Graduate thesis

NTNU
Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences
Department of Public Health and Nursing

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Climate change: is heat exposure during pregnancy associated with adverse pregnancy outcomes in Blantyre, Malawi? A cross-sectional study.

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Supervisor: Jon Øyvind Odland
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Sammendrag

Bakgrunn

Klimaendringer har skadelige effekter på global helse, og gravide kvinner er særlig sårbare. Malawi, som resten av verden, blir varmere og ekstremvær som hetebølger blir mer vanlig. Høye temperaturer øker risikoen for flere svangerskapskomplikasjoner. Studien vår har som mål å undersøke om økte temperaturer og økt frekvens av hetebølger gjennom svangerskapet påvirker forekomst av negative svangerskapsutfall i Malawi.

Metode

Denne tverrsnittsstudien brukte data på svangerskapsutfall fra Queen Elizabeth Central Hospital i Blantyre, Malawi, mellom 2015 og 2022. Temperaturdata ble hentet fra det malawiske Department of Climate Change and Meteorological Services. Odds ratio (OR) for maternell død, dødfødsel og svangerskapskomplikasjoner ble beregnet gitt eksponering for en eller flere hetebølger (kategorisk variabel), antall hetebølgedager og kumulativ varme over en predefinert terskel (kontinuerlige variabler). Alle analyser ble utført med maksimum og minimum temperatur, og for eksponering kort tid før fødsel eller gjennom svangerskapet. Alle analyser ble gjennomført ujustert, samt justert for maternell alder, HIV-status og paritet.

Resultat

Data fra 743 svangerskap ble inkludert. Eksponering for hetebølger og høye temperaturer gjennom svangerskapet økte oddsen for dødfødsel (kategorisk OR 2.07-2.44, kontinuerlig OR 1.03-1.08), eklampsi (kontinuerlig OR 1.04-1.05), og infeksjoner (kategorisk OR 1.65-1.66, kontinuerlig OR 1.02-1.05). Hetebølger og økte temperaturer den siste uken av svangerskapet økte oddsen for maternell død (kategorisk OR 3.78-4.00, kontinuerlig OR 1.12), preterm fødsel (kontinuerlig OR 1.08), og eklampsi (kategorisk OR 2.55, kontinuerlig OR 1.16-1.17). Oddsen for hastekeisersnitt ble redusert etter heteeksponering (kategorisk OR 0.11-0.31, kontinuerlig OR 0.55-0.94).

Konklusjon

Hetebølger og høye temperaturer var assosiert med økt forekomst av maternell død, dødfødsel og svangerskapskomplikasjoner. Gravide kvinner og fosteret er særlig sårbare i en verden med økende temperaturer. Det finnes tiltak for å redusere risikoen, og disse bør implementeres for å minimere påvirkningen av klimaendringer på den globale mor-barn-helsen.

Abstract

Background

Climate change has detrimental effects on human health globally, and pregnant women are particularly vulnerable. Malawi, like the rest of the world, is getting warmer and extreme weather events such as heatwaves are becoming more common. Excess heat increases the risk of several pregnancy complications. Our study aimed to investigate whether increased temperatures and frequency of heatwaves in pregnancy influence the occurrence of adverse pregnancy outcomes in Malawi.

Method

This cross-sectional study used data on pregnancy outcomes from Queen Elizabeth Central Hospital in Blantyre, Malawi, between 2015 and 2022. Temperature data were retrieved from the Malawian Department of Climate Change and Meteorological Services. The odds ratio (OR) of maternal death, stillbirth, and pregnancy complications was calculated given exposure to one or more heatwaves (categorical variable), number of heatwave days and cumulative heat above a predefined threshold (continuous variables). All analyses were performed with maximum and minimum temperatures, and after exposure close to delivery and exposure throughout pregnancy. All analyses were performed unadjusted and adjusted for maternal age, HIV status and parity.

Results

Data from 743 pregnancies were included. Exposure to heatwaves and high temperatures throughout pregnancy increased the odds of stillbirth (categorical OR 2.07-2.44, continuous OR 1.03-1.08), eclampsia (continuous OR 1.04-1.05), and infections (categorical OR 1.65-1.66, continuous OR 1.02-1.05). Heatwaves and high temperatures in the last week of pregnancy increased the odds of maternal death (categorical OR 3.78-4.00, continuous OR 1.12), preterm birth (continuous OR 1.08), and eclampsia (categorical OR 2.55, continuous OR 1.16-1.17). The odds of emergency section decreased after exposure to heat (categorical OR 0.11-0.31, continuous OR 0.55-0.94).

Conclusion

Heatwaves and high temperatures were associated with an increased frequency of maternal death, stillbirth, and pregnancy complications. Pregnant women and their fetus are highly vulnerable to the effects of a warming world. Actions to mitigate this risk are available and should be taken to reduce the impact of climate change on global maternal and child health.

Background

Climate change is the greatest threat to global health in the 21st century (1). The global average temperature in 2021 was 1.2°C warmer than pre-industrial temperatures, and the past seven years are the warmest on record (2). The 2021 report of the Lancet Countdown on health and climate change called a code red for a healthy future, emphasizing the devastating consequences of climate change on human health and well-being (2). The most vulnerable groups, such as the elderly, children, pregnant women, people with chronic diseases, and people in low-income countries are less resistant to the consequences of climate change (3–5).

Climate change already has a devastating impact on health in Malawi and other African countries (6). The rate of temperature increase is higher in Africa than the global average, and heatwaves are already more frequent (7). Models predict that the intensity, duration and frequency of heatwaves and other natural disasters will continue to increase in the coming decades (7,8). Malawi faced its worst flood in 50 years in 2015, and the worst drought in 35 years occurred in 2016 (9). Tropical storms and cyclones rarely used to affect Malawi, but struck the southern parts of the country in early 2022. This led to an extensive cholera outbreak, loss of food security and homes, loss of hydroelectric power generation, and placed hundreds of people in emergency shelters (10). Consequences of natural events vary between regions with different climatic conditions and vulnerability (11). Africa is highly vulnerable to these shocks because of high exposure, low adaptive capacity, and poorly developed infrastructure and healthcare services (7,11,12). The mortality related to climate events is also higher in areas where HIV/AIDS is more prevalent, like Malawi (13,14).

Heatwaves are by some considered the “silent killer” because we can’t directly see their dire effects like we can see the disastrous nature of floods and storms (10). There is no standard definition of heatwaves, but it is often defined as a period of consecutive days with high temperatures. Heatwaves cause the most deaths of all climate disasters, with people living in poverty at particular risk (15). Temperatures in the extreme percentiles of the local climate are harmful, and at least three consecutive days of high temperatures are associated with increased morbidity (8). The human body is dependent on lower night-time temperatures to cool down; therefore, increasing nocturnal temperatures are contributing to the burden of heat morbidity (12).

Pregnancy is a vulnerable state with risk of complications for both mother and fetus. Good maternal health, a favourable environment and access to healthcare are crucial for a healthy pregnancy. The global lifetime risk of maternal death was reduced by 38% between 2000 and 2017 (16). Mortality is highest in the least developed countries, and Sub-Saharan Africa accounts for 66% of maternal deaths globally (16). The most frequent obstetric causes of maternal death in Sub-Saharan Africa are hemorrhage, hypertensive disorders and infections, many of these preventable with the right resources and skills (17,18). In Malawi, pregnancy complications are the second most common cause of death for women of childbearing age (19). The prevalence of postpartum hemorrhage is about 2%, chorioamnionitis 30% and endometritis 0.8% according to a recent meta-analysis (20). In the same meta-analysis, the rate of preeclampsia and eclampsia was 0.7%, while a population-based estimation in Lilongwe found that 2.3% of the women had preeclampsia (21). Bacterial uterine infections are the cause of most infection-related maternal deaths (17). Caesarean sections account for 7.7% of all births in Malawi and are generally known to increase the risk of infections (17,22).

Neonatal conditions are the fifth leading cause of death globally, and preterm birth is the most common cause of death among children under the age of five (19). Preterm birth rates are increasing globally, and Sub-Saharan Africa contributes to almost 30% of the total preterm births in the world (23). Malawi is estimated to have one of the highest preterm birth rates in the world; a recent meta-analysis found a rate of 13.5% (20,21). Sub-Saharan Africa has among the highest rates of stillbirth in the world (24). Malawi’s rate decreased by almost 30% from 2000 to 2019, however, there are still approximately 10,000 stillbirths annually (25). These deaths are often a consequence of maternal complications (17).

Climate change threatens to reverse the last decades’ advances in maternal and child health in Africa (26,27). Extreme temperatures and heatwaves are associated with an increased risk of adverse pregnancy outcomes (4,15,18,28). Women with risk factors such as multiple pregnancies, low or high age, malaria, or HIV might be particularly vulnerable (4). Exposure of pregnant women to extreme weather influences the fetus and is associated with adverse health outcomes for the child throughout life (28). The pathogenic effect of heat in pregnancy is not fully understood. Different biological mechanisms probably play a part since outcomes differ in nature and have distinct sensitive periods (29). Physiological changes in pregnancy lower the ability to thermoregulate and increase heat production (30). These changes are counteracted by mechanisms to protect against hyperthermia such as decreased threshold for sweating, lower core temperature, increased plasma volume and bloodstream to the body surface (29). During abnormal heat exposure, these mechanisms might be overwhelmed (26,30).

