Malaria hotspots in Rwanda- relative influence of climate variability and interventions

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Abstract
Despite intense malaria interventions and associated decline of malaria transmission in Rwanda; potential for malaria transmission remain in highly endemic areas. As response, an integrated malaria control was introduced based on local ecology, malaria epidemiology and socio-economic factors. This strategy intends to sustain the achievements in malaria reduction by effective interventions in the areas of the most needs. Pinpointing malaria hotspots can be therefore seen as a well timed support towards local initiative in malaria elimination. As malaria is both sensitive to environmental and socio-economic factors, it is equally important to assess the extent to which malaria is the interplay of climate variability and interventions in Rwanda highlands. Malaria and interventions related data were gathered from Rwandan Ministry of Health. Climate data were provided by Rwanda Meteorological Agency. Hotspot analysis was used to examine the spatial clusters of malaria. Correlation and regression analysis were also performed to test the association between climatic variables and malaria; and to investigate the relative influence of climate and interventions in two research areas with differing malaria endemicity. Persistent hotspots partially overlap with the locations of malaria vector breeding sites in eastern and south-east lower lands. In unstable transmission highlands, a moderate association between climate variability and malaria was evidenced. In high endemic and stable malaria transmission settings, a lack of a strong association between malaria and climate variability was identified. Those findings suggest that malaria interventions would have masked the expected relationship between climate and malaria in highly endemic areas. Maintaining malaria interventions in highlands and more targeting intervention to malaria hotspots can be an efficient way of reducing in Rwanda.

Key words: Climate variability, malaria hotspots, interventions, Rwanda

1. Background
The greatest burden of malaria occurs in the endemic regions where the disease is continuously present in the community. These regions are characterized by suitable environment to interactions between the Anopheles mosquito, malaria parasites and human hosts due poor housing that offers little protection from mosquitoes (Grover-Kopec et al., 2005). Over the past decade, public health planners have beefed up their efforts to eradicate malaria, rolling out insecticide-treated bed nets, increasing indoor residual spraying, and boosting access to artemisinin-combination therapy (Dolgin, 2010). Despite these intense interventions, malaria continues to be among the top killers in the developing world.

In 2012, there were approximately 562,000 malaria-related deaths in Africa, continuing a slow decline since 2004 (WHO, 2013). In many parts of Sub-Saharan Africa, a decreasing malaria transmission was associated with interventions and reduced vector densities induced by change in rainfall (Meyrowitsch et al., 2011). Malaria burden remains however higher and particularly impacts young children and pregnant women (Roll Back Malaria, 2010). While existing interventions were not able to eliminate malaria in highly endemic areas, malaria elimination is only possible in low to moderate transmission settings where vectors are endophile and where sustained interventions are achieved. In high transmission settings where vectors are exophile, new tools that target the outdoor biting and exophile mosquitoes are also required (Griffin et al., 2010).

In Rwanda, malaria distribution is heterogeneous and varies across the landscapes which reduce the efficacy of exiting malaria elimination strategies. Recent successes of scaling up of malaria interventions in Rwanda have revealed the policy gaps. As an example, a result from an entomological survey of more than 50% exophile Entomological Inoculation Rate (EIR) in some areas indicates potential transmission gaps that area not addressed by exiting interventions (Hakizimana et al., 2010). In some areas, asymptomatic malaria is associated with low socio-economic conditions and ineffective use of bed nets (Gahutu et al., 2011). In other areas, malaria hotspots are clustered around the water-based agro-ecosystems (Rulisa et al., 2013). In high endemic zones, malaria is still perceived as a health concern by local communities (Ingabire et al. 2014) despite the intense intervention (Karema et al., 2012; Otten et al., 2009). In remote rural areas, poverty was blamed as the influencing factor of malaria transmission (Ingabire et al., 2014). Efforts to locally eliminate malaria in the most endemic districts should focus on
improving house structures to limit indoor malaria transmission; and on effective implementation of insecticide-treated bed nets and indoor residual spraying (Bizimana et al., 2015; Kateera et al., 2015b).

