

The Effects of Climate on Hospitalization for Respiratory Diseases by Age Group

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Abstract

It examined the relationship between temperatures and hospital admissions for respiratory diseases in the city of Campo Grande, Brazil, during 2008-2014, we used a distributed lag of the nonlinear model (DLNM) to examine the nonlinear effects of temperature on admissions hospital for respiratory diseases by age group. Nonlinear temperature effects were found in hospitalization for respiratory diseases by age group. Both hot and cold effects can last longer - a statistically

significant relationship between the extreme temperatures and hospital admissions in all age groups in the gap. The heat had a greater impact on the elderly, while those aged 5-60 years were more sensitive to cold temperatures. The greatest risk of cumulative effects of heat was observed among those over 65 years at lag 0-25 (HR 1.509, 95% CI: 1.209 to 1.883), while those aged 5-60 years were at greater risk of exposure the extreme temperatures of cold lagged 0-25 (RR 1.482, 95% CI: 1.231 to 1.785). This study provides useful data for policy managers' decisions to better manage the health impacts of hot and cold temperatures.

Keywords: hospital admission, respiratory, temperature, time series analysis, Brazil

Introduction

It is widely accepted that climate change is occurring and that it is caused mainly by increased emissions of anthropogenic greenhouse gases, particularly over the last few decades [1]. Global mean temperature increased by 0.07 °C per decade between 1906 and 2005, compared with 0.13 °C per decade from 1956 to 2005 [1]. Not only has the average global surface temperature increased, but the frequency and intensity of temperature extremes have also changed [1, 2]. Heat wave episodes have been associated with significant health impacts worldwide [3-15]. In addition, episodes of extreme cold (cold spells) are a concern in high-latitude regions, such as Russia [16,17], the Czech Republic [17] and the Netherlands [18].

The effect of ambient temperature on morbidity is a significant public health issue. Increased hospitalizations have been associated with exposure to extreme ambient temperatures, especially during heat waves and cold spells [19-21]. Both heat- and cold-related morbidities occur more frequently among the elderly, as they are more vulnerable to temperature extremes [13, 22, 23]. In addition, urban residents are exposed to higher temperatures than residents of surrounding suburban and rural areas because of the “heat island effect” resulting from high thermal absorption by dark paved surfaces and buildings, heat emitted from vehicles and air conditioners, lack of vegetation and trees, and poor ventilation [24-26]. People living in urban areas have been found to be at a higher risk of morbidity from ambient heat exposure [26]. The effect of temperature on morbidity is likely to become more severe as the number of elderly people increases (from 737 million persons >60 years old in 2009 to 2 billion by 2050 globally) and the proportion of urban residents increases (by approximately 18% of over the next 40 years). Furthermore, climate change will continue for at least the next several decades, even under the most optimistic scenarios [1].

Few studies have examined the impacts of temperatures on respiratory admissions in Campo Grande city, MS, Brazil. It is necessary to quantify the

relationship between temperature and respiratory diseases in order to better manage this increasing health problem. In this study, we examined the effects of temperature on respiratory hospital admission by age groups in Campo Grande city during 2008-2014.

Materials and method

Study location

The city of Campo Grande, MS (20° 27'16 "S, 54° 47'16" W, 650 m) is located on the plateau called Maracajú-Campo Grande, 150 miles from the start of the largest floodplain in the world, the Pantanal (139 111 km²), with an estimated population of 850,000 inhabitants [Souza A, Pavão H, Lastoria G, et al. 2010]. The climate in the region of Campo Grande, is the type with moderate temperatures ranging from 17.8 °C minimum, 29.8 °C maximum and average of 22.7 °C, rainfall annual average 1469 mm, average relative humidity is 72.8% and average elevation of 532 meters.

Data Collection

In this analysis, hospitalization data were collected from the Department of Informatics (DATASUS) of the health agencies of the SUS (Unified Health System). The available data came from the Hospital Information System of SUS (SIH / SUS), managed by the Ministry of Health, through the Department in Health Care, in conjunction with the State Departments of Health and the Municipal Health and processed by Datasus at the Executive Department of the Ministry of Health.

All hospitalizations occurred in the period between January 1, 2008 to December 31, 2014. The respiratory diseases investigated were coded according to the International Classification of Diseases (ICD) 10th Revision (ICD10, J10 to J18). We also stratified the respiratory morbidity by age groups (0-4, 5-60, and >60 years). Daily weather data and ozone (O₃) concentration from same period in Campo Grande were obtained from the Institute of Physics, Federal University of South Mato Grosso (UFMS).

Statistical models

Studies have shown that the extreme temperature can not only affect current day's morbidity but also influence the several following days' morbidity [27-29]. Also, the relationship between temperature and morbidity is non-linear [29]. In this study, a distributed lag non-linear model (DLNM) was fitted to examine the relationship between temperature and daily hospital admissions for respiratory diseases. The DLNM is developed on the basis of "cross-basis" function, which allows simultaneously estimating the non-linear effect of temperature at each lag and the non-linear effects across lags [30]. Most recently, the method has been applied worldwide to identify a non-linear exposure-response association and delayed effects or harvesting [31].

