

ISSN: 2348-5906

CODEN: IJMRK2

IJMR 2024; 11(5): 40-48

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<https://www.dipterajournal.com>

Received: 05-08-2024

Accepted: 13-09-2024

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Spatial distribution and ecological niche modelling of lymphatic filariasis (*Wuchereria bancrofti* (Cobbold, 1877) in the context of climate and global change (Benin, West Africa)

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DOI: <https://doi.org/10.22271/23487941.2024.v11.i5a.803>

Abstract

Lymphatic filariasis is an endemic parasitic disease transmitted to humans by mosquitoes and constitutes a public health problem in Benin. In 2000, the prevalence of infection covered 50 municipalities across the country, with the highest prevalence observed in the southern and central departments of the country. In order to contribute to the sanitary protection of the human populations of Benin, we estimated the potential distribution of the lymphatic filariasis pathogen *Wuchereria bancrofti* under current and future climatic conditions. Five different algorithms were used for the modeling: Maxent, GLM, GAM, BRT, and RF. The best prediction performance was obtained by Maxent and BRT. This has led to the merging of the models of the two algorithms in order to achieve more reliable results. The current potential distribution of *Wuchereria bancrofti* with Maxent and BRT has shown high suitability in Benin countries. The current potential distribution of *Wuchereria bancrofti* is concentrated in the south, reflecting the current distribution of the species: lymphatic filariasis risk areas. Projections of Maxent and BRT in future conditions showed a potential distribution less than that of current conditions, although an emergence of new risk areas for lymphatic filariasis is likely to appear in the north of the country. The predictions of Maxent and BRT made it possible to anticipate the evolution of the risk areas of lymphatic filariasis in the decades to come.

Keywords: Lymphatic filariasis, Maxent, BRT, *Wuchereria bancrofti*, Benin, Africa

Introduction

Arthropods are by far the most numerous phylum in the animal kingdom, and are responsible for 18% of the world's most fatal infectious and parasitic diseases [1]. Arthropods belong to different orders, but are mostly hematophagous, characterized by taking a blood meal through the bite of homeothermic animals, including man. Among these arthropods, mosquitoes are the most formidable, both in terms of their abundance [2] and the diseases they carry. Vector-borne diseases transmitted by mosquitoes have recently undergone a major resurgence [3] and now account for 28% of emerging diseases [4], placing a heavy burden on public health and the global economy [3, 4]. The incidence of these diseases has risen almost fourfold in the last 50 years, and their occurrence has increased markedly since the 1980s [4]. Some of these diseases mainly affect the poorest populations, living in remote rural areas of tropical Africa. The people who suffer from them, because they lack significant political power, are not a priority for public health. As a result, many of these diseases are neglected, with few or no control interventions available for case management, leading the WHO to refer to them as Neglected Tropical Diseases (NTDs). Yet (NTDs) affect around one billion people worldwide. However, WHO has drawn up a list of 17 priority neglected tropical diseases, including lymphatic filariasis (LF), a disfiguring parasitic disease caused by filaria (*Wuchereria bancrofti*), which is involved in 95% of cases [5]. The remaining cases are attributed to *Brugia malayi* (Brug, 1927) and, more rarely, to *Brugia timori* [6]. *Wuchereria bancrofti* is transmitted by mosquitoes of the *Culex*, *Anopheles* or *Aedes* genus. LF is characterized by lymphedema

or hydrocoele. It remains asymptomatic for a long time after infection, in most cases during childhood. These filaria residing in the lymphatic vessels dilate and obstruct them, causing swelling of one or more limbs. Lymphatic vessels in the lower part of the body are particularly affected, for example in the groin, genitals and thighs.

In 2010, an estimated 120 million people in 72 countries were infected, and around 1.39 billion lived in areas where filariasis is endemic and mass treatment is necessary. Nearly 40 million people suffer from the disabling and stigmatizing clinical manifestations of this disease: 15 million of them suffer from lymphedema (elephantiasis) and 25 million men from genitourinary edema, mainly scrotal hydrocoele. In Benin, LF is endemic in several municipalities, and the only strategy adopted to control and eliminate it is mass treatment with Ivermectin and Albendazole. Although this strategy has eliminated LF in some of Benin's municipalities, the disease remains endemic in many others.

In 2000, LF was mapped throughout the country. This was a cross-sectional study designed to determine the prevalence of the disease in the country. At the end of this mapping exercise, 50 of the country's 77 municipalities, including Cotonou and Porto-Novo cities, were identified as endemic. Following the 2000 mapping, a LF elimination plan was launched in 2002. This plan made it possible to control the disease in several municipalities, with satisfactory results. However, a recent survey carried out by the "Programme National de Lutte contre les Maladies Transmissibles (PNLMT)" in 13 municipalities in Benin in April 2018 reported that four municipalities still remain endemic in the Zou department. In order to facilitate decision-making, and to better guide control interventions in the prevention and eradication of LF in Benin, this study proposes to produce risk maps for the disease spread through spatial distribution and ecological niche modeling of the pathogen and incriminating vector. Which vector populations in the study area are involved in LF transmission, and what are their characteristics? What is the risk map for the spread of the disease in the context of climate and global change? These are the research questions that guided our investigations into potential LF vectors.

