

# Effects of air temperature on the risk of death from COPD in major microregions in Brazil: a time series study

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## ABSTRACT

Objective: To evaluate the association between the risk of death from COPD and air temperature events in ten major Brazilian microregions. Methods: This was a time series analysis of daily COPD deaths and daily mean air temperatures between 1996 and 2017. Using distributed nonlinear lag models, we estimated the cumulative relative risks of COPD mortality for four temperature percentiles (representing moderate and extreme cold and heat events) in relation to a minimum mortality temperature, with a lag of 21 days, in each microregion. Results: Significant associations were found between extreme air temperature events and the risk of death from COPD in the southern and southeastern microregions in Brazil. There was an association of extreme cold and an increased mortality risk in the following microregions: 36% (95% Cl, 1.12-1.65), in Porto Alegre; 27% (95% Cl, 1.03-1.58), in Curitiba; and 34% (95% Cl, 1.19-1.52), in São Paulo; whereas moderate cold was associated with an increased risk of 20% (95% CI, 1.01-1.41), 33% (95% CI, 1.09-1.62), and 24% (95% CI, 1.12-1.38) in the same microregions, respectively. There was an increased COPD mortality risk in the São Paulo and Rio de Janeiro microregions: 17% (95% CI, 1.05-1.31) and 12% (95% CI, 1,02-1,23), respectively, due to moderate heat, and 23% (95% CI, 1,09-1,38) and 32% (95% CI, 1,15-1,50) due to extreme heat. Conclusions: Non-optimal air temperature events were associated with an increased risk of death from COPD in tropical and subtropical areas of Brazil.

Keywords: Pulmonary disease, chronic obstructive/mortality; Temperature; Climate.

# **INTRODUCTION**

In 2019, COPD was the fourth leading cause of death in Brazil according to the Global Burden of Disease.<sup>(1)</sup> In addition, COPD prevalence in the Americas is the highest among WHO regions.<sup>(2)</sup> At the same time, climate change has already been a reality, including in Brazil,<sup>(3)</sup> and the new challenge is to study the relationship between chronic diseases and environmental variables. Furthermore, extreme air temperatures are a risk factor for the occurrence and exacerbation of lung diseases, as well as mortality, and, according to the Intergovernmental Panel on Climate Change, this exposure will become more frequent and intense with the progression of the climate transition.<sup>(4,5)</sup>

It is still unclear whether the effect of air temperature on COPD has a higher association with cold or warm temperatures. A national level Chinese study using a similar methodology to that in this study found that colder air temperatures were more often associated with the occurrence of death from COPD,<sup>(6)</sup> whereas a study involving 12 cities in the USA, using a different methodology, estimated that the effect of heat during

Considering the relative lack of research on this topic in Brazil, the objective of this study was to investigate the relationship between air temperature and COPD mortality in several geographic microregions that are representative of all macroregions in Brazil.

## **METHODS**

In this time series study, the relationship between daily mean air temperature and the number of daily deaths from COPD in ten Brazilian microregions was evaluated. The two largest microregions of each of the five Brazilian macroregions (North, Northeast, Central-West, Southeast, and South) were selected, except in the Central-West macroregion, where the first and third largest microregions were selected due to the geographical proximity of the second largest (Goiânia) to the first one (Brasília). Thus, the selected microregions were the following: Belém and Manaus

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summer was responsible for an increase of up to 25% in COPD deaths.<sup>(7)</sup> In addition to these studies,<sup>(6,7)</sup> the relationship between temperature and different COPD outcomes has been studied all over the world.<sup>(8)</sup>

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(North), Salvador and Fortaleza (Northeast), Campo Grande and Brasília (Central-West), São Paulo and Rio de Janeiro (Southeast), and Porto Alegre and Curitiba (South). The study comprised a total of 105 Brazilian municipalities, representing different climate regions in the country, within a period of 22 years (from January 1, 1996, to December 31, 2017).

