The impact of heatwaves on mortality in Australia: a multi-city study

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The impact of heatwaves on mortality in Australia: a multi-city study

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ABSTRACT

Objectives: This study assessed the impact of heatwave on mortality in the three largest Australian cities: Brisbane, Melbourne and Sydney.

Methods: Daily data on climatic variables and mortality for these three cities during the period 1988 to 2009 were obtained from relevant government agencies. A consistent definition of a heatwave was used for these cities. Generalized additive Poisson regression models were fitted to assess the impact of heatwaves on mortality after adjustment for confounders.

Results: Total mortality increased mostly within the same day (lag 0) or a lag of one day (lag 1) during almost all heatwaves in three cities. Using the heatwave definition (HWD) as the 95 percentile of mean temperature for two or more consecutive days in the summer season, the relative risk for total mortality at lag 1 in Brisbane, Melbourne and Sydney was 1.13 (95% confidence interval (CI): 1.08 – 1.19), 1.10 (95% CI: 1.06 – 1.14) and 1.06 (95% CI: 1.01 – 1.10), respectively. Using the more stringent HWD - the 99 percentile of mean temperature for two or more consecutive days in the summer season, the relative risk of total mortality at the lags of 0-2 days in Brisbane and Melbourne was 1.40 (95% CI: 1.29 – 1.51) and 1.47 (95% CI: 1.36 – 1.59), respectively. Elderly, particularly females, were more vulnerable to the impact of heatwaves.

Conclusion: A consistent and significant increase in mortality was observed during heatwaves in the three largest Australian cities, but the impacts of heatwave varied with age, gender, the HWD and geographic area.

ARTICLE SUMMARY

Article focus

- Although the health impact of heatwaves has been increasingly investigated over recent years, little is known about the geographic difference of the heatwave-health relationship in the southern hemisphere.
- This study assessed the heatwave - mortality relationship in the three largest Australian cities: Sydney, Melbourne and Brisbane, and quantified the mortality impacts of heatwaves across these areas.

Key messages

- There was a consistent and significant increase in mortality during heatwaves in the three largest Australian cities, but the impacts of heatwave varied with age, sex, the definition of heatwave and geographic area.
- The impacts of heatwave appeared to occur rapidly and there were no apparent long-term lag effects

Strengths and limitations of this study

- This is the first multi-city study on the mortality impacts of heatwaves in the south hemisphere.
- The key limitation is that the potential confounding effects of air pollution (e.g., O_3) were not controlled, as these data were not complete for the whole study period in all three cities.

INTRODUCTION

It is well known that exposure to extreme temperatures has a significant impact on human health. For example, the 2003 heatwave caused over 70,000 excess deaths in Europe.[1, 2] A number of epidemiological studies have shown that the relationships between temperatures and mortality are often non-linear, with a J, U or V shape.[3-9] However, the key reasons why there are different non-linear curves in different population remain unknown. In addition, exposure to extreme temperatures usually does not reach the highest mortality at the same day, and often show lagged effects.[10, 11] Some of this difference may be explained by inconsistent definitions, methodology as well as possibly population differences. Different heatwave definitions have been used in previous studies since there is currently no standard definition for heatwave.[7, 10, 12]

Some studies have estimated the mortality effects of heatwaves across many countries, cities or communities, and determined how mortality increased during heatwaves.[1-6, 8, 10, 13] Different research methods for estimating mortality associated with heatwaves have been used in previous studies. For example, a descriptive approach has been applied to compare the number of deaths between heatwave and non-heatwave days,[14] a time-series analysis has been widely used to estimate mortality risks in association with hot or cold temperature,[10, 11] and a case-crossover analysis is also another increasingly popular method used in this field.[7, 15, 16] However, recent evidence suggests that time-series analysis is still an effective and possibly the most applicable method for investigating the health impact of time-varying environmental exposures.[17-19]

The most Australia capital cities are located along the coast. There is a wide variation in climatic conditions across Australia. Most previous Australian studies have analysed the relationship between temperature and mortality for only one city and no research, to date, has been conducted to examine the health impact of heatwaves across different cities.[16, 19-24] To better understand how temperature affects mortality in different locations, this study assessed the

temperature - mortality relationship in the three largest Australian cities: Brisbane, Melbourne and Sydney, and attempted to quantify the impact of heatwaves on mortality in these areas.

METHODS

Brisbane, Melbourne and Sydney are the capital cities of Queensland, Victoria and New South Wales, respectively, in Australia. These three metropolitan cities are all located on the south east coast of the continent (Figure 1). There are about 2.2, 4.2 and 4.6 million residents for Brisbane, Melbourne and Sydney, respectively, in June 2011.[25] Together, they represent approximately half of the Australia population of 22.3 million.[25]

[Figure 1 about here]

Data Collection

We obtained mortality data between 1988 and 2009 for Brisbane, Melbourne and Sydney from the Australian Bureau of Statistics (ABS). Due to privacy protection reason, the data obtained from the ABS were limited for the Statistical Division of usual residence by gender and two age groups (i.e., 0-75 and 75+) for the three metropolitan areas. In order to calculate the mortality rate, the corresponding populations by gender and the two age groups from 1988 to 2009 in the three cities were also extracted from the ABS database. Supplemental Table 1 presents the average of population size and percentage of 75 + years old by gender between 1988 and 2009.

Daily climate data on maximum and minimum temperatures and relative humidity for the same period (1988 – 2009) were acquired from the Australian Bureau of Meteorology. We selected all available meteorological stations located within ≤ 30 km of each city's centre (including 7 stations for Brisbane, 7 stations for Melbourne and 11 stations for Sydney). There were approximately 1.4°C to 5.1°C differences for maximum or minimum temperature between meteorological stations of each city. The daily climate data for each city were averaged from selected meteorological stations. When there was a missing value (≤ 1.3%) for a particular meteorological station, observations recorded from the remaining weather stations were used to compute the daily average values.

Data Analysis

Previous studies have found that mean temperature was a slightly better predictor of mortality than maximum or minimum temperature in Brisbane.[26] Thus in this study, we used mean temperature as an indicator of exposure. Daily mean temperatures (i.e., averaged values of maximum and minimum temperatures) were used to investigate the effects of heatwaves on mortality in these three cities. A heatwave was defined as the mean temperature above a heat threshold (i.e., 90, 95 and 99 percentiles of mean temperature) for two or more consecutive days in the summer season (1st December to the end of February of next year). A binary heatwave variable (1 or 0) was used for each day (e.g., 1 for the heatwave days meant that temperatures were equal to or higher than the 99 percentile for two or more consecutive days; 0 for non-heatwave days). A Poisson generalised additive model (GAM) was used to examine both single (e.g., lag 0, 1 and 2) and cumulative lag effects (lag 0 -2) of heatwaves on mortality for each city, after adjustment for humidity and population as confounding factors. The "mgcv" package in R software (version 2.14.1) was used to fit the time series GAM.

RESULTS

Table 1 describes the statistical summary of climatic variables and health outcomes for each city in summer seasons. The highest mean temperature reached 33.6°C in Brisbane (22 Feb. 2004), 35.5°C in Melbourne (29 Jan. 2009) and 33.2°C in Sydney (1 Jan. 2006). However, Brisbane had the higher

average mean temperature (24.8°C) than Melbourne (19.7°C) and Sydney (22.5°C). Similar patterns were observed for the average maximum and minimum temperatures.

[Table 1 about here]

Table 2 indicates the heatwave days and threshold (°C) using different percentiles of mean temperatures. Overall, Brisbane had more heatwave days than Melbourne and Sydney across all heatwave definitions during the study period. This is not unexpected and may simply be because Brisbane is further north with subtropical climatic conditions. Supplemental Figure 1 shows the distribution of daily mortality data by mean temperature for each city. The temperature-mortality relations appeared to be a U shape across three cities.

[Table 2 about here]

Figure 2 shows the distributed lag structure (lag 0 to lag 2) of the heatwave effects on mortality using 95% percentiles of mean temperature as the HWD. Heatwave-related mortality mostly occurred within the same day (lag 0) or a lag of one day (lag 1) for almost all heatwaves in the three cities. Heatwaves also appeared to have greater impacts on female and total mortality. For example, the relative risk for total mortality in Brisbane, Melbourne and Sydney was 1.13 (95% confidence interval (CI): 1.08 – 1.19), 1.10 (95% CI: 1.06 – 1.14) and 1.06 (95% CI: 1.01 – 1.10), respectively, at lag 1. A similar pattern was found if mean temperatures were replaced with maximum temperatures in the heatwave definition in these cities (results not shown).

[Figure 2 about here]

Table 3 reveals the relative risks (RR) of daily mortality during heatwaves using different percentiles of mean temperature as thresholds for cumulative lag effects (lag 0 – 2 days) in three cities after adjustment for relative humidity and population size. Heatwaves appeared to have greater impacts on female and total mortality, especially for female aged 75 and over, regardless of which definition of heatwave was used. However, heatwaves appeared to affect local residents more in Brisbane and Melbourne than Sydney, which may be because Sydney had fewer prolonged hot days than other cities. For example, no heatwave was recorded in Sydney during the study periods if the definition of 99th percentile of mean temperature for 2 or more consecutive days was used (Table 2).

[Table 3 about here]

DISCUSSION

This is the first study to use locally defined definitions to investigate the relationship between heatwaves and mortality in different Australian cities. The principal finding of this study is that there was a consistent and statistical significant relationship between hot temperatures and mortality in the three largest Australian cities: Brisbane, Melbourne and Sydney.

Several mortality studies have reported the impact of heatwaves on mortality.[10, 27, 28] The results of this study support the findings from previous research. In general, heatwaves are associated with significantly increased mortality and the greatest effects occurred at lag 1across all three cities. However, heatwaves appeared to affect mortality more in Brisbane and Melbourne than Sydney. This may be due to the fact that Sydney had fewer prolonged hot days than Brisbane and Melbourne (Table 2). Additionally, adaptation (e.g., more usage of air conditioning in Sydney) and people's behaviour may also play a role.

Our results show that the elderly (≥ 75), especially females, were more vulnerable to heatwave effects than others in these cities. This finding supports previous studies that the female elderly were particularly vulnerable to heat effects.[29, 30] There may be an adverse effect of menopause on thermoregulation, in addition to its effects on cardiovascular fitness.[30] Some important social factors (e.g., living alone or low income) may also explain differences in mortality patterns between males and females during heatwaves.[31, 32]

We investigated both single and cumulative lag effects since some studies have identified the increased risk for temperature-related mortality from exposure occurring on the same day or a few days previously.[10, 11, 15, 16] In this study, we found that the strongest heatwave impact usually occurred on the same day or the next day across all three cities. Thus, we concur with the notion that heatwaves usually have acute and dramatic impacts on mortality. In addition, we found that the minimum mortality temperature thresholds differed across the three cities, i.e., 24.3^{o}C (the 61 percentile of mean temperature), 21.3^{o}C (the 54 percentile of mean temperature) and 23.6^{o}C (the 64 percentile of mean temperature) for Brisbane, Melbourne and Sydney, respectively. This suggests that residents living in different climate zones do have different minimum mortality temperature thresholds, even within the same country.

The findings of this study are comparable to some previous multi-city studies (e.g., US or Europe).[8, 13] There are three similarities across these studies: 1. the similar magnitude of heatwave effects were observed; 2. the impacts of heatwave occurred rapidly and there were no apparent long-term lag effects; and 3. Elderly are more vulnerable to the impacts of heatwave than others. However, there are also some differences across these studies. For example, a previous study[8] found that mortality increased more during heatwaves in early summer than those in late summer, but our results show that higher mortality was resulted from heatwaves in mid or late summer for all three cities, which may be because more intense heatwaves usually occur in mid or late summer in Australia.

There were two key limitations in this study. Only the aggregated data were used while individual exposure and outcome data would give a more precise estimate of the health impacts of a heatwave event, but unfortunately individual data were not available. We did not control for the potential confounding effects of air pollution (e.g., O_3), as these data were not complete for the whole study period in all three cities. However, previous studies have reported the health impacts of a heatwave as occurring independent of air pollution.[33]

CONCLUSION

A consistent and significant increase in mortality was observed during heatwaves in the three Australian metropolitan cities, but the impacts of heatwave varied with age, gender, the definition and geographic area. Extreme hot temperatures appeared to directly result in an increased risk of mortality in these cities. The most vulnerable groups were the elderly, especial female, aged 75 and over. By better understanding heatwave effects on mortality, local government and communities can develop appropriate public health strategies and increase their adaptive capacity to prevent and mitigate the impact of heatwave.

Table 1 Summary of the daily climatic variables and mortality in summer season[a] (1988 – 2009)

	Brisbane				Melbourne				Sydney			
Variable	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max
Male (All)	12	3.9	2	38	27	5.7	11	52	32	7.1	6	74
(0-74)	6	2.8	0	17	13	4.6	1	33	16	5.9	2	47
(75+)	6	2.8	0	25	14	4.4	2	34	15	4.5	3	32
Female (All)	12	4.1	1	40	26	5.7	10	79	30	6.7	9	70
(0-74)	4	2.1	0	13	8	3.3	1	21	10	3.8	1	32
(75+)	8	3.3	0	30	18	5.0	3	64	21	5.4	5	42
Total	24	6.2	4	68	54	8.6	23	127	62	11.1	20	136
MaxT* (^{o}C)	29.3	2.3	20.1	40.1	25.6	5.8	13.9	46.7	27.1	4.0	16.6	44.0
MeanT † (^{o}C)	24.8	1.9	18.3	33.6	19.7	3.9	10.9	35.5	22.5	2.7	15.1	33.2
MinT‡ (^{o}C)	20.3	2.2	11.9	27.1	13.8	3.3	5.8	27.6	18.0	2.3	9.8	25.8
RH§ (%)	70.2	8.7	30.2	96.8	65.0	11.6	19.7	95.6	70.0	11.0	28.1	98.1

[a] 1st December to the end of February of next year
* maximum temperature, † mean temperature, ‡ minimum temperature, § relative humidity

Table 2 Summaries of heatwave definitions (HWDs) used in different cities (1988 – 2009)

HWD[a]	Heatwave days and threshold					
	Brisbane		Melbourne		Sydney	
99%	11	29.7 °C	4	30.1 °C	0	29.6 °C
95%	70	28.0 °C	56	27.2 °C	37	27.3 °C
90%	153	27.2 °C	128	25.3 °C	118	26.1 °C

[a] HWDs were defined as the mean temperature above the percentiles (i.e., 90th, 95th or 99th centile) for two or more consecutive days in the summer season (1st December to the end of February of next year).

