Final Report

Project Title:

Ecological niche modelling of strongyloidiasis, hookworm infection and opisthorchiasis in Thailand

By Dr.Apiporn Thinkhamrop

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Ecological niche modelling of strongyloidiasis, hookworm infection and opisthorchiasis in Thailand

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Abstract

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1. Abstract:

Strongyloidiasis, hookworm infection and opisthorchiasis are public health problem Thailand caused by soil-transmitted helminthes: *Strongyloides stercoralis*, *Necator americanus*, and carcinogenic liver fluke: *Opisthorchis viverrini* respectively. The correctly defining disease distribution and disease risk map is an important step in the control and prevention of diseases. This study use geographical information systems (GIS) and remote sensing (RS) technologies within the MaxEnt ecological niche modeling program to determine the climatic and environmental factors (Bioclim, NDVI, NDWI, LST, precipitation, tmin, tmax, tmean, altitude, Land cover, soil texture and soil pH) on transmission patterns of strongyloidiasis, hookworm infection and opisthorchiasis. Disease case occurrence points are from the literature reviews. Climatic and environmental data are compiled from MODIS satellite imagery, and WorldClim data for Thailand. A range of climate variables was used: the Hadley Global Environment Model 2 - Earth System (HadGEM2-ES) climate change model and also the IPCC scenarios A2a for 2050 and 2070.

The MaxEnt model's internal jackknife analyses of variable importance indicated that land cover had the highest percent contribution (22.5%). Maximum temperature in October (12.2%), Mean temperature of driest quarter (9.6%), precipitation of coldest quarter (9.6%) and normalized difference vegetation index (8.9%) were the most important individual variables influencing distribution of *S. stercoralis* in Thailand. The current distribution predicted for *S. stercoralis* in Thailand are primarily in southern and some parts of central, northern and northeastern Thailand. For hookworm infection, land cover had the highest percent contribution (24.1%). Altitude (15.1%), Minimum temperature in October (13.2%), Mean temperature of driest quarter (9.3%), were the most important individual variables influencing distribution of hookworm in Thailand. Suitable climatic and environmental conditions for hookworm are mainly in southern and some parts of central, northern and northeastern Thailand.

The current distribution of *O. viverrini* is significantly affected by precipitation and minimum temperature. According to current conditions, parts of Thailand climatically suitable for *O. viverrini* are mostly in the northeast and north, but the parasite is largely absent from southern Thailand. Under future climate change scenarios, the distribution of *O. viverrini* in 2050 should be significantly affected by precipitation, maximum temperature and mean temperature of the wettest quarter, whereas in 2070, significant factors are likely to be precipitation during the coldest quarter, maximum and minimum temperatures. Maps of predicted future distribution revealed a drastic decrease in presence of *O. viverrini* in the northeast region.

The information gained from this study should be a useful reference for implementing long-term prevention and control strategies for *S. stercoralis*, hookworm and *O. viverrini* in Thailand.

Keywords : *S. stercoralis*, hookworm, *O. viverrini*, ecological niche modeling, climate change

2. Introduction

Human strongyloidiasis and hookworm infection are neglected tropical diseases (NTDs) caused by soil-transmitted helminthes infections (*Strongyloides stercoralis*, *Necator americanus and Ancylostoma duodenale*, respectively). These diseases cause public health problem in the worldwide especially developing countries of Asia, Africa and Latin America [1]. *S. stercoralis* is able to maintain itself for decades within its host and may cause a lethal hyperinfection syndrome among immunosuppressed patients [2] [3], whereas hookworm infection is a leading cause of anemia and potentially result in growth retardation as well as intellectual and cognitive impairments especially in child [4]. Strongyloidiasis and hookworm infection have been extensively studied in Thailand especially in Northeast Thailand where the prevalence of *S. stercoralis* and hookworm was 28.9% % and 12.7%, respectively [5] . In Thailand, most of strongyloidiasis and hookworm infection patients were infected by walking barefoot over contaminated soil. The larvae of *S. stercoralis* and hookworm become infective only under favorable conditions, socio-economic and environmental factors are key to *S. stercoralis* and hookworm development and therefore to possible transmission to humans.

Opisthorchiasis, a food-borne trematode infection caused by the liver fluke *Opisthorchis viverrini* remains a major public health threat in many parts of Southeast Asia including Thailand, Lao PDR, Cambodia and some villages in South Vietnam [6,7]. *O. viverrini* has been extensively studied in Thailand where an estimated 8 million people are infected with the liver fluke [8]. *Opisthorchis viverrini* is classified as a group 1 biological carcinogen and can induce several biliary diseases including the most fatal bile-duct cancer, cholangiocarcinoma (CCA), [9,10]. Thailand has the highest incidence of CCA in the world. This liver fluke is transmitted by eating raw, fermented or insufficiently cooked cyprinoid fish caught from natural water bodies. Cyprinoid fish are frequently infected with metacercaria, the infective stage of *O. viverrini*, by contact with cercariae released from the first intermediate snail host, *Bithynia* spp.

It has long been known that climatic conditions affect epidemic diseases. Climate change is a significant driver of change in spatial patterns of parasitism and disease, as parasite distributions are directly influenced by environmental conditions such as temperature and precipitation. These changes may impact parasite survival and reproduction, as well as the availability of their transmission environment and any required intermediate hosts [11,12,13]. The Intergovernmental Panel on Climate Change (IPCC) estimates that there will be a 0.2 °C increase in temperature for each future decade [14]. Any temperature increase can greatly affect the prevalence of vector-borne parasitic diseases [15], while precipitation affects the dissemination of water-borne disease [13]. Climate change projections show increasing temperature across Thailand [16].

The correctly understanding epidemiology and spatial distribution is an important step in the control and prevention of diseases. Recent studies have used ecological niche modeling (ENMs) as a tool to predict risk areas and distribution patterns of diseases such as blastomyosis [17], malaria [18], leishmaniasis [19,20,21]. Maximum Entropy software (MaxEnt) is a general-purpose ecologic niche modeling software that is able to predicted species geographic distribution when only occurrence data is available for analysis [22,23,24]. Climate and environmental conditions affect epidemic diseases and significant driver to alter spatial patterns of parasitism and disease, as parasite distributions are directly influenced by environmental conditions such as temperature and precipitation. These changes may impact the survival, reproduction, as well as the availability and means of their transmission environment.

3. Objectives

The specific objectives of this study are to (1) determine the environmental and climate factors (Bioclim, NDVI, NDWI, LST, precipitation, tmin, tmax, tmean, altitude, Land cover, soil texture and soil pH) on distribution patterns of strongyloidiasis and hookworm infection in Thailand, (2) develop a risk map modeling for strongyloidiasis, hookworm infection and opisthorchiasis based on environmental and climate factors (3) investigate potential distributions of opisthorchiasis under projected climate conditions for 2050 and 2070.

4. Research methodology

4.1 *Strongyloides stercoralis* , hookworm and *O. viverrini* occurrence data records

Thailand is located is located in the latitudes 5° 37′ and 20° 27′ N and longitudes 97° 22′ and 105° 37′ E, which has been known as a main endemic area of STHs. A systematic literature review of *S. stercoralis* and hookworm infection was conducted to review all of research articles which published between 1970 and 2014. The publications were identified in PubMed, endnote, google and Thai-TCI by using the search terms “Thailand* AND helminth (OR Hookworms*, OR Strongyloides*)” both in English and Thai languages.

Occurrence data records of *O. viverrini* infections were obtained from two national surveys which conducted in 2009 and 2014 by the Department of Disease Control, Ministry of Public Health, Thailand, identified 426 villages and other sites where infections of *O. viverrini* occurred. These surveys were carried out in 77 provinces of Thailand [25,26]. There are 237 occurrence points of *S. stercoralis*, 822 points of hookworm and 426 points of *O. viverrini* were geocoded and then transformed into geographic coordinates (Global Coordinate System, WGS84) using ArcGIS version 10.4 (ESRI Inc., Redlands, CA, USA) (Figure 1).

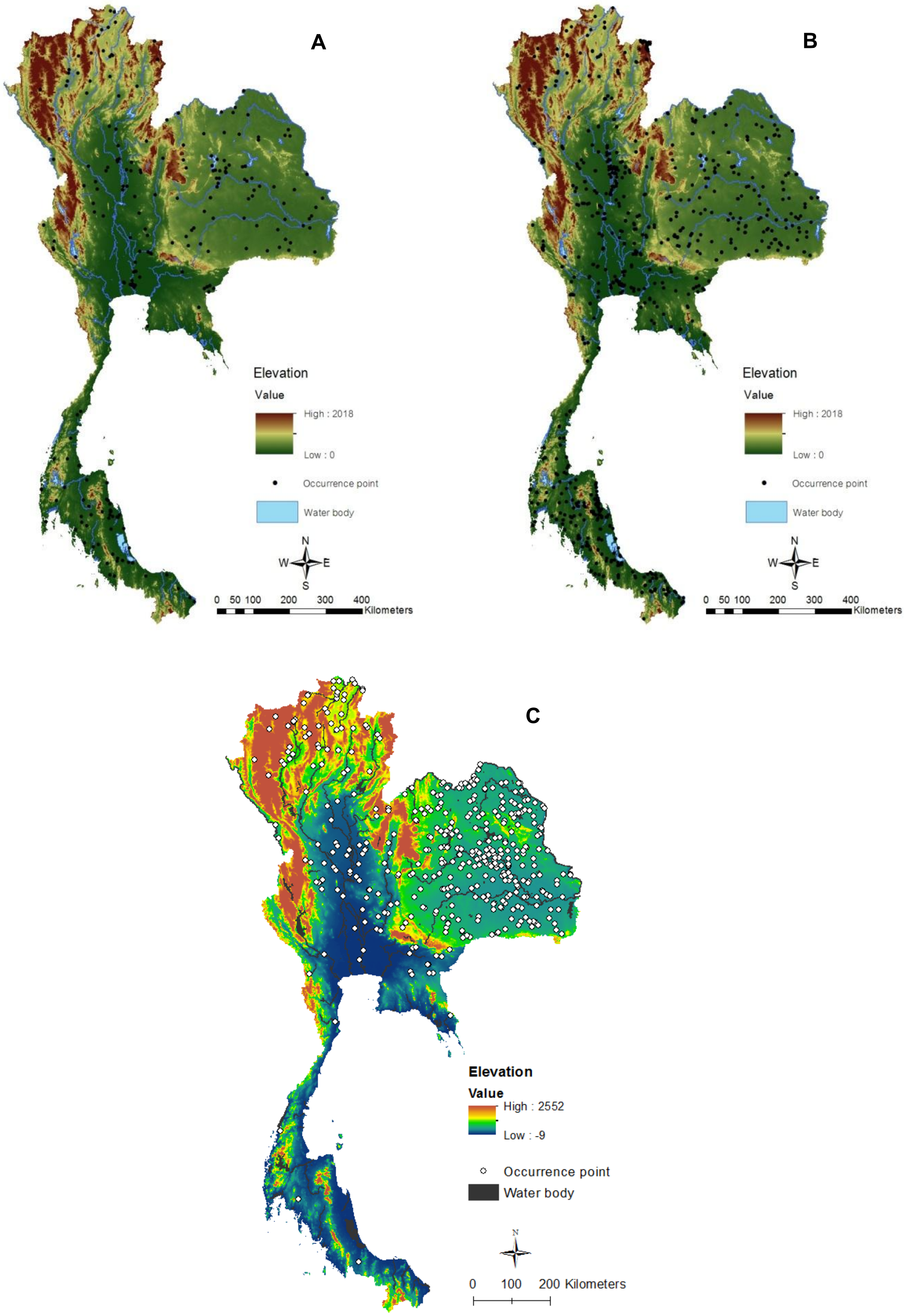


Figure 1 Occurrence point records of *S. stercoralis* (A), hookworm (B) and *O. viverrini* (C) in Thailand as baseline data.

