

# Extreme heat increases the risk of intrapartum-related asphyxia: evidence from maternal-neonatal cohorts in West Africa

**Anna Dimitrova**

[anna.k.dimitrova@gmail.com](mailto:anna.k.dimitrova@gmail.com)

Barcelona Institute for Global Health <https://orcid.org/0000-0003-2715-9276>

**Nathalie Beloum**

MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine, The Gambia

**Toussaint Rouamba**

Institut de Recherche en Sciences de la Santé–Clinical Research Unit of Nanoro (IRSS-CRUN), Nanoro, Burkina Faso

**Bully Camara**

MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine, The Gambia

**Usman Nakakana**

MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine, The Gambia

**Joel Bognini**

Institut de Recherche en Sciences de la Santé–Clinical Research Unit of Nanoro (IRSS-CRUN), Nanoro, Burkina Faso <https://orcid.org/0000-0002-8465-2895>

**Athanase Somé**

Institut de Recherche en Sciences de la Santé–Clinical Research Unit of Nanoro (IRSS-CRUN), Nanoro, Burkina Faso

**Hawanatu Jah**

MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine, The Gambia

**Ebrahim Ndure**

MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine, The Gambia

**Hannah Blencowe**

London School of Hygiene and Tropical Medicine, London, UK

**Marie-Laure Volvert**

Department of Women and Children's Health, School of Life Course and Population Sciences, King's College London, London, UK

**Peter von Dadelszen**

King's College London

**Helen Brotherton**

MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine, The Gambia

**Christian Bottomley**

London School of Hygiene and Tropical Medicine, London, UK

**Halidou Tinto**

Institut de Recherche en Sciences de la Santé–Clinical Research Unit of Nanoro (IRSS-CRUN), Nanoro, Burkina Faso

**Umberto D'Alessandro**

MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine, The Gambia

**Anna Roca**

ISGlobal, Campus Hospital Clínic-Universitat de Barcelona, Barcelona, Spain

---

**Article**

**Keywords:**

**Posted Date:** August 3rd, 2026

**DOI:** <https://doi.org/10.21203/rs.3.rs-10130591/v1>

**License:**  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

**Additional Declarations:** There is **NO** Competing Interest.

---

# Abstract

Intrapartum-related asphyxia (IRA) is a major cause of neonatal mortality and long-term neurodevelopmental impairment, yet little is known about the role of environmental stressors. Using clinical cohort data from 13,803 births in The Gambia and Burkina Faso linked to ERA5 temperature data, we applied a time-stratified case-crossover design to investigate the short-term effects of heat exposure on IRA. Exposure to extreme daytime heat in the days preceding delivery was associated with increased odds of IRA, with stronger associations observed at higher temperature thresholds and longer exposure durations. Among live births, the most extreme multi-day heat events nearly doubled the odds of IRA. No associations were observed for minimum temperatures. These findings suggest that extreme heat may act as an acute trigger of intrapartum complications and highlight the need to strengthen maternal and newborn health systems in regions facing increasing heat exposure.

## Introduction

Intrapartum-related asphyxia (IRA), resulting from inadequate oxygen transfer during labour, is a major cause of stillbirth, neonatal mortality, and long-term neurodevelopmental impairment<sup>1–5</sup>. The burden is disproportionately concentrated in low- and middle-income countries, especially in sub-Saharan Africa (SSA)<sup>3,4,6–9</sup>, where consistent access to timely and high-quality obstetric and neonatal care remains limited<sup>3,10</sup>.

Despite its importance, the determinants of IRA remain poorly understood. Studying IRA requires detailed antepartum, intrapartum, and immediate postnatal information collected at or immediately after delivery, including indicators of fetal distress and neonatal resuscitation. However, these indicators are often unavailable or inconsistently recorded in routine facility data. As a result, many studies rely on proxy measures such as Apgar scores, which are themselves rarely available from large population-based datasets or even in routine facility data. This scarcity of high-quality standardized intrapartum data has constrained large-scale analyses of IRA and its risk factors.

Heat exposure during pregnancy has been increasingly associated with adverse perinatal outcomes, including preterm birth, stillbirth, and neonatal mortality<sup>11–14</sup>. However, evidence on whether acute heat exposure can trigger intrapartum complications leading to asphyxia remains limited. This question is particularly relevant in SSA, where both climate vulnerability and health system constraints are substantial<sup>8,14–16</sup>. The region has experienced faster warming than the global average, alongside an increasing frequency and intensity of extreme heat events<sup>17,18</sup>. At the same time, access to high-quality intrapartum care remains inadequate in many settings<sup>19–21</sup>. This is particularly the case in West and Central Africa, which bear the highest burden of stillbirths and neonatal mortality globally<sup>22,23</sup>.

In this study, we investigate the association between ambient heat exposure in the days preceding delivery and the risk of IRA using clinical delivery data from three maternal cohorts in The Gambia and Burkina Faso. By linking individual birth records to high-resolution temperature estimates and applying a

time-stratified case-crossover design, we estimate the short-term effects of extreme heat exposure and explore heterogeneity across population subgroups.

## Results

### Baseline characteristics

We analysed 14,252 births from three maternal cohorts conducted in The Gambia and Burkina Faso between 2013 and 2022. Birth records were linked to ERA5 temperature data, and associations between short-term heat exposure and IRA, defined as a 1-minute Apgar score <7 including intrapartum stillbirths, were estimated using a time-stratified case-crossover design.

Of 14,252 births available for analysis, we excluded births with missing information on date of birth, 1-minute Apgar score, or place of delivery ( $n=289$ ; Figure 1). We also excluded: (i) births with congenital anomalies ( $n=137$ ) because such conditions may independently affect neonatal outcomes and Apgar scores through non-hypoxic pathways, potentially introducing misclassification of IRA; and (ii) macerated stillbirths ( $n=23$ ), as they indicate antepartum fetal death that may have occurred days before delivery and therefore likely fall outside the exposure window of interest. Among the 13,803 births included in our study population, we identified 491 cases of IRA (3.6%), of which 408 were among live births and 83 cases were stillbirths (17% of IRA cases).

Among the 491 IRA cases, the time-stratified case-crossover design identified 1,674 referent days (ratio 1:3.4). Exposure frequencies and temperature thresholds corresponding to each heat definition are shown in Supplementary Table S1.

