



Full length article

The burden of premature births attributed to heat across 13 countries

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ABSTRACT

Background: Climate change threatens global health, particularly among vulnerable populations such as pregnant individuals and their newborns. Evidence linking heat to premature birth is largely based on single-location studies or heterogeneous meta-analyses, leaving important gaps regarding underrepresented regions, preterm subgroups, and the role of maternal and infant characteristics. **Objectives:** To quantify the association between heat and preterm birth (PTB) across multiple countries, assess gestational-age-specific effects, and identify maternal vulnerability factors. **Methods:** We analysed 36.6 million births occurring during the warm season from 250 locations in 13 countries to assess heat effects on PTB. Distributed lag non-linear models (DLNM) with quasi-Poisson regression estimated heat-PTB associations and the fraction of PTB attributable to heat. Gestational-age subcategories (extreme, very, late, and at-term) and socio-economic vulnerability profiles were also examined. **Results:** Overall, 1.4% (95% CI: 1.3–1.5) of PTB were attributable to heat (855 PTB per million births), with national burdens from 628 to 1,347 PTB per million. Higher susceptibility was suggested for younger, single, non-primiparous, less-educated, and socio-economically deprived mothers, and among female fetuses. Late PTB

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showed the largest risk; at-term births also displayed a small but consistent heat-related increase. **Conclusions:** This large analysis of heat-related PTB using harmonized individual-level data indicates that heat increases PTB risk, with variations across countries and climates. It also shows that heat can trigger labour beyond the typical PTB window, affecting pregnancies not usually considered clinically vulnerable. Overall, these findings underscore the need for strategies to mitigate heat-related risks during pregnancy, particularly among socio-economically vulnerable populations.

1. Introduction

The progressive anthropogenic warming of the climate poses unprecedented challenges to public health, primarily affecting the most vulnerable (Romanello et al., 2024). Increasing evidence indicates that pregnant individuals and their newborns are among this particularly susceptible subpopulation (Roos et al., 2021).

Exposure to heat during pregnancy has been associated with an increased risk of maternal morbidity and adverse birth outcomes (Bonell et al., 2022; Chersich et al., 2020; Jiao et al., 2023). Although the exact biological mechanism remains uncertain, previous research suggests that high temperatures may trigger a series of responses in pregnant individuals such as inflammation, oxidative stress and vasoconstriction, all of which can harm the placenta, disrupt intrauterine growth and/or trigger labour (Samuels et al., 2022).

Epidemiological studies from Europe, North America, and Asia have shown that exposure to elevated ambient temperatures increases the risk of preterm birth (PTB) (i.e., babies born alive before 37 completed gestational age weeks) (Bont et al., 2022; Cheng et al., 2020; Darrow et al., 2024; Sun et al., 2019; Vicedo-Cabrera et al., 2014). Despite the extensive research on this topic, knowledge gaps remain, such as the role of specific maternal characteristics or evidence in more vulnerable populations in the Global South (Lakhani et al., 2024; Meherali et al., 2024; Nyadanu et al., 2024). In particular, it is still unclear whether vulnerability to heat is the same across different endpoints of gestational duration, as subgroups other than standard PTB have been barely studied (Bont et al., 2022). Additionally, estimates are heterogeneous mainly because existing studies used different designs, methods, and temperature metrics (Chersich et al., 2020).

Globally, 15 million babies (approx. 11% of all pregnancies) are born preterm each year, and the number is increasing (Chawanpaiboon et al., 2019). Understanding the impact of heat on preterm birth (PTB) remains a priority in neonatal health, given the associated high risk of mortality and morbidity in the mother and neonate (Saigal and Doyle, 2008). According to a recent report of the United Nations, PTB is the leading cause of infant mortality worldwide (i.e., 18% of all deaths among children under the age of five and 35% of all neonatal deaths) (UN Inter-Agency Group for Child Mortality Estimation (UN IGME), 2024). PTB has also been associated with a range of lifelong morbidities, imposing significant psychological and financial burdens on the affected families and substantial costs for healthcare systems (Lai and Lorch, 2023).

We aim to address existing knowledge gaps on the relationship between ambient temperature and maternal health by performing the most extensive multi-country assessment to date on the impact of heat on PTB. These findings have implications for understanding potential health impacts, as global temperatures continue to rise due to climate change (IPCC, 2022). In particular, we apply state-of-the-art methods in climate epidemiology to quantify the prematurity burden associated with exposure to heat during the last days of gestation in 250 locations from 13 countries distributed across different regions of the world. Additionally, we explore the role of various maternal and fetal characteristics on the relationship between heat exposure and PTB, as well as the potential triggering effect of heat for labour by estimating the heat-related risk of birth at different gestational lengths, including at-term births (ATB).

2. Methods

2.1. Data collection

Individual data on gestational age in completed weeks and date of birth for all births occurring in 250 locations across 13 countries were provided by the respective national Public Health or Statistical registries. The data covered overlapping periods of at least three years from 1 January 1979 to 31 December 2019. Whenever available, these sources also provided maternal and fetal characteristics, including maternal age in three categories based on absolute cutoffs (<25, 25–34, ≥35), maternal age in tertiles, maternal education (lower secondary or less, higher secondary, university), marital status (single, non-single), socioeconomic status (low, non-low), fetal sex (male/female), parity (0, ≥1), and ethnicity (Caucasian/non-Caucasian). Data collection was coordinated within the Multi-country Multi-city (MCC) collaborative research network, the largest data consortium on climate change and health research (Gasparrini et al., 2024), along with external partners in Australia, Brazil, Israel, Japan, and the US.

We limited our study population to live-born singleton births with gestational ages between 22 and 42 completed weeks, the standard period of fetal viability, and defined preterm births (PTB) as live births with reported gestational age below 37 completed weeks (World Health Organization, 2016). We aggregated data in each community to obtain daily counts of PTB and at-term births (ATB), classified into gestational age categories as follows: extreme, very, late, and standard PTB (22–27, 28–31, 32–36, and < 37 weeks, respectively), and early and full ATB (37–38 and ≥ 39 weeks, respectively) (World Health Organization, 2023). For analyses of fetal and maternal characteristics as effect modifiers in the heat–PTB association, daily counts were also stratified by these categories.

