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Extreme heat, preterm birth, and stillbirth: A global analysis across 14 lower-middle income countries

Sara McElroy [a,b,c,*], Sindana Ilango [a,b,c,d], Anna Dimitrova [a,b,c], Alexander Gershunov [a,b,c], Tarik Benmarhnia [a,b,c]

[a] University of California, San Diego-Herbert Wertheim School of Public Health, United States
[b] San Diego State University, United States
[c] Scripps Institution of Oceanography, United States
[d] University of Washington, United States

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ABSTRACT

Stillbirths and complications from preterm birth are two of the leading causes of neonatal deaths across the globe. Lower- to middle-income countries (LMICs) are experiencing some of the highest rates of these adverse birth outcomes. Research has suggested that environmental determinants, such as extreme heat, can increase the risk of preterm birth and stillbirth. Under climate change, extreme heat events have become more severe and frequent and are occurring in differential seasonal patterns. Little is known about how extreme heat affects the risk of preterm birth and stillbirth in LMICs. Thus, it is imperative to examine how exposure to extreme heat affects adverse birth outcomes in regions with some of the highest rates of preterm and stillbirths. Most of the evidence linking extreme heat and adverse birth outcomes has been generated from high-income countries (HICs) notably because measuring temperature in LMICs has proven challenging due to the scarcity of ground monitors. The paucity of health data has been an additional obstacle to study this relationship in LMICs. In this study, globally gridded meteorological data was linked with spatially and temporally resolved Demographic and Health Surveys (DHS) data on adverse birth outcomes. A global analysis of 14 LMICs was conducted per a pooled time-stratified case-crossover design with distributed-lag nonlinear models to ascertain the relationship between acute exposure to extreme heat and PTB and stillbirths. We notably found that experiencing higher maximum temperatures and smaller diurnal temperature range during the last week before birth increased the risk of preterm birth and stillbirth. This study is the first global assessment of extreme heat events and adverse birth outcomes and builds the evidence base for LMICs.

1. Introduction

Adverse pregnancy outcomes, including preterm birth and still birth, annually affect nearly 19 million women worldwide. The World Health Organization (WHO) states that these outcomes are increasing every year (Chawanpaiboon et al., 2019). Preterm birth (defined as a live birth before 37 weeks gestation) increases risk of several adverse health outcomes later in life, including respiratory diseases, neurodevelopment and growth impairments, and other morbidities, which places a substantial burden on health care systems (Undela et al., 2019; Anderson and Doyle, 2003). Stillbirth is defined as fetal death after 28 weeks gestation or at least 1000-grams at birth, and there are an estimated 2.6 million stillbirths each year, one every 16 s (WHO, 2018). Lower- to middle-income countries (LMICs) experience the highest rates of these adverse birth outcomes. Of the ten countries with the highest rates of preterm birth, nine are LMICs (Blencowe et al., 2016). Furthermore, 98% of the global number of stillbirths take place in LMICs (Aminu et al., 2014; WHO UNICEF UNFPA, 2012). The large proportion of adverse birth outcomes occurring in LMICs may be due to deficiency in access to health care and lack of education and resources dedicated to pregnancy health (Ngandu et al., 2020). Environmental determinants constitute one set of modifiable risk factors than can be intervened on at the population-level. These adverse birth outcomes can be avoided given that heat impacts are preventable with evidence-based warning systems, heat advisories and action plans that inform the public of measures that can be taken to mitigate exposure.

* Corresponding author.
E-mail address: s1mcelroy@health.ucsd.edu (S. McElroy).

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Previous studies examining preterm birth and stillbirth have identified the role of environmental risk factors such as outdoor air pollution (Chang et al., 2011; DeFranco et al., 2015), ambient temperature (Auger et al., 2011; Auger et al., 2014), rainfall variability (Chacón-Montalván et al., 2021), wildfires (Abdo et al., 2019), and ice storms (Auger et al., 2011). In the context of climate change, we have seen an increase in severity and duration of extreme weather events such as heat waves (Luber and McGeehin, 2008; Deschênes and Moretti, 2009). Pregnant women are particularly vulnerable to extreme heat and are at a high risk of heat related health conditions, including heat stroke, respiratory conditions, and adverse birth outcomes (Filippidou and Koukouliata, 2011; Balbus and Malina, 2009). Previous literature suggests extreme heat may trigger preterm birth or stillbirth notably through the following biological mechanisms: 1) decrease in the ratio of body surface area to body mass (Sun et al., May 2019), 2) dehydration (Dadvand et al., 2011; Bouchama and Knochel, 2002), and 3) birth defects such as heart conditions (Basu et al., 2016).

