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Title: Modification of temperature-related human mortality by area-level socioeconomic and demographic characteristics in Latin American cities

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Author contributions

All authors conceptualized the analysis. MB and BNS completed formal analysis. MB created the original draft of the manuscript. ADR and DAR are senior investigators and provided supervision. All authors contributed to writing and manuscript editing.

Declaration of interests

The authors declare no competing interests.

Data availability

Links to the ERA5-Land, WorldPop and Global Urban Footprint source datasets used to estimate population-weighted ambient temperature, as well as final daily temperature outputs, are available at <u>https://github.com/Drexel-UHC/</u> salurbal_heat. Vital registration and population data for Brazil, Chile and Mexico were downloaded from publicly available repositories of statistical agencies in each country. Vital registration and population data for Argentina, Costa Rica, El Salvador, Guatemala, Panama and Peru were obtained directly from statistical agencies in each country. A link to these agency websites can be accessed via https://drexel.edu/lac/data-evidence/data-acknowledgements.

Code availability

Requests for the code used in this study should be made to the corresponding author

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Abstract

Background: In Latin America, where climate change and rapid urbanization converge, nonoptimal ambient temperatures contribute to excess mortality. However, little is known about arealevel characteristics that confer vulnerability to temperature-related mortality.

Objectives: Explore city-level socioeconomic and demographic characteristics associated with temperature-related mortality in Latin American cities.

Methods: The dependent variables quantify city-specific associations between temperature and mortality: heat- and cold-related excess death fractions (EDF, or percentages of total deaths attributed to cold/hot temperatures), and the relative mortality risk (RR) associated with 1°C difference in temperature in 325 cities during 2002-2015. Random effects meta-regressions were used to investigate whether EDFs and RRs associated with heat and cold varied by city-level characteristics, including population size, population density, built-up area, age-standardized mortality rate, poverty, living conditions, educational attainment, income inequality, and residential segregation by education level.

Results: We find limited effect modification of cold-related mortality by city-level demographic and socioeconomic characteristics and several unexpected associations for heat-related mortality. For example, cities in the highest compared to the lowest tertile of income inequality have all-age cold-related excess mortality that is, on average, 3.45 percentage points higher (95% CI: 0.33, 6.56). Higher poverty and higher segregation were also associated with higher cold EDF among those 65 and older. Large, densely populated cities, and cities with high levels of poverty and income inequality experience smaller heat EDFs compared to smaller and less densely populated cities, and cities with little poverty and income inequality.

Discussion: Evidence of effect modification of cold-related mortality in Latin American cities was limited, and unexpected patterns of modification of heat-related mortality were observed. Socioeconomic deprivation may impact cold-related mortality, particularly among the elderly. The findings of higher levels of poverty and income inequality associated with lower heat-related mortality deserve further investigation given the increasing importance of urban adaptation to climate change.

Keywords: temperature-related mortality; urban health; Latin America; climate change

1. Introduction

Associations of extreme hot and cold ambient temperatures with human mortality have been widely documented in global and regional studies.^{1–7} An estimated 5 million deaths per year globally are associated with non-optimal temperatures, accounting for 9% of all deaths.¹ The temperature-mortality burden varies spatially,³ with urban areas being particularly vulnerable to extreme heat because of how growing urban populations and the urban heat island effect interact with advancing climate change.⁸

An urgent area of research and a public health opportunity is identifying population characteristics that confer vulnerability to (or protection from) heat or cold-related mortality. Multiple cities in Europe and beyond have adopted heat action plans in the aftermath of the 2003 heatwave in Europe that led to an estimated 70,000 excess deaths.⁹ In addition to coordinating response efforts in case of an emergency, these plans help identify vulnerable populations and provide them with necessary care in the event of a heat wave.⁹ The reduction of cold-related mortality also presents a public health opportunity because excess deaths associated with cold outnumber those associated with hot temperatures and make up the majority of temperature-related mortality worldwide.¹ Efforts at reducing cold-related mortality have targeted energy insecurity and subpar home insulation.¹⁰

Vulnerability to non-optimal temperatures is a function of exposure, physiological sensitivity, and adaptive capacity.¹¹ Socioeconomic and demographic characteristics relate to each of these pillars of vulnerability. They can modify an individual's vulnerability to heat or cold by influencing the intensity of their exposure to extreme temperatures. For example, persons whose occupations involve working outside may be exposed to high temperatures at disproportionately higher rates compared to those who work inside.¹² Ethnic and racial minorities, as well as the poor, tend to live

in hotter neighborhoods than non-minorities and the more affluent.^{13,14} Furthermore, an individual's socioeconomic position is correlated with the presence of underlying medical conditions¹⁵ and thus shapes biological susceptibility to extreme temperatures.¹⁶ Socioeconomic characteristics also impact one's adaptive capacity by determining one's ability to achieve thermal comfort when temperatures are extremely hot or cold (e.g., having access to air conditioning or space heaters or weatherized homes).¹⁷ At the area-level, densely populated and segregated areas may not have adequately equipped and staffed medical facilities to treat temperature-related health episodes, resulting in worse mortality outcomes. Finally, elevated temperatures in densely built-up areas caused by the urban heat island effect may also exacerbate vulnerability to heat.¹⁸

A number of individual factors have been shown to modify vulnerability to non-optimal temperatures including age,^{6,19–21} sex,^{12,22} low socioeconomic position,^{22,23} and pre-existing health conditions.^{21–24} However, a recent systematic review²⁵ reported that the evidence of effect modification of temperature-related mortality by area-level characteristics is limited. In particular, the authors reviewed 207 studies and concluded that the evidence of effect modification by area-level factors, including socioeconomic conditions, is either limited or suggestive.²⁵ Furthermore, they found weak evidence that factors such as population density, housing quality and availability of healthcare facilities modify the association between temperature and mortality.² Another limitation stems from the fact that most studies on the topic originate in North America and Europe,^{21,26,27} followed by a few studies in Asia,^{22,28,29} and a handful of studies in Latin America.^{7,20,30–32} Little is known about determinants of hot- or cold- temperature vulnerability within middle- and low-income countries and more broadly within the countries of the global South, which have inherently different temperature regimes and may have different adaptive capacities than high income countries.^{4,33} We hypothesize that better socioeconomic conditions –

low levels of poverty, total mortality, income inequality, residential segregation and better living conditions, as well low population density and small built-up area – are associated with smaller excess mortality attributed to non-optimal temperatures in Latin American cities.