**Table 1:** Description of the study population.

| Characteristic                          | Overall<br>(N=13,803) | IRA<br>(N=491) | non-IRA<br>(N=13,312) | p-value <sup>3</sup> |
|-----------------------------------------|-----------------------|----------------|-----------------------|----------------------|
|                                         | n                     | n (%)          | n (%)                 |                      |
| <b>Country</b>                          |                       |                |                       | 0.01                 |
| Burkina Faso                            | 5,346                 | 163 (3.0)      | 5,183 (97)            |                      |
| The Gambia                              | 8,457                 | 328 (3.9)      | 8,129 (96.1)          |                      |
| <b>Residence</b>                        |                       |                |                       | <0.001               |
| Rural/peri-urban                        | 6,219                 | 184 (3.0)      | 6,035 (97)            |                      |
| Urban                                   | 7,584                 | 307 (4.0)      | 7,277 (96)            |                      |
| <b>Season of birth</b>                  |                       |                |                       | 0.9                  |
| Dry                                     | 8,978                 | 318 (3.5)      | 8,660 (96.5)          |                      |
| Wet                                     | 4,825                 | 173 (3.6)      | 4,652 (96.4)          |                      |
| <b>Time of birth<sup>1</sup></b>        |                       |                |                       | <0.001               |
| Day                                     | 6,648                 | 281 (4.2)      | 6,367 (95.7)          |                      |
| Night                                   | 6,711                 | 201 (3.0)      | 6,510 (97)            |                      |
| Unknown                                 | 444                   | 9              | 435                   |                      |
| <b>Birthweight category<sup>2</sup></b> |                       |                |                       | <0.001               |
| Low                                     | 1,292                 | 75 (5.8)       | 1,217 (94.2)          |                      |
| Normal                                  | 12,487                | 411 (3.3)      | 12,076 (96.7)         |                      |
| Unknown                                 | 24                    | 5              | 19                    |                      |
| <b>Delivery mode</b>                    |                       |                |                       | <0.001               |
| Cesarian section                        | 280                   | 47 (17)        | 233 (83)              |                      |
| Vaginal birth                           | 13,513                | 441 (3.3)      | 13,072 (96.7)         |                      |
| Unknown                                 | 10                    | 3              | 7                     |                      |
| <b>Birth outcome</b>                    |                       |                |                       | <0.001               |
| Live birth                              | 13,720                | 408 (3.0)      | 13,312 (97)           |                      |
| Stillbirth                              | 83                    | 83 (100)       | 0 (0)                 |                      |

Notes: <sup>1</sup> Daytime hours were defined as 07:00–18:00 and nighttime hours as 18:00–07:00; <sup>2</sup> low birthweight was defined as <2.5 kg. <sup>3</sup> P-values are based on Pearson's Chi-squared test.

# IRA and extreme heat

Figure 2 summarizes associations between heat exposure and IRA across multiple temperature thresholds and exposure durations. Among all IRA cases (including both live births and stillbirths), increased odds of IRA were observed for extreme heat exposure defined as maximum daily temperature above the 90th percentile sustained for at least three consecutive days (OR = 1.80; 95% CI: 1.08–2.98; Figure 2, Panel A). More generally, effect estimates tended to increase with both higher temperature thresholds and longer exposure durations. No association or trend was observed between IRA and heat exposure based on daily minimum temperature (Figure 2, Panel C).

Among IRA cases restricted to live births, associations were stronger and more consistent. Increased odds of IRA were observed for heat events defined as maximum daily temperatures above the 85th percentile (OR = 1.68; 95% CI: 1.03–2.72; Figure 2, Panel B). Effect estimates increased with both higher temperature thresholds and longer durations of exposure. The largest effect was observed for temperatures above the 95th percentile sustained for three or more consecutive days (OR = 1.97; 95% CI: 0.99–3.90; Figure 2, Panel B). As in the full sample, no association or trend was found between IRA and daily minimum temperature among live births (Figure 2, Panel D).

## Subgroup differences in the association between heat exposure and IRA

Results from the subgroup analyses restricted to live births are presented in Figure 3. Associations between heat exposure and IRA were generally stronger among nighttime than daytime deliveries, particularly for heat events defined using maximum temperatures above the 80th percentile. For exposure on the day of delivery, the odds of IRA were elevated among nighttime deliveries (OR 1.88, 95% CI 1.01–3.52), whereas no association was observed among daytime deliveries (OR 0.64, 95% CI 0.37–1.09;  $p$ -interaction=0.01). Similar heterogeneity was observed for heat events lasting two consecutive days, with ORs of 2.02 (95% CI 1.10–3.72) and 0.75 (95% CI 0.44–1.28) for nighttime and daytime deliveries, respectively ( $p$ -interaction=0.02). However, these differences were not evident at higher temperature thresholds.

Some heterogeneity was also observed by delivery mode. Associations tended to be stronger among births delivered by caesarean section than among vaginal deliveries, with a statistically significant interaction for heat exposure above the 85th percentile on the day of delivery ( $p$ -interaction=0.02). Although effect estimates were generally larger during the dry season than the wet season, interaction tests provided no evidence that these differences were statistically significant. Likewise, no statistically significant heterogeneity was observed by country, residence, or birthweight.

Analyses based on minimum daily temperature showed little evidence of effect modification across subgroups. The only statistically significant interaction was observed for nighttime deliveries exposed to minimum temperatures above the 80th percentile for three or more consecutive days (OR 2.15, 95% CI 1.09–4.21), compared with daytime deliveries (OR 0.77, 95% CI 0.43–1.40;  $p$ -interaction=0.03).

These findings should be interpreted cautiously. The observed patterns were not consistent across alternative heat definitions, and the number of exposed observations within some subgroup-specific heat categories was small (Supplementary Tables S2–S7), limiting statistical power and increasing the possibility that some findings reflect chance variation rather than true effect heterogeneity.

