Association of high ambient temperature with daily hospitalization for cardiorespiratory diseases in Brazil: A national time-series study between 2008 and 2018

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Abstract

Further research is needed to examine the nationwide impact of temperature on health in Brazil, a region with particular challenges related to climate conditions, environmental characteristics, and health equity. To address this gap, in this study, we looked at the relationship between high ambient temperature and hospital admissions for circulatory and respiratory diseases in 5,572 Brazilian municipalities between 2008 and 2018. We used an extension of the two-stage design with a case time series to assess this relationship. In the first stage, we applied a distributed lag non-linear modeling framework to create a cross-basis function. We next applied quasi-Poisson regression models adjusted by $PM_{2.5}$, O_3, relative humidity, and time-varying confounders. We estimated relative risks (RRs) of the association of heat (percentile 99^{th}) with hospitalization for circulatory and respiratory diseases by sex, age group, and Brazilian regions. In the second stage, we applied meta-analysis with random effects to estimate the national RR. Our study population includes 23,791,093 hospital admissions for cardiorespiratory diseases in Brazil between 2008 and 2018. Among those, 53.1% are respiratory diseases, and 46.9% are circulatory diseases. The robustness of the RR and the effect size varied significantly by region, sex, age group, and health outcome. Overall, our findings suggest that i) respiratory admissions had the highest RR, while circulatory admissions had inconsistent or null RR in several subgroup analyses; ii) there was a large difference in the cumulative risk ratio across regions; and iii) overall, women and the elderly population experienced the greatest impact from heat exposure. The pooled national results for the whole population (all ages and sex) suggest a relative risk of 1.29 (95% CI: 1.26; 1.32) associated with respiratory admissions. In contrast, national meta-analysis for circulatory admissions suggested robust positive associations only for people aged 15-45, 46-65, >65 years old; for men aged 15-45 years old; and women aged 15-45 and 46-65 years old. Our findings are essential for the body of scientific evidence that has assisted policymakers to promote health equity and to create adaptive measures and mitigations.

Keywords

Temperature; Heat; Hospitalization; Respiratory diseases; Cardiovascular diseases

1. INTRODUCTION

Exposure to high ambient temperature has been linked to increased risk of several adverse health outcomes, causing significant excess morbidity and mortality (Phung et al., 2016). Between 2000 and 2019, non-optimal ambient temperatures were associated with more than 5 million deaths per year globally, of which 0.91% of all deaths were related to heat exposure (Zhao et al., 2021). Cardiorespiratory diseases have often been identified as an important public health concern in the context of climate-related health effects (Carreras et al., 2015; Ferreira et al., 2019; Jacobson et al., 2021), given that exposure to extreme temperatures may disturb heart rate (Kaldur et al., 2016), change blood pressure (Radin et al., 2018), increase respiratory infections (D'Amato et al., 2018), and contribute to the development of chronic conditions such as chronic obstructive pulmonary disease – COPD (Tsuji et al., 2019).

So far, multiple investigations of the health effects of ambient temperature were essential for the creation of the initial body of solid scientific evidence that has helped policymakers to create adaptive measures and mitigations (Tong and Ebi, 2019). However, there is still a gap in the literature, given that most of the studies were performed in the USA, numerous European countries, China, and Australia (Rocque et al., 2021; Song et al., 2017). According to a review study focused on South America (de Sousa et al., 2018), in the year 2018, there were very few climate-related health effects studies in the continent, which Brazil, the most studied country in the region, had only 8 investigations. Among those investigations in Brazil, dengue was the main outcome, and only 2 studies considered cardiorespiratory diseases (de Souza et al., 2012; Kleinfelder et al., 2009). To update this review study in South America, we searched the literature for studies related to cardiorespiratory hospital admissions in Brazil after 2018. We found 5 studies, of which two looked at the association between heatwaves and risk of hospitalization in 1,814 Brazilian municipalities (Zhao et al., 2019f, 2019d); one focused on heat exposure and hospitalization for Chronic Obstructive Pulmonary Disease (COPD) in 1,642 municipalities (Zhao et al., 2019b); and other two studies focused on the associations between temperature variability and hospitalization for cardiac arrhythmia (Zhao et al., 2019a) and ischemic heart disease (Zhao et al., 2019g) in 1,814 Brazilian municipalities. More investigations are still required in South America, particularly in Brazil, in order to promote health equity under global scenarios suggesting that extreme temperature events will continue increasing their magnitude, intensity, and frequency (Fiore et al., 2012; IPCC, 2014; Mahowald, 2011).

From a methodological point of view, there is still a lack of studies related to cardiorespiratory hospital admissions in Brazil that consider: i) a study population from all Brazilian municipalities (total 5,572), since the Brazilian studies mentioned above have accounted only for part of the country, less than 50% of the total municipalities; and ii) a modeling framework that considers covariates related to air quality and humidity, since the literature from other countries has suggested these variables as important control factors for the association between health outcomes and weather (Danesh Yazdi et al., 2022; Weinberger et al., 2021), and there is no study in Brazil to date that accounts for these covariates.

Besides the methodological gap, there are the public health issues. First, there are significant differences in the quality of health/environment and health care among different population groups in Brazil, which negatively affects health/environment equity. Second, cardiorespiratory diseases represent a large fraction of the Brazilian burden of diseases. According to the Ministry of Health in Brazil, in 2020 circulatory and respiratory diseases were responsible for 357,741 and 148,773 deaths, respectively. By comparison, according to the World Health Organization (WHO, 2014), in 2012 circulatory and respiratory diseases were responsible for 17.5 and 4 million deaths globally, respectively.

