



Exposure to hot and cold temperatures and ambulance attendances in Brisbane, Australia: A time series study

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Article focus:

- To examine the relationship between exposure to hot and cold temperatures and ambulance attendances.
- To contribute to the literature concerning effects of climate change on non-fatal health outcomes, specifically ambulance attendances.

Key messages:

- Hot and cold ambient temperatures affected ambulance attendances for a variety of health outcomes.
- There were differences in the temperature–attendance relationship for different medical conditions.

Strengths:

- This study adds to the limited literature examining the effects of temperature on non-fatal health outcomes.
- Ambulance attendance data could be useful for the development of weather/health early warning systems.

Limitations:

- Misclassification bias might exist due to non-standardised coding in administrative ambulance data.
- The location of attendance may not always correspond with the location where the patient received the majority of exposure.

ABSTRACT

Objectives:

To investigate the effect of hot and cold temperatures on ambulance attendances.

Design:

An ecological time series study.

Setting and participants:

The study was conducted in Brisbane, Australia. We collected information on 783 935 daily ambulance attendances, along with data of associated meteorological variables and air pollutants, for the period of 2000–2007.

Outcome measures:

The total number of ambulance attendances was examined, along with those related to cardiovascular, respiratory and other non-traumatic conditions. Generalised additive models were used to assess the relationship between daily mean temperature and the number of ambulance attendances.

Results:

There were statistically significant relationships between mean temperature and ambulance attendances for all categories. Acute heat effects were found with a 1.17% (95% CI: 0.86%, 1.48%) increase in total attendances for 1 °C increase above threshold (0–1 days lag). Cold effects were delayed and longer lasting with a 1.30% (0.87%, 1.73%) increase in total attendances for a 1 °C decrease below the threshold (2–15 days lag). Harvesting was observed following initial acute periods of heat effects, but not for cold effects.

Conclusions:

This study shows that both hot and cold temperatures led to increases in ambulance attendances for different medical conditions. Our findings support the notion that ambulance attendance records are a valid and timely source of data for use in the development of local weather/health early warning systems.

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INTRODUCTION

The effect of climate change on human health has received much attention in response to projected scenarios of both increasing and more variable global temperatures.[1, 2] It is important to examine these effects as not only will it increase knowledge of the relationships between temperature and human health, but this information will also inform public health policy which seeks to minimise the adverse impacts of climate change on the population, particularly in terms of major chronic conditions such as cardiovascular and respiratory disease.[3]

To date, a large body of research has been devoted to examining the effects of temperature on mortality for different populations, with a particular focus on vulnerable subgroups such as the elderly and frail.[4, 5] Studies have examined the effects of hot and cold temperatures in terms of same-day and extended periods of exposure (e.g., heatwaves), the apparent variation in responses between populations living in different climates, and the presence of lagged responses to exposure.[6–9] Another important area of study relates to the non-linear nature of the temperature–health relationship, which is sometimes interpreted through the existence of temperature ‘comfort zones’, above and below which the health risk due to increasing or decreasing temperature increases dramatically.[10]

As opposed to research into fatal health events, there has been much less attention into research of non-fatal health outcomes. To date, only a few studies have concentrated on hospital and/or emergency department admissions data, collected from either hospital or health department information systems.[11–13] A number of benefits to using non-fatal event data have been suggested, from the ability to conduct more targeted health intervention strategies throughout the community,[14] to the development of early-warning assessment systems.[15–17] In such applications, other forms of morbidity data such as ambulance

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3 attendance records have been cited as being potentially useful for the purposes of capturing
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5 those events that, while not leading to immediate death, are important precursors to such
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7 incidents and therefore to effective public health intervention strategies.
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11 There have been few attempts to examine the effect of temperature on ambulance
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13 attendances.[18–20] A number of studies have reported a strong relationship between same
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15 day temperature and emergency admissions by ambulance for cerebrovascular disease[21,
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17 22] and respiratory disease.[23] A study of ambulance response calls and extreme heat in
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19 Toronto[24] examined the spatial variation in calls across the city, noting that increased call
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21 rates during hot periods were related to day-of-week factors and associated population
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23 movements. Two recent studies from Toronto[25] and Italy[26] both attempted to quantify
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25 the temperature–ambulance attendance relationship for cardiovascular and respiratory disease
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27 and heat/cold exposure, after controlling for seasonality, air pollution, and day-of-week
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29 factors. They found an increase in ambulance attendances for cardiovascular, respiratory and
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31 other non-traumatic diseases in relation to exposure to temperatures during the summer
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33 period.
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39 To date, there exists a lack of research examining the effects of temperature on morbidity,
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41 particularly ambulance attendances, and no studies have been conducted in a sub-tropical
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43 climate to assess both cold and hot temperature effects on ambulance attendances. This study
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45 therefore examined the relationship between ambient temperature and ambulance attendances
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47 in Brisbane, Australia.
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49 **METHODS**

50 **The study population**

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3 Brisbane is the capital city of Queensland, located on the east coast of Australia (27° 30'
4 south and 153° 00' east). It has a sub-tropical climate and generally experiences mild winters
5 and hot summers. The population increased over the study period from 0.88 million in 2000
6 to 1.01 million in 2007.
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12 Data on meteorological factors, air pollution and ambulance attendances in Brisbane,
13 Australia for the period from 1 January 2000 to 31 December 2007 were obtained from
14 relevant government agencies. As postcode was the only available geographical location
15 identifier, a list of postcodes for the City of Brisbane was obtained from the Australian
16 Bureau of Statistics and Brisbane City Council to define the area and population of the study.
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24 **Ambulance attendance data**

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27 Anonymised ambulance attendance data were supplied by the Queensland Ambulance
28 Service (QAS), the main provider of out-of-hospital emergency care and ambulance transport
29 in Queensland. The variables extracted from each anonymised attendance record were the
30 date of attendance, sex and age of the patient, postcode of attendance event and the health
31 assessment of the patient, recorded using a specific coding system. The data were collected
32 from the ambulance information management system utilised by the QAS. Ethical approval
33 was obtained prior to the collection of this data.
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44 In this study, we calculated the daily number of attendance events for groups of health
45 assessment codes related to cardiovascular, respiratory or other non-traumatic attendances
46 that may have been related to ambient temperature exposure.
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50 **Exposure data**

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53 Daily meteorological data from a central monitoring station were obtained from the Bureau
54 of Meteorology, which consisted of observations of daily mean temperature (calculated as the
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3 average of the daily minimum and maximum temperatures) and humidity. Air pollution data
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5 were obtained from the Department of Environment and Resource Management and
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7 consisted of hourly mean concentrations of ozone (O₃), nitrogen dioxide (NO₂), sulphur
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9 dioxide (SO₂) and particulate matter of size less than 10µm (PM₁₀) from eight monitoring
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11 sites throughout Brisbane. Daily mean values were then calculated for all meteorological and
12
13 environmental data; when a particular station lacked daily environmental data, the average
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15 across the remaining stations was calculated. Daily mean temperature was used in the
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17 analysis, following several previous studies that have shown it to perform as well as or better
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19 than other temperature measures.[27–29]
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24 **Statistical analysis**

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27 To better understand the nature of the association between ambulance attendances and
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29 temperature, we initially examined the exposure–response curve using generalised additive
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31 models. The relationship between same-day temperature and attendances was analysed using
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33 a natural cubic spline with four degrees of freedom (dfs). The model also adjusted for the
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35 possible confounding effects of humidity, O₃, NO₂, SO₂ and PM₁₀ by using separate cubic
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37 splines with four dfs each. The selection of dfs was based on previous research.[30] To
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39 control for any secular trends and seasonal effects other than temperature, time was
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41 incorporated using a cubic spline with five dfs per year. Effects from both day-of-week and
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43 public holidays were incorporated through dummy variables to control for calendar effects.
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47 To derive specific estimates of heat and cold slopes, we applied a distributed lag non-linear
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49 model (DLNM) with either a “V” or “U” shape linear threshold.[10, 31] This involved
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51 specifying a single or double threshold for temperature, and then estimating a log-linear
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53 change in risk of ambulance attendances above (or below) the hot (or cold) threshold/s. To
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55 examine the nature of delayed effects of temperature on ambulance attendances, a natural
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3 cubic spline was used to incorporate lagged effects up to 27 days.[9] An approximate range
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5 for threshold value/s was selected for each attendance group. These ranges were partitioned
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7 into 0.5 °C increments, and the DLNM model was applied iteratively using each value across
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9 the range. The thresholds were then selected based on the model of best fit (lowest deviance)
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11 across the values. Using the DLNM with these thresholds, cold effects (1 °C decrease in
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13 temperature below the threshold) and heat effects (1 °C increase in temperature above the
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15 threshold) were graphically examined across lags. Based on an examination of the general
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17 nature of the exposure–response relationship for lags up to 27 days, parametric effect
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19 estimates were obtained using a lag-stratified approach[10] for the following lag periods: the
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21 average of lag days 0–1, 2–15 and 16–27. Estimates of the percent change in ambulance
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23 attendance corresponded to a 1 °C increase (or decrease) in temperature above (or below) the
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25 threshold/s. There were no missing values in the ambulance attendance data, and very few
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27 missing environmental data after aggregation over all available stations (0.24% temperature
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29 data and 0.44% humidity data). All analyses were conducted in SAS V9.2 and R V2.12.2.
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34 35 **RESULTS**

