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Exposure to extreme temperatures during pregnancy and birth weight: evidence from Chile (2011 – 2020)

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Abstract:	Background: Exposure to extreme temperatures during pregnancy can have adverse effects on birth weight, however, there is little evidence from Latin America. Methods: We conducted a population-based cohort design using secondary information from birth records: 2011-2020. Mean, minimum, and maximum daily temperatures were obtained from meteorological stations in 26 municipalities representing different climatic zones of Chile. Temperature percentiles were calculated for each climatic zone and assigned for the entire pregnancy, trimester, and gestational week based on residence, date of birth and gestational age. General additive models (GAM) and distributed lag nonlinear models (DLNM) were used, using the 50th percentile for comparison. All models adjusted for month and year of last menstrual cycle and maternal and paternal: age, education level, and employment status. Results: Exposure to cold mean temperatures (≤10th percentile) in the total pregnancy period and each trimester was associated with a lower mean birth weight (-28.7 gram for the total period, -45.9, -36.1, and -83.4 g for trimester 1, 2, and 3, respectively), whereas exposure to warm mean temperatures was associated with higher birth weight (21.3 g for >90th percentile). For extreme temperatures, exposure to both cold (≤10th percentile for minimum) and hot (>90th percentile for maximum) in the total pregnancy period related to lower birth weight: -48.7 g (95% CI -49.7; -47.6) and -17.48 g (95% CI -18.5; -16.4), respectively, with similar effects by trimester. We observed similar results in DLNM models, with more consistent effects later in pregnancy. Discussion: Lower birth weight was consistently observed for exposure to cold temperatures, as was exposure to extreme heat. Exposure to warmer mean temperatures related to higher birthweight. Differing results from the Chilean population highlight the importance of understanding regional impacts of climate change on child health.

Date: December 22, 2024

To: Editor-in-Chief
Science of the Total Environment

Re: New Original Research Article: “Exposure to extreme temperatures during pregnancy and birth weight: evidence from Chile (2011 – 2020)”

We respectfully submit for your review our original research article titled “Exposure to extreme temperatures during pregnancy and birth weight: evidence from Chile (2011 – 2020)”.

The objective of our study was to evaluate the relationship between exposure to both average and extreme temperatures (minimum and maximum) and birth weight using available data from government meteorological stations representing a variety of climatic zones and birth records available in Chile. We analyzed 330,118 term births between 2011 and 2020, explored windows of exposure (total pregnancy period, trimester, and gestational week), in attempt to increase evidence on the potential perinatal health effects of climate change in Chile.

Exposure to extreme temperatures during pregnancy can have adverse effects on birth weight, however, there is little evidence from Latin America. Our analysis of nearly 300,000 births from 5 climatic zones in Chile showed that exposure to cold temperatures and extreme heat, were related to lower birth weight among infants born at term. Exposure to warmer mean temperatures, however, related to slightly higher birthweight. Differing results from our sample of births from Chile highlight the importance of understanding regional impacts of climate change on maternal and child health.

I certify that all authors have participated substantially either in the conception, design of this work, and writing of this manuscript. All authors have reviewed the manuscript submitted for publication, approve it for publication, and take public responsibility for its content. There are no conflicts of interests to report.

This manuscript is only being submitted to the *Science of the Total Environment* and has not been published elsewhere. If accepted, it will not be published elsewhere including electronically in the same form, in English or in any other language, without the written consent of the copyright-holder.

My Co-Authors and I thank you for your time in reviewing this article, which we herewith submit for consideration.

Sincerely,

Estela Blanco, PhD, MPH, MA
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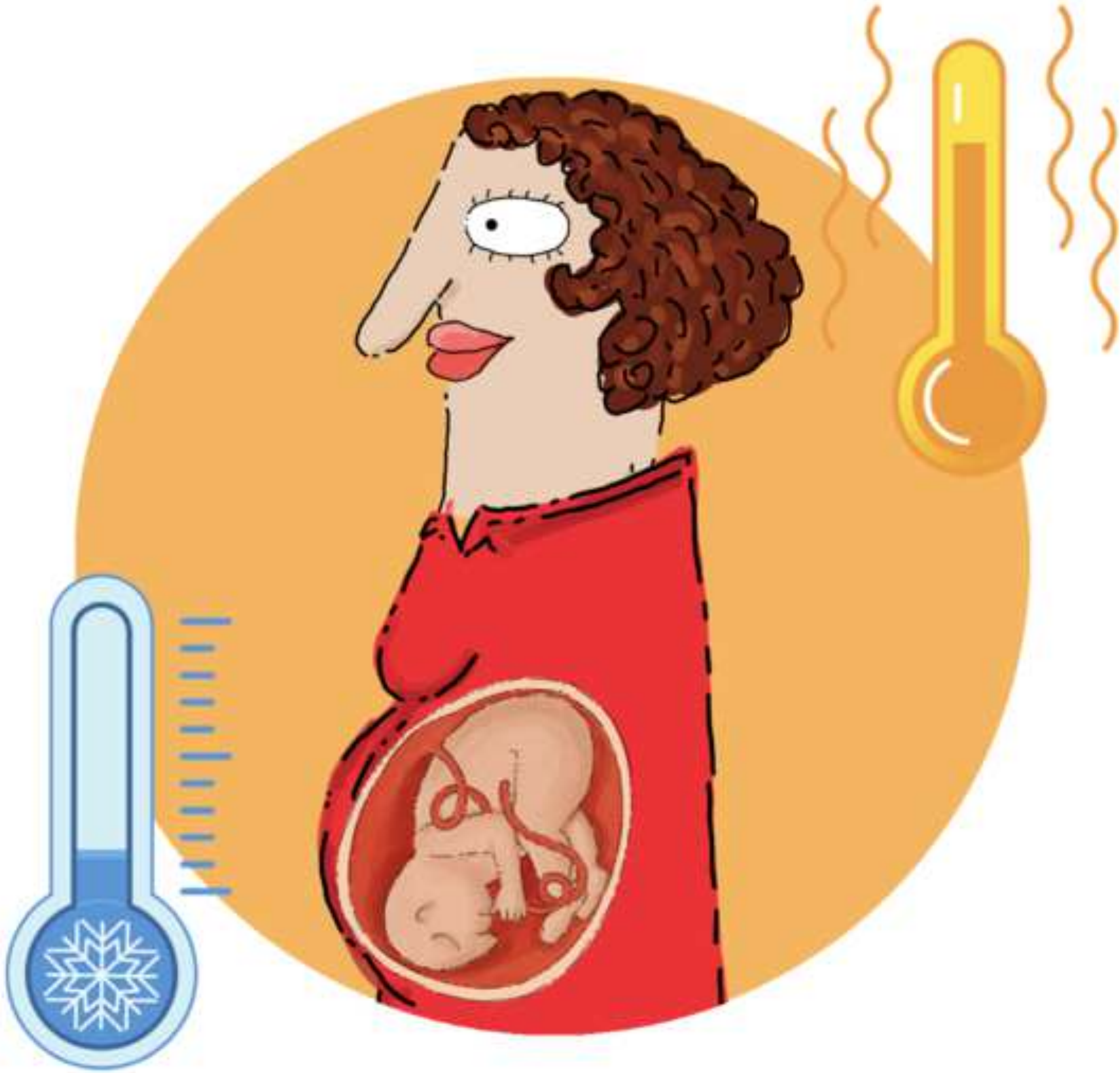
Graphical Abstract



Highlights

- Temperature exposure during pregnancy may influence birth weight.
- Limited evidence is available from diverse climatic zones and the Global South.
- Lower birth weight was observed for exposure to extreme temperatures.
- Exposure to warmer mean temperatures related to higher birthweight.
- Health impacts of climate change should be evaluated in diverse regions.