4.2 Environmental and climate data layers

MODIS earth observing satellite time series data were used to investigate regional remote sensing features that may influence *S. stercoralis*, hookworm and *O. viverrini* distribution in Thailand. MODIS is a multispectral sensor on board the Terra satellite designed for regional scale studies with 36 bands at 250, 500 or 1000 m spatial resolution. The United States Geological Survey (USGS) generates a number of data products available free via the Internet from the USGS EROS Data Center. MODIS data products on land surface temperature (LST), normalized difference vegetation index (NDVI), normalized difference water index (NDWI). These data were obtained for the time period 1 January 2001 through 31 December, 2014 at a resolution of 0.25 km^2 and were processed to produce a mosaic covering the study area in Thailand using ArcGIS 10.4 (ESRI Inc., Redlands, CA, USA). Nearly cloud-free scenes were available during the dry season and late cold season. Altitude data were obtained from WorldClim database (www.worldclim.org). Similarity, soil pH and soil texture were obtained from https://soilgrids.org and land cover was obtained from http://www.iscgm.org/.

Current and future climatic data including 19 bioclimatic variables, precipitation, monthly minimum, maximum and mean temperatures, were downloaded from the WorldClim database (http://www.worldclim.org/), available at approximately 1 km2 (30 arc-seconds) spatial resolution (Table 1). Future climate scenario data for 2050 and 2070 (A2a emission scenario) from the global climate model of the Hadley Global Environment Model 2 - Earth System (HadGEM2-ES) was used to assess the effects of climate change. These future climate projections are based on IPCC 5AR assessment data and were calibrated and statistically downscaled using the data for 'current' conditions. Projections, grid cell size and spatial extent were processed to ensure consistency in ASCII format for MaxEnt analysis for all environmental and climatic data layers using ArcGIS 10.4 All files were projected and geo-referenced in the same system re-sampled to a grid cell size of 1 km2 spatial resolution at earth surface and converted to ASCII format.

4.3 Ecological Niche Models

MaxEnt software was used for model construction (version 3.3.3k, Available from https://www.cs.princeton.edu/~schapire/maxent/). Variables initially considered included Worldclim data (19 BioClim variables, altitude), MODIS environmental data (LST, NDVI, NDWI), land cover, soil texture and soil pH (Table 1). Data layers represented the main factors that were hypothesized to be important determinants of the distribution range of *S. stercoralis*, hookworm and *O. viverrini* in Thailand. MaxEnt analysis was run using 75% of records as training data to construct the model and the remaining 25% for testing the model. MaxEnt was initially run including all environmental and climatic variables. Of all variables, the top 12 significantly correlated environmental variables were identified and selected based on percent contribution to the model. MaxEnt was then re-run including only the top 12 variables to develop the final model. The MaxEnt modeling procedure assessed the importance of the variables contributing to *S. stercoralis*, hookworm and *O. viverrini* distribution through jackknife analysis of contribution of environmental and climatic variables to the model, the average values of area under the curve (AUC) of 10 model iterations and the average percentage contribution of each variable to the model. The performance of the model was evaluated by deriving the AUC values of the receiver operator characteristic (ROC) plot analysis within MaxEnt [22,23,27]. AUC values range from 0.5 to 1, where the former value indicates a model no different from chance and the latter gives increasingly good discrimination as it approaches 1, i.e. 0.5-0.6 = no discrimination; 0.6-0.7 = discrimination; 0.7-0.8 = acceptable; 0.8-0.9 = excellent; 0.9-1.0 = outstanding [22,23,24].

Table 1. Environmental and climate variables used for the construction of the *S. stercoralis*, hookworm and *O. viverrini* distribution niche model.

Variable	Explanation	Data source
BIO1	Annual mean temperature	WorldClim
BIO2	Mean diurnal range	WorldClim
BIO3	Isothermality	WorldClim
BIO4	Temperature seasonality	WorldClim
BIO5	Maximum temperature of warmest month	WorldClim
BIO6	Minimum temperature of coldest month	WorldClim
BIO7	Temperature annual range	WorldClim
BIO8	Mean temperature of wettest quarter	WorldClim
BIO9	Mean temperature of driest quarter	WorldClim
BIO10	Mean temperature of warmest quarter	WorldClim
BIO11	Mean temperature of coldest quarter	WorldClim
BIO12	Annual precipitation	WorldClim
BIO13	Precipitation of wettest month	WorldClim
BIO14	Precipitation of driest month	WorldClim
BIO15	Precipitation seasonality	WorldClim
BIO16	Precipitation of wettest quarter	WorldClim
BIO17	Precipitation of driest quarter	WorldClim
BIO18	Precipitation of warmest quarter	WorldClim
BIO19	Precipitation of coldest quarter	WorldClim
Tmin	Minimum temperature	WorldClim
Tmax	Maximum temperature	WorldClim
Tmean	Mean temperature	WorldClim
Alt	Altitude	WorldClim
Lu	Land cover	ISCGM
Soil tex	Soil texture	Soilgrids
Soil pH	Soil pH	Soilgrids
LST	Land surface temperature	MODIS
NDVI	Normalized difference vegetation index	MODIS
NDWI	Normalized difference water index	MODIS

5. Results

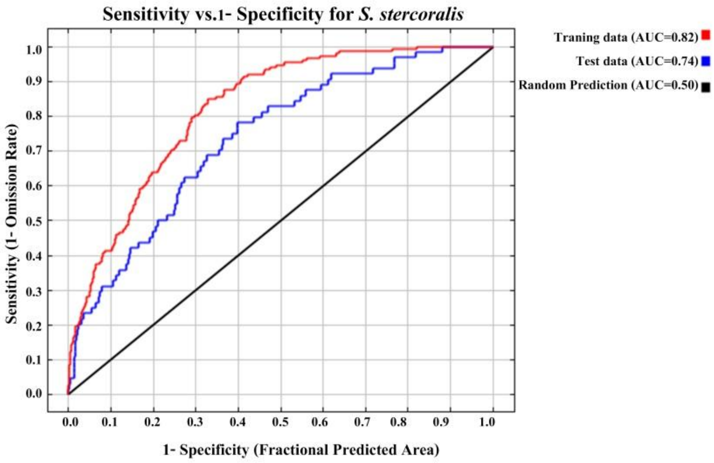
5.1 Ecological niche modelling of strongyloidiasis and hookworm infection in Thailand

In Figure 3 the receiver operating curve (ROC) of both training and test data, are shown. The red (training) line shows the “fit” of the model to the training data. The blue (testing) line indicates the “fit” of the model to the testing data, and is the real test of the models predictive power.

For strongyloidiasis, the AUC is 0.82 (Figure 2) which indicates a model of 82% validity. The MaxEnt model’s internal jackknife analyses of variable importance indicated that land cover had the highest percent contribution (22.5%). Maximum temperature in October (12.2%), Mean temperature of driest quarter (9.6%), precipitation of coldest quarter (9.6%) and normalized difference vegetation index (8.9%) were the most important individual variables influencing distribution of *S. stercoralis* in Thailand (Table 2). Figure 3A shows the current distribution predicted by MaxEnt for *S. stercoralis* in Thailand. Suitable climatic and environmental conditions are primarily in southern and some parts of central, northern and northeastern Thailand. The jackknife evaluation procedure indicated that land cover was the strongest predictor for the presence of *S. stercoralis* (Figure 4A).

For hookworm infection, the AUC is 0.78 (Figure 2) which indicates a model of 78% validity. The MaxEnt model’s internal jackknife analyses of variable importance indicated that land cover had the highest percent contribution (24.1%). Altitude (15.1%), Minimum temperature in October (13.2%), Mean temperature of driest quarter (9.3%), were the most important individual variables influencing distribution of hookworm in Thailand (Table 2, Figure 3). Figure 3B shows the current distribution predicted by MaxEnt for hookworm in Thailand. Suitable climatic and environmental conditions are mainly in southern and some parts of central, northern and northeastern Thailand. The jackknife evaluation procedure indicated that land cover was the strongest predictor for the presence of hookworm (Figure 4B).

A



B

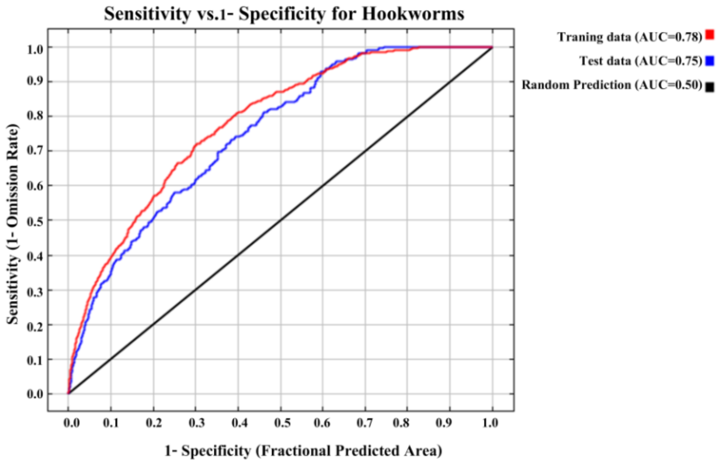


Figure 2 The average area under the curve (AUC) for 10 MaxEnt runs. The red line is the mean value for the 10 MaxEnt runs and the blue bar represents ± 1 standard deviation. The mean AUC value of 0.82 indicates an excellent model for *S. stercoralis* (A) and mean AUC value of 0.78 indicates acceptable model for hookworm (B).