It is impossible to predict the health impact of climate change on future generations (28). Malawi, like the rest of the world, will suffer from increased temperatures and heatwaves in the years to come. Young women and those with low socioeconomic status are particularly vulnerable to heat exposure (4,31), which means Malawian women are at risk. There are few studies on the effect of heat on pregnancy outcomes in low-income countries. The excess mortality and morbidity associated with heat exposure is approaching zero in some high- and middle-income countries (26). Measures to accomplish this in a low-income setting are available, but research is needed on how to do this effectively. This underlines the necessity of more knowledge about the relationship between heat exposure and pregnancy in low-income countries. Our study aimed to describe the effects of increasing temperatures on pregnancy outcomes in Malawi.

Objective and hypothesis

The objective was to examine if increased ambient temperature and frequency of heatwaves throughout pregnancy are associated with adverse pregnancy outcomes in women giving birth at Queen Elizabeth Central Hospital (QECH) in Blantyre, Malawi.

H_0: Increased temperature and frequency of heatwaves during pregnancy do not influence pregnancy outcomes.

H_1: Increased temperature and frequency of heatwaves influence pregnancy outcome.

Methods

Study design and setting

This was a cross-sectional study conducted in Blantyre, Malawi, using meteorological and secondary clinical data. Temperature data were obtained from the Malawian Department of Climate Change and Meteorological Services. Data on pregnancy outcomes were obtained from a pre-existing dataset of an observational study (32) conducted at the QECH. This dataset had records of patients from 2015-2022.

Study population

This study included the records of all pregnant women who had delivery outcomes from the prior observational study.

Women with severe pregnancy complications other than those analysed and multiple pregnancies were excluded, as well as those more likely to have pregnancy complications regardless of heat exposure because of underlying disease or age under 15 years.

Data management and collection

The data collection is described in detail by the original researchers (32). Briefly, handwritten patient files from women giving birth at QECH between 2015-2022 were consecutively selected and reviewed retrospectively. Data from the files were extracted manually and digitized with Open Data Kit software.

A copy of the data set was obtained from the original researchers using a flash drive. All patient information was anonymized before our retrieval and stored safely. After organizing the data in Microsoft Excel, we imported the data to R-studio. This software was used to extract data on maternal and fetal outcomes, pregnancy complications, age, parity, HIV status and mode of delivery.

Maximum and minimum temperatures in our study period were extracted from the Chichiri and Bvumbwe meteorological stations, located in central Blantyre and south of Blantyre, respectively. We calculated the daily maximum and minimum temperatures using the mean of the measurements from these stations. In this way, the temperature estimates were representative of a larger geographical area.

Definitions

Individual outcome variables were any record of maternal infection, preterm birth, preeclampsia, eclampsia/HELLP syndrome (henceforth eclampsia), antepartum or postpartum hemorrhage (henceforth hemorrhage), emergency caesarean sections, stillbirth, and maternal death (in this study: maternal condition at discharge or closure of report). All diagnoses were set by clinicians in line with local and World Health Organization criteria (33–37) and documented in the patient files. We extracted diagnoses from the data set. Maternal infection included those with infection and sepsis, meningitis, endometritis, and chorioamnionitis as defined in the original study (32).

The exposure variables were one or more heatwaves (yes/no), number of heatwave days and cumulative heat. Heatwaves were defined as a period of at least three consecutive days with temperatures higher than the 95th percentile of the study period (2015-2022) in accordance with previous studies (4,38,39). We also included the year 2014 because women giving birth in early 2015 were pregnant in 2014. Heatwaves overlapping with a woman's exposure period were included. The number of heatwave days was the sum of all days included in a heatwave in the given exposure period. If only one or two days in a heatwave overlapped with the exposure period these days were included. Cumulative heat was the sum of the anomaly between all days (independent of heatwaves) above the 95th percentile in the study period. Heat exposure from both maximum (Tmax) and minimum (Tmin) temperatures was assessed. The Tmax is suitable to study the effect of warm days, while the Tmin represents warm nights.

Accordingly, the following metrics for measuring heat effect were studied; the categorical Tmax heatwaves and Tmin heatwaves, and the continuous Tmax heatwave days, Tmin heatwave days, Tmax cumulative heat and Tmin cumulative heat. All metrics were examined during a short-term exposure period, defined as the last six days before admission to hospital and admission day, and the long-term exposure period, defined as the last 37 weeks before hospital admission. Thus, we had a measurement of the acute effects of heat and the heat burden for each pregnancy, assessed through hot days and warm nights. Women with preterm births were excluded when looking at long-term exposure because it was not possible to estimate with certainty the duration of their pregnancy.

Statistical analysis

Demographic data were presented as median (interquartile range) for continuous variables and frequencies (percentages) for categorical variables. Exposure to heatwaves was presented as pie charts, and the number of heatwave days and excess temperature were presented as bar charts or histograms. Separate diagrams were made for long-term and short-term exposure.

We used logistic regression to determine the association between exposure to each of the six heat metrics and adverse pregnancy outcomes in the short-term and long-term periods. Analyses were performed unadjusted and adjusted for maternal age, parity, and HIV status.

All analyses were conducted in Rstudio using R version 4.2.1. Tables were made with gtsummary (40) and visualizations were made with ggplot2 (41) packages for R.

Ethical considerations

Ethical clearance for the data collection was obtained for the original study from the College of Medicine Research Ethics Committee (COMREC – Ref P.09/21/3412) and the Regional Committee for Medical and Health Research Ethics Central (REK) in 2021 (REK 322956).

Results

Study characteristics

The data material contained information about 804 women giving birth at QECH from March 2015 to March 2022. We excluded 44 women because they had severe pregnancy complications other than those we analysed (ectopic pregnancy, uterine perforation), multiple pregnancies, age under 15 years or underlying disease (Kaposi sarcoma, hematological malignancy, AIDS, hypertension, diabetes, or kidney disease). After removal of 17 duplicates, a total of 743 women remained for analysis. All women were included in the short-term exposure analysis, but 46 women with preterm births were excluded from the long-term exposure analysis.

The median age of the study group was 24 years, 42% of the women were primiparous, and 18% were HIV reactive (Table 1). These characteristics were similar across all exposure groups. The most prevalent outcomes were preeclampsia (11.3%) and infection (10.1%). More than half (52.1 %) of the women delivered by caesarean section. Only two of the 37 women with severe hypertensive disease had HELLP syndrome (data not shown).

Occurrence of heatwaves

Between 2014 and 2022 the 95th percentile of the maximum temperature was 32.1°C, while the 95th percentile of the minimum temperature was 20.6°C. There were 18 heatwaves in the study period using the maximum temperatures and 12 heatwaves using the minimum temperatures.

Looking at the long-term exposure, 312 women were exposed to one or more heatwaves using the maximum temperatures, whereas 304 women were exposed using the minimum temperatures. Notice that 302 of these individuals were exposed to one or more heatwaves using both the maximum and minimum temperatures (Figure 1A). The women were exposed to between 1-23 heatwave days with a remarkable peak of 15 days using the maximum temperatures, and between 1-25 warm nights with a peak of 13 days using the minimum temperatures (Figure 2). The cumulative heat exposure ranged from 1-40 additional degrees above threshold using the maximum temperatures and from 1-58 additional degrees using the minimum temperatures (Figure 3).

Looking at short-term exposure, 81 women were exposed to one or more heatwaves using the maximum temperatures, while 83 women were exposed using the minimum temperatures. Of these, 59 women were exposed to heatwaves using both maximum and minimum temperatures (Figure 1B). Most women were exposed to seven heatwave days when looking at the maximum temperatures, and one warm night looking at the minimum temperatures (Figure 4). They experienced between 1-19 additional degrees above threshold using maximum temperatures, and 1-13 additional degrees using minimum temperatures (Figure 5).

The association between heat exposure and maternal death and stillbirth

Pregnant women exposed to extreme daytime temperatures the last six days before hospital admission were more likely to die (Table 3), whereas rates of stillbirth increased after daytime and nighttime heat exposure 37 weeks before admission (Table 2).

Analyses showed a fourfold increased odds of maternal death after exposure to one or more heatwaves using maximum temperatures six days before admission (unadjusted odds ratio (uOR) 3.78, 95% CI 1.18-10.5). The association was still significant after adjusting for age, HIV, and parity (adjusted OR (aOR) 4.00, 95% CI 1.05-12.8). There was also a dose-response relationship between high daytime temperatures and maternal death: adjusted analysis showed 12% increased odds of maternal death for each degree above 32.1°C the last six days before admission (aOR 1.12, 95% CI 1.00-1.23). Those aged 16-20 or above 30 and multipara women were particularly vulnerable (Figure 6). The unadjusted analysis was not significant for this association (Table 3 and Figure 6).

Exposure of the mother to heatwaves the last 37 weeks before admission using both maximum and minimum temperatures more than doubled the odds of stillbirth (Tmax uOR 2.07, 95% CI 1.08-4.10, Tmin uOR 2.44, 95% CI 1.26-4.90). The association was no longer significant in the adjusted (Figure 7). Furthermore, there was a relationship between an increasing number of heatwave days, cumulative heat, and stillbirth for both hot days and warm nights. The odds of stillbirth increased by 7-8 % for each heatwave day the mother was exposed to and 3-5 % for each degree above the threshold value throughout pregnancy (Table 2). This result was consistent in the adjusted analysis, except for the cumulative heat measurement using maximum temperatures (Figure 7).

The association between heat exposure and pregnancy complications

Women exposed to heat during the last 37 weeks or the last 6 days before admission experienced significantly more eclampsia, preterm birth, and infections (Tables 2 and 3).

