Predicted distribution and burden of podoconiosis in Cameroon.

Abstract

Background: Understanding the number of cases of podoconiosis, its geographical distribution and the population at risk are crucial to estimating the burden of this disease in endemic countries. We assessed each of these using nationwide data on podoconiosis prevalence in Cameroon.

Methods: We analysed data arising from two cross-sectional surveys in Cameroon. The first survey was conducted in the North West region of Cameroon in 2014 and the second corresponds to a nationwide mapping survey carried out in 2017. The assembled survey dataset was combined with a suite of environmental and climate data and analysed within a robust statistical framework, which included machine learning-based approaches and geostatistical modelling. The environmental limits, spatial variation of predicted prevalence, population at risk and number of cases of podoconiosis were each estimated.

Results: A total of 214,729 records of individuals screened for podoconiosis were gathered from 748 communities in all 10 regions of Cameroon. Of these screened individuals, 882 (0.41%; 95%CI 0.38-0.44) were living with podoconiosis. High environmental suitability for podoconiosis was predicted in three regions of Cameroon (Adamawa, North West and North). The national population living in areas environmentally suitable for podoconiosis was estimated at 5.2 (95% CI: 4.7-5.8) million, which corresponds to 22.3% of Cameroon's population in 2015. The largest proportion (32.2%) of the population at risk was found in North West region. Countrywide, in 2015, the number of adults estimated to be suffering from podoconiosis was 41,556 (95% Confidence Interval [CI], 1,170- 240,993). Four regions (Central, Littoral, North and North West) contributed 61.2% of the cases. A total of 94 out of 189 health districts are predicted to have more than 100 podoconiosis cases, however, in only 20 health districts would the predicted number exceed 500.

Conclusion: In Cameroon, podoconiosis is more widely distributed than was initially expected. The number of cases and the population at risk may pose a challenge to the national health system. Strengthening of the health system for early diagnosis of podoconiosis, morbidity management and follow up of cases is of utmost necessity. Promotion of footwear use and regular foot hygiene through social mobilization should be at the forefront of any intervention plan. Elimination of podoconiosis requires firm political will, policy formulation, operational and financial commitment by the Cameroonian Ministry of Health and donors.

Introduction

At the heart of Sustainable Development Goals (SDGs) for health is the principles of Universal Health Coverage (UHC), to promote physical and mental health well-being and to extend life expectancy for all [1].Neglected tropical disease affect the bottom billion people and their services can be a gateway to UHC[2]. Podoconiosis, a neglected tropical disease is one of the principal causes of tropical lymphedema [3, 4], which leads to massive swelling of the lower legs with the subsequent suffering to those affected [3, 5]. It is primarily a disease of barefooted individuals, who are more exposed to certain soil chemicals that trigger the lymphedema [3]. The disease is found in highland areas of tropical Africa, Central America and limited areas of India (north-west) and south-eastern Asia, according to the World Health Organization (WHO) [6, 7]. However, the actual geographical distribution and burden remain unknown in most endemic areas. Determining the burden and geographical distribution of podoconiosis is of utmost important to guide resource allocation and to monitor and evaluate the impact of prevention and control interventions put in place [3, 6]. Additionally, estimating the number of potential cases has shown to help strengthen active surveillance and inform national control strategies and case enrolment [8, 9].

Podoconiosis is caused by long-term exposure to red clay soils, with mineral particle-induced inflammation on a background of genetic susceptibility [10-15]. Interactions between genetic and environmental factors trigger an inflammatory response that leads to lymphoedema and fibrosis [3]. It is hypothesized that mineral particles that penetrate bare skin are engulfed by macrophages in the lower limb lymphatics and induce an inflammatory response in the lymphatic vessels. This is followed by fibrosis and obstruction of the vessel lumen leading to oedema of the lower leg, which progresses to elephantiasis [3].

Certain type of soils such as clay and silt soils have proven to be associated with a higher risk of podoconiosis [11-13]. Thus, soils with fine texture and sticky in nature are more easily able to penetrate the skin and become absorbed into the body [16]. Rainfall, altitude, terrain slope and some types of land cover have been found to favour the occurrence of podoconiosis [11-13]. All these factors ultimately contribute to the type of soils generated [12].

Nowadays, the availability of geographical data on soil composition, climate (i.e. temperature and precipitation) and topography, primarily derived from remotely-sensed data, and the development of robust statistical and modelling approaches, are making study of the relative contribution of all these environmental factors possible [8, 12, 13]. Studies conducted in Ethiopia, a country that is thought to bear the highest burden of podoconiosis, have enabled identification of up to eight environmental factors (elevation and derived slope, annual precipitation, EVI, clay and silt content of the top soil, population density and distance from water bodies) driving the distribution of podoconiosis across the country [12]. Other research carried out in Ethiopia, but on a more local scale, showed that soil chemicals such as smectite quartz and mica, present in clay-rich soils, were strongly associated with the occurrence of podoconiosis [13]. However, it is reasonable to think that these factors, and others that may not have been reported yet, do not equally influence the distribution of podoconiosis everywhere. Therefore, identifying environmental factors that determine the distribution of podoconiosis in distinctive geographic areas should be considered a prerequisite for delineating the global distribution of podoconiosis [3, 6, 12].

In Cameroon, another podoconiosis-endemic country, a few studies have been conducted in the north-west of the country [17-19]. Yet, the presence of this non-filarial elephantiasis elsewhere in the country and the environmental drivers underpinning its distribution remain to be determined.

Building upon our previous modelling experience in Ethiopia [8, 11, 12], we used podoconiosis prevalence data collected in two surveys in Cameroon to: i) identify the environmental drivers of podoconiosis, ii) determine its geographical limits and finally, iii) estimate the disease burden in environmentally suitable areas.

