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# Predictive and epidemiologic modeling of the spatial risk of human onchocerciasis using biophysical factors: A case study of Ghana and Burundi

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ABSTRACT

Although recent efforts taken have substantially contained human onchocerciasis in many African countries, published reports indicate a recrudescence of the disease. To understand this problem, biophysical factors that favor the establishment of human onchocerciasis in Ghana and Burundi—countries identified as threat locations of recrudescence for neighboring countries—were analyzed. Data pertaining to the prevalence of human onchocerciasis in both countries was obtained from published sources. Findings in this study suggest that there was a gradient in prevalence of onchocerciasis in geographic locations near the water streams. The predictive models suggest that rainfall, humidity, and elevation were statistically significant for Burundi data while in Ghana, only the effect of elevation was highly significant ($p < 0.0001$). In 2010, the estimated at-risk population was 4,817,280 people (19.75% of the total population) and 522,773 people (6.23% of the total population) in Ghana and Burundi, respectively. Findings can help in the effective design of preventive control measures.



## 1. Introduction

Human onchocerciasis is an important blindness-causing disease due to a nematode (worm) called *Onchocerca volvulus* and transmitted by *Simulium* black flies (Vieira et al., 2007). Human onchocerciasis (river blindness) is the second leading infectious cause of blindness in the world as well as in Sub-Saharan Africa (Etya'alé, 2002; Alonso et al., 2009), and 123 million people are at risk in all endemic areas (Udall, 2007). The insect vector transmitting human onchocerciasis, *Simulium damnosum*, can fly over 12 km from its breeding site (Babatimehi, 2008), to seek for a human host for a blood meal in order to produce new batch of eggs, yet few studies have used this range in their spatial framework.

Table 1 summarizes key epidemiological, clinical and biological information about the human onchocerciasis. The adult worms normally have average life cycle ranging from 9 to 11 years (Shibuya et al., 2000) and are typically found in 'nodules' swellings, which are often subcutaneous and situated over bony prominences (Lévêque et al., 2003; Hopkins, 2005). The blindness-causing disease was first observed by O'Neill in Ghana in 1875 (Burnham, 1998). Once in the human body, the female adults of *O. volvulus* yield millions of microfilaria that are responsible of various clinical and dermatological manifestations, including blindness and onchodermatitis, thickening and atrophy of the skin and pigmentry aberrations, such as, leopard skin (Okoye and Onwuliri, 2007; Babatimehi, 2008). It is also known to lead to weight loss, changes in the immune system, growth arrest and susceptibility of epilepsy (Burnham, 1998; Pion et al., 2009).

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**Table 1**
Key epidemiological, clinical, and biological information about the human onchocerciasis.

| Epidemiological information | Clinical and Dermatological information | Molecular information |
|---|---|---|
| Over 17 million of people infected by human onchocerciasis are distributed in Africa. Latin America, and Yemen[a] | In infected individuals, early manifestations of the disease might appear one to three years after the transmission of the infective larvae[h] | The genus of Onchocerca consists of 28 species among which *O. volvulus* causes human onchocerciasis. the rest are parasites of ungulate mammals[m] |
| *0. volvulus,* which is the human onchocerciasis parasite, was first observed by O'Neill in Ghana in 1875[b] | Ocular lesions include night blindness visual field loss and constriction, irreversible blindness, punctuate and sclerosing keratitis. optic nerve atropy[i] | Two strains of *O. volvulus* were found to be distributed in West Africa in the savannah regions and in rain forest areas: a blinding savannah parasite strain transmitted by savanna members of *Simulium damnosum* and non-blinding forest strain, transmitted by forest members[n] |
| Adult female of *O. volvulus* have a life span of 9–11 years[c] | Skin lesions include pruritus, subcutaneous nodules, papular dermatitis, generalized lichenified onchodermatitis. leopard skin, and atrophy of the skin[j] | |
| The insect vectors *Simulium damonosum* breed in fast flowing (0.1–2.5 ms-1: 0.7–2 ms-1; 2.4–3.0 ms-1) and well oxygenated rivers[d] | In forest areas, onchocercal skin disease affects all age groups of infected people, and constitute the most important public health problem[k] | Sensitive methods of detection of *O. volvulus* presence in human body include polymerase chain reaction (PCR). and topical application of diethylcarbamazine (DEC) patch[o] |
| Onchocerciasis is most frequent among farmers, fishermen, and sand diggers[e] | Onchocerciasis causes troublesome itching weight loss, changes in the immune system, nanism, epilepsy, hyposexual dwarfism[l] | |
| Highest historical prevalence were recorded in west African countries including Ghana. Nigeria. Liberia, and parts of Mali[f] | | |
| Prevalence is higher among subjects aged of 50 years or above, lower within individuals aged of 20 to 29. and higher in males than females[g] | Severe troublesome itching causes bleeding and pain of the infected people when scratching their body with materials such as stones, twigs or knives[k] | |

[a] Hoerauf et al. (2003).
[b] Burnham (1998).
[c] Shibuya et al. (2000).
[d] Opoku (2006), Leveque et al. (1988) (1985), and Gnmewald (1981).
[e] Jacobi et al. (2010), Etya'ale (2001), and Burnham (1998).
[f] Udall (2007).
[g] Okonkwo et al. (2010).
[h] Etya'ale (2001).
[i] Basáñez et al. (2006), Etya'ale (2001), and Burnham (1998).
[j] Babatimehi (2008), Okoye and Onwuliri (2007), Emukah et al. (2004), and Burnham (1998).
[k] Remme (2004).
[l] Pion et al. (2009), Burnham (1998), and Etya'ale (2001).
[m] Morales-Hojas et al. (2006), Morales-Hajos et al. (2007), Keddie et al. (1998).
[n] Adewale et al. (2005), Duerr et al. (2004), Morales-Hajos et al. (2007), Keddie et al. (1998), and Ogunrinade et al. (1999).
[o] Boatin et al. (2002), Morales-Hajos et al. (2007), Keddie et al. (1998).

Onchocerciasis is a rural disease since it mainly affects villagers and is most frequent among agricultural workers, fishermen, and sand diggers (Burnham, 1998; Etya'ale, 2001; Jacobi et al., 2010). It has largely contributed to the depopulation of agricultural fertile lands, low agricultural productivity, and destabilization of the socio-economic development in poorest regions in the world. The 34 endemic countries are primarily distributed in Africa, the Middle East, South America, and Central America. Of the 30 endemic Sub-Saharan African countries (Etya'alé, 2002), 11 are located in Sub-Saharan West Africa, including Ghana, Nigeria, Liberia, and parts of Mali. The West African countries have the highest historical prevalence of onchocerciasis (Udall, 2007; Opara et al., 2008). Given these facts, onchocerciasis still poses a disease burden to rural communities and remains a serious public health problem and burden to socioeconomic development in Africa (Opoku, 2000; Alonso et al., 2009).

Against this background, there were concerted efforts by the International Scientific Community for Onchocerciasis Control that resulted in the initiation of two programs: (1) Onchocerciasis Control Program (OCP) that ran from 1974 to 2002 (Lévêque et al., 2003) and (2) the African Program for Onchocerciasis Control (APOC) setup in 1995 and is still ongoing. The APOC program builds upon the earlier successes of the OCP.

