

Original Contribution

Human–Wildlife Interactions Predict Febrile Illness in Park Landscapes of Western Uganda

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Abstract: Fevers of unknown origin complicate treatment and prevention of infectious diseases and are a global health burden. We examined risk factors of self-reported fever—categorized as “malarial” and “non-malarial”—in households adjacent to national parks across the Ugandan Albertine Rift, a biodiversity and emerging infectious disease hotspot. Statistical models fitted to these data suggest that perceived nonmalarial fevers of unknown origin were associated with more frequent direct contact with wildlife and with increased distance from parks where wildlife habitat is limited to small forest fragments. Perceived malarial fevers were associated with close proximity to parks but were not associated with direct wildlife contact. Self-reported fevers of any kind were not associated with livestock ownership. These results suggest a hypothesis that nonmalarial fevers in this area are associated with wildlife contact, and further investigation of zoonoses from wildlife is warranted. More generally, our findings of land use–disease relationships aid in hypothesis development for future research in this social-ecological system where emerging infectious diseases specifically, and rural public health provisioning generally, are important issues.

Keywords: Fevers of unknown origin, Malaria, Human–wildlife interactions, Protected areas, Central Africa

INTRODUCTION

Febrile illnesses are a major health burden across much of the tropics (Naing and Kassim 2012; Acestor et al. 2012). Syndromic fever may result from a number of common

illnesses, including malaria, pneumonia, typhoid fever, invasive nontyphoidal salmonellosis, and influenza (Chandramohan et al. 2002; Källander et al. 2004; Feikin et al. 2011; Prasad et al. 2015). In addition to common febrile illnesses, a number of other less common infections cause fever. For example, fever and other nonspecific symptoms (e.g., weakness, headache, digestive and respiratory upset) are associated with acute bacterial zoonoses such as leptospirosis, Q fever, brucellosis, and rickettsial fevers (Parola 2011; Crump et al. 2013; Dreyfus et al. 2016).

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Indeed, a wide variety of zoonotic pathogens result in high fever. Since the majority (> 70%) of emerging human infectious diseases originate from wildlife reservoirs (Jones et al. 2008; Hassell et al. 2017), rural populations living adjacent to wildlife refugia like protected areas may face a heightened risk of acquiring novel febrile illnesses.

In sub-Saharan Africa, protected areas (hereafter, parks) are the predominant conservation management strategy (Naughton-Treves et al. 2005; Chape et al. 2005; Coad et al. 2015). Conservation planning increasingly adopts whole-landscape approaches to promote ecosystem health inclusive of both parks and the surrounding matrix of human-dominated lands (DeFries and Rosenzweig 2010). However, many parks protecting exceptional biodiversity exist alongside high-density human populations dependent on natural resources for their livelihoods (Myers et al. 2000; Ferraro 2002; Naughton-Treves et al. 2011; Salerno et al. 2017). As a result, rural people living directly adjacent to parks frequently interact with wildlife and wildlife habitat (Brashares et al. 2011; MacKenzie and Hartter 2013; Salerno et al. 2016). Moreover, healthcare services adjacent to parks are often poorly provisioned (Chapman et al. 2015). This environment may facilitate the emergence of new diseases from wildlife, since human population density, forest cover, and rate of land-use change are all risk factors for emergence of novel zoonoses (Allen et al. 2017).

A central public health challenge exists in the inability to diagnose pathogens causing generalized syndromic fever (Petti et al. 2006; Uneke 2008). In rural communities in malaria-endemic areas, the majority of malaria cases are diagnosed and treated within the home and only present to health centers when home treatment fails (Amexo et al. 2004). Many rural health centers lack the diagnostic capabilities to adequately identify the etiology of fevers that are nonmalarial in nature, and therefore clinical misdiagnosis of malaria is common (Moerman et al. 2003; Nankabirwa et al. 2009). Zoonotic emergence events thus may be misdiagnosed or go unnoticed if they are associated with generalized febrile illness or other common diseases. Clinical misdiagnoses also result in elevated mortality risk from nonmalarial diseases for incorrectly diagnosed patients, in addition to wasted healthcare resources (Rooth and Björkman 1992; Reyburn et al. 2004).

The Ugandan Albertine Rift is a biodiversity (Brooks et al. 2004) and emerging infectious disease hotspot (Jones et al. 2008). Here, a dense human population occupies small farms alongside parks and forest fragments, and interaction between humans and wildlife occurs frequently

(Paige et al. 2014; Hartter et al. 2016). One of the most intimate exposures to wildlife in this region occurs because households living adjacent to parks and forest fragments routinely guard their crops from raiding wildlife, most commonly from primates, elephants, and wild pigs (Naughton 1998; MacKenzie et al. 2015). These interactions lead to both direct contact with wild animals and indirect contact with feces left in and around fields (Goldberg et al. 2008). Consumption and hunting of wild animals also occurs, but much less frequently than in Central and West Africa (Paige et al. 2014). Through these transmission pathways and others (e.g., resource collection and livestock grazing in parks and forest fragments), humans, wildlife, and livestock are known to share a number of common pathogens diverse in life cycle and mode of transmission (Rwego et al. 2008; Salyer et al. 2012; Ghai et al. 2014a, b). While numerous studies have examined how interactions with wildlife and protected areas affect human enteric pathogen infections in this region (e.g., Goldberg et al. 2008; Rwego et al. 2008), there is limited research attempting to understand how wildlife interactions and park proximity affect infections that often manifest as generalized fever (Paige et al. 2016).

Here, we report associations between self-reported febrile illness, wildlife contact, and proximity to park boundaries as part of a multi-objective study. We investigate two main questions in the Ugandan Albertine Rift by fitting statistical models to household-reported syndromic survey data: (1) do respondents perceive a difference in the cause of fever as malarial *versus* nonmalarial in a manner that allows for inferences regarding risk factors and (2) more specifically, are these perceived causes of fever associated with personal wildlife interactions and/or household proximity to park boundaries? Our study uses syndromic surveillance (May et al. 2009) of perceived malarial fever and nonmalarial fever, as defined by respondent perceptions of fever origin in cases which caused missed work or other significant changes in daily activity. These self-diagnoses are reported through household surveys. Cases are not specifically associated with diagnostic confirmation, although surveys report if respondents typically seek diagnostic confirmation. Our data show that perceptions of fever origin (malarial vs. nonmalarial) directly influence healthcare-seeking behavior, and thus the opportunity to diagnose nonmalarial febrile diseases as they emerge (Uzochukwu and Onwujekwe 2004; Lester et al. 2016). Such low-cost, exploratory research should guide coordinated investigation that integrates ecological, veterinary,

and epidemiological sciences (Travis et al. 2014; see also Pattanayak et al. 2006).

METHODS

Study Region and Survey Design

We conducted surveys in households bordering four national parks in western Uganda: Kibale, Queen Elizabeth, Murchison Falls, and Rwenzori Mountains (Fig. 1, Table 1). As part of a larger study investigating human–environment–climate interactions in a multipark landscape (Hartter et al. 2016), we administered quantitative surveys to 981 households. Households were randomly selected within 5 km of park boundaries using a geographical random sampling procedure (Goldman et al. 2008). Surveys were administered between 2012 and 2014 in order to quantify various characteristics related to health, livelihoods, and interactions with parks and wildlife. A single survey was administered per household to either household heads or spouses. All questions related to health and wildlife contact pertain specifically to individual respondents; livelihood-related questions such as land or cattle ownership may pertain to the immediate household. Surveys were administered in the local languages by experienced field technicians. See Supplementary Material for sampling and survey details.

In surveys conducted adjacent to Kibale and Queen Elizabeth National Parks, questions yielded three variables describing self-reported illness: the *annual frequency of perceived malarial fever* (0, 1, 2, 3, 4+); the method typically used, if any, to *assess fever origin* (i.e., get diagnostic test at a health facility with treatment, rely on self-diagnosis based upon symptoms alone plus treatment, or self-diagnose symptoms without treatment); and, for the fever cases that were believed to be something other than malaria, the *annual frequency of perceived nonmalarial fever* (0, 1, 2, 3, 4+). In surveys conducted adjacent to two additional national parks, Murchison Falls and Rwenzori Mountains, the single question regarding nonmalarial fever was not asked. Analyses including these Murchison–Rwenzori data therefore examined only relationships between self-reported perceived malarial fever and independent variables of interest. With the exception of the variable regarding nonmalarial fever, survey questions and protocols were identical across the entire sample.

Hereafter, we use “two-park sample” to refer to analyses conducted on Kibale and Queen Elizabeth National Parks data where questions regarding both perceived

malarial and nonmalarial fever were collected ($n = 617$). We use “four-park sample” to refer to analyses that included all four national parks but pertain only to perceived malarial fever ($n = 981$). For all questions regarding fever, respondents were asked to generalize their answers for a typical year (see “Case Definitions and Risk Factors” section below). Respondents were not asked specifically about other symptoms associated with fever cases, nor about the relationship between frequency and severity. Questions on fever frequency were specific to the respondent, not the entire household. All cases were self-reported and measured through household surveys; data do not include medical records or diagnostic information.

