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Severe Flooding and Malaria Transmission in the Western Ugandan Highlands: Implications for Disease Control in an Era of Global Climate Change

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(See the editorial commentary by Caminade, McIntyre, and Jones on pages 1300–1.)

Background. There are several mechanisms by which global climate change may impact malaria transmission. We sought to assess how the increased frequency of extreme precipitation events associated with global climate change will influence malaria transmission in highland areas of East Africa.

Methods. We used a differences-in-differences, quasi-experimental design to examine spatial variability in the incidence rate of laboratory-confirmed malaria cases and malaria-related hospitalizations between villages (1) at high versus low elevations, (2) with versus without rivers, and (3) upstream versus downstream before and after severe flooding that occurred in Kasese District, Western Region, Uganda, in May 2013.

Results. During the study period, 7596 diagnostic tests were performed, and 1285 patients were admitted with a diagnosis of malaria. We observed that extreme flooding resulted in an increase of approximately 30% in the risk of an individual having a positive result of a malaria diagnostic test in the postflood period in villages bordering a flood-affected river, compared with villages farther from a river, with a larger relative impact on upstream versus downstream villages (adjusted rate ratio, 1.91 vs 1.33).

Conclusions. Extreme precipitation such as the flooding described here may pose significant challenges to malaria control programs and will demand timely responses to mitigate deleterious impacts on human health.

Keywords. Malaria; climate change; epidemiology; Uganda; disasters; flooding.

The effect of global climate change on the incidence of vector-borne diseases, including malaria, is of both great interest and debate [1, 2]. Many analyses have suggested that rising global temperatures may result in a resurgence of malaria [3–5]. One region that has received particular attention is the East African highlands. A number of studies have attributed a resurgence of malaria in this region, especially at higher altitudes, to warming surface temperatures and changing rainfall patterns [5–8]. Others, however, are more skeptical of long-term impacts on climate [9, 10].

In addition to rising global temperatures, the manifold effects of climate change also entail an increased frequency of weather extremes, such as droughts and floods [11, 12]. Approximately 50% of global disasters between 2003 and 2012 were attributable to extreme precipitation and flooding [13]. Populations in developing countries are thought to be particularly at risk of adverse health consequences from floods, given unregulated land use in flood-prone areas, limited public-health infrastructure, and inadequate emergency response capability [14].

Over the past 100 years, East Africa has become wetter on average by around 10%–20% [15]. The frequency of major flood events in this region has also been increasing [16]. Uganda is not only expected to see a relatively large increase in the mean annual temperature, but the country may also experience increases in extreme precipitation [8, 15, 17]. Like warming temperatures, weather extremes—particularly heavy precipitation and flooding—have been associated with increasing malaria transmission [18]. Changing precipitation patterns can have both short-term and long-term effects on vector habitats and disease transmission [4, 19]. However, there is little empirical evidence outside of field reports and mathematical models about the relationship between individual flood events and malaria transmission.

On 1 May and again on 5 May 2013, heavy rains exacerbated existing glacial snowmelt [20, 21] and submerged 9 subcounties of Kasese District, Western Region, Uganda. Using this event as a natural experiment, we sought to estimate the temporal and spatial changes in malaria epidemiology associated with flooding in this rural, malaria-endemic area of western Uganda. The overall objective of the study was to estimate the excess burden

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of malaria attributable to flooding and, more specifically, to identify the geographic areas most vulnerable to postflood epidemic malaria, using the method of differences in differences.

METHODS

Study Site

The Bugoye Level III Health Center (BHC), located in Kasese District (0° 18′ N, 30° 5′ E), functions as the primary referral center for the Bugoye subcounty, serving a rural population of approximately 50 000 residents. Clinical officers, nurses, midwives, and laboratory technicians from the Ugandan Ministry of Health staff the health center, and care is available at no cost to patients. Malaria rapid diagnostic tests (mRDTs) were first introduced at the BHC in 2011 [22].

The climate in Bugoye permits year-round malaria transmission. There are semiannual transmission peaks that occur December–February and May–July, following the end of the traditional rainy seasons [23]. The geography of the Bugoye subcounty is also highly varied. Narrow river valleys and steep hillsides with elevations up to 2000 m define the westernmost villages of the subcounty along the boundary of the Rwenzori National Park. In contrast, the villages located to the east and southeast are composed of relatively level terrain at elevations nearly 1000 m lower than those to the west. Three large rivers—the Mubuku to the north, the Nyabyagi to the south, and the Sabo, which bisects the middle of the subcounty—flow down the hillsides from west to east.

