaling, on average, 106,313 deaths in this month. Thus, it is essential not to lose context and whilst focusing on countering the Covid-19 pandemic, also ensure that other healthcare demands and their conditioning factors are not neglected, and that instead of spreading panic, contribute to people's awareness.

Disaster circumstances, such as pandemics, require swift and informed decision-making by authorities across all areas of activity. And it is precisely during these events that new guidelines are recommended and public policies are created to manage future events. As an example, with the Influenza A pandemic in 2009, the notification of cases of severe acute respiratory syndrome became mandatory in Brazil (38). Even so, with each new event, new demands arise that still need attention from public authorities, such as the availability of data from the Mortality Information System in near real time. We hope that the analyses presented here can help provide more context to the mortality patterns associated with the Covid-19 crisis, and foster increased agility in the availability of data by the responsible bodies, which would allow research teams from across the world to further contribute to our understanding of this global health challenge.

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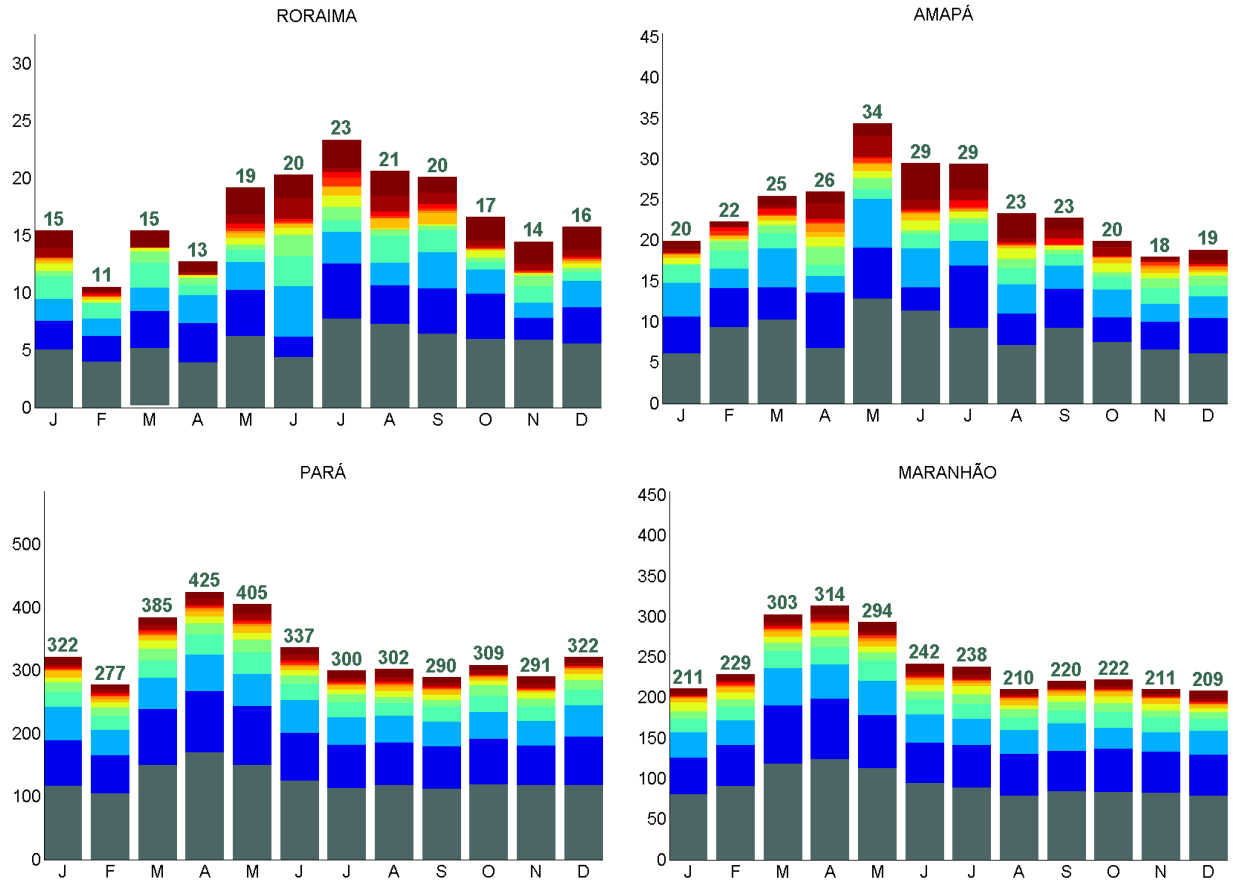
Supplementary Material

Figure 1. Average number of monthly deaths from respiratory causes (2014-2018), by state.