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38 Figure 1 shows the distribution of attendance events through time for all attendance
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40 categories, meteorological and air pollution variables. A strong, increasing secular trend was
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42 apparent for total attendance events over the study period, with a similar but slightly weaker
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44 trend for cardiovascular and other non-traumatic attendances. A strong seasonal pattern was
45
46 observed for respiratory attendances, with increases during the cooler months. A sharp spike
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48 in total attendance events occurred during early 2004, which corresponded to a severe
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50 heatwave in Brisbane at that time.[32] Strong seasonality was observed in temperature, along
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52 with O₃ and NO₂ concentrations, with weaker seasonality present in both relative humidity
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54 and SO₂ concentrations. There was no apparent seasonal pattern for PM₁₀.
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[Figure 1 here]

Table 1 shows that for the period of study from 2000–2007 there were 783, 935 ambulance attendances, of which 15.3%, 8.7% and 7.1% were cardiovascular, respiratory and other non-traumatic conditions respectively. Daily mean temperature for the period ranged from 9 °C to 34.2 °C.

Table 1: Summary statistics for daily ambulance attendances, meteorological and air pollution variables in Brisbane, 2000–2007

Variable	No. days	Mean	Minimum	25 th Percentile	Median	75 th percentile	Maximum
Total (783 935 counts)	2922	268.3	104	210	283.5	325	432
Cardiovascular (120 041 counts)	2922	41.1	11	34	41	48	77
Respiratory (68 535 counts)	2922	23.5	3	18	23	29	62
Other non-traumatic (55 822 counts)	2922	19.1	1	12	18	25	60
Mean temperature (°C)	2915	20.5	9	17.1	21	23.7	34.2
Relative humidity (%)	2909	71.4	23.8	66.3	72.6	78.5	96.3
PM ₁₀ (µg/m ³)	2922	19.7	4.7	14.9	18.4	22.6	166.8
Ozone (ppm)	2922	0.0144	0.0014	0.0107	0.0137	0.0174	0.0353
Sulphur dioxide (ppm)	2922	0.0015	0	0.0009	0.0013	0.0019	0.0085
Nitrogen dioxide (ppm)	2922	0.0116	0.0014	0.0077	0.0109	0.0151	0.0333

Table 2 shows the correlation coefficients between all attendances and environmental variables. There exists significant, although weak, correlation between temperature, humidity and air pollutants. Temperature and NO₂ were found to have the strongest correlation across all variables.

Table 2: Spearman correlations between environmental variables for Brisbane, 2000–2007

	O3	PM10	SO2	NO2
Temperature	0.132 **	0.033	-0.162 **	-0.670 **
O3		0.106 **	-0.119 **	-0.225 **
PM ₁₀			0.273 **	0.305 **
SO ₂				0.397 **

** $P < 0.001$

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3 Through the use of a DLNM with a linear threshold model for temperature, it was found that
4
5 the exposure–response relationship for total, cardiovascular and respiratory attendances was
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7 described by a “V” shape with a threshold temperature (of minimum attendance count) of
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9 22 °C. The other non-traumatic attendance group was best described by a “U” shape with a
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11 large comfort zone between 15.5 °C and 28 °C.
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15 There were similar patterns of lagged effects of both hot (a 1 °C increase above the threshold)
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17 and cold (a 1 °C decrease below the threshold) temperatures on the number of ambulance
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19 attendances across all groups (Figure 2). Cold effects were found to be delayed, generally
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21 occurring 2–3 days following exposure for all groups. The other non-traumatic attendance
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23 group was an exception, with effects not occurring until approximately 5–8 days after
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25 exposure. The respiratory and other non-traumatic groups also displayed signs of acute cold
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27 effects, although these were not statistically significant. Heat effects were found to be acute
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29 across all groups, occurring within 0–2 days following exposure.
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33 [Figure 2 here]
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37 We calculated parametric effect estimates for the average of lags 0–1, 2–15 and 15–27 (Table
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39 3). There were significant heat effects over lags 0–1, with a 1 °C increase in temperature
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41 above 22 °C associated with a 1.17% (95% CI: 0.86%, 1.48%) increase in total ambulance
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43 attendances. The largest heat effect found was for the other non-traumatic attendance group,
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45 with a 1 °C increase in temperature resulting in a 20.56% (95% CI: 15.15%, 26.10%)
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47 increase in attendances.
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50 We found that the hot effects on all groups displayed characteristics consistent with
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52 harvesting, with a significant decrease in attendances for total (–0.82%, 95% CI: –1.35%, –
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54 0.30%), cardiovascular (–1.85%, 95% CI: –3.06%, –0.64%) and respiratory (–1.99%, 95%
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CI: -3.72%, -0.25%) categories over lags 2–15, which followed the immediate increases in ambulance attendance observed over the first few days of exposure.

Table 3: Temperature effects on ambulance attendances in Brisbane, Australia. Effects given as percent change per 1 °C above or below threshold (Threshold stated in brackets for each category)

	Lag in days	Attendance category (95% C.I)			
		Total (22 °C)	Cardiovascular (22 °C)	Respiratory (22 °C)	Other (15.5/28 °C)
Heat effect	0–1	1.17 (0.86, 1.48)	0.45 (-0.26, 1.16)	-0.38 (-1.40, 0.63)	20.56 (15.15, 26.10)
	2–15	-0.82 (-1.35, -0.30)	-1.85 (-3.06, -0.64)	-1.99 (-3.72, -0.25)	-12.37 (-27.06, 2.48)
	16–27	-0.47 (-0.97, 0.04)	-0.35 (-1.51, 0.81)	-0.72 (-2.38, 0.94)	3.19 (-10.30, 16.83)
Cold effect	0–1	-0.16 (-0.40, 0.08)	-0.62 (-1.17, -0.06)	0.63 (-0.09, 1.34)	-0.38 (-2.12, 1.38)
	2–15	1.30 (0.87, 1.73)	1.63 (0.64, 2.62)	3.65 (2.38, 4.92)	3.40 (0.43, 6.37)
	16–27	0.12 (-0.28, 0.53)	-1.1 (-2.03, -0.16)	0.9 (-0.30, 2.11)	6.49 (3.62, 9.36)

Cold effects over lags 2–15 were found for all categories, with the largest increases in attendances associated with respiratory (3.65%, 95% CI: 2.38%, 4.92%), and other non-traumatic (3.40%, 95% CI: 0.43%, 6.37%) groups. The other non-traumatic attendance group also showed significant cold effects from 15 days onward (6.49%, 95% CI: 3.62%, 9.36%). There was no apparent harvesting observed in cold effects, except for the CV group.

DISCUSSION

In this study, we examined the relationship between temperature and ambulance attendances using time series modelling techniques. Cold and heat effects were observed for all attendance categories. There was a “V” or “U” shaped relationship between daily mean temperature and ambulance attendances, with statistically significant increases in different attendance categories for a 1 °C change in temperature from the thresholds. Cold effects were found to be delayed in onset but last longer than heat effects, which were immediate and short-lived.

There have been few studies of the effects of ambient temperature on ambulance attendances.

