



# Temporal change in the impacts of ambient temperature on preterm birth and stillbirth: Brisbane, 1994–2013



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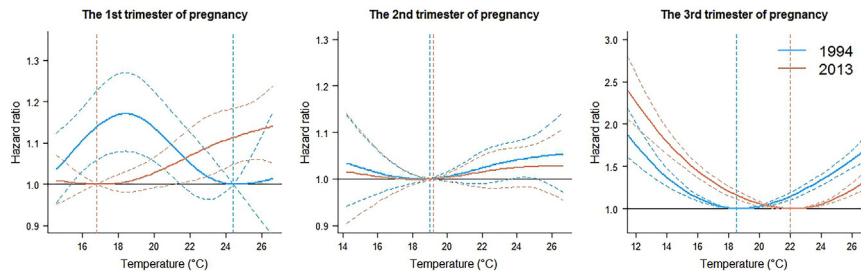
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## HIGHLIGHTS

- Both low and high temperatures at trimester 3 increase the risk of preterm birth.
- Both low and high temperatures at trimester 2 increase the risk of stillbirth.
- Pregnant women may have adapted to high but not low temperature over time.

## GRAPHICAL ABSTRACT



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## ABSTRACT

**Background:** Pregnant women are susceptible to ambient temperature which may associate with adverse birth outcomes. These associations might change over time due to adaptation. However, no evidence is available worldwide.

**Objectives:** To examine the effects of ambient temperature at three trimesters of pregnancy on preterm birth and stillbirth, and evaluate the effect changes during 1994–2013.

**Methods:** Information on birth outcomes and meteorological parameters during 1994–2013 were obtained in Brisbane, Australia. Cox proportional hazards models were employed to evaluate the effects of mean temperature during each trimester of pregnancy on preterm birth and stillbirth. An interaction term between time and temperature was used to assess the potential changes in effects of temperature over time.

**Results:** Both low and high temperatures at the 3rd trimester of pregnancy significantly increased the risk of preterm birth, with similar hazard ratios (HRs) [95% confidence intervals (CIs)] for low [1.21 (1.16, 1.27)] and high [1.21 (1.16, 1.26)] temperatures in comparison with thresholds. Increased risk of stillbirth was significantly associated with both low and high temperatures at the 2nd trimester of pregnancy, and lower HRs were observed for low temperature [1.23 (1.04, 1.45)] than high temperature [1.47 (1.24, 1.74)], in comparison with thresholds. The effects of low temperature became stronger, whereas the effects of high temperature became weaker from 1994 to 2013 for both preterm birth and stillbirth.

**Conclusions:** Both low and high ambient temperatures during pregnancy increase the risks of preterm birth and stillbirth. Pregnant women should have adapted to high temperature but not low temperature.

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## 1. Introduction

During past decades, climate change has been estimated to cause enormous health and economic losses in various ways (McMichael

et al., 2006; Patz et al., 2005), and the impact of ambient temperature on health is of increasing public concern (Basu, 2009; Ye et al., 2012). Both low and high ambient temperatures are associated with a wide range of adverse health outcomes, including cardiovascular diseases, respiratory diseases, infectious diseases, and mental health issues (Carder et al., 2005; Hajat and Haines, 2002; Hansen et al., 2008; Xiao et al., 2017). The relationships between temperature and health could also be modified by social and demographic factors, and for example, children and the elderly are more vulnerable to ambient temperature compared with adults (Ye et al., 2012). In addition, latest studies indicate that pregnant women are particularly susceptible to non-optimal temperature during pregnancy leading to a higher risk of adverse birth outcomes, including preterm birth (Auger et al., 2017; Basu et al., 2017).

Environmental factors during pregnancy including variations of temperature may have impacts on adverse birth outcomes (Dadvand et al., 2014). As previously reported, the effects of temperature on health may change over time because of adaptation to local climate, and for example, a multi-country study demonstrated weakened effects of heat on mortality in 2006 than that in 1993 (Gasparrini et al., 2015). Recent studies have provided evidence of relationships between ambient temperature and adverse birth outcomes, highlighting the need for further research (Kloog et al., 2015; Konkel et al., 2017). Some studies indicated temperature could affect birth outcomes through several ways: heat may trigger inflammatory processes during pregnancy by increasing the production of proinflammatory cytokines and heat stress may induce the production of oxytocin and prostaglandin (Schifano et al., 2013). In addition, low temperature is related to peripheral vasoconstriction and hypertensive disorders of pregnancy, which might alter uteroplacental perfusion and adversely affect the developing fetus (Van Zutphen et al., 2014). However, the mechanisms have not been fully understood, including which trimester of pregnancy is most susceptible to ambient temperature and whether the associations between ambient temperature and adverse birth outcomes has changed or not during past decades.

