Research Article

**Climate change and health transitions:
Evidence from Antananarivo, Madagascar**

Jordan D. Klein

Anjarasoa Rasoanomenjanahary

Contents

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Jordan D. Klein[1]

Anjarasoa Rasoanomenjanahary[2]

Abstract

BACKGROUND
Global climate change poses grave risks to population health, especially in low- and middle-income countries (LMICs). It both threatens the sustainability of nascent epidemiological transitions and raises prospects for counter transitions driven by indirect climate impacts on mortality, such as those from reemerging infectious diseases and by direct impacts of extreme climatic events.

OBJECTIVE
We investigate how the relationship between climate and mortality has changed as Antananarivo, Madagascar, progressed through the stages of the epidemiological transition, focusing on enteric infection mortality in children under 5.

METHODS
Using death registration, precipitation, and temperature time series data spanning over four decades, we model the climate–cause-specific mortality relationships during each stage of the epidemiological transition using generalized additive models.

CONCLUSIONS
While we find that childhood enteric infection mortality has become less sensitive to low rainfall and higher temperatures, it has become more sensitive to heavy rainfall. Mortality from other causes has also become less sensitive to high temperatures but has become slightly more sensitive to heavy rainfall while significantly more sensitive to low temperatures.

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[1] Office of Population Research, Princeton University, Princeton, NJ, USA. Email: jdklein@princeton.edu.
[2] Bureau municipal d'hygiène de la Commune urbaine d'Antananarivo, Antananarivo, Madagascar.
Email: anjarasoa.maharavo@gmail.com.

CONTRIBUTION
This is the first multidecade climate–mortality study of a city in sub-Saharan Africa outside of South Africa.

1. Introduction

1.1 Climate change and health

Climate change poses severe threats to human health globally, particularly in more vulnerable populations in low- and middle-income countries (LMICs). For instance in economically disadvantaged populations in Africa the projected loss of healthy life years due to climate change is anticipated to be 500 times higher than in better-off populations in Europe (Barrett, Charles, and Temte 2015). The health impacts of climate change encompass higher temperatures and precipitation extremes. Direct effects include an increased risk of death from heat stress (Takahashi, Honda, and Emori 2007), drowning and acute trauma (Ahern et al. 2005; Alderman, Turner, and Tong 2012), and malnutrition (Patz, Grabow, and Limaye 2014; Stanke et al. 2013), following extreme heat, flooding, and drought, respectively. These climate extremes can also indirectly affect mortality through environmental mediators, contributing to higher risk of getting an infectious disease.

Enteric infections – diseases of the gut often acquired through exposure to water contaminated with pathogens (Mahmud et al. 2020) – disproportionately affect certain global populations. They are most fatal among children under 5 in Africa, the Middle East, and South Asia (Kolstad and Johansson 2011) and are notably climate sensitive (Costello et al. 2009; Mahmud et al. 2020) (see Figure 1a). Previous research links precipitation extremes with enteric infections (Mahmud et al. 2020; Shuman 2010). Heavy rainfall increases the risk of specific enteric infections, primarily in regions with inferior water and sanitation infrastructure where sewage lines and water treatment plants can easily be overwhelmed by runoff and contaminate drinking water (Alderman, Turner, and Tong 2012; Bastaraud et al. 2020; Shuman 2010). Conversely, low rainfall can enhance enteric infection risk due to water scarcity, leading to poor sanitation and potential exposure to contaminated water (Atabati et al. 2020; Saad et al. 2018; Shuman 2010; Stanke et al. 2013). Temperature also influences enteric disease risk (Howard et al. 2016; Mahmud et al. 2020), partly through higher temperatures boosting the replication rates and survival of waterborne pathogens (Philipsborn et al. 2016).

Climate factors can also affect enteric infection risk through their impact on nutrition (see Figure 1b). High temperatures – as well as low and high levels of precipitation – correlate with lower crop yields (Kahn 2016; Alderman, Turner, and Tong 2012). This decrease in food supply heightens food prices, reduces household purchasing power, and

increases malnutrition rates, especially in infants and young children. Malnutrition increases disease susceptibility, particularly to enteric infections (Atabati et al. 2020; Mahmud et al. 2020; Stanke et al. 2013). Existing literature further finds climatic factors shaping the risk of enteric infection mortality through their impacts on host immunity, population displacement, and health system disruptions (Mahmud et al. 2020).

Figure 1:　　　Key relationships between climate and enteric infections

(a)　　　Through contaminated water exposure
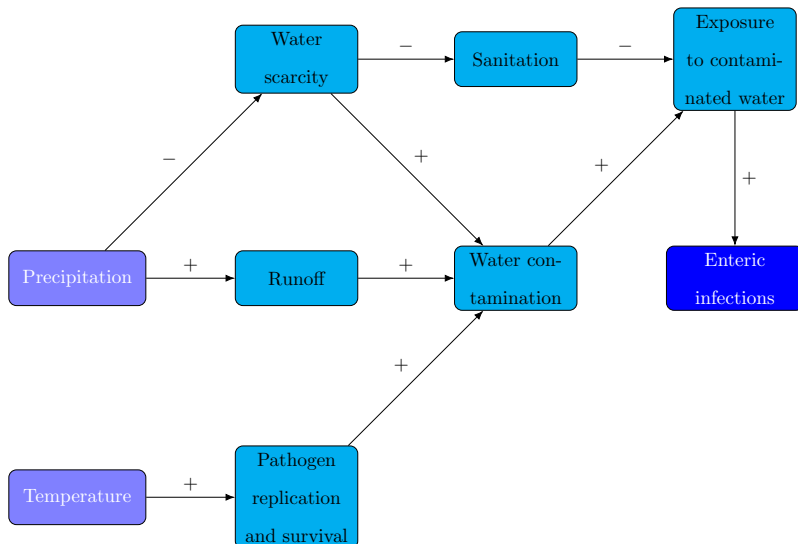
(b)　　　Through malnutrition
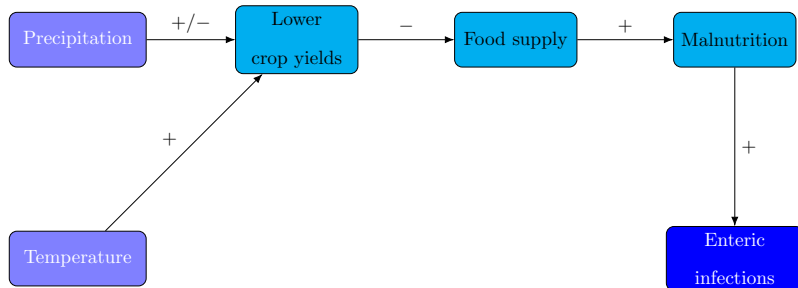
Sources: Alderman, Turner, and Tong (2012); Atabati et al. (2020); Bastaraud et al. (2020); Howard et al. (2016); Kahn (2016); Philipsborn et al. (2016); Saad et al. (2018); Shuman (2010); Stanke et al. (2013).

1.2 Antananarivo, Madagascar's epidemiological transition

Among the parts of the world most vulnerable to climate change and its health impacts is Madagascar, where global climate change has been associated with a rise in temperatures and an increase in the frequency of floods and droughts (Schlüter et al. 2020). Its rapidly growing capital, Antananarivo (18°55′ S, 47°32′ E), has a population over 1,200,000 (IN-STAT 2020) and experiences a mild oceanic climate of the subtropical highland variety (Köppen climate classification Cwb) with distinct cooler dry and warmer rainy seasons (Climate-Data.org 2020) (see Figure A-1, appendix). During this warmer rainy season the city experiences higher levels of enteric infection prevalence (Cassel-Beraud et al. 1990). Additionally, in recent years it has experienced increasing temperatures during the cooler dry season, delays to the start of the rainy season (Bastaraud et al. 2020), and an increasing frequency of deadly floods (Floodlist 2019, 2020) (see Figure A-2 and Table A-1, appendix).

Over the past several decades Antananarivo has undergone the classic epidemiological transition as described by Omran (Masquelier et al. 2014; Omran 2001). According to this framework societies transition through three sequential stages in which childhood infectious disease mortality – especially from waterborne enteric infections – plays a significant role. The transition begins with an age of pestilence and famine characterized by high and fluctuating mortality due to infectious disease epidemics. This is followed by an age of receding epidemics, where mortality declines, and concludes with an age of degenerative and 'manmade' diseases, where the disease burden shifts toward non-communicable diseases (NCDs) that primarily afflict older adults, with mortality further declining and then stabilizing at a lower level. Since Omran's initial work, the theory has expanded to include a more broadly defined concept of health transitions, encompassing additional phases, multiple variants, and counter transitions where mortality increases rather than declines (Frenk et al. 1989).