A Toronto study[25] reported large increases in ambulance response calls during the summer

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3 period. Similarly, a multi-city analysis in Italy[26] found an increasing risk of ambulance
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5 dispatches for increasing temperature, with the largest same-day heat effects occurring for
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7 other non-traumatic and respiratory conditions. However, no cold effect was observed in their
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9 study. The short-term nature of the heat effects in these studies has been observed more
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11 generally. Heat effects on both cardiovascular and respiratory diseases are often observed to
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13 be immediate and short-term,[25, 33] with the strongest heat effects recorded in the first one
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15 to three days following exposure, before decreasing in magnitude.[34] We found similar
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17 trends across all attendance categories, with a heat effect observed immediately following
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19 exposure. In terms of cold temperature effects, we found a significantly increased risk for all
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21 attendance categories. The cold effects on cardiorespiratory attendances are consistent with
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23 most previous studies.[35–37] While this result differs with the those from the Italian
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25 study,[26] based on our results the short exposure lags considered in that study may have
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27 resulted in an underestimation of the cold effect. Our findings of lagged effect of cold
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29 temperatures of up to 15 days following exposure corroborate observations from previous
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31 research.[35, 38]
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37 A common pattern across all categories was the slight drop in heat effects between 2 and 15
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39 days, consistent with the harvesting phenomenon found in studies of temperature and
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41 mortality.[6] The occurrence of such an effect has a clear physiological explanation in terms
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43 of fatal health outcomes, however it is less clear as to what would cause this displacement in
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45 out-of-hospital attendances. One factor may be due to an initial large number of transfers and
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47 subsequent admissions of seriously ill patients to hospital. Once there, it would be expected
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49 that such people would spend a number of days in hospital, thereby removing high risk
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51 individuals from the general population that would further utilise ambulance services.
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56 An interesting finding was the differences in temperature effects on different categories of
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58 ambulance attendance. In our study, for same-day temperature exposure there was a slight,
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3 non-significant decrease and increase in heat effect for respiratory and cardiovascular
4 attendances, respectively. In particular, the direction of effect on respiratory attendances is in
5 line with previous results that show a protective effect of hot temperatures on pre-admission
6 respiratory morbidity.[39] This finding may be due to the fact that in our study, respiratory
7 tract infections made up a large proportion of respiratory attendances, conditions that are
8 more prevalent in cooler weather.[23, 36] The other non-traumatic attendance category
9 displayed a significantly larger heat effect. This is likely a result of either the higher
10 temperature threshold identified for this sub-group, or the fact it contained a large percentage
11 of attendances that were related to psychiatric issues, which have been identified as being
12 strongly influenced by high temperatures.[40]
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26 This study has a number of strengths. Firstly, given the current lack of research into
27 temperature effects on ambulance attendances, the study contributes to an understanding of
28 how pre-hospital health conditions are affected by changes in temperature. Secondly,
29 ambulance attendances often occur for conditions that do not require hospital admission nor
30 cause death. This implies that ambulance attendance data may be useful in surveillance
31 systems as they provide the ability to monitor health outcomes that will not be captured in
32 mortality or admissions data.
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42 Limitations of the study should also be acknowledged. Firstly, compared to other types of
43 health outcomes such as mortality, hospital admissions and emergency admissions, the
44 available coding regime was limited for ambulance attendances and therefore the risk of
45 misclassification of health outcomes was potentially higher here than for other types of health
46 outcomes. As the primary purpose of the ambulance data set is for administrative and
47 performance evaluation purposes, codes are not required at the level of detail seen in a
48 hospital setting, as a more thorough diagnosis is made once the patient is admitted. Therefore
49 the relevant attendance categories were necessarily grouped together. Secondly, the postcode
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3 variable in our dataset reflected the location of attendance, not the residential area of the
4 patient. Therefore the location of attendance may not closely correspond with the location
5 where the patient received the majority of exposure. Finally, the implementation of a new
6 information system and coding regime in 2006 may have produced some measurement error
7 in the data. However, sensitivity analyses using data from each year separately and also data
8 from before the new system was implemented (2000–2005) were found to make little
9 difference to the results.
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19 This research may have several implications, within both the research domain and public
20 health policy arena. Firstly, this study has shown that the effects of ambient temperature on
21 ambulance attendances in a sub-tropical climate are similar to those found in both hospital
22 admissions and mortality data.[5] However, some specific effects on ambulance attendances
23 were found to differ with those on hospital admissions or mortality, and also between the
24 different attendance categories; it would therefore be useful to compare different exposure–
25 response relationships in future research.[18] In terms of public health policy,[24] examining
26 ambulance attendances rather than admission or mortality data would potentially help to pick
27 up not only early signs of temperature effects, but also effects on health conditions that
28 cannot be examined through analysis of mortality and hospital admissions data.
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42 This study found significant effects of both cold and hot temperatures and lagged effects of
43 up to 15 days on cardiorespiratory attendances, which contributes to the currently limited
44 research of temperature effects on ambulance attendances. The use of ambulance data in
45 epidemiological research is needed in order to assess a wider range of non-fatal health
46 outcomes, with its analysis particularly useful in the development of more responsive early
47 warning and health surveillance systems.
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11
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13
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15
16 revision of the manuscript. DC read and revised the manuscript. All authors read and
17
18 approved the final manuscript.
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30 **Data sharing statement:** No additional data available.
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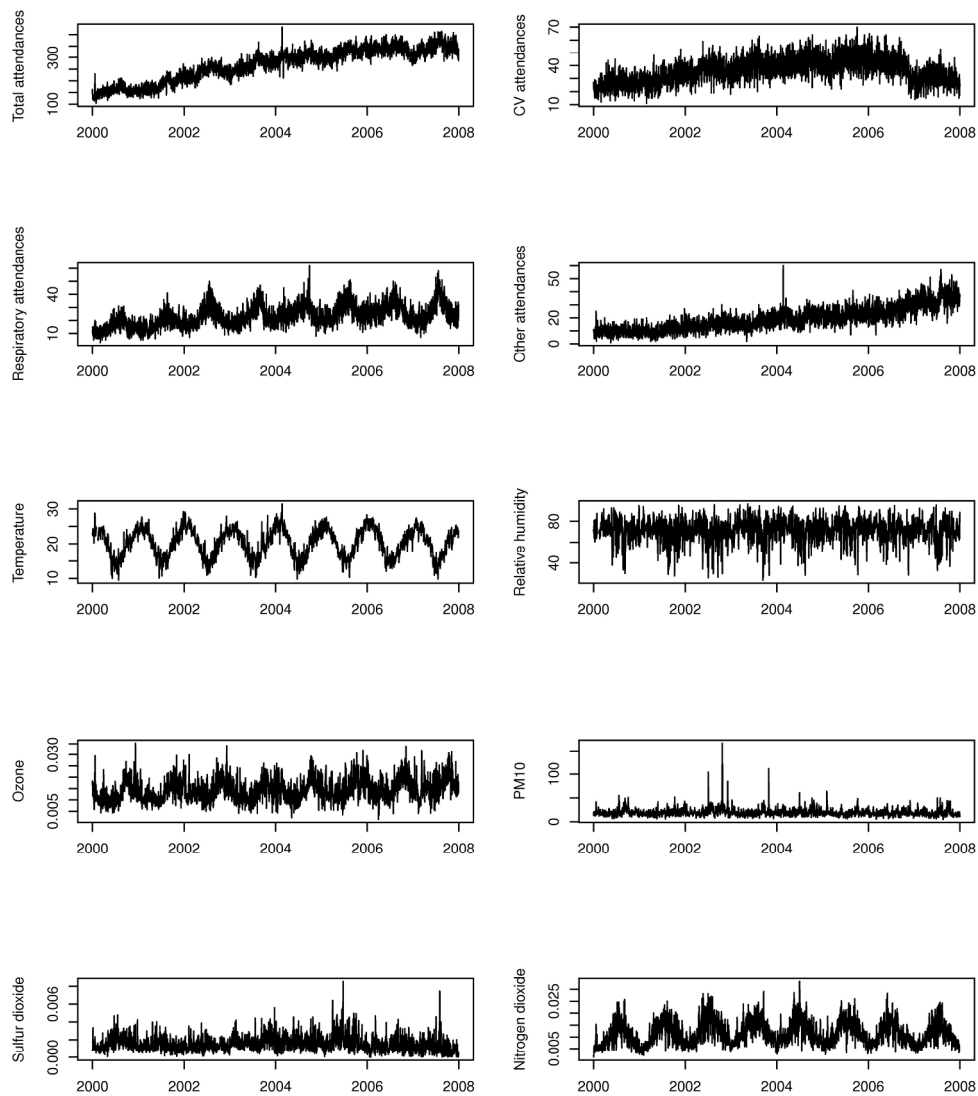
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4 **List of Figures:**
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8 **Figure 1:** Distributions of ambulance attendance counts, temperature and air pollutants
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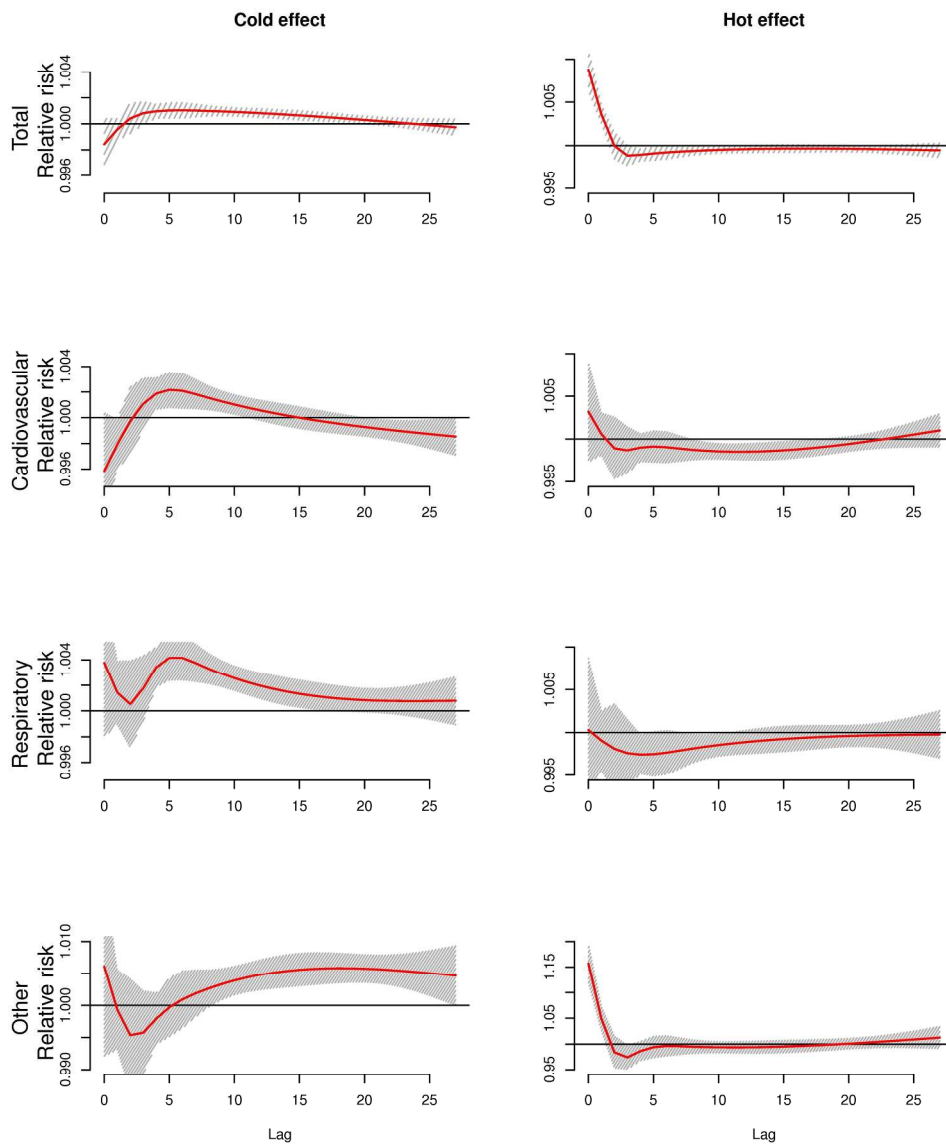
10 **Figure 2:** Lagged effects for a 1 °C decrease (left) and increase (right) in mean temperature
11 below (and above) the threshold temperature for total, cardiovascular, respiratory and other
12 non-traumatic attendances. The shaded region corresponds to the 95% confidence interval
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Distributions of ambulance attendance counts, temperature and air pollutants
235x281mm (300 x 300 DPI)