Three years following the end of the OCP program, however, Cote d'Ivoire and Ghana were identified to be a threat location of recrudescence of onchocerciasis for neighboring countries. Indeed, the 2005 epidemiological surveillance revealed high prevalence rates (up to 41%) of human onchocerciasis in the southern region of Cote d'Ivoire (APOC, 2006). Some of the cases of recrudescence were reported through entomological and epidemiological surveillance systems (Taylor et al., 2009), while a possible emergence of resistant adult parasite population was cited in Ghana (Osei-Atweneboana et al., 2007).

The application of new technologies, such as geographical information systems (GIS), enables the compilation, organization, and analysis of risk factors for human onchocerciasis. For example, the Rapid Epidemiology Mapping of Onchocerciasis (REMO) under the APOC program, uses GIS to map and model potential risk areas based on river basins. Disease models explaining the spatial patterns of human onchocerciasis in Sub-Saharan Africa have facilitated the effective design of preventive control strategies. Habitats of black flies have also been accurately identified and in one study, maps showing black flies habitats relative to human onchocerciasis were used to identify communities that were susceptible and at high risk (Noma et al., 2002). The GIS provides baseline information about the geographic distribution and prevalence of human onchocerciasis. The tool helps with the identification of endemic communities so that they can effectively be targeted for prevention and treatment. The analytical capability of this tool was one of the incentives for undertaking this study.

Another incentive was related to the need to investigate biophysical factors that favor the establishment of human onchocerciasis in Ghana. The primary goal of this study was to identify potential risk areas for human onchocerciasis using relevant biophysical factors and provide a strong spatial framework that can help in advancing our knowledge about the habitats of the black flies. We hypothesize that human onchocerciasis is prevalent among rural communities living in close proximity to water streams. To achieve this, relevant epidemiological and biophysical data were compiled for Ghana and Burundi.

## 2. Materials and methods

### 2.1. Study area and design

Ghana is located in West Africa on the Gulf of Guinea between latitudes 4°35′N and 11°5′N and longitudes 3°5′W and 1°10′E with a total land area of about 239,000 km$^2$. Situated close to three neighboring countries (Burkina Faso in north, Cote d'Ivoire in west, and Togo in east) and in the south is Atlantic Ocean. It has tropical humid conditions with three key hydroclimatic zones, namely the South-Western, the Coastal, and the Volta basin system (Dazé, 2007); the Volta lake represents about 5 percent of the total land area (Tamakloe, 2003). Temperatures range from 18 °C to 40 °C and at present has an average annual temperature above 24 °C (Cameron, 2011). The mean minimum and maximum rainfalls are 900 mm (South-East region) and 2000 mm (South West region), respectively (Tamakloe, 2003). The highest altitude is 883 m and half of the country lies below 152 m above sea level (Ghana National Commission for UNESCO, xxxx). The total population of Ghana was estimated at 24,392,000 in 2010 (United Nations, Department of Economic and Social Affairs).

Burundi is located in the east-central Africa with a total land area of about 27,834 km$^2$. It lies between latitudes 2°20′ and 4°27′S and longitudes between 28°50′ and 30°53′E. It is part of the Albertine Rift, a western extension of Great Rift Valley, altitude varies from 775 m to 2670 m. It is bordered by three countries, Tanzania to the East and South, Rwanda to the North, and the Democratic Republic of Congo to the West (Nkurunziza et al., 2010; Ndayishimiye et al., 1992). A tropical highland climate predominates in Burundi and is subject to significant daily temperature variations due to differences in altitude (Nkurunziza et al., 2010). Temperatures vary from 16 °C in the highest mountain areas to 23 °C in areas near the Lake Tanganyika and the average temperature in the central plateau is 20 °C. Rainfall is irregularly and unevenly distributed, falling heavily in the North-West, many areas receiving between 130 cm and 160 cm per year (Nkurunziza et al., 2010, 2011). The total population was 8,383,000 in 2010 (United Nations, Department of Economic and Social Affairs) and is predominately rural (Nkurunziza et al., 2011).

In this retrospective design, we analyzed a number of biophysical factors that favor the establishment of human onchocerciasis in Ghana and Burundi. A predictive model of biophysical factors and epidemiological model were constructed using GIS, geostatistical/spatial interpolation techniques, and a two-stage process through the use of a principal component analysis (PCA) and generalized linear mixed model (GLMM) with spatially autocorrelated errors.

### 2.2. Datasets

Data pertaining to the prevalence of human onchocerciasis in Ghana and Burundi was obtained for the period 2004 and 1985–1992, respectively. Table 2 provides a list of spatial datasets used to build disease models for human onchocerciasis.

Biophysical factors, including temperature (°C), humidity (%), rainfall (mm), elevation (m), rivers, and land cover were obtained from multiple sources (Table 2). The temperature, rainfall and humidity were obtained from an online World Weather Database (http://www.tutiempo.net). Given that the climatic data are reported on a monthly basis from January to December, the average of the monthly mean temperature, humidity and rainfall were compiled for all endemic communities. The locations of eight weather stations (two stations are located in Burundi and the others are located in the neighboring countries) in Burundi and 11 weather stations in Ghana were encoded as point spatial features. Elevation data and mosaic images were obtained at 30 × 30 m spatial resolution from the ASTER, United States Geological Survey website (http://demex.cr.usgs.gov/DEMEX/).

Epidemiological data about 20 endemic communities in Ghana were obtained from a published report (Osei-Atweneboana et al., 2007). The epidemiological database contained 2501 individuals, including the nodule prevalence before Ivermectin treatment. For Burundi data was compiled using two sources: the first one was from Newell (1995) and the second one was from Newell et al. (1997). The first source contained published reports of human onchocerciasis in Burundi, while the second one contained published reports of prevalence and intensity of human onchocerciasis in the provinces of Bururi, Cibitoke, and Bubanza. The second source drew from a sample population collected in 33 administrative units between 1990 and 1992.

**Table 2**
A list of spatial datasets used for analysis and model development.

| Data | Source | Spatial or temporal resolution | Description |
|---|---|---|---|
| Temperature<br>Humidity<br>Rainfall<br>Longitude and latitude of the weather stations | http://www.tutiempo.net/en/Climate/ | At city level | The website provides historical climate data on each country in the world. The data are described using 11 climate variables including the average annual and monthly temperature, humidity, and rainfall. The locations of each weather station are also provided. |
| Digital Elevation Model (DEM) | http://demex.cr.usgs.gov/DEMEX/ | 30 × 30 m | Data were downloaded in longitude and latitude geographic coordinate system, and GeoTIFF format. The Geoid reference was WGS84/EGM96 |
| Human onchocerciasis prevalence data | Ghana: Osei-Atweneboana et al. (2007) | At village level | 20 endemic communities in Ghana for the year of 2004 included 2501 individuals, and nodule prevalence |
| | Burundi: Newell (1995) and Newell et al. (1997) | At village level | Data for Burundi also contained nodule prevalence and in some cases the villages' population. The compiled data covered the period of 1985–1992 |
| Land cover of Ghana | http://www.fao.org/geonetwork/srv/en/main.home | Temporal resolution:January 2005–December 2005 | The ESRI Shapefile format was downloaded in in ArcGIS 9.3. The original data with 46 classes was reclassified into nine classes using the global cover legend of FAO in order to identify agricultural zones<br>Geographic Coordinate System: GCS_WGS_1984<br>Scale: 1:3,600,000 |

Endemic communities for Ghana and Burundi were geocoded using place locations/reference files obtained from the US National Geospatial-Intelligence Agency website. A GIS map (Fig. 2) showing endemic communities relative to weather stations was developed and used in further geographical analysis.