We controlled for seasonality and long-term trend using a natural cubic spline with 7 df per year for time. The day of week was also included as an indicator in our analysis to control any confounding weekly pattern. Public holiday was controlled as a binary variable. We also control for relative humidity and ozone concentration. We evaluated the model fit using Akaike's Information Criterion for quasi-Poisson (Q-AIC). We used mean temperature to assess temperature effects in this analysis since it was found to be a better predictor (i.e. had lower Q-AIC values) than the maximum and minimum temperatures.

We used a DLNM with 5 degrees of freedom natural cubic for temperature (knots at equally-spaced percentiles by default) and with 4 degrees of freedom natural cubic for lags (knots at equally-spaced values in the log scale of lags by default) [31]. The median value of the mean temperature (24.2 °C) was used as the reference value (centering value) to calculate the relative risks. A maximum lag of 25 was used to completely capture the overall temperature effect and adjust for a possible harvesting effect. We examined and plotted cumulative relative risks with temperature for lag 0, lags 0-2, 0-14 and 0-25.

Hot and cold effects separately on relative risks of age-specific hospital admissions for respiratory diseases, were also examined. For hot effects, we calculated relative risks associated with the 99th percentile of temperature (high temperature) relative to the 75th percentile of temperature. For cold effects, we calculated relative risks associated with the first percentile of temperature (cold temperature) relative to the 25th percentile of temperature. The cumulative effects of hot and cold temperatures along the lags were then estimated separately.

Sensitivity analysis were conducted by varying the df for time from 6-12 per year, the maximum lag days from 14-30 days, and the df for temperature and lags from 3 to 6. All statistical tests and modeling were preformed using the R software, version 3.0.1. Distributed lag non-linear models were fitted through “dlnm” package [30].

Results

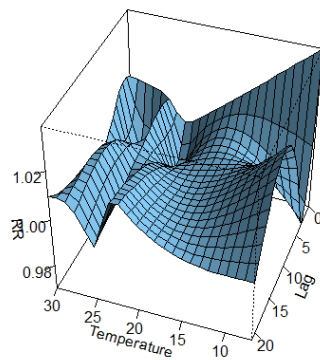
During the study period (January 1, 2008 to December 31, 2014) the total number of hospital admissions for respiratory diseases was 4486. Table 1 shows the statistical summary for hospital data, weather and ozone levels.

	Mean	SD	Min	25th	Median	75th	Max
<i>Meteorological</i>							
Mean temperature(°C)	23.50	3.51	7.00	22.10	24.20	25.73	30.81
Maximum temperature(°C)	30.07	3.87	10.90	28.40	30.80	32.59	39.50

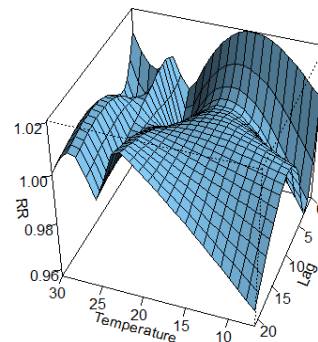
Minimum temperature(°C)	18.85	3.62	4.30	17.30	19.90	21.39	26.88
Relative humidity (%)	66.06	16.12	19.16	55.00	67.81	78.83	98.00
Ozone	17.56	7.59	0.66	12.97	16.44	20.73	52.76
Respiratory hospital admission							
All	10.54	3.29	2.00	8.00	10.00	12.00	23.00
0-4 y	5.06	1.75	1.00	4.00	5.00	6.00	13.00
5-60 y	2.67	1.21	0.00	2.00	2.00	3.00	8.00
>60 y	2.80	1.07	0.00	2.00	3.00	3.00	7.00

Table 1. Descriptive analysis of respiratory hospital admission, ozone, and weather conditions in Campo Grande, Brazil During 2008 to 2014.

The 3-D plots show the non-linear relationships between mean temperature and age-specific hospital admissions for respiratory diseases along 25 lag days (Fig. 1). For total hospital admissions, there was no evident effect of temperature, but both low and high temperatures were associated with increased numbers of total hospital admission. We observed that both low and high temperatures were associated with increased numbers of respiratory hospitalization in those older than 60 years, while relative risks of admissions higher at cold temperatures in other age groups.