Throughout most of the 20th century Antananarivo was in the first stage of the epidemiological transition (see Figure 2). Its first water treatment plant – constructed in 1927 (Japan International Cooperation Agency 2019) – was insufficient to meet the needs of its rapidly growing and urbanizing population, which expanded from less than 200,000 to approximately 700,000 by 1993 (INSTAT 2020). Water contamination was high (Bastaraud et al. 2020), and enteric infections were the second leading cause of death (Masquelier et al. 2014). Mortality peaked in 1986 with life expectancy hitting lows of 46 and 62.4 in males and females, respectively. However, following the 1986 mortality crisis and a 1993 water treatment plant upgrade, Antananarivo transitioned into the second stage. According to Bastaraud et al. (2020) and Masquelier et al. (2014), water quality improved significantly, and infectious disease mortality in particular dropped sharply. Currently Antananarivo appears to be in the third stage of degenerative and manmade diseases (see

Figure A-3 and Table A-2, appendix). By 2008–2012 NCDs became the leading causes of death with enteric infections not even placing in the top ten.

Figure 2:   **Antananarivo's epidemiological transition**
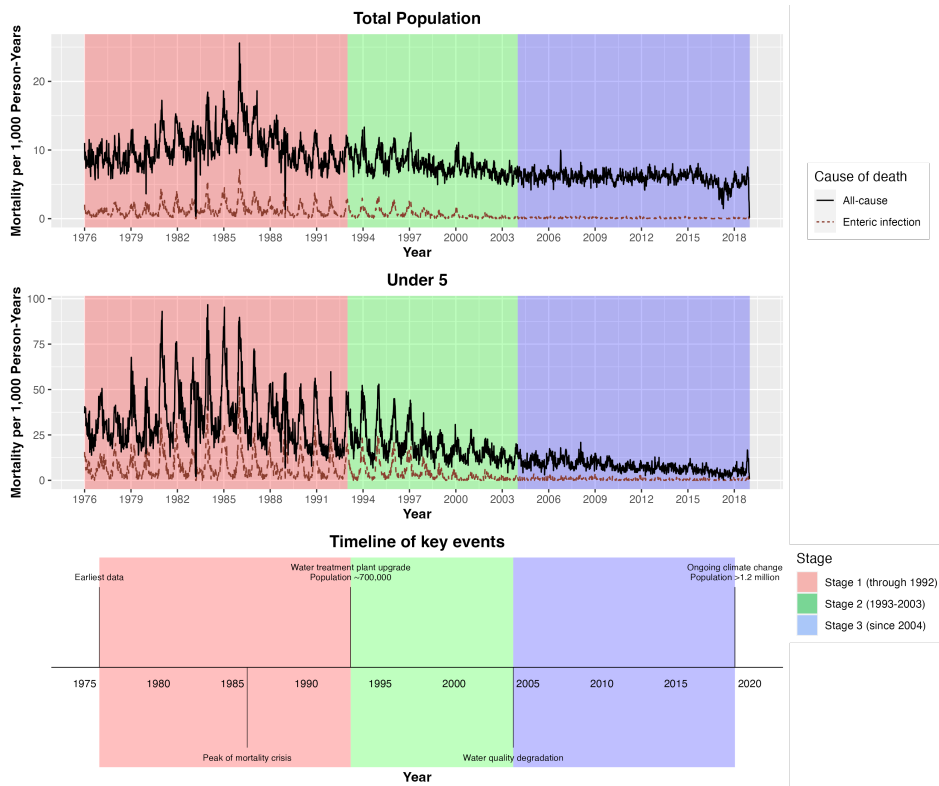
Note: Weekly time series of all-cause and enteric infection mortality in the total population and children under 5 with an accompanying timeline of concurrent events during the three stages of the city's epidemiological transition (1976–2018).

Since 2004 Antananarivo's water treatment infrastructure has been more vulnerable to heavy rainfall and increasingly unable to meet quality standards (Bastaraud et al. 2020). While additional water treatment plants have been installed and used in recent years and new ones are being constructed (Takouleu 2020), challenges with providing quality water remain. This is further complicated by Antananarivo's continued rapid population growth, unplanned urban development, and accelerating climate change.

Despite this increase in water contamination, enteric infection mortality has remained well below its pretransition levels, likely kept down by interventions like antimicrobials and oral rehydration therapy, which treat disease on the individual level and reduce infection fatality rates, rather than interventions like improved water and sanitation infrastructure, which reduce incidence on the population level (Masquelier et al. 2014). Epidemiological transitions driven by the former types of interventions are less durable than those driven by the latter and are liable to reversal (Frenk et al. 1989), especially in light of increasing threats posed by antimicrobial resistance: Antibiotic-resistant serotypes of common enteric pathogens have been prevalent in Antananarivo for several decades (Cassel-Beraud et al. 1990; Rasamiravaka 2020). This brings the sustainability of Antananarivo's epidemiological transition into question and suggests the city may be vulnerable to a new transition stage or a counter transition characterized by reemerging infectious diseases as theorized by Barrett et al. (1998) and Olshansky et al. (1998).

1.3 Research aims

We investigate the potential vulnerability of Antananarivo to a counter health transition characterized by increasing mortality from reemerging childhood enteric diseases – that is, indirect mortality impacts of climate, direct impacts of climatic extremes, or some combination thereof (Barrett, Charles, and Temte 2015; Barrett et al. 1998; Patz et al. 1996). Thereupon we examine how the relationships between the precipitation and temperature and mortality from enteric infections in children under 5 and other causes of death inclusive of direct climate-related mortality in the general population have changed as the city went through the three stages of the epidemiological transition.

Our focus is on enteric infection mortality – overwhelmingly concentrated in children under 5 – due to its exceptional sensitivity to climate. This focus also considers the central roles it plays in epidemiological transition theory and the role it played in historical transitions (Omran 2001; Szreter 1988, 1997). This is especially the case in Antananarivo, where enteric infections were the leading infectious cause of death at the beginning of the time period from which we have data when the city was in the first stage of its epidemiological transition (Masquelier et al. 2014). Furthermore, although previous literature analyzes the climate–enteric infection relationship (Hashizume et al. 2007; Luque Fernandez et al. 2009; Philipsborn et al. 2016) – including in Antananarivo (Cassel-Beraud et al. 1990) – it has received less attention there than other climate sensitive infectious diseases like vector-borne diseases (Ihantamalala et al. 2018a, 2018b). Ours is the first study to quantitatively dissect this relationship in Antananarivo. We employ a novel approach by focusing on mortality rather than reported cases as our outcome. Additionally, direct climate-related mortality has yet to be studied in less climatically di-

verse environments like Antananarivo, and this is the first long-run climate–mortality study in a sub-Saharan African city outside of South Africa.

We hypothesize that enteric infection mortality increases following precipitation extremes – especially heavy rainfall – with temperature playing a smaller secondary role. Based on the findings of Bastaraud et al. (2020) that water quality was more sensitive to rainfall before the treatment plant upgrade in 1993 and after its increasing inability to meet quality requirements since 2004, we expect we may see greater sensitivity of enteric infection mortality to climate during the first and third stages of the epidemiological transition but with heterogeneity in the extent of this sensitivity due to climate adaptation. In addition to water treatment infrastructure, such climate adaptation encompasses access to medicines to treat climate-related diseases, supply-and-demand side responses of farmers and consumers to the impacts of climate on food production (Kahn 2016), and physiological acclimatization (Achebak, Devolder, and Ballester 2018, 2019). Since recent years have seen more deadly floods, we suspect mortality from other causes may have become more sensitive to extreme precipitation highs during the third epidemiological transition stage. We measure extreme precipitation-related mortality under the umbrella of all other causes since causes of death from floods spanning drowning, acute trauma, injuries, toxic exposure, and NCDs (Alderman, Turner, and Tong 2012) are so varied and difficult to classify. In contrast despite rising temperatures being associated with climate change (Schlüter et al. 2020), temperatures in Antananarivo are still too mild to pose a substantial risk of direct mortality from extreme heat (Climate-Data.org 2020).

2. Methods

2.1 Data

2.1.1 Mortality

Our primary outcomes of interest in this study are weekly enteric infection mortality in children under 5 and all-age cause-deleted mortality (i.e., mortality from all other causes). To calculate these variables we obtained the 1976–2018 death registration time series from the Antananarivo Municipal Office of Hygiene (the Bureau municipal d'hygiène, or BMH), which includes the date of death, age at death, and cause of death according to International Classification of Diseases (ICD) codes, a standardized system of diagnostic codes maintained by the World Health Organization (WHO) (World Health Organization 2019). While Antananarivo's death registration data are timely and complete (Masquelier et al. 2019), they are of lower quality with regards to cause-of-death encoding. Masquelier et al. (2019) find that 31% of deaths registered from 1976 to 2015 use what the WHO denotes "major garbage codes," while in our own analyses we find that the vast majority

of enteric disease deaths (84.12%) do not identify a specific pathogen. This precludes us from considering pathogen-specific mortality.

