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Maternal exposure to heatwave and preterm birth in Brisbane, Australia

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Objective To quantify the short-term effects of maternal exposure to heatwave on preterm birth.

Design An ecological study.

Setting A population-based study in Brisbane, Australia.

Population All pregnant women who had a spontaneous singleton live birth in Brisbane between November and March in 2000–2010 were studied.

Methods Daily data on pregnancy outcomes, meteorological factors, and ambient air pollutants were obtained. The Cox proportional hazards regression model with time-dependent variables was used to examine the short-term impact of heatwave on preterm birth. A series of cut-off temperatures and durations were used to define heatwave. Multivariable analyses were also performed to adjust for socio-economic factors, demographic factors, meteorological factors, and ambient air pollutants.

Main outcome measure Spontaneous preterm births.

Results The adjusted hazard ratios (HRs) ranged from 1.13 (95% CI 1.03–1.24) to 2.00 (95% CI 1.37–2.91) by using different heatwave definitions, after controlling for demographic, socio-economic, and meteorological factors, and air pollutants.

Conclusions Heatwave was significantly associated with preterm birth: the associations were robust to the definitions of heatwave. The threshold temperatures, instead of duration, could be more likely to influence the evaluation of birth-related heatwaves. The findings of this study may have significant public health implications as climate change progresses.

Keywords Hazards ratio, heatwave, preterm birth, survival analysis.

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Introduction

According to the definition of the World Health Organization, preterm birth is defined as a live childbirth occurring at <37 completed weeks or 259 days of gestation.[1] Children who are born preterm are more likely to experience early death, respiratory illnesses, neurodevelopmental disorders, lower cognitive abilities, and even increased behavioural problems.[2–5] In addition to possible physical and psychological damage to a child's health, preterm birth may also increase the economic burdens of the families in terms of increased healthcare costs and/or educational expenditure.[6]

There are three types of preterm birth: spontaneous preterm birth; medically indicated preterm birth, as well as maternal elective preterm birth; and caesarean preterm birth.[7,8]

Preterm birth is associated with a variety of factors, including genetic, sociodemographic, behavioural, and environmental factors.[9–12] In recent decades, the impact of ambient temperature on preterm birth has been increasingly recognised.[13–16] However, the findings on how, and to what extent, ambient temperature might influence gestational age have been inconsistent. A time-stratified, case-crossover analysis of almost 60 000 births in California between May and September in 1999–2006 found that a 5.6°C increase in the weekly average apparent temperature (i.e. the cumulative average weekly lag) increased the incidence of preterm delivery by 8.6% (95% CI 6.0–11.3%).[14] By contrast, a time-series analysis of short-term effects of meteorological factors on preterm births in London, using a large data set that included 482 568 births, covering a period of 13 years, revealed that the risk of preterm birth did not increase when pregnant women were exposed to higher temperatures.[15]

Although the exact biological mechanism by which heatwave leads to preterm birth is still unknown, several animal experiments and human trials have been performed to investigate this issue. An animal study on maternal endocrine and fetal metabolic responses to heat stress showed that heat stress could induce the hypersecretion of antidiuretic hormone (ADH) and oxytocin (OT), which either individually or collectively might decrease uterine blood flow, shift fetal metabolic pathways from anabolic to catabolic, and then result in preterm birth (Figure 1).[17]

Climate change has been accelerating over recent years.[18] Heatwave will be one of the important public health challenges of this century as a consequence of the overall global warming, and the increased frequency, intensity, and duration of extreme events. The definition of heatwave generally involves two indispensable aspects: the temperature exceeding a specific absolute temperature or percentile of the temperature distribution, and the prolonged duration of the heat event.[19] Some previous studies that focused on the association between heatwave and health outcomes such as

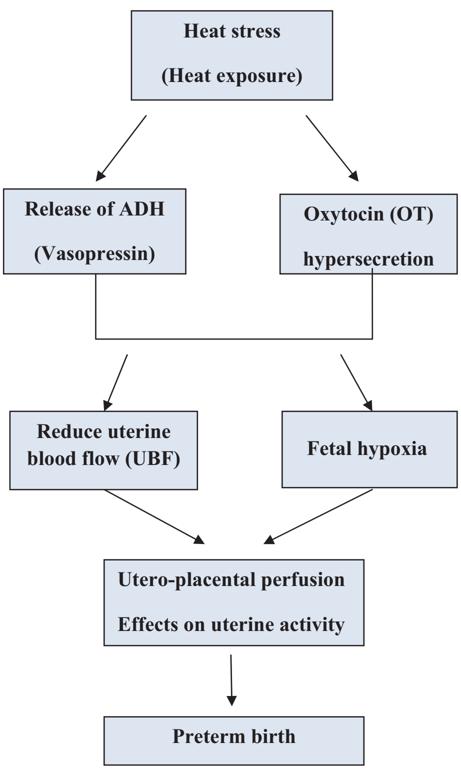

Figure 1. Possible biological mechanisms for heat-related preterm birth (summarised from Dreiling et al.[17]). ADH, antidiuretic hormone.