### 2.3. Statistical and spatial analytical elements of the disease model

Fig. 1 shows three components of data analysis. These include spatial interpolation, statistical analysis, and accounting for spatial autocorrelation. Data processing and analysis was accomplished by using Microsoft Office Excel 2007 and SAS 9.2. In addition, the study compared the performance of three sets of interpolation and variogram algorithms in ArcGIS 9.3 to discover the best set to characterize and interpolate biophysical factors (Table 3). The three sets included ordinary kriging, cokriging, and inverse distance weighted (IDW) methods. Risk modeling of human onchocerciasis was accomplished by using GIS and statistical analysis methods.

Climatic variables, such as average monthly mean temperature, average monthly mean humidity, and average monthly mean rainfall, were used in estimating wet season parameters. Elevation data served as a co-variate for Cokriging. A number of climatic surface maps were derived to represent the following time slices 1985–1992, 2004, 2010, and 2005–2010.

The next step was to use PCA to identify biophysical variables exhibiting maximum variances relative to endemic communities. The model is useful in explaining the variance–covariance structure of a set of variables, through a few linear combinations of these variables, called principal components (Johnson and Wichern, 1998). A two-stage process including the PCA and spatial GLMM model was followed; in the first-stage, the explanatory variables included humidity, temperature, rainfall, and elevation. Using mean threshold values for each variable reported in Table 6, surface values were extracted and then these were reclassified into binary values, with optimal area being assigned the value of 1 while non-optimal areas were assigned the value of 0. Optimal locations had favorable characteristics that enable the establishment and development of *Simulium damnosum*, the vector of *Onchocerca volvulus*.

The PCA models with the principal components of biophysical factors that most explain the spatial distribution of human onchecerciasis were identified. The key elements of these models are defined by the values of $a_{11}$ and $a_{12}$ that maximize the variance of $P_1$. The second principal component is defined by the values of $a_{21}$ and $a_{22}$ that maximize the variance of $P_2$, but $P_2$ must be uncorrelated with $P_1$ and so forth, with each successive principal component uncorrelated with all preceding ones. The first principal component explains the most variance followed by the second and so forth. The components of the primary PCA model are defined as follows:

$$\begin{cases} P_1 = a_{11}(Y_1 - \overline{Y}_1) + a_{12}(Y_2 - \overline{Y}_2) + \cdots a_{1m}(Y_m - \overline{Y}_m) \\ P_2 = a_{21}(Y_1 - \overline{Y}_1) + a_{22}(Y_2 - \overline{Y}_2) + \cdots a_{2m}(Y_m - \overline{Y}_m) \\ \\ P_m = a_{m1}(Y_1 - \overline{Y}_1) + a_{m2}(Y_2 - \overline{Y}_2) + \cdots a_{mm}(Y_m - \overline{Y}_m) \end{cases}$$

$P_1, P_2, \ldots, P_m$ are called principal components, $a_{ij}$ are called eigenvectors and represent the proportions of each explanatory variables, $Y_1, Y_2, \ldots, Y_m$ are the explanatory variables and $Y_1$ bar, $Y_2$ bar, …, $Y_m$ bar are the mean of the explanatory variables.

The second-stage involved the use of a spatial GLMM to identify the strongest biophysical predictors of human onchocerciasis. The prevalence rates in the endemic communities served as the health outcome (dependent variable) while rainfall, temperature, humidity, and elevation were biophysical predictors. Prevalence rates were further

