International Journal of Primatology (2022) 43:74–91
https://doi.org/10.1007/s10764-021-00223-5

# The Risks of Yellow Fever to Asian Primates

Júlio César Bicca-Marques[1] · Rafael Magalhães Rabelo[2,3] · Marco Antônio Barreto de Almeida[4] · Lilian Patrícia Sales[5]

Received: 15 October 2020 / Accepted: 19 April 2021 / Published online: 27 May 2021
© Springer Science+Business Media, LLC, part of Springer Nature 2021

## Abstract

Infectious diseases are a growing threat to the conservation of nonhuman primates. In the case of diseases shared with humans, the risk is higher where habitat loss and fragmentation facilitate proximity to wildlife. Yellow fever (YF) is an infectious disease transmitted by mosquito vectors between primates in a sylvatic cycle or between humans in an urban cycle. Whereas YF does not compromise the survival of primates in Africa, where the disease is native and endemic, it has caused significant losses in Atlantic Forest primate populations in South America. Given that Asia is free of YF, we anticipate maps of infection risk for 80 species of Asian primates based on biotic and abiotic predictors of YF environmental suitability. Specifically, we used data on climate, forest cover, and the potential distribution of the mosquitoes that act as vectors in YF sylvatic cycles. We found that Malaysia, Singapore, Indonesia, Brunei, and portions of southern India are high-risk zones for the occurrence of the YF virus. Four primate species have their ranges located completely within YF high-risk zones and an additional 44 species include high-risk zones within their distributions. We found that YF is a potential threat to wildlife worldwide, and that Asian primates can become particularly vulnerable if the YF virus is introduced into the region. Given the documented negative effects of YF on primates that are not immune to the disease, we stress the urgency of global control policies, such as mass human vaccination and safer travel protocols, to prevent the spread of the YF virus.

**Keywords** Alien species · Conservation · Haplorrhini · Health · Infectious diseases · Strepsirrhini

## Introduction

Infectious diseases (hereafter diseases) shared with humans have long been known to cause high mortality in nonhuman primate (hereafter primate) populations (Balfour

Handling Editor: Paul Garber

✉ Júlio César Bicca-Marques
jcbicca@pucrs.br

Extended author information available on the last page of the article

1914; Collias and Southwick 1952; Formenty *et al.* 1999; see also Ryan and Walsh 2011; Wallis and Lee 1999). Yet, diseases were not officially recognized as major threats to the conservation of primates until recently. This situation is illustrated by the lack of any primate listed among the 54 mammals in the 2006 IUCN Red List of Threatened Species for which diseases were considered a major threat (Pedersen *et al.* 2007). Whereas most primate researchers and conservationists have focused their efforts on understanding and lowering the most pervasive impacts of habitat loss, habitat fragmentation, and hunting (Cowlishaw and Dunbar 2000), a few have proposed strategies to avoid the transmission of diseases from humans to primates even before the full recognition of diseases as critical threats to conservation (Wallis and Lee 1999; see also Bicca-Marques and Calegaro-Marques 2014; Wolfe *et al.* 1998).

Outbreaks of Ebola in chimpanzee (*Pan troglodytes*) and gorilla (*Gorilla beringei* and *G. gorilla*) populations in Africa (Bermejo *et al.* 2006; Formenty *et al.* 1999; Walsh *et al.* 2003) were critical in highlighting the importance of health surveillance of populations of threatened primate species (Wolfe *et al.* 1998). Since then, addressing disease prevention has gained momentum in primate research and conservation (Chapman *et al.* 2005; Estrada *et al.* 2017, 2018; Gillespie *et al.* 2008; Nunn and Altizer 2006; Nunn and Gillespie 2016). Outbreaks of other diseases, such as the yellow fever (hereafter YF) in South America (Almeida *et al.* 2012, 2014; Bicca-Marques *et al.* 2017; Holzmann *et al.* 2010; Moreno *et al.* 2013) and the Kyasanur Forest Disease in Asia (Shah *et al.* 2018), have reinforced the need to monitor the health of wild populations and to study the impact of diseases on their long-term viability.

Within this context, YF is an important disease to investigate. First, its causative agent, the YF virus, evolved in Africa sometime in the past 1500 yr (95% probability = 288–1304 yr; Bryant *et al.* 2007), where primates coevolved with it and developed resistance (Monath and Vasconcelos 2015). Second, it was introduced in the Americas between 300 and 400 yr ago during the trade of enslaved African humans (Bryant *et al.* 2007; Hanley *et al.* 2013), where it is currently endemic in 13 countries (WHO 2020b) and where its impacts on primates have been much higher than recorded in Africa. Third, YF never established itself in Asia (Hanley *et al.* 2013; Klitting *et al.* 2018; Kuno 2021), despite the likely existence of biotic and abiotic conditions to maintain its cycle (Monath and Vasconcelos 2015). This absence has been explained by the putative cross-immunity between the YF virus and other arboviruses, particularly the dengue virus. A less likely hypothesis, among others, is the lower competence of mosquito vectors (Amaku *et al.* 2011; Valentine *et al.* 2019). Although only few Asian primates are known to be susceptible to experimental infection with the YF virus (e.g., *Macaca mulatta*: Stokes *et al.* 1928; Theiler and Anderson 1975), its introduction in Asia could be catastrophic given the primates' lack of prior contact, as we describe in the text that follows for platyrrhines. An importation of human cases of YF from Angola into China in 2016 (Song *et al.* 2018; Wang *et al.* 2016; Wilder-Smith and Leong 2017) did not result in secondary in-country infection (Barrett 2018) but warned about its risk of introduction and spread in Asia given the presence of mosquito vectors and dense populations of unvaccinated people (Monath *et al.* 2016).

Yellow fever is a disease of great concern to public health. Despite the existence of a safe vaccine, tens of thousands of humans die in Africa and the Americas every year because there is no specific and effective treatment (WHO 2020b). Most infected

unvaccinated people are asymptomatic or develop a mild, harmless form of the disease. Those people who develop the severe or the fatal form and die represent *ca.* 6% of the infected population (Johansson *et al*. 2014). In the Americas, YF can follow an urban cycle that involves the original African mosquito vector *Aedes aegypti* and humans as hosts and a sylvatic cycle that is maintained by native *Haemagogus* spp. and *Sabethes* spp. mosquitoes and primates as hosts. Humans enter the sylvatic cycle accidentally (Abreu *et al*. 2019; Cardoso *et al*. 2010; Hanley *et al*. 2013; Monath and Vasconcelos 2015). Whereas the urban cycle has not generated cases throughout the continent of South America since the 1950s (Vasconcelos 2002), except for a localized and controlled resurgence in Paraguay in 2008, sylvatic outbreaks occur periodically outside the endemic region (Monath and Vasconcelos 2015). The two most recent extra-Amazonian sylvatic YF outbreaks occurred in center-west, southeast and southern Brazil between 2007 and 2009 and between 2014 and 2021 (Almeida *et al*. 2012; Bicca-Marques 2009; Bicca-Marques and Freitas 2010; Hill *et al*. 2020; Jesus *et al*. 2020; Moreno *et al*. 2011, 2013; Romano *et al*. 2019).

Thousands of deaths of howler monkeys (*Alouatta* spp.) during these outbreaks (Almeida *et al*. 2012, 2014; Bicca-Marques and Freitas 2010; Bicca-Marques *et al*. 2017; Hill *et al*. 2020; Holzmann *et al*. 2010; Moreno *et al*. 2011, 2013; Possamai *et al*. 2019; Romano *et al*. 2019) confirmed their long-known high susceptibility to the YF virus (Balfour 1914; Collias and Southwick 1952). After the 2007–2009 outbreak, the conservation status of *Alouatta guariba clamitans* changed from Endangered to Critically Endangered in Argentina and from Near Threatened to Vulnerable in Brazil, while that of *Alouatta caraya* changed from Least Concern to Vulnerable in Argentina and to Near Threatened in Brazil, and from Vulnerable to Endangered in the southernmost Brazilian state of Rio Grande do Sul (see Bicca-Marques *et al*. 2020).

