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Epidemiology of the zoonotic malaria *Plasmodium knowlesi* in changing landscapes

Running title: Land use and spatial epidemiology of *Plasmodium knowlesi*

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Abstract.

Within the past two decades, incidence of human cases of the zoonotic malaria *Plasmodium knowlesi* has increased markedly. *P. knowlesi* is now the most common cause of human malaria in Malaysia and threatens to undermine malaria control programmes across Southeast Asia. The emergence of zoonotic malaria corresponds to a period of rapid deforestation within this region. These environmental changes impact the distribution and behaviour of the simian hosts, mosquito vector species and human populations, creating new opportunities for *P. knowlesi* transmission. Here, we review how landscape changes can drive zoonotic disease emergence, examine the extent and causes of these changes across Southeast and identify how these mechanisms may be impacting *P. knowlesi* dynamics. We review the current spatial epidemiology of reported *P. knowlesi* infections in people and assess how these demographic and environmental changes may lead to changes in transmission patterns. Finally, we identify opportunities to improve *P. knowlesi* surveillance and develop targeted ecological interventions within these landscapes.

Keywords.

Plasmodium knowlesi, emerging diseases, land use change, deforestation, spatial epidemiology

1. Introduction.

The zoonotic malaria, *Plasmodium knowlesi*, is an emerging disease driven by changing patterns of land use. Carried by long- and pig-tailed macaques (*Macaca fascicularis* and *M. nemestrina*) and transmitted by the *Anopheles* Leucosphyrus Group of mosquitoes, the geographical range of *P. knowlesi* is limited by the distribution of the mosquito vectors and simian hosts (Moyes et al., 2014, Moyes et al., 2016). *P. knowlesi* was first described in macaques in the 1930s with only one naturally acquired human infection reported in the twentieth century (Knowles and Das Gupta, 1932, Chin et al., 1965). However, in 2004, the use of molecular diagnostics identified a large number of human infections with *P. knowlesi* in Malaysian Borneo previously misdiagnosed by microscopy (Singh et al., 2004). Since detection of this cluster, reported incidence of *P. knowlesi* has increased markedly, with *P. knowlesi* now the most common cause of human malaria in Malaysia and identified across Southeast Asia (Singh et al., 2004, William et al., 2014, William et al., 2013). These rising numbers of human *P. knowlesi* cases correspond to a period of rapid and extensive environmental change within endemic areas. Land use changes, such as deforestation and agricultural expansion, may increase spatial overlap between people, macaques and mosquitoes and have been proposed as the main cause of this emergence (Singh and Daneshvar, 2013, Lee et al., 2011, Moyes et al., 2016).

These changing disease dynamics threaten to undermine regional malaria elimination efforts. The potential threat of simian malaria to malaria elimination has been recognised since the first Global Malaria Eradication campaign in the 1960s (Coatney, 1963). This is most pronounced in Malaysia where *P. knowlesi* emergence has reversed decades of progress in reduction of malaria cases (Barber et al., 2017). The first malaria eradication programme in Malaysia began in 1961, reducing transmission of non-zoonotic malaria species primarily through vector control. This led to a precipitous decline in

transmission from the 1980s onwards, culminating in Malaysia moving to the elimination phase in 2011 (Chin et al., 2020b). While Malaysia has now not reported any indigenous cases of human malaria since 2017, thousands of human *P. knowlesi* cases are reported in Malaysia annually (Chin et al., 2020b). The World Health Organization has recently recognised the regional importance of *P. knowlesi* to malaria elimination and instigated the formation of an Evidence Review Group to identify key knowledge gaps and possible interventions (World Health Organisation Regional Office for Western Pacific, 2017). Critical to these initiatives is understanding how deforestation and other ecological changes may alter future *P. knowlesi* transmission dynamics and human risks.