Materials and Methods

Study area: In 2020, the Programme National de Lutte contre les Maladies Transmissibles (PNLMT) in its epidemiological monitoring report reported that of Benin's twelve (12) departments, LF remains endemic in four (04) municipalities (Covè, Ouinhi, Zagnanado and Za-kpota) of the ZOU department^[7]. The Zou department is located between 7° 11' north and 1° 59' east, and bordered to the north by the Collines department, to the south by the Atlantic and Ouémé departments, to the east by the Plateau department and to the west by the Couffo department and the Republic of Togo. It covers an area of 5,243 km², including (Covè municipality (525 km²); Zagnanado (750 km²); Ouinhi (483 km²) and Za-kpota (409 km²)). The study area is characterized by a transitional climate between the sub-equatorial and humid tropical Sudano-Guinean climates of northern Benin. Average annual rainfall varies between 900 and 1,200 mm. There are two rainy seasons (March to July and August to October) and the vegetative growth period varies between 80 and 100 days. The soils are ferralitic clayey-sandy bar soils, highly degraded but very well drained, with low retention capacity.

The four endemic communities are located in two health zones, CoZO (Covè, Zagnanado, Ouinhi) and ZoBoZo (Zogbodomey, Bohicon, Zakpota). This study was carried out in these two health zones. However, historical data from other localities where LF was endemic were also used.

Survey of the presence and abundance of potential LF vectors in relation to disease transmission

In the four study municipalities, mosquitoes were captured using aerosol spraying. This method involves spraying habitats (rooms with closed openings) with pyrethrin to collect the mosquito species found there. An aerosol spray was applied to paralyze mosquitoes resting inside dwellings, so that they could be collected on white sheets spread out on the floor or other flat surfaces in the dwelling. Mosquitoes in the room are stunned and fall onto the sheet. They are collected and packed in Petri dishes. In the field, an entomologist had identified the various species collected on the same day and isolated the vectors of lymphatic filariasis. The presence and abundance of vectors is then assessed. Information on the vectors (genus, species, abundance) was recorded on a collection sheet.

Modeling the spatial distribution and ecological niche of the pathogen and potential LF vectors

Occurrence data: Occurrence data on LF were collected through a survey of sick or recovered subjects with complications of the disease. Information on the subjects was obtained from the focal points of the zone hospitals in the health zones concerned by this study. Collaboration with community relays made it easier for us to locate subjects. The health data collected included patient age, sex, profession, ethnicity, place of origin, geographical coordinates and disease status. Occurrence data on *Culex* and *Anopheles* vectors, derived from field data, were also used to model spatial distribution and ecological niche. Additional data can be downloaded from the GBIF website (<https://doi.org/10.15468/dl.sq88f9>). These data were then merged to form a single database in an Excel file, analyzed and processed using R version 4.0.2 and Excel. Processing consisted of cleaning up occurrences, taxonomic verification, projection of coordinates, deletion of erroneous points of presence and duplicates, and correction of various errors and omissions, in order to obtain a clean, geo-referenced dataset suitable for use. For the correction operations, the Catalogue of Life database (www.catalogueoflife.org) was used for taxonomic verification. The Géolocate platform (www.geolocate.org) and Google Earth software (<https://earth.google.com>) were also used to verify the geographical coordinates of the patients' places of origin.

In order to reduce potential sampling bias, spatial filtering is performed on the dataset. Using the 'spThin' package in R^[8], the presence data is filtered to space the data at 5 kilometers. In the end, 125 hits were obtained to run the models.

Environmental data

Fifteen bioclimatic variables (bio1-bio7 and bio10-bio17) were downloaded from the Wordclim website (<http://www.worldclim.org/current>) at a resolution of 2.5 minutes^[9, 10] (Table 1). Future variables were downloaded from the Africlim website^[11], https://webfiles.york.ac.uk/KITE/AfriClim/GeoTIFF_150s/ under the rcp4.5 and rcp8.5 scenarios, to 2055. The AfriClim

database was chosen for future projections because it is better adapted to the ecological realities of Africa than general circulation models [11]. A collinearity test was performed on the variables previously downloaded from WorldClim with the "SP Thin" module of the R software [8]. Only selected variables were considered in the modelling process.