Several studies have found that pregnant women are particularly susceptible to adverse health outcomes if exposed to extreme heat during the last week of pregnancy (Chang et al., 2011; Dadvand et al., 2011; Ha et al., 2017; Li et al., 2018; Rappazzo Kristen et al., 2014; Sexton et al., 2021). More specifically, experiencing an extreme heat event toward the end of gestational period can trigger the mother to give birth soon after. Previous literature also highlights the heterogeneity in heat conditions and contextual factors that could influence birth outcomes, which necessitates the expansion of this research into lesser studied regions (McElroy et al., 2020; Xu et al., 2016). Moreover, most existing studies have been conducted in high-income countries in North America, Europe, and Asia (Sun et al., May 2019; Basu et al., 2010; Guo et al., 2018; Li et al., 2018). A recent systematic review by Cherish et. al published in 2020 examining the associations between high temperatures and adverse birth outcomes found 48 studies that investigated the relationship between heat and preterm birth and only eight papers that examined heat and stillbirth (Chersich et al., 2020) All these studies were conducted in upper-middle- and high-income countries. Drawing inferences from these studies and extrapolating them to women in LMICs could be invalid because of the vastly different social, demographic, and meteorological environments to which women in LMICs are exposed.

The lack of studies in LMICs that have examined the relationship between extreme heat and adverse birth outcomes could be attributed to methodological challenges in measuring exposure levels (Ostro et al., 2018). Previous studies in high-income-countries (HICs) have mainly relied on ground monitor meteorological station networks, which most LMICs lack the resources and infrastructure to build and maintain (Rees et al., 2019). As a result, LMICs rarely engage in routine and comprehensive meteorological data collection, which poses problems in assessing acute exposure levels of heat. Furthermore, the few studies (Molina and Saldarriaga, 2017, Grace et al., 2015; Nori-Sarma et al., 2019) conducted in LMICs relied on national monthly or annual averages of exposure which hampers examination of acute exposure periods with fine geographic resolution. In this study, we addressed these limitations and methodological challenges by using globally gridded meteorological product to measure exposure to heat with fine spatiotemporal resolution. Data on adverse birth outcomes was obtained from the Demographic and Health Surveys (DHS), a nationally representative household-based survey piloted by the US Agency for International Development, which were linked with the meteorological data. With the release of the newest phase of the DHS survey date of birth (or date of death) were recorded, which had not been previously done. This allows us to perform more detailed analyses, i.e., using daily measurements that can reveal critical temperature thresholds of susceptibility. This study is the first to quantify acute heat effects on risk of preterm birth and stillbirth in 14 LMICs.

2. Materials and methods

2.1. *Description of study population:*

Fourteen LMICs (Angola, Benin, Burundi, Ethiopia, Haiti, Malawi, Nepal, Nigeria, Philippines, South Africa, Tajikistan, Timor-Leste, Uganda, and Zimbabwe) spanning various climate zones were included in these analyses. These countries were selected because they participated in the most recent DHS survey round (phase 7), which was completed between 2014 and 2018 and contained data for at least one of the outcomes of interest (preterm birth or stillbirth). These surveys are nationally representative and provide detailed maternal and child health information which is standardized across countries. Women ages 15–49 responded to questionnaires about their complete birth histories, which included information about birth weight, duration of pregnancy, date of birth (day, month, year) and infant mortality. In addition, individual- and household-level data, such as household wealth, education level, prenatal care, and health insurance status, are recorded. DHS also provides global positioning system (GPS) data for each primary sampling unit (PSU). A PSU is defined as a city block in an urban area and a village in a rural area. Surveyors used global positioning system devices to collect geospatial information to identify the central point of the populated area of each PSU (Aliaga and Ren, 2006). To ensure respondent confidentiality, GPS coordinates were randomly displaced by the DHS survey. The displacement is carried out so that urban PSUs contain a minimum of 0 and maximum of 2 km of error and rural PSUs contain a minimum of 0 and a maximum of 5 km of positional error with a further 1% of the rural clusters displaced a minimum of 9 and a maximum of 10 km (USAID, 2013).

All women aged 15 to 49 in these countries were considered for the analysis if they answered questions about their birth histories, household demographics, and health practices. Women who were interviewed across the 14 countries had birth history data ranging from 2009 to 2018.

2.2. *Linking of health and meteorological data:*

For this study we linked two data sources: The DHS and global gridded temperature. The latitude and longitude for each PSU within the DHS surveys was used as the spatial linking component. Even though these surveys are cross-sectional in nature, the retrospective information on previous births allows us to observe multiple birth outcomes over time within each village. Moreover, the newest phase of the DHS surveys included birth date at the daily-level compared to previous surveys which only recorded month and year of birth, thus allowing us to determine a 7-day period prior to birth as our exposure window.

We matched the DHS data with geographically gridded weather data that included maximum and minimum temperature from the Climate Prediction Center's (CPC) Global Daily Temperature data provided by NOAA/OAR/ESRL Physical Science Laboratory in Boulder Colorado (https://psl.noaa.gov/) (Kloog et al., 2015). This temperature data is globally gridded at a 0.5°x 0.5° (~55x55 km) spatial resolution and at 24-hour temporal resolution and utilizes the Sheppard Algorithm. Previous epidemiological studies have utilized the CPC Global Daily Temperature and found it a valid measure of temperature (Wellenius et al., 2012).