Title: Exposure to extreme temperatures during pregnancy and birth weight: evidence from Chile (2011 – 2020)

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ABSTRACT

Background: Exposure to extreme temperatures during pregnancy can have adverse effects on birth weight, however, there is little evidence from Latin America.

Methods: We used birth records in 2011-2020. Mean, minimum, and maximum daily temperatures were obtained from meteorological stations in 26 municipalities representing different climatic zones of Chile. Temperature percentiles were calculated for each climatic zone and assigned for the entire pregnancy, trimester, and gestational week, using the 50th percentile for comparison. General additive models and distributed lag nonlinear models (DLNM) adjusted for month and year of last menstrual cycle and maternal and paternal: age, education, and employment.

Results: Exposure to cold mean temperatures (≤10th percentile) in the total pregnancy period and each trimester was associated with a lower mean birth weight (-28.7 gram for the total period, -45.9, -36.1, and -83.4 g for trimester 1, 2, and 3, respectively), whereas exposure to warm mean temperatures was associated with higher birth weight (21.3 g for >90th percentile). For extreme temperatures, exposure to both cold (≤10th percentile for minimum) and hot (>90th percentile for maximum) in the total pregnancy period related to lower birth weight: -48.7 g (95% CI -49.7; -47.6) and -17.48 g (95% CI -18.5; -16.4), respectively, with similar effects by trimester. In DLNM, consistent effects were observed later in pregnancy.

Discussion: Lower birth weight was observed for exposure to cold temperatures and extreme heat. Exposure to warmer mean temperatures related to higher birthweight. Differing results from Chile highlight understanding regional impacts of climate change on child health.

Keywords: extreme temperature, perinatal health, climate change, pregnancy

INTRODUCTION

Climate change is the greatest threat to human health. Climate changes include larger and more frequent heat waves, wildfires, and storms, among other extreme weather events (1). The health effects of climate change are many and varied (2). Studies of the health effects of climate change have focused on differential risks among certain subgroups of the population, for example, older adults, people with underlying health conditions, and, to a lesser extent, children. Pregnant women, the fetus, and the newborn, by comparison, have received less attention (3,4). Pregnancy is a period of extraordinary change and exposures during the fetal period have the potential to affect short- and long-term health (5,6). Improving maternal and child health is a focus of local, regional, and global public policy, underlining the importance of identifying the health effects of climate change in these vulnerable populations.

The perinatal period begins at 23 weeks of gestation and continues until 7 days after birth. It is considered a critical period for the future health of the mother and child. Despite significant improvements in maternal mortality worldwide, maternal morbidity remains high, with some adverse pregnancy and childbirth outcomes increasing in many regions and others where prevalence reduction has not progressed (7–12). One of the first markers of newborn health is birth weight, which summarizes aspects of maternal nutrition and prenatal care (13). Deviations in this indicator, whether due to underweight or excess, are associated with negative health effects.

In Latin America, the prevalence of low birth weight (birth weight <2,500 g) has been estimated to be between 7 and 10% (12), while in Chile, despite a slight increase over the years (4.6% in 1991 versus 6.3% in 2016), the prevalence is lower (14). Low birth weight is attributed to up to 60% of neonatal deaths. At the national level, it has been shown that the mortality rate for children with low birth weight is 10 times higher than the mortality rate for children with normal weight (15). In addition, it is associated with later problems in the life cycle, such as childhood asthma, metabolic syndrome, type 2 diabetes, and cardiovascular diseases in adulthood (13,16).

There is evidence that ambient temperature influences birth weight, with more evidence for heat (4,17–20). While the exact biological mechanisms are unclear, animal models have demonstrated alterations in thermoregulation among pregnant females due to thermal stress, where low birth weight is hypothesized to be an adaptation mechanism (21). In addition, inflammatory responses to hypo- or hyperthermia have also been described, which would be involved in the reduction of uterine blood flow, affecting placental growth (22,23). In terms of human evidence, one study identified a reduction of 16.7 g of birth weight for each increase of 8ºC (24). Regarding the risk of term low birth weight at term (tLBW), another study showed a 13% increase in risk for each increase of 5°C (17). A recent article focused on ambient temperatures in Latin American cities in Brazil, Chile and Mexico and found lower birth weight associated with exposure to higher temperatures overall, but when separated by country, only observed lower average birth weights for exposure to cold temperatures in Chile, with a positive trend for higher temperatures (25). Although there is some evidence, additional research is needed from more diverse climatic zones.

Most previous studies have used absolute temperature to evaluate health effects; however, recent work has used temperature percentiles as a way to consider the potential of individual and population-level adaptation to temperature (26). This may be especially important using information from different climatic zones present within a geographic area. The average behavior and the number and intensity of extreme events can vary latitudinally, so for example, according to historical data from the Climate Risk Atlas for Chile (27), the average maximum temperature varies between 22° in the extreme north of Chile (desert) and only 7° in the southern zone (cold steppe). Using this methodology, Basagaña and colleagues found a U-shape negative relationship between temperature and birth weight in Israel, with lower birth weights associated with exposure to both lower (-56 g for ≤10^{th} vs. 41st–50th percentile) and higher temperatures (-65 g >90^{th} vs. 41st–50th percentile) over the entire pregnancy period (26). Furthermore, questions remain about windows of vulnerability to the potential effects on birth weight from exposure to extreme temperatures during gestation. The same study from Israel (26) and another conducted in the US (18), found greater effects in the initial and final weeks of gestation for exposure to higher temperatures, with less consistency for colder temperatures. More study is needed to clarify these relationships, as understanding whether timing of exposure influences the magnitude of effect is helpful for elucidating potential biological mechanisms and, potentially, for the design of interventions.

The objective of the current study was to evaluate the relationship between exposure to both average and extreme temperatures (minimum and maximum) and birth weight using available data from government meteorological stations representing a variety of climatic zones and birth records available in Chile. We analyzed 330,118 term births between 2011 and 2020, explored windows of exposure (total pregnancy period, trimester, and gestational week), in attempt to increase evidence on the potential perinatal health effects of climate change in Chile.

METHODS

We conducted a population-based cohort design using secondary information from births in Chile obtained from the Department of Statistics and Health Information (DEIS) and National Statistics Institute. In compliance with Article 29 of Law 17.374, all records remained anonymous and confidential. Records contain information from birth certificates including demographic characteristics of both parents and child. We evaluated births between 2011 and 2020 for the municipalities with available temperature date (described below). Infants born at term (≥ 37 weeks gestation), who had complete information on gestational age, birthweight and covariates were included in analyses (n=330,118). To avoid fixed-cohort bias (28), we limited the sample to infants whose estimated first week of gestation was 1-1-2011 and who were able to be born at term by 12-31-2020. A detailed summary of sample sizes associated with each inclusion criterion can be found in the Supplemental Material (Figure S1).

Our main analyses focused on term birth weight (tBW), measured in grams (g). Additional analyses were conducted for term low birth weight (tLBW), defined as a birth weight <2,500 g among infants born ≥ 37 weeks. In Chile, gestational age is determined using reported date of last menstrual period and via ultrasound conducted in the first trimester in the primary care setting (29).

Exposure assessment

Daily temperature (mean, minimum, and maximum) from meteorological stations located throughout Chile and maintained by the Meteorological Department of Chile (DMC for initials in Spanish) was obtained. We selected based on availability and completeness of data during the period of interest; data from a total of 26 municipalities representing different climatic zones of Chile was downloaded. Temperature sensors maintained by the DMC are installed at a height of 1.5 meters, in accordance with the international standard. We note that 9 of the 27 DMC monitoring stations used are located at small regional airports that range between 4 and 18 kms from the center of the municipality. A map of municipalities represented (Figure S2) and the coordinates of each temperature monitoring station (Table S1) are shown in Supplemental Material.