Data on mortality from COPD were collected via the Brazilian Ministry of Health Information Department, specifically retrieved from the Mortality Information System<sup>(9)</sup> based on the primary cause of death (COPD) which was defined in accordance with the Tenth Edition of the International Classification of Diseases (codes J41-J44).<sup>(6)</sup>

Daily mean temperature data were estimated from the ERA-Interim reanalysis, developed by the European Center for Medium-Term Weather Forecasting, which provides four daily air temperature values at points on a uniform horizontal grid with approximately 13 km of space between them.<sup>(10,11)</sup> This reanalysis model is conceived from a forecasting system combined with the assimilation of meteorological information from ships, satellites, planes, radars, radiosondes, and surface meteorological stations.<sup>(12)</sup> By calculating the mean of the four values of air temperature, we obtained the mean daily temperatures for those points. Then, to obtain the daily mean temperature for the microregions, we calculated the mean value of all points identified within the territory of each microregion.

Although data from meteorological stations are more reliable, their irregular distribution, incomplete time series, and large territorial gaps from such stations make a time series analysis unfeasible. Thus, the data from ERA-Interim solve these difficulties due to a correlation equal to or greater than 96% when compared with data from existing surface meteorological stations.<sup>(13)</sup> In addition, air temperature means are the most used data as parameters for analysis in climate and health studies. Although there is variation in air temperature within each microregion, the mean daily air temperature is representative of the temperature behavior in each microregion.<sup>(13)</sup>

To study the association between daily COPD deaths and mean daily air temperature, generalized additive models were fitted with a negative binomial distribution together with a natural cubic spline of time with eight degrees of freedom per year to adjust for long-term trend and seasonality, as well as days of the week to adjust for short-term seasonality.

For inferential analysis and modeling, which characterizes the focus of the present study, distributed lag nonlinear models were used.<sup>(14)</sup> After selecting a natural spline with five degrees of freedom for the exposure-response function, a polynomial function with one intercept and four degrees of freedom for the lag-response function, and 21 days of lag, we estimated, for each microregion, the cumulative relative risks of death from COPD in percentiles of air temperature distribution with the minimum mortality temperature (MMT)—that is, the reference temperature at which there is minimum risk of mortality in the accumulated lag<sup>(15)</sup>—corresponding to the total accumulated risk. The 2.5th and 10th percentiles were chosen to represent, respectively, extreme cold and moderate cold, as were the 90th and 97.5th percentiles to represent moderate heat and extreme heat.

We estimated the fractions and numbers of events attributable to non-optimal temperatures, accumulated up to the 21st day, with the forward method<sup>(16)</sup> of current exposure to future risks. We calculated the following components:

- a. Attributable risk (AR) to extreme cold (between the lowest temperature and the 2.5th percentile)
- b. AR to moderate cold (between the 2.5th and 10th percentiles)
- c. AR to mild cold (between the 10th percentile and the MMT)
- d. AR to mild heat (between MMT and the 90th percentile)
- AR to moderate heat (between the 90th and 97.5th percentiles)
- f. AR to extreme heat (between the 97.5th percentile and the highest temperature)

We analyzed the residuals of the models to detect possible serial autocorrelations and performed a sensitivity analysis to assess the robustness of the main model against the ones produced with many different parameter alterations (supplementary Table S1 and Figure S1). The R software, version 3.4.0 (The R Project for Statistical Computing, Vienna, Austria) was used, especially the *dlnm* package.<sup>(17)</sup> The related scripts are available on Github (https://github.com/ joao-med/COPD-Temperature).

Due to the public nature of the data, the research was exempted from approval by a research ethics committee in accordance with Resolution No.510 of the Brazilian National Health Council.

# RESULTS

We analyzed a total of 208,169 COPD deaths in ten Brazilian microregions, ranging from 3,812 deaths in the Campo Grande microregion, with 0 to 5 daily cases, and 67,806 deaths in the São Paulo microregion, with 0 to 26 daily cases (Table 1 and Figure 1).

