



## Climate change and preterm birth: A narrative review

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### ABSTRACT

The sizable and multifactorial risks to human health posed by climate change are both increasingly well understood and broadly accepted. One critical aspect of human health that has received comparatively scant attention in this area is the increased risk of preterm birth, deriving from the direct and indirect effects climate change. Preterm birth, delivery prior to 37 weeks' completed gestation, impacts more than 15 million pregnancies every year. The healthcare costs of caring for preterm infants and their families exceed tens of billions of dollars annually. As such, prematurity conveys significant costs to preterm birth survivors, their families, and society.

Climate change is predicted to exert a host of direct and indirect impacts on pregnancy health that translate to an increased risk of preterm delivery, perinatal death, and long-term morbidity. We identified seven impacts of climate change, namely, temperature, precipitation, air quality, food insecurity, displacement, range of vector-borne diseases, and socio-economic inequality, that jointly and individually have the potential to convey an elevated risk of adverse pregnancy outcomes and preterm birth. We performed a literature review using these terms. We present data in a narrative review to highlight the material risk of shortened pregnancy duration posed by climate change. In particular, although targeted interventions may offset some impacts of climate change, it is increasingly apparent that the meta-system impacts exerted by climate change mean that effective and long-term actions by which a significant reduction in pregnancy health risks may be achieved require: (i) tackling the root cause of climate change itself; and (ii) considering vulnerable populations, such as pregnant women, in multi-sectorial climate adaptation plans. Given the potential risk posed to pregnancy health by preterm birth, we advocate for prematurity/pregnancy health to be considered as a critical factor in the assessment of climate change interventions.

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## Climate change and preterm birth

Prematurity presently exerts an outsized negative impact on individual and societal health (Goldenberg et al., 2008, Goldenberg et al., 2018, Organisation WH 2018, Romero et al., 2014). Preterm birth risk co-localizes with regions most susceptible to and poorly equipped to cope with climate change (Organisation WH 2018, Lawn et al., 2010). Not only does preterm birth exert acute (i.e. in the perinatal period) adverse effects on health, there is increasing evidence that the degree to which one is born preterm alters one's risk of developing non-communicable diseases, such as heart failure (Carr et al., 2017) and lung disease (Bui et al., 2022), in later life. Of note, poorer cardio-pulmonary health in later life is likely to make an individual's adaptation to a warming climate even more difficult, and may result in an increased risk of hospitalisation, health system resource utilisation, and early death.

The overarching aim of this paper was to review the growing but underappreciated body of evidence linking direct and indirect climate change effects to an increased risk of preterm birth (Patz et al., 2005, McMichael et al., 2006, Costello et al., 2009). Although an increasing number of original and review articles have emphasised the importance of climate change to preterm birth risk, many of these have focused largely, if not exclusively, on temperature effects (Poursafa et al., 2015, Bekkar et al., 2020, Carolan-Olah and Frankowska, 2014, Guo et al., 2018, Sun et al., 2020, DeNicola et al., 2019, Chersich et al., 2020, Sun et al., 2019). In the present narrative review, we sought to provide a broader assessment of the interconnected direct and indirect factors that have the potential to increase preterm birth risk. This evidence should serve to stimulate rapid and ambitious transformative actions not only to halt and reverse climate crisis but also to increase the adaptive capacity and resilience of vulnerable populations and health systems (Roos et al., 2021, Rylander et al., 2013).

The following approach was taken in assembling the data presented. Following a review of two landmark papers from the climate change literature (Patz et al., 2005, McMichael et al., 2006), and technical documents from the World Health Organisation (Organisation WH 2021), the World Food Program (FAO I, UNICEF, WFP and WHO 2021), and the World Bank (Group, 2021), we identified seven key climate change impacts (temperature, precipitation, air quality, food insecurity, displacement, range of vector-borne diseases, and socio-economic inequality). Rather than being exhaustive, this selection was chosen to highlight the broad array of climate change factors that likely act to increase the risk of preterm delivery. We then performed an unstructured literature search for each of these sub-topics using Scopus®, PubMed, and Google Scholar, and assembled evidence from peer-reviewed publications and reports from expert agencies (including the World Health Organisation, the World Bank, the World Food Program) to support our contention that each of these impacts (individually and in concert) act to materially increase the risk of adverse pregnancy outcomes and, in particular, preterm birth.

Of particular note is their complex, interacting nature on preterm risk. This observation suggests that, although targeted interventions (i.e., adapting crop genetics to tolerate higher heat stress and improving vector control programs) may achieve some benefit, effective long-term solutions must include actions not only for limiting increases in global temperature but also for strengthening individual and societal adaptive capacities.

We suggest that pregnancy health and, in particular, the risk of preterm birth must be included as an important rationale for managing climate change. Given the broad scope of topics to be covered, the paper will commence with brief introductions to Climate Change and Preterm Birth as individual concepts before progressing to highlight how the changing climate acts to increase the risk of shortened pregnancy.

## Climate change

Climate change is broadly accepted as progressive (as opposed to cyclical) alterations in key environmental determinants such as temperature and rainfall, driven as a result of increasing atmospheric concentrations of heat-trapping “greenhouse gases,” including carbon dioxide, methane, nitrous oxide, and fluorinated gases (e.g., hydro-fluorocarbons) (Nations, 2022, Agency, 2022). Although natural phenomena such as volcanic eruptions and solar activity can impact climatic conditions, there is now a strong consensus for the view that the primary driver of climate change from the late 18<sup>th</sup> Century (i.e., the start of the industrial revolution) onward was, and remains, human activity (Patz et al., 2005, Nations, 2022). In addition to the burning of fossil fuels that release heat-trapping gases into the atmosphere, multiple facets of human activity, including the clearance of land (Malhi et al., 2008), the construction of urban dwellings (Tong et al., 2021), and agriculture (Johnson and Johnson, 1995), contribute to the process of climate change. The most salient marker of climate change is the increase in average global temperatures (Masson-Delmotte et al., 2018). The International Panel on Climate Change (IPCC) estimated that, by 2017, human activity had increased global temperatures by approximately 1 °C (likely  $\pm 10\%$ ) over and above the period from 1850 to 1900. Earlier IPCC estimates have placed projected year 2100 global average temperature increases in the range of 1.4–5.8 °C with a doubling in pre-industrial atmospheric carbon levels; more recent estimates have a lower upper limit of around 4–4.5 °C (Masson-Delmotte et al., 2018). Temperature changes, thus their potential impacts, are predicted to be unequally distributed, with central and eastern North America, central and southern Europe, western and central Asia, and southern Africa experiencing the strongest extreme warming. Tropical regions are predicted to see the largest and earliest increase in the number of exceptionally hot days. It is presently predicted that avoiding the worst extremes of climate change, thus the adverse effects on human health, requires a 45% reduction in 2010 CO<sub>2</sub> emissions by 2030 and net-zero CO<sub>2</sub> emissions by approximately 2050 (Masson-Delmotte et al., 2018). Whether this goal can be achieved remains to be seen; however, the impact of inaction is clear, given projections suggesting that an additional 0.5 °C warming will result in an increased frequency of exposure to heatwaves for more than 400 million people and to extreme heatwaves for another 65 million (Masson-Delmotte et al., 2018).