Women exposed to one or more heatwaves close to delivery using the maximum temperatures had increased odds of developing eclampsia (uOR 2.5, 95% CI 1.05-5.55). The association was no longer significant after adjustment for maternal age, parity, and HIV status (Figure 8). For nightly temperatures, the odds of developing eclampsia increased by 16-17 % per degree above 20.6°C (uOR 1.17, 95% CI 1.03-1.31; aOR 1.16, 95% CI 1.00-1.31). The effect of high nightly temperatures was also present in the long-term analysis, where the odds of eclampsia increased by 4% per degree above 20.6°C (uOR 1.04, 95% CI 1.02-1.06; aOR 1.04, 95% CI 1.01-1.06). Furthermore, the long-term analysis of maximum temperatures showed that the odds of eclampsia increased by 5 % per heatwave day (uOR 1.05, 95% CI 1.01-1.10, aOR 1.05, 95% CI 1.00-1.10) (Tables 2 and 3).

There was a small but significant association between cumulative heat and preterm birth using maximum temperatures the last six days before admission in the adjusted analysis; the odds increased by 8 % for each degree above 32.1°C (aOR 1.08, 95% CI 1.00-1.15). This result was not significant in the unadjusted analysis (Figure 9). There was also a tendency towards a positive association for all other temperature metrics (Table 3).

Being exposed to excessive daytime heat throughout pregnancy was associated with increased odds of infection: a 65% increase after exposure to one or more heatwaves (uOR 1.65, 95% CI 1.03-2.70), 5% for each heatwave day (uOR 1.05, 95% CI 1.01-1.08) and 2% per degree above 32.1°C (uOR 1.02, 95% CI 1.00-1.04). This result was not significant in the adjusted analysis (Figure 10). After long-term exposure to high nightly temperatures the odds of infection increased by 65% after exposure to one or more heatwaves (uOR 1.65, 95% CI 1.02-2.68) and 3% per degree above 20.6°C (uOR 1.03, 95% CI 1.01-1.05). The association with heatwaves was not significant in the adjusted analysis (Figure 11).

The association between heat and emergency caesarean section

Heat exposure throughout pregnancy and the last six days before admission significantly reduced the odds of emergency section (Tables 2 and 3). This relationship was consistent through analysis of all heatwave metrics, also in the adjusted analyses. The association was strongest for heatwave as a categorical variable after both long-term (Tmax and Tmin uOR 0.17, 95% CI 0.12-0.24) and short-term exposure (Tmin uOR 0.12, 95% CI 0.06-0.24, Tmax uOR 0.31, 95% CI 0.18-0.53).

Discussion

This is one of very few studies exploring the effect of heatwaves and extreme temperatures on pregnancy outcomes in a low-income country. We found significant associations between heat exposure in pregnancy and several complications indicating that heat is a risk factor for adverse pregnancy outcomes. Namely, high daily and nightly temperatures throughout pregnancy increased the odds of stillbirth, while high daily temperatures close to delivery increased the odds of maternal death. The odds of developing eclampsia was elevated after heat stress throughout pregnancy and close to delivery. Maternal infections were more common after long-term exposure to high temperatures. There was a small association between short-term exposure to high daily temperatures and preterm birth. Surprisingly, exposure to heat in pregnancy seemed to protect against emergency sections independent of the length of exposure.

Stillbirth and preterm delivery

The increased odds of stillbirth after heat exposure seen in our study is in line with results from multiple reviews (4,42–44). Chersich et al. found a 5% increased odds of stillbirth per degree rise in temperature in their meta-analysis, similar to our 3 % and 5 % increased odds per degree for high daily and nightly temperatures respectively. However, we looked at the effect of cumulative heat above a threshold while the meta-analysis looked at the effect of total cumulative temperatures. One study among 14 lower-middle-income countries, including Malawi, found an increased risk of stillbirth after heat exposure during the last seven days of pregnancy (29). We did not find an association between heat exposure close to delivery and stillbirth, but our results are imprecise since we do not know the exact date of delivery.

Stillbirths are often caused by maternal complications (17). Consequently, an increased risk of maternal complications, such as infections, placental abruption, and hypertensive disease, can increase the risk of stillbirth. The odds of eclampsia and infection were elevated after long-term heat exposure in our study, and this might partly explain the increased odds of stillbirth. Animal studies have proposed that a 1.5-2 °C increased core temperature of the mother is teratogenic (30). The mechanisms are not fully understood, but placental cell damage and abruption are associated with heat exposure and can lead to stillbirth (29,45).

Numerous studies have investigated the relationship between heat exposure in pregnancy and preterm birth (4,29,46,47). Several find a risk of preterm birth after extreme heat close to delivery, consistent with our finding of 8% increased odds of preterm birth per additional degree in the last week of pregnancy. Our finding concerned high daily temperatures, but high nightly temperatures are suggested to be more predictive for preterm birth (4). Due to limitations of our data we have not analysed the effect of heat exposure throughout pregnancy, which would have been interesting as previous studies indicate that this can provoke preterm births (4,48). Proposed mechanisms are that heat stress can lead to increased fetal heart rate and oxidative stress, releasing endotoxins, cortisol, adrenaline and inflammatory markers triggering uterine contractions and preterm birth (29,30,49).

Maternal death, eclampsia, preeclampsia, infection, and hemorrhage

Studies investigating the relationship between heat exposure in pregnancy and maternal death are lacking compared to research on preterm birth, stillbirth, and birth weight. However, it is known that heatwaves increase mortality in general (8) and pregnant women are more vulnerable (15) supporting our results showing increased maternal death after short-term exposure to heat. As Chersich et al. point out, the association between mortality and heat exposure is likely as heat is associated with common causes of maternal death, such as hemorrhage (50), infection (51), eclampsia (43) and caesarean sections (26). We did not find any association between hemorrhage and heat exposure, and surprisingly women exposed to excess heat had fewer emergency sections. We found increased odds of eclampsia and infection after heat exposure close to delivery. This suggests that eclampsia and infection are mediators for maternal death, although we have not analysed the association between eclampsia, infection, and maternal death.

We found increased odds of eclampsia after heat exposure in the last week of pregnancy, consistent with studies reporting more eclampsia after exposure to heatwaves during the third trimester (50,52). Additionally, a study found increased hospitalization because of hypertension in pregnancy on hot days (53). Our long-term results are in line with literature suggesting an increased risk of eclampsia and preeclampsia after exposure to excess heat throughout pregnancy (43). However, we did not find significant associations with preeclampsia. Mechanisms behind these effects are unclear, but it is hypothesized that heat exposure influences vascularization and placentation in the first trimester (54), demonstrated by laboratory trials showing an effect on trophoblast cell migrations (52).

To our knowledge, little research is done to support the association we found between excess heat and maternal infection. One study found a dose-response relationship between heat and group B streptococci (GBS) colonization in the warmest month (51). Maternal GBS colonization is linked to maternal bacteraemia, endometritis and chorioamnionitis, and is the leading cause of life-threatening neonatal infection. Another study found an increased number of emergency department visits for pregnant women due to infections or parasitic diseases following warm days (53), supporting our results. HIV was associated with infection in our adjusted analysis; however, these results are imprecise and not significant. Widespread access to antiretroviral treatment and adjunctive HIV care may explain the low impact of HIV in our study (22).

Despite postpartum hemorrhage being the major obstetric cause of maternal death, there are few studies assessing the risk of hemorrhage following exposure to high temperatures. Our study found no associations between heat exposure and hemorrhage, in contrast with one previous study that showed higher odds of placental abruption during warm seasons, with socioeconomically disadvantaged women at particular risk (45). Another observed more uterine bleeding after exposure to heatwaves in the first trimester (50). Heat exposure may trigger inflammatory responses or the coagulation system, leading to placental abruption and hemorrhage (45). High temperatures can disrupt safe storage of heat-sensitive medications such as oxytocin, especially in a low-resource setting, increasing the risk of post-partum hemorrhage (26,55).

Unexpectedly, our analysis showed that heat exposure protected against emergency caesarean sections. There is little previous research on this outcome, but since excess heat is associated with adverse pregnancy outcomes this was a surprising result (4,15,26). The prevalence of caesarean sections was much higher in our material than the national average (52.1 vs 7.7%) (22). Accordingly, our result could be due to irregularities in the way our data was collected and should be interpreted with caution.

Strengths and limitations

There are several strengths in our study. We had access to a relatively large sample size, and the study design is well-adapted to investigate the relationship between heat exposure and pregnancy outcomes. Using temperature data from two meteorological stations means we are covering a larger geographical area which is more representative of where the women lived. We cannot be certain that the women stayed in this area because we do not have information about the residential address, but we assume that this is the case for most of them. We looked at different heat metrics, meaning that we investigated both if there was a simple association and a dose-response relationship between excess heat and the outcomes. We also studied maximum temperatures reflecting daytime heat and minimum temperatures reflecting warm nights.

There are several limitations to consider. There is a possibility of selection bias due to the secondary nature of the dataset, as the variables collected were not purposely tailored to answer our research question. Additionally, the original study mentions a possible selection bias in the data retrieval (32). QECH is a local hospital for Blantyre and a referral hospital for complicated pregnancies from Southern Malawi. Because of this, the results might overestimate the frequency of complications. Some of the logistic regression analyses have wide confidence intervals, suggesting imprecise results. Furthermore, we lacked information about factors that should have been adjusted for, such as socioeconomic status, physical labour and if the pregnant woman had means to cool down during pregnancy (for example access to air conditioning).

Because information on the date of delivery and gestational age was not available in the dataset, we estimated the exposure window from admission date. The exposure intervals are therefore imprecise. Furthermore, most of our data are from the end of 2019, so changes in hospital procedures or available resources can affect the distribution of outcomes. This also means that many women have the same exposure periods, which can explain the uneven distribution of heatwave days. Our data and analyses were not able to detect sensitive periods for heat exposure, other than to see if the last week of pregnancy was of significance. In our short-term analyses, it is probable that women exposed to heatwaves close to delivery gave birth in the warms periods in Malawi and therefore were compared mostly to women giving birth in the colder seasons. Accordingly, seasonal changes other than heat can influence our results.