Methods

Podoconiosis prevalence data

We compiled a database of 748 geo-located prevalence records of podoconiosis in Cameroon (Figure 1). Podoconiosis prevalence data were assembled from two cross-sectional surveys conducted in Cameroon. The first survey, conducted in the North West region of Cameroon in 2014, was a cross-sectional study involving stratified and cluster sampling. The sampling design and findings of this survey are detailed in a separate publication [20]. Briefly, at least 50% of the communities from all the health areas in each of the 19 health districts of the region were screened for lymphedema of the lower limbs. Preliminary community screening was carried out by trained community health workers (CHIs), and final confirmation of podoconiosis was done by expert research assistants and health personnel following a standardized clinical diagnosis algorithm [19, 21]. Overall, in the 19 Health Districts of the North West region of Cameroon, 204,551 individuals from 672 communities were investigated for podoconiosis.

The second study was a nationwide cross-sectional survey conducted in 40 Health Districts from all 10 regions of Cameroon [22]. In this survey, seventy-six communities were randomly selected, with 10,178 individuals from 4,603 households screened for podoconiosis. Field workers used the same validated clinical diagnosis algorithm to confirm podoconiosis cases as that used in the first survey.

Explanatory environmental variables

Data on extrinsic determinants of podoconiosis was assembled from remotely sensed environmental datasets (Figure 1S). Geographic coordinates of each community were used to extract from gridded maps estimates on silt and clay soil fraction, pH of the soil, slope, precipitation, elevation, land surface temperature, distance to stable lights, enhanced vegetation index (EVI), and distance to water surfaces (water bodies and streams).

Raster datasets of averaged Enhanced Vegetation Index (EVI) and land surface temperature (LST) for the period 2000-2015 were obtained from the African Soil Information System (AfSIS) project [23]. This project generates time series average products for several environmental indicators such as vegetation indices and LST using MODIS data.

Information on rainfall was extracted from a synoptic gridded map of annual precipitation calculated from monthly total precipitation gridded datasets obtained from WorldClim database [24]. This database provides a set of global climate layers obtained by interpolation of precipitation data for the period 1950–2000 collected in weather stations distributed across the world [25]. From the Consortium for Spatial Information (CGIAR-CSI), we obtained a raster dataset of elevation at $1km^2$ [26]. This elevation layer resulted from processing and resampling the gridded digital elevation models (DEM) derived from the original 30-arcsecond DEM produced by the Shuttle Radar Topography Mission (SRTM). The elevation raster was processed to calculate terrain slope in degrees.

Soil data including silt and clay fraction and soil-pH of the top soil, were obtained from the ISRIC-World Soil Information project [27]. This project provides gridded maps of soil composition at 250m resolution worldwide. We also generated continuous surfaces of straight line distance (Euclidean distance) in km to the nearest water body and permanent rivers based on the Global Database of Lakes, Reservoirs and Wetlands [28] and Digital Global Chart [29] respectively.

Finally, night-light emissivity for 2013 captured by the Operational Linescan System instrument on board a satellite of the Defence Meteorological Satellite Programme was used as a proxy measure of poverty across Cameroon [30]. This instrument measures visible and infrared radiation emitted at night-time, resulting in remote imagery of lights on the ground. This information has been correlated with gross domestic product in developed countries [31, 32] and, although far from precise, would provide an indirect measure of poverty in developing countries [33].

Input grids were resampled to a common spatial resolution of 1km^2 using nearest neighbour approach and clipped to match the geographic extent of a map of Cameroon, and eventually aligned to it. Raster manipulation and processing was undertaken using *raster* package in R v3.3.2 and final map layouts created with ArcGIS 10.3 software (ESRI Inc., Redlands CA, USA).

Environmental modelling using machine learning approaches

An ensemble of distribution models was generated based on the reported occurrence of podoconiosis in the surveyed communities and the environmental factors. Communities were reclassified as endemic (1) or non-endemic (0) for podoconiosis based on records of confirmed podoconiosis cases. We used two machine learning based algorithms available within the BIOMOD framework [34] to obtain those ensembles of predicted distribution: generalized boosted regression tree modelling (BRT) and random forest (RF). The latter was run using the parameters set by default in the *biomod2* R package [34] whereas for the former, the learning rate (l*r)* and tree complexity (*tc*), key parameters in BRT models, were set enabling the model to account for up to four potential interactions and slowing it down enough (lr: 0.005) to get the model converged without over-fitting the data. This tuning was undertaken using the *gbm* package in R v3.3.2.

All these models are intended to discriminate the suitability of the environment for the presence of podoconiosis, and for this they need to be trained with presence and absence records. From this first modelling exercise, we had to make some decisions regarding the community data to be used due to differences on sampling design between the two cross-sectional surveys. Whilst the first survey dataset was obtained during an intensive screening exercise in a region known to be endemic for podoconiosis, the nationwide cross-sectional survey was intended to be geographically representative of disease distribution across the country. Therefore, the unbalanced representation of communities at North West region was compensated by selecting a random subset (75%) of “positive” communities (reporting podoconiosis cases) from this region and generating a set of background points or pseudo-absences [35] for the whole dataset (Figure 1). Background points were randomly selected with the underlying geographical bias as the occurrence data, as some authors have recommended it [36]. For this, we created a sampling bias surface by counting the number of occurrence records within each grid cell (1km x 1km resolution) and then extrapolated these data across Cameroon using kernel density estimation. We used *kernlab*, *ks* and *sm* R packages for running this process. Lastly, we generated the background points (n=500) from random locations weighted by the sampling bias surface [37, 38]. In order to maximise the ability of the model to discriminate between suitable and unsuitable areas, regression weights were used to down-weight pseudo-absence records, so that the summed weights of the absence and pseudo-absence records matched that of the presence records.

Figure 1 approximately here

Models were calibrated using an 80% random sample of the initial data and evaluated against the remaining 20% data using the area under the curve (AUC) of the receiver operation characteristic (ROC), the true skill statistic (TSS) [39] and the proportion correctly classified (PCC). Projections were performed 100 times, each time selecting a different 80% random sample while verifying model accuracy against the remaining 20%. The evaluation statistics (AUC and TSS) were used to select the models to be assembled based on the matching between predictions and observations. Here, models with AUC < 0.8 or TSS values < 0.7 were disregarded when assembling the final model.