All



0-4

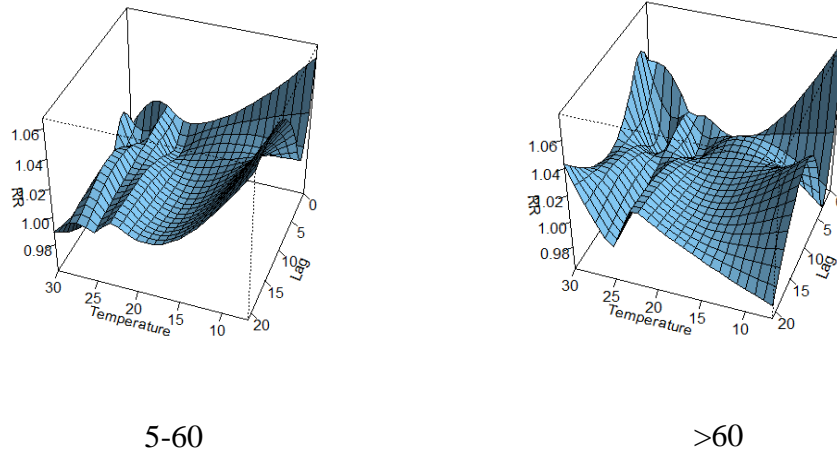
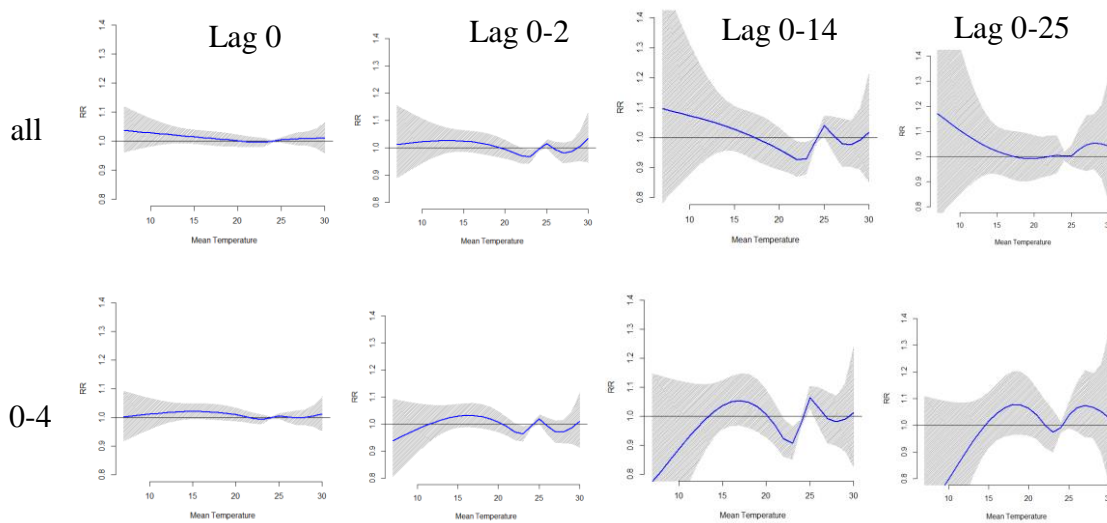


Figure 1. The three-dimensional plot of the association between mean temperature and age-specific hospital admissions along 25 lags

Figure 2 shows the temperature effects of current day (lag 0) and cumulative effects on age-specific hospital admissions at lags 0–2, 0–14, and 0–25. The effects of temperature on all age groups were non-linear. For the effects of extreme hot temperature, the cumulative risks on hospitalizations at lag 0–27 were highest among the elderly, while the cumulative effects of extreme cold temperature were highest among those aged 5-60 years. Figure 3 and 4 show the hot and cold effects on age-specific hospitalizations along the lags. Heat effects increased at long lag days for all sub-groups except for those aged 5–60 years old and lasted longer in those older than 60 years. Cold effects were found to be more immediate.



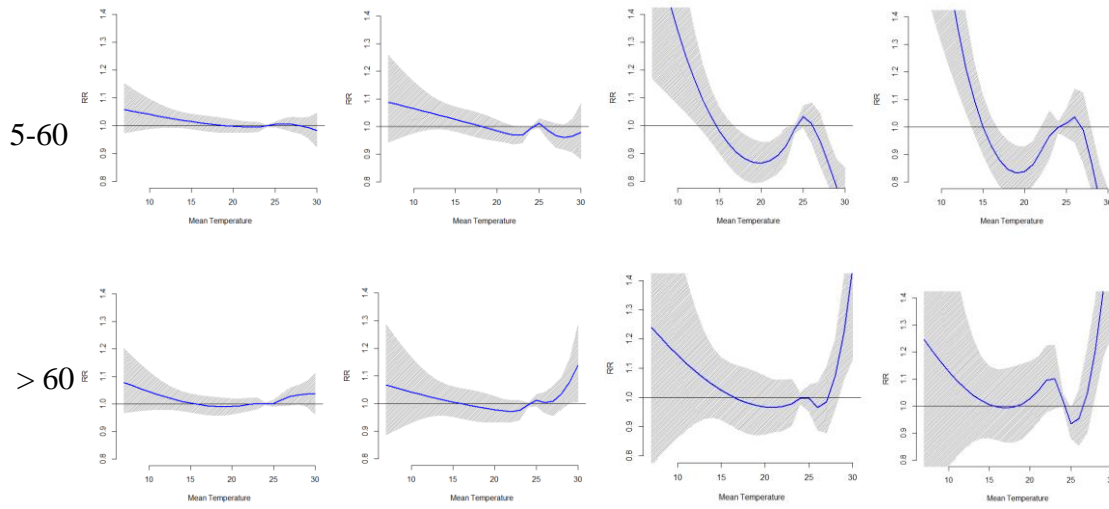


Figure 2. Exposure-response curves of maximum temperature and age-specific hospital admissions along the lags

