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Climate and Health Africa Conference

Admire Chikandiwa

Senior Researcher: Wits Planetary Research Institute, and **Senior Medical Registrar**, Department of Obstetrics and Gynaecology, Wits University

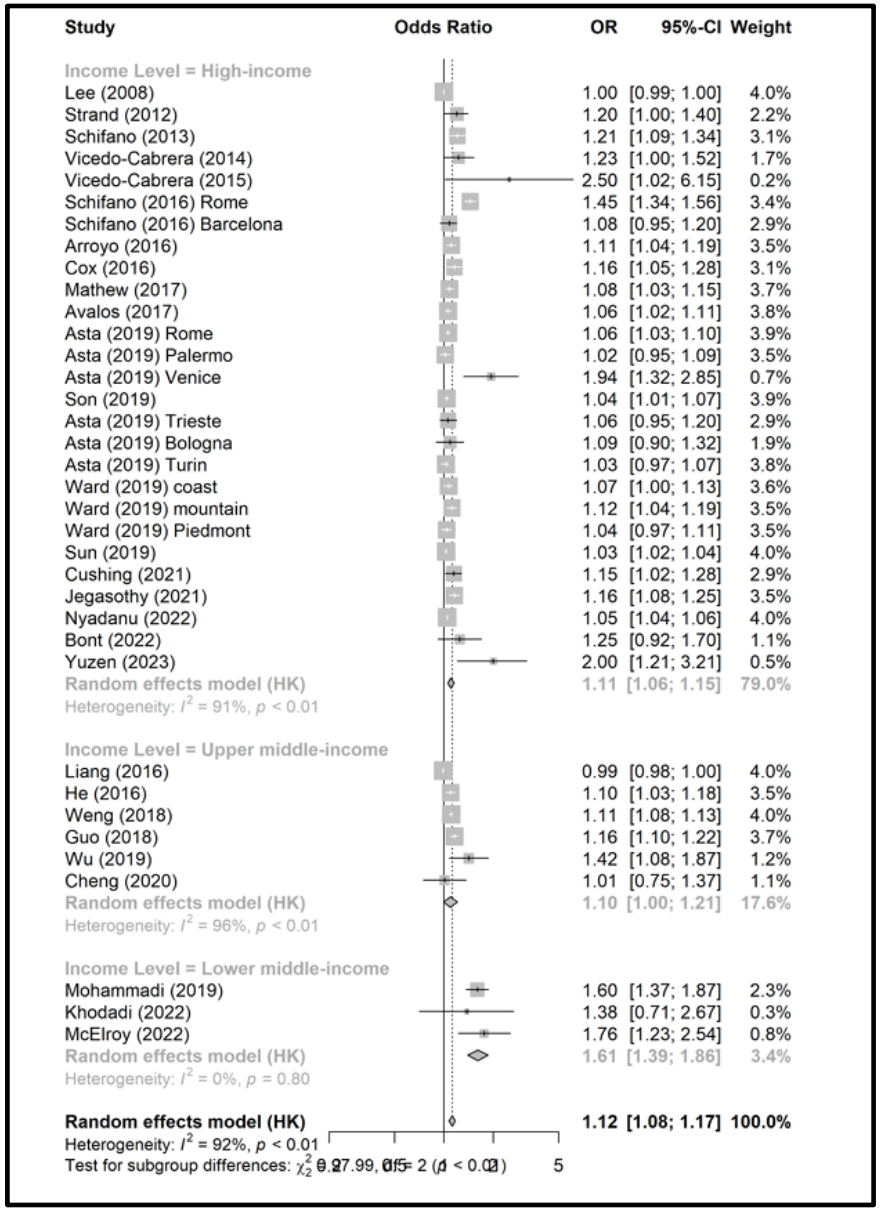
Biological pathways from heat exposure to preterm birth and other adverse maternal and child health: longitudinal studies across three countries in sub-Saharan Africa

HE²AT center

Outline

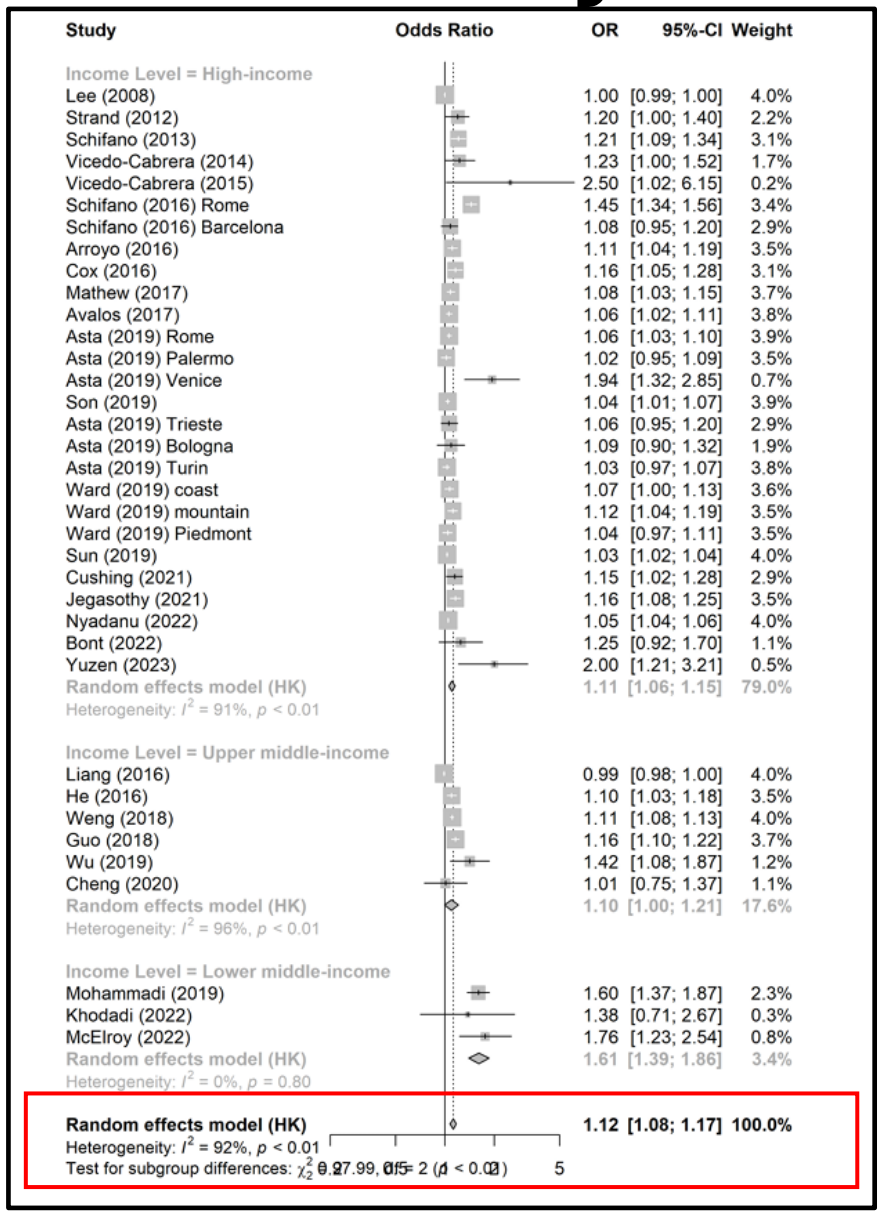
- Background and study rationale
- Cross-cutting activities and synergies across the studies
- Contribution to evidence and policy