The municipalities included in this study are distributed across continental Chile, a region spanning multiple climate regions. We used a spatially resolved map of Köppen-Geiger climate zones to identify the predominant climate in each municipality (30). Then, we classified municipalities into five distinctive climate zone categories: desert (Northern zone); temperate dry with hot summer (Center zone); temperate dry with warm summer (Center-south zone; temperate with no dry season (South-austral and insular zone); and cold steppe (Austral zone). Details of which municipalities and number of births for the study period in each climatic zone can be found in Supplemental Material (Table S2).

Temperature percentiles were calculated for each climatic zone and assigned for the entire pregnancy, trimester, and gestational week based on municipality of residence, date of birth and gestational age. We conducted analyses for mean temperatures, comparing percentiles of low (≤10, 11-20, 21-30, and 31-40) and high (51-60, 61-70, 71-80, 81-90, and >90) mean temperatures to the 41-50th percentile for each exposure window. In addition, we analyzed exposure to extreme cold (≤10, 11-20, 21-30, and 31-40 of minimum temperatures) and hot (51-60, 61-70, 71-80, 81-90, and >90 of maximum temperatures) compared to the 41-50th percentile of minimum and maximum temperatures, respectively.

Statistical analysis

We estimated Generalized Additive Models (GAM) for tBW (linear link function) and tLBW (logit link function), assessing the effects of our three temperature metrics (mean, minimum, and maximum) over the total pregnancy period and by trimester. All models were adjusted for covariates, including maternal and paternal age, education, employment status, and month and year of the last menstrual cycle, to account for seasonal and time trends. We also fitted distributed lag nonlinear models (DLNM), using the dlnm R package version 2.4.7 (31), to explore the effect of temperature by gestational week. Our DLNM models were built as an extension of the GAM, given that nonlinear relationships have been previously described (18, 23), maintaining the same covariate adjustments.

Formally, the DLNM approach is based on the construction of a *cross-basis* function that simultaneously defines the exposure-response and lag-response relationships across the pregnancy periods. Y_t represents the outcome at time t (tBW or tLBW). The model is specified as follows (32):

$$g(E[Y_t]) = \alpha + \beta X_t + s_j(T_t) + \sum_{l=1}^{L} s_l(T_{t-l}) + Z_t \gamma$$

where $g()$ is the link function (identity for linear model and logit for binary outcome), T_t represents temperature metric (mean, minimum, maximum) at time t, $s_j(T_t)$ represents a smooth function of the temperature metric over time, and $\sum_{l=1}^{L} s_l(T_{t-l})$ is the lag structure up to lag L, which captures the delayed effects of temperature exposure. Z_t represents a vector of covariates (infant sex, maternal and paternal age, education, employment status, month, and year of last menstrual cycle), and γ is the corresponding vector of coefficients. For DLNM models, we used a cross-basis function to simultaneously model the exposure-response and lag-response relationships for each temperature metric, using natural cubic splines for the lag-response dimension with 2 knots and strata for the exposure-response function, as recommended by previous studies (26).

We conducted additional analyses using a two-stage design to better understand the relationship between temperature and birthweight by climatic zone. First, we estimated models for each climatic zone and then pooled estimates using meta-analytic techniques (33). We calculated best linear unbiased predictions (BLUPs) to adjust original estimates for each climatic zone. As this was an exploratory analysis only, we focused on term birth weight and exposures in the entire pregnancy period only. All models included the same adjustment variables as the GAM models. R code used to conduct all analyses is provided in Supplemental Material. Our study was reviewed and approved by the Institutional Review Board at Universidad Mayor.

RESULTS

Average birth weight was 3381.9 g (SD=433.3), with 2.0% of births classified as tLBW. Table 1 provides additional descriptive information of the sample. During the total pregnancy period, median temperature for the sample was 14.9 degrees and varied between 9.9 (10^{th} percentile) and 18.4 (90^{th} percentile) degrees. When considering climatic zone, greater variability in exposure was observed. Median daily temperature in the desert climatic zone was 17.0 and varied between 14.6 (10^{th} percentile) and 19.7 (90^{th} percentile), while in the cold steppe climatic zone, the 50^{th}, 10^{th} and 90^{th} percentile of mean daily temperatures were 6.5, 5.1 and 8.0, respectively. Table 2 provides summary statistics for the three exposure metrics for the entire sample and for each climatic zone during the entire pregnancy period; Figure S3 shows distribution of temperatures across climatic zones. Additional summary statistics (all temperature deciles) for exposure metrics during the entire pregnancy period and by trimester per climatic zone can be found in Tables S2-S5.

Birth weight: exposure in total pregnancy period and by trimester

Compared to exposure to the 41-50^{th} percentile in the total pregnancy period, exposure to cold mean temperatures (≤10th percentile) was associated with a lower mean birth weight (-28.6, 95% CI -29.7; -27.6 g, see Table S6), whereas exposure to warmer temperatures (>90th percentile) was associated with a higher birth weight (21.3, 95% CI 20.2; 22.4 g, Table S6) see Figure 1, Panel A. For trimester of pregnancy (Figure 1, Panel

B), exposure to the coldest mean temperatures (≤10th percentile) in the third trimester related to the lowest birth weight (-83.4, 95% CI -91.8; -74.9 g, see Table S7); estimates for each trimester were very similar for percentiles 21-30 and 31-40 compared to the reference group (Table S7). For warmer temperatures (>50th percentile), exposure in the first and third trimester were consistently related to higher birthweight. Estimates for the second trimester were less consistent (Figure 1, Panel B) and of smaller magnitude (-0.2 g, 95% CI -10.4; 10.0 g, for >90th percentile, see Table S7).

For extreme temperatures in the entire pregnancy period, exposure to both cold (≤10th percentile of minimum temperatures) and hot (>90th percentile of maximum temperatures) related to lower birth weight (Figure 1, Panel C and E): -48.6 g (95% CI -49.6; -47.6) and -17.4 g (95% CI -18.5; -16.4), respectively (see Table S6). In trimester-specific analysis, we observed similar patterns for extreme temperatures (Figure 1, Panel D and E). For the coldest minimum temperature (≤10th percentile), the strongest effect was observed for exposure in the third trimester (-63.0, 95% CI -71.0; -55.0), with first and second trimesters having similar magnitudes of effects (Table S8). For maximum temperatures, estimates were similar for each trimester <80th percentile, after which we observed slightly more pronounced effects in the first and third trimesters (Figure 1, panel F). For example, exposure to >90th percentile of maximum temperatures in the first and third trimester, compared to 41-50th percentile, related to the following reductions in birth weights: -51.1 (95% CI -59.3; -42.8) and -64.8 (-73.4; -56.2) g, respectively (Table S9).

Birth weight: exposure by week of gestation

Using DLNMs, we observed a negative relationship with exposure to mean temperatures ≤10th percentile compared to the 41-50th percentile early in pregnancy (gestational weeks 1-10) and again starting at week 16 through the end of pregnancy (Figure 2, Panel A), with estimates for exposure starting in week 25 being very similar. For example, exposure in week 25 and 34 were -5.2 g (95%CI -7.0; -3.3) and -5.5 g (95%CI -7.5; -3.4). For exposure to mean temperatures >90th percentile, we observed a positive relationship for exposure throughout pregnancy, with the strongest effects early and late in pregnancy: 6.1 g (95% CI 2.8; 9.2) in week 1 and 6.2 g (95% CI 3.1; 9.3). Table S10 provides exact estimates for these comparisons for each week.