This study uses daily mortality records from 326 cities in nine Latin American countries, combined with daily temperature data and information on cities' socioeconomic and demographic characteristics to examine the extent to which associations between non-optimal temperatures and mortality are modified by characteristics such as poverty, living conditions, inequality, and segregation, among others.

2. Methods

2.1. Study area

The study sample consists of cities from the *Salud Urbana en América Latina* (SALURBAL) project. The goal of SALURBAL, an interdisciplinary multinational collaboration, is to investigate the social and environmental determinants of health in Latin American cities.³⁴ The SALURBAL project includes a total of 371 cities that represent urban agglomerations covering the apparent urban extent or built up area with at least 100,000 residents.³⁴ This study is based on 326 cities in Argentina, Brazil, Chile, Costa Rica, El Salvador, Guatemala, Mexico, Panama, and Peru. Due to unavailable daily mortality data from Colombia and Nicaragua, cities in these two countries were excluded from the analysis. Figure 1 depicts the location of the cities used in this study.

2.2. Data sources

2.2.1. Mortality data

Individual mortality records were obtained from the vital registration systems in each country for the 2002-2015 period and included date of death, municipality of residence, age at death, and cause of death classified according to the World Health Organization Global Health Estimate (GHE) classifications.³⁵ We conducted analysis for all-cause (GHE tiers I., II., III.) and cardiovascular (II.G.) mortality, as non-optimal temperatures have been associated with cardiovascular deaths.³⁶ Analyses considered deaths at any age, as well as stratification by age at death (<65 and 65+ years).

2.2.2. City characteristics

Guided by the theoretical frameworks on vulnerability to temperature-related mortality,³⁷ we extracted and/or calculated the following city-level characteristics from the countries' census bureaus, national statistical offices, or analogous organizations: population, population density, crude mortality rate per 10,000 residents averaged across the entire study period, percentage of built up area, living conditions score, poverty, Gini index of income inequality, and a measure of residential segregation by education – isolation index. Total mortality rate was used as a proxy of the underlying level of population health; lower population health is considered a vulnerability factor for temperature-related mortality.²⁵ The isolation index, a measure of residential segregation, characterizes potential contact between social groups, with higher values indicating low levels of exposure of one population group to a different group within an area.³⁸ In all of the sample countries but Brazil, the isolation index measured the extent to which two population groups by educational attainment – those with incomplete primary education vs. university education – are exposed to each other in a city. For Brazil, the isolation index was based on income.

Table 1 contains descriptions of the city-level characteristics used in the study. The year of

measurement for each indicator (varies by country) is presented in Supplementary Material Table

S1.

Table 1. Description of the socioeconomic and demographic effect modifiers of temperaturerelated mortality

Variable name	Variable name Description [§]					
Population	Population The number of residents in a city					
Population density	The number of city residents per km ² of city built-up area					
Percentage of built-up area	Percentage of city area (within the city administrative boundary) classified as built-up by the Global Urban Footprint project					
Total mortality rate	Total number of all-cause all-age deaths per 1,000 city residents					
Living conditions score	 A composite score based on the census measures of: Proportion of households with piped water access inside the dwelling; 	326 326				
	 Proportion of households with more than 3 people per room (reverse coded); Proportion of the population aged 15 to 17 attending school. The score³⁹ is computed as a sum of z-scores of the constituent variables. Higher values indicate better living conditions. 					
Poverty	The proportion of the population in the city living in households with household income below the national income poverty line.	320				
Gini index of income inequality	Income-based Gini index of income inequality. Measures the deviation of a country's income distribution from a perfectly equal distribution. The Gini index of '0' signifies perfect equality; '1' means maximum inequality.	296				
Isolation index	A measure of residential segregation. Measures the extent to which a social group resides in neighborhoods where they are exposed only to other members of the same social group. ^{38,40} In all countries except Brazil, the isolation index compared two population groups: those with primary incomplete education and those with university completed education. The isolation index in Brazil is income based. The index ranges from 0 (complete integration) to 1 (complete segregation). Higher values denote higher levels of segregation.	303				

[§]A table detailing the temporal resolution for each indicator (varies by country) is available in Supplementary Material Table S1.

2.2.3. Temperature data

Temperature data was obtained from the land surface component of the 5th generation of European ReAnalysis (ERA5), also known as ERA5-Land, produced by the European Centre for Medium-Range Weather Forecasts (ECMWF) and publicly available.⁴¹ ERA5-Land supplies hourly temperature at 2 meters above land surface for the global extent at 9x9 km spatial resolution.

