Ecosystem change, market participation, and human health in villages proximate to Parc National de Marojejy

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Abstract

Human activities, including agricultural practices, have marked impacts on ecosystems that can affect food security, health, and livelihoods. These changes can affect human health by increasing infectious disease transmission between humans and animals. Furthermore, increased engagement with market economies through selling cash crops and purchasing consumer goods (i.e., market integration) can alter diet and behaviors, which may contribute to chronic diseases. The area around the Parc National de Marojejy in the SAVA region of northeast Madagascar has undergone considerable land use and economic changes in recent decades. Using One Health and evolutionary medicine frameworks, we conducted several empirical studies in multiple villages to explore linkages among animal and human health, ecosystem change, and market integration. We employed a range of methods including household and social network surveys, focus groups, and biological samples from humans, and wild and domestic animals. We confirmed the presence of infectious disease agents such as *Leptospira, Blastocystis,* canine hookworm (*Ancylostoma ceylanicum*), human hookworm (*Necator americanus*), hantaviruses, astroviruses, paramyxoviruses, and coronaviruses. Among chronic diseases, hypertension was high among the study population, and people tend to exhibit short and fragmented sleep. Access to healthcare remains a challenge in the region, but participation in vanilla markets could lower these barriers by providing health insurance through vanilla certification schemes. We found that variation in land use, shared habitats, contact points, and social networks can all influence the potential for disease transmission. We are currently engaged in more in-depth studies in additional villages to better understand how environmental changes and economic development in Madagascar are contributing to a changing health landscape.

Key words: One Health, evolutionary medicine, land-use change, infectious disease, chronic disease

Résumé détaillé

Les activités humaines, y compris les pratiques agricoles, ont des impacts remarquables sur les écosystèmes qui peuvent affecter la sécurité alimentaire, la santé et les moyens de subsistance. Ces changements peuvent affecter la santé humaine en augmentant la transmission des maladies infectieuses entre les humains et les animaux. En outre, la participation (intégration) accrue au marché peut modifier le régime alimentaire et le comportement, ce qui peut contribuer à favoriser les maladies chroniques. Compte tenu du changement rapide de l'utilisation des terres, de la participation au marché et du changement climatique en cours dans de nombreux pays à faible et moyen revenu, il est crucial de comprendre comment ces changements affectent la santé humaine et d'utiliser les informations qui en découlent pour identifier les actions que les communautés locales et les décideurs politiques pourraient prendre pour améliorer le bien-être humain. La zone autour du Parc National de Marojejy dans la Région SAVA du Nord-est de Madagascar a subi des changements considérables en matière d'utilisation des terres et d'économie au cours des dernières décennies. La « seule santé » examine d'abord comment les activités humaines influencent les animaux, y compris les animaux domestiques et sauvages (qui peuvent inclure des espèces sauvages

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introduites) et l'environnement ; et comment ceux-ci ont à leur tour un impact sur la santé et le bien-être humain. La médecine évolutive considère comment le processus évolutif rend les humains (et les autres animaux) vulnérables aux maladies infectieuses et non infectieuses, et fournit ainsi un aperçu des raisons ultimes pour lesquelles « pourquoi nous tombons malades ». En utilisant les cadres « la seule santé » et « médecine évolutive », plusieurs études empiriques ont été menées dans plusieurs villages pour explorer les liens entre la santé animale et humaine, le changement des écosystèmes et l'intégration aux marchés. Une gamme de méthodes a été utilisée, notamment des enquêtes auprès des ménages et les réseaux sociaux, des groupes de discussion et de prélèvement des échantillons biologiques chez les humains et les animaux sauvages et domestiques.

Des traces des agents pathogènes telles que *Leptospira*, *Blastocystis*, l'ankylostome canin (*Ancylostoma ceylanicum*), l'ankylostome humain (*Necator americanus*), les hantavirus, les astrovirus, les paramyxovirus et les coronavirus sont trouvées. Parmi les maladies chroniques, les cas d'hypertension sont élevés dans la population étudiée et les gens ont tendance à avoir un sommeil court et fragmenté. L'accès aux soins de santé reste un défi dans la région, mais la participation aux marchés de la vanille pourrait réduire ces obstacles en fournissant une assurance maladie par le biais de programmes de certification de la vanille. Il a été constaté au cours de l'étude que les variations dans l'utilisation des terres, les habitations partagées, les points de contact et les réseaux sociaux peuvent tous influencer la potentialité de transmission de la maladie.

Actuellement, des études plus approfondies dans d'autres villages afin de mieux comprendre comment les changements environnementaux et le développement économique à Madagascar contribuent à l'évolution du paysage sanitaire sont en cours. C'est une recherche sur la modélisation des facteurs écologiques et socio-économiques qui influencent la propagation des maladies autour des villages et au sein du parc et elle étudie aussi les multiples hypothèses concernant la façon dont les activités humaines impliquant l'utilisation des terres affectent la transmission des maladies zoonotiques. Ce travail s'étend à un ensemble plus vaste des villages autour du parc pour étudier comment l'intégration du marché influence les schémas de déplacement humain et favorise la transmission des maladies infectieuses.