Daily time series data on mean temperature (Tmean) for each location were obtained via the MCC collaborative network or from the respective national meteorological agencies. The study locations cover four of the five major Köppen–Geiger climate zones: Tropical, Arid, Temperate, and Continental (Kottek et al., 2006).

2.2. Statistical analysis

We used a two-stage design to assess the PTB risk associated with heat during the last four days of gestation (lag 0–4), restricting analyses to the five warmest consecutive months in each country (“warm season”; 36.6 million births). These analyses were drawn from a total dataset of 86 million births from 250 locations in 13 countries, with the remaining data used to derive control variables (see sTable 1 and sTable 2). Stage one analysed outcomes at the location level, while stage two pooled location-specific estimates via meta-analysis. The PTB burden was then quantified using established health impact assessment methods. Further details are presented in the following subsections.

2.2.1. First stage

A time-stratified conditional quasi-Poisson regression model (Turner and Firth, 2007) with distributed lag non-linear models (DLNM) (Gasparrini, 2014) was fitted to each outcome in each location during the warm season. This approach, equivalent to a time-stratified case-crossover design, compares exposure at the time of the event with related non-event periods, allowing control for long-term and seasonal

trends (Nyadanu et al., 2022a). Case and control periods were matched within the same calendar month and year.

Seasonality in births, driven by location-specific conception patterns, can cluster pregnancies in late gestation, creating potential residual confounding. To address this, we applied the pregnancy-at-risk approach (Vicedo-Cabrera et al., 2014), incorporating a weighted offset based on gestational age to account for the probability of delivery at each week, proven effective to this aim (Huang et al., 2023).

DLNM, strongly recommended for analysing the short-term effects of heat on PTB (Nyadanu et al., 2024), was applied to capture the nonlinear relationship between daily mean temperature and PTB risk, accounting for delayed effects. This model uses basis functions in two dimensions to estimate both the exposure–response and lag–response associations while mitigating, to some extent, multicollinearity.

Our model, formulated for standard PTB without loss of generality, was

$$Y_t \sim \text{quasi-Poisson}(\mu_t)$$

$$\log\left(\frac{\mu_t}{Z_t}\right) = \alpha_{st} + \eta \text{cb}(T\text{mean})_t + \delta \text{dow}_t + \gamma \log(W_t)$$

where, Y_t is the observed number of PTB on day t and Z_t is the number of pregnancies at risk of being born preterm on day t ; α_{st} (introduced through the “eliminate” function in “gnm” package) is the intercept for stratum, st , in which t is included, with strata defined as the same calendar month of the same year; cb is the matrix representing the bidimensional cross-basis function used to assess the non-linear and delayed exposure-lag-response association between $T\text{mean}$ and PTB accounting for 4 days of lag after exposure and η the respective coefficients. $T\text{mean}$ was defined on a percentile scale rather than on the absolute scale; accordingly, results are consistently interpreted in terms of percentiles. The exposure–response relationship was modelled as a natural cubic spline with two internal knots placed at the 50th and 90th percentiles of location-specific temperature distribution and the lag–response relationship was modelled as two strata, lag 0–1 and 2–4; dow is the day of the week indicator and δ the respective coefficients. At last, W_t , as proposed by Vicedo-Cabrera, et al. (Vicedo-Cabrera et al., 2014), is the ratio between a propensity to be born –weighted offset and the offset itself,

$$W_t = \sum_{j=22}^{36} \frac{Z_{ij} W^j}{Z_t}$$

where Z_{ij} is the number of pregnancies at gestational week j (22–36 weeks) on day t , and W^j is the conditional probability of birth at week j conditional on reaching week j . The weighted offset W_t ranks contributions of pregnancies by gestational age, with higher weeks carrying a greater probability of delivery. Including $\log(W_t)$ alongside the crude Z_t offset provides a flexible alternative to directly using the weighted offset, allowing the coefficient (γ) to reflect the relative importance of each gestational subgroup (Vicedo-Cabrera et al., 2014).

In our analysis, we used a relatively short maximum lag of 4 days, focusing on acute impacts as supported by previous studies (Darrow et al., 2024; Khosravipour and Golbabaie, 2024). The lag–response shape (strata) was chosen conservatively to capture potential immediate effects (Khosravipour and Golbabaie, 2024). The function (ns) and number of knots for the exposure–response curve were based on the linear or J-shaped patterns reported in prior warm-season studies (Nyadanu et al., 2022b). Sensitivity analyses varying knot number and positions showed minimal impact on results (not shown).

Additionally, we conducted stratified analyses by fetal and maternal characteristics using this first-stage approach to each of their respective categories, with Z_t and W_t recalculated for each subset. We also replicated the standard PTB model for each of the other GA categories—extreme, very and late PTB, as well as early and full ATB.

2.2.2. Second stage

In the second stage, location-specific temperature–PTB curves were pooled using a multilevel multivariate random-effects *meta*-analytical model (Sera et al., 2019). The model assumed a hierarchical structure with locations nested within countries as the random effect, and the warm-season temperature range ($rgT\text{mean}$) in each location as a fixed-effects *meta*-predictor. This model was selected based on the minimum Akaike Information Criterion from a set of plausible models previously applied in similar contexts to control for climate-related heterogeneity (e.g., we tested location nested within the interaction of country and climate zone as a random effect, and the possible inclusion of mean temperature as a fixed-effects *meta*-predictor). Heterogeneity across locations was assessed using the Cochran Q test and the I^2 index (Higgins and Thompson, 2002). The resulting pooled curve, covering lag 0–4, represents the global association between heat and PTB.

Using the same *meta*-analytical framework, we derived country- and climate zone-specific PTB curves based on their respective average temperature ranges, to examine climate-based differences. These curves were then used to estimate moderate and extreme heat effects, defined as the percentage change (ch%, 95% CI) in PTB when $T\text{mean}$ increased from a reference percentile to the 75th and 95th percentiles, respectively. The reference was set at the minimum-effect percentile, denoted as the MMT in line with standard DLNM terminology. The MMT was restricted to the 1st–50th percentile range to minimise the influence of extreme values.