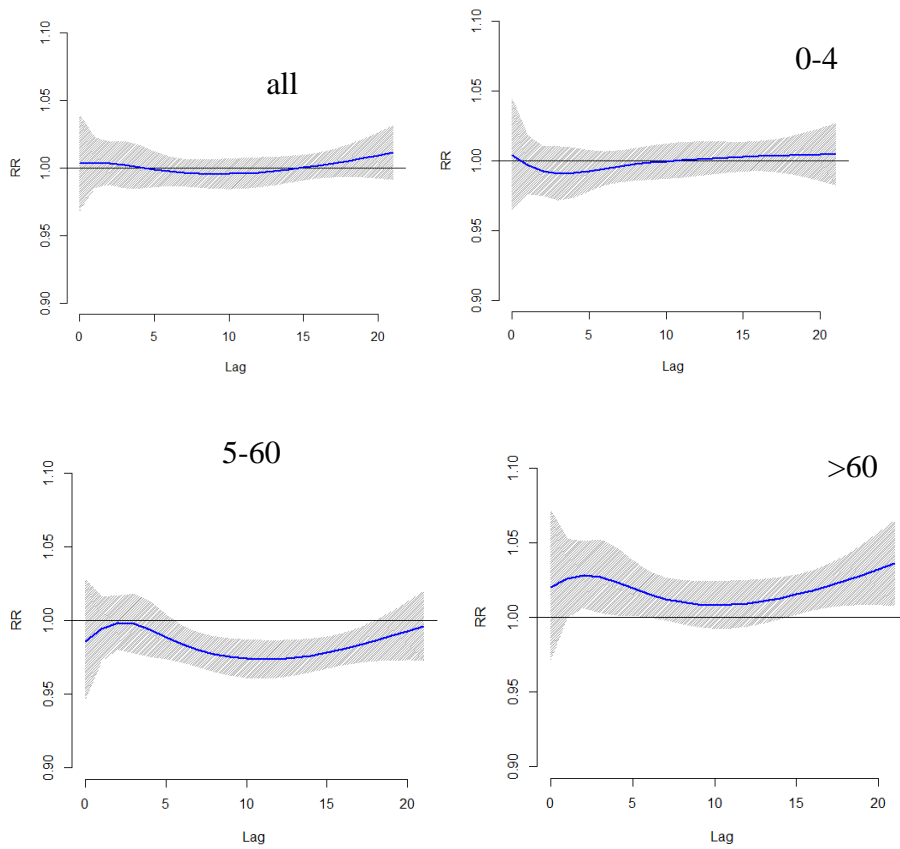


Figure 3. The estimated hot effects of maximum temperature (99th relative to 75th percentile) on age-specific morbidities along the lags