The flooding of May 2013, considered the worst since April 1966, swept away houses, cattle, and infrastructure, including multiple bridges, the municipal wastewater treatment facility, and the district hospital. More than 1000 houses were destroyed, and nearly 10 000 residents were displaced [24]. Heavy rains caused overflowing of the Mubuku and Sabo rivers in the Bugoye subcounty, one of 9 affected subcounties in the region.

Study Design

We used a quasi-experimental design and differences-in-differences regression analysis to examine malaria diagnostic testing results and malaria-related hospitalizations before and after severe flooding in Kasese District. Results of malaria diagnostic tests, defined as either microscopy or mRDT, were obtained from health center laboratory registries. Information on patients admitted with a diagnosis of malaria was collected from inpatient medical records. For each record, we abstracted the following information: age, sex, village of residence, and diagnostic test result.

To estimate associations between geographic factors and malaria risk, we completed village-level geographic information system (GIS) mapping of the subcounty and surrounding environs, composing an area of approximately 55 km^2. These data were entered into ArcGIS (Redlands, California) to create a reference map, from which we calculated the mean elevation and area of each village. We divided the data into quartiles based on mean elevation (Figure 1) and defined villages by the presence or absence of a flood-affected river within or along the village boundaries. In a secondary analysis based on observed geographical trends, we subdivided the villages with flood-affected rivers into 2 categories: "upstream" (defined as <6 km from the river source) and "downstream" (>6 km).

Of the 32 villages in the subcounty, we included 31 villages in the analyses. We excluded 1 village, where international relief organizations established temporary camps with healthcare services for individuals displaced by flooding. We included 2 villages outside of the Bugoye subcounty but for which BHC is the closest medical center. Village populations were taken from the 2014 national census, from which we estimated a 3% annual population growth rate [25]. Villages that are traditionally subdivided for administrative purposes, such as Muramba 1 and Muramba 2, were considered 1 village for the analysis.

Statistical Analysis

To assess the impact of flooding on malaria transmission, we selected 2 primary outcomes of interest: (1) the *P. falciparum* test positivity rate (PfPR), defined as the percentage of malaria diagnostic tests positive for *P. falciparum* malaria per 100 tests conducted [26], and (2) the incidence rate of severe malaria, as measured by the number of malaria-related inpatient admissions per village per month, using 2014 census data to provide village-level population offsets. Our primary explanatory variable of interest was calendar time, which we divided into a 12-month "preflood" period (May 2012 to April 2013) and a 12-month "postflood" period (June 2013 to May 2014).

We first graphically depicted trends in diagnostic test results and inpatient malaria admissions rates over calendar time to examine patterns of malaria outcomes in relation to the flooding. We then compared malaria incidence before and after the flood by fitting generalized linear models and estimated the incidence rate ratio (IRR) of hospitalization before and after the flood, using generalized negative binomial regression models. We accounted for clustering within villages, using a clustered sandwich estimator. We added potentially confounding covariates in multivariable models including age, sex, the presence of an affected river in the village, mean village elevation, and rainy versus dry season. We included in multivariable regression models all variables that were significant in univariable models with a prespecified P value of <.25 [27]. A resulting P value of <.05 in final models was considered statistically significant.

We then used the method of difference in differences [28] to examine the preflood and postflood differences in malaria incidence according to the presence or absence of a flood-affected river within or along the village boundaries, the proximity to the river source (upstream vs downstream), and the mean village elevation. Differences-in-differences models have been