Howlers, marmosets (*Callithrix* spp.), and capuchin monkeys (*Sapajus* spp.) were the most frequent taxa among the 23,270+ primate deaths recorded by the Brazilian Ministry of Health from July 2014 to June 2019 (Romano *et al*. 2019), a number that is certainly underestimated given that most primate deaths that occur in the interior of forests go unnoticed to local inhabitants, health, and environmental authorities. This later outbreak is also believed to have caused a 32% decline in the wild population of the Endangered *Leontopithecus rosalia* from 3700 individuals before the outbreak in 2014 to 2516 after it in 2018 (Dietz *et al*. 2019). The largest population of the Critically Endangered *Brachyteles hypoxanthus* decreased nearly 10% from 324 to 293 individuals in just 6 mo (October 2016–April 2017), whereas another, smaller population declined 26% from 34 to 25 individuals (Strier *et al*. 2019). The populations of the three primates syntopic with the larger *B. hypoxanthus* population showed greater losses. The Endangered *Callithrix flaviceps* decreased by >90%, the Vulnerable *Alouatta guariba clamitans* by >80%, and the Near Threatened *Sapajus nigritus* by 40%–50% between 2015 and 2017/2018 (Possamai *et al*. 2019). A population of the Near Threatened *Callicebus nigrifrons* was estimated to decrease by almost 80% after the same outbreak (Berthet *et al*. *unpublished*). This widespread impact of YF on platyrrhine monkeys even after ca. 400 yr of the introduction of the virus in the continent led the Vulnerable *A. guariba* to be included in the 2018–2020 list of the 25 world's most endangered primates (Buss *et al*. 2019) as an ambassador for warning about the risk of diseases to primate populations.

In addition to highlighting the need to better understand the role of each component of the sylvatic cycle, these later outbreaks provided critical data for improving our understanding of the factors that may facilitate the occurrence and spread of extra-Amazonian outbreaks of sylvatic YF. Modeling environmental suitability of the YF virus in the state of Rio Grande do Sul, Brazil based on the distribution of primate hosts, mosquito vectors and the occurrence of YF-related primate deaths during the 2008–2009 outbreak identified rainfall, air humidity, ambient temperature, and wind speed as important environmental predictors of YF distribution. While the first three variables modulate vector reproduction and density, wind speed facilitates the dispersal of infected vectors through the landscape (Almeida *et al*. 2019b).

Rainfall, temperature, altitude, and diversity of primate hosts were also associated with the occurrence of human cases of YF in South America (Hamrick *et al*. 2017). Similarly, temperature, rainfall, and vegetation cover were critical factors in the modeling of the global distributions of two mosquito vectors. Whereas India and other parts of eastern Asia are predicted as highly suitable for the mosquito *Aedes aegypti*, eastern China and Japan are particularly suitable for *Aedes albopictus* (Kraemer *et al*. 2015). Authors focusing on modeling the global distribution of YF have identified highly suitable areas in eastern Thailand and areas of lower suitability in parts of Malaysia and Indonesia (Rogers *et al*. 2006). Large areas of lower suitability were also identified in Cambodia, India, Laos, Myanmar, Papua New Guinea, the Philippines, and Vietnam (Shearer *et al*. 2018). These models have used environmental (mainly vegetation) variables and the distributions of vectors and primate hosts to identify regions suitable for the introduction of the YF virus that could also impact humans (e.g., Shearer *et al*. 2018).

Here we assess the suitability of the distribution ranges of Asian primates for the establishment of sylvatic YF cycles based on abiotic and biotic conditions. We begin by estimating the worldwide habitat suitability for the major mosquito vectors and combine this information with environmental gradients to predict the potential distribution of the YF virus. Then we assess the percentage of the distribution of each Asian primate species that is suitable for the establishment of YF as a proxy of their risk upon the introduction of the YF virus and compare this risk between taxonomic families and conservation status categories. We further explore our findings in light of the risk of different pathways for the introduction of the YF virus, the challenges of the required mitigating strategies, and the potential consequences for the conservation of Asian primates.

## Methods

### Data Collection

We modeled the global environmental suitability for the mosquito vectors involved in the sylvatic YF cycles in the Americas and Africa and in the Zone of Emergence in Africa, where other mosquito species are responsible for virus spillover into humans, who replace nonhuman primates as primary hosts (Fig. 1). We adopted a conservative approach of focusing on the sylvatic vectors because our aim was to assess the invasion of Asian forests by the YF virus and the *Aedes*, *Haemagogus* and *Sabethes* mosquitos

as "prerequisites" for the establishment of sylvatic cycles of the disease. We used the mosquitoes involved in the sylvatic cycles in Africa and South America as proxies for Asian sylvatic mosquitoes because of missing information on the efficacy of the latter as YF vectors (Kuno 2021). We decided not to model the suitability for the urban vector so as not to lose focus on the risks of establishing sylvatic cycles. This decision was also supported by the lack of evidence of infected *Aedes aegypti* in those urban and periurban areas in Brazil where primates have died of yellow fever (Abreu *et al*. 2019; Cunha *et al*. 2020; Sacchetto *et al*. 2020).

To establish the environmental conditions likely to drive the occurrence and potential distribution of sylvatic vectors, we first obtained biological data for those mosquito species available in online data repositories [Global Biodiversity Information Facility (GBIF) (www.gbif.org) and SpeciesLink (splink.cria.org.br)]. After removing duplicate occurrences and those outside land masses, we grouped the mosquito records by genus, resulting in a mean of 1670 ± SD 1450 records (*Aedes*: 699 records, *Haemagogus*: 3,846, *Sabethes*: 466). We used the occurrence data to model the global environmental suitability for each mosquito genus.

We generated 9999 random points within a previously estimated YF polygon (Hanley *et al*. 2013) to create a proxy of global suitability for the occurrence of the disease. We then assumed that the random points encompass the conditions that allow the simultaneous occurrence and interaction among the YF virus, vectors, and hosts. However, our assumption of a homogeneous probability of disease occurrence across the entire YF polygon increases commission error and uncertainty. To circumvent these positional issues, we removed YF occurrences that fell outside of landscapes with

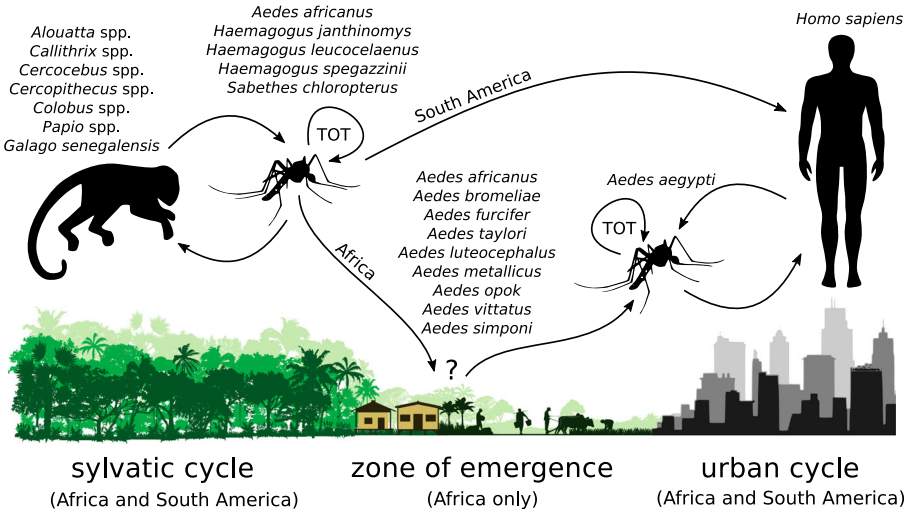


**Fig. 1** Sylvatic transmission, spillover, and urban transmission of the YF virus. In Africa, virus transmission occurs among mosquitoes (mainly *Aedes africanus*) by transovarial transmission process (TOT) and from mosquitoes to wild nonhuman primates in the sylvatic cycle. During the rainy season it reaches a "zone of emergence." Once the virus reaches humans, virus transmission is sustained and amplified by *Aedes aegypti* in urban areas. In South America, the sylvatic cycle is sustained by *Haemagogus* and *Sabethes* vector species and platyrrhine primates as hosts, especially *Alouatta* spp., which are highly susceptible and develop clinical disease. Eventual transmission to humans (without passing through a "zone of emergence") promotes the spillover to urban areas, where the cycle is also sustained and amplified by *A. aegypti*.

<30% forest cover based on estimates of tree cover from the literature (Hewson *et al.* 2019). Therefore, we approximate our YF occurrences to the regions where YF sylvatic cycles are more likely to take place.