Average (numbers above the bars) number of deaths attributed to respiratory diseases in each Brazilian state, from 2014 to 2018. Colors correspond to the age groups. The order of the figures follows the latitude gradient (from north to south) of the capitals of each state. The color code is available in Figure 1, main text (these charts, along with charts on mortality incidence per state, are available for download in the Supplementary Material 2).



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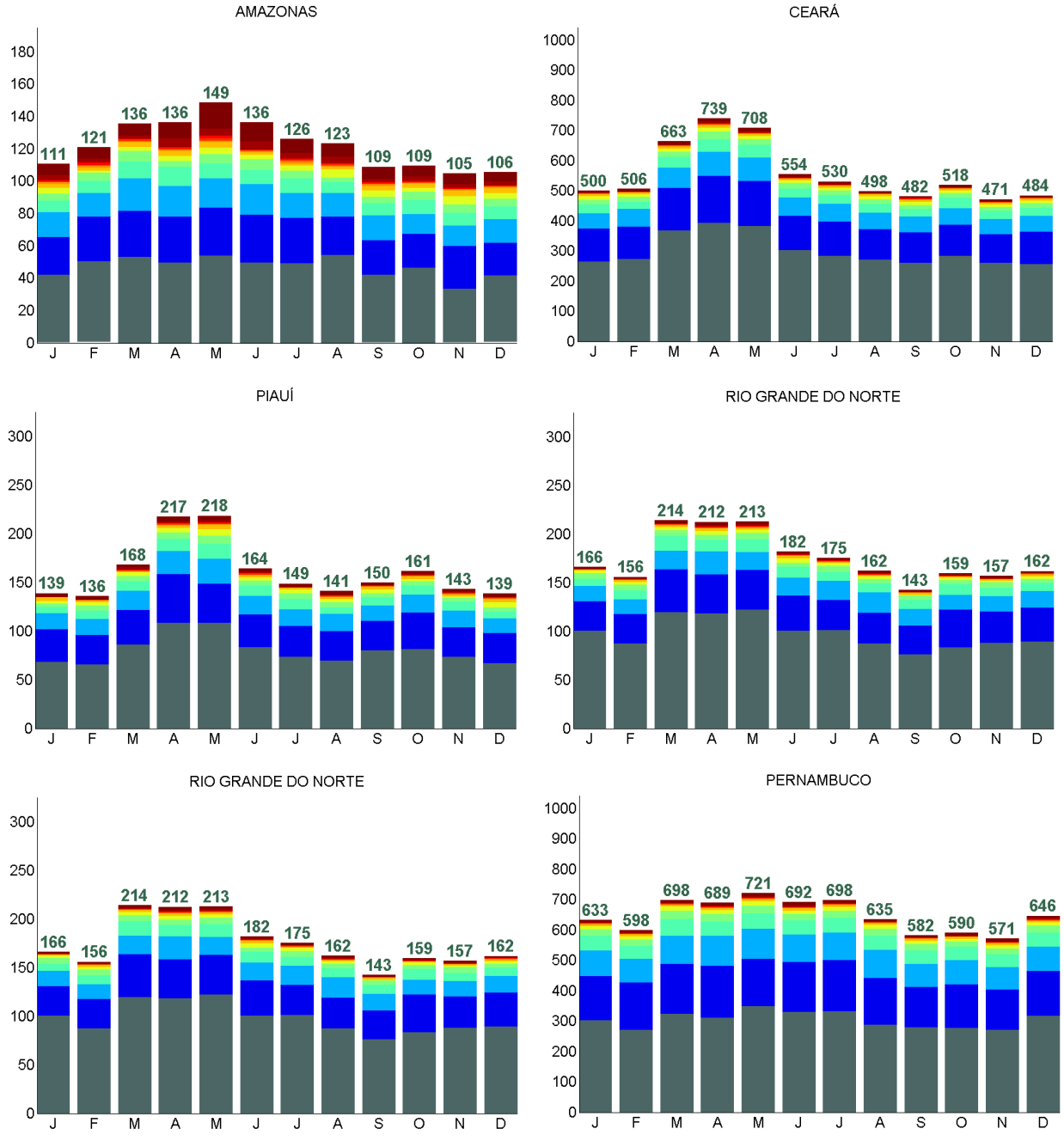