Implications

These results contribute to existing evidence suggesting healthcare providers and policymakers should take action to protect pregnant women from heat. The findings in our study are especially worrisome because projections show that temperatures will increase faster in Africa than the global average. Women in low-income countries are particularly vulnerable to heat and have few possibilities to protect themselves from exposure. There are effective measures to reduce the risks associated with extreme heat for pregnant women (26). These include behavioural changes, like maintaining hydration and shifting workloads from pregnant women to other family members during hot periods, and adaption of homes and health facilities to improve passive cooling. Resources to implement these should be made available. Further research is needed to understand the biological mechanisms behind heat stress in pregnancy (43).

Conclusion

In conclusion, the findings in this study demonstrate that heat exposure has a significant impact on pregnancy outcomes at QECH in Blantyre, Malawi. Pregnant women are at increased risk of heat-related illness and other complications affecting both mother and fetus. It is important for healthcare providers and policymakers to be aware of the potential effects of high temperatures and heatwaves on pregnant women and to take steps to mitigate the risks and provide support to those who may be affected. All things considered, our study adds to the growing pile of evidence that climate change is and will be threatening maternal and fetal health. Urgent actions are necessary to decrease emissions and secure the well-being of mothers all over the world.

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	Short-term exposure			Long-term exposure		
	Total N = 743	**Heatwave Tmax N = 81**	**Heatwave Tmin N = 83**	**Total N = 697**	**Heatwave Tmax N = 312**	**Heatwave Tmin N = 304**
Demographics						
Age median (IQR)	24 (20, 29)	24 (20, 30)	25 (20, 32)	24 (20, 29)	23 (19, 30)	23 (20, 30)
Primipara n (%)	293 (42%)	27 (39%)	28 (40%)	272 (41%)	120 (42%)	116 (41%)
HIV reactive n (%)	126 (18%)	15 (19%)	13 (16%)	117 (18%)	44 (15%)	41 (14%)
Complications related to pregnancy and childbirth n (%)						
Preeclampsia	84 (11,3%)	9 (11%)	10 (12%)	80 (11%)	30 (9.6%)	29 (9.5%)
Eclampsia/HELLP	37 (5.0%)	8 (9.9%)	8 (9.6%)	36 (5.2%)	20 (6.4%)	21 (6.9%)
Preterm birth	46 (6.2%)	7 (8.6%)	6 (7.2%)	---	---	---
Hemorrhage	46 (6.2%)	3 (3.7%)	5 (6.0%)	45 (6.5%)	21 (6.7%)	20 (6.6%)
Infection	75 (10,1%)	11 (14%)	10 (12%)	75 (11%)	42 (13%)	41 (13%)
Maternal and perinatal mortality n (%)						
Maternal death	17 (2.3%)	5 (6.2%)	4 (4.8%)	16 (2.3%)	8 (2.6%)	9 (3.0%)
Stillbirth	41 (5.6%)^{8}	4 (5.0%)	5 (6.1%)	39 (5.7%)^{8}	24 (7.8%)	25 (8.3%)
Mode of delivery n (%)						
Vaginal	356 (47.9%)	60 (74.0%)	69 (83.1%)	330 (47.3%)	230 (73.7%)	224 (73.7%)
Elective section	39 (5.2%)	2 (2.5%)	2 (2.4%)	38 (5.5%)	6 (1.9%)	6 (2.0%)
Emergency section	346 (46.6%)	19 (23.5%)	12 (14.5%)	327 (46.9%)	76 (24.4%)	74 (24.3%)
Unspecified section	2 (0.3%)	0 (0 %)	0 (0%)	2 (0.3%)	0 (0%)	0 (0%)

Table 1: Overview of patient characteristics. The short-term and long-term exposure overall groups are the same, except that women with preterm birth are removed from the long-term exposure groups. Continuous variables are reported as median (25^{th},75^{th} percentile)^{m} and categorical variables as number n (%)^{m}, where *m* is the number of missing data points. Abbreviations: IQR, interquartile range; Tmax, maximum temperature; Tmin, minimum temperature.

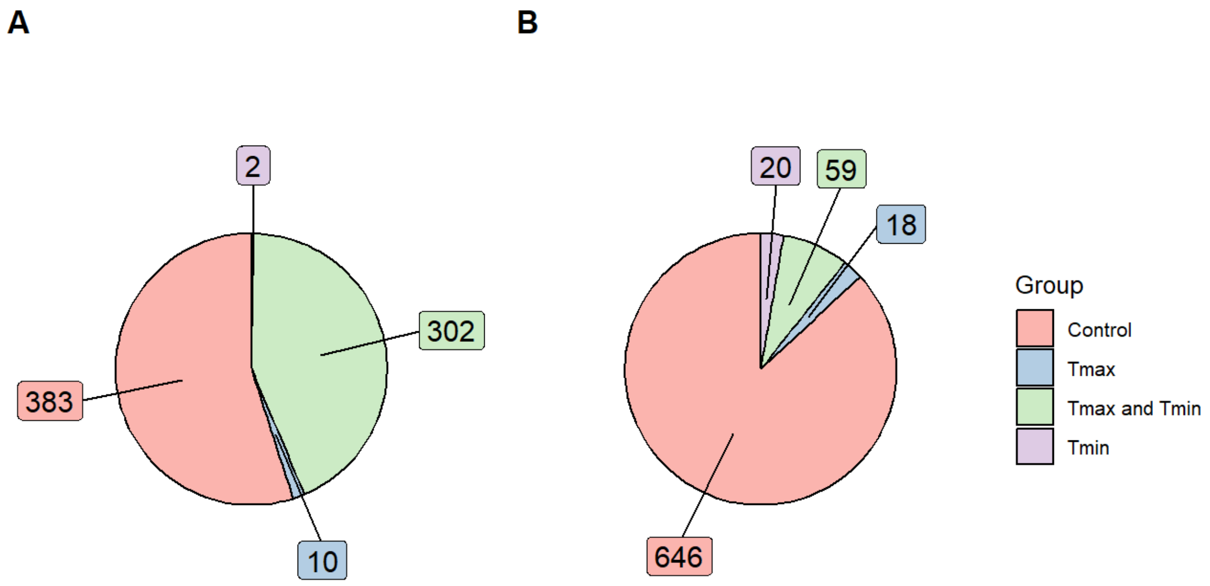

Figure 1: Overview of women exposed to one or more heatwaves 37 weeks before admission (A) and six days before admission (B). Control groups were not exposed to any heatwaves, the Tmax group was exposed to one or more heatwaves using the maximum temperatures, the Tmin group was exposed to one or more heatwaves using the minimum temperatures, and the Tmax and Tmin group was exposed to one or more heatwaves using both maximum and minimum temperatures. Abbreviations: Tmax, maximum temperature; Tmin, minimum temperature.

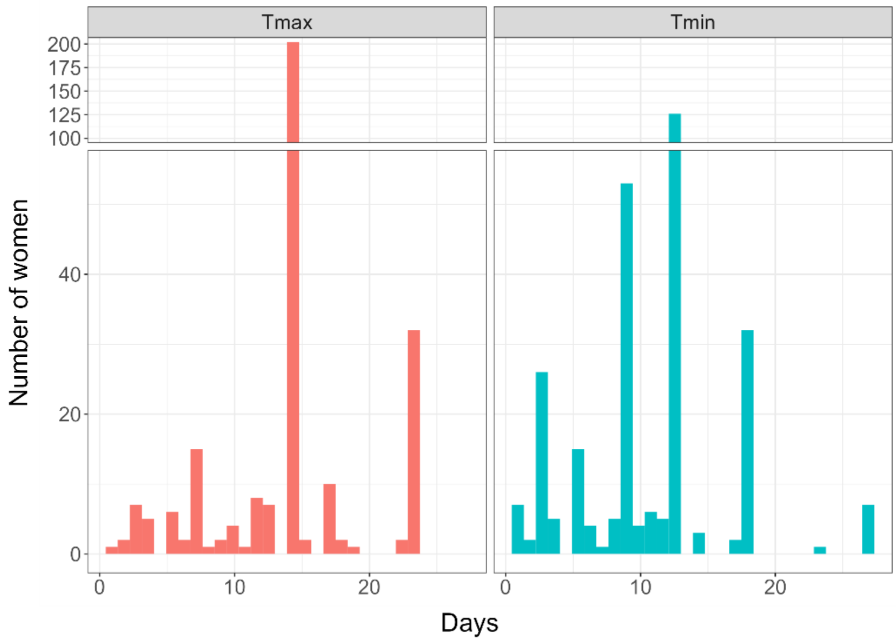

Figure 2: Long-term exposure shown as number of heatwave days using maximum (left panel) and minimum (right panel) temperatures. The x-axis shows number of heatwave days, while the y-axis shows the number of women exposed. 385 women were not exposed to any heatwave days using the maximum temperature, and 393 women were not exposed using the minimum temperatures. Abbreviations: Tmax, maximum temperature; Tmin, minimum temperature.

