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Brief Research Article

# Preliminary Risk Maps for Transmission of Kyasanur Forest Disease in Southern India

**A. Townsend Peterson[1], Gautam Talukdar[2]**

[1]University Distinguished Professor, Biodiversity Institute, University of Kansas, Lawrence, Kansas 66045, USA, [2]Scientist, Wildlife Institute of India, Dehradun, Uttarakhand, India

## Summary

Kyasanur forest disease is known to be transmitted across forested regions of Southern India. The disease appears to be hosted in wild mammals and transmitted by tick vectors although the diversity and identity of host and vector species remain unclear. The area across which risk exists of contracting the disease through transfer from the hosts or vectors, however, has never been mapped in detail, such that the area that surveillance, education, and investment in diagnostic facilities should cover remains unknown. This contribution uses known occurrences of the disease from the year 2000 till date to create and test a correlational ecological niche model that translates into preliminary transmission risk maps, which are summarized in terms of risk presented in each district in the region, as well as across peninsular India.

**Key words:** Ecological niche, Kyasanur forest disease, map, moderate resolution imaging spectroradiometer, normalized difference vegetation index, transmission risk

## Introduction

Kyasanur forest disease (KFD) is caused by KFD virus, which is a member of the virus family *Flaviviridae*.[1] Discovered in 1957, it was isolated from a sick monkey from the Kyasanur Forest of Karnataka in Southern India.[2,3] Diverse tick species,[4,5] perhaps particularly hard ticks in the genus *Haemaphysalis*,[6] vector KFD among diverse wild mammals[5,7-9] and occasionally humans.[2,10] KFD outbreaks in humans are frequently presaged by high fatality rates in local primate populations.[10] A recent Indian Council of Medical Research publication[11] gives a full summary of aspects of the etiology and natural history of the disease.

The transmission area of KFD is simultaneously well known and poorly known. That is, to the best of our knowledge, no detailed map of potential transmission areas has been developed. All maps to date consist of (a) points of known occurrence, (b) broad and overly general outlines lacking detail entirely, or simply (c) outlines of states in which the disease has been documented. The point maps clearly underestimate risk areas, whereas the general outlines and state maps overestimate them. As such, a detailed, quantitative, data-driven risk-mapping effort is in order, which can be achieved using correlational ecological niche modeling[12] – development of such a preliminary risk map is the purpose of this contribution.

Ecological niche model development requires (a) data on known occurrences of the species or phenomenon in question, (b) a hypothesis regarding the area relevant and accessible to the species or phenomenon,[13] and (c) data describing environmental variation across the relevant area. For this study, we assembled occurrence data from the ProMED archives (http://www.promedmail.org/), over the period January 1, 2000–March 1, 2016. We used "kyasanur" as a search term, and reviewed each ProMED post for confirmed or strongly suspected KFD cases in humans. We used specific village names whenever possible, up to and including the smallest local districts (called *taluks*), but no areas coarser than that. We translated site names into geographic coordinates

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**Address for correspondence:** Prof. A. Townsend Peterson, Biodiversity Institute, The University of Kansas, Lawrence, Kansas 66045, USA. E-mail: town@ku.edu



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through consultation of Google Earth (https://www.google.com/earth/); sites that could not be located with confidence were excluded from the analysis. Our final sample size for occurrence data in the defined period was 31 records of sites (many more cases, of course, occurred, in many cases with multiple cases at individual sites; others were not reported in detail in ProMED). For lack of concrete knowledge of biogeographic barriers relevant to this virus distribution, but considering the possibility of movements of mammal reservoir taxa, we defined a relevant area (= the area that has been accessible to the species over relevant time periods or M)[13] as the area within 220 km of known occurrences of KFD; we note that additional risk areas may exist beyond the limits of this area, which we assess in a final analysis.

Environmental variation across Southern Indian landscapes was characterized using information expressed in multitemporal normalized difference vegetation indices from the moderate resolution imaging spectroradiometer sensor.[14] We used 1 year (2013) of data, comprising 23 16-day composite images at 250 m resolution. To reduce both the overall dimensionality of the environmental space and the collinearity among environmental dimensions, we used principal components analysis of the 23 images and retained for analysis only the first 8 components, which together explained > 99% of the overall variation in the environmental landscape of the region of interest [Figure 1 shows a visualization of variation in the first three of these principal components].