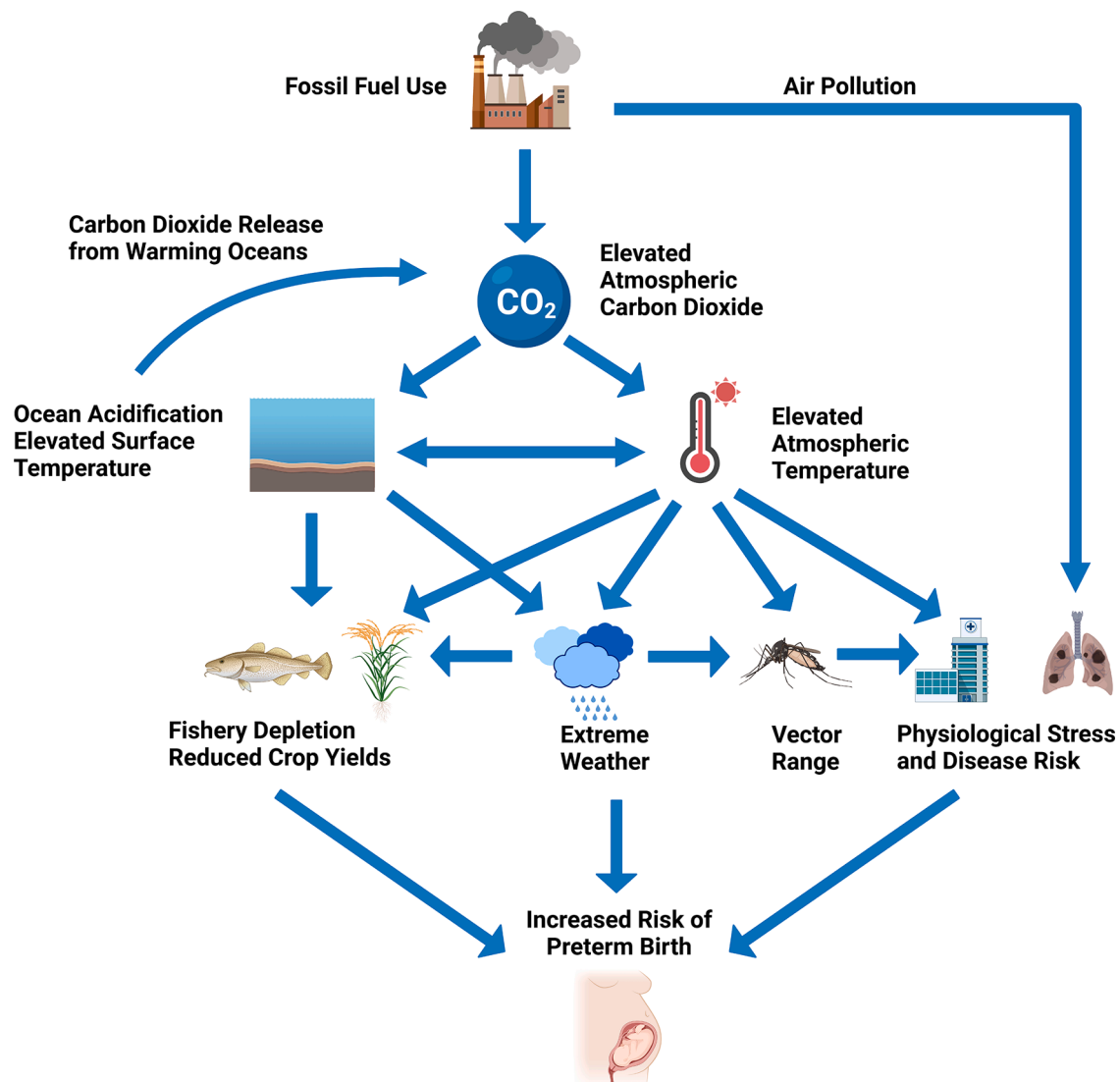
A warming planet manifests as a diverse, interconnecting suite of changes to terrestrial (e.g., soil salinity (Corwin, 2021) and moisture content (Berg and Sheffield, 2018), flooding risk (Kundzewicz et al., 2014), and erosion risk (Nearing et al., 2004)), marine (e.g., oxygenation (Matear et al., 2000), acidification (Hoegh-Guldberg et al., 2007), and water temperature (Johnson and Lyman, 2020)), and atmospheric (methane (Schaefer, 2019) and CO<sub>2</sub> (NASA 2021) content) ecosystems. Although temperature impacts some regions more than others, modeling suggests that greater increases in temperature correlate with more severe perturbations to ecosystems (Masson-Delmotte et al., 2018). These “phenotypic expressions” of a changing climate adversely impact human health and wellbeing in a number of ways. Direct changes include the increased incidence of environmental stressors such as extremes of temperature (McElroy et al., 2022) and precipitation (Chacón-Montalván et al., 2021, Rocha and Soares, 2015, Sun et al., 2020) (which vary depending on geographic location), resulting in more frequent storms, flooding, drought, and fires. Indirect impacts include the effects of altered crop and fishery productivity and increasing pathogen and vector ranges as well as altered plant and animal species' diversity and ranges. Climate change-driven societal impacts, such as economic loss, health system stress, social disruption, and forced displacement (individual and at a population level), similarly exert adverse effects on human health (Patz et al., 2005, Costello et al., 2009, Wheeler and Braun, 2013). Each of these interacting climate change-derived factors has the potential to increase a given population's risk of preterm birth (Fig. 1). Consequently, these factors should be

considered when designing short- and long-term pregnancy health policies and when making climate-resilient societies and health systems. Likewise, climate actions should consider benefits to pregnancy health in order to prioritize those interventions with the largest gains for pregnant women and future generations.

#### Preterm birth

Preterm birth (i.e., delivery before completion of the 37<sup>th</sup> week of gestation) already accounts for more than one million deaths each year (Goldenberg et al., 2008, Goldenberg et al., 2018, Lawn et al., 2010). Of the 15 million estimated preterm births worldwide each year, the highest rates are identified in economically disadvantaged communities in the United States and in Southern/South-East Asia and Sub-Saharan Africa (Goldenberg et al., 2008, Goldenberg et al., 2018, Lawn et al.,

2010). The impact of prematurity on resources is sizable, with estimates of an annual \$26.4 billion in direct healthcare costs in the United States (Romero et al., 2014). The cost of providing acute care for a single extremely early preterm infant can comfortably exceed that of a healthy term infant by nearly \$150,000.00 (Mangham et al., 2009). Comparably lower rates of prematurity are reported in higher-resource countries and in those with socialized healthcare systems providing comprehensive antenatal care, notably Denmark, Norway, and Sweden (Blencowe et al., 2013). Prematurity may be stratified into four gestational age-dependent categories, namely, extremely preterm (<28 weeks of gestation; around 5% of cases), very preterm (28–31 weeks of gestation; around 15% of cases), and moderate preterm (32–33 weeks of gestation; around 20% of cases), with the residual considered as late or near preterm (34–36 weeks of gestation) (Romero et al., 2014). Preterm birth can also be categorized phenotypically as spontaneous preterm labor