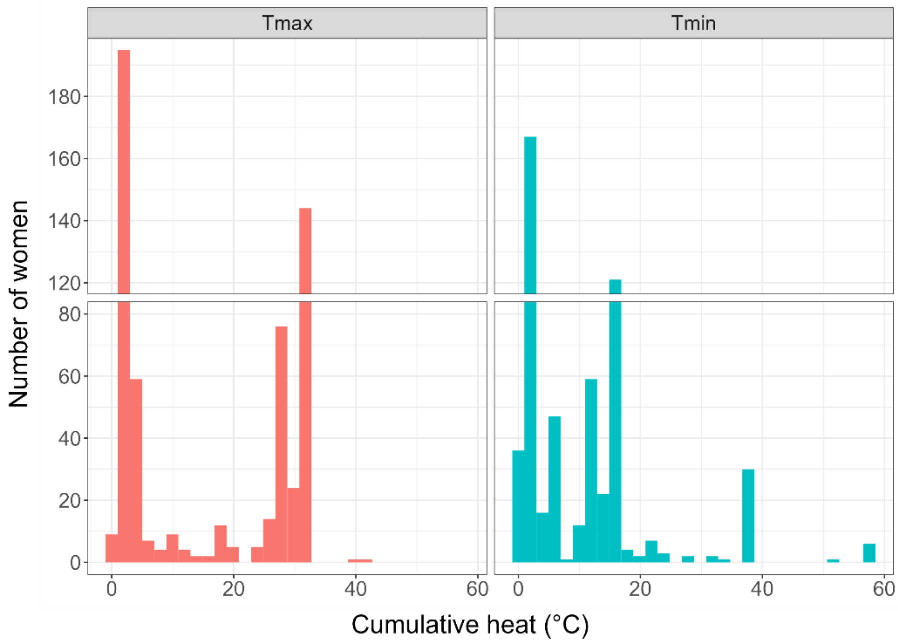

Figure 3: Long-term exposure shown as cumulative heat above the threshold using maximum (left panel, threshold 32.1˚C) and minimum (right panel, threshold 20.6 ˚C) temperatures. The x-axis shows the cumulative number of degrees (Celsius) above the threshold, while the y-axis shows the number of women exposed. A total of 697 women were included. Abbreviations: Tmax, maximum temperature; Tmin, minimum temperature.

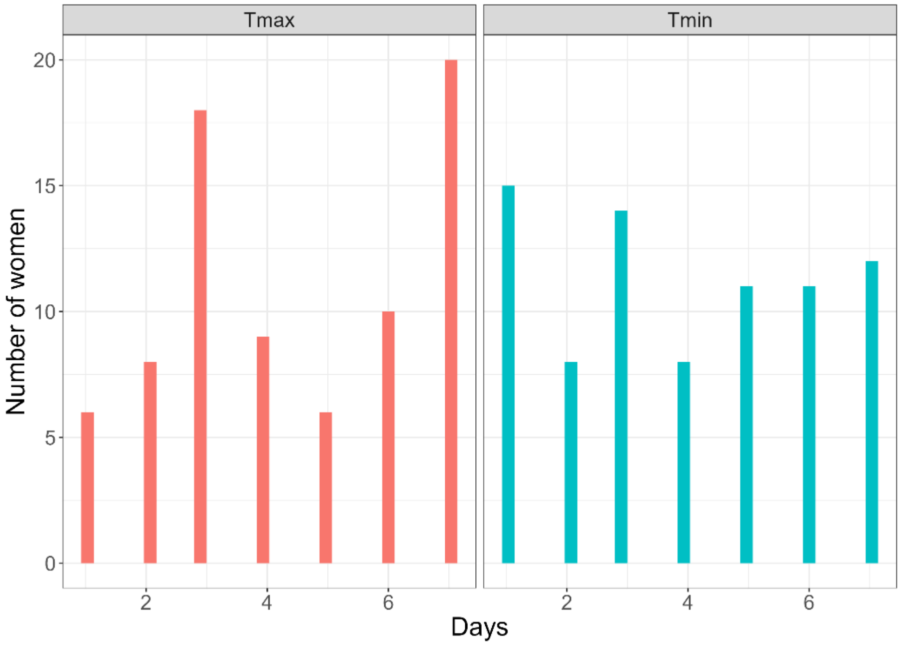

Figure 4: Short-term exposure shown as number of heatwave days using maximum (left panel) and minimum (right panel) temperatures. The x-axis shows the number of heatwave days, while the y-axis shows the number of women exposed. 666 women were not exposed to any heatwave days using the maximum temperatures and 664 women were not exposed using the minimum temperatures. Abbreviations: Tmax, maximum temperature; Tmin, minimum temperature.

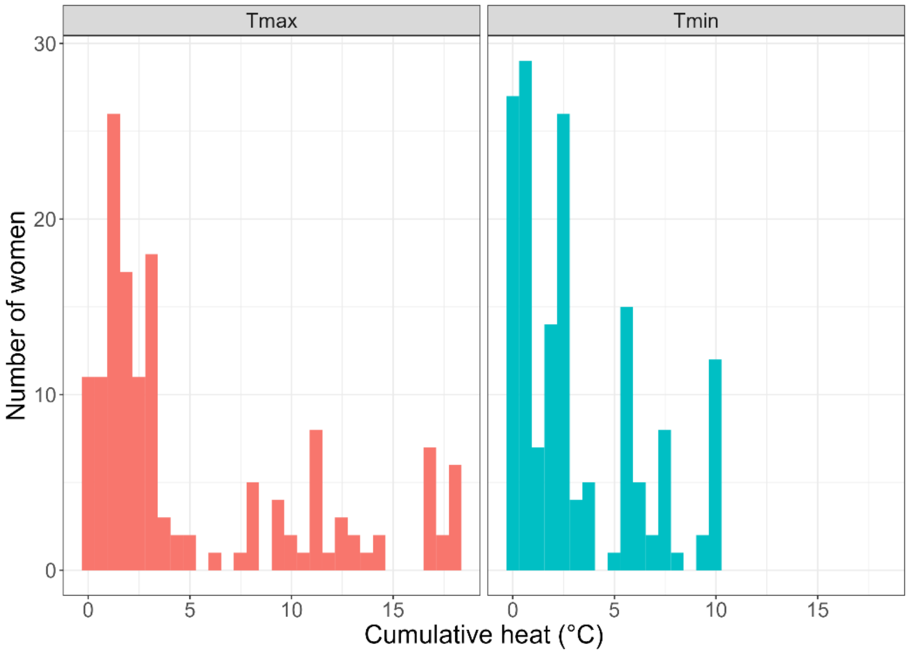

Figure 5: Short-term exposure shown as cumulative heat above the threshold using maximum (left panel, threshold 32.1˚C) and minimum (right panel, threshold 20.6 ˚C) temperatures. The x-axis shows the cumulative number of degrees (Celsius) above the threshold, while the y-axis shows the number of women exposed. A total of 743 women were included. Abbreviations: Tmax, maximum temperature; Tmin, minimum temperature.

Long-term exposure		Tmax			Tmin		
		Heatwave	Heatwave days	Cumulative heat	Heatwave	Heatwave days	Cumulative heat
Perinatal and maternal death							
Stillbirth	Unadjusted	**2.07 (1.08-4.10, 0.032)**	**1.07 (1.03-1.12, <0.001)**	**1.03 (1.00-1.05, 0.023)**	**2.44 (1.26-4.90, 0.009)**	**1.08 (1.03-1.13, <0.001)**	**1.05 (1.03-1.08, <0.001)**
	Adjusted	1.65 (0.80-3.49, 0.2)	**1.07 (1.02-1.12, 0.005)**	1.02 (1.00-1.05, 0.076)	2.04 (0.98-4.36, 0.059)	**1.08 (1.03-1.13, <0.001)**	**1.05 (1.02-1.08, <0.001)**
Maternal death	Unadjusted	1.24 (0.45-3.41, 0.7)	1.00 (0.93-1.06, >0.9)	1.00 (0.97-1.04, 0.8)	1.68 (0.62-4.76, 0.3)	1.01 (0.93-1.08, 0.9)	1.02 (0.98-1.06, 0.3)
	Adjusted	1.45 (0.47-4.62, 0.5)	1.00 (0.92-1.08, >0.9)	1.01 (0.97-1.05, 0.7)	2.22 (0.72-7.54, 0.2)	1.01 (0.92-1.09, 0.8)	1.03 (0.98-1.07, 0.2)
Complications related to pregnancy							
Eclampsia/HELLP	Unadjusted	1.58 (0.81-3.14, 0.2)	**1.05 (1.01-1.10, 0.025)**	1.02 (1.00-1.05, 0.073)	1.87 (0.95-3.76, 0.071)	1.03 (0.98-1.08, 0.2)	**1.04 (1.02-1.06, <0.001)**
	Adjusted	1.49 (0.73-3.08, 0.3)	**1.05 (1.00-1.10, 0.029)**	1.02 (1.00-1.05, 0.10)	1.83 (0.90-3.81, 0.10)	1.03 (0.98-1.08, 0.3)	**1.04 (1.01-1.06, 0.007)**
Preeclampsia	Unadjusted	0.71 (0.44-1.14, 0.2)	0.97 (0.94-1.01, 0.12)	0.99 (0.97-1.00, 0.15)	0.71 (0.43-1.14, 0.2)	0.97 (0.93-1.00, 0.089)	0.98 (0.95-1.00, 0.071)
	Adjusted	0.65 (0.38-1.07, 0.094)	0.97 (0.93-1.00, 0.072)	0.98 (0.96-1.00, 0.093)	0.65 (0.38-1.08, 0.10)	0.96 (0.92-1.00, 0.083)	0.97 (0.94-1.00, 0.062)
Hemorrhage	Unadjusted	1.09 (0.59-1.99, 0.8)	1.00 (0.96-1.04, 0.9)	1.00 (0.97-1.02, 0.8)	1.04 (0.56-1.90. >0.9)	1.00 (0.95-1.05, >0.9)	1.01 (0.98-1.03, 0.7)
	Adjusted	1.06 (0.55-2.03, 0.9)	0.99 (0.95-1.04, 0.7)	1.00 (0.97-1.02, 0.7)	1.00)0.51-1.91, >0.9)	0.96 (0.92-1.00, 0.083)	1.00 (0.97-1.03, 0.8)
Infection	Unadjusted	**1.66 (1.03-2.70, 0.040)**	**1.05 (1.01-1.08, 0.004)**	**1.02 (1.00-1.04, 0.034)**	**1.65 (1.02-2.68, 0.043)**	1.03 (0.99-1.06, 0.13)	**1.03 (1.01-1.05, <0.001)**
	Adjusted	1.27 (0.74-2.18, 0.4)	1.03 (1.00-1.07, 0.071)	1.01 (0.99-1.03, 0.3)	1.27 (0.74-2.17, 0.4)	1.02 (0.98-1.06, 0.2)	**1.03 (1.01-1.05, 0.009)**
Mode of delivery							
Emergency section	Unadjusted	**0.17 (0.12-0.24, <0.001)**	**0.88 (0.86-0.90, <0.001)**	**0.94 (0.92-0.95, <0.001)**	**0.17 (0.12-0.24, <0.001)**	**0.88 (0.86-0.91, <0.001)**	**0.93 (0.92-0.95, <0.001)**
	Adjusted	**0.16 (0.11-0.23, <0.001)**	**0.87 (0.85-0.89, <0.001)**	**0.93 (0.92-0.95, <0.001)**	**0.18 (0.13-0.25, <0.001)**	**0.87 (0.85-0.90, <0.001)**	**0.93 (0.91-0.95, <0.001)**

