

EPIDEMIOLOGY

Socioecological vulnerability and the risk of zoonotic disease emergence in Brazil

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In developing countries, outbreaks of zoonotic diseases (ZDs) result from intertwined ecological, socioeconomic, and demographic processes that shape conditions for (i) increased contact between vulnerable human population and wildlife in areas undergoing environmental degradation and (ii) the rapid geographic spread of infections across socially vulnerable regions. In Brazil, recent increases in environmental and social vulnerabilities, amplified by economic and political crises, are potential triggers for outbreaks. We discuss Brazilian features that favor outbreaks and show a novel quantitative method for zoonotic risk assessment. Using data on nine ZDs from 2001 to 2019, we found that the most significant causal variables were vegetation cover and city remoteness. Furthermore, 8 of 27 states presented low-level risk of ZD outbreaks. Given the ZD-bushmeat connection, we identified central hunted mammals that should be surveilled to prevent spillover events. The current challenge is to coordinate intersectoral collaboration for effective One Health management in megadiverse countries with high social vulnerability and growing environmental degradation like Brazil.

INTRODUCTION

Brazil currently combines socioecological vulnerabilities and an ongoing economic and political crisis that make the country a potential incubator of the next pandemic. This current crisis is characterized by the disregard for scientific evidence and attacks on conservation organizations, the flexibilization of environmental laws, and the replacement of institutional mechanisms promoting biodiversity conservation by destructive environmental policies (1, 2). A set of bills recently sent to the Brazilian Congress illustrate the destructive environmental policies that have been proposed: mining in Indigenous lands and protected areas, reduction of environmental licensing requirements, public forest concessions to private initiatives, legalization of illegal land claims, incentives to oil and gas extraction, changes in the implementation of Indigenous people's constitutional rights, and weaker gun control laws, among others (3). In an ideological inversion, Brazilian environmental policies recently moved from a historical leadership position to a global environmental threat, as suggested by the upward trend in Amazon deforestation rates, 182% above the target in 2020 (4). At the end of the same year,

almost one-third of Pantanal, the world's largest tropical wetland, burned down because of an annual increase of 508% in fire occurrence compared to the 2012–2019 average (5). Meanwhile, the coronavirus disease 2019 (COVID-19) pandemic disproportionately affected Brazilian regions showing higher social deprivation (5). Increasing extreme poverty in COVID-19 times (6) and the recent environmental setbacks may form a perfect storm in which ecological and socioeconomic vulnerabilities converge to drastically increase the risks of emerging infectious disease outbreaks (7).

Several authors have already drawn attention to the risk of a deadly pathogen emerging from the Amazon rainforest. Changes in land-use patterns, which increase social vulnerability and disrupt ecosystem functioning, also affect pathogen transmission cycles, broadening the risk of contact between humans and previously isolated wildlife that represent pathogen reservoirs and vectors (8–10). The Brazilian terrestrial territory has a subcontinental scale and encompasses several biomes—Amazon and Atlantic rainforests, Pantanal (wetlands), Cerrado (savannah), Caatinga (tropical dry forest), and Pampa (grasslands)—that hold an extremely rich biota. The megadiversity of all Brazilian biomes extends to parasites and pathogens, which represents an enormous pool of potential emerging zoonotic diseases (ZDs) (11). The need to predict the ZD emergence challenges us to understand how anthropogenic pressures on ecosystems and associated social vulnerability promote risks arising from contact between humans, domestic animals/livestock, and zoonotic pathogens that circulate in high-tolerating wild terrestrial mammals of human presence and that may become epidemic agents. These efforts are crucial as the ongoing large-scale habitat loss and fragmentation amplifies socioecological vulnerabilities and, hence, epidemic risks across the country.

Here, we raise a red flag for the current risks of ZD emergence in Brazil based on a novel risk assessment method combined with datasets summarizing key historical, environmental, and socioeconomic drivers of zoonosis dynamics. In addition, we performed network analyses to depict the interactions among pathogens and the most hunted mammal species in Brazil, shedding light on the

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most critical pathways for zoonotic spillover from wildlife to humans and discussing the implications for public health policies.