## Robustness analysis

We observed modest associations between heat exposure and the occurrence of birth in both the non-IRA sample and the full cohort, particularly at extreme maximum temperatures above the 95th percentile (Supplementary Figure S1). However, these effect sizes were substantially smaller than those observed for IRA. Among the full sample, ORs ranged from 1.09 (95% CI: 1.02-1.16) for at least one day with maximum daily temperatures above the 85<sup>th</sup> percentile to 1.14 (95% CI: 1.02-1.28) for temperatures above the 95<sup>th</sup> percentile sustained for at least two consecutive days. Additionally, we found no consistent association between post-delivery heat exposure and IRA (Supplementary Figure S2) in our second robustness analysis.

## Discussion

Using high-quality clinical cohort data and a time-stratified case-crossover design, we found that exposure to extreme ambient heat on the day of delivery and the preceding days is associated with increased odds of IRA in West Africa, with stronger and more consistent effects observed among live births. Associations increased with both higher temperature percentiles and longer exposure durations, consistent with a dose–response relationship. For the most extreme heat events sustained over up to three consecutive days, the odds of IRA were nearly doubled. The smaller effect sizes observed in analyses including stillbirths may reflect differences in the timing and mechanisms of fetal compromise, as stillbirths could be influenced by heat exposure outside the short exposure window examined in this study.

Our findings are consistent with the limited epidemiological evidence linking heat exposure to adverse intrapartum outcomes. Two previous studies provide relevant evidence. A large population-based cohort in northwest China reported a 13.9–47.0% increased risk of intrapartum severe asphyxia, defined as 5-minutes Apgar score  $\leq 3$ , following exposure to extreme heat during late pregnancy<sup>39</sup>. The study was based on 182,322 births of which 1575 had severely asphyxia according to the definition. Similarly, a time-stratified case-crossover study in São Paulo, Brazil, using population-based birth registry data (several million singleton births), found that exposure to high ambient temperatures (95th vs 50th percentile) around the time of delivery was associated with an 8% increase in the odds of asphyxia, defined as 5-minute Apgar score  $\leq 7$ , among low-risk births<sup>40</sup>. The stronger effects observed in our study may reflect the use of prospectively collected cohort data or potentially greater vulnerability to heat exposure in West African settings. In addition, our use of 1-minute rather than 5-minute Apgar scores

may capture more immediate intrapartum compromise, whereas 5-minute scores can be influenced by neonatal resuscitation and post-delivery stabilisation.

Beyond these epidemiological studies, supporting evidence comes mainly from small physiological studies. In rural Gambia, a cohort study of 92 pregnant subsistence farmers found that high environmental heat was associated with signs of fetal strain, including elevated fetal heart rate and altered umbilical artery resistance, suggesting compromised fetal circulation under heat stress<sup>41</sup>. Similar alterations in placental blood flow under maternal heat exposure have been reported in both a field-based study in The Gambia and a clinical cohort study in China<sup>42,43</sup>. Several biological mechanisms support a plausible link between acute maternal heat exposure and intrapartum fetal compromise. Heat stress can impair placental function and reduce uteroplacental perfusion through cardiovascular strain, dehydration, and thermoregulatory responses that redistribute maternal blood flow toward the skin<sup>41,44</sup>. During labour, when uterine contractions intermittently reduce oxygen delivery<sup>45,46</sup>, this diminished placental reserve may limit fetal tolerance to hypoxic stress, increasing the risk of adverse intrapartum outcomes<sup>46–48</sup>.

In addition to direct physiological pathways, behavioural and health-system factors may also contribute to the observed associations<sup>49</sup>. Extreme heat may delay care-seeking during labour, particularly where travel to facilities is physically demanding or transport infrastructure is limited. Evidence from India suggests that heat exposure is associated with reduced maternal healthcare utilization during pregnancy<sup>50</sup>. Heat may also affect the quality of intrapartum care by increasing fatigue, cognitive strain, and reduced work capacity among healthcare workers, potentially compromising timely monitoring and intervention during labour. These challenges may be especially important in low-resource West African settings where staffing and facility capacity are already constrained. Because our analysis was restricted to facility-based deliveries, the observed associations may underestimate the broader impacts of extreme heat, particularly for women delivering at home or facing barriers to accessing skilled obstetric care during heat events.

The observed heterogeneity in effects further supports a multifactorial pathway linking heat exposure to IRA. Stronger associations among cesarean deliveries may reflect underlying obstetric complications, such as fetal distress or obstructed labour<sup>52</sup>, which can increase susceptibility to hypoxic stress and amplify the effects of acute heat exposure. Elevated associations during nighttime deliveries may reflect impaired recovery from daytime heat exposure and cumulative thermal stress, compounded by poor sleep, persistent indoor heat retention in poorly ventilated settings common in LMICs, and maternal physiological strain associated with hot nights. Differences in labour management or reduced staffing during night shifts may further contribute through less intensive monitoring or delayed obstetric intervention. However, these sub-group findings were not consistent across all heat definitions and should be interpreted cautiously.

Our robustness analyses suggest that the observed associations are unlikely to be driven solely by shifts in the timing of delivery. Although heat exposure was modestly associated with birth timing, consistent

with evidence linking heat to preterm labour<sup>34–38</sup>, these effects were substantially smaller than those observed for IRA. Prematurity is an established risk factor for IRA<sup>54,55</sup> and may increase susceptibility to acute intrapartum stressors, including heat exposure. However, the stronger associations observed in our study for IRA compared to overall birth timing suggest that preterm birth alone is unlikely to explain our findings and that additional mechanisms are likely involved. The lack of consistent associations between post-delivery heat exposure and IRA further supports the temporal specificity of the relationship.

Our findings are particularly relevant for sSA, where rising heat exposure<sup>17,18</sup> coincides with limited access to high-quality intrapartum care, especially in rural areas<sup>10,16,20,21</sup>. Coverage of essential services remains low, with only 15% of hospitals equipped to provide basic neonatal resuscitation<sup>10</sup>. The burden is especially pronounced in West Africa, which has one of the highest stillbirth and neonatal mortality rates globally<sup>22</sup>. Beyond early neonatal deaths, IRA is a major cause of long-term neurodevelopmental impairment, including cerebral palsy and cognitive disability, imposing substantial lifelong social and economic burdens in low-resource settings<sup>1,2,5</sup>. While therapeutic hypothermia improves outcomes in high-income settings, trials in sSA and South Asia have not demonstrated benefit<sup>56</sup>, highlighting the limited availability of effective treatments for IRA in these contexts. As extreme heat events become more frequent, the observed increased risks could translate into a considerable rise in preventable mortality and disability, underscoring the urgent need to strengthen intrapartum care and develop context-appropriate treatments for IRA in climate-vulnerable settings.

