Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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1. Introduction

Mortality owing to coronavirus disease (COVID-19), caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is considered avoidable because some collective and individual measures can help prevent the infection, and appropriate health assistance greatly reduces the mortality risk. Nevertheless, mortality risk varies according to some individual and geographic risk factors, resulting in health inequity observed in several parts worldwide since the beginning of the pandemic [1,2]. In Brazil, COVID-19 was first reported in the city of São Paulo on February 25, 2020 [3]. Until 3 August, 4 months after the first reported death, the disease had already resulted in 2,962,442 confirmed cases and 99,572 deaths in the country [4]. Currently, the United States of America and Brazil are the epicentres of the disease.

Brazil is the fifth country worldwide in terms of surface area and population and is classified as having an upper-middle-income economy [5]. Almost 60% of the Brazilian population is concentrated in 6% of the large cities, among which São Paulo is the largest. The Brazilian Unified Health System guarantees healthcare for all citizens as well as for thousands of foreigners residing or passing through the country [6]. Despite this universal healthcare, geographic differences in mortality rates across different areas have been observed on a national and intra-urban scale. Spatial heterogeneity in population characteristics such as age, underlying health, household densities, partial lack of sanitation, socio-economic status, contact networks, and mobility patterns [7] has emerged as a potential propellant of the spatiotemporal
spread of the disease.

Since the beginning of the pandemic, mapping disease occurrence and spread has become a powerful tool to track the disease and establish measures to slow down the transmission of the infection both locally and globally [8]. Web-based Geographical Information Systems have allowed near real-time monitoring using map-centric dashboards [9–11]. Despite advances in the use of technology to reduce the impact of the pandemic, little is known about the spatiotemporal patterns of COVID-19 mortality, especially in intra-urban settings. Studying the spatiotemporal dynamics of mortality instead of the cases may help better evaluate inequity. All health disadvantages accumulated over decades of life, owing to any kind of deprivation, increase the risk of mortality due to COVID-19. The lack of a robust spatiotemporal analysis undermines the comprehension of mitigation strategies to potentialise disease-control efforts. Thus, this study aimed to unveil the spatiotemporal dynamics of COVID-19 mortality in a higher spatial resolution (in the city of São Paulo), considering the socio-economic context of the population. This approach may shed light on the urgent need for solid evidence on health inequities during the COVID-19 outbreak.

2. Materials and methods

2.1. Study area and data acquisition

This ecological study, based on COVID-19 secondary mortality data, was delineated in the city of São Paulo, state of São Paulo, Brazil (Fig. 1). In 2020, the estimated population of this city was 11,869,660 inhabitants, and the mean demographic density was 7803 inhabitants/km² [12].

When using COVID-19 data, underreporting is always an issue that deserves attention, even for mortality. To minimise the effect of possible sub-notification of deaths, we analysed confirmed and suspected deaths due to COVID-19. Thus, mortality data comprised confirmed and suspected deaths that occurred between 15 March and June 13, 2020, extracted on 18 June from the Mortality Information System (SIM), the Mortality Information Improvement Program (PRO-AIM) of the Epidemiology and Information Coordination (CEInfo) of the São Paulo Health Secretariat (SMS-SP). Confirmed deaths due to COVID-19 corresponded to the code B34.2 (coronavirus infection disease), according to the International Classification of Diseases Tenth Revision (ICD-10). Suspected deaths were coded as U04.9 (corresponding to severe acute respiratory syndrome).

The places of residence of the COVID-19 deaths were geocoded with CEInfo/SMS-SP using its databases and Google Maps API geocoding script (that uses public places as the base map). The resulting geocoded addresses were validated by comparing the road or Zone Improvement Plan (ZIP code), whenever the record was allocated using the original ZIP code. Geocoded data were assigned to the 310 sample areas of the Brazilian Institute of Geography and Statistics, for which demographic and socio-economic census data are available [13]. We considered these areas as the spatial units in our models (Fig. 1).