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Lagged effects for a 1 °C decrease (left) and increase (right) in mean temperature below (and above) the threshold temperature for total, cardiovascular, respiratory and other non-traumatic attendances. The shaded region corresponds to the 95% confidence interval
238x288mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	4–5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6–7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8–10
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8–9
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	n/a
		(b) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8–9
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	8–9
Bias	9	Describe any efforts to address potential sources of bias	9, 15
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9–10
		(b) Describe any methods used to examine subgroups and interactions	9–10
		(c) Explain how missing data were addressed	n/a
		(d) If applicable, explain how loss to follow-up was addressed	n/a
		(e) Describe any sensitivity analyses	16
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	11
		(b) Indicate number of participants with missing data for each variable of interest	11
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	
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	13
		(b) Report category boundaries when continuous variables were categorized	n/a
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	16
Discussion			
Key results	18	Summarise key results with reference to study objectives	10–13
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13–15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15–16
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	17

*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.



Exposure to hot and cold temperatures and ambulance attendances in Brisbane, Australia: A time series study

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Keywords:	PUBLIC HEALTH, ACCIDENT & EMERGENCY MEDICINE, EPIDEMIOLOGY

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7 **Type of Manuscript:** Research article

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9 **Title:** Exposure to hot and cold temperatures and ambulance attendances in Brisbane,
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11 **Australia: A time series study**

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17 **Keywords:** Ambulance attendances, Distributed lag non-linear model, Morbidity,
18 Queensland Ambulance Service, Temperature
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21 **Word count:**

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24 Abstract: 230
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27 Main document: [2947](#)
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Article focus:

- To examine the relationship between exposure to hot and cold temperatures and ambulance attendances.
- To contribute to the literature concerning effects of climate change on non-fatal health outcomes, specifically ambulance attendances.

Key messages:

- Hot and cold ambient temperatures affected ambulance attendances for a variety of health outcomes.
- There were differences in the temperature–attendance relationship for different medical conditions.

Strengths:

- This study adds to the limited literature examining the effects of temperature on non-fatal health outcomes.
- Ambulance attendance data could be useful for the development of weather/health early warning systems.

Limitations:

- Misclassification bias might exist due to non-standardised coding in administrative ambulance data.
- The location of attendance may not always correspond with the location where the patient received the majority of exposure.

ABSTRACT**Objectives:**

To investigate the effect of hot and cold temperatures on ambulance attendances.

Design:

An ecological time series study.

Setting and participants:

The study was conducted in Brisbane, Australia. We collected information on 783 935 daily ambulance attendances, along with data of associated meteorological variables and air pollutants, for the period of 2000–2007.

Outcome measures:

The total number of ambulance attendances was examined, along with those related to cardiovascular, respiratory and other non-traumatic conditions. Generalised additive models were used to assess the relationship between daily mean temperature and the number of ambulance attendances.