2.3. *Temperature measures:*

We considered three measurements of temperature in our analyses: daily maximum (Tmax), minimum (Tmin), and diurnal temperature range (Tmax - Tmin), specific to each PSU. These three metrics were selected to examine how extreme heat effects birth outcomes. Diurnal temperature range (that is highly correlated with humidity) was used to assess how humid nighttime heat events may play a role in risk of adverse birth outcomes. Each daily temperature value measure was linked with daily individual cases of preterm births and stillbirths using information about the geographic coordinates of survey participants and timing of birth.

2.4. Exposure and outcome classification:

Preterm birth status was obtained via the “duration of pregnancy” question in the birth history questionnaire. Duration of pregnancy is reported in months and any birth that was recorded as less than 9 months of gestation is considered preterm; about 6% of all births in our sample classified as preterm. Stillbirths were obtained per the questions “Is the child alive or dead at time of interview?” and “Age at death” within the birth history questionnaire. If the child was not alive at the time of interview and age of death indicated that the child died at birth, then this child was considered stillborn.

2.5. Time-stratified case-crossover with distributed nonlinear lag design:

A time-stratified case-crossover design was utilized to estimate the acute risk of extreme heat and preterm birth and stillbirth. This approach has been well established in the literature to estimate acute health effects of environmental exposures and has been widely applied to estimate associations between short-term exposure to extreme heat and health outcomes (Kloog et al., 2015; Kloog et al., 2015; Wellenius et al., 2012; Zanobetti et al., 2014; Di et al., 2017). This design allows for the control of any time-fixed confounders such as maternal age, nutrition, access to health care, wealth, education, etc. Individual adverse birth outcome events are the unit of observation, or case day, and environmental data on the date of the adverse birth outcome event is compared with three control days. These analyses match case days to a control day of the same day of the week, in the same month and year as the adverse birth outcome. Matching on day of the week controls for potential week-varying confounders such as the week/weekend difference in temperature and rates of adverse birth outcomes. Matching by month and year controls for potential confounding by seasonality and long term trends (Navidi, 1998). We applied distributed-lag nonlinear models (DLNM) with the case-crossover logistic model to assess the nonlinear and lagged associations between temperature and adverse birth outcomes up to 7 days before the birth date. The nonlinear and lagged temperature and adverse birth outcome associations were modeled using spline functions. A spline function incorporates multiple polynomial segments joined by knots to make a continuous curve. The number of knots can be adjusted to increase or decrease smoothness of the curve. We chose knot placement using quantiles of the temperature distributions (see Appendix A). Our final model of nonlinear temperature-adverse birth outcome relationship used b-splines with one knot at the 40th quantile of the temperature distribution. Different knot placements were assessed for the temperature-preterm birth and temperature-stillbirth associations. The model with the lowest Akaike Information Criterion (AIC) was chosen for the analysis (See Appendix A). The lagged adverse birth outcome relationship was modeled using natural cubic splines with 2 knots placed at equally spaced values in the log scale and could lag up to 7 days. This 7-day window of high susceptibility was identified in previous literature (Basu et al., 2016; Ha et al., 2017; Li et al., 2018; Bekkar et al., 2020). Since the study design controls for time-invariant confounders the only covariates that need to be controlled for in the model are time-varying meteorological variables (humidity and wind speed). A pooled case-crossover analysis with random effects across all PSUs and countries was performed for both preterm birth and stillbirth. These pooled data combined all cases (preterm and stillbirths) across all countries.

2.6. Effect modification:

As an exploratory analysis, we assessed if the relationship between temperature and birth outcomes was modified by maternal education (low vs. high), household wealth (low vs. high quantiles), and rural/urban residence. The DHS survey developed a measure of household wealth, which is constructed based on a Principal Component Analysis (PCA) and using detailed information about household assets, building characteristics, and overcrowding. We used wealth quintiles in the stratified analyses. As models focusing on continuous temperature metrics did not converge, we instead focused on two heat wave definitions. If there was a day when the maximum temperature was greater than or equal to the 80th, and 90th percentiles of the PSU-specific temperature distribution, the day was considered to be a heat day.

3. Results

In total, 103,535 births were included in this study across the 14 countries. There were 5882 preterm birth cases and 1210 stillbirth cases. The distribution of preterm birth and stillbirth cases by country are depicted in Table 1. The highest rate of preterm births was in Malawi (10.4%) while the lowest rate occurred in Nigeria (1%). The highest proportion of stillbirths were recorded in Ethiopia (3.5%) and the lowest in Tajikistan (0.6%). These percentages are the proportion of adverse outcomes within the total number of births given of women who participated in the DHS survey. Temperature distributions for each country can be seen in Table 1. Fig. 1 depicts the gridded distribution of temperature thresholds for the 95th percentile for all countries included in the study.

