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Predicting the potential distribution of hemorrhagic fever with renal syndrome in Southwest China using the ecological niche modeling

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Abstract

Background: Hemorrhagic fever with renal syndrome (HFRS) severely burdens China's public health. With its complex topography and rich biodiversity, Southwest China has historically incubated this natural focal disease. Currently, traditional environmental factors associated with transmission here are increasingly eclipsed by anthropogenic forces, notably population agglomeration. Driven by these shifting dynamics, HFRS incidence and endemic ranges are expanding, yet systematic, regional-scale assessments remain scarce. Consequently, this study employs ecological niche modeling to map potential high-risk zones. Ultimately, we aim to explore the primary factors associated with HFRS prevalence amid the complex interplay of natural environments and human activities.

Methods: Surveillance data of HFRS cases in Southwest China from 2014 to 2023 were obtained from the China Information System for Disease Control and Prevention (CISDCP). A Maximum Entropy (MaxEnt) model was constructed by integrating occurrence records with multisource environmental variables, including meteorological, socioeconomic, and land cover factors. Model performance was evaluated using the Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC), and the Jackknife test was employed to quantify the contribution of each variable.

Results: The MaxEnt model demonstrated robust predictive performance with a mean AUC of 0.902. Population density was identified as the predominant predictor (73.5% contribution), followed by the Normalized Difference Vegetation Index (NDVI) in May (9.2%) and annual mean temperature (5.8%). The spatial distribution of risk exhibited a core aggregation with sporadic dispersion pattern, with high-risk zones concentrated in the Chengdu-Chongqing

urban agglomeration and localized clusters in Yunnan Province. Response curves revealed a sigmoidal positive correlation between population density and disease risk. Meteorological factors, such as temperature and precipitation, exhibited non-linear inverted U-shaped or U-shaped relationships, constraining the spatial boundaries of transmission.

Conclusions: The spatial heterogeneity of HFRS in Southwest China is jointly driven by anthropogenic activities and natural environmental constraints. Human population density is identified as a primary factor associated with amplified transmission risk, which may reflect the human behavior amplification effect in natural focal diseases. These findings suggest a strategic shift from blanket prevention to precision control, prioritizing active surveillance in densely populated urban fringes and areas undergoing infrastructure development.

Keywords

Hemorrhagic fever with renal syndrome; Ecological niche modeling; MaxEnt; Southwest China; Risk assessment; Population density; Spatial heterogeneity.

Background

Hemorrhagic fever with renal syndrome (HFRS) is a natural focal disease caused by hantavirus infection, characterized primarily by acute onset, rapid disease progression, and a high mortality rate [1, 2]. China is one of the countries most severely affected by HFRS globally [3, 4]. Since the 1980s, the annual reported case count exceeded 100,000 for many years, placing a sustained and significant burden on the public health system [5, 6]. Although the national HFRS incidence rate in China has declined significantly in recent years following the implementation of comprehensive control measures—such as vaccination, reservoir host

control, and health education—this trend does not indicate that epidemic risk has been eliminated, given the continued occurrence of sporadic cases and localized clusters [7, 8]. Notably, the epidemiological pattern of HFRS is not static but rather undergoes continuous evolution, driven by the interplay of natural environmental and socioeconomic factors [9, 10].

Particularly in the context of global warming, alterations in temperature and precipitation patterns can indirectly modulate hantavirus transmission risk by influencing the population dynamics and habitat distribution of reservoir hosts such as rodents [11, 12], thereby contributing to a geographical shift in high-risk areas [7, 10]. Against this backdrop, the epidemiological pattern of HFRS, traditionally predominant in northern regions, is currently exhibiting new characteristics of spatial variation [7, 9]. In recent years, the epidemiological dynamics of HFRS in Southwest China have attracted increasing attention due to rising incidence and the region's unique ecological landscape. While traditional high-incidence areas have long been concentrated in Northeast China and the North China Plain [13], Southwest China has recently exhibited an upward trend in reported cases and a gradual expansion of the endemic range, emerging as a potential high-risk region that warrants attention within the national prevention and control framework [14, 15, 16].

The study area is characterized by complex topography, featuring the coexistence of plateaus, mountains, and basins, diverse climatic types, and significant ecological heterogeneity; consequently, its natural conditions differ markedly from traditional HFRS-endemic areas [17]. This unique physiographical and climatic context may result in distinct reservoir species compositions, transmission pathways, and environmental associated factors compared to the northern endemic areas, thereby shaping a region-specific pattern of

HFRS transmission [14, 18, 19]. Previous studies have demonstrated that meteorological factors, socioeconomic factors, and land cover variables are closely associated with the occurrence of HFRS [20]. However, existing literature has largely concentrated on specific HFRS-endemic cities in southwestern China, with a primary emphasis on analyzing demographic characteristics and the spatiotemporal dynamics of the epidemic [14, 21, 22, 23]. Consequently, systematic and quantitative assessments regarding the distributional characteristics of HFRS risk factors and projected risk patterns at a holistic regional scale remain insufficient [7]. Given these limitations, it is imperative to conduct a comprehensive analysis of multidimensional influencing factors at a broader spatial scale. Therefore, this study aims to systematically identify the combined effects of meteorological, socioeconomic, and land cover variables on the occurrence of HFRS in southwestern China, delineate potential disease risk zones, and quantify the population exposed to varying levels of risk, thereby providing a scientific basis for comprehensively assessing the associated public health burden and formulating region-specific prevention and control strategies.

Methods

Study area

Southwestern China is located between approximately 97°21'–110°11' E and 21°08'–34°19' N, situated at the eastern margin of the Qinghai-Tibet Plateau and encompassing the main body of the Yunnan-Guizhou Plateau. The region covers a total area of approximately 1.14 million km² (Fig. 1). The region exhibits diverse climatic types, predominantly characterized by a subtropical monsoon climate alongside features of a plateau mountain climate. The mean

annual temperature ranges from 8 to 20°C, with annual precipitation typically falling between 800 and 1800 mm. Notably, significant vertical climate differentiation is observed in local alpine valley areas [17]. According to the 2021 provincial statistical yearbooks and data from the Seventh National Population Census, the permanent resident population totaled approximately 198 million by the end of 2020. The population distribution is characterized by relative concentrations in basins, plains, and urban areas, in contrast to the sparsely populated mountainous regions.

Data collection

Surveillance data regarding HFRS cases in Southwest China spanning from 2014 to 2023 were sourced from the Infectious Disease Reporting System of the Chinese Center for Disease Control and Prevention (China CDC). All reported cases were confirmed strictly following the standardized diagnostic criteria formulated by the national CDC [24].

The base map was obtained from the National Platform for Common Geospatial Information Services (<https://www.tianditu.gov.cn/>; Map Approval No. GS(2024)0650), featuring polygon vector layers for provincial, prefectural, and county-level administrative divisions. Population data for southwestern China were derived from the Seventh National Population Census conducted in 2020, accessed via the National Bureau of Statistics of China (<https://www.stats.gov.cn/sj/pcsj/rkpc/7rp/zk/indexce.htm>). Population density was calculated by dividing the population size by the land area of each county.

Environmental variables

To investigate the environmental risk factors influencing the spatiotemporal distribution of HFRS in recent years, we collected data on a range of environmental variables, including

meteorological factors and land cover (Table 1). The selection of these variables was informed by prior studies and expert consultation regarding their potential impact on the spatiotemporal variation of the HFRS epidemic.