Table 3 Relative risk of mortality by different HWDs for cumulative lag effects (lag 0-2) in three cities, 1988 -2009

HWD[a]	RR[†] [95% CI[*]] Brisbane	Melbourne	Sydney
Male (All)			
99%	**1.32 [1.17 - 1.48]**	**1.37 [1.22 - 1.53]**	n/a[‡]
95%	1.04 [0.99 - 1.10]	1.00 [0.96 - 1.04]	1.03 [0.99 - 1.08]
90%	1.01 [0.97 - 1.05]	1.02 [0.99 - 1.05]	**1.04 [1.01 - 1.06]**
(0 - 74)			
99%	**1.29 [1.10 - 1.53]**	**1.37 [1.15 - 1.63]**	n/a
95%	1.04 [0.96 - 1.12]	0.96 [0.91 - 1.02]	**1.07 [1.01 - 1.13]**
90%	0.99 [0.93 - 1.04]	1.00 [0.96 - 1.04]	**1.04 [1.00 - 1.08]**
(75+)			
99%	**1.33 [1.13 - 1.56]**	**1.38 [1.19 - 1.61]**	n/a
95%	1.05 [0.97 - 1.13]	1.04 [0.98 - 1.09]	0.99 [0.92 - 1.05]
90%	1.03 [0.97 - 1.08]	1.03 [0.99 - 1.07]	**1.03 [1.00 - 1.07]**
Female (All)			
99%	**1.45 [1.30 - 1.61]**	**1.57 [1.41 - 1.74]**	n/a
95%	**1.13 [1.07 - 1.19]**	**1.11 [1.07 - 1.15]**	1.03 [0.98 - 1.07]
90%	**1.06 [1.02 - 1.10]**	**1.05 [1.02 - 1.07]**	**1.05 [1.03 - 1.08]**
(0 - 74)			
99%	1.08 [0.86 - 1.34]	**1.46 [1.18 - 1.81]**	n/a
95%	1.06 [0.96 - 1.17]	**1.10 [1.03 - 1.18]**	0.97 [0.90 - 1.05]
90%	1.04 [0.96 - 1.11]	1.04 [0.99 - 1.09]	1.04 [0.99 - 1.09]
(75+)			
99%	**1.61 [1.42 - 1.82]**	**1.63 [1.44 - 1.85]**	n/a
95%	**1.15 [1.08 - 1.22]**	**1.12 [1.07 - 1.17]**	**1.06 [1.01 - 1.12]**
90%	**1.07 [1.02 - 1.12]**	**1.05 [1.01 - 1.08]**	**1.06 [1.03 - 1.09]**
Total			
99%	**1.40 [1.29 - 1.51]**	**1.47 [1.36 - 1.59]**	n/a
95%	**1.09 [1.05 - 1.13]**	**1.06 [1.03 - 1.09]**	**1.03 [1.00 - 1.07]**
90%	**1.04 [1.01 - 1.07]**	**1.03 [1.01 - 1.05]**	**1.04 [1.03 - 1.06]**

[a] HWDs were defined as different percentiles (i.e., 90th, 95th or 99th centile) of mean temperature for two or more consecutive days in the summer season.
[*]confidence interval, [†]relative risk, [‡] not applicable

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Contributors ST contributed to the design and co-ordinated the study. XW conducted the data analyses. ST and XW wrote the first draft of the article. All authors critically reviewed and approved the final manuscript.

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Competing interests There is no conflict of interest.

Ethics approval An ethical approval was granted by the Human Research Ethics Committee, Queensland University of Technology, Australia.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

REFERENCES

1. Le Tertre A, Lefranc A, Eilstein D, et al. Impact of the 2003 heatwave on all-cause mortality in 9 French cities. Epidemiology 2006;17:75-9.
2. Robine JM, Cheung SL, Le Roy S, et al. Death toll exceeded 70,000 in Europe during the summer of 2003. C R Biol 2008;331:171-8.
3. McMichael AJ, Wilkinson P, Kovats RS, et al. International study of temperature, heat and urban mortality: the 'ISOTHURM' project. Int. J. Epidemiol. 2008;37:1121-31.
4. Knowlton K, Rotkin-Ellman M, King G, et al. The 2006 California heat wave: impacts on hospitalizations and emergency department visits. Environ. Health Perspect. 2009;117:61-7.
5. O'Neill MS, Zanobetti A, Schwartz J. Modifiers of the temperature and mortality association in seven US cities. Am. J. Epidemiol. 2003;157:1074-82.
6. Stafoggia M, Forastiere F, Agostini D, et al. Vulnerability to Heat-Related Mortality: A Multicity, Population-Based, Case-Crossover Analysis. Epidemiology 2006;17:315-23
7. Tong S, Wang XY, Barnett AG Assessment of heat-related health impacts in Brisbane, Australia: comparison of different heatwave definitions. *PLoS ONE* 2010;5: e12155. doi: 10.1371/journal.pone.0012155.
8. Anderson GB, Bell ML. Heat Waves in the United States: Mortality Risk during Heat Waves and Effect Modification by Heat Wave Characteristics in 43 U.S. Communities. Environ. Health Perspect. 2011;119:210-8.
9. Hajat S, Kosatky T. Heat-related mortality: a review and exploration of heterogeneity. J. Epidemiol. Community Health 2010;64:753-60.
10. Anderson BG, Bell ML. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology 2009;20:205-13.
11. Yu W, Mengersen K, Hu W, et al. Assessing the relationship between global warming and mortality: lag effects of temperature fluctuations by age and mortality categories. Environ Pollut 2011;159:1789-93.

12. Gasparrini A, Armstrong B. The impact of heat waves on mortality. Epidemiology 2011;22:68-73.

13. Baccini M, Kosatsky T, Analitis A, et al. Impact of heat on mortality in 15 European cities: attributable deaths under different weather scenarios. J. Epidemiol. Community Health 2011;65:64-70.

14. Grize L, Huss A, Thommen O, Schindler C, Braun-Fahrlander C. Heat wave 2003 and mortality in Switzerland. Swiss Med Wkly 2005;135:200-5.

15. Basagana X, Sartini C, Barrera-Gomez J, et al. Heat Waves and Cause-specific Mortality at all Ages. Epidemiology 2011;22:765-72.

16. Wang XY, Barnett AG, Yu W, et al. The impact of heatwaves on mortality and emergency hospital admissions from non-external causes in Brisbane, Australia. Occup. Environ. Med. 2012;69:163-9.

17. Guo Y, Barnett AG, Zhang Y, et al. The short-term effect of air pollution on cardiovascular mortality in Tianjin, China: comparison of time series and case-crossover analyses. Sci. Total Environ. 2010;409:300-6.

18. Tong S, Wang XY, Guo Y Assessing the short-term effects of heatwaves on mortality and morbidity in Brisbane, Australia: comparison of case-crossover and time series analyses. *PLoS ONE* 2012;7: e37500. doi: 10.1371/journal.pone.0037500.

19. Guo Y, Barnett AG, Tong S. Spatiotemporal model or time series model for assessing city-wide temperature effects on mortality? Environ. Res. 2013;120:55-62.

20. Williams S, Nitschke M, Weinstein P, et al. The impact of summer temperatures and heatwaves on mortality and morbidity in Perth, Australia 1994-2008. Environ Int 2012;40:33-8.

21. Schaffer A, Muscatello D, Broome R, Corbett S, Smith W Emergency department visits, ambulance calls, and mortality associated with an exceptional heat wave in Sydney, Australia, 2011: a time-series analysis. *Environ Health* 2012;11. doi: 10.1186/1476-069x-11-3.

22. Vaneckova P, Beggs PJ, Jacobson CR. Spatial analysis of heat-related mortality among the elderly between 1993 and 2004 in Sydney, Australia. Soc. Sci. Med. 2010;70:293-304.

23. Huang C, Barnett AG, Wang X, Tong S. Effects of extreme temperatures on years of life lost for cardiovascular deaths: a time series study in brisbane, australia. Circ Cardiovasc Qual Outcomes 2012;5:609-14.

24. Guest CS, Willson K, Woodward AJ, et al. Climate and mortality in Australia: retrospective study, 1979-1990, and predicted impacts in five major cities in 2030. Clim Res 1999;13:1-15.

25. ABS. Australian Burean of Statistics: Regional Population Growth, Australia, 2011 http://www.abs.gov.au/ausstats/abs@.nsf/mf/3218.0.

26. Vaneckova P, Neville G, Tippett V, et al. Do Biometeorological Indices Improve Modeling Outcomes of Heat-Related Mortality? J. Appl. Meteor. Climatol. 2011;50:1165-76.

27. Schifano P, Leone M, De Sario M, et al. Changes in the effects of heat on mortality among the elderly from 1998-2010: results from a multicenter time series study in Italy. *Environ Health* 2012;11: 58. doi: 10.1186/1476-069x-11-58.

28. Barnett AG, Tong S, Clements AC. What measure of temperature is the best predictor of mortality? Environ. Res. 2010;110:604-11.

29. Yu W, Vaneckova P, Mengersen K, Pan X, Tong S. Is the association between temperature and mortality modified by age, gender and socio-economic status? Sci. Total Environ. 2010;408:3513-8.

30. Hajat S, Kovats RS, Lachowycz K. Heat-related and cold-related deaths in England and Wales: who is at risk? Occup. Environ. Med. 2007;64:93-100.

31. Kim Y, Joh S. A vulnerability study of the low-income elderly in the context of high temperature and mortality in Seoul, Korea. Sci. Total Environ. 2006;371:82-8.

32. Stafoggia M, Forastiere F, Agostini D, et al. Factors affecting in-hospital heat-related mortality: a multi-city case-crossover analysis. J. Epidemiol. Community Health 2008;62:209-15.

33. Tong S, Ren C, Becker N. Excess deaths during the 2004 heatwave in Brisbane, Australia. Int. J. Biometeorol. 2010;54:393-400.

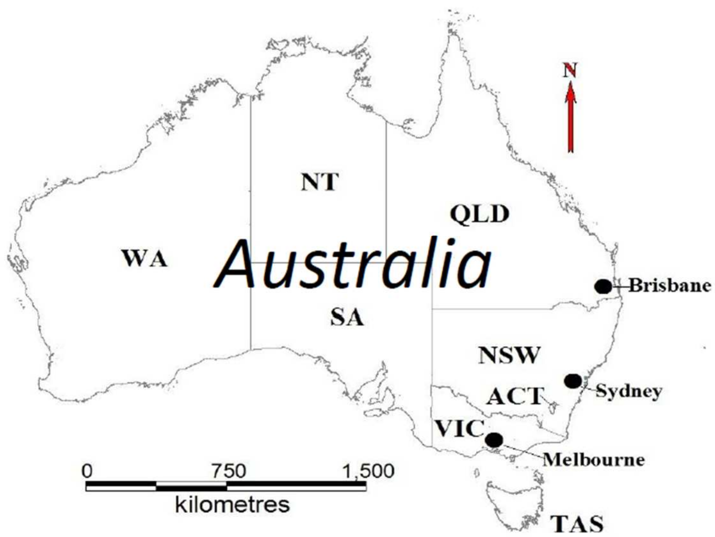


Figure 1 Locations of Brisbane, Melbourne and Sydney in Australia
254x190mm (96 x 96 DPI)

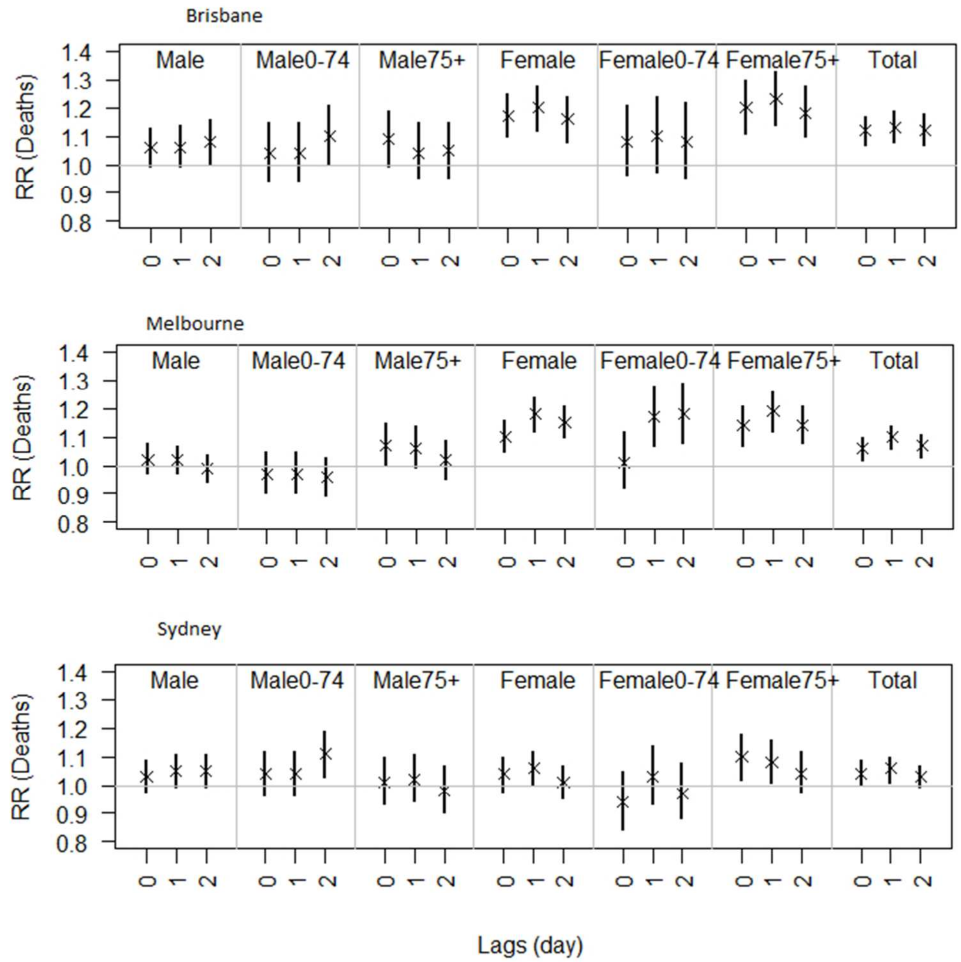
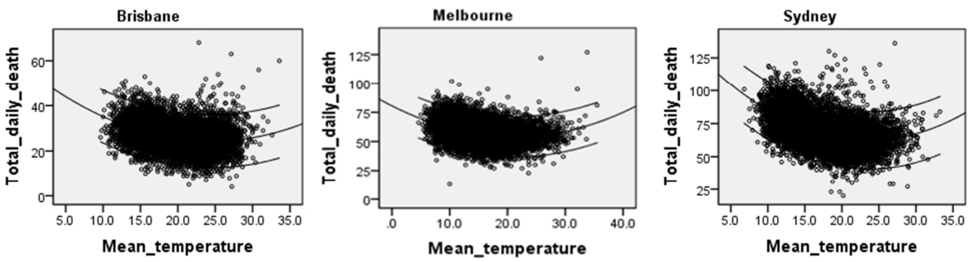


Figure 2 Distributed lag structure of the heatwave effects on mortality by sex, age and city. Cross symbols denote the mean relative risk (RR), and the vertical lines represent the 95% confidence intervals
185x186mm (96 x 96 DPI)

Supplemental Table 1 Average population size and percentage of older people (75+) between 1988 and 2009

City	Total	Male	% 75+ (M*)	Female	% 75+ (F†)
Brisbane	1,603,742	792,809	3.6	810,933	5.9
Melbourne	3,423,855	1,688,942	4.1	1,734,914	6.4
Sydney	3,996,444	1,978,055	4.0	2,018,389	6.4

*Male, †Female



Supplemental Figure 1 The distribution of daily mean temperature (oC) and mortality (1988 – 2009)
234x67mm (96 x 96 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract √
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found √
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported √
Objectives	3	State specific objectives, including any prespecified hypotheses √
Methods		
Study design	4	Present key elements of study design early in the paper √
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection √
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants N/A
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable √
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group √
Bias	9	Describe any efforts to address potential sources of bias √
Study size	10	Explain how the study size was arrived at √
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why √

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding √
		(*b*) Describe any methods used to examine subgroups and interactions √
		(*c*) Explain how missing data were addressed √
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed N/A *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy N/A
		(*e*) Describe any sensitivity analyses √

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed N/A
		(b) Give reasons for non-participation at each stage N/A
		(c) Consider use of a flow diagram N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders √
		(b) Indicate number of participants with missing data for each variable of interest √
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time N/A
		Case-control study—Report numbers in each exposure category, or summary measures of exposure N/A
		Cross-sectional study—Report numbers of outcome events or summary measures N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included √
		(*b*) Report category boundaries when continuous variables were categorized √
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period √
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses √
Discussion		
Key results	18	Summarise key results with reference to study objectives √
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias √
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence √
Generalisability	21	Discuss the generalisability (external validity) of the study results √

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based √

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

The impact of heatwaves on mortality in Australia: a multi-city study

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The impact of heatwaves on mortality in Australia: a multi-city study

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ABSTRACT

Objectives: This study assessed the impact of heatwave on mortality in the three largest Australian cities: Brisbane, Melbourne and Sydney.

