



## The association between ambient temperature and the risk of preterm birth in China



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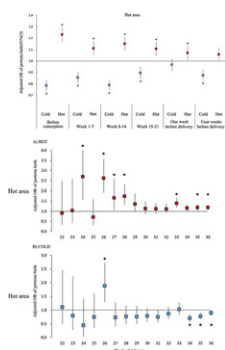
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### HIGHLIGHTS

- The largest study to date on the relationship between temperature and preterm birth in China.
- Covering a wide range of 132 cities in China.
- Long-term and short-term exposures to temperature at different stages of pregnancy were studied.
- Hot exposure may be a risk factor for preterm birth, and cold exposure may be a protective factor for preterm birth.

### GRAPHICAL ABSTRACT



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### ABSTRACT

**Background:** With the gradual increase of global warming, the impact of extreme temperatures on health has become a focus of attention, however, its relationship with preterm birth remains unclear.

**Objectives:** To investigate the association between exposure to extreme temperatures and preterm birth.

**Methods:** Temperature exposures and birth outcomes of 1,020,471 pregnant women from 132 cities in China were investigated. The pregnancy process was divided into different pregnancy periods. Study areas were divided into three categories (cold, medium, and hot areas) according to the local average temperature by cluster analysis. Average temperature data for each province used in the cluster analysis came from the China Statistical Yearbook 2013. Logistic regression was used to compare the effects of exposure to hot and cold conditions on the outcomes of pregnancy in different periods and regions.

**Results:** A total of 1,020,471 singleton births were included, of which 73,240 (7.2%) were preterm births. Compared with moderate temperatures (5th to 95th percentile), heat exposure (>95th percentile) in different periods of pregnancy increased the risk of preterm birth in hot areas. The most obvious increase was during the 3 months before pregnancy (odds ratio (OR) = 1.229, 95% confidence interval (CI): 1.166–1.295). In contrast to heat exposure, cold exposure (<5th percentile) in hot areas reduced the risk of preterm birth; the protective effect was most pronounced in the 3 months before pregnancy (OR = 0.784, 95% CI: 0.734–0.832). In medium and cold areas cold exposure also reduced the risk of preterm birth. The effect of exposure to extreme ambient temperatures throughout the entire pregnancy on preterm birth was similar to those of the periods above.

**Conclusions:** Acute and chronic exposure to extreme temperatures may affect the risk of preterm birth. Extreme heat is a risk factor for preterm birth and extreme cold is a protective factor.

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## 1. Introduction

Recent studies have shown that the incidence of preterm birth worldwide is about 10% (Beck et al., 2010), which is considered a major global health problem. The World Health Organization has defined preterm birth as a live baby who is born before 37 weeks of pregnancy (Listed, 1977). Preterm birth is an important cause of perinatal morbidity and mortality and may lead to a variety of complications, such as neurologic and developmental disabilities (Frey and Klebanoff, 2016). Many surviving preterm children also face life-long difficulties, including learning disabilities and vision and hearing problems (Marlow et al., 2005). Therefore, prevention of preterm birth is a serious and urgent challenge. Although many risk factors and interventions have been explored, preterm birth rates continue to increase in nearly all countries with reliable data (Blencowe et al., 2012); therefore, further study of the risk factors for preterm birth is required.

The increases in global warming and extreme weather have received much attention in recent years, and many studies have been conducted on diseases that may be related to environmental factors (Barnett, 2007). As a special population, the ability of pregnant women to maintain a balanced body temperature is very limited. Owing to the physical and mental stress caused by pregnancy, these women are more vulnerable to environmental factors (Flouris, 2011). The impact of extreme ambient temperature exposure during pregnancy is of great public health concern, and its potential relationship with preterm birth is particularly important.

The current findings regarding the relationship between ambient temperature and preterm birth are inconsistent. Research has shown that short-term heat exposure increases the risk of preterm birth (Patrizia et al., 2013). Extreme cold exposure had been found to raise the risk of preterm birth (He et al., 2016). Other studies have yielded the opposite conclusion that exposure to extreme cold temperatures is not associated with premature birth (Vicedo-Cabrera et al., 2015). These differing results may be related to differences in study design, geographic location, population, length of exposure window, cutoff value, and may also be related to regional adaptability, such as people from hot areas are more tolerant of heat than those from cold regions (Guo, 2014). The detailed mechanism of the influence of environmental temperatures on preterm birth remains to be elucidated; there is no clear conclusion at present.