Table 1: Significance of the different bioclimatic variables from Worldclim 2.1

Code	Bioclimatic variables
BIO1	Annual Mean Temperature
BIO2	Mean Diurnal Range (Mean of monthly (max temp - min temp))
BIO3	Isothermality (BIO2/BIO7) (* 100)
BIO4	Temperature Seasonality (standard deviation *100)
BIO5	Max Temperature of Warmest Month
BIO6	Min Temperature of Coldest Month
BIO7	Temperature Annual Range (BIO5-BIO6)
BIO8	Mean Temperature of Wettest Quarter
BIO9	Mean Temperature of Driest Quarter
BIO10	Mean Temperature of Warmest Quarter
BIO11	Mean Temperature of Coldest Quarter
BIO12	Annual Precipitation
BIO13	Precipitation of Wettest Month
BIO14	Precipitation of Driest Month
BIO15	Precipitation Seasonality (Coefficient of Variation)
BIO16	Precipitation of Wettest Quarter
BIO17	Precipitation of Driest Quarter
BIO18	Precipitation of Warmest Quarter
BIO19	Precipitation of Coldest Quarter

Algorithms and models calibration

The species distribution model (SDM) method was chosen in this study because of its ability to predict species occurrence based on environmental characteristics [12-15], species responses to environmental change [13-16], and SDM provides graphical user interface (GUI) making them click-and-run algorithms and particularly friendly to users with less computational expertise. Algorithms used include generalized linear models (GLM), generalized additive models (GAM) [17, 18], maximum entropy modeling (MaxEnt) [19, 20], random forests (RF) [21, 22] and boosted regression trees (BRT) [23].

GLMs are an extension of "simple" linear regression models, which predict the response variable as a function of several predictor variables. GLMs find the equation that best predicts the occurrence of a species for the values of the environmental variables. The model has three important components: the probability distribution of the response variable, the linear predictor (LP), and the link function [17].

GAMs are an extension of GLMs such that predictor variables can be modeled non-parametrically in addition to linear and polynomial terms for other predictors. Therefore, GLMs are useful when the relationship between variables is expected to

be of a more complex form, not easily fitted by standard linear or nonlinear models, or when there is no a priori reason to use a particular model [17, 24].

MaxEnt is a stand-alone Java application for modeling the geographic distribution of species; an algorithm that predicts a greater proportion of species occurrence and is more useful for exploration purposes aimed at discovering new species ranges [25]. The unique feature of this algorithm is its ability to work with both continuous and categorical data [19].

BRT models are a combination of two techniques: decision tree algorithms and boosting methods [26]. This statistical method is particularly suited to explore ecological variables and to optimize prediction performance [23]. Fitting multiple trees in BRT overcomes the biggest drawback of single-tree models: their relatively poor predictive performance. Moreover, it is flexible and easy to read [26]. Moreover, BRTs take into account collinearity between variables.

RFs are recognized as one of the best technical modeling distributions measured by its predictive power [27, 28], including specifically in the context of niche modeling [16]. Its specificity is its ability to compare two types of data (presence/absence and abundance data).

For the execution of algorithms, a collinearity test was performed for the bioclimatic variables selection with the module "SP Thin" in R software [8]. This allowed to retain four bioclimatic variables which are: Bio 12, Bio 1, Bio 15, and Bio 2. The algorithms were executed in R software [29]; more precisely in the module sdm. To fit the models, the 05 algorithms are used with 10 replications, 10,000 background points was randomly generated and cross validation was used as replication method. Then to evaluate the models performance using the get_evaluations function, we focused on True Skill Statistic (TSS), Receiving Operator Curves (ROC), and Area under the Curve (AUC). The values of AUC were interpreted as proposed [30-32] : $0.50 \leq AUC \leq 0.70$: the model has low accuracy; $0.70 \leq AUC \leq 0.90$: the model has moderate accuracy; $AUC > 0.90$: the model has high accuracy. COR and TSS values can range from -1 to +1. The standard deviation was calculated in order to assess the variability of AUC and TSS values around their means. The results of distributions generated by the models were mapped using QGIS 3.24.2 software.

Results

Presence and abundance of potential LF vectors associated with disease transmission in the study area

In the field, the various mosquito captures carried out really attest to the presence of vectors. A total of three vectors were identified after capture. These were *Anopheles gambiae*, *Culex quinquefasciatus* and *Anopheles funestus* (Figure 1).