Methods: Daily data on climatic variables and mortality for these three cities during the period 1988 to 2009 were obtained from relevant government agencies. A consistent definition of a heatwave was used for these cities. Generalised additive models were fitted to assess the impact of heatwaves on mortality after adjustment for confounders.

Results: Total mortality increased mostly within the same day (lag 0) or a lag of one day (lag 1) during almost all heatwaves in three cities. Using the heatwave definition (HWD) as the 95th centile of mean temperature for two or more consecutive days in the summer season, the relative risk for total mortality at lag 1 in Brisbane, Melbourne and Sydney was 1.13 (95% confidence interval (CI): 1.08 – 1.19), 1.10 (95% CI: 1.06 – 1.14) and 1.06 (95% CI: 1.01 – 1.10), respectively. Using the more stringent HWD - the 99th centile of mean temperature for two or more consecutive days, the relative risk of total mortality at the lags of 0-2 days in Brisbane and Melbourne was 1.40 (95% CI: 1.29 – 1.51) and 1.47 (95% CI: 1.36 – 1.59), respectively. Elderly, particularly females, were more vulnerable to the impact of heatwaves.

Conclusion: A consistent and significant increase in mortality was observed during heatwaves in the three largest Australian cities, but the impacts of heatwave varied with age, gender, the HWD and geographic area.

ARTICLE SUMMARY

Article focus

- Although the health impact of heatwaves has been increasingly investigated over recent years, little is known about the geographic difference of the heatwave-health relationship in the Southern Hemisphere.
- This study assessed the heatwave - mortality relationship in the three largest Australian cities: Sydney, Melbourne and Brisbane, and quantified the mortality impacts of heatwaves across these areas.

Key messages

- There was a consistent and significant increase in mortality during heatwaves in the three largest Australian cities, but the impacts of heatwave varied with age, sex, the definition of heatwave and geographic area.
- The impacts of heatwave appeared to occur rapidly and there were no apparent long-term lag effects.

Strengths and limitations of this study

- This is the first multi-city study on the mortality impacts of heatwaves in the Southern Hemisphere; and the similarities and differences in the heatwave - mortality relationship across the three largest Australian cities were quantified.
- The key limitation is that the potential confounding effects of air pollution were not controlled, as these data were not complete for the whole study period in all three cities.

INTRODUCTION

It is well known that exposure to extreme temperatures has a significant impact on human health. For example, the 2003 heatwave caused over 70,000 excess deaths in Europe.[1, 2] A number of epidemiological studies have shown that the relationships between temperatures and mortality are often non-linear, with a J, U or V shape.[3-9] However, the key reasons why there are different non-linear curves in different population remain unknown. In addition, exposure to extreme temperatures usually does not reach the highest mortality at the same day, and often show lagged effects.[10, 11] Some of this difference may be explained by inconsistent definitions, methodology as well as possibly population differences. Different heatwave definitions have been used in previous studies since there is currently no standard definition for heatwave.[7, 10, 12]

Some studies have estimated the mortality effects of heatwaves across many countries, cities or communities, and determined how mortality increased during heatwaves.[1-6, 8, 10, 13] Different research methods for estimating mortality associated with heatwaves have been used in previous studies. For example, a descriptive approach has been applied to compare the number of deaths between heatwave and non-heatwave days,[14] a time-series analysis has been widely used to estimate mortality risks in association with hot or cold temperature,[10, 11] and a case-crossover analysis is also another increasingly popular method used in this field.[7, 15, 16] However, recent evidence suggests that time-series analysis is still an effective and possibly the most applicable method for investigating the health impact of time-varying environmental exposures.[17-19]

The most Australia capital cities are located along the coast. There is a wide variation in climatic conditions across Australia. Most previous Australian studies have analysed the relationship between temperature and mortality for only one city and no research, to date, has been conducted to examine the health impact of heatwaves across different cities.[16, 19-24] To better understand how temperature affects mortality in different locations, this study assessed the

temperature - mortality relationship in the three largest Australian cities: Brisbane, Melbourne and Sydney, and attempted to quantify the impact of heatwaves on mortality in these areas.

METHODS

Brisbane, Melbourne and Sydney are the capital cities of Queensland, Victoria and New South Wales, respectively, in Australia. These three metropolitan cities are all located on the south east coast of the continent (Figure 1). There are about 2.2, 4.2 and 4.6 million residents for Brisbane, Melbourne and Sydney, respectively, in June 2011.[25] Together, they represent approximately half of the Australia population of 22.3 million.[25]

[Figure 1 about here]

Data Collection

We obtained mortality data between 1988 and 2009 for Brisbane, Melbourne and Sydney from the Australian Bureau of Statistics (ABS). Due to privacy protection reason, the data obtained from the ABS were limited for the Statistical Division of usual residence by gender and two age groups (i.e., 0-75 and 75+) for the three metropolitan areas. In order to calculate the mortality rate, the corresponding populations by gender and the two age groups from 1988 to 2009 in the three cities were also extracted from the ABS database. Supplemental Table 1 presents the average of population size and percentage of 75 + years old by gender between 1988 and 2009.

Daily climate data on maximum and minimum temperatures and relative humidity for the same period (1988 – 2009) were acquired from the Australian Bureau of Meteorology. We selected all available meteorological stations located within ≤ 30 km of each city's CBD (7 stations for Brisbane, 7 stations for Melbourne and 11 stations for Sydney). We calculated the daily averages of climatic variables using all records from meteorological stations in each city. This approach is used

in previous research.[18] There were approximately 1.4°C to 5.1°C differences for maximum or minimum temperature between meteorological stations of each city. When there was a missing value (≤ 1.3%) for a particular meteorological station, observations recorded from the remaining weather stations were used to compute the daily average values.

Data Analysis

Previous studies have found that mean temperature was a slightly better predictor of mortality than maximum or minimum temperature in Brisbane.[26] Thus in this study, we used mean temperature as an indicator of exposure. Daily mean temperatures (i.e., averaged values of maximum and minimum temperatures) were used to investigate the effects of heatwaves on mortality in these three cities. A heatwave was defined as the mean temperature above a heat threshold (i.e., 90, 95 and 99 percentiles of mean temperature) for two or more consecutive days in the summer season (1st December to the end of February of next year). A binary heatwave variable (1 or 0) was used for each day (e.g., 1 for the heatwave days meant that temperatures were equal to or higher than the 99 percentile for two or more consecutive days; 0 for non-heatwave days). A Poisson generalised additive model (GAM) was used to examine both single (e.g., lag 0, 1 and 2) and cumulative lag effects (lag 0 -2) of heatwaves on mortality for each city, after adjustment for humidity and population as confounding factors. The "mgcv" package in R software (version 2.14.1) was used to fit the time series GAM.

RESULTS

Table 1 describes the statistical summary of climatic variables and health outcomes for each city in summer seasons. The highest mean temperature reached 33.6°C in Brisbane (22 Feb. 2004), 35.5°C in Melbourne (29 Jan. 2009) and 33.2°C in Sydney (1 Jan. 2006). However, Brisbane had the higher

average mean temperature (24.8^{o}C) than Melbourne (19.7^{o}C) and Sydney (22.5^{o}C). Similar patterns were observed for the average maximum and minimum temperatures.

[Table 1 about here]

Table 2 indicates the heatwave days and threshold (^{o}C) using different percentiles of mean temperatures. Supplemental Table 2 also provided the heatwave days separated by early summer and later summer. Overall, Brisbane had more heatwave days than Melbourne and Sydney across all heatwave definitions during the study period. This is not unexpected and may simply be because Brisbane is further north with subtropical climatic conditions. Supplemental Figure 1 shows the distribution of daily mortality data by mean temperature for each city. The temperature-mortality relations appeared to be a U shape across three cities.

[Table 2 about here]

Figure 2 shows the distributed lag structure (lag 0 to lag 7) of the heatwave effects on mortality using 95% percentiles of mean temperature as the HWD in three cities after adjustment for relative humidity and population size. Heatwave-related mortality mostly occurred within the same day (lag 0) or a lag of one day (lag 1) in the three cities. Heatwaves also appeared to have greater impacts on female and total mortality. For example, the relative risk for total mortality in Brisbane, Melbourne and Sydney was 1.13 (95% confidence interval (CI): 1.08 – 1.19), 1.10 (95% CI: 1.06 – 1.14) and 1.06 (95% CI: 1.01 – 1.10), respectively, at lag 1. A similar pattern was found if mean temperatures were replaced with maximum temperatures in the heatwave definition in these cities (results not shown).

[Figure 2 about here]

Table 3 reveals the relative risks (RR) of daily mortality during heatwaves using different percentiles of mean temperature as thresholds for cumulative lag effects (lag 0 – 2 days) in three cities after adjustment for relative humidity and population size. Heatwaves appeared to have greater impacts on female and total mortality, especially for female aged 75 and over, regardless of which definition of heatwave was used. However, heatwaves appeared to affect local residents more in Brisbane and Melbourne than Sydney, which may be because Sydney had fewer prolonged hot days than other cities. For example, no heatwave was recorded in Sydney during the study periods if the definition of 99th percentile of mean temperature for 2 or more consecutive days was used (Table 2).

[Table 3 about here]

DISCUSSION

This is the first study to use locally defined definitions to investigate the relationship between heatwaves and mortality in different Australian cities. The principal finding of this study is that there was a consistent and statistical significant relationship between hot temperatures and mortality in the three largest Australian cities: Brisbane, Melbourne and Sydney.

Several mortality studies have reported the impact of heatwaves on mortality.[10, 27, 28] The results of this study support the findings from previous research. In general, heatwaves are associated with significantly increased mortality across all three cities. However, heatwaves appeared to affect mortality more in Brisbane and Melbourne than Sydney. This may be due to the fact that Sydney had fewer prolonged hot days than Brisbane and Melbourne (Table 2). Additionally, adaptation (e.g., more usage of air conditioning in Sydney) and people's behaviour may also play a role. Supplemental Table 2 shows that the total number of deaths (i.e., 4,566) during heatwave periods in the late summer was greater than that in the early summer. For example, if the heatwave was defined as the 95th centile for two or more consecutive days, 4,566 people died during heatwave periods across three cities in the late summer, compared with 2720 died in the early summer.

Our results show that the elderly (≥ 75), especially females, were more vulnerable to heatwave effects than others in these cities. This finding supports previous studies that the female elderly were particularly vulnerable to heat effects.[29, 30] There may be an adverse effect of menopause on thermoregulation, in addition to its effects on cardiovascular fitness.[30] Some important social factors (e.g., living alone or low income) may also explain differences in mortality patterns between males and females during heatwaves.[31, 32]

We investigated both single and cumulative lag effects since some studies have identified the increased risk for temperature-related mortality from exposure occurring on the same day or a few days previously.[10, 11, 15, 16] In this study, we found that the strongest heatwave impact usually occurred on the same day or the next day across all three cities (Figure 2). Thus, we concur with the notion that heatwaves usually have acute and dramatic impacts on mortality.

The findings of this study are comparable to some previous multi-city studies (e.g., US or Europe).[8, 13] There are three similarities across these studies: 1. the similar magnitude of heatwave effects were observed; 2. the impacts of heatwave occurred rapidly and there were no apparent long-term lag effects; and 3. Elderly are more vulnerable to the impacts of heatwave than others. However, there are also some differences across these studies. For example, a previous study[8] found that mortality increased more during heatwaves in early summer than those in late summer, but our results show that higher mortality was resulted from heatwaves in mid or late summer for all three cities (Supplemental Table 2), which may be because more intense heatwaves usually occur in mid or late summer in Australia.

There were two key limitations in this study. Only the aggregated data were used while individual exposure and outcome data would give a more precise estimate of the health impacts of a heatwave event, but unfortunately individual data were not available. We did not control for the potential confounding effects of air pollution (e.g., O_3), as these data were not complete for the whole study period in all three cities. However, previous studies have reported the health impacts of a heatwave as occurring independent of air pollution.[33]

CONCLUSION

A consistent and significant increase in mortality was observed during heatwaves in the three Australian metropolitan cities, but the impacts of heatwave varied with age, gender, the definition and geographic area. Extreme hot temperatures appeared to directly result in an increased risk of mortality in these cities. The most vulnerable groups were the elderly, especial female, aged 75 and over. By better understanding heatwave effects on mortality, local government and communities can develop appropriate public health strategies and increase their adaptive capacity to prevent and mitigate the impact of heatwave.

Table 1 Summary of the daily climatic variables and mortality in summer season[a] (1988 – 2009)

	Brisbane				Melbourne				Sydney			
Variable	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max
Male (All)	12	3.9	2	38	27	5.7	11	52	32	7.1	6	74
(0-74)	6	2.8	0	17	13	4.6	1	33	16	5.9	2	47
(75+)	6	2.8	0	25	14	4.4	2	34	15	4.5	3	32
Female (All)	12	4.1	1	40	26	5.7	10	79	30	6.7	9	70
(0-74)	4	2.1	0	13	8	3.3	1	21	10	3.8	1	32
(75+)	8	3.3	0	30	18	5.0	3	64	21	5.4	5	42
Total	24	6.2	4	68	54	8.6	23	127	62	11.1	20	136
MaxT* (°C)	29.3	2.3	20.1	40.1	25.6	5.8	13.9	46.7	27.1	4.0	16.6	44.0
MeanT † (°C)	24.8	1.9	18.3	33.6	19.7	3.9	10.9	35.5	22.5	2.7	15.1	33.2
MinT‡ (°C)	20.3	2.2	11.9	27.1	13.8	3.3	5.8	27.6	18.0	2.3	9.8	25.8
RH§ (%)	70.2	8.7	30.2	96.8	65.0	11.6	19.7	95.6	70.0	11.0	28.1	98.1

[a]1st December to the end of February of next year
*maximum temperature, †mean temperature, ‡minimum temperature, §relative humidity

Table 2 Heatwave definition (HWD) used in three cities (1988 – 2009)

HWD[a]	Heatwave days and threshold					
	Brisbane		Melbourne		Sydney	
99%	11	29.7 °C	4	30.1 °C	0	29.6 °C
95%	70	28.0 °C	56	27.2 °C	37	27.3 °C
90%	153	27.2 °C	128	25.3 °C	118	26.1 °C

[a] HWD were defined as the mean temperature above the percentiles (i.e., 90th, 95th or 99th centile) for two or more consecutive days in the summer season (1st December to the end of February of next year).