Missing ERA5-Land pixels (30% of cities contained ≥ 1 missing pixels) were imputed using a random forest regression model that included resampled ERA5 temperature (31 km resolution), elevation, and aspect, with further modeling of residuals using kriging for spatial interpolation. For each SALURBAL city we computed population-weighted mean daily temperature for every day during the study period. The computation is described in detail in Kephart et al.⁷

3. Statistical analysis

We estimated effect modification of temperature-related mortality by city characteristics in three stages using an approach similar to that in Sera et al.²⁷ Specifics of the first and second stage analyses, and their results, are available elsewhere.⁷ Briefly, we estimated associations between daily mean temperature and daily mortality counts for every city using distributed lag nonlinear conditional Poisson models. We estimated the associations for all-cause deaths and for deaths from cardiovascular disease. The models accounted for lags from 0-21 days, and controlled for seasonality by including terms for day of week, month and year.^{7,42} Next, for each city we obtained summaries that quantified the temperature-mortality associations. To do so, the city-specific nonlinear curves of the temperature-mortality association were used to identify the observed optimal temperature from a human health perspective (also known as minimum mortality temperature (MMT)), defined as the daily mean temperature in a city corresponding to the temperature at which rates of mortality were lowest. We used the MMT for each city to estimate the excess death fraction (EDF), representing the percent of total deaths observed in a city during the study period that occurred during days with mean temperatures above (heat EDFs) or below (cold EDFs) the MMT, and can be attributed to non-optimal temperature. Extreme heat or extreme cold EDFs refer to the fraction of total deaths that occurred on days on which temperatures were $\ge 95^{\text{th}}$ percentile or $\le 5^{\text{th}}$ percentile of the city-specific daily temperature distribution and can be attributed to non-optimal

temperature, respectively. We also estimated the relative risk (RR) of mortality associated with a 1°C change in city mean daily temperature below the 5th or above the 95th percentile of the cityspecific temperature distribution. The relative risk approximates the steepness of the non-linear temperature-mortality curves under extremely hot and extremely cold temperatures. While EDFs describe the relative contribution of non-optimal temperatures to mortality in a city, RRs characterize the magnitude of the association. The log relative risk of mortality due to 'extreme cold' was computed as the difference in the log-risk of mortality at the 1st and 5th percentiles of city-specific distribution of daily temperatures divided by the difference in degrees Celsius between the 1st and 5th percentiles of the temperature distribution. The log RR due to 'extreme heat' was computed similarly: difference between the log- risk of mortality at the 99th and 95th percentiles of the city-specific distribution of daily temperatures divided by the difference in degrees Celsius between the 99th percentile and 95th percentile of the temperature distribution. The resulting estimated relative risk of mortality due to extreme cold, for example, can be interpreted as a change in the relative risk of mortality associated with a 1°C decrease in mean daily temperature below the 5th percentile of the temperature distribution. Additional details of the first and second stage analyses and results are described and reported elsewhere.⁷

The third stage of our analysis and the primary analysis of this paper estimated effect modification of the temperature-attributed excess death fractions and the relative risk of mortality by city-level socioeconomic characteristics by implementing random effects meta-regressions.^{27,43} We ran separate models for each combination of the predictor variables with either the EDFs or RRs for heat/extreme heat or cold/extreme cold as the dependent variables. Because the dependent variable (EDF from the second stage) represents an association between temperature and mortality, results from the meta-regressions with city-level characteristics can be interpreted as effect modification

estimates. To accommodate potential non-linearity of the associations between the levels of cityspecific socioeconomic and demographic characteristics and temperature-related mortality, we modeled each predictor measure as a three-level categorical variable, with categories based in tertiles (low, medium, high) of the respective observed distributions. All meta-regressions were adjusted for continuous measures of city daily mean temperature and mean temperature range (measured over all observed timepoints), and country (Central American countries were as aggregated into one group) based on a priori hypotheses that these variables might confound associations. The modeling was done using packages "dlnm"⁴⁴ and "mvmeta"⁴⁵ in the R environment for statistical computing (version 4.1.1).

3.1. Additional analyses

Analysis by age group, cardiovascular mortality, and climate characteristics

We estimated meta-regressions for the six mortality outcomes (EDF due to cold and heat; EDF due to extreme cold and extreme heat; relative risk of mortality due to extreme cold and extreme heat) among those ages 65+ only. In addition, we also estimated excess deaths associated with hot and cold temperatures for cardiovascular (CVD) deaths. Finally, in order to analyze whether effect modification by city characteristics varied depending on the cities' climatic conditions, we stratified the cities by 1) Köppen climate zones (arid, tropical and temperate); and 2) category of inter-annual temperature variation (annual temperature range: >10°C and \leq 10°C).

3.2. Sensitivity analysis

We undertook several sensitivity analyses to assess the robustness of the results. First, we compared the results from the all-age models to the results with adjustment for the proportion of population 65 and older as the older age group may disproportionally contribute to mortality

relative to its population size. Second, we re-estimated the meta-regressions for each socioeconomic and demographic indicator while adjusting for population and population density to assess the robustness of our results to the city size and population distributions in cities. Third, for each effect modifier we re-estimated the meta-regressions including non-linear spline terms for mean daily temperature and temperature range.

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4. Results

4.1. Sample characteristics

Table 2 presents summary statistics for the cities included in the analysis. An analogous countryspecific table can be found in Supplementary Material Table S1. Our analysis included a total of 15,364,950 deaths in 326 cities in nine Latin American countries representing over 2.9 billion person-years of risk observed in the analysis. The annual mean temperature varied by city (Figure 1), with the hottest annual temperatures observed in the cities in Brazil and Central America (median city annual temperatures: 22.2° C and 23.8° C, respectively), and the lowest annual temperatures observed in Chilean cities (13.7° C).

We observed high variability in socioeconomic indicators between the cities in general, as well as between cities within countries. The highest levels of city income inequality were observed in Brazil (median Gini index=0.55), while in the rest of the countries it hovered around 0.4. According to the living conditions score (a measure describing piped water access in a dwelling, overcrowding, and the proportion of 15–17-year-olds attending school), cities with the most suboptimal living conditions in our sample are located in Central America and Peru. Indeed, the median proportion of households with piped water access is slightly higher in Central American cities – 76%, compared with 97% in Brazil. Peruvian and Central American cities also had the highest levels of overcrowding, with the median city proportion of households with more than three people per room at about 10%.