Overall, we find an increased risk of preterm birth among women who were exposed to extreme heat within the seven days before giving birth (Fig. 2). The distributed lag nonlinear model identified a range of temperatures that increased the risk of preterm birth. When pooling estimates from all countries, the rate of preterm birth increased when women were exposed to temperatures higher than 20 °C and the same risk decreased at temperatures below 20 °C, which was the point of overall minimum effect. We also explored potential lagged effects in the seven days before birth. Supplementary Figure S1 depicts the estimated risk ratio by temperature unit at specific lags (1, 3, 5, and 7 days) and by varied temperatures (13.3, 22.1, 32.7, and 35.2), corresponding to the 1st, 5th, 95th, and 99th percentiles of the temperature distribution, using 20 °C as the reference temperature. The results suggest that hotter temperatures have a more immediate effect on preterm birth than lagged effects. For, example lagging the exposure by 5 or 7 days (Figure S1 (C)) shows minimal effect on preterm birth compared to the risk of exposure with zero to one day of lag (Figure S1 (A)). Similarly, the graphs showing risk by distribution of temperature confirm an immediate increased risk of preterm birth at hotter temperature 32.7–35.2 °C (Figure S1 (G, H)). However, at moderate temperatures there was no

Table 1
Outcome and exposure summary statistics for each country included in the study.

Country	Total number of births	Number of preterm births	Number of stillbirths	Mean >= 95th threshold °C
Angola	7447	146	69	32.34
Benin	7956	763	75	37.43
Burundi	7856	231	57	28.22
Ethiopia	1113	123	39	32.08
Haiti	6530	522	49	34.35
Malawi	9380	970	82	31.39
Nigeria	33924	356	542	36.96
Nepal	3553	74	30	32.89
Philippines	2130	222	25	33.35
South Africa	3548	457	49	33.32
Tajikistan	3786	137	22	32.68
Timor-Leste	4353	446	52	33.81
Uganda	8825	1343	92	31.78
Zimbabwe	3134	92	27	32.89

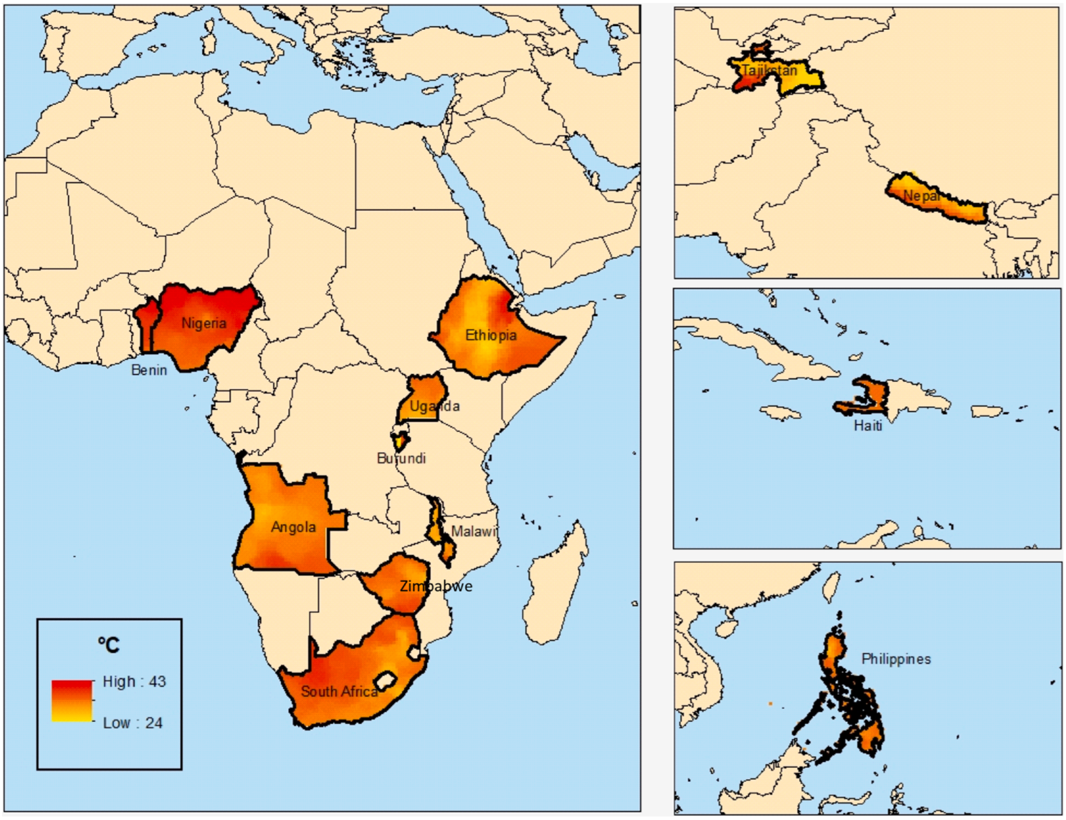

Fig. 1. Map of countries that participated in Phase 7 of the DHS survey included in this study and spatial distribution of temperature thresholds (daily temperature greater than 95th percentile at the PSU level).

observed lagged effect.