deaths and emergency hospital admissions showed that even a small change in the definition of heatwave can lead to considerable differences in the risk estimates of heatwave.[20,21] To our knowledge, several studies have examined the associations between high temperature or heat stress and preterm birth,[14,22,23] but none of them have taken the duration of heat events into account. This study investigated the effects of heatwave on preterm birth during the period 2000–2010 in Brisbane, Australia. In addition, we examined how the birth-related effects of heatwave changed when different temperature thresholds and durations were used to define a heatwave.

Methods

Birth cohort

Data on all singleton births in Brisbane from 1 January 2000 to 31 December 2010 were collected from the Data Collections Unit (DCU) of the Queensland Health Statistics Centre, which records antenatal, intrapartum, and postpartum data for all live births and stillbirths of at least 20 weeks of gestation, and/or at least 400 g in weight, born in Queensland. The data set we collected included the following variables: date of birth, gestational age in weeks, gender of baby, weight of baby, onset of labour (spontaneous, induced, and caesarean), mother's residential area (postcode), maternal age group, marital status, indigenous status, and parity. We only included spontaneous live births, which accounted for 56% of all births in this study, in order to gain a more accurate estimation of gestational effects attributed to heatwave, as most induced and caesarean births were medically indicated. In addition, to focus on heatwave exposure, as in another study,[14] only spontaneous births that occurred in warm seasons (1 November–31 March) were used in our final analysis.

Environmental exposure

As the earliest conception date of pregnant women in the birth cohort was 13 March 1999, we collected environmental data for 1999–2010 to obtain information on environmental exposure for the whole pregnancy period. Data on meteorological factors, including daily maximum temperature, relative humidity, and ambient barometric pressure, from eight monitoring stations in Brisbane during 1999–2010 were obtained from the Australian Bureau of Meteorology. We used nine definitions of heatwave in this study through combining a series of cut-off percentiles and different durations: daily maximum temperature exceeding the 90th, 95th, and 98th percentiles of daily maximum temperature distribution of the study period for at least 2, 3, or 4 consecutive days (Table 1). We estimated the effects of heatwave exposure of pregnant women during their last gestational weeks before delivery.

Table 1. Summary of heatwave events during summer seasons in the period 1999–2010 using different heatwave definitions (HWDs) in Brisbane, Australia

HWDs	Cut-off percentile and temperature (°C)	Duration (days)	Number of heatwave events
1	90th (30.38)	2	281
2	90th (30.38)	3	190
3	90th (30.38)	4	129
4	95th (31.32)	2	115
5	95th (31.32)	3	60
6	95th (31.32)	4	31
7	98th (32.52)	2	37
8	98th (32.52)	3	11
9	98th (32.52)	4	2

We also acquired data on ambient air pollutants, including particulate matter with a diameter <10 μm (PM_{10}), ozone (O_3), carbon monoxide (CO), and nitrogen dioxide (NO_2) from five stations in Brisbane, as many previous investigations have found that ambient air pollution could affect birth outcomes.[24–26] The air pollution data were provided by the Queensland Department of Environment and Resource Management. Weekly average levels of meteorological factors and ambient air pollution exposures were calculated by using the original daily data.

In addition, we also acquired data on the Social Economic Index for Areas (SEIFA) from the Australian Bureau of Statistics (ABS) to estimate maternal socio-economic status. SEIFA is a product developed by the ABS that ranks areas in Australia according to relative socio-economic advantage and disadvantage. The index is based on information from the 5-yearly census, and consists of four sub-indexes. In this study we used SEIFA data released in 2001 and 2006 to represent the maternal economic status of the births that occurred during 2000–2005 and 2006–2010, respectively. SEIFA data was linked to the birth records by year and area postcode.