We thus identify enteric infection deaths regardless of causal agent using ICD ninth edition (ICD-9) codes (World Health Organization 1978) 001–009 in the 1976–2015 BMH data. In the 2016–2018 data BMH denotes cause of death using ICD tenth edition (ICD-10) codes (World Health Organization 2019) in addition to written descriptions. To find the most accurate cause-of-death identification method for this time period, we forecast enteric disease mortality from 2016 to 2018 using 1976–2015 data with an autoregressive integrated moving average and find that enteric disease deaths identified using ICD-10 codes A00–A09 are closer to this forecast than enteric disease deaths identified using keywords from the written descriptions based on root mean squared error. After obtaining weekly enteric infection deaths, we subtract them from weekly all-cause mortality to obtain cause-deleted mortality. We also analyze all-cause mortality as an outcome itself to assess the robustness of our results to the aforementioned encoding issues. We standardize all-age cause-deleted and all-cause mortality using the 2000 age distribution of Antananarivo.

2.1.2 Climate

Our exposures of interest are total weekly precipitation and weekly mean of daily maximum temperature. We calculate these variables using daily precipitation and maximum temperature from Climate Hazards Group InfraRed Precipitation with Station (CHIRPS) (Funk et al. 2015) and Climate Hazards Group InfraRed Temperature with Station (CHIRTS) (Funk et al. 2019) data, respectively. We obtained CHIRPS precipitation daily time series from 1981 to 2018 averaged over four administrative divisions that cover Antananarivo: Ambohidrantrimo, Antananarivo-Atsimondrano, Antananarivo-Avaradrano, and Antananarivo-Renivohitra. We obtained CHIRTS temperature daily time series from 1983 to 2016 at the closest available coordinates to Antananarivo: $18°52'30.0''S$ $47°37'30.0''E$.

2.2 Models

We fit models of our outcomes of interest – under-5 enteric infection mortality and cause-deleted mortality – as functions of total precipitation and mean daily maximum temperature during individual weeks in the past or every week between a specified point in the past and the present, denoting these simple and cumulative lag models respectively (see Table 1). Informed by previous work finding an up to eight-week lag between climatic events and water contamination/enteric disease cases – but with substantial heterogeneity in the precise timing (Bastaraud et al. 2020; Hashizume et al. 2007; Luque Fernandez et al. 2009) – we fit our models with temperature and precipitation lags of zero to eight

weeks, finding the lag with the best fit. We perform robustness checks of our models using all-cause mortality as the outcome (see Table C-1, appendix).

Table 1:   **List of models**

Model	Outcome[a]	Climate lag terms[b]
1	< 5 enteric infection	Simple lag
2		Cumulative lag
3	All ages cause-deleted	Simple lag
4		Cumulative lag

Notes:[a] Outcome of interest.   [b] Whether the model was fitted using simple or cumulative lag terms for precipitation and temperature (0 to 8 weeks).

We selected negative binomial generalized additive models (GAMs) with a log-link function as the modeling approach uniquely well suited to our analysis, where our outcomes of interest are an overdispersed count variable with high degrees of variation over time, and we are interested in exploring their complex nonlinear relationships with our exposures (Hastie and Tibshirani 1990). Specifically, we expect the mortality effects of precipitation and temperature to change at different levels, with mortality increasing at both extreme highs and lows. Complex nonlinear relationships like these – where simpler linear models do not suffice – are common in the climate–health literature (Grace 2017; Hashizume et al. 2007; Schlüter et al. 2020). Consequently GAMs have been used extensively in previous work modeling the relationship between climatic extremes and enteric diseases (Li et al. 2013; Ma et al. 2013; Chen et al. 2012) and how the seasonality of mortality changed over time during Antananarivo's epidemiological transition (Schlüter et al. 2020). This latter work by Schlüter et al. (2020) especially inspires our modeling approach as we similarly seek to model how the dynamics of mortality changed during the city's transition. GAMs help achieve a balance between complexity and interpretability in modeling these systems (Ross 2019). Since they rely on nonparametric smoothing functions, they allow for greater flexibility in uncovering underlying patterns in the data compared to easier-to-interpret linear methods commonly used in the climate–mortality literature, such as binned models (Grace 2017; Geruso and Spears 2018; Barreca et al. 2016; Barreca 2012; Carleton 2017). We do, however, acknowledge this trade-off in our ultimate selection of GAMs. Additionally, since binned models look at the effect of cumulative exposure to precipitation or temperature falling within a certain range over an entire time interval, they do not allow us to examine the impacts of different time lags on the climate–enteric infection relationship in the way zero-to-eight-week lag-fitted GAMs do.

In our models we use person-years of exposure – either in the population under 5 or all ages – as an offset, derived from age-disaggregated population data from Madagascar's Institut National de la Statistique (INSTAT) (INSTAT 2020). INSTAT conducted censuses in 1975, 1993, and 2018 with a provisional count in 2009 (Masquelier et al. 2014). We use estimates provided by Bruno Masquelier (personal communication, April 3, 2020) and linear interpolation for intercensal population estimates. We then calculate person-years of exposure in each age group by dividing its estimated population in a given year by epidemiological weeks. We control for seasonality with month fixed effects, longer term changes in climate and mortality – the latter mediated through unobserved variables (see Figure 3) – with year fixed effects, and mortality in the previous week with first-order autoregressive terms. We explore how the relationship between climate and mortality evolved as Antananarivo went through the first (1983–1992), second (1993–2003), and third stages (2004–2016) of Omran's epidemiological transition (Masquelier et al. 2014; Omran 2001) by fitting our climate terms by stage. Our smoothing parameter estimation method is a restricted maximum likelihood estimation. We perform model selection by finding the precipitation and temperature lag terms that minimize the Bayesian information criterion (Schwarz 1978).

Our model specification is as follows:

$$log(Y_t) = log(PY_t) + f_1(Y_{t-1}) + i.year_t + i.month_t$$
$$+ f_2(tmax_{t-j}, i.period_t) + f_3(prcp_{t-j}, i.period_t) + \epsilon_t \tag{1}$$

refers to models with simple climate lag terms (1, 3, 5, and 7 in Tables 1 and C-1), and

$$log(Y_t) = log(PY_t) + f_1(Y_{t-1}) + i.year_t + i.month_t$$
$$+ f_2\left(\frac{\sum_{j=0}^{J} tmax_{t-j}}{J+1}, i.period_t\right) + f_3\left(\sum_{j=0}^{J} prcp_{t-j}, i.period_t\right) + \epsilon_t \tag{2}$$

refers to models with cumulative climate lag terms (2, 4, 6, and 8 in Tables 1 and C-1).

Y_t is the outcome of interest – enteric infection, cause-deleted, or all-cause mortality in children under 5 or in all age groups – at week t. Y_{t-1} is a first-order autoregressive term, the outcome of interest in the previous week. $log(PY_t)$ is the person-years of exposure offset, $i.year_t$ and $i.month_t$ are year and month fixed effects, respectively, and ϵ_t is the error term. f_1, f_2, and f_3 are smoothing functions of the autoregressive term, $tmax$ is the weekly mean of daily maximum temperature, and $prcp$ is the total weekly precipitation. Inclusion of $i.period_t$ in the smoothing function indicates smoothing functions were fitted for each stage of the epidemiological transition separately. The subscript j indicates lags for precipitation and temperature. Equation 1 fits simple lag terms – rainfall/temperature in the single week specified. Equation 2 fits cumulative lag terms – total

rainfall/average temperature between week J, taking a maximum value of eight, and the current week t.

To ensure the robustness of our results to alternative model specifications we replicate all our analyses with year-by-month fixed effects, modeling precipitation and temperature separately, and precipitation–temperature interaction, as well as easier-to-interpret methods such as linear models with fixed effects and distributed lags (see Table G-1, appendix) and binned models with fixed effects (see Table H-1, appendix). Further details on our specification of these models are provided in the appendix (see Year-by-month fixed effect models, Separate precipitation and temperature models, Precipitation–temperature interaction models, Linear distributed lag models, and Binned models). We performed all analyses in R (R Core Team 2023) using the packages mgcv (Wood 2017), lfe (Gaure 2013), and itsadug (van Rij et al. 2022) to fit and visualize our models.