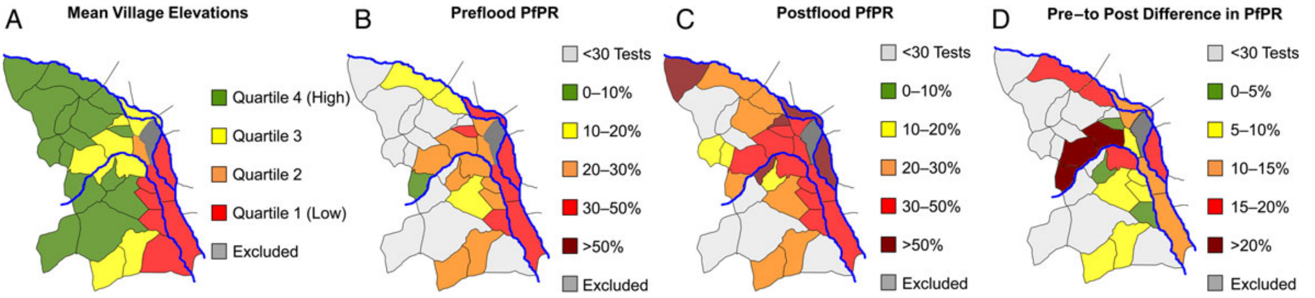

Figure 1. *A*, Mean village elevations divided in quartiles, highlighting the generally higher terrain to the west of the subcounty and the lower terrain to the southeast between the Mubuku and Sabo rivers. *B*, *Plasmodium falciparum* test positivity rate (PfPR) in each village before the flood, with the highest rates in villages at lower elevation and along the major rivers. *C*, PfPR in each village after the flood, with relatively high positivity rates in the majority of villages. *D*, Absolute difference in the PfPR from the preflood to postflood periods. The PfPR for villages with <30 tests performed in the respective period is not shown.

increasingly used in public health to study the effects of external events or policies at different times by treating the event as a quasi-experiment [29, 30]. Whereas conventional observational studies are valid only if there are no underlying secular trends in the outcomes of interest, the difference-in-differences study design addresses this problem by using a comparison group that is experiencing the same trends but is not exposed to the event or policy. This method allows the investigator to subtract out background changes.

Finally, we calculated the topographic convergence index (TCI) [31], which estimates drainage patterns based on a mathematical measurement of upslope drainage and the slope of the terrain for our geographic area of interest. High values indicate areas with large upslope drainage area and relatively low slope, leading to higher potential for water to slow or stagnate. As the slope increases or the upslope drainage area decreases, the potential for water to pool in these regions drops, indicated by a drop in the TCI. All data were analyzed with Stata 12.1 (College Station, TX).

Ethics Statement

Ethical approval of the study was provided by the institutional review boards of Partners Healthcare and the Mbarara University of Science and Technology. Informed consent was not required by the ethical review committees because of the programmatic nature of original data collection and retrospective review of data.

RESULTS

Diagnostic Test Positivity Rate

A total of 10 134 individuals underwent diagnostic testing for malaria by mRDT and/or microscopy during the study period. Village of residence information was not available for 630 test results (6.2%). Missing data were more common in the postflood than the preflood period (6.7% vs 5.2%; $P = .004$). We excluded data from 1858 individuals (18.3%) who presented for testing from villages outside of the defined study area.

Complete clinical and demographic information was available for 7596 individuals who presented from villages in the defined study area during the observation period (Table 1). The median age of those undergoing testing was 13 years, with approximately 2 in 3 being female. The majority of those who had a malaria diagnostic test performed (6757 [89.0%]) presented from villages containing a flood-affected river.

More than twice as many patients underwent malaria testing in the postflood period as compared to the preflood period (5285 vs 2311). The test positivity rate increased from 25.8%

Table 1. Characteristics of Patients Undergoing Diagnostic Testing for Malaria During Each Study Period

Variable	Preflood Period	Postflood Period	*P* Value
Patients tested	2311 (30.4)	5285 (69.6)	. . .
Age, y			
Median (IQR)	14 (2.5–25)	13 (4–27)	.068
>15	1098 (47.5)	2443 (46.3)	
5–15	453 (19.6)	1403 (26.6)	<.001
<5	760 (32.9)	1436 (27.2)	
Male sex	879 (38.1)	1968 (37.3)	.66
Rainy season[a]	1148 (49.7)	2696 (51.0)	.28
Village of residence			
Contains flood-affected river	2060 (89.1)	4697 (88.9)	.75
Elevation quartile			
4 (highest)	359 (14.9)	792 (15.0)	
3	780 (33.8)	1775 (33.6)	
2	464 (20.1)	1004 (19.0)	.64
1 (lowest)	722 (31.2)	1713 (32.4)	
Diagnostic testing			
RDT			
Performed	1850 (80.1)	4881 (92.4)	<.001
Positive result	421 (22.8)	1894 (38.8)	<.001
Microscopy			
Performed	475 (19.9)	586 (7.6)	<.001
Positive result	179 (37.8)	313 (53.4)	<.001

Data are no. (%) of patients, unless otherwise indicated.