In all microregions analyzed, the lowest mean air temperatures were identified in the middle of the year (months of June and July) except in Manaus, Belém, and Fortaleza microregions. Meanwhile, the highest mean air temperatures occurred at the end and the beginning of the year (between October and March). These variations correspond to winters (lower temperatures) and late summers (higher temperatures) in the southern hemisphere. During the studied period, the lowest mean air temperature was in the Curitiba microregion (18.7°C), whereas the highest one was in the Fortaleza microregion (27.3°C). In addition, the highest and the lowest air temperatures were found

Table 1. Distribution of daily mortality from COPD in the Brazilian microregions studied, 1996-2017.	f daily mortality	r from COPD in the E	3razilian microreg	ions studied,	1996-2017.					
Variable					Micro	Microregion				
	Brasília	Campo Grande	Porto Alegre	Curitiba	São Paulo	Rio de Janeiro	Salvador	Fortaleza	Belém	Manaus
<b>Population</b> <sup>a</sup>	2,411,628	820,088	3,598,717	2,977,488	2,977,488 13,468,309	11,210,768	336,7109	318,1579	2,047,843	1,874,407
				00	<b>COPD</b> deaths					
Total number	6,906	3,812	30,232	17,616	67,806	54,916	7,070	7,224	8,130	4,457
Mean annual number	314	173	1374	801	3,082	2,496	321	328	370	203
Mean annual rate $^{\flat}$	13.02	21.13	38.19	26.89	22.88	22.27	9.54	10.32	18.05	10.81
				Daily	Daily distribution					
Minimum value	0	0	0	0	0	0	0	0	0	0
25th percentile	0	0	2	-	9	5	0	0	0	0
Median	-	0	Υ	2	80	7	-	-	-	0
Mean	-	0	4	2	80	7	-	-	-	-
75th percentile	-	-	5	S	10	8	-	-	2	-
Maximum value	9	5	17	12	26	20	9	7	80	9
Mean daily rate <sup>b</sup>	0.04	0.06	0.10	0.07	0.06	0.06	0.03	0.03	0.05	0.03
<sup>a</sup> Average population for the period. <sup>b</sup> Rates per 100,000	or the period.	Rates per 100,000 p	population.							

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in the Campo Grande (32.7°C) and Curitiba (4.5°C) microregions, respectively. Simultaneously, the MMT varied from 17.9°C to 28.5°C in the Curitiba and Belém microregions, respectively (Table 2 and Figure 1).

There was an association between COPD deaths and air temperature, especially in the most populous microregions such as São Paulo, Rio de Janeiro, and Porto Alegre \_(the first two in the Southeast macroregion and the last one in the South one). These three microregions had the highest mean daily death rates (Table 1), which contributed to a more reliable estimate of the relative risks (Table 3 and Figure 2).

The percentile attributable to extreme cold showed an increased risk of death from COPD of 36%, 27%, and 34%, respectively, in the Porto Alegre, Curitiba, and São Paulo microregions, while moderate cold showed a significant increase of 20%, 33%, and 24% in the same microregions. Furthermore, an increased risk of moderate heat was estimated to be 17% and 12%, respectively, in the São Paulo and Rio de Janeiro microregions. Regarding extreme heat, the microregions that showed significant results were Campo Grande, São Paulo, and Rio de Janeiro, with increases in the mortality risk of 55%, 23%, and 32%, respectively (Table 3).

The fraction of COPD deaths attributable to cold air temperature over the entire study period (from 1996 to 2017) was 8.83% in the São Paulo microregion, whereas, in the Porto Alegre microregion, with the combination of extreme and moderate cold temperatures, that value was 3.35%. Regarding heat, the attributable fraction was 3.21% in the São Paulo microregion. Considering extreme heat only, the attributable fraction was 1.40% in the Campo Grande microregion, whereas that was 1.86% in the Rio de Janeiro microregion, considering both extreme and moderate heat (Table 4).