Statistical analysis

Survival analysis was used in this study to explore the influence of heatwave on spontaneous preterm birth. Several studies have used the Cox proportional hazards (PHs) regression model to investigate the birth effects of environmental factors such as temperature and air pollution.[13,24] The authors in these studies believed that survival analysis combined the advantages of cohort and time-series studies, as this model allows for the simultaneous examination of the impact of both subject-specific (e.g. individual behaviour risk factors) and time-related factors (e.g. air pollution, humidity, and other meteorological factors). Furthermore, the power of the survival analysis is increased compared with a case-crossover approach because all the subjects are examined.[24,25,27]

Preterm birth was defined as a live birth occurring at <37 completed weeks of gestation, according to the definition of the World Health Organization.[1] We used the Cox PHs regression model (Cox regression), which is widely used in survival analysis, with time-dependent covariates to estimate the acute effects of heatwave.[28] Cox regression has been used in epidemiological studies to analyse time-to-event data, with censoring. The standard Cox regression model assumes a constant hazard ratio (HR) over time: in other words, the effects on survival of covariates should be time independent. However, in our study, we must consider that values of covariates such as heatwave exposure at different times of the whole pregnancy period were not fixed, and so we fitted the Cox regression model with time-dependent covariates as follows:

$$h[t, X_I, X_i(t)] = h_0(t)\exp[\beta_I X_I + \beta_d X_i(t)]$$

where $h_0(t)$ is the baseline hazard function, being the hazard function for individuals with all explanatory variables equal to zero; X_I refers to the values of time-independent variables such as the baby's gender, mother's age, and parity; $X_i(t)$ are the values of the time-dependent variables (meteorological factors and air pollutants); and β_I and β_d are vectors of model parameters for time-independent and time-dependent covariates.[29]

Heatwave exposure in this study was assigned as a binary value (yes/no), which indicated whether they experienced at least one heatwave event in the last gestational weeks before delivery.

Preterm birth is the outcome of interest in this study. We divided the whole pregnancy period into gestational weeks and assumed that within each of these, time-dependent variables such as weekly air pollution levels could be fixed. Consequently, the birth states of each pregnant woman were represented by a series of intervals of 1-week duration. Within each interval, a censoring variable was created that was 0 if a preterm birth did not occur, and 1 if a preterm birth occurred. For example, if one delivery occurred at 36 weeks of gestation, the pregnancy would be recorded as 36 intervals, with the final censoring variable equal to 1; if a delivery occurred at 38 weeks of gestation, the pregnancy would be recorded as 38 intervals with all values of censoring variable equal to 0.

We classified maternal age into three groups, <20, 20–34, and >34 years, and treated age groups as stratified variables in the model, as previous studies have found a nonlinear relationship between maternal age and birth outcomes: i.e.

women younger than 20 years or older than 34 years were more likely to suffer from adverse birth outcomes, such as preterm birth, low birthweight, and even stillbirth.[30,31] Indigenous status (yes/no), marital status (yes/no), parity (primiparity/multiparity), baby's gender (male/female), as well as SEIFA scores were entered into the model to adjust for demographic factors and areal socio-economic status. In addition, we used both single-pollutant and multi-pollutant models to adjust for the confounding effects of air pollution. To control for long-term trends, we added 'year' as a factor variable into the model.

We restricted the study to warm seasons so as to control the effects of seasonality of birth; meanwhile, a factor variable 'Month' was also included in the model.

The graphical methods, which used cumulative sums of the martingale-based residuals, were performed to check the proportionality assumptions of the Cox models used in our study.[32,33] The results of the PH assumption on all covariates showed that for heatwave and most of other covariates, except relative humidity, the standardized and the observed score processes fluctuated randomly around zero, and the *P* values of the Kolmogorov-type supremum tests were larger than 0.05, which indicated that the PH assumptions on most variables were satisfied (Figures S1–S13). However, when we removed relative humidity from the model the estimates of heatwave barely changed. All analyses were conducted using SAS 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

A total of 275 465 singleton live births occurred between 1 January 2000 and 31 December 2010 in Brisbane.