2.2.3. Maternal and fetal characteristics

In this sub-analysis, for each maternal or fetal characteristic, we pooled the PTB exposure–response curves across categories, treating each category as a level of a factor (F_c). A joint *meta*-analysis was then performed following the approach of Sera et al. (2019) (Sera et al., 2019). The model assumed a hierarchical structure with locations nested within the interaction between country and F_c as the random effect. The fixed-effects component included F_c , $rgT\text{mean}$, and their interaction ($F_c \times rgT\text{mean}$). The contribution of each characteristic was evaluated using a multivariate Wald test on the $F_c + F_c \times rgT\text{mean}$ terms, representing the total effect of F_c (Hayes, 2017).

This joint *meta*-analytic model was selected to approximate the results that would have been obtained by separately *meta*-analysing the location-specific exposure–response curves for each category using the main model, ensuring a conservative approach. Inclusion of interaction terms in both fixed and random components allows for potential differential effects across categories, as would occur if each category were analysed individually. Sensitivity analyses comparing both *meta*-analytical approaches (see sFig. 7) confirmed high robustness, except for the Caucasian ethnicity category.

2.2.4. Heat as a trigger of labour

We conducted a joint *meta*-analysis pooling curves for all GA categories, examining completed gestational weeks as a continuous metric of heat-related delivery risk. The dose–response *meta*-analytical model (Sera et al., 2019) assumed locations nested within the interaction between country and F_e as the random effect, with F_e identifying each GA category. The fixed-effects component included $rgT\text{mean}$ plus a natural spline of gestational week ($g\text{week}$), with an internal knot at 32, the midpoint of the 22–42 week range. Each $g\text{week}$ was assigned to the midpoint of its category interval (e.g., extreme PTB = 24.5 weeks). This approach allows derivation of non-linear heat-related delivery risk across all gestational weeks.

This model approximates results that would have been obtained by separately *meta*-analysing each GA category, important as differences between GA groups may reflect intrinsic vulnerabilities beyond gestational age. Sensitivity analyses comparing this continuous approach with categorical (F_e) and separate *meta*-analyses confirmed high robustness (see sFig. 8).

2.2.5. PTB burden

We applied health impact assessment (HIA) methods to convert the exposure–response relationships between heat and PTB into attributable burdens at regional and national levels. Compared with relative risks, these burden estimates provide more intuitive metrics, facilitating clearer communication to both the public and policymakers.

We followed standard procedures to calculate attributable numbers (AN) and fractions (AF) in the DLNM context (Gasparrini and Leone, 2014). Briefly, for each day t in each location, the overall cumulative RR for that day's temperature, with MMT as reference, was used to estimate the fraction and number of PTB attributable to heat (i.e., temperatures above the MMT) over the following four days. The total AN of PTB due to heat was obtained by summing daily AN_{*t*} contributions from days exceeding MMT. Empirical CIs (eCIs) for AN were derived using Monte Carlo simulations assuming a multivariate normal distribution of the reduced coefficients. Location-specific AN estimates and simulations were then aggregated to the national level to calculate AF and 95% CIs.

Overall cumulative risk and MMT were derived from Best Linear Unbiased Prediction (BLUP) curves for each location from our meta-analytical PTB model. BLUP curves combine pooled coefficients with a shrinkage estimate of city-specific deviations, balancing local and population-level information (Gasparrini et al., 2012). Burden results were also expressed as PTB rates per million live births by dividing AN by the total number of births in each location and multiplying by one million—equivalent to multiplying the AF by the location-specific PTB incidence.

All analyses were conducted in R (version 4.3.3 for Windows) using the gnm (Turner and Firth, 2007), dlnm (Gasparrini and Armstrong, 2013) and mixmeta (Sera and Gasparrini, 2022) packages.

3. Results

3.1. Study locations and birth dataset

Table 1 shows the descriptive statistics from each country. Our study included 86 million births from 250 locations across 13 countries worldwide, out of them 36.6 million took place in the warm season. Each location contributed an average of 24 years of data (with a minimum of 3 years) between 1979 and 2019.

Our study locations, although unevenly distributed, cover most of the regions of the globe, including North America (Canada, US), South America (Brazil, Chile, Ecuador, Paraguay), Southern Europe (Italy, Spain), Western Europe (Switzerland) and Northern Europe (Estonia), Middle East (Israel), Eastern Asia (Japan) and Oceania (Australia). This allowed us to assess the heat-PTB impact in populations with distinct characteristics and climates. PTB was defined as a live birth with reported gestational age below 37 completed gestational age weeks. On average, 6.9% of all births during the warm season were born preterm,

Table 1

Descriptive summary.

Country	Cities	Period	Warmer months	Temperature	Births	PTB
Australia	3	2001–2019	November- March	21.8	527.3	5.34%
Brazil	27	2010–2018	November- March	25.7	3,617.7	11.57%
Canada	19	1986–2012	May- September	16.7	2,032.4	6.12%
Chile	11	1992–2018	November- March	16.3	1,746.5	5.88%
Ecuador	2	2013–2019	December- April	21.4	234.5	9.08%
Estonia	4	2004–2018	May- September	14.7	50.2	4.77%
Israel	22	2000–2014	June- October	26.0	368.1	5.59%
Italy	6	2001–2019	May- September	23.1	211.9	6.16%
Japan	47	1979–2018	May- September	23.2	20,464.1	4.24%
Paraguay	1	2017–2019	November- March	27.0	10.5	10.44%
Spain	52	1990–2014	May- September	21.2	1,763.8	6.65%
Switzerland	16	2008–2017	May- September	15.8	345.0	4.09%
USA	40	1981–2018	May- September	25.0	5,239.9	9.33%

Number of cities, warm season definition, mean temperature during warm season (°C), total number of births during warm season (thousands) and preterm birth (PTB) percentage during the warm season.

ranging by country between 4.1% (Switzerland) and 11.6% (Brazil). Regarding climate, Estonia and Paraguay had the coldest and hottest warm seasons, with mean temperatures of 14.7 °C and 27 °C, respectively, during the warm season. By location, we can observe (Fig. 1) that warmer locations—those showing higher absolute temperatures in the warm season—, mainly in South America and North America, reported higher PTB percentages. Climate zone (Kottek et al., 2006) patterns shown in sFig. 1.