Ecological niche models were calibrated using maximum entropy routines implemented in Maxent version 3.3.3 k[15] with 10 random bootstrap replicates; initial model runs were based on a testing scheme designed to assess the model's ability to predict across unsampled areas. occurrences were sorted by latitude, and the northernmost 25% and southernmost 25% of occurrence data were used to calibrate the model, and the middle 50% were used in partial receiver operating characteristic (ROC) analyses,[16] using an online testing facility.[17] Final models were calibrated using all available occurrence data, with 10 replicate bootstrap analyses; we used the median of the logistic outputs across the 10 replicates as a suitability measure. Thresholds for interpretation as high- and moderate-risk areas were set using a modified least training presence thresholding approach[18] that allowed an acceptable omission error ($E$) of no more than $E = 10\%$ (moderate risk) or $E = 20\%$ (high risk) omission.[16]

Finally, in light of indications from initial analyses that risk areas might extend more broadly than our model calibration area, we explored the implications of our models more broadly across peninsular India. We outlined an area that included all of peninsular India, and recalculated the principal components as described above. We again calibrated models across the area within 220 km of known occurrences but transferred models across the broader area. To avoid known complications of model transfers,[19] we specified "no clamping" and "no extrapolation" in Maxent model transfer process, and we used the jackknife process to reduce the inclusion of variables in these final models (we used only components 1, 2, 5, and 6). Full details of the niche modeling methodology are available in a recent methodological synthesis.[12]

The spatially partitioned test of the model's predictions indicated excellent predictive ability of the models [Figure 2]. That is, the spatial distribution of occurrences in the middle 50% of the latitudinal distribution of KFD occurrences was anticipated closely by the model based on the northern and southern quartiles of the occurrences. All 1000 partial ROC random replicate analyses yielded area under the curve ratios above the critical value of 1.0, such that the model predictions were statistically significantly better than random predictions ($P < 0.001$).

Final models [Figure 3] indicated a narrow corridor of highly suitable areas for KFD transmission, running north–south along the coast of the Arabian Sea, coinciding with forested areas, and skirting around higher elevation areas [Figure 3]. The greatest concentrations of highly suitable areas were in southern coastal parts of Karnataka and even more into Kerala. Curiously, KFD cases were documented only recently in Kerala;[20] previously, the disease was known to occur only

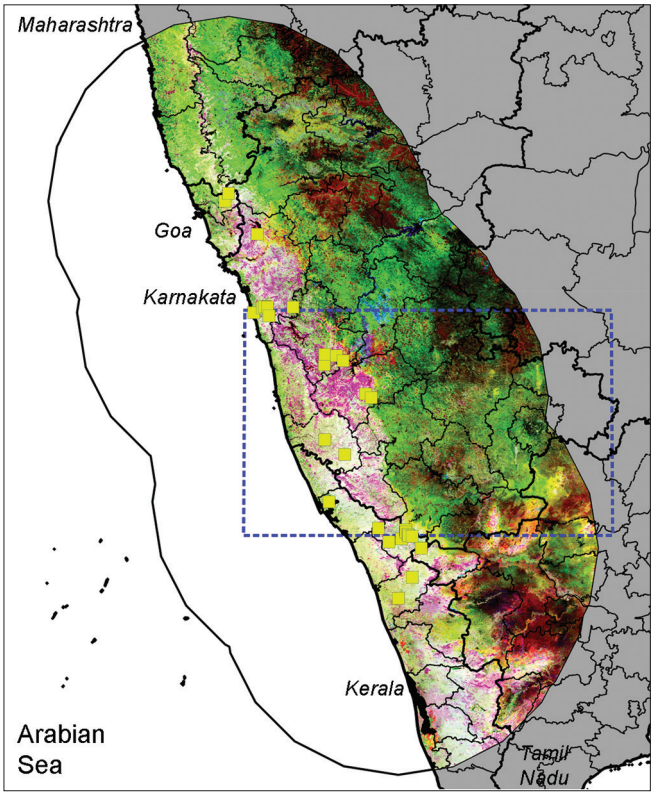


**Figure 1:** Known occurrence points (2000–2016, drawn from ProMED archives) plotted on a visualization of environmental variation across the region within 220 km of known occurrences of Kyasanur forest disease in humans. The visualization plots the first three principal components of the overall multitemporal moderate resolution imaging spectroradiometer normalized difference vegetation index data set as red, green, and blue, to provide a visualization of environmental diversity.

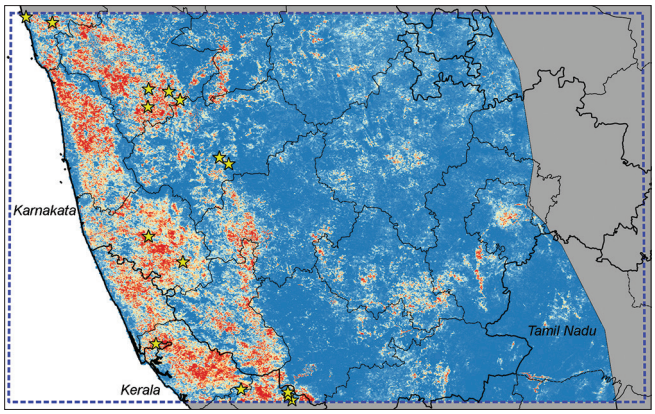


**Figure 2:** Test of niche model predictions across the middle 50% of the latitudinal distribution of human cases (2000–2016) of Kyasanur forest disease. Model predictions shown as a color ramp from blue (low suitability) to red (high suitability); independent test data shown as yellow stars; blue dashed box = test region. The model was calibrated with case data from farther north (25%) and farther south (25%), such that predictions and test data are independent of one another. The prediction resulted highly statistically significant based on partial receiver operating characteristic analyses.