This study has several strengths. It uses high-quality clinical data with detailed information on perinatal outcomes, enabling a more specific definition of IRA than is possible in most population-based datasets. In addition, outcome data were collected in real time during labour by trained clinical staff, minimising the potential for recall bias. The use of a time-stratified case-crossover design reduces confounding by time-invariant individual characteristics and accounts for seasonality and long-term trends. The use of location-specific temperature percentiles allows for comparability across climatically distinct settings. However, some limitations should also be considered. First, the use of the 1-minute Apgar score as a proxy for IRA may introduce some misclassification, as Apgar scores reflect overall neonatal condition rather than a direct measure of hypoxia. However, this approach is widely used in settings where more detailed clinical diagnostics are unavailable. Second, temperature exposure was assigned at the facility level using gridded reanalysis data, which may not fully capture individual-level exposure, particularly indoor conditions.

In summary, our findings provide evidence that acute exposure to extreme heat in the days preceding delivery increases the risk of IRA in West Africa. These results support the hypothesis that extreme heat may act as a short-term trigger of intrapartum complications that compromise fetal oxygenation, particularly in settings with limited capacity for continuous intrapartum monitoring and neonatal care. As climate change intensifies the frequency and severity of heat events, heat-related intrapartum complications may become an increasingly important contributor to neonatal morbidity and mortality.

Strengthening intrapartum care, improving access to timely obstetric interventions and neonatal resuscitation, and incorporating heat exposure into maternal health risk assessment and early warning systems could help reduce preventable adverse birth outcomes.

## Data and methods

### Clinical data

This analysis uses data from three studies conducted in West Africa.

- i. The PregnAnZI-1 trial was a phase III, double-blind, placebo-controlled randomized clinical trial conducted in The Gambia. Overall, 829 women were recruited during labour at a single urban health facility between April 2013 and 2014. Clinical data were collected by study staff at delivery and during the follow-up visits conducted up to 28 days postpartum. The intervention was given during labour and did not have any effect on the Apgar score<sup>24</sup>.
- ii. PregnAnZI-2 was conducted in The Gambia and Burkina Faso between October 2017 and May 2021, with the same design as PregnAnZI-1<sup>24,25</sup>. Approximately 12,000 women were recruited at the time of labour across multiple health facilities in the two countries (urban in The Gambia and rural in Burkina Faso).
- iii. The PRECISE study is a prospective pregnancy cohort established across three countries in sSA to investigate placental disorders and adverse birth outcomes in low-resource settings<sup>26,27</sup>. Recruitment took place between June 2019 and December 2022. Pregnant women were enrolled during antenatal care and followed through delivery, with detailed clinical, demographic and biological data collected to characterize maternal health, pregnancy complications, and perinatal outcomes in both urban and rural populations. We used data from the Gambian study sites (rural and peri-urban), as this analysis focuses on West African populations.

Eligible women provided written informed consent during antenatal care visits, and eligibility was subsequently confirmed at the time of admission for delivery.

Low 1-minute Apgar score (Apgar-1' < 7) was used as a proxy for IRA. The Apgar score is a standardised clinical assessment of a newborn's condition after birth, based on five components (heart rate, respiratory effort, muscle tone, reflex response, and skin colour) each scored from 0 to 2, with a total score ranging from 0 to 10. Health facility staff were trained to assess and record Apgar scores at delivery. We used the 1-minute Apgar score because it directly reflects the newborn's condition immediately after labour and delivery, and it is not influenced by neonatal resuscitation efforts, for which detailed data were unavailable.

### Temperature data

Gridded daily maximum and minimum near-surface air temperature data were obtained from the ERA5 reanalysis dataset at a spatial resolution of 0.25° × 0.25°. The geographic coordinates of the

corresponding health facilities were used to link the individual births with the temperature data. To enable comparison across study populations located in climatically distinct regions, absolute temperature values were converted into location-specific temperature percentiles using the long-term temperature distributions for the period 2000–2021. Extreme heat exposure was defined using binary indicators based on percentile thresholds of the local temperature distribution (80th, 85th, 90th, and 95th percentiles) and exposure durations spanning the day of delivery and the two preceding days (lags 0-2).

### Estimation strategy

We apply a time-stratified case-crossover design, in which each IRA case day is matched to referent days within the same day of the week, month, and year, thereby controlling for seasonality, long-term trends, and time-invariant confounders. Associations between heat exposure and IRA were estimated using conditional logistic regression, which accounts for the matched nature of the data. For example, if an IRA case occurred on the first Monday of January 2021, the referent days for that case would be the remaining Mondays in January 2021, resulting in three to four matched referent days per case. The design compares exposure during the hazard period immediately preceding delivery with exposure during referent periods for the same individual, allowing each case to serve as their own control. As a result, all time-invariant characteristics, including maternal sociodemographic factors, underlying health status, household conditions, and stable community-level characteristics, are inherently accounted for by design, as these factors remain constant across the matched case and referent periods. This self-matched design is widely used in environmental epidemiology to investigate the short-term effects of transient exposures, such as temperature and air pollution, on acute health outcomes<sup>28–33</sup>.

### Assessment of effect heterogeneity

To investigate whether the association between heat exposure and IRA varied across population subgroups, we fitted conditional logistic regression models including interaction terms between heat exposure and country, residence (urban vs rural/peri-urban), season of delivery (dry vs wet), time of delivery (daytime vs nighttime), birthweight (normal vs low), and delivery mode (cesarean section vs vaginal birth). Statistical evidence of heterogeneity was assessed using Wald tests of the interaction terms.

### Robustness analysis

We evaluated the robustness of the analysis using two complementary approaches. First, to assess whether the observed associations reflect a true increase in the risk of IRA rather than a shift in the timing of delivery, we repeated the analyses among births without IRA (“healthy” cases) and in the full cohort using the same modelling framework. This approach evaluates whether heat exposure is associated with an increased likelihood of delivery on hot days—potentially driven by heat-induced preterm or early labour—rather than a specific increase in intrapartum complications. Previous studies have shown that exposure to high ambient temperatures can increase the risk of preterm birth<sup>34–38</sup>, raising the possibility of selection effects in case-only analyses.