Results:

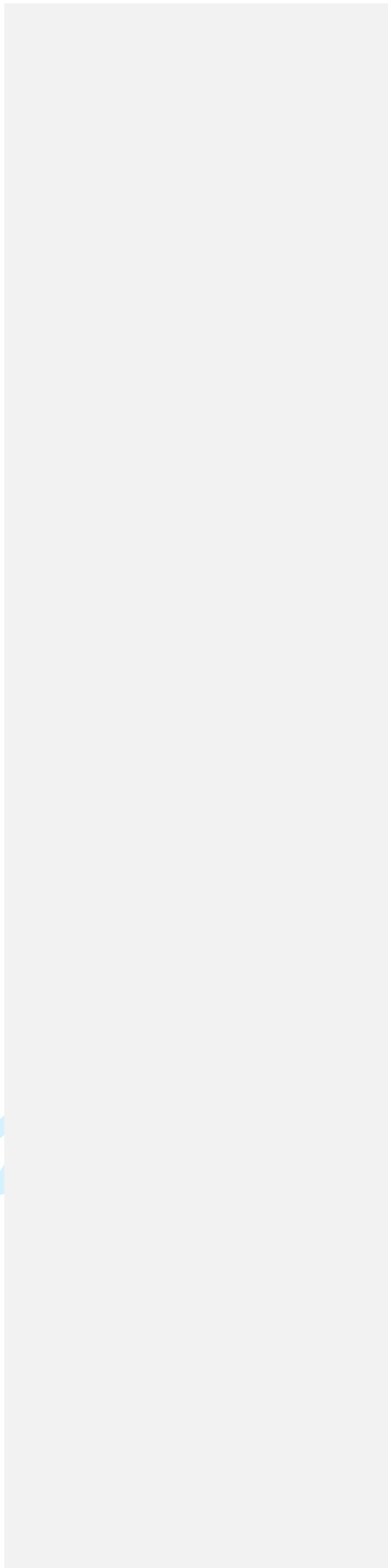
There were statistically significant relationships between mean temperature and ambulance attendances for all categories. Acute heat effects were found with a 1.17% (95% CI: 0.86%, 1.48%) increase in total attendances for 1 °C increase above threshold (0–1 days lag). Cold effects were delayed and longer lasting with a 1.30% (0.87%, 1.73%) increase in total attendances for a 1 °C decrease below the threshold (2–15 days lag). Harvesting was observed following initial acute periods of heat effects, but not for cold effects.

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Conclusions:

This study shows that both hot and cold temperatures led to increases in ambulance attendances for different medical conditions. Our findings support the notion that ambulance attendance records are a valid and timely source of data for use in the development of local weather/health early warning systems.

For peer review only



INTRODUCTION

The effect of climate change on human health has received much attention in response to projected scenarios of both increasing and more variable global temperatures.[1, 2] It is important to examine these effects as not only will it increase knowledge of the relationships between temperature and human health, but this information will also inform public health policy which seeks to minimise the adverse impacts of climate change on the population, particularly in terms of major chronic conditions such as cardiovascular and respiratory disease.[3]

To date, a large body of research has been devoted to examining the effects of temperature on mortality for different populations, with a particular focus on vulnerable subgroups such as the elderly and frail.[4, 5] Studies have examined the effects of hot and cold temperatures in terms of same-day and extended periods of exposure (e.g., heatwaves), the apparent variation in responses between populations living in different climates, and the presence of lagged responses to exposure.[6–9] Another important area of study relates to the non-linear nature of the temperature–health relationship, which is sometimes interpreted through the existence of temperature ‘comfort zones’, above and below which the health risk due to increasing or decreasing temperature increases dramatically.[10]

As opposed to research into fatal health events, there has been much less attention into research of non-fatal health outcomes. To date, only a few studies have concentrated on hospital and/or emergency department admissions data, collected from either hospital or health department information systems.[11–13] A number of benefits to using non-fatal event data have been suggested, from the ability to conduct more targeted health intervention strategies throughout the community,[14] to the development of early-warning assessment systems.[15–17] In such applications, other forms of morbidity data such as ambulance

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7 attendance records have been cited as being potentially useful for the purposes of capturing
8 those events that, while not leading to immediate death, are important precursors to such
9 incidents and therefore to effective public health intervention strategies.
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12 There have been few attempts to examine the effect of temperature on ambulance
13 attendances.[18–20] A number of studies have reported a strong relationship between same
14 day temperature and emergency admissions by ambulance for cerebrovascular disease[21, 22]
15 and respiratory disease.[23] A study of ambulance response calls and extreme heat in
16 Toronto[24] examined the spatial variation in calls across the city, noting that increased call
17 rates during hot periods were related to day-of-week factors and associated population
18 movements. Two recent studies from Toronto[25] and Italy[26] both attempted to quantify
19 the temperature–ambulance attendance relationship for cardiovascular and respiratory disease
20 and heat/cold exposure, after controlling for seasonality, air pollution, and day-of-week
21 factors. They found an increase in ambulance attendances for cardiovascular, respiratory and
22 other non-traumatic diseases in relation to exposure to temperatures during the summer
23 period.
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37 To date, there exists a lack of research examining the effects of temperature on morbidity,
38 particularly ambulance attendances, and no studies have been conducted in a sub-tropical
39 climate to assess both cold and hot temperature effects on ambulance attendances. This study
40 therefore examined the relationship between ambient temperature and ambulance attendances
41 in Brisbane, Australia.
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46 47 **METHODS**

48 49 **The study population**

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7 Brisbane is the capital city of Queensland, located on the east coast of Australia (27° 30'
8 south and 153° 00' east). It has a sub-tropical climate and generally experiences mild winters
9
10 (average minimum and maximum temperature: 9.7 °C, 21.3 °C) and hot summers (average
11 minimum and maximum temperature: 20.8 °C, 28.7 °C). The population increased over the
12
13 study period from 0.88 million in 2000 to 1.01 million in 2007.
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17 Data on meteorological factors, air pollution and ambulance attendances in Brisbane,
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19 Australia for the period from 1 January 2000 to 31 December 2007 were obtained from
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21 relevant government agencies. As postcode was the only available geographical location
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23 identifier, a list of postcodes for the City of Brisbane was obtained from the Australian
24
25 Bureau of Statistics and Brisbane City Council to define the area and population of the study.
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27 **Ambulance attendance data**

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29 Anonymised ambulance attendance data were supplied by the Queensland Ambulance
30
31 Service (QAS), the main provider of out-of-hospital emergency care and ambulance transport
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33 in Queensland. The variables extracted from each anonymised attendance record were the
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35 date of attendance, sex and age of the patient, postcode of attendance event and the health
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37 assessment of the patient, recorded using a specific coding system. The data were collected
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39 from the ambulance information management system utilised by the QAS. Ethical approval
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41 was obtained prior to the collection of this data.
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44 In this study, we calculated the daily number of attendance events for groups of health
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46 assessment codes related to cardiovascular, respiratory or other non-traumatic attendances
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48 that may have been related to ambient temperature exposure.
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50 **Exposure data**

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7 Daily meteorological data from a central monitoring station were obtained from the Bureau
8 of Meteorology, which consisted of observations of daily mean temperature (calculated as the
9 average of the daily minimum and maximum temperatures) and humidity. Air pollution data
10 were obtained from the Department of Environment and Resource Management and
11 consisted of hourly mean concentrations of ozone (O₃), nitrogen dioxide (NO₂), sulphur
12 dioxide (SO₂) and particulate matter of size less than 10µm (PM₁₀) from eight monitoring
13 sites throughout Brisbane. Daily mean values were then calculated for all meteorological and
14 environmental data; when a particular station lacked daily environmental data, the average
15 across the remaining stations was calculated. Daily mean temperature was used in the
16 analysis, following several previous studies that have shown it to perform as well as or better
17 than other temperature measures.[27–29]

28 **Statistical analysis**

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31 To better understand the nature of the association between ambulance attendances and
32 temperature, we initially examined the exposure–response curve using generalised additive
33 models. The relationship between same-day temperature and attendances was analysed using
34 a natural cubic spline with four degrees of freedom (dfs). The model also adjusted for the
35 possible confounding effects of humidity, O₃, NO₂, SO₂ and PM₁₀ by using separate cubic
36 splines with four dfs each. The selection of dfs was based on previous research.[30] To
37 control for any secular trends and seasonal effects other than temperature, time was
38 incorporated using a cubic spline with five dfs per year. Effects from both day-of-week and
39 public holidays were incorporated through dummy variables to control for calendar effects.