Regarding the attributable deaths for different mean air temperatures during the studied period, the São Paulo microregion had the most significant results: the range corresponding to moderate cold and mild cold might have been responsible for, respectively, 1,267 (95% CI, 770-1,727) and 4,108 deaths (95% CI, 1,631-6,525). Meanwhile, the number of deaths attributable to mild and moderate heat were, in this order, 1,097 (95% CI, 50-2,032) and 771 (95% CI, 361-1,169). On the other hand, extreme heat might have been responsible for 412 deaths (95% CI, 226-562) in the Rio de Janeiro microregion, which showed the most significant result between 1996 and 2017.

In the Fortaleza and Salvador microregions, no associations were present in any lag. However, associations with extreme cold or extreme heat were present in almost all lags in all of the other microregions (Figures S2 and S3).

#### DISCUSSION

The present study carried out a comprehensive analysis of the Brazilian territory and population,

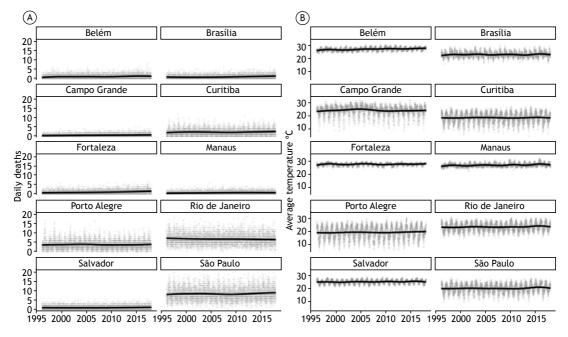


Figure 1. Daily distribution of deaths from COPD (J41-44) and mean temperatures (°C) between 1996 and 2017 in the microregions studied. Each day is represented as a gray dot, and the line on each graph represents the time trend.

evaluating the impact of air temperature on COPD mortality in tropical and subtropical areas. Moreover, due to the scarcity of material available with similar analyses, we expanded the knowledge on health and climate, bringing important information for better decision making and consequent improvement of public health. We investigated ten Brazilian microregions, located in all macroregions and representing the major climate types of the country, with an estimated number of 27,090,704 people and 208,169 deaths from COPD during the period between 1996 and 2017. Furthermore, we identified a significant association between extreme air temperature events and the risk of death from COPD in the southern and southeastern microregions of the country, with an emphasis on the microregion of São Paulo, where there was the highest number of recorded deaths. In this microregion, 1,836 deaths were attributable to exposure to non-optimal air temperature conditions in the period analyzed, and the risk of death from COPD increased significantly in both cold and warm moderate and extreme temperature events, regardless whether below or above the MMT.

Another important feature that strengthens our analysis is the use of distributed lag nonlinear models that capture complex relationships between the relationship of air temperature and COPD deaths,<sup>(14,18)</sup> by calculating nonlinear relationships and exposure implications from a lagged perspective. This methodology also provides relative and attributable risk estimation for different temperatures and lags.<sup>(14,19)</sup>

To compare our research with the various results presented around the world, it is worth noting that a similar study in China published in 2018 found a fraction of 12.6% (95% CI, 10.31-12.57) of COPD deaths attributable to air temperature, presenting a curve where most of the deaths were due to colder temperatures.<sup>(6)</sup> Likewise, for the same air temperature conditions, we found an attributable fraction of 12.04% (95% CI, 4.8-18.98) in the São Paulo microregion and an analogous modeled curve.