The final assemble model was obtained by estimating the mean of probabilities across the selected models per grid cell. The range of uncertainties was also calculated by estimating the confidence intervals around the mean of probabilities across the ensemble per grid cell. The resulting predictive map quantifies the environmental suitability for podoconiosis. In order to convert this continuous metric into a binary map outlining the distribution limits, a threshold value of suitability was determined, above which transmission was assumed to be possible. Based on the ROC curve, the threshold value that represents a better trade-off between sensitivity, specificity and PCC was determined.

In addition, partial dependence functions were performed separately for both modelling approaches (BRT & RF) to visualise dependencies between the probability of podoconiosis occurrence and covariates. The partial dependence function shows the marginal effect of each covariate on the response after averaging the effects of all other covariates.

Geostatistical modelling to estimate disease burden

Empirical data and spatially matched covariates were then used within a geostatistical framework. We develop a geostatistical model to predict podoconiosis prevalence in environmentally suitable areas, as delineated by first modelling exercise, at village level across Cameroon. We let podoconiosis risk depend on the suite of measured risk factors mentioned above. We included spatial random effects in order to account for spatial variation in podoconiosis prevalence between villages that is not explained by the explanatory variables. We carried out validation of the model using a variogram-based procedure which tests the compatibility of the adopted spatial structure with the data. More details are provided in the supplementary material (Text 1S). The analysis was carried out using the R package *PrevMap*, which implements parameter estimation and spatial prediction of geostatistical models. This model was applied to produce continuous predictions of prevalence of podoconiosis among adults (≥15 years old) at $1km^2$ spatial resolution and probability maps of exceeding a 1% prevalence threshold, which was used to define podoconiosis endemicity. We checked the validity of the assumed covariance model for the spatial correlation using the Monte Carlo algorithm and empirical semi-variogram as described in the supplemental file (Figure 2S). Additionally, maps of the number of standard errors (SEs) from the posterior mean prevalence of podoconiosis (≥15 years) and number of cases were generated for each 1km × 1km grid location.

Gridded maps of both population density and age structure were obtained from the WorldPop project [40, 41]. We used these gridded surfaces of population estimates to compute the potential affected adult population (older than 15). An output raster dataset computing the estimated number of podoconiosis cases per grid cell was obtained by multiplying the $1km^2$ raster dataset of predictive prevalence with the corresponding adult population density surface. The same procedure was used to estimate the uncertainty range of affected population using the gridded surfaces of 95% confidence interval for predicted prevalence. These surfaces were then used to extract the aggregate number of people with podoconiosis and uncertainty range by administrative area (health districts and regions).

Results

Main outcomes of surveys

A total of 214,729 records of individuals screened for podoconiosis in 748 clusters were assembled for the current analysis from all 10 regions of Cameroon. Of the 214,729 screened individuals, 882 (0.4%; 95%CI 0.38-0.44) were positive for podoconiosis. Of the 748 clusters, 59.2% (443/748) recorded zero cases of podoconiosis. On average the number of individuals screened per cluster was 273, with 83% screening 100 or more individuals (Table 1).

Table 1 approximately here

Factors associated with podoconiosis occurrence

Figures 3S to 6S in the supplementary file show the marginal effect of each covariate on the probability of podoconiosis occurrence, whilst the relative contribution of each predictor variable on the outcome (podoconiosis prevalence) is summarized in Figure 7S (supplementary file 2). Both marginal effect plots and covariate contribution have been estimated separately for BRT and RF assemble models. Briefly, six of 11 selected environmental covariates were the major contributors to the assemble models: silt and clay fraction of top soil, precipitation, elevation, slope and distance to stable night lights (Figure 5S). In both modelling approaches, when the silt fraction exceeds 25% the probability of podoconiosis occurrence increases. The association of probability of podoconiosis and annual precipitation is steadily high over 1,000mm and sharply decreases when the annual mean rainfall goes beyond 2,000mm-2,500mm. Areas located between 1,000masl (meters above sea level) and 2,000masl are most suitable for the occurrence of podoconiosis. Slope above 10 degrees and clay fraction of the top soil exceeding 40% seem to prevent the occurrence of podoconiosis (Figures 3S to 6S).

Environmental limits of podoconiosis in Cameroon

High environmental suitability of podoconiosis was predicted in three Regions of Cameroon (Adamawa, North West and North). Absence of podoconiosis was predicted in much of South West, Littoral, East, Central and South regions (Figure 2). A suitability cut-off of 0.43 (0.39-0.45, for 95%CI lower and upper bounds, respectively) with a sensitivity of 99.6% and specificity 99.8% provided the best discrimination between presence and absence records in the training data, and therefore this threshold value was used to reclassify the predictive risk map into a binary map outlining the potential environmental limits of occurrence (Figure 8S, supplementary file 2). Uncertainty was calculated as the range of the 95% confidence interval in predicted probability of occurrence for each pixel (Figure 2) indicating high uncertainty in the northern part of the Extreme North region. Cross-validation analysis for the BRT and RF ensemble models using a 20% held-out subsample indicated their high predictive performance, with AUC values of 0.92 (95%CI: 0.9-0.94) and 0.96 (95%CI: 0.95-0.97) respectively. This high performance is also consistent through the true skill statistic, with TSS values of 0.78 (95%CI: 0.75-0.82) and 0.82 (95%CI: 0.8-0.86) for the BRT and RF models respectively.

Figure 2 approximately here

Predicted prevalence, population at risk and estimation of podoconiosis burden

The national population living in areas environmentally suitable for podoconiosis is estimated to be over 5.2 (95% CI: 4.7–5.8) million, which corresponds to 22.3% of Cameroon's population in 2015. The largest portion (32.2%) of the most-at-risk population live in the North West Region.