40
41 To derive specific estimates of heat and cold slopes, we applied a distributed lag non-linear
42 model (DLNM) with either a “V” or “U” shape linear threshold.[10, 31] This involved
43 specifying a single or double threshold for temperature, and then estimating a log-linear
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7 change in risk of ambulance attendances above (or below) the hot (or cold) threshold/s. To
8 examine the nature of delayed effects of temperature on ambulance attendances, a natural
9 cubic spline was used to incorporate lagged effects up to 27 days.[9] An approximate range
10 for threshold value/s was selected for each attendance group. These ranges were partitioned
11 into 0.5 °C increments, and the DLNM model was applied iteratively using each value across
12 the range. The thresholds were then selected based on the model of best fit (lowest deviance)
13 across the values. Using the DLNM with these thresholds, cold effects (1 °C decrease in
14 temperature below the threshold) and heat effects (1 °C increase in temperature above the
15 threshold) were graphically examined across lags. Based on an examination of the general
16 nature of the exposure–response relationship for lags up to 27 days, parametric effect
17 estimates were obtained using a lag-stratified approach[10] for the following lag periods: the
18 average of lag days 0–1, 2–15 and 16–27. Estimates of the percent change in ambulance
19 attendance corresponded to a 1 °C increase (or decrease) in temperature above (or below) the
20 threshold/s. There were no missing values in the ambulance attendance data, and very few
21 missing environmental data after aggregation over all available stations (0.24% temperature
22 data and 0.44% humidity data). All analyses were conducted in SAS V9.2 and R V2.12.2.

37 38 **RESULTS**

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41 Figure 1 shows the distribution of attendance events through time for all attendance
42 categories, meteorological and air pollution variables. A strong, increasing secular trend was
43 apparent for total attendance events over the study period, with a similar but slightly weaker
44 trend for cardiovascular and other non-traumatic attendances. A strong seasonal pattern was
45 observed for respiratory attendances, with increases during the cooler months. A sharp spike
46 in total attendance events occurred during early 2004, which corresponded to a severe
47 heatwave in Brisbane at that time.[32] Strong seasonality was observed in temperature, along
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with O₃ and NO₂ concentrations, with weaker seasonality present in both relative humidity and SO₂ concentrations. There was no apparent seasonal pattern for PM₁₀.

[Figure 1 here]

Table 1 shows that for the period of study from 2000–2007 there were 783, 935 ambulance attendances, of which 15.3%, 8.7% and 7.1% were cardiovascular, respiratory and other non-traumatic conditions respectively. Daily mean temperature for the period ranged from 9 °C to 34.2 °C.

Table 1: Summary statistics for daily ambulance attendances, meteorological and air pollution variables in Brisbane, 2000–2007

Variable	No. days	Mean	Minimum	25 th Percentile	Median	75 th percentile	Maximum
Total (783 935 counts)	2922	268.3	104	210	283.5	325	432
Cardiovascular (120 041 counts)	2922	41.1	11	34	41	48	77
Respiratory (68 535 counts)	2922	23.5	3	18	23	29	62
Other non-traumatic (55 822 counts)	2922	19.1	1	12	18	25	60
Mean temperature (°C)	2915	20.5	9	17.1	21	23.7	34.2
Relative humidity (%)	2909	71.4	23.8	66.3	72.6	78.5	96.3
PM ₁₀ (µg/m ³)	2922	19.7	4.7	14.9	18.4	22.6	166.8
Ozone (ppm)	2922	0.0144	0.0014	0.0107	0.0137	0.0174	0.0353
Sulphur dioxide (ppm)	2922	0.0015	0	0.0009	0.0013	0.0019	0.0085
Nitrogen dioxide (ppm)	2922	0.0116	0.0014	0.0077	0.0109	0.0151	0.0333

Table 2 shows the correlation coefficients between all attendances and environmental variables. There exists significant, although weak, correlation between temperature, humidity and air pollutants. Temperature and NO₂ were found to have the strongest correlation across all variables.

Table 2: Spearman correlations between environmental variables for Brisbane, 2000–2007

	O3	PM10	SO2	NO2
Temperature	0.132 **	0.033	-0.162 **	-0.670 **
O3		0.106 **	-0.119 **	-0.225 **
PM ₁₀			0.273 **	0.305 **
SO ₂				0.397 **

** $P < 0.001$

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9 Through the use of a DLNM with a linear threshold model for temperature, it was found that
10 the exposure–response relationship for total, cardiovascular and respiratory attendances was
11 described by a “V” shape with a threshold temperature (of minimum attendance count) of
12 22 °C. The other non-traumatic attendance group was best described by a “U” shape with a
13 large comfort zone between 15.5 °C and 28 °C.
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19 There were similar patterns of lagged effects of both hot (a 1 °C increase above the threshold)
20 and cold (a 1 °C decrease below the threshold) temperatures on the number of ambulance
21 attendances across all groups (Figure 2). Cold effects were found to be delayed, generally
22 occurring 2–3 days following exposure for all groups. The other non-traumatic attendance
23 group was an exception, with effects not occurring until approximately 5–8 days after
24 exposure. The respiratory and other non-traumatic groups also displayed signs of acute cold
25 effects, although these were not statistically significant. Heat effects were found to be acute
26 across all groups, occurring within 0–2 days following exposure.
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35 [Figure 2 here]
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38 We calculated parametric effect estimates for the average of lags 0–1, 2–15 and 15–27 (Table
39 3). There were significant heat effects over lags 0–1, with a 1 °C increase in temperature
40 above 22 °C associated with a 1.17% (95% CI: 0.86%, 1.48%) increase in total ambulance
41 attendances. The largest heat effect found was for the other non-traumatic attendance group,
42 with a 1 °C increase in temperature resulting in a 20.56% (95% CI: 15.15%, 26.10%)
43 increase in attendances.
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50 We found that the hot effects on all groups displayed characteristics consistent with
51 harvesting, with a significant decrease in attendances for total (–0.82%, 95% CI: –1.35%, –
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0.30%), cardiovascular (−1.85%, 95% CI: −3.06%, −0.64%) and respiratory (−1.99%, 95% CI: −3.72%, −0.25%) categories over lags 2–15, which followed the immediate increases in ambulance attendance observed over the first few days of exposure.

Table 3: Temperature effects on ambulance attendances in Brisbane, Australia. Effects given as percent change per 1 °C above or below threshold (Threshold stated in brackets for each category)

	Lag in days	Attendance category (95% C.I)			
		Total (22 °C)	Cardiovascular (22 °C)	Respiratory (22 °C)	Other (15.5/28 °C)
Heat effect	0–1	1.17 (0.86, 1.48)	0.45 (−0.26, 1.16)	−0.38 (−1.40, 0.63)	20.56 (15.15, 26.10)
	2–15	−0.82 (−1.35, −0.30)	−1.85 (−3.06, −0.64)	−1.99 (−3.72, −0.25)	−12.37 (−27.06, 2.48)
	16–27	−0.47 (−0.97, 0.04)	−0.35 (−1.51, 0.81)	−0.72 (−2.38, 0.94)	3.19 (−10.30, 16.83)
Cold effect	0–1	−0.16 (−0.40, 0.08)	−0.62 (−1.17, −0.06)	0.63 (−0.09, 1.34)	−0.38 (−2.12, 1.38)
	2–15	1.30 (0.87, 1.73)	1.63 (0.64, 2.62)	3.65 (2.38, 4.92)	3.40 (0.43, 6.37)
	16–27	0.12 (−0.28, 0.53)	−1.1 (−2.03, −0.16)	0.9 (−0.30, 2.11)	6.49 (3.62, 9.36)

Cold effects over lags 2–15 were found for all categories, with the largest increases in attendances associated with respiratory (3.65%, 95% CI: 2.38%, 4.92%), and other non-traumatic (3.40%, 95% CI: 0.43%, 6.37%) groups. The other non-traumatic attendance group also showed significant cold effects from 15 days onward (6.49%, 95% CI: 3.62%, 9.36%). There was no apparent harvesting observed in cold effects, except for the CV group.

DISCUSSION

In this study, we examined the relationship between temperature and ambulance attendances using time series modelling techniques. Cold and heat effects were observed for all attendance categories. There was a “V” or “U” shaped relationship between daily mean temperature and ambulance attendances, with statistically significant increases in different attendance categories for a 1 °C change in temperature from the thresholds. Cold effects were found to be delayed in onset but last longer than heat effects, which were immediate and short-lived.