Table 2: Analysis of the association between heat metrics during the last 37 weeks of pregnancy and pregnancy outcome. A total of 697 women were included. Results are reported as odds ratio (95% confidence interval, p-value). Significant results are in **bold.** Analyses were adjusted for age, parity, and HIV status. Abbreviations: Tmax, maximum temperature; Tmin, minimum temperature.

Short-term exposure		Tmax			Tmin		
		Heatwave	Heatwave days	Cumulative heat	Heatwave	Heatwave days	Cumulative heat
Perinatal and maternal outcomes							
Stillbirth	Unadjusted	0.93 (0.27- 2.41, 0.9)	1.00 (0.78-1.20, >0.9)	1.00 (0.89-1.09, >0.9)	1.18 (0.40-2.85, 0.7)	0.97 (0.72-1.20, 0.8)	1.01 (0.84-1.17, 0.9)
	Adjusted	0.96 (0.22-2.82, >0.9)	1.01 (0.78-1.23, 0.9)	1.00 (0.88-1.09, >0.9)	1.20 (0.34-3.21, 0.7)	0.99 (0.72-1.24, >0.9)	1.00 (0.79-1.17, >0.9)
Maternal death	Unadjusted	**3.78 (1.18-10.5, 0.015)**	1.19 (0.92-1.45, 0.11)	1.09 (0.98-1.19, 0.053)	2.67 (0.74-7.77, 0.093)	1.22 (0.93-1.49, 0.094)	1.16 (0.95-1.35, 0.092)
	Adjusted	**4.00 (1.05-12.8, 0.025)**	1.22 (0.92-1.53, 0.10)	**1.12 (1.00-1.23, 0.021)**	2.80 (0.61-9.60, 0.13)	1.23 (0.86-1.58, 0.2)	1.18 (0.94-1.41, 0.085)
Complications related to pregnancy							
Preterm	Unadjusted	1.61 (0.64-3.52, 0.3)	1.14 (0.96-1.31, 0.10)	1.07 (0.99-1.14, 0.056)	1.28 (0.48-2.92, 0.6)	1.10 (0.90-1.29, 0.3)	1.07 (0.92-1.21, 0.3)
	Adjusted	1.68 (0.61-3.91, 0.3)	1.15 (0.97-1.33, 0.078)	**1.08 (1.00-1.15, 0.034)**	1.66 (0.55-4.16, 0.3)	1.10 (0.87-1.31, 0.4)	1.08 (0.92-1.23, 0.3)
Eclampsia/HELLP	Unadjusted	**2.55 (1.05-5.55, 0.026)**	1.14 (0.94-1.33, 0.13)	1.03 (0.93-1.11, 0.5)	2.05 (0.81-4.60, 0.10)	1.16 (0.95-1.36, 0.11)	**1.17 (1.03-1.31, 0.009)**
	Adjusted	2.22 (0.80- 5.29, 0.094)	1.12 (0.91-1.32, 0.2)	1.04 (0.93-1.12, 0.4)	1.66 (0.55-4.16, 0.3)	1.09 (0.84-1.33, 0.4)	**1.16 (1.00-1.31, 0.026)**
Preeclampsia	Unadjusted	1.04 (0.47-2.08, >0.9)	1.02 (0.87-1.17, 0.7)	1.02 (0.96-1.09, 0.5)	1.16 (0.54-2.25, 0.7)	1.05 (0.89-1.20, 0.6)	1.04 (0.92-1.15, 0.5)
	Adjusted	0.96 (0.38-2.07, >0.9)	1.01 (0.85-1.17, >0.9)	1.01 (0.94-1.08, 0.7)	1.09 (0.46-2.28, 0.8)	1.01 (0.83-1.19, 0.9)	1.00 (0.87-1.13, >0.9)
Hemorrhage	Unadjusted	0.59 (0.14-1.66, 0.4)	0.88 (0.63-1.10, 0.4)	0.98 (0.86-1.07, 0.6)	1.03 (0.35-2.46, >0.9)	0.96 (0.72-1.17, 0.7)	0.93 (0.73-1.10, 0.5)
	Adjusted	0.76 (0.18-2.19, 0.7)	0.92 (0.66-1.14, 0.5)	0.99 (0.87-1.08, 0.9)	1.01 (0.29-2.65, >0.9)	0.98 (0.72-1.22, 0.9)	0.96 (0.74-1.13, 0.7)
Infection	Unadjusted	1.57 (0.75-3.01, 0.2)	1.11 (0.96-1.26, 0.12)	1.06 (0.99-1.12, 0.058)	1.34 (0.62-2.61, 0.4)	1.09 (0.93-1.25, 0.2)	1.10 (0.99-1.21, 0.066)
	Adjusted	1.51 (0.63-3.22, 0.3)	1.10 (0.93-1.26, 0.2)	1.06 (0.99-1.12, 0.087)	1.13 (0.45-2.48, 0.8)	1.07 (0.88-1.26, 0.4)	1.08 (0.95-1.21, 0.2)
Mode of delivery							
Emergency section	Unadjusted	**0.31 (0.18-0.53, <0.001)**	**0.76 (0.66-0.85, <0.001)**	**0.89 (0.84-0.94, <0.001)**	**0.12 (0.06-0.24, <0.001)**	**0.61 (0.49-0.73, <0.001)**	**0.73 (0.64-0.82, <0.001)**
	Adjusted	**0.30 (0.16-0.24, <0.001)**	**0.76 (0.65-0.86, <0.001)**	**0.89 (0.84-0.95, <0.001)**	**0.11 (0.05-0.23, <0.001)**	**0.55 (0.41-0.70, <0.001)**	**0.73 (0.63-0.83, <0.001)**

Table 3: Analysis of the association between heat metrics during the last six days before admission and pregnancy outcome. A total of 743 women were included. Results are reported as odds ratio (95% confidence interval, p-value). Significant results are in **bold**. Analyses were adjusted for age, parity and HIV status. Abbreviations: Tmax, maximum temperature; Tmin, minimum temperature.

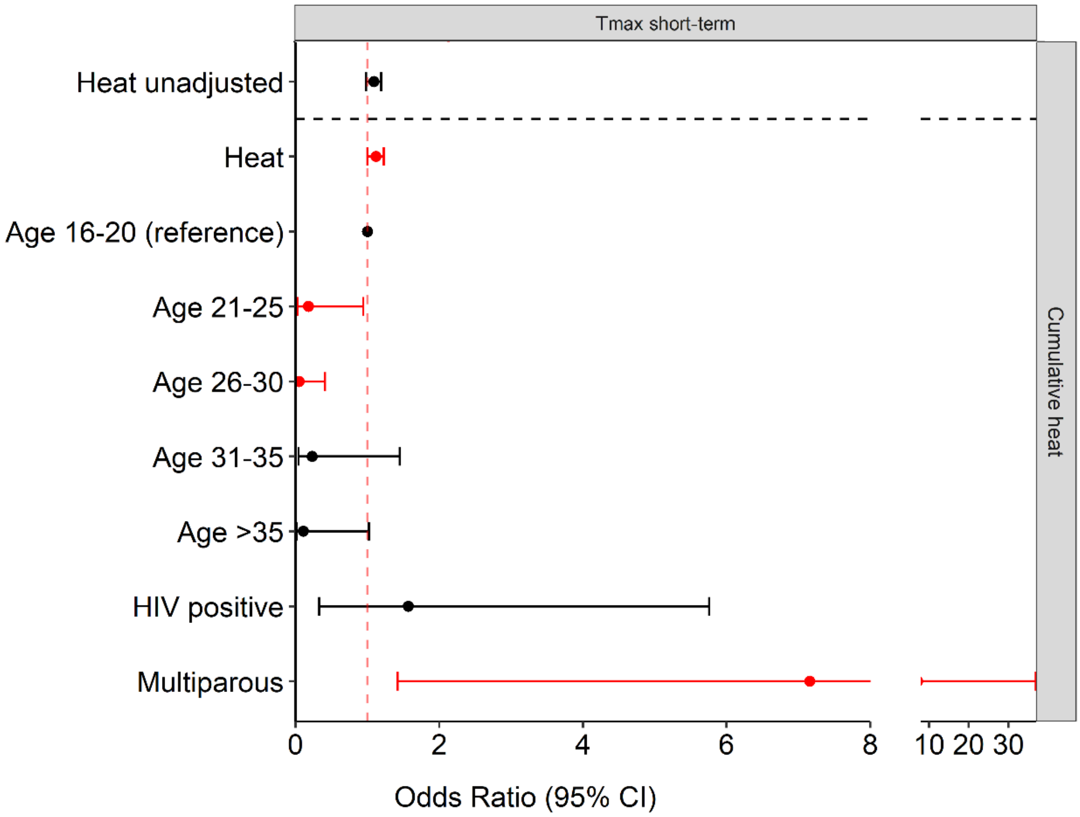

Figure 6: Odds of **maternal death** per 1˚C above the threshold (32.1˚C) six days before admission to hospital using maximum temperatures. Unadjusted analysis is shown above the stapled horizontal line, adjusted analysis is below. Results are reported as odds-ratio with 95% confidence interval. Significant results are in red. Notice that the x-axis is modified for easier interpretation. The red dotted line represents an odds-ratio of one, results overlapping with this line are not significant. A total of 743 women are included. Abbreviations: Tmax, maximum temperature.