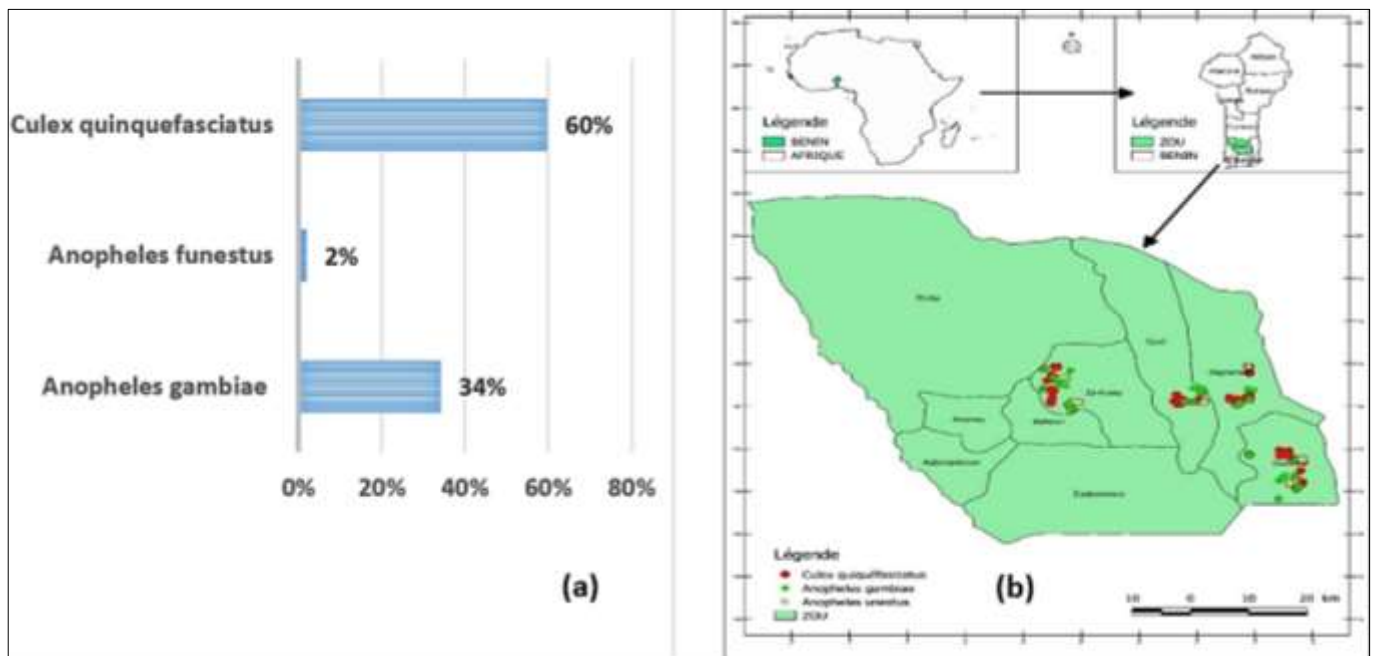


Fig 1: Vectors caught in the field: a) percentage of different vectors caught; b) spatial distribution of vectors caught.

A total of 547 *Anopheles gambiae*, 29 *Anopheles funestus* and 958 *Culex quinquefasciatus* were captured.

Culex quinquefasciatus was the most abundant vector, with 958 occurrences (Table 2).

Table 2: Diversity and abundance of mosquito species caught by commune

Municipalities	<i>Anopheles gambiae</i>	<i>Anopheles funestus</i>	<i>Culex quinquefasciatus</i>
Covè	132	0	253
Ouinhi	192	0	497
Za_kpota	72	0	105
Zagnanado	151	29	103
Total	547	29	958

Culex quinquefasciatus is the most abundant vector species, followed by *Anopheles gambiae*. It is clearly established that the abundance of *Culex quinquefasciatus* is linked to the presence of cases of lymphatic filariasis. This confirms WHO's assertion that "lymphatic filariasis is transmitted by

different types of mosquitoes, primarily of the *Culex* genus and secondarily by the *Anopheles* and *Aedes* genus". Figure 2 shows the spatial distribution of cases of lymphatic filariasis. A total of 43 occurrences of the disease were collected in the field.

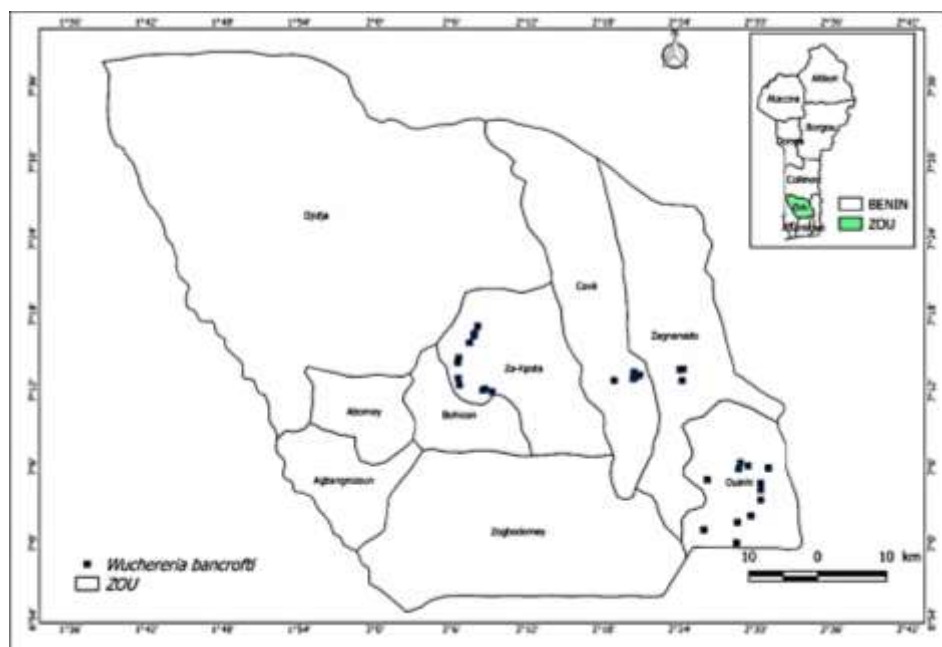


Fig 2: Spatial distribution of LF cases

Modeling the spatial distribution and ecological niche of LF

MaxEnt Models: Figure 3a shows the projected spatial distribution of LF risk areas in the present in Benin. These risk areas, shown in red, cover practically all of southern Benin. The abundance of occurrence data in southern Benin bears witness to Maxent's accuracy and performance in predicting the true presence of the disease.