The number of spontaneous births was 154 785 (56% of all singleton live births). Fifteen births were excluded because they lacked gestational age information. The prevalence of preterm birth was 6.4%. The gestational age ranged from 20 to 43 weeks of gestation, and the mean gestational age was 39.20 weeks of gestation. Only spontaneous births that occurred between November and March, of which the total number was 50 848, were used in the final analysis. Table 2 shows the summary statistics of the demographic factors and the proportions of preterm birth that occurred in different subgroups. The majority of mothers were non-indigenous (97.31%). The ages of the mothers ranged from 15 to 44 years, and most (78.24%) were 20–34 years old. The majority (84.17%) were married. The percentages of primiparity and multiparity were 57.22 and 42.78%, respectively. Chi-square tests showed that the proportions of preterm birth in the indigenous population (10.46%) were considerably higher than in the non-indigenous population (6.48%) ($P < 0.05$), and women older than 34 years as well as primiparae were more likely to experience preterm birth. The proportions of preterm birth varied significantly according to the marital status of the mothers (Table 2).

Table 3 shows the summary statistics of the meteorological factors and air pollutants during 1999–2010 in Brisbane.

Table 2. Characteristics of the 50 848 spontaneous births that occurred between November and March during the period 2000–2010 in Brisbane, Australia

Factors	Number of births	Percentage (%)	Full-term births	Preterm births	Proportion of preterm births (%)	*P*
Indigenous status						
Indigenous	1367	2.69	1224	143	10.46	<0.0001*
Non-indigenous	49 481	97.31	46 277	3204	6.48	
Age group						
<20 years	3300	6.49	3074	226	6.85	<0.0001*
20–34 years	39 781	78.24	37 276	2505	6.30	
>34 years	7767	15.27	7151	616	7.93	
Marital status						
Divorced/separated/widowed	839	1.65	773	66	7.87	0.005*
Married/cohabiting	42 799	84.17	40 047	2752	6.43	
Never married	7210	14.18	6681	529	7.34	
Baby's gender						
Male	26 078	51.29	24 231	1847	7.08	<0.0001*
Female	24 770	48.71	23 270	1500	6.06	
Parity						
Primiparity	21 755	42.78	20 235	1520	6.99	0.002*
Multiparity	29 093	57.22	27 266	1827	6.28	

*Chi-square test, $P < 0.05$.

Table 3. Summary statistics of the meteorological and air pollution variables in Brisbane in the period 2000–2010

Variables	Minimum	Q1	Median	Q3	Maximum
Meteorological factors					
Maximum temperature (°C)	14.00	23.09	26.06	28.51	37.85
Relative humidity (%)	13.71	49.62	57.12	64.25	95.88
Air pressure (kPa)	993.84	1011.47	1015.24	1018.78	1030.80
Air pollutants					
PM_{10} ($\mu g/m^3$)	3.17	14.04	17.66	21.86	965.89
CO (ppm)	0.017	0.296	0.544	0.842	3.483
O_3 (ppm)	0.002	0.012	0.016	0.020	0.043
NO_2 (ppm)	0.001	0.004	0.006	0.010	0.025

Q1, lower quartile; Q3, upper quartile.

We excluded environmental data before 13 March 1999, as all the pregnant women's gestational periods started after this date. The average weekly maximum temperature ranged from 14.00 to 37.85°C during the study period, the medians of weekly concentrations of PM_{10}, CO, O_3, and NO_2 were 17.66 $\mu g/m^3$, 0.544 ppm, 0.016 ppm, and 0.004 ppm, respectively (Table 3).

Figure 2 shows the time series variations of all meteorological factors and air pollutants. The yearly variations in these variables were quite consistent over the study period, except for PM_{10}, which had a dramatic increase in September 2009 because of a dust storm in Brisbane on 23 September 2009.

Several exploratory analyses were also performed. Table 4 shows that the distributions of relative humidity, air pressure, air pollutants, and SEIFA scores (the index of socio-economic disadvantage) in heatwave days and non-heatwave days differed (Student's *t*-test, $P < 0.05$).

Table 5 summarises the proportions of preterm birth by women's heatwave exposure in their last gestational weeks before delivery. Increased proportions of preterm birth for women exposed to heatwave were observed when using five heatwave definitions, although the chi-square tests showed that these differences were not statistically significant.

Table 6 shows that when women were exposed to heatwave, the proportions of preterm birth differed from those in women not exposed to heatwave in the indigenous subgroup, in women older than 34 years of age, and in women who were married or in stable cohabiting relationships (chi-square test, $P < 0.05$).

We examined the HRs of preterm birth for women who experienced at least one heatwave event in their last gestational weeks by using a series of cut-off percentiles and durations to define a heatwave. Compared with the model that was unadjusted for pollutants, the results of single-pollutant models showed that the HRs of preterm birth for women exposed to heatwave in their last gestational weeks changed to some extent when different air pollutants were added into the model separately (Table S1).