Heat and preterm birth systematic review



Lakhoo et al., 2024 Nature Medicine, under review

Heat and preterm birth systematic review



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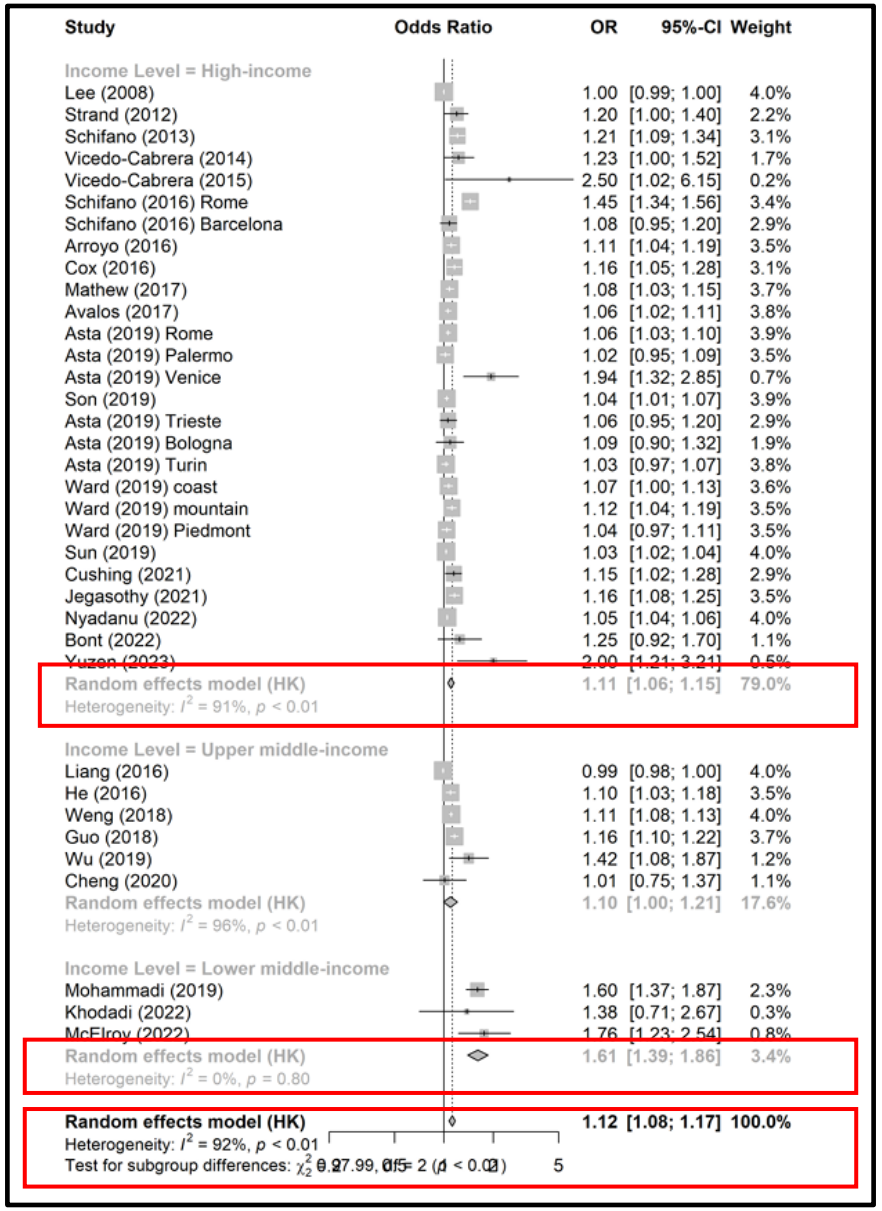


Lakhoo et al., 2024 Nature Medicine, under review

Knowledge gaps

- About 200 studies report linkages between heat exposure and pregnancy outcomes

- Almost none have investigated the underlying biological pathways

- Plausible biological sequelae of heat exposure include:

    - Epigenetic and immunological changes;
    - Sympathetic nervous system activation and release of hormones that trigger labour;
    - Dehydration, aberrant placental implantation and impaired placental flow;
    - Altered foetal membrane integrity and microbiome

Samuels et al., International Journal of Biotechnology, 2022

Preterm birth definition and sequelae

Definition: Birth before 37 completed weeks of gestation

- Leading cause of death and disability in children under 5 years worldwide
- Prevalence of preterm birth in sub-Saharan Africa is **10.9%**