3.2. Risk of prematurity associated with heat

The resulting pooled overall exposure–response curve for temperature and PTB is shown in Fig. 2 A, suggesting that on average, across the 250 locations, the risk of PTB increases almost linearly with rising temperatures in the warm season. In particular, assuming the 1st percentile as reference, the risk of PTB increases by 2.80% (95%CI: 0.51%, 5.15%) at moderate heat days (i.e. 75th percentile) during the following 4 days, and by 3.80% (95%CI: 0.61%, 7.08%) for extreme heat days (i.e., 95th percentile). Lag-specific estimates show the highest risk in the first stratum (0–1 days after exposure; sFig. 2).

As illustrated in Fig. 2 B, moderate heat was associated with increased PTB risk in all countries, ranging from 2.39% (95%CI: 0.38%, 4.44%) in Brazil to 3.31% (95%CI: 0.30%, 6.40%) in Canada. Regarding extreme heat, estimates were more imprecise and no risk was observed in tropical countries. Canada showed the highest risk (6.00% (95%CI: 1.80%, 10.37%)), while Ecuador showed the lowest (−0.15% (95%CI: −3.36%, 3.16%)). Apart from the tropical climate, the risk of extreme heat is of higher magnitude than the risk of moderate heat although, as mentioned, it is less precise. Note that the 1st percentile in all country-specific curves was used as the reference, as it showed the lowest PTB risk (MMT percentile), except Brazil and Ecuador, which had 28th and 30th percentiles, respectively. Estimates are reported in sTable 3, and pooled curves in sFig. 3 and sFig. 4.

Stratified analyses revealed patterns suggesting that specific maternal and fetal characteristics may modulate the heat-PTB association (Fig. 2 C). In particular, we found that mothers younger than 24 years, with non-university education, low socioeconomic status and single, who were multiparous, as well as pregnancies with female fetuses, may have higher heat-related PTB risk (Fig. 2 C). Nevertheless, the statistical significance, evaluated by the multivariate Wald test, was only confirmed for education and marital status (sTable 4) (pooled curves in sFig. 5).

3.3. Heat as a trigger of labour

Previous evidence suggests that the risk of mortality and morbidity gradually increase as the newborn's gestational age decreases, thus indicating that the 37-week cutoff is somewhat arbitrary (Saigal and

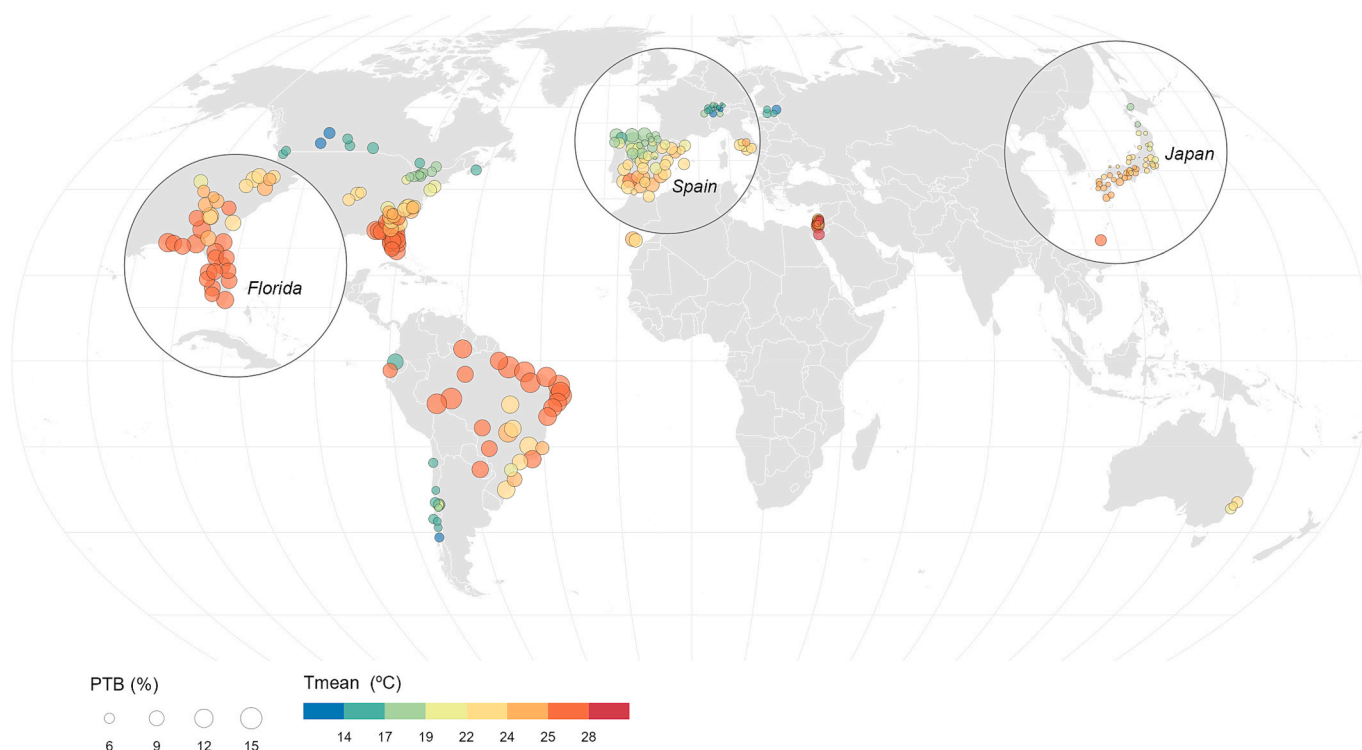


Fig. 1. Mean temperature and preterm birth (PTB) percentage during the warm season across 250 locations in 13 countries (1979–2019).

Doyle, 2008; Stewart et al., 2019). In this analysis, we aimed to explore whether and how heat could shorten gestation, with a particular focus on different Gestational Age (GA) categories of prematurity and two categories of at-term births.

sFig. 6 shows the distribution of all births and PTB by gestational category and country of study. In our sample, 68% of the 36.6 million births taking place in the warm season were full ATB and 26% early ATB. In comparison, most of the PTB were late PTB (5.2%), and only 0.56% and 0.29% were very and extreme PTB, respectively, with similar patterns in each country-specific distribution (see sFig. 6).