RESULTS AND DISCUSSION

Challenges for predicting the risk of new epidemics in a megadiverse and socially heterogeneous country

The expansion of anthropogenic activities over natural habitats shapes landscape mosaics in which human populations surround isolated forest patches. Confined animal populations within fragmented habitat patches are particularly prone to trigger disease epidemics because of their frequently high local density and the adverse effects of habitat degradation on animal nutrition and immunology (12, 13). Anthropogenic agroecosystems attract generalist wild mammals and synanthropic species that forage on crops or regenerating vegetation, such as rodents and pigs, or prey on livestock/poultry, such as carnivores [garden hunting hypothesis (14)]. These mammals interact with wildlife, humans, and domestic animals or livestock in different ways, setting up the conditions for spillover events (15). Prevalent socioeconomic activities, such as logging, hunting/poaching, agriculture, and cattle breeding, also modulate conditions for ZD outbreaks. For example, the incidence of malaria and leishmaniasis correlates with deforestation activities per se (16), whereas, in deforested areas, forestry and agricultural activities favor hantavirus and yellow fever transmission (17, 18). Inferring general drivers of ZD outbreaks is challenging, as pathogens also vary regarding their natural history and vector types (or lack of vectors), sylvatic cycle environments (e.g., terrestrial and aquatic), and reservoirs (e.g., small or large animals). On the other hand, comparative

studies provide evidence that outbreaks of disparate ZDs result from similar ecological, socioeconomic, and demographic processes, such as rapid deforestation and urbanization, conservation policies, and human demographic flows (16, 19).

Despite the recent advances in the identification of general drivers of emerging infectious diseases, predicting zoonotic risks and their outcomes in Brazil is challenging for different reasons. First, the interplay of ecological and socioeconomic processes shaping spillover events, the pathogen's potential for geographical spread, and its outcomes in hospitalization and deaths vary widely over the country. For example, although the Amazon and Cerrado biomes show a high number of hospitalization cases caused by schistosomiasis, leishmaniasis, leptospirosis, malaria, rabies, trypanosomiasis, and yellow fever, both regions have marked differences in the corresponding number of deaths (Fig. 1). Lower mortality in the Amazon is likely associated with the pervasiveness and copying capacity of the public health care system (Sistema Único de Saúde) to diagnose and treat tropical diseases even in remote towns inside the rainforest (20, 21). A second major challenge is that surveillance and epidemiological data refer mostly to the introduced diseases, and there is poor knowledge concerning native pathogens. Although most ZDs currently circulating in Brazil have been introduced from other continents, either during pre-Columbian times [e.g., malaria (22)] or after mercantilist globalization [e.g., dengue, Zika, and yellow fever (23, 24)], other infections have been acquired by humans when they arrived in tropical America and entered the transmission cycle of native zoonotic parasites [e.g., Chagas disease (25, 26)]. Therefore, increased ecological and social vulnerabilities may create the conditions for amplifying the impacts of spillover events. Our early warning