Mots clés : One Health, médecine évolutive, changement d'affectation des terres, maladies infectieuses, maladies chroniques

Introduction

Human activities, including agricultural practices, have marked impacts on ecosystems that can affect food security, health, and livelihoods. For example, emerging evidence suggests that land use change alters mammalian community ecology in ways that augment infectious disease prevalence, potentially increasing zoonotic disease transmission to humans (Keesing *et al*., 2010; Civitello *et al*., 2015). Agricultural intensification often leads to economic development at the cost of landcover change, as subsistence communities change their traditional agricultural practices to produce more commercial crops for market sale. This increased participation in markets (or "market integration") can improve livelihoods and reduce poverty (Boughton *et al*., 2002), yet it may also be associated with increased infectious and non-infectious disease prevalence (Godoy *et al*., 2005; Lea *et al*., 2021). Given the rapid land use change, market participation, and climate change underway in many low- and middle-income countries, it is vitally important to understand how these changes impact human health, and to use this understanding to identify actions that local communities and policy makers could take to improve well-being (Keesing *et al*., 2010; Pattanayak *et al.*, 2017).

Madagascar is an important location for investigating the connections among land use change, market integration, and health. The island is recognized as one of the five leading biodiversity hotspots, yet despite decades of conservation efforts, loss of natural forests has continued at a rapid pace (Waeber *et al*., 2016; Vieilledent *et al*., 2018; Eppley *et al*., 2023). Moreover, a wide range of diseases infect Madagascar's wildlife, humans, and domesticated animals, including plague, typhoid, malaria, dengue fever, schistosomiasis, rabies, leptospirosis, and giardiasis (Barmania, 2015; Nunn *et al*., 2022). Furthermore, as agricultural practices change and Madagascar's rural population has increased market production of cloves, coffee, vanilla, and many other cash crops (Laney & Turner, 2015; Carrière *et al*., 2022; Danthu *et al*., 2022), transitions in diet and behavior may have contributed

to increases in chronic non-infectious diseases, such as cardiovascular illnesses (Ibrahim & Damasceno, 2012; Liebert *et al.*, 2013; Manus *et al*., 2018; Lea *et al.*, 2020; Wade, 2023, unpublished data).

In this contribution, we present One Health and evolutionary medicine as frameworks for investigating interactions involving land use change, socio-economic change, and human health. One Health is particularly important in low resource settings like Madagascar, where there is frequent contact between farmers, livestock, and wildlife (Herrera *et al*., 2020). Evolutionary medicine is important because it engages with occurring market transitions, which are associated with changes in lifestyles that contribute to disease. An important component of socioeconomic change that we consider is "market integration," which we define as the transition from subsistence agriculture to greater production of cash crops and purchase of consumer goods. To illustrate the value of these frameworks, we also provide an overview of several empirical studies that we and our colleagues conducted recently in rural communities around the Parc National de Marojejy in the SAVA Region of northeastern Madagascar. We conclude with some general observations about interconnections between human and animal health, changes in environmental systems, and market participation.

Research frameworks

One Health

One Health draws on public health, veterinary medicine, and environmental sciences to focus an interdisciplinary lens on complex interdependencies among human, animal, and environmental health (Zinsstag *et al*., 2023). In 2022, the One Health High-Level Expert Panel (OHHLEP *et al.*, 2022) proposed this definition: "One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent." Ecology and evolution are central to these efforts, as they describe the interactions among species and how organisms, including infectious diseases, respond to these selective pressures. Likewise, social science perspectives are essential to One Health research, because these fields provide insights into human behavior in the context of social and environmental change.

Research in One Health explicitly considers how human activities influence animals and the environment, including both domesticated and wild animals (which can include introduced feral species), and how these interactions impact human health and well-being. One Health has become an important component of global health, with a growing recognition of the importance of One Health perspectives for understanding the spillover of infectious diseases from domesticated and wild animals to humans, the evolution of antimicrobial resistance, and the challenges of food security in changing environments, including in the context of climate change (Zinsstag *et al*., 2018, 2023). The perspectives, findings, and approaches of One Health have influenced an array of recent research studies on Madagascar, including zoonotic disease from cattle (zebu), the reemergence of plague in humans, and the health of lemurs (Nunn *et al*., 2022). Several of the studies described later in this contribution are influenced by the One Health approach.

Evolutionary medicine

Evolutionary medicine considers how the evolutionary process makes humans (and other animals) vulnerable to infectious and non-infectious disease, and thus provides insights to the ultimate reasons for "why we get sick" (Neese & Williams, 1996). Like One Health, evolutionary medicine represents the convergence of different research fields, especially involving interdisciplinary collaborations among evolutionary biologists, clinicians, and public health practitioners. Evolutionary medicine arises from the realization that evolution is central to the most pressing global health challenges, such as changes in antimicrobial resistance, or the emergence of infectious diseases and their adaptation to human populations. Evolutionary medicine also provides crucial insights to the origins of obesity, aging, and mental health disorders (Neese, 2008; Stearns, 2012).