Meteorological data for southwestern China spanning from 2014 to 2023 were obtained from the China Meteorological Data Service Centre (<https://data.cma.cn/>). The meteorological variables included in this study comprised the multi-year mean relative humidity, multi-year mean temperature, and multi-year mean precipitation. Using ArcGIS 10.8 software (ESRI, Redlands, CA, USA), raster layers representing the mean meteorological data for the 2014–2023 period were generated via the Kriging interpolation method.

Elevation data were derived from a nationwide Digital Elevation Model (DEM) with a spatial resolution of $1\text{ km} \times 1\text{ km}$, obtained from the National Earth System Science Data Center

(<http://www.geodata.cn/data/datadetails.html?dataguid=201519481253546&docid=1301>).

Additionally, slope and aspect variables were calculated from the elevation data using ArcGIS 10.8 software.

Land use data for the year 2013 were obtained from the National Earth System Science Data Center (<https://www.geodata.cn/>), provided as a raster layer with a spatial resolution of $1\text{ km} \times 1\text{ km}$. Although these data slightly precede the case collection period (2014–2023), they maintain strong representativeness, as the macro-scale land cover patterns and regional ecological landscapes in Southwest China remained relatively stable over this decade, thereby serving as a reliable baseline without diminishing the model's explanatory power.

Data for the Normalized Difference Vegetation Index (NDVI) were obtained from the

National Tibetan Plateau Data Center (<https://www.tpdc.ac.cn/>). As the most widely used vegetation index, NDVI indicates vegetation growth status and coverage, thereby comprehensively reflecting the environmental conditions of the region.

All environmental variable datasets were projected to a unified geographic coordinate system and converted into raster format. Subsequently, the data were resampled to a consistent spatial resolution of 1 km and clipped to the extent of the study area using vector boundary data in ArcGIS 10.8.

Statistical methods

Prior to model construction, to ensure the robustness and interpretability of the analytical results, we constructed an initial set of variables by systematically reviewing existing literature to screen for potential environmental factors associated with the occurrence of HFRS. All candidate variables were entered into the MaxEnt model for a preliminary run, with the number of replicates set to 1. The Jackknife test was subsequently employed to evaluate the contribution and importance of each variable to the model. To prevent model overfitting and potential interference with result interpretation caused by the coexistence of highly correlated variables, we subsequently conducted a multicollinearity test using Spearman's rank correlation analysis, establishing a threshold of 0.8 ($|r| \geq 0.8$) [25]. For pairs of highly correlated variables, selection was prioritized based on contribution metrics derived from the preliminary model run: the variable with the higher contribution was retained, while the lower-contributing variable was excluded. Ultimately, a final set of variables that were mutually independent and possessed significant explanatory power for HFRS transmission risk was selected to construct the final model.

Ecological niche modeling

Model construction

In this study, the Maximum Entropy (MaxEnt, version 3.4.3) model was employed for ecological niche modeling. Based on the principle of maximum entropy, this model predicts the probability of presence in specific habitats by integrating geographic occurrence records of HFRS cases with environmental background points; it is widely recognized as a robust machine learning method characterized by high predictive accuracy [26, 27].

Model training and parameter optimization:

To construct a high-precision predictive model, the key eco-environmental factors identified during the screening process were incorporated into the MaxEnt model. In terms of data partitioning, 75% of the HFRS occurrence records were randomly selected as the training set for model calibration, while the remaining 25% were reserved as the test set for model validation [28, 29].

To minimize random errors associated with single simulations and enhance the stability of the results, the model was executed with 10 replicates, and the final output was derived from the average of these 10 runs. Apart from these specific settings, all other parameters were maintained at the software's default values. Default settings were retained because previous studies have demonstrated their robustness in ecological niche modeling when sufficient occurrence records are available [30].

Model performance evaluation:

The predictive performance of the model was evaluated primarily using the Receiver Operating Characteristic (ROC) curve and the Area Under the ROC Curve (AUC) [31]. The

AUC values range from 0 to 1, with a value closer to 1 indicating superior predictive performance. Specifically, an AUC of 0.5 represents a random prediction. The performance levels are categorized as follows: 0.5–0.6 is considered poor; 0.7–0.8 is fair; 0.8–0.9 is good; and 0.9–1.0 is excellent [32]. Furthermore, a threshold-dependent binomial test was employed, utilizing the omission rate as a test statistic to comprehensively evaluate the statistical significance of the model and assess the potential for overfitting [33].

Analysis of environmental variable importance

To identify the key driving factors influencing the distribution of HFRS, the Jackknife test was employed to quantitatively evaluate the contribution of each environmental variable to the model gain, thereby identifying the dominant variables containing the most critical information [34]. Additionally, response curves were utilized to analyze the non-linear response patterns of the predicted probability of HFRS occurrence to variations in individual variables, thereby elucidating the quantitative relationships between environmental factors and disease risk [33, 35].

Risk zonation and population exposure assessment

The output of the MaxEnt model consists of continuous probability values ranging from 0 to 1, representing the environmental suitability for the occurrence of HFRS (i.e., the potential risk). The continuous suitability values predicted by MaxEnt were reclassified into three risk levels (low, medium, and high risk) following the classification scheme proposed by Acharya et al. (2018), where suitability values ≤ 0.29 , 0.29–0.45, and > 0.45 represent low-, medium-, and high-risk areas, respectively. This approach has been previously applied in ecological niche modeling studies and facilitates interpretation of spatial risk patterns. Finally, a spatial overlay

analysis was performed using ArcGIS software to integrate the reclassified risk zonation map with population raster data. This process allowed for the quantitative estimation of the size and spatial distribution characteristics of the population exposed to varying risk levels at both the prefectural and regional scales [36].

Results

Descriptive analysis results

The mean annual incidence rate in Southwestern China was 0.19 per 100,000 population, with the rate reaching 0.32 per 100,000 in 2023. Furthermore, HFRS cases exhibited pronounced seasonal fluctuations, characterized by a primary peak during the spring-summer period (April–June) and a secondary peak during the autumn-winter period (November–January). In terms of geographic distribution, the Liangshan Yi Autonomous Prefecture in Sichuan Province, along with the Dali Bai Autonomous Prefecture and Chuxiong Yi Autonomous Prefecture in Yunnan Province, were identified as the primary high-incidence areas. Collectively, these three regions accounted for 62.60% of the total cases reported in Southwestern China. Demographic analysis indicated that males and farmers aged 20–60 years constituted the primary high-risk groups. The incidence rate among males was 45.01 per 100,000 population, significantly exceeding that among females (1.76 per 100,000 population). Furthermore, significant heterogeneity in incidence rates was observed across prefecture-level cities, with cases predominantly concentrated in mountainous regions and ethnic autonomous prefectures.

Correlation between risk factors and HFRS cases

The results of the correlation analysis are presented in Fig. 2. Based on the modeling results, key ecological environmental variables influencing HFRS transmission risk—including monthly mean Normalized Difference Vegetation Index (NDVI) (specifically for May and August, with a cumulative contribution of 10.4%), land use (specifically 2013 data, 3.1%), annual mean temperature (0.5%), annual precipitation (1.9%), population density (utilizing 2020 data, 69.2%), annual mean relative humidity (4.1%), and slope (1.1%)—were selected to construct the predictive model for HFRS transmission risk in the southwest region.