Table 2 Percent contributions of the climatic and environmental variables in the MaxEnt model for STHs distribution

Variables	Percent contribution	
	S. stercoralis	**Hookworms**
Land cover (LC)	27	24.1
Prec11 Precipitation in November	3.5	8.1
Normalized difference water index (NDWI)	-	5
Prec8 Precipitation in August	-	1.2
Tmax5 Maximum temperature in May	2.8	-
Bio16 Precipitation of wettest quarter	4.2	4.9
Prec12 Precipitation in December	-	1.7
Altitude (Alt)	-	15.1
Tmin10 Minimum temperature in October	-	13.2
Bio9 Mean temperature of driest quarter	9.6	9.3
Tmin11 Minimum temperature in November	-	8.9
Bio13 Precipitation of wettest month	-	5.1
Normalized difference vegetation index (NDVI)	8.9	3.4
Tmax10 Maximum temperature in October	12.2	-
Bio19 Precipitation of coldest quarter	9.6	-
Bio18 Precipitation of warmest quarter	7.7	-
Land surface temperature (LST)	5.7	-
Prec7 Precipitation in July	5.3	-
Prec1 Precipitation in January	3.5	-

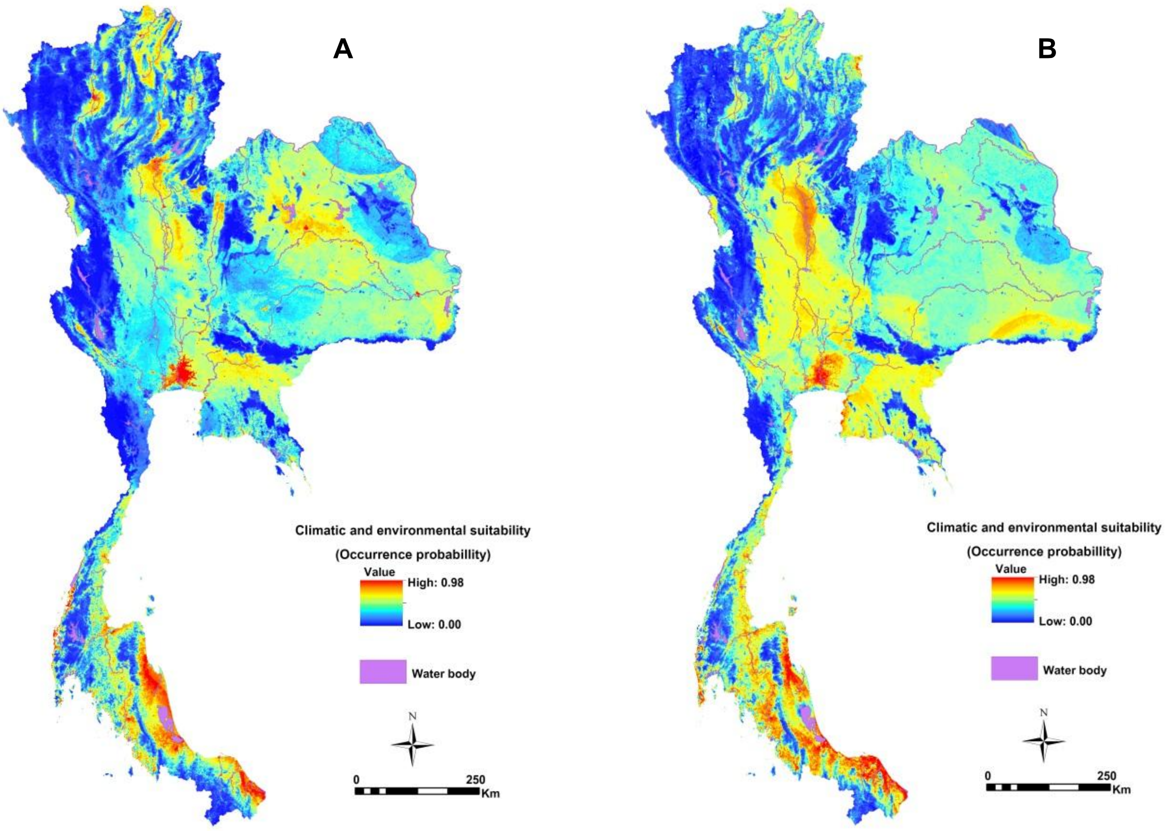
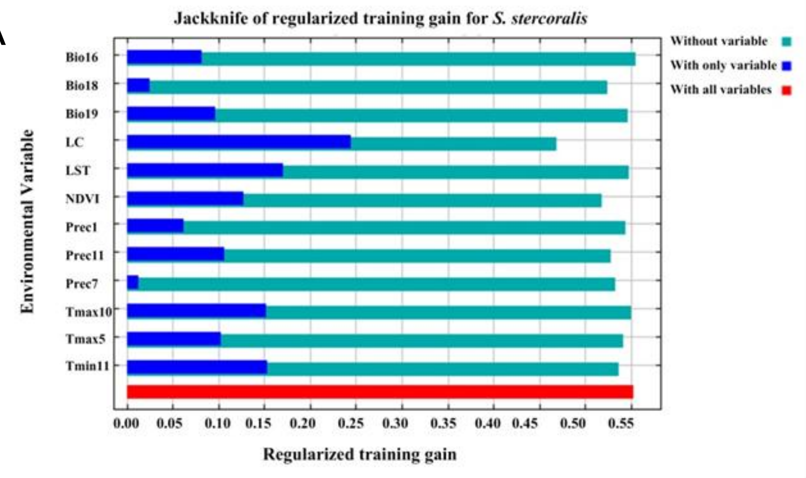


Figure 3 Predicted suitable distributions for *S. stercoralis* (A) and hookworm (B).

A



B

Figure 4 Relative predictive power of different bioclimatic variables based on the jackknife of regularized training gain in Maxent models for *S. stercoralis* (A) and hookworm (B).

5.2 Climatic niches of *O. viverrini* distribution under current climate

Based on known occurrences of *O. viverrini* and current climate data, we generated geographic distribution maps predicting areas where the parasite might occur. Predictive models performed better than random. The training AUC values were greater than 0.8 for *O. viverrini* under the current and future climatic conditions (Figure 5). These modeling results were considered to be of an excellent standard. The current distributions of *O. viverrini* were significantly affected by precipitation and minimum temperature, especially the precipitation in October (35.8%), minimum temperature in July (18.8%) and precipitation of coldest quarter (Bio19, 15%)(Table 3). The liver fluke could tolerate a broad range of precipitation in October, varying from a minimum of 41 mm to a maximum of 356 mm (Appendix C).

Figure 6A shows the current distribution predicted by MaxEnt for *O. viverrini* in Thailand. Suitable climatic conditions are primarily in northeastern and some parts of northern Thailand, but the parasite is largely absent from the southern part of the country. The jackknife evaluation procedure indicated that the precipitation in October was the strongest predictor for the presence of *O. viverrini* (Figure 7). Using the response curve (Figure 8A), the probability of *O. viverrini* presence decreased with an increase in precipitation in October, but increased with increasing minimum temperature in July.

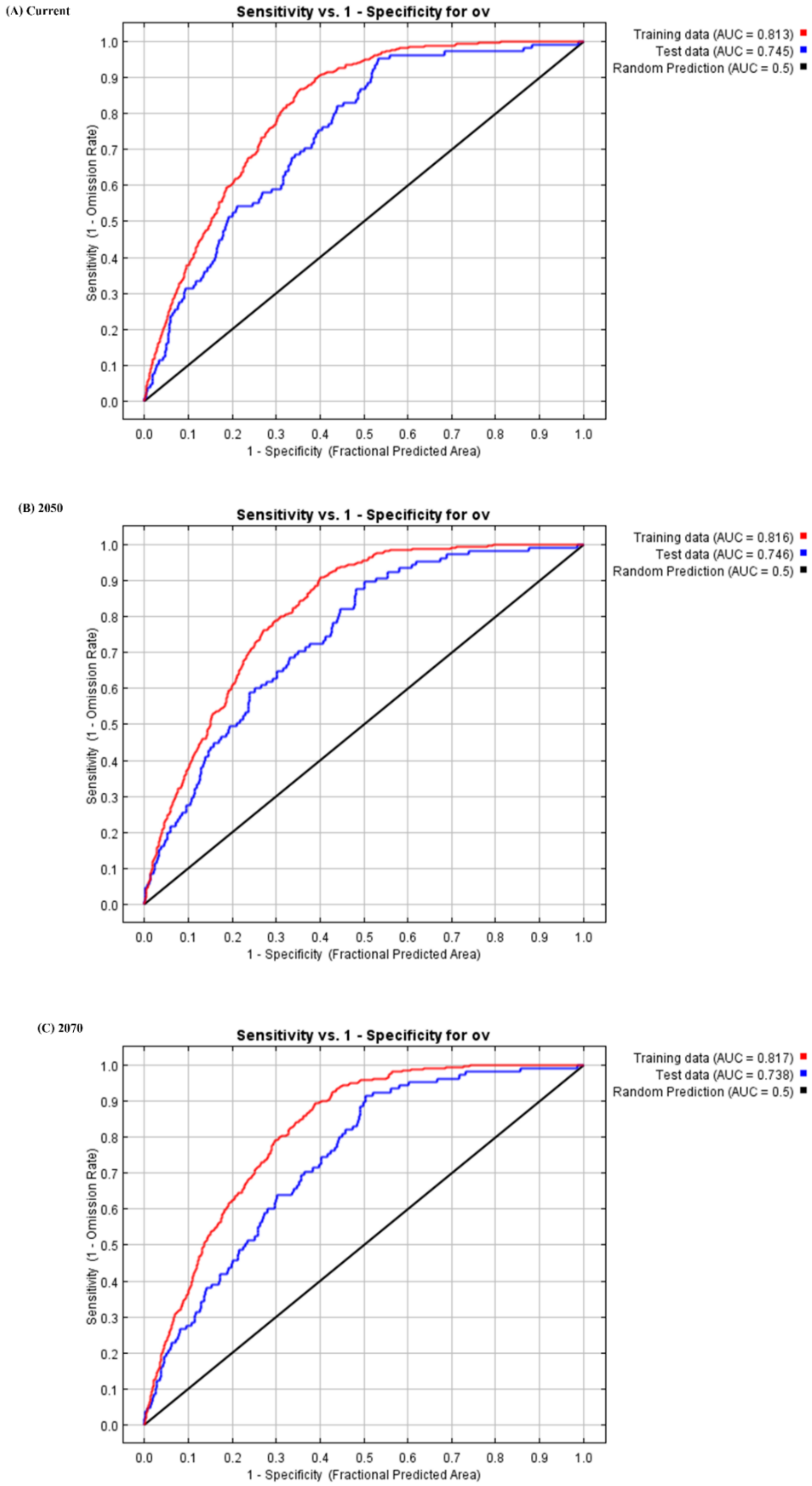


Figure 5 The average area under the curve (AUC) for 10 MaxEnt runs. The red line is the mean value for the 10 MaxEnt runs and the blue bar represents ± 1 standard deviation. The mean AUC value of 0.81 indicates a very good model.