Regarding the risk of death from COPD, an American study found by means of logistic regression models a 19% increased chance among elderly individuals with COPD of dying on the same day when the maximum temperature was lower than or equal to the 1st percentile, as compared with patients without COPD.<sup>(20)</sup> This finding is consistent with our results of COPD mortality risk at the extremely cold temperature (in percentile) in the Porto Alegre, Curitiba, and São Paulo microregions. In turn, a study with data between 1980 and 2000 in New Zealand reported that the mortality rate was 18% higher in winter than that expected when compared with other months, 31% of excess deaths being attributable to respiratory disease.<sup>(21)</sup> Finally, a large study in Taiwan found that a 5°C decrease in mean daily temperature correlated significantly with increased hospital admissions due to COPD on the same day and on the 28 consecutive days.<sup>(22)</sup>

Considering that the likely mechanisms influencing COPD mortality would first have to lead to an exacerbation of the disease, exposure to low air temperatures might facilitate this event by several means. Since an increase in morbidity and mortality is already expected in winter,<sup>(18,23)</sup> some explanations are usually pointed out, such as those indicating the relationship between cold temperature and decreased

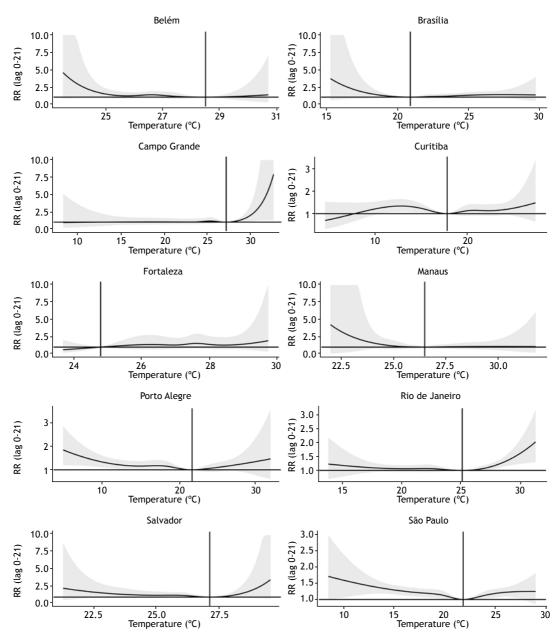
Table 2. Distribution of daily mean temperature (in °C) and temperatures related to minimum risks accumulated up to lag 21 (days) in the Brazilian microregions studied, 1996-2017.	in temperati	ure (in <sup>o</sup> C) and temp	peratures related	to minimum r	'isks accumulate	ed up to lag 21 (days	) in the Brazi	ilian microregi	ons studied,	1996-2017.
Distribution					Microregion	gion				
	Brasília	Campo Grande	Porto Alegre	Curitiba	São Paulo	Rio de Janeiro	Salvador	Fortaleza	Belém	Manaus
Minimum value	15.3	8.3	4.9	4.5	8.4	13.8	21.3	23.7	23.5	22.0
1st percentile	18.5	13.4	8.0	9.3	12.7	16.9	22.5	24.8	24.5	24.2
2.5th percentile	19.2	15.6	9.6	10.8	13.9	17.9	22.9	25.2	24.8	24.5
10th percentile	20.4	19.9	12.7	13.6	16.3	19.6	23.6	26.0	25.4	25.1
25th percentile	21.5	22.8	16.0	16.1	18.4	21.2	24.4	26.7	26.1	25.7
Median	22.7	24.8	19.8	19.0	20.8	23.4	25.7	27.4	26.9	26.5
Mean	22.8	24.3	19.3	18.7	20.6	23.4	25.6	27.3	27.0	26.6
75th percentile	24.1	26.5	23.0	21.7	23.1	25.7	26.8	27.9	27.9	27.3
90th percentile	25.5	27.9	24.9	23.4	24.6	27.4	27.4	28.3	28.7	28.2
97.5th percentile	27.1	29.4	26.6	24.8	26.1	28.7	28.0	28.7	29.3	29.4
99th percentile	27.9	30.2	27.5	25.5	26.8	29.4	28.3	29.0	29.6	30.0
Maximum value	29.7	32.7	31.9	27.6	29.0	31.3	29.5	29.7	30.7	31.8
Minimum mortality temperature	20.9	27.2	21.7	17.9	21.8	25.1	27.1	24.8	28.5	26.5