Table 3 Relative risk of mortality by different heatwave definition (HWD) for cumulative lag effects (lag 0-2) in three cities, 1988 -2009

		RR[†] [95% CI[*]]	
HWD[a]	Brisbane	Melbourne	Sydney
Male (All)			
99%	**1.32 [1.17 - 1.48]**	**1.37 [1.22 - 1.53]**	n/a[‡]
95%	1.04 [0.99 - 1.10]	1.00 [0.96 - 1.04]	1.03 [0.99 - 1.08]
90%	1.01 [0.97 - 1.05]	1.02 [0.99 - 1.05]	**1.04 [1.01 - 1.06]**
(0 - 74)			
99%	**1.29 [1.10 - 1.53]**	**1.37 [1.15 - 1.63]**	n/a
95%	1.04 [0.96 - 1.12]	0.96 [0.91 - 1.02]	**1.07 [1.01 - 1.13]**
90%	0.99 [0.93 - 1.04]	1.00 [0.96 - 1.04]	**1.04 [1.00 - 1.08]**
(75+)			
99%	**1.33 [1.13 - 1.56]**	**1.38 [1.19 - 1.61]**	n/a
95%	1.05 [0.97 - 1.13]	1.04 [0.98 - 1.09]	0.99 [0.92 - 1.05]
90%	1.03 [0.97 - 1.08]	1.03 [0.99 - 1.07]	**1.03 [1.00 - 1.07]**
Female (All)			
99%	**1.45 [1.30 - 1.61]**	**1.57 [1.41 - 1.74]**	n/a
95%	**1.13 [1.07 - 1.19]**	**1.11 [1.07 - 1.15]**	1.03 [0.98 - 1.07]
90%	**1.06 [1.02 - 1.10]**	**1.05 [1.02 - 1.07]**	**1.05 [1.03 - 1.08]**
(0 - 74)			
99%	1.08 [0.86 - 1.34]	**1.46 [1.18 - 1.81]**	n/a
95%	1.06 [0.96 - 1.17]	**1.10 [1.03 - 1.18]**	0.97 [0.90 - 1.05]
90%	1.04 [0.96 - 1.11]	1.04 [0.99 - 1.09]	1.04 [0.99 - 1.09]
(75+)			
99%	**1.61 [1.42 - 1.82]**	**1.63 [1.44 - 1.85]**	n/a
95%	**1.15 [1.08 - 1.22]**	**1.12 [1.07 - 1.17]**	**1.06 [1.01 - 1.12]**
90%	**1.07 [1.02 - 1.12]**	**1.05 [1.01 - 1.08]**	**1.06 [1.03 - 1.09]**
Total			
99%	**1.40 [1.29 - 1.51]**	**1.47 [1.36 - 1.59]**	n/a
95%	**1.09 [1.05 - 1.13]**	**1.06 [1.03 - 1.09]**	**1.03 [1.00 - 1.07]**
90%	**1.04 [1.01 - 1.07]**	**1.03 [1.01 - 1.05]**	**1.04 [1.03 - 1.06]**

[a] HWD were defined as different percentiles (i.e., 90[th], 95[th] or 99[th] centile) of mean temperature for two or more consecutive days in the summer season.
[*]confidence interval, [†]relative risk, [‡] not applicable

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Contributors ST contributed to the design and co-ordinated the study. XW conducted the data analyses. ST and XW wrote the first draft of the article. All authors critically reviewed and approved the final manuscript.

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Competing interests There is no conflict of interest.

Ethics approval An ethical approval was granted by the Human Research Ethics Committee, Queensland University of Technology, Australia.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

REFERENCES

1. Le Tertre A, Lefranc A, Eilstein D, et al. Impact of the 2003 heatwave on all-cause mortality in 9 French cities. Epidemiology 2006;17:75-9.

2. Robine JM, Cheung SL, Le Roy S, et al. Death toll exceeded 70,000 in Europe during the summer of 2003. C R Biol 2008;331:171-8.

3. McMichael AJ, Wilkinson P, Kovats RS, et al. International study of temperature, heat and urban mortality: the 'ISOTHURM' project. Int. J. Epidemiol. 2008;37:1121-31.

4. Knowlton K, Rotkin-Ellman M, King G, et al. The 2006 California heat wave: impacts on hospitalizations and emergency department visits. Environ. Health Perspect. 2009;117:61-7.

5. O'Neill MS, Zanobetti A, Schwartz J. Modifiers of the temperature and mortality association in seven US cities. Am. J. Epidemiol. 2003;157:1074-82.

6. Stafoggia M, Forastiere F, Agostini D, et al. Vulnerability to Heat-Related Mortality: A Multicity, Population-Based, Case-Crossover Analysis. Epidemiology 2006;17:315-23

7. Tong S, Wang XY, Barnett AG Assessment of heat-related health impacts in Brisbane, Australia: comparison of different heatwave definitions. *PLoS ONE* 2010;5: e12155. doi: 10.1371/journal.pone.0012155.

8. Anderson GB, Bell ML. Heat Waves in the United States: Mortality Risk during Heat Waves and Effect Modification by Heat Wave Characteristics in 43 U.S. Communities. Environ. Health Perspect. 2011;119:210-8.

9. Hajat S, Kosatky T. Heat-related mortality: a review and exploration of heterogeneity. J. Epidemiol. Community Health 2010;64:753-60.

10. Anderson BG, Bell ML. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology 2009;20:205-13.

11. Yu W, Mengersen K, Hu W, et al. Assessing the relationship between global warming and mortality: lag effects of temperature fluctuations by age and mortality categories. Environ Pollut 2011;159:1789-93.

12. Gasparrini A, Armstrong B. The impact of heat waves on mortality. Epidemiology 2011;22:68-73.

13. Baccini M, Kosatsky T, Analitis A, et al. Impact of heat on mortality in 15 European cities: attributable deaths under different weather scenarios. J. Epidemiol. Community Health 2011;65:64-70.

14. Grize L, Huss A, Thommen O, Schindler C, Braun-Fahrlander C. Heat wave 2003 and mortality in Switzerland. Swiss Med Wkly 2005;135:200-5.

15. Basagana X, Sartini C, Barrera-Gomez J, et al. Heat Waves and Cause-specific Mortality at all Ages. Epidemiology 2011;22:765-72.

16. Wang XY, Barnett AG, Yu W, et al. The impact of heatwaves on mortality and emergency hospital admissions from non-external causes in Brisbane, Australia. Occup. Environ. Med. 2012;69:163-9.

17. Guo Y, Barnett AG, Zhang Y, et al. The short-term effect of air pollution on cardiovascular mortality in Tianjin, China: comparison of time series and case-crossover analyses. Sci. Total Environ. 2010;409:300-6.

18. Tong S, Wang XY, Guo Y Assessing the short-term effects of heatwaves on mortality and morbidity in Brisbane, Australia: comparison of case-crossover and time series analyses. *PLoS ONE* 2012;7: e37500. doi: 10.1371/journal.pone.0037500.

19. Guo Y, Barnett AG, Tong S. Spatiotemporal model or time series model for assessing city-wide temperature effects on mortality? Environ. Res. 2013;120:55-62.

20. Williams S, Nitschke M, Weinstein P, et al. The impact of summer temperatures and heatwaves on mortality and morbidity in Perth, Australia 1994-2008. Environ Int 2012;40:33-8.

21. Schaffer A, Muscatello D, Broome R, Corbett S, Smith W Emergency department visits, ambulance calls, and mortality associated with an exceptional heat wave in Sydney, Australia, 2011: a time-series analysis. *Environ Health* 2012;11. doi: 10.1186/1476-069x-11-3.

22. Vaneckova P, Beggs PJ, Jacobson CR. Spatial analysis of heat-related mortality among the elderly between 1993 and 2004 in Sydney, Australia. Soc. Sci. Med. 2010;70:293-304.

23. Huang C, Barnett AG, Wang X, Tong S. Effects of extreme temperatures on years of life lost for cardiovascular deaths: a time series study in brisbane, australia. Circ Cardiovasc Qual Outcomes 2012;5:609-14.

24. Guest CS, Willson K, Woodward AJ, et al. Climate and mortality in Australia: retrospective study, 1979-1990, and predicted impacts in five major cities in 2030. Clim Res 1999;13:1-15.

25. ABS. Australian Burean of Statistics: Regional Population Growth, Australia, 2011 http://www.abs.gov.au/ausstats/abs@.nsf/mf/3218.0.

26. Vaneckova P, Neville G, Tippett V, et al. Do Biometeorological Indices Improve Modeling Outcomes of Heat-Related Mortality? J. Appl. Meteor. Climatol. 2011;50:1165-76.

27. Schifano P, Leone M, De Sario M, et al. Changes in the effects of heat on mortality among the elderly from 1998-2010: results from a multicenter time series study in Italy. *Environ Health* 2012;11: 58. doi: 10.1186/1476-069x-11-58.

28. Barnett AG, Tong S, Clements AC. What measure of temperature is the best predictor of mortality? Environ. Res. 2010;110:604-11.

29. Yu W, Vaneckova P, Mengersen K, Pan X, Tong S. Is the association between temperature and mortality modified by age, gender and socio-economic status? Sci. Total Environ. 2010;408:3513-8.

30. Hajat S, Kovats RS, Lachowycz K. Heat-related and cold-related deaths in England and Wales: who is at risk? Occup. Environ. Med. 2007;64:93-100.

31. Kim Y, Joh S. A vulnerability study of the low-income elderly in the context of high temperature and mortality in Seoul, Korea. Sci. Total Environ. 2006;371:82-8.

32. Stafoggia M, Forastiere F, Agostini D, et al. Factors affecting in-hospital heat-related mortality: a multi-city case-crossover analysis. J. Epidemiol. Community Health 2008;62:209-15.

33. Tong S, Ren C, Becker N. Excess deaths during the 2004 heatwave in Brisbane, Australia. Int. J. Biometeorol. 2010;54:393-400.

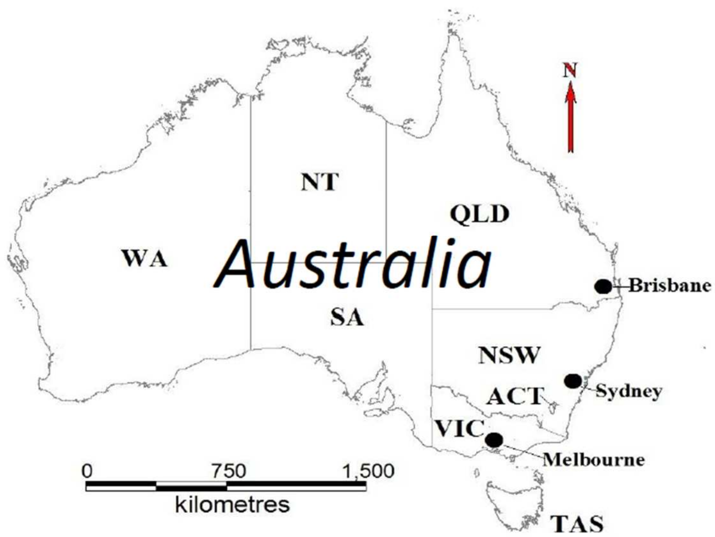


Figure 1 Locations of Brisbane, Melbourne and Sydney in Australia
254x190mm (96 x 96 DPI)

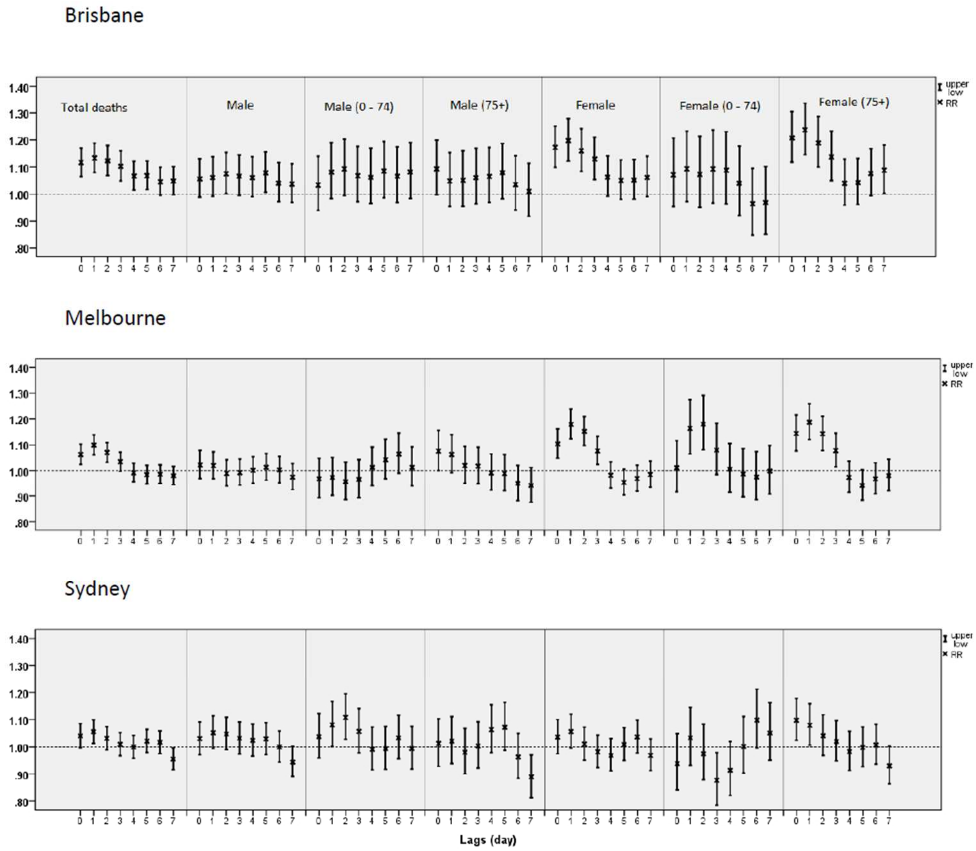


Figure 2 Distributed lag structure of the heatwave effects on mortality by sex, age and city. Cross symbols denote the mean relative risk (RR), and the vertical lines represent the 95% confidence intervals
271x236mm (96 x 96 DPI)

Supplemental Table 1 Average population size and percentage of older people (75+) between 1988 and 2009 in three cities

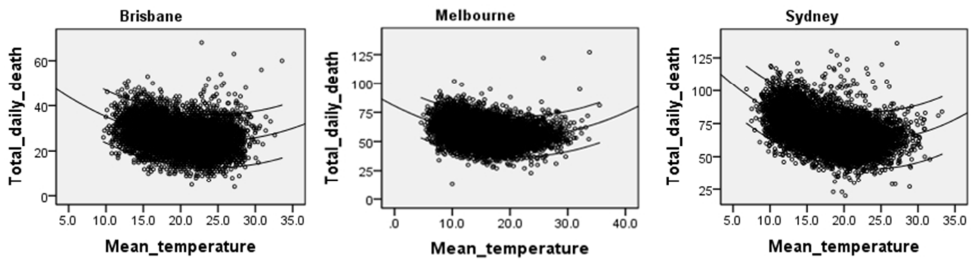
City	Total	Male	% 75+ (M*)	Female	% 75+ (F†)
Brisbane	1,603,742	792,809	3.6	810,933	5.9
Melbourne	3,423,855	1,688,942	4.1	1,734,914	6.4
Sydney	3,996,444	1,978,055	4.0	2,018,389	6.4

*Male, †Female

Supplemental Table 2 Heatwave (HW) days and the total number of deaths in three cities (1988 – 2009)

City	HWD[a]	1988 - 2009	HW days	Total deaths	HW days in each months
Brisbane	90%	Early summer[b]	71	1,615	45 in December, 65 in January
		Late summer[c]	82	2,073	and 43 in February
	95%	Early summer[b]	31	733	19 in December, 29 in January
		Late summer[c]	39	1,093	and 22 in February
	99%	Early summer[b]	6	168	3 in December, 5 in January
		Late summer[c]	5	205	and 3 in February
Melbourne	90%	Early summer[b]	49	2,734	25 in December, 51 in January
		Late summer[c]	79	4,597	and 52 in February
	95%	Early summer[b]	19	1,098	7 in December, 23 in January
		Late summer[c]	37	2,152	and 26 in February
	99%	Early summer[b]	0	N/A	0
		Late summer[c]	4	333	4 in January
Sydney	90%	Early summer[b]	54	3,592	21 in December, 59 in January
		Late summer[c]	64	3,914	and 38 in February
	95%	Early summer[b]	13	889	7 in December, 23 in January
		Late summer[c]	24	1,321	and 8 in February
	99%	Early summer[b]	0	N/A	0
		Late summer[c]	0	N/A	0

[a] HWD were defined as the mean temperature above the percentiles (i.e., 90th, 95th or 99th centile) for two or more consecutive days in the summer season (1st December to the end of February of next year).
[b] between 1st Dec. and 15th Jan.
[c] between 16th Jan and end of Feb.