As noted above, evolutionary medicine is relevant for understanding human health on Madagascar because it engages with evolutionary mismatch, which reflects a situation in which the environments and lifestyles of people today differ radically from those of our hunting-and-gathering ancestors (Manus, 2018). These mismatches exist globally and are accelerated by economic change and market integration, which is occurring throughout Madagascar. Other vulnerabilities emerge because of tradeoffs that arise in the evolutionary process,

such as when a gene provides benefits early in life at some cost late in life (antagonistic pleiotropy, which is responsible for aging; Austad & Hoffman, 2018). Evolutionary medicine also considers ways of using these evolutionary perspectives to improve human health and reduce suffering from disease. Examples involve innovative approaches to the challenges of evolution of resistance to antibiotics (Roemhild & Schulenberg, 2019), cancer chemotherapies (Gatenby & Brown, 2020), and insecticides (Blanford *et al*., 2011).

Research setting

Madagascar's economy depends heavily on agriculture, with 83% of the nation's households engaged in the agricultural sector (INSTAT, 2021). While agriculture is an essential part of the rural economy, agricultural productivity is constrained by limited uptake of modern agricultural practices, poor transportation and marketing infrastructure, and high vulnerability to climate change (World Bank Data, 2019). As one of the world's 10 poorest nations, 79% of the Malagasy population lives below the international poverty line (Bustamante *et al*., 2018). Access to western-style healthcare is often challenging or largely non-existent in rural areas, with 40% of the population living relatively far from primary healthcare clinics, i.e., Centre de Santé de Base (CSB) organized by the Ministère de la Santé Publique, which provide basic primary and obstetric care (Barmania, 2015). Because of distances involved and need for patient support at the centers, individuals seeking healthcare often travel with multiple family members, who must miss work to support their loved ones. This adds to the financial burden of disease and discourages healthcare seeking behavior (Bustamante *et al*., 2018).

This contribution reports on several studies conducted in multiple villages around the Parc