An elevated risk of preterm birth was also identified among pregnant women who experienced diurnal temperature ranges (i.e., difference between daily maximum and minimum temperatures) of less than 16 °C (Fig. 2). There was no lagged effect observed for the diurnal range and preterm birth relationship (see Supplementary Figure S2). We did not identify any effects of temperature on preterm births when using minimum temperature to define extreme heat (See Appendix B).

As for stillbirth, our results indicate an increased risk among pregnant women who experienced hot temperatures within the seven days prior to giving birth. The hot temperature-stillbirth nonlinear association showed a window of temperatures, 20–30 °C, where a pregnant woman is more susceptible to stillbirths as compared to the risk of stillbirth at the identified reference temperature of 20 °C. A decreased risk of stillbirth was observed for temperatures less than the reference temperature (Fig. 3). Supplementary Figure S3 depicts the estimated RR by temperature at specific lags (1, 3, 5, and 7 days) and by lag at specific temperatures (13.3, 22.1, 32.7, and 39), corresponding to the 1st, 5th, 95th, and 99th percentiles of the temperature distribution, using 20 °C as the reference. These graphs present the lagged effect of extreme heat on stillbirth. As temperatures increase, there is a lagged effect of three and five days (Figure S3 (B, C)). This pattern is further pronounced on days with temperatures at the top percentile; we see an increase in stillbirth risk at the lags three to five days (Figure S3 (H)). As temperatures decrease, this lagged effect is attenuated until there is no lagged effect at colder temperatures (see Figure S3 (E, F, G)).

An increase in stillbirth was observed for pregnant women who experienced a day within the week prior to giving birth with smaller diurnal temperature ranges (RR = 2.1, 95% CI 1.01, 4.02). The window of elevated risk was found to be for diurnal temperature range less than 16°C (Fig. 3). The lagged structure of the stillbirth-temperature relationship can be seen in Supplementary Figure 4. There is an immediate effect of small diurnal temperature ranges on risk of stillbirth as seen in Figure S4 (E). For days with recorded 10 °C diurnal temperature range, there was an increased risk of stillbirth throughout the 7-day lag period. As the diurnal temperature range increased, there was no observed lagged risk. Similarly, we did not identify any effect on stillbirth when using minimum temperature metrics to define extreme heat (see Appendix B).

The results of the effect modification analyses revealed that the risk for preterm birth and stillbirth vary by level of maternal education, household wealth, and type of place of residence. The general pattern for the three heat have definitions was that pregnant women living in rural areas, from less wealthy housholds, and with low education levels were at greater risk for preterm birth and stillbirth than their counterparts (See Figs. S5, S6, S7).

4. Discussion

We brought to attention new evidence on the relationship between extreme heat and adverse birth outcomes in countries where the evidence is scarce. This is the first study examining the effect of acute exposure to extreme heat on the risk of preterm and stillbirths in multiple LMICs, drawing data from the large and nationally representative surveys. We overcame the sparse vital records available in LMICs by utilizing the DHS surveys.

Overall, we found a consistent and positive association between extreme heat beyond specific thresholds and risk of preterm birth and stillbirth in LMICs. Similar patterns of increased risk of preterm birth and stillbirth were observed when using multiple metrics to examine ambient temperature (maximum temperature and diurnal temperature range). Our findings indicate that pregnant women start experiencing increased risks of adverse birth outcomes when they experience temperatures greater than 20 °C. As temperatures rise, this risk grows and