As malaria transmission potentials remain in Rwanda, national malaria control programme has an ambitious goal of making Rwanda free malaria country. This goal aims to reduce malaria morbidity to pre-elimination levels of less than 5% malaria positivity rate by 2018 (USAID, 2014). The adopted strategy consists of addressing the gaps of previous interventions by using focused and targeted approaches to malaria elimination. This strategy also needs to sustain the progress so far made by scaling up and targeting the effective malaria interventions from health facilities to community level (USAID, 2014). In line with these local initiatives towards malaria elimination, pinpointing the geographical areas where malaria occurrence is high may be a well time support to malaria elimination in Rwanda. By identification the locations of malaria hotspots and underlying factors, malaria elimination would be much easier and more effective (Dolgin, 2010). This can improve understanding of decision-makers on spatio-temporal dynamics of malaria incidence with implications on interventions.

As Rwanda is closer to elimination phase, malaria transmission hotspots can be identified and targeted as part of effort to its elimination. While interventions targeted to malaria hotspots would be an efficient way (Bousema et al., 2013), identifying hotspots is complicated by many factors affecting malaria transmission, ranging from ecological conditions to human and socioeconomic factors (Bejon et al., 2013). Evolving approaches to identify malaria hotspots analysis have been proposed. Malaria incidence data are frequently used for hotspots detection (Bejon et al., 2010; Bousema et al., 2010; Kreuels et al., 2008). Local Getis-Ord (G) statistics (Getis and Ord, 1992) are also among the approaches that are gaining the credibility in hotspots analysis. Applied to spatial epidemiology, they help to assess malaria clustering in small areas called hotspots coldspots (Cromley and McLafferty, 2012).

Since malaria is greatly influenced by climatic conditions (Bayoh and Lindsay, 2004; Githeko, 2007; Sutherst, 2004), it is widely assumed that malaria transmission increases as a result of climate variability in Rwanda highlands (Hammerich et al., 2002; Henninger, 2013; Loevinsohn, 1994). Projections indicate that highlands that were formerly unsuitable for malaria will become epidemic, whereas lower-lands will have a decreasing risk of epidemic malaria (Ermert et al., 2012). Other factors like drug resistance, control programs, public health facilities, living standards, population movements and migration are accountable for malaria upsurge (Nabi and Qader, 2009). Recognizing that malaria is sensitive to climate and interventions, it is equally worth to assess the relative role of climate variability and interventions on malaria under pace of climate variability in Rwanda. The research hypothesis is that climate effect on malaria incidence in Rwanda was masked by intense interventions in the last decade.

2. Methodology

2.1. Study area description

Epidemiological strata of malaria in Rwanda have been proposed by Meyus et al. (1962) when the country was divided into four malaria ecozones based on elevation, climate, parasite prevalence rates and Anopheles mosquitoes. This stratification was confirmed 20 years later by Ivorra-Cano (1982). A malaria endemicity map for Rwanda was recently published by Malaria Atlas Project in 2011 (Gething et al., 2011). Geographically, Rwanda has two distinct malaria zones. In highlands, malaria is characterized by seasonal peaks of low and unstable transmission during the rainy season, while the rest of the country is marked by a stable transmission (Karema et al., 2012). Figure 1 shows the spatial distribution of malaria prevalence in Rwanda.
Figure 1: Spatial distribution of malaria prevalence in Rwanda
Source: Rwanda Demographic Health Survey

Figure 1 shows malaria endemicity levels within the limits of stable transmission based on rainfall, temperature, land cover and urban-rural settings (Gething et al., 2011). According to Demographic and Health Survey (National Institute of Statistics of Rwanda, 2012), malaria in Rwanda is highly endemic in eastern lowlands and in Bugarama plain in West-South of Rwanda. Bottom valleys are also likely considered as malaria endemic pockets. Highlands exhibit a very low endemicity or absence of malaria transmission (Gething et al., 2011). This spatial distribution of malaria influences the selection of appropriate methods for malaria control. Figure 1 also shows the location of Gikonko and Bungwe as study sites for investigating the relationships between malaria and climate variability.

### 2.2. Health centre catchment areas

In Rwanda, most of malaria cases are reported and treated at health centre level. The distance is the most influencing factor of malaria treatment seeking behavior because patients tend to go to nearest health facility. Using health center geographic coordinates, health centre catchment areas were delineated. Based on rivers, water bodies, flooded areas and slope as impedance for reaching the health facilities, a cost layer was defined and health catchment areas delineated using ArcGIS 10.2 software. The delineated catchment areas were used later in this study as reference units to visualize malaria incidence at country level.

### 2.3. Climate and malaria data

To explore linkages between malaria and climate variability, monthly rainfall and temperature data were collected from meteorological stations. Monthly malaria cases were provided by Rwanda Ministry of Health. The data consisted of population microscopy tested malaria infection and number of positive malaria cases recorded at each health centre. The data were pooled as per GIS data format and records were attached to health centre catchment area using the common identifier. Annual malaria cases were visualized and mapped at health centre catchment level to gain an overview of spatial distribution of malaria incidence at national level.