We identified a sensitive gestational window for moderate heat between week 31 and week 40, and a slightly extended period (from week 30 to week 41) for extreme heat (Fig. 3 A). We then predicted the risk for each endpoint and consistently, found a higher risk for late PTB, whereas risks for extreme and very PTB were lower and highly imprecise for extreme PTB. Specifically, moderate heat was associated with a 2.21% (95%CI: 0.73%, 3.71%) increase in the risk of late PTB, which rose to 3.84% (95%CI: 1.64%, 6.08%) for extreme heat. Interestingly, heat would also increase the chances of at-term birth, with an increase at extreme heat of 3.66% (95%CI: 2.21%, 5.14%) and 2.97% (95%CI: 1.03%, 4.94%), for the early and full ATB, respectively (Fig. 3 B).

3.4. Prematurity burden attributed to heat

Table 2 shows the PTB burden attributed to heat during the warm season overall and by country. Overall, we estimated that 1.41% (95% CI: 1.29, 1.52) of PTB can be attributed to heat during the warm season. The prevalence of prematurity in each location was then translated into an overall PTB rate of 855 (95%CI: 781, 921) per million live births. By country, the lowest heat-PTB rate was observed in Switzerland, 628 (95%CI: 509, 743), while the highest was in Paraguay, 1347 (95%CI: 340, 2348). By location, burdens ranged from 501 (95%CI: 48, 934) in Antofagasta (Chile) to 1726 (95%CI: 676, 2768) in Leon (Spain). (Fig. 4, sFig. 9 with the corresponding AF).

4. Discussion

This study confirms that pregnant people and their newborns are particularly vulnerable to high temperatures and highlights heat as an important environmental factor contributing to a substantial prematurity burden. Specifically, we estimated that 855 PTBs per million births across 250 locations in 13 countries are attributable to heat, corresponding to 1.41% of warm-season PTBs. This magnitude is comparable to the contribution of some well-established risk factors in high-income countries, such as overweight and obesity; for example, the fraction of PTB attributed to overweight/obesity and smoking was estimated at 3.6% in Germany (Reiss et al., 2015). Notably, our estimate is similar to the impact of malaria (1.92%) and exceeds that of maternal smoking (0.16%) in LMICs (Bryce et al., 2022).

Our findings are consistent with previous country-specific epidemiological assessments in Europe, Asia, and North America, which have shown increased PTB risk associated with heat (Bont et al., 2022; Cheng et al., 2020; Darrow et al., 2024; Sun et al., 2019; Vicedo-Cabrera et al., 2014). However, heat-attributable PTB estimates have rarely been reported. Sun et al. reported that 0.17% of all PTB in the US were attributable to heat, corresponding to 154 PTBs per million births (Sun et al., 2019), while Nyadanu et al. estimated over twice this excess (360 per million) in Australia (Nyadanu et al., 2022b), and 881 heatwave-PTBs per million births (2.6% of warm-season PTBs) were reported in China (Zhang et al., 2022). Considering differences in methods and study design, our estimated burden is broadly comparable with these previous findings.

We observed differences in risks across countries, suggesting that contextual factors such as climate, socioeconomic characteristics and healthcare infrastructure may modulate the vulnerability of pregnant women to heat. Specifically, locations in a continental climate, such as in Canada or Estonia, showed a larger extreme heat-PTB risk, while we identified weaker associations in tropical countries like Brazil or Ecuador. Differences in heat exposure (i.e., duration and severity of events) and preparedness and adaptive capacity (e.g., early warning systems) may potentially influence vulnerability across locations (IPCC,