Therefore, further research is needed to examine the nationwide impact of temperature on health in Brazil, a region with particular challenges related to climate conditions, environmental characteristics, and health equity. This is essential to help policymakers to promote health equity and create adaptive measures and mitigations. To address this gap, in this study we examined the association (controlling for spatiotemporal variation, air pollution, and relative humidity) of high ambient temperature with daily hospital admissions for circulatory and respiratory diseases in 5,572 Brazilian municipalities between 2008 and 2018.

2. MATERIALS AND METHODS

2.1. Hospital admission data

Hospital admission data were provided by Brazilian Ministry of Health. We accessed individual hospitalizations nationwide in Brazil at a municipality-level over 11 years (January 1, 2008, and December 31, 2018). Our sample included 129,978,694 hospitalization records (all cases).

Hospital admission data included the date of the event, home municipality, age, sex, and principal diagnosis according to the International Classification of Diseases, version 10 (ICD-10) codes. There are 5,572 municipalities in Brazil, which are grouped into five regions: North, Northeast, Midwest, Southeast, and South (Figure S1).

We accounted only for hospitalizations due to respiratory diseases (ICD-10 codes J00-J99) and circulatory diseases (ICD-10 codes I00-I99). This filter yielded 12,621,970 (9.71% of the total hospitalizations in Brazil) records of hospitalizations for respiratory diseases and 11,169,123 (8.59% of the total hospitalizations in Brazil) hospitalizations for circulatory diseases.

We grouped the hospital admission data by summing the number of hospitalizations for each municipality and the date between January 1, 2008, and December 31, 2018. We also stratified the number of hospitalizations by sex and age group (15-45, 46-65, and >65 years). Each group representing the number of hospitalizations consists of a complete time series of equally distributed observations in each municipality and on each day of the study period.

2.2. Temperature data

Temperature data was retrieved from satellite remote sensing, specifically from the European Centre for Medium-Range Weather Forecasts (ECMWF). The data includes surface temperature (°C) derived from ERA5-Land, with a spatial resolution of 9km and temporal resolution of 6 hours. Brazil has a total land area of approximately 8,515,767 km^2. The smallest municipality in terms of land area is located in the state of Minas Gerais (Southeast region), with a land area of 3.5 km^2, while the largest is located in the state of Pará (North region), with a land area of 159,533 km^2. On average, a municipality in Brazil has a land area of approximately 1,526 km^2, with a standard deviation of 3,465 km^2. The median land area of a municipality in Brazil is approximately 487 km^2.

We calculated the daily mean temporal resolution for surface temperature. Finally, we aggregated the temperature data to the municipality level using a zonal mean, taking into account the geographic location of the boundaries of each Brazilian municipality.

2.3. Covariates

We considered two groups of covariates – air pollutants and weather conditions. For air pollutants, we considered particulate matter with an aerodynamic mass diameter below 2.5 μm

($PM_{2.5}$), measured in µg/m³; and tropospheric ozone (O_3), measured in ppb. Air pollution data were also obtained from satellite observations by ECMWF. The ECMWF employs the Copernicus Atmosphere Monitoring Service (CAMS). The CAMS service runs ensemble models using several satellite observations and emission inventories amongst other predictors.

The air pollution data have a spatial resolution of 12.5 km and a temporal resolution of 6 hours. We calculated the temporal resolution for the daily mean and then aggregated the data by the municipality using a zonal mean. For weather conditions, we considered relative humidity (%), which had the same source and spatiotemporal resolution as for the temperature data.

The validation for the CAMS global model is reported by (Inness et al., 2018). Particularly for $PM_{2.5}$, they validate the CAMS global model using ground observations from the Aerosol Robotic Network (AERONET). AERONET has over 500 stations worldwide that measure spectral Aerosol Optical Depth (AOD) using sun photometers. Approximately 27 AERONET stations are located in Brazil. The validation estimates the mean bias and standard deviation of the satellite's instruments (included in the CAMS model for aerosols) relative to AERONET data. In South America, the bias of the satellite's instruments is slightly smaller, with an approximate bias of -0.006 ± 0.128. Another investigation shows that the CAMS estimates in South America have a root mean square error (RMSE) of 0.268 (compared to AERONET stations) (Gueymard and Yang, 2020). Previous studies have shown that AERONET observation sites in South America have significant representativity for AOD measured by Moderate Resolution Imaging Spectroradiometer (MODIS) aboard TERRA and AQUA satellites (Hoelzemann et al., 2009), which is an instrument included in the CAMS model.

The relationship between AOD and $PM_{2.5}$ is based on the remote sensing process of detecting aerosols (fine solid and/or liquid particles suspended in the air). In short, the radiation interacts with aerosols in the atmosphere resulting in distortion. This distortion is estimated by the radiative transfer model and can be converted into aerosol loading, defined as AOD (Kumar et al., 2007). Given that AOD and $PM_{2.5}$ are based on the primary source (presence of aerosols in the atmosphere), there is a strong positive relationship between AOD and $PM_{2.5}$. Several studies have explored this relationship (Naresh, 2010; Xie et al., 2015; Xu and Zhang, 2020; Yang et al., 2019). Models predicting fine particle using AOD retrievals and ground-based measurements have reported good performance across regions worldwide, including a cross-validated R^2 of 0.73 in Switzerland (de Hoogh et al., 2018), 0.87 in China (Hu et al., 2019), 0.88 in Northeastern USA

(Kloog et al., 2014), and 0.82 in Brazil (Gonçalves et al., 2018). The CAMS global model is considered one of the strongest models used in air pollution and epidemiological studies.