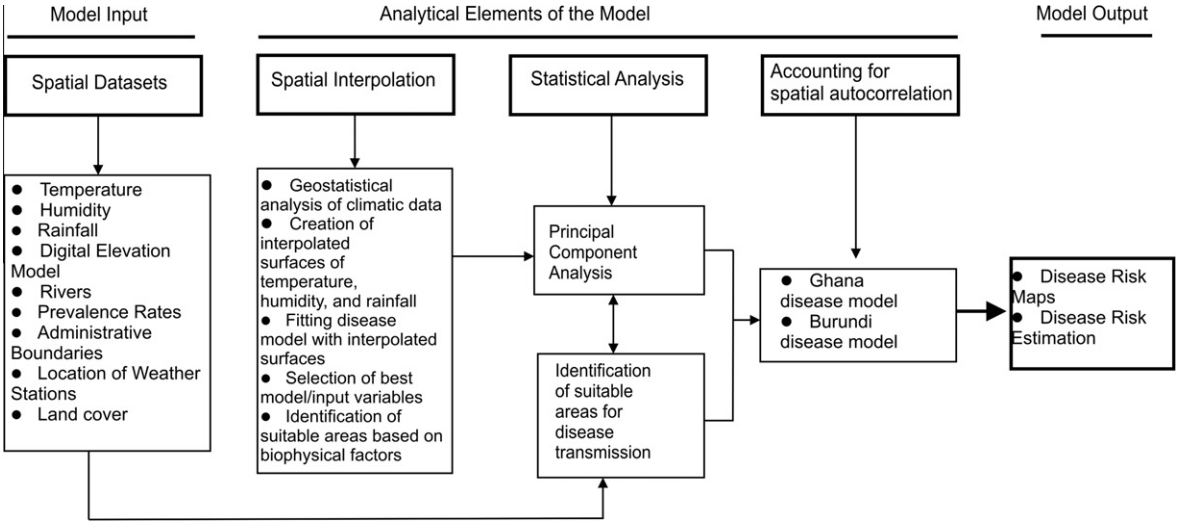


**Fig. 1.** Methodological framework for spatial modeling and risk prediction of human onchocerciasis.

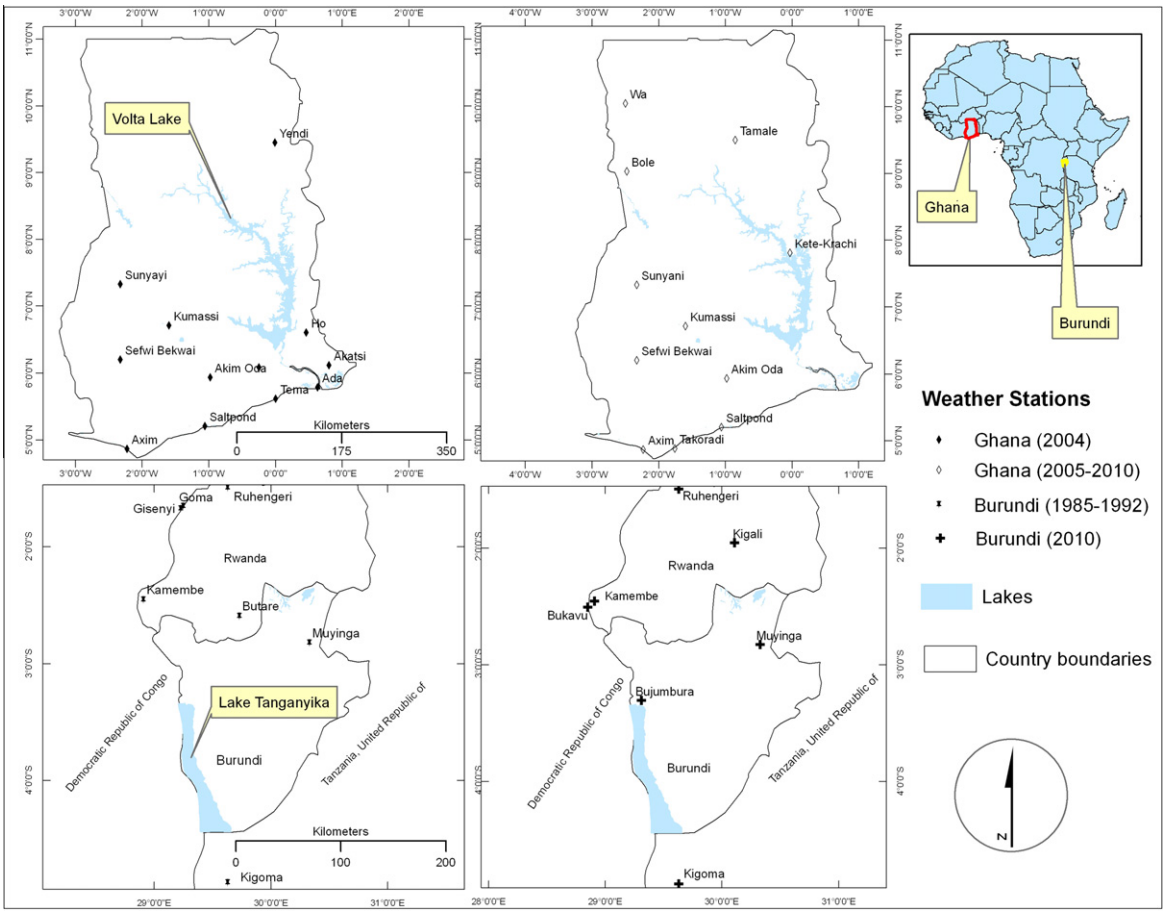


**Fig. 2.** Location of study area, endemic communities, weather stations, and major population centers.

specified by a pair of $(X, Y)$ geographic coordinates and the spatial covariance was assumed to be distance between locations of two endemic communities. This was best represented using a spherical spatial covariance structure that allows for modeling of spatially autocorrelated errors.

**Table 3**
An error matrix of the performance of three spatial interpolation methods.

| Variables | Statistics* | Kriging | | Co-kriging** | | Inverse distance weighted | |
|---|---|---|---|---|---|---|---|
| | | Burundi 2010 | Ghana 2005–2010 | Burundi 2010 | Ghana 2005–2010 | Burundi 2010 | Ghana 2005–2010 |
| Temperature | Mean | 0.108 | −0.004 | 0.42 | −0.066 | 0.742 | 0.033 |
| | RMSE | 4.52 | 0.505 | 5.073 | 0.742 | 4.897 | 0.623 |
| Humidity | Mean | −0.237 | 0.07 | 0.045 | 0.215 | 0.694 | 0.851 |
| | RMSE | 17.947 | 1.764 | 18.675 | 2.766 | 26.906 | 3.2 |
| Rainfall | Mean | −0.06 | 0.867 | 0.51 | 0.772 | −0.0059 | 1.089 |
| | RMSE | 45.22 | 8.258 | 62.758 | 7.043 | 63.688 | 9.718 |

* When the statistic has a mean near zero or when the root mean square error (RMSE) is very small then model is selected.
** Elevation was used as the co-variate for co-kriging.

Two diseases models (Models 1 and 2) show predicted risk maps. Model 1 represents the disease risk estimates for Ghana and Burundi based on the spatial GLMM model without accounting proximity to water streams. Model 2 is the disease risk estimates for both countries relative to the water streams. The final maps were produced using the regression coefficients and they illustrate the spatial risk of onchocerciasis and potential dispersal patterns of black flies.

The total population at risk was estimated by multiplying at risk areas of human onchocerciasis with population density. The estimation was accomplished by using population density values from the Department of Economic and Social Affairs of the United Nations.

## 3. Results

An initial investigation of which of the three spatial interpolation methods (ordinary kriging, co-kriging, and IDW) would most fit the three climatic variables (humidity, temperature, and rainfall) in relation to endemic communities for both Ghana and Burundi yielded varied prediction errors (Table 3). The three interpolated climatic and elevation surfaces are presented in Fig. 3. The analysis of residual values showed that ordinary kriging method had the least prediction errors for the 2004 and 2005–2010 datasets in Ghana. However, the error terms varied in some cases. For example in Burundi, the co-kriging method yielded the best results for temperature and humidity data for both periods while the IDW method provided the best results for rainfall.

A summary of possible linear combinations from the PCA models is given in Table 5. The biophysical average values for elevation, humidity, rainfall and temperature were 240.26 m, 75.12%, 33 mm and 27 °C, respectively, for Ghana, while for Burundi the values were 1553 m (elevation), 71% (humidity), 20 mm (rainfall), and 24 °C (temperature). These values were used in defining parameters for each of the biophysical variable as shown in Table 6. Empirical thresholds for establishment of vector were provided in Table 4. Final maps for Model 1 show the optimal biophysical factors for the vector establishment and disease (Fig. 4).

The PCA modeling process yielded four principal components ($PC_1$, $PC_2$, $PC_3$, and $PC_4$). $PC_1$ only explained 64% and 56% of the total variance of human onchocerciasis in Ghana and Burundi, respectively while $PC_2$ explained 31% (Ghana) and 22% (Burundi) of the total variance. Although the first two principal components $PC_1$ and $PC_2$ explained 95% of the variability in human onchocerciasis in Ghana, an analysis of the PCA model for Burundi showed three principal components encapsulating 97% of the variability of human onchocerciasis. It was determined that $PC_2$ best explained the co-variance of environmental variables in endemic communities.

The risk of human onchocerciasis is represented by the probability of being bitten by a disease vector, *Simulium damnosum, which* in turns infects the human subject with *Onchocerca volvulus*. The risk is evident, especially, where optimal conditions exist for the establishment of the vector and disease. Different biogeographical regions exhibit different biophysical characteristics, but the existence of a host (i.e., human settlements) and optimal biophysical factors are crucial for the vector establishment.

The spatial GLMM indicates that the strongest biophysical predictors of human onchocerciasis for Burundi were rainfall, humidity, and elevation; Ghana only had elevation as the strongest (Table 7). In both countries, temperature was less influential. However, the Burundi Model Likelihood Ratio Test is insignificant suggesting that the predictor coefficients are equal and that accounting for spatial autocorrelation is unnecessary. Simply put, the predictors for Burundi do not seem to exhibit spatial dependency, so we opted for the logistic model without a spatial structure, which suggests that rainfall, humidity, and humidity were still significant. The spatial risk map for Burundi is therefore based on this model. The maps of predicted risk show potential patterns and the spatial risk of human onchocerciasis without water streams (Fig. 4).