In the future to 2055, scenario 4.5 indicates that disease-risk

areas cover fewer departments in southern Benin (Atlantique, Zou, collines) and a few departments in northern Benin (Alibori, Atacora) (Figure 3b. Figure 3c) shows the projection according to scenario 8.5, and the risk areas of the disease cover the departments of Atlantique, collines, Alibori and Atacora.

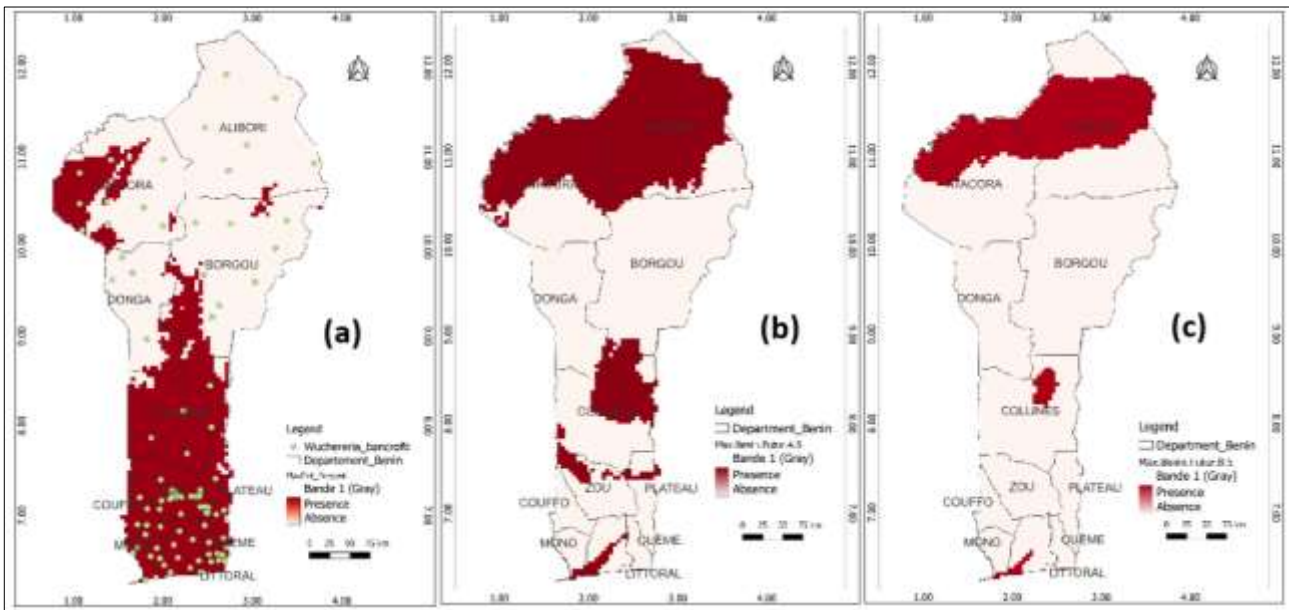


Fig 3: Projected spatial distribution of disease-risk areas in the present (a) and future, according to scenario 4.5 (b) and scenario 8.5 (c) by 2055.

GLM Models

Figure 4 shows the projected spatial distribution of disease-risk zones in the present at the scale of Benin. The disease-risk areas shown in red cover the departments of Atlantique, Littoral, Ouémé, Zou, Mono, Couffo and Plateau.

In the future, by 2055, the disease-risk areas according to scenarios 4.5 and 8.5 cover the whole of Africa, including Benin.

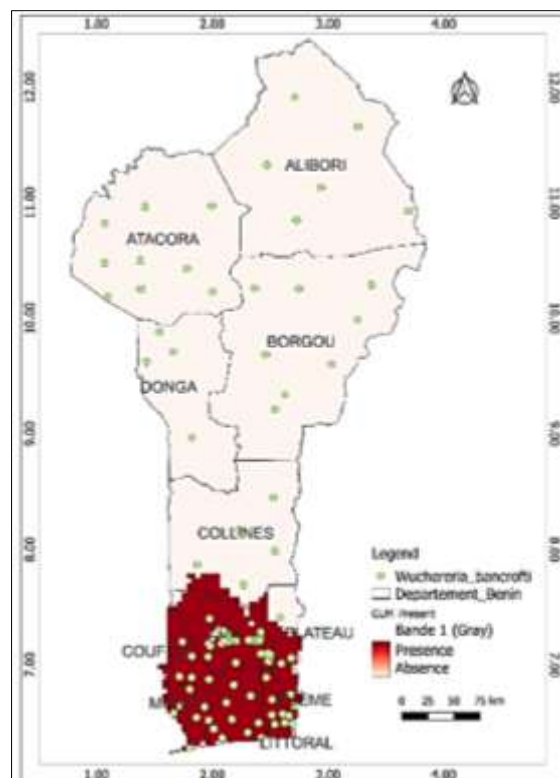


Fig 4: Projection of the spatial distribution of disease-risk areas in the present

BRT Models

Figure 5 (a) shows the projected spatial distribution of disease-risk areas under present climatic conditions. The disease risk areas shown in red cover southern Benin (the departments of Atlantique, Littoral, Collines, Ouémé, Zou,

Mono, Couffo and Plateau). In the future, by 2055, scenarios 4.5 and 8.5 present the same results. The disease risk areas cover fewer departments in southern Benin (Zou, Atlantique, Couffo, Mono, Plateau, part of the hills) and a tiny part of the Alibori department (Figure 5b).