We then estimated the influence of environmental variables on the distributions of mosquitoes and the YF virus. To do so, we defined which predictors are most likely to affect the species' macroscale distributions. Climate acts as a physiological filter to restrict and, therefore, determine species distribution at large geographical scales, whereas vegetation modulates habitat use and species occurrence. We incorporated multiple environmental dimensions, including climatic, vegetation, and topographic predictors, as mediators of habitat suitability. Climate information was obtained at WorldClim version 2 (https://worldclim.com/version2) in the form of 19 gridded spatial files encompassing a wide range of conditions that species are likely to experience in the wild (Fick and Hijmans 2017). These are called "bioclimatic predictors." Vegetation was obtained as NASA Earth Observations (https://neo.sci.gsfc.nasa.gov/) in the form of gridded estimates of Normalized Difference Vegetation Index (NDVI) and Net Primary Productivity (NPP) (Electronic Supplementary Material [ESM] Table SI). We reprojected the layers of these variables to a Robinson projection (datum WGS 84) at a 0.5-degree resolution (pixel size of *ca.* 55 $km^2$). Given the correlation between most of these variables, we reduced their multidimensionality into few axes via a principal component analysis (PCA).

## Statistical Analysis

**Predicting the Environmental Suitability for Mosquito Vectors and the YF Virus** We established the relationship between the mosquitoes' patterns of occurrence and the environmental variables by summarizing the environmental information with a PCA, as mentioned earlier. We then selected the PCA axes that cumulatively explained 85% of the variation in data (ESM Table SII) and used the first four PCA axes as environmental predictors in our modeling (ESM Fig. S1). We performed the characterization of each species' environment using a Poisson Point Process Model (hereafter PPM). A PPM is a point pattern analysis that evaluates how point density (or intensity) changes as a function of covariates according to a statistical model (Renner *et al.* 2015). This approach is robust to the presence of spatial nonindependence of data while still providing useful predictions of species' distributions (Graham *et al.* 2008). Basically, this model uses a logistic equation to predict point intensity as a log-linear function of its predictor variables. Therefore, we assumed that the modeled point density for vectors or for the YF virus at a given pixel represents the degree of habitat suitability for them at that location. We modeled the point density for vectors as

$$\log(\lambda_i) = \alpha + \beta 1 * \mathrm{PCA1}_i + \beta 2 * \mathrm{PCA2}_i + \beta 3 * \mathrm{PCA3}_i + \beta 4 * \mathrm{PCA4}_i$$

where $\lambda_i$ is the modeled point density for each mosquito genus at pixel $i$, $\alpha$ is the point density when all covariates are zero, and $\beta$ are the parameters by which the point density increases or decreases for each 1 unit of change in environmental covariates $\mathrm{PCA}_i$. Poisson regression models, including PPM, are equivalent to many popular methods of species distribution modeling such as Maxent, logistic regression, and Poisson generalized linear model (Aarts *et al.* 2012; Renner and Warton 2013).

After fitting the vector models of habitat suitability, we evaluated their accuracy in predicting known occurrences. To do so, we used a repeated subsampling technique that separates the dataset into "training" and "testing," setting 75% of the data to train the model and the remaining 25% to validate it, repeating this procedure 100 times for each model. Training and testing should ideally use independent datasets to evaluate the accuracy of species distribution models (Araújo *et al*. 2019). However, as often is the case of data from tropical and megadiverse regions, the paucity and inconsistency of yellow fever records in South America prevented us from using this approach. Then, we evaluated the model ability to discriminate presences from absences using the area under the receiver operating characteristic curve (AUC; Fielding and Bell 1997) and the true skills statistics (TSS; Allouche *et al*. 2006).

While AUC is a threshold-independent metric, TSS relies on the selection of a threshold of occurrence probability in which the relationship between commission (false positive) and omission (false negative) errors are minimized (Allouche *et al*. 2006; Fielding and Bell 1997). Both metrics provide a single value of model accuracy. AUC ranges from 0 to 1, and TSS ranges from −1 to +1. An AUC of 0.5 and a TSS of 0 indicate that the model's ability to discriminate presences from absences equals a random distribution. Therefore, AUC >0.5 and TSS >0 indicate that the model discriminates presences from absences above chance level. A value of +1 indicates perfect discrimination for both metrics. It is usually accepted that an AUC >0.8 and a TSS >0.5 indicate good model fit (Almeida *et al*. 2019b; Cavalcante *et al*. 2020; Sales *et al*. 2020). We selected the threshold that maximizes accuracy to convert continuous predictions of habitat suitability into binary estimates of "suitable" vs. "unsuitable" cells from global raster files (Liu *et al*. 2005). We therefore identified regions of the world suitable for the survival of the sylvatic mosquitoes using these layers.

Then, assuming that the mosquito vectors are obligatory elements for the occurrence of sylvatic YF cycles, we included their regional predicted environmental suitability as predictor variables in the modeling of the regions suitable for the YF virus. We transformed the predicted mosquito intensity in regions where the respective species is currently absent into zero (i.e., *Haemagogus* spp. and *Sabethes* spp. in Africa and Southeast Asia, and African *Aedes* spp. in Latin America) before including the vector layers in the model. We performed this transformation to predict a more realistic scenario of YF suitability. Therefore, we modeled the YF virus point density as

$$\log(\lambda_i) = \alpha + \beta 1 * \mathrm{PCA1}_i + \beta 2 * \mathrm{PCA2}_i + \beta 3 * \mathrm{PCA3}_i + \beta 4 * \mathrm{PCA4}_i + \beta 5 * Aedes_i + \beta 6 * Haemagogus_i + \beta 7 * Sabethes_i$$

where $\lambda_i$ is the modeled virus point density at pixel $i$, $\alpha$ is the point density when all covariates are zero, and $\beta$ are the parameters by which the YF virus intensity increases or decreases with each 1 unit in abiotic/biotic covariates. We performed a model selection based on the Akaike's (1974) information criterion (AIC) to distinguish among models with different subsets of predictors. We compared the fit (AIC value) of the potential distribution models of the YF virus with different combinations of predictor variables assuming that models with $\Delta$AIC <2 were similarly supported by the data. After selecting and fitting the best model, we evaluated model accuracy using

the TSS as described earlier. Then, we predicted the suitability for the YF virus across the distribution of Asian primates.

**Assessing the Potential Vulnerability of Primates to the Introduction of the YF Virus in Asia** We used the predicted worldwide suitability for the YF virus to assess the potential vulnerability of 80 Asian primate species to the disease. We accomplished this by measuring the proportion of each species' range that overlapped regions considered suitable for YF occurrence, should the YF virus be introduced into Asia. However, some species in the Philippines and other small islands included pixels with missing environmental data. Therefore, we suggest that our results should be interpreted from a conservation biogeography perspective in which individual species estimates should be analyzed with caution, especially those from locations with missing information. We obtained range maps for the species from the International Union for Conservation of Nature (IUCN) database (www.iucnredlist.org). We performed all GIS procedures and statistical modeling in R version 3.4.4 (R Development Core Team 2018).

## Ethical Note

We based this study on data from the cited literature and from online repositories (www.gbif.org, splink.cria.org.br, www.iucnredlist.org). We did not collect field or captive data for this study and the research adhered to all legal and institutional requirements. The authors declare that they have no conflict of interest.

**Data Availability** Occurrence data sets for mosquito vectors and example codes are available as Electronic Supplementary Material.

## Results

We found that only the first two PCA axes had significant effects on the three mosquito vector taxa (ESM Tables SI and SII). The strongest, negative effect of PCA1 on the global mosquito distribution (ESM Tables SI and SII and Fig. S2) was associated with higher annual mean temperature and precipitation, and higher vegetation cover (negative values) and with a wider annual temperature range and higher seasonality (positive values; ESM Table SIII). Areas presenting these environmental conditions are more suitable for the potential occurrence of African *Aedes* spp. in Latin America and of South American *Haemagogus* spp. and *Sabethes* spp. in Africa and Southeast Asia (Fig. 2).