Second, we conducted a negative control analysis using post-delivery heat exposure (+4, +5, and +6 days after the event), which cannot plausibly influence IRA. Any association observed in this analysis would therefore indicate bias arising from unmeasured time-varying factors or misspecification of the temporal structure of the model, rather than a causal effect.

## Ethics approval

Ethical approval for the included studies was obtained from the relevant institutional review boards. The PregnAnZI-2 trial was approved by The Gambia Government/Medical Research Council Unit The Gambia (MRCG) Joint Ethics Committee, the Comité d’Ethique pour la Recherche en Santé, Burkina Faso, the Ministry of Health of Burkina Faso, and the London School of Hygiene & Tropical Medicine Ethics Committee. PregnAnZI-1 was approved by the joint Gambia Government/Medical Research Council Ethics Committee. The PRECISE study was approved by the King's College London Research Ethics Committee (Ref HR-17/18–7855) and The Gambia Government/Medical Research Council Joint Ethics Committee (Ref SCC 1619). Written informed consent was obtained from all participants during antenatal care visits before enrolment, and eligibility was confirmed at the time of admission for delivery. The present secondary analysis was covered under the original study approvals and data-sharing agreements.

## Declarations

## Data availability

The individual-level clinical data analysed in this study are not publicly available because they contain sensitive participant information and are subject to ethical and data-sharing restrictions imposed by the original studies. De-identified data may be made available to qualified researchers upon reasonable request and subject to approval by the corresponding study investigators and relevant ethics committees. Requests for access to the PregnAnZI datasets should be directed to the MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine. Requests for access to the PRECISE data should be made through the PRECISE Network in accordance with its data-sharing policies. Summary data supporting the findings of this study are available from the corresponding author upon reasonable request.

## Code availability

The code required to reproduce the analyses presented in this study is publicly available in a GitHub repository at <https://github.com/annakdim/Heat-and-IRA>.

**Alternative Corresponding Author:** Anna Roca

**Funding:** The PregnAnZI-2 trials were funded by a grant from UK Research and Innovation under the Joint Global Health Trial Scheme (JGHT; reference No. MC\_EX\_MR/P006949/1) and UK MRC and the UK Department for International Development (DFID) under the MRC/DFID Concordat agreement (reference number MR/J010391/1) and is also part of the EDCTP2 programme supported by the European Union. The PRECISE Network was funded by the UK Research and Innovation Grand Challenges Research Fund GROW Award scheme (grant number: MR/P027938/1). The funders had no role in the design and conduct of the study, or the decision to submit the manuscript for publication.

## References

1. Hong J, Crawford K, Jarrett K, Triggs T, Kumar S (2024) Five-minute Apgar score and risk of neonatal mortality, severe neurological morbidity and severe non-neurological morbidity in term infants – an Australian population-based cohort study. *Lancet Reg Health West Pac* 44
2. Persson M, Razaz N, Tedroff K, Joseph KS, Cnattingius S (2018) Five and 10 minute Apgar scores and risks of cerebral palsy and epilepsy: population based cohort study in Sweden. *BMJ* 360
3. Lee ACC et al (2013) Intrapartum-related neonatal encephalopathy incidence and impairment at regional and global levels for 2010 with trends from 1990. *Pediatr Res* 74(Suppl 1):50–72
4. United Nations Inter-agency Group for Child Mortality Estimation (UN IGME) (2024) *Levels & Trends in Child Mortality: Report 2025 – Estimates Developed by the United Nations Inter-Agency Group for Child Mortality Estimation*. <https://data.unicef.org/resources/levels-and-trends-in-child-mortality-2025/>
5. Zhang S, Li B, Zhang X, Zhu C, Wang X (2020) Birth Asphyxia Is Associated With Increased Risk of Cerebral Palsy: A Meta-Analysis. *Front Neurol* 11
6. Kakooza-Mwesige A et al (2017) Prevalence of cerebral palsy in Uganda: a population-based study. *Lancet Glob Health* 5:e1275–e1282
7. Wudu MA et al (2025) Incidence and predictors of mortality among neonates admitted with birth asphyxia to neonatal intensive care units in Ethiopia: a systematic review and meta-analysis. *BMC Pediatr* 25:140
8. Adekanbi AO, Olayemi OO, Fawole AO, Afolabi KA (2015) Scourge of intra-partum foetal death in Sub-Saharan Africa. *World J Clin Cases: WJCC* 3:635
9. United Nations Inter-agency Group for Child Mortality Estimation (UN IGME). *Standing Up for Stillbirth: Current Estimates and Key Interventions* (2025)
10. Wall SN et al (2010) Reducing Intrapartum-Related Neonatal Deaths in Low- and Middle-Income Countries-What Works? *Semin Perinatol* 34:395–407
11. Lakhoo DP et al (2025) A systematic review and meta-analysis of heat exposure impacts on maternal, fetal and neonatal health. *Nat Med* 31:684–694
12. Shankar K et al (2023) Associations between ambient temperature and pregnancy outcomes from three south Asian sites of the Global Network Maternal Newborn Health Registry: A retrospective