Abbreviations: IQR, interquartile range; RDT, rapid diagnostic test.

[a] Defined as March–May and September–November.

to 39.4% from the preflood to the postflood period (unadjusted relative risk [RR], 1.53; 95% confidence interval [CI], 1.42–1.65; $P < .001$; Supplementary Table 1). This relationship remained statistically significant after adjustment for confounding variables, such that 47% more tests were positive in the postflood period than the preflood period (adjusted RR [ARR], 1.47; 95% CI, 1.36–1.58; $P < .001$). When analyzed by month, the increased percentage of tests with positive results was most pronounced in November, typically a low transmission period, when the percentage of tests with positive results increased from approximately 7.3% to 33.6% from the preflood to the postflood period (ARR, 4.30; 95% CI, 2.33–7.92; $P < .001$; Figure 2).

We identified significant interaction effects between geographic characteristics and malaria test positivity (Table 2), which we subsequently explored in the differences-in-difference analysis.

Presence of a Flood-Affected River

In the preflood period, the test positivity rate was 25.8% in villages that bordered a flood-affected river and 25.5% in those that did not. In the postflood period, test positivity rates were statistically similar in those villages farther from a river (PfPR, 27.0%; $P = .66$) but were significantly higher in villages bordering the flood-affected rivers (PfPR, 40.9%; $P < .001$). Using a regression model stratified by the presence or absence of a river and adjusted for confounding variables, we see that there was little relative change from the preflood to post flood period in villages farther from a river (ARR, 1.03; 95% CI, .81–1.33; $P = .78$) but a significantly higher risk of a positive test in those villages bordering a flood-affected river (ARR, 1.53; 95% CI, 1.41–1.66 $P < .001$). Overall, there was an increase of 30% in the risk of an individual having a positive malaria diagnostic test result in the postflood period in villages bordering a flood-affected river, compared with villages farther from a river (ARR, 1.30; 95% 1.16–1.46; $P < .001$).

Upstream Versus Downstream

Among those villages bordering a flood-affected river, in the preflood period, the test positivity rate was 29.1% in the downstream villages and 21.3% in the upstream villages. In the postflood period, however, the test positivity rate was 40.4% ($P < .001$) in the downstream villages and 41.6% ($P < .001$) in the upstream villages. Again, using a regression model stratified by the relative location of the village along the river and adjusted for confounding variables, we found that there was larger relative change from the preflood to the postflood period in upstream villages (ARR, 1.91; 95% CI, 1.67–2.20; $P < .001$), compared with downstream villages (ARR, 1.33; 95% CI, 1.20–1.46; $P < .001$). In the postflood period, there was no difference in the risk of an individual having a positive malaria diagnostic test result in the upstream villages, compared with the downstream villages (ARR, 0.98; 95% 0.95–1.01; $P = .24$), whereas in the preflood period, upstream villages were relatively protected.

Elevation

The effect of elevation was largely consistent between the preflood and postflood periods, with higher elevations experiencing a lower risk of malaria transmission during both periods (Table 2).