Records, including the basic cause of death, age, sex, date of death according to the epidemiological week (EW) [14], and the sample areas of residence, were obtained after addressing a formal request to the São Paulo Electronic Information System (e-SIC database, protocol 48567). Their data information is hosted in an open session on the municipality’s transparency portal for public access [15]. Here, we named this information the e-SIC database. It was not necessary to submit this study to an ethics committee because we did not have access to personal data, such as names and addresses. The use of secondary data without personal identification and in a public domain dispenses the need for prior approval from the Ethics Committee on Research with Human Beings (as per Resolution No. 510/2016 of the National Health Council) [16].

We also used the data available in the TabNet and named this information as the ‘TabNet database’. The TabNet database is an application, available at <https://www.prefeitura.sp.gov.br/cidade/secretarias/saude/tabnet/>., provided by the Municipal Health Department of São Paulo. It was developed by DataSUS. This application provides free access (to any user) to population databases and to database information systems of SUS (such as the SIM), which is supplied by the Secretariat’s Program (PRO-AIM). Through the TabNet database application, it is possible to perform tabulations and to cross several variables of interest such as EW, sex, age group, and specific cause. The databases are updated periodically. Notably, the data sources of the TabNet and e-SIC database are SIM. However, only the e-SIC database is subdivided according to sample area.

To measure the socio-economic condition of the population, since individual-level data are not available in the mortality database, we used a socio-economic index elaborated for health research. The Socio-economic Index of the Geographic Context for Health Studies (GeoSES) [17] was developed using principal component analysis, starting with 41 variables. The index conceives the socio-economic condition by considering seven parameters based on the theoretical background [18, 19]: education, mobility, poverty, wealth, income, segregation, and deprivation of resources and services. The index was defined on three scales: national, Federative Unit, and intra-municipal. Fig. 1 presents GeoSES for the sample areas of the city of São Paulo. It shows that the areas with the best socio-economic conditions (GeoSES equal to or close to 1) are located in the central part of the city and that the socio-economic conditions deteriorate towards the periphery, where they reach the worst levels (GeoSES equal to or close to −1). It has been shown to be useful in studies of mortality due to avoidable causes of deaths in individuals aged 5–74 years due to interventions at the Brazilian health system on a national scale as well as mortality due to circulatory system diseases in the city of São Paulo [17]. This index is publicly available at https://opendatasus.saude.gov.br/dataset/geoses.

2.2. Data analysis

We used the information of confirmed (B34.2) and suspected (U04.9) deaths due to COVID-19 available for the entire city of São Paulo from the 11th to 29th EWs to calculate the weekly mortality rates of confirmed (B34.2), suspected (U04.9), and total (B34.2 + U04.9) COVID-19 deaths. This was similarly done using the e-SIC database from

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**Fig. 1.** a) South America, Brazil, State of São Paulo, city of São Paulo. b) Distribution of socio-economic Index of the Geographic Context for Health Studies (GeoSES) according to the sample area and delimited by administrative districts, city of São Paulo, 2010.
the 11th to 12th EW. We excluded (from the information e-SIC database) COVID-19 deaths that occurred in the 25th EW because data from this week were incomplete (it was extracted on June 18, 2020, and it contained only part of the 25th EW information). These rates were obtained by dividing the respective numbers of deaths in each week by the total population of the city and presented as death per 100,000 inhabitants per week. In this sequence, we obtained the mortality rates for confirmed, suspected, and total COVID-19 deaths according to sex and age for the entire period from the 11th to 12th EW using the Tabnet and e-SIC databases. The comparisons between the data from these two sources were useful to evaluate the completeness of the data we used for the spatial and spatiotemporal analysis. For the calculation of the mortality rates according to sex and age, we excluded the data without these information.