Several other studies have used ECMWF data as source for $PM_{2.5}$ and meteorology predictions (temperature and humidity), including investigations in i) Portugal on the association between prevailing circulation patterns and particles - PM_{10} and $PM_{2.5}$ (Cavaleiro et al., 2021), ii) Bavaria, Germany, on the relationship between weather variables and ambulatory visits due to chronic obstructive pulmonary disease (Ferrari et al., 2012), iii) Africa on potential predictability of malaria (Tompkins and di Giuseppe, 2015), and iv) in Brazil on the potential for a dengue epidemic during the 2014 World Cup (Lowe et al., 2014) and on the associations of PM2.5-related wildfire emissions and hospital admissions (Weeberb J Requia et al., 2021), birth weight (Requia et al., 2022a), preterm birth (Requia et al., 2022b), and birth defects (Weeberb J. Requia et al., 2021).

Regarding the validation of O_3, it was made by comparing the reanalysis data with surface measurements from observations from the WMO's Global Atmosphere Watch (GAW) program (Galbaly et al., 2013). Their findings support that mean CAMS reanalysis O_3 agrees with the surface data to within 10% for most years and has a smaller bias in the period after 2003.

2.4. Statistical analysis

We used an extension of the two-stage design with a case time series (Gasparrini et al., 2022) to assess the association of low and high ambient temperature with daily hospital admissions for circulatory and respiratory diseases in Brazil between 2008 and 2018. Specifically, we performed the first stage by Brazilian region by using municipality-level series. In the second stage, we estimated the national effects. The statistical analysis in each stage is explained below.

In the first stage, we applied a distributed lag non-linear modeling (DLNM) framework (Gasparrini et al., 2010) to create a cross-basis function. This function represents an association with ambient temperature, allowing non-linearity and temporal dependencies through the lag component. We defined the cross-basis function with natural cubic splines for the temperature exposure-response, and two internal knots (at the 10^{th}, 75^{th}, and 90^{th} temperature percentiles) to represent non-linearity in the exposure-response relationships. We accounted for the lagged effect of temperature up to 3 days of lag (0-3 days) by using interger as parameterization function. This lag was chosen based on a previous study in Brazil on ambient heat and hospitalization for COPD

(Zhao et al., 2019c). Although this choice has a support in the literature, we are aware that this is still a sensitive decision, given that other studies have chosen other lags, including 7 days of lag and even more. Therefore, in the sensitivity analysis we tested the robustness of our results by considering other lags (this is detailed below). Finally, given that this is a time series data, in this cross-basis function, we accounted for a list of municipalities defining groups of observations. All these parameters for the cross-basis function were chosen based on the Akaike Information Criterion (AIC).

Then, we included the cross-basis function in a generalized conditional quasi-Poisson regression model, controlling for $PM_{2.5}$, O_3, relative humidity, and time-varying confounders. The confounding effect of long-term trends was modeled through smooth function of the year (natural splines with knots every 3 years). Also, in the quasi-Poisson model, we defined a stratum to control for temporal trends and seasonality within each municipality. We used a time-stratified sampling to define strata based on the day of the week, month, calendar year, and municipality of the time series.

The analyses were stratified by sex, age group (15-45, 46-65, and >65 years), health outcome (respiratory and circulatory hospital admissions), and Brazilian regions (North, Northeast, Midwest, Southeast, and South). We estimated specific relative risks (RRs) and 95% confidence interval (CI) for each one of these sub-group analyses. The RRs were derived over 3 days of lag (overall cumulative effect) at extreme percentile defined as 99th to represent the extreme heat associations. Here, we used the temperature of minimum risk of hospitalizations (MRH) as reference, defined as the risk increment at percentiles 1st and 99th of the joint temperature distribution relative to MRH.

In the second stage, we applied meta-analysis to estimate the RRs at the national level. Heterogeneity was examined using the I-squared (I^2) statistic. A p-value >0.05 and/or I^2 <50% was considered homogeneous.

We used R software, version 4.0.2, including the R packages “dlnm” (Distributed Lag Non-Linear Models) for the distributed lag modeling framework, “gnm” (Generalized Nonlinear Models) for the generalized conditional quasi-Poisson regression model, and “mixmeta” for the meta-analysis.

2.5. Sensitivity analysis

We performed sensitivity analysis by changing some modeling assumptions. First, we adjusted the model only for temporal trends by removing the control for $PM_{2.5}$, O_3, and relative humidity. Then, we tested a model controlling only for $PM_{2.5}$, another model with only O_3, and another one controlling only for humidity. Finally, we tested the sensitivity of our results by changing 5, 7, 10, 15, 20, 25, and 30 days of lag.

3. RESULTS

Our study population includes 23,791,093 hospitalizations for circulatory and respiratory diseases in Brazil between 2008 and 2018. Among those, 12,621,970 (53%) were people hospitalized due to respiratory diseases 11,169,123 (47%) due to circulatory diseases. Men were the most affected group, representing 52.7% for respiratory admissions and 50.2% for circulatory admissions. For the age group, patients aged >65 had the highest proportion, with 25.8% hospitalized due to respiratory diseases and 45.1% due to circulatory diseases (Table 1).