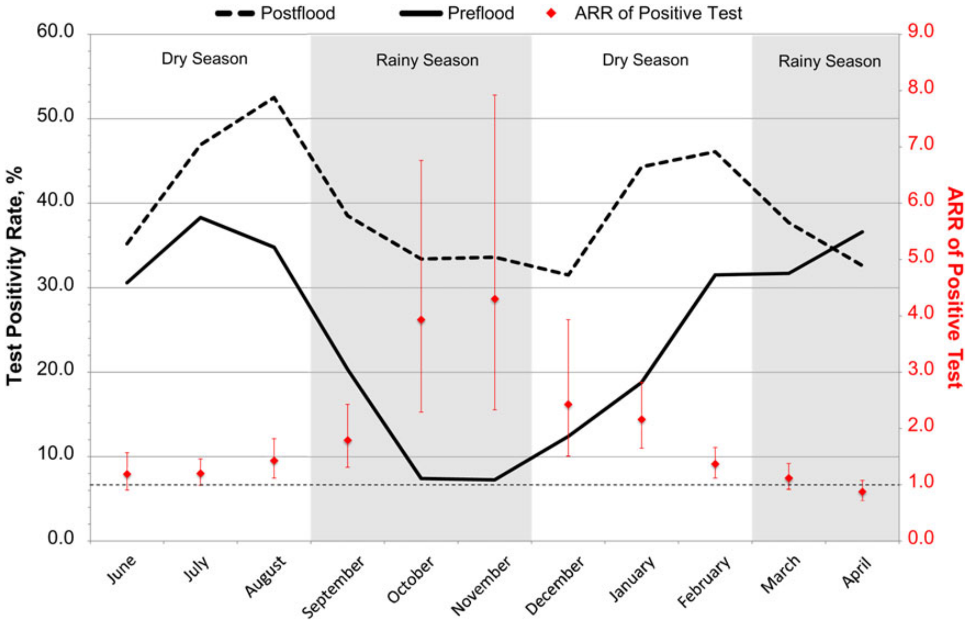

Figure 2. Change in test positivity by month before and after flooding. Abbreviation: ARR, adjusted risk ratio.

Table 2. Interactions Between Village Characteristics and Study Periods and the Risk of a Positive Malaria Test Result

	Preflood Period		Postflood Period		
Characteristic	RR	*P* Value	RR	*P* Value	Interaction *P* Value
Contains river	1.01	.92	1.50	<.001	.003
Location from river					
Downstream	Reference		Reference		<.001
Upstream	0.86	<.001	1.02	.41	
Elevation quartile					
1 (lowest)	Reference		Reference		
2	0.76	.005	0.70	<.001	.44
3	0.73	<.001	0.96	.24	.004
4 (highest)	0.60	<.001	0.59	<.001	.90

Abbreviation: RR, relative risk.

Individual Villages

In addition to the overall increase in the test positivity rate from the preflood to the postflood period at the subcounty level, significant increases were identified in 8 individual villages (Figure 3*A*). A flood-affected river was present in all 8 villages with significant changes in the relative malaria risk. The greatest magnitude of effect was observed in the upstream villages. When the results of changes in the risk of a positive test result at the village level were overlaid on the convergence index (Figure 4), we see that the villages with the largest relative risk for an increase in the test positivity rate were upstream villages, which generally have well-organized, branching drainage networks. In contrast, the downstream villages, which were less impacted in the postflood period, generally had disorganized drainage networks consistent with the more level terrain.

Malaria Admissions

Over the study period, 1744 patients were admitted to the inpatient ward with a diagnosis of malaria. Only 25 patients (1.4%) did not have village of residence information included in the clinical record. We excluded 229 individuals (13.1%) who presented for testing from villages outside of the defined study area and 200 patients (11.5%) who presented from the village where the temporary camps were established.

Relevant demographic and clinical data was available for >98% of included individuals. The only significant difference in the demographic characteristics of admitted patients was a greater proportion of patients aged 5–15 years old in the postflood period, with a lower proportion of those <5 years of age (Supplementary Table 3).

The number of patients admitted with a diagnosis of malaria increased by >50% in the postflood period (781 vs 504; $P < .001$). Additionally, malaria-related admissions as a proportion of all medical admissions increased significantly (54.1% vs 45.4%; $P < .001$). After adjustment for the presence of a river and mean village elevation, the incidence rate ratio (AIRR) of admissions for malaria remained significantly higher in the postflood periods, compared with the preflood period (AIRR, 1.40; 95% CI, .1.16–1.69; $P < .001$; Supplementary Table 2). Similar to the trends seen with PfPR, we found that all 5 villages that experienced increasing incidence of malaria admissions after the flood were in close proximity to a flood-affected river (Figure 3*B*). We found trends in the interaction effects between flooding, the presence of a river, the relative location along the river (upstream vs downstream), or village elevation on the rates of malaria admission, but these associations did not reach the threshold of statistical significance.