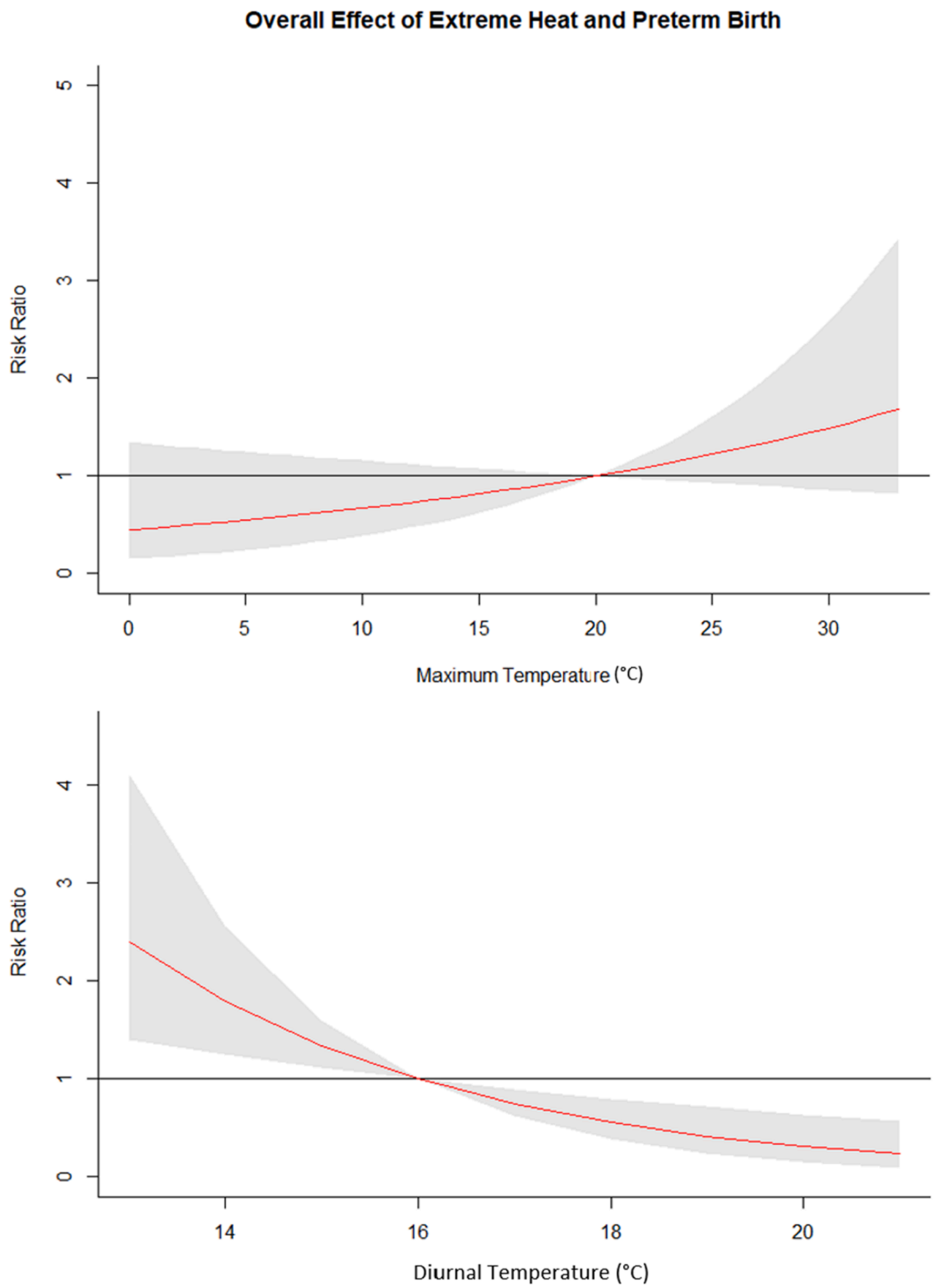

Fig. 2. Overall effect of distributed lag nonlinear case-crossover curve with reference at 20 °C for maximum temperature and diurnal temperature range with reference at 16 °C and preterm birth.

culminates at tempertatures greater 30 °C. Additionally, we identified a heightened risk for preterm birth and stillbirth in pregnant women who have lower levels of education and live in rural areas as compared to pregnant women with higher education and living in urban areas.

Our findings from the lagged analyses suggest there are different critical windows of susceptibility to preterm birth and stillbirth due to heat exposure. An immediate effect of high temperatures is observed for preterm birth. In contrast, increased risk of stillbirth is observed three to five days after the extreme temperature. These observed differences in the critical period of exposure could be time could be explained by differing biological mechanisms behind each adverse birth outcome. Further research is needed to determine the biological mechanisms into these different critical windows of susceptibility to preterm birth and stillbirth, but previous studies have proposed several hypotheses of how extreme heat might cause these outcomes.

Throughout the pregnancy, the additional weight gained may decrease the ratio of body surface area to body mass, which in turn may limit a woman's capacity to retain heat (Sun et al., 2019). In addition, heat production could increase due to fetal growth and metabolism (Grace et al., 2015). Thus, the ability of pregnant women to cope with heat stress may be limited due to the increase in internal heat production and the decrease in capacity for heat stress, which could trigger spontaneous labor. Furthermore, other studies have proposed that extreme heat might lead to a heightening in hormones of the hypothalamic–pituitaryadrenal axis, such as cortisol (Malmkvist et al., 2009; Ansari et al., 2014). This is one of the primary pathways which has been linked with activation of uterine contractions, which could potentially lead to preterm birth (Dreiling et al., 1991). Heat can also lead to dehydration, which in turn increases the viscosity of the blood, elevating cholesterol levels, and shifting blood flow from the developing fetus to