Short-term sequelae: Admission to Neonatal High Care and Intensive Units

- Respiratory Distress Syndrome, neonatal jaundice, sepsis, early neonatal death
- Cost of care around $32,000 in first year of life

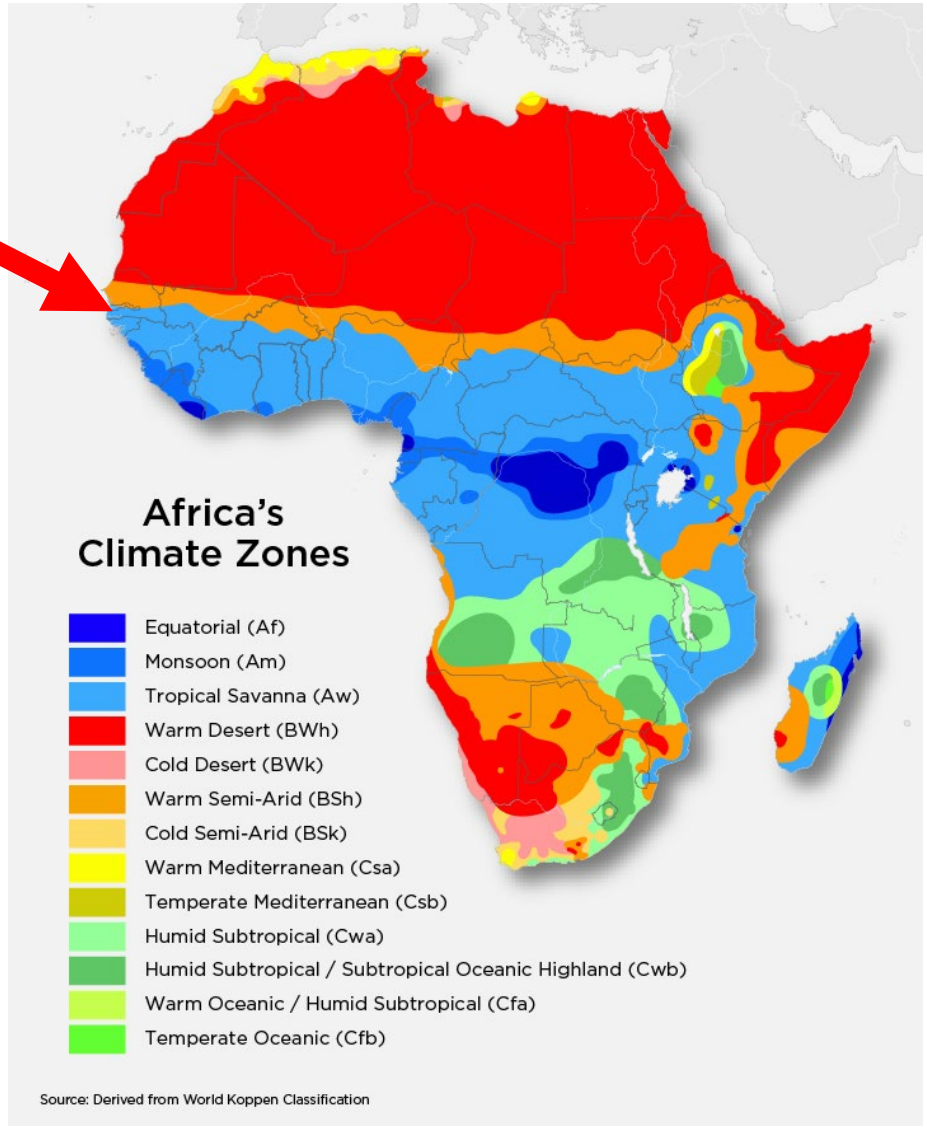
Long-term sequelae: Early development of adult-onset diseases

- Cancers, cardiovascular disease, insulin resistance and obesity
- Neurological and social disability

https://www.who.int/news-room/fact-sheets/detail/preterm-birth

Study location and characteristics

Brikama & Basse
The Gambia
N=670



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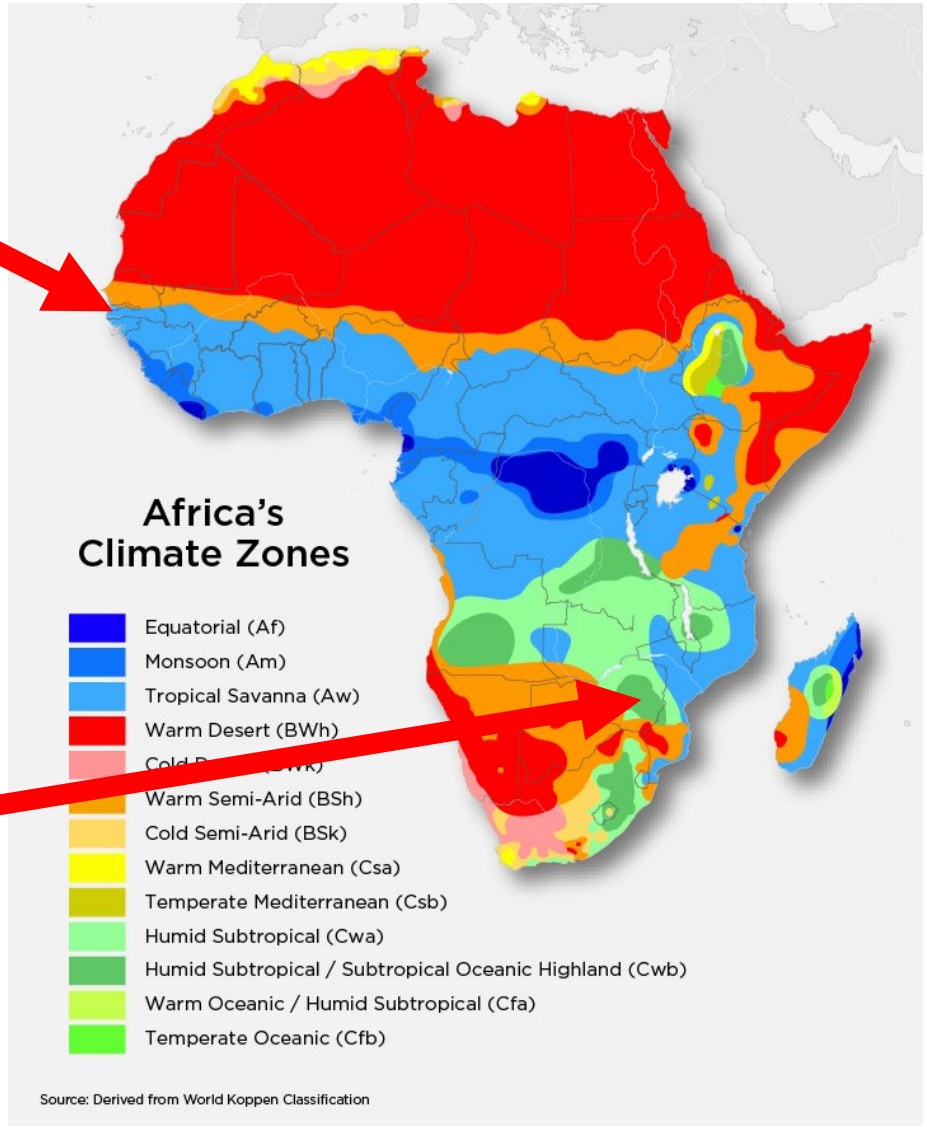