Finally, the model that was adjusted for all air pollutants (CO, O_3, NO_2, and PM_{10}) and all other confounding factors was used. We only reported the results of multivariable analysis.

Figure 3 shows the HRs of preterm birth for women who experienced heatwaves. For most definitions used, we observed a statistically significant increase in the HRs of preterm birth for women who had experienced at least one heatwave event in the last gestational weeks in warm seasons, after controlling confounding factors. Hazard ratios of preterm birth ranged from 1.13 (95% CI 1.03–1.24) to 2.00 (95% CI 1.37–2.91), which showed that even a minor change in the heatwave definitions may affect the assessment of the relationship between heatwave and preterm birth (Figure 3).

For 4 days of consecutive exposure, when higher cut-off percentiles were used to define a heatwave, we found that the HRs increased from 1.13 (95% CI 1.03–1.24) to 2.00 (95% CI 1.37–2.91). However, for the cut-off percentiles used to define a heatwave (the 90th and 95th percentiles), HRs did not increase markedly with the longer duration of heatwave exposure, but did increase for the 98th percentile from 3 days to 4 days of duration (Figure 3).

Discussion

Main findings

In general, a positive association between heatwave exposure in the last gestational weeks and occurrence of preterm birth was found in this study after controlling for a range of potential confounding factors. Meanwhile, we also observed the changes of effect estimates of heatwave using a series of heatwave definitions. The highest HR of preterm birth for women who had experienced at least one heatwave event in the last gestational weeks was 2.00 (95% CI 1.37–2.91), when defining heatwave as a daily maximum