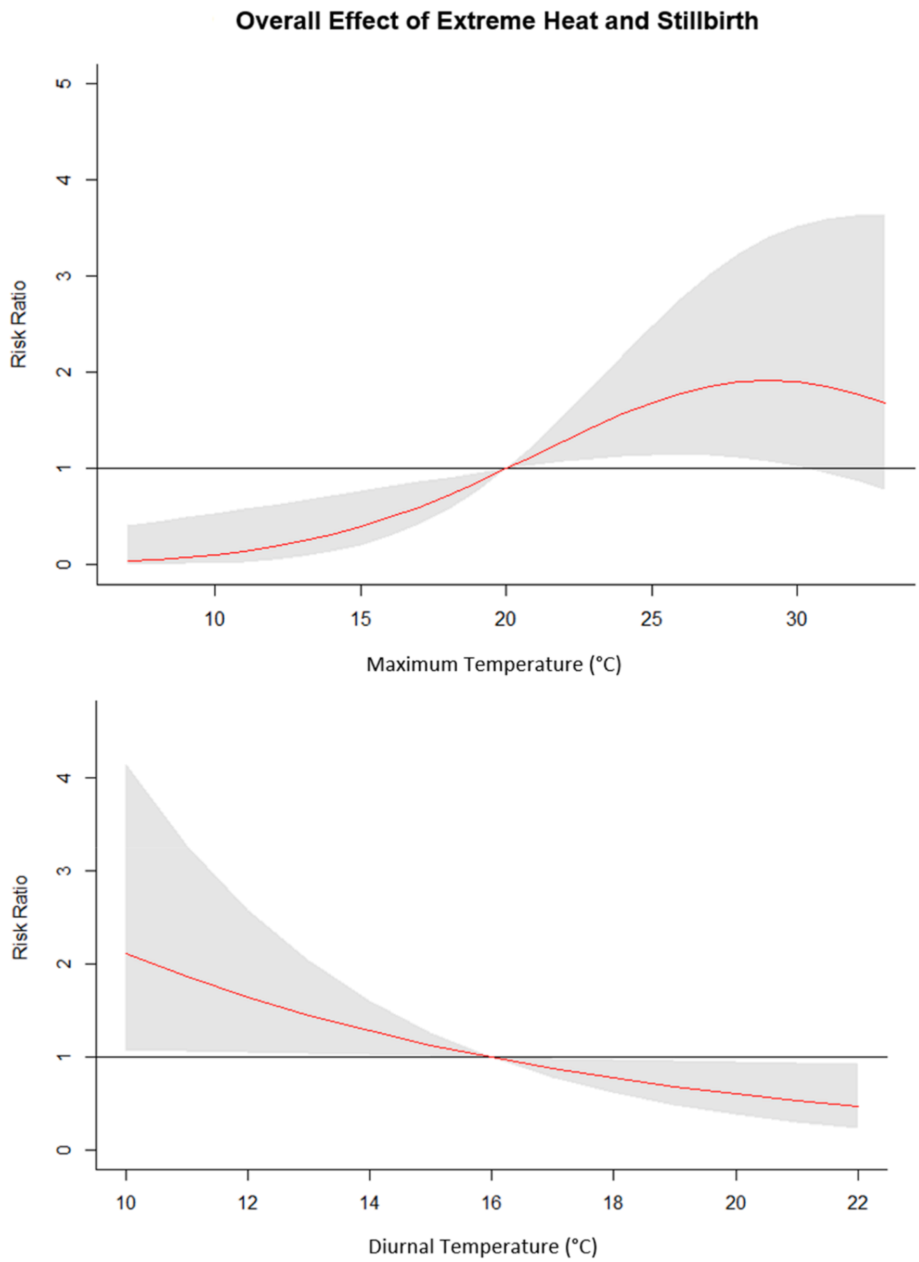

Fig. 3. Overall effect of distributed lag nonlinear case-crossover curve with reference at 20 °C for maximum temperature and diurnal temperature range with refernce at 16 °C and stillbirth.

the skin's surface to lower the body's internal temperature. These processes of physiologic changes may decrease uterine oxygen and induce labor (Dadvand et al., 2011; Bouchama and Knochel, 2002).

There are very few studies that have examined how exposure to extreme heat influences risk of stillbirth (Asamoah et al., 2018; Bekkar et al., 2020; Ranjbaran et al., 2020). One of the postulated mechanisms is that heat exposure may cause hyperthermia, which can cause damage to cells, the placenta, and vascular systems, resulting in cell death (Li et al., 2003). Finally, maternal deficiency in vitamin D could lead to musculoskeletal problems, which in turn could lead to the unviability of the fetus (Palermo and Holick, 2014).

We also identified that days with smaller diurnal temperatures increased the risk of preterm birth. Days with smaller differences between maximum and minimum temperatures (i.e. diurnal temperature range, which is highly correlated with humidity (Tian-Bao, 2014)) were found to have an impact on preterm birth risk. Indeed, nighttime heat events can be explained by various mechanisms including high levels of humidity, associated with attenuated temperature advection (Thomas et al., 2020). In our changing climate, diurnal temperature ranges have been gradually decreasing and it is predicted this pattern will continue in the future (Hartmann et al., 2013) because when the atmosphere warms it also holds more water, which leads to higher humidity. This finding elucidates that these pregnant women are at risk of adverse birth outcomes not only from experiencing high temperatures but also when they experience hot days followed by warm nights.

Almost all the previous evidence about extreme heat and its effect on adverse birth outcome risk has come from HICs. Two systematic reviews of temperature exposure during pregnancy and birth outcomes conducted by Zhang et al. in 2017 and Bekkar et al. in 2020 identified 36 epidemiologic studies (Bekkar et al., 2020; Zhang et al., 2017). The reviewed literature included 36 studies examining adverse birth outcomes, of which the vast majority were from Europe, North America, Asia (Israel, China, and Japan), and Australia, while only study focused on Africa (Ghana) (See Appendix Table 1.) Twenty-four out of the 36 studies examined preterm birth and temperature, 14 studies assessed the effect of temperature on birth weight, and only eight studies examined the relationship between temperature and stillbirth. Overall, we found similar or slightly higher effect sizes for preterm birth and stillbirth compared to the studies conducted in HICs.