DISCUSSION

Our results demonstrate a significant and sustained increase in malaria transmission following catastrophic flooding in a rural, highland area of western Uganda. We observed an increase of approximately 30% in the risk of an individual having a positive

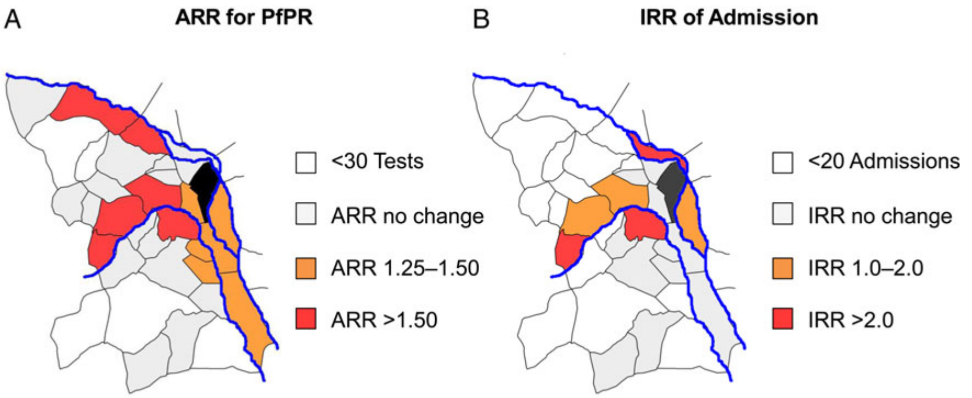

Figure 3. Map demonstrating the relationships between river distribution and changes in malaria risk in the preflood versus postflood periods. A dose-response effect of flood and distance to major rivers can be seen, whereby the regions closest to rivers and at the highest altitudes had the greatest relative increase in positive malaria test results and malaria-related admissions following the flood. Villages without direct access to rivers and at lower elevations were generally less affected. Abbreviations: ARR, adjusted risk ratio; PfPR, *Plasmodium falciparum* test positivity rate.

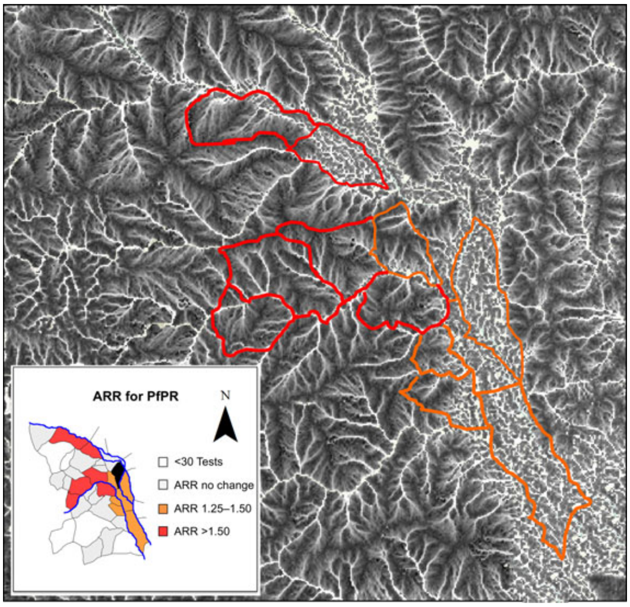

Figure 4. Overlay of the adjusted relative risk of a positive malaria test result on the topographic convergence index (TCI). Areas in white represent wet areas, where precipitation is expected to converge. The image demonstrates the well-organized, branching drainage networks seen in the westernmost or upstream villages, compared with the flat lowlands in the east, where runoff can be expected to accumulate. Abbreviations: ARR, adjusted risk ratio; IRR, incident risk ratio; PfPR, *Plasmodium falciparum* test positivity rate.

malaria diagnostic test in the postflood period in villages bordering a flood-affected river compared with villages farther from a river. Among villages bordering a flood-affected river, we saw a larger relative impact on upstream versus downstream villages (ARR, 1.91 vs 1.33). We also observed a 40% increase in the incidence rate of malaria admission in the postflood period, using the conventional preflood versus postflood analysis, but did not observe similar changes using the differences-in-differences model, a finding that may reflect the smaller absolute number of admissions from affected areas. Overall, these results suggest that the increasingly frequent extreme precipitation events associated with global climate change have great potential to adversely affect malaria-related health in highland areas of East Africa.