Study location and characteristics

Brikama & Basse
The Gambia
N=670

Shurugwi
Zimbabwe
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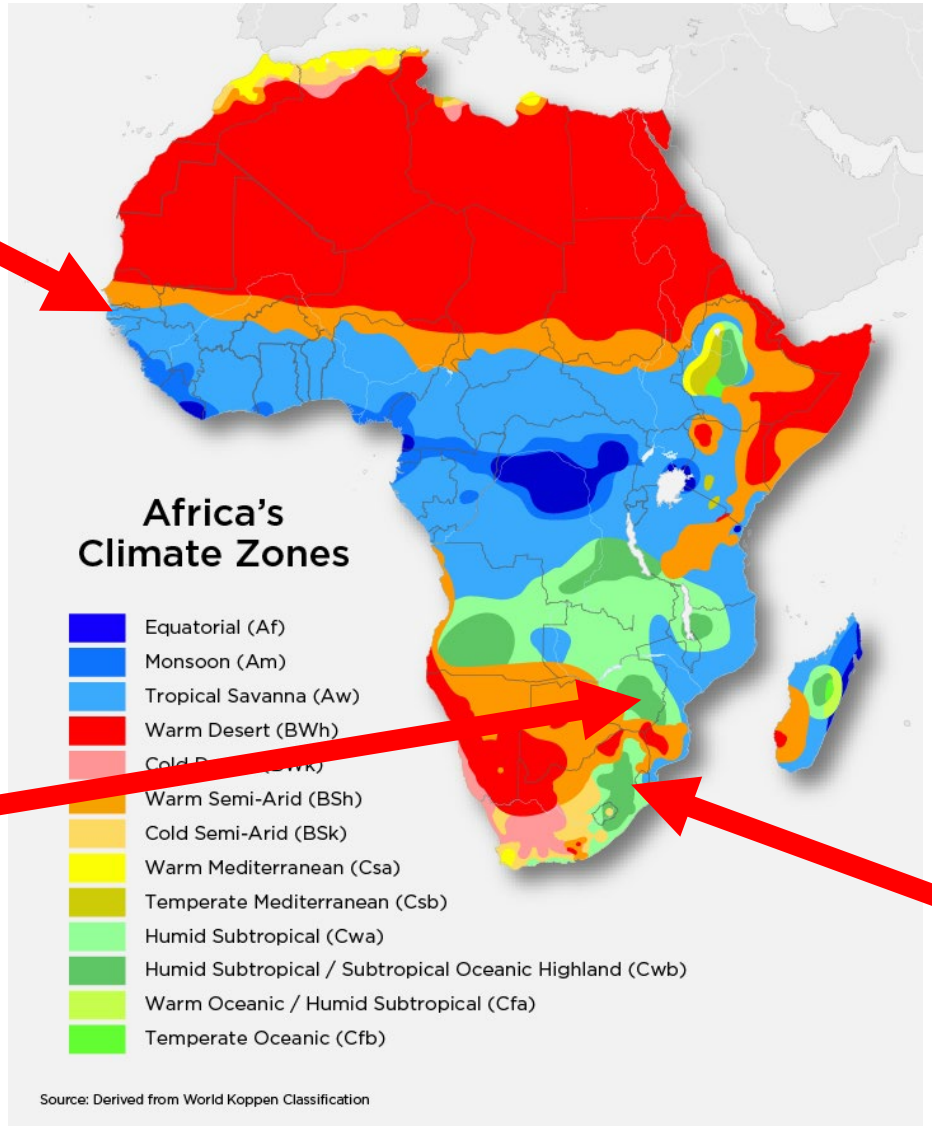
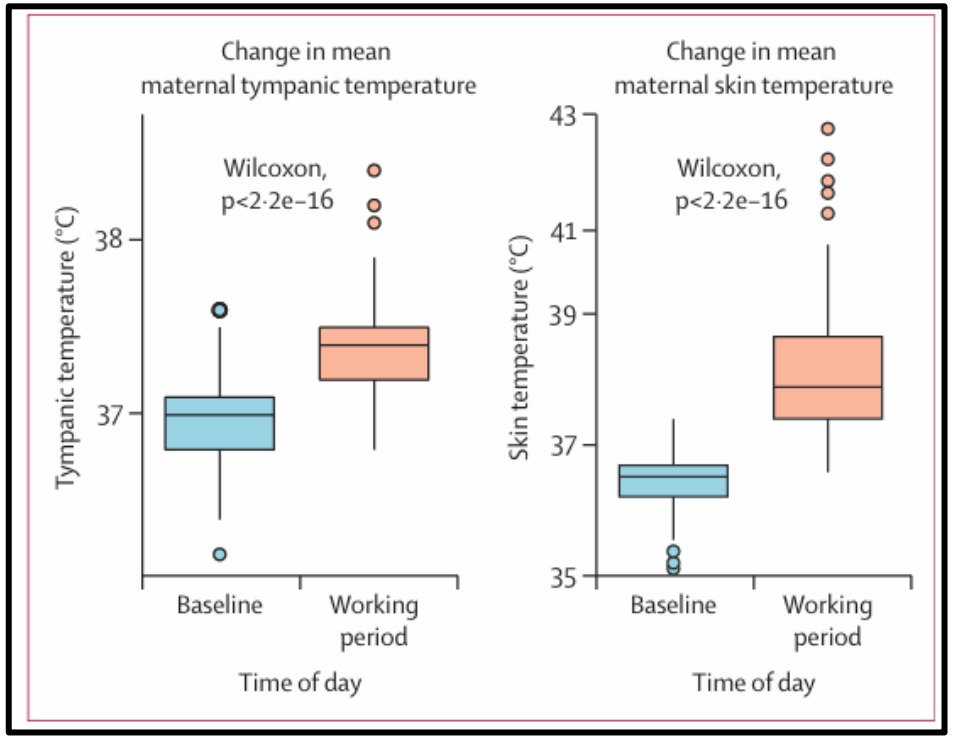
Johannesburg
South Africa
N=200