- cohort study. *BJOG* 130:124–133
13. Dalugoda Y, Kuppa J, Phung H, Rutherford S, Phung D (2022) Effect of Elevated Ambient Temperature on Maternal, Foetal, and Neonatal Outcomes: A Scoping Review. *Int J Environ Res Public Health* 19
  14. Moodley Y, Asare K, Tanser F, Tomita A (2024) Maternal exposure to heat and its association with miscarriage in rural KwaZulu-Natal, South Africa: A population-based cohort study. *Women's Health* 20
  15. Prince MB, Frimpong B, Russo S (2021) Prenatal Exposure to Heat Waves and Child Health in Sub-Saharan Africa.
  16. Gyapong BB, Jones A, Bassett S, Anderson J (2025) The quality of intrapartum care in sub-Saharan Africa: a systematic scoping review. *Afr J Midwifery Womens Health* 19:1–17
  17. Intergovernmental Panel on Climate Change (IPCC) (2023) Climate Change 2021 – The Physical Science Basis: Working Group I Contribution to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change. *Climate Change 2021 – The Physical Science Basis* <https://doi.org/10.1017/9781009157896> doi:10.1017/9781009157896
  18. World Meteorological Organization (WHO). State of the Climate in Africa 2023. 1–33 (2024)
  19. Jena BH, Jaldo MM, Demesa YY, Kebede BA, Melaku LM (2025) Magnitude of neonatal mortality and its association with maternal and child health care in sub-Saharan Africa: a systematic review and meta-analysis. *Archives of Public Health* 2025 83:1 83, 219-
  20. Wan S et al (2023) A descriptive analysis of the coverage of newborn care services among women who delivered in health facilities in 17 sub-Saharan African countries. *BMC Pregnancy Childbirth* 23:256
  21. Chauke L (2025) Improving access to emergency obstetric care in low- and middle-income countries. *Best Pract Res Clin Obstet Gynaecol* 98:102572
  22. Hug L, Alexander M, You D, Alkema L (2019) National, regional, and global levels and trends in neonatal mortality between 1990 and 2017, with scenario-based projections to 2030: a systematic analysis. *Lancet Glob Health* 7:e710–e720
  23. Hug L et al (2021) Global, regional, and national estimates and trends in stillbirths from 2000 to 2019: a systematic assessment. *Lancet* 398:772–785
  24. Camara B et al (2022) Pre-delivery administration of azithromycin to prevent neonatal sepsis and death: a phase iii double-blind randomized clinical trial (PregnAnZI-2 trial). *Int J Clin Trials* 9:34
  25. Roca A et al (2023) Effect of Intrapartum Azithromycin vs Placebo on Neonatal Sepsis and Death: A Randomized Clinical Trial. *JAMA* 329:716–724
  26. Von Dadelszen P et al (2020) The PRECISE (PREgnancy Care Integrating translational Science, Everywhere) Network's first protocol: deep phenotyping in three sub-Saharan African countries. *Reproductive Health* 2020 17:1 17, 51-

27. Craik R et al (2025) PREgnancy Care Integrating translational Science, Everywhere (PRECISE): a prospective cohort study of African pregnant and non-pregnant women to investigate placental disorders – cohort profile. *BMJ Open* 15:e091831
28. Dimitrova A et al (2024) Temperature-related neonatal deaths attributable to climate change in 29 low- and middle-income countries. *Nature Communications* 2024 15:1 15, 1–11
29. Tobias A, Kim Y, Madaniyazi L (2024) Time-stratified case-crossover studies for aggregated data in environmental epidemiology: a tutorial. *Int J Epidemiol* 53
30. Janes H, Sheppard L, Lumley T (2005) Case-crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. *Epidemiology* 16:717–726
31. Maclure M (1991) The Case-Crossover Design: A Method for Studying Transient Effects on the Risk of Acute Events. *Am J Epidemiol* 133:144–153
32. Cortes TR et al (2025) Ambient temperature and non-accidental mortality: A nationwide space–time-stratified case-crossover study within the 100 million Brazilian Cohort. *Environ Int* 205:109892
33. Wang Y et al (2022) Health threat of PM2.5-bound trace elements exposure on asthma hospital admission: A time-stratified case-crossover study. *Environ Int* 170:107604
34. Part C et al (2023) Effects of ambient temperature on preterm birth, stillbirth, and low Apgar score in Soweto, South Africa: A case-crossover analysis. *ISEE Conference Abstracts* (2023)
35. Ilango SD et al (2020) Extreme heat episodes and risk of preterm birth in California, 2005–2013. *Environ Int* 137:105541
36. Samuels L et al (2022) Physiological mechanisms of the impact of heat during pregnancy and the clinical implications: review of the evidence from an expert group meeting. *Int J Biometeorol* 1:3
37. Syed S, O'Sullivan TL, Phillips KP (2022) Extreme Heat and Pregnancy Outcomes: A Scoping Review of the Epidemiological Evidence. *International Journal of Environmental Research and Public Health* Vol. 19, Page 2412 19, 2412 (2022)
38. Chersich MF et al (2020) Associations between high temperatures in pregnancy and risk of preterm birth, low birth weight, and stillbirths: systematic review and meta-analysis. *BMJ* m3811 10.1136/bmj.m3811
39. Tang Z, Wu M, Song G, Yang R, Wang Y (2021) Impact of ambient temperature exposure on newborns with low Apgar scores in northwest China. *Environ Sci Pollut Res* 28:36367–36374
40. Del Carretto M et al (2025) Short-term ambient heat exposure and low APGAR score in newborns: A time-stratified case-crossover analysis in São Paulo state, Brazil (2013–2019). *PLOS Global Public Health* 5:e0004557
41. Bonell A et al (2022) Environmental heat stress on maternal physiology and fetal blood flow in pregnant subsistence farmers in The Gambia, west Africa: an observational cohort study. *Lancet Planet Health* 6:e968–e976
42. Bonell A et al (2023) A feasibility study of the use of UmbiFlow™ to assess the impact of heat stress on fetoplacental blood flow in field studies. *Int J Gynecol Obstet* 160:430–436