Given that the Model 1 does not accurately represent the potential zones of transmission threat of human onchocerciasis (river blindness is predominately common among the rural community near a water stream) there is a need to further refine it. To refine this model, it was assumed that human onchocerciasis will most likely occur in villages that are in close proximity to water streams away from the cities. It was further assumed that there is a specific flying distance range (12 km) from the rivers, where the insects are most likely to breed (Babatimehi, 2008); this distance range represents the high risk areas for disease transmission. A 12 km buffer zone around the water streams was used to represent the flight distance range and dispersal of the black flies. Figs. 5 and 6 illustrate the

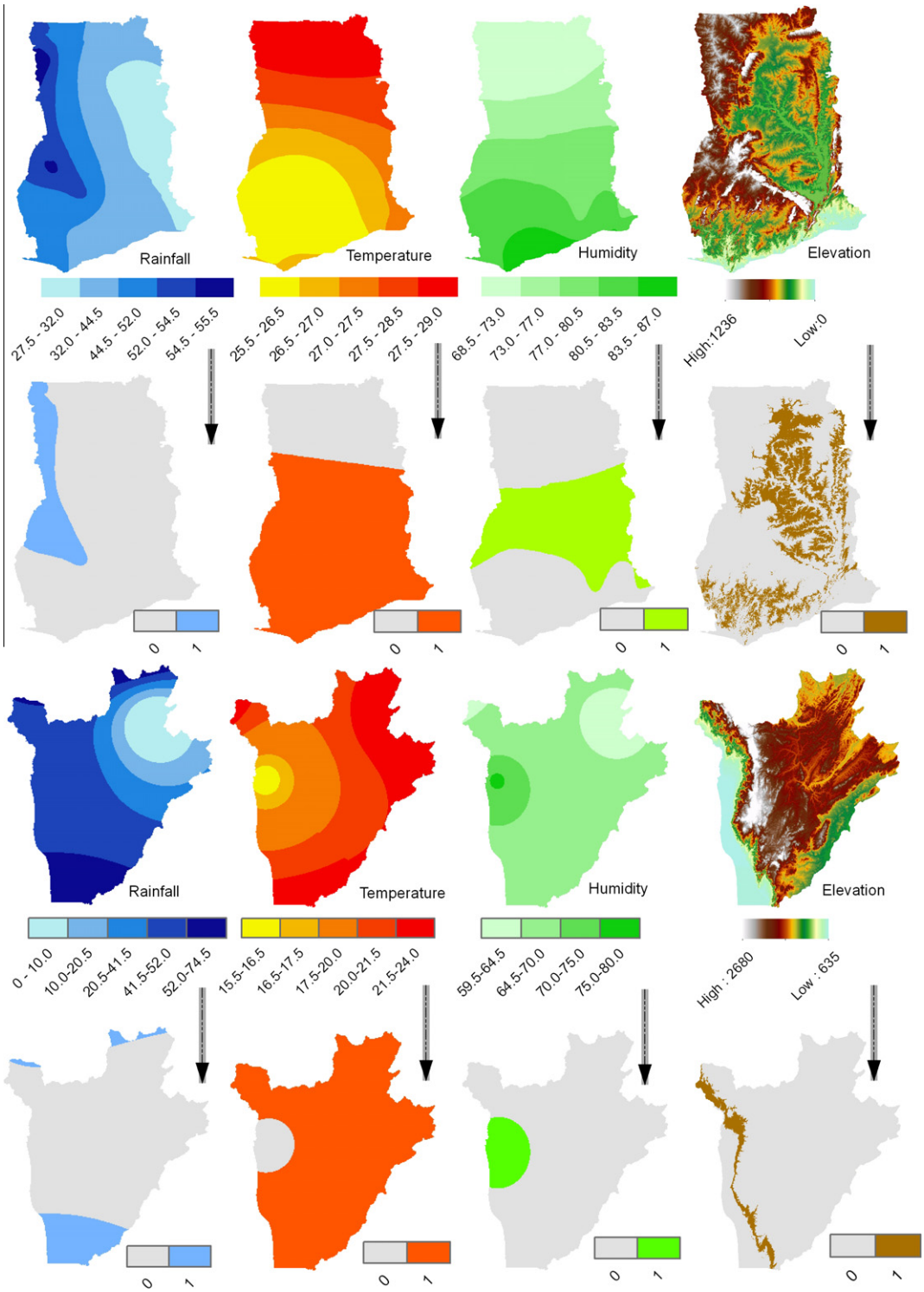


**Fig. 3.** Spatial interpolation of Climate data and extraction of suitable habitats in Ghana (2005–2010) and Burundi (2010). In Ghana, ordinary kriging was used as the best interpolation method. In Burundi, co-kriging was used to interpolate temperature and humidity, and inverse distance weighted for rainfall.

refined disease models from Model 1 of human onchocerciasis. These maps represent the high risk areas and potential biogeographic regions and epidemiologic patterns of human onchocerciasis relative to at-risk population.

The final task after deriving the refined disease models was to estimate the population by region that is at risk of human onchocerciasis. The boundary layer containing the geographical regions was linked to the refined disease

**Table 4**
Thresholds values of optimal biophysical variables for *Simulium damnosum*.

| Variables | Values | Boolean | Ref. | Values | Boolean | Ref. |
|---|---|---|---|---|---|---|
| Humidity (%) | 75–80 | 1 | 1 | 75–80 | 1 | 1 |
| | <75 or > 80 | 0 | | <75 or > 80 | 0 | |
| Temperature (°C) | 20–28 | 1 | 2 | 18–22 | 1 | 5 |
| | <20 or > 28 | 0 | | <18 or > 22 | 0 | |
| Rainfall (mm) | Heavy (May–June) | 1 | 3 | Wet season (October–May) | 1 | 6 |
| | Light | 0 | | Light | 0 | |
| Elevation (m) | 95–142 | 1 | 4 | 820–1110 | 1 | 5 |
| | <95 or > 142 | 0 | | <820 or > 1110 | 0 | |
| Ghana | | | | Burundi | | |

1: Nwoke (1988); 2: Opoku (2006) and Gebre-Michael et al. (2005), Nwoke (1988); 3: Opoku (2006); 4: The values were defined using PCA; 5: Lakwo et al. (2006); 6: The values were defined based on the information provided by the World Weather Information Service (www.worldweather.org).

**Table 5**
Principal component analysis: possible linear combinations of the independent variables.

| | $PC_1$ | | $PC_2$ | | $PC_3$ | | $PC_4$ | |
|---|---|---|---|---|---|---|---|---|
| | Ghana 2004 | Burundi 1985–1992 | Ghana 2004 | Burundi 1985–1992 | Ghana 2004 | Burundi 1985–1992 | Ghana 2004 | Burundi 1985–1992 |
| Elevation | −0.54 | −0.39 | 0.35 | 0.52 | 0.76 | 0.74 | 0.02 | 0.18 |
| Humidity | −0.33 | 0.64 | 0.73 | 0.09 | −0.58 | 0.08 | 0.1 | 0.76 |
| Rainfall | 0.5 7 | 0.47 | 0.33 | −0.43 | 0.23 | 0.65 | 0.71 | −0.41 |
| Temperature | 0.52 | 0.47 | 0.47 | 0.73 | 0.17 | −0.16 | −0.69 | −0.47 |
| Eigengenvalues | 2.55 | 2.25 | 1.23 | 0.87 | 0.16 | 0.77 | 0.05 | 0.11 |
| Proportion | 0.6391 | 0.5619 | 0.3079 | 0.2173 | 0.0399 | 0.1939 | 0.0131 | 0.0269 |
| Cumulative proportion | 0.6391 | 0.5619 | 0.9469 | 0.7792 | 0.9868 | 0.9731 | 1 | 1 |

maps. Areas that fall within disease maps were identified and then estimates were derived. Table 8 presents the estimated population at risk of human onchocerciasis. The estimated total land area at risk of human onchocerciasis was 47,228 $km^2$ and 3314 $km^2$ for Ghana and Burundi, respectively. The estimated total population that is at risk is 4,817,280 (Ghana) and 997,470 (Burundi).