Table 2 provides the descriptive statistics for temperature and the covariates (relative humidity and air pollutants) in Brazil during our study period. Between 2008 and 2018, the mean ambient temperature was 23.59°C (sd = 3.79°C), with a minimum of 1.25°C and a maximum of 34.92°C. Relative humidity had a mean of 77.76% (sd = 13.64%). For air pollutants, we estimated a mean concentration of 10.01μg/m³ (sd = 8.28μg/m³) for $PM_{2.5}$ and 20.07ppb (sd = 7.01ppb) for O_3 (Table 2). Figure 1 shows Brazil's spatial distribution of ambient temperature and hospital admissions in the study period.

Table 1 – Descriptive characteristics of hospital admission events in Brazil, 2008-2018.

Health outcome	Age	Number of hospital admissions (%)[1]		
		Men	**Women**	**All sex**
Respiratory hospital admissions	15-45	1,029,372 (8.16)	1,023,403 (8.11)	2,052,775 (16.26)
	46-65	988,490 (7.83)	910,468 (7.21)	1,898,958 (15.04)
	>65	1,630,513 (12.92)	1,632,364 (12.93)	3,262,877 (25.85)
	All ages[2]	6,646,890 (52.66)	5,975,080 (47.34)	12,621,970 (100)
Circulatory hospital admissions	15-45	790,658 (7.08)	1,026,640 (9.19)	1,817,298 (16.27)
	46-65	2,362,171 (21.15)	2,052,674 (18.38)	4,414,845 (39.53)
	>65	2,516,053 (22.53)	2,522,032 (22.58)	5,038,085 (45.11)
	All ages[2]	5,611,256 (50.24)	5,557,867 (49.76)	11,169,123 (100)

Notes: [1] the percentages were based on the total number of hospital admissions in Brazil between 2008 and 2018, which for respiratory hospital admissions were 12,621,970 cases, and for circulatory admissions were 11,169,123 cases. [2] this includes people under 15 years old.

Table 2 – Summary statistics for temperature and covariates (humidity and air pollutants) in Brazil, 2008-2018.

Variable	**Min**	**Q1**	**Mean**	**SD**	**Q3**	**Max**
Temperature (°C)	1.25	21.60	23.59	3.79	26.23	34.92
Relative humidity (%)	20.00	69.75	77.76	13.64	88.50	100
$PM_{2.5}$ (µg/m³)	3.03	5.05	10.01	8.28	11.85	61.35
O_3 (ppb)	3.36	15.22	20.07	7.01	24.77	39.15

Note 1: summary statistics were calculated considering the values at the municipality level averaged across the entire country in the study period.

Note 2: Minimum (Min), first quartile (Q1), standard deviation (SD), third quartile (Q3), and maximum (Max).

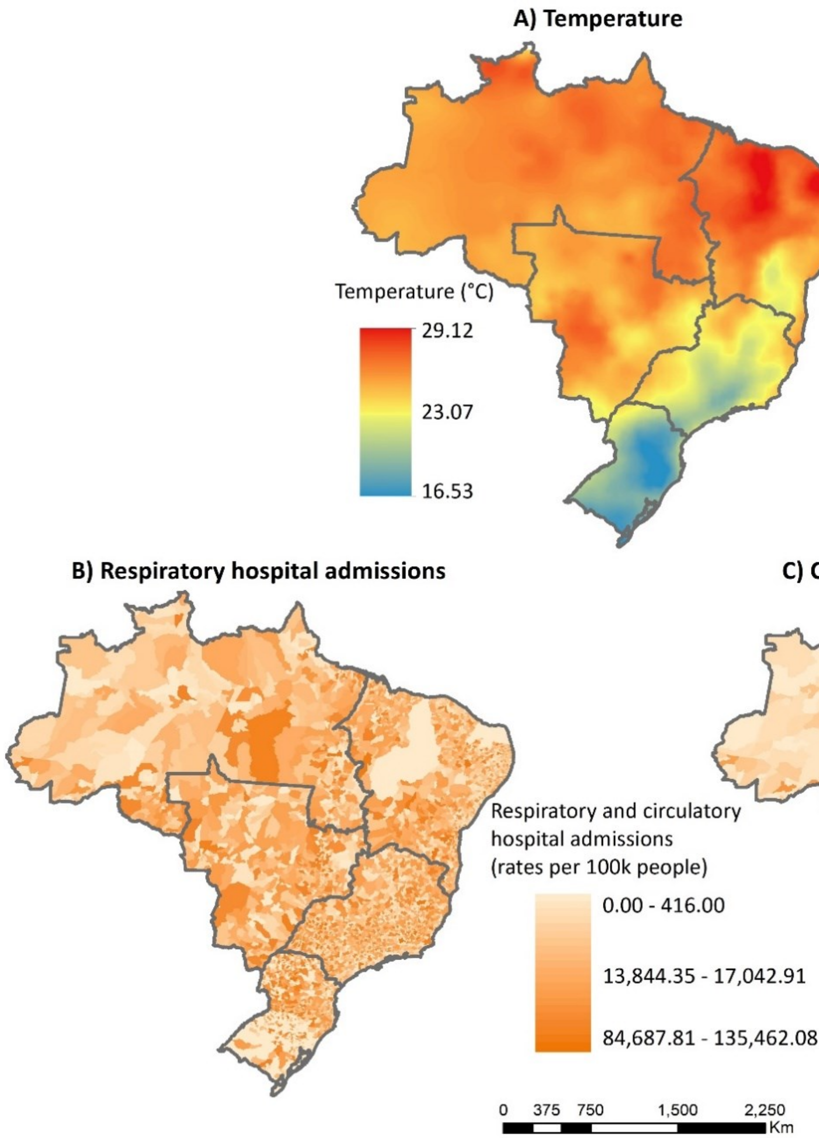

Figure 1 – Spatial variation of ambient temperature (average between 2008-2018) and cardiorespiratory hospital admissions (sum between 2008-2018) in Brazil. Note 1: the polygons in gray represent the Brazilian regions. Note 2: we used the total population in each municipality to calculate the rates.