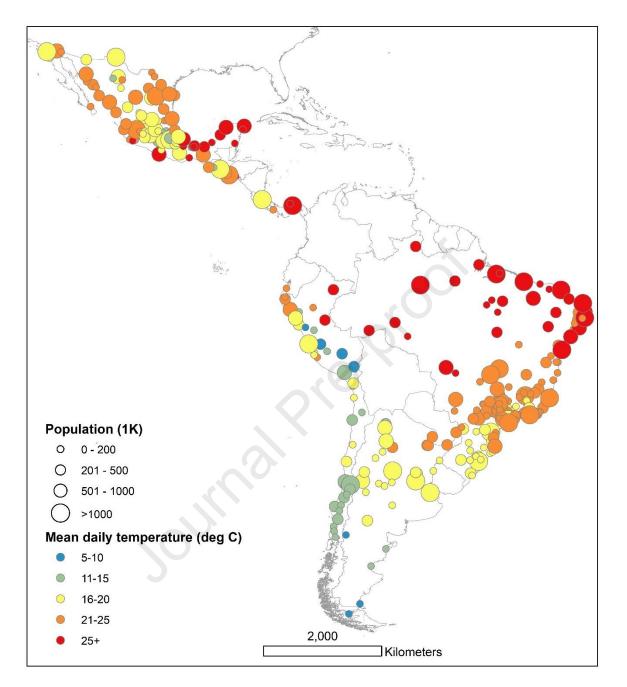


Figure 1. City-specific mean daily temperature and population size

Correlations between demographic and socioeconomic indicators

The demographic and socioeconomic indicators used in the study describe different aspects of cities' socioeconomic environments, but they exhibit several correlation patterns (Figure 2). The highest levels of correlation are observed between segregation (isolation index) and the Gini index of income inequality, as well as between the living conditions score and Gini income inequality. Poverty prevalence is not strongly correlated with the inequality and segregation measures, meaning that the most unequal and segregated cities are not necessarily the poorest. On the other hand, living conditions are associated with both segregation and the Gini index. The strongest negative correlations are observed between poverty and the living conditions score, which is expected. We observe moderate correlations between population density, segregation, and income inequality. As Figure 2 shows, the main exposure variable – mean daily temperature – is strongly and positively correlated with income inequality and isolation index.

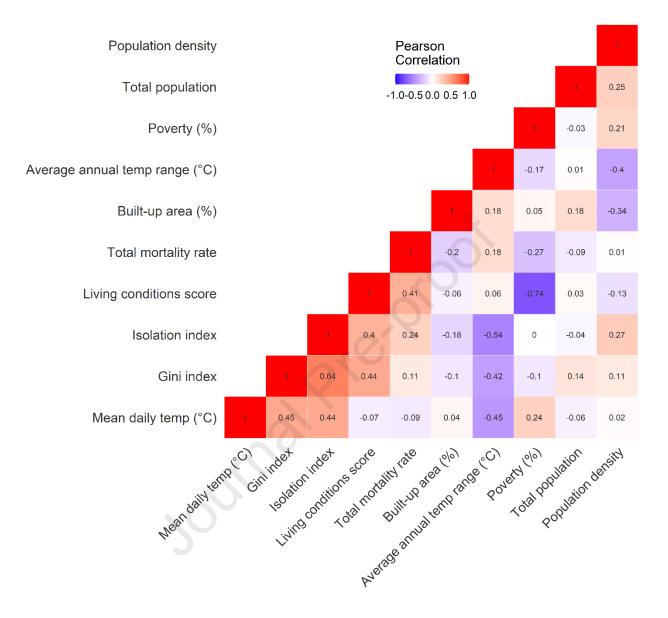


Figure 2. Correlations between pairs of the temperature, socioeconomic, and demographic indicators used in the study

Variable	N cities [‡]	Mean	SD	Min	Median	Max
Daily temperature (°C)	326	20.44	4.49	4.93	20.94	27.82
Annual temperature range (°C)	326	14.01	7.19	3.20	13.56	34.25
Total deaths Socioeconomic and demographic effect modifiers	326	47,132	137,125	2,518	16,912	1,594,830
Population (1K)	326	778	2,060	104	271	20,888
Population density per km ²	326	6,901	2,751	2,657	6,124	23,051
Population >65 years (%)	326	6.76	1.81	1.59	6.69	12.84
Built-up area (%)	326	59.09	6.84	18.72	59.85	71.83
Total mortality rate per 1,000 residents	326	5.47	1.19	1.28	5.36	9.27
Living conditions score: Households with piped water inside the	326	0.01	1.76	-5.87	0.33	2.31
dwelling (%) Overcrowding: households with more	326	87.40	13.18	33.41	92.60	99.71
than 3 people per room (%)	326	5.97	4.78	0.32	4.19	26.24
15-17 yo attending school (%)	326	79.40	8.17	45.75	82.25	91.96
Poverty (%)	320	30.64	15.78	4.40	28.25	71.10
Gini index of income inequality	296	0.50	0.08	0.29	0.51	0.68
Isolation index	303	0.29	0.16	0.09	0.26	0.70

Table 2. Descriptive statistics for temperature, mortality, and socioeconomic and demographic variables for the Latin American cities included in the analysis[§]

[§]Supplementary Material Table S1 contains summary statistics by country, including the years of data for every country.

[‡]The number of cities varied by variable because of data availability.