Anthropogenic environmental changes affect the distribution of people, animal reservoirs and disease vectors, impacting infectious disease risks (Gottdenker et al., 2014, Kilpatrick and Randolph, 2012). These have been linked to altered dynamics and geographical distribution of malaria and other zoonotic and vector-borne diseases globally (Guerra et al., 2006, Hahn et al., 2014, Yasuoka and Levins, 2007). Current levels of landscape change are unprecedented, with pathogen emergence from wildlife populations in altered ecosystems threatening global health. Understanding how ecological changes driven by human activity can modify the epidemiology of these diseases is vital to predicting future disease risks and designing effective public health measures. In addition to posing a major threat to malaria elimination, *P. knowlesi* exemplifies an emerging disease driven by environmental change. Here, we review how ecological changes impact disease emergence, describe spatial distribution of human *P. knowlesi* infections, define the extent of landscape change across Southeast Asia and examine mechanisms through which landscape impacts *P. knowlesi* risks. We additionally assess potential future changes in transmission pathways and opportunities to improve surveillance and control for this emerging zoonotic malaria species within these rapidly changing landscapes.

2. Ecological change and mechanisms of disease emergence and transmission

Deforestation has been identified as one of the key drivers of *P. knowlesi* emergence and likely to shape changing risks of *P. knowlesi* and other simian malarias. There is an increasing body of evidence documenting the complex relationship between land use and land cover changes and disease emergence; changes in human disease risk as a result of forest clearance is governed by physical changes to the environment, knock-on effects to ecological communities and by human behaviours and activity in areas where land use change occurs (Table 1). Within this section, we review the key mechanisms through which landscape change impacts disease transmission in relation to *P. knowlesi*.

[Insert Table 1 here]

2.1 Biodiversity impacts

High biodiversity areas like tropical forests are often considered “hotspots” for emerging diseases due to the large pool of novel enzootic pathogens. However, the impacts of biodiversity on infectious disease are difficult to generalise, and have caused a great deal of debate - both dilution and amplification effects have been ascribed to high levels of biodiversity. There is evidence that in different circumstances high biodiversity can limit the transmission of infectious diseases, whether emerging or established (Luis et al., 2018).

Spread of pathogens with density-dependent transmission may be amplified when species diversity is high if there is no compensatory reduction in abundance of a host species (Dobson, 2004). However, high host diversity in frequency-dependent and vector-mediated pathogens can in some circumstances

buffer disease spread as infection rates within species populations remain relatively low (Dobson, 2004). Transmission of most vector-borne diseases is considered to be frequency-dependent as it is reliant on the actions of the vector (e.g. biting rate); high diversity is predicted to reduce disease risk in these instances, due to differences between species in their competence as hosts (Ferrari et al., 2011).

Shifts in community structures as a result of environmental change could be more important than natural biodiversity gradients and explain inconsistencies in observation of a “dilution effect”; the effect is more likely to be observed where biodiversity levels have fallen due to ecological disruption, including through land use and land cover change, than in areas where low biodiversity is a result of community assembly and ecological drift (Halliday et al., 2020). Biodiversity loss in degraded ecological communities tends to be non-random. The species that survive or are able to recolonise areas after events leading to biodiversity loss usually have fast life history strategies that prioritise reproduction, growth and dispersal rather than protection against disease, and often therefore have disproportionate roles in pathogen spread (Lacroix et al., 2014). In Sao Paulo, predicted biodiversity loss caused by sugarcane expansion and subsequent dominance of generalist rodents in the environment is expected to increase risk of Hantavirus pulmonary syndrome from 1.3% to 1.5% and place 20% more people at risk of contracting the disease (Prist et al., 2017).

The loss of the preferred host of a vector can change their feeding behaviours, including shifts towards human hosts. For example, in Kenya, experimental plots with large herbivores excluded were associated with elevated human biting rates of *Aedes mcintoshi*, a primary vector of Rift Valley Fever virus; however, when evaluated with a decline in abundance of the vector, overall vectorial capacity in exclusion zones was half of that in plots populated by large herbivores (Tchouassi et al., 2020). These contradictory effects demonstrate that changes to community structure are not uniform in their

influence and should be evaluated in combination when evaluating overall changes to disease risk. Land use and land cover change can also facilitate the arrival and establishment of invasive species in affected areas, bringing with them new disease risks. Not only do invasive species often cause a decline in species richness, but they can introduce novel pathogens or strains of a disease to a location (Crowl et al., 2008). Invasive species also provide the opportunity for pathogen host-switching, amplifying the transmission of disease and potentially increasing pathogen evolution speed, which is thought to be greater where multiple transmission cycles exist and interact (Wilcox and Ellis, 2006, Parrish et al., 2008, Jacquot et al., 2016).