**Fig. 1.** Schematic model of interacting direct and indirect effects of climate change on pregnancy outcomes. The use of fossil fuels acts to generate atmospheric greenhouse gases (e.g. CO<sub>2</sub> and methane), increasing average atmospheric temperatures and harmful atmospheric pollution, and reducing ocean surface pH. Increased atmospheric temperatures also increase ocean surface temperatures, reducing CO<sub>2</sub>-sink capacity and disrupting fishery stocks. Both changes in atmospheric and ocean temperatures increase the likelihood of extreme weather events (increased and decreased precipitation, more frequent and stronger storm systems with greater land penetration), which combine with elevated temperatures to disrupt crop yields, and increase the risk of crop loss, and make human habitat disruption more likely. These changes have economic (adverse impacts on agricultural and fishery industries), health (poor nutrition) and migration effects, each of which individually and jointly impact pregnancy health and preterm risk. Extreme weather events in turn, along with elevated temperatures, alter disease vector range and risk of exposure, exert maternal physiological stress (directly through climatic effects and indirectly through social and habitat disruption) and increase disease risk. Each of these factors, individually and in concert act to increase the risk of preterm birth. Notably, many of the regions most likely to be impacted by these cascading impacts are those least equipped to adopt mitigation strategies. Image created using Biorender.com.

with intact membranes (~40% of cases) and as preterm prelabor rupture of the membranes (about 30% of cases), with the residual considered as medically indicated (i.e., due to maternal disease or fetal distress) (Goldenberg et al., 2008, Romero et al., 2014). Of late, the importance of a healthy pregnancy continuing to 39 weeks of gestation has become increasingly apparent, given the increased risk of developmental deficit observed even in children born at 37 weeks and 38 weeks of gestation (Vogel et al., 2018).

The risk of death and serious disease increases proportionally to the degree of prematurity, as does the resource demand for requisite clinical care (Stoll et al., 2010, Stoll et al., 2015, Swamy and Skjærven, 2008, Cheong et al., 2020). Babies born in the late preterm period (especially closer to term) generally require far more modest levels of support—predominantly brief and non-invasive in nature—than those born early in gestation (Goldenberg et al., 2008, Stoll et al., 2010, Stoll et al., 2015, Glass et al., 2015). Late preterm neonates also have far lower rates of acute (i.e., respiratory distress, infection) and long-term (i.e., brain injury, blindness, bronchopulmonary dysplasia) injuries than early preterm deliveries (Stoll et al., 2010, Stoll et al., 2015, Doyle et al., 2017, Saigal and Doyle, 2008, Siffel et al., 2021). Similarly, the potential for long-term personal and societal losses (due to lost individual economic opportunity and increased call on healthcare) increases with the degree of prematurity among survivors. Preterm birth is considered a syndrome; a wide range of factors are considered to increase the risk of preterm delivery, including poverty, low educational attainment, tobacco exposure, poor access to antenatal care, drug and alcohol abuse, black race, maternal stress, infection, very high maternal body mass index (BMI), advanced maternal age, short maternal stature, and placental disorders (Romero et al., 2014, Blencowe et al., 2013, Iams, 2014). For a detailed review of the etiology of preterm birth and derived outcomes, works by Goldenberg et al. (2008), Romero et al. (2014), Lawn et al. (2010), and Vogel et al. (2018) are excellent references.

Although the exact causes of preterm birth remain unresolved (one of the strongest maternal predictors of preterm risk is a previous preterm delivery (Romero et al., 2014)), infectious and inflammatory processes and maternal stress have been linked to an elevated risk (Kemp, 2014), especially in early deliveries. Of note, many of the regions with the most extensive potential exposure to climate change, and already possessing many of the climatic risk factors believed to elevate the risk of prematurity in the maternal population, are also those with the least ability (lack of resources, infrastructure, and technical expertise) to respond to climate-change phenomena and to the likely increase in preterm deliveries that will result (Goldenberg et al., 2018, Blencowe et al., 2013). These same regions are also often those less well-equipped to effectively manage the long-term consequences of prematurity. Preterm birth is associated with deficits in executive function and academic achievement as well as in attention, motor, and language skills; these developmental challenges often require specialized intervention during the school years and, if left untreated, likely will influence an individual's socio-economic opportunity over the life-course (Vogel et al., 2018, Stoll et al., 2015, Saigal and Doyle, 2008, Siffel et al., 2021, Anderson et al., 2016, Chawanpaiboon et al., 2019). Preterm infants are also at an elevated risk of a range of chronic diseases, including cardiovascular disease (increased risk of hypertension and stroke), kidney disease (reduced nephron counts and reduced glomerular filtration rate), reduced insulin sensitivity, and pulmonary insufficiency, with the degree of risk proportional to the degree of prematurity (Vogel et al., 2018, Stoll et al., 2015, Saigal and Doyle, 2008, Siffel et al., 2021, Anderson et al., 2016, Chawanpaiboon et al., 2019). As such, not only does preterm birth place a significant burden on the individual and on society acutely but also continues to exert a deleterious impact in the long-run.

### Climate change impact 1: temperature

As a result of climate change, the frequency, duration, and severity of extreme weather events such as heatwaves are increasing rapidly (Luber

and McGeehin, 2008, Hoegh-Guldberg et al., 2019). Pregnant women are particularly vulnerable to extreme heat and are at a high risk of heat-related health conditions that may include heat stroke and adverse birth outcomes (Carolan-Olah and Frankowska, 2014, Balbus and Malina, 2009, Spolter et al., 2020, Bouchama and Knoche, 2002). Specifically, experiencing heatwaves during the second half of pregnancy has been consistently associated with preterm birth (Dadvand et al., 2011, Ha et al., 2017, Li et al., 2018, Vicedo-Cabrera et al., 2014). Several systematic reviews from the last decade highlighted the association between exposure to high temperatures and adverse birth outcomes, particularly preterm birth (Poursafa et al., 2015, Carolan-Olah and Frankowska, 2014, Chersich et al., 2020, Kuehn and McCormick, 2017, Zhang et al., 2017, Strand et al., 2011, Beltran et al., 2013). Luton and colleagues reported an increase in the frequency (17.5% vs. 4.4% at the same time the previous year) of oligohydramnios in term pregnancies during the August 2003 heatwave that affected Paris (Luton et al., 2004). Oligohydramnios is considered a marker of fetal compromise and elevated risk of injury (Seol et al., 2021). It can derive from both abnormalities (i.e. renal disease), uteroplacental insufficiency, and may be impacted by maternal hydration status (Luton et al., 2004, Seol et al., 2021). A meta-analysis performed by Chersich and collaborators showed that the odds of preterm birth during a heatwave were 1.16-fold higher than on non-heatwave days (95% confidence interval [CI], 1.10–1.23;  $I^2=44.7\%$ ) (Luber and McGeehin, 2008). In addition, this study also suggested that the average odds of preterm birth increased by 1.05 for each 1 °C increase in temperature (95% CI, 1.03–1.07), thus indicating a dose-response association. In fact, preterm birth rates rise progressively in tandem with increasing levels of temperature or with longer durations of heat exposure (Chersich et al., 2020).

The effect of temperature on pregnancy outcome is particularly relevant in low-income and lower-middle-income countries where preterm birth rates are high (Chawanpaiboon et al., 2019). McElroy et al. recently reported that high temperatures increased the risk of preterm birth in lower-income to middle-income countries (McElroy et al., 2022). This study considered data from 14 lower-middle-income countries spanning various climate zones, and the results suggested that the risk of preterm birth increased progressively when (i) pregnant women were exposed to maximum temperatures higher than 20 °C, and/or (ii) they experienced smaller diurnal temperature ranges (less than 16 °C). Furthermore, they found an increased risk of preterm birth when women were exposed to extreme heat within the seven days before giving birth, suggesting that hotter temperatures have a more immediate than lagged effect on late preterm birth (McElroy et al., 2022). In addition, the association of temperature and preterm birth among pregnant women in low socioeconomic regions might be especially relevant in some subgroups with reduced physiological capacities for coping with high temperatures, including women with a multiple pregnancy, obesity, malaria, mental health problems, and other chronic conditions (Basu et al., 2017, Basu et al., 2010).