As only one suspected COVID-19 death occurred during the 11th EW, we restricted our spatial and spatiotemporal analysis from the 12th to 24th EW, and spatial or spatiotemporal architecture was considered in all models developed. We first modelled the confirmed and total COVID-19 deaths using spatiotemporal models involving only the intercept and random effects that account for spatial and temporal autocorrelation and the interaction between them. The spatial dependence was modelled considering the Besag–York–Mollié (BYM) model with two components representing the spatially structured and non-structured random effects [20,21]. These two components were considered independent from one another and followed the parameterisation proposed previously [22]. The temporal dependence was modelled using a non-structured random effect and a structured random effect provided by a random walk autoregressive model of first order (RW1). The interaction between space and time was modelled considering spatial and temporal non-structured random effects [21].

The number of confirmed and total COVID-19 deaths per EW and per sample area was modelled using Poisson and zero-inflated Poisson probability distributions with a latent Gaussian Bayesian model approach. We considered the expected confirmed and total COVID-19 deaths for each EW and for each spatial unit as offsets in these models. The expected deaths were estimated with indirect standardisation, considering the age and sex structure of each sample area and the mortality rates for the entire study period and city. This enabled us to interpret the outcomes of our analysis as relative risks (RR) concerning non-informative priors for the fixed effects and priors with penalised splines. We considered the entire city variate in each EW. To this end, we considered spatial models with spatial random effects, the intercept, BYM spatial random effects, and GeoSES as a covariate. The spatial dependence was modelled considering the Besag–York–Mollié (BYM) model with two components representing the spatially structured and non-structured random effects [20,21]. These two components were considered independent from one another and followed the parameterisation proposed previously [22]. The temporal dependence was modelled using a non-structured random effect and a structured random effect provided by a random walk autoregressive model of first order (RW1). The interaction between space and time was modelled considering spatial and temporal non-structured random effects [21].

Finally, we used a spatial approach to model the confirmed and total COVID-19 death per EW to evaluate the role of the socio-economic covariate (GeoSES) in these models and obtained the corresponding RR. We also used the spatiotemporal models, considering socio-economic variables (GeoSES). Table 2 shows the spatiotemporal RR and the 95% credibility intervals for GeoSES obtained for the models with confirmed and total COVID-19 deaths. In both models, it is noted that a high socio-economic variable (GeoSES) is associated with a higher risk of COVID-19 deaths. Apart from the fact that the RR is greater for the total deaths than for the confirmed ones, the distribution of the RR is similar between them, and it follows the behaviour of the temporal RR. In the first two EWs, the sample areas presented lower values of RR that increased over time. However, this increase occurred with greater intensity in peripheral areas. We also used the spatiotemporal models, considering socio-economic variables (GeoSES). Table 2 shows the spatiotemporal RR and the 95% credibility intervals for GeoSES obtained for the models with confirmed and total COVID-19 deaths. In both models, it is noted that a high socio-economic level protected against the risk of mortality due to COVID-19.
concluded that it remains a critical component of the outbreak control caution because they may not be COVID-19-related and, on the other hand, could be considered as one of the strengths of the study. This is the first population-based study on the evolution of the spatiotemporal pattern of COVID-19 mortality in the intra-urban setting of the largest city of Brazil. Using two different datasets, analysing the confirmed and confirmed plus suspected deaths separately, we were able to evaluate how uncertainty would impact the association between the RR and the socio-economic condition. The robust EW models clearly showed when the high risk of death shifted from areas with the best to those with the worst socio-economic conditions in the city of São Paulo. The risk of death was the highest among men aged >70 years; this is similar to data from China and the United States [27]. Recently, Souza et al. [3] analysed the Brazilian population and found that most COVID-19 deaths were of men and that the most frequent comorbidities were cardiovascular disease and diabetes. Behavioural factors, especially social status, that may prejudice adherence to lockdown measures, have been shown to be potentially crucial in determining susceptibility to SARS-CoV-2 [28,29]. This unequal death ratio in men may be interpreted considering many factors: the comparatively higher prevalence of comorbidities (i.e., hypertension, diabetes, cardiovascular disease, and chronic lung disease) [30], higher risk behaviours (i.e., smoking and alcohol use), occupational exposure [31], and sex differences in immune responses [32]. However, there may be other social and behavioural characteristics that favour women as reported in previous studies, which proposed that women are more likely than men to adopt hand hygiene practices [33] and to seek preventive care [34].