While acknowledging the limitations, we include self-diagnoses as they are the best available measure in this area. Among communities in malaria-endemic regions, the knowledge of malaria and its symptomatology is high. Knowledge acquisition is both heuristic in nature given the frequent exposure to the disease in their environment, and it is also informed by experience with clinical diagnostics and treatment; indeed, approximately one-half of our sample typically seeks clinical care for what they perceive as malaria. Multiple studies from the region and elsewhere demonstrate that this knowledge base allows for households to fairly accurately self-diagnose malaria versus other fever-causing diseases in both children and adults (e.g., Ahorlu et al. 1997; Dunyo et al. 2000; Yé et al. 2007; Birhanu et al. 2016; see also Maheu-Giroux et al. 2011). More importantly, these pre-diagnostic data are critical in understanding care-seeking behavior (McCombie 2002). Throughout, we are explicit in presenting model results as coefficient effects on *perceived* fever outcomes.

Case Definitions and Risk Factors

We define fever through respondent recall of high-intensity fevers, and we recorded their perceptions of fever origin; the two-park sample includes malarial and nonmalarial fevers, while the four-park sample includes only malarial fevers. During surveys, enumerators asked respondents to specifically consider only fevers they thought to be severe, such as those causing missed work or other significant changes in daily activity, and the annual frequency of these fever cases. Because the study goals focused on perceptions, respondents were not given criteria or syndromic classifications with which to define their fevers (see May et al. 2009). In the two-park sample, preliminary survey results showed the distribution of fever responses was highly

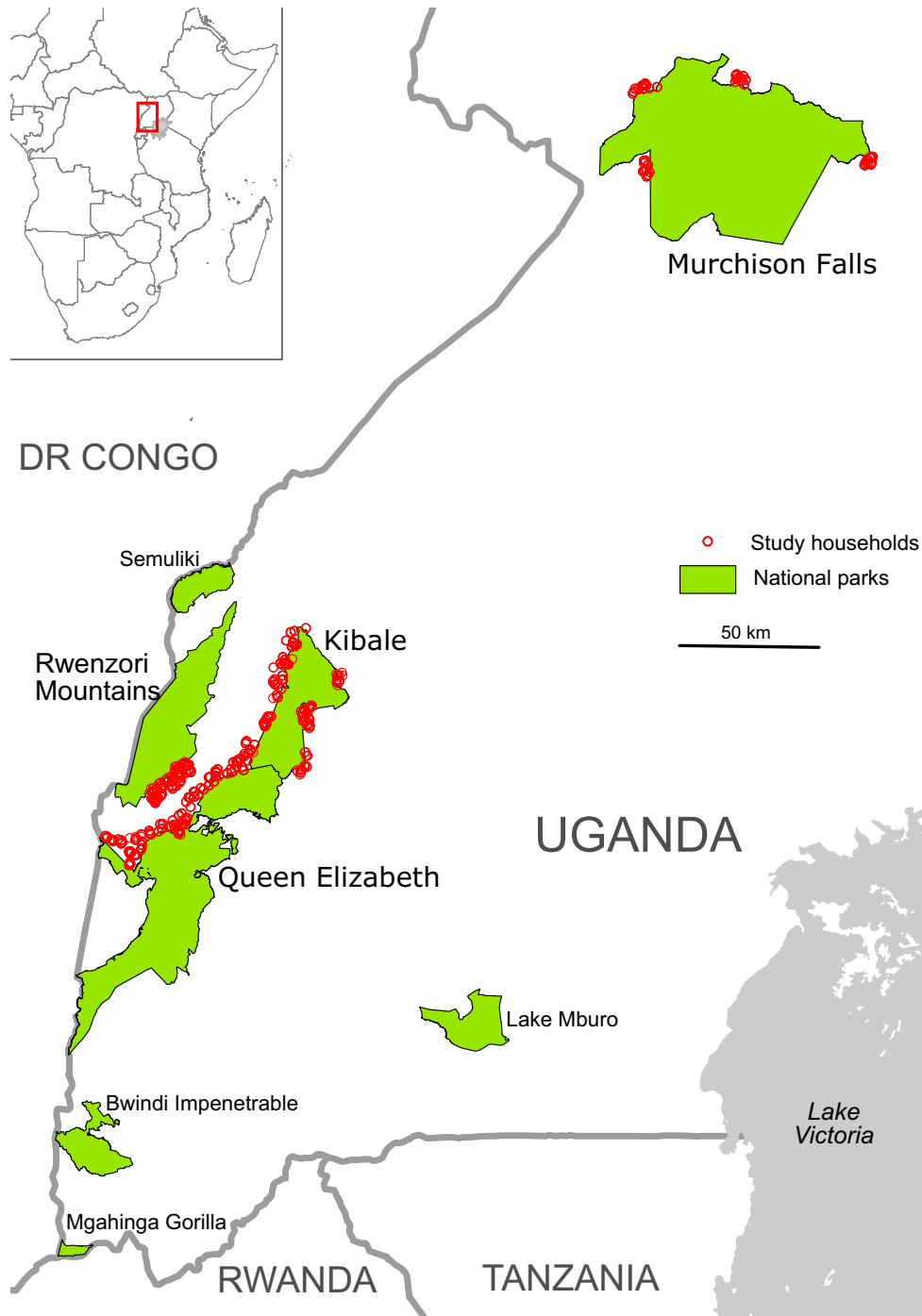


Figure 1. Study region in western Uganda. Household surveys were conducted at sites adjacent to four national parks (green polygons): Murchison Falls, Kibale, Rwenzori Mountains, and Queen Elizabeth. Sample households (red points) were selected within 5 km of park boundaries using a geographically randomized method.

skewed toward three or more incidents per year. Therefore, we postcoded both malaria and nonmalaria responses into binary indicators of four or more incidents of fever per year (i.e., the response category of greater than or equal to four; see Supplementary Table S1 for more details including the

distribution of fever responses). Thus, in the two-park sample, households were assigned to one of four possible (multinomial) categories regarding experience of fever (Table 2). In the four-park sample, where data do not exist for nonmalarial fever, we examined only the binary out-

Table 1. Site-Level Summary Information. Biophysical data are reported from Uganda Wildlife Authority (UWA), Africa Rainfall Climatology v2 (Novella and Thiaw 2012), and the WorldPop project (Stevens et al. 2015). Ethnic groups are reported from survey data (groups in parentheses are minorities in the park area).

National park	
Kibale	Area: 795 km ² . Precipitation: 1050–1425 mm year ⁻¹ . Elevation: 1100–1590 m asl Primary ethnic groups: Bakiga, Batoro (Basongora, Bakonjo, Bafumbira, Banyarwanda) Dominant landcover: mid-altitude tropical forest Human population density within 5 km of boundary: 278 people per km ²
Queen Elizabeth	Area: 1978 km ² . Precipitation: 800–1400 mm year ⁻¹ . Elevation: 900–1300 m asl Primary ethnic groups: Basongora, Bakonjo (Bafumbira, Bakiga, Batoro) Dominant landcover: Savanna woodland and mid-altitude tropical forest Human population density within 5 km of boundary: 196 people per km ²
Murchison Falls	Area: 3877 km ² . Precipitation: 1000–1500 mm year ⁻¹ . Elevation: 500–1300 m asl Primary ethnic groups: Acholi, Aluru, Bagungu (Paluo, Rangi) Dominant landcover: savanna woodland Human population density within 5 km of boundary: 165 people per km ²
Rwenzori Mountains	Area: 995 km ² . Precipitation: 2000–3000 mm year ⁻¹ . Elevation: 500–5109 m asl Primary ethnic groups: Bakonjo (Bakiga, Batoro) Dominant landcover: mid- to high-altitude tropical forest Human population density within 5 km of boundary: 490 people per km ²

come of frequent perceived malarial fever versus infrequent or no fever.

We examined associations of these response variables (Table 2a–d) with a set of epidemiological risk factors (Table 3). Specifically, we considered frequency of wildlife contact and distance to park boundary as focal predictor variables. In terms of wildlife contact, the explicit objectives of this study involve testing for associations between perceived fever and direct contact with wildlife, following on research from the region identifying multiple sources of risk: frequent and direct physical contact with animals (nonhuman primates in particular) and feces (Goldman et al. 2008; Hartter, unpublished data); human, wildlife, and livestock sharing multiple pathogens and antibiotic resistance (Goldberg et al. 2008); households spending significant time in fields guarding crops and in forests gathering resources (MacKenzie et al. 2015); households identifying health as a severe livelihood risk (Hartter et al. 2016); poor access to health services in the areas of farms and fragmented forests directly adjacent to park boundaries (Chapman et al. 2015). The survey recorded the general frequency of direct contact, handling, or being bitten by wild animals from the park or forest as categorical responses. The second focal predictor, distance to park, is the linear distance between the location of the household and

the nearest park boundary. See Supplementary Material for further details on risk factors.

In terms of additional covariates, in order to determine if contact with animals overall (not specifically wildlife) was associated with fever, we considered the type of livestock owned by the household. Acknowledging that respondents' past experiences with health care influence perceptions of current illness, we considered whether or not respondents typically seek diagnostic tests at a health center (e.g., rapid test, diagnostic microscopy) to confirm when they suspect they have malaria. Finally, we considered land area owned, quality of house construction, mean annual temperature, and distance to nearest household neighbor to control for the known effects of household wealth (Bhutta et al. 2014), climate (Githeko and Ndegwa 2001; Hay et al. 2002; Patz et al. 2005), and human density (Allen et al. 2017) on health and disease.