Table 3. Relative risks and respective 95% CIs (accumulated up to 21 days) of death from COPD due to exposure to mean temperatures in the microregions studied, taking as a reference

Mean					Micro	Microregion				
temperature	Brasília	Campo Grande	Porto Alegre	Curitiba	São Paulo	São Paulo Rio de Janeiro	Salvador	Fortaleza	Belém	Manaus
Extreme cold	1.18	1.03	1.36	1.27	1.34	1.09	1.59	1.15	1.61	1.36
	(0.94; 1.48)	(0.62; 1.71)	(1.12; 1.65)	(1.03; 1.58)	(1.19; 1.52)	(0.95; 1.25)	(0.89; 2.85)	(0.82; 1.59)	(0.97; 2.68)	(0.78; 2.37)
Moderate cold	1.02	1.04	1.20	1.33	1.24	1.06	1.41	1.35	1.24	1.15
	(0.94; 1.10)	(0.67; 1.60)	(1.01; 1.41)	(1.09; 1.62)	(1.12; 1.38)	(0.94; 1.19)	(0.85; 2.34)	(0.68; 2.70)	(0.82; 1.87)	(0.70; 1.88)
Moderate heat	1.31	1.05	1.10	1.15	1.17	1.12	1.03	1.30	1.00	1.07
	(0.96; 1.78)	(0.94; 1.18)	(0.92; 1.30)	(0.92; 1.43)	(1.05; 1.31)	(1.02; 1.23)	(0.95; 1.10)	(0.69; 2.43)	(0.94; 1.07)	(0.71; 1.60)
Extreme heat	1.36	1.55	1.17	1.22	1.23	1.32	1.25	1.33	1.05	1.09
	(0.97; 1.91)	(0.97; 1.91) (1.07; 2.25)	(0.96; 1.43)	(0.93; 1.59)	(1.09; 1.38)	(0.96; 1.43) (0.93; 1.59) (1.09; 1.38) (1.15; 1.50) (0.92; 1.71) (0.69; 2.56)	(0.92; 1.71)	(0.69; 2.56)	(0.73; 1.53)	(0.66; 1.82)







**Figure 2.** Accumulated relative risk (RR) curves by temperature. The gray margins indicate the confidence interval of the measurement, the vertical line indicates the minimum mortality temperature, and the lines below the x-axis indicate single measurements of temperature.

lung function,<sup>(18)</sup> infection by viral agents,<sup>(21)</sup> direct effect of cold on bronchoconstriction, and decreased mucociliary clearance that may result in exacerbation of COPD progressively.<sup>(20)</sup>

Regarding warmer air temperatures, the moderate heat percentile in the São Paulo microregion was found to be a risk factor for COPD mortality, as was in the Rio de Janeiro one. By the possible effect of heat, the aforementioned American study estimated that the effect of increasing air temperatures during summer was responsible for an increase of up to 25% in the causes of death from COPD.<sup>(7)</sup> Accordingly, another research carried out specifically in New York City found, through a generalized additive model, that each 1°C above the temperature of 29°C (75th percentile) meant a 7.6% increase in the risk of hospital admission for COPD with a 3-day lag.<sup>(24)</sup> Finally, another American study estimated a 4.7% increase in the risk of same-day COPD hospitalization among the elderly for every 5.6°C increase in mean ambient temperature during summer.<sup>(25)</sup>

Concerning this issue, heat exposure is related to events that may lead to bronchoconstriction mediated by cholinergic factors,<sup>(8)</sup> hyperventilation in extreme Table 4. Fractions and numbers (95% CIs) of COPD deaths attributable to exposure to mean temperatures in the microregions studied, 1996-2017.