The spatial distribution of suspected and confirmed deaths due to COVID-19 in the city of São Paulo shows inequalities, with spatial dependence and positive correlation associated with socio-economic factors of the areas. This is remarkably similar to the results of Maciel et al. [35]. Our findings reveal that the socio-economic condition acts as a protective factor against the risk of mortality due to COVID-19. In the models considering only confirmed deaths and all deaths, an increase of one unit in the socio-economic indicator represented a 25% and 33% decrease in the risk of mortality, respectively. The first observation is that, when considering all deaths, the protective effect of the socio-economic level is more evident, showing that there must be a higher incidence of suspected deaths in the less favoured areas than in the most favoured areas (in areas with better socio-economic level). The spatial distribution of suspected and confirmed deaths due to COVID-19 in the city of São Paulo shows inequalities, with spatial dependence and positive correlation associated with socio-economic factors of the areas. This is remarkably similar to the results of Maciel et al. [35]. Our findings reveal that the socio-economic condition acts as a protective factor against the risk of mortality due to COVID-19. In the models considering only confirmed deaths and all deaths, an increase of one unit in the socio-economic indicator represented a 25% and 33% decrease in the risk of mortality, respectively. The first observation is that, when considering all deaths, the protective effect of the socio-economic level is more evident, showing that there must be a higher incidence of suspected deaths in the less favoured areas than in the most favoured areas (in areas with better socio-economic level). The spatial distribution of suspected and confirmed cases of COVID-19 and severe acute respiratory infection with unknown aetiology, with per capita income in the metropolitan region of São Paulo. They found that the COVID-19 cases were more associated with better levels than the latter. They pointed out because there is a delay in the confirmation of suspected cases, and consequently, some of the suspected deaths are later confirmed to be COVID-19-related deaths. Furthermore, some of the suspected cases would be considered as confirmed COVID-19-related deaths if the case definition was not strict (as the required test is often not available or is not performed within the appropriate window time). From this perspective, the amplitudes of variation in rates and RR obtained from confirmed and total deaths could be considered as lower and upper limits (or vice versa) for the magnitudes of these measures.

The elderly population represents one of the groups that are more prone to COVID-19 in the city of São Paulo. The risk of death was the highest among men aged >70 years; this is similar to data from China and the United States [27]. Recently, Souza et al. [3] analysed the Brazilian population and found that most COVID-19 deaths were of men and that the most frequent comorbidities were cardiovascular disease and diabetes. Behavioural factors, especially social status, that may prejudice adherence to lockdown measures, have been shown to be potentially crucial in determining susceptibility to SARS-CoV-2 [28,29]. This unequal death ratio in men may be interpreted considering many factors: the comparatively higher prevalence of comorbidities (i.e., hypertension, diabetes, cardiovascular disease, and chronic lung disease) [30], higher risk behaviours (i.e., smoking and alcohol use), occupational exposure [31], and sex differences in immune responses [32]. However, there may be other social and behavioural characteristics that favour women as reported in previous studies, which proposed that women are more likely than men to adopt hand hygiene practices [33] and to seek preventive care [34].