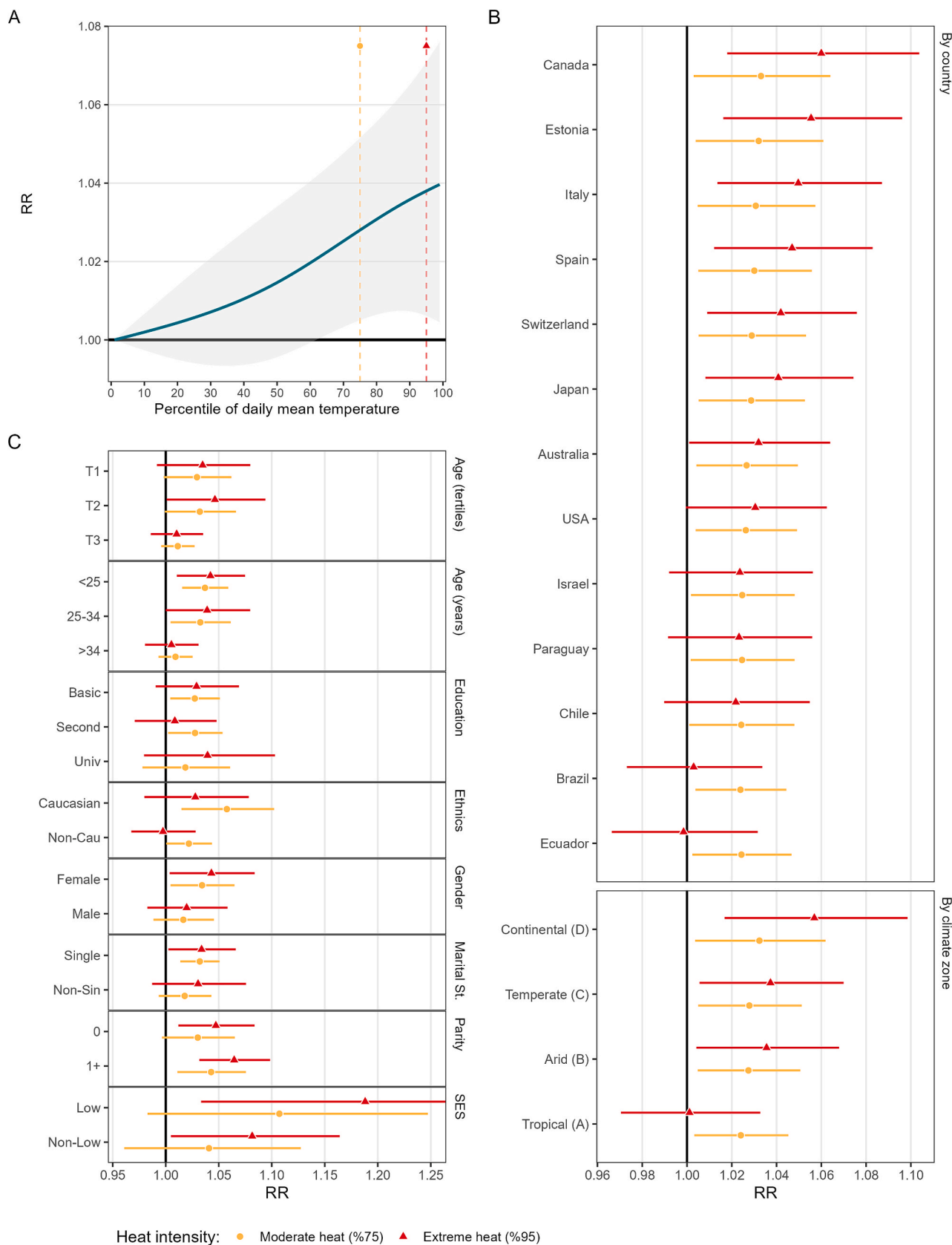


Fig. 2. Heat-Preterm birth (PTB) association in the warm season of 250 locations in 13 countries (1979–2019). A: Overall Relative Risk (RR) of PTB by temperature percentile, using the 1st percentile as reference; dashed orange and red lines mark moderate and extreme heat (75th and 95th percentiles), respectively; shaded area indicates 95% confidence interval (CI). B: RR at moderate and extreme heat by country and climate zone (bars: 95% CI). C: RR at moderate and extreme heat by maternal and foetal characteristics (bars: 95% CI). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

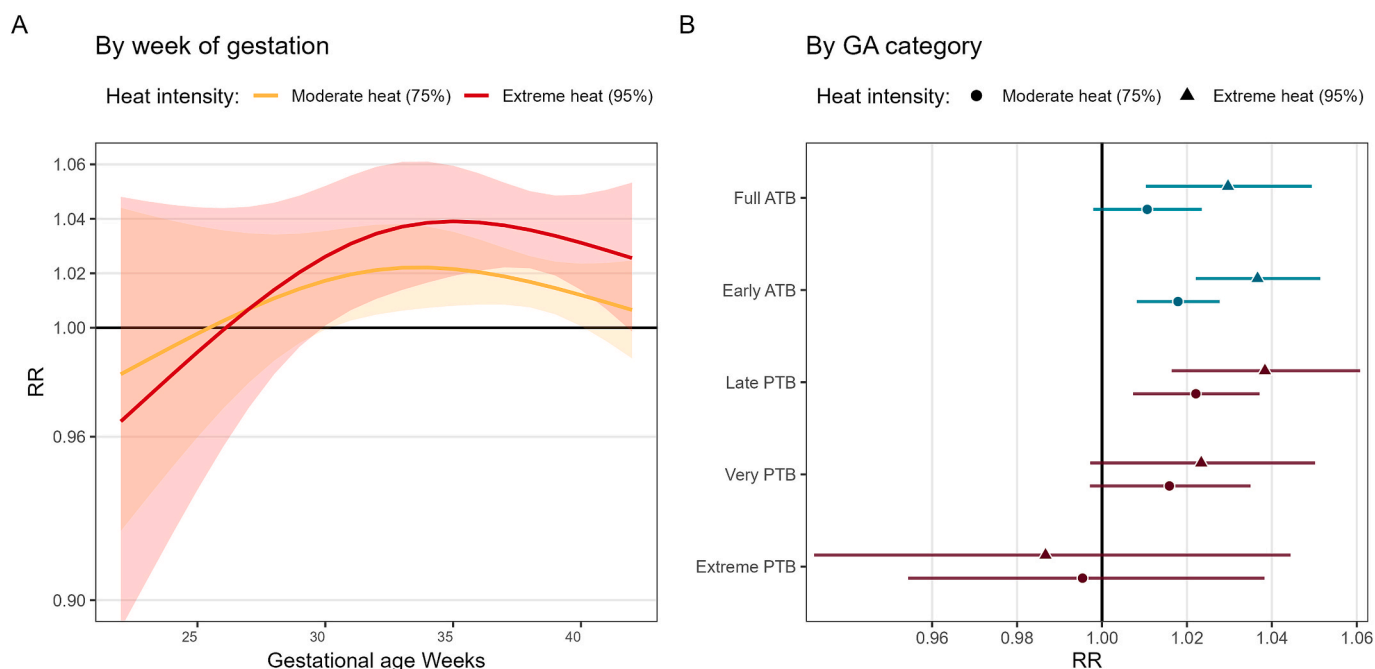


Fig. 3. Risk of birth associated with moderate and extreme heat exposure during the warm season in 245¹ locations (13 countries, 1979–2019). A: Heat-related birth risk by completed gestational week (orange: moderate heat, red: extreme heat); shaded areas indicate 95% CI. B: Risk by Gestational Age (GA) category: extreme PTB (22–27 weeks), very PTB (28–31), late PTB (32–36), early ATB (37–38), full ATB (39–42); bars: 95% CI. ¹The complete set unless five locations — Qiryat Shmona and Tiberias (Israel), Rieti (Italy), and Teruel (Spain) —not achieving model convergence for ‘Extreme PTB’. Prematurity burden attributed to heat. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

2022), as reflected in the different geographical patterns of our PTB rates. Recent reviews also suggest that the country’s income level may be a relevant driver of differences in heat-PTB risk across populations, with larger risks observed in low-income countries (Lakhoo et al., 2025; Nyadanu et al., 2024).

Some maternal and fetal characteristics appeared to modulate heat-related PTB risk. In particular, younger mothers with non-university education and low socioeconomic status seemed more vulnerable to heat in terms of increased risk of PTB, in agreement with previous studies (Chersich et al., 2020; Son et al., 2019; Syed et al., 2022). Socioeconomically disadvantaged individuals are more likely to live in areas more affected by the urban heat island effect, have limited adaptive capacity and face other environmental stressors that may interact with heat (Hsu et al., 2021). Single and Caucasian mothers showed higher PTB risks from heat, similarly to a study in the US (Sun et al., 2019). However, these findings should be interpreted with caution due to larger imprecision in the estimates. As suggested by a systematic review (Chersich et al., 2020), female fetuses might be more vulnerable than males. Finally, unlike a recent Australian study (Jegasothy et al., 2022), we did not find clear evidence of high vulnerability among women of different parity.