The predicted prevalence map showed heterogeneous distribution of podoconiosis burden across Cameroon (Figure 3). The highest prevalence of podoconiosis is predicted in four regions (Adamawa, North West, North and in some part of Extreme North). In the remaining regions, the distribution of podoconiosis would be focal and prevalence low. Nationally, we estimated 41,556 adults (95%CI, 1,170- 240,993) to be living with podoconiosis in 2015 in Cameroon (Table 2). Four regions (Central, Littoral, North and North West) contributed 61.2% of the absolute number of cases (Figure 4). The greatest proportion of all individuals with podoconiosis resided in the Central Region (17.6%). The South and East regions contributed marginally to the total number of people with podoconiosis. At least one case of podoconiosis was estimated in 170 of 189 Health Districts. A total of 94 Health Districts reported ≥100 podoconiosis cases and only 20 had more than 500 predicted cases of podoconiosis (Table 1S). We have also estimated the continuous probability of exceeding 1% podoconiosis prevalence (the threshold considered for intervention) across the endemic areas (Figure 5). Most of the areas have low probability of exceeding 1%, and only a few restricted areas at the North-West region would potentially exceed that threshold.

Figure 3 & 4 approximately here

Discussion

Podoconiosis is a highly neglected disease that is often underreported in endemic countries [3, 42]. Understanding the occurrence of podoconiosis is crucial for identifying populations at risk and to estimate the number of cases in order to scale up interventions [3]. Here, we used data on podoconiosis prevalence to model the environmental suitability, estimate the population at risk and the number of cases of podoconiosis in Cameroon. We quantified the relationship of climate, environmental and meteorological factors to the spatial distribution of podoconiosis. Our model prediction suggests marked ecological limits separating the broad areas of environmental suitability in western, central and northern parts of Cameroon from the southern and eastern parts of the country, which are considered to be free of podoconiosis.

Despite estimating a large number of individuals living in the predicted podoconiosis risk zone (5.2 million), the total number potentially affected would be relatively small (41,556 adults). This makes us think that the disease could be controlled and eliminated in Cameroon if the appropriate interventions are put in place in the most-at-risk areas. However, current intervention efforts in the country cover only a fraction of the population potentially at risk [3].

We believe this work increases insight into the epidemiology of podoconiosis and simultaneously has practical consequences for the Cameroon health system. First, the identification of areas at risk and quantification of disease burden presented in this work should support more comprehensive plans for podoconiosis control in Cameroon. The risk maps presented can help set priority areas for intervention, and lead to more rational use of available resources. Health services and surveillance systems in these at-risk areas should be prepared to diagnose podoconiosis cases correctly and provide the necessary health care that patients require. Ensuring health workers are well trained in the diagnosis and management of podoconiosis is essential.

Second, we have extended the understanding of the environmental drivers of podoconiosis. In addition to the factors identified in previous work [11, 22, 42] such as precipitation, elevation and soil composition, we have found that land surface temperature, distance from stable night-light and pH of the soil may contribute to the risk of podoconiosis occurrence. The results here indicate that, although the same suite of environmental and climatic factors drive the distribution of podoconiosis in different settings, there is spatial variation in their effect and relative contribution. The interplay among podoconiosis risk, climate, environment, and socio-economic development is inevitably complex. Our analysis highlights the fact that a focus on simple, single factors fails to adequately explain the risk of podoconiosis. This study provides an analytic framework for developing podoconiosis risk model and estimating the disease burden in other potentially endemic countries. Ultimately, it will also contribute to constructing continental and global risk maps and to estimation of the actual burden of podoconiosis at global scale [6].

Our results show that podoconiosis is present in other regions of Cameroon besides the historical endemic North West region [22]. Most of the areas where high prevalence of podoconiosis is documented are in the Cameroon Volcanic Line (CVL) [43]. The CVL is a 1,600 km chain of volcanoes, that extends along the border region of eastern Nigeria and includes islands such as São Tomé & Príncipe [44], and Bioko [16], which are also endemic for podoconiosis. These volcanic activities occurred over 1 million years ago [43], with subsequent weathering and generation of soils. Dense tropical forest has flourished over these rich soils for thousands of years, and become highly rich in clay and silt because of the decomposition of organic matter.

Podoconiosis is a significant public health problem in Cameroon, yet is still unknown to the formal health system. Although the disease was reported four decades ago [17, 45], there has been no systematic effort to map the distribution and quantify the burden in the country. The failure of many national health agencies to prioritize podoconiosis might be because of a lack of international donor assistance. Nationally, there are only small-scale interventions accessible to a fraction of patients in the North-West region of the country. Exposure to soil is common: in rural areas of Cameroon, shoes are not worn regularly [45]. They are preserved for special occasions such as attending weddings, church ceremonies and weekly markets [46]. In a survey conducted in the North West region only a handful of interviewees reported wearing shoes during farm-related activities such as planting, harvesting and working on a rice farm [20]. This is likely to have contributed to the continued presence of the disease in environmentally suitable areas. The lack of attention by national agencies and international partners and difficulties in ensuring access to preventive methods such as shoes [47] are listed among the major challenges for podoconiosis elimination.

This study had some limitations. First, most of the prevalence data gathered for this study came from the North West region of the country, which may have introduced geographical bias in the analysis. We mitigated the impact of this bias by generating more random background points around areas with more dense distribution of communities reporting podoconiosis cases. Furthermore, the nationwide mapping survey was designed to capture the potential variation of podoconiosis risk across the country. Thus, although sparse, surveyed communities were selected from the various ecological settings existing in the country. Second, although we accounted for the most significant environmental predictors when constructing our models, we did not include important risk factors which operate at individual or household level, such as shoe wearing practice and household socioeconomic status [11, 13, 48]. We tried to minimize this limitation by including a proxy measure of poverty (night-light emissivity) [33]. However, the wide confidence intervals around the estimates of prevalence and disease burden point to important risk factors which we may not yet be taking into account.