Figure 2 shows the overall cumulative effect over 3 days of lag for heat (percentile 99^{th}) exposure to ambient temperature in Brazil (results from meta-analysis). The results indicate robust positive associations for respiratory hospital admissions in all subgroup analyses during heat exposure. The pooled national results for the whole population (all ages and sex) suggest a relative risk of 1.29 (95% CI: 1.26; 1.32) associated with respiratory admissions during heat exposure (Figure 2). In contrast, national meta-analysis for circulatory admissions suggested robust positive associations only for people aged 15-45, 46-65, >65 years old; for men aged 15-45 years old; and women aged 15-45 and 46-65 years old (Figure 2). For circulatory admissions, the pooled national RR for the whole population was 1.01 (95% CI: 0.99; 1.02). We present in the Supplementary Materials (Table S2) all the national average relative risk (from the primary analysis, for all sub-group analyses) along with the estimated heterogeneity test from the meta-analysis.

There is consistency between the results of the primary analysis and the results of the sensitivity analysis that considered different covariates in the statistical model (Figure S2). Overall, the primary coefficients (model adjusted for $PM_{2.5}$, O_3, humidity, and temporal factors) associated with cardiorespiratory admissions (Figure S2, panel A) are stable across the different models, including model adjusted only for $PM_{2.5}$ (Figure S2, panel B), model adjusted only for O_3 (Figure S2, panel C), model adjusted only for humidity (Figure S2, panel D), and model adjusted only for temporal terms (Figure S2, panel E). In contrast, the results from our primary analysis (3 days of lag) were sensitive to different lags (Figure S3). Overall, we can observe that the higher lags (5, 7, 10, 15, 20, 25, and 30 days of lag) the higher inconsistency of the coefficients (Figure S3). Table S3 in Supplementary Materials shows all the RR values at national level from the primary model and sensitivity analysis (different covariates and different lagas for all subgroups and health outcomes.

Figure 3 shows the overall cumulative effect (primary model) over 3 days of lag in each Brazilian region. The reference of the RR in Figure 3 is based on the minimum risk temperature (MRT), which is reported in Supplementary Materials (Table S1) with all the coefficients (RR) for all sub-group analyses and health outcomes. The results suggest a substantial increase in hospital admission risk for respiratory diseases (all ages and sex) in all regions, with relative risks reaching 1.26 (95% CI: 1.21; 1.31) in the North region, 1.27 (95% CI: 1.24; 1.30) in the Northeast, 1.35 (95% CI: 1.31; 1.40) in the Midwest, 1.30 (95% CI: 1.28; 1.31) in the Southeast, and 1.28 (95% CI: 1.25; 1.31) in the South region. For circulatory diseases (all ages and sex), we found robust associations only in the South region [1.05 (95% CI: 1.02; 1.07)] and Southeast region [1.02 (95% CI: 1.01; 1.03)] (Figure 3). Table S4 in Supplementary Materials shows all the RR values from the primary model and sensitivity analysis (different covariates and different lags) for all sub-groups, health outcomes, and regions.

In Figure S4, we show the bi-dimensional exposure-lag-response association stratified by regions for circulatory and respiratory admissions and for the overall analysis (all ages and sex). Note that Figure 4 only illustrates a summary of the association between ambient temperature and hospital admissions over the lags 1-3 with limited ability to inform inferential information, given that the uncertainty is not shown in the 3-D charts. In Figure 4, we show the overall cumulative exposure-responses.