Analyses

We fitted three statistical models that together address the two main research questions: (1) do respondents perceive a difference in the cause of fever as malarial *versus* non-malarial in a manner that allows inferences regarding risk factors and (2) more specifically, are these perceived causes

Table 2. Case Definitions for Perceived Fever Variables. In the two-park sample bordering Kibale and Queen Elizabeth National Parks only, respondents were asked about both perceived malarial and perceived nonmalarial fevers. Postcoding of the two questions regarding reported perceived malarial fevers (column 1) and perceived nonmalarial fevers (row 1) assigns each household to one of four possible fever outcomes. In the larger four-park sample, households were asked only about malaria, and responses were categorized as either frequent perceived malarial fever (b) vs. infrequent or no fever (d). Respondents were asked only to consider fevers which they thought to be severe (i.e., resulted in lost work and/or significant change in activity).

	Respondent reports four or more episodes of perceived nonmalarial fever	Respondent reports infrequent (< 4) or no perceived nonmalarial fever
Respondent reports four or more episodes of perceived malarial fever	Frequent combined fever (a)	Frequent malarial fever (b)
Respondent reports infrequent (< 4) or no perceived malarial fever	Frequent nonmalarial fever (c)	Infrequent or no fever (d)

of fever associated with wildlife interactions and household proximity to park boundaries?

Our first two models used only data from the two-park sample including self-diagnosis of both malarial and nonmalarial fever. First, we estimated a binomial regression model predicting any form of fever reported by household as predicted by wildlife contact and proximity to park boundary, while controlling for livestock contact, household wealth, climate, and human density. The modeled outcome variable corresponded to case definitions of any frequent fever (Table 2a, b, or c) versus infrequent or no fever (Table 2d). This model therefore ignored patient self-diagnoses and was the most inclusive fever outcome variable (i.e., if a household reported any type of fever). Thus, we considered that this model would identify general associations between fever and the household-level predictor covariate risk factors (Table 2; also, Supplementary Material). Results are reported in the “[Binomial Model in the Two-Park Sample](#)” section.

Second, also in the two-park sample, we estimated a multinomial logistic regression model (Venables and Ripley 2002) predicting the four fever case definitions (Table 2) using the same suite of predictors (Table 3; also, Supplementary Material). We considered that this model allows for self-diagnosis and is fitted to perceived malarial vs. nonmalarial fever outcomes. Results are reported in the “[Multinomial Model in the Two-Park Sample](#)” section. In both the two-park models, we do not impose a multilevel structure in the data because the park landscape is continuous between Kibale and Queen Elizabeth National Parks, and varying (i.e., random) effects would not gain

separation (see Supplementary Material, Fig. 1, and Table 1; also McElreath 2015).

Since fever is widely (but not exclusively) synonymous with malaria in this region (Chipwaza et al. 2014; Ghai et al. 2016), we then fitted a third model to the complete sample from all four parks testing whether perceived malarial fever alone yielded consistent associations with the same set of independent variables used in the first two models. As stated above, the difference in samples is due to the question regarding perceived nonmalarial fever being omitted in the households adjacent to Murchison Falls and Rwenzori Mountains National Parks. For this model, we used multilevel binomial logistic regression to predict frequent malaria, with varying intercept effects accounting for unobserved differences in fever among each of the four parks (Chung et al. 2013), using the same suite of predictors (Table 3; also, Supplementary Material). Results are reported in the “[Perceived Malarial Fever Across All Parks](#)” section.

All fitted models produced raw coefficient estimates on the log-odds scale. We report results as coefficient plots with 95% confidence intervals and as model-wide prediction plots of focal coefficients with 95% confidence bands. For estimates with consistent (i.e., significant) associations at the 95% interval, we report the log-odds values and intervals in text (we also note estimates where the intervals cross zero but are unclear in Figs. 2 and 4). Analyses were conducted in the R Statistical Environment (R Core Team 2016). Code and data to reproduce analyses are deposited at the Zenodo archive (DOI: [10.5281/zenodo.1044466](https://doi.org/10.5281/zenodo.1044466)).

Table 3. Risk Factors Predicting Fever. The same set of predictor variables are included in all fever models. For continuous, integer, and binary variables, mean values are reported in parentheses, along with standard errors and variable class. For categorical variables, category proportions are reported.

Predictor variable	Description of variable
Proximity to park boundary	Linear distance in kilometers between household and park boundary (2.11 [0.04]; continuous)
Frequency of human–wildlife contact	How often the respondent comes into direct contact with wildlife or wild animal feces (ordered category: none (0.36), less than monthly (0.14), monthly (0.44), weekly (0.06)). Details of interactions (wildlife species, location (farm vs. home), type of contact (bitten vs. contacting feces)) were not recorded
Use of diagnostic test to confirm fever cause	Whether or not the respondent typically gets tested using rapid diagnostic kits or blood smear versus self-diagnosing symptoms and either taking medication or not (0.44 [0.016]; binary)
Livestock ownership	Whether or not a household owns each of four livestock species: cattle (0.15 [0.012]), sheep/goats (0.66 [0.015]), chickens (0.80 [0.013]), pigs (0.24 [0.014]))
Total land owned	Includes both farmed and fallowed land, in acres (5.35 [0.181]; continuous)
Quality of house	Whether or not a house is categorized as high-income construction (see MacKenzie 2012); 0.13 [0.011]; binary)
Mean temperature	Mean annual temperature in degrees Celsius based on spatially explicit data of monthly averages (Hijmans et al. 2005); 21.11 [0.067]; continuous)
Distance to nearest household	Linear distance in kilometers between survey household and nearest neighboring household in sample (see Supplementary Material; 0.08 [0.005]; continuous)

RESULTS

Perceived Malarial and Nonmalarial Fever

Binomial Model in the Two-Park Sample

Our first, most conservative model aggregated household responses into a general measure of fever (case definitions a, b, or c vs. d in Table 2; i.e., a binomial response variable of frequent fever). Ignoring self-diagnosis (of malarial vs. nonmalarial of fever origin), the model estimated that wildlife contact and distance to park did not predict a change in log-odds of frequent fever (Supplementary Figure S1). The linear term for wildlife contact suggested slight increased odds of fever, but the estimate was imprecise at 95% confidence. Higher temperature (0.06 [0.03, 0.09]) and lower wealth (− 0.11 [− 0.21, 0]) predicted increased odds of frequent fever.

Multinomial Model in the Two-Park Sample

The model including self-diagnosis separated fever into four response categories: frequent malarial and frequent nonmalarial fever (i.e., combined fever), frequent malarial

with infrequent nonmalarial fever, frequent nonmalarial with infrequent malarial fever, and infrequent fever of both types (Table 2). Although using the same data as the binomial model above (“[Binomial Model in the Two-Park Sample](#)” section), this multinomial model accounting for respondent self-diagnosis yielded more precise estimates (Fig. 2).

In terms of focal predictors, higher frequency of direct contact with wildlife predicted increased odds of frequent combined fever (both malarial and nonmalarial, linear term: 0.99 [0.12, 1.86]; Table 2 case (a); Fig. 3a) and frequent nonmalarial fever alone (1.17 [0.19, 2.16]; Table 2, case (c); Fig. 3c). Higher frequency of wildlife contact did not predict increased or decreased odds of malarial fever alone (− 0.01 [− 0.90, 0.87]; Table 2, case (b); Fig. 3b). The multinomial model treated the four-level ordered factor of direct wildlife contact as three orthogonal polynomials (note the segmented linear trend in Fig. 3a–c). Despite an apparent reduction in the effect size of “High” frequency wildlife contact on combined fever and nonmalarial fever (Fig. 3a, c, respectively), the linear term for wildlife contact was positive and significant at 95% confidence.

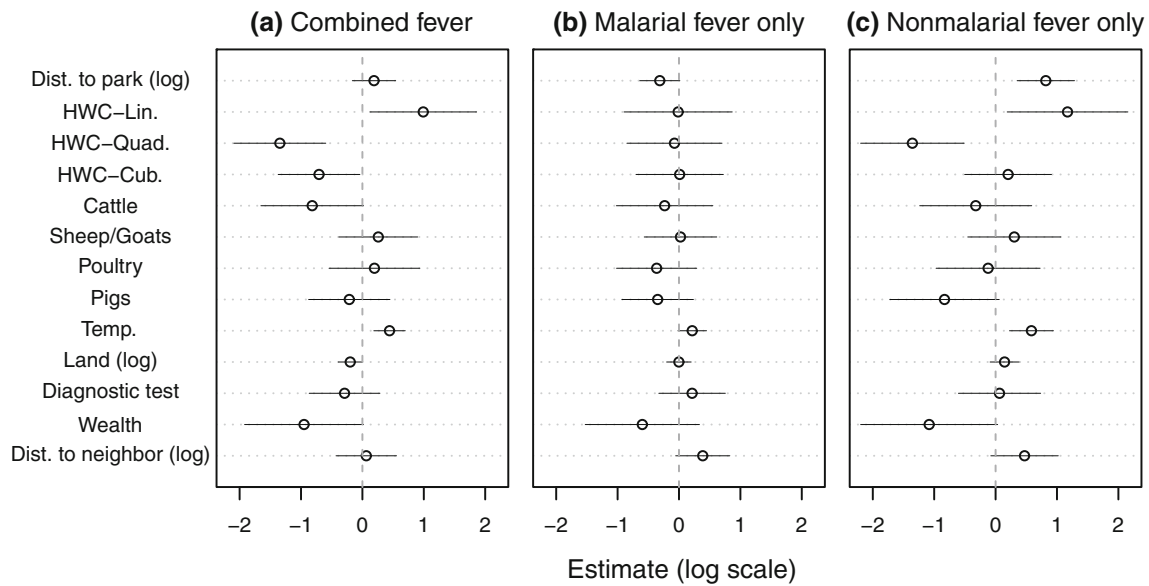


Figure 2. Household level coefficient estimates from the multinomial model (Kibale and Queen Elizabeth). Coefficients for corresponding outcomes [combined fever (a); malaria only (b); nonmalarial fever only (c)] are estimated with respect to the reference category of no or infrequent fever of any kind. HWC-Lin, HWC-Quad, and HWC-Cub estimates are the orthogonal polynomial terms representing the four-level human–wildlife contact ordered factor variable. Estimates are plotted with 95% confidence intervals.