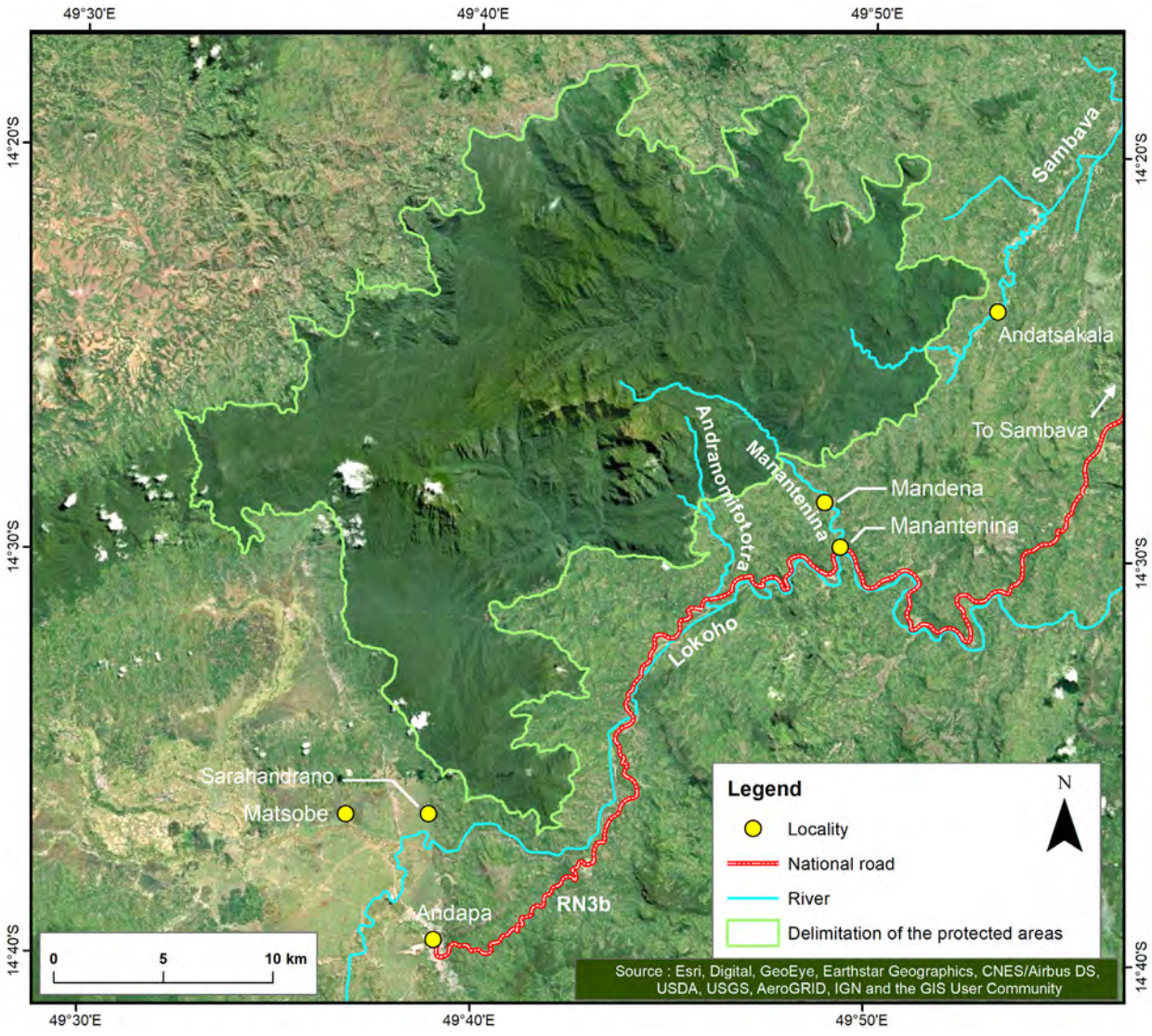

Figure 1. Map showing location of study villages near the Parc National de Marojejy.

Table 1. Summary of demographic and agricultural statistics, separated by village in northeast Madagascar. Data from Kramer *et al*. (2020) and Herrera *et al*. (2021).

	Manantenina	Mandena	Matsobe
Number of survey respondents	150	94	110
Mean age of respondent, years	41.4	45.6	45.5
Median household size	4	4	4
Median land size, estimated hectares	5	2	6
Median vanilla harvest (in kg)	20	10	17.5
Median rice harvest (in kg)	300	456	900
% respondents growing rice	70	80	82
% respondents growing vanilla	87	92	45
% collecting fuelwood	86	97	65
% respondents completed primary school	81	79	84
% respondents farming as main activity	90	86	91
% respondents with bank account	71	76	66

National de Marojejy in the SAVA Region (Figure 1). To provide context for these studies, three of these villages (Mandena and Manantenina in Sambava District and Matsobe in Andapa District) are described in some detail. The villages were selected based on their proximity to the national park. The park provides water and maintenance of meteorological systems to surrounding settlements (Goodman *et al.,* 2023, herein). Residents of the villages collect fuelwood, construction wood, wild game, and other products from the park (personal observation, 2022). In addition, because Mandena is the only entry point for tourists who wish to visit the park, a number of villagers find occasional work as tourist guides and porters. Between 2012 and 2016, there were 1399 visitors to the national park per year (Goodman *et al.,* 2023, herein).

Household surveys were conducted in each village to collect information on agricultural activity, demographic information and health conditions, and access to healthcare. The surveys were conducted in the local dialect by Malagasy research assistants and students, accompanied by one or more researchers from Duke University. Verbal consent was obtained and responses were recorded with Qualtrics software using Samsung tablets. In addition, several focus groups on agricultural activity and health were held in each village. Further details are provided elsewhere (Herrera *et al*., 2021).

Baseline socioeconomic data are reported in Table 1 for 354 respondents in the three villages. The mean age of respondents was 44 and the average household size was 4. The surveyed farmers reported median landholdings that ranged from 2 ha in Mandena to 6 ha in Matsobe. Approximately four-fifths of respondents completed primary school. Farming was the main activity for most respondents (86-91%). The two most important agricultural crops in the area were reported as rice and vanilla, but many other crops were produced by the rural residents. Approximately three-fourths of respondents grew rice, with median rice harvests much higher in Matsobe than in the other two villages. Vanilla was grown by most respondents in Manantenina (87%) and Mandena (82%), but only by 45% of those living in Matsobe. Fuelwood collection in degraded forests within and outside the national park was a common activity in all three villages. Relatively few respondents (9-21%) had bank accounts. Up to 76% of respondents reported that they had experienced food insecurity in their household at some time during the past three years.

Research studies

In this section, we present several research projects conducted in villages adjacent to the Parc National de Marojejy. These include studies that engage with both One Health and evolutionary medicine, along with global health projects more generally. Most of these research projects have provided Duke University and Malagasy students with unique training opportunities, resulting in multiple theses and publications.

Zoonotic disease transmission

We conducted a number of studies on the transmission of organisms between non-human animals and humans. In one study, we investigated the effects of human land use on the prevalence of *Leptospira* in small mammals living in and around Mandena (Herrera *et al*., 2020). A variety of species of *Leptospira* infect a range of mammals, including humans, with human infections potentially resulting in life-threatening disease. Black rats, which exist in high abundance throughout the agricultural areas around Marojejy, are known to be reservoirs of

Leptospira, which is waterborne and can persist in the soil. This transmission mode provides abundant opportunities for cross-species infections to occur from a small mammal host to humans, particularly in the context of farming.

To investigate the role of land use change in shaping mammalian communities and the *Leptospira* lineages that they harbor, we captured 530 small mammals around Mandena, including various tenrecs, native rodents, and especially introduced mice, rats, and shrews. The introduced small mammals were more abundant in more anthropogenically impacted habitats, such as rice fields, the village, and forest fragments. We found 36% of sampled individuals were infected with *Leptospira* (192 of the 530 animals tested), with most of those infections (168) occurring in introduced species. Two species of *Leptospira* were identified: *L. interrogans*, which was found in native and introduced species, especially *Rattus*, and *L. kirschneri*, only found in the introduced house mouse (*Mus musculus*). These results provide new insights to risks of human infection from this neglected tropical disease, including the impacts of land use change on infection risk. The results also revealed the protective role of the national park on small mammals, with native species occurring at higher abundance within Marojejy.