### 2.4. Testing spatial autocorrelations
We draw on Tobler’s law of spatial autocorrelation by which near things are more similar (Tobler, 1970). Based on Tobler’s law, spatial statistic was performed to identify clusters of malaria incidence (Cromley and McLaugherty, 2012). The local Gi* statistics (Getis and Ord, 1992) were calculated for each year using the following formula:

$$ Gi^* (d) = \sum_{j} W_{ij} (d) x_j / \sum x_j $$

Where, $W_{ij}$ is a spatial weight matrix at a given distance lag in kilometers (d) ($W_{ij}(d)$) when the distance from the health centre catchment area j to i is within d, otherwise $W_{ij}(d)$ is 0 (Getis and Ord, 1995; Getis and Ord, 1996). The Gi* statistics compare the local mean (like malaria cases for each health catchment area and the neighboring zones) to the global mean (malaria case for all health catchment areas). Getis-Ord Gi* statistics is a local indicator of spatial autocorrelation which uses spatial neighboring principle to detect the clusters of geographic phenomena (Getis and Ord, 1995). Getis-Ord Gi* statistics were calculated for annual malaria cases at health centre catchment areas, leading to Z-score and p value which indicate whether malaria incidence is clustered or not (Table 1).

### Table 1: Analysis clustering for different years using

<table>
<thead>
<tr>
<th>Year</th>
<th>Observed</th>
<th>Expected</th>
<th>Variance</th>
<th>Z-score</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>3.266</td>
<td>0.001</td>
</tr>
<tr>
<td>2008</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>6.684</td>
<td>0.000</td>
</tr>
<tr>
<td>2009</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>7.138</td>
<td>0.000</td>
</tr>
<tr>
<td>2010</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>4.922</td>
<td>0.000</td>
</tr>
<tr>
<td>2011</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>7.076</td>
<td>0.000</td>
</tr>
<tr>
<td>2012</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>3.500</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Z-scores and p-values measure if spatial clusters are more pronounced than expected in a random distribution. A high positive z-score and a small p-value indicate a spatial cluster of high values. A low negative z-score and a small p-value indicate a spatial cluster of low values. The higher (or lower) the z-score value, more intense is the cluster of malaria distribution. A z-score near zero indicates no apparent spatial clustering (Getis and Ord, 1992). Z-score associated values showed that malaria was intensively clustered in Rwanda for the years 2009, 2010 and 2008. For all years, Z-score and p-values give the probability that they were not generated by a random process. When p-value is very small, it means that there is a low probability that the spatial pattern results from a random process.

### 2.5. Hotspots analysis

Hotspot analysis is a spatial statistics analysis technique for identification of clusters of spatial phenomena. These spatial phenomena are depicted as points in a map and refer to event or object locations. A hotspot is also an area with higher concentration of events compared to the expected number given a random distribution of the events (Chakravorty, 1995). In this study, hotspot analysis was performed to identify the locations of higher or lower malaria cases than expected under the null hypothesis of spatial randomness or a concentration of malaria that cannot be explained by chance. The presence of hotspots and coldspots in Rwanda from 2007 to 2012 was performed in ArcGIS 10.2 software. A high and positive Z score value, indicate that the health centre catchment area i is surrounded by a health centre catchment area with relatively high malaria cases, whereas high but negative Z-score values indicate that the centre catchment area i is surrounded by an area with relatively low (cold spot) malaria cases.

#### 2.6. Correlation and regression analysis

To investigate linkage between climate variability and malaria, a case study approach was adopted in two sites with differing malaria endemicity (Bungwe and Gikonko in Burera and Gisagara districts respectively). The main aim was to examine the extent to which malaria is the interplay of climate variability and malaria interventions in highland communities. Spearman correlation analysis was firstly performed using the SPSS statistics 22.0 to investigate the association between precipitations, temperature and monthly malaria cases were transformed by one month lag in order to account for the life cycle of 14 days for *Plasmodium falciparum* (Kleinschmidt, 2001), and the time by which the larvae develop in adult and infective mosquito (Martens and Chris, 2005). The assumption was that malaria infected people for a given month were bitten by mosquitoes in previous month (Nkurunziza et al., 2010). While the correlation coefficients examined the degree of relationship between climatic variables and malaria cases, multiple linear regression analysis was also applied to identify variables that would be the best predictors of malaria. The model for multiple linear regression analysis for a given n observations is given by the formula:

$$ Y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + ... + \beta_p x_{ip} + \epsilon_i $$