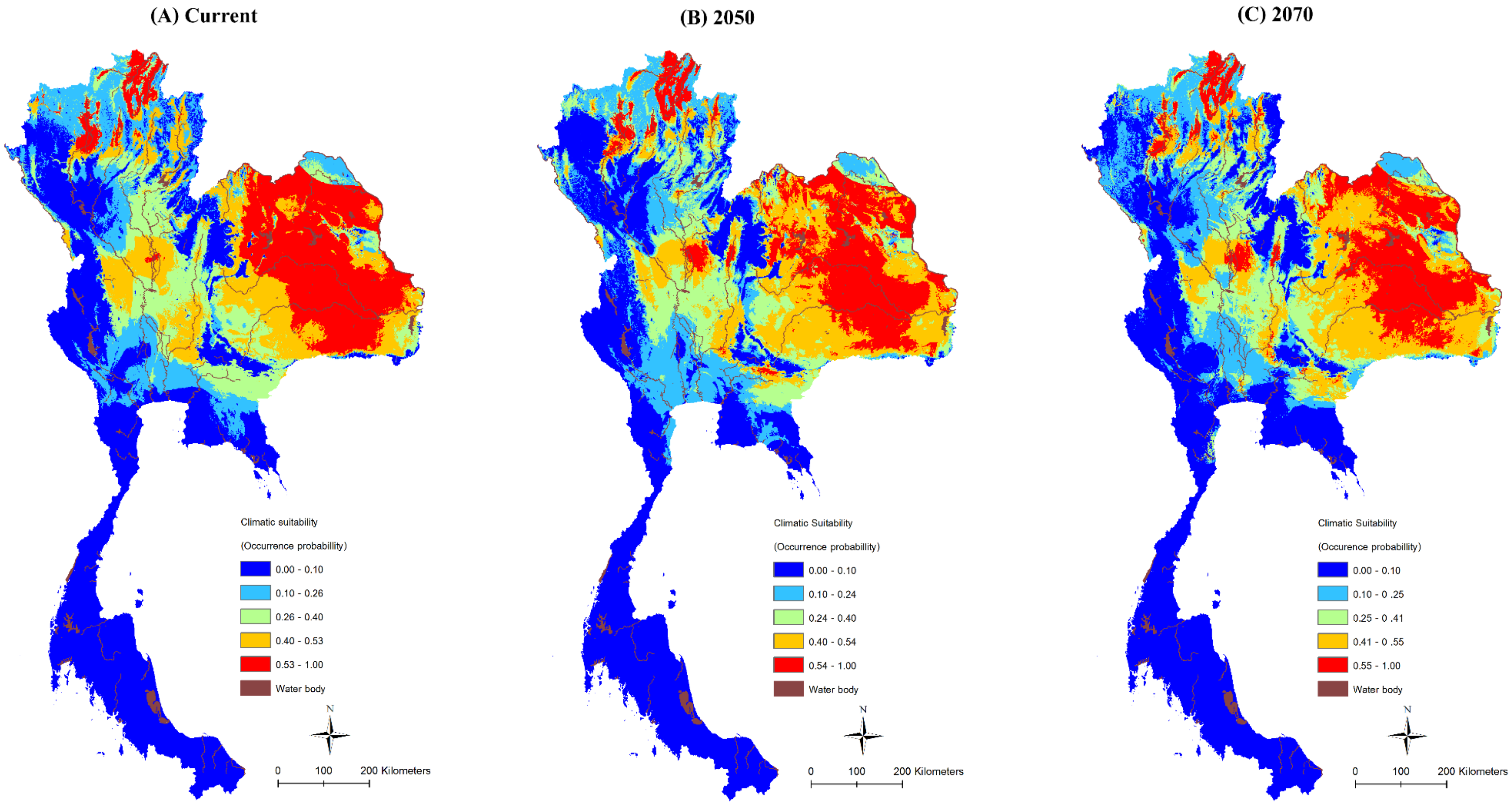


Figure 6 Predicted current (A) and future (2050 (B), 2070 (C) suitable distributions for *O. viverrini*

5.3 Consensus projections of the geographic distribution of the climatic niches for future periods

The predicted distribution of *O. viverrini* in 2050 was significantly affected by precipitation in October (32.3%), maximum temperature in May (29%) and mean temperature of the wettest quarter (6.7%), whereas in 2070, predicted distribution was largely affected by precipitation of coldest quarter (28.8%), maximum temperature in May (24.1%) and minimum temperature in July (14.8%)(Figure 7, Table 3). The climatic profiles for *O. viverrini* distribution in 2050 and 2070 are shown in Appendices D and E, respectively. The future distribution map revealed a drastic decrease in suitability in northeastern Thailand (Figure 6B and 6C). By 2050, the presence of *O. viverrini* is predicted to decrease with an increase in precipitation in October, but to increase with increasing maximum temperature in May and mean temperature of the wettest quarter (Figure 8B). By 2070, presence of *O. viverrini* is likely to decrease with increasing precipitation in the coldest quarter, but to increase with maximum temperature in May and minimum temperature in July (Figure 8C).

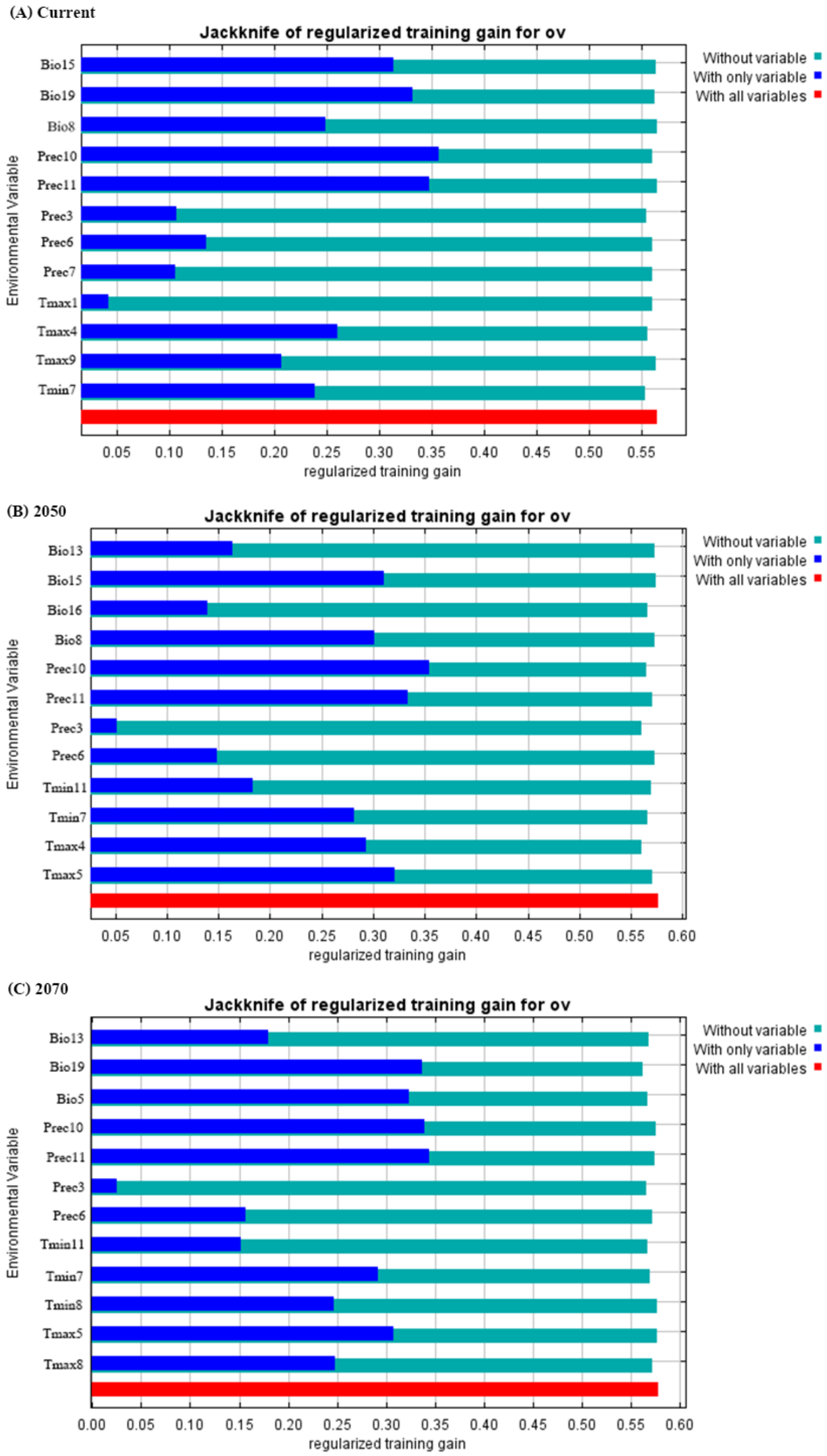


Figure 7 Relative predictive power of different bioclimatic variables based on the jackknife of regularized training gain in Maxent models for *O. viverrini* in current (A), 2050 (B) and 2070 (C)