In another study, we considered the potential role of domesticated animals in zoonotic disease transmission. For this, we investigated the skin microbiome on cattle (zebu) and their owners as a proxy for disease transmission across species (Manus *et al*., 2017). We hypothesized that we would see greater similarity in the microorganisms on the cattle and their owners, particularly on parts of the body that are associated with human-animal contact, such as the hands of herders and the cows' torsos. We failed to find support for this association. Instead, we found that microbes on the ankles of humans were more similar to those on the cattle, suggesting that the ground and low vegetation are the principal transmission pathway for microbial transfer. We also did not find compelling evidence that the skin microbiome of humans differed based on whether they owned cattle.

We also studied hygienic behaviors that are relevant in the context of zoonotic infectious disease, using both surveys and additional studies of the skin microbiome. In the microbiome study, we investigated how access to antibacterial soap influences the communities of organisms on human hands, with implications for disease transfer (Yu *et al*., 2018). We implemented an experimental approach in which one group of villagers was given antibacterial soap, and their skin microbiome was compared to another group that did not have access to the same type of soap. We found that antibacterial soap led to marked changes in the composition of the skin microbiome, but not to the number of bacteria on the skin. We hypothesized that the large exposure to domesticated animals and their microbes in this population may lead to continued colonization of the human skin microbiome, even with the use of antibacterial products.

In a more recent study, we investigated the predictors of infection with *Blastocystis*, a common intestinal microorganism, in Mandena (Anaeme, 2022, unpublished data). This protozoan is spread through a fecal-oral route, and is known to have reservoirs in domesticated and wild animals. Its effects are also variable depending on the strain of *Blastocystis* and host characteristics. As such, it is a good organism for investigating zoonotic disease outcomes. The research used survey data on animal interactions, hygienic practices, and demographics. *Blastocystis* infection was assessed in human fecal samples using DNA metabarcoding.

We found that the prevalence of *Blastocystis* was high in Mandena, with 119 of 183 sampled individuals showing evidence of *Blastocystis* (64%). We also found evidence of multiple genetic variants of *Blastocystis* in these samples, with some people harboring up to 34 different genetic variants. Predictors of infection and variant number included hygienic factors - such as washing hands without soap, and animal contact, such as owning a cat or coming into contact with rodents. However, the genetic variants in humans living in Mandena were not the same as those sampled in the non-human animals in this village, suggesting that transmission between them is not common. This work was limited to one village; ongoing research is expanding this research to multiple villages, with larger samples in each village.

We have a number of other projects on infectious diseases in the region, with many of them involving zoonoses. In one village, for example, we found that 23% of people show evidence of infection with canine hookworm (*Ancylostoma ceylanicum*), indicating a high rate of transmission from dogs to people (Titcomb, 2022, unpublished data). Remarkably, 47% of people sampled in this village have infection with the human hookworm (*Necator americanus*), with similarly high prevalence in other villages. Likewise,

in terrestrial small mammals, we find evidence for hantaviruses, astroviruses, paramyxoviruses, and some coronaviruses in bats. Additional research will be needed to determine which, if any, of these are zoonotic. We are currently completing our lab work on these samples from humans, domesticated animals, bats, and non-volant small mammals across three villages to better understand the drivers of these infectious diseases, particularly in relation to shared habitats, water sources, and contact points.

Domesticated animals also have the potential to introduce infectious agents into wildlife, both in the park and around its borders. Among the domesticated animals we are studying for zoonotic diseases, dogs would be most likely to enter the park, and thus are worth studying in the context of introducing new infectious diseases to wild animals within the national park boundaries (Rasambainarivo *et al*., 2017). In this context, we have evidence of both *Leptospira* and canine hookworm infections in dogs sampled in the villages in which we are studying zoonotic diseases. Using GPS data loggers, we are also collecting data on dog ranging patterns, along with movement data on their owners. All of these projects investigate infection in relation to land use change, environmental health, and socioeconomic data, thus engaging with One Health approaches to understand infectious diseases at the human-animal-environment interface.

Barriers to healthcare access

Previous research has shown that there were several significant obstacles to healthcare in rural Madagascar, including the need for transportation to clinics, financial constraints in paying for healthcare and medicine, and unreliable healthcare quality (Bustamante *et al*., 2018). We examined healthcare access in two of the villages described above, Manantenina and Matsobe (France, 2019, unpublished data). In addition to focus groups and household surveys, a Quality of Care Assessment was conducted for all known local health centers (CSBs) along 53 km of road between the two villages. The assessment was based on the WHO Service Availability and Readiness Assessment (SARA), a tool used to assess the health facility “readiness” of clinics to treat the communities they serve (World Health Organization, 2015). The assessment is largely based on availability of essential medicines, other consumables, and basic medical equipment. The clinics in closest proximity to Manantenina (outside of the village) and Matsobe (within the village) had readiness scores of 61 and 68, which were near the median of the nine evaluated clinics. Thus, the clinics were similarly positioned to provide healthcare services.