43. Yuan X et al (2026) The association of heat stress with fetal umbilical artery blood flow: a birth cohort study in Beijing, China. *Environ Res* 288:123167
44. Périard JD, Eijsvogels TMH, Daanen HA (2021) M. Exercise under heat stress: thermoregulation, hydration, performance implications, and mitigation strategies. *Physiol Rev* 101:1873–1979
45. Wray S et al (2021) Hypoxia and reproductive health: Hypoxia and labour. *Reproduction* 161:F67–F80
46. Turner JM, Mitchell MD, Kumar S (2019) The physiology of intrapartum fetal compromise at term. *Am J Obstet Gynecol* 221
47. Acharya G, Sitras V (2009) Oxygen uptake of the human fetus at term. *Acta Obstet Gynecol Scand* 88:104–109
48. Frenken MWE, van der Woude DAA, Dieleman JP, Oei SG, van Laar J (2022) O. E. H. The association between uterine contraction frequency and fetal scalp pH in women with suspicious or pathological fetal heart rate tracings: A retrospective study. *Eur J Obstet Gynecol Reproductive Biology* 271:1–6
49. Kouanda S et al (2026) Heat and its effects on maternal and neonatal health care: Evidence from Burkina Faso. *Public Health* 252
50. Dey AK, Dimitrova A, Raj A, Benmarhnia T (2025) The effect of extreme temperatures on healthcare utilization during pregnancy: Findings from a nationally representative survey in India. *Environ Res* 285:122410
51. Haksari EL et al (2025) Neonatal mortality and survival of low-birth-weight infants at hospitals in indonesia, a multi center study. *Scientific Reports* 2025 15:1 15, 31607-
52. Chu K et al (2012) Cesarean Section Rates and Indications in Sub-Saharan Africa: A Multi-Country Study from Medecins sans Frontieres. *PLoS ONE* 7:e44484
53. Guigma KH, Todd M, Wang Y (2020) Characteristics and thermodynamics of Sahelian heatwaves analysed using various thermal indices. *Climate Dynamics* 2020 55:11 55, 3151–3175
54. Wang Y, Xiao S, Zhang S, Qiu C (2025) Incidence of neonatal asphyxia and associated risk factors: a systematic review and cumulative meta-analysis. *BMC Pediatr.* 25
55. Jikamo B et al (2025) Epidemiology of perinatal asphyxia among newborns in Ethiopia: a systematic review and meta-analysis of incidence and risk factors. *Maternal Health, Neonatology and Perinatology* 2025 11:1 11, 42-
56. Thayyil S et al (2021) Hypothermia for moderate or severe neonatal encephalopathy in low-income and middle-income countries (HELIX): a randomised controlled trial in India, Sri Lanka, and Bangladesh. *Lancet Glob Health* 9:e1273–e1285

## Figures

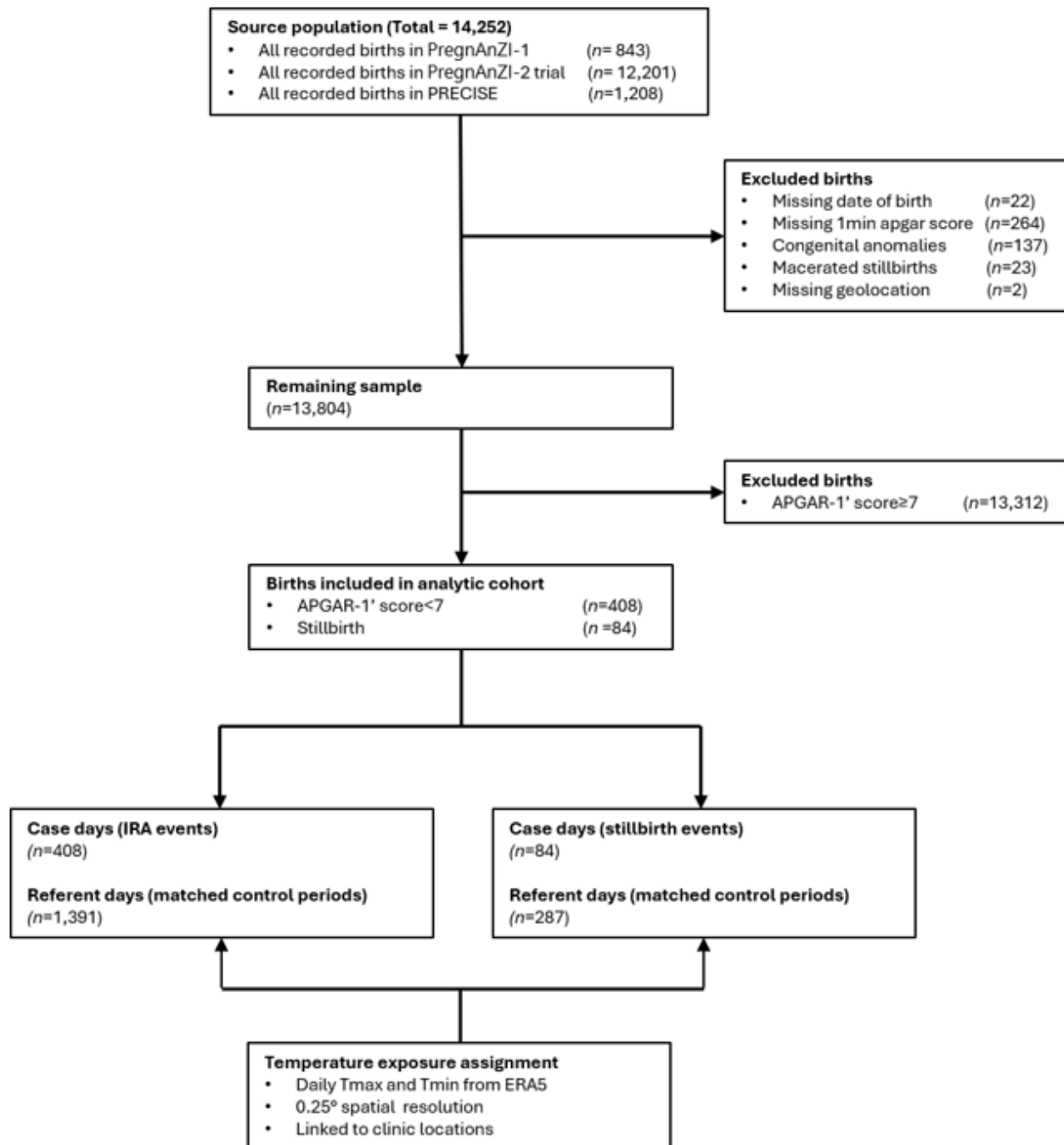


**Figure 1**

**Study population selection.** The flow diagram shows the number of births assessed for eligibility, exclusions due to missing outcome, missing birth date, missing birth location, or other exclusion criteria, and the final analytic sample used in the case-crossover analysis of heat exposure and intrapartum-related asphyxia (IRA).

*Notes:* IRA, intrapartum-related asphyxia. Referent days were selected using a time-stratified case-crossover design matched on weekday, month, and year.