After controlling for other factors, increasing linear distance between households and park boundaries predicted increased odds of nonmalarial fever alone (0.82 [0.35, 0.24]; Table 2, case (c); Fig. 3f); the distance estimate was positive for combined fever but imprecise at 95% confidence (0.19 [− 0.16, 0.54]; Table 2, case (a); Fig. 3d). In terms of malaria (Table 2, case (b)), closer proximity to park boundary predicted increased odds of malarial fever when nonmalarial fever was infrequent (although the confidence interval slightly crosses the indifference line, − 0.31 [− 0.64, 0.01]; Fig. 3e).

Livestock ownership did not consistently predict increased or decreased odds of fever (Fig. 2). This was true for the coefficient estimates of each of the livestock species included in the model. Interestingly, cattle ownership suggested lower combined malaria and nonmalarial fever (− 0.82 [− 1.65, 0.02]; Table 2, case (c)), but the effect was imprecise at 95% confidence, and most likely reflects greater household wealth rather than a factor related directly to disease transmission.

In terms of additional covariates in the multinomial model, temperature predicted increased odds of fever across all fever cases although with less confidence for malarial fever (combined fever, 0.44 [0.19, 0.70]; malarial fever, 0.21 [− 0.01, 0.45]; nonmalarial fever, 0.58 [0.23, 0.94]). Land ownership and higher quality house con-

struction predicted decreased odds of fever in general though not universally (Fig. 2). Households that typically sought diagnostic tests to confirm fever were not predicted to experience increased or decreased odds of any fever (but see Fig. 4); again, the diagnostic test variable measures typical respondent behavior and is not linked directly to reported fever cases. As a proxy for population density, distance to nearest household neighbor did not consistently predict increased or decreased odds of any fever at 95% confidence, although estimates may suggest a positive association with perceived malarial and nonmalarial fevers alone.

Perceived Malarial Fever Across All Parks

Only the malarial fever model was fitted to the complete four-park sample (see Methods). In this model predicting perceived malarial fever, higher frequency of direct contact with wildlife did not predict increased or decreased odds of malaria (Figs. 4 and 5a). Closer proximity to park boundaries predicted increased odds of malarial fever (− 0.30 [− 0.52, − 0.07]; Figs. 4 and 5b). These results are consistent with those from the multinomial model fitted to the two-park sample (Figs. 2 and 3).

The four-park model included varying intercept effects for each of the four parks. These effects estimate the

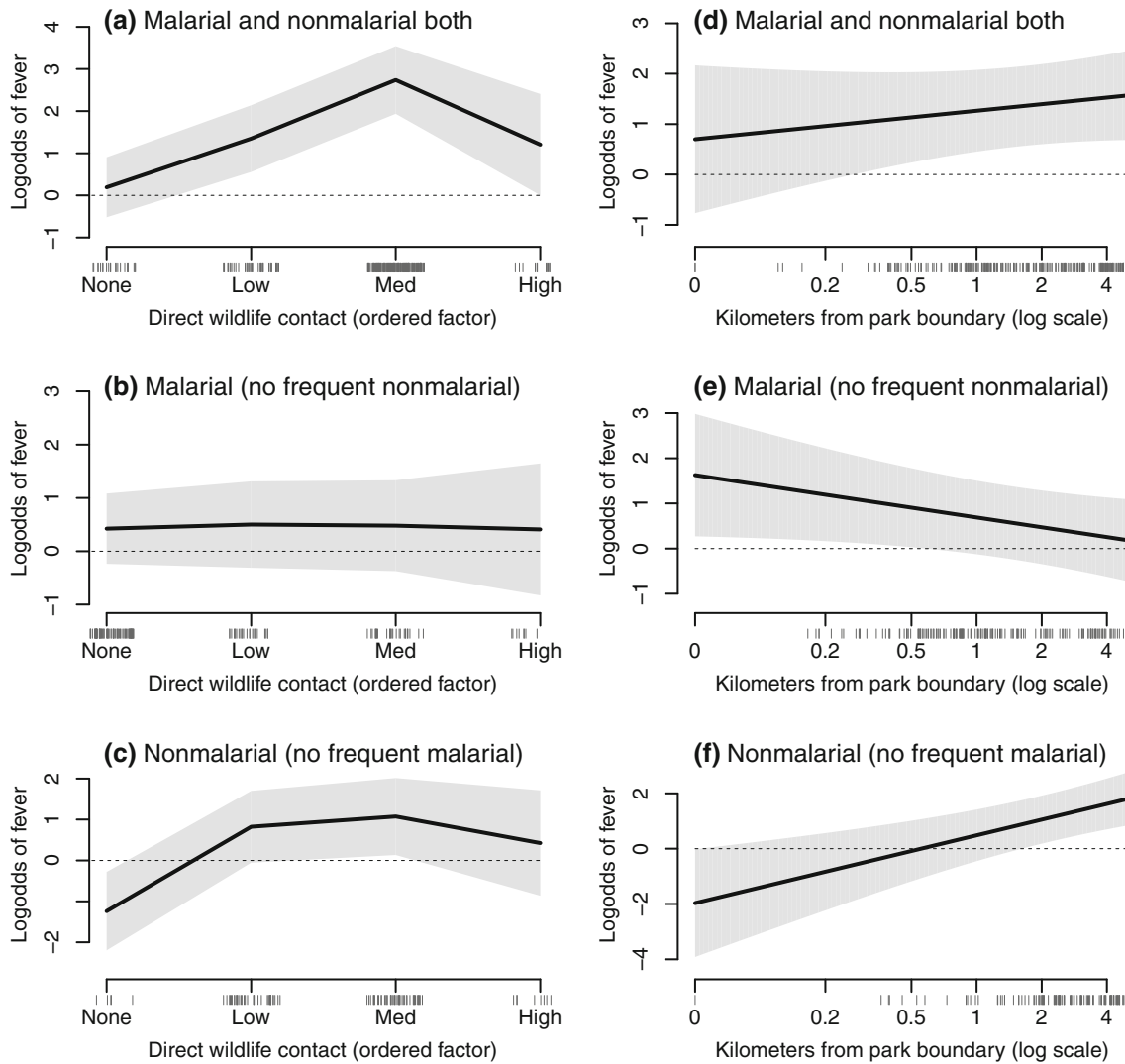


Figure 3. Multinomial model predictions of fever associated with frequency of wildlife contact and distance to park boundary. Frequency of wildlife contact (left three panels a–c) and linear distance between household location and park boundary (right three panels d–f) predicted the log-odds of a particular fever case definition [malarial and nonmalarial fevers both (top a, d); malarial fevers only (middle b, e); nonmalarial fevers only (bottom c, f)] relative to the reference response of infrequent or no fever. Therefore, corresponding y-axis values are interpretable as the log-odds of a particular fever case relative to infrequent or no fever of any kind, or in more general terms how relatively common a particular fever case is (indifference value of no more or less common is 0, dashed horizontal line). Coefficient estimates (black trend lines) are from the single multinomial model fitted to the two-park sample. Coefficient estimates are plotted with model-averaged predictions at 95% confidence (gray bands), with all other model covariates held and their mean or modal values. Direct wildlife contact observations and household distances to park (gray tick marks) are displayed below the x-axes.

unobserved differences in fever explained by the differences among the four park sites (McElreath 2015), such as dominant landcover, elevation, or distance to market (e.g., Supplementary Table S2). The estimates are relatively small in magnitude apart from Queen Elizabeth households (Kibale, 0.04; Murchison Falls, 0.05; Rwenzori 0.11). Households near Queen Elizabeth National Park may experience decreased odds of malarial fever (-0.21), after

accounting for household-level differences. Confidence intervals around varying effects estimates are unreliable and not estimated by the model; effects are too small to be perceptible when plotted, and so we omit them from Fig. 5.