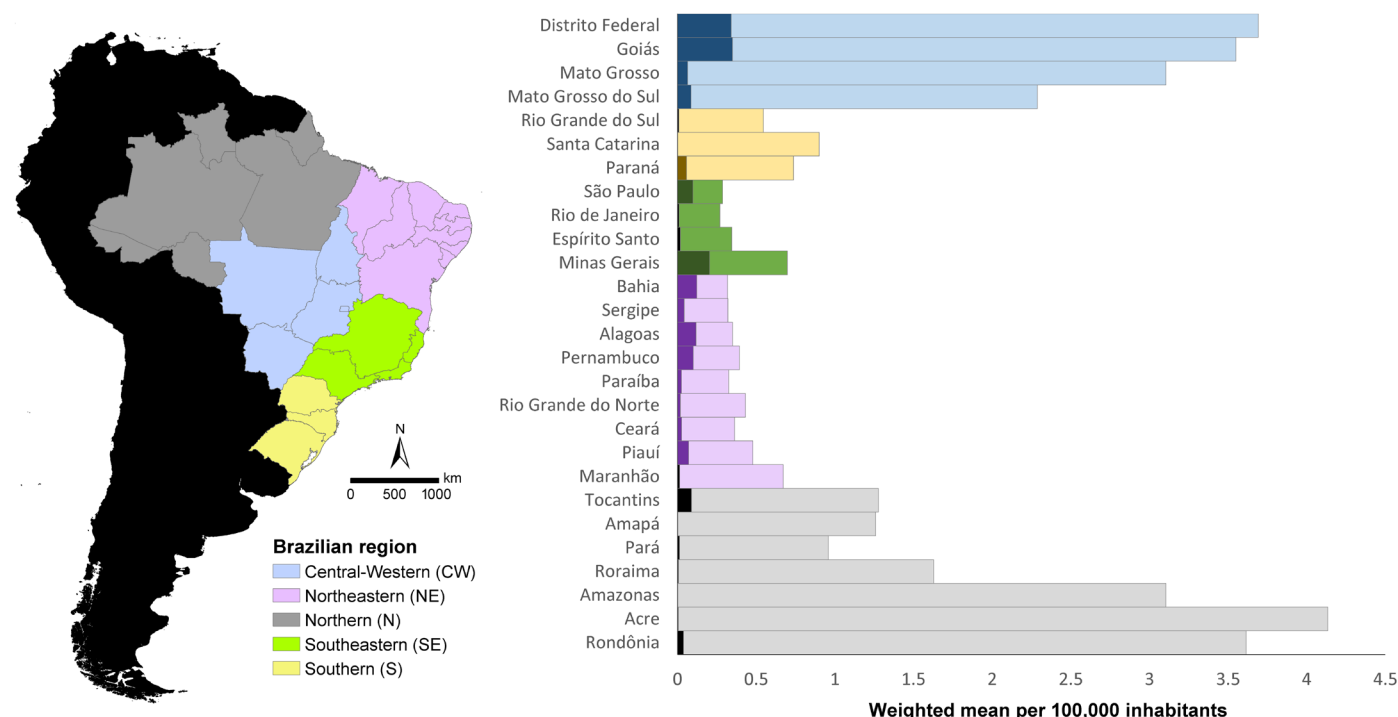


Fig. 1. Weighted mean of deaths (darker bars) versus the weighted mean of hospitalizations (lighter bars) per 100,000 inhabitants due to ZDs in Brazilian states from 2001 to 2019. The following ZDs were included: schistosomiasis, leishmaniasis (cutaneous and visceral), leptospirosis, malaria, rabies, trypanosomiasis, and yellow fever. The number of zoonoses in each state was used as a weight to calculate mean deaths and hospitalizations. Main bar colors (blue, yellow, green, lavender, and gray) denote Brazilian administrative regions and correspond to the colored map (left). Inner divisions at each region represent the state's boundaries.

and coping capabilities demand a clear definition of the hot spot areas for pathogen surveillance and the identification of critical reservoir species for monitoring.

Assessing the risk of ZDs' emergence with epidemic potential in Brazil and their major potential biological sources

The socioeconomic of the COVID-19 pandemic shows that strategies preventing outbreaks of novel pathogens should be a priority for public policies worldwide because they are cost effective and can save millions of human lives. Although global predictions include Brazil as a hot spot of emerging ZDs (27), the country is often considered well prepared for preventing and managing epidemic outbreaks (28). However, the rapid spread of the COVID-19 pandemic across the country and the overwhelming number of related deaths showed that the Brazilian preparedness for handling epidemiological emergencies may be highly overrated. Although the country's public health system is well structured, its organization and services are highly biased toward highly populated urban centers. Vast regions of the countryside remain unassisted in many aspects of health policies, including a weak or lack of epidemiological surveillance (1). Another important and recently experienced aspect is the vulnerability to misguided public policy actions made by current governments (1).

Considering the urgent need of monitoring zoonotic risks in megadiverse regions under increasing socioecological degradation, we here applied a new analytical framework to predict ZD epidemic risks in Brazil. In doing so, we considered several drivers of zoonotic risks, including proxies for changing patterns of land use, terrestrial mammalian species richness, social welfare, and the geographical connectivity of Brazilian cities and towns. First, we gathered data on relevant variables for ZD outbreaks based on the INFORM protocol for risk assessment of humanitarian crises and disasters (<https://drmkc.jrc.ec.europa.eu/inform-index>). These variables encompass the critical process of exposure, vulnerability, and coping capacity (Table 1). Second, we performed structural equation modeling (SEM; path analysis) to understand the direct dependencies among various socioeconomic, infrastructural, environmental, and biodiversity variables, providing causal inferences on the processes shaping the emergence of ZDs. The response variable was the mean cases of ZDs by state. We weighted these means by the number of infectious ZDs notified on SINAN (Notifiable Diseases Information System) per 100,000 inhabitants, from 2001 to 2019. Therefore, our response variable accounts for the different ZDs in each Brazilian state and their population sizes. We included the following zoonoses, subject to compulsory notification according to Brazilian law, in this assessment: Chagas disease, yellow fever, spotted fever, integumental and visceral leishmaniasis, hantavirus, leptospirosis, malaria, and rabies. We assume that the processes underlying the geographical spread and epidemiological patterns of these zoonoses could be extrapolated to novel pathogens emerging from wildlife. Our assumption is based on previous studies showing strong and general relationships between the emergence of zoonoses and land use, environmental changes, human density, and mobility (16, 29). To assign a category risk to each Brazilian state, we calculated a weighted mean from the scaled values of the variables included in the final SEM model, using the SEM coefficients as weights. Therefore, the zoonotic risk categories correspond to the weighted mean quartiles so that low risk refers to values between the minimum and the second quartile (50th percentile) and medium risk refers to values between the second and third quartiles (75th percentile). High risk refers to

values between the third quartile and the maximum value (Table 2 and fig. S1).