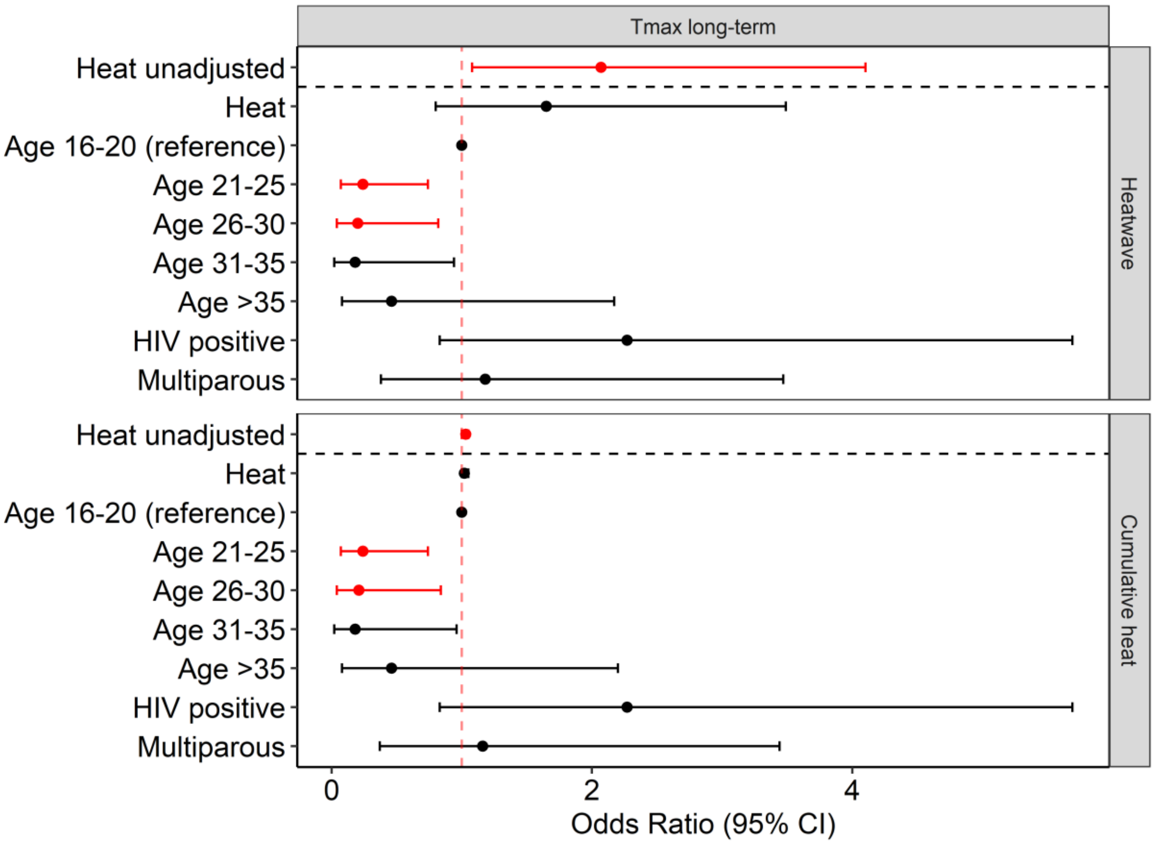

Figure 7: Odds of **stillbirth** if exposed to one or more heatwaves and per 1˚C above the threshold (32.1˚C) throughout pregnancy using maximum temperatures. Unadjusted analysis is shown above the stapled horizontal line, adjusted analysis is below. Results are reported as odds-ratio with 95% confidence interval. Significant results are in red. The red dotted line represents an odds-ratio of one, results overlapping with this line are not significant. A total of 697 women are included. Abbreviations: Tmax, maximum temperature.

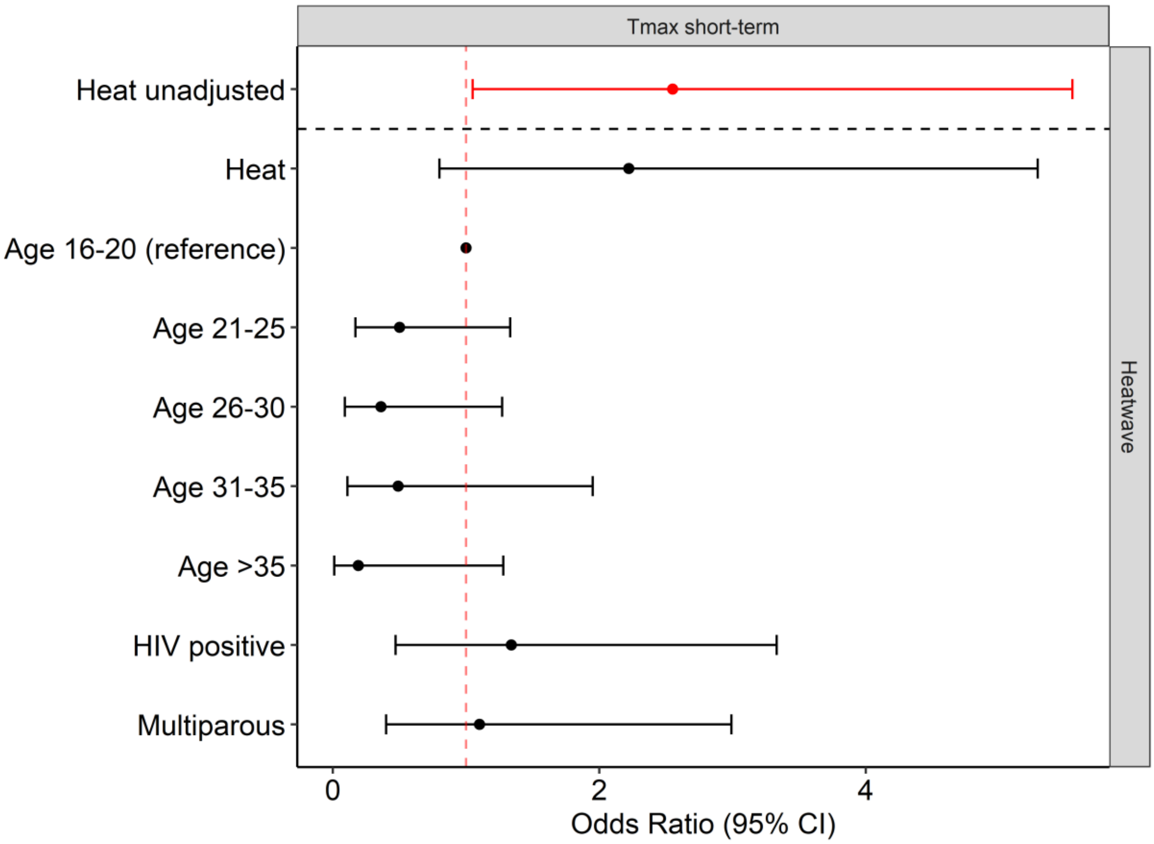

Figure 8: Odds of **eclampsia** if exposed to one or more heatwaves six days before admission to hospital using maximum temperatures. Unadjusted analysis is shown above the stapled horizontal line, adjusted analysis is below. Results are reported as odds-ratio with 95% confidence interval. Significant results are in red. The red dotted line represents an odds-ratio of one, results overlapping with this line are not significant. A total of 697 women are included. Abbreviations: Tmax, maximum temperature.