There are a few studies on the relationship between long-term exposure to heat or cold and birth outcomes; however, there are no studies on the relationship between exposure to environmental factors and preterm birth in different periods of pregnancy for the entire Chinese population. The purpose of this study was to explore the effects of exposure to extreme environmental temperatures during pregnancy on preterm birth.

## 2. Methods

### 2.1. Study population

The data used in the study were obtained from the National Free Pre-pregnancy Checkups Project (NFPCP). The NFPCP is a national health service that has been supported by the National Health and Family Planning Commission and the Ministry of Finance of the People's Republic of China since 2010, aiming to provide free pre-pregnancy medical examinations and follow-up of pregnancy outcomes for couples of childbearing age throughout the country. The NFPCP covered only rural couples from 2010 to 2012 and was further expanded to urban couples in 2013. Our study covered 132 cities in 30 provinces of China; the details are given in Fig. 1.

Women aged 15 to 49 years old who participated in the NFPCP between January 2010 and December 2013 were included in this study. Participants were enrolled by trained staff. Date of Age, number of previous pregnancies, alcohol consumption, exposure to secondhand

smoke, and other information were collected by qualified nurses using structured questionnaires in face-to-face interviews. Physical characteristics of women of childbearing age, such as pre-pregnancy body mass index, were collected through physical examinations, and pregnancy outcome information was obtained by follow-up investigation for all participants. A total of 1,122,456 women with pregnancy outcome data were enrolled in the NFPCP. The analysis was restricted to all singleton births. After removal of multiple pregnancies, miscarriages and stillbirths, a total 1,020,471 women were included in the current analysis. Of these 955,284 (93.6%) were rural inhabitants and 65,187 (6.4%) were urban inhabitants. The details are given in Fig. 2.

The Institutional Research Review Board of the National Research Institute for Family Planning approved the study protocols and forms, in accordance with the relevant guidelines and regulations. Informed consent was obtained from all NFPCP participants.

### 2.2. Temperature exposure

Hourly temperature and humidity data for each city were obtained from the National Meteorological Information Center of the China Meteorological Administration and were linked to each woman of childbearing age, based on residential address data collected by the NFPCP.

Because the etiology threshold window for the effects of temperature exposure on risk of preterm birth is still unclear, several exposure windows were explored. The windows of average daily temperature exposure were set to 3 months before pregnancy (91 days before the last menstrual date), the first 1–7 weeks of pregnancy, weeks 8–14 of pregnancy, weeks 15–21 of pregnancy, and the entire pregnancy period (length of the entire pregnancy is estimated from the menstrual date and date of delivery), to explore the effect of long-term ambient temperature exposures on preterm birth (Ha et al., 2016). In addition, to explore the effects of short-term exposure on preterm birth, the exposure windows were also set to 1 week before delivery and 4 weeks before delivery (Strand et al., 2012).

As the study covered a number of cities across China, temperature exposures were categorized by local temperature distributions among study participants in each pregnancy window, to reflect regional adaptability. An average temperature distribution for each location and each pregnancy window was created, and the exposures were defined based on the following cutoff values: cold (<5th percentile), hot (>95th percentile), and moderate (5th to 95th percentile) (Liang et al., 2016). The study areas were divided into three categories as cold, medium, and hot areas according to the local average temperature by cluster analysis. Average temperature data for each province used for cluster analysis came from the China Statistical Yearbook 2013; details are provided in Table A1.

### 2.3. Outcome and covariates

All results and covariate information were obtained from the NFPCP. The primary outcome of this study was preterm birth, defined as delivery at <37 weeks, compared with full-term birth (delivery at ≥37 weeks) (van Vliet et al., 2017). The gestational age was calculated as the number of weeks between the date of the last menstrual period and date of delivery. Covariate variables included maternal age, body mass index before pregnancy, infant sex, exposure to alcohol and secondhand smoke during pregnancy, number of previous pregnancies, the month of pregnancy, humidity, and the average per capita gross domestic product (GDP) of each city from 2010 to 2013. Maternal age was categorized into several groups: <20, 20–24, 25–29, 30–34 and ≥35 years. Body mass index before pregnancy was calculated as weight in kilograms divided by height in meters squared (kg/m<sup>2</sup>) and categorized as underweight (<18.5), normal weight (18.5–23.9), overweight (24–27.9) and obese (≥28) (Ramos et al., 2017).

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