Our study identified a number of geographical factors of postflood malaria that may inform emergency response and malaria control programs. First, the observed impacts of the flood were most pronounced in villages along flood-affected rivers. This finding is consistent with previous work showing that most productive breeding sites are usually located close to rivers and streams [32, 33] and that households in close proximity to breeding sites generally exhibit higher adult mosquito densities [34].

Second, we found the greatest relative increase in malaria test positivity in upstream areas. When we overlaid the postflood malaria risk map on TCI results (Figure 4), we found that the upstream villages were generally those with organized, branching drainage systems. Under normal conditions, these areas are well drained, and accessible surface water is largely limited to fast-moving streams that are unsuitable breeding habitats [35, 36]. However, during periods of extreme, prolonged precipitation, well-drained areas may become saturated to the extent that stagnant pools are formed, creating ideal habitats for the *Anopheles* vector [32, 35]. Despite the greater relative impact on upstream villages, the absolute effect of the flood was most pronounced in lower downstream villages. In such areas, stagnant pools are a permanent feature of the terrain, which favors stable breeding habitats and malaria transmission even in the absence of flooding.

Third, we observed a 3-month lag between the flooding and the peak of the postflood malaria epidemic. This delay may be the result of heavy rainfall flushing out existing breeding sites. Lyndsay et al hypothesized that such a flushing effect could explain the lower postflood malaria prevalence in northeastern Tanzania seen after the heavy precipitation of the 1997–1998 El Nino southern oscillation [37]. However, as the floodwaters recede, the vectors can reestablish productive habitats in new areas typically with a delay of 6–8 weeks, although this may vary by geographic and climactic conditions [38]. In Mozambique, for example, malaria incidence peaked approximately 1 month after flooding, while in northeastern Kenya and southwest Uganda, peak incidence was seen 2–3 months after flooding, which is consistent with our findings [39–41]. In our study, the impact of flooding on malaria transmission was greatest during what is typically the low transmission season, with a >4-fold increased risk of a positive malaria test in the postflood period, compared with the preflood period (Figure 2). We hypothesize that this "unseasonal epidemic" was due to surface waters from the flood that accumulated and persisted, allowing mosquito larvae to complete the full life cycle at times and in areas not normally hospitable to breeding [42].

Our study has a number of important policy and programmatic implications. First, the initial delay between the flood and the postflood epidemic may provide an important opportunity for targeted interventions to mitigate the postflood epidemic [43]. Additionally, our results show that control efforts must be sustained, as the effects of the flood on malaria transmission may continue for up to 1 year after the initial event. Finally, our study demonstrates the importance of understanding local microenvironments. Most of the villages we studied averaged <2 km^2 in size, yet we observed stark contrasts in both the preflood and postflood epidemiology of malaria, even between neighboring villages.

Our study has a number of methodological limitations. While more robust than conventional preevent versus postevent analyses, the difference-in-differences study design relies on the assumption that preexisting trends in malaria transmission would have been the same in the postflood period in the absence of severe flooding. Differential trends in the exposed and unexposed villages in the period leading up to the flooding