We used information on birth outcomes and weather conditions in Brisbane, Australia from 1994 to 2013 to assess the effects of ambient temperature at different stages of pregnancy on the risk of preterm birth and stillbirth. We also examined whether there was any change over time in the studied associations.

## 2. Material and methods

### 2.1. Birth outcome data

Data on birth outcome and maternal information were collected in metropolitan area of Brisbane, Australia from Queensland Health Perinatal Data Collection Unit (<https://www.health.qld.gov.au/hsu/collections/pdc>) during 1 July 1994 through 31 December 2013. Birth records identified by all hospitals (public and private) were submitted to this database, as well as voluntary reports of homebirths. The database and participants have been previously reported (Li et al., 2016). Relevant variables of birth information included in this study were status of the baby at birth (stillbirth, preterm birth, and live full-term birth), gender (male vs. female), and number of births (single vs. multiple). Maternal information included were gestational weeks, previous pregnancy (yes vs. no), medical conditions during pregnancy (yes vs. no), maternal age at admission (<35 years vs. ≥35 years), and smoking status (smokers vs. non-smokers). In this study, the effects of ambient temperature on preterm birth and stillbirth were modelled separately. Preterm birth was defined as live birth with gestational age <37 weeks (Goldenberg et al., 2008). Stillbirth was defined as the loss of a foetus who shows no signs of life at birth and is at least 20 weeks in gestation or 400 g in birthweight if gestation unknown (<http://www.slhd.nsw.gov.au/RPA/neonatal/html/Newprot/stillbirths.html>).

### 2.2. Meteorological data

Meteorological data were obtained from Queensland Department of Environment and Heritage Protection (<https://www.ehp.qld.gov.au/>). Daily data of mean temperature, maximum temperature, minimum temperature, and mean relative humidity were used in this study. To explore which stage of pregnancy is most susceptible to ambient temperature, moving averages of mean, maximum and minimum daily temperature and relative humidity were calculated for all mothers in the database during each of three trimesters of pregnancy (first trimester: week 1 to week 12; second trimester: week 13 to week 28; third trimester: week 29 to birth).

### 2.3. Statistical analyses

Cox proportional hazards models were employed to evaluate the effects of temperature exposure during pregnancy on the risk of preterm birth and stillbirth. Considering the nonlinear effects of meteorological factors, a natural cubic spline with 3 degrees of freedom was used for temperature or relative humidity during each trimester (Qin et al., 2017; Zhan et al., 2017). Apart from meteorological variables, other potential confounders were also controlled in the models, including gender of baby, number of births, previous pregnancy, medical conditions during pregnancy, maternal age at admission, and smoking status. Models were fitted for preterm birth and stillbirth separately and each of three trimesters of pregnancy separately. Survival time for each participant was defined as the period from the middle time point of each trimester to the date of birth.

To examine the potential changes in effects of temperature on birth outcomes during 1994–2013, time-varying models were developed based on the basic models described above, and the original spline variables in the basic models were replaced by the interaction variables between time and spline variables (Gasparrini et al., 2015). Interaction variables are expressed as following:

$$Int_{1994} = (year\ of\ date - 1994) / (2013 - 1994) * ob_i;$$

$$Int_{2013} = (year\ of\ date - 2013) / (2013 - 1994) * ob_i;$$

where  $Int_{1994}$  and  $Int_{2013}$  are centred spline variables at the years of 1994 and 2013, respectively;  $ob_i$  is the spline variable of temperature at trimester  $i$  of pregnancy. With the time-varying models, the effects of temperature on birth outcomes in 1994 and 2013 were examined and compared. In this study, hazard ratios (HRs) at 5th, 25th, 75th and 95th percentiles of temperature at each trimester of pregnancy (defined as low, moderate low, moderate high and high temperatures, respectively) and corresponding 95% confidence intervals (CIs) were calculated, with reference to the minimum-prevalence temperature (threshold).

### 2.4. Sensitivity analyses

To test the robustness of the results, sensitivity analyses were performed by changing the degrees of freedom of temperature (3 to 6 degrees). Data on particles with aerodynamic diameter < 10 μm (PM<sub>10</sub>) and sulphur dioxide (SO<sub>2</sub>) were only available after year 2000. Thus, we included them to the model to check whether the main findings were changed or not. All statistical analyses were carried out with R software (version 3.3.3, R Core Team, 2017).

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