Model Evaluation

The close proximity between the average omission rate of the test data and the predicted omission rate indicated that the trained model was statistically significant; furthermore, the mean Area Under the Curve (AUC) value for 10 replicate runs was 0.902 (Standard Deviation [SD] = 0.017), demonstrating that the MaxEnt model exhibited high predictive sensitivity and accuracy with robust performance. (Figs. 3–5)

Key predictive variables for HFRS

The relative contribution analysis based on the MaxEnt model revealed significant differences in the explanatory power of various variables regarding the spatial distribution of Hemorrhagic Fever with Renal Syndrome (HFRS). Specifically, population density, the Normalized Difference Vegetation Index for May (NDVI5), and annual mean temperature were identified as the top three predictors in the model, with relative contributions of 73.5%, 9.2%, and 5.8%, respectively, accounting for a cumulative contribution of 88.5%. Furthermore, results from the Jackknife test confirmed that population density yielded the highest model gain when used in isolation. Response curve analysis further elucidated the

non-linear relationships between key variables and the probability of HFRS occurrence. Specifically, population density demonstrated a significant positive correlation with HFRS risk, and its response curve exhibited a typical sigmoidal or threshold growth pattern: in the low-density range, the probability of occurrence rose exponentially with increasing population; once population density reached approximately 2500 people/km², environmental suitability rapidly ascended to high values, maintaining a probability above 0.65, and plateaued at a high level beyond approximately 19,000 people/km². Furthermore, visual assessment of the risk distribution (Figure 7) indicates that the higher risk zones associated with population density are largely distributed along the peripheral extension zones of urban agglomerations (i.e., urban-rural fringes) rather than strictly within central urban cores. Regarding environmental factors, vegetation indices (NDVI5 and NDVI8) generally exhibited a negative relationship with HFRS occurrence, though moderate suitability was maintained within specific ranges (0.1–0.8 for NDVI5, and 0.25–0.75 for NDVI8). Meteorological factors displayed non-linear responses: relative humidity showed a bimodal relationship (peaks at 65% and 82%), precipitation exhibited a U-shaped relationship (lowest risk at 1210–1640 mm), and mean temperature presented an inverted U-shaped relationship peaking between 10–16 °C. Slope exhibited an overall weak inverted U-shaped relationship with the probability of HFRS occurrence, reaching a relative high in predicted risk at approximately 17–23.5°, with a corresponding response probability of 0.7–0.8. Analysis of land cover types indicated that impervious surfaces and forests were associated with the highest HFRS occurrence probabilities, followed by cropland and shrubland, whereas grassland and water bodies exhibited relatively lower predicted risks.(Fig. 6)

Risk of HFRS occurrence:

Figure 7 illustrates the spatial heterogeneity of the potential HFRS risk in Southwest China as predicted by the MaxEnt model. The results indicated that the distribution of HFRS within the study area exhibited significant spatial clustering characteristics. Based on the reclassification standards, the study area was dominated by low-risk areas, covering 91.0% of the total area; whereas high- and medium-risk areas accounted for 3.0% and 6.0%, respectively. Table 2 further quantifies the exposed areas and the size of the population at risk within different administrative units across each risk level. The high-risk areas exhibited a spatial distribution pattern characterized by "core aggregation with sporadic dispersion." The primary cluster was situated in the northeastern part of the study area (specifically, the Sichuan Basin and its vicinity), encompassing densely populated urban agglomerations such as the main urban districts of Chongqing, Chengdu, Deyang, Mianyang, and Nanchong. Furthermore, significant high-risk areas with a punctuate distribution and weak spatial continuity were identified in Yunnan Province in the southwestern region, predominantly concentrated in the central part of Dali Bai Autonomous Prefecture, Chuxiong Yi Autonomous Prefecture, and parts of Baoshan City. The medium-risk areas are predominantly distributed in annular or band-like patterns along the periphery of high-risk zones, forming an ecotone that transitions from high-risk to low-risk areas. These regions are concentrated in the peripheral extension zones of the Chengdu-Chongqing urban agglomeration, as well as in Chuxiong Yi Autonomous Prefecture and Yuxi City in central Yunnan Province. In contrast, low-risk areas extensively cover the western and southern margins of the study area, particularly in higher-elevation regions such as Ganzi Tibetan Autonomous Prefecture, Aba Tibetan and Qiang Autonomous Prefecture,

and the southern part of Pu'er City. (Fig. 7)

Spatial uncertainty of MaxEnt predictions

The standard deviation map (Fig. 8) demonstrated generally low prediction uncertainty across Southwest China. Most pixels showed very low or low standard deviation values, indicating high consistency among the 10 replicate MaxEnt runs. Moderate uncertainty was mainly observed in several mountainous transitional areas, whereas high and very high uncertainty were confined to a limited number of localized patches. Overall, the small spatial extent of high-uncertainty areas suggests that the model predictions were robust and spatially stable.

Discussion

Based on HFRS case data from Southwest China spanning 2014–2023, this study utilized the Maximum Entropy (MaxEnt) model to systematically characterize potential high-risk zones and key environmental drivers of hemorrhagic fever with renal syndrome (HFRS), effectively bridging the knowledge gap regarding the lack of systematic, quantitative risk assessments at a holistic regional scale in this region [37].

The results indicate robust model performance, with HFRS incidence risk exhibiting significant spatial heterogeneity at the regional scale [38]; high-risk zones are not uniformly distributed but are concentrated in areas characterized by prominent interactions between specific ecological conditions and human activities, revealing the spatial patterns where the natural environment and human exposure co-drive disease transmission. Concurrently, natural environmental variables, such as vegetation indices and temperature, exhibited clear threshold effects. These relationships may reflect ecological conditions favorable for reservoir host

habitats and HFRS transmission. Spatially, the study identified a risk pattern characterized by higher density in the north versus sparsity in the south, featuring the coexistence of core clustering and multi-point sporadic occurrences [39]. Specifically, it confirmed a contiguous high-risk zone anchored by the Chengdu-Chongqing urban agglomeration, along with localized sporadic risk patches in regions such as Yunnan.

The results indicate that population density was the predominant predictor, yielding the highest percent contribution. This aligns with findings from other high-incidence regions in China [10, 13], where urbanization and population aggregation drive HFRS transmission. The sigmoidal response curve substantiates the 'human behavior amplification effect' in densely populated areas. Specifically, urban-rural fringes characterized by habitat fragmentation favor commensal rodents like *Rattus norvegicus* [40], which are gradually replacing sylvatic foci [7]. Additionally, floating populations in these areas face increased contact with infected rodents, sustaining transmission risks [13]. In Southwest China, the unique 'mountainous urbanization' pattern—lacking geographical buffer zones between settlements and natural ecosystems—further exacerbates this overlap. Importantly, while the model identifies population density as the strongest predictor, it should not be strictly treated as a demonstrated causal mechanism. Alternative explanations must be considered, as densely populated areas typically correlate with higher levels of urbanization, greater surveillance intensity, improved healthcare access, and varying socioeconomic factors, all of which naturally elevate the probability of clinical diagnosis and case reporting.

The non-linear response of NDVI indicates that HFRS risk peaks in areas with intermediate vegetation density (e.g., cultivated lands), reflecting a trade-off between host

survival resources and human contact opportunities [9]. Extremely high NDVI areas restrict human-rodent contact [41] and exhibit a biodiversity dilution effect [42]. Temporally, the peak risk associated with NDVI5 coincides with intensive spring and summer agricultural activities [43]. In contrast, NDVI8 exhibits a lagged effect, where abundant autumn food resources drive the winter migration of wild rodents into human settlements, triggering the secondary epidemic peak [7, 44, 45].