## 4. Discussion

Predictive risk maps of human onchocerciasis were constructed using GIS, geostatistical, PCA, and spatial GLMM models. These maps show potential biogeographic regions and epidemiologic patterns relative to at-risk population. Three major findings of this study are as follows:

1. Human onchocerciasis displays non-homogenous patterns that is suggestively associated with favorable biophysical factors, which enable disease vector and host establishment.
2. The predictive risk maps show the total land area and at risk population estimates for human onchocerciasis, with Ghana being more vulnerable than Burundi.
3. High risk areas and epidemiologic patterns of the disease vector and host are evident mostly in rural settings and close to water streams.

Findings in this study suggest that there was a gradient in prevalence of onchocerciasis in geographic locations that are in close proximity to water streams. Also, the predictive models after accounting for spatial autocorrelation suggest that rainfall, humidity, and elevation were statistically significant for Burundi data while in Ghana, only the effect of elevation was highly significant ($p < 0.0001$). This study generates new insights about the spatial patterns of human onchocerciasis. The findings are in agreement with reports in published studies (Osei-Atweneboana et al., 2007; Taylor et al., 2009).

In 2010, the estimated at-risk population was 4,817,280 people (or 19.75% of the total population) and 522,773 people (or 6.23% of the total population) in Ghana and Burundi, respectively. The findings suggest that geographic locations in the southwestern region of Ghana are at a high risk of human onchocerciasis, including Bronga-Ahafo, Ashanti, and the Eastern regions. The highest estimates of at risk population were observed in Bronga-Ahafo (1,711,527 people), Ashanti (1,499,265 people), and Eastern region (976,248 people). The estimates are consistent with the Special Intervention Zones (SIZ) in Ghana (APOC, 2006; Taylor et al., 2009). Taylor et al. (2009) reported 3,200,000 people to be at risk of river blindness in 2008. There is a slight overestimation in our models because of population density overlaps in urban and rural areas. Another approach would have been to use the rural population density reported by the Ministry of Food and Agriculture of Ghana of 56.2 persons per square kilometers in 2000. With the United Nations projected growth rate of 0.5% between 2005 and 2010, the rural population density would be 59.07 persons per square kilometers. Thus, the total estimate of the population at risk would be at

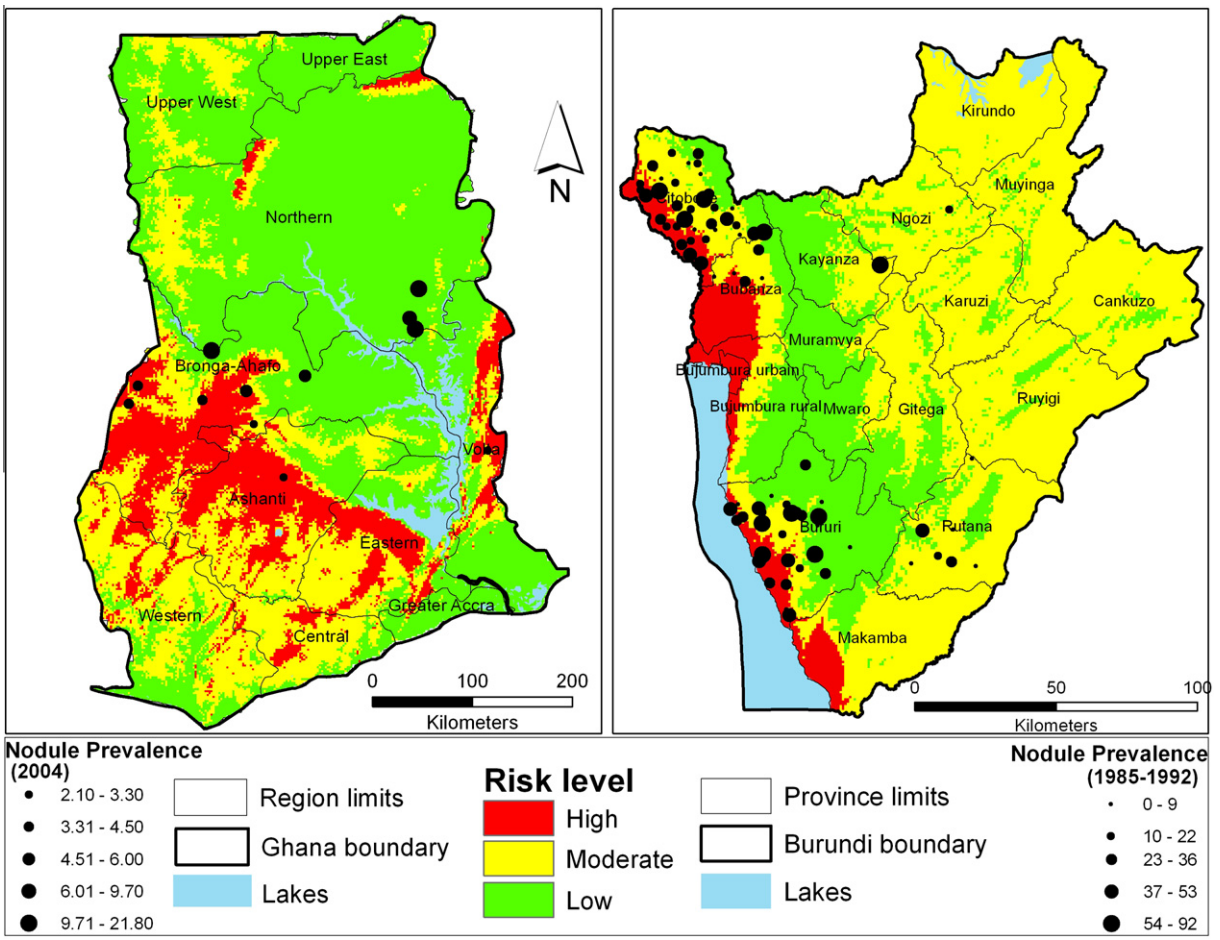


**Fig. 4.** Spatial risk models of Onchocerciasis in Ghana (a) and in Burundi (b) based on the Model 1 without accounting for water streams. The black dots represent endemic communities reported in 2004 (a) and between 1985 and 1992 (b). The endemic communities, which were based on published reports, appear to fit the disease models.

**Table 6**
Principal component parameters estimation.

| Variables | Parameters | $PC_1$ | | $PC_2$ | | $PC_3$ |
|---|---|---|---|---|---|---|
| | | Ghana 2004 | Burundi 1985–1992 | Ghana 2004 | Burundi 1985–1992 | Burundi 1985–1992 |
| Constant | $b_0$ | 121.81 | 85 | −162.48 | −222.67 | −309.82 |
| Elevation | $b_1$ | −0.54 | −0.39 | 0.35 | 0.52 | 0.74 |
| Humidity | $b_2$ | −0.33 | 0.64 | 0.73 | 0.09 | 0.08 |
| Rainfall | $b_3$ | 0.57 | 0.47 | 0.33 | −0.43 | 0.65 |
| Temperature | $b_4$ | 0.52 | 0.47 | 0.47 | 0.73 | −0.16 |

All biophysical variables have different level of significance on the different principal components. While $PC_2$ presents a positive impact of the variables on the occurrence of river blindness in Ghana in 2004, rainfall seem to negatively affect the disease transmission in Burundi for the period of 1985–1992.