This is the first comprehensive assembly of contemporary data on podoconiosis occurrence and prevalence in Cameroon. We have applied new modelling approaches to maximize the predictive power of these data [49, 50]. However, data on podoconiosis is scant both in space and time compared to other infectious diseases and NTDs, such as soil-transmitted helminth infections [51, 52], malaria [53] and lymphatic filariasis [54]. The production of fine resolution maps of podoconiosis is contingent upon the availability of geo-referenced data. Conducting standalone podoconiosis surveys could be costly and integrating podoconiosis surveys with other standard surveys such as malaria indicator surveys, demographic and health surveys and other ongoing NTD mapping and evaluation surveys could be critical to leverage resources. Strengthening the routine surveillance of podoconiosis within the national health system framework is important to ensure sustainable data sources and to detect incident cases. A simplified case definition of podoconiosis can be included in the integrated diseases surveillances systems in endemic countries, to heighten the index of suspicion among health care providers.

Conclusion

The distribution of podoconiosis in Cameroon is wider than initially thought, according to our predictive models. The number of cases and population at risk may pose a challenge to the national health system in Cameroon. The findings presented here indicate the need for rapid scale up of interventions for those at risk and in need of care services. Promotion of footwear and foot hygiene through social mobilization will be important. Morbidity management and disability prevention services should be made accessible to those suffering from the condition. This can be achieved through the integration of care management services into the primary health system and other similar ongoing interventions. The results presented here may help decision makers to make evidence-based plans and evaluate performance.

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Tables & Figures

Table 1. General description of podoconiosis surveys conducted in Cameroon in 2014 and 2017

Table 2. Estimated number of podoconiosis cases and population at risk among adults in Cameroon in 2015.

Figure 1. Distribution of surveyed community and background points for podoconiosis across Cameroon.

Figure 2. Ensemble of predicted environmental suitability models for podoconiosis and corresponding uncertainty of prediction. Uncertainty was calculated as the range of the 95% confidence interval in predicted probability of occurrence for each pixel and rescaling to a 0-1 scale.

Figure 3. Predicted podoconiosis prevalence maps of Cameroon; mean predicted prevalence (A) and, lower (B) and upper 95% CI bounds (C).

Figure 4. Estimated number of adults (≥15 years old) with podoconiosis across Cameroon: estimated number of cases (A) and, lower (B) and upper 95% CI bounds (C)

Figure 5. Map of probability of exceeding 1% podoconiosis prevalence in Cameroon.

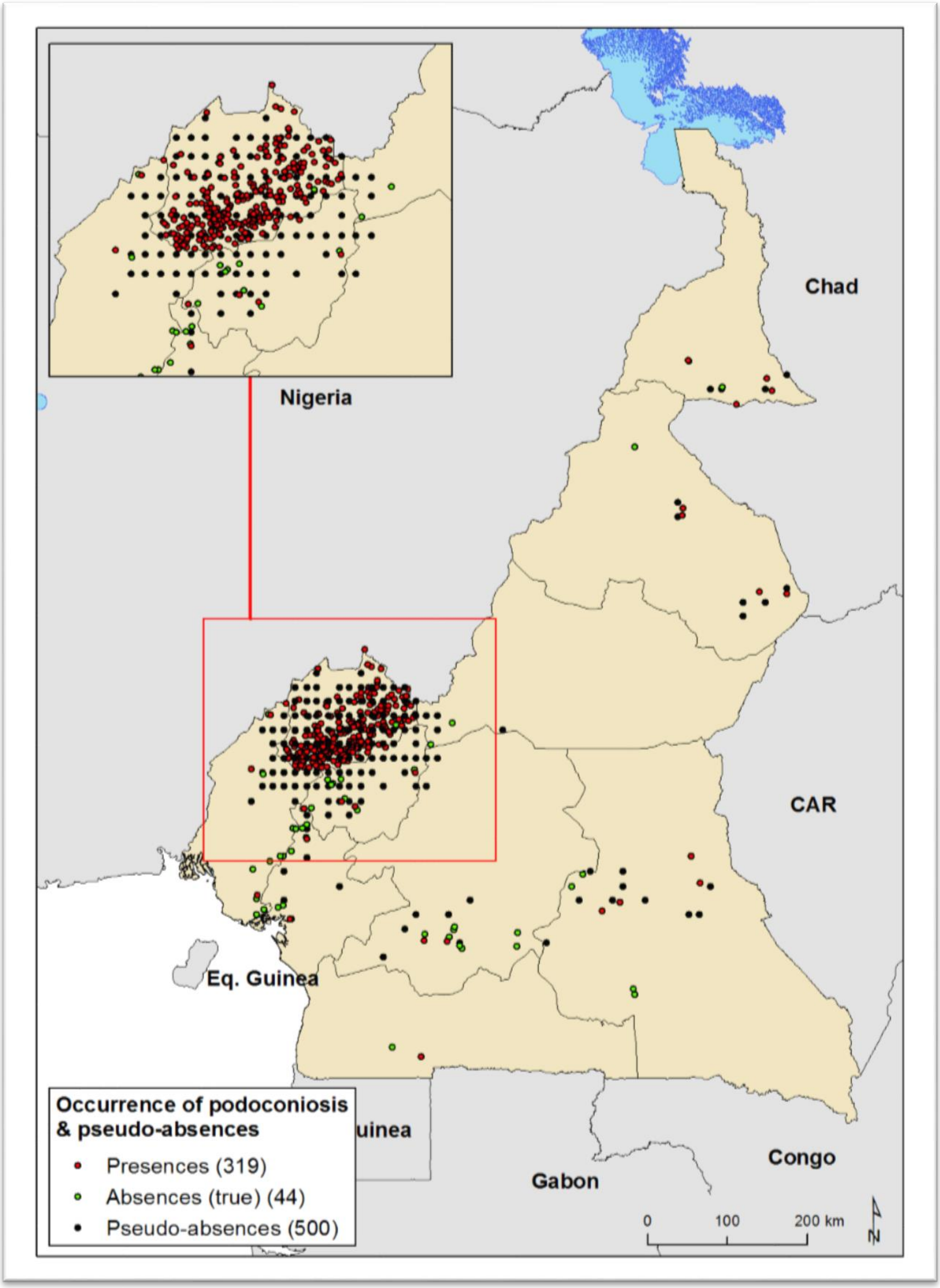
Table 1

Region	Clusters surveyed	Total surveyed	Podoconiosis cases
Adamawa	2	320	0
Central	10	1,932	4
East	8	1,195	4
Extreme North	5	803	5
Littoral	9	1,228	4
North	5	692	7
North West	681	205664	849
South	2	435	1
South West	14	1,137	3
West	12	1,323	5
Total	748	214,729	882