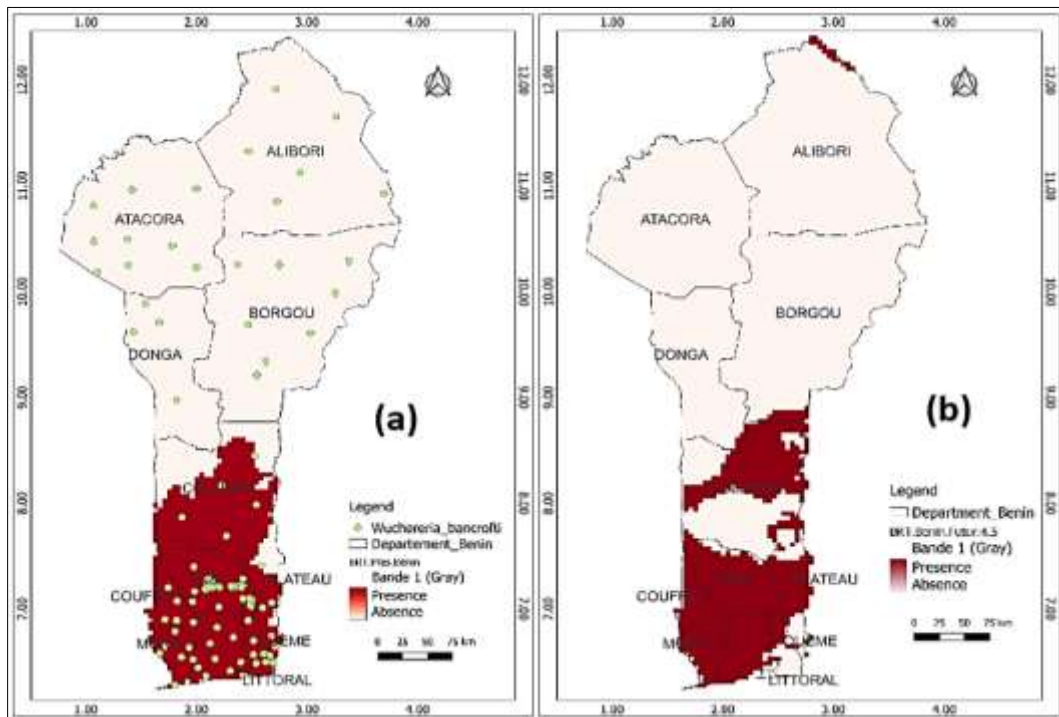


Fig 5: Projected spatial distribution of disease-risk areas in the present (a) and in the future by 2055 for scenarios 4.5 and 8.5 (b)

RF Models

Figure 6 a shows the projected spatial distribution of disease-risk areas in the present for Benin. The disease-risk areas shown in red cover the departments of Zou, Couffo, Mono,

Plateau, Atlantique, Littoral and Collines. In the future to 2055, for scenarios 4.5 and 8.5, the disease-risk zones cover all departments except part of Alibori (Figure 6b).