The final SEM model shows only significant causal links between variables ($P < 0.05$; table S1) and explains 80.9% (R^2) of the variation in the mean cases of ZDs (Fig. 2). Zoonotic epidemic risks, as inferred from the observed mean number of ZD cases, are positively associated with vegetation loss (path analysis coefficient = 0.30), mammalian richness (0.47), and remoteness (0.72) and negatively related to urban afforestation (−0.33) and vegetation cover (−0.82). The mapping of zoonotic epidemic risks based on our SEM model reveals that, from 27 states, only 29.63% ($n = 8$) are at low risk of zoonotic outbreaks according to our assessment. Our results support previous studies showing that the states where the Amazon rainforest is the prevailing habitat type represent the major concern regarding zoonotic risks (Fig. 3A). For example, the Maranhão state in the Northeastern region presents 34% of its territory covered by the Amazon rainforest and shows a higher zoonotic risk, whereas its neighbor, Ceará state (where the Caatinga dry forests prevail), shows a lower risk (Table 2 and Fig. 3B). Although most low-risk states are in the Northeastern region, other relevant cold spots include the Central-Western state of Goiás and the Southern states of Paraná and the Rio Grande do Sul (Table 2 and Fig. 3A). An important feature shared by all low-risk states is the higher connectivity among cities (Table 2), reflecting easier accessibility to large urban centers and, consequently, to more specialized health care when necessary.

Beyond spillover: Human mobility as a key process bridging pathogen sources and superspreader cities

For zoonotic spillover events to become epidemics, several factors should be aligned, including pathogen dynamics in the reservoir host; the ecological, epidemiological, and behavioral determinants of pathogen exposure; and the social factors affecting susceptibility to infection and transmissibility potential (15). Pathogen spillover among wild hosts increases with primary host population density, as suggested by hantavirus infection dynamics (30). However, spillover events alone are not enough to trigger the epidemic spread of ZDs, as a minimum density of infective human individuals is required for an epidemic to begin (31). After that, human flows over geographic transportation networks become a key codeterminant in shaping large-scale epidemiological patterns from a few superspreader locations (32).

Human mobility patterns across Brazilian territories show a highly complex and hierarchical organization (33), with intense people flows from smaller to larger cities for services, provisioning of goods, and business, which continuously connects ZD sources and highly populated regions. In addition, medium- to long-distance flows of patients pursuing high-complexity health care are widespread across the country (34). This socioeconomic dependence of towns and smaller cities on regional centers or state capitals amplifies the epidemic potential for geographical spread and has shaped the introduction and heterogeneous patterns of cases and deaths during the interiorization of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) in Brazil, for example (32). Therefore, to increase public health coping capacity, early detection and fast-response mechanisms should (i) track which regions facing increasing human-wildlife contacts are more prone to become sources of local ZD outbreaks and (ii) assess the risks of a local outbreak becoming epidemic or pandemic based on the geographical connectivity of different local hot spots of ZD sources.

Table 1. Factors included in the present ZDs' risk analysis in the 27 Brazilian states from 2001 to 2019. IBGE, Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística; www.ibge.gov.br); IUCN, International Union for Conservation of Nature (www.iucn.org); Mapbiomas, multi-institutional initiative to map Brazilian land use and cover (mapbiomas.org/en); DATASUS, Informatics Department of the Brazilian Unified Health System (Departamento de Informática do Sistema Único de Saúde; datasus.saude.gov.br).

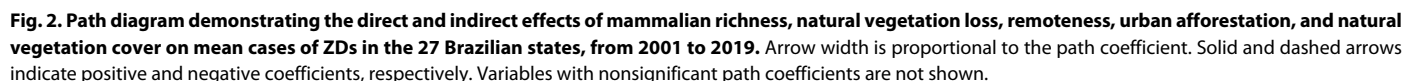
Risk component	Main category	Variable category	Variable name	Rationale for inclusion	Data source
Exposure	ZD drivers	Animal	Proportion of livestock treated for zoonoses	Indication of parasites and pathogens potentially in contact with the human population	IBGE
			Richness of wild mammals	Indication of natural hosts maintaining natural parasite-host cycles, suggesting ecosystem health status	IUCN
		Environment	Proportion of cultivated area	The presence of crops acts as a filter for biodiversity, favoring generalist vertebrate species, frequently considered competent hosts	IBGE
			Proportion of natural vegetation cover	Indication of ecosystem preservation	Mapbiomas
			Natural vegetation loss	Indication of ecosystem preservation	Mapbiomas
Vulnerability	Social	Housing	Urban afforestation	Measured in urban areas, an indication of housing quality (e.g., local temperature and biodiversity persistence)	IBGE
			Exposure to domestic waste	Indication of housing quality and proximity to potential vectors (e.g., mosquitoes and rats)	IBGE
			Exposure to sewer	Indication of housing quality (e.g., mosquitoes and rats)	IBGE
	Economic	Gross domestic product	Mean gross domestic product	Indication of resources available to cope with epidemics	IBGE
Coping capacity	Infrastructure	Health professionals	Number of health professionals per 100,000 inhabitants	Indication of health care availability	DATASUS
		Health services sites	Number of health facilities per 100,000 inhabitants	Indication of health care availability	DATASUS
		Accessibility	City remoteness	Indication of specialized health care availability	IBGE