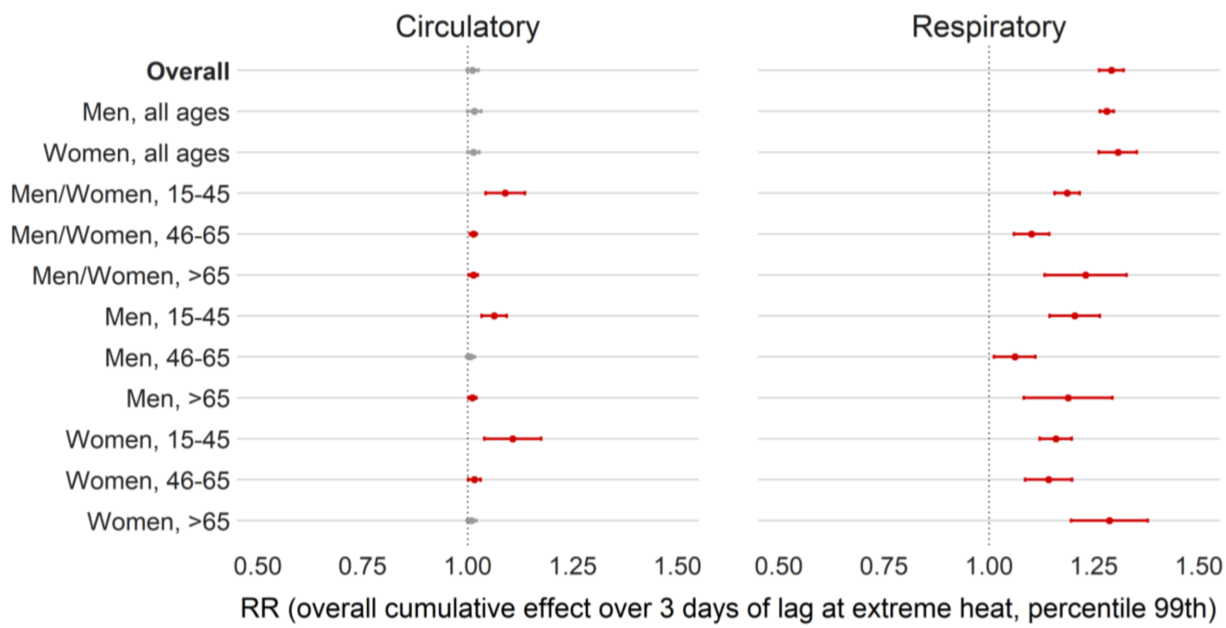

Figure 2 - Relative risks (95%CI) heat (percentile 99th) exposure in Brazil (results from meta-analysis) stratified by health effects, age, and sex.

Note 1: This is the overall cumulative effect over 3 days of lag (summing all the contributions up to the maximum lag).

Note 2: gray color represents the insignificant coefficients (which the RR includes the value 1) and red color represents the significant positive associations.

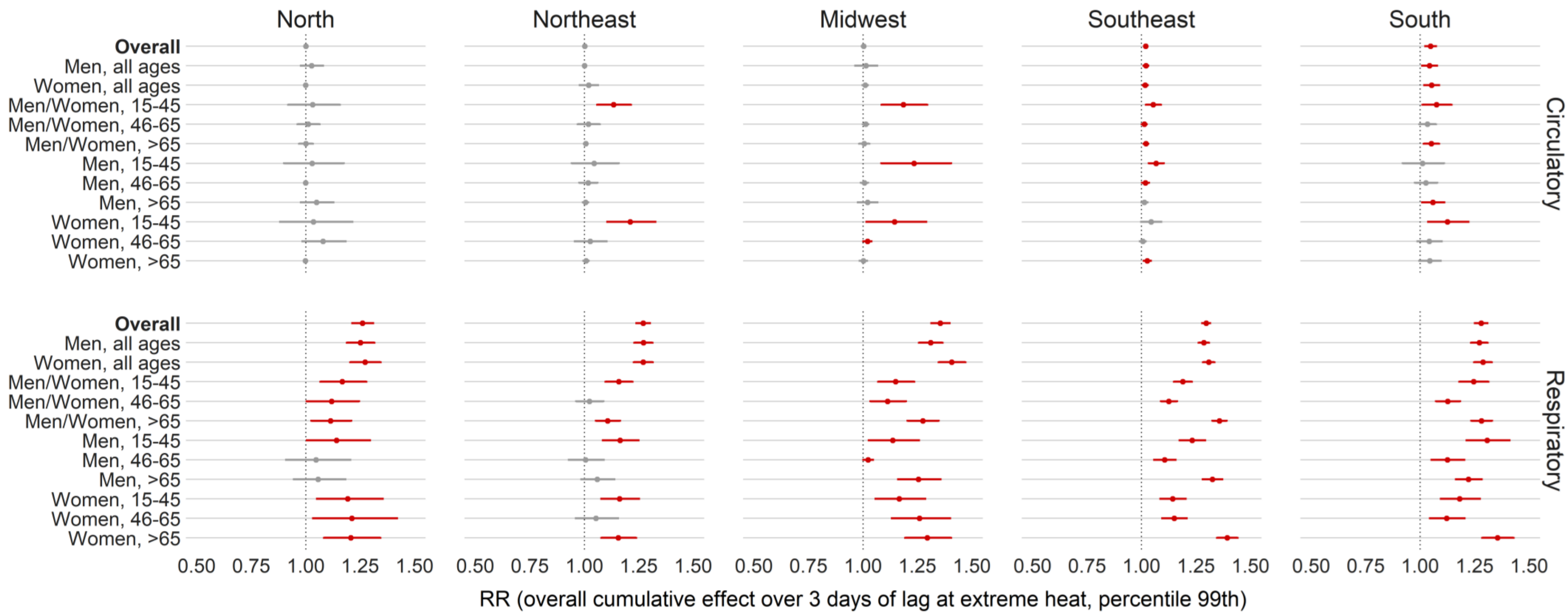

Figure 3 – Relative risks (95%CI) for heat (percentile 99[th]) exposure stratified by regions, health effects, age, and sex.

Note 1: This is the overall cumulative effect over 3 days of lag (summing all the contributions up to the maximum lag).
Note 2: gray color represents the insignificant coefficients (which the RR includes the value 1) and red color represents the significant positive associations.
Note 3: The reference of the RR is based on the minimum risk temperature (MRT), which varied depending on the subgroup analysis. It varied from 23 to 31°C in the North region, 21 to 31°C in the Northeast, 16 to 31°C in the Midwest, 14 to 26.9°C in the Southeast, and 8 to 9.4°C in the South. In Table S1, we show the MRT for each subgroup.