Climatic and meteorological factors similarly bounded transmission risks through complex, non-linear ecological pathways rather than simple unidirectional mechanisms [13, 39]. The inverted U-shaped relationship for mean temperature (peaking at 10-16 °C) and the U-shaped relationship for precipitation indicate that optimal, mild weather conditions maximize rodent breeding and human agricultural exposure [7]. Conversely, extreme temperatures (> 25 °C) reduce human-rodent contact through heat stress and restricted outdoor activities [46]. Furthermore, while extreme precipitation anomalies (droughts or floods) can drive commensal migration and elevate indoor infection risks [47], moderate, sustained rainfall suppresses population density through ecological counter-balancing (e.g., burrow inundation or ectoparasite proliferation) [48]. Finally, the bimodal distribution of relative humidity reflects a dual dependency, balancing the requirements of regional agricultural cycles against the detrimental effects of hot, humid environments on the long-term stability of lipid-enveloped viruses [49, 50, 51]. These findings suggest that early warning strategies must incorporate seasonally differentiated interventions, emphasizing indoor rodent eradication during dry or extreme weather periods.

This finding stands in marked contrast to the majority of studies focusing on the plains

regions of China (e.g., the Guanzhong Plain and the Northeast China Plain). Previous research generally suggests that flat terrain with a slope of less than 10° is conducive to mechanized cultivation and irrigation, thereby representing areas characterized by the highest rodent density and the most frequent human-rodent contact [52]. However, the skewing of risk towards intermediate slopes observed in this study may be attributed to the unique vertical agriculture and mountainous settlement patterns in the southwest region. Due to the scarcity of flat terrain resources, extensive agricultural activities (e.g., terraced fields and drylands) and rural settlements are compelled to extend onto the hillsides [53]. According to a study by Yang et al. on the distribution of traditional villages in the southwest region, a substantial number of settlements are situated on gentle to intermediate slopes. This terrain not only facilitates natural drainage and prevents waterlogging but also falls precisely within the suitable nesting habitat range of wild rodents, such as *Apodemus agrarius* [54, 55].

Therefore, moderate slope zones effectively constitute a unique "human-rodent-environment" interface specific to the southwest mountainous regions, rather than acting as geographical barriers. In terms of land cover types, this study identified that impervious surfaces and woodlands exhibited the highest probability of HFRS occurrence. The elevated risk associated with impervious surfaces underscores the role of rapid urbanization in driving HFRS transmission; notably, a recent study by Xiang et al., based on 34 years of surveillance data in China, indicated that the expansion of impervious surfaces has superseded certain natural factors, emerging as the primary predictor variable for HFRS transmission [56]. This is primarily attributed to the fact that urbanization in the southwest region is often accompanied by the persistence of urban villages and aging residential

neighborhoods; characterized by suboptimal sanitation, these areas are prone to harboring commensal rodent-borne foci dominated by *Rattus norvegicus*. A review by Li et al. further emphasizes that the expansion of impervious surfaces during urbanization effectively provides stable shelters for commensal rodents by modifying microhabitats (e.g., sewers and refuse accumulation sites), thereby prolonging viral transmission chains within anthropogenic environments [40]. Furthermore, the elevated risk associated with woodlands elucidates the characteristics of mixed-type foci within the region. In contrast to the distinct separation between urban areas and forests observed in the northern plains, mountainous cities in the southwest often exhibit a mosaic landscape described as cities within forests and houses within mountains. This ecotone, resulting from the high proximity between woodlands and residential zones, significantly increases the probability of residents (particularly peripheral farmers) encountering wild rodent hosts—primarily *Apodemus agrarius* inhabiting forest edges—during foraging or agricultural activities. Consequently, the dual high risk attributed to both impervious surfaces and woodlands in this study substantively reflects the complex reality of the spatial overlap and interplay between commensal and wild rodent-borne foci in the southwest region.

In addition to natural and conventional socioeconomic determinants, the potential impact of large-scale infrastructure development—such as the construction of highways and water conservancy hubs—on the transmission risk of HFRS cannot be overlooked. Such high-intensity anthropogenic disturbances alter land cover and hydrological characteristics, thereby directly inducing the fragmentation and restructuring of rodent habitats. Taking the Three Gorges Project as a case in point, long-term ecological monitoring has demonstrated

that water impoundment in the reservoir area has precipitated a significant insularization effect [19]. As water levels rise periodically, the resulting inundation of low-elevation habitats compels reservoir hosts, such as *Rattus norvegicus*, to undergo a forced migration toward unsubmerged islands or peripheral high-altitude agricultural zones; this displacement precipitates an acute, short-term surge in local rodent density, thereby intensifying interspecific competition and accelerating the turnover of dominant species [57, 58]. Similarly, in the context of large-scale infrastructure development recently undertaken in Yunnan Province—particularly water conservancy projects—rodents may be driven to migrate toward construction camps or surrounding residential areas in search of foraging resources and new habitats [14, 22, 59, 60]. This process significantly amplifies the likelihood of human exposure to infected hosts and their excreta, highlighting the critical need to prioritize the prevention of emergent infectious foci triggered by drastic ecological transformations, particularly during the construction phase and within resettlement areas. The spatial uncertainty analysis further indicated that the MaxEnt model produced highly consistent predictions across the 10 replicate runs. Areas with elevated uncertainty were mainly confined to transitional zones between different suitability classes, whereas the core high-risk regions exhibited relatively low uncertainty. These findings further support the robustness and reliability of the predicted HFRS risk distribution.

This study is subject to certain limitations: First, it is important to note that MaxEnt was originally developed for species distribution modeling. While applied here to disease occurrence, disease records are influenced not only by environmental suitability but also by surveillance intensity, healthcare access, reporting practices, diagnostic capacity, and human

behavior. Consequently, the predicted suitability may partially reflect reporting patterns rather than true transmission risk. Second, given that this study was conducted as an ecological analysis at the population level, it delineates environmental risks on a regional scale rather than quantifying individual exposure levels; consequently, caution must be exercised during result interpretation to avoid the ecological fallacy. In addition, a temporal mismatch existed between some environmental variables and the disease occurrence data. For example, land-use data from 2013 were used to characterize environmental conditions associated with HFRS cases reported during 2014–2023. Although land-use patterns generally change gradually at the regional scale and may exert lagged effects on disease transmission, this temporal inconsistency may still introduce uncertainty into model predictions.

Finally, several methodological limitations should be acknowledged. Due to data availability constraints, the model did not directly incorporate important biological and public health determinants. In particular, HFRS is a typical rodent-borne zoonotic disease, yet key host ecological variables, including rodent distribution, host population abundance, species composition, infection prevalence, and hantavirus circulation characteristics, were unavailable for the entire study area and therefore could not be incorporated into the model. Likewise, important public health factors such as vaccination coverage, surveillance sensitivity, healthcare accessibility, diagnostic capacity, and health-seeking behavior were not included.