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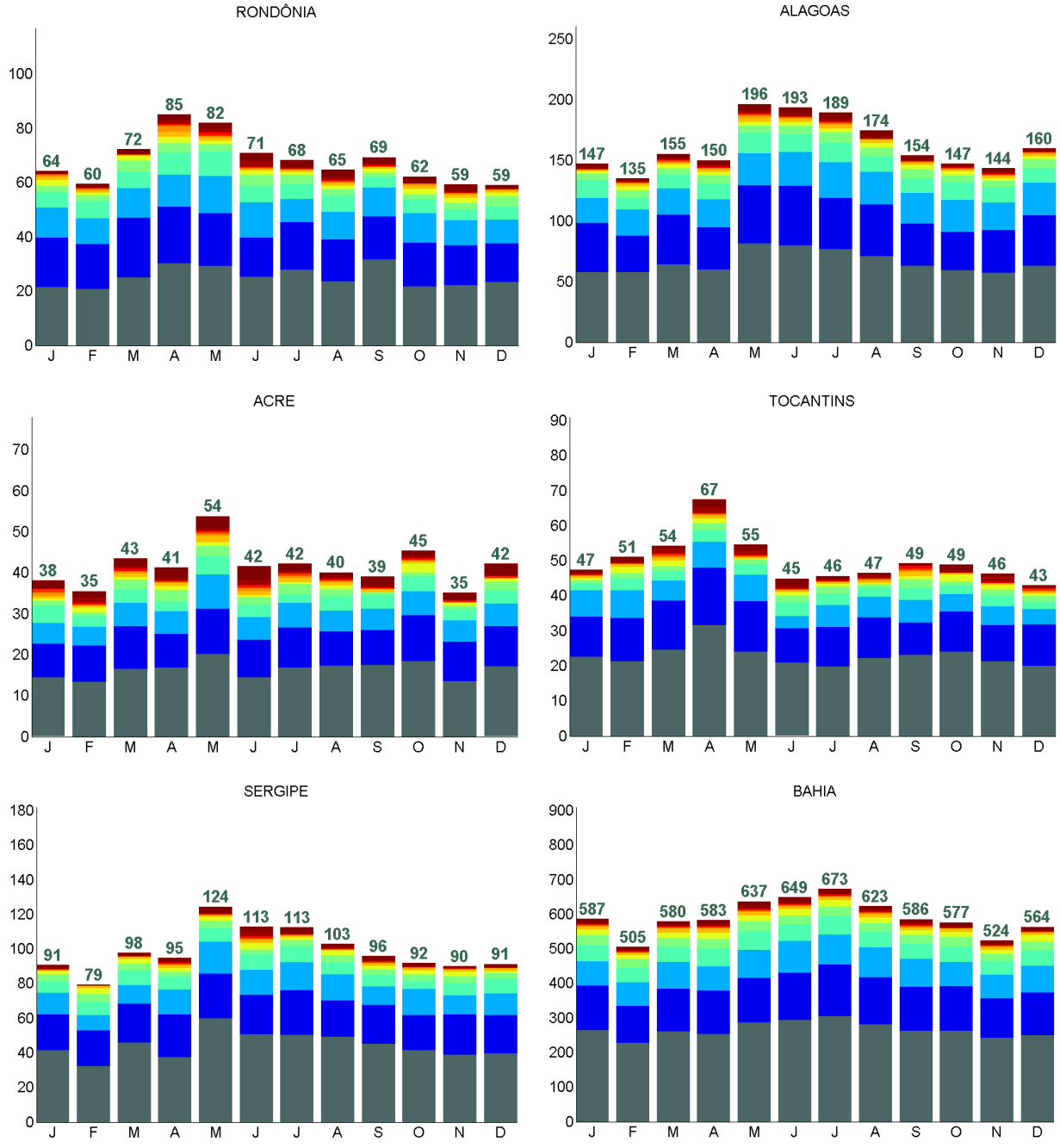