Our risk assessment method assigned the higher risk level to six states from the Northern region (Acre, Amapá, Rondônia, Roraima, Amazonas, and Maranhão) and to one state from Central-Western (Mato Grosso). These states are partially or entirely covered by the Amazon rainforest (Fig. 3, A and B). In general, these states show the lowest levels of urban afforestation, the highest mammal richnesses,

and the highest levels of city remoteness (Table 2). The high-risk group also includes states with the highest vegetation cover (Amazonas) and the highest vegetation loss (Mato Grosso) (Fig. 3, A and B, and Table 2). Conversely, low risk was assigned to eight states, including most from Northeastern (within Atlantic Forest and Caatinga biomes) and Southern (within Atlantic Forest and Pampa biomes) regions

Table 2. Risk assessment based on the positive and negative effects of city afforestation, mammal richness, city remoteness, natural vegetation cover, and vegetation loss on the mean cases of ZDs per 100,000 inhabitants in the 27 Brazilian states, from 2001 to 2019. Categories of a low, medium, and high risk for each variable based on its quantiles: Low, value between the minimum observed value to the second quantile (50th percentile); Medium, value between the second to the third quantile (75th percentile); High, value between the third quantile to the maximum value. Bold values represent the minimum and maximum values for each variable.

Region	State	Mean zoonotic cases	Afforestation (%)	Mammal richness	Remoteness (%)	Vegetation cover (ha)	Vegetation loss (ha)	Risk level assigned
Northern	Acre (AC)	374.97	20	241	45	14,670,090.03	868,181.04	High
	Amapá (AP)	187.32	0	195	56	13,684,978.11	508,430.65	High
	Amazonas (AM)	121.47	30	438	71	149,532,235.20	1,981,027.71	High
	Pará (PA)	122.69	27	288	27	101,947,243.40	11,466,461.87	Medium
	Rondônia (RO)	181.81	40	239	23	16,076,036.59	3,424,908.24	High
Northeastern	Roraima (RR)	171.09	45	245	40	21,418,462.04	1,250,192.48	High
	Tocantins (TO)	115.15	79	194	32	19,807,760.66	2,565,649.35	Medium
	Alagoas (AL)	11.68	59	145	0	465,322.48	160,954.08	Low
	Bahia (BA)	44.22	54	226	6	32,689,566.13	5,765,322.26	Medium
	Ceará (CE)	37.63	79	137	0	10,794,396.20	1,236,874.00	Low
	Maranhão (MA)	96.95	51	187	13	24,100,065.94	6,999,336.01	High
	Paraíba (PB)	5.51	80	151	0	3,262,857.26	660,182.01	Low
	Pernambuco (PE)	13.77	54	156	1	5,132,406.11	655,572.29	Medium
	Piauí (PI)	23.44	70	156	24	22,043,502.96	1,440,398.65	Medium
	Rio Grande do Norte (RN)	6.27	58	125	0	2,923,858.40	696,825.44	Low
Southeastern	Sergipe (SE)	10.10	50	114	0	479,454.95	274,116.00	Low
	Espírito Santo (ES)	19.29	58	173	0	1,215,414.01	81,842.01	Medium
	Minas Gerais (MG)	20.42	68	269	4	24,114,461.08	2,248,188.59	Medium
	Rio de Janeiro (RJ)	3.66	60	190	0	1,372,636.08	49,981.02	Medium
	São Paulo (SP)	5.90	81	222	0	5,382,844.08	478,037.04	Medium
Southern	Paraná (PR)	13.54	77	190	0	5,767,018.90	391,339.89	Low
	Rio Grande do Sul (RS)	7.53	82	153	1	13,863,748.76	4,211,494.82	Low
	Santa Catarina (SC)	14.17	44	159	0	4,721,413.89	219,999.22	Medium
Central-West	Distrito Federal (DF)	2.70	37	129	0	259,434.78	14,896.05	Medium
	Goiás (GO)	15.04	78	183	1	12,590,629.75	1,539,269.42	Low
	Mato Grosso (MT)	208.70	59	257	65	60,049,531.23	12,720,723.82	High
	Mato Grosso do Sul (MS)	29.84	96	195	27	14,782,805.64	1,463,539.43	Medium