Consequently, the environmental variables used in this study should be regarded primarily as indirect proxies for the ecological processes underlying HFRS transmission. Although climatic, vegetation, land-use, and topographic factors influence host habitats and opportunities for human–rodent contact, they cannot directly characterize the biological

mechanisms governing pathogen maintenance and transmission. Moreover, although MaxEnt has been widely applied in infectious disease ecology, it was originally developed for species distribution modeling and primarily estimates environmental suitability. Therefore, the predicted suitability surfaces generated in this study may reflect not only ecological conditions favorable for HFRS occurrence but also spatial heterogeneity in case detection and reporting. As a result, the identified high-risk areas should be interpreted as regions environmentally suitable for reported HFRS occurrence rather than direct representations of actual transmission intensity. Additionally, while default MaxEnt settings demonstrated robust performance in our study, future studies may further explore parameter optimization to potentially enhance model predictive accuracy. Future studies integrating rodent surveillance data, host infection indicators, hantavirus circulation information, ecological variables, epidemiological data, and health-system indicators may provide a more comprehensive assessment of disease risk.

Conclusions

Hemorrhagic Fever with Renal Syndrome (HFRS) remains a significant natural focal disease posing a threat to public health in Southwest China. Based on the Maximum Entropy (MaxEnt) model, this study systematically characterized the potential geographical distribution patterns and key driving mechanisms of HFRS across the region at a regional scale. Our findings demonstrate that HFRS prevalence is driven by the dual influence of natural environmental factors and anthropogenic activities. Specifically, human population density emerged as the primary predictor, highlighting the amplification effect of human activities on transmission

risk, whereas natural variables such as vegetation indices, temperature, and topography constrained the spatial boundaries of natural foci through non-linear mechanisms. The risk prediction maps constructed in this study provide visually intuitive decision-making support for regional public health authorities. Our findings may help inform future precision prevention and control strategies. Enhanced surveillance could be prioritized in the fringe areas of the Chengdu – Chongqing urban agglomeration, mountainous terraced agricultural regions, and major infrastructure development areas, while seasonally targeted rodent control and vaccination programs may also be considered according to local epidemiological conditions.

Declarations

Ethics approval and consent to participate

This study did not involve any human intervention or clinical trials. The use of hemorrhagic fever with renal syndrome (HFRS) case data was based on routine public health surveillance activities in China. According to national regulations, such surveillance data are exempt from institutional ethics review. Therefore, ethics approval was not required for this study. As all data were anonymized and contained no personal identifiers or private health information, the requirement for informed consent was also deemed unnecessary. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the

corresponding author on reasonable request.

Competing interests

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Authors' contributions

QC,YX, and WZ conceived and designed the study. DZ, ZZ, and YW collected and organized the data. LZ, Z Zheng, RQ, and FS analyzed the data. DZ wrote the original draft of the manuscript. QC,YX, and WZ reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Figure Legends

Figure 1. Map of the study area. The figure illustrates the geographical location and elevation gradient of Southwest China.

Figure 2. Displays a heatmap illustrating the pairwise Pearson correlation coefficients among different environmental variables in Southwest China.

Figure 3. Averaged omission and predicted area for the MaxEnt model of HFRS in Southwest China.

Figure 4. Receiver operating characteristic (ROC) curve for the MaxEnt model of HFRS in Southwest China.

Figure 5. Results of the Jackknife test evaluating the relative importance of predictor variables to the HFRS risk prediction in Southwest China.

Figure 6. Response curves for the probability of HFRS presence. The curves illustrate the mean response of 10 replicate MaxEnt runs (blue) and the mean $\pm$ one standard deviation (grey). The x-axis represents the value of each predictor variable, while the y-axis represents the predicted probability of HFRS occurrence.

Figure 7. Environmental suitability maps for HFRS in Southwest China.

Figure 8. Spatial uncertainty of MaxEnt model predictions for HFRS in Southwest China.

Table 1 Definitions and types of environmental variables

Variable classification	Variable name	Definition	Resolution	Variable type
Climatic	MAT	Annual Mean Temperature	1km	Continuous
	AAP	Annual Average Precipitation	1km	Continuous
	RH	Average Annual Relative Humidity	1km	Continuous
	LD	Land Cover	1km	Categorical
	DEM	Digital Elevation Model	1km	Continuous
	Aspect	Terrain Aspect	1km	Continuous
Geographical	Slope	Terrain Slope	1km	Continuous
	NDVI3	Normalized Difference Vegetation Index in March	1km	Continuous
	NDVI5	Normalized Difference Vegetation Index in May	1km	Continuous
	NDVI7	Normalized Difference Vegetation Index in July	1km	Continuous
	NDVI8	Normalized Difference Vegetation Index in	1km	Continuous

August

NDVI9

Normalized Difference

1km

Continuous

Vegetation Index in

September

Socioeconomic

DP

Density of population

1km

Continuous

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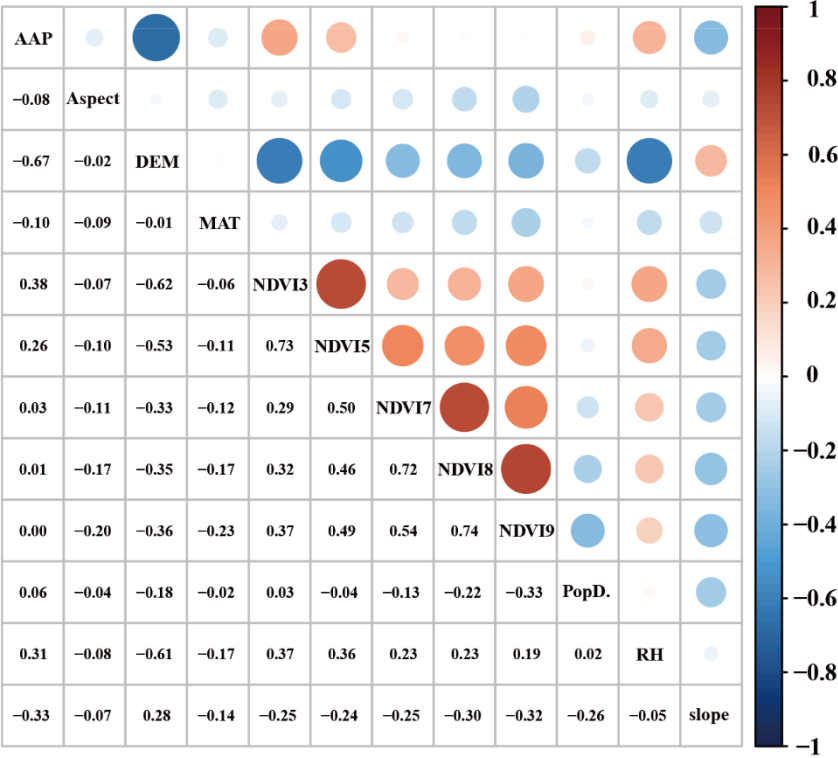
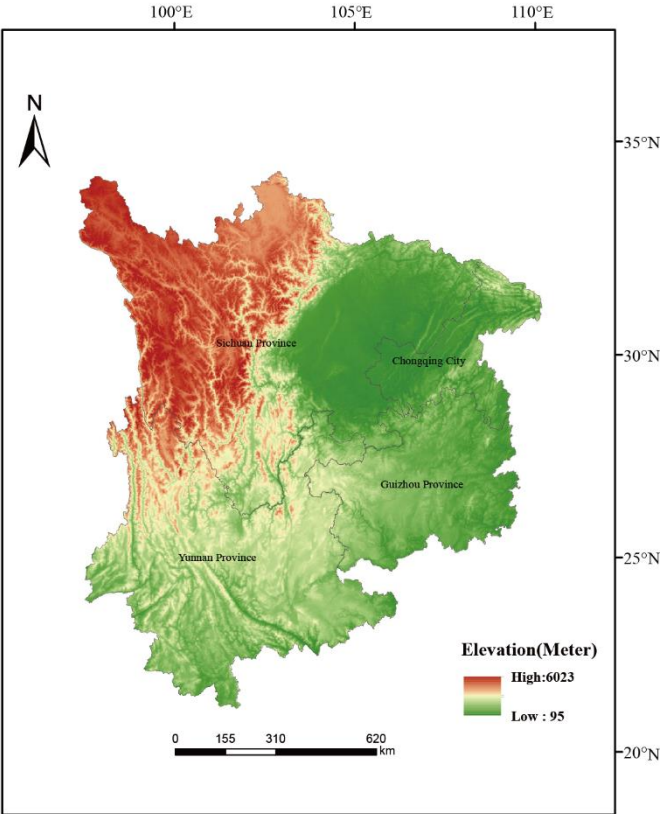
Table 2 Exposed areas and the size of the population at risk across different suitability classes