Supplemental Figure 1 The distribution of daily mean temperature (oC) and mortality (1988 – 2009)
234x67mm (96 x 96 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract √
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found √
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported √
Objectives	3	State specific objectives, including any prespecified hypotheses √
Methods		
Study design	4	Present key elements of study design early in the paper √
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection √
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants N/A
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable √
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group √
Bias	9	Describe any efforts to address potential sources of bias √
Study size	10	Explain how the study size was arrived at √
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why √

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding √
		(*b*) Describe any methods used to examine subgroups and interactions √
		(*c*) Explain how missing data were addressed √
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed N/A *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy N/A
		(*e*) Describe any sensitivity analyses √

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed N/A
		(b) Give reasons for non-participation at each stage N/A
		(c) Consider use of a flow diagram N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders √
		(b) Indicate number of participants with missing data for each variable of interest √
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time N/A
		Case-control study—Report numbers in each exposure category, or summary measures of exposure N/A
		Cross-sectional study—Report numbers of outcome events or summary measures N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included √
		(*b*) Report category boundaries when continuous variables were categorized √
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period √
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses √
Discussion		
Key results	18	Summarise key results with reference to study objectives √
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias √
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence √
Generalisability	21	Discuss the generalisability (external validity) of the study results √
Other information		

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based √

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

The impact of heatwaves on mortality in Australia: a multi-city study

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The impact of heatwaves on mortality in Australia: a multi-city study

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Word count: 1,985

ABSTRACT

Objectives: This study assessed the impact of heatwave on mortality in the three largest Australian cities: Brisbane, Melbourne and Sydney.

Methods: Daily data on climatic variables and mortality for these three cities during the period 1988 to 2009 were obtained from relevant government agencies. A consistent definition of a heatwave was used for these cities. Generalised additive models were fitted to assess the impact of heatwaves on mortality after adjustment for confounders.

Results: Total mortality increased mostly within the same day (lag 0) or a lag of one day (lag 1) during almost all heatwaves in three cities. Using the heatwave definition (HWD) as the 95th centile of mean temperature for two or more consecutive days in the summer season, the relative risk for total mortality at lag 1 in Brisbane, Melbourne and Sydney was 1.13 (95% confidence interval (CI): 1.08 – 1.19), 1.10 (95% CI: 1.06 – 1.14) and 1.06 (95% CI: 1.01 – 1.10), respectively. Using the more stringent HWD - the 99th centile of mean temperature for two or more consecutive days, the relative risk of total mortality at the lags of 0-2 days in Brisbane and Melbourne was 1.40 (95% CI: 1.29 – 1.51) and 1.47 (95% CI: 1.36 – 1.59), respectively. Elderly, particularly females, were more vulnerable to the impact of heatwaves.

Conclusion: A consistent and significant increase in mortality was observed during heatwaves in the three largest Australian cities, but the impacts of heatwave appeared to vary with age, gender, the HWD and geographic area.

ARTICLE SUMMARY

Article focus

- Although the health impact of heatwaves has been increasingly investigated over recent years, little is known about the geographic difference of the heatwave-health relationship in the Southern Hemisphere.
- This study assessed the heatwave - mortality relationship in the three largest Australian cities: Sydney, Melbourne and Brisbane, and quantified the mortality impacts of heatwaves across these areas.

Key messages

- There was a consistent and significant increase in mortality during heatwaves in the three largest Australian cities, but the impacts of heatwave appeared to vary with age, sex, the definition of heatwave and geographic area.
- The impacts of heatwave occurred rapidly and there were no apparent long-term lag effects.

Strengths and limitations of this study

- This is the first multi-city study on the mortality impacts of heatwaves in the Southern Hemisphere; and the similarities and differences in the heatwave - mortality relationship across the three largest Australian cities were quantified.
- The key limitation is that the potential confounding effects of air pollution were not controlled, as these data were not complete for the whole study period in all three cities.

INTRODUCTION

It is well known that exposure to extreme temperatures has a significant impact on human health. For example, the 2003 heatwave caused over 70,000 excess deaths in Europe.[1, 2] A number of epidemiological studies have shown that the relationships between temperatures and mortality are often non-linear, with a J, U or V shape.[3-9] However, the key reasons why there are different non-linear curves in different population remain unknown. In addition, exposure to extreme temperatures usually does not reach the highest mortality at the same day, and often show lagged effects.[10, 11] Some of this difference may be explained by inconsistent definitions, methodology as well as possibly population differences. Different heatwave definitions have been used in previous studies since there is currently no standard definition for heatwave.[7, 10, 12]

Some studies have estimated the mortality effects of heatwaves across many countries, cities or communities, and determined how mortality increased during heatwaves.[1-6, 8, 10, 13] Different research methods for estimating mortality associated with heatwaves have been used in previous studies. For example, a descriptive approach has been applied to compare the number of deaths between heatwave and non-heatwave days,[14] a time-series analysis has been widely used to estimate mortality risks in association with hot or cold temperature,[10, 11] and a case-crossover analysis is also another increasingly popular method used in this field.[7, 15, 16] However, recent evidence suggests that time-series analysis is still an effective and possibly the most applicable method for investigating the health impact of time-varying environmental exposures.[17-19]

The most Australia capital cities are located along the coast. There is a wide variation in climatic conditions across Australia. Most previous Australian studies have analysed the relationship between temperature and mortality for only one city and no research, to date, has been conducted to examine the health impact of heatwaves across different cities.[16, 19-24] To better understand how temperature affects mortality in different locations, this study assessed the

temperature - mortality relationship in the three largest Australian cities: Brisbane, Melbourne and Sydney, and attempted to quantify the impact of heatwaves on mortality in these areas.

METHODS

Brisbane, Melbourne and Sydney are the capital cities of Queensland, Victoria and New South Wales, respectively, in Australia. These three metropolitan cities are all located on the south east coast of the continent (Figure 1). There are about 2.2, 4.2 and 4.6 million residents for Brisbane, Melbourne and Sydney, respectively, in June 2011.[25] Together, they represent approximately half of the Australia population of 22.3 million.[25]

[Figure 1 about here]

Data Collection

We obtained mortality data between 1988 and 2009 for Brisbane, Melbourne and Sydney from the Australian Bureau of Statistics (ABS). Due to privacy protection reason, the data obtained from the ABS were limited for the Statistical Division of usual residence by gender and two age groups (i.e., 0-75 and 75+) for the three metropolitan areas. In order to calculate the mortality rate, the corresponding populations by gender and the two age groups from 1988 to 2009 in the three cities were also extracted from the ABS database. Supplemental Table 1 presents the average of population size and percentage of 75 + years old by gender between 1988 and 2009.

Daily climate data on maximum and minimum temperatures and relative humidity for the same period (1988 – 2009) were acquired from the Australian Bureau of Meteorology. We selected all available meteorological stations located within ≤ 30 km of each city's CBD (7 stations for Brisbane, 7 stations for Melbourne and 11 stations for Sydney). We calculated the daily averages of climatic variables using all records from meteorological stations in each city. This approach is used

in previous research.[18] There were approximately 1.4°C to 5.1°C differences for maximum or minimum temperature between meteorological stations of each city. When there was a missing value (≤ 1.3%) for a particular meteorological station, observations recorded from the remaining weather stations were used to compute the daily average values.

Data Analysis

Previous studies have found that mean temperature was a slightly better predictor of mortality than maximum or minimum temperature in Brisbane.[26] Thus in this study, we used mean temperature as an indicator of exposure. Daily mean temperatures (i.e., averaged values of maximum and minimum temperatures) were used to investigate the effects of heatwaves on mortality in these three cities. A heatwave was defined as the mean temperature above a heat threshold (i.e., 90, 95 and 99 percentiles of mean temperature) for two or more consecutive days in the summer season (1st December to the end of February of next year). A binary heatwave variable (1 or 0) was used for each day (e.g., 1 for the heatwave days meant that temperatures were equal to or higher than the 99 percentile for two or more consecutive days; 0 for non-heatwave days). A Poisson generalised additive model (GAM) was used to examine both single (e.g., lag 0, 1 and 2) and cumulative lag effects (lag 0 -2) of heatwaves on mortality for each city, after adjustment for humidity and population as confounding factors. The "mgcv" package in R software (version 2.14.1) was used to fit the time series GAM.

RESULTS

Table 1 describes the statistical summary of climatic variables and health outcomes for each city in summer seasons. The highest mean temperature reached 33.6°C in Brisbane (22 Feb. 2004), 35.5°C in Melbourne (29 Jan. 2009) and 33.2°C in Sydney (1 Jan. 2006). However, Brisbane had the higher

average mean temperature (24.8°C) than Melbourne (19.7°C) and Sydney (22.5°C). Similar patterns were observed for the average maximum and minimum temperatures.

[Table 1 about here]

Table 2 indicates the heatwave days and threshold (°C) using different percentiles of mean temperatures. Supplemental Table 2 also provided the heatwave days separated by early summer and later summer. Overall, Brisbane had more heatwave days than Melbourne and Sydney across all heatwave definitions during the study period. This is not unexpected and may simply be because Brisbane is further north with subtropical climatic conditions. Supplemental Figure 1 shows the distribution of daily mortality data by mean temperature for each city. The temperature-mortality relations appeared to be a U shape across three cities.

[Table 2 about here]

Figure 2 shows the distributed lag structure (lag 0 to lag 7) of the heatwave effects on mortality using 95% percentiles of mean temperature as the HWD in three cities after adjustment for relative humidity and population size. Heatwave-related mortality mostly occurred within the same day (lag 0) or a lag of one day (lag 1) in the three cities. Heatwaves also appeared to have greater impacts on female and total mortality. For example, the relative risk for total mortality in Brisbane, Melbourne and Sydney was 1.13 (95% confidence interval (CI): 1.08 – 1.19), 1.10 (95% CI: 1.06 – 1.14) and 1.06 (95% CI: 1.01 – 1.10), respectively, at lag 1. A similar pattern was found if mean temperatures were replaced with maximum temperatures in the heatwave definition in these cities (results not shown).

[Figure 2 about here]

Table 3 reveals the relative risks (RR) of daily mortality during heatwaves using different percentiles of mean temperature as thresholds for cumulative lag effects (lag 0 – 2 days) in three cities after adjustment for relative humidity and population size. Heatwaves appeared to have greater impacts on female and total mortality, especially for female aged 75 and over, regardless of which definition of heatwave was used. However, heatwaves appeared to affect local residents more in Brisbane and Melbourne than Sydney, which may be because Sydney had fewer prolonged hot days than other cities. For example, no heatwave was recorded in Sydney during the study periods if the definition of 99th percentile of mean temperature for 2 or more consecutive days was used (Table 2).

[Table 3 about here]

DISCUSSION

This is the first study to use locally defined definitions to investigate the relationship between heatwaves and mortality in different Australian cities. The principal finding of this study is that there was a consistent and statistical significant relationship between hot temperatures and mortality in the three largest Australian cities: Brisbane, Melbourne and Sydney.

Several mortality studies have reported the impact of heatwaves on mortality.[10, 27, 28] The results of this study support the findings from previous research. In general, heatwaves are associated with significantly increased mortality across all three cities. However, heatwaves appeared to affect mortality more in Brisbane and Melbourne than Sydney. This may be due to the fact that Sydney had fewer prolonged hot days than Brisbane and Melbourne (Table 2). Additionally, adaptation (e.g., more usage of air conditioning in Sydney) and people's behaviour may also play a role. Supplemental Table 2 shows that the total number of deaths during heatwave periods in the late summer was greater than that in the early summer. For example, if the heatwave was defined as the 95th centile for two or more consecutive days, 4,566 people died during heatwave periods across three cities in the late summer, compared with 2720 died in the early summer. Our results show that the elderly (≥ 75), especially females, were more vulnerable to heatwave effects than others in these cities. This finding supports previous studies that the female elderly were particularly vulnerable to heat effects.[29, 30] There may be an adverse effect of menopause on thermoregulation, in addition to its effects on cardiovascular fitness.[30] Some important social factors (e.g., living alone or low income) may also explain differences in mortality patterns between males and females during heatwaves.[31, 32]

We investigated both single and cumulative lag effects since some studies have identified the increased risk for temperature-related mortality from exposure occurring on the same day or a few days previously.[10, 11, 15, 16] In this study, we found that the strongest heatwave impact usually occurred on the same day or the next day across all three cities (Figure 2). Thus, we concur with the notion that heatwaves usually have acute and dramatic impacts on mortality.

The findings of this study are comparable to some previous multi-city studies (e.g., US or Europe).[8, 13] There are three similarities across these studies: 1. the similar magnitude of heatwave effects were observed; 2. the impacts of heatwave occurred rapidly and there were no apparent long-term lag effects; and 3. elderly are more vulnerable to the impacts of heatwave than others. However, there are also some differences across these studies. For example, a previous study[8] found that mortality increased more during heatwaves in early summer than those in late summer, but our results show that higher mortality was resulted from heatwaves in mid or late summer for all three cities (Supplemental Table 2), which may be because more intense heatwaves usually occur in mid or late summer in Australia.