Voriable Autoroo	Average					Microsoften					
Adriabile	temperature	Brasília Camp	Campo Grande	Porto Alegre	Curitiba	São Paulo	Rio de Janeiro	Salvador	Fortaleza	Belém	Manaus
	:			1.22		0.90				1.13	
	Extreme cold	I	I	(0.55; 1.74)	I	(0.44; 1.24)	I	I	I	(0.02; 1.69)	I
	Modements cold			2.13	2.43	1.87					
	wonerate coto	I	I	(0.58; 3.36)	(0.78; 3.93)	(1.16; 2.52)	I	I	I	I	I
					4.12	6.06					
	שוות רחום	I	I	I	(1.32; 6.80)	(2.34; 9.75)	I	I	I	I	I
Attribute for attion 0/	titld boot					1.62					
Attributable fraction, %	MILD NEAL	I	I	I	I	(0.20; 3.03)	I	I	I	I	I
	4					1.14	1.11				
	moderate neat	I	I	I	I	(0.50; 1.73)	(0.44; 1.69)	I	I	I	I
			1.40			0.45	0.75				
	באנו פווופ חפמו	I	(0.30; 1.94)	I	I	(0.16; 0.71)	(0.39; 1.02)	I	I	I	I
	ŀ		1.4	3.35	6.55	12.04	1.86			1.13	
	וסנמו	I	(0.30; 1.94)	(1.13; 5.10)	(2.10; 10.73)	(4.80; 18.98)	(0.83; 2.71)	I	I	(0.02; 1.69)	I
				368		607				92	
	EXTREME COLD	I	I	(144; 524)	I	(312; 848)	I	I	I	(6; 137)	I
				644	428	1,267					
	Moderate cold	I	I	(144; 1015)	(125; 663)	(770; 1,727)	I	I	I	I	I
	11:14 Cold				726	4,108					
		I	I	I	(199; 1,155)	(1,631; 6,525)	I	I	I	I	I
Attack aldatidiates	the boot					1,097					
ALLI IDULADIE UEALIIS, II		I	I	I	I	(50; 2,032)	I	I	I	I	I
	Moderate heat					771	612				
	שחחבו מרב וובמר	I	I	I	I	(361; 1,169)	(254; 940)	I	I	I	I
	Extramo host		53			305	412				
	באנו הוווה ווהמו	I	(13; 73)	I	I	(86; 478)	(226; 562)	I	I	I	I
	Total		53	1,012	1,154	8,155	1,024			92	
	וטרמו	I	(13; 73)	(288; 1,539)	(324; 1,818)	(3,210; 12,779)	(480; 1,502)	I	I	(6; 137)	I
Extreme cold: temperature between the 0th percentile and the 2.5th percentile. Moderate cold: temperature between the 2.5th percentile and the 10th percentile. Mild cold: temperature between the 10th percentile and MMT. Light heat: temperature between the 90th percentile. Moderate heat: temperature between the 97.5th percentile and the 97.5th percentile and the 100th percentile and the 97.5th percentile. Moderate heat: temperature between the 97.5th percentile. Moderate heat: temperature between the cold and heat	ture between the he 10th percentile xtreme heat: tem	Oth perce and MMT. perature t	entile and the 2.5 Light heat: tempe between the 97.51	5th percentile. Perture between th percentile an	Moderate cold: the MMT and t d the 100th pe	temperature be the 90th percenti rcentile. Attribut	stween the 2.5th ile. Moderate heat: able fraction: prop	percentile a temperatur portion of d	nd the 10th re between aaths attribu	n percentile. M the 90th perce utable to cold	lild cold: ntile and and heat
from 1996 to 2017. Attributable deaths: number of deaths	ibutable deaths: r	number of	deaths attributab	attributable to cold and heat.	leat.						