Table 2

	Estimated population at risk			Estimated podoconiosis burden		
Regions	**Population Estimates**	**Lower bound**	**Upper bound**	**Adult estimated cases**	**Lower Bound**	**Upper Bound**
Adamawa	381,666	361,913	420,270	2,305	49	13,831
Central	400,747	306,628	431,475	7,303	176	43,138
East	80,736	72,706	97,824	899	22	5,293
Extreme North	547,793	493,820	613,170	5,134	112	30,902
Littoral	618,549	491,969	749,893	6,186	237	34,237
North	595,335	504,622	757,766	5,840	128	35,152
North West	1,678,461	1,649,810	1,719,003	6,089	271	32,011
South	126,695	120,569	131,644	840	19	5,043
South West	203,965	193,811	229,278	2,521	59	14,867
West	583,260	546,435	652,894	4,441	99	26,519
Grand Total	**5,217,208**	**4,742,282**	**5,803,216**	**41,556**	**1,170**	**240,993**

Figure 1



Nigeria
Chad
CAR
Eq. Guinea
uinea
Gabon
Congo
Occurrence of podoconiosis & pseudo-absences
Presences (319)
Absences (true) (44)
Pseudo-absences (500)
0
100
200 km
N

Figure 2

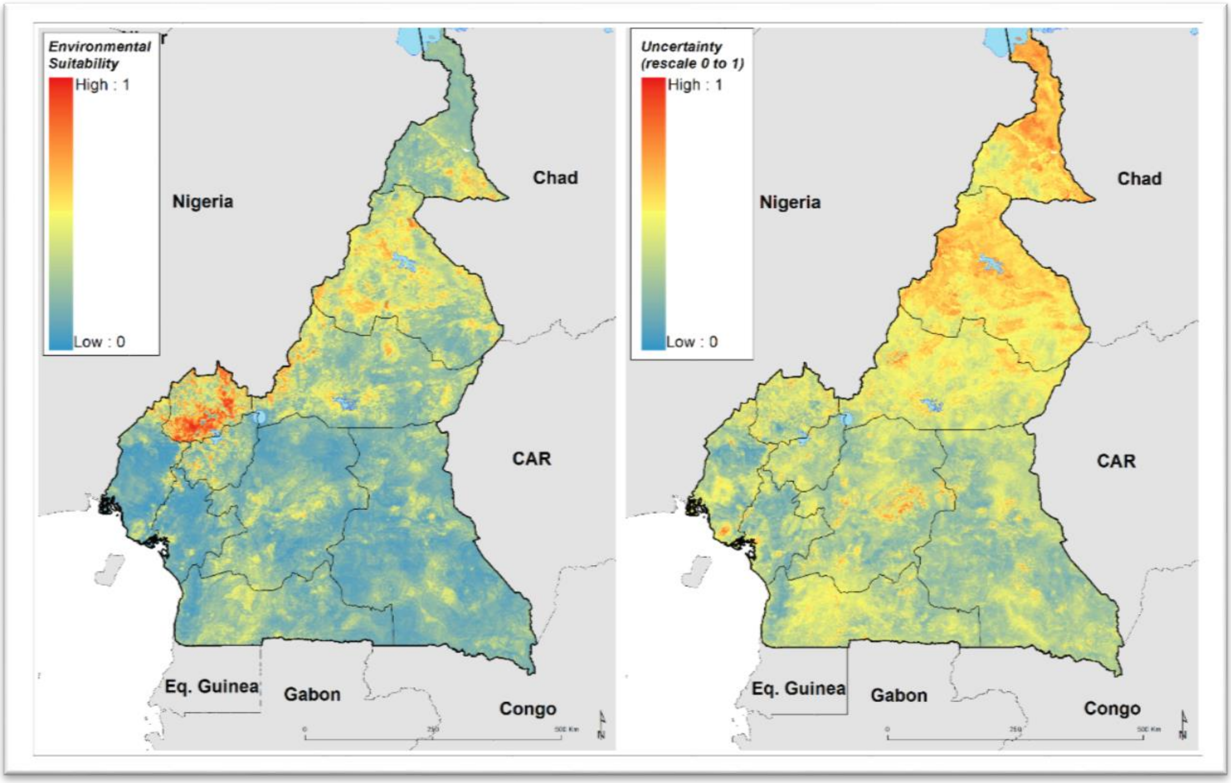

Environmental Suitability
High : 1
Low : 0
Nigeria
Chad
CAR
Eq. Guinea
Gabon
Congo
Uncertainty (rescale 0 to 1)
High : 1
Low : 0
Nigeria
Chad
CAR
Eq. Guinea
Gabon
Congo