The mechanisms by which exposure to extreme heat might trigger or cause preterm birth are not fully elucidated. One theory, demonstrated in animal models, is that heat can lead to dehydration in pregnant women, which, in turn, could increase viscosity of the blood and decrease uterine blood flow, thus elevating the levels of antidiuretic hormones and oxytocin that would induce labor (Bouchama and Knoche, 2002, Dadvand et al., 2011, Stan et al., 2013). Other studies proposed that heat stress, like different types of stress, might lead to an overactivation of the hypothalamic-pituitary-adrenal axis, elevating the levels of corticotropin-releasing hormone and cortisol, which have been associated with uterine contractions and preterm labor (Malmkvist et al., 2009, Rees et al., 2016, Costello et al., 2018, Smith and Nicholson, 2007, Dreiling et al., 1991). Another proposed explanation is that the additional weight gained throughout pregnancy may decrease the ratio of body surface area to body mass, limiting pregnant women's capacity to release heat (Sun et al., 2019). In addition, the fetus itself also contributes to maternal heat stress through its metabolic rate (Wells, 2002).

Thus, the increase in internal heat production and the decrease in capacity for heat loss limited the ability of pregnant women to manage heat stress, potentially making them more vulnerable to extreme heat. Finally, high temperatures may also change the behavior of pregnant women and, consequently, change their exposure to other potential labor-inducing factors. For example, high temperatures may induce changes in nutrition, physical activity, exposure to infectious agents or vectors, and time spent indoors with consequent exposure to ambient air pollutants (Spolter et al., 2020).

## Climate change impact 2: food insecurity

Climate change increases the risk of malnutrition in pregnancy by threatening the three basic components of food security as detailed by the United Nations Food and Agriculture Organization in the 1996 Rome World Food Summit Report: food availability, stability of food supply, and access to food (Nations FaAOotU 1996). Malnutrition derives from the consumption of either an insufficient (undernutrition), an excessive (associated with obesity and a host of non-communicable diseases), or an inadequately balanced (e.g., poor quality) diet of macronutrients (i.e., protein, carbohydrate, fats) and micronutrients (e.g., zinc, iron, folate, vitamins B6, C, E) (Organisation WH 2021, Mousa et al., 2019). All three forms of malnutrition are associated with adverse pregnancy outcomes and an increase in the risk of preterm birth and low-birthweight infants (Mousa et al., 2019). Sub-optimal maternal nutrition and preterm birth are also associated with an increased risk of childhood obesity and non-communicable diseases in later life.

Climate-change effects increase the likelihood of all three forms of malnutrition in women of reproductive age, especially in regions with existing high rates of preterm birth. According to a recent report by the United Nations Food and Agriculture Organization, nearly 2.37 billion people did not have access to adequate food supplies in 2020 (FAO I, UNICEF, WFP and WHO 2021). Around 12% of the world's population was graded as severely food insecure (gone a day or more without eating), and a little over one-third of the global population could not afford to consume a healthy diet due to a combination of rising food prices and inadequate income (FAO I, UNICEF, WFP and WHO 2021). Accordingly, an estimated 100 million children and 600 million adults were obese in 2015, with prevalence doubling in 70 countries since 1980 (Collaborators et al., 2017). Changes in climate—specifically warming temperatures and altered rainfall patterns—likely exacerbate the risk of maternal malnutrition during the periconceptual period and during pregnancy itself.

There is good evidence that reductions in overall calorific intake, as well as perturbations in dietary balance and/or nutrient composition, increase the risk of preterm birth and low-birthweight infants (Bloomfield, 2011). Work by Richterman and colleagues in Haiti, for example, identified extreme household hunger as a risk factor for preterm birth (adjusted odds ratio [aOR] 1.57; 95% CI, 1.09–2.26) (Richterman et al., 2020). Bater et al. reported that, in Uganda, severe food insecurity and failure to take iron supplementation were associated with significantly increased odds of a preterm delivery (Bater et al., 2020). Similarly, in the United States, mothers exposed to food insecurity were reported to have a three-fold increase in the risk of delivering a low-birthweight infant (Borders et al., 2007). Mothers in Bangladesh reporting food insecurity had 38% higher odds of delivering a small-for-gestational-age (SGA) infant (Chowdhury et al., 2018). Low maternal BMI has been shown to increase the risk of preterm delivery in multiple studies (Bloomfield, 2011). This finding is of additional concern as (i) poor maternal diet is also associated with stunting and reduced growth in offspring (Prendergast and Humphrey, 2014), and (ii) short maternal stature is an additional risk factor for preterm birth (Group CHERGS-f-G-APBW 2015). Thus, poor pregnancy health may be transmitted between generations of a population.

A poor diet (high in fat and sugar) similarly increases the risk of preterm birth (Grieger et al., 2014). Obesity has been shown to

differentially increase the risk of preterm birth dependent on the magnitude of BMI excess. A review by Torloni and colleagues concluded that a BMI of 25–34.9 (pre-obese and obese I groups) was protective for delivery by spontaneous preterm birth. However, obese II women (BMI 35–40) had a general increase in preterm delivery risk, and obese III (BMI >40) women had an even higher risk of very early preterm delivery (Torloni et al., 2009). Interestingly, short maternal stature (itself a risk factor for preterm birth) may also exacerbate the risk of preterm birth in tandem with obesity (Mehraban et al., 2022).

Noting the link between inflammation, preterm birth, and fetal brain injury, Lee and colleagues reported that, in a cohort of Bangladeshi women, a low intake of B, D, and E group vitamins, iron, and zinc was associated with increased levels of the cytokine interleukin-8 in cord blood (Lee et al., 2021). Again, in rural Bangladesh, supplementation of maternal diet with multiple micronutrients was shown to reduce the risk of preterm birth and low birthweight, relative to iron-folate supplementation alone (West et al., 2014). Similarly, a periconceptual diet high in protein and fruits (fish, meat, chicken, fruit, grains) has been associated with a reduction in the likelihood of preterm birth (Grieger et al., 2014).

Climate change increases the likelihood of adverse pregnancy diets, especially in regions with fragile access to food supplies. Increases in atmospheric CO<sub>2</sub> concentrations (from around 180 parts per million in 1850 to around 417 parts per million in 2022) may benefit crop yields of some species under optimal growth conditions (i.e., water, temperature) via improved photosynthesis and water conservation (DaMatta et al., 2010). As such, crop yields in regions currently temperature sub-optimal for growth may improve. However, yields in other regions with deteriorating temperature and precipitation profiles are predicted to fall, and the overall impact of climate change on crop yield is predicted to be negative (DaMatta et al., 2010). Drought and heat shock/temperature stress are primary factors of concern regarding the yield of key crops. In an analysis of studies published between 1980 and 2015, Daryanto and colleagues reported that, at a 40% water reduction, wheat yield was reduced by 20.6% and maize yield by 39.3% (Daryanto et al., 2016). This finding is of particular importance given that maize and wheat crops constitute over 50% of the world's cereal production and that yield increases of 60% and 110%, respectively, are predicted as necessary to meet 2050 demands (Daryanto et al., 2016). Moreover, many key growing regions for both maize and wheat are predicted to experience hotter, drier conditions consistent with decreased yield. In particular, low-income and middle-income countries in tropical regions with higher baseline temperatures may be especially susceptible to crop disruption due to climate change. In addition to adverse growing conditions, alterations in the range of invasive pests such as the fall army worm (Díaz-Álvarez et al., 2021, Paudel Timilsena et al., 2022), and competitive plants such as the bellyache bush (Moshobane et al., 2022, Roberts and Biology, 2021), may further reduce crop and livestock yields in some regions.