To investigate health-seeking behaviors for acute onset illnesses, survey respondents were asked about the prevalence of fever in their household in the last three months and the actions taken to treat fever. In both villages, respondents reported similar levels of fever within the last three months (45% and 43%). Respondents in Manantenina were much less satisfied with their healthcare access as compared to those in Matsobe, citing the following issues as the principal problem for higher rates than respondents in Matsobe: distance to the clinic (69% vs 16%), not wanting to travel alone to the clinic (83% vs 20%), and cost of care (93% vs 79 %). However, despite reporting barriers as a major impediment more frequently, respondents in Manantenina were more likely to seek medical treatment when related to fever (82% vs 57%). This may be because 51% of the respondents in Manantenina had health insurance, while no one in Matsobe reported that they had health insurance.

Among the respondents who sought care with a medical professional at the onset of a fever, 27% in Manantenina and Matsobe received a diagnosis for their fever, and the majority treated their illness with medication (93% vs 96%, respectively). This suggests that future healthcare policy should focus on reducing the barriers to accessing care, including transportation and distance to clinics.

Vanilla cultivation, market integration, and access to healthcare

Vanilla is a popular and lucrative commercial crop in the SAVA Region due to suitable growing conditions and the global demand for natural (plant grown) versus artificially produced vanilla. High vanilla prices motivated farmers in the region to expand production of this crop in the previous decade (Hänke *et al*., 2018). From 2012 to 2018, the Madagascar price for cured vanilla increased from about $50 to $600 per kilogram. In addition, the proportion of vanilla produced under environmental and social certification increased, and several companies and NGOs launched sustainability certification programs that include rural development activities and price support schemes (Andriamparany *et al*., 2021). Farm income in rural SAVA initially improved due to higher vanilla prices; however, prices started falling after

2018, and by 2020 were 50% below their peak level (Khan *et al*., 2021).

To better understand the vanilla economy and socioeconomic status of villages near the Parc National de Marojejy, household surveys were conducted among farmers in Manantenina and Matsobe villages in 2019 (France, 2019, unpublished data; Metz, 2020, unpublished data). The two villages reported very different levels of involvement in vanilla sustainability certification programs, with 61% enrolled in Manantenina and only 6% in Matsobe. Respondents in both villages had positive views of certificate programs, with the level of satisfaction higher in Manantenina. In Manantenina, half of the respondents had healthcare coverage, with most receiving this coverage through an affiliation with a vanilla certification program. In focus groups, farmers in both villages were positive about healthcare access provided by certification programs. One farmer in Manantenina reported, "*each [program] member has a health insurance card … when a member gets sick, they can go to the hospitals that work with [the program*]" (Munshi, 2020, unpublished data, translated from Malagasy).

Our research group also used survey data from Manantenina to construct a wealth index for each household. We then applied regression analysis to explore the relationship among vanilla production, wealth, and healthcare access (Metz, 2020, unpublished data). These analyses revealed a positive relationship between vanilla production and wealth. However, we found no evidence that either variable had an impact on health status or healthcare access. One limitation was our focus on a single village. A more definitive analysis will need to examine these relationships in more villages and with larger samples. It also would be important to use longitudinal data that accounted for the price variability of vanilla over time.

Our team also piloted several choice experiment questions in Mandena to better understand farmers' decisions about participating in vanilla sustainability certificate programs (Kramer *et al*., 2018). Choice experiments are used by social scientists to better understand decision making, and the relative importance of different attributes of a program (Holmes *et al*., 2017). The choice experiments in this study provided a series of hypothetical choices among certificate programs with varying attributes. The four attributes were a price premium for growing certified vanilla, advance payment on some of the premium, health insurance, and an agronomic training program to provide farmers with information on best practices for vanilla cultivation. The results from nearly 100 farmers suggest strong enthusiasm for vanilla certification programs, consistent with observed enrollment levels. The most important attribute in our experiment was access to health insurance.

Social networks and potential disease transmission

Infectious diseases spread through direct contact between individuals as well as indirect contacts involving (1) environmental overlap for parasites that are transmitted through soil or water or (2) overlap in shared areas that harbor many vectors, such as mosquitoes that transmit malaria. These contacts are dependent on social networks and movement patterns, which can be studied to understand the spread of both disease and information about controlling disease.