In the four-park model, respondents who typically sought health center tests to diagnose fever were predicted to report significantly less frequent malaria (-0.30 [$-0.60, 0$]). This is unsurprising, but the result is more

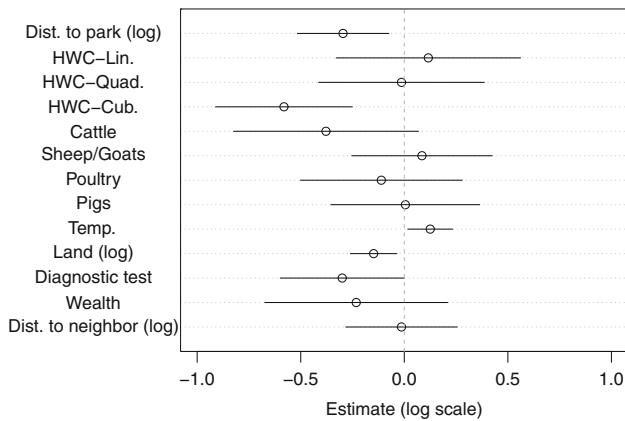


Figure 4. Household level coefficient estimates from the multilevel binomial model predicting perceived malaria fitted to the four-park sample. HWC-Lin, HWC-Quad, and HWC-Cub estimates are the orthogonal polynomial terms representing the four-level human-wildlife contact ordered factor variable. Estimates are plotted with 95% confidence intervals.

precise than the less-certain estimate of the multinomial model (Fig. 2). Distance to nearest neighbor and livestock ownership did not predict higher or lower odds of malaria; the effect of cattle is negative yet imprecise (-0.38 [$-0.82, 0.07$]). Higher temperature (0.13 [$0.02, 0.23$]) and larger land holdings (-0.15 [$-0.26, -0.04$]) positively and negatively predicted odds of malaria, respectively.

DISCUSSION

Despite the risks of emerging disease associated with wild animal reservoirs, little is known about how contact with wildlife and proximity to their refugia affect human rates of febrile illness in local populations (Woolhouse 2002; Bengis et al. 2004; Paige et al. 2016). Here, we report three key findings regarding respondent perceptions of malarial and nonmalarial fever origin along with risk factors including wildlife interactions and household proximity to park boundaries. First, direct contact with wildlife is associated with perceived nonmalarial fever. Second, interaction with wildlife and their habitat differentially affects perceived nonmalarial and malarial fevers. Finally, increasing proximity of households to parks increases the odds of malarial fevers and decreases the odds of nonmalarial fevers. Taken together, these findings suggest that contact with wildlife and their habitat in this region plays a role in the dynamics and perceived risk of human febrile illness.

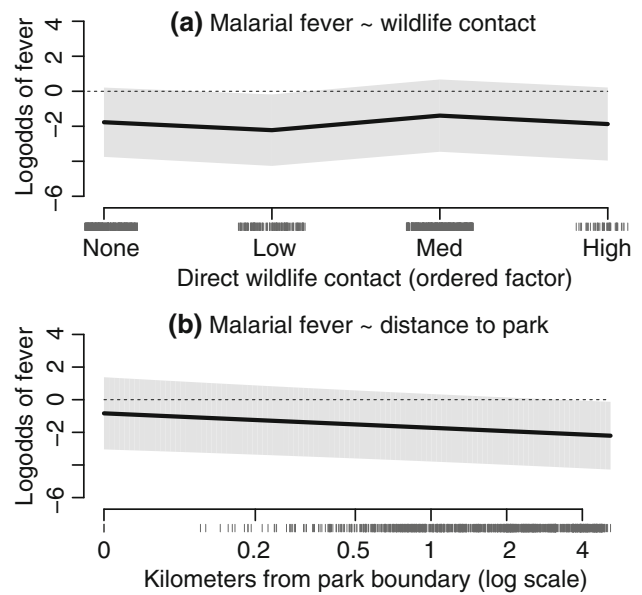


Figure 5. Multilevel model predictions of fever associated with frequency of wildlife contact and park proximity. A multilevel binomial model was fitted to the complete four-park data and estimated the same household-level coefficients as the multinomial model. The two panels show the log-odds of respondents experiencing frequent malarial fever, given changes in wildlife contact frequency (a) and park proximity (b). Coefficient estimates (black lines) are plotted with model-averaged predictions at 95% confidence (gray bands), with all other model covariates held and their mean or modal values. The model includes varying intercept effects adjustments for individual parks; these varying effects estimates are small in magnitude and not discernable from the mean (black lines) and so are not plotted. Direct wildlife contact observations and household distances to park (gray tick marks) are displayed below the x-axes.

Our analyses show that more frequent wildlife contact predicts higher incidence of perceived nonmalarial fevers when compared to malarial fevers alone or less frequent fever of any kind. This finding and the study region's status as a global hotspot of zoonotic disease emergence reinforces the need to further investigate zoonotic causes of nonmalarial fever in the area (Allen et al. 2017; Jones et al. 2008); numerous other studies found linkages between wildlife contact and zoonotic infections (e.g., Wolfe 2005; Morse et al. 2012; Jones et al. 2013). In Uganda, humans interact predominantly with cercopitheid monkeys like baboons (*Papio anubis*), vervet monkeys (*Chlorocebus pygerythrus*), and red-tailed monkeys (*Cercopithecus ascanius*) through crop-raiding events where animals are chased from fields or houses (Naughton 1998; Hill 2000; MacKenzie et al. 2015). Indeed, primate diversity is

exceptionally high in Kibale National Park, and high in the other parks, and multiple species inhabit unprotected forest fragments (C. Chapman and T. Butynski, personal communication; also Onderdonk and Chapman 2000; Salerno et al. 2017), although models estimated relatively small differences in reported fever among parks. Based on our experience, interaction with primates is the most common interaction reported in our study region. Wildlife contact also occurs with dead primates that are hunted or purchased for meat, or trapped as vermin (M. Mahero, personal observation), although not as frequently as in West Africa (Paige et al. 2014), and our survey did not explicitly address bushmeat hunting or consumption. Contact with numerous rodent species is common (T. Gillespie, unpublished data), and surveyed households report rodent feces in homes, but this may not be consistently reported as wildlife contact. Overall, future research is warranted that builds upon our findings by establishing the wildlife species and types of contact that pose the greatest risk of zoonotic fever transmission, including how this risk varies across parks and habitat types (Daszak et al. 2007).

Models that evaluated perceived malarial versus nonmalarial fevers from Kibale and Queen Elizabeth National Parks suggest that interaction with natural habitat is differentially associated with perceived fever origin. Specifically, perceived nonmalarial fevers are predicted by increasing frequency of wildlife encounters and greater distance from parks. In contrast, perceived malarial fevers are not associated with wildlife encounters but are predicted by decreasing distance from parks. These results suggest strong, opposing effects of natural environment on the two fever types. Perceptions indeed affect the likelihood that treatment and/or confirmatory testing is actively sought, which reinforces the need for both malarial and nonmalarial diagnostic capacity (Crump et al. 2013). This need is greatest in under-resourced settings with variable environments undergoing rapid landcover change, as is the case in our study region (Salerno et al. 2017), and throughout many areas of sub-Saharan Africa (Chipwaza et al. 2014; Chapman et al. 2015; Salerno 2016). Importantly, this result also corroborates previous findings that individuals interacting more extensively with wildlife and their refugia may experience greater risk of being misdiagnosed with regionally common illnesses like malaria, rather than novel illnesses that may be introduced by contact with natural landscapes (Kansiime et al. 2014).

In contrast to our expectations, we show that perceived malarial fever increased as households approached the park

boundary, while nonmalarial fevers decreased with park proximity. With respect to malarial fevers, we anticipated decreased malaria reporting closer to parks because the primary vector and parasite in the region is human-specific, yet there is a high presence of wildlife-specific vectors at park boundaries which compete with and reduce the presence of human-specific vectors (Krief et al. 2012). In contrast to expectations, our findings of higher malaria closer to parks may be tied to more rapid landcover change at boundaries, where malaria burdens are conventionally anticipated to increase following forest removal because of increases in favorable vector habitat such as irrigated cultivation or livestock footprints (Guerra et al. 2006). In practice, however, the relationship between proximity to forested areas and malaria varies considerably within and between landscapes (Valle and Clark 2013). Pattanayak et al. (2006) review no fewer than five potential pathways whereby habitat cover and clearing may relate to malaria incidence; we propose that their candidate pathways of changing vector-host ecology and local climate are most likely at play, and we agree that outcomes attributed to local conditions may idiosyncratically affect the vector, parasite, and human behavior.

We report higher temperature associated with more frequent malarial and/or nonmalarial fever in all models. This is consistent with mean temperatures across our sites being slightly lower than the estimated malaria optimum (Mordecai et al. 2013). Both the two-park and the four-park sample provide strong evidence for higher malarial fever closer to park boundaries. In Uganda, significant climate change-induced fluctuations that lead to more variable temperature and humidity (Diem et al. 2016) may have shifted malaria vector or parasite preferences toward the more thermally stable, damper areas around parks. Additionally, changes in human behavior in households living adjacent to parks, notably outdoor sleeping to prevent crop damage from nocturnally raiding animals, may contribute to higher reported malaria near parks, though we do not have data to evaluate this hypothesis. Further research is needed to tease apart these biophysical habitat–fever relationships, which is important given that the Albertine Rift is expected to experience a significant increase in malaria transmission under near-term climate projections (Ryan et al. 2015).