4.2. Excess mortality associated with temperature

According to a meta-regression of city-specific temperature-mortality associations, 5.75% (95% CI: 5.31, 6.07) of deaths at all ages and from all causes are associated with non-optimal temperatures during the 2002-2015 study period.⁷ Out of 5.75%, 0.67% (95% CI: 0.58, 0.74) deaths were associated with heat (the cumulative effect of all temperatures above MMT), whereas cold (cumulative effect of temperatures below MMT) accounted for 5.09% (95% CI: 4.64, 5.47) of the deaths.⁷

4.3. Effect modification of temperature-related mortality by city-level socioeconomic characteristics

In this section, we describe associations between city-level socioeconomic and demographic characteristics and: (1) excess death fractions (EDF) related to cold and heat; (2) relative risk (RR) of mortality due to extreme cold and extreme heat. The estimates in Figure 3 can be interpreted as a percentage-point difference in the EDF associated with differences in city characteristics. The reference category for each indicator are cities with desirable levels of the indicator (e.g., low poverty, high living conditions score, etc.). In the case of population, population density, and % built-up area, the reference are cities with low (bottom tertile) absolute values of these characteristics. All of the results below are adjusted by country, mean daily temperature, and average annual temperature range.

Cold-related mortality

Higher levels of socioeconomic deprivation were associated with higher EDF from cold (left panel of Figure 3; quantitative estimates and confidence intervals are in Supplementary Material Table S2). Specifically, cities with low and medium levels of living conditions and with medium and high levels of poverty, income inequality, and segregation have larger cold-related EDF than cities with more desirable levels of these indicators, though the differences are not statistically significant. Results for the excess mortality associated with extreme cold (Figure S1 and Table S3 in the Supplementary Material) showed that cities with the highest income inequality have on average 0.41 percentage point higher EDF from extreme cold (95% CI: 0.04, 0.77) relative to cities with the lowest income inequality.

Results for the relative risk of mortality attributed to extreme cold are presented in Figure 4 (left panel; quantitative estimates and confidence intervals are in Supplementary Material Table S4). We find that a 1°C-decrease in the mean daily temperate below the 5th percentiles of the city-specific temperature distribution in cities with high levels of poverty and high residential

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segregation is associated with larger relative risk of extreme cold-related mortality, though the associations do not reach statistical significance.

Heat-related mortality

Associations with EDFs from heat were smaller in magnitude as compared to associations with cold EDFs. Higher socioeconomic deprivation, population, and population density were associated with lower excess mortality due to heat (Figure 3). Cities in the top tertile of population size have, on average, heat EDF 0.35 percentage points lower (95% CI: -0.59, -0.11) than cities in the bottom tertile. The effect modification for population density is similar in magnitude: in the most densely populated cities heat EDF is on average 0.33 percentage points smaller (95% CI: -0.57, -0.09) relative to the least densely populated cities. As Figure 3 also shows, EDFs due to heat are higher in cities in the top tertile of the mortality rate distribution compared to cities with the lowest levels of mortality. Specifically, the heat EDF in cities with the highest mortality rates in the sample is, on average, 0.3 percentage points higher (95% CI: 0.04, 0.60) than in cities with the lowest mortality rate. Finally, cities with medium and high poverty, and medium and high income inequality have lower heat EDF relative to cities with desirable levels of these indicators. For example, cities with the highest income inequality (those in the top tertile of the Gini index) have, on average, heat EDF that is 1.23 percentage points lower (95% CI: -1.96; -0.50) than cities with the least income inequality. The estimates for poverty and isolation index are similar in magnitude. The results for the EDF associated with extreme heat (Figure S1 and Table S3 in the Supplementary Material) largely resembled the results for EDF due to heat described above.

As for the relative risk of mortality attributed to extreme heat (Fig. 4, right panel), in cities with medium and high income inequality a 1°C increase in mean daily temperature above the 95th percentile is associated with the relative risk of mortality that is 1% and 2% higher, respectively

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(95% CI: [0.99, 1.05] and [0.97; 1.04]) than in cities with low income inequality, though the associations are not statistically significant. Unlike for excess mortality dur to heat and extreme heat, the total mortality rate was not a statistically significant modifier of the relative risk of morality due to extreme heat.

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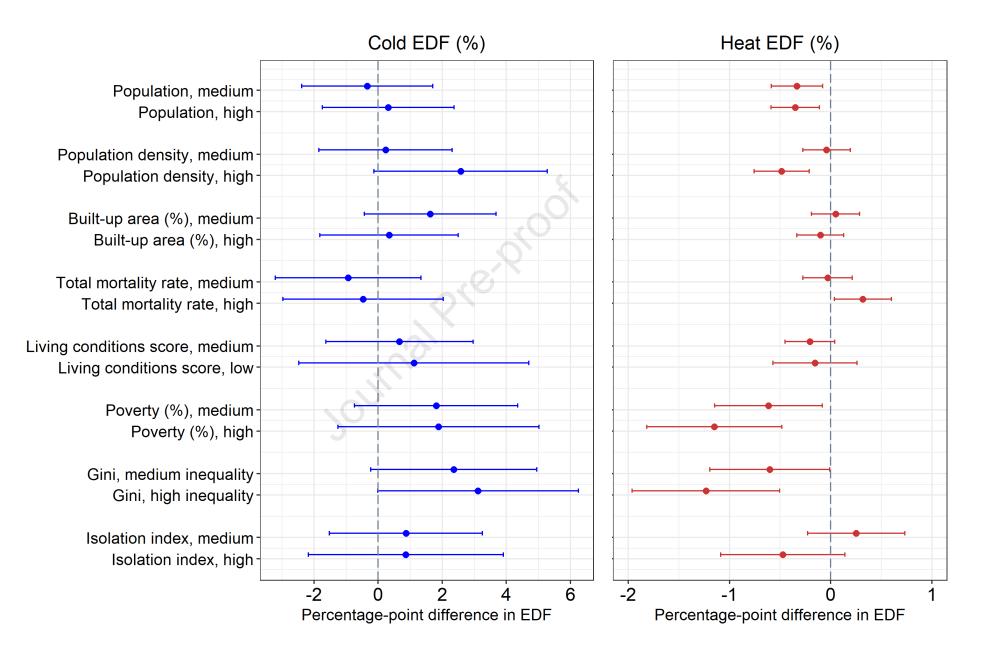