Increasing temperature and drought conditions may also modulate the composition of key food crops, such as soybeans, wheat, barley, and rice. Increasing temperature has been shown to alter crop carbohydrate composition (DaMatta et al., 2010). In soybean seeds, an increase in experimental temperature decreased the leaf photosynthetic rate, sugar and starch content, seed weight, and yield (Zhang et al., 2016). In barley, elevations in temperature are predicted to reduce yield (Cammarano et al., 2019) and have been shown to reduce grain size and starch content. Xiong et al. reported an analysis of differential effects of elevated daytime and night-time temperatures on rice yield and quality; yield reductions were linked to an increase in photorespiration and a decrease in photosynthesis (Xiong et al., 2017). These changes were accompanied by a reduction in the head rice percentage and poorer quality (chalky) grains that are less attractive to consumers and achieve a lower price (Xiong et al., 2017). Increases in atmospheric CO<sub>2</sub> have also been associated with reductions in the mineral content (especially iron and zinc) in both rice and wheat (Chumley and Hewlings, 2020). In

addition to plants, animal-derived protein similarly plays an important role in a diversified pregnancy diet, and access to this valuable resource is likely to be impacted by climate change. Reduced availability and increased feed prices, reduced pasture availability and quality, reduced livestock health due to an increase in disease and parasites, and the direct impacts of extreme weather (heat, lack of water) may equate to reduce meat product yields (Thornton et al., 2009). Similarly, elevated temperatures are associated with reduced milk volume and/or quality (protein and fat composition) in goats, cows, and camels. These same effects may also have a sizable adverse effect on animal reproduction, further exacerbating supply limitations and negatively impacting periconceptual and pregnancy diets.

### Climate change impact 3: altered rainfall

An increased risk of preterm birth has been linked to rainfall extremes, including flooding and storm activity (Chen et al., 2021). A common theme amongst studies assessing the impacts of extreme weather events on pregnancy wellbeing is that, similar to many other climate-change phenomena, the adverse impacts appear to concentrate in those regions where individuals have the least capacity to manage and to adapt to the external stress (Chacón-Montalván et al., 2021). Stress on the family unit, displacement, injury, exposure to disease (disruption to sanitation services, water-borne disease), economic loss, and disruption to healthcare access all likely contribute to an increased risk of preterm birth.

A warming climate (particularly warming ocean temperatures) has been linked to an increase in the frequency and the intensity of tropical cyclones. In an assessment of tropical cyclone impacts in East and South East Asia, between 1979 and 2016, Chen and colleagues reported a significant increase in inland impacts; tropical cyclones were sustained (>17 m/s) for 2–9 h longer and penetrated 30–190 km further inland (Chen et al., 2021). The authors predicted that the year 2100 would see a near doubling of destructive impact on inland Asian regions, with increases in tropical cyclone landfall intensity, sustained duration, and inland penetration of 2 m/s (6% increase), 4.9 h (56% longer), and 92 km (50% further), respectively (Chen et al., 2021). Noting that tropical cyclone activity has increased around 13% over the past four decades, Sun and colleagues assessed the impact of tropical cyclones on births in 378 counties of the United States between 1989 and 2002 (Sun et al., 2020). They reported that the risk of preterm birth was positively associated with high peak wind speed (>17.2 m/s), adjacency to the path of the storm (<60 km), and exposure to cumulative rainfall over 100 mm. Notably, the strongest association was seen in early (i.e., high-risk) preterm births and in mothers living in areas scoring highly for social vulnerability (Sun et al., 2020). These data are in line with an assessment of extreme precipitation and preterm birth risk in Puerto Rico (Yu et al., 2018). The impact of Hurricane Katrina on pregnancy outcomes in the United States' Gulf Coast states was complex (Hamilton et al., 2009); significant decreases in very preterm births in Federal Emergency Management Authority (FEMA)-designated parishes in Louisiana were reported in the 12 months following the disaster, whereas significant increases in very preterm births were reported in designated parishes in Alabama over the same period. The authors noted that this observation might be due to the relocation of at-risk women in Louisiana (Hamilton et al., 2009).

Assessing the association between flooding and adverse pregnancy outcomes in Amazonia, Chacon-Montalvan et al. reported a significant association between extreme rainfall, preterm birth, intrauterine growth restriction (IUGR), and a mean reduction of 183 g in birthweight (Chacón-Montalván et al., 2021). Noting the complex interplay of flooding on economic opportunity, parental stress, sanitation, transport, and food access, the authors concluded that such an extreme event poses a particular risk for disadvantaged individuals living in remote areas. They also noted that proposed coping strategies, such as cultivating fast-growing crops, were insufficient to address the increased risks to

pregnancy health (Chacón-Montalván et al., 2021). An assessment of birth outcomes before and after the 1997 Red River flood in North Dakota revealed a significant increase in low birthweight and preterm deliveries following the flood (Tong et al., 2011). Interestingly, a similar pattern was not observed following the Calgary floods of 2013, with the authors suggesting that the provision of universal prenatal care and the magnitude of the disaster may have offset adverse effects of the event on pregnant women (Hetherington et al., 2021).

### Climate change impact 4: altered disease range

Several factors are globally altering the environmental conditions that affect the development and dynamics of vector-borne diseases, particularly those spread by mosquitos (Franklinos et al., 2019). Rising temperatures, increased rainfalls and humidity, the globalization of humankind with massive human migrations, and urban encroachment on rural/natural areas are (i) increasing the geographic range and lengthening the season of different vectors; (ii) creating more and better areas for vector breeding; (iii) accelerating their developmental dynamics; and (iv) exposing people to pathogens to which they are not immune, thus bringing vector-borne diseases to new regions and favoring their spreading. (Franklinos et al., 2019, O'Kelly and Lambert, 2020)

More than 80% of the global population is at risk of a vector-borne disease (Franklinos et al., 2019). Pregnant women represent the single largest vulnerable group due to both pregnancy-related immune modulation and to the impact of infection on two human lives simultaneously (O'Kelly and Lambert, 2020). Several physiological mechanisms, including changes in hormone levels and immune system characteristics, have been proposed to increase the susceptibility of pregnant women to infections (Kourtis et al., 2014, Pazos et al., 2012). However, for most vector-borne diseases, the complex interactions between pathogen, mother, placenta, and fetus are poorly understood.

In malaria-endemic areas, pregnant women are at particular risk of acquiring malaria, which has adverse consequences on birth outcomes, including delivery of an SGA infant and preterm birth (Chua et al., 2021, Nkwabong et al., 2020). Interestingly, preterm deliveries have been associated with *Plasmodium falciparum* infection during early and late pregnancies (Nkwabong et al., 2020, Elphinstone et al., 2019, Moore et al., 2017). Several factors significantly increase the risk of this outcome, including systemic inflammation (Fried et al., 2017) and periconceptual iron supplementation (Brabin et al., 2019). Of note, the precise mechanisms linking malaria in pregnancy with preterm birth remain unclear. It has been proposed that VAR2CSA, a unique variant surface antigen expressed in *Plasmodium falciparum*-infected erythrocytes, mediates their sequestration in the placenta and the activation of syncytiotrophoblasts.

