Title: Malaria exposure and pregnancy outcomes in Sub-Saharan Africa.
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Abstract
Despite the high burden of malaria in sub-Saharan Africa, research has been hindered by a lack of detailed incidence data with high spatial and temporal resolution. To study the impact of *in utero* exposure to malaria on pregnancy outcomes we circumvent this problem by using detailed reproductive histories from the Demographic and Health Surveys and combine that data with an index of exposure to malaria based on climatic variables. We use Linear Probability Models to estimate the impact of exposure to malarious conditions during different months of gestation on birth weight. Preliminary results show that the relationship between exposure to malarious conditions and birthweight depends on context (malaria endemicity and immunity). This paper provides a framework for predicting potential future impacts of climate change on malarial outbreaks and pregnancy outcomes and can be used to predict locations and months with high risk of malaria transmission.

Extended Abstract:

The burden of malaria is especially high in sub-Saharan Africa (SSA). Approximately 90% of the 212 million malaria cases and 92% of the 429,000 malaria deaths occur in SSA (WHO 2016). Pregnant women are particularly vulnerable to the causes and adverse outcomes associated with malaria. Pregnant individuals are more attractive to mosquitoes compared to non-pregnant individuals, and severe malaria (when organ dysfunction occurs) is more common in pregnant women ((Schantz-Dunn and Nour 2009; Marchesini and Crawley, 2004). The majority of social science research focused on malaria is based on historical data and typically focuses on the long-term effects of malaria exposure during pregnancy outcomes (Barreca 2010; Cutler et al. 2010; Venkataramani 2012). However, with increased public health campaigns and education about the treatment and prevention of malaria, much has changed over the past decades.

In this article, we aim to investigate the relationship between in utero exposure to malaria and birth weight in sub-Saharan Africa covering the period from 1990-2010 [we are extending the dataset to add more years]. We build on related research and use detailed environmental data to construct spatially and temporally varying measures of malaria risk (Kudamatsu et al. 2009 and Tansler et al. 2003). We use different data which we believe improves the measurement of malarious conditions. Furthermore, we run analyses to test which aspects of the malarious conditions index are driving our results.

To conduct this analysis, we rely on georeferenced health survey data from the Demographic and Health Surveys (DHS) and include all African countries with spatially referenced data. This results in detailed information on 200K+ pregnancies representing 19 different countries. Using detailed remotely sensed based rainfall data (CHIRPS) and monthly temperature data (Princeton meteorologic forcing dataset), we create a monthly binary malaria index (BMI) that considers a range of climate characteristics to estimate increased risk of malaria exposure and merge this with the DHS data. Because adverse health outcomes related to malaria can also be impacted by individual outcomes, including the timing and duration of the exposure to malaria, we also consider individual-level variability within a given community (or malarial zone). In this way we can identify the in-utero periods that are most critical for malaria prevention while also considering the unique individual-level characteristics that intensify or reduce the risks associated with exposure to malaria while pregnant.

We hypothesize that malaria will have a larger impact on fetal loss and other pregnancy outcomes in areas with epidemic/seasonal malaria and relatively low immunity compared to endemic areas. This is motivated by the Kudamatsu et al. (2016) finding that infant mortality was 2.8-3.7 percentage points higher among infants whose mothers were exposed to more than six months of malarious weather conditions in the year before their births, but this was only significant in low malaria-transmission settings. We also hypothesize that malaria incidence will have a stronger effect on primigravidae (first order births) than on multigravida women (Desai et al. 2007). The impact on first order births is because maternal immunity diminishes especially during first pregnancies (Schantz-Dunn and Nour 2009).

Preliminary results show that the relationship between exposure to malarious conditions and birthweight (BW) depends on context (malaria endemicity and immunity). For instance, each additional month of malarious exposure in endemic area is associated with 21.8 grams increase in BW; each additional month of malarious exposure in epidemic area is associated with -7.7 grams decrease in BW; while each additional month of malarious exposure in malaria free area is associated with -34.3 grams decrease in BW.

Data and Methods

Source of Demographic Data

We use reproductive data from the Demographic and Health Surveys (DHS). Although the DHS is typically cross-sectional, the retrospective birth histories have been widely used to investigate health at birth and later infant outcomes (Dorélien 2015, Kudamatsu et al. 2016, Grace et al. 2015, Davenport et al. 2017. Grace et al. 2017). Specifically, our DHS data comes from 36 surveys from 19 sub-Saharan African countries with both calendar and georeferenced data. The survey dates range from 1990-2010 (between 2010 and 2015 info on migration history was not included), however the earliest conceptions took place in May 1985 and the latest conceptions took place in November 2008. Our sample consists of over 200,000 thousand conceptions resulting in live births.