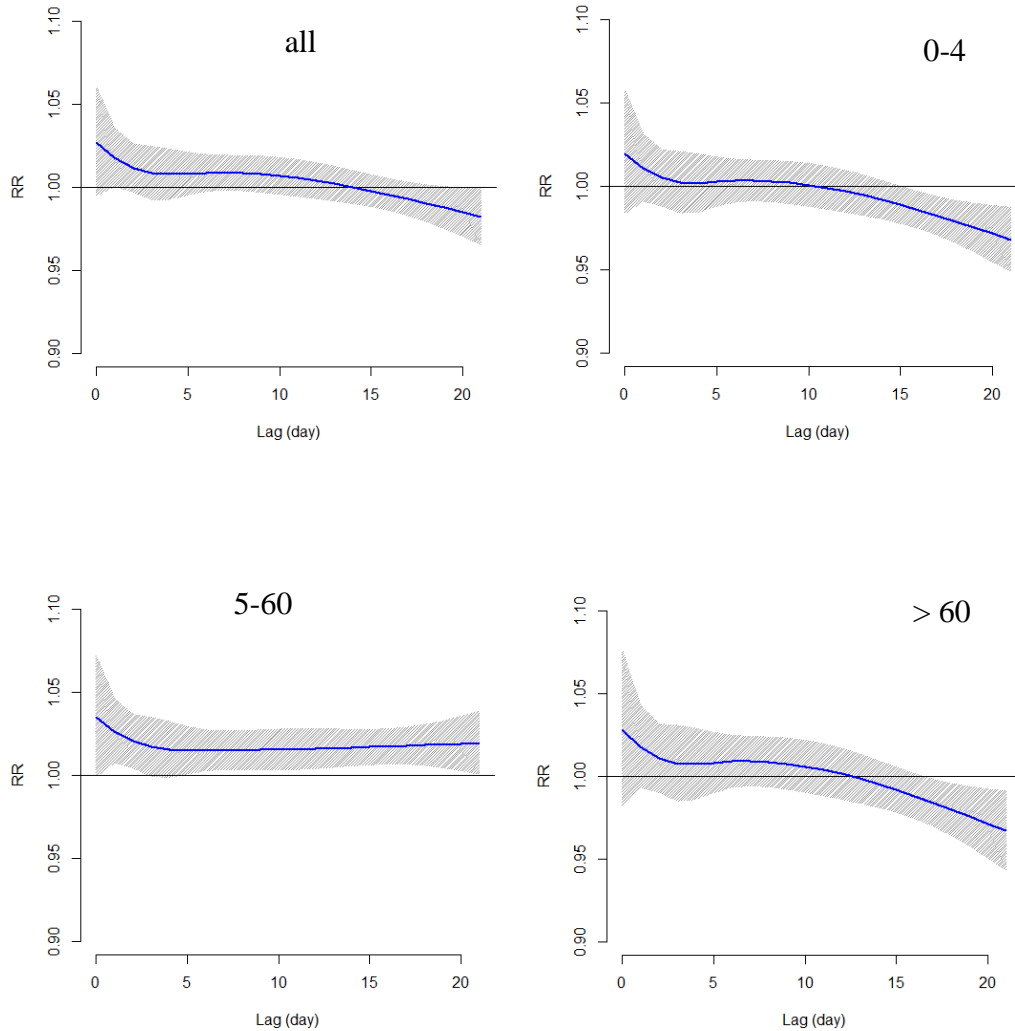


Figure 4. The estimated cold effects of maximum temperature (1st relative to 25th percentile) on age-specific morbidities along the lags

The cumulative hot and cold effects on age-specific respiratory hospitalizations along the lags were presented in Table 2 and 3. Both high and low temperatures had no statistically significant association with increased hospitalizations in all age groups at lag 0. Heat had a greater impact on the elderly, whereas those aged 5-60 years were more sensitive to cold temperatures. The highest cumulative risk of heat effects was observed among those older than 65 years at lag 0–25 (RR 1.509, 95% CI: 1.209-1.883). The highest risk of cold effect on respiratory hospitalizations was found in those aged 5- 60 years at lag 0–25 (RR 1.482, 95% CI: 1.231-1.785).

	Lag0	Lag0-2	Lag0-14	Lag0-25
All	1.003 (0.968-1.038)	1.010(0.952-1.071)	0.982 (0.873- 1.105)	1.021(0.871-1.197)
0-4 y	1.003 0.964 1.044	0.993 0.929 1.060	0.958 0.839 1.099	0.986 0.823 1.182
5-60 y	0.985 0.945 1.027	0.978 0.913 1.047	0.772 0.674 0.885	0.702 0.584 0.845
> 60 y	1.020 0.971 1.071	1.076 0.992 1.167	1.268 1.076 1.494	1.509 1.209 1.883

The bold-faced data means statistically significant ($p < 0.05$).

Table 2. The cumulative relative risks of hot effects on age-specific hospital admissions for respiratory diseases.

	Lag0	Lag0-2	Lag0-14	Lag0-25
All	1.027 0.994 1.060	1.057 1.001 1.116	1.141 1.000 1.301	1.065 0.898 1.263
0-4 y	1.019 0.983 1.057	1.035 0.973 1.102	1.037 0.888 1.210	0.891 0.729 1.088
5-60 y	1.034 0.998 1.072	1.084 1.021 1.150	1.306 1.130 1.510	1.482 1.231 1.785
> 60y	1.027 0.982 1.075	1.057 0.978 1.141	1.124 0.933 1.355	0.973 0.764 1.239

The bold-faced data means statistically significant ($p < 0.05$).

Table 3. The cumulative relative risks of hot effects on age-specific hospital admissions for respiratory diseases.

Sensitivity analysis

We varied the df for time (range 6-12 per year) to investigate the influence of seasonality, and found the results scarcely varied (data not shown). We altered the maximum lag days from 14-30 days, and the temperature effects were similar (data not shown). Additionally, the df for temperature and lags from 3 to 6 were changed, which also gave similar estimated effects.

Discussion

This study examined the effects of temperature on respiratory hospital admissions by age groups in Campo Grande city, Brazil, during 2004-2014. We found that the temperature-morbidity relationship was non-linear for respiratory disease in all age groups. Although we did not observe immediate temperature effects on respiratory hospitalization, lag effects of both high and low temperatures were apparent. The elderly was found to be at higher risk during extreme hot days, whereas those aged 5-60 years were more sensitive to cold temperatures.

Previous studies have observed acute temperature effects on mortality [27, 29, 32] and morbidity. The hot temperatures had short-term effects on mortality and morbidity [32], whereas the cold effect were normally delayed and lasted several days [33]. In this analysis, we found acute cold effects (lag 0-2) on respiratory diseases and this may be in part because people in the city of Campo Grande with tropical weather patterns might not used to cold weather. Studies in Europe and USA have confirmed that cold temperatures tend to have greater impacts on mortality in warmer cities than in cold cities [34].