Despite not being included in the final model, health care access and the availability of trained professionals are important factors for preventing and coping with any health emergency. Our results show the need to integrate both ecosystem/landscape (mammalian richness, vegetation loss, and vegetation cover) and urbanization characteristics (remoteness and urban afforestation) in the planning of public health policies. Preventive strategies for ZD outbreaks require collaboration among different sectors, including the federal government (environmental, health, and agricultural agencies), agribusiness (including animal farming), and society. Nationwide laboratory confirmation of zoonotic agents circulating in wildlife, livestock, and humans is one of the needed strategies to promote human, animal, and environmental health. In addition, it is paramount to ensure the public health and educative programs at smaller scales (individual, family, and community levels) to inform the Brazilian population about the risks associated with several forms

Identifying critical species representing potential ZD sources requires us to focus on processes that increase the likelihood of human-wildlife contacts, such as deforestation and associated bushmeat hunting and consumption (13). Although target species vary across regions because of the turnover in species composition and abundances, bushmeat hunting and trading are pervasive throughout Brazil (35). The bushmeat trade is a process connecting ZD sources and dense susceptible urban populations (36, 37). Several ongoing processes increase the potential of bushmeat hunting and trading as a potential source of epidemics. For example, declining game species populations along with socioeconomic changes increasing extreme poverty and hunger are leading local communities to intensify the use of wildlife as food sources and expand their hunting areas (38, 39). The replacement of natural habitats by commodity plantations and unplanned urbanization also represents