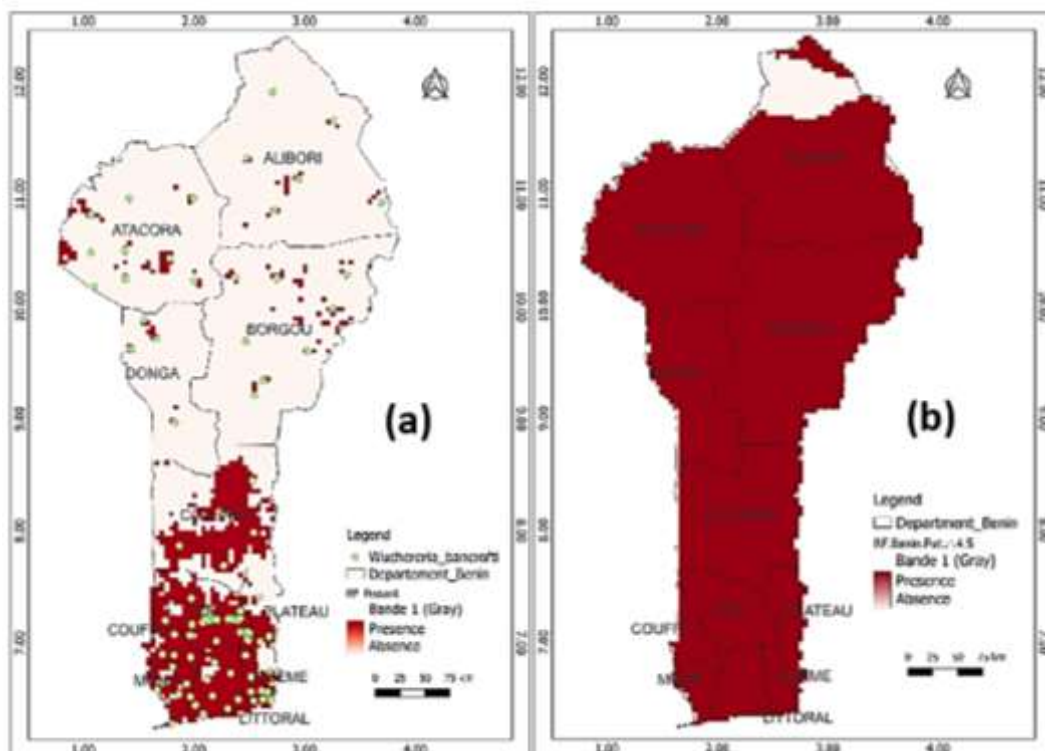


Fig 6: Projected spatial distribution of disease-risk areas in the present (a) and in the future by 2055 for scenarios 4.5 and 8.5 (b)

GAM Models

In present, Figure 7a shows the projected spatial distribution of disease-risk areas of Benin scale. The disease risk areas presence cover southern Benin. In the future to 2055, scenario 4.5, the disease risk areas cover all the departments of

southern Benin (Zou, Atlantique, Collines) and part of the departments of Alibori and Atacora (Figure 7 b). Scenario 8.5 indicates that disease-risk areas cover all southern Benin departments (Zou, Atlantique, Collines) and virtually all Alibori and Atacora departments (Figure 7 c).

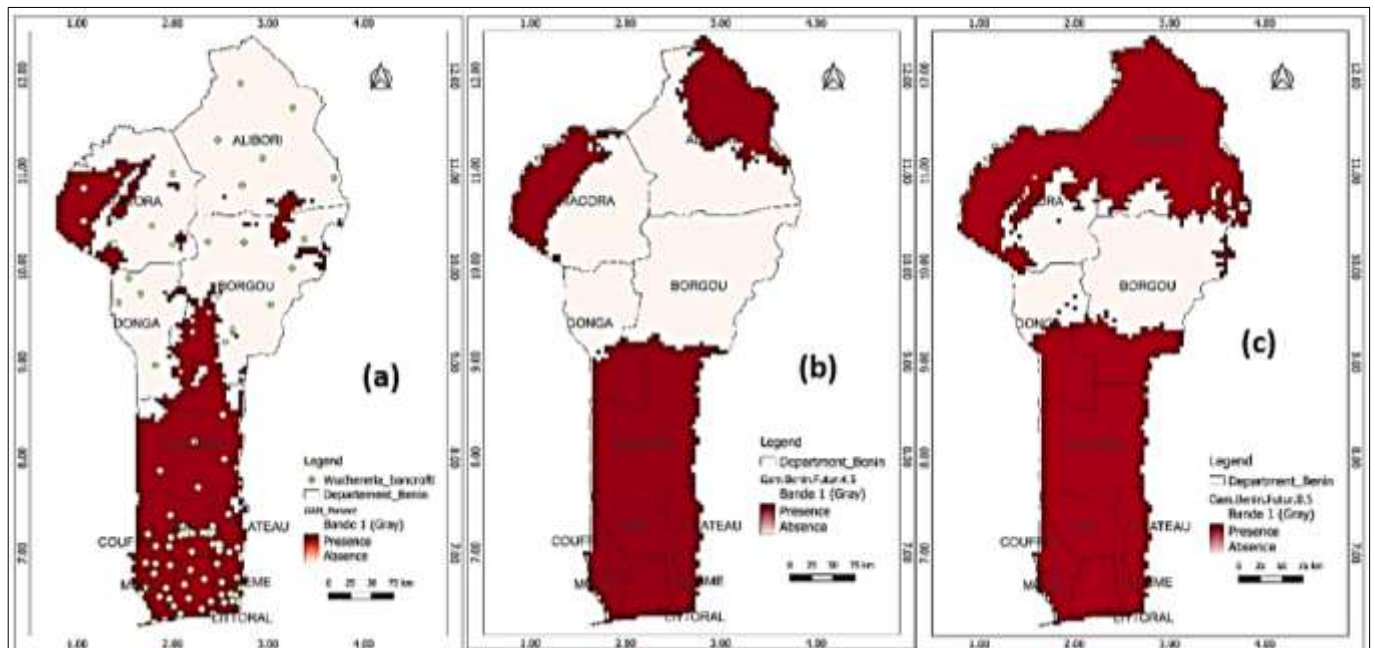


Fig 7: Projected spatial distribution of disease-risk areas in the present (a) and in the future, according to scenario 4.5 (b) and scenario 8.5 (c) by 2055.