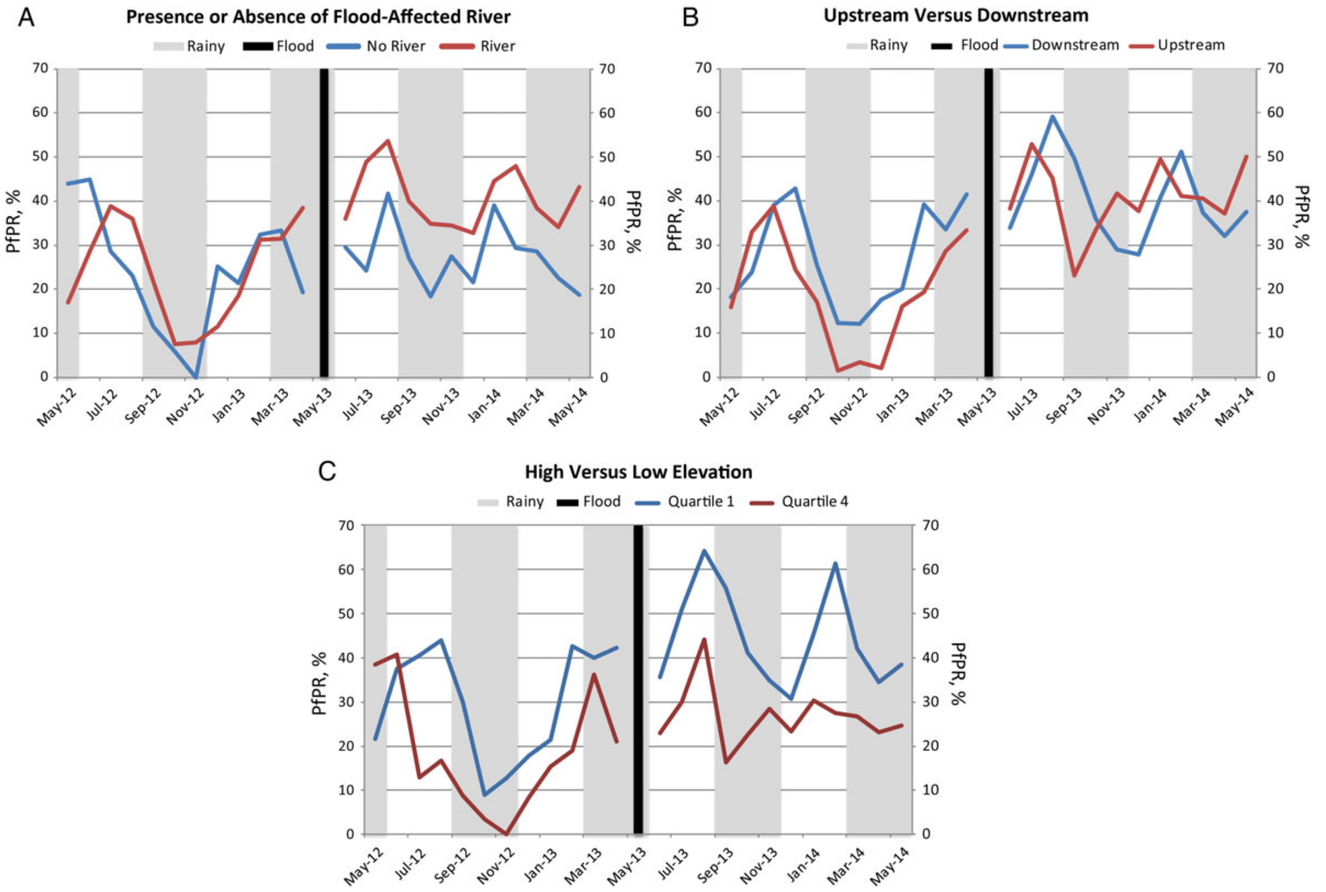

Figure 5. Monthly trends in diagnostic test positivity rate in the preflood and postflood periods between villages with and those without a flood-affected river (*A*), villages upstream and those downstream from the river source (*B*), and at high (quartile 4) and low (quartile 1) elevations (*C*). Abbreviation: PfPR, *Plasmodium falciparum* test positivity rate.

would have biased our results. We assessed these trends prior to the "shock" of the flood by examining the parallel trends and presenting graphical displays of the raw data that clearly demonstrate this assumption was met (Figure 5).

Second, because we abstracted information from routinely collected clinical records, our study is subject to error in programmatic medical record data collection. In general, missing clinical or demographic data was rare, and we did not observe a differential rate of missing data by geographic location, although there was a small increase in the postflood period as compared to the preflood period (6.7% vs 5.2%; $P = .004$).

Finally, it is not possible to attribute this specific event to climate change or to predict whether similar events will occur in this or other flood-prone malaria-endemic areas. However, changing precipitation patterns over the last century and increasing frequency of extreme flooding events both in East Africa and other regions mandate increased attention to relationships between such events and human health [5, 8, 11, 16].

In summary, we have observed increased malaria transmission and morbidity following a major flood event in a highland area of western Uganda. These findings highlight that extreme weather conditions during periods of increased global weather emergencies have great potential to adversely affect human health in malaria-endemic and epidemic-prone areas. Events such as the flooding described here may pose significant challenges to malaria control and elimination programs, and will demand timely and sustained responses to prevent and mitigate deleterious impacts on human health.

Supplementary Data

Supplementary materials are available at http://jid.oxfordjournals.org. Consisting of data provided by the author to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the author, so questions or comments should be addressed to the author.

Notes

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