Figure 3: **Directed acyclic graph of the posited relationship between exposures (temperature and precipitation) and outcome (climate-related mortality)**
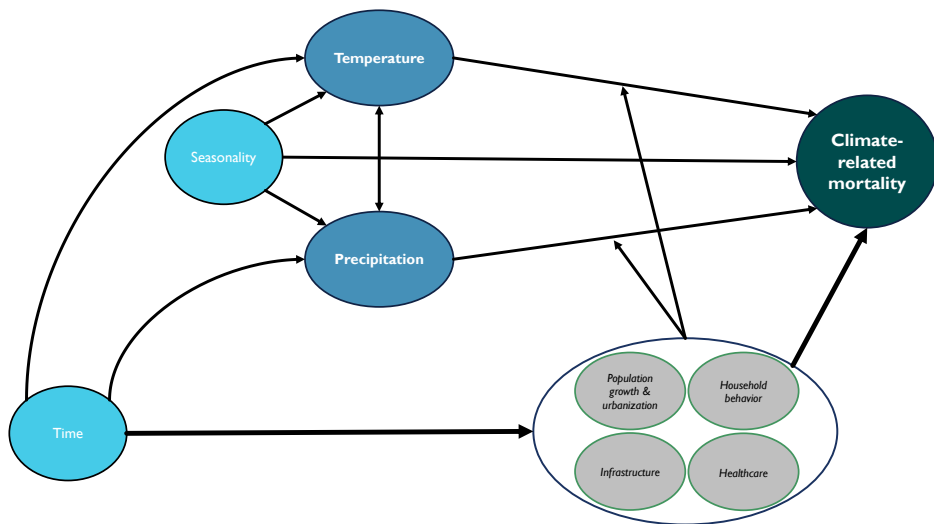
3. Results

### 3.1 Under-5 enteric infection mortality

During the first stage of the epidemiological transition we observe a mildly negative or null relationship between precipitation and under-5 enteric infection mortality when looking at a simple five-week or cumulative zero-to-seven-week lag model, respectively (see Figures 4a and 5a; Tables B-1 and B-2, appendix). These results could suggest that mortality increased following acute episodes of low precipitation – such that all else being equal, in the five weeks following a week with 0 millimeters of precipitation we could expect a mortality rate of on average about 25 per 100,000 person-years higher than in the five weeks after a week with 200 millimeters of precipitation – but not following longer term periods of low precipitation. However, caution must be exercised when interpreting these findings due to their wide confidence intervals and high degree of uncertainty. In most of our robustness checks we consistently find a mildly negative association between precipitation and under-5 enteric infection mortality during the first stage of the epidemiological transition, regardless of the precipitation lag terms (see Figures D-1a, D-2a, E-1a, and E-2a and Tables D-1, D-2, E-2, and E-4, appendix). Nevertheless, as Antananarivo progressed through the second and third stages of the epidemiological transition despite under-5 enteric infection mortality declining overall (see Figure A-3 and Table A-2, appendix), we observe it becoming more sensitive to higher precipitation. This relationship appears to be most pronounced when considering precipitation with a cumulative lag during the third epidemiological transition stage, where we may expect a mortality rate after a seven-week period with 1,000 millimeters of total precipitation on average almost 100 per 100,000 person-years higher than after a seven-week period with 0 millimeters of precipitation.

Figure 4: **Predicted weekly under-5 enteric infection mortality from total precipitation five weeks prior (a) and mean of daily maximum temperature eight weeks prior (b)**

(a)

(b)
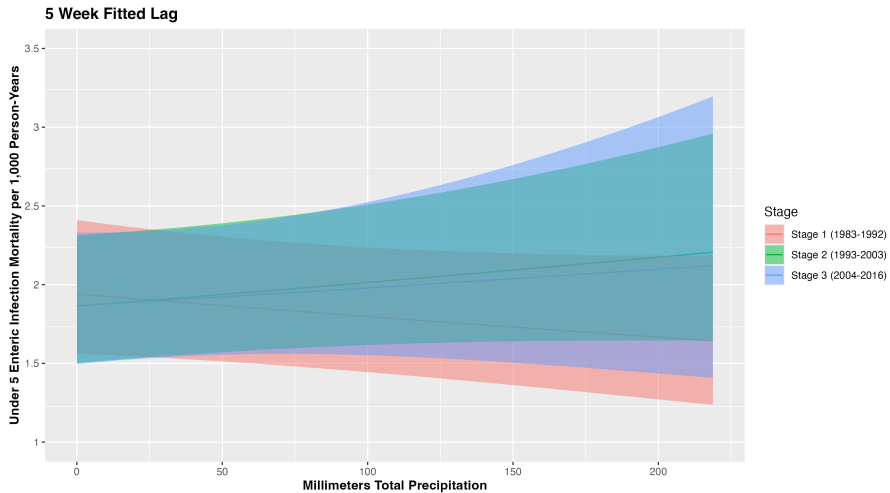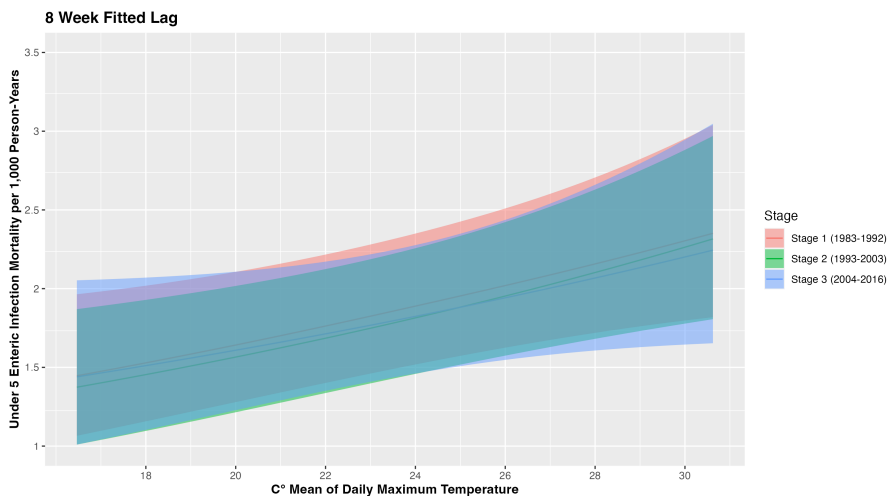
Notes: Fitted generalized additive model 1 (see Table 1). Date set to January 2000, and autoregressive and climate terms not plotted to their mean values. Shaded regions indicate 95% confidence intervals.

Figure 5: **Predicted weekly under-5 enteric infection mortality from total precipitation over the preceding seven weeks (a) and mean of daily maximum temperature over the preceding three weeks (b)**
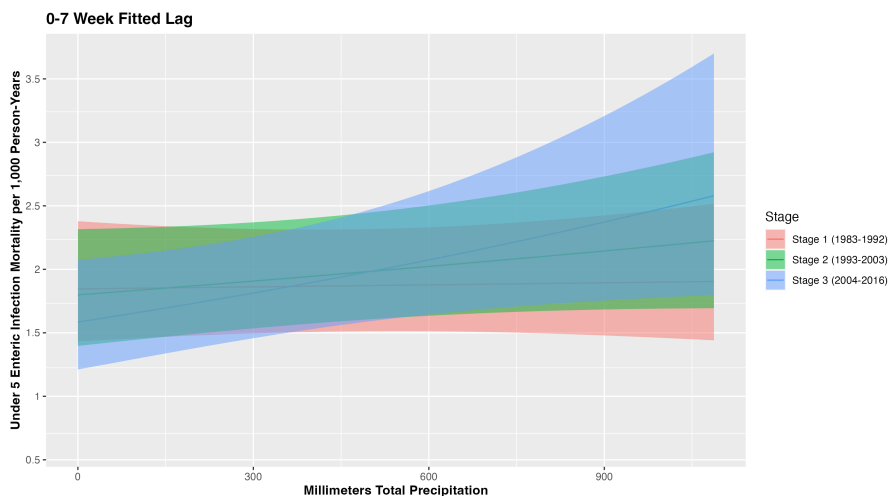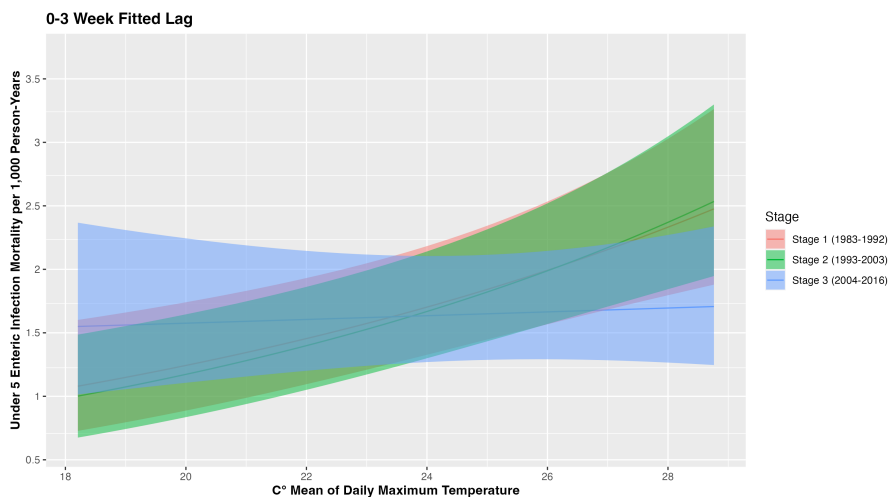
(a)

(b)

Notes: Fitted generalized additive model 2 (see Table 1). Date set to January 2000, and autoregressive and climate terms not plotted to their mean values. Shaded regions indicate 95% confidence intervals.