Figure 3. Difference in excess death fractions (EDF) of all-cause mortality associated with cold and hot temperatures by levels of the socioeconomic and demographic characteristics of Latin American cities. Cold temperatures are defined as those below the minimum mortality temperature. Hot temperatures are defined as those above the minimum mortality temperature. Point estimates and 95% confidence intervals are obtained from the random effects meta-regressions that include a socioeconomic indicator, city-level mean daily temperature and mean annual temperature range, and country. Separate meta-regressions were fitted for each indicator. The socioeconomic characteristics were categorized as low, medium, and high according to the tertiles of their distribution. The reference category for each effect modifier are cities with desirable levels of the indicator (e.g., low poverty, high living conditions, etc.). In the case of population, population density, and % urban area, the reference are cities with low (bottom tertile) values of these characteristics. Refer to Table 1 for variables' definition. Supplementary Material Table S2 contains the estimates and confidence intervals shown in the figure. The analysis is based on 326 cities for all variables except poverty (n=320 cities), Gini index (n=296), and isolation index (n=303).

index (n=303).

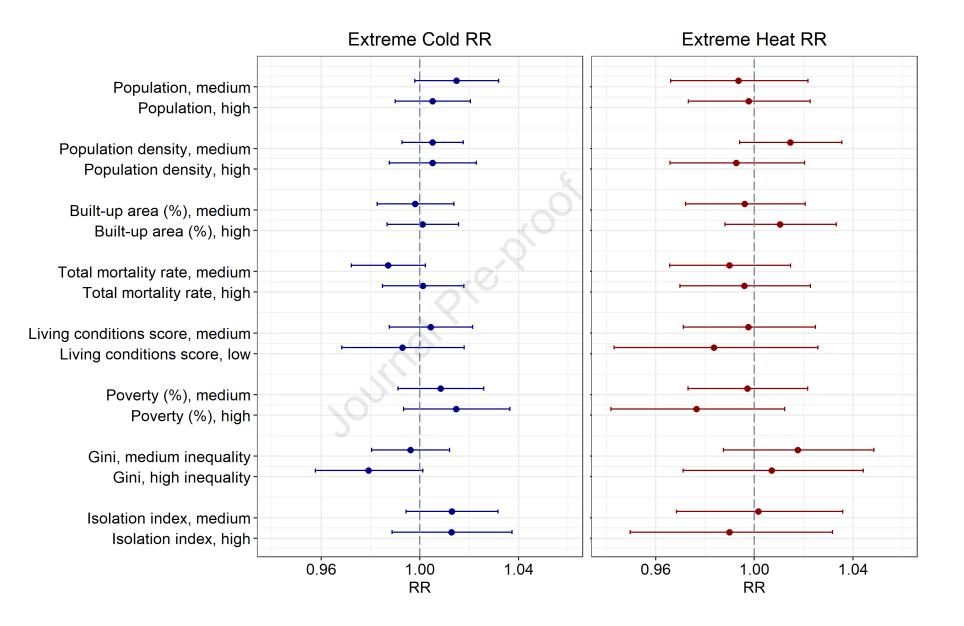


Figure 4. Relative risk (RR) of all-cause mortality per 1°C more extreme cold and hot temperatures by levels of the socioeconomic characteristics of Latin American cities. RR for extreme cold was computed by dividing the difference in log-relative risk of mortality between temperatures at the 1^{st} and 5^{th} percentile of the city-specific daily mean temperature distribution by the difference in degrees Celsius between the 1st percentile and 5th percentile of the temperature distribution, and exponentiating the quotient. RR for heat was analogously obtained as the difference between the log-relative risk of mortality at the 99th and 95th percentile of the city-specific observed distribution of daily temperatures divided by the difference in degrees Celsius between the 99th percentile and 95th percentile of the temperature distribution, and exponentiating the quotient. For extreme cold, the results can be interpreted as a change in the relative risk of mortality associated with a 1°C decrease in mean daily temperature below the 5th percentile of the temperature distribution. For extreme heat, the results present an estimated change in the relativ^e risk of mortality associated with a 1°C increase in daily mean temperature above the 95th percentile of the temperature distribution. Point estimates and 95% confidence intervals are obtained from the random effects meta-regressions that include a socioeconomic indicator, mean daily temperature, mean annual temperature range, and country group. Separate metaregressions were fitted for each socioeconomic indicator. The reference category for each socioeconomic effect modifier are cities with desirable levels of the indicator (e.g., low poverty, high living conditions score, etc.). In the case of population, population density, and % urban area, the reference are cities with low absolute values (bottom tertile) of these characteristics. The analysis is based on 326 cities for all variables except poverty (n=320 cities), Gini index (n=296), and isolation index (n=303). Supplementary Material Table S4 contains the estimates and confidence intervals shown in the figure.

4.4. Additional analyses: age groups, CVD mortality, and city climatic conditions

For those aged 65+ most of the estimates for the socioeconomic effect modifiers of temperaturerelated mortality did not differ substantially from the above-described results for all ages (Figures S2-S4 in Supplementary Material). However, the cold-related excess mortality fractions among those 65 and older were greater in magnitude in the poorest in most segregated cities, compared to the all-age excess mortality in the poorest in most segregated cities. Specifically, excess mortality associated with cold among the elderly is 5.79 percentage points higher (95% CI: 0.52, 11.06) in the poorest cities and 5.34 percentage points higher (95% CI: 0.88, 9.80) in the most segregated cities, relative to less poor and less segregated cities. Corresponding EDF estimates for all-age mortality do not exceed 3% (Figure 3).

The results for cardiovascular mortality (Figure S5 in Supplementary Material) demonstrate effect modification by one city-level indicator: cities with poor levels of living conditions tend to have more excess deaths attributed to cold (but not heat) than cities with optimal living conditions.