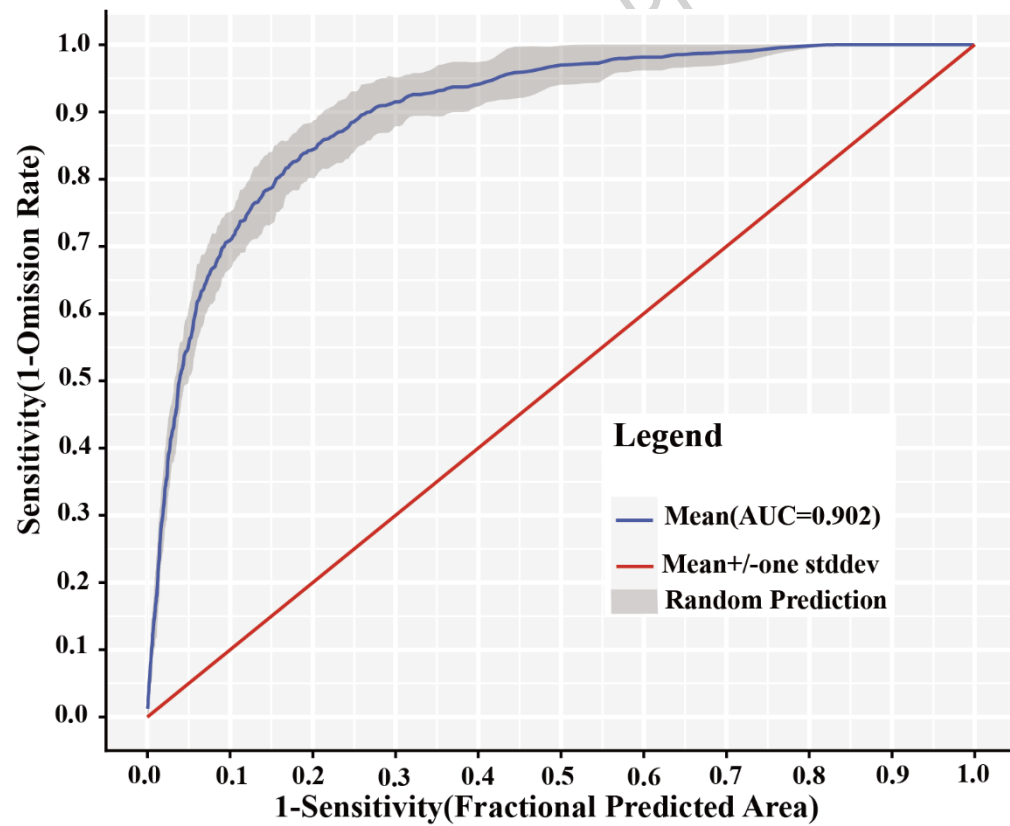
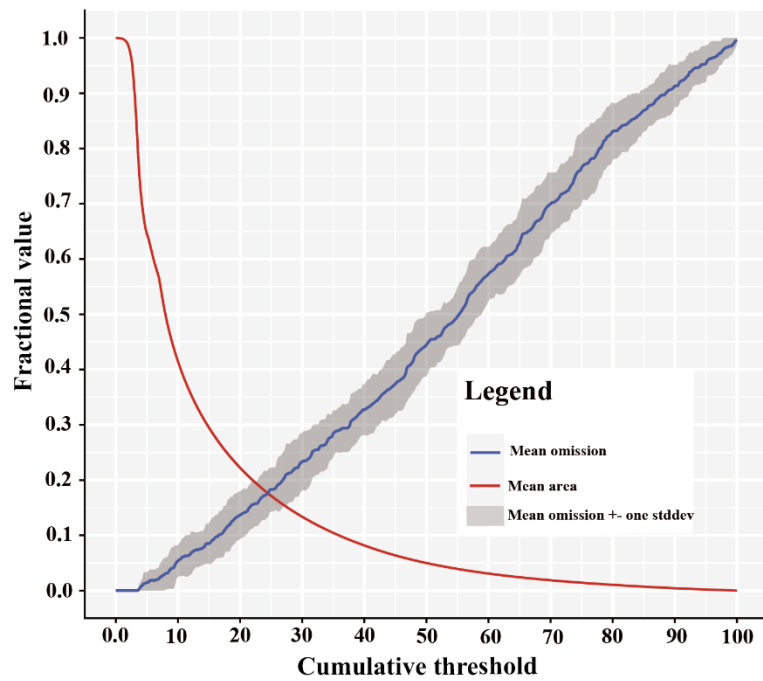
City	Risk Level	Area (Km ²)	Population
Aba Autonomous Prefecture	Low risk	64148.80	863570
	Medium risk	138.08	32451
	High risk	83.38	60255
Anshun City	Low risk	5333.83	445736
	Medium risk	715.60	1033754
	High risk	499.90	893389
Baoshan City	Low risk	12696.65	418597
	Medium risk	394.59	1116926
	High risk	237.70	1043290
Bazhong City	Low risk	9009.76	456072
	Medium risk	317.36	388940
	High risk	129.10	2630567
Bijie City	Low risk	17154.23	1139997
	Medium risk	1464.60	1313159
	High risk	720.18	4380090
Chengdu City	Low risk	6333.15	3317118
	Medium risk	2840.07	10443407
	High risk	1674.04	2254486
Chongqing City	Low risk	53804.59	4938018
	Medium risk	5008.24	12597443
	High risk	2892.51	12846107
Chuxiong Yi Autonomous Prefecture	Low risk	15973.42	418412
	Medium risk	2462.96	1827308
	High risk	1608.98	525276
Dali Bai Autonomous Prefecture	Low risk	16294.71	418741
	Medium risk	1942.58	577549
	High risk	1795.09	2583274
Dazhou City	Low risk	11177.37	1559124
	Medium risk	1113.99	1421821
	High risk	378.37	2844087
Dehong Autonomous Prefecture	Low risk	7604.23	252024
	Medium risk	90.61	206762
	High risk	29.62	771338
Deyang City	Low risk	2660.93	1545818
	Medium risk	1495.32	1580534
	High risk	350.75	718619