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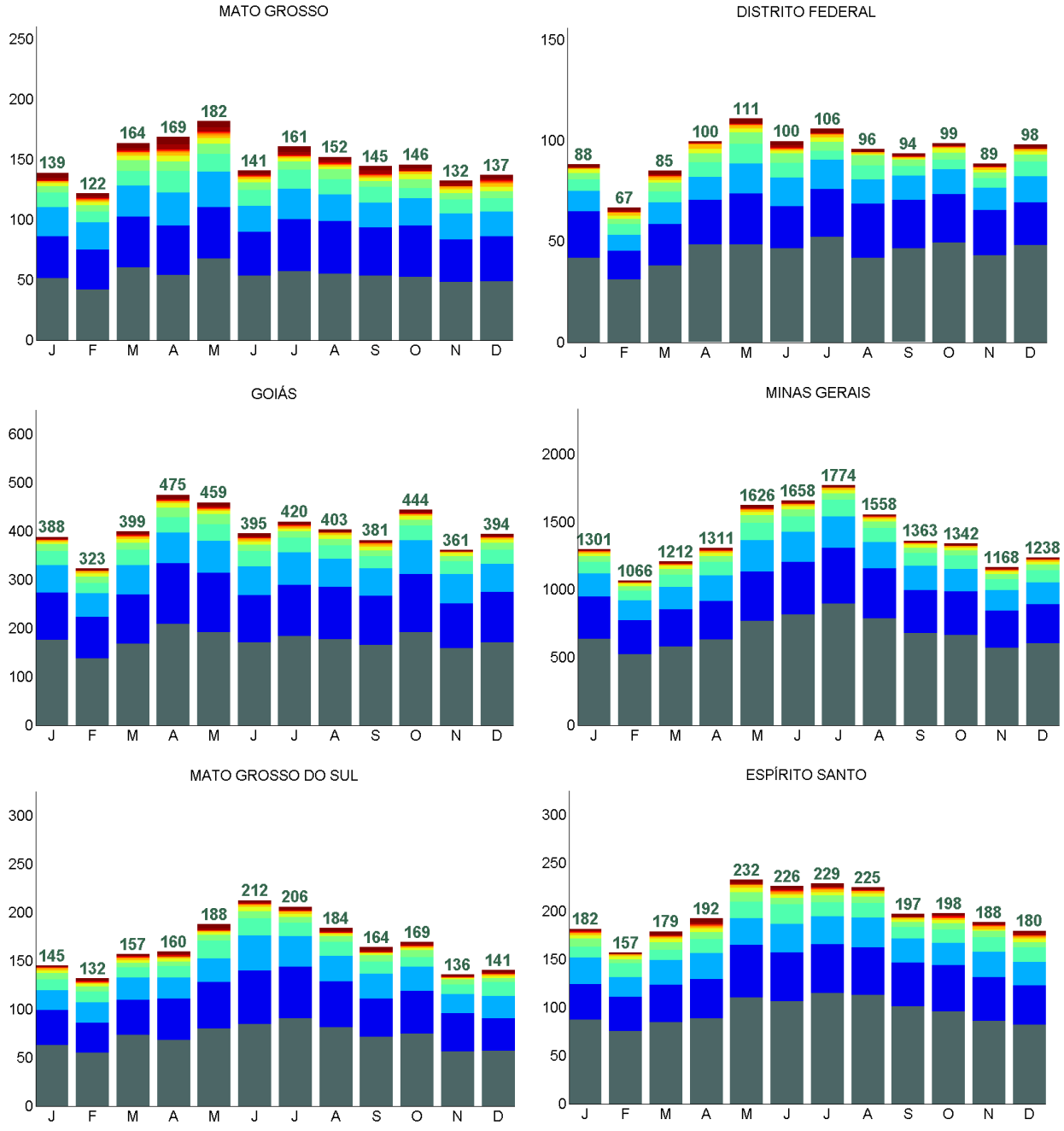