We also find that increasing distance between households and park boundaries was associated with higher overall reported combined fever and nonmalarial fever. This result seems initially at odds with our finding that

wildlife contact predicts nonmalarial fever. However, in Uganda, rural landscapes are a patchwork of agricultural land, protected parks, and numerous unprotected fragments that also support wildlife populations (Chapman et al. 2013; Salerno et al. 2017). Recent work shows that unlike wildlife in protected areas, wildlife inhabiting fragments overlap with human-influenced habitat in both forests and adjacent farmlands (Paige et al. 2016) and are known to harbor higher parasite burdens than animals inhabiting protected areas (Gillespie and Chapman 2006). We suggest that the observed pattern of higher nonmalarial fever farther from park boundaries may be driven by wildlife with higher disease burden in this habitat and greater risk of transmission of zoonotic febrile pathogens through overlap of wildlife and human habitat, even in the absence of direct contact. For example, adjacent to our study region in the Democratic Republic of the Congo, time spent in forests harvesting resources even in the absence of primate contact was associated with simian foamy virus infection (Switzer et al. 2012), although infection does not cause fever. Fragmented landscapes could indeed maintain unique ecologies of disease presence and transmission (Guivier et al. 2014; Marcantonio et al. 2015; Scinachi et al. 2017). Unpacking these fever–habitat associations should be central to follow-up investigations.

Our study has notable limitations, and we remain cautious in interpreting findings. Principally, we report associations with respondent perceptions of febrile illness, and cases are not confirmed through laboratory or other diagnostic methods. As a precaution, in the two-park sample, we first implemented a conservative approach regarding the accuracy of perceived fever origin by fitting a binomial model that ignored respondent self-diagnosis and considered fever of any type. Then as a less-conservative approach, we fitted a multinomial model that assumed respondents could accurately distinguish between malarial and nonmalarial fevers. While both assumed accurate respondent self-reporting regarding fever generally, the second model additionally considered perceived fever origin. Comparing these models allows us to infer the value of considering self-diagnostic data in future efforts. Specifically, the first model, which considered fever of either type as a generalized response variable, did not yield precise estimates of risk factors. Using the same data, the second model predicted clear relationships which only emerged after separating the two fever types by self-diagnostic reports. This is suggestive of respondent perceptions containing meaningful information on fever origin.

In addition, surveys were not designed to assess health outcomes as their primary goal. Clear limitations exist with the sampling frame, specifically that questions regarding nonmalarial fever were only asked in households near Kibale and Queen Elizabeth National Parks. Our primary objective with this paper was therefore to explore relevant associations between wildlife and habitat interactions and household experience with fever. Validation of a syndromic approach to assessing household fever risk, independent of local healthcare capacity, could present a cost-effective method to enhance fever surveillance in a dynamic, resource limited, landscape.

To conclude, our results suggest that interactions with natural and human-influenced habitat may considerably and variably affect the risk of acquiring febrile pathogens. In many developing countries, poor access to and quality of health care are often-cited challenges in park-adjacent rural areas (Chapman et al. 2015). Our findings, along with others (Goldberg et al. 2008; Ghai et al. 2014a), highlight the potential for significant but less-understood challenges from disease transmission at the people–park interface. Science-based policy must critically evaluate land and natural resource use decisions, health capacity, emerging zoonotic disease risk, and biodiversity conservation. Indeed, this is one of the ecosystem health Grand Challenges of our time (Travis et al. 2014). Our findings further reinforce the call for a multidisciplinary team-based approach—integrating ecological, veterinary, and epidemiological sciences—to understand relationships between human health and natural systems (Daszak et al. 2007).

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REFERENCES

- Acestor N, Cooksey R, Newton PN, Ménard D, Guerin PJ, Nakagawa J, Christophel E, González IJ, Bell D (2012) Mapping the aetiology of non-malarial febrile illness in Southeast Asia through a systematic review—terra incognita impairing treatment policies. *PLoS ONE* 7:e44269. <https://doi.org/10.1371/journal.pone.0044269>
- Ahorlu CK, Dunyo SK, Afari EA, Koram KA, Nkrumah FK (1997) Malaria-related beliefs and behaviour in Southern Ghana: implications for treatment, prevention and control. *Trop Med Int Health* 2:488–499
- Allen T, Murray KA, Zambrana-Torrel C, Morse SS, Rondinini C, Di Marco M, Breit N, Olival KJ, Daszak P (2017) Global hotspots and correlates of emerging zoonotic diseases. *Nat Commun* 8(1):1124. <https://doi.org/10.1038/s41467-017-00923-8>
- Amexo M, Tolhurst R, Barnish G, Bates I (2004) Malaria misdiagnosis: effects on the poor and vulnerable. *Lancet* 364:1896–1898. [https://doi.org/10.1016/S0140-6736\(04\)17446-1](https://doi.org/10.1016/S0140-6736(04)17446-1)
- Bengis R, Leighton F, Fischer J, Artois M, Morner T, Tate C (2004) The role of wildlife in emerging and re-emerging zoonoses. *Rev Sci Tech-Off Int Epizoot* 23:497–512
- Bhutta ZA, Sommerfeld J, Lassi ZS, Salam RA, Das JK (2014) Global burden, distribution, and interventions for infectious diseases of poverty. *Infect Dis Poverty* 3:21. <https://doi.org/10.1186/2049-9957-3-21>
- Birhanu Z, Abebe L, Sudhakar M, Dissanayake G, Yihdego YY, Alemayehu G, Yewhalaw D (2016) Malaria related perceptions, care seeking after onset of fever and anti-malarial drug use in malaria endemic settings of southwest Ethiopia. *PLoS ONE* 11:e0160234. <https://doi.org/10.1371/journal.pone.0160234>
- Brashares JS, Golden CD, Weinbaum KZ, Barrett CB, Okello GV (2011) Economic and geographic drivers of wildlife consumption in rural Africa. *Proc Natl Acad Sci* 108:13931–13936. <https://doi.org/10.1073/pnas.1011526108>
- Brooks TM, Hoffman DM, Burgess N, Plumptre A, Williams S, Gereau RE, Mittermeier RA, Stuart S (2004) Eastern afro-montane. In: *Hotspots Revisited: Earth's Biologically Richest and Most Endangered Ecoregions*, Mittermeier RA, Robles-Gil P, Hoffmann M, Pilgrim JD, Brooks TM, Mittermeier CG, Lamoreux JL, Fonseca G (editors), Mexico: Cemex, pp 241–242
- Chandramohan D, Jaffar S, Greenwood B (2002) Use of clinical algorithms for diagnosing malaria. *Trop Med Int Health* 7:45–52
- Chape S, Harrison J, Spalding M, Lysenko I (2005) Measuring the extent and effectiveness of protected areas as an indicator for meeting global biodiversity targets. *Philos Trans R Soc B Biol Sci* 360:443. <https://doi.org/10.1098/rstb.2004.1592>
- Chapman CA, Ghai R, Jacob A, Koojo SM, Reyna-Hurtado R, Rothman JM, Twinomugisha D, Wasserman MD, Goldberg TL (2013) Going, going, gone: a 15-year history of the decline of primates in forest fragments near Kibale National Park, Uganda. In: *Primates in Fragments: Complexity and Resilience*, Marsh KL, Chapman AC (editors), New York, NY: Springer, pp 89–100
- Chapman CA, van Bavel B, Boodman C, Ghai RR, Gogarten JF, Hartter J, Mechak LE, Omeja PA, Poonawala S, Tuli D, Goldberg TL (2015) Providing health care to improve community perceptions of protected areas. *Oryx J Fauna Preserv Soc* 49:636–642. <https://doi.org/10.1017/s0030605313001592>
- Chipwaza B, Mugasa JP, Mayumana I, Amuri M, Makungu C, Gwakisa PS (2014) Community knowledge and attitudes and health workers' practices regarding non-malaria febrile illnesses in eastern Tanzania. *PLoS Negl Trop Dis* 8:e2896. <https://doi.org/10.1371/journal.pntd.0002896>
- Chung Y, Rabe-Hesketh S, Dorie V, Gelman A, Liu J (2013) A nondegenerate penalized likelihood estimator for variance parameters in multilevel models. *Psychometrika* 78:685–709
- Coad L, Leverington F, Knights K, Geldmann J, Eassom A, Kapos V, Kingston N, de Lima M, Zamora C, Cuadros I, Nolte C, Burgess ND, Hockings M (2015) Measuring impact of protected area management interventions: current and future use of the global database of protected area management effectiveness. *Philos Trans R Soc B Biol Sci*. <https://doi.org/10.1098/rstb.2014.0281>
- Crump JA, Morrissey AB, Nicholson WL, Massung RF, Stoddard RA, Galloway RL, Ooi EE, Maro VP, Saganda W, Kinabo GD, Muiruri C, Bartlett JA (2013) Etiology of severe non-malaria febrile illness in northern Tanzania: a prospective cohort study. *PLoS Negl Trop Dis* 7:e2324. <https://doi.org/10.1371/journal.pntd.0002324>
- Daszak P, Epstein JH, Kilpatrick AM, Aguirre AA, Karesh WB, Cunningham AA (2007) Collaborative research approaches to the role of wildlife in zoonotic disease emergence. In: *Wildlife and Emerging Zoonotic Diseases: The Biology, Circumstances and Consequences of Cross-Species Transmission*, Childs JE, Mackenzie JS, Richt JA (editors), Berlin, Heidelberg: Springer, pp 463–475
- DeFries R, Rosenzweig C (2010) Toward a whole-landscape approach for sustainable land use in the tropics. *Proc Natl Acad Sci U S A* 107:19627–19632. <https://doi.org/10.1073/pnas.1011163107>
- Diem JE, Hartter J, Salerno J, McIntyre E, Stuart Grandy A (2016) Comparison of measured multi-decadal rainfall variability with farmers' perceptions of and responses to seasonal changes in western Uganda. *Reg Environ Change*. <https://doi.org/10.1007/s10113-016-0943-1>
- Dreyfus A, Dyal JW, Pearson R, Kankya C, Kajura C, Alinaitwe L, Kakooza S, Pelican KM, Travis DA, Mahero M, Boulware DR, Mugisha L (2016) Leptospira seroprevalence and risk factors in health centre patients in Hoima District, Western Uganda. *PLoS Negl Trop Dis* 10:e0004858. <https://doi.org/10.1371/journal.pntd.0004858>
- Dunyo SK, Afari EA, Koram KA, Ahorlu CK, Abubakar I, Nkrumah FK (2000) Health centre versus home presumptive diagnosis of malaria in southern Ghana: implications for home-based care policy. *Trans R Soc Trop Med Hyg* 94:285–288. [https://doi.org/10.1016/S0035-9203\(00\)90324-9](https://doi.org/10.1016/S0035-9203(00)90324-9)
- Feikin DR, Olack B, Bigogo GM, Audi A, Cosmas L, Aura B, Burke H, Njenga MK, Williamson J, Breiman RF (2011) The burden of common infectious disease syndromes at the clinic and household level from population-based surveillance in rural and urban Kenya. *PLoS ONE* 6:e16085. <https://doi.org/10.1371/journal.pone.0016085>
- Ferraro PJ (2002) The local costs of establishing protected areas in low-income nations: Ranomafana National Park, Madagascar. *Ecol Econ* 43:261–275
- Ghai RR, Chapman CA, Omeja PA, Davies TJ, Goldberg TL (2014) Nodule worm infection in humans and wild primates in Uganda: cryptic species in a newly identified region of human transmission. *PLoS Negl Trop Dis* 8:e2641. <https://doi.org/10.1371/journal.pntd.0002641>
- Ghai RR, Simons ND, Chapman CA, Omeja PA, Davies TJ, Ting N, Goldberg TL (2014) Hidden population structure and cross-species transmission of whipworms (*Trichuris* sp.) in humans