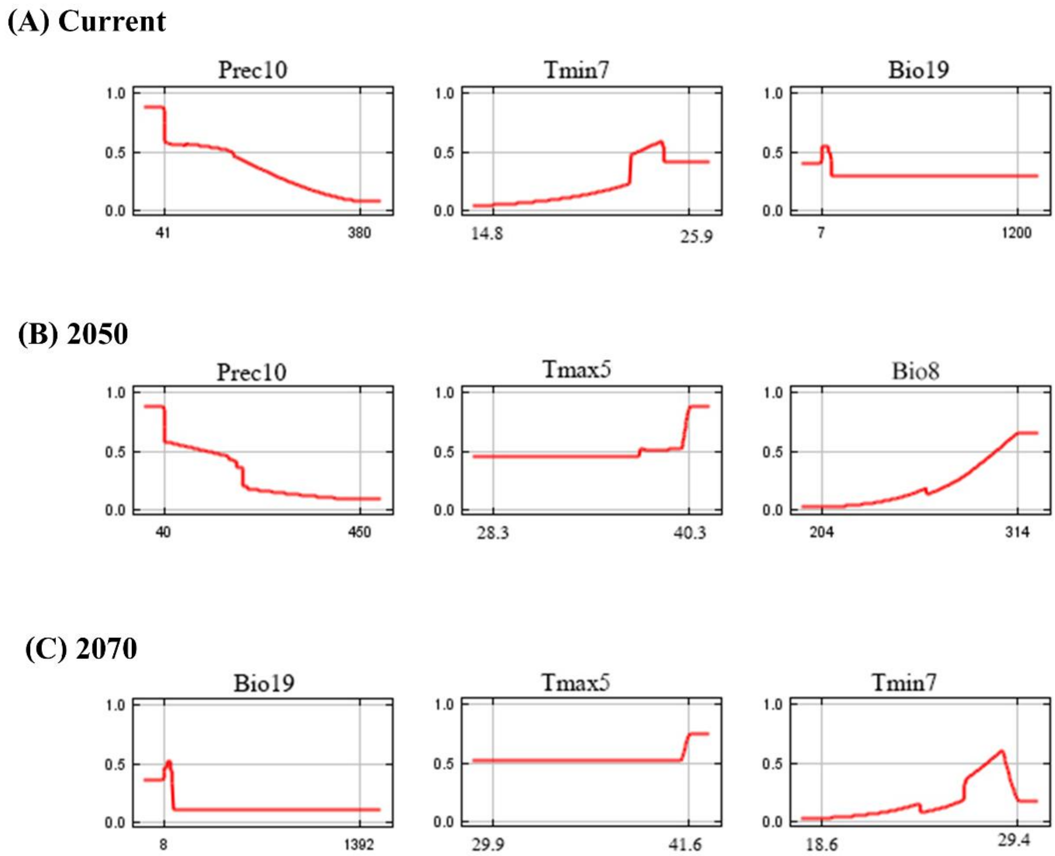


Figure 8 Response curves showing the relationships between the probability of presence and three top climatic predictors of *O. viverrini* in current (A), 2050 (B) and 2070 (C)

6. Conclusion and Discussion

We present the first to use MaxEnt model-based estimates of suitable distribution for *S. stercoralis*, hookworm and *O. viverrini* based on climatic and environmental factors in Thailand at high spatial resolution. Model validation recommended excellent predictive ability of our final models.

Our results indicate that several climatic and environmental predictors are significantly associated with *S. stercoralis* and hookworm infections. Land cover, altitude temperature and precipitation were identified as important predictors explaining the geographical distribution of *S. stercoralis* and hookworms, suggesting these factors are important driver of hookworm survival and transmission [28,29,30].

Land cover with paddy field, cropland and other vegetation mosaic are the most suitable for *S. stercoralis* distribution in Thailand, similar with the study of Khieu et al. (2014) show that land cover class corresponding to paddy field or croplands was associated with an increased risk for *S. stercoralis* infection [31]. Previous research established a relationship between land cover and the occurrence of hookworm transmission [32]. The result shows that land cover with were significantly associated with the spatial distribution of hookworm infection.

Hookworm distribution is negative affected by altitudes, hookworm prevalence were found to decrease with increasing altitude [33]. Our result finding that suitable area for hookworm mostly areas are in southern part of Thailand with low altitude. High prevalence of hookworm diseases are confined to the coastal plain below 150 m above sea level [34,35,36], but higher altitudes (above 500 m) have low prevalence of hookworm infections [37].

High or low humidity is depended by rainfall or precipitation, relationship between rainfall and *S. stercoralis* and hookworm prevalence is well-established [29]. Infection prevalence of *S. stercoralis* was significantly decreased with increasing rainfall [31]. Strongyloidiasis is prevalent in southern part of Thailand with low altitude and long rainy season resulting in stool submersion in water inhibiting growth and development of *S. stercoralis* filariform larva in the environment [38]. With rainfall being important in the transmission of hookworm infection, heavy rainfall might cause wash out hookworm eggs from the soil [39,40,41]. The water retaining properties of the soil to maintain hookworm larvae is associated with amount of rainfall. This water is restricted to the thin film around individual soil particles when the soil dries out [42]. The hookworm infective larval stage remains inactive in the moisture film until it responds to the necessary stimuli which facilitate contact with its human host [36]. Critical low and high temperatures effect to development, hatching and survival of *S. stercoralis* and hookworm eggs and larvae. Suitable temperatures for development of *S. stercoralis* and hookworm eggs to be infective stages are 20-30 °C [28,43,44].

Climate change will alter the spatial patterns of parasites worldwide [45]. In Thailand, clear evidence exists that temperatures have already increased and that rainfall patterns have changed [16]. Our analyses demonstrated that the current distribution of *O. viverrini* is significantly affected by precipitation and minimum temperature. Under the future climate-change scenarios, the distribution of *O. viverrini* in 2050 was affected by precipitation, maximum temperature and mean temperature of the wettest quarter, whereas in 2070, precipitation of the coldest quarter, maximum and minimum temperatures are the most important variables. Warmer temperatures, in particular, should support faster reproduction and longer transmission seasons of parasites with environmental reservoirs and stages; therefore, one would expect higher parasite species richness and infection rates with increasing temperature [46,47,48]. The distribution of human bacteria and helminths exhibit a positive correlation with monthly temperature ranges [12]. Precipitation is also important to consider. Guernier et al. (2004) found that the maximum annual range of precipitation corresponded positively with human parasite richness, indicating that regions with distinct dry and wet seasons may harbor more parasites. Many parasites require water or humid conditions to complete their life cycle [12], and will respond to increasing precipitation. Many helminths produce fragile eggs that cannot withstand harsh arid conditions [49], therefore drier climates can interfere with egg development. The results of this study identify the importance of climatic factors in explaining national geographical distribution of *O. viverrini* and indicate that MaxEnt is a useful tool for defining such distributions in endemic areas and for predicting distributions in areas with similar climatic conditions. Climate models are therefore suitable for assisting health planning decisions and monitoring progress on a national level. This is particularly important in data-scarce regions where resources and health data are limited, and effective resource allocation and planning are needed to have a significant impact on sustained disease control programmes.

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7. Appendix

Appendix A Climatic and environment profile of *S. stercoralis* based on its current occurrence

Variables	Max.	Min.	Mean	SD
Land cover	Paddy field Cropland / Other Vegetation Mosaic	-	-	-
Tmax10 Maximum temperature in October (°C)	32.40	28.10	30.95	0.65
Bio19 Precipitation of coldest quarter (mm)	1204.00	10.00	200.97	330.56
Tmin11 Minimum temperature in November (°C)	23.30	15.70	20.47	1.94
Normalized difference vegetation index	0.87	0.09	0.51	0.15
Bio18 Precipitation of warmest quarter (mm)	836.00	196.00	371.29	109.48
Land surface temperature	30.20	19.64	25.13	1.78
Prec7 Precipitation in July (mm)	553.00	94.00	202.01	82.90
Bio16 Precipitation of wettest quarter (mm)	1648.00	457.00	816.14	235.41
Prec1 Precipitation in January (mm)	196.00	1.00	29.51	49.52
Prec11 Precipitation in November (mm)	518.00	5.00	108.33	155.87
Tmax5 Maximum temperature in May (°C)	35.60	30.80	33.79	0.94

Appendix B Climatic and environment profile of hookworm based on its current occurrence

Variables	Max.	Min.	Mean	SD
Land cover	Paddy field Cropland / Other Vegetation Mosaic	-	-	-
Altitude	1255.00	2.00	128.78	180.94
Tmin10 Minimum temperature in October (°C)	24.50	15.50	22.51	1.28
Bio9 Mean temperature of driest quarter (°C)	27.90	16.60	25.03	2.09
Tmin11 Minimum temperature in November (°C)	23.70	12.70	20.72	2.01
Prec11 Precipitation in November (mm)	540.00	3.00	135.24	168.93
Bio13 Precipitation of wettest month (mm)	635.00	187.00	330.60	87.08
Normalized difference water index	0.67	0.06	0.42	0.12
Bio16 Precipitation of wettest quarter (mm)	1776.00	442.00	824.95	240.11
Normalized difference vegetation index	0.89	-0.09	0.56	0.15
Prec12 Precipitation in December (mm)	510.00	1.00	83.83	137.62
Prec8 Precipitation in August (mm)	619.00	87.00	218.88	92.18

Appendix C Climatic profile of *O. viverrini* based on its current occurrence

Variable	Mean	Suitable range*
Prec10 Precipitation in October (mm)	111.60	41-356
Tmin7 Minimum temperature in July (°C)	23.70	19.20-24.70
Bio19 Precipitation of coldest quarter (mm)	32.45	8-604
Bio8 Mean temperature of wettest quarter (°C)	27.35	22.7-28.40
Prec6 Precipitation in June (mm)	201.65	80-592
Bio15 Precipitation seasonality (mm)	86.84	51-104
Tmax9 Maximum temperature in September (°C)	30.98	26.50-32.30
Tmax4 Maximum temperature in April (°C)	35.52	31.80-38.10
Prec11 Precipitation in November (mm)	22.88	3-324
Prec7 Precipitation in July (mm)	223.67	97-660
Prec3 Precipitation in March (mm)	35.63	10-83
Tmax1 Maximum temperature in January (°C)	29.95	24.90-32.30

*Suitable range: The range of environmental factors which allow *O. viverrini* distribution.

Appendix D Climatic profile of *O. viverrini* based on its occurrence data in 2050

Variable	Mean	Suitable range*
Prec10 Precipitation in October (mm)	114.89	40-397
Tmax5 Maximum temperature in May (°C)	38.59	33.60-40.10
Bio8 Mean temperature of wettest quarter (°C)	30.27	25.30-31.30
Prec6 Precipitation in June (mm)	181.75	75-546
Tmax4 Maximum temperature in April (°C)	38.23	34.70-40.90
Bio16 Precipitation of wettest quarter (mm)	710.93	461-1747
Bio15 Precipitation seasonality (Coefficient of Variation)	91.66	62-106
Tmin7 Minimum temperature in July (°C)	26.54	21.80-27.70
Bio13 Precipitation of wettest month (mm)	303.34	203-676
Prec3 Precipitation in March (mm)	35.04	10-69
Prec11 Precipitation in November (mm)	22.50	2-364
Tmin11 Minimum temperature in November (°C)	22.41	17.70-26.30

* Suitable range: The range of environmental factors which allow *O. viverrini* distribution.