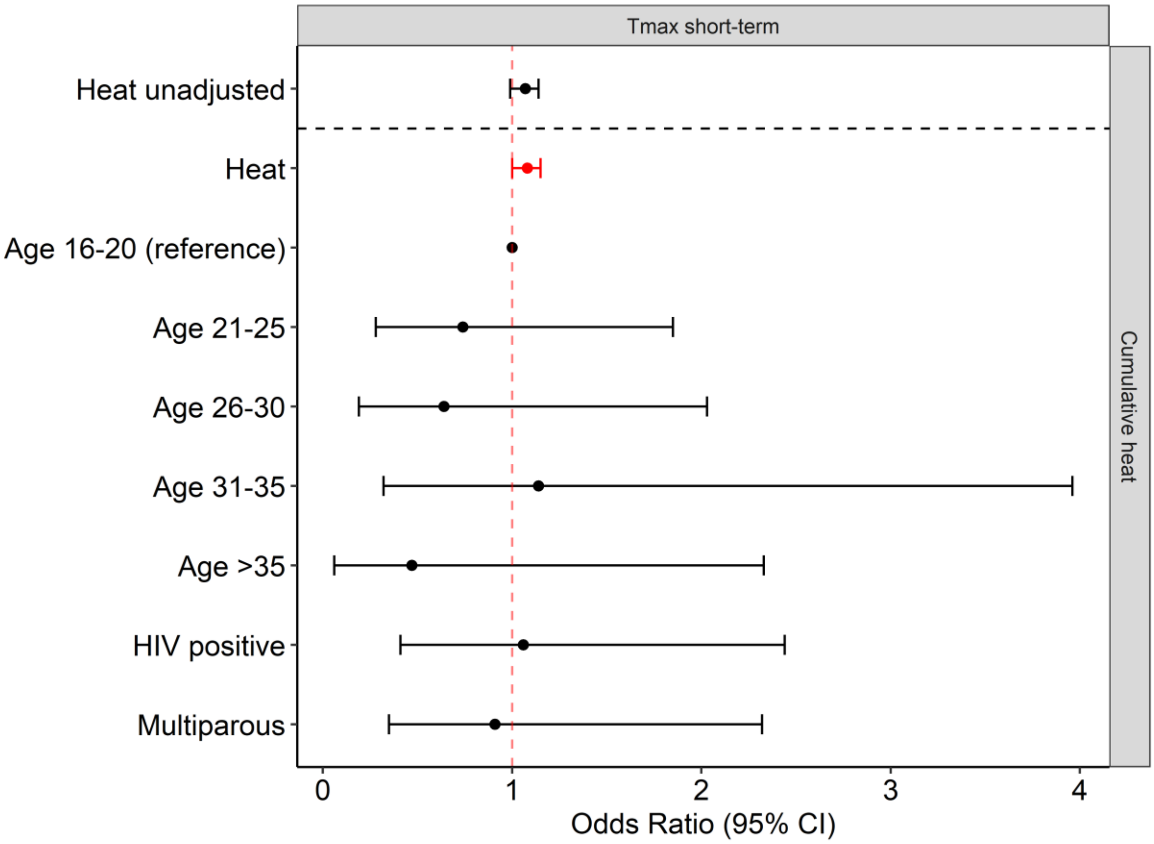

Figure 9: Odds of **preterm delivery** per 1˚C above the threshold (32.1 ˚C) throughout pregnancy using maximum temperatures. Unadjusted analysis is shown above the stapled horizontal line, adjusted analysis is below. Results are reported as odds-ratio with 95% confidence interval. Significant results are in red. The red dotted line represents an odds-ratio of one, results overlapping with this line are not significant. A total of 743 women are included. Abbreviations: Tmax, maximum temperature.

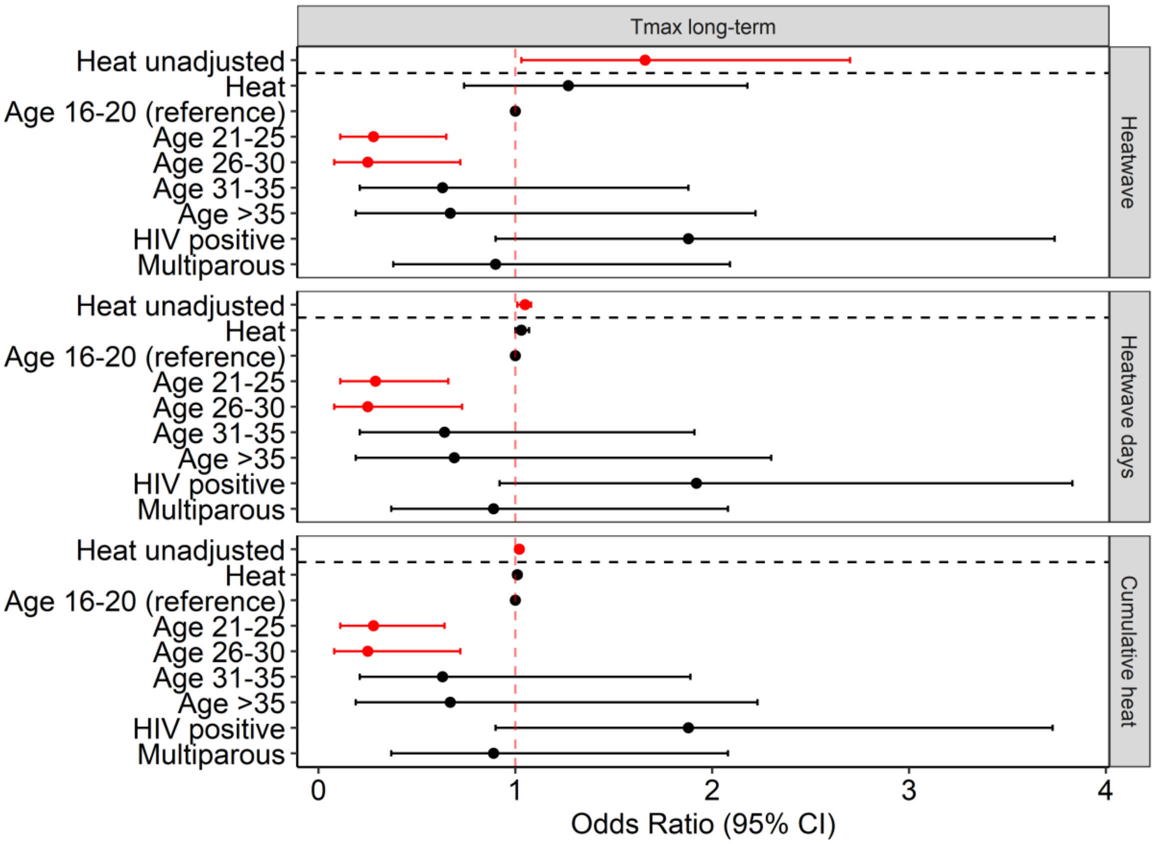

Figure 10: Odds of **infection** if exposed to one or more heatwaves, per heatwave day and per 1˚C above the threshold (32.1 ˚C) throughout pregnancy using maximum temperatures. Unadjusted analysis is shown above the stapled horizontal line, adjusted analysis is below. Results are reported as odds-ratio with 95% confidence interval. Significant results are in red. The red dotted line represents an odds-ratio of one, results overlapping with this line are not significant. A total of 697 women are included. Abbreviations: Tmax, maximum temperature.

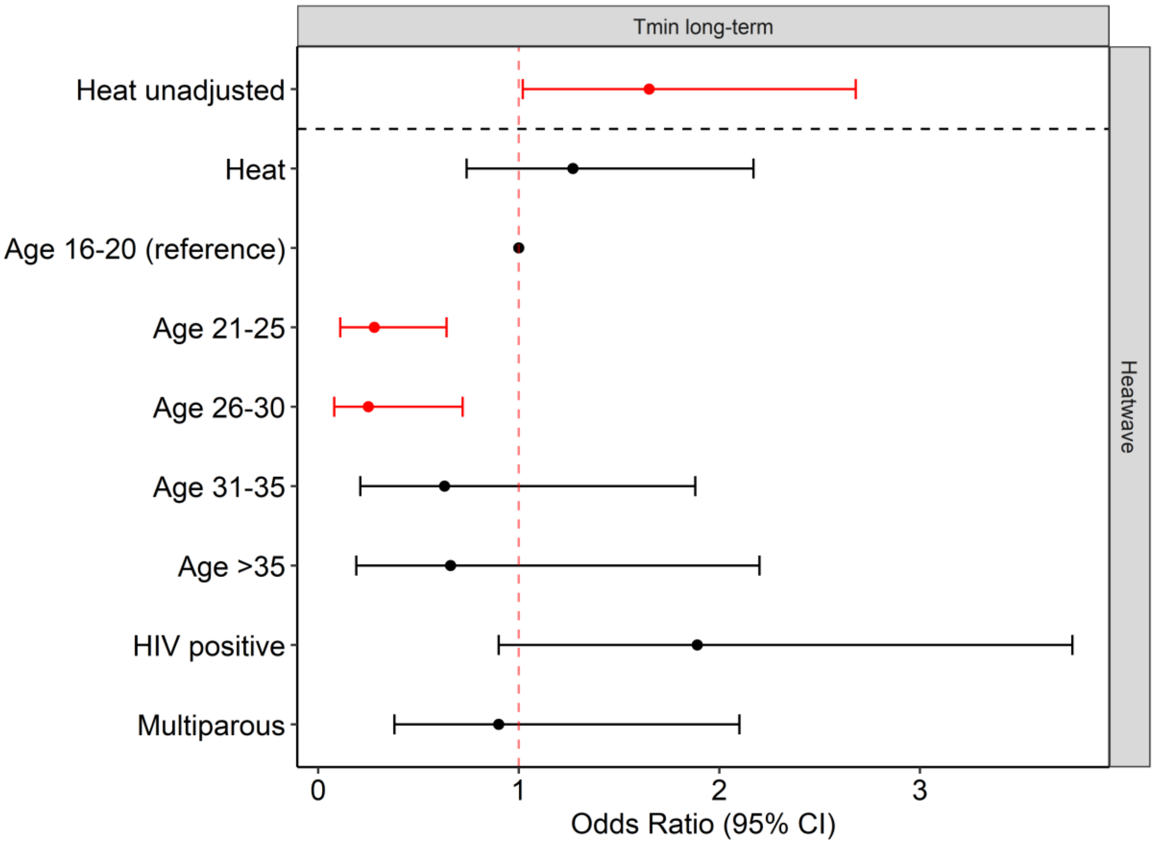

Figure 11: Odds of **infection** if exposed to one or more heatwaves throughout pregnancy using minimum temperatures. Unadjusted analysis is shown above the stapled horizontal line, adjusted analysis is below. Results are reported as odds-ratio with 95% confidence interval. Significant results are in red. The red dotted line represents an odds-ratio of one, results overlapping with this line are not significant. A total of 697 women are included. Abbreviations: Tmax, maximum temperature.

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