There were some limitations in this study. We did not control for the potential confounding effects of air pollution (e.g., O_3), as these data were not complete for the whole study period in all three cities. However, previous studies have reported the health impacts of a heatwave as occurring independent of air pollution.[10, 33] A relatively small number of heatwave days may explain why the differences in heat effects between the three cities as well as the subpopulations were not statistically significant as their 95% confidence intervals were overlapped each other. Additionally, the mortality data for three cities only included two age groups (0 – 74, 75&+) by gender. Thus, we were unable to divide the data into smaller age groups.

CONCLUSIONS

A consistent and significant increase in mortality was observed during heatwaves in the three Australian metropolitan cities, but the impacts of heatwave appeared to vary with age, gender, the heatwave definition and geographic area. Extreme hot temperatures appeared to directly result in an increased risk of mortality in these cities. The most vulnerable groups were the elderly, especial female aged 75 and over. By better understanding heatwave effects on mortality, local government and communities can develop appropriate public health strategies and increase their adaptive capacity to prevent and mitigate the impact of heatwave.

Table 1 Summary of the daily climatic variables and mortality in summer season[a] (1988 – 2009)

	Brisbane				Melbourne				Sydney			
Variable	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max
Male (All)	12	3.9	2	38	27	5.7	11	52	32	7.1	6	74
(0-74)	6	2.8	0	17	13	4.6	1	33	16	5.9	2	47
(75+)	6	2.8	0	25	14	4.4	2	34	15	4.5	3	32
Female (All)	12	4.1	1	40	26	5.7	10	79	30	6.7	9	70
(0-74)	4	2.1	0	13	8	3.3	1	21	10	3.8	1	32
(75+)	8	3.3	0	30	18	5.0	3	64	21	5.4	5	42
Total	24	6.2	4	68	54	8.6	23	127	62	11.1	20	136
MaxT* (^oC)	29.3	2.3	20.1	40.1	25.6	5.8	13.9	46.7	27.1	4.0	16.6	44.0
MeanT † (^oC)	24.8	1.9	18.3	33.6	19.7	3.9	10.9	35.5	22.5	2.7	15.1	33.2
MinT‡ (^oC)	20.3	2.2	11.9	27.1	13.8	3.3	5.8	27.6	18.0	2.3	9.8	25.8
RH§ (%)	70.2	8.7	30.2	96.8	65.0	11.6	19.7	95.6	70.0	11.0	28.1	98.1

[a]1st December to the end of February of next year
*maximum temperature, †mean temperature, ‡minimum temperature, §relative humidity

Table 2 Heatwave definition (HWD) used in three cities (1988 – 2009)

HWD[a]	Heatwave days and threshold					
	Brisbane		Melbourne		Sydney	
99%	11	29.7 °C	4	30.1 °C	0	29.6 °C
95%	70	28.0 °C	56	27.2 °C	37	27.3 °C
90%	153	27.2 °C	128	25.3 °C	118	26.1 °C

[a] HWD were defined as the mean temperature above the percentiles (i.e., 90th, 95th or 99th centile) for two or more consecutive days in the summer season (1st December to the end of February of next year).

Table 3 Relative risk of mortality by different heatwave definition (HWD) for cumulative lag effects (lag 0-2) in three cities, 1988 -2009

HWD[a]	RR[†] [95% CI[*]]		
	Brisbane	Melbourne	Sydney
Male (All)			
99%	**1.32 [1.17 - 1.48]**	**1.37 [1.22 - 1.53]**	n/a[‡]
95%	1.04 [0.99 - 1.10]	1.00 [0.96 - 1.04]	1.03 [0.99 - 1.08]
90%	1.01 [0.97 - 1.05]	1.02 [0.99 - 1.05]	**1.04 [1.01 - 1.06]**
(0 - 74)			
99%	**1.29 [1.10 - 1.53]**	**1.37 [1.15 - 1.63]**	n/a
95%	1.04 [0.96 - 1.12]	0.96 [0.91 - 1.02]	**1.07 [1.01 - 1.13]**
90%	0.99 [0.93 - 1.04]	1.00 [0.96 - 1.04]	**1.04 [1.00 - 1.08]**
(75+)			
99%	**1.33 [1.13 - 1.56]**	**1.38 [1.19 - 1.61]**	n/a
95%	1.05 [0.97 - 1.13]	1.04 [0.98 - 1.09]	0.99 [0.92 - 1.05]
90%	1.03 [0.97 - 1.08]	1.03 [0.99 - 1.07]	**1.03 [1.00 - 1.07]**
Female (All)			
99%	**1.45 [1.30 - 1.61]**	**1.57 [1.41 - 1.74]**	n/a
95%	**1.13 [1.07 - 1.19]**	**1.11 [1.07 - 1.15]**	1.03 [0.98 - 1.07]
90%	**1.06 [1.02 - 1.10]**	**1.05 [1.02 - 1.07]**	**1.05 [1.03 - 1.08]**
(0 - 74)			
99%	1.08 [0.86 - 1.34]	**1.46 [1.18 - 1.81]**	n/a
95%	1.06 [0.96 - 1.17]	**1.10 [1.03 - 1.18]**	0.97 [0.90 - 1.05]
90%	1.04 [0.96 - 1.11]	1.04 [0.99 - 1.09]	1.04 [0.99 - 1.09]
(75+)			
99%	**1.61 [1.42 - 1.82]**	**1.63 [1.44 - 1.85]**	n/a
95%	**1.15 [1.08 - 1.22]**	**1.12 [1.07 - 1.17]**	**1.06 [1.01 - 1.12]**
90%	**1.07 [1.02 - 1.12]**	**1.05 [1.01 - 1.08]**	**1.06 [1.03 - 1.09]**
Total			
99%	**1.40 [1.29 - 1.51]**	**1.47 [1.36 - 1.59]**	n/a
95%	**1.09 [1.05 - 1.13]**	**1.06 [1.03 - 1.09]**	**1.03 [1.00 - 1.07]**
90%	**1.04 [1.01 - 1.07]**	**1.03 [1.01 - 1.05]**	**1.04 [1.03 - 1.06]**

[a] HWD were defined as different percentiles (i.e., 90th, 95th or 99th centile) of mean temperature for two or more consecutive days in the summer season.
[*]confidence interval, [†]relative risk, [‡] not applicable
Adjusted for relative humidity, days of week and population size

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Contributors: ST contributed to the design and co-ordinated the study. XW conducted the data analyses. ST and XW wrote the first draft of the article. All authors critically reviewed and approved the final manuscript.

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REFERENCES

1. Le Tertre A, Lefranc A, Eilstein D, et al. Impact of the 2003 heatwave on all-cause mortality in 9 French cities. Epidemiology 2006;17:75-9.

2. Robine JM, Cheung SL, Le Roy S, et al. Death toll exceeded 70,000 in Europe during the summer of 2003. C R Biol 2008;331:171-8.

3. McMichael AJ, Wilkinson P, Kovats RS, et al. International study of temperature, heat and urban mortality: the 'ISOTHURM' project. Int. J. Epidemiol. 2008;37:1121-31.

4. Knowlton K, Rotkin-Ellman M, King G, et al. The 2006 California heat wave: impacts on hospitalizations and emergency department visits. Environ. Health Perspect. 2009;117:61-7.

5. O'Neill MS, Zanobetti A, Schwartz J. Modifiers of the temperature and mortality association in seven US cities. Am. J. Epidemiol. 2003;157:1074-82.

6. Stafoggia M, Forastiere F, Agostini D, et al. Vulnerability to Heat-Related Mortality: A Multicity, Population-Based, Case-Crossover Analysis. Epidemiology 2006;17:315-23

7. Tong S, Wang XY, Barnett AG Assessment of heat-related health impacts in Brisbane, Australia: comparison of different heatwave definitions. *PLoS ONE* 2010;5: e12155. doi: 10.1371/journal.pone.0012155.

8. Anderson GB, Bell ML. Heat Waves in the United States: Mortality Risk during Heat Waves and Effect Modification by Heat Wave Characteristics in 43 U.S. Communities. Environ. Health Perspect. 2011;119:210-8.

9. Hajat S, Kosatky T. Heat-related mortality: a review and exploration of heterogeneity. J. Epidemiol. Community Health 2010;64:753-60.

10. Anderson BG, Bell ML. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology 2009;20:205-13.

11. Yu W, Mengersen K, Hu W, et al. Assessing the relationship between global warming and mortality: lag effects of temperature fluctuations by age and mortality categories. Environ Pollut 2011;159:1789-93.

12. Gasparrini A, Armstrong B. The impact of heat waves on mortality. Epidemiology 2011;22:68-73.

13. Baccini M, Kosatsky T, Analitis A, et al. Impact of heat on mortality in 15 European cities: attributable deaths under different weather scenarios. J. Epidemiol. Community Health 2011;65:64-70.

14. Grize L, Huss A, Thommen O, et al. Heat wave 2003 and mortality in Switzerland. Swiss Med Wkly 2005;135:200-5.

15. Basagana X, Sartini C, Barrera-Gomez J, et al. Heat Waves and Cause-specific Mortality at all Ages. Epidemiology 2011;22:765-72.

16. Wang XY, Barnett AG, Yu W, et al. The impact of heatwaves on mortality and emergency hospital admissions from non-external causes in Brisbane, Australia. Occup. Environ. Med. 2012;69:163-9.

17. Guo Y, Barnett AG, Zhang Y, et al. The short-term effect of air pollution on cardiovascular mortality in Tianjin, China: comparison of time series and case-crossover analyses. Sci. Total Environ. 2010;409:300-6.

18. Tong S, Wang XY, Guo Y Assessing the short-term effects of heatwaves on mortality and morbidity in Brisbane, Australia: comparison of case-crossover and time series analyses. *PLoS ONE* 2012;7: e37500. doi: 10.1371/journal.pone.0037500.

19. Guo Y, Barnett AG, Tong S. Spatiotemporal model or time series model for assessing city-wide temperature effects on mortality? Environ. Res. 2013;120:55-62.

20. Williams S, Nitschke M, Weinstein P, et al. The impact of summer temperatures and heatwaves on mortality and morbidity in Perth, Australia 1994-2008. Environ Int 2012;40:33-8.

21. Schaffer A, Muscatello D, Broome R, et al. Emergency department visits, ambulance calls, and mortality associated with an exceptional heat wave in Sydney, Australia, 2011: a time-series analysis. *Environ Health* 2012;11. doi: 10.1186/1476-069x-11-3.

22. Vaneckova P, Beggs PJ, Jacobson CR. Spatial analysis of heat-related mortality among the elderly between 1993 and 2004 in Sydney, Australia. Soc. Sci. Med. 2010;70:293-304.

23. Huang C, Barnett AG, Wang X, et al. Effects of extreme temperatures on years of life lost for cardiovascular deaths: a time series study in brisbane, australia. Circ Cardiovasc Qual Outcomes 2012;5:609-14.

24. Guest CS, Willson K, Woodward AJ, et al. Climate and mortality in Australia: retrospective study, 1979-1990, and predicted impacts in five major cities in 2030. Clim Res 1999;13:1-15.

25. ABS. Australian Burean of Statistics: Regional Population Growth, Australia, 2011 http://www.abs.gov.au/ausstats/abs@.nsf/mf/3218.0.

26. Vaneckova P, Neville G, Tippett V, et al. Do Biometeorological Indices Improve Modeling Outcomes of Heat-Related Mortality? J. Appl. Meteor. Climatol. 2011;50:1165-76.

27. Schifano P, Leone M, De Sario M, et al. Changes in the effects of heat on mortality among the elderly from 1998-2010: results from a multicenter time series study in Italy. *Environ Health* 2012;11: 58. doi: 10.1186/1476-069x-11-58.

28. Barnett AG, Tong S, Clements AC. What measure of temperature is the best predictor of mortality? Environ. Res. 2010;110:604-11.

29. Yu W, Vaneckova P, Mengersen K, et al. Is the association between temperature and mortality modified by age, gender and socio-economic status? Sci. Total Environ. 2010;408:3513-8.

30. Hajat S, Kovats RS, Lachowycz K. Heat-related and cold-related deaths in England and Wales: who is at risk? Occup. Environ. Med. 2007;64:93-100.

31. Kim Y, Joh S. A vulnerability study of the low-income elderly in the context of high temperature and mortality in Seoul, Korea. Sci. Total Environ. 2006;371:82-8.

32. Stafoggia M, Forastiere F, Agostini D, et al. Factors affecting in-hospital heat-related mortality: a multi-city case-crossover analysis. J. Epidemiol. Community Health 2008;62:209-15.

33. Tong S, Ren C, Becker N. Excess deaths during the 2004 heatwave in Brisbane, Australia. Int. J. Biometeorol. 2010;54:393-400.

Manuscript title:

The impact of heatwaves on mortality in Australia: a multi-city study

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Keywords: climate changes, heatwaves, mean temperature, mortality, time series analysis.

Word count: 1,~~950~~985

ABSTRACT

Objectives: This study assessed the impact of heatwave on mortality in the three largest Australian cities: Brisbane, Melbourne and Sydney.

Methods: Daily data on climatic variables and mortality for these three cities during the period 1988 to 2009 were obtained from relevant government agencies. A consistent definition of a heatwave was used for these cities. Generalised additive models were fitted to assess the impact of heatwaves on mortality after adjustment for confounders.

Results: Total mortality increased mostly within the same day (lag 0) or a lag of one day (lag 1) during almost all heatwaves in three cities. Using the heatwave definition (HWD) as the 95th centile of mean temperature for two or more consecutive days in the summer season, the relative risk for total mortality at lag 1 in Brisbane, Melbourne and Sydney was 1.13 (95% confidence interval (CI): 1.08 – 1.19), 1.10 (95% CI: 1.06 – 1.14) and 1.06 (95% CI: 1.01 – 1.10), respectively. Using the more stringent HWD - the 99th centile of mean temperature for two or more consecutive days, the relative risk of total mortality at the lags of 0-2 days in Brisbane and Melbourne was 1.40 (95% CI: 1.29 – 1.51) and 1.47 (95% CI: 1.36 – 1.59), respectively. Elderly, particularly females, were more vulnerable to the impact of heatwaves.

Conclusion: A consistent and significant increase in mortality was observed during heatwaves in the three largest Australian cities, but the impacts of heatwave ~~varied~~appeared to vary with age, gender, the HWD and geographic area.

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ARTICLE SUMMARY

Article focus

- Although the health impact of heatwaves has been increasingly investigated over recent years, little is known about the geographic difference of the heatwave-health relationship in the Southern Hemisphere.
- This study assessed the heatwave - mortality relationship in the three largest Australian cities: Sydney, Melbourne and Brisbane, and quantified the mortality impacts of heatwaves across these areas.

Key messages

- There was a consistent and significant increase in mortality during heatwaves in the three largest Australian cities, but the impacts of heatwave ~~varied~~appeared to vary with age, sex, the definition of heatwave and geographic area.
- The impacts of heatwave ~~appeared to occur~~occurred rapidly and there were no apparent long-term lag effects.

Strengths and limitations of this study

- This is the first multi-city study on the mortality impacts of heatwaves in the Southern Hemisphere; and the similarities and differences in the heatwave - mortality relationship across the three largest Australian cities were quantified.
- The key limitation is that the potential confounding effects of air pollution were not controlled, as these data were not complete for the whole study period in all three cities.