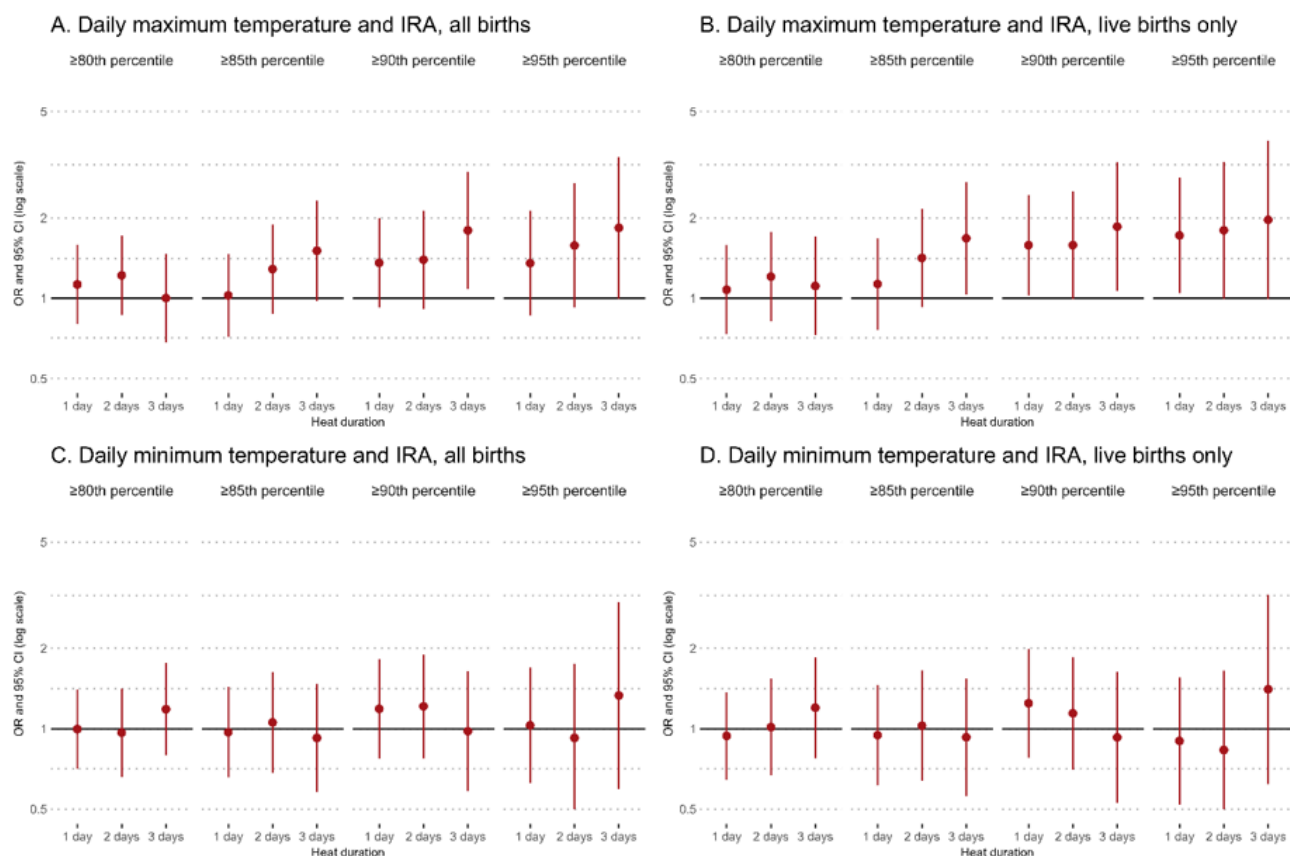


**Figure 2**

Associations between heat exposure and intrapartum-related asphyxia (IRA) by temperature threshold and exposure duration. Panels show maximum daily temperature for all births (A) and live births only (B), and minimum daily temperature for all births (C) and live births only (D). ORs and 95% CIs are reported in Supplementary Tables S8–S11.

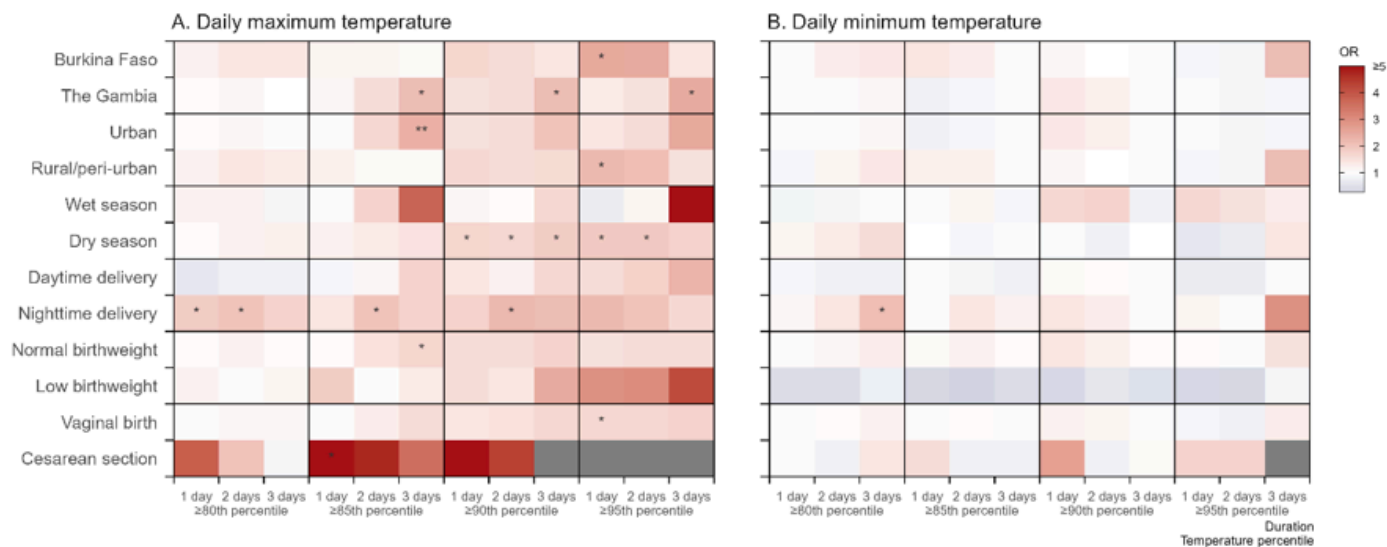


**Figure 3**

Associations between heat exposure and intrapartum-related asphyxia (IRA) among live births by subgroup and heat definition. Asterisks indicate statistical significance (\* $p<0.05$ ; \*\* $p<0.01$ ).

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryInformation.docx](#)