Appendix E Climatic profile of *O. viverrini* based on its occurrence data in 2070

Variable (unit)	Mean	Suitable range*
Bio19 Precipitation of coldest quarter (mm)	35.21	9-675
Tmax5 Maximum temperature in May (°C)	40.05	34.90-41.40
Tmin7 Minimum temperature in July (°C)	27.87	23.10-28.90
Prec6 Precipitation in June (mm)	169.22	74-567
Prec11 Precipitation in October (mm)	142.24	55-457
Bio13 Precipitation of wettest month (mm)	289.79	209-698
Bio5 Maximum temperature of warmest month (°C)	40.17	36-42.10
Tmax8 Maximum temperature in August (°C)	36.45	30.40-37.80
Tmin11 Minimum temperature in November (°C)	23.98	19.40-27.90
Prec3 Precipitation in March (mm)	43.78	10-107
Prec11 Precipitation in November (mm)	24.33	3-379
Tmin8 Minimum temperature in August (°C)	27.73	22.70-29

* Suitable range: The range of environmental factors which allow *O. viverrini* distribution.

8. Output (Acknowledge the Thailand Research Fund)

8.1 International Journal Publication

We have 1 international publication in Parasitology research and 1 manuscript preparation.

1. Suwannatrai A, Pratumchart K, Suwannatrai K, Thinkhamrop K, Chaiyos J, Kim CS, Suwanweerakamtorn R, Boonmars T, Wongsaroj T, Sripa B (2017) Modeling impacts of climate change on the potential distribution of the carcinogenic liver fluke, *Opisthorchis viverrini*, in Thailand. Parasitol Res 116: 243-250., IF 2.329
2. Mapping of soil-transmitted helminth infections in Thailand under current and future climate and environmental condition (**Manuscript in preparation**)

8.2 Application

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8.3 Others e.g. national journal publication, proceeding, international conference, book chapter, patent

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ORIGINAL PAPER

Modeling impacts of climate change on the potential distribution of the carcinogenic liver fluke, *Opisthorchis viverrini*, in Thailand

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Abstract Global climate change is now regarded as imposing a significant threat of enhancing transmission of parasitic diseases. Maximum entropy species distribution modeling (MaxEnt) was used to explore how projected climate change could affect the potential distribution of the carcinogenic liver fluke, *Opisthorchis viverrini*, in Thailand. A range of climate variables was used: the Hadley Global Environment Model 2—Earth System (HadGEM2-ES) climate change model and also the IPCC scenarios A2a for 2050 and 2070. Occurrence data from surveys conducted in 2009 and 2014 were obtained from the Department of Disease Control, Ministry of Public Health, Thailand. The MaxEnt model performed better than random for *O. viverrini* with training AUC values greater than 0.8 under current and future climatic conditions. The current distribution of *O. viverrini* is significantly affected by precipitation and minimum temperature. According to current conditions, parts of Thailand climatically suitable for *O. viverrini* are mostly in the northeast and north, but the parasite is largely absent from southern Thailand. Under future climate change scenarios, the distribution of *O. viverrini* in 2050 should be significantly affected by precipitation, maximum temperature, and mean temperature of the wettest quarter, whereas in 2070, significant factors are likely to be precipitation during the coldest quarter, maximum, and minimum temperatures. Maps of predicted future distribution revealed a drastic decrease in presence of *O. viverrini* in the northeast region. The information gained from this study should be a useful reference for implementing long-term prevention and control strategies for *O. viverrini* in Thailand.

Keywords *Opisthorchis viverrini* · Climate change · MaxEnt · Modeling · Distribution · Thailand

Electronic supplementary material The online version of this article (doi:10.1007/s00436-016-5285-x) contains supplementary material, which is available to authorized users.

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Introduction

It has long been known that climatic conditions affect epidemic diseases. Climate change is a significant driver of change in spatial patterns of parasitism and disease, as parasite distributions are directly influenced by environmental conditions such as temperature and precipitation. These changes may impact parasite survival and reproduction, as well as the availability of their transmission environment and any required intermediate hosts (Brooker et al. 2006; Guernier et al. 2004; Wu et al. 2016). The Intergovernmental Panel on Climate Change (IPCC) estimates that there will be a 0.2 °C increase in temperature for each future decade (IPCC 2007). Any temperature increase can greatly affect the prevalence of vector-borne parasitic diseases (Houghton et al. 1990), while precipitation affects the dissemination of water-borne disease (Wu et al. 2016). Climate change projections show increasing temperature across Thailand (Marks 2011).

The liver fluke, *Opisthorchis viverrini*, causes opisthorchiasis, which has a key public health impact in Thailand, Lao P.D.R., Cambodia and southern Vietnam (Keiser and Utzinger 2005; Sithithaworn et al. 2012). More infected people (an estimated 8 million) live in Thailand than in any other country (Sripa et al. 2011). *O. viverrini* is classified as a group 1 biological carcinogen and can induce several biliary diseases including the most fatal bile-duct cancer, cholangiocarcinoma (CCA) (Brindley et al. 2015; IARC 1994). Thailand has the highest incidence of CCA in the world. This liver fluke is transmitted by eating raw, fermented or insufficiently cooked cyprinoid fish caught from natural water bodies. Cyprinoid fish are frequently infected with metacercaria, the infective stage of *O. viverrini*, by contact with cercariae released from the first intermediate snail host, *Bithynia* spp.

To further opisthorchiasis control and elimination in Thailand, it is necessary to understand the climate niche of *O. viverrini* and define distribution of this disease under current and future climate conditions. Species distribution models (SDMs), which predict the relationship between species records at sites and the environmental and/or spatial characteristics of those sites, have been frequently used to define and predict disease distribution (Franklin 2009). Maximum entropy algorithm software (MaxEnt) has been developed for modeling species distributions from presence-only species records and has shown a high predictive power for both large and very small sample sizes (Elith et al. 2011; Hernandez et al. 2006; Phillips et al. 2006). In this study, the MaxEnt model was used to define the current distribution of *O. viverrini* in Thailand and to investigate potential distributions under projected climate conditions for 2050 and 2070.

Materials and methods

Study area and climate

Thailand (513,115 km^2 of land area) is located in the tropics between latitudes 5° 37′ and 20° 27′ N and longitudes 97° 22′ and 105° 37′ E. The Thai climate is controlled by tropical monsoons, and the weather is generally hot and humid across most of the country throughout most of the year. While Thailand's seasons are generally divided into the dry season (March to May), cold season (November to February), and rainy season (June to October), in reality, it is relatively hot most of the year. The weather in central, northern, and northeastern Thailand is determined by these three seasons, whereas the southern, coastal regions of Thailand feature only rainy and dry seasons. During the dry season, day temperatures may reach 42 °C, whereas during the cold season, the daytime temperature may drop to 0–10 °C. However, the average temperature of the whole country all the year round ranges from 24 to 34 °C, and the annual rainfall is about 1000–4000 mm (Thai Meteorological Department 2015).

Occurrence data records

Data obtaining from two national surveys conducted in 2009 and 2014 by the Department of Disease Control, Ministry of Public Health, Thailand identified 426 villages and other sites where infections of *O. viverrini* occurred. These surveys were carried out in 77 provinces of Thailand (MOPH 2009; MOPH 2014) (Fig. 1). The *O. viverrini* occurrence points were geocoded and then transformed into geographic coordinates (Global Coordinate System, WGS84) using ArcGIS (ESRI Inc., Redlands, CA, USA).

Climatic data

The WorldClim data are derived from measurements of altitude, temperature and rainfall from weather stations across the globe (period 1950–2000). Current and future climatic

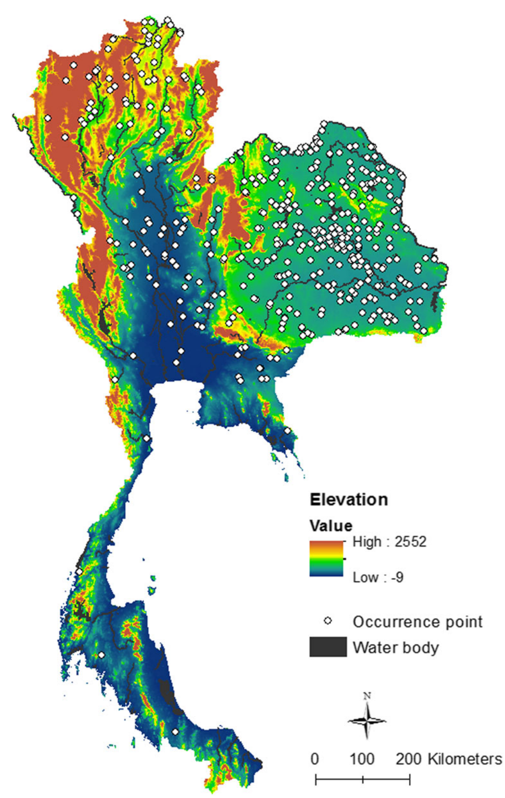


Fig. 1 *Opisthorchis viverrini* occurrence point records in Thailand in 2009 and 2014 as baseline data

data including 19 bioclimatic variables, precipitation, and monthly minimum, maximum, and mean temperatures were downloaded from the WorldClim database (http://www.worldclim.org/), available at approximately 1 km^2 (30 arc-seconds) spatial resolution (Hijmans et al. 2005) (Table 1). Future climate scenario data for 2050 and 2070 (A2a emission scenario) from the global climate model of the Hadley Global Environment Model 2—Earth System (HadGEM2-ES) was used to assess the effects of climate change. These future climate projections are based on IPCC 5AR assessment data and were calibrated and statistically downscaled using the data for 'current' conditions.

Climatic niche modeling

Climatic niche modeling (CNM) was developed to define the relationship between the geographic distribution of *O. viverrini* and those climate factors that may be related to the disease. MaxEnt (version 3.3.3k; http://www.cs.princeton.edu/wschapire/maxent/) was employed to model present and future potential distributions of *O. viverrini*. The MaxEnt modeling procedure assessed the importance of the variables contributing to *O. viverrini* distribution through the following: (i) the average percentage contribution of each climatic variable to the model, (ii) jackknife analysis of contribution of each variable to the model, and (iii) the average values of area under the curve (AUC) of 10 model iterations (Mischler et al. 2012).

MaxEnt statistical analysis was done to develop a probability surface for *O. viverrini* human prevalence points based on 2009 and 2014 baseline data. Ten iterations of the model were run including all climatic variables, with 75 % of the points used as training data and the 25 % of the points set aside to test the model. Of all variables, the top 12 significantly correlated climatic variables were identified and selected based on percent contribution to the model. MaxEnt was then re-run including only these 12 variables to develop the final model. The AUC values of the receiver operator characteristic (ROC) plot analysis within MaxEnt were used to evaluate the accuracy of the model (Hernandez et al. 2006; Phillips et al. 2006; Phillips and Dudík 2008). AUC values range between 0.5 and 1, which the former value indicates a model no different from chance and the latter gives increasingly good discrimination as it approaches 1, for example: 0.5–0.6 = no discrimination, 0.6–0.7 = unacceptable, 0.7–0.8 = acceptable, 0.8–0.9 = excellent, 0.9–1.0 = outstanding, 1 = perfect (Mischler et al. 2012; Phillips et al. 2006).