For extreme temperatures, we found a consistent negative effect for exposure the coldest temperatures later in pregnancy between gestational weeks 28 to 37 (Figure 2, Panel C). For example, exposure to <=10th percentile of minimum temperature, compared to the 41-50th percentile, in gestational week 28, related to -1.9 g birth weight (95% CI -3.5; -0.3, see Table S11). For maximum temperatures negative associations were observed for exposure to the >90th compared to the 41-50th percentile across all weeks of gestation (Figure 2, Panel D), with the strongest associations later in pregnancy beginning in gestational week 27 (week 27, -3.1 g, 95% CI -4.9; -1.2, Table S12) and increasing in magnitude until term (week 37, -11.0 g, 95% CI -14.4; -7.7, Table S12). The entire exposure-lag response for each exposure metric (mean, minimum, and maximum temperatures) can be visualized in Figure S8.

Term low birth weight (tLBW): exposure in total pregnancy period and by trimester

The associations with tLBW and temperature percentiles during the gestational period showed similar results. Compared to the reference group (41-50th percentile), exposure to cold mean temperatures (≤10th percentile) was associated with a higher likelihood of low birth weight (OR 1.10, 95% CI 1.08; 1.12), while exposure to warmer temperatures (>90th percentile) was linked to a decreased likelihood of low birth weight (OR 0.93, 95% CI 0.91; 0.95), see Figure 3 (Panel A) and Table S6. For analysis by trimester (Figure 3, Panel B), exposure to cold temperatures (≤10th percentile) during the third trimester was associated with the highest odds of tLWB (OR 1.45, 95% CI 1.25; 1.68). However, estimates for warmer temperatures (>90th percentile) in the first, second and third trimesters were less consistent and of smaller magnitude (e.g., first trimester OR 0.88, 95% CI 0.75; 1.04, second trimester OR 1.00, 95% CI 0.84; 1.18 and third trimester OR 1.03, 95% CI 0.88; 1.19, Table S7).

Exposure to extreme temperatures during the entire pregnancy period temperatures was associated with an increased risk of tLBW. Specifically, exposure to extremely cold temperatures (≤10th percentile of minimum temperatures) was associated with an OR of 1.26 (95% CI 1.24; 1.29), and exposure to extremely hot temperatures (>90th percentile) was associated with an OR of 1.12 (95% CI 1.09; 1.14), see Figure 3 panels C and E and Table S6. Results were consistent when evaluated by trimester, with the third trimester showing the strongest association for extremely cold temperatures (OR 1.49, 95% CI 1.30; 1.72, Table S8) and extremely hot temperatures (OR 1.58, 95% CI 1.35; 1.85, Table S9) (Figure 3 panels D and F).

Term low birth weight (tLBW): exposure by week of gestation

The DLNMs analysis showed an inverse relationship with cold mean temperatures (≤10th percentile versus 41-50th percentile) during early pregnancy, particularly in the first 4 weeks (Figure 4, Panel A), and between weeks 21 and 32, with similar magnitudes of effects: OR 1.06, 95% CI 1.01; 1.12 for week 1 and OR 1.04, 95% CI 1.01; 1.07 for week 28 (See Table S10). For hot mean temperatures (>90th percentile), no significant associations were detected (Figure 4, Panel B and Table S10).

For extreme temperatures, DLNMs analysis revealed that exposure to extremely cold temperatures (≤10th percentile of minimum) was associated with a non-significant slightly elevated risk of tLBW throughout the pregnancy (Figure 4, Panel C), with ORs remaining close to 1.01 for most of the gestational period (e.g., week 10: OR 1.01, 95% CI 0.98; 1.04, Table S11). For hot temperatures (>90th percentile of maximum), starting around week 30, a gradual increase in ORs was noted, with estimates reaching statistical significance for weeks 32-37 (Figure 4, Panel D). The highest effect observed in week 35 (OR 1.06, 95% CI 1.01; 1.11, Table S12), indicating a slightly higher risk of tLBW during late gestation for exposure to extreme hot temperatures (>90th percentile of maximum).

Two-stage analysis

The results of our two-stage analysis, in which we analyzed the effect of exposure to average daily mean, minimum and maximum temperatures in the entire pregnancy period on tBW by climatic zone, are summarized graphically in Figure 5. Overall, lower temperatures (Panel A) were associated with reduced birth weight, particularly in desert regions (-228.1 g; 95% CI: -310.2, -146.1) and cold steppe regions (-95.8 g; 95% CI: -204.8, 13.3). Heat conditions (Panel B) were linked to greater birth weight in desert regions (350.7 g; 95% CI: 145.1, 556.4) but lower birth weight in temperate dry, hot summer regions (-265.6 g; 95% CI: -473.7, -57.5). For extreme temperatures, pooled estimates indicate a moderate negative effect on birth weight across all climatic zones during cold and heat extremes. Effects were particularly marked for both extreme cold (minimum) and hot (maximum) temperatures in the desert zone and, for hot temperatures, for the temperate dry, hot summer climatic zone (Figure 5, Panels C and D).

DISCUSSION

In our study of nearly 300,000 births from 26 municipalities and 5 climatic zones in Chile, we found consistent associations between exposure to low temperatures (<10^{th} percentile) during gestation and lower birth weight. Our cold temperature results were consistent using both daily mean temperatures and extreme cold temperatures, estimated using daily minimum temperatures. Associations for exposures to warmer temperatures were more nuanced. When evaluating daily mean temperatures, exposure to temperatures above the 50^{th} percentile in the entire pregnancy period related to slightly higher birth weights. However, when maximum temperatures were used as the metric of interest, exposure to temperatures above the 50^{th} percentile were associated with lower birth weights.

Our cold temperature results are in agreement with recent work from Israel (26), however at least two main differences can be appreciated. First, we found more modest effects (-28 versus -56 g). A large study focused on births in the U.S. found an even smaller (6 g) decrement in birth weight, associated with exposure to low temperatures (<= 10^{th} percentile) during the total pregnancy period (34). A modest reduction in birth weight may not have any clinical importance on the individual level, however, at the population level it signifies an environmental problem in a vulnerable population group, where prevention can reduce the population mean risk involved in avoiding the public health consequences of low birth weight (35). Moreover, the impact takes on greater importance when temperature extremes (both cold and hot) are common and escalating (36,37). Second, while we also found the strongest associations for exposures to colder temperatures in the later weeks of pregnancy (starting in gestational week 16), our results suggested additional susceptibility in the early weeks of pregnancy. Specifically, using mean temperature, we observed a lower birth weight for exposures to cold mean temperatures in gestational weeks 1-10. Direct comparisons with other studies are difficult considering differences in methodologies, nevertheless, another study from the U.S., did not find a relationship with exposure to colder temperatures in early pregnancy and risk of tLBW (38). Another study using data from cities in Mexico, Brazil and Chile, did not identify any cold-temperature effects for tBW (25). While we caution against over-interpretation of our results, these differences make clear that additional studies are needed from a variety of climatic regions, as identifying windows of increased risk is important for thinking about public health interventions.