We did not observe substantial differences in the associations between temperature-related mortality (both for excess death fractions and relative risk) and city characteristics among cities in arid, temperate, and tropical climate zones (Figures S6-S8 in the Supplementary Material), as well as in cities with different levels of mean annual temperature range (results not shown).

5. Discussion

Limited evidence for effect modification

Overall, our results show limited effect modification of cold- and heat-related mortality in Latin American cities by city-level demographic and socioeconomic characteristics. However, socioeconomic deprivation, in particular income inequality and poverty, may be associated with higher excess mortality due to cold. As our supplementary analyses show, income inequality is associated with higher excess mortality attributed to extreme cold among all-age all-cause deaths. Elevated excess mortality due to cold is also observed among the elderly (65+) in the poorest and most segregated cities. We find no clear pattern of effect modification for the relative risk of mortality associated with a 1°C decrease in temperature below the 5th percentile.

We observe smaller heat EDF for large and more densely populated cities compared to cities with small population and sparsely populated cities. Surprisingly, our results show that cities with high income inequality and high poverty have lower heat EDF compared to cities with desirable levels of these indicators. We also find that cities with low total mortality rate tend to have smaller excess mortality due to heat and extreme heat, and find no modification of the relative risk of mortality associated with a 1°C increase in temperature above the 95th percentile.

We hypothesized that desirable socioeconomic characteristics – such as low levels of poverty, income inequality, residential segregation, and high standards of living conditions, as well as small

% built-up, low population, and low population density – would be associated with smaller excess mortality and smaller relative risk of mortality due to non-optimal temperatures. Cities with a desirable socioeconomic environment likely consist of individuals with lower vulnerability to health risks from non-optimal temperatures along all three dimensions of vulnerability.¹⁶ For example, city residents with at least secondary education are likely to avoid exposure to excessively hot and cold temperatures through employment in jobs that do not entail working outside, may live in areas further away from the urban heat island, and are more likely to afford air conditioning. Conversely, in cities with a high prevalence of poverty, the adaptive capacity to cold and hot temperatures may be compromised because of the difficulty of affording heating, air conditioning, and healthcare. Likewise, high socioeconomic position as a correlate of underlying health conditions may indicate reduced biological susceptibility to non-optimal temperatures among well-off individuals.

Power to detect associations between EDFs and city characteristics varies by heat or cold EDFs. Higher between-city variability in cold EDF than in heat EDF observed in the analysis makes it more likely to identify factors, including socioeconomic and demographic conditions, that explain the variability in cold EDFs. In other words, limited variability in between-city heat EDF may be a limiting factor in detecting conclusive patterns of effect modification for heat-related mortality.

Evidence from existing studies

While multiple studies have demonstrated the contribution of higher- and lower-than-optimal temperatures to mortality all over the globe,^{1,2,7} to date few studies have analyzed effect modification of temperature-related mortality, and the analyses of effect modification outside of the Global North are even scarcer.⁴ Still, our finding of no large-scale effect modification of temperature-related mortality by city-level socioeconomic characteristics is in line with several

other studies based in the Europe,^{26,46} Asia,⁴⁷ Latin America,^{20,31} and Australia.⁴⁸ A study by Sera et al.²⁷ included 37 cities from Brazil, Mexico, Chile and Colombia alongside 303 cities from Southeast Asia and the Global North. The authors also found no effect modification of excess deaths fractions associated with cold temperatures by any city-level characteristics they considered, including unemployment rate, gross domestic product, poverty, Gini index, hospital bed rates, and life expectancy, among others. However, the authors found that higher income inequality (Gini index), population, and population density were associated with larger fractions of deaths attributed to heat, whereas we find the opposite. It is worth mentioning that Sera et al. modeled the above-mentioned city characteristics as continuous variables whereas we modeled them as categorical variables with three levels to detect non-linear associations. Among the studies based in Latin America, a study from Sao Paulo by Gouveia et al.²⁰ found no effect modification of the relative risk of mortality due to cold and heat by a composite index based on income, educational attainment, and living conditions. An analysis of vulnerability to heat-related mortality in Sao Paulo, Santiago, and Mexico City found that the vulnerability by education and sex varied widely between cities.³¹ Another study from a warm city – Hong Kong – showed a 0.65% increase in the relative risk of mortality associated with a 3°C increase in average daily temperature above 28.2°C for areas of Hong Kong with low socioeconomic status, although the association was not statistically significant (95% CI: 0.998-1.909).²⁸

Some of our results are also in contrast to several studies from China,²² Japan,²⁹ and France,⁴⁹ among others, that found higher cold-related²² and heat-related^{29,49} mortality in socioeconomically deprived areas. Results from a study based in Mexico revealed lower vulnerability to cold-related mortality among individuals in the top quartiles of personal income distribution, though no effect modification for heat was found.⁵⁰

Our study is among the first to explore city socioeconomic characteristics as effect modifiers of temperature-related mortality in Latin America, so barring a few exceptions we cannot compare the observed results with other studies in the same region. However, the use of community- or area-wide effect modifiers, which ignore within-city and between-person or -neighborhood heterogeneity in socioeconomic wellbeing, potentially contributes to the findings of no effect modification.^{20,46,47} Future work should examine temperature-related mortality in relation to within-city heterogeneity in socioeconomic indicators.

Explaining smaller heat EDF for cities with high income inequality

The finding of lower heat-related EDF in cities with high income inequality as measured by the Gini coefficient is in contrast to our expectation and requires replication and confirmation. Cities in the highest 30% of income inequality distribution are almost exclusively concentrated in Brazil - 92 cities in Brazil and 6 cities in Mexico and tend to be the hottest cities in our sample (as also indicated by the positive correlation between Gini and daily mean temperature (r=0.44). It is possible that hotter cities are more adapted to high temperatures and that our controls for city temperature and temperature range were insufficient to address this confounding effect. We reestimated the models using cubic splines for temperature and temperature range as a more rigorous control of the observed temperature distribution, but that did not change the results. We also acknowledge that data on healthcare use, which was not available, could potentially help us explain the surprising result. However, despite accounting for average daily temperature and temperature range, it is possible that the observed counterintuitive relationship may be due to the high levels of acclimatization to higher temperatures among the highly unequal cities that also happen to be among the hottest in our analytical sample. Finally, these results may also be explained by unobserved confounders related to inequality and MMT.