The relationships between temperature and mortality have been examined in different parts of the world, such as USA, Europe and Australia [35-38], but there is little evidence in Brazil. Studies showed that effects of temperature on morbidity/mortality varied by population and region [38, 39, 16, 35]. In this study, both extreme cold and high temperatures had significant effects on age-specific respiratory hospital admission. A recent study has showed that cities with median or lower income (e.g., Bangkok, Mexico City, São Paulo, Delhi, Santiago, and Cape Town) are at higher risks of temperature-related mortality [40].

The variation of human responses to climate changes appears to be directly associated to questions of individual and collective vulnerability. Variables such as age, health profile, physiological resilience and social-economic status directly contribute to the human responses to climate variables. Factors which increase vulnerability include population growth, poverty and environmental degradation, which affect especially children, with an increase in respiratory and diarrheic diseases resulting from settlement of people in frequently inadequate locations [41].

Atmospheric conditions may influence the transport of micro-organisms, as well as pollutants originating in fixed and mobile sources, and the production of pollen [42]. Effects of climate changes may be aggravated, depending on the physical and chemical characteristics of the pollutants and climatic conditions such as temperature, humidity and precipitation. These characteristics define the time period during which pollutants remain in the atmosphere, and they can be transported long distances in favorable conditions such as high temperatures and low humidity. These pollutants associated with climatic conditions can affect the health of populations far from the pollution generating sources.

The alterations in temperature, humidity and rainfall may increase the effects of respiratory diseases, as well as alter exposition to atmospheric pollutants. Given the evidence of the relation between health effects due to climatic variations and the levels of atmospheric pollution, such as episodes of thermal inversion, increases in pollution levels and an increase in respiratory problems, it seems inevitable that long-term climate changes will affect human health at a global level.

This study has two major strengths. Firstly, this study investigated the effects of temperature on respiratory morbidity by age group using an advanced statistical approach (DLNM) in Campo Grande city, Brazil. The advanced statistical approach can flexibly examine effects of temperature on morbidity. For example, it can smooth temperature and lag at the same time. Secondly, we used ten years' data which had high quality (no missing data for mortality). We also adjusted for a range of confounders including relative humidity and air pollutants. However, some limitations of the study should be noted. First, this is an ecological study in

which exposure misclassification might occur as detailed spatial information was unavailable in this study. In addition, with this study design it was not possible to control other time-varying confounding variables such as intake of alcohol, smoking rates and use of medications.

Conclusions

This study examined the effects of temperature on hospital admissions for respiratory diseases by age group in the city of Campo Grande, Brazil. The relationship between temperature and respiratory morbidity by age group was non-linear. Both hot and cold temperatures were associated with increased risk of respiratory morbidity. Both hot and cold effects can last longer. Heat-related risk in older people (> 60 years) was higher than those in other age groups. These results demonstrate that extreme temperatures influence the health of vulnerable populations in Campo Grande city.

References

- [1] IPCC. Fifth assessment report. Intergovernmental Panel on Climate Change; 2014.
- [2] WHO. 2008. Protecting health from climate change. World Health Day 2008. Geneva:World Health Organization.
- [3] A Souza, Fernanda A Andrade, Pelumi E Oguntunde, Milica Arsic, Debora A.S Silva, Climate indicators and the impact on morbidity and mortality of acute respiratory infections, *Advanced Studies in Medical Sciences*, **6** (2018), 5-20. <https://doi.org/10.12988/asms.2018.863>
- [4] A Souza, Association Between Aerosols And Hospitalizations For Respiratory Diseases (Associação Entre Aerossóis E Internações Por Doenças Respiratórias), *Revista Brasileira De Climatologia*, **19** (2016), 352-365. <https://doi.org/10.5380/abclima.v19i0.45088>
- [5] A Souza, D. A. Santos, Temperature as a risk factor for hospital admissions in 70 cities MS, *Ciência e Natura*, **38** (2016), 1512-1522. <https://doi.org/10.5902/2179460x21277>
- [6] A. Souza, H. Pavão, G. Lastoria, et al., Respiratory hospitalizations associated with atmospheric pollution in the city of Campo Grande-MS, Brazil, *Revista De Biociencias-Unitau*, (2010), 43-49.
- [7] A. Souza, D. A. S. Santos, F. Aristone, M. Kovač, M. Berislav, M. Brunislav, H. G. Pavao, J. C. Pires, P. V. Ikefuti, Impacto De Fatores Meteorológicos Sobre

As Concentrações De Ozônio Modelados Por Análise De Séries Temporais E Métodos Estatísticos Multivariados, *Holos*, **5** (2017), 2.