Several previous studies have identified an inverse relationship between exposures to warmer temperatures during gestation and birth weight (18,25,26,34). For exposure to extreme heat, using maximum daily temperatures, we found an inverse relationship in our large sample from a variety of climatic zones in Chile. On the other hand, we found a positive association between exposure to greater mean temperatures (>50th percentile) and tBW. This result was especially apparent for exposures in the first and third trimester of pregnancy. Other studies have found modest positive relationships between exposure to warmer temperatures and tBW, however these associations were observed for later pregnancy only (23,39). We hypothesize that the reason we see the inverse relationship when only using maximum temperatures relates to a potential threshold of effect. For example, the 90th percentile of daily mean temperatures for the study conducted in Israel ranged between 23 and 28 degrees Celsius (26), compared to 16 and 18 degrees in our study. By comparison, the 90th percentile of daily maximum temperatures in our study were between 27 and 34 degrees. While far from resolving this quandary, our two-stage analysis helped to identify that the positive association between warmer mean temperatures and tBW was present for the desert climatic zone only. This suggests that a more specific analysis using smaller geographic areas may be warranted.

For our exposure metrics we used data from government maintained meteorological stations. Meteorological monitoring networks provide reliable, continuous measurements of temperature usually over large periods of time. However, monitoring stations have limited spatial coverage as they are scarce and are spread throughout large geographic areas, limiting the study to 26 Chilean communes. Future studies might benefit from using non-traditional sources of temperature data with more complete spatial coverage, including satellite-derived land surface temperature or modelled temperature. Nevertheless, there are important tradeoffs between these data in terms of granularity, coverage, and accuracy that need to be evaluated and considered for its use in exposure assessment of ambient temperature. For example, land surface temperature data have continuous global coverage at high spatial resolution over large periods of time. However, land surface temperature measures the temperature at the surface canopy (i.e., tree tops, roofs, bare ground), and while its spatial behavior correlates well with that of daytime air temperature (measured two meters above the ground), the two exhibit important data differences, as surface temperature can exceed 50° even when air temperature is below 30° (40). On the other hand, modelled temperature data might have good spatial and temporal granularity, but the accuracy of predictions will depend on the quality of training data, modelling decisions, and statistical approaches used. Future studies should explore the potential of these alternative data sources, evaluating strengths and limitations and the implications of its use in environmental health research. This is particularly relevant in regions like Latin America, where monitoring stations are sparse.

Our study had several limitations. First, there are several potential points for exposure misclassification. We assigned exposure based on maternal residence reported on birth certificates. While mobility during pregnancy has been reported to be high in the U.S. and Canada (41,42), there are no similar published reports of the phenomenon in Chile. Local evidence, not specific to the pregnancy population, shows that internal migration is uncommon in Chile (6.2%) and is most prevalent among men aged 25-54 with no children (43). Nevertheless, we expect that this bias, if present, to be non-differential. In addition, we assigned exposure at the level of municipality using temperature records from meteorological monitoring stations that were not necessarily located in the urban center, where the largest proportion of the population is located. In fact, 9 of the 27 stations used in the current analysis were located at small regional airports. Studies from Chile (44) and around the world (45,46) have illustrated the urban heat island effect, in which higher temperatures are experienced in densely populated areas compared to rural areas outside of urban centers. Along these lines, there may be important differences between areas within the same city or commune, which cannot be represented by a single registry, representing a potential for future studies. Thus, our results, especially for higher temperatures, may be attenuated. Furthermore, while we did have some information on variables known to influence adverse birth outcomes, such as maternal and paternal age (47,48), parental education level (49), and social vulnerability (50,51), many individual-level variables were not available (e.g., maternal morbidities). Additionally, the lack of data on indoor exposures and air conditioning use may have led to greater imprecision in our findings. Another potential limitation is spatial autocorrelation, specifically that temperature exposure might not be independent across regions. Ignoring spatial autocorrelation in models could lead to biased standard errors and invalid inference. Two final limitations should be noted. We were unable to adjust for air pollution in our models, as reliable measures were not available for all municipalities used in the analysis, a common reality in the Global South (52). Finally, we were unable to account for pregnancy loss in our analysis, which may have attenuated results (53,54).

Several strengths should also be noted. We used data from 5 different climatic zones. Chile is an extremely diverse country in terms of climatic zones (55), making it necessary to consider zone in analysis. In addition, relative measures of temperature were used, which may better relate to biological mechanisms of health effects and individual and population-level adaptation to temperature (20,56). That is, we may expect greater health effects when temperatures deviate from common levels (50th percentile). Finally, we took advantage of large administrative datasets. In particular, birth data is highly standardized, with nearly all births in Chile occurring in hospitals using a standard of care birth protocol (57).

Although there is evidence report regarding associations between temperature and newborn health, additional research is needed from more diverse climatic zones. To our knowledge, this is only the third published report from South America. One study focused on the Andean regions of Peru, Bolivia, and Colombia and found a negative relationship between exposure to increased relative temperature and birth weight (20). The only other study with information from Chile, focused on cities in Mexico, Brazil and Chile and, while authors concluded that exposure to warmer temperatures in pregnancy related to lower birth weight overall, results were inconclusive for Chile (25). In our analysis, we were able to include additional municipalities and climatic zones, as we used a different source for exposure assignment and evaluated exposure based on percentile of temperature for each climatic zone, which may better adjust for adaptation. Clearly, more studies from Latin America and the Global South are needed. From a scientific perspective, it is important to test whether a relationship described in other countries and regions is maintained, after considering local conditions, health habits, underlying risk factors and resilience of the population, among other aspects. Having locally produced evidence also serves to raise national awareness. In Chile, several branches of the government have taken on the task of understanding the potential threats of climate change (40, 41) with mention of rising temperatures, but nowhere is the health of the newborn mentioned.

Our analysis of nearly 300,000 births from 5 climatic zones in Chile between 2011 and 2020 showed that exposure to cold temperatures and extreme heat, were related to lower birth weight among infants born at term. Exposure to warmer mean temperatures, however, related to slightly higher birthweight. Differing results from our sample of births from Chile highlight the importance of understanding regional impacts of climate change on maternal and child health.

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Table 1. Characteristics of singleton term births in Chile: 2011-2020 (n = 330,118).

Variable	% (n)
Gestational age (Weeks)*	38.7 (1.0)
Birth weight (g*)	3381.9 (433.6)
Term low birth weight	2 (6602)
Newborn sex, male	51 (167247)
Maternal age	
<=20	14 (45263)
20-29	45 (148549)
30-39	37 (123609)
>=40	4 (12562)
Unknown	0.04 (135)
Maternal education	
No education	0.06 (212)
Primary	8 (26132)
Secondary	52 (170869)
College	40 (132768)
Unknown	0.04 (137)
Mother employed	50 (164124)
Paternal age	
<=20	6 (20466)
20-29	35 (115904)
30-39	38 (125456)
40-49	10 (33085)
>=50	1 (4620)
Unknown	9 (30587)
Paternal education	
No education	0.05 (149)
Primary	7 (23664)
Secondary	47 (154810)
College	37 (120929)
Unknown	9 (30566)
Father employed	75 (246722)
Climatic zones	
Desert	29 (96918)
Temperate dry, hot summer	20 (65224)
Temperate dry, warm summer	29 (94832)
Temperate, no dry season	17 (57402)
Cold steppe	5 (15742)

* Mean (standard deviation).