We found strong accuracy in all model validation, which indicates that our models showed robust support from the data (Table I). The best explanatory models of the suitability for the YF virus ($\Delta$AICc <2) included the four PCA axes and the distributions of the mosquito taxa as predictors (ESM Table SIV). Therefore, the inclusion of the distribution of the mosquito vectors improved the predictive performance of the YF virus models. Those models correctly identified YF endemic

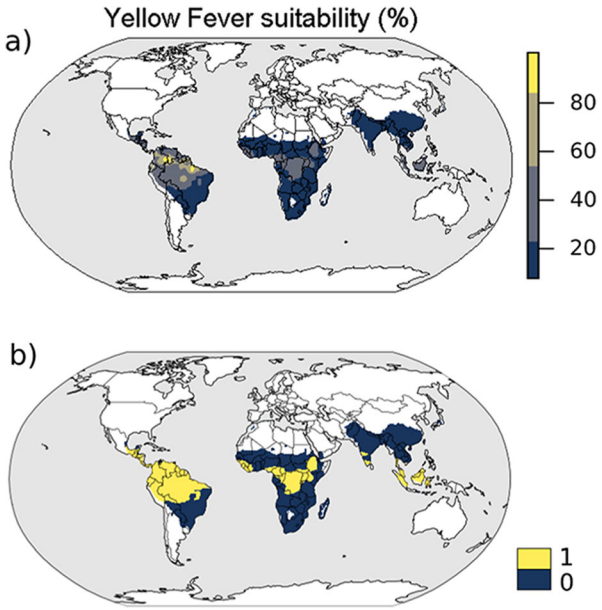


**Fig. 2** Predictions of habitat suitability for the YF virus at the extent of occurrence of Asian primates. Estimates were calculated with Poisson point process models (PPMs) calibrated with environmental information on climate and vegetation, in addition to the occurrence of the vectors of the virus (*Aedes*, *Haemagogus*, and *Sabethes* mosquitoes) in Africa and the Americas. The upper map (**a**) shows the global distribution of suitable environments in a continuous projection (in %), whereas the bottom map (**b**) shows it in the binary projection used to estimate the risk of YF to the species.

regions in Africa and Latin America and predicted southern India and portions of Southeast Asia (Malaysia, Singapore, Indonesia, and Brunei) as regions considered suitable for the YF virus (Fig. 2). Similar to the mosquito models, suitability for the YF virus was higher in regions with higher temperature, precipitation, and vegetation cover, and wider temperature variation on a global scale. According to this model, suitability for the YF virus was higher in regions with higher suitability for *Aedes* spp. and, particularly, *Haemagogus* spp., but lower in regions with higher suitability for *Sabethes* spp. (ESM Fig. S3).

The range size of the studied Asian primates spans from 16 km$^2$ for the Critically Endangered *Nomascus hainanus* to 6,661,788 km$^2$ for the Least Concern *Macaca mulatta* (ESM Table SV). Forty-four Asian primates (55% of the analyzed species) were considered exposed to the risk of YF, should the virus be introduced into the forests of the region. From those, four species had their ranges completely overlapping high-risk zones for the YF virus. They are the Critically Endangered *Pongo tapanuliensis*, the Vulnerable *Presbytis hosei*, and the Data Deficient *Tarsius lariang* and *Tarsius pumilus*. In addition, 25 species had ≥50% of their ranges exposed to the risk of YF (Fig. 3a and ESM Table SV). Most Tarsiidae and Hominidae species were found to be at risk of exposure to the YF virus (Fig. 3b). Most primates in our sample (68 out of 80) are threatened or Near Threatened with extinction (13 Critically Endangered, 25 Endangered, 22 Vulnerable, 8 Near Threatened; ESM Table SV). A greater proportion of Vulnerable (55%), Near Threatened (50%), and Data Deficient (50%) species have at least 50% of their ranges exposed to the risk of YF compared

**Table I** Evaluation and accuracy of habitat suitability models

| | Validation metric | | Recommended threshold |
|---|---|---|---|
| | AUC | TSS | |
| *Aedes* spp. | 0.79 | 0.57 | 0.04 |
| *Haemagogus* spp. | 0.81 | 0.67 | 0.07 |
| *Sabethes* spp. | 0.84 | 0.70 | 0.08 |
| Yellow fever | 0.86 | 0.58 | 0.15 |

Habitat suitability models of mosquito YF vectors (*Aedes* spp., *Haemagogus* spp. and *Sabethes* spp.) were built from georeferenced species' occurrences and validated using the area under the receiver operating characteristic curve (AUC) and the true skills statistics (TSS; see the text for details). The recommended threshold is the one that minimizes omission and commission errors.

with species in the other categories of conservation status (Endangered, 28%; Critically Endangered, 23%; Least Concern, 12%; Fig. 3c).

## Discussion

Yellow fever is an African-borne disease that has decimated native populations of Latin-American primate species that are not adapted to the YF virus. Here we modeled the potential global distribution of YF based on abiotic and biotic conditions suitable for the establishment of sylvatic cycles of the disease. We found that the tropical belt, especially warm and humid environments, is highly suitable for the occurrence of YF, as has also been reported by other authors (e.g., Rogers *et al*. 2006; Shearer *et al*. 2018). Southern India and Southeast Asia (Malaysia, Singapore, Indonesia, and Brunei) have highly suitable areas for the YF virus, potentially threatening most of its primate fauna. We also found that 55% of the Asian primates that composed our sample ($n$ = 44), including threatened species and species from all primate families, live in regions with favorable conditions for the occurrence of the disease. The entire distribution of many species is included within these high-risk zones. Across the known distributional limits of the remaining 36 species (45% of our sample), the estimated risk of YF was considered low (<16%). However, limitations on environmental data may have biased risk assessments for some species, so that areas predicted as low risk of YF should not be considered risk-free for conservation planning and preventive strategies.

Asian people and primates are naïve to the YF virus. Assuming that common exposure to dengue and other arboviruses promotes the cross-immunity, the introduction of the YF virus into the continent may result in milder consequences than those seen in the Americas (Amaku *et al*. 2011; Wolfe *et al*. 2001). There is also experimental evidence that individuals of *Macaca mulatta* previously exposed to the dengue virus showed reduced levels of viremia when challenged with the YF virus (Theiler and Anderson 1975). In this respect, laboratory evidence of natural infection with dengue and/or other arboviruses in wild populations of *Macaca fascicularis*, *Macaca fuscata*, *Macaca nemestrina*, *Macaca sinica*, *Presbytis melalophos*, *Trachypithecus cristatus*, *Trachypithecus obscurus*, and *Pongo pygmaeus* (see review by Valentine *et al*. 2019) is compatible with the existence of sylvatic cycles of these diseases in Asian forests