Results

Climatic niches of *O. viverrini* distribution under current climate

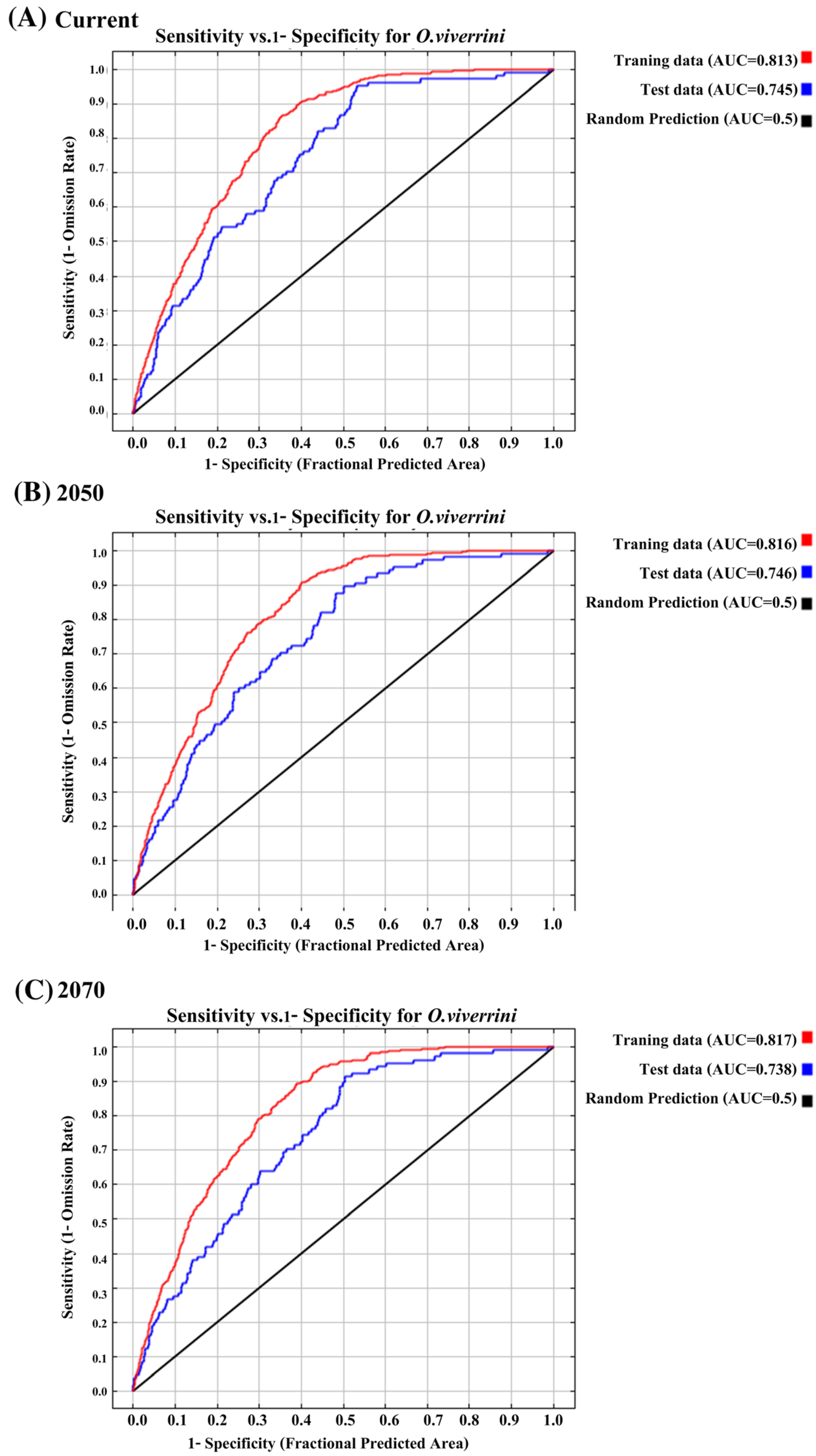
Based on known occurrences of *O. viverrini* and current climate data, we generated geographic distribution maps predicting areas where the parasite might occur. Predictive models performed better than random. The training AUC values were greater than 0.8 for *O. viverrini* under the current and future climatic conditions (Fig. 2). These modeling results were considered to be of an excellent standard. The current distributions of *O. viverrini* were significantly affected by precipitation and minimum temperature, especially the precipitation in October (35.8 %), minimum temperature in July (18.8 %), and precipitation of coldest quarter (Bio19, 15 %) (Table 2). The liver fluke could tolerate a broad range of precipitation in October, varying from a minimum of 41 mm to a maximum of 356 mm (Appendix A).

Figure 3a shows the current distribution predicted by MaxEnt for *O. viverrini* in Thailand. Suitable climatic conditions are primarily in northeastern and some parts of northern Thailand, but the parasite is largely absent from the southern part of the country. The jackknife evaluation procedure

Table 1 Climatic data used in this study

Annual mean temperature (BIO1)	Precipitation of wettest month (BIO13)
Mean diurnal range (BIO2)	Precipitation of driest month (BIO14)
Isothermality (BIO3)	Precipitation seasonality (BIO15)
Temperature seasonality (BIO4)	Precipitation of wettest quarter (BIO16)
Max temperature of warmest month (BIO5)	Precipitation of driest quarter (BIO17)
Min temperature of coldest month (BIO6)	Precipitation of warmest quarter (BIO18)
Temperature annual range (BIO7)	Precipitation of coldest quarter (BIO19)
Mean temperature of wettest quarter (BIO8)	Monthly precipitation (Prec)
Mean temperature of driest quarter (BIO9)	Monthly minimum temperature (Tmin)
Mean Temperature of warmest quarter (BIO10)	Monthly mean temperature (Tmean)
Mean temperature of coldest quarter (BIO11)	Monthly maximum temperature (Tmax)
Annual precipitation (BIO12)	

Fig. 2 The average area under the curve (AUC) for 10 MaxEnt runs. The *red line* is the mean value for the 10 MaxEnt runs, and the *blue line* represents ±1 standard deviation. The mean AUC value of 0.81 indicates an excellent model



indicated that the precipitation in October was the strongest predictor for the presence of *O. viverrini* (Fig. 4). Using the response curve (Fig. 5a), the probability of *O. viverrini* presence decreased with an increase in precipitation in October but increased with increasing minimum temperature in July.

Consensus projections of the geographic distribution of the climatic niches for future periods

The predicted distribution of *O. viverrini* in 2050 was significantly affected by precipitation in October (32.3 %), maximum

Table 2 Percent contributions of the climatic variables in the MaxEnt model for *Opisthorchis viverrini* distribution

Variables	Percent contribution		
	Current	2050	2070
Prec10 Precipitation in October	35.8	32.3	5.8
Tmin7 Minimum temperature in July	18.8	4.3	14.8
Bio19 Precipitation of coldest quarter	15	–	28.8
Bio8 Mean temperature of wettest quarter	5.2	6.7	–
Prec6 Precipitation in June	4.9	6.6	10.3
Bio15 Precipitation seasonality (coefficient of variation)	4.6	4.8	–
Tmax9 Maximum temperature in September	3.9	–	–
Tmax4 Maximum temperature in April	3.7	5.1	–
Prec11 Precipitation in November	3.1	1.1	1.3
Prec7 Precipitation in July	2.4	–	–
Prec3 Precipitation in March	1.6	1.8	1.3
Tmax1 Maximum temperature in January	1	–	–
Tmax5 Maximum temperature in May	–	29	24.1
Bio16 Precipitation of wettest quarter	–	4.8	–
Bio13 Precipitation of wettest month	–	2.5	4.1
Tmin11 Minimum temperature in November	–	0.8	1.5
Bio5 Maximum temperature of warmest month	–	–	3.6
Tmax8 Maximum temperature in August	–	–	3.5
Tmin8 Minimum temperature in August	–	–	0.9

temperature in May (29 %), and mean temperature of the wettest quarter (6.7 %), whereas in 2070, predicted distribution was largely affected by precipitation of coldest quarter (28.8 %), maximum temperature in May (24.1 %), and minimum temperature in July (14.8 %) (Table 2). The climatic profiles for *O. viverrini* distribution in 2050 and 2070 are shown in

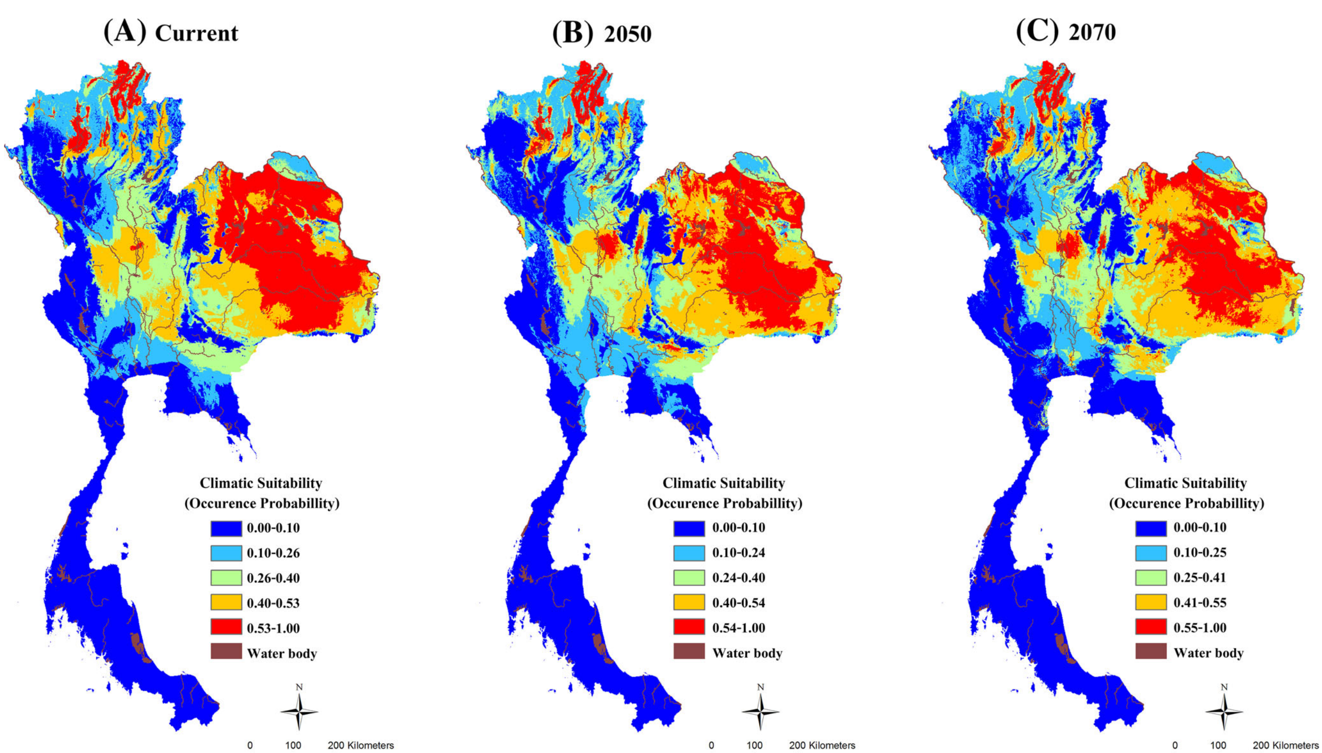


Fig. 3 Predicted current and future (2050, 2070) suitable distributions for *Opisthorchis viverrini*