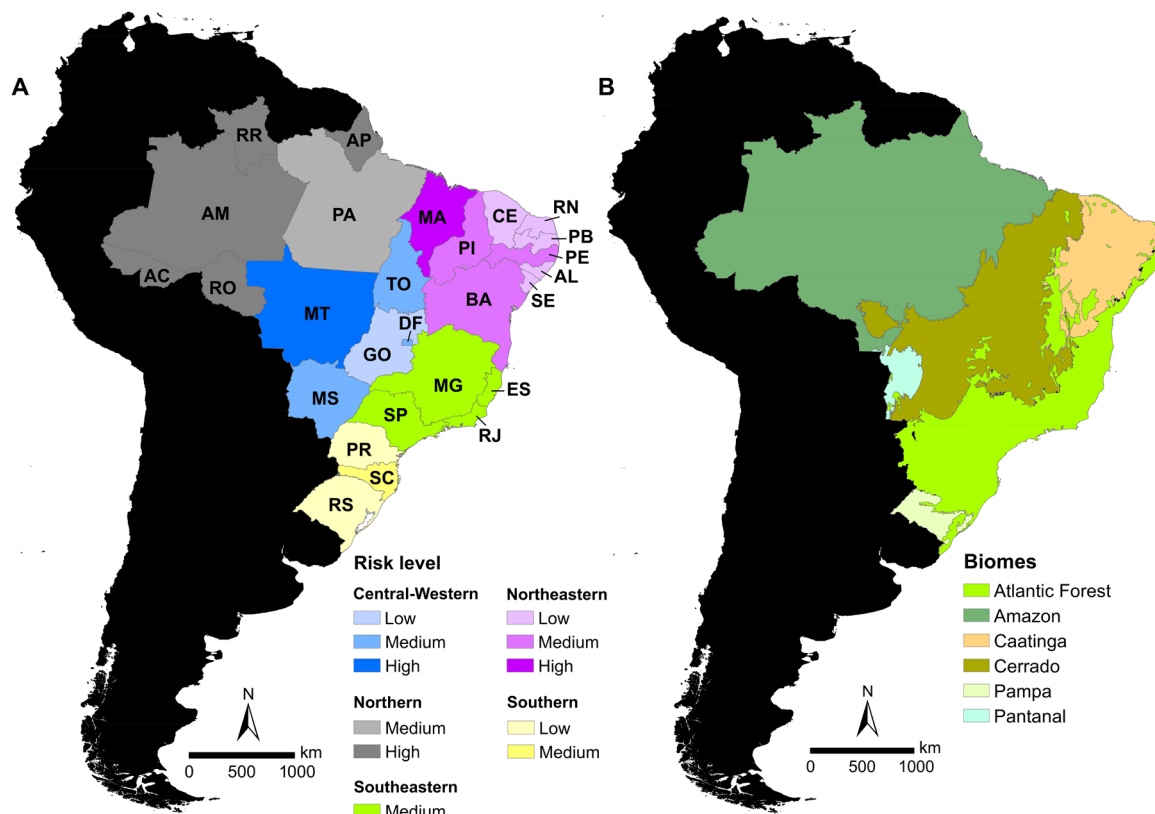


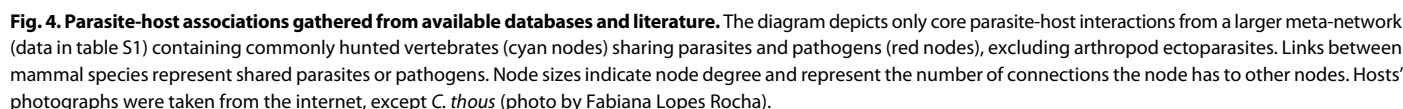
Fig. 3. ZD risk assessment in Brazilian states and biomes. Maps showing (A) the risk level of each Brazilian state based on the effects of mammalian richness, natural vegetation loss, remoteness, urban afforestation, and natural vegetation cover on mean cases of ZDs and (B) the geographic range of Brazilian biomes. Brazilian states: AC, Acre; AL, Alagoas; AM, Amazonas; AP, Amapá; BA, Bahia; CE, Ceará; DF, Distrito Federal; ES, Espírito Santo; GO, Goiás; MA, Maranhão; MG, Minas Gerais; MS, Mato Grosso do Sul; MT, Mato Grosso; PA, Pará; PB, Paraíba; PE, Pernambuco; PI, Piauí; PR, Paraná; RJ, Rio de Janeiro; RO, Rondônia; RN, Rio Grande do Norte; RR, Roraima; RS, Rio Grande do Sul; SC, Santa Catarina; SE, Sergipe; SP, São Paulo; TO, Tocantins.

critical processes negatively affecting social welfare (40) and increasing bushmeat trading (41).

Bushmeat hunting is a relevant factor in shaping observed patterns of emerging zoonoses because it favors direct human–wild animal contact. Although only traditional people and communities are legally allowed to hunt, bushmeat consumption is cultural and widespread across all Brazilian regions. To complement our analyses, we summarized a unique dataset on frequently poached mammal species in Brazil and associated parasites, which represent potential zoonotic agents that deserve surveillance. We gathered the information on wild mammal–pathogen interactions from the Nucleotide database and literature, as specified in table S2. Hence, we provide a network overview of the zoonotic agents interacting with the main poached mammal species (Fig. 4 and table S2). We found 173 parasites interacting with 63 mammals, which can cause at least 76 different diseases, but several pathogen species can cause multiple illnesses (table S2). We built a meta-network using this dataset, which shows bacteria, protozoans, and viruses as the main groups of parasites circulating among all host species. Closeness centrality is a widely used metric to infer species importance in interaction networks [including parasite–host ones (42)], and we used it as a proxy for inferring reservoir roles and parasite zoonotic potential (43). The protozoans *Leishmania* spp. (closeness centrality $C = 0.45$) and *Trypanosoma* spp. ($C = 0.38$) are the most central parasites in the meta-network, infecting a high diversity of host species (Fig. 4).

Host species shared by the highest number of different parasites are the crab-eating fox, usually killed for control (*Cerdocyon thous*; $C = 0.40$); the peri-urban opossum species (*Didelphis* spp.; $C = 0.39$); and an armadillo group highly appreciated as bushmeat (*Dasypus* spp.; $C = 0.38$) (Fig. 4). These species also have the highest values for other centrality metrics (harmonic closeness, betweenness, and eigenvalue; table S3) Capuchin monkey (*Sapajus apella*; $C = 0.36$), however, exclusively hosts most hemorrhagic fever viruses (Fig. 4 and table S2), contributing to its highest betweenness centrality value (table S3). Although there is likely a sampling bias toward more abundant species, such as the crab-eating fox and capuchin monkeys, it is also important to consider that more abundant species may also interact more frequently with humans, as these species occur even in urban areas and city parks. Therefore, topologically central host species represent sentinels whose monitoring and surveillance can improve tracking spillover events.