We observe a steep positive relationship between temperature and under-5 enteric infection mortality with both eight- and zero-to-three-week lags during the first stage of the epidemiological transition (see Figures 4b and 5b), which is converse to precipitation. According to the latter we may expect a mortality rate over 100 per 100,000 person-years higher on average following a three-week period with a mean daily maximum temperature of 28°C than with a mean daily maximum temperature of 20°C. This strong positive relationship persisted during the second stage. However, by the third stage under-5 enteric infection mortality became less sensitive to temperature. This is especially the case for the cumulative lag model, where we see barely any variation of mortality in response to temperature. This suggests that under-5 enteric infection mortality has become less sensitive to longer periods of higher temperatures, a finding shared by our robustness checks (see Figures D-1b, D-2b, E-1b, and E-2b and Tables E-1 and E-3, appendix).

These findings are consistent with our models of temperature–precipitation interaction. During the first stage of the epidemiological transition, we observe an increase in mortality at higher temperatures and lower precipitation levels (see Figures F-1 through F-6 and Tables F-1 and F-2, appendix). As Antananarivo progressed to the second stage, we find a shift where higher mortality became associated with higher precipitation levels, an association that persists through the third stage. By this final stage of the transition, the relationship between mortality and temperature became greatly attenuated.

3.2 Age-standardized cause-deleted mortality and robustness checks

Compared to the findings for under-5 enteric infection mortality we observe that age-standardized cause-deleted mortality appears to be less sensitive to precipitation. Predicted mortality shows minimal variation with precipitation with a four-week simple lag at all stages of the epidemiological transition (see Figure 6a; Table B-3, appendix). While we do find that cause-deleted mortality became slightly more sensitive to higher levels of precipitation with a zero-to-six-week cumulative lag during the later stages of the epidemiological transition – with expected mortality following a six-week period with 1,000 millimeters of total precipitation about 40 per 100,000 person-years higher than a six-week period with 0 millimeters of precipitation (see Figure 7a; Table B-4, appendix) – there is a great degree of uncertainty in these results. Our broader finding of little variability of mortality with precipitation is widely observed across our robustness checks (see Figures D-3a, D-4a, E-3a, and E-4a and Tables D-3, D-4, E-6, and E-8, appendix).

Figure 6: **Predicted weekly age-standardized cause-deleted mortality from total precipitation four weeks prior (a) and mean of daily maximum temperature eight weeks prior (b)**

(a)

(b)
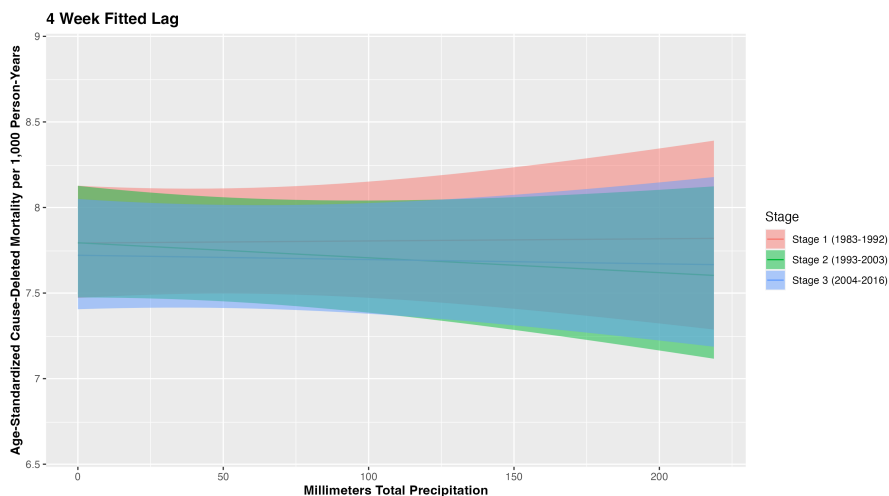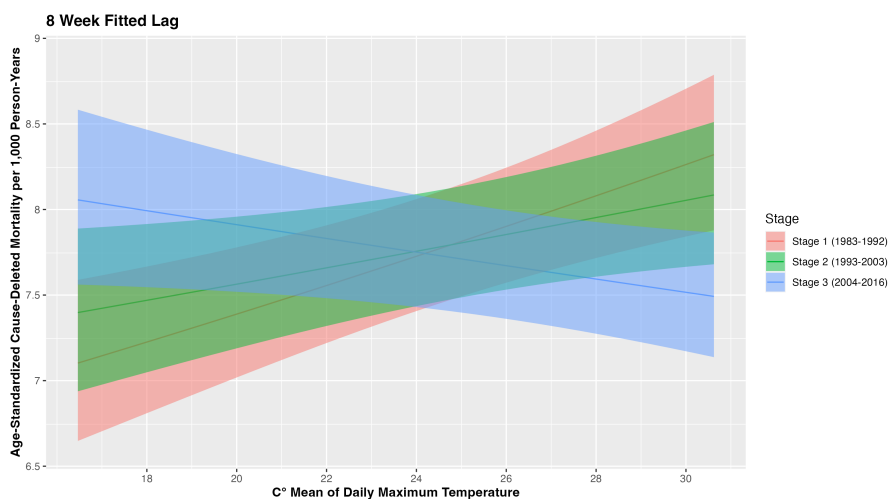
Notes: Fitted generalized additive model 3 (see Table 1). Date set to January 2000, and autoregressive and climate terms not plotted to their mean values. Shaded regions indicate 95% confidence intervals.

Figure 7: **Predicted weekly age-standardized cause-deleted mortality from total precipitation over the preceding six weeks (a) and mean of daily maximum temperature over the preceding eight weeks (b)**
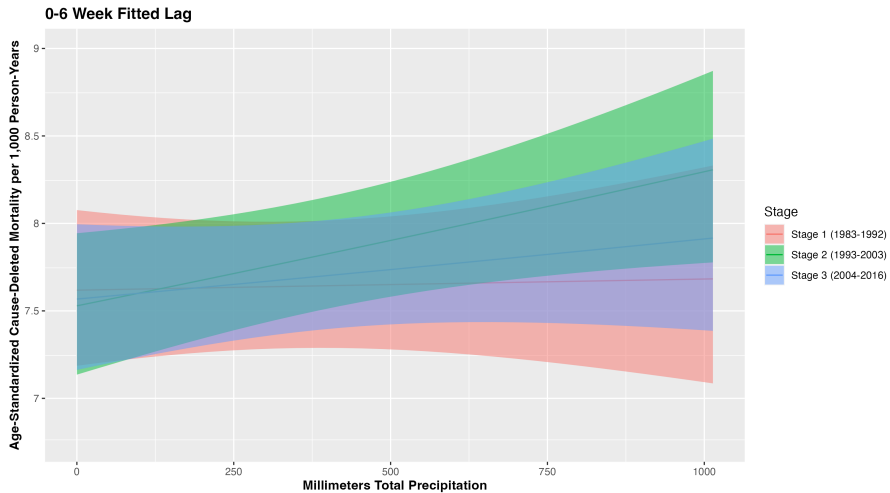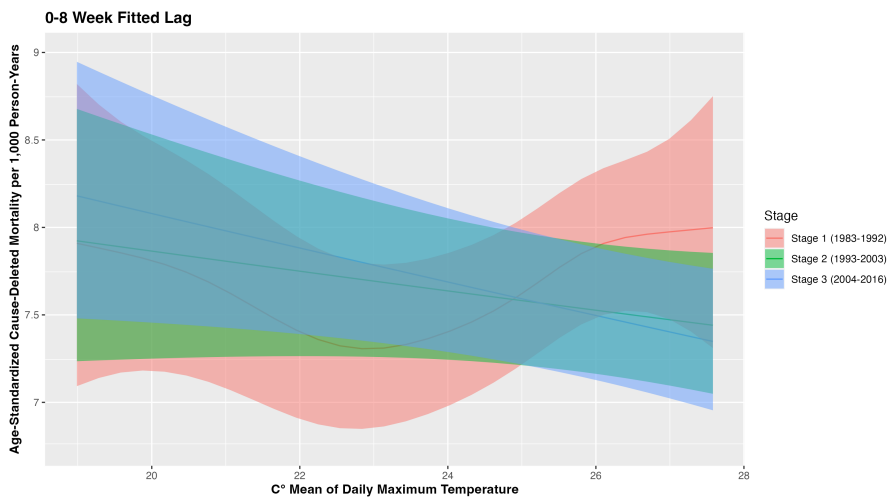
(a)

(b)

Notes: Fitted generalized additive model 4 (see Table 1). Date set to January 2000, and autoregressive and climate terms not plotted to their mean values. Shaded regions indicate 95% confidence intervals.