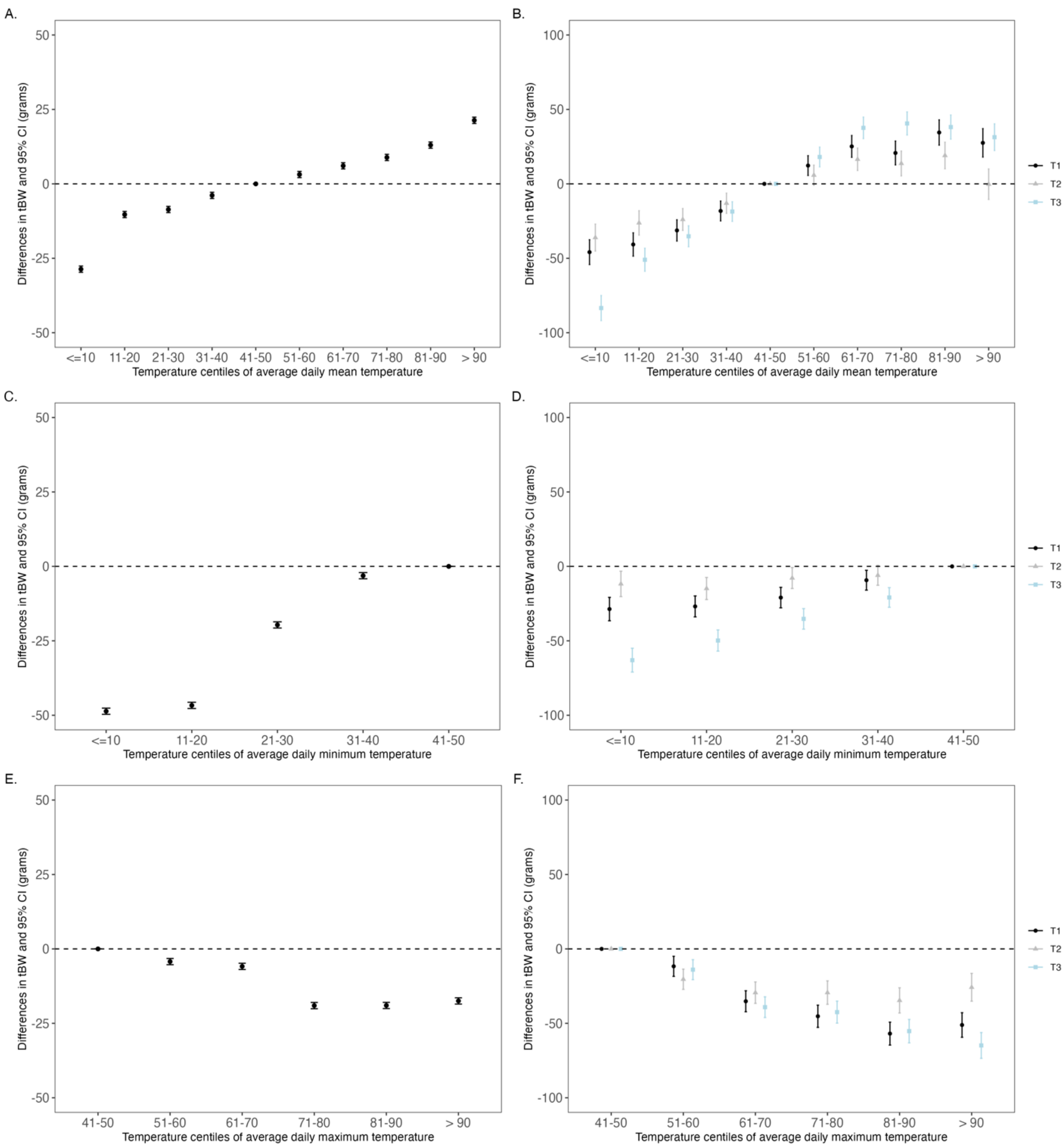
Table 2. Summary statistics of the mean temperatures in every climatic zone during research period (2011-2020) and the distribution in mean term birthweight (tBW, g) and term low birthweight (birthweight <2500 g, >= 37 gestational weeks).

	N	**tBW**	**tLBW**	**Daily Mean Temperature**			**Daily Minimum Temperature**		**Daily Maximum Temperature**	
				10th %ile	**50th %ile**	**90th %ile**	**50th %ile**	**10th %ile**	**50th %ile**	**90th %ile**
Overall	330118	3386.15	2%	9.9	14.9	18.4	6.2	1.5	22.3	27.0
Desert	96918	3352.20	2%	14.6	17.0	19.7	13.6	1.8	21.5	25.2
Temperate dry, hot summer	65224	3383.59	2%	13.5	16.0	18.6	6.5	4.4	26.6	29.1
Temperate dry, warm summer	94832	3395.25	2%	12.4	14.4	17.3	6.5	3.7	23.4	26.4
Temperate, no dry season	57402	3425.16	2%	8.9	10.9	14.1	2.8	0.7	18.1	20.8
Cold steppe	15742	3408.70	2%	5.1	6.5	8.0	0.2	-0.9	12.9	14.9

Note: Overall average temperature for mean: 14.6, min: 7.0 and max: 22.2. All temperature in degrees Celsius.

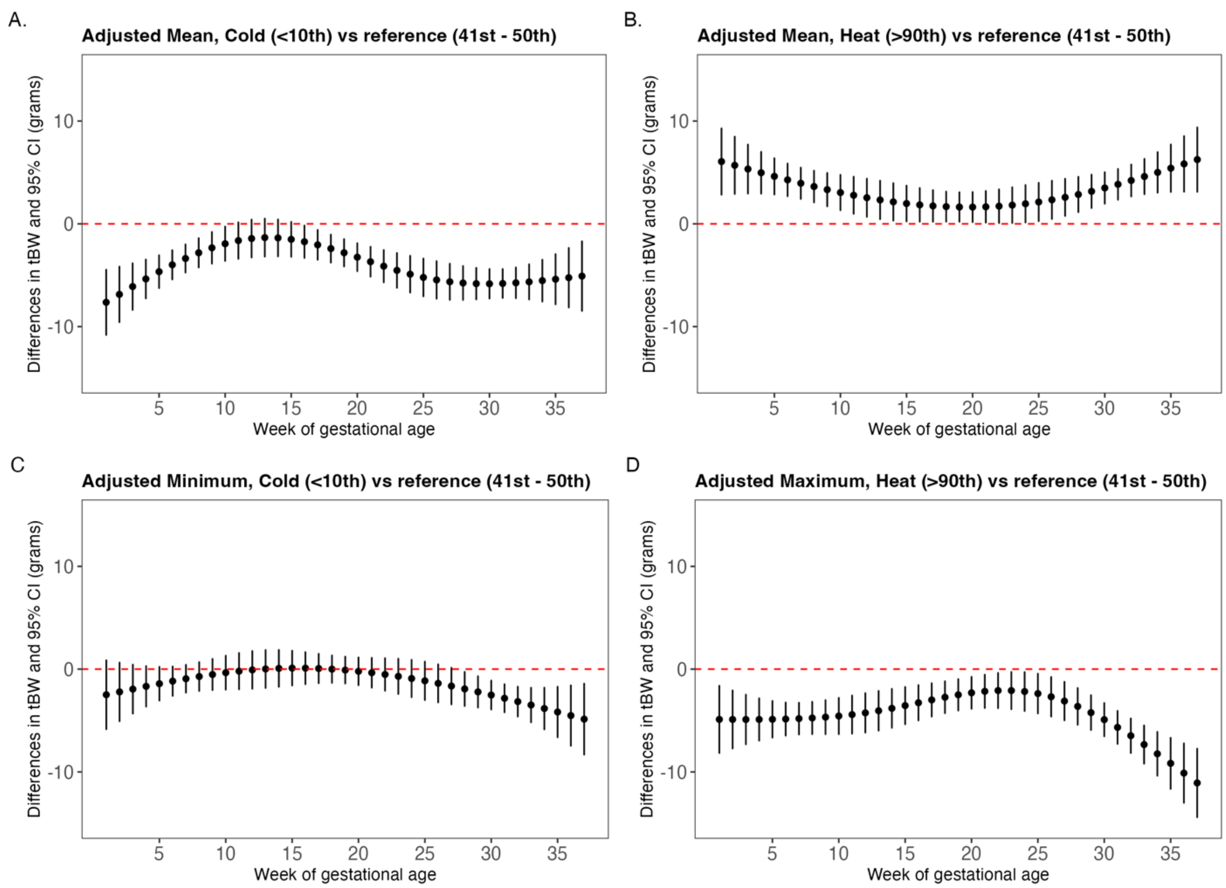
Figures

Figure 1. Estimated differences in mean term birth weight (g) and 95% confidence intervals according to climate zone-specific centiles of average daily mean, minimum and maximum temperature relative to the reference category (41st–50th centile) among singleton term live births during the entire pregnancy (panel A, C, E) and by trimester (panel B, D, F) in the period 2011–2020.