Despite the spillover risk arising from bushmeat consumption, completely banning could affect billions of livelihoods worldwide and exacerbate threats to biodiversity (39). To prevent zoonotic outbreaks related to hunting, it is imperative to ensure the sanitary and food safety of people who use bushmeat for their subsistence (e.g., the traditional people and communities who have the right to hunt in Brazil) through health monitoring of the whole production chain and policies promoting education in good management practices. The commerce of fresh bushmeat in urban conglomerates



To date, major disease outbreaks and epidemics in Brazil have been caused by pathogens introduced into the country (e.g., dengue and yellow fever). However, we show that all regions in Brazil are subject to zoonotic risks emerging from the native biota. These risks are higher in the Amazon rainforest. We also synthesized the most comprehensive database of all pathogens that potentially cause severe damage to public health, such as viral hemorrhagic fevers (e.g., Oropouche, Changuinola, and Mayaro). The few cases of the Sabia virus in São Paulo state in the 1990s were already a wake-up call to promote necessary changes in Brazilian sanitarian surveillance. The

We used the state-level data of the number of communicable ZDs notified on SINAN from the statistics department of the Brazilian

public health care system (DATASUS), spanning from 2001 to 2019. In our dataset, we included the annual number of cases of the following compulsory notification zoonoses: Chagas disease or American trypanosomiasis, yellow fever, spotted fever, skin and visceral leishmaniasis, hantavirus, leptospirosis, malaria, and rabies. Because ZDs vary in occurrence and frequency between all Brazilian states, we used the weighted mean of the number of cases at each state as the response variable using the number of zoonoses occurring at each state (zoonoses richness) as weight. Furthermore, we converted the weighted mean of 100,000 inhabitants to account for differences in human population size between states. We refer to this response variable as mean cases of ZDs throughout the text and embedded in figures.

To understand how environmental and socioeconomic factors influence the mean cases of ZDs throughout the Brazilian territory, we included as predictors annual variables from the Brazilian Institute of Geography and Statistics (IBGE; Instituto Brasileiro de Geografia e Estatística), the multi-institutional initiative to map Brazilian land use and cover (Mapbiomas), and the DATASUS (Table 1). All these predictors have the same temporal spanning of the ZDs data (2001 to 2019). We used data available from the International Union for Conservation of Nature (IUCN) to estimate mammalian richness.

Parasite-host interactions

We assumed the hunting/poaching activities as a primordial route to human-animal contact. In addition, we believed that tracking poaching would be a possible way to understand the potential of parasites circulating in a somewhat constant way because the activity is performed across the entire country, despite being illegal (excepting traditional peoples and wild boar management). Hence, to depict the possible etiologic agents circulating between hunters/poachers and wild mammals, we assembled the parasites and pathogens registered in Brazil's main hunted mammal species through the Nucleotide database and a nonextensive search in the literature (table S2). In the final list, we excluded ectoparasites such as ticks and fleas, which act more as vectors, because our focus was on parasites and pathogens infecting hunted species. We also gathered the hunted mammalian species list from literature (35, 44–47). Using table S2, we built the meta-network of parasite-host interactions and selected the core interactions (i.e., the largest connected component of the network) to demonstrate the pathogens potentially circulating among bushmeat consumers (Fig. 4). To identify central species of parasites and hosts in the meta-network, we measured each node's centrality and showed results for the closeness centrality metric in the section, "Bushmeat hunting and trading as major risk factors for the emergence of ZDs". Closeness centrality measures the reciprocal sum of the length of the shortest paths between each node and all other nodes in the graph. For other centrality metrics results, see table S3.

Structural equation modeling

To understand how the different factors affected the number of zoonotic cases and quantified causal relationships, we used a structural equation model (path analysis, hereafter SEM) considering the relevant components of exposure, vulnerability, and coping capacity (Table 1). SEM aimed to identify the significant factors and to quantify their influence on the mean cases of ZDs (response variable). In addition, we allowed pairwise correlations between all variables to vary (free pathways) to track the interdependencies between variables. In the final model, we considered only significant variables

($P < 0.05$). Last, we used the significant factors from the final SEM and its coefficients describing their relationship with the response variable to perform the risk assessment. For model fitting, we scaled and centered all variables.

Risk assessment

We assigned the categories of low, medium, and high risk for the emergence of ZDs in each Brazilian state by a new approach using weighted means and quantiles. First, we identified which factors from Table 1 explained the mean cases of ZDs and quantified their relationship. Second, we gathered the annual values of the identified factors and calculated their weighted mean for each Brazilian state, using the SEM coefficients of the response variable and each factor as weight. Last, we estimated quantiles and minimum and maximum values of each factor to assign (i) the low category to mean weighted values between the minimum value and the second quartile (50th percentile), (ii) the medium category to values between the second and third quartiles (75th percentile), and (iii) the high category to values between the third quartile and the maximum value. Hence, we proposed a risk assessment approach fully based on quantitative parameters.

SUPPLEMENTARY MATERIALS

Supplementary material for this article is available at <https://science.org/doi/10.1126/sciadv.abo5774>

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Socioecological vulnerability and the risk of zoonotic disease emergence in Brazil

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