Where $Y_i$ is the dependent variable, $\beta_0$ is the intercept, $\beta_1; \beta_2$ and $\beta_p$ are the regression coefficient of each independent variable included in the regression model; $\epsilon_i$ is the random error usually described as residual. It is the difference between observed and predicted values of the dependent variable.
3. Results and discussions

3.1. Malaria hotspots in Rwanda

The presence of statistically significant hot-spots and cold-spots of malaria in Rwanda are shown in Figure 2. A high and positive Z-score value (in red color) indicate that an area is surrounded by areas with high malaria incidence; whereas a high but negative Z-score values (in dark blue color) indicate that the area is surrounded by other areas with low malaria incidence. The health centre catchment areas with Z-score values $>-0.85$ and $\leq -0.20$ (in yellow color) indicate the random malaria distribution.

Hotspot analysis also produces a p-value for each health centre catchment area, reflecting whether the differences between local and global means are statistically significant (Haque et al., 2012).

Figure 2: Hotspots of malaria incidence in Rwanda in 2012

The statistically significant hotspots of malaria incidence were mainly detected in eastern lower lands (Nyagatare, Kirehe, and Bugesera district); in South-East within Gisagara District, and in South-West within Rusuzi District. While local malaria hotspots may be linked to the uniqueness of geographic features of the area, or to climate suitability for malaria transmission, their temporal shifts provides evidence that other factors than climate may be involved. These factors may relate to shared socio-economic and cultural practices. Figure 3 shows the spatial-temporal variation of hot-spots of malaria in Rwanda from 2007 to 2012.
Stable hotspots of malaria may suggest that existing malaria control and prevention measures are unlikely to break malaria transmission cycle in intensely endemic parts where malaria elimination requires targeting interventions (Ferguson et al., 2010). An entomological survey found more than 50% Exophile Entomological Inoculation Rate (EIR) in some areas as example of potential transmission gaps not addressed by exiting interventions (Hakizimana et al., 2010). Malaria transmission hotspots were identified in south east and eastern lower lands near the water-based agro-ecosystems where malaria control should focus on vector breeding sites and engaging in farming communities (Rulisa et al., 2013). Moreover, land use changes may result in malaria hotspots where populations share the same socioeconomic conditions and geographical factors. Approaches to malaria elimination in Rwanda need therefore to consider these changes to adopt new strategies (Cotter et al., 2013).

This study used a spatial statistic approach to quantify malaria clustering intensity. Such approach was used elsewhere for other diseases (Bhunia et al., 2013; Naish and Tong, 2014), but rarely applied to malaria in Rwanda. Recent studies by Rulisa et al., (2013) and Tuyishimire (2013) focused on household and at small scale administrative units. These studies identified local drivers of malaria transmission. There were however unable to compare malaria hotspots at country level in order to effectively guide national malaria control program in targeting interventions in the most risk areas. This study is therefore a fist attempt to implement a spatial statistic approach to malaria hotspots analysis in Rwanda.

The results from study have implications for malaria control and interventions. First, geographic variation of malaria across the country informs decision-makers on high risk malaria zones. Since space-time clusters are mainly located in eastern and south eastern lower lands, this finding is consistent with a pervious study that has identified the local clusters of malaria transmission in Bugesera region near the water-based agricultural ecosystems (Rulisa et al., 2013). Therefore, malaria control in Rwanda needs to maintain and scale-up its efforts in farming communities near the irrigation schemes especially in Gisagara, Bugesera, Kayonza and Nyagatare Districts. In these districts, malaria distribution is
mainly associated to irrigation agricultural practices (Bizimana et al., 2015). Besides, all spatial clusters of malaria in each year are almost intersected with space-time cluster, indicating a highly focal concentration of malaria which can be addressed by more focused and targeted interventions. Second, while it is difficult to determine all reasons for spatial shifts and extent of malaria hotspots over the study period using the available data, it is interesting that an increasing size of hotspot for the years 2009 and 2010 coincided with the period of the reported delay in bed nets provision (Karema et al., 2012). Moreover, climate variability associated with 2009/2010 strong El Niño (Climate Prediction Center, 2014) may be an explanation for intense malaria clustering.