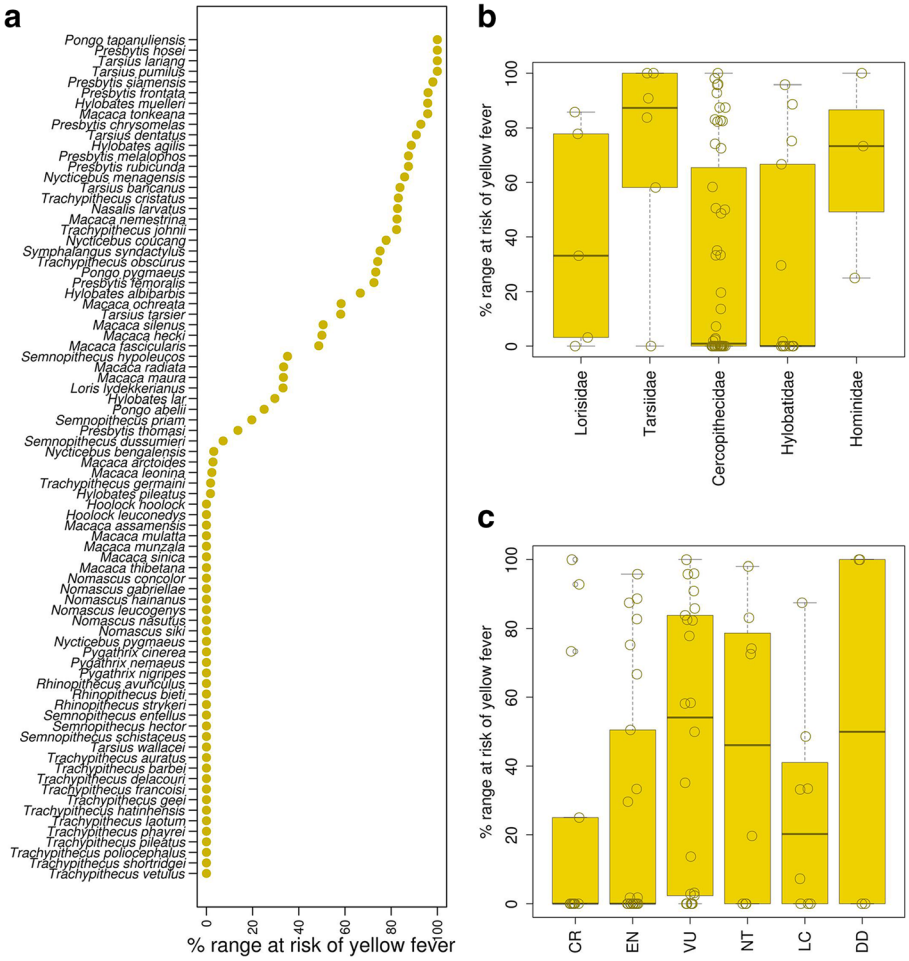


**Fig. 3** Asian primates' vulnerability to YF. Species vulnerability was measured as the percentage of their ranges that is suitable for YF. **(a)** Ranking of the vulnerability of Asian primate species to YF. Comparison of the risk of YF to **(b)** families and **(c)** conservation statuses (according to the IUCN Red List of Threatened Species). The boxes represent the first and third interquartiles, the black horizontal lines within the boxes represent the medians, the whiskers represent the 5th and 95th percentiles, and the open circles represent the primate species.

(Wolfe *et al*. 2001). The existence of cross-immunity would not only lower the impact on primate populations, but it could decrease the risk and speed of YF virus spread (Metcalf and Lessler 2017; see also Almeida *et al*. 2019a). Additionally, the fact that immunity after infection is lifelong (Rogers *et al*. 2006) could lower the risk of establishing sylvatic YF cycles in dengue-endemic areas.

Assuming that Asian primates are susceptible to the YF virus, irrespective of their immunity to dengue and other arboviruses, there is wide variation in the risk across species. Whereas the habitats of most Critically Endangered, Endangered, and Least Concern species do not present optimal conditions for establishment of the YF virus, the habitats of about half of the Vulnerable, Near Threatened, and Data Deficient species are highly suitable for the virus. At the family level, most Tarsiidae and

Hominidae would face a high risk of susceptibility to YF upon the introduction of the virus within their ranges. The case of *Pongo tapanuliensis* may be particularly critical given that its entire small distribution is suitable for YF and that the construction and flooding of a hydroelectric dam will further reduce its habitat by 8% (Sloan *et al*. 2018). Although the entire habitat of *Presbitys hosei* is also suitable for YF, this taxon occupies an area >200 times larger than that of *P. tapanuliensis*. The situation of the Data Deficient *Tarsius lariang* and *Tarsius pumilus* demands particular attention as well. Research on population size and trend across their small ranges is urgent to assess their conservation status. Also, whereas *Pongo pygmaeus* and several other Asian primates exposed to dengue and other arboviruses may benefit from some level of cross-immunity protection against the YF virus, similar evidence of infection appears to be missing for *Tarsius* spp. either because of lack of investigation or because this lineage is more sensitive to arboviruses and infected individuals do not survive.

Prevention of sylvatic outbreaks will require the development of safe and effective vaccines for primates. A successful test of the effectiveness of the 17DD attenuated human YF vaccine for immunizing wild-born captive howler monkeys was recently performed in Brazil (Fernandes *et al*. 2020). However, even if it is proved efficient and safe for other primates and produced in large scale, its delivery needs to consider the potential stress and the risks associated with darting, sedating, capturing, and handling wild primates. Even in the event that an oral vaccine is created, the technical challenges of habituating and baiting wild primates to ensure the ingestion of an appropriate dose by adults, juveniles, and infants are extremely difficult (Ryan and Walsh 2011). In addition, the feasibility of either strategy must take into account the species' behavior; the size of populations; the proportion of habituated individuals or groups; the distribution, characteristics, and accessibility of their habitats; and the logistics, personnel, financial investment, and time required (see Leendertz *et al*. 2017). Finally, it is critical to assess the level of immunity of each target population to avoid large outbreaks. In the case of human YF, transmission is prevented when ≥80% of a population is immunized (WHO 2020b). Additionally, wherever there is a risk of reemergence, new immunization campaigns will be necessary as susceptible individuals are born into the population. In sum, a case-by-case cost-benefit analysis is necessary to assess whether such intervention (Ryan and Walsh 2011) is worth pursuing.

In light of these uncertainties and risks, preventing the introduction of a species is always the best policy (Simberloff 2013). In the case of the YF virus, the strategies needed to avoid its arrival in Asia depend on the pathway of introduction. Immunization of people arriving from YF-endemic countries is a critical strategy. This risk of introduction should be minimized given International Health Regulations mandating the presentation of a certificate of immunization upon arrival in the region (WHO 2020b). However, improper enforcement that allowed the importation of the YF virus into China (Wang *et al*. 2016; Wilder-Smith and Leong 2017) and the recent withdrawal of this requirement by the governments of Laos and Vietnam (WHO 2020a) are particularly worrisome. The widespread presence of *Aedes aegypti* in Asia (Amaku *et al*. 2011; Shearer *et al*. 2018) and the common occurrence of primates in many cities (Bicca-Marques 2017) may facilitate the establishment of urban YF cycles in the ports of entry before the spread of the YF virus to forested regions. This is the pattern that happened with the introduction of YF into the Americas some 400 yr ago (Hanley *et al*. 2013).

Another potential pathway of introduction is via the trade of agribusiness and forestry commodities (Klitting *et al*. 2018) accidentally carrying infected eggs, larvae, or adult mosquito vectors (Chippaux and Chippaux 2018; Kraemer *et al*. 2015), like the long-distance transport and introduction of the urban mosquitoes *Aedes aegypti* and *Aedes albopictus* in new continents via shipping and airfreight (Tatem *et al*. 2006; see also Kraemer *et al*. 2015). Inspection and fumigation of the cargo before unloading is necessary to significantly reduce the risk (Tatem *et al*. 2006).

Lastly, the risk of YF virus introduction via primate trade is probably negligible. Legal exports and illegal trafficking of primates from Africa and South America pose low risk of carrying the YF virus as viremic individuals are infective only during a 4- to 5-day period (Woodall *et al*. 1968), beginning as soon as 2 days after infection (Monath *et al*. 1981). The illegal trade of live primates between Asian countries (Nijman *et al*. 2011), however, could facilitate the spread of the disease upon the establishment of YF sylvatic or urban cycles in the region.

Finally, irrespective of the pathway of introduction, if the YF virus is established in Asian forests, its spread can be facilitated by increases in temperature, rainfall, and air humidity associated with the ongoing climate change, as these climatic conditions have been related to the survival and reproduction of mosquito vectors (Almeida *et al*. 2019b). Southeast Asia is likely to be particularly affected because it is predicted to experience higher frequencies of extreme heat waves and heavy rainfall (ADB 2017). Additionally, taxa currently not expected to face significant risks with the introduction of the YF virus in Asia could be in danger if changes in these abiotic factors increase YF suitability of regions currently at low risk based on our modeling.

In sum, we modeled the areas within the distribution of Asian primates with abiotic and biotic conditions suitable for the establishment of sylvatic YF cycles and their potential consequences for primate conservation. We also explored potential pathways for the introduction of the YF virus in the region and addressed the required measures to avoid this scenario. We expect that our study will be useful for scientists and decision-makers to enforce and propose governmental policies to avoid the importation, establishment, and spread of the YF virus and other infectious organisms. We also recommend funding scientific research examining the vulnerability of Asian primates to the YF virus, the existence of cross-immunity with dengue, and the competence of native Asian sylvatic mosquitoes to act as YF vectors. Finally, we advocate measures aimed at protecting primates and humans from YF, and to model the risk of introducing other emerging infectious diseases afflicting primates (e.g., Ebola and Kyasanur Forest Disease) outside their current distributions.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s10764-021-00223-5.