<https://doi.org/10.15628/holos.2017.5033>

[8] A. Souza, D. A. S. Santos, P. G. Caldin, Poluição Atmosférica Urbana A Partir De Dados De Aerossóis Modis: Efeito Dos Parâmetros Meteorológicos, *Boletim Goiano De Geografia*, **37** (2017), 466.

<https://doi.org/10.5216/bgg.v37i3.50766>

[9] A. Souza, D. A. S. Santos, A. Z. Kofanovski, M. Kovač, Condições Climáticas E O Risco De Exacerbação Da Asma, *Saúde (Santa Maria)*, **43** (2017), 244.

<https://doi.org/10.5902/2236583423462>

[10] A Souza, Débora A. S. Santos, Priscilla V. Ikefuti, Association Between Climate Variables, Pollutants, Aerosols And Hospitalizations Due To Asthma, *O Mundo Da Saúde (Cusc. Impreso)*, 41 (2017), 359-367.

<https://doi.org/10.15343/0104-7809.20174103359367>

[11] B. G. Armstrong, Z. Chalabi, B. Fenn, S. Hajat, S. Kovats, A. Milojevic, P. Wilkinson, Association of mortality with high temperatures in a temperate climate. England and Wales, *J. Epidemiol Community Health*, **65** (2011), 340-345. <https://doi.org/10.1136/jech.2009.093161>

[12] D. Aström, B. Forsberg, K. L. Ebi, J. Rocklöv, Attributing mortality from extreme temperatures to climate change in Stockholm, Sweden, *Nature Climate Change*, **3** (2013), 1050-1054. <https://doi.org/10.1038/nclimate2022>

[13] K. Knowlton, M. Rotkin-Ellman, G. King, H. Margolis, D. Smith, G. Solomon, R. Trent, P. English, The 2006 California heat wave: impacts on hospitalizations and emergency department visits, *Environ Health Perspect.*, **117** (2009), 61-67. <https://doi.org/10.1289/ehp.11594>

[14] L. Bai, G. Ding, S. Gu, P. Bi, B. Su, D. Qin, G. Xu, Q. Liu, The effects of summer temperature and heat waves on heat-related illness in a coastal city of China, 2011-2013, *Environment Research*, **132** (2014), 212-219.

<https://doi.org/10.1016/j.envres.2014.04.002>

[15] P. Michelozzi, G. Accetta, M. De Sario, D. D'Ippoliti, C. Marino, M. Baccini, A. Biggeri, H. Anderson et al., High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities, *Am. J. Respir. Crit. Care Med.*, **179** (2009), 383-389. <https://doi.org/10.1164/rccm.200802-217oc>

[16] B. Revich, D. Shaposhnikov, Excess mortality during heat waves and cold spells in Moscow, Russia, *Occup. Environ. Med.*, **65** (2008), 691-696.

<https://doi.org/10.1136/oem.2007.033944>

- [17] J. Kysely, L. Pokorna, J. Kyncl, B. Kriz, Excess cardiovascular mortality associated with cold spells in the Czech Republic, *BMC Public Health*, **9** (2009), 19. <https://doi.org/10.1186/1471-2458-9-19>
- [18] M. M. Huynen, P. Martens, D. Schram, M. P. Weijnenberg, A. E. Kunst, The impact of heat waves and cold spells on mortality rates in the Dutch population, *Environ. Health Perspect.*, **109** (2001), 463-470. <https://doi.org/10.1289/ehp.01109463>
- [19] K. Juopperi, J. Hassi, O. Ervasti, A. Drebs, S. Näyhä, Incidence of frostbite and ambient temperature in Finland, 1986-1995. A national study based on hospital admissions, *Int. J. Circumpolar Health*, **61** (2002), 352-362. <https://doi.org/10.3402/ijch.v61i4.17493>
- [20] J. Schwartz, J. M. Samet, J. A. Patz, Hospital admissions for heart disease: the effects of temperature and humidity, *Epidemiology*, **15** (2004), 755-761. <https://doi.org/10.1097/01.ede.0000134875.15919.0f>
- [21] J. C. Semenza, J. E. McCullough, W. D. Flanders, et al., Excess hospital admissions during the July 1995 heat wave in Chicago, *Am. J. Prev. Med.*, **16** (1999), no. 4, 269-277. [https://doi.org/10.1016/s0749-3797\(99\)00025-2](https://doi.org/10.1016/s0749-3797(99)00025-2)
- [22] R. S. Kovats, S. Hajat, P. Wilkinson, Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London, UK, *Occup. Environ. Med.*, **61** (2004), 893-898. <https://doi.org/10.1136/oem.2003.012047>
- [23] D. B. Panagiotakos, C. Chrysohoou, C. Pitsavos, P. Nastos, A. Anadiotis, C. Tentolouris, C. Stefanadis, P. Toutouzas, A. Paliatsos, Climatological variations in daily hospital admissions for acute coronary syndromes, *Int. J. Cardiol.*, **94** (2004), 229-233. <https://doi.org/10.1016/j.ijcard.2003.04.050>
- [24] R. G. Barry, R.J. Chorley, *Atmosphere, Weather and Climate*, 8th ed., New York: Methuen & Co. Ltd, 2003.
- [25] S. Hajat, T. Kosatsky, Heat-related mortality: a review and exploration of heterogeneity, *J. Epidemiol. Community Health*, **64** (2010), 753-60. <https://doi.org/10.1136/jech.2009.087999>
- [26] M. S. O'Neill, K. L. Ebi, Temperature extremes and health: impacts of climate variability and change in the United States, *J. Occup. Environ. Med.*, **51** (2009), 13-25. <https://doi.org/10.1097/jom.0b013e318173e122>
- [27] A. Braga, A. Zanobetti, J. Schwartz, The effect of weather on respiratory and cardiovascular deaths in 12 U.S. cities, *Environmental Health Perspective*, **110**