Figure 3

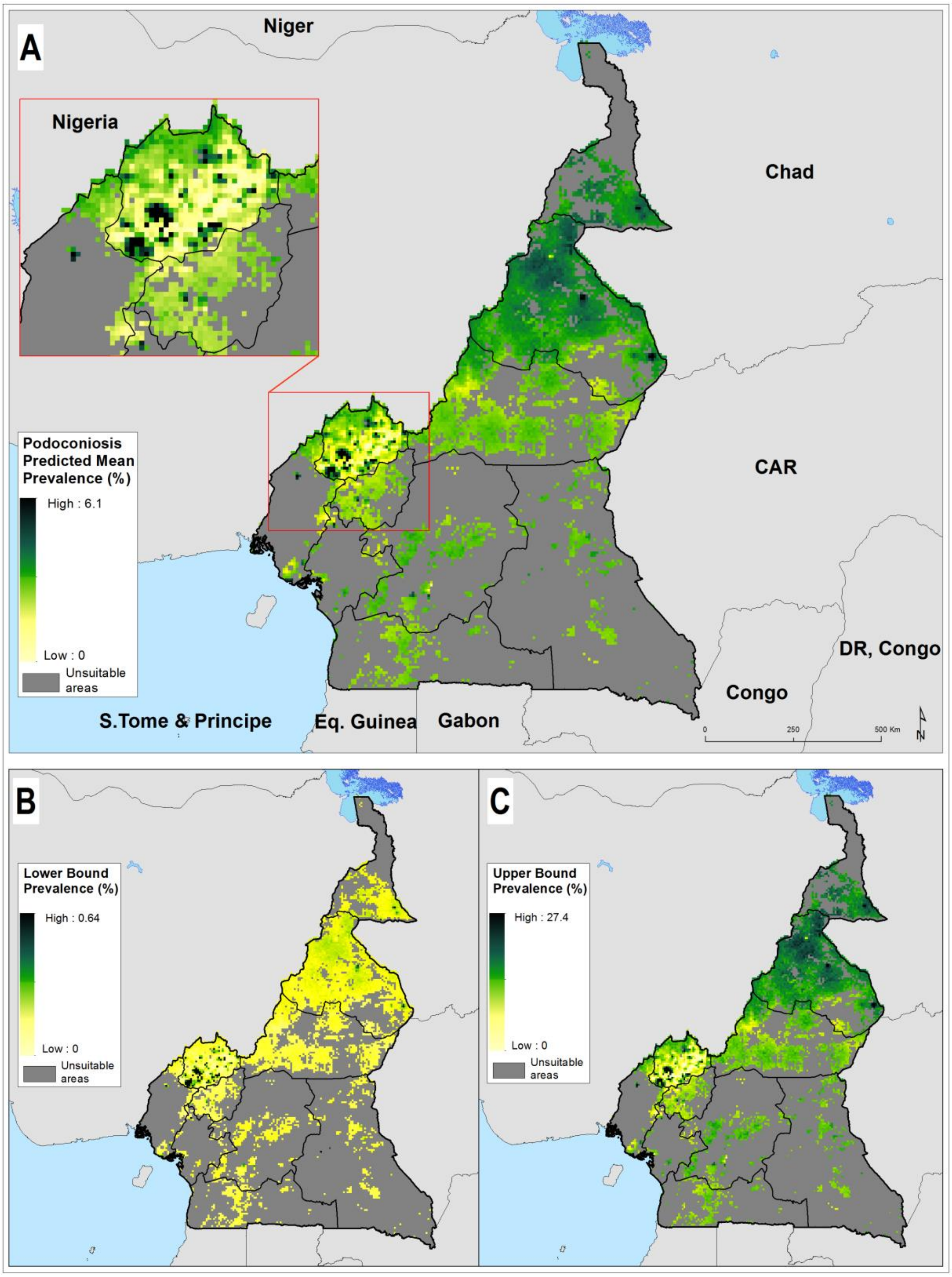

A
Niger
Nigeria
Chad
CAR
Podoconiosis Predicted Mean Prevalence (%)
High : 6.1
Low : 0
Unsuitable areas
DR, Congo
Congo
S.Tome & Principe
Eq. Guinea
Gabon
0
250
500 Km
N
B
Lower Bound Prevalence (%)
High : 0.64
Low : 0
Unsuitable areas
C
Upper Bound Prevalence (%)
High : 27.4
Low : 0
Unsuitable areas