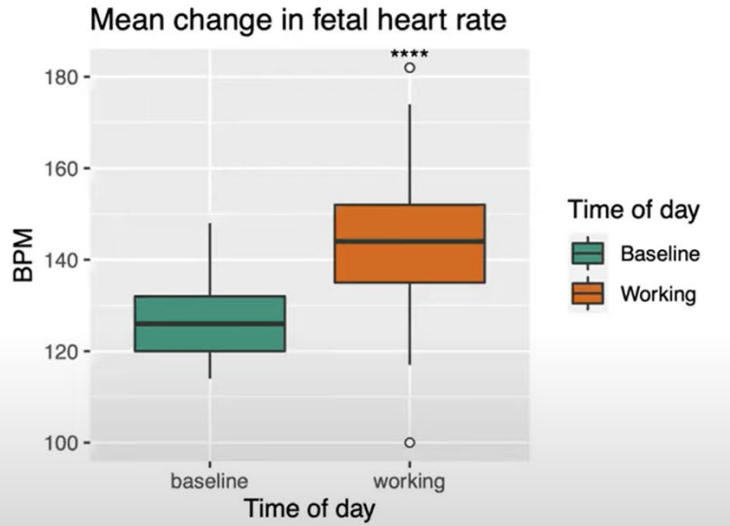


Preliminary work: Basse, Gambia



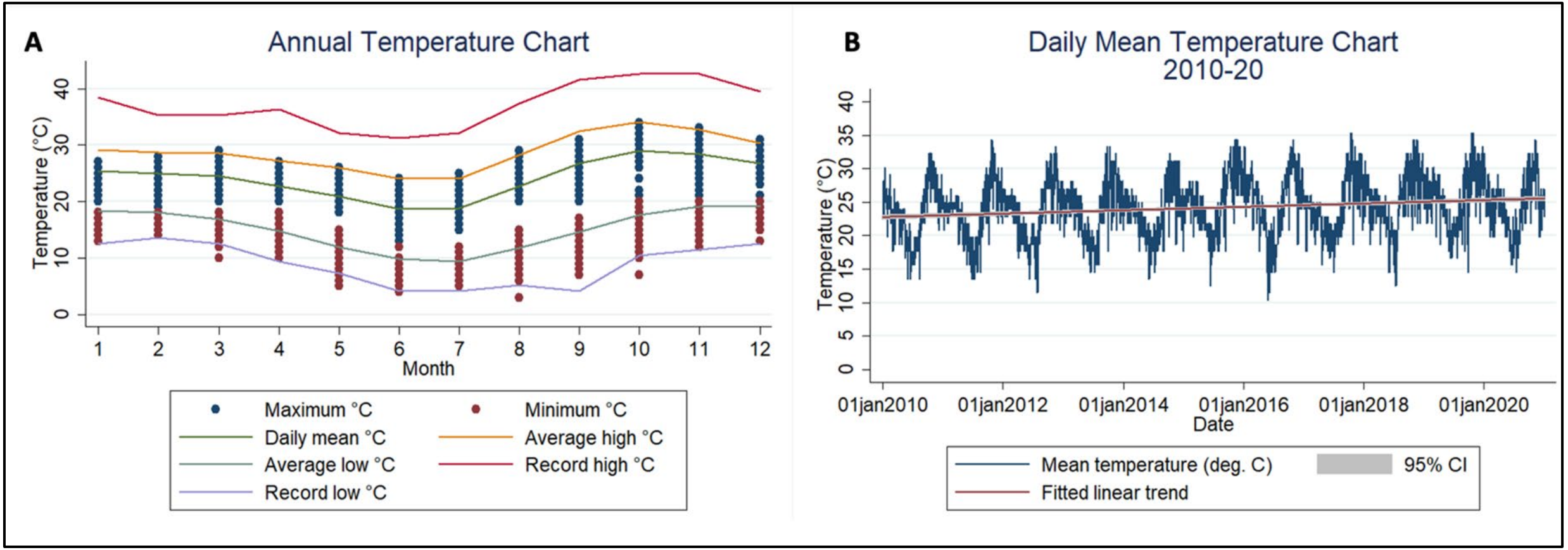
Impact on fetus

- 41/122 (33.6%) episodes of fetal stress
- 21/122 (17%) experienced fetal heart rates >160 or < 115 bpm.
- 22/40 (55%) experienced an increase in RI from baseline