temperature events,<sup>(26)</sup> and release of cytokines such as IL-1 and IL-6.<sup>(3)</sup> In addition to direct relationships, high air temperatures may increase the risk of exacerbations by interacting with variables such as air pollution, ozone level in the atmosphere, and clinical history of cardiovascular disease.<sup>(23,26)</sup>

Epidemiological studies since the 1940s have shown an association between cold temperatures and adverse cardiovascular effects.<sup>(27)</sup> A study in China published in 2023 demonstrated that temperature extremes, either cold or hot, increased the risk of mortality from ischemic heart disease in different regions of the country.<sup>(28)</sup> As for Brazil, a study investigated the relationship between air temperature and mortality from cerebrovascular diseases, in which non-optimal temperatures (either cold or hot) were associated with an increased risk of death in all Brazilian regions.<sup>(29)</sup> However, it should be noted that a clear effect of exposure is not always found in all localities.<sup>(8)</sup> This can be mainly explained by factors such as acclimatization of the local population, intrinsic variations in climate, such as mean air temperature, temperature range, and relative humidity, as well as access to health care services, quality infrastructure, air conditioning, and other socioeconomic factors.<sup>(3,30)</sup> In this context, access to a quality health care services, establishment of bronchodilator therapy, changes in habits, such as smoking cessation and initiation of physical activity, might change the quality of life and life expectancy and could be associated with the response of the disease to different temperatures.<sup>(22)</sup> Furthermore, although our study did not detail the population groups in the microregions, there is evidence in the literature that the elderly, women, and people with a low educational level are more vulnerable to health events, such as deaths from stroke, in non-optimal temperatures.<sup>(29)</sup> Other variables such as COPD stages and number of exacerbations were important limitations of the study, since they represent significant disease prognostic data. However, these clinical variables are not present in mortality databases. Other studies, using different data sources and analysis methods, could add information about the importance of these clinical variables as modifiers of the effect of air temperature on COPD mortality.

Likewise, a recent study on COPD hospitalizations suggested that the lack of association between heat and hospitalizations could be related to higher socioeconomic development and consequent better access to the health care system in the southern region of Brazil.<sup>(3)</sup> In turn, the present study found no significant relationship between heat and COPD mortality in the two southern microregions analyzed (Porto Alegre and Curitiba); in the meantime, cold was associated as a risk factor for mortality. The aforementioned finding does not exclude the possibility that the socioeconomic development of a region is related to the outcome, but it points out that new studies should introduce these variables together with air temperature.

When considering the limitations of the study, although many confounders and trends were controlled by the time scale and models used, the addition of data regarding air pollution, including particulate materials and gases such as nitrogen dioxide, ozone, and sulfur dioxide, could have increased the predictive power of the models.<sup>(8,18,23,24,30)</sup> However, these data are extremely limited in all regions and periods studied. The low daily frequency of deaths in some of the regions studied also made it impossible to estimate the effects of temperature on specific demographic groups by sex and age; considering the importance of this knowledge for public health, a more detailed analysis should be carried out in future studies, using data only from the most populous microregions, such as São Paulo.

In conclusion, this study expands the knowledge about the relationship between air temperature and mortality from COPD and contributes to studies that show significant effects of global warming on both health risk and burden on health care systems after extreme events. Thus, it is necessary to institute preventive measures from the recognition of this phenomenon to create local confrontation guidelines. Thus, it is important to guide the most vulnerable population about measures to mitigate possible deleterious effects on health, in addition to preparing and adapting public services and professionals to the increased demand for health care during such periods.

## **AUTHOR CONTRIBUTIONS**

All authors contributed to study conception and design. JPMG, MCN, and WCMF: material preparation; and data collection and analysis. IMR: material preparation; data collection and analysis; and drafting of the manuscript. All authors reviewed the manuscript and approved the final manuscript.

# **CONFLICTS OF INTEREST**

None declared.

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