2,789,772 people. This estimate represents 11.44% of the 2010 total population and is still below the 2008 national rate of 13.7%. Although we attempted to account for rurality by linking rural name places with disease maps in a GIS, the estimates are still high.

In Burundi, the prediction of risk of onchocerciasis resulted in the identification of five provinces, Citoboke, Bubanza, Bujumbura, Bururi, and Makamba as areas at high risk. The total population at risk estimate in 2010 was 522,773 people. With an estimate of 140,984 people, the province of Bubanza had the highest number of population at risk, followed by the province of Citoboke (106,301 people). In 2006, APOC estimated 1,114,870 people living in four endemic provinces, namely Citoboke, Bubanza, Bururi, and Rutana. Comparing our estimate with the number of population at risk estimated in 2006 by APOC, we noticed a significant decrease of the population at risk of 53.10% between 2006 and 2010. However, we cannot necessarily

**Table 7**
Biophysical predictors of spatial risk of human onchocerciasis.

| Spatial GLMM model with spherical spatial covariance structure | | | | | | | Model without spatial structure: logistic regression model | | |
|---|---|---|---|---|---|---|---|---|---|
| Variables | Ghana* | | | Burundi** | | | Burundi*** | | |
| | Coefficient | *t*-Statistic | *P*-Value | Coefficient | *t*-Statistic | *P*-Value | Coefficient | Wald chi-square | *P*-Value |
| Intercept | −3.1999 | −0.44 | | 3.7554 | 2.65 | | 74.8498 | 5.4121 | 0.0200 |
| Rainfall | −0.00024 | −0.02 | 0.9852 | −0.00025 | −3.85 | 0.0002 | −0.00425 | 6.6317 | 0.0100 |
| Temperature | 0.03285 | 0.17 | 0.8648 | 0.003349 | 1.51 | 0.1338 | 0.0597 | 1.3223 | 0.2502 |
| Humidity | 0.03001 | 0.82 | 0.4168 | −0.04862 | −2.12 | 0.0362 | −0.9769 | 4.2582 | 0.0391 |
| Elevation | 0.001612 | 4.72 | <0.0001 | −0.03834 | −2.33 | 0.0219 | −0.8560 | 5.2754 | 0.0216 |

$N = 100$; *Chi-square = 28.19; $p < 0.0001$; **Chi-square = 0.00; $p = 1.000$; ***Chi-square = 10.2756; $p = 0.0360$.
*Fit statistics-2 Res log likelihood 66.0, AIC 72.0, AICC 72.3, and BIC 79.7.
**Fit statistics-2 Res log likelihood 39.5, AIC 45.5, AICC 45.8, and BIC 53.2.
***Fit statistics (intercept and covariates)-2 Log L34.242, AIC 44.242, and SC 57.268.

relate that decrease to the positive impact of APOC through the distribution of Ivermectin drugs in the endemic communities in Burundi, since our models essentially predict the risk based on biogeographical factors but not on therapeutic coverage from one period to another.

The disease models demonstrate the value, use, and relevance of predictive modeling based on the integration of a variety of methods, including GIS, geostatistical, and a two-stage process using PCA and spatial GLMM model for spatio-environmental modeling. Environmental (biophysical)-sampled predictor variables can be useful in helping identify high disease risk populations. The positive effect of elevation on the distribution of human helminthes was reported by Diggle et al. (2007) after their spatial modeling and prediction of the risk of Loa loa in Cameroon. The effect of rainfall and humidity were reported in recent studies as the main explanatory climatic factors governing the numbers, distribution and intensity of the biting rate of the flies

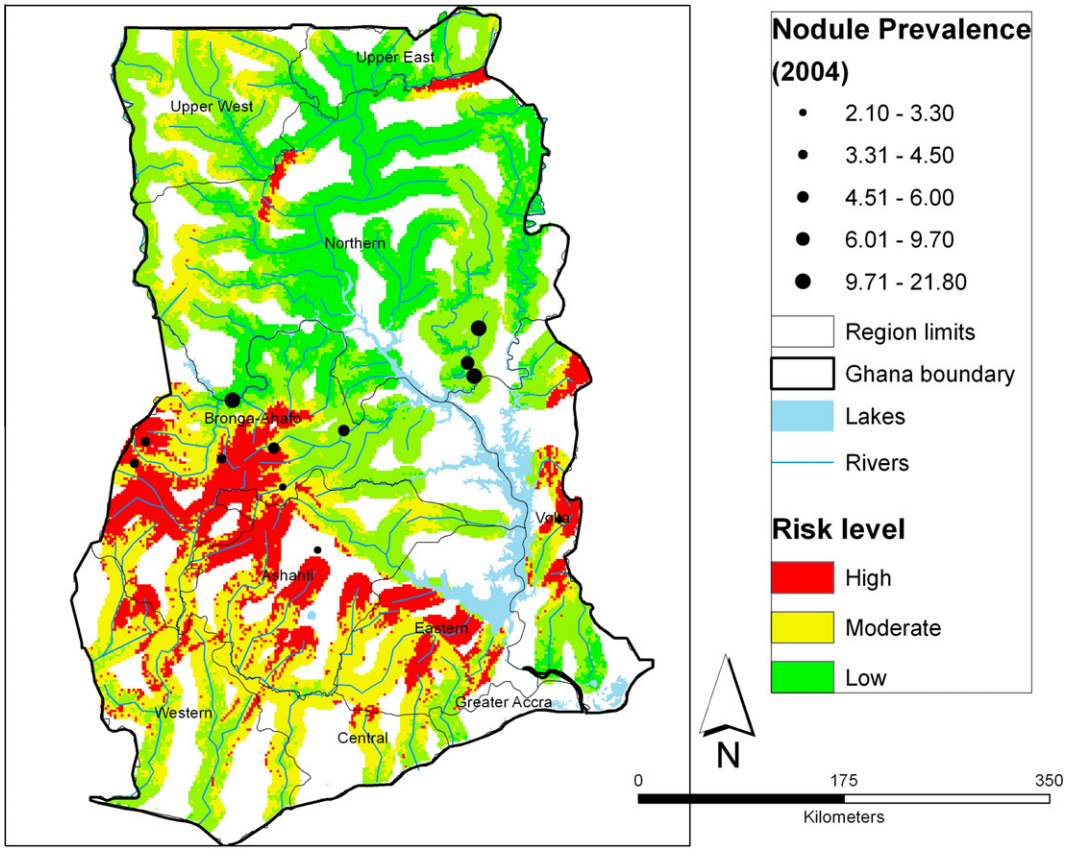


**Fig. 5.** Spatial risk model of Onchocerciasis predicted using spatial GLMM model relative to the water streams. The high risk areas are located within the central and southwards. Also, high risk areas track closely with water streams.