However, these assumptions on malaria hotspots can be taken with caution. They need to be validated by a statistical analysis of relationship between all factors of malaria clustering in specific areas. Recognizing that the drivers of malaria transmission are more complex and varying in heterogeneous landscape, a further study using Geographically Weighted Regression (Brunsdon et al., 1996; Fotheringham et al., 2002) can help to identify the best predictors of malaria incidence in each hotspot if the required data are locally available in Rwanda.

### 3.2. Climate variability and malaria

Spearman correlation analysis showed that monthly malaria is positively correlated with monthly mean and maximum temperature at Bungwe. The positive sign of correlation coefficient means that malaria increases as temperature also increases. This association is not strong in children under five years (R=0.301; p=0.001), probably because of intense interventions with bed nets to pregnant women and young children (Karema et al., 2012). Under climate variability, intensive use of bed nets would have reduced the effect of climate on malaria. In adult people, malaria becomes strongly and positively associated with temperature (R=0.499; p=0.001). This strong association may be explained by ineffective use of bed nets in highlands. According to demographic and health survey, gaps between the bed nets ownership and use are generally higher in highlands (National Institute of Statistics of Rwanda, 2012) despite the high level of national coverage (Karema et al., 2012; Kateera et al., 2015a). Monthly maximum and mean temperature only influence malaria transmission at Bungwe site, indicating that maximum temperature seems to play a key role in highland malaria in (Henninger, 2013).

Monthly malaria case is strongly and negatively associated with interventions in all categories of ages (R=-0.852; p=0.001), meaning that malaria transmission is substantially reduced with large scale distribution of bed nets (Table 2). A rising temperature would enhance the survival chance of malaria parasite and vectors in rainy season, and thus accelerates the transmission dynamics and spread of malaria into populations that are already immunologically more susceptible to infection.

### Table 2: Association between malaria, climate and interventions at Bungwe

<table>
<thead>
<tr>
<th>Climate variables</th>
<th>Malaria in &lt;5 years</th>
<th>Malaria in ≥ 5 years</th>
<th>All ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum temperature</td>
<td>R 0.301**</td>
<td>0.499**</td>
<td>0.497**</td>
</tr>
<tr>
<td></td>
<td>p value 0.001</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Minimum temperature</td>
<td>R -0.017</td>
<td>-0.180*</td>
<td>-0.179*</td>
</tr>
<tr>
<td></td>
<td>p value 0.852</td>
<td>0.044</td>
<td>0.044</td>
</tr>
<tr>
<td>Mean temperature</td>
<td>R 0.251**</td>
<td>0.346**</td>
<td>0.345**</td>
</tr>
<tr>
<td></td>
<td>p value 0.005</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Average rainfall</td>
<td>R -0.114</td>
<td>-0.174</td>
<td>-0.172</td>
</tr>
<tr>
<td></td>
<td>p value 0.205</td>
<td>0.052</td>
<td>0.054</td>
</tr>
<tr>
<td>Bednets ratio to population</td>
<td>R -0.506**</td>
<td>-0.846**</td>
<td>-0.852**</td>
</tr>
<tr>
<td></td>
<td>p value 0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

*From table 2, the most significant explanatory variables of malaria occurrence are highlighted in bold. The sign * means that a significant association at the 0.05 confidence level, and the sign ** shows a significant association at the 0.01 confidence level.*
Although precipitations create mosquitoes’ breeding sites (McMichael and Martens, 1995), malaria was weakly and negatively associated with monthly precipitations at Bungwe. This can be explained by the washing effect of heavy rainfall in humid highlands. Too much rainfall may flush away the breeding larvae, reducing therefore the numbers of malaria vectors (Patz et al., 2003). This finding does not however corroborate the findings from a previous study by Hammerich et al. (2002) who evidenced an increasing malaria incidence in pregnant women and younger children in northern Rwanda highlands as a result of heavy.

Interventions onset with bed nets is strongly and negatively correlated with monthly malaria cases in both hypo-endemic and meso-endemic malaria areas. This was also supported by a remarkable decline of malaria due to a large scale distribution of bed nets between 2006 and 2012 (Karema et al., 2012). As malaria is sensitive to interventions, climate variability in Rwanda might have been counterbalanced by interventions during the last decade. In all age groups, a strong and negative association was evidenced between monthly malaria cases and bed nets ratio to population. The number of malaria incidence decreases as the bed net ratio to population also increases. Between 2005 and 2010, the national coverage of LLINs drastically increased from nearly zero to 76% while the confirmed malaria cases declined by 72% in 2010 (Karema et al., 2012). This impressive performance in malaria control is likely to obscure the expected relationships between malaria transmission and climate.