Finally, we also explored the heat-related risk of delivery across gestational length and found that heat would be a triggering factor of labour with larger risks between 31 and 40 gestational age weeks, corresponding to late PTB and early ATB. Interestingly, though comparatively minor, an increased risk was also observed in full-term births (≥ 39 weeks), in line with findings of previous assessments (Auger et al., 2014; Barreca and Schaller, 2020; Spolter et al., 2020; Yüzen et al., 2023). This evidence supports our hypothesis that heat may trigger delivery not only in fetuses who are inherently more vulnerable due to underlying conditions (e.g., congenital anomalies, intrauterine growth restriction, placental insufficiency) or physiological immaturity, but also in those sufficiently mature and developing optimally. The absence of an association in extreme or very preterm births, also widely documented Auger et al. (2014), may stem from several factors. The extreme frailty of

extreme and very PTB could prioritise other mechanisms, unrelated to environmental factors, such as infections, as drivers of delivery (Moutquin, 2003) and might also lead to a significant number of in-utero fetal deaths, competing with live birth delivery in response to heat (Hajdu, 2025). Also, the lack of an observed effect may result from limited statistical power due to data scarcity.

Several biological mechanisms have been proposed through which heat exposure may increase the risk of delivery, particularly, but not exclusively, during critical windows leading to PTB (Darrow et al., 2024). Pregnant women are especially vulnerable due to physiological and hormonal changes, including increased internal heat production from fetal growth and reduced heat dissipation from weight gain (Baharav et al., 2023). Animal studies suggest mechanisms such as elevated maternal temperature (triggering contractions), dehydration (causing electrolyte imbalances, increased blood viscosity, and reduced utero-placental blood flow), endocrine dysregulation, altered glucose metabolism, and inflammatory or oxidative stress, all contributing to preterm labour (Samuels et al., 2022). Emotional stress may intensify these biological responses (Lin et al., 2017). Alternatively, heat has been linked to maternal morbidities like gestational diabetes and pre-eclampsia, both independent risk factors for PTB (Shashar et al., 2020) and connected with the premature membrane rupture, leading to natural or clinically induced labour (Jiao et al., 2023).

To our knowledge, this is the first multi-site study to provide a comprehensive perspective on the association between heat and PTB across different countries and climates, using a standard and well-established methodology. Nearly a hundred observational studies have examined this topic worldwide, with over a dozen reviews and meta-analyses synthesising their findings. However, methodological differences across primary studies led to extremely heterogeneous pooled estimates (Nyadanu et al., 2024). Our study also contributes to covering existing evidence gaps (Meherali et al., 2024), by including a limited, though non-negligible, number of locations (44 out of 250) from the Global South (Lakhani et al., 2024) and countries barely studied such as Estonia, or with extreme social within-country inequalities such as USA,

Table 2

Preterm birth (PTB) burden attributed to heat during the warm season in the 250 locations (13 countries) included in this study (1979–2019).

Country	PTB AF (CI95%)	PTB Rate (CI95%)
Paraguay	1.28 (0.32, 2.24)	1347 (340, 2348)
USA	1.38 (1.09, 1.67)	1289 (1019, 1555)
Brazil	1.02 (0.78, 1.25)	1174 (900, 1446)
Spain	1.63 (1.38, 1.86)	1080 (919, 1234)
Canada	1.76 (1.4, 2.17)	1078 (854, 1329)
Italy	1.58 (0.76, 2.45)	974 (467, 1511)
Estonia	1.71 (1.03, 2.36)	814 (491, 1124)
Israel	1.43 (1.07, 1.76)	799 (600, 984)
Chile	1.29 (0.79, 1.76)	756 (463, 1035)
Ecuador	0.83 (0.33, 1.35)	748 (295, 1225)
Australia	1.4 (0.59, 2.21)	747 (315, 1177)
Japan	1.56 (1.36, 1.75)	663 (579, 744)
Switzerland	1.53 (1.24, 1.81)	628 (509, 743)
All	1.41 (1.29, 1.52)	855 (781, 921)

PTB AF: PTB fraction attributable to heat(%), PTB Rate: PTB Rate (per million births) attributable to heat. Color scales classify estimates into seven increasing-magnitude categories, from light to dark red.

Brazil or Chile (Chancel et al., 2022). However, the estimates from this assessment should not be considered representative of the risk and burden of prematurity worldwide, as other relevant regions are hardly covered, such as Africa or Asia. The large size and high quality of the individual data used enabled us to conduct a novel yet complex analysis of critical susceptible exposure windows, as well as a detailed assessment by vulnerable subpopulations and across different PTB severity types. We employed a state-of-the-art methodology, specifically a two-stage time series analysis with distributed lag non-linear models, to account flexibly for the potential non-linearities in the association and contribution of past exposures (Gasparrini, 2014). We applied the corrected pregnancy-at-risk approach, as described by Vicedo-Cabrera et al., to account for potential biases due to the seasonality of conception (Vicedo-Cabrera et al., 2014). Finally, this study provides estimates of the burden of PTB associated with heat across countries. These burdens, which facilitate a better understanding of our results for both the public and policymakers, can be key in decision-making processes.

We must acknowledge the presence of a high degree of heterogeneity in the data (i.e., different period lengths, within-country coverage, and information quality), leading to potentially larger uncertainty in the estimates. This heterogeneity, to some extent unavoidable, reflects regional variability in epidemiological capacities, including maternal-birth registries and surveillance systems worldwide. Additionally, we could not exclude programmed deliveries since this information was missing in most of the countries. However, we acknowledge that by restricting to singleton pregnancies, a high proportion of induced births would have been excluded. Also, we cannot rule out some degree of

regionally varying misclassification in PTB diagnosis due to the method used to define gestational age. We could not ascertain whether gestational dating was based on self-reported last menstrual period (LMP), clinical diagnosis, and/or ultrasounds. Compared to first-trimester ultrasonography, other methods may lead to underreporting of PTB, particularly in the extreme and very preterm categories. We also lack information on other relevant biological, socio-demographic, and behavioural factors (e.g., underlying health conditions, access to healthcare, occupation, substance use, and nutrition). In addition, our exposure metric was based on ambient temperature data from fixed weather monitoring stations, which inherently leads to some degree of exposure misclassification due to spatial variability. However, in ecological studies, this represents the average exposure during a day in the study population, only affecting the precision of the estimates. While we relied on a single heat metric, a fuller understanding of heat effects would likely require consideration of alternative measures, such as heat waves, absolute temperatures, or diurnal variability. All the aforementioned limitations may have undoubtedly impacted the results of our study. However, we expect that any remaining exposure and outcome misclassification would be non-differential, likely attenuating the observed effect estimates toward the null.