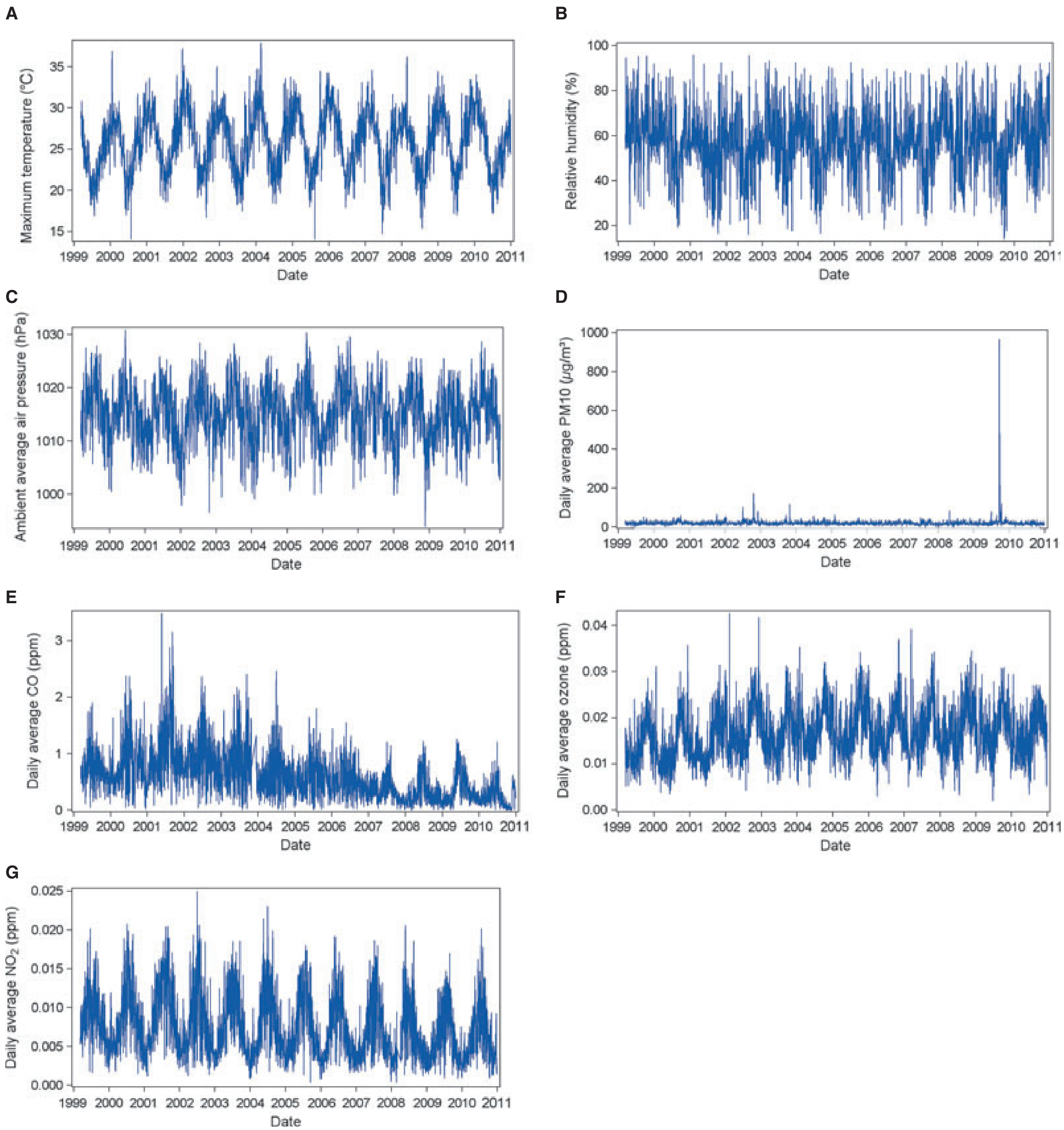

Figure 2. Time series of meteorological and air pollutants during the period 1999–2010 in Brisbane, Australia: (A) daily maximum temperature; (B) daily relative humidity; (C) daily ambient air pressure; (D) daily average PM_{10}; (E) daily average CO; (F) daily average O_3; (G) daily average NO_2.

temperature over the 98th percentile, which lasted for four consecutive days.

Strengths and limitations

This study has several key strengths. Firstly, to our knowledge, this is the first study that takes the duration of heat exposure into account to explore the association between heatwave and preterm birth. Secondly, we excluded the other two types of preterm births to reduce the overestimation of the preterm birth risk of heatwave, as most induced preterm births are unlikely to be attributable to heatwave. Thirdly, we used a series of heatwave definitions with

Table 4. Distribution of environmental factors on heatwave and non-heatwave days

Meteorological factors	Non-heatwave	Heatwave	*P*
Relative humidity (%)	62.31	60.80	<0.0001*
Air pressure (kPa)	1012.8	1010.5	<0.0001*
Air pollutants			
PM_{10} ($\mu g/m^3$)	17.03	20.10	<0.0001*
CO (ppm)	0.491	0.486	0.04*
O_3 (ppm)	0.015	0.017	<0.0001*
NO_2 (ppm)	0.005	0.004	<0.0001*
SEIFA scores			
Index of socio-econonic disadvantage	1004.6	1003.2	0.03*

*Student's *t*-test, $P < 0.05$.

different cut-off percentiles and durations in this study. Our robust findings may shed some light on how the intensity and duration of heatwave might affect an assessment of the birth-related impacts of heatwave. Finally, survival analysis was used in this study to estimate the effects of heatwave on preterm birth.

Several limitations must also be acknowledged. In this study, we used SEIFA data instead of individual data to represent the socio-economic status of the pregnant women, which might produce misclassification bias to some extent. In addition, we did not take into account several confounding factors, such as maternal smoking status, as this kind of individual information had too many missing values in our records. Meanwhile, meteorological and air pollution data obtained at an ecological level might be less representative. However, these measurement errors are very likely to be non-differential, and are therefore likely to result in under-estimation rather than over-estimation of heatwave effects. Finally, a fixed cohort bias occurred in this study. One methodological study suggests that a fixed cohort bias may occur when using a study period based on date of birth, as a fixed cohort could only capture births with longer gestational age at the start period and births with shorter gestational age at the end of study[34]; However, another study showed that this bias could only have minimal impact on their results.[35] In this study we only examined the short-term effects of maternal heatwave exposure in the last week before delivery. As most heatwave events occurred during the summer seasons, we could capture most subjects exposed to heatwave because we extended our study period across the warm seasons.

Interpretation

Eight studies have reported the effects of ambient temperature on gestational age or preterm birth.[13–15,22,23,36–38] Our results are consistent to some extent with the findings of most previous studies, which showed that higher ambient temperature, especially extreme hot weather, might shorten the gestational age or result in preterm birth.[13,14,22,23,36,37] A recent study based on a birth cohort in Barcelona defined an extreme heat event when the heat index (HI) exceeded the 90th, 95th, and 99th percentiles of heat indices, and found a small reduction (0.2 day) in the average length of gestation when the HI on the day of delivery exceeded the 95th percentile (HI_{95} 30.5°C).[22] A survival analysis in Brisbane also found that exposure to high temperatures during the last gestational week was associated with an increase of the risk of preterm birth.[13]