A study of social networks was conducted in Mandena to better understand social relationships and their potential role in public health (Owens, 2019, unpublished data). Using social network aspects associated with friends, agricultural co-workers, and people from whom they might borrow or to whom they may loan money, we created several social networks representing contact patterns among 500 individuals. One of the resultant networks is shown in Figure 2, based on questions related to co-working relationships (Owens, 2019, unpublished data). We found that assortative mixing (homophily) was a predictor of interactions. In particular, gender was a key characteristic in determining connectedness in a network, with individuals of one gender more likely to be connected with others of the same gender in both

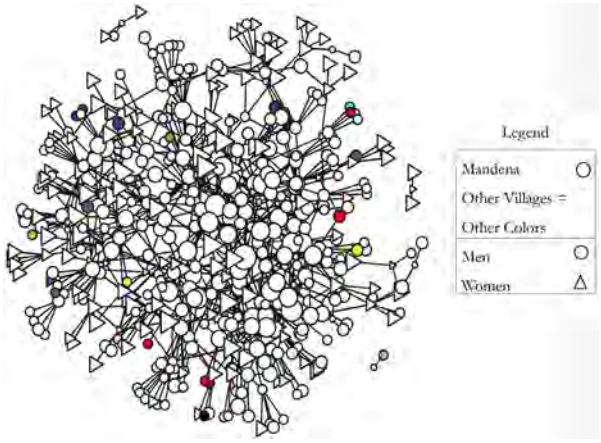

Figure 2. Agricultural social network of 500 people in one village in 2018 (circles = men, triangles = women, size = number of co-workers, color = village).

work and friend networks. We also found that men were more likely to be central in work networks, and the work networks tend to have more connectivity than friend networks, which are often more isolated (Owens, 2019, unpublished data).

We also investigated the implications of assortative mixing for health, information flow, and the structure of social connections in communities that have different ethnic groups, occupations, and educational levels (Lodge, 2020, unpublished data). We focused on social connections in Manantenina, finding evidence for homophily in a number of health-related traits. For example, smokers were more likely to be connected to other smokers on the Manantenina social network; this parallels findings in industrialized countries (Flatt *et al*., 2012). Likewise, social connections were predicted by gender, with men more likely to interact with other men and women more likely to interact with other women. In addition, body mass index was predictive of social connections in some tests, with some other variables, such as blood pressure, showing weak associations.

Across human and animal societies, more socially connected individuals have improved health outcomes (Snyder-Mackler *et al*., 2020). In baboons, for example, females with more high-quality social connections are able to overcome the negative effects of early life hardship (Lea *et al*., 2015) and those with more connections live longer lives (Archie *et al*., 2014). We therefore also investigated whether people who are named by more people on surveys have better health. However, we found no significant effects of social connectedness on several key health measures, including body mass index, heart rate, and blood pressure. Sociality also comes with increased risk of infectious disease (Rifkin *et al*., 2012). Our social networks will be used to assess if this holds true in other villages surrounding the national park.

Evolutionary and ecological perspectives on human sleep

Market economies are thought to have major influences on many aspects of modern lifestyles, including diet, physical activity, and exposure to natural light. Sleep is another behavior that changes radically as populations become engaged in market economies. In high-income, industrialized settings, people are more likely to sleep at sites that are quiet, comfortable, safe, and have good temperature control. They are also more likely to have bright lighting to remain active well past sundown and to use electronic devices with screens, which are commonly used until going to sleep. Evidence suggests that these factors negatively impact sleep, leading to longer latency to fall asleep and poorer sleep quality (Chang *et al*., 2014). Yet other factors, such as better quality of the sleep environment, may improve sleep.

To shine new light on human sleep, we investigated sleep variation in rural farmers in Mandena (Samson *et al*., 2017). These farmers were assumed to spend more time outdoors in natural light, they generally lack access to bright indoor lighting and electronic devices, and given the tropical setting, they experience approximately 12 hours of darkness per day year-round. Thus, we expected that residents of Mandena would go to bed early, sleep longer than those in high-income settings, and rise early. Twenty-one individuals agreed to wear actigraphy devices up to three weeks. These devices have a three-dimensional accelerometer that measures subtle body movements. These data are logged on the device and can be analyzed to provide insights to sleep duration and quality, where the latter is measured as fragmentation of sleep and its efficiency (i.e., percentage of time in bed scored as sleep by the actigraphy algorithms). Because actigraphy cannot effectively quantify the stages of sleep, such as rapid-eye movement (REM), we also used polysomnography on a subset of individuals to measure electrical activity of the brain.

Counter to our initial predictions, our analyses revealed the surprising finding that Mandena residents have even shorter and more fragmented sleep than is found in populations in Italy and the United States that have been studied with comparable methods. In particular, analyses of the actigraphy data revealed that the Mandena study participants went to sleep much earlier (mean = 19:21) and woke up earlier (mean = 5:44) than the Italian population and most other industrialized populations (Samson *et al*., 2017). Despite spending an average of 9.4 hours in bed, however, the actual sleep duration of the Malagasy participants was only 6.5 hours on average, much less than 7.6 and 7.0 hours in the Italian and US populations studied with actigraphy; this difference was less pronounced once we accounted for napping during the day. The short sleep at night reflects a much more fragmented sleep, with substantially lower sleep efficiency (70% vs. 90-94% for the industrialized populations). These findings were confirmed with polysomnography, which also revealed a short duration of REM sleep.