This large multi-site study provides compelling population-based evidence of the adverse effects of heat on preterm delivery. The geographical pattern of risks, coupled with the spatial distribution of PTB rates worldwide, translated into a distinct geographical pattern of burdens, placing at the top countries with pronounced internal social inequalities. Our findings confirm that rising temperatures due to global

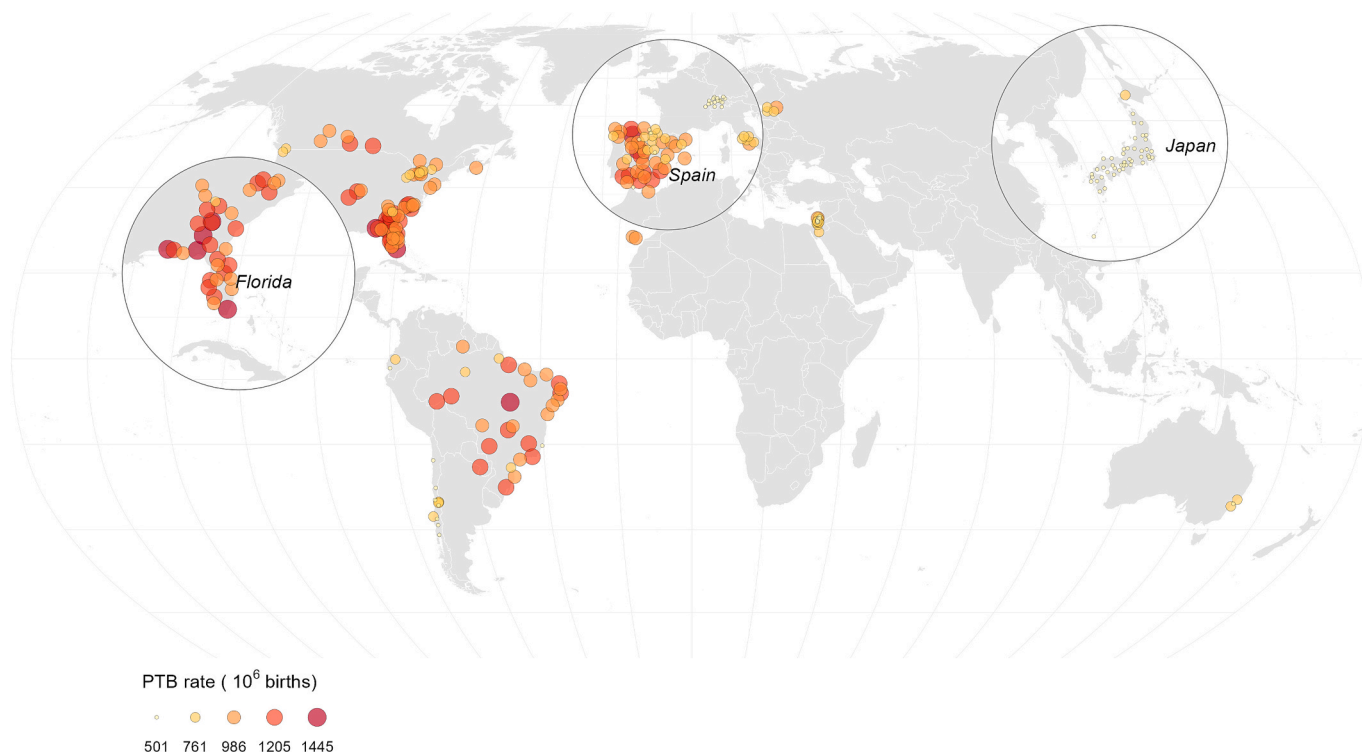


Fig. 4. Burden of preterm birth attributed to heat during the warm season in 250 locations across 13 countries (1979–2019).

warming is undermining years of progress in neonatal/infant health by increasing the risk of adverse birth outcomes. Thus, ambitious strategies to mitigate the effects of climate change on public health are now more imperative than ever.

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Code availability: The R code used to perform the main statistical analyses and generate the figures is available at <https://github.com/ihercar/heat-ptb-mcc>. The repository includes the full analysis pipeline and a synthetic and fictitious dataset that allows users to reproduce and test the code workflow.

CRediT authorship contribution statement

Carmen Iniguez: Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization, Software. **Coral Salvador:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Keren Agay-Shay:** Writing – review & editing, Data curation. **Howard H. Chang:** Writing – review & editing, Formal analysis, Data curation. **Francesca de’Donato:** Writing – review & editing, Data curation. **Yoonhee Kim:** Writing – review & editing, Data curation. **Shoko Konishi:** Writing – review & editing, Data curation. **Eric Lavigne:** Writing – review & editing, Data curation. **Hans Orru:** Writing – review & editing, Data curation. **Martina S. Ragettli:** Writing – review &

editing, Data curation. **Weeberb J. Requia:** Writing – review & editing, Data curation. **Dominic Royé:** Writing – review & editing, Visualization, Data curation. **Tanya Singh:** Writing – review & editing, Formal analysis, Data curation. **Joshua Warren:** Writing – review & editing, Formal analysis, Data curation. **Nicolás Valdés:** Writing – review & editing, Data curation. **Ben Armstrong:** Writing – review & editing, Data curation. **Antonio Gasparrini:** Writing – review & editing, Data curation. **Francesco Sera:** Writing – review & editing, Data curation. **Aurelio Tobías:** Writing – review & editing, Data curation. **Ana Maria Vicedo-Cabrera:** Writing – review & editing, Writing – original draft, Supervision, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2026.110286>.

Data availability

The original datasets analysed in this study contain individual-level health records and are subject to data protection regulations; therefore, they cannot be shared publicly. Access to intermediate outputs may be granted upon reasonable request and in compliance with institutional and legal restrictions.

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