When examining the impact of temperature on cause-deleted mortality, we find a positive relationship during the first stage of the epidemiological transition using an eight-week simple lag (see Figure 6b), where we may expect a mortality rate of on average about 100 per 100,000 person-years higher eight weeks after a week with a mean daily maximum temperature of 30°C than a week with a mean daily maximum temperature of 18°C. However, as the transition progressed to the second stage, this positive association attenuated. By the third stage the relationship became negative, albeit less steep than the initial positive association observed in the first stage, with a predicted mortality rate of on average about 50 per 100,000 person-years lower eight weeks after a week with a mean daily maximum temperature of 30°C than a week with a mean daily maximum temperature of 18°C. In contrast when considering a zero-to-eight-week cumulative lag, we observe higher mortality at both low and high temperature levels during the first stage of the epidemiological transition, and during both the second and the third stages the relationship between temperature and mortality was negative (see Figure 7b). These findings are broadly consistent across our robustness checks and demonstrate that during the first stage of the epidemiological transition short periods of high temperature were followed by increased mortality while longer term periods of both high and low temperature were associated with increased mortality (see Figures D-3b, D-4b, E-3b, and E-4b and Tables E-5 and E-7, appendix). In contrast during the latter stages of the transition only lower temperatures were associated with higher mortality over both the short and long term. These findings are also consistent with our models of temperature–precipitation interaction as we observe a shift toward higher cause-deleted mortality at lower temperatures as Antananarivo progressed through the epidemiological transition and minimal variation of mortality with precipitation over time (see Figures F-7 through F-12 and Tables F-3 and F-4, appendix).

Similar findings when using all-cause mortality as our outcome demonstrate the robustness of our results to potential cause-of-death encoding errors. The climate–mortality relationships in our all-cause mortality models are similar in direction and slope to those in our cause-specific mortality models during the stages of the epidemiological transition (see Figures C-1 through C-4, D-5 through D-8, E-5 through E-8, and F-13 through F-24 and Tables C-2 through C-5, D-5 through D-8, E-9 through E-16, and F-5 through F-8, appendix). In addition to these more difficult-to-interpret GAMs, we obtain qualitatively similar results when using alternative easier-to-interpret methods commonly used in the climate–mortality literature, including linear models with fixed effects and distributed lags (see Figures G-1 through G-16, appendix) and binned models with fixed effects (see Figures H-1 through H-8, appendix).

4. Discussion

4.1 Climate–enteric infection relationship

Our findings support our hypothesis that enteric infection mortality in children under 5 is sensitive to precipitation extremes. However, contrary to our initial expectations we observe that temperature appears to play an equally important role as precipitation in influencing enteric infection mortality. Additionally, while our findings provide some support to our hypothesis that enteric infection mortality would have been more sensitive to climate during the first and third stages of the epidemiological transition, we unexpectedly find the directionality of this sensitivity and the relative importance of precipitation and temperature to shift between these two stages. During the first stage low rainfall and high temperatures were associated with higher mortality, with the latter playing a far more important role. Conversely, by the third stage heavy rainfall was associated with higher mortality, with precipitation now playing the more important role.

Enteric infection prevalence in Antananarivo has been found to be higher during the rainy season, particularly during the first stage of the epidemiological transition (Cassel-Beraud et al. 1990). However, after controlling for seasonality, our analysis reveals interesting patterns. Prior to the 1993 expansion of the water treatment plant, higher enteric infection mortality was associated with low rainfall, while after the treatment plant expansion, higher mortality followed heavy rainfall despite enteric infection mortality declining overall. These findings align with the mechanisms proposed by previous literature (see Figure 1a). In the absence of access to an improved source of water – defined by the WHO as one free from contamination when operating as intended by the nature of its construction or through active intervention (World Health Organization 2017) – households must seek out water from unimproved sources. During periods of low rainfall, when water is scarcer, the potential water sources available to these households are more limited and are more likely to be of poorer quality and more contaminated (Atabati et al. 2020; Saad et al. 2018; Stanke et al. 2013). Although the construction of new infrastructure expanding access to treated water from an improved source – as happened in Antananarivo in 1993 – may help protect against the impacts of low rainfall, such infrastructure is vulnerable to contamination by runoff from heavy rainfall (Shuman 2010). This vulnerability is particularly evident in high-density urban areas in LMICs like Antananarivo, where lower quality water infrastructure struggles to meet the demands of a rapidly growing low-income urban population, exacerbated by the challenges posed by climate change (Alderman, Turner, and Tong 2012; Howard et al. 2016). This is precisely what has been observed in the previous literature as the city's water supply has seen greater spikes in contamination following heavy rainfall in recent years (Bastaraud et al. 2020). Because Antananarivo and Madagascar as a whole are expected to experience a continued increase in the frequency and intensity of heavy rainfall events (Bastaraud et al. 2020; Otto et al.

2022), this state of affairs makes Antananarivo especially vulnerable to a counter health transition driven by increasing mortality from reemerging childhood enteric diseases. The stronger observed association between higher mortality rates and heavy rainfall in our cumulative model compared to the simple lag model suggests that the persistence of heavy rainfall over an extended period of time may be necessary to overwhelm water infrastructure and cause significant damage. The simple lag model in contrast might not capture the cumulative effects of prolonged runoff. Despite these findings it is worth noting that countervailing trends have been identified in certain contexts. In settings with greater access to improved water and sanitation infrastructure there may be a greater vulnerability to low levels of rainfall than to high levels (Alderman, Turner, and Tong 2012; Stanke et al. 2013).

Our finding that enteric disease mortality increased following higher temperatures prior to the 1993 water treatment plant expansion is consistent with the literature. Prevalence of many common deadly enteric diseases – as well as enteric disease overall – is associated with higher temperatures in most settings (Hashizume et al. 2007; Howard et al. 2016; Kolstad and Johansson 2011; Luque Fernandez et al. 2009; Philipsborn et al. 2016; Saad et al. 2018). This is especially the case in settings where access to treated water from improved sources is limited, and drinking water is contaminated by pathogens whose replication and survival are promoted by higher temperatures. That enteric infection mortality became less sensitive to temperature during the latter stages of the epidemiological transition following the water treatment plant expansion therefore also aligns with this literature. However, neither reduced sensitivity of enteric infection mortality to temperature and low rainfall nor low enteric infection mortality overall during the third stage can likely be explained – and almost certainly not fully explained – by the expansion of water treatment infrastructure alone. In addition to seeing larger spikes in contamination following heavy rainfall, the city water supply was of similarly poor quality during the third stage as it was during the first (Bastaraud et al. 2020). Therefore, other modes of adaptation to climate change – including to its impacts on agricultural production – could have also played a role (see Figure 1b).

Our findings of a negative association between precipitation and enteric infection mortality and a positive association between temperature and enteric infection mortality during the first stage of the epidemiological transition may in part be explained by low precipitation and high temperature's negative impacts on crop yields (Kahn 2016; Stanke et al. 2013). These adverse effects on agricultural productivity could have led to malnutrition and subsequently increased the susceptibility of children to mortality from enteric diseases (Atabati et al. 2020; Mahmud et al. 2020). The reduced sensitivity of enteric infection mortality to low rainfall and high temperatures as Antananarivo progressed through the epidemiological transition could therefore, according to the literature, potentially be explained by the adaptation of farmers and consumers to climate impacts on agricultural production over time (Kahn 2016). According to Kahn (2016) such adap-

tation can take the form of farmers moving to new locations less impacted by climatic conditions, changing their inputs and farming methods, and increasing storage while consumers may shift to less expensive foods that are less impacted by low rainfall and high temperature.

Conversely, a potential mechanism of climate adaptation that is unlikely to have played a significant role in reducing overall enteric infection mortality or its sensitivity to low rainfall and high temperature is socioeconomic development. While the precise relationship between standards of living and mortality is not definitively established, standards of living in Madagascar remain below their early 1980s peak (The World Bank 2021). Furthermore, as highlighted in the seminal works of Preston (1975) and Easterlin (1999), economic growth has not historically been the primary driver of mortality declines associated with the epidemiological transition. This crucial role has instead been played by public health interventions and public policy. This has precisely been the case in Antananarivo, where improved access to medicines such as antimicrobials and oral rehydration therapies have likely contributed significantly to both keeping enteric infection mortality rates low overall and to climate adaptation by moderating the mortality impacts of climatic extremes (Masquelier et al. 2014). However, the sustainability of the effect of these medicines on mortality is at risk due to the increasing prevalence of antimicrobial-resistant pathogens in Madagascar (Rasamiravaka 2020).