INTRODUCTION

It is well known that exposure to extreme temperatures has a significant impact on human health. For example, the 2003 heatwave caused over 70,000 excess deaths in Europe.[1, 2] A number of epidemiological studies have shown that the relationships between temperatures and mortality are often non-linear, with a J, U or V shape.[3-9] However, the key reasons why there are different non-linear curves in different population remain unknown. In addition, exposure to extreme temperatures usually does not reach the highest mortality at the same day, and often show lagged effects.[10, 11] Some of this difference may be explained by inconsistent definitions, methodology as well as possibly population differences. Different heatwave definitions have been used in previous studies since there is currently no standard definition for heatwave.[7, 10, 12]

Some studies have estimated the mortality effects of heatwaves across many countries, cities or communities, and determined how mortality increased during heatwaves.[1-6, 8, 10, 13] Different research methods for estimating mortality associated with heatwaves have been used in previous studies. For example, a descriptive approach has been applied to compare the number of deaths between heatwave and non-heatwave days,[14] a time-series analysis has been widely used to estimate mortality risks in association with hot or cold temperature,[10, 11] and a case-crossover analysis is also another increasingly popular method used in this field.[7, 15, 16] However, recent evidence suggests that time-series analysis is still an effective and possibly the most applicable method for investigating the health impact of time-varying environmental exposures.[17-19]

The most Australia capital cities are located along the coast. There is a wide variation in climatic conditions across Australia. Most previous Australian studies have analysed the relationship between temperature and mortality for only one city and no research, to date, has been conducted to examine the health impact of heatwaves across different cities.[16, 19-24] To better understand how temperature affects mortality in different locations, this study assessed the

temperature - mortality relationship in the three largest Australian cities: Brisbane, Melbourne and Sydney, and attempted to quantify the impact of heatwaves on mortality in these areas.

METHODS

Brisbane, Melbourne and Sydney are the capital cities of Queensland, Victoria and New South Wales, respectively, in Australia. These three metropolitan cities are all located on the south east coast of the continent (Figure 1). There are about 2.2, 4.2 and 4.6 million residents for Brisbane, Melbourne and Sydney, respectively, in June 2011.[25] Together, they represent approximately half of the Australia population of 22.3 million.[25]

[Figure 1 about here]

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Data Collection

We obtained mortality data between 1988 and 2009 for Brisbane, Melbourne and Sydney from the Australian Bureau of Statistics (ABS). Due to privacy protection reason, the data obtained from the ABS were limited for the Statistical Division of usual residence by gender and two age groups (i.e., 0-75 and 75+) for the three metropolitan areas. In order to calculate the mortality rate, the corresponding populations by gender and the two age groups from 1988 to 2009 in the three cities were also extracted from the ABS database. Supplemental Table 1 presents the average of population size and percentage of 75 + years old by gender between 1988 and 2009.

Daily climate data on maximum and minimum temperatures and relative humidity for the same period (1988 – 2009) were acquired from the Australian Bureau of Meteorology. We selected all available meteorological stations located within ≤ 30 km of each city's CBD (7 stations for Brisbane, 7 stations for Melbourne and 11 stations for Sydney). We calculated the daily averages of climatic variables using all records from meteorological stations in each city. This approach is used

in previous research.[18] There were approximately 1.4°C to 5.1°C differences for maximum or minimum temperature between meteorological stations of each city. When there was a missing value (≤ 1.3%) for a particular meteorological station, observations recorded from the remaining weather stations were used to compute the daily average values.

Data Analysis

Previous studies have found that mean temperature was a slightly better predictor of mortality than maximum or minimum temperature in Brisbane.[26] Thus in this study, we used mean temperature as an indicator of exposure. Daily mean temperatures (i.e., averaged values of maximum and minimum temperatures) were used to investigate the effects of heatwaves on mortality in these three cities. A heatwave was defined as the mean temperature above a heat threshold (i.e., 90, 95 and 99 percentiles of mean temperature) for two or more consecutive days in the summer season (1st December to the end of February of next year). A binary heatwave variable (1 or 0) was used for each day (e.g., 1 for the heatwave days meant that temperatures were equal to or higher than the 99 percentile for two or more consecutive days; 0 for non-heatwave days). A Poisson generalised additive model (GAM) was used to examine both single (e.g., lag 0, 1 and 2) and cumulative lag effects (lag 0 -2) of heatwaves on mortality for each city, after adjustment for humidity and population as confounding factors. The "mgcv" package in R software (version 2.14.1) was used to fit the time series GAM.

RESULTS

Table 1 describes the statistical summary of climatic variables and health outcomes for each city in summer seasons. The highest mean temperature reached 33.6°C in Brisbane (22 Feb. 2004), 35.5°C in Melbourne (29 Jan. 2009) and 33.2°C in Sydney (1 Jan. 2006). However, Brisbane had the higher

average mean temperature (24.8°C) than Melbourne (19.7°C) and Sydney (22.5°C). Similar patterns were observed for the average maximum and minimum temperatures.

[Table 1 about here]

Table 2 indicates the heatwave days and threshold (°C) using different percentiles of mean temperatures. Supplemental Table 2 also provided the heatwave days separated by early summer and later summer. Overall, Brisbane had more heatwave days than Melbourne and Sydney across all heatwave definitions during the study period. This is not unexpected and may simply be because Brisbane is further north with subtropical climatic conditions. Supplemental Figure 1 shows the distribution of daily mortality data by mean temperature for each city. The temperature-mortality relations appeared to be a U shape across three cities.

[Table 2 about here]

Figure 2 shows the distributed lag structure (lag 0 to lag 7) of the heatwave effects on mortality using 95% percentiles of mean temperature as the HWD in three cities after adjustment for relative humidity and population size. Heatwave-related mortality mostly occurred within the same day (lag 0) or a lag of one day (lag 1) in the three cities. Heatwaves also appeared to have greater impacts on female and total mortality. For example, the relative risk for total mortality in Brisbane, Melbourne and Sydney was 1.13 (95% confidence interval (CI): 1.08 – 1.19), 1.10 (95% CI: 1.06 – 1.14) and 1.06 (95% CI: 1.01 – 1.10), respectively, at lag 1. A similar pattern was found if mean temperatures were replaced with maximum temperatures in the heatwave definition in these cities (results not shown).

[Figure 2 about here]

Table 3 reveals the relative risks (RR) of daily mortality during heatwaves using different percentiles of mean temperature as thresholds for cumulative lag effects (lag 0 – 2 days) in three cities after adjustment for relative humidity and population size. Heatwaves appeared to have greater impacts on female and total mortality, especially for female aged 75 and over, regardless of which definition of heatwave was used. However, heatwaves appeared to affect local residents more in Brisbane and Melbourne than Sydney, which may be because Sydney had fewer prolonged hot days than other cities. For example, no heatwave was recorded in Sydney during the study periods if the definition of 99th percentile of mean temperature for 2 or more consecutive days was used (Table 2).

[Table 3 about here]

DISCUSSION

This is the first study to use locally defined definitions to investigate the relationship between heatwaves and mortality in different Australian cities. The principal finding of this study is that there was a consistent and statistical significant relationship between hot temperatures and mortality in the three largest Australian cities: Brisbane, Melbourne and Sydney.

Several mortality studies have reported the impact of heatwaves on mortality.[10, 27, 28] The results of this study support the findings from previous research. In general, heatwaves are associated with significantly increased mortality across all three cities. However, heatwaves appeared to affect mortality more in Brisbane and Melbourne than Sydney. This may be due to the fact that Sydney had fewer prolonged hot days than Brisbane and Melbourne (Table 2). Additionally, adaptation (e.g., more usage of air conditioning in Sydney) and people's behaviour may also play a role. Supplemental Table 2 shows that the total number of deaths ~~(i.e., 4,566)~~

during heatwave periods in the late summer was greater than that in the early summer. For example, if the heatwave was defined as the 95th centile for two or more consecutive days, 4,566 people died during heatwave periods across three cities in the late summer, compared with 2720 died in the early summer.

Our results show that the elderly (≥ 75), especially females, were more vulnerable to heatwave effects than others in these cities. This finding supports previous studies that the female elderly were particularly vulnerable to heat effects.[29, 30] There may be an adverse effect of menopause on thermoregulation, in addition to its effects on cardiovascular fitness.[30] Some important social factors (e.g., living alone or low income) may also explain differences in mortality patterns between males and females during heatwaves.[31, 32]

We investigated both single and cumulative lag effects since some studies have identified the increased risk for temperature-related mortality from exposure occurring on the same day or a few days previously.[10, 11, 15, 16] In this study, we found that the strongest heatwave impact usually occurred on the same day or the next day across all three cities (Figure 2). Thus, we concur with the notion that heatwaves usually have acute and dramatic impacts on mortality.

The findings of this study are comparable to some previous multi-city studies (e.g., US or Europe).[8, 13] There are three similarities across these studies: 1. the similar magnitude of heatwave effects were observed; 2. the impacts of heatwave occurred rapidly and there were no apparent long-term lag effects; and 3. Elderlyelderly are more vulnerable to the impacts of heatwave than others. However, there are also some differences across these studies. For example, a previous study[8] found that mortality increased more during heatwaves in early summer than those in late summer, but our results show that higher mortality was resulted from heatwaves in mid or late summer for all three cities (Supplemental Table 2), which may be because more intense heatwaves usually occur in mid or late summer in Australia.

There were ~~two key limitations in this study. Only the aggregated data were used while individual exposure and outcome data would give a more precise estimate of the health impacts of a heatwave event, but unfortunately individual data were not available.~~some limitations in this study. We did not control for the potential confounding effects of air pollution (e.g., O_3), as these data were not complete for the whole study period in all three cities. However, previous studies have reported the health impacts of a heatwave as occurring independent of air pollution.[~~33~~10, 33] A relatively small number of heatwave days may explain why the differences in heat effects between the three cities as well as the subpopulations were not statistically significant as their 95% confidence intervals were overlapped each other. Additionally, the mortality data for three cities only included two age groups (0 – 74, 75&+) by gender. Thus, we were unable to divide the data into smaller age groups.

~~CONCLUSION~~

CONCLUSIONS

A consistent and significant increase in mortality was observed during heatwaves in the three Australian metropolitan cities, but the impacts of heatwave ~~varied~~appeared to vary with age, gender, the heatwave definition and geographic area. Extreme hot temperatures appeared to directly result in an increased risk of mortality in these cities. The most vulnerable groups were the elderly, especial female~~,~~ aged 75 and over. By better understanding heatwave effects on mortality, local government and communities can develop appropriate public health strategies and increase their adaptive capacity to prevent and mitigate the impact of heatwave.

Table 1 Summary of the daily climatic variables and mortality in summer season[a] (1988 – 2009)

	Brisbane				Melbourne				Sydney			
Variable	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max
Male (All)	12	3.9	2	38	27	5.7	11	52	32	7.1	6	74
(0-74)	6	2.8	0	17	13	4.6	1	33	16	5.9	2	47
(75+)	6	2.8	0	25	14	4.4	2	34	15	4.5	3	32
Female (All)	12	4.1	1	40	26	5.7	10	79	30	6.7	9	70
(0-74)	4	2.1	0	13	8	3.3	1	21	10	3.8	1	32
(75+)	8	3.3	0	30	18	5.0	3	64	21	5.4	5	42
Total	24	6.2	4	68	54	8.6	23	127	62	11.1	20	136
MaxT* (°C)	29.3	2.3	20.1	40.1	25.6	5.8	13.9	46.7	27.1	4.0	16.6	44.0
MeanT † (°C)	24.8	1.9	18.3	33.6	19.7	3.9	10.9	35.5	22.5	2.7	15.1	33.2
MinT‡ (°C)	20.3	2.2	11.9	27.1	13.8	3.3	5.8	27.6	18.0	2.3	9.8	25.8
RH§ (%)	70.2	8.7	30.2	96.8	65.0	11.6	19.7	95.6	70.0	11.0	28.1	98.1

[a] 1st December to the end of February of next year
*maximum temperature, †mean temperature, ‡minimum temperature, §relative humidity

Table 2 Heatwave definition (HWD) used in three cities (1988 – 2009)

HWD[a]	Heatwave days and threshold					
	Brisbane		Melbourne		Sydney	
99%	11	29.7 °C	4	30.1 °C	0	29.6 °C
95%	70	28.0 °C	56	27.2 °C	37	27.3 °C
90%	153	27.2 °C	128	25.3 °C	118	26.1 °C

[a] HWD were defined as the mean temperature above the percentiles (i.e., 90th, 95th or 99th centile) for two or more consecutive days in the summer season (1st December to the end of February of next year).

Table 3 Relative risk of mortality by different heatwave definition (HWD) for cumulative lag effects (lag 0-2) in three cities, 1988 -2009

HWD[a]		RR[†] [95% CI[*]]		
		Brisbane	Melbourne	Sydney
Male	(All)			
	99%	**1.32 [1.17 - 1.48]**	**1.37 [1.22 - 1.53]**	n/a[‡]
	95%	1.04 [0.99 - 1.10]	1.00 [0.96 - 1.04]	1.03 [0.99 - 1.08]
	90%	1.01 [0.97 - 1.05]	1.02 [0.99 - 1.05]	**1.04 [1.01 - 1.06]**
	(0 - 74)			
	99%	**1.29 [1.10 - 1.53]**	**1.37 [1.15 - 1.63]**	n/a
	95%	1.04 [0.96 - 1.12]	0.96 [0.91 - 1.02]	**1.07 [1.01 - 1.13]**
	90%	0.99 [0.93 - 1.04]	1.00 [0.96 - 1.04]	**1.04 [1.00 - 1.08]**
	(75+)			
	99%	**1.33 [1.13 - 1.56]**	**1.38 [1.19 - 1.61]**	n/a
	95%	1.05 [0.97 - 1.13]	1.04 [0.98 - 1.09]	0.99 [0.92 - 1.05]
	90%	1.03 [0.97 - 1.08]	1.03 [0.99 - 1.07]	**1.03 [1.00 - 1.07]**
Female	(All)			
	99%	**1.45 [1.30 - 1.61]**	**1.57 [1.41 - 1.74]**	n/a
	95%	**1.13 [1.07 - 1.19]**	**1.11 [1.07 - 1.15]**	1.03 [0.98 - 1.07]
	90%	**1.06 [1.02 - 1.10]**	**1.05 [1.02 - 1.07]**	**1.05 [1.03 - 1.08]**
	(0 - 74)			
	99%	1.08 [0.86 - 1.34]	**1.46 [1.18 - 1.81]**	n/a
	95%	1.06 [0.96 - 1.17]	**1.10 [1.03 - 1.18]**	0.97 [0.90 - 1.05]
	90%	1.04 [0.96 - 1.11]	1.04 [0.99 - 1.09]	1.04 [0.99 - 1.09]
	(75+)			
	99%	**1.61 [1.42 - 1.82]**	**1.63 [1.44 - 1.85]**	n/a
	95%	**1.15 [1.08 - 1.22]**	**1.12 [1.07 - 1.17]**	**1.06 [1.01 - 1.12]**
	90%	**1.07 [1.02 - 1.12]**	**1.05 [1.01 - 1.08]**	**1.06 [1.03 - 1.09]**
Total				
	99%	**1.40 [1.29 - 1.51]**	**1.47 [1.36 - 1.59]**	n/a
	95%	**1.09 [1.05 - 1.13]**	**1.06 [1.03 - 1.09]**	**1.03 [1.00 - 1.07]**
	90%	**1.04 [1.01 - 1.07]**	**1.03 [1.01 - 1.05]**	**1.04 [1.03 - 1.06]**

[a] HWD were defined as different percentiles (i.e., 90th, 95th or 99th centile) of mean temperature for two or more consecutive days in the summer season.
[*]confidence interval, [†]relative risk, [‡] not applicable

Adjusted for relative humidity, days of week and population size

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REFERENCES

1. Le Tertre A, Lefranc A, Eilstein D, et al. Impact of the 2003 heatwave on all-cause mortality in 9 French cities. Epidemiology 2006;17:75-9.