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The low socio-economic condition levels demonstrate not only the
vulnerability of the population but also the difficulties health services
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similar to the overall fragility expected from health services in Brazil
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Table 1
Number and mortality rates (per 100,000 inhabitants in fourteen weeks) of
suspected (severe acute respiratory syndrome - U04.9), confirmed (coronavirus
infection disease - B34.2), and total (U04.9 + B34.2) COVID-19 deaths, ac-
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bases, sex, and age. City of São Paulo, 11th to 24th epidemiological weeks, 2020.

| Sex       | Confirmed | Suspect | Total |
|-----------|-----------|---------|-------|
| Male      | 3350      | 2507    | 5857  |
|           | 593.9     | 44.4    | 103.6 |
|           | 3861      | 2228    | 6089  |
|           | 68.3      | 39.4    | 107.7 |
| Female    | 2524      | 2309    | 4833  |
|           | 40.6      | 37.1    | 77.7  |
|           | 2906      | 2099    | 5005  |
|           | 46.7      | 33.8    | 80.5  |
| Total     | 5875      | 4818    | 10,693|
|           | 49.5      | 40.6    | 101.1 |
|           | 6768      | 4330    | 11,098|
|           | 57.0      | 36.5    | 93.5  |

Fig. 3. Posterior means of the temporal relative risks (RR) of COVID 19. City of
São Paulo, 12th to 24th Epidemiological Week, 2020.

Fig. 4. Posterior means of the spatiotemporal relative risks (RR) for confirmed
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103 destinations across 30 countries [37].

Airport, which is the largest in Brazil, with non-stop passenger flights to
is the most populated city in the country, with approximately 12 million
transmission. The city of São Paulo is particularly vulnerable because it
worsened sanitary conditions [47]. This probably explains its fast
started to circulate in the suburbs of the city, with high population density and
epidemic. After these first cases in the richest areas, the virus started
fourth week onwards, when the worst socio-economic level became a
risk factor. Similarly, Souza et al. [3] showed a higher risk of diagnosed
COVID-19 cases in census tracts with higher per capita income in the São
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is the most populated city in the country, with approximately 12 million
inhabitants [48], and it is highly connected with other countries
worldwide via its main airport, the São Paulo-Guarulhos International
Airport, which is the largest in Brazil, with non-stop passenger flights to
103 destinations across 30 countries [37].

In this study, we used SIM instead of the SIVEP Gripe database,
unlike other studies [3]. The recommendation of the State Health
Department [49] to register the notification of death and the monitoring
of mortality using SIM, in practice, leads to a time-lapse between the
event and the use of information. COVID-19 mortality data were
improved in the city of São Paulo with PRO-AIM, using the Laboratory
Environment Manager System (GAL) and Flu Surveillance Information
System (Sivep Gripe). These characteristics, combined with the possi-
ability of assessing home or unattended deaths, motivated the option of
using SIM data (which considered the confirmed and suspected di-
agnoses in analysing mortality due to COVID-19). It is necessary to
emphasise that the recommendation to register confirmed and suspected
deaths due to COVID-19 [49] (that motivated the change of the codes
assigned by the health services since the beginning of the crisis, and
which is applied by SMS-SP to monitor the evolution of events) has not
been applied yet.

Our study findings must be considered in the context of several as-
sumptions and data limitations. We associated patients’ addresses or
postcode to the area-based socio-economic conditions using geo-
localisation. This may provide some insight into the likelihood of
exposure to health factors and COVID-19 risks. This approach is
frequently used as representative of individual socio-economic condi-
tions. Nevertheless, they are not a perfect picture of the individuals’
conditions, and they could underestimate the magnitude of social
disproportion related to individual social measures [50]. Rather, they
are best employed along with individual-level variables to reflect
geographical or aggregate-level risks [38]. We highlight that our spatial
analysis is subject to methodological limitations caused by ecological
fallacy and the modifiable areal unit problem. These constraints are
intrinsic to any spatial analysis that uses aggregated data [51]. Despite
these, our study still contributes to healthcare planning measures and to
future precision studies focusing on the effects of social health factors on
COVID-19 deaths. In addition, one of the strengths of our study was that
it dealt with COVID-19 deaths instead of the cases (owing to the better
accuracy and coverage of the data). When we consider only the cases,
many asymptomatic cases may not be reported and this could hamper
the conclusions.