4.2 Association of climate with deaths from other causes/direct climate-related mortality

Compared to under-5 enteric infection mortality, all-age cause-deleted mortality demonstrates a relatively lower sensitivity to climate, particularly in relation to precipitation. During the initial stage of the epidemiological transition, cause-deleted mortality displayed minimal sensitivity to changes in precipitation levels. Surprisingly, as Antananarivo progressed through the transition, mortality rates continued to exhibit limited sensitivity to precipitation, although a weak association with higher levels of precipitation was observed when looking at cumulative lag models. These findings provide limited support to our hypothesis that precipitation would exhibit a positive association with cause-deleted mortality during the third stage of the epidemiological transition, as suggested by the increased frequency of deadly floods (Bastaraud et al. 2020; Floodlist 2019, 2020). However, it is crucial to note that increased deadliness of floods alone does not necessarily indicate an increase in the sensitivity of mortality to precipitation. Without significant changes in the underlying effect modifiers of this relationship, an increase in the deadliness of floods could simply reflect a higher intensity of rainfall during these events rather than a heightened response of direct climate-related mortality to precipitation.

Nevertheless, evidence suggests that certain underlying effect modifiers may have changed over time, potentially increasing the sensitivity of direct climate-related mortality to heavy rainfall. Notably, ongoing unplanned low-income urban population growth has been identified as a factor that could influence this relationship (Bastaraud et al. 2020). Yet the only small increase in the direct mortality effects of high levels of precipitation observed during the second and third stages of the epidemiological transition in our analyses can likely be explained by the overall low baseline of flood-related mortality in Antananarivo (Floodlist 2019, 2020), particularly in comparison to other causes of death. Thus the small effect size of higher levels of precipitation on cause-deleted mortality – accompanied by a high degree of uncertainty – can be attributed to the minimal increase in the total number of deaths resulting from the low baseline of flood-related mortality.

Unlike precipitation all-age cause-deleted mortality exhibits a significant sensitivity to temperature, a relationship that has undergone changes over time. Although our results support our hypothesis that despite increases in temperature attributed to climate change, temperatures in Antananarivo are still too mild to pose a substantial risk of direct mortality from extreme heat, a closer analysis of our findings reveals a more nuanced picture that warrants further examination.

During the first stage of the epidemiological transition, we observe a positive relationship between temperature and mortality in addition to higher mortality rates following longer periods of low temperatures. The positive association between temperature and mortality during this stage is likely attributable to the impact of other climate-sensitive nonenteric infectious diseases, such as vector-borne diseases, like malaria, that thrive in warmer temperatures (Patz, Grabow, and Limaye 2014; Watts et al. 2021). In Antananarivo a resurgence of malaria occurred in 1984 following a decades-long campaign to control the disease. However, with the introduction of chloroquine chemoprophylaxis in 1988 and DDT spraying in 1993–1995, malaria was brought under control once again (Masquelier et al. 2014). This resurgence in malaria incidence – spanning roughly a decade – coincides with the time period corresponding to the first stage of the epidemiological transition in our analyses (1983–1992).

Similarly, the comparatively smaller role played by low temperatures in cause-deleted mortality during the first stage of the epidemiological transition may be driven by mortality from NCDs such as cardiovascular disease (CVD). CVD has been associated with both hotter and colder temperatures in different contexts, the latter driven by cardiovascular stress due to changes in blood pressure, vasoconstriction, and an increase in blood viscosity at cold temperatures (Barreca 2012; Barreca et al. 2016). In Antananarivo CVD mortality has consistently been higher during colder months (Schlüter et al. 2020). Accordingly, our findings that the positive association between cause-deleted mortality and high temperature inverted while the positive association between cause-deleted mortality and low temperature strengthened may be expected by the decrease in the proportion of mortality caused by infectious diseases relative to NCDs as the city progressed through

the epidemiological transition. However, why mortality has only become less sensitive to high temperatures but not to low temperatures when both are risk factors for NCD mortality requires further explanation.

One potential explanation for this phenomenon could be the adaptation of farmers and consumers in response to the impacts of high temperatures on food production following the mechanisms previously described in 4.1, thus ameliorating the impact of heat on nonenteric infection causes of death linked to malnutrition. A further explanation could be physiological adaptation to higher temperatures over time as the climate steadily becomes warmer (Achebak, Devolder, and Ballester 2018). Previous literature focusing on Spain (Achebak, Devolder, and Ballester 2019) – where CVD mortality has become less sensitive to both high and low temperatures in recent decades – asserts that reduced sensitivity to high temperatures can in part be attributed to acclimatization as the temperature at which mortality is minimized has steadily increased. According to Achebak, Devolder, and Ballester (2019) reduction in the risk of mortality at cold temperatures however can be explained by socioeconomic development. As Madagascar, unlike Spain, has not experienced an increase in income over the past several decades (The World Bank 2021), our finding of a decrease in the risk of mortality at high temperatures but not at low temperatures aligns with Achebak, Devolder, and Ballester (2019)'s framework.

Overall, though our results provide evidence to suggest Antananarivo may be vulnerable to a counter health transition driven by increasing mortality from reemerging enteric infections, the prospects for a counter transition driven by the direct mortality impacts of climatic extremes are far lower, at least for the near future. The more distant future is less certain. In the historical record thus far temperature in Antananarivo has only on rare occasions exceeded 29°C, too low of a level for a substantial risk of extreme heat-related mortality (Barreca 2012; Barreca et al. 2016; Geruso and Spears 2018; Takahashi, Honda, and Emori 2007). However, if the temperature continues to increase and precipitation becomes more extreme, they could have impacts on direct climate-related mortality not heretofore uncovered.

4.3 Limitations

The great uncertainties involved in predicting future climatic conditions are mirrored by those surrounding the precise relationships between climate and health outcomes, particularly childhood enteric disease. The precise mechanisms through which climatic conditions cause different health outcomes are finicky and not completely understood. The results of studies linking the two are often highly dependent on the local contexts in which they are conducted and the methods of analysis they use, such that studies looking at similar outcomes often produce entirely contradictory results (Kolstad and Johansson 2011; Mahmud et al. 2020; Saad et al. 2018; Thindwa et al. 2019). While our results may of-

fer some insight into potential vulnerabilities of urban areas in LMICs to reverse health transitions as climate change accelerates, they should first and foremost be interpreted as specific to the context of Antananarivo from 1983 to 2016, with the understanding that there is a chance that different results could be obtained if different data or statistical modeling methods were used. Nevertheless, we do endeavor to ensure our results are robust to a variety of model specifications.

Though we use enteric infection death registration data in this study, the ideal data with which to evaluate the climate–enteric disease relationship would be pathogen-specific incidence rates at a high temporal and spatial resolution. Even if we keep mortality as our primary outcome, pathogen-specific incidence data would add great value in permitting us to analyze the extent to which changes in enteric infection mortality over time and in response to public health interventions and climate adaptation on one hand and environmental changes on the other have been driven by changes in incidence versus changes in infection fatality rates. However, pathogen-specific incidence data quality, timeliness, and completeness are often poor in resource-limited settings like Madagascar (Randriamiarana et al. 2018), and key pathogens may be missed as a result of limited diagnostic capacity. In contrast mortality data from Madagascar – and from Antananarivo specifically – are of uniquely high quality, particularly with respect to timeliness and completeness. Since 1976 more than 80% of deaths have been reported on the same day or the day after they occur (Masquelier et al. 2014), and Masquelier et al. (2019) estimate that death registration is more than 90% complete. However, the quality of these data is lower with respect to cause-of-death encoding. This could potentially lead to not insignificant numbers of enteric disease deaths being encoded as deaths from other causes and vice versa. This would in turn necessarily bias our calculated enteric disease and cause-deleted mortality rates through over- and underestimation in opposing directions. We analyze the extent to which this phenomenon may be impacting our results by demonstrating their robustness to using all-cause mortality as an outcome. This approach is sound as enteric infection deaths comprise a significant proportion of all deaths in children under 5 while other causes of deaths constitute the vast majority in the entire population (Masquelier et al. 2014).

That these precise cause-of-death encoding errors do not impact our results is in large part due to the fact that we lump individual causes of death together into two very broad categories: enteric infections and all other causes. Our use of cause-deleted mortality as a catch-all category that includes all causes of death other than enteric infections relies on the expectation that the degree to which it changes in response to climate will necessarily capture the diverse causes of direct climate-related mortality. Though crude this choice was informed by similar approaches that use all-cause mortality to estimate the direct mortality impacts of climatic extremes found extensively in the literature (Barreca 2012; Barreca et al. 2016; Geruso and Spears 2018). However, we cannot discount the extent to which cause-deleted mortality's response to climate may also capture indirect

climate-related mortality from causes other than enteric infections, including from other infectious diseases (Barreca 2012). We also cannot discount the possibility that direct climate-related mortality comprises such a small proportion of overall mortality that its sensitivity to climate cannot be detected when lumped in with other causes of death. We could address this by looking at individual direct climate-related causes of death as outcomes, such as drowning, acute trauma, injuries, and toxic exposure (Alderman, Turner, and Tong 2012), but such an approach would necessarily be subject to the aforementioned cause-of-death encoding issues.