Bonell et al., The Lancet Planetary Health, 2022

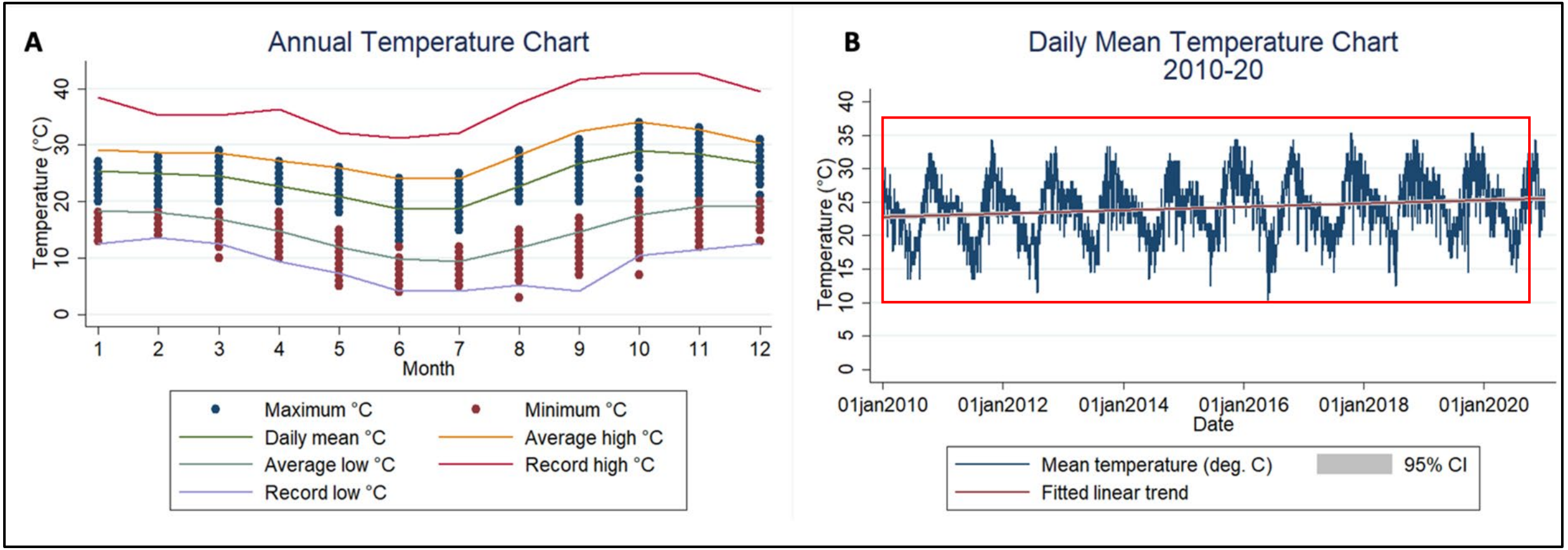
Preliminary work: Shurugwi, Zimbabwe



Climate change in Shurugwi: (A) Intra-annual variation in temperature (B) Average daily temperature by year

Prendergast et al., Study protocol: Extreme heat and preterm birth in rural Zimbabwe

Preliminary work: Shurugwi, Zimbabwe



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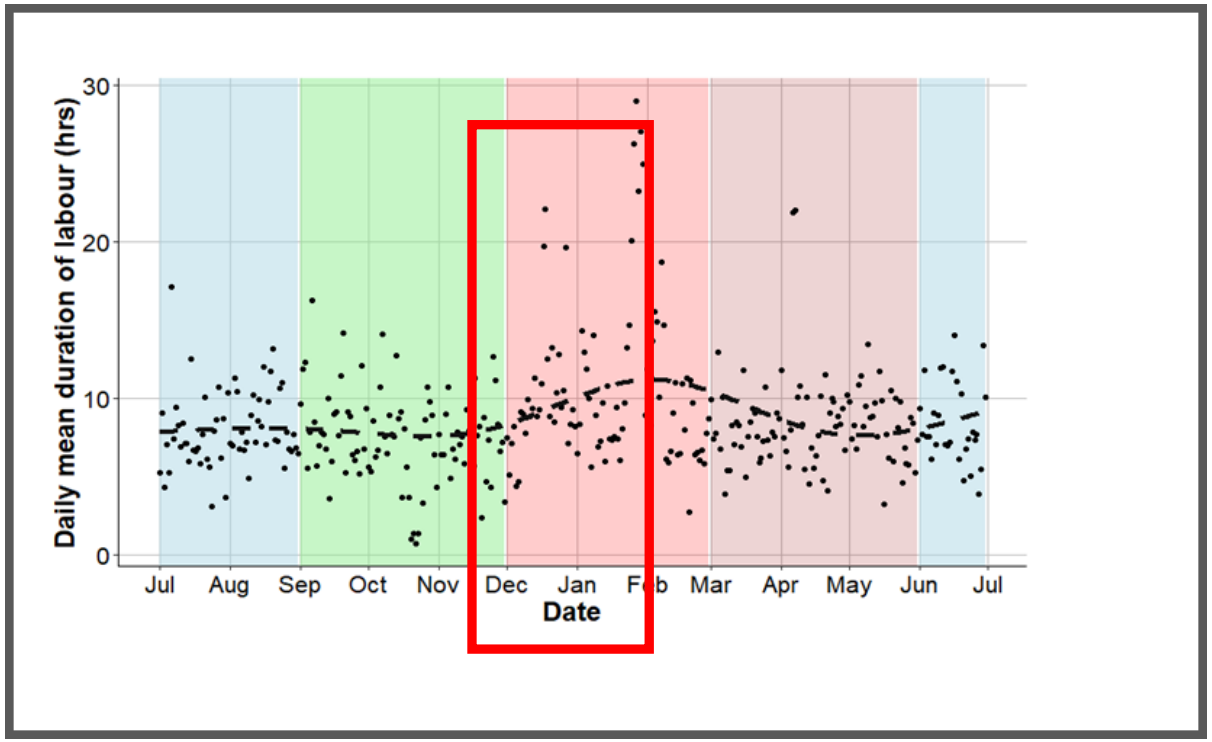
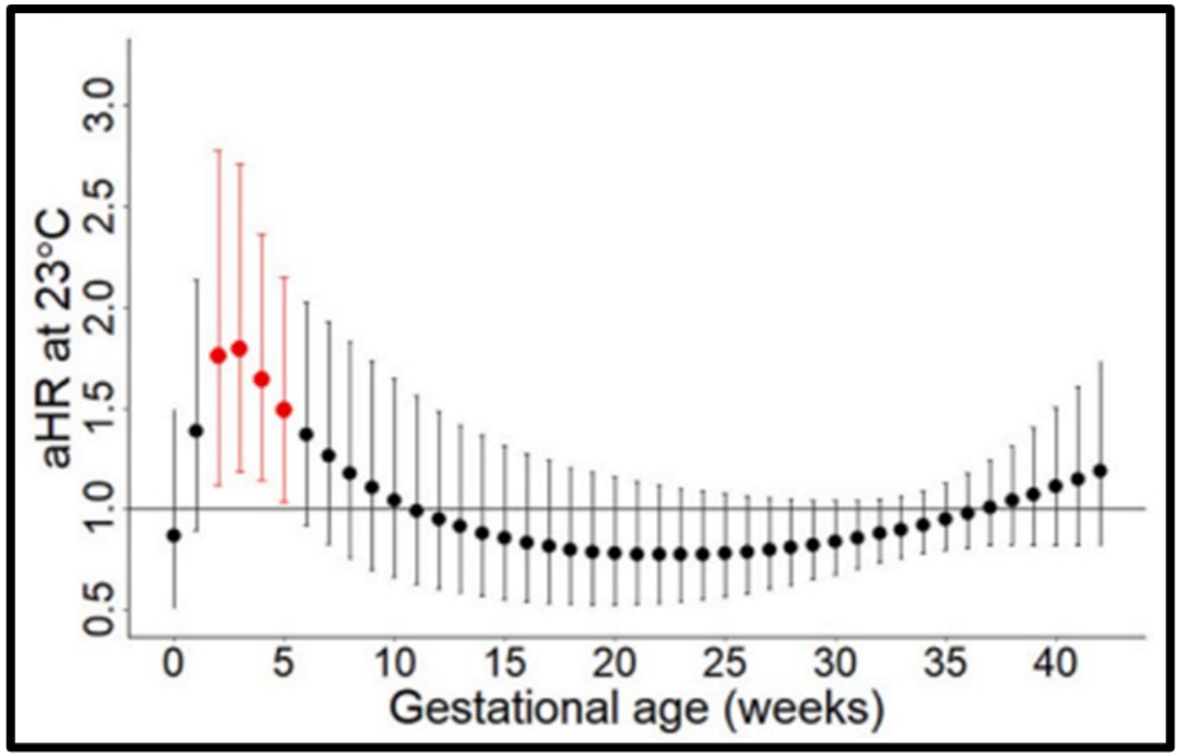
Preliminary work: Johannesburg, RSA