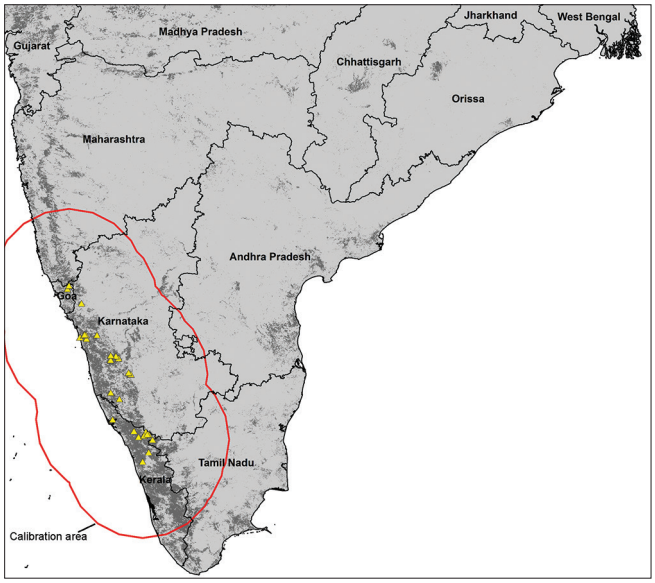


**Figure 4:** Projection of ecological niche models of risk of transmission of Kyasanur forest disease across peninsular India. Areas identified as at risk shown in dark gray; triangles indicate occurrence data, and the red outline shows the area across which models were calibrated.

farther north. Proportional coverage of districts overlapping the study area by high- and moderate-risk areas, according to the model outputs, is listed in the Appendix.

The models presented herein are admittedly based on relatively small sample sizes of sites where cases occurred during 2000–2016 and would ideally be tested and enriched with fuller sets of occurrence data. We are concerned that risk areas may extend farther north, and particularly farther south, as – in the latter direction – models identified high-risk areas even 220 km south of the known cases; this result suggested

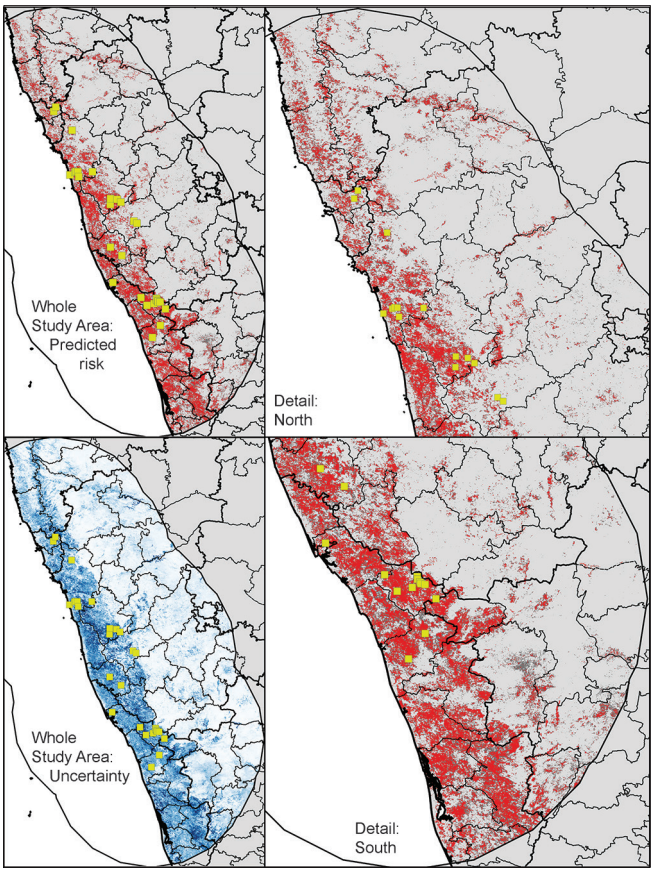


**Figure 3:** Final niche model predictions of areas suitable for Kyasanur forest disease transmission in Southern India. In three panels (upper left and right, lower right, modeled suitability shown as high (red, $E = 20\%$) and moderate (dark gray, $E = 10\%$). Lower left panel shows uncertainty: higher uncertainty in darker shades of blue, calculated as maximum – minimum across all 10 final replicate analyses.

that the risk areas for KFD may be still more broad than the area analyzed in this study. The absence of KFD records from what is at times termed the Southern Ghats (i.e., the Western Ghats south of Thrissur, Kerala) is particularly intriguing, as it coincides with a known biogeographic barrier. We assessed this possibility in our broad-area projections [Figure 4], which indicated that the broad risk areas do not extend much farther north than what was visible in our original models, but that apparently suitable conditions do extend beyond the Palghat Gap into the Southern Ghats.

In sum, we provide the first mapping of occurrences and possible risk of KFD transmission. Our models anticipated independent occurrence data remarkably well such that we have confidence in their predictions. Resources for avoiding infection, assuring successful diagnosis, improving patient care, and efficient case reporting can be allotted across the region using our risk statistics (Appendix) as a preliminary guide.

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## Conflicts of interest

There are no conflicts of interest.

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