2. Robine JM, Cheung SL, Le Roy S, et al. Death toll exceeded 70,000 in Europe during the summer of 2003. C R Biol 2008;331:171-8.

3. McMichael AJ, Wilkinson P, Kovats RS, et al. International study of temperature, heat and urban mortality: the 'ISOTHURM' project. Int. J. Epidemiol. 2008;37:1121-31.

4. Knowlton K, Rotkin-Ellman M, King G, et al. The 2006 California heat wave: impacts on hospitalizations and emergency department visits. Environ. Health Perspect. 2009;117:61-7.

5. O'Neill MS, Zanobetti A, Schwartz J. Modifiers of the temperature and mortality association in seven US cities. Am. J. Epidemiol. 2003;157:1074-82.

6. Stafoggia M, Forastiere F, Agostini D, et al. Vulnerability to Heat-Related Mortality: A Multicity, Population-Based, Case-Crossover Analysis. Epidemiology 2006;17:315-23

7. Tong S, Wang XY, Barnett AG Assessment of heat-related health impacts in Brisbane, Australia: comparison of different heatwave definitions. *PLoS ONE* 2010;5: e12155. doi: 10.1371/journal.pone.0012155.

8. Anderson GB, Bell ML. Heat Waves in the United States: Mortality Risk during Heat Waves and Effect Modification by Heat Wave Characteristics in 43 U.S. Communities. Environ. Health Perspect. 2011;119:210-8.

9. Hajat S, Kosatky T. Heat-related mortality: a review and exploration of heterogeneity. J. Epidemiol. Community Health 2010;64:753-60.

10. Anderson BG, Bell ML. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology 2009;20:205-13.

11. Yu W, Mengersen K, Hu W, et al. Assessing the relationship between global warming and mortality: lag effects of temperature fluctuations by age and mortality categories. Environ Pollut 2011;159:1789-93.

12. Gasparrini A, Armstrong B. The impact of heat waves on mortality. Epidemiology 2011;22:68-73.

13. Baccini M, Kosatsky T, Analitis A, et al. Impact of heat on mortality in 15 European cities: attributable deaths under different weather scenarios. J. Epidemiol. Community Health 2011;65:64-70.

14. Grize L, Huss A, Thommen O, Schindler C, Braun-Fahrlander C. Heat wave 2003 and mortality in Switzerland. Swiss Med Wkly 2005;135:200-5.

15. Basagana X, Sartini C, Barrera-Gomez J, et al. Heat Waves and Cause-specific Mortality at all Ages. Epidemiology 2011;22:765-72.

16. Wang XY, Barnett AG, Yu W, et al. The impact of heatwaves on mortality and emergency hospital admissions from non-external causes in Brisbane, Australia. Occup. Environ. Med. 2012;69:163-9.

17. Guo Y, Barnett AG, Zhang Y, et al. The short-term effect of air pollution on cardiovascular mortality in Tianjin, China: comparison of time series and case-crossover analyses. Sci. Total Environ. 2010;409:300-6.

18. Tong S, Wang XY, Guo Y Assessing the short-term effects of heatwaves on mortality and morbidity in Brisbane, Australia: comparison of case-crossover and time series analyses. *PLoS ONE* 2012;7: e37500. doi: 10.1371/journal.pone.0037500.

19. Guo Y, Barnett AG, Tong S. Spatiotemporal model or time series model for assessing city-wide temperature effects on mortality? Environ. Res. 2013;120:55-62.

20. Williams S, Nitschke M, Weinstein P, et al. The impact of summer temperatures and heatwaves on mortality and morbidity in Perth, Australia 1994-2008. Environ Int 2012;40:33-8.

21. Schaffer A, Muscatello D, Broome R, Corbett S, Smith W Emergency department visits, ambulance calls, and mortality associated with an exceptional heat wave in Sydney, Australia, 2011: a time-series analysis. *Environ Health* 2012;11. doi: 10.1186/1476-069x-11-3.

22. Vaneckova P, Beggs PJ, Jacobson CR. Spatial analysis of heat-related mortality among the elderly between 1993 and 2004 in Sydney, Australia. Soc. Sci. Med. 2010;70:293-304.

23. Huang C, Barnett AG, Wang X, Tong S. Effects of extreme temperatures on years of life lost for cardiovascular deaths: a time series study in brisbane, australia. Circ Cardiovasc Qual Outcomes 2012;5:609-14.

24. Guest CS, Willson K, Woodward AJ, et al. Climate and mortality in Australia: retrospective study, 1979-1990, and predicted impacts in five major cities in 2030. Clim Res 1999;13:1-15.

25. ABS. Australian Burean of Statistics: Regional Population Growth, Australia, 2011 http://www.abs.gov.au/ausstats/abs@.nsf/mf/3218.0.

26. Vaneckova P, Neville G, Tippett V, et al. Do Biometeorological Indices Improve Modeling Outcomes of Heat-Related Mortality? J. Appl. Meteor. Climatol. 2011;50:1165-76.

27. Schifano P, Leone M, De Sario M, et al. Changes in the effects of heat on mortality among the elderly from 1998-2010: results from a multicenter time series study in Italy. *Environ Health* 2012;11: 58. doi: 10.1186/1476-069x-11-58.

28. Barnett AG, Tong S, Clements AC. What measure of temperature is the best predictor of mortality? Environ. Res. 2010;110:604-11.

29. Yu W, Vaneckova P, Mengersen K, Pan X, Tong S. Is the association between temperature and mortality modified by age, gender and socio-economic status? Sci. Total Environ. 2010;408:3513-8.

30. Hajat S, Kovats RS, Lachowycz K. Heat-related and cold-related deaths in England and Wales: who is at risk? Occup. Environ. Med. 2007;64:93-100.

31. Kim Y, Joh S. A vulnerability study of the low-income elderly in the context of high temperature and mortality in Seoul, Korea. Sci. Total Environ. 2006;371:82-8.

32. Stafoggia M, Forastiere F, Agostini D, et al. Factors affecting in-hospital heat-related mortality: a multi-city case-crossover analysis. J. Epidemiol. Community Health 2008;62:209-15.

33. Tong S, Ren C, Becker N. Excess deaths during the 2004 heatwave in Brisbane, Australia. Int. J. Biometeorol. 2010;54:393-400.

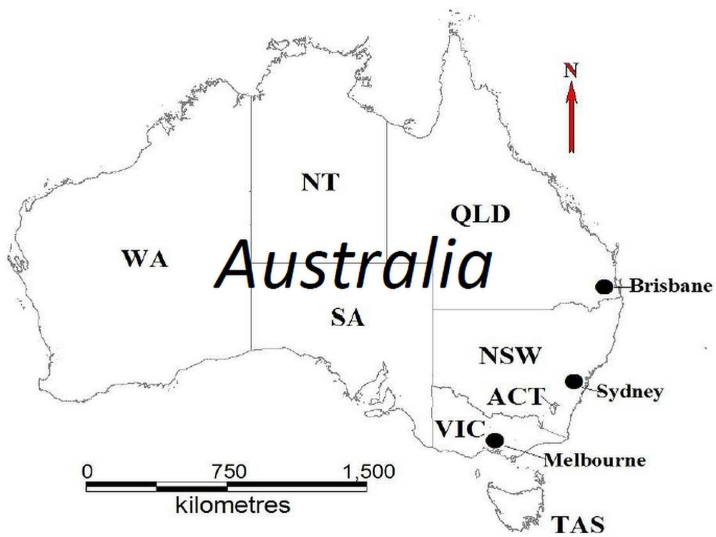


Figure 1 Locations of Brisbane, Melbourne and Sydney in Australia
254x190mm (300 x 300 DPI)

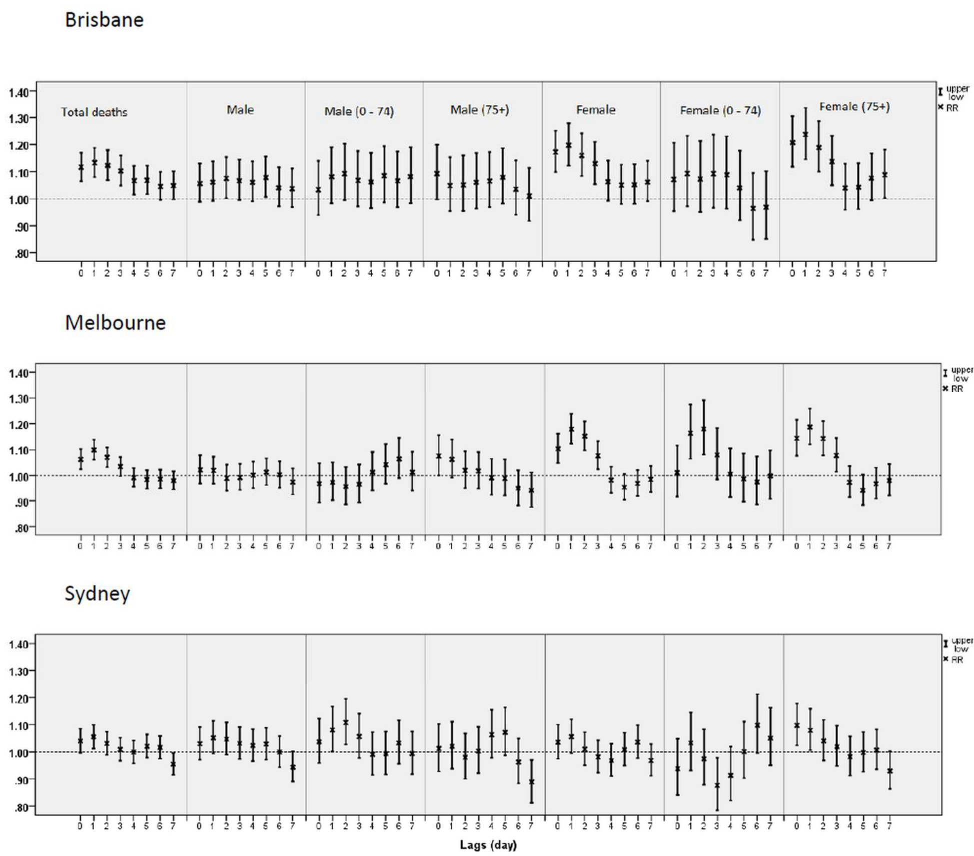


Figure 2 Distributed lag structure of the heatwave effects on mortality by sex, age and city. Cross symbols denote the mean relative risk (RR), and the vertical lines represent the 95% confidence intervals
271x235mm (300 x 300 DPI)

Supplemental Table 1 Average population size and percentage of older people (75+) between 1988 and 2009 in three cities

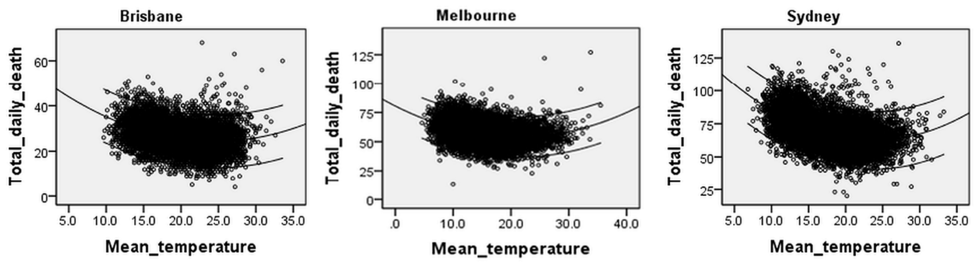
City	Total	Male	% 75+ (M*)	Female	% 75+ (F†)
Brisbane	1,603,742	792,809	3.6	810,933	5.9
Melbourne	3,423,855	1,688,942	4.1	1,734,914	6.4
Sydney	3,996,444	1,978,055	4.0	2,018,389	6.4

*Male, †Female

Supplemental Table 2 Heatwave (HW) days and the total number of deaths in three cities (1988 – 2009)

City	HWD[a]	1988 - 2009	HW days	Total deaths	HW days in each months
Brisbane	90%	Early summer[b]	71	1,615	45 in December, 65 in January
		Late summer[c]	82	2,073	and 43 in February
	95%	Early summer[b]	31	733	19 in December, 29 in January
		Late summer[c]	39	1,093	and 22 in February
	99%	Early summer[b]	6	168	3 in December, 5 in January
		Late summer[c]	5	205	and 3 in February
Melbourne	90%	Early summer[b]	49	2,734	25 in December, 51 in January
		Late summer[c]	79	4,597	and 52 in February
	95%	Early summer[b]	19	1,098	7 in December, 23 in January
		Late summer[c]	37	2,152	and 26 in February
	99%	Early summer[b]	0	N/A	0
		Late summer[c]	4	333	4 in January
Sydney	90%	Early summer[b]	54	3,592	21 in December, 59 in January
		Late summer[c]	64	3,914	and 38 in February
	95%	Early summer[b]	13	889	7 in December, 23 in January
		Late summer[c]	24	1,321	and 8 in February
	99%	Early summer[b]	0	N/A	0
		Late summer[c]	0	N/A	0

[a] HWD were defined as the mean temperature above the percentiles (i.e., 90th, 95th or 99th centile) for two or more consecutive days in the summer season (1st December to the end of February of next year).
[b] between 1st Dec. and 15th Jan.
[c] between 16th Jan and end of Feb.



Supplemental Figure 1 The distribution of daily mean temperature (oC) and mortality (1988 – 2009)
309x90mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract √
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found √
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported √
Objectives	3	State specific objectives, including any prespecified hypotheses √
Methods		
Study design	4	Present key elements of study design early in the paper √
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection √
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants N/A
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable √
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group √
Bias	9	Describe any efforts to address potential sources of bias √
Study size	10	Explain how the study size was arrived at √
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why √

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding √
		(*b*) Describe any methods used to examine subgroups and interactions √
		(*c*) Explain how missing data were addressed √
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed N/A *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy N/A
		(*e*) Describe any sensitivity analyses √

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed N/A
		(b) Give reasons for non-participation at each stage N/A
		(c) Consider use of a flow diagram N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders √
		(b) Indicate number of participants with missing data for each variable of interest √
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time N/A
		Case-control study—Report numbers in each exposure category, or summary measures of exposure N/A
		Cross-sectional study—Report numbers of outcome events or summary measures N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included √
		(*b*) Report category boundaries when continuous variables were categorized √
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period √
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses √
Discussion		
Key results	18	Summarise key results with reference to study objectives √
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias √
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence √
Generalisability	21	Discuss the generalisability (external validity) of the study results √
Other information		

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based √

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.