Analysis of **7996** birth records in Jhb.
Median duration in summer=7.7 hours (IQR=1.8-13.8), winter=6.4 hours (IQR=1.3-12.4),
EMCS for foetal distress=396 (21% of births) versus winter=292 (14% of births)
(Unpublished work)

Ambient temperature during pregnancy and risk of maternal hypertensive disorders: A time-to-event study in Johannesburg, South Africa

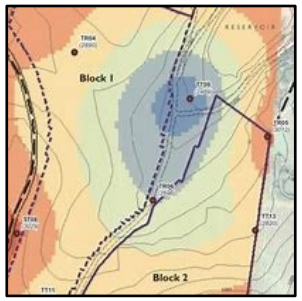
Chérie Part [a,*], Jean le Roux [b], Matthew Chersich [b], Shobna Sawry [b], Véronique Filippi [c], Nathalie Roos [d], Lee Fairlie [b], Britt Nakstad [e,f], Jeroen de Bont [g], Petter Ljungman [g,h], Massimo Stafoggia [i], Sari Kovats [a], Stanley Luchters [j,k,l], Shakoor Hajat [a]

Heat In Pregnancy Study (HIPS):

An observational cohort study of heat stress impacts in pregnancy in The Gambia

Overall aim: to determine the physiological and biochemical changes that occur in pregnancy due to heat stress and how these impact maternal, fetal and newborn health and well-being.

Micro-climate mapping by remote data monitoring: cover regions from where participants will be recruited for the duration of the study



Chronic Heat Prospective Cohort study: Intensive follow-up including wearable devices to measure personal heat, humidity and air pollution exposure

Placenta and microbiome work: fetal size, umbilical doppler assessments, placental hormones, placental histology and rectal swabs for infant microbiota

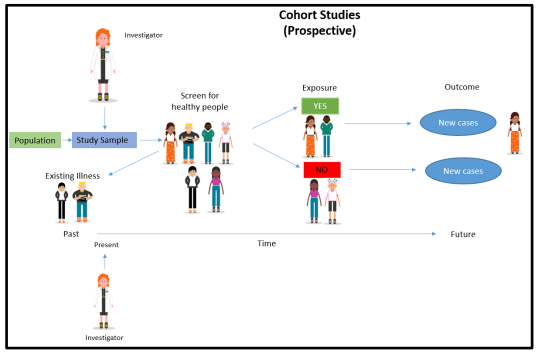
Extreme heat and preterm birth in rural Zimbabwe Study

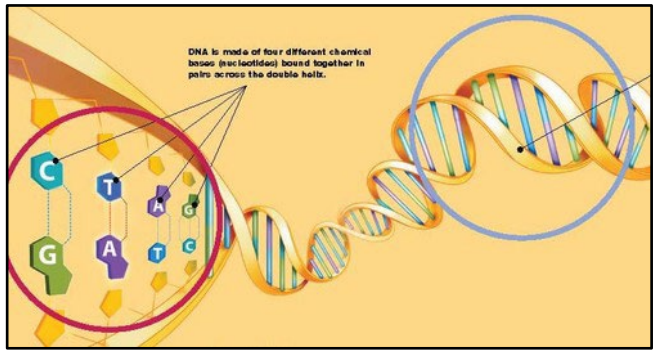
Overall aim: to define the biological mechanisms linking extreme heat with preterm birth