Discussion

Bioecology of *Culex quinquefasciatus*, major vector of lymphatic filariasis, and environmental variables governing its spatial distribution: This study revealed that mosquitoes of the genus *Culex quinquefasciatus* are the most abundant in the environment of lymphatic filariasis patients, with a low presence of *Anopheles gambiae* and *Anopheles funestus*. These results are in line with those of [33-37], describing *C. quinquefasciatus* as the most widespread mosquito in the world, especially in tropical and subtropical zones, and the most important vector of the filarial parasite *Wuchereria bancrofti*. Generally speaking, *C. quinquefasciatus* is the main vector involved. A few other species are vectors, but their role is relatively secondary. These include *Anopheles gambiae* and *Anopheles funestus* [34]. In this study, bioclimatic variables such as bio 12, bio 1, bio 15 and bio 2 were retained and used in the various models. The authors: [38-41], in their work also used these same variables but only with Maxent. They claim that the models take into account relative humidity (air humidity) and larval habitats linked to precipitation. Surface moisture affects survival and development. Indeed, wetlands provide more habitats, favoring adult reproduction and survival of aquatic stages [42]. It is generally agreed that wind has a mechanical effect that induces passive transport of insects [43-45].

Algorithm performance in relation to species biology and ecology: All five modeling techniques (MaxEnt, GLM, BRT, RF, GAM) had a reasonable ability to distinguish between areas of presence and absence (all AUC > 0.75, Table 2).

The AUC makes it possible to rank the different models according to their performance. MaxEnt comes first, with 0.8

AUC and 0.06 standard deviation. Next are GAM, (AUC=0.8 and 0.07 standard deviation); BRT (AUC = 0.79 and 0.07 standard deviation); RF (AUC=0.76 and 0.07 standard deviation) and GLM (AUC = 0.75 and 0.07 standard deviation). Referring to the *Wuchereria bancrofti* occurrence data, the projection in the present testifies to MaxEnt's accuracy and performance in predicting the true presence of risk areas of Lymphatic Filariasis. MaxEnt had the best performance. BRT's and RF's performance is acceptable, but inferior to MaxEnt's in that they didn't consider all areas of presence in the occurrence data. In the present, BRT, RF and GAM were able to predict the true presences of the species with the exception of GLM, which didn't take into account abundance areas of the species like MaxEnt, BRT, RF and GAM. GLM had the weakest projections in both the present and the future, while MaxEnt had the best calibration. These results are in line with those of [29, 46]. These authors in their study found that there is a performance gap between RF / BRT and GAM / MARS. However, in their study they claim that GAM and MARS perform poorly in geographical distribution assessments, with much greater difficulty in predicting in new areas than BRT and RF. This reinforces our best results obtained with MaxEnt and BRT.

Table 2: Model performance

Algorithms	AUC (Ecartype)	COR (Ecartype)	Deviance (Ecartype)	TSS (Ecartype)
MaxEnt	0.8 (0,06)	0.38 (0,07)	1 (0,10)	0.56 (0,12)
GLM	0.75 (0,07)	0.36 (0,09)	0.56 (0,05)	0.53 (0,05)
BRT	0.79 (0,07)	0.39 (0,14)	0.54 (0,04)	0.55 (0,01)
RF	0.76 (0,07)	0.33 (0,11)	0.6 (0,09)	0.47 (0,04)
GAM	0.8 (0,07)	0.41 (0,12)	0.53 (0,07)	0.56 (0,07)

Conclusion

This study reveals that the presence of patients is linked to the presence of vectors, and that the *Culex quinquefasciatus* vector is the most abundant in the various communes studied: Covè, Ouinhi, Zangnando and Za-kpota. The spatial distribution and ecological niche modeling of *Wuchereria bancrofti* revealed that, based on the five (5) algorithms (Maxent, GLM, GAM, BRT, RF) used, the risk areas of the disease extend from southern to central Benin. However, under the effect of climate change, the disease-risk areas are likely to expand considerably by 2055, according to the 4.5 or 8.5 scenarios. Nevertheless, it should be noted that other factors influencing distribution, such as genetic adaptation, mosquito lifespan and mosquito flight capacity, need to be taken into account in order to draw conclusions that will better guide decision-making on disease eradication policy.

We suggest better organization of mass treatment campaigns, raising public awareness of the consequences of the disease and the need to use insecticide-impregnated mosquito nets, awareness campaigns on patient hygiene and management of hydrocele and lymphedema cases, and vector control more focused on *Culex quinquefasciatus*. The resistance of *Culex quinquefasciatus*, the major vector of lymphatic filariasis, suggests studies targeting epidemiological and statistical methods that maximize the programmatic effectiveness of vector control strategies aimed at eradicating lymphatic filariasis.

Author Contributions

Conceptualization, RA, TG, ASL, ET, MD, BA and JCG methodology RA, TG and JCG; software TG. and JCG; formal analysis, RA, TG and JCG; writing original draft preparation RA; writing-review and editing, RA, TG, ASL, ET, MD, BA and JCG supervision JCG; All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

The datasets used in this study are accessible upon reasonable request from the corresponding authors.

Financial support

JRS Biodiversity Foundation in collaboration with the master and Ph. D program in biodiversity informatics in Benin.

Conflict of interests

The authors have not declared any conflict of interests.

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