**Acknowledgments** We thank Alejandro Estrada and Paul A. Garber for inviting us to contribute to this special issue. We also thank two anonymous reviewers and Paul A. Garber for their critical and constructive comments on earlier versions of this article. JCBM also thanks the Brazilian National Council for Scientific and Technological Development/CNPq for a research fellowship (PQ 1C No. 304475/2018-1). RMR also thanks CNPq (No. 142352/2017-9). MABA acknowledges the support of Vivyanne Santiago Magalhães. LPS thanks the Concordia University for a Horizon2020 post-doc fellowship.

**Author Contributions** JCBM conceived the study. JCBM, RMR and MABA designed the study. RMR and LPS analyzed the data. JCBM, RMR, MABA, and LPS wrote the manuscript.

## References


Aarts, G., Fieberg, J., & Matthiopoulos, J. (2012). Comparative interpretation of count, presence-absence and point methods for species distribution models. *Methods in Ecology and Evolution, 3*, 177–187. https://doi.org/10.1111/j.2041-210X.2011.00141.x.

Abreu, F. V. S., Ribeiro, I. P., Ferreira-de-Brito, A., Santos, A. A. C., Miranda, R. M., et al (2019). *Haemagogus leucocelaenus* and *Haemagogus janthinomys* are the primary vectors in the major yellow fever outbreak in Brazil, 2016–2018. *Emerging Microbes & Infections, 8*, 218–231.

ADB (Asian Development Bank) (2017). *A region at risk: The human dimensions of climate change in Asia and the Pacific*. Asian Development Bank. https://doi.org/10.22617/TCS178839-2.

Akaike, H. (1974). A new look at the statistical model identification. *IEEE Transactions on Automatic Control, 19*, 716–723.

Allouche, O., Tsoar, A., & Kadmon, R. (2006). Assessing the accuracy of species distribution models: prevalence, kappa and the true skill statistic (TSS). *Journal of Applied Ecology, 43*, 1223–1232. https://doi.org/10.1111/j.1365-2664.2006.01214.x.

Almeida, M. A. B., Cardoso, J. C., Santos, E., Fonseca, D. F., Cruz, L. L., et al (2014). Surveillance for yellow fever virus in non-human primates in southern Brazil, 2001–2011: A tool for prioritizing human populations for vaccination. *PLoS Neglected Tropical Diseases, 8*, e2741. https://doi.org/10.1371/journal.pntd.0002741.

Almeida, M. A. B., Santos, E., Cardoso, J. C., Fonseca, D. F., Noll, C. A., et al (2012). Yellow fever outbreak affecting *Alouatta* populations in southern Brazil (Rio Grande do Sul State), 2008–2009. *American Journal of Primatology, 74*, 68–76. https://doi.org/10.1002/ajp.21010.

Almeida, M. A. B., Santos, E., Cardoso, J. C., Noll, C. A., Lima, M. M., et al (2019a). Detection of antibodies against Icoaraci, Ilhéus and Saint Louis encephalitis arboviruses during yellow fever monitoring surveillance in non-human primates (*Alouatta caraya*) in southern Brazil. *Journal of Medical Primatology, 48*, 211–217. https://doi.org/10.1111/jmp.12417.

Almeida, M. A. B., Santos, E., Cardoso, J. C., Silva, L. G., Rabelo, R. M., & Bicca-Marques, J. C. (2019b). Predicting yellow fever through species distribution modeling of virus, vector, and monkeys. *EcoHealth, 16*, 95–108. https://doi.org/10.1007/s10393-018-1388-4.

Amaku, M., Coutinho, F. A. B., & Massad, E. (2011). Why dengue and yellow fever coexist in some areas of the world and not in others? *BioSystems, 106*, 111–120. https://doi.org/10.1016/j.biosystems.2011.07.004.

Araújo, M. B., Anderson, R. P., Barbosa, A. M., Beale, C. M., Dormann, C. F., et al (2019). Standards for distribution models in biodiversity assessments. *Science Advances, 5*, eaat4858. https://doi.org/10.1126/sciadv.aat4858.

Balfour, A. (1914). The wild monkey as a reservoir for the virus of yellow fever. *The Lancet, April, 25*, 1176–1178.

Barrett, A. D. T. (2018). The reemergence of yellow fever. *Science, 361*, 847–848. https://doi.org/10.1126/science.aau8225.

Bermejo, M., Rodríguez-Teijeiro, J. D., Illera, G., Barroso, A., Vilà, C., & Walsh, P. D. (2006). Ebola outbreak killed 5000 gorillas. *Science, 314*(5805), 1564.

Bicca-Marques, J. C. (2009). Outbreak of yellow fever affects howler monkeys in southern Brazil. *Oryx, 43*, 173.

Bicca-Marques, J. C. (2017). Urbanization (and primate conservation). In A. Fuentes, M. Bezanson, C. J. Campbell, A. F. Di Fiore, S. Elton, et al (Eds.), *The International Encyclopedia of Primatology* (Vol. 3, pp. 1–5). Wiley-Blackwell. https://doi.org/10.1002/9781119179313.wbprim0153.

Bicca-Marques, J. C., & Calegaro-Marques, C. (2014). Parasite sharing between humans and nonhuman primates and the hidden dangers to primate conservation. *Zoologia, 31*, 313–315.

Bicca-Marques, J. C., Calegaro-Marques, C., Rylands, A. B., Strier, K. B., Mittermeier, R. A., et al (2017). Yellow fever threatens Atlantic Forest primates. *Science Advances, 3*, e1600946 tab-e-letters.

Bicca-Marques, J. C., Chaves, Ó. M., & Hass, G. P. (2020). Howler monkey tolerance to habitat shrinking: Lifetime warranty or death sentence? *American Journal of Primatology, 82*, e23089. https://doi.org/10.1002/ajp.23089.

Bicca-Marques, J. C., & Freitas, D. S. (2010). The role of monkeys, mosquitoes, and humans in the occurrence of a yellow fever outbreak in a fragmented landscape in south Brazil: Protecting howler monkeys is a

matter of public health. *Tropical Conservation Science, 3*, 78–89. https://doi.org/10.1177/194008291000300107.

Bryant, J. E., Holmes, E. C., & Barrett, A. D. T. (2007). Out of Africa: a molecular perspective on the introduction of yellow fever virus into the Americas. *PLoS Pathogens, 3*, e75. https://doi.org/10.1371/journal.ppat.0030075.

Buss, G., Oklander, L. I., Bicca-Marques, J. C., Hirano, Z. M., Chaves, Ó. M., et al (2019). Brown howler monkey, *Alouatta guariba* (Humboldt, 1812). In C. Schwitzer, R. A. Mittermeier, A. B. Rylands, F. Chiozza, E. A. Williamson, et al (Eds.), *Primates in Peril: The World's 25 Most Endangered Primates (2018–2020)* (pp. 94–97). IUCN.

Cardoso, J. C., Almeida, M. A. B., Santos, E., Fonseca, D. F., Sallum, M. A. M., et al (2010). Yellow fever virus in *Haemagogus leucocelaenus* and *Aedes serratus* mosquitoes, southern Brazil, 2008. *Emerging Infectious Diseases, 16*, 1918–1924.

Cavalcante, T., Jesus, A. S., Rabelo, R. M., Messias, M. R., Valsecchi, J., et al (2020). Niche overlap between two sympatric frugivorous Neotropical primates: Improving ecological niche models using closely-related taxa. *Biodiversity and Conservation, 29*, 2749–2763.

Chapman, C. A., Gillespie, T. R., & Goldberg, T. L. (2005). Primates and ecology of their infectious diseases: How will anthropogenic change affect host-parasite interactions? *Evolutionary Anthropology, 14*, 134–144.

Chippaux, J. P., & Chippaux, A. (2018). Yellow fever in Africa and the Americas: A historical and epidemiological perspective. *Journal of Venomous Animals and Toxins including Tropical Diseases, 24*, 1–14. https://doi.org/10.1186/s40409-018-0162-y.

Collias, N., & Southwick, C. (1952). A field study of population density and social organization in howling monkeys. *Proceedings of the American Philosophical Society, 96*, 143–156.

Cowlishaw, G., & Dunbar, R. (2000). *Primate conservation biology*. University of Chicago Press.

Cunha, M. S., Tubaki, R. M., Menezes, R. M. T., Pereira, M., Caleiro, G. S., et al (2020). Possible non-sylvatic transmission of yellow fever between non-human primates in São Paulo city, Brazil, 2017–2018. *Scientific Reports, 10*, 15751.