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7 There have been few studies of the effects of ambient temperature on ambulance attendances.
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9 A Toronto study[25] reported large increases in ambulance response calls during the summer
10 period. Similarly, a multi-city analysis in Italy[26] found an increasing risk of ambulance
11 dispatches for increasing temperature, with the largest same-day heat effects occurring for
12 other non-traumatic and respiratory conditions. However, no cold effect was observed in their
13 study. The short-term nature of the heat effects in these studies has been observed more
14 generally. Heat effects on both cardiovascular and respiratory diseases are often observed to
15 be immediate and short-term,[25, 33] with the strongest heat effects recorded in the first one
16 to three days following exposure, before decreasing in magnitude.[34] We found similar
17 trends across all attendance categories, with a heat effect observed immediately following
18 exposure. In terms of cold temperature effects, we found a significantly increased risk for all
19 attendance categories. The cold effects on cardiorespiratory attendances are consistent with
20 most previous studies.[35–37] While this result differs with the those from the Italian
21 study,[26] based on our results the short exposure lags considered in that study may have
22 resulted in an underestimation of the cold effect. Our findings of lagged effect of cold
23 temperatures of up to 15 days following exposure corroborate observations from previous
24 research.[35, 38]

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40 A common pattern across all categories was the slight drop in heat effects between 2 and 15
41 days, consistent with the harvesting phenomenon found in studies of temperature and
42 mortality.[6] The occurrence of such an effect has a clear physiological explanation in terms
43 of fatal health outcomes, however it is less clear as to what would cause this displacement in
44 out-of-hospital attendances. One factor may be due to an initial large number of transfers and
45 subsequent admissions of seriously ill patients to hospital. Once there, it would be expected
46 that such people would spend a number of days in hospital, thereby removing high risk
47 individuals from the general population that would further utilise ambulance services.
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7 An interesting finding was the differences in temperature effects on different categories of
8 ambulance attendance. In our study, for same-day temperature exposure there was a slight,
9 non-significant decrease and increase in heat effect for respiratory and cardiovascular
10 attendances, respectively. In particular, the direction of effect on respiratory attendances is in
11 line with previous results that show a protective effect of hot temperatures on pre-admission
12 respiratory morbidity.[39] This finding may be due to the fact that in our study, respiratory
13 tract infections made up a large proportion of respiratory attendances, conditions that are
14 more prevalent in cooler weather.[23, 36] The other non-traumatic attendance category
15 displayed a significantly larger heat effect. This is likely a result of either the higher
16 temperature threshold identified for this sub-group, or the fact it contained a large percentage
17 of attendances that were related to psychiatric issues, which have been identified as being
18 strongly influenced by high temperatures.[40]
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21 This study has a number of strengths. Firstly, given the current lack of research into
22 temperature effects on ambulance attendances, the study contributes to an understanding of
23 how pre-hospital health conditions are affected by changes in temperature. Secondly,
24 ambulance attendances often occur for conditions that do not require hospital admission nor
25 cause death. This implies that ambulance attendance data may be useful in surveillance
26 systems as they provide the ability to monitor health outcomes that will not be captured in
27 mortality or admissions data.
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30 Limitations of the study should also be acknowledged. Firstly, compared to other types of
31 health outcomes such as mortality, hospital admissions and emergency admissions, the
32 available coding regime was limited for ambulance attendances and therefore the risk of
33 misclassification of health outcomes was potentially higher here than for other types of health
34 outcomes. As the primary purpose of the ambulance data set is for administrative and
35 performance evaluation purposes, codes are not required at the level of detail seen in a
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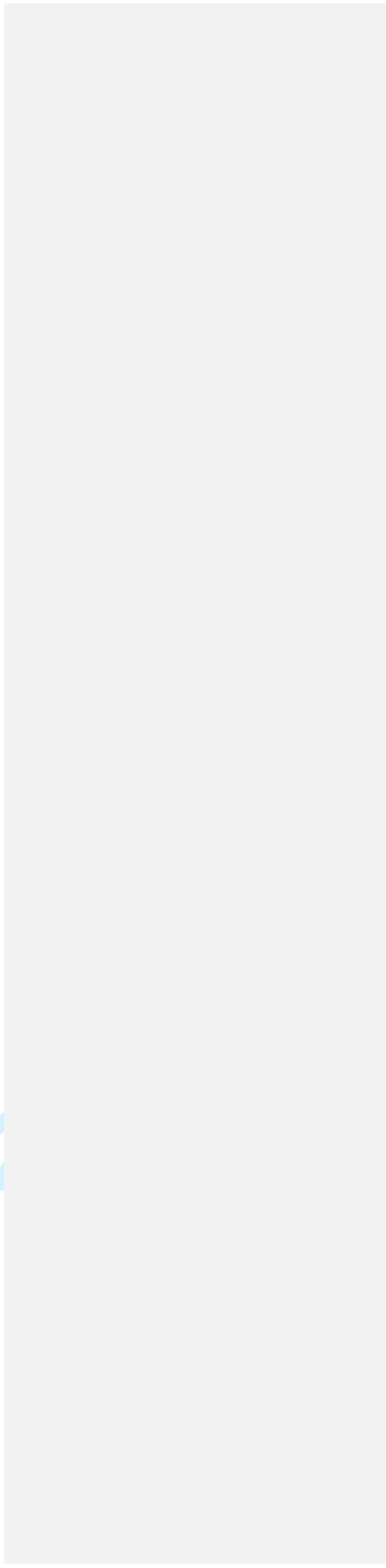
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7 hospital setting, as a more thorough diagnosis is made once the patient is admitted. Therefore
8 the relevant attendance categories were necessarily grouped together. Secondly, the postcode
9 variable in our dataset reflected the location of attendance, not the residential area of the
10 patient. Therefore the location of attendance may not closely correspond with the location
11 where the patient received the majority of exposure. Finally, the implementation of a new
12 information system and coding regime in 2006 may have produced some measurement error
13 in the data. However, sensitivity analyses using data from each year separately and also data
14 from before the new system was implemented (2000–2005) were found to make little
15 difference to the results.
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24 This research may have several implications, within both the research domain and public
25 health policy arena. Firstly, this study has shown that the effects of ambient temperature on
26 ambulance attendances in a sub-tropical climate are similar to those found in both hospital
27 admissions and mortality data.[5] However, some specific effects on ambulance attendances
28 were found to differ with those on hospital admissions or mortality, and also between the
29 different attendance categories; it would therefore be useful to compare different exposure–
30 response relationships in future research.[18] In terms of public health policy,[24] examining
31 ambulance attendances rather than admission or mortality data would potentially help to pick
32 up not only early signs of temperature effects, but also effects on health conditions that
33 cannot be examined through analysis of mortality and hospital admissions data.
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45 This study found significant effects of both cold and hot temperatures and lagged effects of
46 up to 15 days on cardiorespiratory attendances, which contributes to the currently limited
47 research of temperature effects on ambulance attendances. The use of ambulance data in
48 epidemiological research is needed in order to assess a wider range of non-fatal health
49 outcomes, with its analysis particularly useful in the development of more responsive early
50 warning and health surveillance systems.
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For peer review only