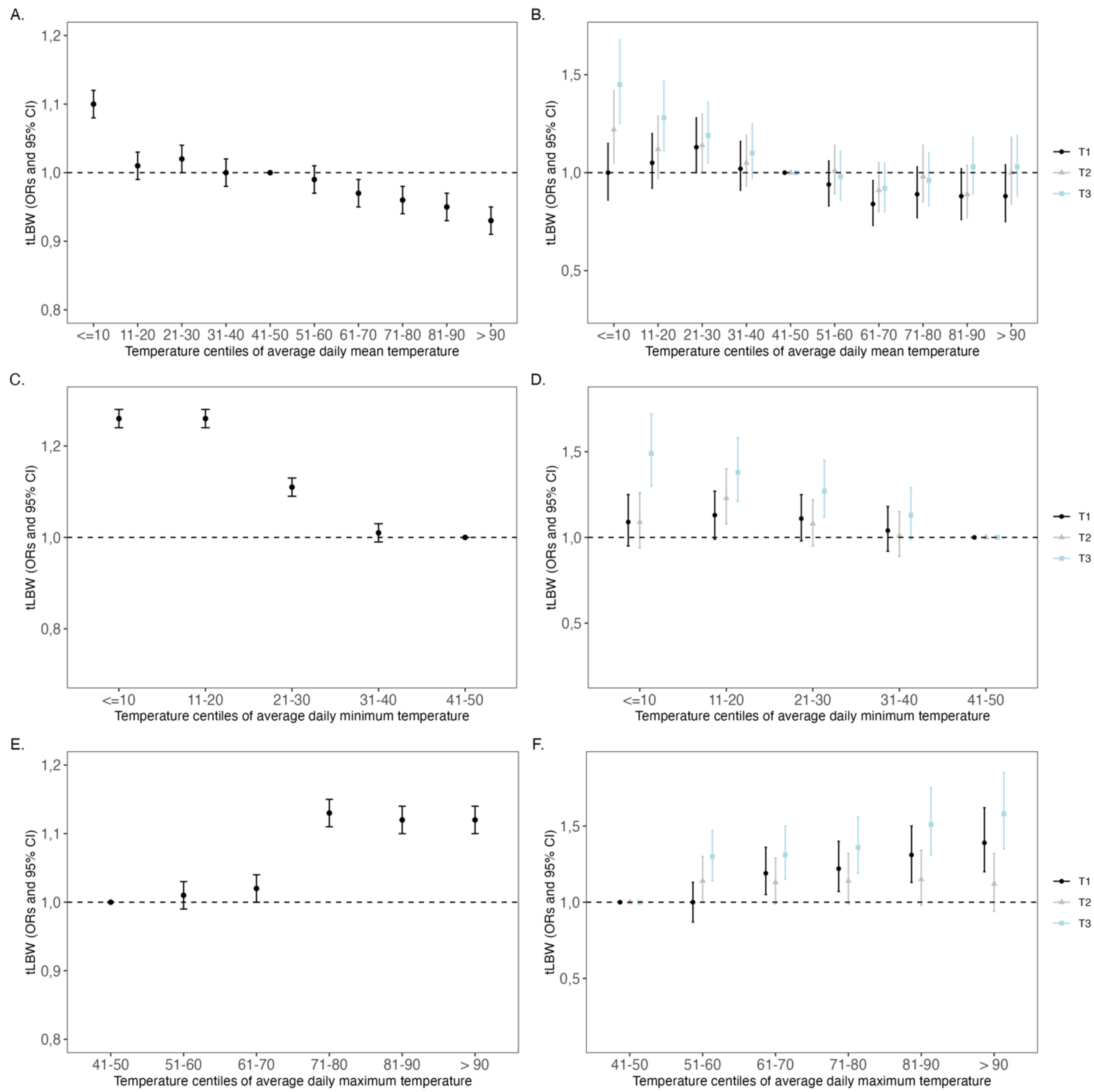
Note: Models estimated using generalized additive model (GAM) with normal distribution and identity link function for tBW. Models were adjusted for: newborn sex, maternal and paternal age, maternal and paternal education, maternal and paternal occupation, year and month of last menstrual period splines (N= 330,118). tBW-term mean birthweight (mean birthweight among births>36 gestational age weeks).

Figure 2. Estimated differences in mean term birth weight (g) and 95% confidence intervals associated with exposure to cold and hot daily mean, minimum and maximum temperatures (≤10th or >90th the percentile for each climate zone, respectively, relative to the 41st–50th centile) during each gestational age week among singleton live births in Chile during the period 2011–2020.



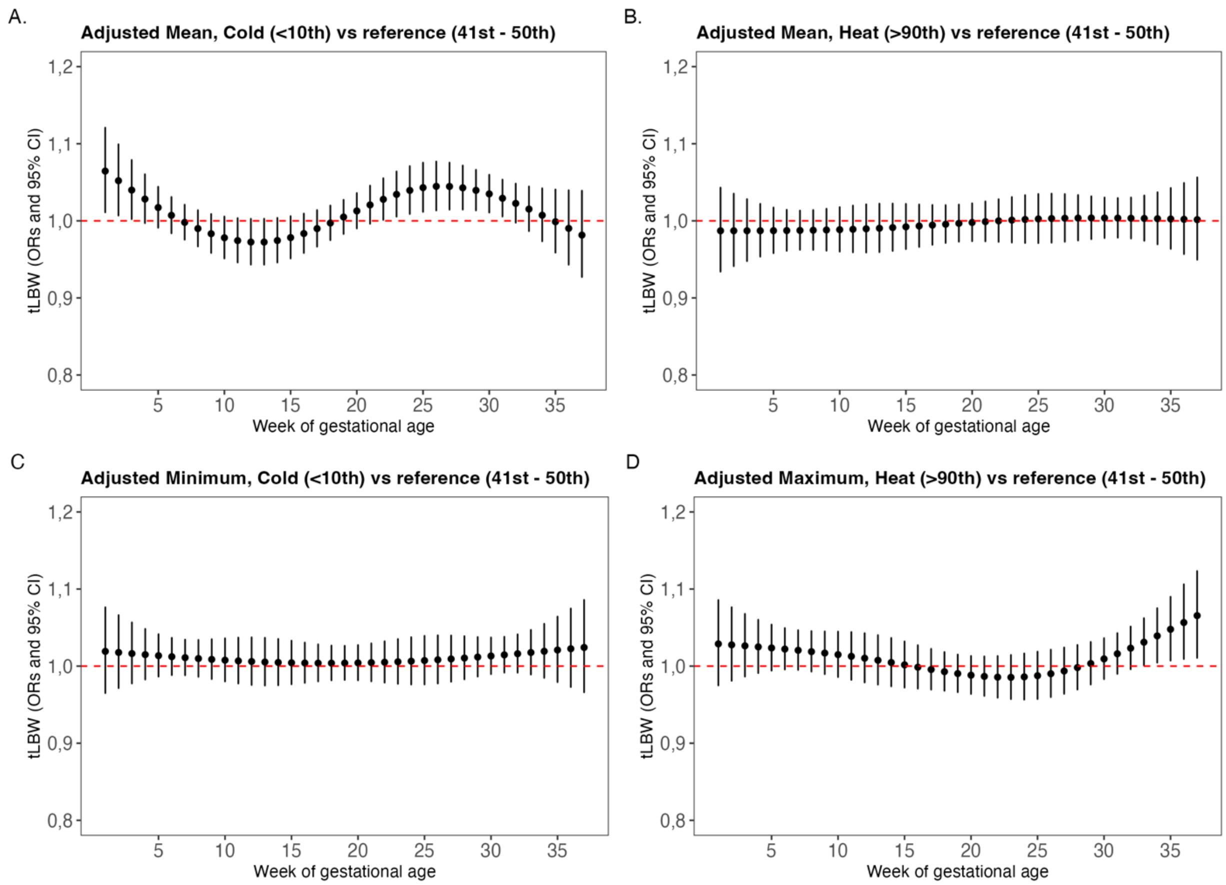
Estimates were derived using distributed lag non-linear models (DLNM, lag-response function modeled as a natural spline with equidistant knots and 2 degrees of freedom, exposure–response function modeled using indicator terms for each decile of the temperature distribution). Models were adjusted for: newborn sex, maternal and paternal age, maternal and paternal education, maternal and paternal occupation, year and month of last menstrual period splines (N= 330,118). Term birthweight is mean birthweight among births >36 gestational age weeks.