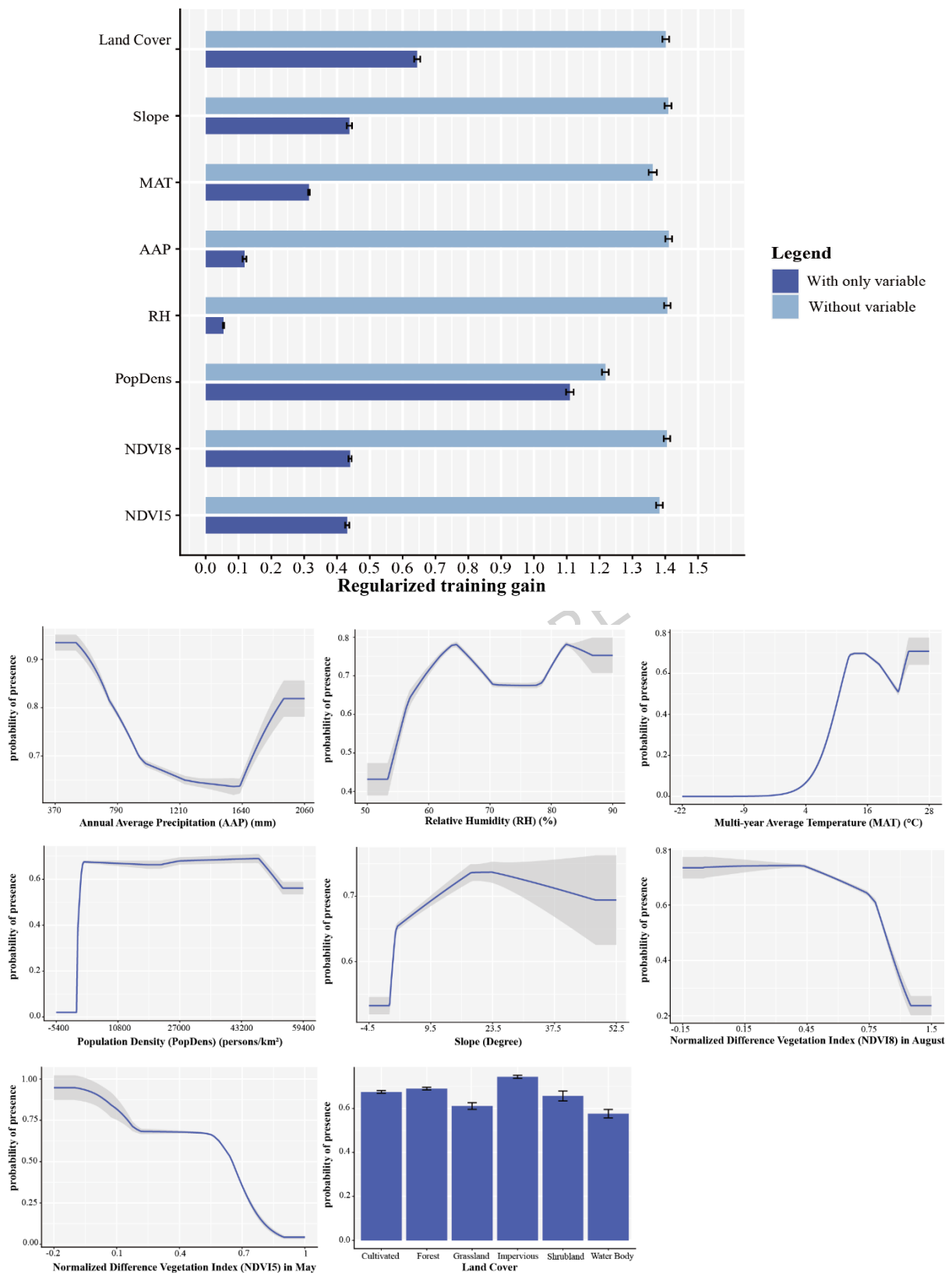
Diqing Tibetan Autonomous Prefecture	Low risk	16605.86	64948
	Medium risk	205.52	112523
	High risk	82.58	242858
Ganzi Tibetan Autonomous Prefecture	Low risk	112754.37	60348
	Medium risk	247.97	88297
	High risk	77.97	987516
Guang'an City	Low risk	3372.18	1214216
	Medium risk	1041.85	1244815
	High risk	385.52	1188051
Guangyuan City	Low risk	12071.61	286676
	Medium risk	318.70	647640
	High risk	180.47	1716316
Guiyang City	Low risk	4473.41	309672
	Medium risk	656.14	3561643
	High risk	641.75	621218
Honghe Autonomous Prefecture	Low risk	20226.34	732451
	Medium risk	1226.83	1970987
	High risk	645.55	1881562
Kunming City	Low risk	11746.94	5517194
	Medium risk	1591.52	496214
	High risk	1487.35	623839
Leshan City	Low risk	8718.07	387945
	Medium risk	413.14	1021837
	High risk	299.53	2003497
Liangshan Yi Autonomous Prefecture	Low risk	40945.86	683604
	Medium risk	1803.40	2079018
	High risk	1010.58	1920737
Lijiang City	Low risk	13126.75	153081
	Medium risk	976.76	897209
	High risk	693.04	242590
Lincang City	Low risk	15895.18	477666
	Medium risk	334.79	765272
	High risk	138.23	1265942
Liupanshui City	Low risk	6415.35	1200019
	Medium risk	389.04	362439
	High risk	254.73	1382781
Luzhou City	Low risk	6986.01	1422804
	Medium risk	1332.95	1914107
	High risk	646.05	1080539
Meishan City	Low risk	4374.80	522426