While many authors believe in a strong association between malaria and climate, climate variability at Gikonko site is not however strongly associated with malaria (Table 3). This finding is consistent with a similar study in the same area (Loevinsohn, 1994).

### Table 3: Association between malaria, climate and interventions at Gikonko

<table>
<thead>
<tr>
<th>Climate variables</th>
<th>Malaria in &lt; 5 years</th>
<th>Malaria in ≥ 5 years</th>
<th>Malaria in all ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum temperature</td>
<td>R -0.005</td>
<td>0.039</td>
<td>0.015</td>
</tr>
<tr>
<td>p value</td>
<td>0.950</td>
<td>0.659</td>
<td>0.860</td>
</tr>
<tr>
<td>Minimum temperature</td>
<td>R <strong>0.216</strong></td>
<td><strong>0.206</strong></td>
<td><strong>0.224</strong></td>
</tr>
<tr>
<td>p value</td>
<td>0.013</td>
<td>0.018</td>
<td>0.010</td>
</tr>
<tr>
<td>Mean temperature</td>
<td>R 0.065</td>
<td>0.086</td>
<td>0.081</td>
</tr>
<tr>
<td>p value</td>
<td>0.456</td>
<td>0.329</td>
<td>0.358</td>
</tr>
<tr>
<td>Average rainfall</td>
<td>R 0.127</td>
<td>0.069</td>
<td>0.091</td>
</tr>
<tr>
<td>p value</td>
<td>0.145</td>
<td>0.434</td>
<td>0.300</td>
</tr>
<tr>
<td>Bednets ratio to population</td>
<td>R <strong>-0.750</strong></td>
<td><strong>-0.628</strong></td>
<td><strong>-0.708</strong></td>
</tr>
<tr>
<td>p value</td>
<td><strong>0.000</strong></td>
<td><strong>0.000</strong></td>
<td><strong>0.000</strong></td>
</tr>
</tbody>
</table>

From table 2, the most significant explanatory variables of malaria occurrence are highlighted in bold. The sign * means that a significant association at the 0.05 confidence level, and the sign ** shows a significant association at the 0.01 confidence level.

Monthly minimum temperature, ranging from 23.1°C to 27.7°C for Gikonko site, exhibits a weak association with malaria at Gikonko. Generally, an optimal temperature for malaria transmission of around 31°C was predicted by most of malaria models as optimum threshold where endemic malaria transmission can occur and spread in free regions (Bayoh and Lindsay, 2004; Parham and Michael, 2010). This threshold is however inconsistent with different locations in Africa where monthly malaria cases were negatively associated with temperature as malaria decreased when temperature get higher than normal. The development of malaria parasites and vectors are generally inhibited at temperatures higher than 23-24°C (Ikemoto, 2008; Mordecai et al., 2013). As monthly maximum temperature was higher than the optimum threshold for malaria transmission at Gikonko site, our results are consistent with these studies in tropical regions of Africa. This indicates that other socioeconomic factors (such as poverty, migration and water based agricultural practices) than the climate variability are accounted for malaria upsurge at Gikonko.

### 3.3. Relative role of climate and interventions

Standardized regression coefficients β (Table 4) represent the change in standard deviations of malaria that result from a change of one standard deviation in...
climate explanatory variables. Since $\beta$ coefficient has a positive sign for maximum temperature ($\beta=0.510$), this implies that an increase of monthly maximum temperature by one unit in standard deviation, while other variables remain constant, would lead to an increase in malaria by 0.510. Thus, change in maximum temperature has a greater relative effect on malaria in low and unstable transmission settings of Bungwe highlands than does a change in minimum temperature and average rainfall. In high transmission areas of Gikonko, climate variability exhibits however a small effect on malaria incidence.