Table 5. Summary of spontaneous preterm births to women exposed and unexposed to heatwave in their last gestational weeks during the period 2000–2010 in Brisbane, Australia

HWDs	Non-heatwave exposure			Heatwave exposure			*P**
	Full-term births	Preterm births	Proportion of preterm birth (%)	Full-term births	Preterm births	Proportion of preterm birth (%)	
1	22 588	1649	6.38	24 913	1698	6.8	0.05
2	30 754	2161	6.57	16 747	1186	6.61	0.83
3	34 997	2489	6.64	12 504	858	6.42	0.38
4	35 043	2460	6.56	12 458	887	6.65	0.98
5	40 055	2826	6.59	7446	521	6.54	0.87
6	43 440	3057	6.57	4061	290	6.67	0.82
7	41 799	2983	6.66	5702	364	6	0.05
8	45 274	3214	6.63	2227	133	5.64	0.06
9	47 068	3315	6.58	433	32	6.88	0.79

*Chi-square test.

Table 6. Proportions of preterm birth stratified by demographic factors for women exposed and unexposed to heatwave (HWD1) during the period 2000–2010 in Brisbane, Australia*

Demographic factors	Non-heatwave exposure			Heatwave exposure			*P* value
	Full-term births	Preterm births	Proportion of preterm birth (%)	Full-term births	Preterm births	Proportion of preterm birth (%)	
Indigenous status							
Indigenous	684	66	8.80	540	77	12.48	0.03*
Non-indigenous	24229	1632	6.31	22 048	1572	6.66	0.12
Age group							
<20 years	1681	123	6.82	1393	103	6.89	0.94
20–34 years	19 457	1282	6.18	17 819	1223	6.42	0.32
>34 years	3775	293	7.20	3376	323	8.73	0.01*
Marital status							
Divorced/separated/widowed	391	30	7.13	382	36	8.61	0.42
Married/cohabiting	20 970	1,381	6.18	19 077	1371	6.70	0.03*
Never married	4985	409	7.58	1696	120	6.61	0.17
Baby's gender							
Male	12 799	931	6.78	11 432	916	7.42	0.04*
Female	12 114	767	5.91	11 156	733	6.17	0.49
Parity							
Primiparity	10 560	760	6.71	9675	760	7.28	0.09*
Multiparity	14 353	938	6.13	12 913	889	6.44	0.28

*Chi-square test, $P < 0.05$.

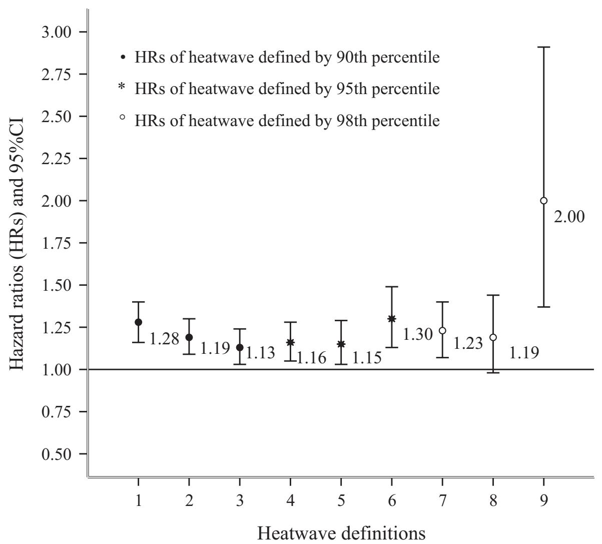

Figure 3. The adjusted hazard ratios of preterm birth for women exposed to at least one heatwave (nine definitions) in their last gestational weeks before delivery in warm seasons during the period 2000–2010 in Brisbane, Australia. Values shown in this figure are adjusted hazard ratios of preterm birth after adjusting for maternal indigenous status, age, marital status, gender of infants, parity, humidity, air pressure, O_3, NO_2, CO, and PM_{10}.