Implications for public health in the face of increasing heat

Despite limited overall evidence of modification of heat-related mortality by city socioeconomic characteristics, the total city-level mortality rate emerged as an effect modifier of excess mortality due to heat and extreme heat, and income inequality emerged as a modifier of cold-related mortality. In this study we used city-specific mortality rate as a measure of population health, though other variables such as life expectancy might be better proxies. The mortality rate may be correlated with higher levels of susceptibility to temperature-related mortality because of underlying chronic conditions. Given that heat-related mortality for all ages does not exceed 1% of all deaths during the study period, this may prove an actionable finding by suggesting that the strategies and interventions that cities are pursuing to reduce mortality at large should also work for reducing mortality associated with heat. Empirical evidence for an increased risk of mortality due to heat among people with pre-existing health conditions such as diabetes, Alzheimer's disease, and dementia has been reported in existing research.^{24,51} A study based in Rio de Janeiro, Brazil.⁵¹ found diabetic illnesses to be the largest contributor to excess temperature mortality. In this case, reducing the prevalence of diabetes would also reduce temperature-related mortality. The authors of a Mexico-based study found that the rollout of Mexico's universal health insurance program called Seguro Popular contributed to a 30% decrease in cold-related deaths among the poor by increasing medical assistance in general as well as expanding insurance coverage to include winter-related illnesses such as pneumonia.⁵⁰ As such, in the face of limited resources, reducing the prevalence of underlying chronic diseases, which would in turn decrease total mortality, will likely be beneficial for reducing temperature-related mortality as well.

A much higher percentage of cold-related than heat-related deaths in Latin America suggests potential for adaptation to colder temperatures. As our findings indicate, socioeconomic

deprivation is associated with higher levels of cold-related mortality, and income inequality in particular is associated with higher excess mortality due to extreme cold. Population's adaptive capacity to withstand the impact of extreme cold may be bolstered by expanding the use of heaters in dwellings and weatherizing homes. Future research should explore the role of energy insecurity in explaining the association of socioeconomic deprivation with cold EDFs.

Limitations

First, between-individual or neighborhood variability in socioeconomic characteristics is likely much higher than the between-city variability exploited in the study. Therefore, an analysis using individual-level mortality outcomes and individual-level socioeconomic characteristics would provide a more robust assessment of effect modification. Relatedly, within-city variability in socioeconomic characteristics is also likely higher than the between-city variability, so an alternative analysis could utilize socioeconomic and demographic data from a level smaller than city – such as neighborhood level, for example. It may be that the temperature-mortality relationship is modified by socioeconomic environment at the neighborhood level, but less so at the city level. Second, no variables describing healthcare provision and accessibility were available for this analysis, whereas the number of hospital beds²⁷ and access to health insurance⁵⁰ may be associated with vulnerability to mortality from extreme temperature exposures. Third, our study did not adjust for nor considered atmospheric humidity as a possible effect modifier. Fourth, while the mortality data covered the period from 2002-2015, the effect modifiers used in the analysis were cross-sectional. Fifth, we utilized city-level measures of temperature, which is an approximation of an individual exposure to temperature. Finally, a recent study⁵² found that land surface temperature may produce statistically different estimates of mortality risk compared to air temperature, which is used in most temperature-mortality studies. Land surface temperature may

represent a better exposure metric for evaluating mortality risk attributed to temperature as it more accurately reflects localized thermal environment, especially in an urban context where dense build-up and high concentrations of impervious surfaces contribute to the heat island effect.⁵²

Strengths

This work explored effect modification of mortality associated with both types of non-optimal temperatures – hot and cold temperatures, as well as analyzed effect modification in relation to the relative risk of mortality associated with changes in temperature. We used population-weighted air temperature, which enabled a more accurate measurement of city-level exposure compared to temperature measures that do not account for population distribution. Our study based on individual mortality records from a large and diverse sample is among the first studies of temperature-related mortality in Latin America, which is an extremely understudied region. While many previous studies of temperature-mortality and its effect modification by area-level socioeconomic characteristics considered a limited number of cities in Latin America and the Global South,^{1,27} cities outside of the Global North have represented a small fraction of the total sample. This study provides evidence for effect modification of temperature-related mortality for hundreds of cities in Latin America's temperate and tropical regions, which have distinct temperature and precipitation regimes from those in the Global North.

Conclusion

The levels of temperature-related mortality in Latin American cities are impacted by socioeconomic characteristics (for cold) and by levels of mortality (for heat). Reducing income inequality and the prevalence of underlying chronic diseases, which would in turn decrease total mortality, and taking particular care of the elderly will likely be beneficial for reducing

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temperature-related mortality in Latin America. Cities should harness local information about vulnerable populations and city-specific determinants of mortality to inform public health programs to protect its populations in the face of climate change.

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Journal Pre-proof

- Limited evidence of effect modification of cold-related mortality in Latin American cities
- High income inequality is associated with greater excess mortality from cold for all ages
- Segregation and poverty are associated with higher excess mortality due to cold among the elderly
- Results for heat-related mortality are opposite of expectations (e.g., higher poverty less heat-related mortality)
- The results for heat-related mortality require further investigation

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Author contributions

All authors conceptualized the analysis. MB and BNS completed formal analysis. MB created the original draft of the manuscript. ADR and DAR are senior investigators and provided supervision. All authors contributed to writing and manuscript editing.