Remotely Sensed Environmental Data

We construct a malaria exposure index using separate gridded datasets for temperature and precipitation. For temperature we use monthly maximum, mean, and minimum air temperatures (0.5° X 0.5° resolution or ~50km) from the Princeton meteorological forcing dataset (Sheffield et al., 2006, Harris et al. 2014). For precipitation, we use monthly average and cumulative rainfall (0.05° X 0.05° resolution or ~5km) from the Climate Hazards groups Infrared Precipitation with Stations (CHIRPS) product (Funk et al. 2015). Both the temperature and precipitation products are generated by combining satellite-based observations with on-the ground meteorological stations.

Binary Malaria Index (BMI)

There exists a lack of monthly malaria incidence data, therefore we will start by creating an index based on the Tanser et al. (2003) and Kudamatsu et al. (2016) methodology. For each month of gestation, a binary malaria index (BMI) is created and assigned a value of one if the following four conditions are met—

1) average rainfall during the month of interest (t_i) and preceding two months is at least 60mm *[$P(t_i) > 60$ mm, for t_i in (t, t-1, t-2)];*
2) rainfall in a least one of these months is at least 80mm [*$P(t_i) > 80$ mm, for at least one of t_i in (t, t-1, t-2)*];
3) the month of interest and none of the preceding 11 months has a minimum temperature below 5 degrees Celsius;

4) the average temperature in the past 3 months exceeds the sum of 19.5C and the standard deviation of monthly average temperature in the past 12 months.

If all these conditions are not met the index takes a value of zero. These conditions are believed to be necessary for the survival of the malaria vectors and parasites (Kudamatsu et al., 2016). The reasoning behind each of these conditions can be found in Kudamatsu et al. (2016) and Tanser et al 2003.

Generating Malaria Endemicity

In addition to coding whether each month of gestation was exposed to malarious conditions or not, we also use the BMI to describe if the DHS cluster is in a malaria free, epidemic, or endemic zone. A cluster is located in an endemic zone if the average annual number of months with malarious conditions is larger than four; epidemic if the average annual number of malarious months is between 1 and 4; and malaria free if the average annual number of malarious months is zero (Kudamatsu et al 2016). To calculate the cluster level endemicity, we created an BMI for every month from January 1985 to December 2010 and computed the average number of months per year for each location (i.e., pixel) and appendix for more details on how this was created). Next, we extracted the 0.05˚ BMI climatology for each of the DHS cluster locations, while including a 10km buffer. All 0.05˚ pixels within 10km buffer were averaged to produce the estimate at the DHS cluster location.

Estimation Strategy

Our main independent variable is an index of malarious exposure based on weather conditions. First, we estimate the impact of *cumulative of exposure* to malarious conditions. Next, we estimate the impact of *exposure during different months of gestation* on the pregnancy outcomes (Deschenes et al. 2009; Wilde et ar. 207). Since malarious exposure is often seasonal, we need to be concerned about endogeneity. Our estimation strategy identifies the causal effects of malarious weather exposure on pregnancy outcomes by focusing on the impacts of seasonal/anomalous conditions which deviate from local average patterns (Dell et al. 2014; Kudamatsu et al. 2016; Dorélien 2016). One way to achieve this is to include fixed effects (FE) or dummy variables for the calendar months into the regression in order to control for seasonally

varying factors. We also include cluster FE to control for unobserved location specific characteristics; and country by year FE to control for unobserved country and time specific trends in malaria exposure. We are not able to include cluster by calendar month FE (which would control for location specific unobserved seasonal trends) because of lack of variation due to the fact that our malaria index is a binary indicator and very seasonal (certain months is some locations are always classified as malarious or not malarious).

- Our treatment variable, malarious conditions, will not capture all exposure to malaria; many women might already be infected with malaria (asymptomatic infections) prior to the malaria season. So, the malarious conditions will most likely represent the impact of new malaria infections.
- Our treatment variable is likely to capture both direct and indirect effects. And although we primarily focus on causal pathways that act through the mother, my treatment variable may also capture the impact of paternal malarial exposure, and effects that are due to household behavioral changes in response to malarious conditions (Sharp et al. 2018; Kudamatsu et al. 2016).
- Because we do not know if the pregnant women are, in fact, infected with malaria, our estimates may be conservative (lower bound estimate of the effect).
- Our study is less likely to suffer from omitted variable bias due to maternal selection.

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