This process leads to the secretion of pro-inflammatory cytokines/chemokines that contribute to placental inflammation and impaired placental function (Chua et al., 2021, Tomlinson et al., 2020). On the other hand, the efforts to eliminate malaria-transmitting mosquitoes include the use of insecticides. DDT (1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane), a still widely used compound against malaria-transmitting mosquitoes in many countries, has been associated with preterm birth and spontaneous abortion (van den Berg et al., 2017, Longnecker et al., 2001). Thus, increased risk of preterm birth in malaria-endemic regions may be associated with both malarial infection and the use of insecticides. Since malaria transmission is mainly constrained by the suitability of the climate for breeding and development of *Anopheles* spp. mosquitoes, it has been predicted that climate changes will shift geographic locations suitable for malaria transmission (Ryan et al., 2020, Caminade et al., 2014). Instead, it has been suggested that, in Africa, climate change could shift disease burden from malaria to arboviruses (Mordecai et al., 2020).

Several arboviruses cause vector-borne infections in pregnancy, including Dengue, Zika, West Nile, Chikungunya (CHIKV), Yellow fever,

and Japanese encephalitis. All are spread by mosquitoes (mainly *Aedes* or *Culex* spp.) and have variable distribution worldwide (Cleton et al., 2015). Dengue, Zika, and CHIKV have more serious implications in pregnancy (Vouga et al., 2019). Dengue infection has been reported from the Americas, Africa, Southeast Asia, Europe, Western Pacific, and Eastern Mediterranean regions, and it has been estimated that 390 million individuals are infected yearly (Bhatt et al., 2013, Bhatt et al., 2021). Dengue infection in pregnant women appears to be more severe when compared to the general population (Machado et al., 2013, Paixao et al., 2018). A meta-analysis showed increased odds [odds ratio (OR) 3.51] of miscarriage for dengue during pregnancy (Paixao et al., 2016). Interestingly, this study also showed that preterm birth was one of the most common adverse pregnancy outcomes. The OR for the association with dengue was 1.71. Another study from Brazil retrospectively reviewed data from 3898 pregnant women with symptomatic dengue and also reported increased odds of preterm delivery (Nascimento et al., 2017). The pathogenesis of Dengue virus infection involves a complex interplay of viral and host factors (Bhatt et al., 2021); thus, detrimental consequences of dengue in pregnancy likely reflect the effects on the mother rather than the fetus. However, a study has shown histopathological changes in the placenta (deciduitis, intervillitis) consistent with viral damage and the presence of viral antigens (Ribeiro et al., 2017).

Zika, a flavivirus that affects tropical areas, is found primarily in Latin America. As with the Dengue virus, its transmission is facilitated by mosquitoes *Aedes*, and the mechanisms underlying its spread are similar to those of other vector-borne diseases. Most Zika patients are asymptomatic during infection, and some may develop mild viral symptoms. One of the most relevant differences between Dengue and Zika viruses that arises in pregnancy is the transplacental transfer of Zika and its tropism for the developing fetal nervous system, which can result in severe congenital defects (Bustamante et al., 2019). On the other hand, the association of Zika virus infection during pregnancy with pregnancy outcomes is controversial. Many studies suggest that Zika virus infection in pregnant women is associated with an increased risk of having an SGA neonate but does not increase the risk of preterm deliveries (Ospina et al., 2020, Chibueze et al., 2017, Cooper et al., 2019).

The CHIKV virus is a mosquito-borne infection that causes significant morbidity. A prospective study during the CHIKV outbreak on Réunion Island in 2005–2006 in women infected during pregnancy with CHIKV ( $n = 658$ ) and non-infected women ( $n = 628$ ) showed no significant difference in adverse events such as preterm delivery, low birthweight, miscarriage, or stillbirth. However, they did show an increased risk of hospitalization (40% versus 29%) (Fritel et al., 2010). It must be noted that the majority of CHIKV infections included in the study occurred in the first and second trimesters. Similarly, an observational study found no differences in the risk for preterm delivery between pregnant women infected with the CHIKV virus during pregnancy and pregnant women who were not infected (Foeller et al., 2021). Interestingly, a recent study during the CHIKV infection epidemic in Kassala, eastern Sudan, demonstrated that the rates of miscarriage (19.3% vs. 1.4%,  $P < 0.001$ ) and preterm birth (13.9% vs. 2.8%,  $P = 0.003$ ) were significantly higher in pregnant women with confirmed CHIKV infection compared to the rate in the community (Ali et al., 2021).

In all of these arboviral diseases, transmission is highly sensitive to climatic conditions, especially temperature, rainfall, and relative humidity (Colon-Gonzalez et al., 2021). Studies on the potential impacts of climate change on Dengue suggest a significant expansion of the geographic regions at risk during this century (Naish et al., 2014). Interestingly, studies suggest that climate change will affect not only the dynamics of mosquito development but also virus replication in the vectors and mosquito-human interactions (Naish et al., 2014, Morin et al., 2013, Dhiman et al., 2010).

## Climate change impact 5: displacement and migration

In addition to the COVID-19 pandemic, climate crises, political unrest, and war have increased the forced and protracted displacement of affected populations. Setting aside the currently accelerating displacement of significant numbers of Ukrainian refugees, the United Nations High Commissioner for Refugees projects that almost 1.5 million persons are in need of global resettlement in 2022, the vast majority forcibly displaced by war and conflict (UNHCR 2021). Forced and protracted displacement further exacerbates the risks of pregnancy complications; preterm birth; maternal and infant mortality among vulnerable pregnant women due to physical and mental stress; lack of access to primary healthcare, nutrition, and housing; psychological and physical traumas; and the ever-present threat of exploitation and gender-based violence (Boswall, 2015, Hersh and Obser, 2016, Rohwerder, 2016). Pregnant women in transit may refuse urgent medical care out of concerns of being separated from their social groups or of missing transportation to the next destination; communication barriers; perceptions of healthcare staff as untrustworthy; and cultural barriers, including treatment by male healthcare providers (Eapen et al., 2016). The experience of physical and psychological stress puts forcibly displaced pregnant women at higher risk of preterm birth and significant morbidity and mortality. Other risks to vulnerable displaced women and girls include increased vulnerability to early marriage, exploitation and trafficking, and lack of access to contraception and treatment for sexually transmitted diseases, leading to unplanned pregnancies and the perpetuation of the cycle of pregnancy complications, including preterm birth (Rohwerder, 2016).

Several systematic reviews highlighted the significantly increased incidence of low birthweight among migrant women settled in European countries compared to native populations (OR 1.42) and preterm birth <37 weeks (aOR, 1.24). The likelihood of preterm birth was higher among Asian and African migrant women (aOR 1.14–1.29), lower among migrant women from South America (aOR 0.83), and similar among migrant women from Europe and North Africa (Bollini et al., 2009, Gagnon et al., 2009, Pedersen et al., 2014). Preterm birth outcomes are positively influenced by maternal education and negatively affected by the duration of residence in the receiving country, where five-year increases in residence significantly increased preterm birth (aOR 1.14), probably as an indirect effect of ongoing psychosocial stress (De Maio, 2010).