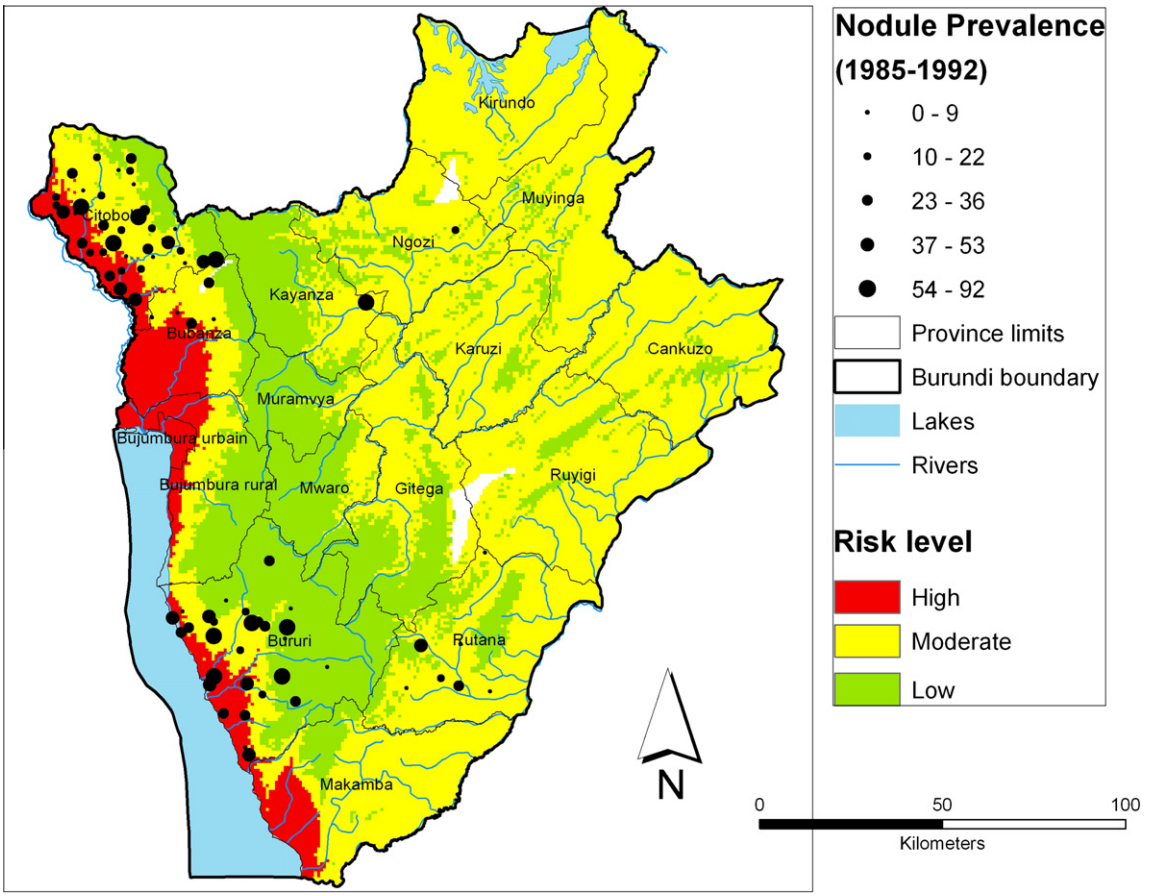


**Fig. 6.** Spatial risk model of Onchocerciasis predicted using Model 1 relative to the water streams in Burundi for the year of 2010. The map shows the North-West and South-West portions of the country have the highest risk for human onchocerciasis.

**Table 8**
Estimated population at risk of onchocerciasis in Ghana for the period 2005–2010 and in Burundi for the year of 2010.

| | Regions of Ghana | | | | | |
|---|---|---|---|---|---|---|
| | Bonga-Ahafo | Ashanti | Northern | Eastern | Volta | Total |
| Area at risk ($km^2$) | 16779.67 | 14698.7 | 2037.69 | 9571.06 | 4141.14 | 47228.24 |
| Population density ($/km^2$) | | | | | | 102 |
| Population at risk | 1711527 | 1499265 | 207844 | 976248 | 422396 | 4,817,280 |
| | Province of Burundi | | | | | |
| | Citoboke | Bubanza | Bujumbura | Bururi | Makamba | Total |
| Area at risk ($km^2$) | 353.159 | 468.385 | 335.962 | 281.993 | 297.288 | 1736.786831 |
| Population density ($/km^2$) | | | | | | 301 |
| Population at risk | 106301 | 140984 | 101125 | 84880 | 89483 | 522,773 |

(Gebre-Michael et al., 2005; Lakwo et al., 2006; Opoku, 2006). Assessing the potential impact on human health from waterborne and vector-borne infections, Hunter (2003) reported the positive effects of increased temperature and heavy rainfall on the distribution of vector and the effectiveness of pathogen transmission. However, due to certain climatic preferences that favor the homerange of black flies, it is possible predicted risk maps may not reflect future climate changes. Also, the fluctuations of climatic conditions at different geographic scales may influence the biodiversity and adaptations of black flies species.

This study has some limitations in spite of providing a comprehensive picture of human onchocerciasis relative to the black flies's habitat. The study did not account for socioeconomic factors, such as gender and age. In fact, Okwa et al. (2009) acknowledge that the prevalence of onchocerciasis increases with age. In a study of socioeconomic factors among women in a rural Guinea savannah ecotype of Nigeria, they reported an increase in

the prevalence among women of advanced age (51 years and over). This was further confirmed by Okonkwo et al. (2010) after examining 450 farmers in a rural setting of Nigeria. This study reported the highest infection rates among human subjects aged of 50 years and over in comparison to the age bracket between 20 and 29. Although, that could be specific to the rural regions in Nigeria, most studies have reported that agricultural workers, fishermen, and sand diggers were the most susceptible because of the nature of their daily work (Burnham, 1998; Etya'ale, 2001; Jacobi et al., 2010). In addition, the rates are normally higher in males than females (Okonkwo et al., 2010).

Another concern is related to the epidemiological data used for this study (Osei-Atweneboana et al., 2007). The sample in this study was based on microfilarial loads collected from the infected rural communities, which were assessed using skin snips. This is a standard method for onchocerciasis diagnosis involving the use of microscopical detection of microfilariae (Borsboom et al., 2003; Remme, 2004; Wanji et al., 2005; Ozoh et al., 2007; Mas et al., 2006; Lipner et al., 2006; Katabarwa et al., 2008; Rebecca et al., 2008; Kogi and Bulus, 2010). Although we recognize that this method is widely used its efficacy is still questionable. Weil et al. (2000) has shown that the examination is not sufficiently sensitive for detection of early infections of onchocerciasis or low microfilariae densities. The pain associated with sample collections makes it unpopular among endemic populations (Boatin et al., 2002), this can lead underestimation of the disease risk. Alternative diagnosis methods such as polymerase chain reaction (PCR) and topical application of diethylcarbamazine (DEC) patch were found to be more sensitive than skin snips (Boatin et al., 2002).

The last concern is related to the number of weather stations used for spatial prediction of climate data in Burundi. Only two weather stations (Bujumbura and Muyinga) were available for Burundi. To overcome this problem, we used six additional weather stations distributed in the neighboring countries (Democratic Republic Congo, Tanzania and Rwanda). It was reasonable to use these stations because of their proximity to Burundi. However, when we analyzed the root-mean-square errors (RMS) of the predicted climate data in Burundi in 2010, we noticed that the RMS values were largely greater than 1 (4.52 as minimum value and 63.68 as the maximum), suggesting an underestimation. This could partly be due to a sample size. Ghana only had 11 weather stations. We do not think this presents a major problem to this analysis given the number of weather stations in Africa. In addition, the spatial distribution of temperature, humidity, and rainfall is generally homogenous. Despite the homogeneity, a more robust spatial interpolation model would require a reasonable sample size. For future studies, we suggest the use of school weather stations and additional field measurements/sensors for calibration of these models.

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