Dietz, J. M., Hankerson, S. J., Alexandre, B. R., Henry, M. D., Martins, A. F., et al (2019). Yellow fever in Brazil threatens successful recovery of Endangered golden lion tamarins. *Scientific Reports, 9*, 12926.

Estrada, A., Garber, P. A., Mittermeier, R. A., Wich, S., Gouveia, S., et al (2018). Primates in peril: the significance of Brazil, Madagascar, Indonesia and the Democratic Republic of the Congo for global primate conservation. *PeerJ, 6*, e4869. https://doi.org/10.7717/peerj.4869.

Estrada, A., Garber, P. A., Rylands, A. B., Roos, C., Fernandez-Duque, E., et al (2017). Impending extinction crisis of the world's primates: Why primates matter. *Science Advances, 3*, e1600946. https://doi.org/10.1126/sciadv.1600946.

Fernandes, A. T. S., Moreira, S. B., Gaspar, L. P., Simões, M., Cajaraville, A. C. R. A., et al (2020). Safety and immunogenicity of 17DD attenuated yellow fever vaccine in howler monkeys (*Alouatta* spp.). *Journal of Medical Primatology*. https://doi.org/10.1111/jmp.12501.

Fick, S. E., & Hijmans, R. J. (2017). WorldClim 2: New 1-km spatial resolution climate surfaces for global land areas. *International Journal of Climatology, 37*, 4302–4315. https://doi.org/10.1002/joc.5086.

Fielding, A. H., & Bell, J. F. (1997). A review of methods for the assessment of prediction errors in conservation presence/absence models. *Environmental Conservation, 24*, 38–49.

Formenty, P., Boesch, C., Wyers, M., Steiner, C., Donati, F., et al (1999). Ebola virus outbreak among wild chimpanzees living in a rain forest of Côte d'Ivoire. *Journal of Infectious Diseases, 179*(Suppl 1), S120–S126.

Graham, C. H., Elith, J., Hijmans, R. J., Guisan, A., Townsend Peterson, A., et al (2008). The influence of spatial errors in species occurrence data used in distribution models. *Journal of Applied Ecology, 45*, 239–247.

Gillespie, T. R., Nunn, C. L., & Leendertz, F. H. (2008). Integrative approaches to the study of primate infectious diseases: Implications for biodiversity conservation and global health. *Yearbook of Physical Anthropology, 51*, 53–69.

Hamrick, P. N., Aldighieri, S., Machado, G., Leonel, D. G., Vilca, L. M., et al (2017). Geographic patterns and environmental factors associated with human yellow fever presence in the Americas. *PLoS Neglected Tropical Diseases, 11*, e0005897. https://doi.org/10.1371/journal.pntd.0005897.

Hanley, K. A., Monath, T. P., Weaver, S. C., Rossi, S. L., Richman, R. L., & Vasilakis, N. (2013). Fever versus fever: The role of host and vector susceptibility and interspecific competition in shaping the current and future distributions of the sylvatic cycles of dengue virus and yellow fever virus. *Infection Genetics Evolution, 19*, 292–311. https://doi.org/10.1016/j.meegid.2013.03.008.

Hewson, J., Crema, S. C., González-Roglich, M. Tabor, K., & Harvey, C. A. (2019). New 1 km resolution datasets of global and regional risks of tree cover loss. *Land, 8*, 14.

Hill, S. C., Souza, R., Thézé, J., Claro, I., Aguiar, R. S., et al (2020). Genomic surveillance of yellow fever virus epizootic in São Paulo, Brazil, 2016-2018. *PLoS Pathogens, 16*, e1008699. https://doi.org/10.1371/journal.ppat.1008699.

Holzmann, I., Agostini, I., Areta, J. I., Ferreyra, H., Beldomenico, P., & Di Bitetti, M. S. (2010). Impact of yellow fever outbreaks on two howler monkey species (*Alouatta guariba clamitans* and *A. caraya*) in Misiones, Argentina. *American Journal of Primatology, 72*, 475–480. https://doi.org/10.1002/ajp.20796.

Jesus, J. G., Gräf, T., Giovanetti, M., Mares-Guia, M. A., Xavier, J., et al (2020). Yellow fever transmission in non-human primates, Bahia, Northeastern Brazil. *PLoS Neglected Tropical Diseases, 14*, e0008405. https://doi.org/10.1371/journal.pntd.0008405.

Johansson, M. A., Vasconcelos, P. F., & Staples, J. E. (2014). The whole iceberg: estimating the incidence of yellow fever virus infection from the number of severe cases. *Transactions of the Royal Society of Tropical Medicine and Hygiene, 108*, 482–487. https://doi.org/10.1093/trstmh/tru092.

Klitting, R., Gould, E. A., Paupy, C., & Lamballerie, X. (2018). What does the future hold for yellow fever virus? (I). *Genes, 9*(291), 12–16.

Kraemer, M. U. G., Sinka, M. E., Duda, K. A., Mylne, A. Q. N., Shearer, F. M., et al (2015). The global distribution of the arbovirus vectors *Aedes aegypti* and *Ae. albopictus*. *eLife, 4*, e08347. https://doi.org/10.7554/eLife.08347.

Kuno, G. (2021). The absence of yellow fever in Asia: History, hypotheses, vector dispersal, possibility of YF in Asia, and other enigmas. *Viruses, 12*, 1349. https://doi.org/10.3390/v12121349.

Leendertz, S. A. J., Wich, S. A., Ancrenaz, M., Bergl, R. A., Gonder, M. K., et al (2017). Ebola in great apes: Current knowledge, possibilities for vaccination, and implications for conservation and human health. *Mammal Review, 47*, 98–111. https://doi.org/10.1111/mam.12082.

Liu, C., Berry, P. M., Dawson, T. P., & Pearson, R. G. (2005). Selecting thresholds of occurrence in the prediction of species distributions. *Ecography, 28*, 385–393. https://doi.org/10.1111/j.0906-7590.2005.03957.x.

Metcalf, C. J. E., & Lessler, J. (2017). Opportunities and challenges in modeling emerging infectious diseases. *Science, 357*, 149–152. https://doi.org/10.1126/science.aam8335.

Monath, T. P., Brinker, K. R., Chandler, F. W., Kemp, G. E., & Cropp, C. B. (1981). Pathophysiologic correlations in a rhesus monkey model of yellow fever with special observations on the acute necrosis of B cell areas of lymphoid tissues. *The American Journal of Tropical Medicine and Hygiene, 30*, 431–443. https://doi.org/10.4269/ajtmh.1981.30.431.

Monath, T. P., & Vasconcelos, P. F. C. (2015). Yellow fever. *Journal of Clinical Virology, 64*, 160–173. https://doi.org/10.1016/j.jcv.2014.08.030.

Monath, T. P., Woodall, J. P., Gubler, D. J., Yuill, T. M., Mackenzie, J. S., et al (2016). Yellow fever vaccine supply: A possible solution. *The Lancet, 387*, 1599–1600.

Moreno, E. S., Rocco, I. M., Bergo, E. S., Brasil, R. A., Siciliano, M. M., et al (2011). Reemergence of yellow fever: Detection of transmission in the State of São Paulo, Brazil, 2008. *Revista da Sociedade Brasileira de Medicina Tropical, 44*, 290–296. https://doi.org/10.1590/S0037-86822011005000041.

Moreno, E. S., Spinola, R. M. F., Tengan, C. H., Brasil, R. A., Siciliano, M. M., et al (2013). Yellow fever epizootics in non-human primates, São Paulo State, Brazil, 2008–2009. *Revista do Instituto de Medicina Tropical de São Paulo, 55*, 45–50. https://doi.org/10.1590/S0036-46652013000100008.

Nijman, V., Nekaris, K. A. I., Donati, G., Bruford, M., & Fa, J. (2011). Primate conservation: measuring and mitigating trade in primates. *Endangered Species Research, 13*, 159–161. https://doi.org/10.3354/esr00336.

Nunn, C. L., & Altizer, S. (2006). *Infectious diseases in primates: Behavior, ecology and evolution*. Oxford University Press.

Nunn, C. L., & Gillespie, T. R. (2016). Infectious disease and primate conservation. In S. A. Wich & A. J. Marshall (Eds.), *An introduction to primate conservation* (pp. 157–173). Oxford University Press.