Most studies reviewed the described suboptimal prenatal care provision and worse maternal health outcomes for migrant women, with large effect sizes attributed to organizational, socio-cultural, and communication barriers; wariness toward healthcare providers and Western medicine; and a sense of discrimination. In situations of perceived discrimination, significantly increased risks of stillbirth and perinatal mortality among migrants compared to native women (relative risk 1.7–2.8) have been described (Gagnon et al., 2009, Small et al., 2014). Asylum-seeking migrant women had greatest vulnerability to poor birth outcomes. IUGR and preterm birth affected up to 15% of asylum-seeking women, who also suffered high rates of other perinatal complications (Gissler et al., 2009, Hadgkiss and Renzaho, 2014). Exposure to extreme levels of stress from forced displacement and migration likely increases preterm birth via alterations in hypothalamic-pituitary-adrenal function, resulting in fluctuations in cortisol and corticotrophin-releasing hormone levels. This outcome appears to be time-based, with Liu et al. reporting the highest risk of preterm birth  $\leq 36$  weeks of gestation in the first year of residency in host countries compared to years 2–5 among female refugees, although the risk of very preterm birth (22–32 weeks) was highest in years 3–5 of residency (Liu et al., 2014).

Wanigaratne et al. further described a higher incidence of preterm birth among secondary refugees who settled in North America, the women who have resided in at least two different countries after leaving their country of birth, compared to primary refugees, the women who

arrived directly at their host country, probably related to prolonged psychosocial stress among the former due to a longer duration of migration, unsettlement, non-integration, and deprivation (Wanigaratne et al., 2016, Pottie et al., 2007, Kramer et al., 2009, Yehuda and Minireview, 2011). Open hostility and refusal to integrate refugee populations significantly increase preterm birth by 58% among secondary refugees versus a 12% increase among primary refugees (adjusted cumulative OR, 1.58 vs. 1.12), compared to non-refugees, and significantly higher incidences of very preterm birth (22–32 weeks) and moderate preterm birth (>32–36 weeks) were observed in secondary refugees compared to non-refugees (Wanigaratne et al., 2016, Urquia et al., 2015, Urquia and Gagnon, 2011).

### Climate change impact 6: air pollution

In recent times, interest has increased in studying preterm birth risk factors associated with environmental pollutants, such as pesticides, metals, hydrocarbons, and gases, among others.

In 2019, a systematic review summarized the contaminants that have been implicated in the etiopathogenesis of preterm birth (Porpora et al., 2019). The elements that contribute to air pollution have a central role (Maisonet et al., 2004, Parker et al., 2011, Shah and Balkhair, 2011). It has been observed that suspended particles with a diameter of less than 2.5 µm are capable of being transferred from the maternal lung into the systemic and even the placental circulation. These particles impair function (Pfarrer et al., 1999, Wylie et al., 2017) and may increase the risk of premature birth and other pathologies, including preeclampsia (Harrabi et al., 2006, Jedrychowski et al., 2012), in patients exposed to air pollutants. The longest studied air pollutant is tobacco, and its association with preterm birth has been known for more than 50 years (Goldstein et al., 1964). It has been observed that even passive smokers or patients exposed to cigarette toxins, but who were not active smokers, have a higher risk of preterm birth and low-birthweight newborns (Crane et al., 2011, Ion et al., 2015, Salmasi et al., 2010, Ward et al., 2007).

A recent study analyzed the records of almost 600,000 pregnant patients exposed to different concentrations of the most significant air pollutants in China (Zhou et al., 2022). This study demonstrated a positive association between preterm birth with the following pollutants: PM<sub>10</sub> 1,103 (95% CI: 1080–1127), PM<sub>2.5</sub> 1160 (95% CI: 1134–1186), SO<sub>2</sub> 1535 (95% CI: 1508–1563), NO<sub>2</sub> 1617 (95% CI: 1587–1647) and CO 1358 (95% CI: 1335–1382), NO<sub>2</sub> being the largest contributor to the risk of preterm birth caused by air pollutants (26.5%) and the third trimester the most sensitive exposure window. A new meta-analysis also evaluated the correlation between maternal air pollutant exposure and preterm birth, including more than 60 studies, and found the same association (Ju et al., 2021). In addition, the findings in these studies showed that the exposure of PM<sub>2.5</sub>, PM<sub>10</sub>, and O<sub>3</sub> in the entire pregnancy was positively correlated with risk of moderate preterm birth (32–35 weeks of gestation), very preterm birth (28–31 weeks of gestation), and extremely preterm birth (before 28 weeks of gestation) (Zhou et al., 2022, Ju et al., 2021). Moreover, a retrospective cohort study in California concluded that PM<sub>2.5</sub> exposure during the last trimester of pregnancy was associated with increased risk of preterm birth (<34 weeks of gestation); women in the highest quartile of exposure had increased risk of delivery at 32–33 weeks (OR 1.15, 95% CI 1.06–1.24), 28–31 weeks (OR 1.30, 95% CI 1.19–1.43), 24–27 weeks (OR 2.05, 95% CI 1.75–2.39), and 20–23 weeks (OR 2.84, 95% CI 2.29–3.53) of gestation compared to women in the lowest quartile (Padula et al., 2014).

Another substance to which we are constantly exposed is bisphenol A (BPA) through different products, e.g., plastic, polycarbonate, medical equipment, dental filling materials, glasses, and personal care products. Studies have shown that the greater the exposure to this product, the greater the risk of preterm birth (Namat et al., 2021, Pergialiotis et al., 2018, Suvorov and Waxman, 2015). This association was statistically

significant only if the exposure occurred in the third trimester, when the increase of BPA concentration decreases the gestational age by 1.36 (–2.21, –0.52) days, and there was no association when exposure occurred in the first and second trimesters (Namat et al., 2021).

The mechanisms involved in adverse fetal outcomes, with the various contaminants, could be explained by direct damage of DNA. Chemical compounds may bind to DNA and form covalent adducts, generating modifications in gene expression (Perera et al., 1992). Other studies suggest that intrauterine exposure to air pollution is associated with increased levels of DNA adducts in the placenta and fetal blood (Topinka et al., 1997). An additional process involved pollutants that could change genic expression through epigenetic changes such as DNA methylation, acetylation, ubiquitination, and histone modifications (Hou et al., 2012). Alternatively, toxic compounds may activate inflammatory pathways that increase oxidative stress, producing substances that affect placental function. In particular, trophoblast proliferation and differentiation may be compromised, increasing vascular reactivity and leading to adverse perinatal outcomes (Myatt and Cui, 2004). Moreover, findings suggest that substances, such as BPA, may induce pathological changes in the placenta, disrupting its metabolic activity, stimulating apoptotic or anti-apoptotic signals in the trophoblast, and increasing its fusion while inhibiting trophoblast migration and invasion—all mechanisms that may be involved in the pathophysiology of preterm birth (Adu-Gyamfi et al., 2022).

Other pollutants implicated in preterm birth and IUGR are polycyclic aromatic hydrocarbons (waste from the combustion process of cars and industries), exposure to which preterm birth is directly and proportionally associated (Choi et al., 2008, Guo et al., 2012). Contaminants in water and treatment of drinking water with chlorine that leads to the release of disinfection by-products (trihalomethanes, chloroform, bromoform, and haloacetic acids) have also been postulated as potential risk factors for preterm birth; however, the evidence is controversial (Grellier et al., 2010, Hoffman et al., 2008, Yang et al., 2007).