Two cohorts: evaluate association between extreme heat and preterm birth

Nested sub-study: explore associations between extreme heat and inflammatory pathways underlying preterm birth

Human fetal chip model: provide a cellular level understanding of the response of foetal membranes to environmental changes in heat





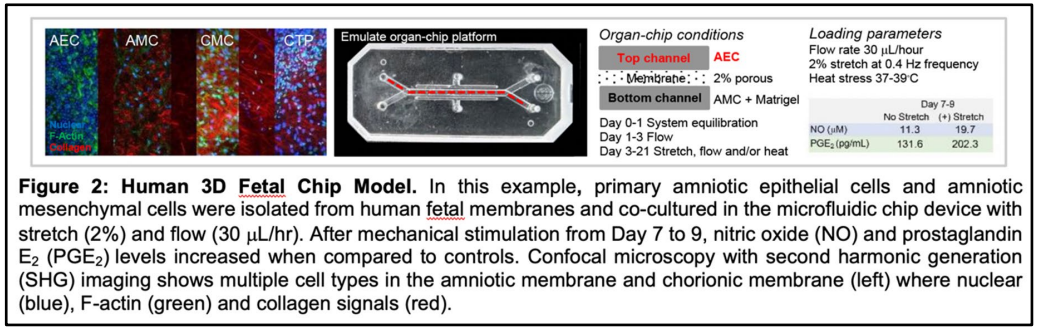


Figure 2: Human 3D Fetal Chip Model. In this example, primary amniotic epithelial cells and amniotic mesenchymal cells were isolated from human fetal membranes and co-cultured in the microfluidic chip device with stretch (2%) and flow (30 µL/hr). After mechanical stimulation from Day 7 to 9, nitric oxide (NO) and prostaglandin E_2 (PGE_2) levels increased when compared to controls. Confocal microscopy with second harmonic generation (SHG) imaging shows multiple cell types in the amniotic membrane and chorionic membrane (left) where nuclear (blue), F-actin (green) and collagen signals (red).

Bio-HEAT study:

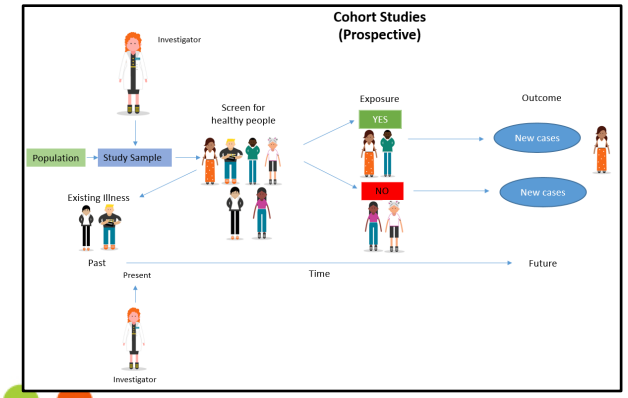
Investigating the Biological pathways from HEAT exposure to preterm birth and other adverse maternal and child health outcomes

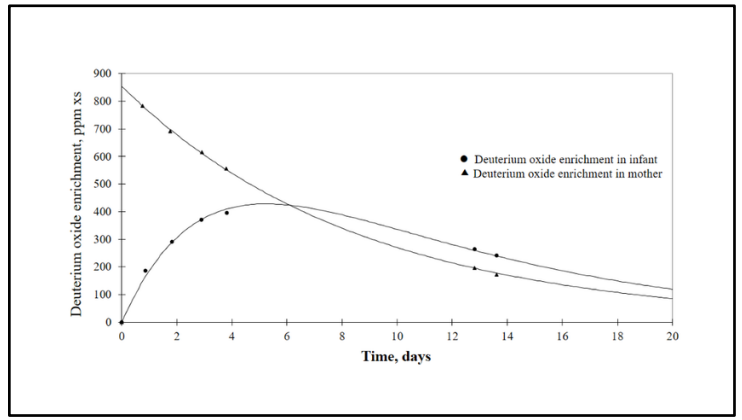
Overall aim: to understand the causal relations between heat exposure and pregnancy, intrapartum and postpartum outcomes

Pregnant women cohort: elucidate the biomarkers and other factors mediating preterm birth in extreme heat.

Intrapartum cohort: explore the impact of potential protective interventions (space cooling, hydration) on outcomes using a historical comparative analysis.

Breast feeding cohort: explore the breast-feeding frequency, breast milk composition and breastmilk volumes changes with ambient temperature





Summary of the three studies

Study	Inflammatory biomarkers	Genetics and Epigenetics	Other innovative work
HIPS study (The Gambia)	**Placental hormones**: PAPP-A,PLGF, **Immune markers**: TNF- and IL-6	Placenta and Infant epigenetics	Infant rectal microbiome and Placental work
Extreme heat and preterm birth in rural Zimbabwe	**Multiplex inflammatory panel by Luminex**: CRP, IL-4-13, TNF, CCL3 **Lipid profiles**: Resolvins, eicosanoids **Intestinal inflammation/barrier function**: I_FABP, Neopterin, myeloperoxidase, LBP	DAMPS and PAMPS: S100B, hsp70, hsp90	Human fetal chip model
Bio-Heat study (South Africa)	**Immune markers**: IL-6 and other cytokines **Sympathetic system**: cortisol and adrenaline	Epigenetics	Intra-partum protective interventions and breast milk sub-study

Anticipated outcomes

- Rigorous evidence from rural and urban settings, across 2 African regions
- Understanding of the pathways from heat exposure and preterm birth, and variation in these across regions and populations
- Synthesised findings from these and other related studies
- Inform the development of targeted and evidence-based interventions

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- https://www.lshtm.ac.uk/research/centres-projects-groups/gambia-heat-in-pregnancy-study#:~:text=While%20thermoregulation%20in%20pregnancy%20is,rate%20and%20placental%20blood%20flow.
- Find grants awarded | Grant Funding | Wellcome

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