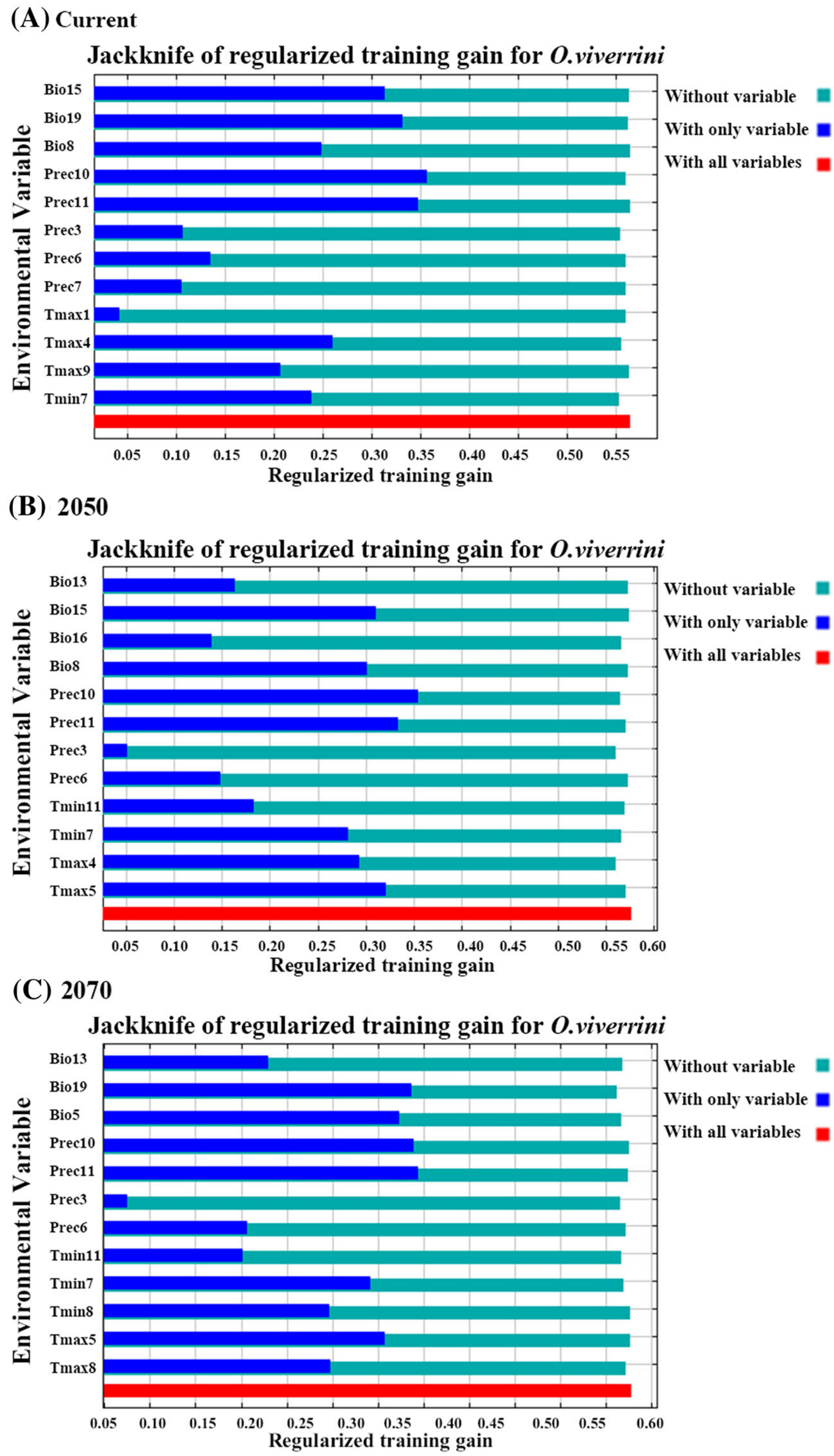


Fig. 4 Relative predictive power of different bioclimatic variables based on the jackknife of regularized training gain in MaxEnt models for *Opisthorchis viverrini*

Appendices B and C, respectively. The future distribution map revealed a drastic decrease in suitability in northeastern Thailand (Fig. 3b, c). By 2050, the presence of *O. viverrini* is predicted to decrease with an increase in precipitation in October but to increase with increasing maximum temperature in May and mean temperature of the wettest quarter (Fig. 5b). By 2070, the presence of *O. viverrini* is likely to decrease with increasing precipitation in the coldest quarter but to increase with maximum temperature in May and minimum temperature in July (Fig. 5c).

Discussion

Climate change will alter the spatial patterns of parasites worldwide (Costello et al. 2009). In Thailand, clear evidence

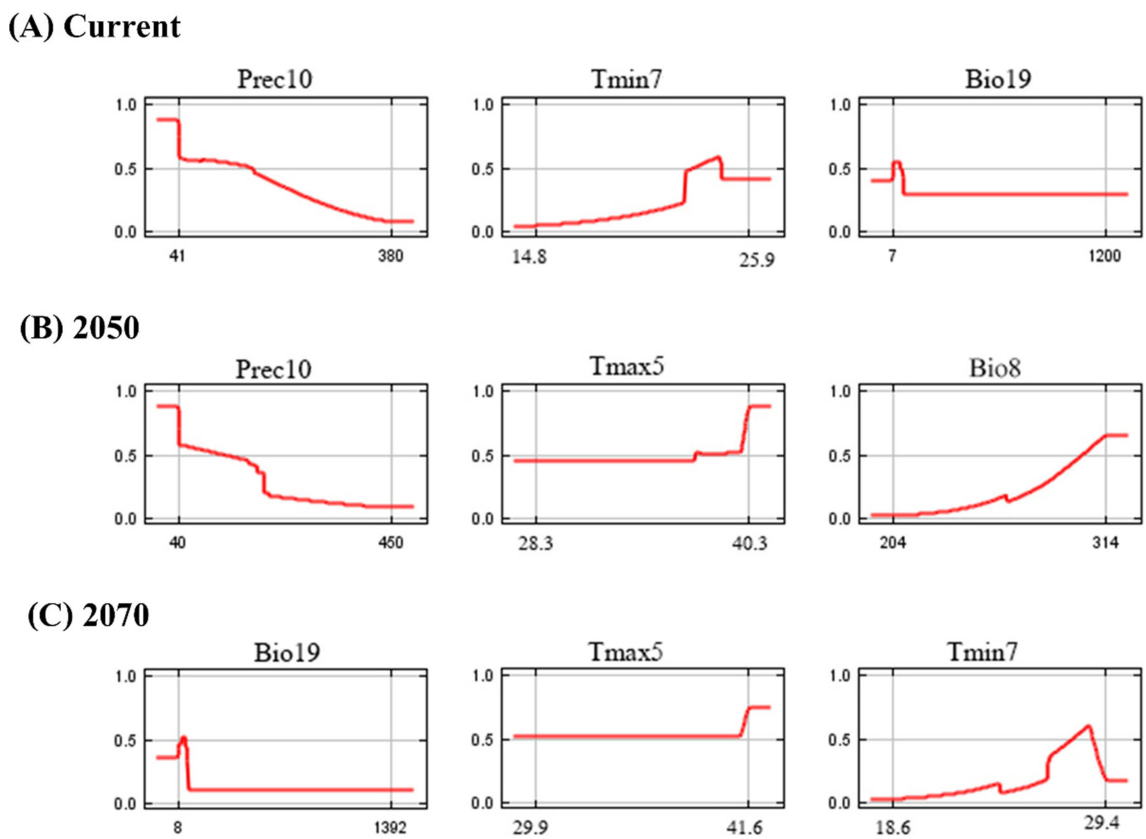


Fig. 5 Response curves showing the relationships between the probability of presence and the three top climatic predictors of *Opisthorchis viverrini*

exists that temperatures have already increased and that rainfall patterns have changed (Marks 2011). Our analyses demonstrated that the current distribution of *O. viverrini* is significantly affected by precipitation and minimum temperature. Under the future climate change scenarios, the distribution of *O. viverrini* in 2050 should be affected by precipitation, maximum temperature, and mean temperature of the wettest quarter, whereas for 2070, precipitation of the coldest quarter and maximum and minimum temperatures are the most important variables. Parasite reproduction rate should increase (shorter generation times) as temperatures rise. Similarly, transmission seasons are likely to lengthen. Given that distributions of many human pathogens are positively correlated with monthly temperature ranges (Guernier et al. 2004), these effects will probably lead to increasing parasite species richness and prevalences in the years ahead (Allen et al. 2002; Hoberg et al. 2008; Larsen and Roepstorff 1999). Precipitation is another major environmental variable. Many parasites require moist or wet conditions at some point in their life-cycles. Guernier et al. (2004) presented evidence that regions of the world with distinct wet and dry seasons may be home to greater numbers of human parasites. In contrast, regions with persistent arid conditions are less suitable for survival of parasites and their fragile eggs and other transmission stages (Roberts and Janovy 2000). The results of this study identify the importance of climatic factors in explaining national geographical distribution of *O. viverrini* and indicate that MaxEnt is a useful tool for defining such distributions in endemic areas and for predicting distributions in areas with similar climatic conditions. Therefore, climate models are necessary tools for national level policy decisions regarding health planning and progress monitoring. These models become especially powerful in data-scarce regions for effective resource allocation and planning for sustained disease control.

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