Table 4: Regression coefficients for malaria and climate at Bungwe and Gikonko

<table>
<thead>
<tr>
<th>Sites</th>
<th>Models</th>
<th>Climate variable</th>
<th>Standardized $\beta$</th>
<th>St.Error</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bungwe</td>
<td>1</td>
<td>Maximum temperature</td>
<td><strong>0.510</strong></td>
<td>15.94</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minimum temperature</td>
<td>-0.215</td>
<td>29.28</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rainfall</td>
<td>-0.008</td>
<td>0.25</td>
<td>0.919</td>
</tr>
<tr>
<td>Gikonko</td>
<td>1</td>
<td>Rainfall</td>
<td>0.207</td>
<td>0.361</td>
<td>0.015</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Rainfall</td>
<td>0.213</td>
<td>0.354</td>
<td>0.011</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minimum temperature</td>
<td>0.204</td>
<td>27.649</td>
<td>0.015</td>
</tr>
</tbody>
</table>

Despite the climate suitability at Gikonko, high vectors density and malaria endemicity, the lack of discernable effect of climate variability on malaria may be linked to acquired immunity which counterbalances the effect of increased mosquito biting exposure (Yamana et al., 2013). Without the acquired immunity from prior exposure to malaria infection, change in climate variables would significantly have a larger effect on climate induced malaria in high transmission areas of Rwanda. This finding from Bungwe and Gikonko sites shows that temperature effect on malaria appears to be nonlinear (Alonso et al., 2011). Increased variations in temperature, when the maximum is close to upper limit for malaria vectors and parasites, tend to reduce malaria transmission; while increased variations of mean temperature near the minimum boundary increases the transmission (Paaijmans et al., 2010).

Table 5: Regression coefficients for malaria, climate and interventions at Bungwe and Gikonko

<table>
<thead>
<tr>
<th>Models</th>
<th>Variables</th>
<th>Standardized $\beta$</th>
<th>St.Error</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bungwe</td>
<td>Maximum temperature</td>
<td>-0.027</td>
<td>12.473</td>
<td>0.654</td>
</tr>
<tr>
<td></td>
<td>Minimum temperature</td>
<td>0.073</td>
<td>19.670</td>
<td>0.156</td>
</tr>
<tr>
<td></td>
<td>Rainfall</td>
<td>-0.073</td>
<td>0.156</td>
<td>0.138</td>
</tr>
<tr>
<td></td>
<td><strong>Interventions</strong></td>
<td><strong>-0.878</strong></td>
<td><strong>108.401</strong></td>
<td><strong>0.000</strong></td>
</tr>
<tr>
<td>Gikonko</td>
<td>Interventions</td>
<td>-0.640</td>
<td>150.464</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td><strong>Interventions</strong></td>
<td><strong>-0.635</strong></td>
<td><strong>146.726</strong></td>
<td><strong>0.000</strong></td>
</tr>
<tr>
<td></td>
<td>Maximum temperature</td>
<td>0.183</td>
<td>21.570</td>
<td>0.005</td>
</tr>
</tbody>
</table>

When combining climate variables and interventions (Table 5), only interventions were strongly and negatively associated with malaria. However, the absence of significant association between climate variability and malaria would have been masked by effective malaria interventions. Even if malaria interventions would have masked the known relationship between climate and malaria in Rwanda highlands, this needs further investigation with data that are relatively distributed over a long period and more locations.

Because some variance in malaria incidence may be explained simply by chance, it was necessary to look at the Adjusted R square instead of R squared to from the regression model to examine the percentage of variability in malaria incidence that is explained by monthly maximum and minimum temperature, monthly rainfall and interventions.

When using only climate variables, Adjusted R square was less than 0.50 (Adjusted $R^2=0.277$) at Bungwe. This implies that climate variables only explain 27.7% of variability in malaria (Table 6). When climate variables were combined and interventions incorporated into the model, Adjusted $R^2$ showed an improved performance (Adjusted $R^2=0.725$). This also indicates that malaria in Bungwe highlands and in middle altitude areas of Gikonko is also explained by other socioeconomic factors than only the climate variability. These factors may be related to interventions with bed nets, land use changes, population movements and migrations. Consequently, in low transmission settings of highlands, targeted interventions can greatly improve malaria control. Malaria elimination in Rwanda highlands may therefore be feasible with bednets that are accurately targeted to malaria hotspots in hyper endemics districts.
Table 6: Summary of regression models between malaria and climate and interventions at Bungwe and Gikonko