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14
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17 revision of the manuscript. DC read and revised the manuscript. All authors read and
18 approved the final manuscript.
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25
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30 **Data sharing statement:** No additional data available.
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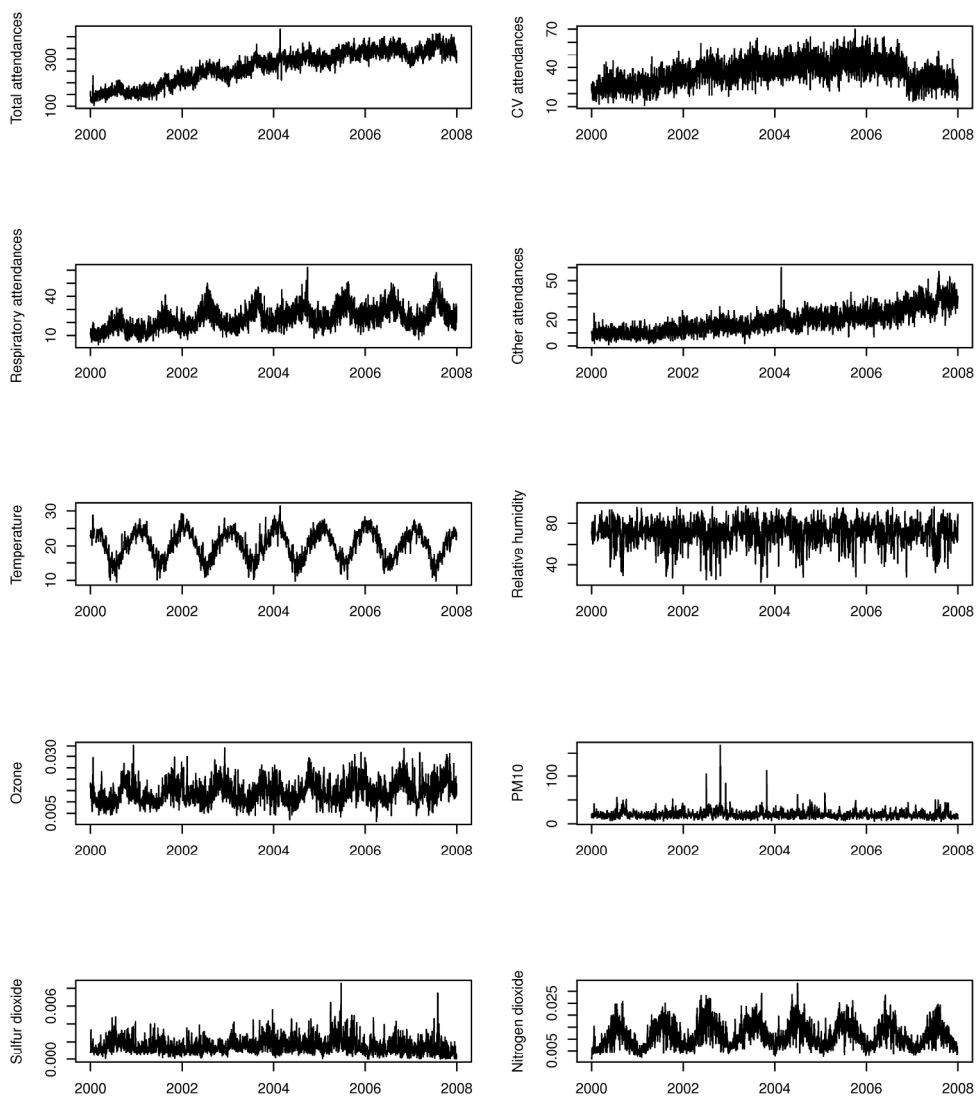
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8 **List of Figures:**
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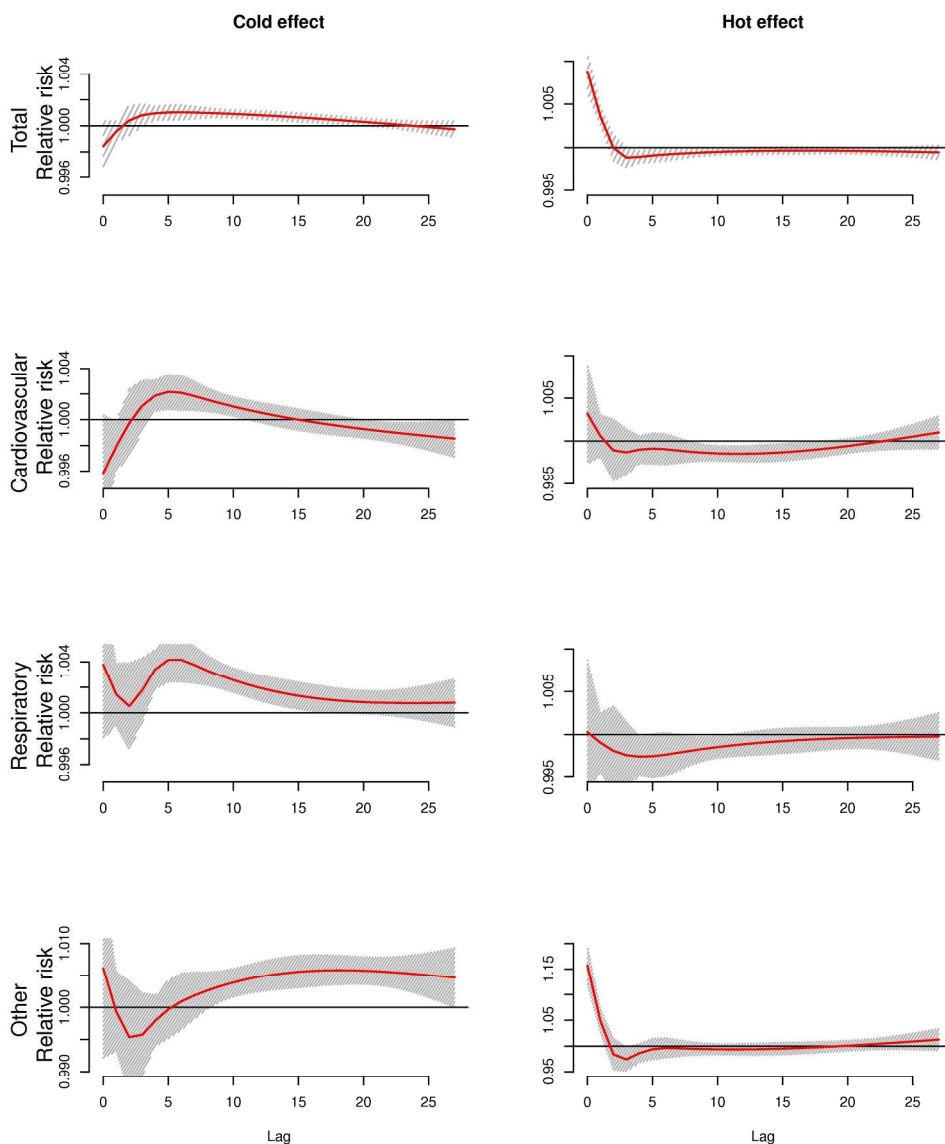
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11 **Figure 1:** Distributions of ambulance attendance counts, temperature and air pollutants

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13 **Figure 2:** Lagged effects for a 1 °C decrease (left) and increase (right) in mean temperature
14 below (and above) the threshold temperature for total, cardiovascular, respiratory and other
15 non-traumatic attendances. The shaded region corresponds to the 95% confidence interval
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Distributions of ambulance attendance counts, temperature and air pollutants
235x281mm (300 x 300 DPI)



Lagged effects for a 1 °C decrease (left) and increase (right) in mean temperature below (and above) the threshold temperature for total, cardiovascular, respiratory and other non-traumatic attendances. The shaded region corresponds to the 95% confidence interval
 238x288mm (300 x 300 DPI)

Table 3: Unadjusted temperature effects on ambulance attendances in Brisbane, Australia. Effects given as percent change per 1 °C above or below threshold (Threshold stated in brackets for each category)

	Lag in days	Attendance category (95% C.I)			
		Total (22 °C)	Cardiovascular (22 °C)	Respiratory (22 °C)	Other (15.5/28 °C)
Heat effect	0-1	1.51 (0.54, 2.49)	0.81 (-0.15, 1.77)	0.29 (-0.93, 1.51)	23.52 (13.23, 34.31)
	2-15	-0.49 (-1.96, 0.99)	-1.25 (-2.70, 0.21)	-1.16 (-3.00, 0.69)	-27.55 (-53.20, -1.41)
	16-27	1.02 (-0.21, 2.24)	1.12 (-0.09, 2.33)	1.89 (0.36, 3.43)	-0.95 (-23.62, 22.16)
Cold effect	0-1	-0.57 (-1.27, 0.14)	-0.68 (-1.36, 0.01)	-0.03 (-0.81, 0.75)	-3.52 (-6.61, -0.39)
	2-15	0.86 (-0.22, 1.93)	1.71 (0.66, 2.76)	3.83 (2.63, 5.02)	-0.97 (-5.82, 3.89)
	16-27	1.10 (0.26, 1.93)	0.08 (-0.73, 0.90)	2.79 (1.86, 3.72)	5.81 (1.60, 10.03)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	4–5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6–7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8–10
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8–9
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	n/a
		(b) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8–9
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	8–9
Bias	9	Describe any efforts to address potential sources of bias	9, 15
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9–10
		(b) Describe any methods used to examine subgroups and interactions	9–10
		(c) Explain how missing data were addressed	n/a
		(d) If applicable, explain how loss to follow-up was addressed	n/a
		(e) Describe any sensitivity analyses	16
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	11
		(b) Indicate number of participants with missing data for each variable of interest	11
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	
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	13
		(b) Report category boundaries when continuous variables were categorized	n/a
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	16
Discussion			
Key results	18	Summarise key results with reference to study objectives	10–13
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13–15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15–16
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	17

*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.