- and non-human primates in Uganda. *PLoS Negl Trop Dis* 8:e3256. <https://doi.org/10.1371/journal.pntd.0003256>
- Ghai RR, Thurber MI, El Bakry A, Chapman CA, Goldberg TL (2016) Multi-method assessment of patients with febrile illness reveals over-diagnosis of malaria in rural Uganda. *Malar J* 15: 460. <https://doi.org/10.1186/s12936-016-1502-4>
- Gillespie TR, Chapman CA (2006) Prediction of parasite infection dynamics in primate metapopulations based on attributes of forest fragmentation. *Conserv Biol* 20:441–448
- Githeko AK, Ndegwa W (2001) Predicting malaria epidemics in the Kenyan highlands using climate data: a tool for decision makers. *Glob Change Hum Health* 2:54–63. <https://doi.org/10.1023/A:1011943131643>
- Goldberg TL, Gillespie TR, Rwego IB, Estoff EL, Chapman CA (2008) Forest fragmentation as cause of bacterial transmission among nonhuman primates, humans, and livestock, Uganda. *Emerg Infect Dis* 14:1375–1382
- Goldman A, Hartter J, Southworth J, Binford M (2008) The human landscape around the island park: impacts and responses to Kibale National Park. In: *Science and Conservation in African Forests: The Benefits of Longterm Research*, Wrangham R, Ross E (editors), Cambridge: Cambridge University Press
- Guerra CA, Snow RW, Hay SI (2006) A global assessment of closed forests, deforestation and malaria risk. *Ann Trop Med Parasitol* 100:189–204. <https://doi.org/10.1179/136485906X91512>
- Guivier E, Galan M, Henttonen H, Cosson J-F, Charbonnel N (2014) Landscape features and helminth co-infection shape bank vole immunoheterogeneity, with consequences for Puumala virus epidemiology. *Heredity* 112:274–281
- Hartter J, Dowhaniuk N, MacKenzie CA, Ryan SJ, Diem JE, Palace MW, Chapman CA (2016) Perceptions of risk in communities near parks in an African biodiversity hotspot. *Ambio*. <https://doi.org/10.1007/s13280-016-0775-8>
- Hassell JM, Begon M, Ward MJ, Fèvre EM (2017) Urbanization and disease emergence: dynamics at the wildlife–livestock–human interface. *Trends Ecol Evol* 32:55–67. <https://doi.org/10.1016/j.tree.2016.09.012>
- Hay SI, Cox J, Rogers DJ, Randolph SE, Stern DI, Shanks GD, Myers MF, Snow RW (2002) Climate change and the resurgence of malaria in the East African highlands. *Nature* 415:905–909. <https://doi.org/10.1038/415905a>
- Hijmans RJ, Cameron SE, Parra JL, Jones PG, Jarvis A (2005) Very high resolution interpolated climate surfaces for global land areas. *Int J Climatol* 25:1965–1978. <https://doi.org/10.1002/joc.1276>
- Hill CM (2000) Conflict of interest between people and baboons: crop raiding in Uganda. *Int J Primatol* 21:299–315. <https://doi.org/10.1023/a:1005481605637>
- Jones BA, Grace D, Kock R, Alonso S, Rushton J, Said MY, McKeever D, Mutua F, Young J, McDermott J, Pfeiffer DU (2013) Zoonosis emergence linked to agricultural intensification and environmental change. *Proc Natl Acad Sci* 110:8399–8404
- Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, Daszak P (2008) Global trends in emerging infectious diseases. *Nature* 451:990–993. <https://doi.org/10.1038/nature06536>
- Källander K, Nsungwa-Sabiiti J, Peterson S (2004) Symptom overlap for malaria and pneumonia—policy implications for home management strategies. *Acta Trop* 90:211–214. <https://doi.org/10.1016/j.actatropica.2003.11.013>
- Kansiime C, Mugisha A, Makumbi F, Mugisha S, Rwego IB, Sempa J, Kiwanuka SN, Asimwe BB, Rutebemberwa E (2014) Knowledge and perceptions of brucellosis in the pastoral communities adjacent to Lake Mburo National Park, Uganda. *BMC Public Health* 14:242. <https://doi.org/10.1186/1471-2458-14-242>
- Krief S, Levrero F, Krief J-M, Thanapongpichat S, Imwong M, Snounou G, Kasenene JM, Cibot M, Gantier J-C (2012) Investigations on anopheline mosquitoes close to the nest sites of chimpanzees subject to malaria infection in the Ugandan highlands. *Malar J* 11:116–139
- Lester J, Paige S, Chapman CA, Gibson M, Holland Jones J, Switzer WM, Ting N, Goldberg TL, Frost SDW (2016) Assessing commitment and reporting fidelity to a text message-based participatory surveillance in rural western Uganda. *PLoS ONE* 11:e0155971. <https://doi.org/10.1371/journal.pone.0155971>
- MacKenzie CA (2012) Accruing benefit or loss from a protected area: location matters. *Ecol Econ* 76:119–129. <https://doi.org/10.1016/j.ecolecon.2012.02.013>
- MacKenzie CA, Hartter J (2013) Demand and proximity: drivers of illegal forest resource extraction. *Oryx* 47:288–297. <https://doi.org/10.1017/S0030605312000026>
- MacKenzie CA, Sengupta RR, Kaoser R (2015) Chasing baboons or attending class: protected areas and childhood education in Uganda. *Environ Conserv* 42:373–383. <https://doi.org/10.1017/S0376892915000120>
- Maheu-Giroux M, Casapia M, Gyorkos TW (2011) On the validity of self-reports and indirect reports to ascertain malaria prevalence in settings of hypoendemicity. *Soc Sci Med* 72:635–640. <https://doi.org/10.1016/j.socscimed.2010.12.007>
- Marcantonio M, Rizzoli A, Metz M, Rosà R, Marini G, Chadwick E, Neteler M (2015) Identifying the environmental conditions favouring west Nile virus outbreaks in Europe. *PLoS ONE* 10:e0121158. <https://doi.org/10.1371/journal.pone.0121158>
- May L, Chretien J-P, Pavlin JA (2009) Beyond traditional surveillance: applying syndromic surveillance to developing settings—opportunities and challenges. *BMC Public Health* 9: 242. <https://doi.org/10.1186/1471-2458-9-242>
- McCombie S (2002) Self-treatment for malaria: the evidence and methodological issues. *Health Policy Plan* 17:333–344
- McElreath R (2015) *Statistical Rethinking: A Bayesian Course with Examples in R and Stan*, Boca Raton: Chapman & Hall/CRC Press
- Moerman F, Lengeler C, Chimumbwa J, Talisuna A, Erhart A, Coosemans M, D'Alessandro U (2003) The contribution of health-care services to a sound and sustainable malaria-control policy. *Lancet Infect Dis* 3:99–102. [https://doi.org/10.1016/S1473-3099\(03\)00518-8](https://doi.org/10.1016/S1473-3099(03)00518-8)
- Mordecai EA, Paaijmans KP, Johnson LR, Balzer C, Ben-Horin T, de Moor E, McNally A, Pawar S, Ryan SJ, Smith TC, Lafferty KD (2013) Optimal temperature for malaria transmission is dramatically lower than previously predicted. *Ecol Lett* 16:22–30. <https://doi.org/10.1111/ele.12015>
- Morse SS, Mazet JA, Woolhouse M, Parrish CR, Carroll D, Karesh WB, Zambrana-Torrel C, Lipkin WI, Daszak P (2012) Prediction and prevention of the next pandemic zoonosis. *Lancet* 380:1956–1965. [https://doi.org/10.1016/S0140-6736\(12\)61684-5](https://doi.org/10.1016/S0140-6736(12)61684-5)
- Myers N, Mittermeier RA, Mittermeier CG, da Fonseca GAB, Kent J (2000) Biodiversity hotspots for conservation priorities. *Nature* 403:853–858. http://www.nature.com/nature/journal/v403/n6772/supinfo/403853a0_S1.html
- Naing C, Kassim AIBM (2012) Scaling-up attention to nonmalaria acute undifferentiated fever. *Trans R Soc Trop Med Hyg* 106:331–332. <https://doi.org/10.1016/j.trstmh.2012.03.003>