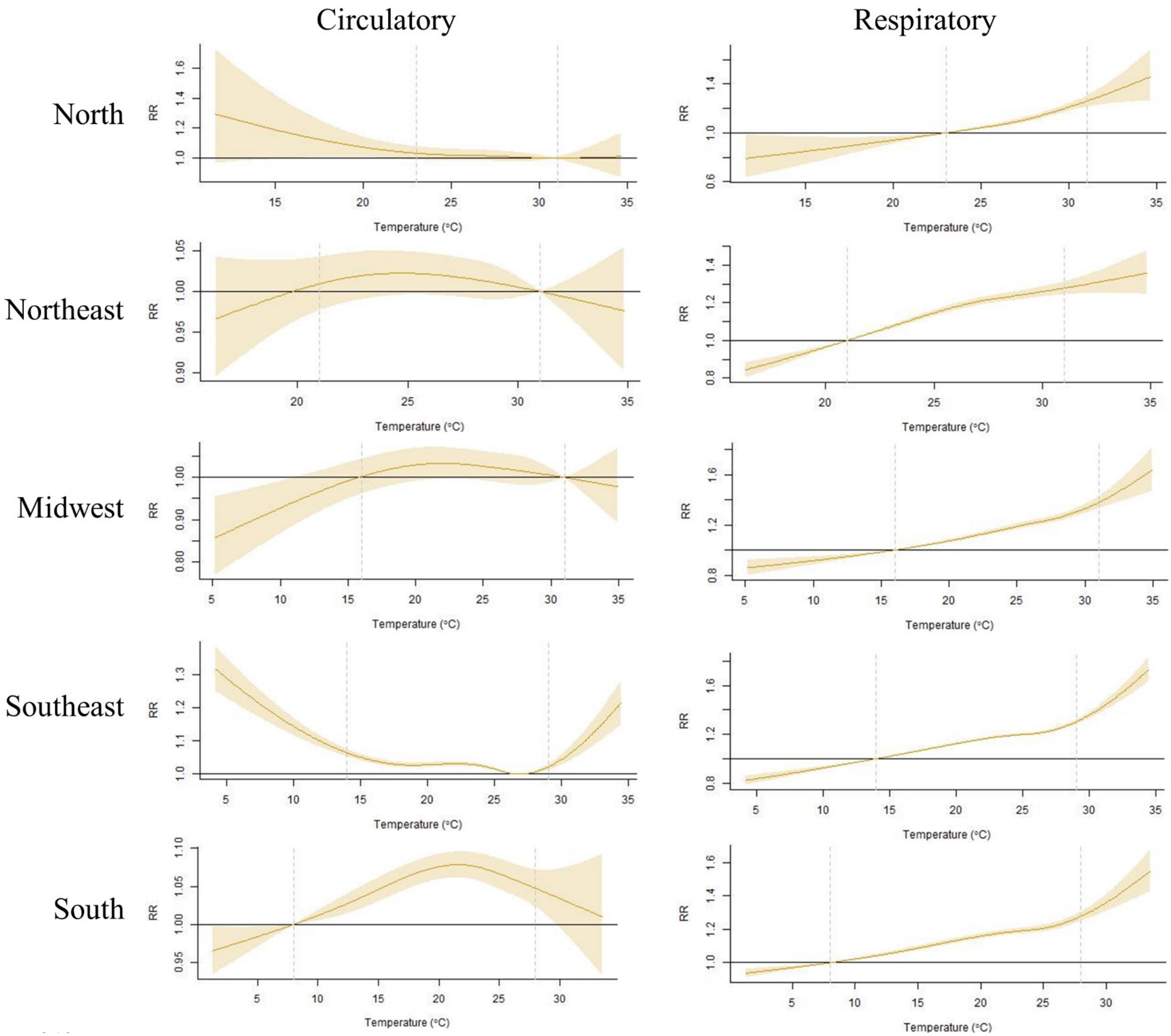

Figure 4- Cumulative risk ratio (95%CI) in ambient temperature for circulatory and respiratory hospital admissions for the overall population. Charts are stratified by health outcome and regions.

Note 1: The reference of the RR is based on the minimum risk temperature (MRT), which for circulatory diseases is 30.8°C in the North region, 31°C in the Northeast, 31°C in the Midwest, 26.9°C in the Southeast, and 8°C in the South. For respiratory diseases, it is 23°C in the North region, 21°C in the Northeast, 16°C in the Midwest, 14°C in the Southeast, and 8°C in the South.

Note 2: Vertical lines indicate the 1st and 99th percentile.

4. DISCUSSION

Our results indicate substantial association of high ambient temperature with daily hospitalization for cardiorespiratory diseases in Brazil. The robustness of the RR and the effect size varied significantly by region, sex, age group, and health outcome (circulatory and respiratory admissions). Overall, our findings suggest that i) the highest RR occurred for respiratory admissions; ii) the RR in several subgroup analyses for circulatory admissions was either null or inconsistent; iii) there is a large difference in the cumulative risk ratio (curves shown in Figure 4) between regions; and iv) overall, women and the elderly population were the most impacted by heat exposure.