(2002), 859–863. <https://doi.org/10.1289/ehp.02110859>

[28] A Zanobetti, Generalized additive distributed lag models: quantifying mortality displacement, *Biostatistic*, **1** (2000), 279-292.
<https://doi.org/10.1093/biostatistics/1.3.279>

[29] Y. Guo, A. G. Barnett, X. Pan, W. Yu, S. Tong, The impact of temperature on mortality in tianjin, china: a case-crossover design with a distributed lag nonlinear model, *Environ. Health Perspect.*, **119** (2011), 1719-1725.
<https://doi.org/10.1289/ehp.1103598>

[30] A. Gasparrini, B. Armstrong, M. Kenward, Distributed lag non-linear models, *Statistics in Medicine*, **29** (2010), 2224-2234.
<https://doi.org/10.1002/sim.3940>

[31] L Bai, Cirendunzhu, A. Woodward, D. Zhaxisangmu, B. Chen, Q. Liu, Temperature, hospital admissions and emergency room visits in Lhasa, Tibet: a time-series analysis, *Sci. Total Environ.*, **490** (2014), 838-48.
<https://doi.org/10.1016/j.scitotenv.2014.05.024>

[32] R. Basu, J. Same, Relation between elevated ambient temperature and mortality: A review of the epidemiology evidence, *Epidemiologic Reviews*, **82** (2002), 61-76. <https://doi.org/10.1093/epirev/mxf007>

[33] G. Anderson, M. Bell, Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States, *Epidemiology*, **20** (2009), 205-213.
<https://doi.org/10.1097/ede.0b013e318190ee08>

[34] A. Analitis, K. Katsouyanni, A. Biggeri, M. Baccini, B. Forsberg, L. Bisanti, U. Kirchmayer, F. Ballester, E. Cadum, P. G. Goodman, A. Hojs, J. Sunyer, P. Tiittanen, P. Michelozzi, Effects of cold weather on mortality: results from 15 European cities within the PHEWE project, *Am. J. Epidemiology*, **168** (2008), 1397–1408. <https://doi.org/10.1093/aje/kwn266>

[35] W. Yu, W. Hu, K. Mengersen, Y. Guo, X. Pan, D. Connell, S. Tong, Time course of temperature effects on cardiovascular mortality in Brisbane, Australia, *Heart*, **97** (2011), 1089-1093. <https://doi.org/10.1136/hrt.2010.217166>

[36] F. C. Curriero, K. S. Heiner, J. M. Samet, et al., Temperature and mortality in 11 cities of the eastern United States, *Am. J. Epidemiology*, **155** (2002), 80-87.
<https://doi.org/10.1093/aje/155.1.80>

[37] M. Baccini, A. Biggeri, G. Accetta, et al., Heat effects on mortality in 15 European cities, *Epidemiology*, **19** (2008), 711-719.
<https://doi.org/10.1097/ede.0b013e318176bfcd>

[38] J. Rocklöv, B. Forsberg, The effect of temperature on mortality in Stockholm 1998—2003: A study of lag structures and heatwave effects, *Scandinavian Journal Of Public Health*, **36** (2008), 516-523.
<https://doi.org/10.1177/1403494807088458>

[39] A. El-Zein, M. Tewtel-Salem, G. Nehme, A time-series analysis of mortality and air temperature in Greater Beirut, *Sci. Total Environ.*, **330** (2004), 71-80.
<https://doi.org/10.1016/j.scitotenv.2004.02.027>

[40] Y. Guo, A. Gasparri, B. Armstrong, et al., Global variation in the effects of ambient temperature on mortality: a systematic evaluation, *Epidemiology*, **25** (2014), 781-789. <https://doi.org/10.1097/ede.000000000000165>

[41] A. J. McMichael, Global climate change and health: an old story writ large, in *Climate Change and Human Health. Risks And Responses*, McMichael AJ, Campbell- Lendrum DH, Corvalan CF, Ebi KL, Githenke A, Scheraga JD, et al, editors, Geneva: WHO 2003, 1-17.

[42] R Basu, High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008, *Environ Health*, **8** (2009), 40.
<https://doi.org/10.1186/1476-069x-8-40>

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