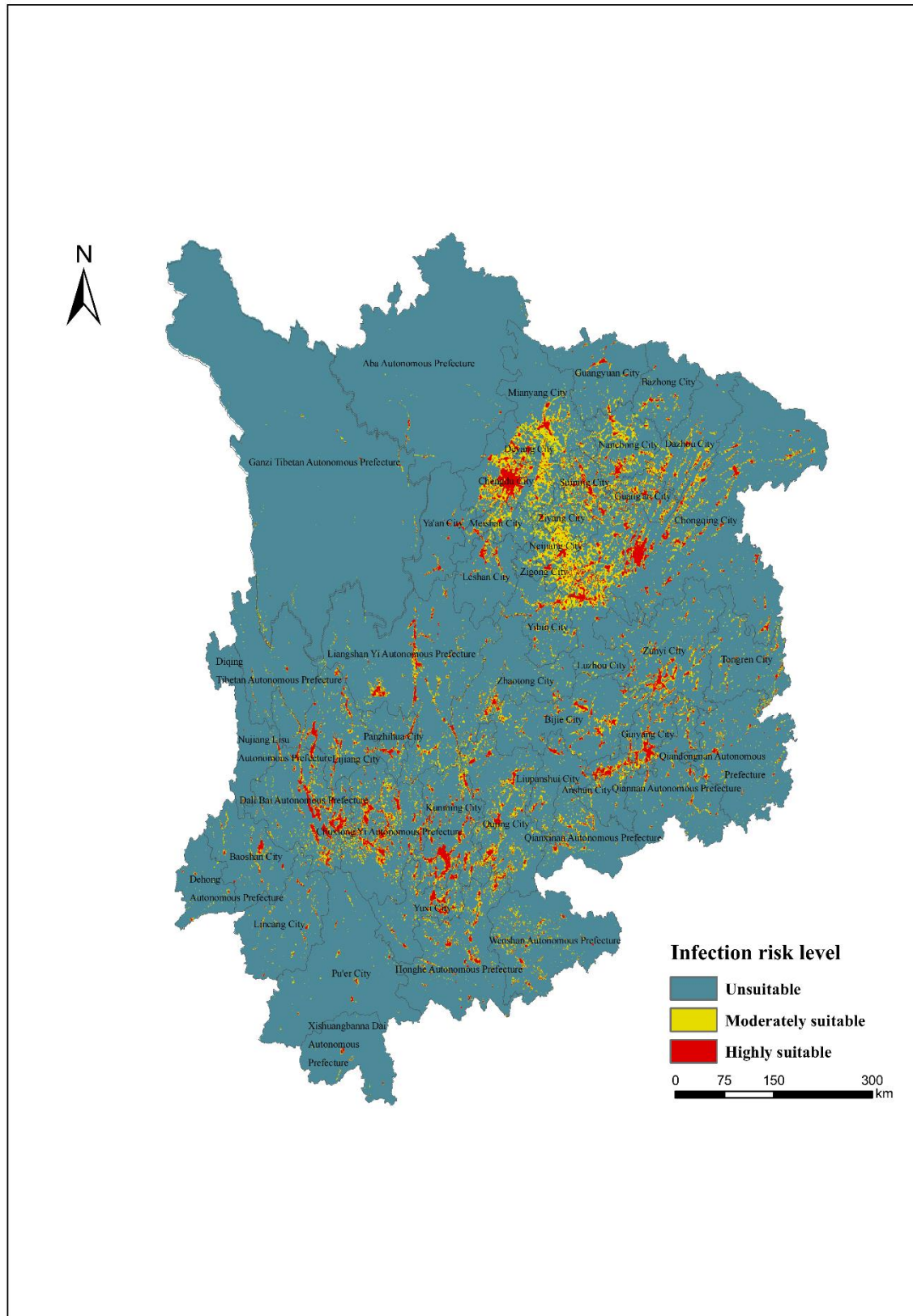
	Medium risk	784.63	1650396
	High risk	185.03	941987
Mianyang City	Low risk	13360.78	1550337
	Medium risk	1826.73	1569747
	High risk	406.25	1784364
Nanchong City	Low risk	7115.02	2083446
	Medium risk	1870.51	1988060
	High risk	536.54	2561136
Neijiang City	Low risk	1589.79	1994654
	Medium risk	2084.48	786386
	High risk	333.94	1080528
Nujiang Lisu Autonomous Prefecture	Low risk	10280.27	403128
	Medium risk	76.27	46458
	High risk	47.79	99869
Panzhihua City	Low risk	4693.79	144593
	Medium risk	340.54	924825
	High risk	271.94	194555
Pu'er City	Low risk	30114.53	380651
	Medium risk	170.92	609960
	High risk	80.48	1615439
Qiandongnan Autonomous Prefecture	Low risk	20639.10	470009
	Medium risk	641.64	795713
	High risk	278.45	2359910
Qiannan Autonomous Prefecture	Low risk	17308.98	818276
	Medium risk	849.60	544416
	High risk	358.34	1993493
Qianxinan Autonomous Prefecture	Low risk	10808.20	587998
	Medium risk	715.12	700802
	High risk	252.04	1608285
Qujing City	Low risk	17200.38	1429105
	Medium risk	2279.27	2621900
	High risk	988.51	2005189
Suining City	Low risk	2419.86	1102506
	Medium risk	1114.34	1541239
	High risk	492.17	790030
Tongren City	Low risk	12240.14	571704
	Medium risk	618.14	588681
	High risk	216.81	2057432
Wenshan Autonomous Prefecture	Low risk	20471.39	634780

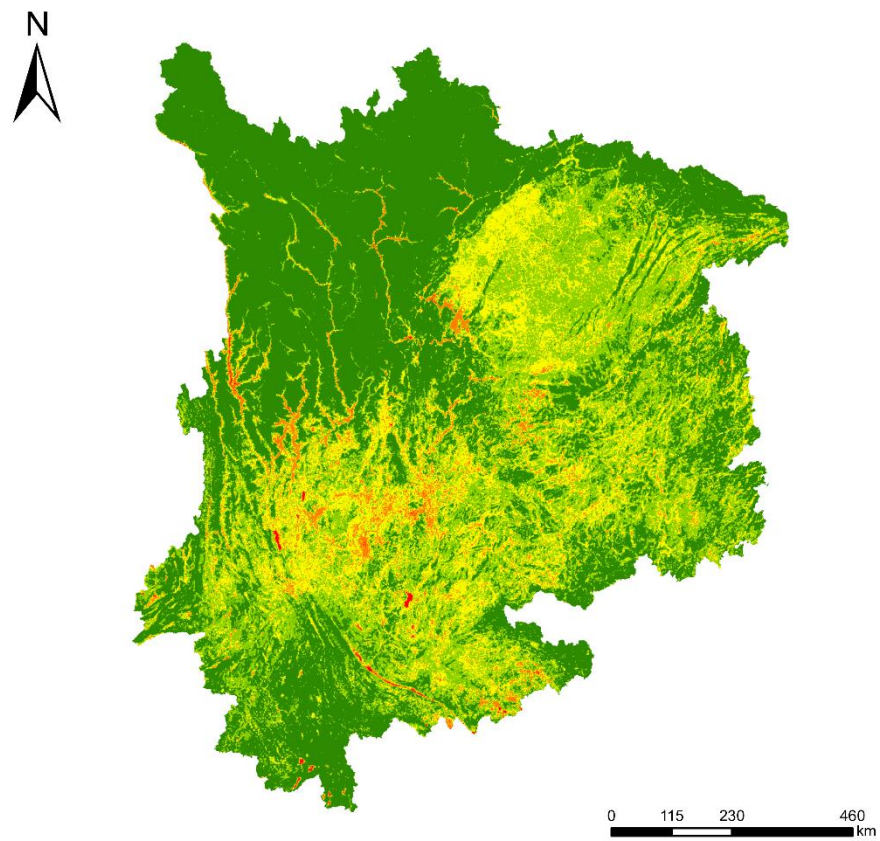
Xishuangbanna Dai Autonomous Prefecture	Medium risk	907.29	714726
	High risk	280.13	2255825
	Low risk	12731.40	73619
Ya'an City	Medium risk	66.07	173908
	High risk	38.61	903974
	Low risk	10939.91	171705
Yibin City	Medium risk	151.87	480347
	High risk	173.54	929566
	Low risk	8313.22	953216
Yuxi City	Medium risk	1064.58	1017000
	High risk	366.90	2737904
	Low risk	8950.16	332595
Zhaotong City	Medium risk	771.18	1623218
	High risk	657.00	441248
	Low risk	15073.80	937994
Zigong City	Medium risk	844.96	713230
	High risk	414.69	3827060
	Low risk	2052.85	977347
Ziyang City	Medium risk	1003.06	878237
	High risk	192.66	976697
	Low risk	2969.68	1204434
Zunyi City	Medium risk	1185.09	455753
	High risk	150.45	1111978
	Low risk	19915.94	1196192
	Medium risk	1601.37	2170286
	High risk	950.48	3043821









**Standard deviation of predicted suitability**

0.000002946 - 0.004107658 Very low SD

0.010264725 - 0.019842386 Moderate SD

0.046523013 - 0.174453199 Very high SD

0.004107658 - 0.010264725 Low SD

0.019842386 - 0.046523013 High SD