Besides those stemming from the measurement and construction of our outcome variables, we must also address limitations to this study from the variables we omit from our analyses. These include variables that both mediate the changes in mortality we observe over time and modify the effects of climatic drivers on mortality on both the individual/household and community levels (see Figure 3). Some of these key individual/household-level variables include access to medicines and adherence to treatment regimens, health-seeking behavior, access to and sources of water and sanitation, sanitation and hygiene practices, household construction materials, income, ethnic group, and sex/gender. Key community-level variables include neighborhood (or fokontany in the case of Antananarivo), population density, topography, ground permeability, community-level water and sanitation infrastructure, and prevalence of antimicrobial-resistant pathogen serotypes. Several of these factors are instrumental in undergirding the classical epidemiological transition and could potentially play key roles in facilitating a counter health transition. Unfortunately data on many of them are sparse in low-resource settings like Madagascar. During the time period covered by our climate data (1983–2016) only one full household census was conducted in 1993 with a provisional count in 2009 (Masquelier et al. 2014). Other data sources like the Demographic and Health Surveys (DHS) could help fill in the gaps, but they are only marginally less sparse, with only four full DHS surveys and three malaria indicator surveys conducted during this time period and none of them before 1992 (The DHS Program 2021). Data with such sparsity are especially problematic in rapidly changing environments like Antananarivo. While not ideal, we do attempt to control for changes in these omitted variables over time with year fixed effects and address their potential effect modification of the climate–mortality relationship by fitting our climate terms by stage of the epidemiological transition. This of course relies on the certainly oversimplified expectation that the omitted effect modifiers are roughly constant during each stage of the transition and change uniformly between them.

We must also address the fact that the delineation of the stages of the epidemiological transition and assigning them start and end points is by necessity an arbitrary process. Omran's epidemiological transition theory itself is ill defined and cannot be operationalized without substantial ambiguity (Mackenbach 1994). This is because the epidemiological transition theory is not a grand unified theory of epidemiology espous-

ing a set of universal laws governing how disease and mortality patterns change across time and space. Rather, it is most useful as a framework for stimulating further inquiry in describing and explaining how these patterns may change over time in different settings–precisely how we have applied it in this study. Therefore, there are as many models of how societies progress through the epidemiological transition as there are societies, and what precisely demarcates the ages of pestilence and famine, receding pandemics, and degenerative manmade diseases nor when they begin and end in different societies is universally agreed upon (Omran 2001). There is nothing that specifically required us to demarcate the beginning or end of each stage where we did. We made these delineations informed by our observation of three clear periods where mortality appears to be high and fluctuating (through 1992), declining (1993–2003), and stable at a lower level (since 2004, see Figure 2). We were also informed by the work of Bastaraud et al. (2020), which identifies 1993 and 2004 as breakpoints in drinking water quality coinciding with a treatment plant upgrade and an increasing inability of water infrastructure to meet the needs of the population respectively.

Finally, although we consider the effects of temperature and precipitation on mortality separately, we caution against interpreting them in isolation from one another. Precipitation and temperature are not independent, and in addition to having complex relationships with mortality, they have complex relationships with each other (Trenberth and Shea 2005). We address this in our analyses by demonstrating the consistency of our results across models with temperature–precipitation interaction.

4.4 Future directions

These limitations point to several potentially rewarding areas for future research. Advancing our understanding of the precise mechanisms through which climate influences health – particularly mortality – would benefit from additional research that models the impacts of climate on individual direct and indirect causes of death, provided the availability of death registration data of sufficient quality. We understand that various climatic drivers increase the risk of illness from different pathogens through mechanisms that require further exploration (Kolstad and Johansson 2011; Mahmud et al. 2020; Thindwa et al. 2019). Given death registration data that identifies specific pathogens, it would be possible to generate pathogen specific models of the climate-enteric disease mortality relationship. Additionally, modeling mortality from individual causes like heat stress, drowning, and malnutrition could reveal the direct effects of climate on mortality, which may be obscured when modeling measures of mortality that group diverse causes together.

A more detailed examination of the roles played by omitted variables at each stage along the causal chain from water contamination to enteric infection mortality is also

necessary. Several factors may enable or prevent water contamination by enteric disease-causing pathogens from leading to higher enteric disease mortality. These factors include those that mediate the effect of water contamination on enteric disease incidence, such as household water source. They also include those that control the infection fatality rate by influencing the effect of disease incidence on mortality, such as use of oral re-hydration therapy, antimicrobial medicines, and the prevalence of antimicrobial-resistant pathogen serotypes that determine pathogen susceptibility to these medicines. For instance if households use bottled drinking water, they may be less affected by contamination levels of the public water supply network. Likewise, if they use oral rehydration therapy, children may be less affected by illness from enteric infections. Considering the potential reversibility of the protective effects of some of these variables – especially the use of antimicrobial medicines – future work that examines their roles as drivers of the epidemiological transition and modifiers of the climate–enteric disease mortality relationship could significantly contribute to our understanding of the vulnerability of Antananarivo and similar low-income urban areas globally to counter health transitions from reemerging enteric infectious diseases and the potential role of climate change.

While Antananarivo might be more vulnerable to a counter health transition from reemerging infectious diseases than the direct mortality impacts of a more extreme climate, this phenomenon is not expected to be universal across low-income urban areas worldwide. Undertaking similar studies to the one conducted here – modeling how the climate sensitivity of direct and indirect climate-related causes of death in low-income urban agglomerations has evolved over time – could prove immensely valuable. This is particularly relevant for urban areas in more climatically diverse settings – such as tropical and coastal regions – where climatic conditions may be more extreme, resulting in direct climate-related mortality playing a more significant role.

5. Conclusion

Antananarivo has gone through a remarkable transformation over the past several decades. Water infrastructure has been improved, access to essential medicines expanded, and consequently mortality – particularly from childhood enteric infections and infectious diseases overall – has dropped sharply while life expectancy has increased significantly (Masquelier et al. 2014). Alongside these improvements other forms of climate adaptation, such as farmer and consumer responses to climate impacts on food production and physiological acclimatization (Kahn 2016; Achebak, Devolder, and Ballester 2018, 2019), have likely helped reduce the sensitivity of enteric infection mortality to both low rainfall and higher temperatures.

However, numerous challenges loom on the horizon. As the city's meteoric population growth continues unabated and climate change takes its toll on substandard infras-

tructure (Barrett, Charles, and Temte 2015; Bastaraud et al. 2020; Howard et al. 2016), water supplies are insufficient to meet population needs and increasingly vulnerable to contamination with disease-causing pathogens following heavy rainfall. Adding to these problems is the growing uncertainty about the continued effectiveness of commonly used medicines due to the proliferation of antimicrobial-resistant pathogens. These three factors – climate change, antimicrobial resistance, and rapid, unplanned low-income urbanization – intertwine and exacerbate each other (MacFadden et al. 2018; Howard et al. 2016; Sellers 2020; Rasamiravaka 2020). Consequently, overall mortality – particularly childhood enteric disease mortality – has grown more sensitive to heavy rainfall events in recent years. These events are projected to increase in frequency and severity as climate change accelerates. This situation underlines Antananarivo's vulnerability to a counter health transition driven by rising mortality from reemerging childhood enteric diseases, setting a worrying precedent for other urban areas in LMICs.

A secondary challenge facing Antananarivo is that posed by stagnant living conditions (The World Bank 2021). While the epidemiological transition and the subsequent shift of disease burden away from infectious diseases towards NCDs – along with climate adaptation – may have decreased mortality's sensitivity to high temperatures, Madagascar's stagnant living standards may have contributed to a sustained sensitivity to lower temperatures (Achebak, Devolder, and Ballester 2018, 2019). Nevertheless, the climate–disease relationship – particularly regarding childhood enteric diseases – remains complex and insufficiently understood (Kolstad and Johansson 2011; Mahmud et al. 2020; Thindwa et al. 2019), and the underlying mechanisms are likely highly dependent on local contexts (Saad et al. 2018).

Despite these uncertainties our ongoing research to deepen our understanding of this relationship in different contexts should not delay urgently needed action. Measures are required to ameliorate the negative impacts of climate change on health and more specifically on childhood enteric disease mortality. One of the most effective policy levers for reducing the health impacts of climate change is mitigation through emissions reductions. With the global south emitting far fewer greenhouse gases per capita, and yet it is projected to endure far more severe health impacts from climate change, it is the responsibility of the global north to lead these emissions reductions. Alongside mitigation adaptation is equally important. Urban areas in LMICs with inadequate water and sanitation infrastructure must continue to build new capacity and receive the necessary funding to do so. It is also vital to increase access to essential medicines, improve antimicrobial stewardship to slow the emergence of resistant pathogens, make food systems more climate resilient, and raise living standards. The threat of climate change catalyzing counter health transitions from reemerging childhood enteric infectious diseases remains grave and uncertain. Through mitigation, adaptation, and further research, we can shed light on this darkness and reduce some of this uncertainty.

6. Acknowledgements

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