Figure 4

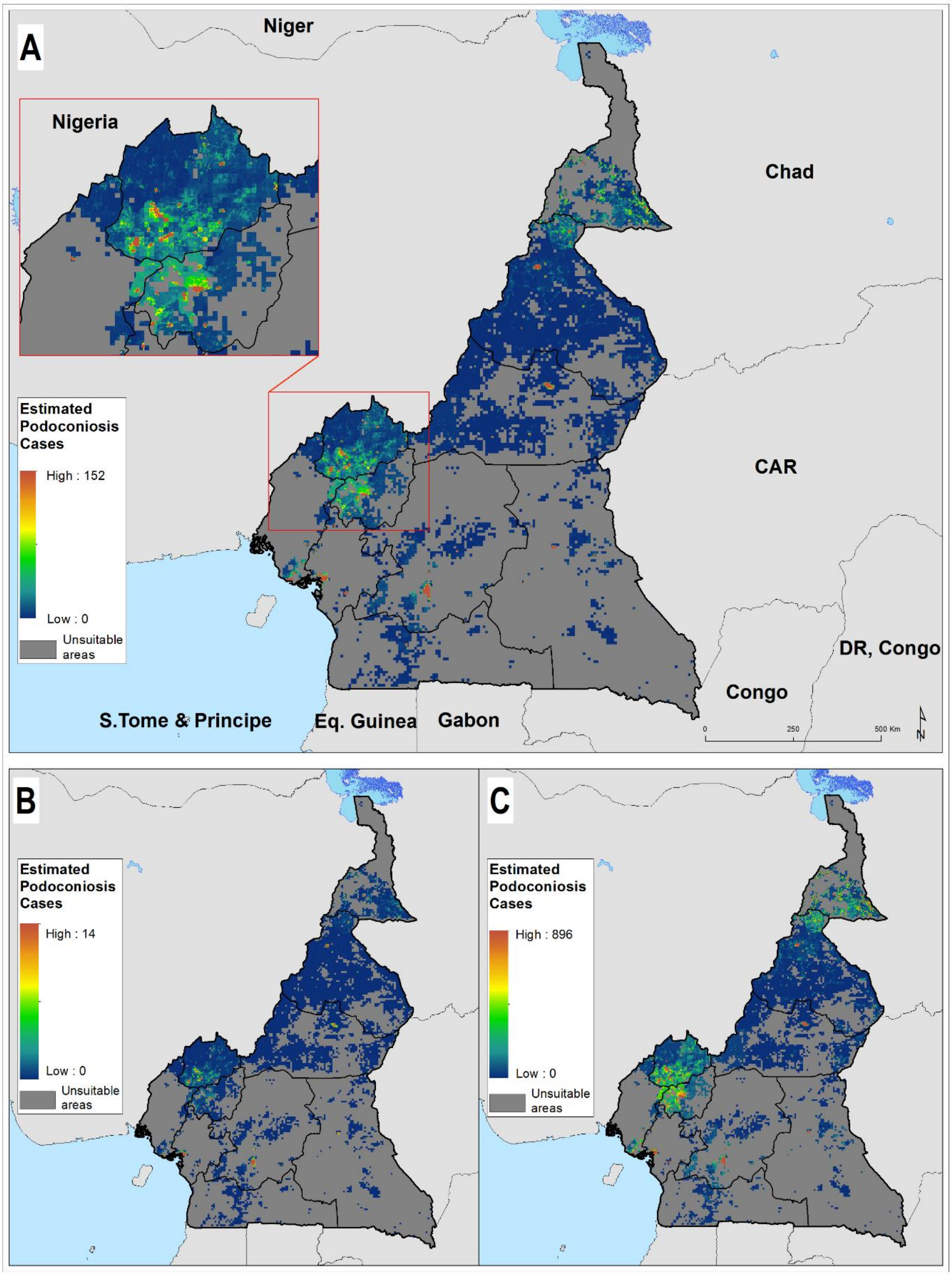
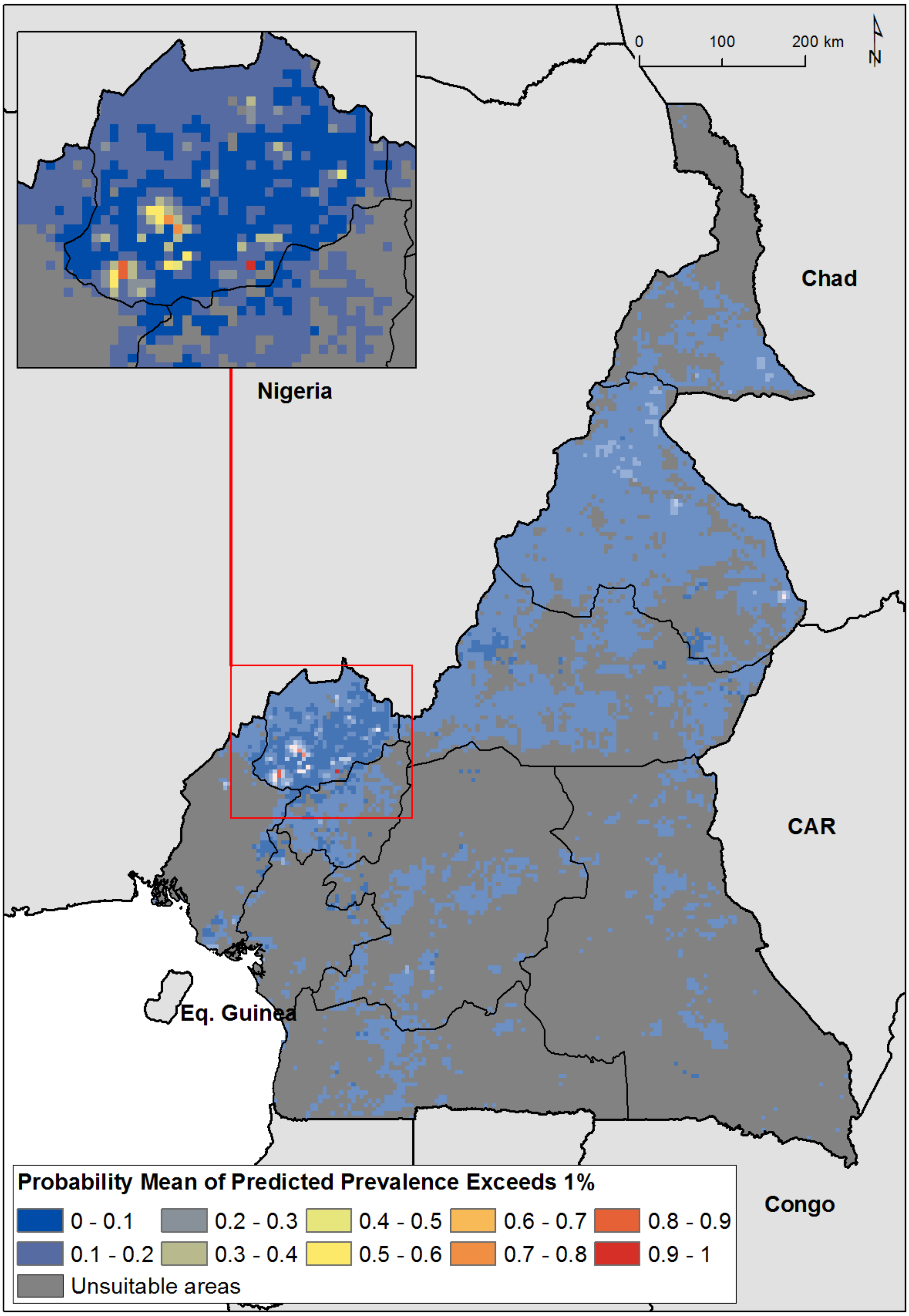

A
Niger
Nigeria
Chad
CAR
Estimated Podoconiosis Cases
High : 152
Low : 0
Unsuitable areas
DR, Congo
Congo
S.Tome & Principe
Eq. Guinea
Gabon
0
250
500 Km
B
Estimated Podoconiosis Cases
High : 14
Low : 0
Unsuitable areas
C
Estimated Podoconiosis Cases
High : 896
Low : 0
Unsuitable areas

Figure 5



0
100
200 km
N
Chad
Nigeria
CAR
Eq. Guinea
Congo
Probability Mean of Predicted Prevalence Exceeds 1%
0 - 0.1
0.2 - 0.3
0.4 - 0.5
0.6 - 0.7
0.8 - 0.9
0.1 - 0.2
0.3 - 0.4
0.5 - 0.6
0.7 - 0.8
0.9 - 1
Unsuitable areas