<table>
<thead>
<tr>
<th>Models</th>
<th>R</th>
<th>R²</th>
<th>Adj. R²</th>
<th>Std. Error</th>
<th>R² Change</th>
<th>Change Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>F Change</td>
</tr>
<tr>
<td>Bungwe</td>
<td>1. Predictors: (Constant), rainfall, min. temperature and maximum temperature</td>
<td>0.542</td>
<td>0.294</td>
<td>0.277</td>
<td>173.543</td>
<td>0.294</td>
</tr>
<tr>
<td></td>
<td>2. Predictors: (Constant), Bednets ratio to population, rainfall, min. temperature and max. temperature</td>
<td>0.856</td>
<td>0.734</td>
<td>0.725</td>
<td>107.078</td>
<td>0.734</td>
</tr>
<tr>
<td>Gikonko</td>
<td>1. Predictors: Constant, Bed nets ratio to population</td>
<td>0.640</td>
<td>0.409</td>
<td>0.405</td>
<td>229.935</td>
<td>0.409</td>
</tr>
<tr>
<td></td>
<td>2. Predictors: (Constant), Bednets ratio to population, minimum temperature</td>
<td>0.665</td>
<td>0.443</td>
<td>0.434</td>
<td>224.165</td>
<td>0.033</td>
</tr>
</tbody>
</table>

At Gikonko site, regression analysis has identified bed nets ratio to population and minimum temperature as best predictors of malaria. Since Adjusted R square 0.405 for bed nets ratio to population, and of 0.434 for both bednets ratio to population and minimum temperature are less than 0.50, this reveals some gaps that are not addressed by existing malaria interventions high transmission areas of Rwanda. Other social factors beyond climate variability and interventions are playing a key role. Moreover, since individuals are more infected regardless of environmental factors of their location, little difference is to be expected in malaria incidences between locations of households. The above results have an implication for national malaria control in high transmission settings like Gikonko where potentials for malaria transmission remain and malaria elimination is not nearly to be achieved.

It is worth to note that is only climate variability cannot be blamed for increasing malaria in Rwanda. This calls for bringing the development of the country’s population structures into the analysis. In particular, deforestation by a high population growth rate and internal migrations, change in settlement structures, land use changes (Guerra et al., 2006) through expansion of irrigated areas provide conducive environment for anopheles mosquito (Teklehaimanot and Pushpa, 1999). This accommodates malaria vectors because what happened on rice paddies in concert with local climate variability is exactly what many studies have been warning against for creation of breeding sites for Anopheles mosquito (Ijumba and Lindsay, 2001; Ijumba et al., 2002).

4. Concluding remarks
This study firstly applied a spatial statistic based approach to assess malaria clustering in small areas called hotspots in Rwanda. The persistent hotspots of malaria incidence partially overlap with the location of vector breeding sites that might favor higher exposure of local communities to mosquitoes' bites. This study demonstrates the need to generate space time malaria incidence map which can help in prioritizing malaria interventions in the areas of the most needs. Although malaria hotspots identification is a useful tool to guide public health decision-makers, the used approach is however without limitations and comes along with some challenges. First, malaria reporting based on health centre level may have missed some malaria cases. However, the underreporting is likely to be random both in location and in demographic characteristics due to the large efforts and attention for malaria surveillance and reporting system in Rwanda. Second, the use of health centre catchment areas may not be appropriate as it might not capture the exposure or malaria infection due to unknown locations of households. A third limitation is that the study did not statistically explore the drivers of malaria in the hotspots. Recognizing that the drivers of malaria transmission are more complex and varying across the heterogeneous landscapes of Rwanda, a further study using geographically weighted regression may be useful to identify the best predictors of malaria in each hotspot if required data are locally available. Despite these limitations, the research findings have significant implications for eliminating malaria in Rwanda.

Another objective of this study was to instigate the relative influence of climate variability and malaria in Rwanda. With regard to this aim, the study result how that relationship between climate variability and malaria varies according to the locations. There is therefore no doubt that malaria outbreaks were related to climate variability in Rwanda. In hypo-endemic and unstable transmission highlands, malaria was significantly associated with maximum temperature of the previous month. Conversely, too
much rainfall was likely to flush away breeding larvae, reducing the numbers of malaria vectors, and then decreasing malaria transmission. In hyper-endemic areas, malaria cases were only associated with minimum temperature. Other climate variables were however not strongly associated with malaria incidence because the maximum temperature at Gikonko site was higher than the optimum threshold temperature for malaria transmission. However there are other aspects that play an important role in malaria transmission. Therefore, malaria elimination in Rwanda cannot be made based on the forecasts using only climate parameters. Besides, most of the recent malaria resurgence can be explained by other factors than climate variability including malaria intervention, livelihoods activities and migrations.

Finally, since only two study areas for a period of ten years were used, one can consider data to be probably insufficient to detect the relationships between the climate variables and malaria at country level. This study suggests that the effect of interventions masked the known relationship between climate and malaria incidence, even if further research with data for a longer period and more locations is needed to validate the above findings.

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