5. Conclusions

We used models with spatial and spatiotemporal architectures to
investigate the patterns of confirmed and total (confirmed and sus-
p ected) COVID-19 deaths in the city of São Paulo. The obtained results,
after considering both categories, showed differences regarding the
magnitude of the rates and RR. However, there were no differences with
respect to the derived conclusions. The risk of mortality due to COVID-
19 was the highest between the 20th and 23rd EW, followed by an

Table 2

| COVID-19 deaths | Covariate | RR posterior means | 95% Credible Interval (CI) |
|-----------------|-----------|--------------------|----------------------------|
|                 |           | 0.025  | 0.975 quantil | quantil |
| Confirmed       | Intercept | 0.82   |               |        |
|                 | GeoSES    | 0.75   | 0.69          | 0.82   |
| Total           | Intercept | 0.74   | 0.71          | 0.77   |
|                 | GeoSES    | 0.67   | 0.62          | 0.72   |

This may be because all the infected subjects had been abroad [46]. In
the first two weeks, the best socio-economic conditions was presented as
a risk factor. Then, there was a change in the spatial pattern from the
fourth week onwards, when the worst socio-economic level became a
risk factor. Similarly, Souza et al. [3] showed a higher risk of diagnosed
COVID-19 cases in census tracts with higher per capita income in the São
Paolo metropolitan region during the early phase of the COVID-19 epidemic. After these first cases in the richest areas, the virus started
circulate in the suburbs of the city, with high population density and
worsened sanitary conditions [47]. This probably explains its fast
transmission. The city of São Paulo is particularly vulnerable because it
is the most populated city in the country, with approximately 12 million
inhabitants [48], and it is highly connected with other countries
worldwide via its main airport, the São Paulo-Guarulhos International
Airport, which is the largest in Brazil, with non-stop passenger flights to
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5. Conclusions

We used models with spatial and spatiotemporal architectures to
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19 was the highest between the 20th and 23rd EW, followed by an

Fig. 5. Posterior means of the spatiotemporal relative risks (RR) for total COVID-19 deaths by sample areas of the city of São Paulo, 12th to 24th Epidemiology Weeks, 2020.

Fig. 6. Posterior means of the relative risks and 95% credible interval for the socio-economic covariate obtained with spatial models for confirmed and total COVID-19 deaths, according to each one of the epidemiologic weeks. City of São Paulo, 12th to 24th Epidemiology Week, 2020.
apparent stabilisation of the temporal trend. However, we did not rule out a possible future rise in mortality. A high socio-economic level was shown to protect against the risk of mortality due to COVID-19 throughout the study period. However, this was not a uniform pattern, since we identified a shift in the risk of mortality due to COVID-19 in the city of São Paulo over time. We had the highest risk in the best socio-economic contexts during the first two EWs that then shifted to the worst contexts from the 16th EW. Concerning sex and age, men and elderly individuals were at the highest risk of mortality due to COVID-19. Our study corroborated the relationship between COVID-19 mortality and socio-economic conditions, revealing the importance of integrating geographic screening, in areas with higher risk of death, when planning better actions to face the pandemic.

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CRediT authorship contribution statement

Patricia Marques Moralejo Bermudi: Data curation, Formal analysis, Methodology, Software, Writing - original draft, Writing - review & editing.
Camila Lorenz: Investigation, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing.
Breno Souza de Aguiar: Conceptualization, Data curation, Validation, Visualization, Writing - original draft, Writing - review & editing.
Marcelo Antunes Failla: Conceptualization, Data curation, Validation, Visualization, Writing - original draft, Writing - review & editing.
Ligia Vizeu Barroso: Conceptualization, Investigation, Project administration, Supervision, Validation, Visualization - original draft, Writing - review & editing.
Francisco Chiaraavalli-Neto: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Supervision, Writing - original draft, Writing - review & editing.

Declaration of competing interest

I declare no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tmaid.2020.101945.

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