### Climate change impact 7: socio-economic inequality

Socio-economic inequality, arising from a systemic lack of public healthcare investment and accessibility, negatively impacts poorer communities' ability to prevent and treat diseases, and the relational processes are consistently identified as a critical factor influencing the risk of preterm birth via poor nutritional intake, delays in seeking medical attention, and detrimental habits (Heaman et al., 2013, Smith et al., 2015, Shankardass et al., 2014, Aizer and Currie, 2014). Such inequalities have been exacerbated by the COVID19 pandemic, particularly in moderate to higher-income countries, leading to increasing rates of preterm birth among socio-economically disadvantaged women (Bernstein, 2021). In communities where economic inequality increased due to job and opportunity loss, illness, and pandemic measures, preterm birth rates were higher than communities where economic inequalities remained stable (Wallace et al., 2016). Measures to relieve acute economic hardship related to the sweeping social changes forced by the COVID19 pandemic included enhanced provision of healthcare and access to services as well as economic relief in terms of income supplements to low-income individuals. This relief, in general, has positively influenced birth outcomes, though there are certainly barriers to equitable distribution (Enns et al., 2021, Thongkong et al., 2017, Lim et al., 2010, Guanais, 2013, Shei, 2013).

Greater income inequality in high-income countries appears to increase the risk of poor birth outcomes, including preterm birth. The rise in the risk of preterm birth is especially pronounced in communities of medium to high inequality, compared to preterm birth risk in communities of low inequality (23% vs. 7% respectively, according to Huynh et al.) (Nkansah-Amankra et al., 2010, Huynh et al., 2005, Fujiwara et al., 2013). Life-course perspective analyses suggest that income inequalities pre-dating pregnancy and experienced during pregnancy both enhance the risk of preterm birth. Wallace et al. found that the incidence



of spontaneous and iatrogenic preterm birth increases in communities with increasing income inequality, by contrast with a lower incidence of preterm birth in communities in which the income gap remained stable or narrowed (12.3% vs. 10.9%, respectively) (Wallace et al., 2016). The presence of a widening income gap between social classes is a key element accounting for higher preterm birth rates, independent of unemployment and poverty levels, rather than the initial degree of inequality and magnitude of the income gap (Nkansah-Amankra et al., 2010, Fujiwara et al., 2013, Blumenshine et al., 2010, Lu and Halfon, 2003, Daoud et al., 2015).

Socially disadvantaged women are more likely to be in low-wage employment, which may not offer access to paid medical and maternity leave for pregnancy complications. This detriment clearly reduces the capacity of women who experience preterm labor to comply with prescribed medical treatment, typically including hospitalization and physical rest. This type of experience fuels a vicious cycle of unstable employment, financial instability, poor perinatal outcomes, and enduring socio-economic inequalities, particularly distinct in the wake of the COVID19 pandemic (Bernstein, 2021).

Interventions that can break this cycle include a guarantee of access to maternal health services, extension of governmental healthcare funding, and additional support to low-income and middle-income women (Shankardass et al., 2014, Aizer and Currie, 2014, Brownell et al., 2018). Unconditional income supplements granted to low-income pregnant women are associated with reduced incidence of preterm birth and low birthweight and with improved breast-feeding initiation, thus narrowing the birth-outcome gap with higher-income women (absolute reduction in inequities of almost 2%). Even without precise knowledge of how the income supplement is expended, expanding prenatal income supplements may be critical for attaining population-level equity in birth outcomes (Brownell et al., 2018).

Government healthcare expenditure prioritizing pregnant low-income women during the pandemic contributed to better birth outcomes (Lim et al., 2010, Guanais, 2013, Shei, 2013, Cuestas et al., 2021). Expanding healthcare access and cash support for families of need in low-income and middle-income countries are associated with reduced perinatal complications and improved birth outcomes (Enns et al., 2021). The reduction in preterm birth and low birthweight is mirrored in low-income communities within high-income countries, which likewise receive financial support. For example, preterm birth and low birthweight were reduced by 17% to 19% among First Nations communities in Canada, in which there is typically a two-times higher incidence of preterm birth than in non-indigenous communities, following unconditional prenatal income supplementation (Enns et al., 2021, Chen et al., 2015). It is important to note that the impact of additional financial support may differ in urban and rural communities, and it may be limited by pre-existing health inequalities (Brownell et al., 2018, Cuestas et al., 2021).

## Conclusions

Ensuring women have access to optimal pregnancy conditions is critical to achieving a healthy start to life for all children. Premature birth remains a leading global cause of both perinatal death and childhood diseases, whose effects persist long into adulthood and significantly compromise the individual quality of life and socio-economic opportunities. Of particular concern, a number of the outcomes associated with poor pregnancy health and prematurity (i.e., stunting, SGA, reduced socio-economic achievement) predispose subsequent generations to increased risk of pregnancies impacted by preterm birth (Prendergast and Humphrey, 2014).

Climate change is rightly viewed as posing a significant risk to human health and wellbeing, and the risks it conveys are now widely appreciated. Despite this awareness, we are only beginning to grasp the extent of the first-order and second-order risks to pregnancy duration exerted by a warming climate. As discussed above, increased risks of

prematurity are directly and indirectly exacerbated by climate change: rising temperatures place additional heat stress on mothers (i.e., HPA axis activation, oxidative stress) and may alter behavior (i.e., reduced exercise, avoidance of healthcare visits) in ways that increase the risk of preterm delivery. Extreme weather events not only increase the likelihood of socio-economic disadvantage and inequality, stress and displacement but also impact crop diversity, food security, and nutritional quality. Both individually and synergistically, each of these factors negatively impacts pregnancy health and increases the risk of preterm delivery.

Two key areas are of particular concern in devising risk management strategies to offset climate-change harm on pregnancy. First, many of the regions most likely to be exposed to the worst extremes of climate change are regions that already report some of the highest rates of preterm birth and, due to socio-economic factors, are worst placed to implement mitigation strategies to offset these impacts. Remarkably, these regions have the least capability to cope with long-term impacts of prematurity on their populations. Second, the interconnected nature of factors that increase the risk of prematurity may mean that targeted interventions may offer only transient or modest benefits. For example, adapting crops to tolerate more extreme weather events (i.e., lack of rainfall or number of extreme heat days) may be beneficial in resolving impacts of sub-optimal nutrition on pregnancy, but it will not address the risk posed to pregnancies by heat stress, reduced physical activity during pregnancy, altered disease vector ranges, or the socio-economic impacts of increased cooling costs on households.

Because of this synergy, it seems reasonable to conclude that while mitigation strategies are a laudable short-term approach to protecting an optimal pregnancy duration and minimizing the risk of prematurity, significant attention must be given to (i) addressing the root causes of climate change itself through a broad multisectoral and transformative approach, and (ii) designing climate adaptation plans that prioritize vulnerable populations, such as pregnant women, to improve the overall resilience of such societies and to accelerate progress toward sustainable development goals (Morton et al., 2019, Spiering and Barrera, 2021). Moreover, pregnancy health and prematurity must be included as a key metric in climate-change risk assessments to human health, and as a rationale for efforts to minimize, as much as possible, devastating potential effects on future generations.

## Authorship contribution statement

Conceptualisation: MK, MC, SI

Writing – Original Draft: LB, SI, MB, CM, MK

Writing – Review and Editing: LB, SI, RR, MB, CM, MC, MK

## Condensation

Climate Change acts directly and indirectly to increase population-level risk of preterm birth, with the greatest impact likely in lower resource jurisdictions.

## Disclosure statement

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### Declaration of interests

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.

### Data availability

No data was used for the research described in the article.

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