2.2 Habitat fragmentation

Habitat fragmentation is often defined as the breaking up of an expansive landscape to form several, smaller patches of habitat separated by an unlike matrix (Wilcove et al., 1986). It can influence the spread of disease by altering the physical structure of an area, as well as the diversity, composition, and dynamics of its community (Collinge, 1996). Habitat fragmentation has been linked to increased infection rates in vectors and hosts, vector prevalence, and frequency of spillover events (Barros and Honorio, 2015, Rulli et al., 2017).

Habitat fragmentation alters conditions within the forest structure and increases the amount of “edge” habitat where the environment is different from intact forest, graduating from the patch’s edge to its primary forest core (Laurance and Yensen, 1991). Edge effects change abiotic variables such as light, airflow, temperature, humidity, and soil moisture and encroach different distances into forest interiors; there is evidence of airflow differences reaching 240m in, whereas it is difficult to detect changes in humidity, temperature and light far beyond 50m (Chen et al., 1995, Chen et al., 1999). The differing

degrees to which these factors reach into the forest and interact with each other makes it difficult to disentangle their effects, but there is still evidence that altered environmental conditions can influence factors related to the spread of zoonotic disease. These transitional zones between ecosystems are known as ecotones and when connecting wild spaces to manmade or settled environments are often areas of increased contact between pathogens, hosts and vectors.

Fragmentation creates smaller, isolated habitat patches with less “core” area in favour of “edge”, increasing likelihood of interactions between animals and vectors living within the forest, and humans living on its outskirts (Wilkinson et al., 2018). Yellow fever virus is an example of a pathogen associated with forest ecotone environments. In non-urban areas the virus typically transmits enzootically between non-human primates and mosquitoes in a canopy-level sylvatic cycle deep in the forest (Valentine et al., 2019). Human encroachment and settlement in forest fringes has created habitat that supports *Aedes* mosquitoes able to bridge the ecological gap between sylvatic and peri-urban transmission cycles (Couto-Lima et al., 2017).

In the Brazilian Amazon, Barros & Honório (2015) found that larval “hotspots” for *A. darlingi* are associated with aquatic habitats at forest fringes, leading to high malarial rates in those living in proximity to forest fragment fringes. Those living within 400m of a hotspot were subject to a 2.6 times higher risk of malaria; these people were often recent settlers who resided in closest proximity to the forest fringe ecotone (Barros and Honorio, 2015). Exacerbated disease risk in forest edge environments has been attributed to more frequent encroachment of forest by people living in these areas, but interactions and mixing between humans, hosts, vectors and pathogens in the ecotones themselves are also likely to be related to spillover risk (Despommier et al., 2006).

Fragmentation can have conflicting influences on disease: in Eastern Zambia, tsetse flies responsible for the spread of human and animal trypanosomiasis are lowest in numbers in areas with the greatest amount of fragmentation (Ducheyne et al., 2009) and in Malawi, tsetse flies are near-absent outside of protected areas where natural vegetation has not been cleared (Van den Bossche et al., 2000). However, this reduction in numbers does not necessarily translate into decreased risk of trypanosomiasis; tsetse flies in fragmented areas live longer and are more likely to be infected. A study on impact of habitat fragmentation on tsetse fly populations by Mweempwa et al. (2015) found that infection rates were highest in the most fragmented site (14.5%), followed by the least fragmented (7.6%), and lowest at an intermediate level of fragmentation (4.8%). Combined with the longevity of flies in the most fragmented areas, trypanosomiasis infection risk was not significantly different in the least and most fragmented sites, despite an eight-fold reduction in tsetse density between the two; this was attributed to differences in entomological inoculation rates (EIR) as a result of increased temperature in fragmented areas (Mweempwa et al., 2015). In European bank voles, carriage of Puumala hantavirus is higher in animals living in larger more connected environments than smaller areas isolated from other suitable habitat, implying fragmentation would reduce prevalence of the disease in this species (Guivier et al., 2011). The effect of environmental change on disease is complex and dependent on the response of vector and host species; understanding the ecology of animals involved in the transmission cycle is vital in order to predict how altering a landscape will impact disease dynamics.