Our findings are consistent with the literature. In Spain (Iñiguez et al., 2021), the pooled overall heat effect for circulatory hospitalizations had a null relative risk [in our study it was null too] and with no statistical significance for respiratory admissions (RR = 1.04, 95% CI: 0.97;1.11) [in our study it was 1.29 (95% CI: 1.26; 1.32)]. Similar to our study and this study in Spain, which the risk for circulatory diseases was mostly statistically insignificant, in California, USA, robust associations related to heat wave was found only for respiratory admissions [1.09 (95% CI: 1.07; 1.12] (Sherbakov et al., 2018). In contrast, a recent national study in the USA did not find robust associations for either circulatory or respiratory admissions (Bernstein et al., 2022).

Previous studies in Brazil also found similar results. Xu et al. (2020), (Zhao et al., 2019e), and (Zhao et al., 2019f) looked at the associations between heat exposure and hospitalizations in Brazil and observed either protective effect or inconsistent associations for circulatory admissions and robust positive associations for respiratory diseases. They also found a wider confidence interval with a larger margin of error in the North region. We observed the same issue in our analysis (Figure 3). We suggest that this is a result of a smaller sample size and a higher variability in the North region. Another study by Xu et al. (2020) and (Zhao et al., 2019e) found that the attributable burden was greatest in the Midwest and Northeast. In our study, Midwest had the highest RR as well [1.35 (95% CI: 1.31; 1.40)], while Northeast and North had the lowest RR, 1.27 (95% CI: 1.24; 1.30) and 1.26 (95% CI: 1.21; 1.31), respectively. The literature has shown mixed results related to the spatial variability of the risk. Another Brazilian study, for example, focused on the association between ambient heat and hospitalization for COPD and reported that the effect was stronger in the Midwest and Southeast regions and minimal in the Northeast (Zhao et al., 2019c). Mixed results were also observed by these Brazilian studies (Xu et al., 2020; Zhao et al., 2019e, 2019c, 2019f) in the analysis stratified by sex and age groups.

This large difference in the risk between regions is explained by the spatial distribution of the environmental and socioeconomic conditions in Brazil. The Brazilian regions are very heterogeneous between each other in terms of temperature and also social/economic factors. As we mentioned in the introduction, there are substantial disparities in the environmental conditions and quality of public health across Brazilian regions, which negatively impacts health equity and it is an important determinant of the heat impacts on hospital admissions. Brazil has different types of biomes (Amazon forest, Cerrado, Atlantic forest, Caatinga, Pampa, and Pantanal) that are strongly correlated with ambient temperature (LYRA et al. 2016; Salazar et al. 2007). For example, the Caatinga biome (mainly located in the northeastern region) has become warmer and drier in the recent years, while the temperature in the South region had a slight variation (Costa et al. 2020; Da Silva et al. 2019). Regarding sociodemographic conditions, according to the last census, Northeast is the region with the lowest average income and the Southeast the one with the highest average income. While the Southeast concentrates the largest urban areas and industries, the Northeast region has the highest rural population in Brazil, with more than a quarter of the population living in the countryside.

The regional risk observed in our study highlights the importance of considering the spatial distribution of environmental and socioeconomic conditions when designing policies and interventions to mitigate the health effects of heat waves. The fact that certain biomes and regions are more vulnerable to the impacts of high temperature suggests that targeted interventions may be necessary to address the health equity concerns. Additionally, the disparities in income and rural-urban divide across regions are also crucial factors that must be taken into account when designing interventions. Overall, these findings underscore the need for a holistic approach that considers both the environmental and social determinants of health in order to promote health equity and reduce the impacts of heat waves in Brazil.

Our study has some limitations. First, because of individual perception and decision to seek medical attention after symptoms of cardiorespiratory disease, some individuals went to the hospital on the first day of exposure, some others waited until symptoms became too severe and went to the hospital five days after exposure, some others had acute symptoms but did not go to the hospital, etc. Because we used a time series framework, this problem may have influenced our findings. Second, there is the possibility of some residual bias, even after adjustment for air pollution, humidity, spatiotemporal factors, and stratification of the analysis by sex and age. Third, the predicted temperature, especially the concentration of air pollutants (the main covariate considered in our analyses) may have introduced some errors in the exposure measurement. In addition, there is the possibility of exposure misclassification given the coarse spatial resolution of the temperature and air pollution measurements. Fourth, this is a ecological study which cannot attribute individual level associations for temperature and hospitalization risk. Also, our study design does not capture the cause-and-effect relationship between exposure to heat and cardiorespiratory disease. We only assessed the association of high ambient temperature with daily hospitalization for cardiorespiratory diseases.

Although these limitations exist, our study has some strengths. First, our sample includes more than 23 million hospitalizations nationwide over 11 years. This sample size provides high statistical power and enhances the generalizability of our findings to the Brazilian population. Second, we used a modeling method that flexibly describes associations that have potentially nonlinear and lagged effects in time series data. Environmental stressors, such as exposure to temperature, frequently demonstrate time-lagged effects, requiring specific models that account for the temporal dimension of the exposure-response relationship. Third, we accounted for spatiotemporal trends in our model by using a time-stratified sample to define strata based on the day of the week, month, calendar year, and community in the time series. This approach reduces the effects of confounding factors associated with the spatiotemporal trend by controlling for time-dependent risk factors within municipalities, including the day of the week, season, and long-term trends, through matching.

5. CONCLUSIONS

Our findings suggest that extreme heat is associated with a significant increase in daily hospital admissions, particularly among the elderly population. These results have important implications for policymakers, as they can help inform adaptive measures and mitigation strategies to reduce the adverse effects of climate change on public health in Brazil. Overall, our study contributes to the growing body of evidence highlighting the urgent need for action to address the serious climate change challenges facing South America.

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