This study is one of the first studies that examined environmental risk factors for preterm birth and stillbirth in a comprehensive set of LMICs. We found that acute exposure to extreme heat is a critical risk factor for both adverse birth outcomes. Previous studies examining the effect of temperature on adverse birth outcomes in LMICs have relied on coarse temporal exposure data. This study incorporated distributed lag nonlinear models in tandem with the classic case-crossover design to capture these nonlinear and lagged acute relationships of temperature and adverse birth outcomes. While we relied on an ecological study design given that we did not have access to representative birth certificate data or to dedicated cohort studies, it will be important for future studies to explore the role of extreme heat on birth outcomes capitalizing on distinct sources of data and individual-level study designs.

Since extreme heat events display distinct spatial and temporal patterns, it is important for early warning systems to utilize real-time or close to real-time temperature data on a local scale. Besides utilizing remote sensing data, the use of low-cost sensors has been suggested to obtain more accurate exposure data in LMICs (Longo et al., 2017). The advancement of meteorological sensing technologies and increasing access to mobile phones and the internet provides numerous opportunities for research in LMICs.

Pregnant women should be targeted by early warning systems through dedicated actions. For example, in areas where women mainly work outside for their livelihoods, a simple recommendation to stay indoors (if they have access to air conditioning) or remain in the shade on extreme heat days can reduce exposure. Another example, the Conditional Cash Transfer (CCT) has recently been suggested as a viable strategy to deal with the effects of extreme weather events (Pega et al., 2015). In addition, training, and skill development for additional sources of income in places where heat waves occur frequently could be implemented.

Additional research is needed to support and maintain the proposed early warning systems, particularly the systematic collection of epidemiologic data on health risks associated with extreme heat events. We know that incorporating local evidence into early warning systems works in reducing adverse health outcomes. This study provides local epidemiologic data that has elucidated spatial and temporal aspects of extreme heat exposure and associated risks across 14 LMICs. Our results can help inform decision-makers about the temperature thresholds at which risks for pregnant women become elevated.

We acknowledge some limitations concerning the analyses that were implemented in this study. First, all exposures were assigned per globally gridded meteorological data that were previously validated. Our measurements are only as good as the data available, which could lead to potential exposure misclassification. Yet, using remote sensing information may reduce the risk of exposure misclassification compared to the previously standard use of ground monitors. LMICs have a very small number of ground monitors and extrapolating from these very few measurements is likely to produce less accurate exposure data then the CPC Global Daily Temperature gridded measurements. However, these data are independent from the outcome of interest and any exposure misclassification is non-differential. Second, we did not examine the impact of co-occurring extreme weather events such as drought and dust storms. Additional research needs to examine how these co-occurring events may contribute to the risk of preterm birth and stillbirth. Third, this study relied on a selective sample of mothers who were willing to participate in the DHS survey and survived to the time of interview. Given that LMICs have high rates of maternal mortality, future studies need to better account for selective survival. All outcomes were based on self-reports of survey participants. Women were asked to report on their birth histories over the previous five years, which can introduce recall bias especially for preterm births (Kloog et al., 2015) which may explain the surprisingly low rates in some countries. Next, we acknowledge how imprecise a monthly assessment of preterm birth is, which most likely introduced outcome misclassification into our study. This outcome misclassification most likely contributted to our imprecise effect estimates. Nonetheless, we are confident that this choice of measurement was a necessary trade-off for the ability to examine preterm birth and stillbirth risk across geographical regions on a daily scale. Finally, there was no information in the survey that distinguished between the type and timing of stillbirths. Stillbirths can happen before the onset of labor or during labor or delivery (Feresu et al., 2005). Thus, we had to assume that the stillbirth happened on the day of death reported in the survey, which could introduce some bias into our analyses.

4.1. Conclusion

Our study is one of the first to examine the link between acute exposure to heat in LMICs and the risk of preterm birth and stillbirth. Due to climate change, extreme heat events have become more frequent, intense, and longer-lasting in recent decades — a trend projected to accelerate in the future. LMICs lack the infrastructure to deal with extreme heat and so it is especially important to study how heat affects pregnancy outcomes, as as pregnant women are among the most vulnerable population groups. Our results indicated elevated risks of adverse birth outcomes across LMICs due to heat exposure. Continued research into the mechanisms that are driving this association is crucial to ultimately reduce the number of neonatal deaths worldwide.

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Author contribution

Sara McElroy: Conceptualization, Data Curation, Formal Analysis, Methodology, Drafting the manuscript, Visualization. **Tarik Benmarhnia:** Conceptualization, Methodology. **Anna Dimitrova:** Methodology. Revising the manuscript critically for important intellectual content: Sara McElroy, Sindana Ilango, Anna Dimitrova, Alexander Gershunov, and Tarik Benmarhnia.

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.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2021.106902.

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