In this study, we identified heatwave as a period in which the daily maximum temperatures exceeded certain percentiles of the temperature distribution for two or more consecutive days. For a given percentile, the effects did not increase when the duration of the heatwave changed, excepting the 98th percentile, in which an increasing trend arose after a change in the duration of the heatwave from 3 to 4 days. On the other hand, when the duration of the heatwave was 4 days, there was a dose–response effect with the increased cut-off percentiles. A recent study defined heatwave as two or more consecutive days of daily mean temperatures that are higher than the 95% percentile of the warm season temperatures for that community, and explored the effects of heatwave on mortality in 43 communities in the USA. The results of the study found that, on average, the mortality risk increased by 2.49% with every 1°F increase in heatwave intensity, and by 0.38% for every 1-day increase in the duration of the heatwave.[21] Both our study and the study of 43 US communities hint that proper relative thresholds, instead of duration, for defining heatwaves is more likely to assist in the evaluation of the health-related effects of heatwave.[21]

Our results were partially inconsistent with the characteristic of mortality effects of heatwave, however, as there is a greater mortality risk with more intensive temperatures or longer durations of heat.[21,39] One potential explanation is that when a heatwave becomes more intense for a short period, pregnant women might be more likely to alter their behaviours to protect themselves from heatwave exposure, which is effective to some extent, but that when the intensity or duration of heatwave increases past a certain degree, mere behavioural changes won't be able to protect women from the impacts of the heatwave.

In addition to the possible mechanism mentioned above,[17] several studies have proposed that activation of the maternal–fetal hypothalamic–pituitary–adrenal axis triggered by heat stress could also cause preterm birth.[40,41] A study in Denmark found that the increased corticotrophin-releasing hormone and cortisol secreted by the placenta, which could be activated by heat stress, were associated with preterm birth.[42] Furthermore, studies also found a significant increase of serum heat-shock protein (HSP70) levels in women with preterm birth and pre-eclampsia, as human cells and tissues may produce HSP70 rapidly to recover structural and functional damage caused by the incorrect folding of proteins.[43–46]

The associations in this study were robust to the definitions of heatwave, persisted after adjustment for confounding factors, followed a dose–response relationship with increasing temperature, and were consistent with other international studies. In addition, there are plausible biological mechanisms that can explain the association: all of these factors supported the interpretation that the relationship between short-term heatwave exposure and preterm birth is causal.

Conclusion

In conclusion, heatwave was significantly associated with preterm birth, but the effect estimates were influenced by the intensity and duration of the heatwaves. The findings of this study showed that it is important for pregnant women to reduce heatwave exposure, which may have significant public health implications as climate change progresses. A number of measures can be implemented to reduce the risk of preterm birth associated with heatwave exposure.[47] First, information related to heat stress and birth outcomes, as well as recommendations on how to reduce heatwave exposure, should be widely disseminated by health-related organisations. Second, a community-based heat health warning system should be developed and implemented in a timely way to alert pregnant women. Interventions like changing the thermal capacity of living places and providing special supportive services to pregnant women during heatwave can also be developed and implemented.[47]

In addition, more animal experiments and human trials on the biological mechanisms should be performed in the future to help us improve our understanding of the causal relationship between heatwave and preterm birth.

Disclosure of interests

The authors declare that they have no conflicting interests.

Contribution to authorship

ST designed the study. JW, GW, and YG collated and analysed the data. JW wrote the first draft of the article. JW, ST, GW, and XP contributed to the interpretation of the analyses and revision of the article. All authors approved the final article for publication.

Details of ethics approval

Ethical approval was authorised by the Human Research Ethics Committee of Queensland University of Technology. The Queensland Health approved the Public Health Act (PHA) application for the collection of birth data.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figures S1–S13. Plots checking the proportional hazard assumptions for all variables.

Figure S1. Checking proportional hazards assumptions for heatwave (HWD 4).

Figure S2. Checking proportional hazards assumptions for SEIFA scores Variable "disvin" in this figure refers to index of socio-economic disadvantage.

Figure S3. Checking proportional hazards assumptions for maternal age.

Figure S4. Checking proportional hazards assumptions for Indigenous status.

Figure S5. Checking proportional hazards assumptions for marital status.

Figure S6. Checking proportional hazards assumptions for baby's gender.

Figure S7. Checking proportional hazards assumptions for parity.

Figure S7. Checking proportional hazards assumptions for parity.

Figure S8. Checking proportional hazards assumptions for relative humidity.

Figure S9. Checking proportional hazards assumptions for air pressure.

Figure S10. Checking proportional hazards assumptions for PM10.

Figure S11. Checking proportional hazards assumptions for O3.

Figure S12. Checking proportional hazards assumptions for CO.

Figure S13. Checking proportional hazards assumptions for NO2.

Table S1. Hazard ratios (HRs) of preterm birth of single-pollutant models for women who experienced a heatwave in their last gestational weeks in a birth cohort during 2000-2010, Brisbane, Australia. ■

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