Thus, this non-industrialized population has poorer sleep than would be expected in an

industrialized population. We hypothesized that this relates to several factors. First, the quality of the sleep environment in the home is often better for industrialized populations, especially those who would volunteer for a sleep study. In contrast, we found that many people in Mandena are sleeping in crowded indoor spaces and with less comfortable bedding. Second, the high human density in Malagasy villages creates substantial noise that disrupts sleep, including noise from animals (dogs), crying babies, and social interactions that occur throughout the night. Even if this noise is not noted as bothersome to some in the village because they are habituated to it, it was correlated with disrupted sleep in Mandena (Samson *et al*., 2017). Finally, the threat of theft around vanilla harvesting time is high, which would suggest that market integration in this village may also contribute to poor sleep, as it does (for different reasons) in industrialized settings.

Hypertension

A core finding from evolutionary medicine is that evolutionary mismatch impacts human health, i.e., that changes to human lifestyles, including those associated with economic integration, also result in changes to health. High blood pressure or hypertension is an example of negative health changes resulting from market integration. Hypertension results from a combination of environmental and genetic factors, with important lifestyle variables that include diet, exercise, sleep, and psychosocial stress. It is reasonable to expect that market integration will covary with many of these risks, while also providing income for people to purchase processed foods and alcohol that contribute to hypertension. In addition, hypertension commonly increases with age. Thus, as populations age globally, the incidence of hypertension is expected to increase. Finally, some studies have suggested potential links between malaria infection and hypertension, particularly when infection occurs early in life (Etyang *et al*., 2016). In one study at two sites Kenya and one in the United States, for example, Etyang *et al*. (2016) found that individuals with sickle cell trait, which confers resistance to malaria, had lower blood pressure as adults, but only in one Kenyan site with malaria. Given the high prevalence of malaria in the areas surrounding Marojejy (Meekers & Yukich, 2016), this infectious disease may also contribute to higher rates of hypertension, especially when combined with effects of market integration later in life.

To investigate hypertension around the Marojejy Massif region, we recruited 513 adult participants from Mandena (Manus *et al*., 2018). From these volunteers, we collected data on blood pressure and other health related variables, such as body mass index and socioeconomic variables. We documented an unexpectedly high prevalence of hypertension: 49% of 513 subjects exhibited hypertension, where using the diagnostic definition based on updated guidelines from the American Heart Association (Whelton *et al*., 2018). We also found that blood pressure increased with age and body mass index, but did not vary with gender. We were unable to discern any effects of tobacco and alcohol use or household size (as a possible marker of stress), although sample sizes were smaller than the overall cohort. A recent expansion of this study to two other villages (Sarahandrano and Andatsakala) confirmed the high prevalence of hypertension in the local rural population, yet there was no evidence that perceived experiences of stress, particularly stressful events that are unexpected or beyond one's control, influence blood pressure (Wade, 2023, unpublished data). This more recent study also investigated salt intake in Andatsakala, but did not find an association with hypertension.

Conclusion

The area around the Parc National de Marojejy has undergone considerable land use change in recent decades, including the loss of native forest, with this change accompanied by increased planting of commercial crops. It is important to understand how these environmental and economic changes impact human health and well-being. One Health and evolutionary medicine are two frameworks that are helpful for understanding these linkages. From a One Health perspective, a wide range of infectious diseases are found in wildlife, domesticated animals, and humans in the region. The land use changes underway may have the potential to increase the transmission of diseases from, for example, wild mammals to humans; we have documented some evidence of that risk. From an evolutionary medicine perspective, it is important to recognize that the changes in diet and behavior resulting from greater participation in agricultural and consumer goods markets may have contributed to chronic, non-infectious diseases.

The empirical studies summarized in this contribution explored some of the linkages among animal and human health, ecosystem change and

market participation. We confirmed the presence of infectious pathogens in humans and other animals, including *Leptospira, Blastocystis,* canine hookworm (*Ancylostoma ceylanicum*), human hookworm (*Necator americanus*), hantaviruses, astroviruses, paramyxoviruses, and coronaviruses. These studies provided new insights into the risk of zoonotic disease transmission and the potential for human infectious diseases to also infect animals. One study found that access to healthcare remains challenging for many in the SAVA Region due to constraints of transportation and care cost. Other studies showed participation in vanilla markets has the potential to lower barriers to healthcare through health insurance associated with vanilla certification schemes. Several studies explored how shared habitats, contact points, and social networks are influencing the potential for disease transmission. Hypertension and fragmented sleep are generally viewed as problems of industrialized societies, but our research has shown surprisingly high levels of both in villages around Marojejy, suggesting that lifestyle changes underway in SAVA, may be contributing to greater chronic disease.

We are currently engaged in more in-depth studies to better understand how environmental changes and economic development in Madagascar are contributing to a changing health landscape. Our research is modeling the ecological and socioeconomic factors that influence disease spread around villages and within the park and investigating multiple hypotheses concerning how human land use activities affect zoonotic disease transmission. This work is expanding to a larger set of villages around the park to investigate how market integration influences patterns of human movement and drives the transmission of infectious disease. All of this work will continue to use One Health and evolutionary medicine approaches to better understand these important changes underway in rural Madagascar.

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