Figure 3. Adjusted ORs and 95% confidence intervals for term low birth weight according to climate zone-specific centiles of average daily mean, minimum and maximum temperature relative to the reference category (41st–50th centile) among singleton term live births during the entire pregnancy (panel A, C, E) and by trimester (panel B, D, F) in the period 2011–2020.



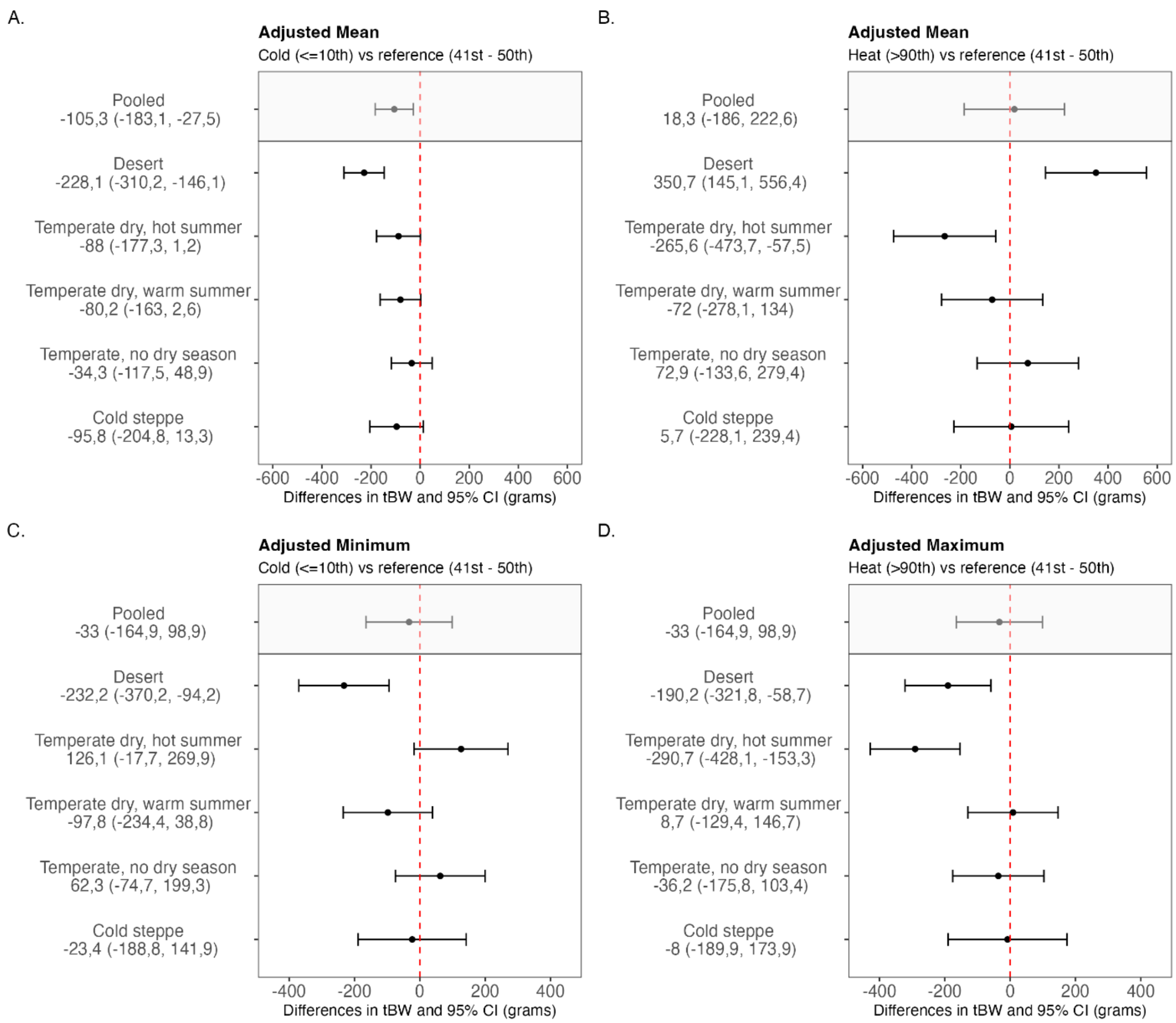
Note: Estimates were derived by generalized additive model (GAM) with binomial family and logit link function for term low birth weight. Models were adjusted for: newborn sex, maternal and paternal age, maternal and paternal education, maternal and paternal occupation, year and month of last menstrual period splines (N= 330,118). Term low birthweight was defined as births>36 gestational age weeks with birthweight <2500 g.

Figure 4. Adjusted ORs and 95% CI for tLBW in association with extreme cold and hot daily mean, minimum and maximum temperatures (≤10th or >90th the percentile for each climate zone, respectively, relative to the 41st–50th centile) during each gestational age week among singleton live births in Chile during the period 2011–2020.



Estimates were derived using distributed lag non-linear models (DLNM, lag-response function modeled as a natural spline with equidistant knots and 2 degrees of freedom, exposure–response function modeled using indicator terms for each decile of the temperature distribution). Models were adjusted for: newborn sex, maternal and paternal age, maternal and paternal education, maternal and paternal occupation, year and month of last menstrual period splines (N= 330,118). Term low birthweight was defined as births>36 gestational age weeks with birthweight <2500 g.

Figure 5. Two Stage estimated differences in mean term birth weight (g) and 95% confidence intervals according to climate zone-specific centiles of average daily mean (Panels A and B), minimum (Panel C), and maximum (Panel D) temperature relative to the reference category (41st–50th centile) among singleton term live births in Chile 2011-2020. Estimates were calculated for exposure in the entire pregnancy period.



Note: Estimates were derived using a generalized additive model (GAM) with a normal distribution and identity link function for tBW. Models were adjusted for: newborn sex, maternal and paternal age, maternal and paternal education, maternal and paternal occupation, year and month of last menstrual period splines (N= 330,118). Term birth weight represents birth weight for infants born after 36 weeks gestation.

Declaration of interests

☐The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☒The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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