- Nankabirwa J, Zurovac D, Njogu J, Rwakimari J, Counihan H, Snow R, Tibenderana J (2009) Malaria misdiagnosis in Uganda—implications for policy change. *Malar J*. <https://doi.org/10.1186/1475-2875-8-66>
- Naughton L (1998) Predicting patterns of crop damage by wildlife around Kibale National Park, Uganda. *Conserv Biol* 12:156–168. <https://doi.org/10.1111/j.1523-1739.1998.96346.x>
- Naughton-Treves L, Alix-Garcia J, Chapman CA (2011) Lessons about parks and poverty from a decade of forest loss and economic growth around Kibale National Park, Uganda. *Proc Natl Acad Sci U S A* 108:13919–13924. <https://doi.org/10.1073/pnas.101332108>
- Naughton-Treves L, Holland MB, Brandon K (2005) The role of protected areas in conserving biodiversity and sustaining local livelihoods. *Annu Rev Environ Resour* 30:219–252. <https://doi.org/10.1146/annurev.energy.30.050504.164507>
- Novella NS, Thiaw WM (2012) African rainfall climatology version 2 for famine early warning systems. *J Appl Meteorol Climatol* 52:588–606. <https://doi.org/10.1175/JAMC-D-11-0238.1>
- Onderdonk DA, Chapman CA (2000) Coping with forest fragmentation: the primates of Kibale National Park, Uganda. *Int J Primatol* 21:587–611. <https://doi.org/10.1023/A:1005509119693>
- Paige SB, Bleecker J, Mayer J, Goldberg T (2016) Spatial overlap between people and non-human primates in a fragmented landscape. *EcoHealth*. <https://doi.org/10.1007/s10393-016-1194-9>
- Paige SB, Frost SDW, Gibson MA, Jones JH, Shankar A, Switzer WM, Ting N, Goldberg TL (2014) Beyond bushmeat: animal contact, injury, and zoonotic disease risk in western Uganda. *EcoHealth* 11:534–543. <https://doi.org/10.1007/s10393-014-0942-y>
- Parola P (2011) *Rickettsia felis*: from a rare disease in the USA to a common cause of fever in sub-Saharan Africa. *Clin Microbiol Infect* 17:996–1000. <https://doi.org/10.1111/j.1469-0691.2011.03516.x>
- Pattanayak S, Dickinson K, Corey C, Murray B, Sills E, Kramer R (2006) Deforestation, malaria, and poverty: a call for transdisciplinary research to support the design of cross-sectoral policies. *Sustain Sci Pract Policy* 2(2):45–56
- Patz JA, Campbell-Lendrum D, Holloway T, Foley JA (2005) Impact of regional climate change on human health. *Nature* 438:310–317. <https://doi.org/10.1038/nature04188>
- Petti CA, Polage CR, Quinn TC, Ronald AR, Sande MA (2006) Laboratory medicine in Africa: a barrier to effective health care. *Clin Infect Dis* 42:377–382. <https://doi.org/10.1086/499363>
- Prasad N, Murdoch DR, Reyburn H, Crump JA (2015) Etiology of severe febrile illness in low- and middle-income countries: a systematic review. *PLoS ONE* 10:e0127962. <https://doi.org/10.1371/journal.pone.0127962>
- R Core Team (2016) R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing. <https://www.R-project.org/>.
- Reyburn H, Mbatia R, Drakeley C, Carneiro I, Mwakasungula E, Mwerinde O, Saganda K, Shao J, Kitua A, Olomi R, Greenwood BM, Whitty CJ (2004) Overdiagnosis of malaria in patients with severe febrile illness in Tanzania: a prospective study. *BMJ*. <https://doi.org/10.1136/bmj.38251.658229.55>
- Rooth I, Björkman A (1992) Fever episodes in a holoendemic malaria area of Tanzania: parasitological and clinical findings and diagnostic aspects related to malaria. *Trans R Soc Trop Med Hyg* 86:479–482
- Rwego IB, Isabirye-Basuta G, Gillespie TR, Goldberg TL (2008) Gastrointestinal bacterial transmission among humans, mountain gorillas, and livestock in Bwindi Impenetrable National Park, Uganda. *Conserv Biol* 22:1600–1607. <https://doi.org/10.1111/j.1523-1739.2008.01018.x>
- Ryan SJ, McNally A, Johnson LR, Mordecai EA, Ben-Horin T, Paaijmans K, Lafferty KD (2015) Mapping physiological suitability limits for malaria in africa under climate change. *Vector-Borne Zoonotic Dis* 15:718–725. <https://doi.org/10.1089/vbz.2015.1822>
- Salerno J (2016) Migrant decision-making in a frontier landscape. *Environ Res Lett* 11:044019
- Salerno J, Borgerhoff Mulder M, Grote MN, Ghiselli M, Packer C (2016) Household livelihoods and conflict with wildlife in community-based conservation areas across northern Tanzania. *Oryx* 50:702–712. <https://doi.org/10.1017/S0030605315000393>
- Salerno J, Diem JE, Dowhaniuk N, Goldman A, MacKenzie CA, Omeja PA, Palace MW, Reyna-Hurtado R, Ryan SJ, Hartter J (2017) Park isolation in anthropogenic landscapes: land change and livelihoods at park boundaries in the African Albertine Rift. *Reg Environ Change*. <https://doi.org/10.1007/s10113-017-1250-1>
- Salyer SJ, Gillespie TR, Rwego IB, Chapman CA, Goldberg TL (2012) Epidemiology and molecular relationships of *Cryptosporidium* spp. in people, primates, and livestock from western Uganda. *PLoS Negl Trop Dis* 6:e1597
- Scinachi CA, Takeda GACG, Mucci LF, Pinter A (2017) Association of the occurrence of Brazilian spotted fever and Atlantic rain forest fragmentation in the São Paulo metropolitan region, Brazil. *Acta Trop* 166:225–233. <https://doi.org/10.1016/j.actatropica.2016.11.025>
- Stevens FR, Gaughan AE, Linard C, Tatem AJ (2015) Disaggregating census data for population mapping using random forests with remotely-sensed and ancillary data. *PLoS ONE* 10:e0107042. <https://doi.org/10.1371/journal.pone.0107042>
- Switzer WM, Tang S, Ahuka-Mundeki S, Shankar A, Hanson DL, Zheng H, Ayouba A, Wolfe ND, LeBreton M, Djoko CF, Tamoufe U, Esteban A, Heneine W, Peeters M, Wright LL, Muyembe-Tamfum JJ, Wemakoy EO, Mulembakani P, Hoff NA, Rimoin AW (2012) Novel simian foamy virus infections from multiple monkey species in women from the Democratic Republic of Congo. *Retrovirology* 9:100. <https://doi.org/10.1186/1742-4690-9-100>
- Travis DA, Sriramarao P, Cardona C, Steer CJ, Kennedy S, Sreevatsan S, Murtaugh MP (2014) One Medicine One Science: a framework for exploring challenges at the intersection of animals, humans, and the environment. *Ann N Y Acad Sci* 1334:26–44. <https://doi.org/10.1111/nyas.12601>
- Uneke C (2008) Concurrent malaria and typhoid fever in the tropics: the diagnostic challenges and public health implications. *J Vector Borne Dis* 45:133–142
- Uzochukwu BS, Onwujekwe OE (2004) Socio-economic differences and health seeking behaviour for the diagnosis and treatment of malaria: a case study of four local government areas operating the Bamako initiative programme in south-east Nigeria. *Int J Equity Health* 3:6
- Valle D, Clark J (2013) Conservation efforts may increase malaria burden in the Brazilian Amazon. *PLoS ONE* 8:e57519. <https://doi.org/10.1371/journal.pone.0057519>
- Venables WN, Ripley BD (2002) *Modern Applied Statistics with S, 4th ed.*, New York: Springer

Wolfe ND (2005) Bushmeat hunting, deforestation, and prediction of zoonotic disease. *Emerg Infect Dis J* 11(12):1822–1827

Woolhouse ME (2002) Population biology of emerging and re-emerging pathogens. *Trends Microbiol* 10:S3–S7

Yé Y, Kimani-Murage E, Kebaso J, Mugisha F (2007) Assessing the risk of self-diagnosed malaria in urban informal settlements of Nairobi using self-reported morbidity survey. *Malar J* 6:71. <https://doi.org/10.1186/1475-2875-6-71>