Pedersen, A. B., Jones, K. E., Nunn, C. L., & Altizer, S. (2007). Infectious diseases and extinction risk in wild mammals. *Conservation Biology, 21*, 1269–1279.

Possamai, C. B., Mendes, S. L., & Strier, K. B. (2019). Decline of a primate community following a yellow fever outbreak in the Brazilian Atlantic Forest. *American Journal of Primatology, 82*(Suppl.1), 36–37.

R Development Core Team (2018). *R: A language and environment for statistical computing* (Vol. 3). R Foundation for Statistical Computing.

Renner, I. W., Elith, J., Baddeley, A., Fithian, W., Hastie, T., et al (2015). Point process models for presence-only analysis. *Methods in Ecology and Evolution, 6*, 366–379. https://doi.org/10.1111/2041-210X.12352.

Renner, I. W., & Warton, D. I. (2013). Equivalence of MAXENT and Poisson point process models for species distribution modeling in ecology. *Biometrics, 69*, 274–281. https://doi.org/10.1111/j.1541-0420.2012.01824.x.

Rogers, D. J., Wilson, A. J., Hay, S. I., & Graham, A. J. (2006). The global distribution of yellow fever and dengue. *Advances in Parasitology, 62*, 181–220.

Romano, A. P. M., Ramos, D. G., Pinna, F. V., Rossi, J. C. N., Passos, P. H. O., & Said, R. F. C. (2019). Reemergência e manutenção extra-amazônica da febre amarela no Brasil, 2014 a 2019: Principais desafios para a vigilância, a prevenção e o controle. In M. da Saúde (Ed.), *Saúde Brasil 2019 uma Análise da Situação de Saúde com Enfoque nas Doenças Imunopreveníveis e na Imunização* (pp. 307–329). Ministério da Saúde.

Ryan, S. J., & Walsh, P. D. (2011). Consequences of non-intervention for infectious disease in African great apes. *PLoS ONE, 6*, e29030. https://doi.org/10.1371/journal.pone.0029030.

Sacchetto, L., Silva, N. I. O., Rezende, I. M., Arruda, M. S., Costa, T. A., et al (2020). Neighbor danger: Yellow fever virus epizootics in urban and urban-rural transition areas of Minas Gerais state, during 2017–2018 yellow fever outbreaks in Brazil. *PLoS Neglected Tropical Infectious Diseases, 14*, e0008658.

Sales, L., Culot, L., & Pires, M. M. (2020). Climate niche mismatch and the collapse of primate seed dispersal services in the Amazon. *Biological Conservation, 247*, 108628. https://doi.org/10.1016/j.biocon.2020.108628.

Shah, S. Z., Jabbar, B., Ahmed, N., Rehman, A., & Nasir, H. (2018). Epidemiology, pathogenesis, and control of a tick-borne disease - Kyasanur Forest Disease: Current status and future directions. *Frontiers in Cellular and Infection Microbiology, 8*, 1–19. https://doi.org/10.3389/fcimb.2018.00149.

Shearer, F. M., Longbottom, J., Browne, A. J., Pigott, D. M., Brady, O. J., et al (2018). Existing and potential infection risk zones of yellow fever worldwide: A modelling analysis. *The Lancet, 6*, e270–e278.

Simberloff, D. (2013). *Invasive species: What everyone needs to know*. Oxford University Press.

Sloan, S., Supriatna, J., Campbell, M. J., Alamgir, M., & Laurance, W. F. (2018). Newly discovered orangutan species requires urgent habitat protection. *Current Biology, 28*, R1–R3.

Song, R., Guan, S., Lee, S. S., Chen, Z., Chen, C., et al (2018). Late or lack of vaccination linked to importation of yellow fever from Angola to China. *Emerging Infectious Diseases, 24*, 1383–1386. https://doi.org/10.3201/eid2407.171868.

Stokes, A., Bauer, J. H., & Hudson, N. P. (1928). The transmission of yellow fever to macacus rhesus: Preliminary note. *Journal of the American Medical Association, 90*, 253–254.

Strier, K. B., Tabacow, F. P., Possamai, C. B., Ferreira, A. I. G., Nery, M. S., et al (2019). Status of the northern muriqui (*Brachyteles hypoxanthus*) in the time of yellow fever. *Primates, 60*, 21–28.

Tatem, A. J., Hay, S. I., & Rogers, D. J. (2006). Global traffic and disease vector dispersal. *Proceedings of the National Academy of Sciences of the USA, 103*, 6242–6247. www.pnas.orgcgi. https://doi.org/10.1073/pnas.0508391103.

Theiler, M., & Anderson, C. R. (1975). The relative resistance of dengue-immune monkeys to yellow fever virus. *The American Journal of Tropical Medicine and Hygiene, 24*, 115–117.

Valentine, M. J., Murdock, C. C., & Kelly, P. J. (2019). Sylvatic cycles of arboviruses in non-human primates. *Parasites & Vectors, 12*, 463. https://doi.org/10.1186/s13071-019-3732-0.

Vasconcelos, P. F. C. (2002). Yellow fever in South America. In *International colloquium on invertebrate pathology and microbial control*, *8; International conference on* Bacillus thuringiensis *6; Annual meeting of the Sip*, *35*. (Documentos, 184). (pp. 49–54). Embrapa.

Wallis, J., & Lee, D. R. (1999). Primate conservation: The prevention of disease transmission. *International Journal of Primatology, 20*, 803–826.

Walsh, P. D., Abernethy, K. A., Bermejo, M., Beyersk, R., De Wachter, P., et al (2003). Catastrophic ape decline in western equatorial Africa. *Nature, 422*, 611–614.

Wang, L., Zhou, P., Fu, X., Zheng, Y., Huang, S., et al (2016). Yellow fever virus: Increasing imported cases in China. *Journal of Infection, 73*, 377–380.

WHO (World Health Organization). (2020a). Countries with risk of yellow fever transmission and countries requiring yellow fever vaccination (July 2020). https://www.who.int/publications/m/item/countries-with-risk-of-yellow-fever-transmission-and-countries-requiring-yellow-fever-vaccination-(july-2020) (accessed September 20, 2020).

WHO (World Health Organization). (2020b). Yellow fever. Fact sheet. https://www.who.int/en/news-room/fact-sheets/detail/yellow-fever (accessed August 8, 2020).

Wilder-Smith, A., & Leong, W. Y. (2017). Importation of yellow fever into China: Assessing travel patterns. *Journal of Travel Medicine, 24*, 1–4. https://doi.org/10.1093/jtm/tax008.

Wolfe, N. D., Escalante, A. A., Karesh, W. B., Kilbourn, A., Spielman, A., & Lal, A. A. (1998). Wild primate populations in emerging infectious disease research: The missing link? *Emerging Infectious Diseases, 4*, 149–158. https://doi.org/10.3201/eid0402.980202.

Wolfe, N. D., Kilbourn, A. M., Karesh, W. B., Rahman, H. A., Bosi, E. J., et al (2001). Sylvatic transmission of arboviruses among Bornean orangutans. *The American Journal of Tropical Medicine and Hygiene, 64*, 310–316.

Woodall, J. P., Dykes, J. R. W., & Williams, M. C. (1968). The reaction of a species of colobus monkey to inoculation with yellow fever virus. *Annals of Tropical Medicine & Parasitology, 62*, 528–535. https://doi.org/10.1080/00034983.1968.11686594.

## Affiliations

**Júlio César Bicca-Marques[1] · Rafael Magalhães Rabelo[2,3] · Marco Antônio Barreto de Almeida[4] · Lilian Patrícia Sales[5]**

1 Laboratório de Primatologia, Escola de Ciências da Saúde e da Vida, Pontifícia Universidade Católica do Rio Grande do Sul, PUCRS, Porto Alegre, RS, Brazil

2 Programa de Pós-Graduação em Ecologia, Instituto Nacional de Pesquisas da Amazônia, INPA, Manaus, AM, Brazil

3 Grupo de Pesquisa em Ecologia de Vertebrados Terrestres, Instituto de Desenvolvimento Sustentável Mamirauá, Tefé, AM, Brazil

4 Centro Estadual de Vigilância em Saúde, Secretaria da Saúde do Estado do Rio Grande do Sul, Porto Alegre, RS, Brazil

5 Department of Biology, Concordia University, Montréal, QC, Canada