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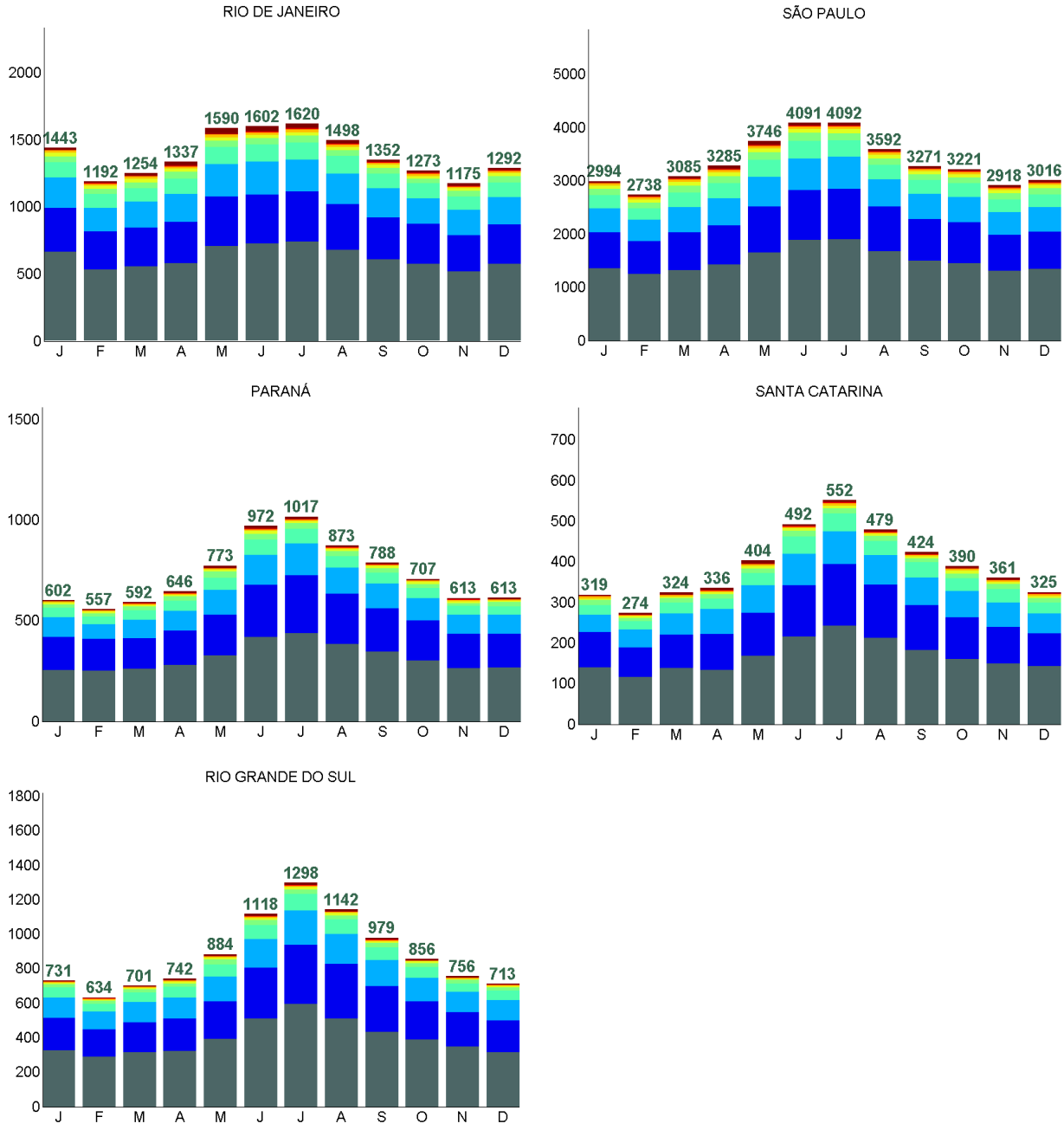

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Supplementary Material 2. Original data from historical mortality series

Data on respiratory mortality data for the years 2014-2018, aggregated by federation unit, age group and month are available at Brasil_Obitos_respiratorios_2014_2018 .xls.

To reproduce the graphs and latitudinal analyzes performed here in the Epipoi program (14) (www.epipoi.info) it is also necessary to download a file containing the latitude and longitude of the capitals of the Brazilian states: Brasil_Latitudes_Longitudes_capitais_dos_estados.xls. To perform the analyses of incidence, it is also necessary to load the population file Brasil_Populacao_interpolada_por_mes_2014_2018.xls (obtained from the interpolation of population census data, from IBGE, with the software Popweaver (33))

The table used in the time series shown in Supplemental Figure 3 is available at Obitos_Brasil_2014-2018_por_grupos_de_causas .xls

Other available resources:
Figures of the average monthly deaths from respiratory causes (2014-2018) by state
Average incidence of monthly deaths from respiratory causes (2014-2018) by state

Supplementary Figure 3.

Upper chart: dynamic (updated daily) deaths by Covid-19 are represented, per month, on the same scale (deaths refer to the cumulative up to that date of the month). Sources: DATASUS (11) and Panel Coronavirus (https://covid.saude.gov.br/).

Lower chart, average (numbers above the bars) number of deaths from different causes in each Brazilian state, from 2014 to 2018. Disease categories: infectious and parasitic diseases (A00-99, B00-99), neoplasms (C00-99, D00-48), diabetes (E10-14), diseases of the nervous system (F00-99, G00-99), circulatory (I00-99), respiratory (J00-99), digestive system (K00-99), genitourinary (N00-99), transport accidents (V00-99), suicides (X60-84), violence (aggression, X85-Y09), external causes other than transport accidents, suicides and violence (such as poisoning, asphyxiation and complications in the use of medications; W00-99, X0-59, Y10-99, S00-99, T00-99) and others (other death codes).

https://public.tableau.com/views/Dashboard_Covid-19_Auto/StoryBilingual?:display_count=y&:origin=viz_share_link

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Supplementary Figure 4

Monthly average of incidence (per 100,000 population) of respiratory death of each state of Brazil of years 2014-2018 per latitude