2.3 Physical changes to the environment

Altering landscapes can change the physical characteristics of an environment. This can include very localised changes in variables such as temperature, wind flow and the chemical composition of water, soil and air, or act on a greater scale: regional weather patterns can be affected in the long term by land

cover conversion, especially in tropical areas (Feddema et al., 2005). Land use and land cover change can significantly influence surface fluxes of heat and water vapour, as well as result in greenhouse gas emissions and changes in carbon sink availability, and is an important climate forcing particularly in regional projection models (Quesada et al., 2017).

Logging can alter environmental conditions within a forest to different degrees depending on the intensity of the operation and the method used, and create novel habitats conducive to the spread of zoonotic diseases (Walsh et al., 1993, Inada et al., 2017). Removing trees reduces the number of leaves falling into ponds and streams, and without the tannins released during decomposition of the organic matter, acidity is decreased and turbidity increased, enhancing algal growth (Herrera-Silveira and Ramirez-Ramirez, 1996). Many mosquito larvae feed on algae; combined with greater sunlight and warmth from decreased canopy cover, these conditions create favourable breeding sites for mosquitoes (Tuno et al., 2005, Kweka et al., 2016).

The mosquito *Anopheles gambiae* is the primary vector of malaria in sub-Saharan Africa. Decreased canopy cover increased the abundance of *A. gambiae* larvae, and artificial experiments by Afrane et al. revealed much higher larval survivorship in sunlit pools than in the shaded conditions associated with intact forest (Afrane et al., 2006). Vittor et al. found that biting rates of *Anopheles darlingi*, an important vector for malaria in the Americas, were 278-times higher (after controlling for human population) in areas in the Amazon basin that have experienced over 80% deforestation than areas where deforestation was lower than 30% (Vittor et al., 2009).

Changes to the physical environment can also reduce disease risk. The black fly, *Simulium woodi*, is a vector for human onchocerciasis (river blindness). The Tanzanian population of black flies rapidly

declined between 1963 and 1985, with the mean-biting catch falling by 87% in this time. Muro & Raybould, attributed this to a loss of suitable, cool, shaded breeding habitat due to deforestation. This period also saw a reduction in the percentage of mature *S. woodi* infected with the disease-causing agent, the nematode *Onchocerca volvulus*, from 17% to 3% (Muro and Raybould, 1990). While this decline plateaued, 25 years later populations had not recovered, suggesting deforestation in the area had a significant and long-term impact on vector numbers (Kalinga and Post, 2011).

2.4. Socio-economic changes and development

Land use and land cover change, especially for extractive industries and conversion to agriculture, creates economic opportunity and can attract large numbers of migrant workers and settlers. When this economic migration introduces a novel population of immunologically naive humans to an area, increased levels of some diseases can be observed, especially in the early stages of settlement and forest clearance. Yellow fever outbreaks in the Angola and Democratic Republic of Congo have been associated with high population mobility combined with low vaccine coverage, for example (Kraemer et al., 2017). This dynamic has also been used to explain the meteoric rise in malaria cases associated with development in the Brazilian Amazon (dubbed “frontier malaria”), from around 8,000 cases per annum in 1970 to 615,000 in 2000 (Barbieri et al., 2005). Patterns of initial increased disease risk followed by reduction in infection have been explained by the different landscape patterns and human behaviour associated with early as compared to late stages of land cover change. Initial encroachment tends to involve small-scale agriculture and resource extraction, creating large amounts of forest-edge and increasing human exposure to pathogens, hosts and vectors, as more time is spent in forest and forest edge (MacDonald and Mordecai, 2019). As settlements become more established, they often grow in size and distance from forest habitat and develop stronger social institutions with better access to

healthcare and disease prevention measures (de Castro et al., 2006). Additionally, forest edge habitat decreases as agricultural land is consolidated and intensification begins to take precedence over expansion, reducing deforestation rates (MacDonald and Mordecai, 2019).

Land use change is often accompanied by the building of infrastructure that can influence disease risks; this is particularly well documented for roads and for water management systems such as irrigation and dams. These can exacerbate fragmentation, create environmental conditions and novel habitats that may be suitable for vectors of disease, and facilitate the spread of people, animals and pathogens (Wolfe et al., 2005, Wilcox and Ellis, 2006). For example, trenches formed along roadsides can increase the amount of standing water and therefore breeding sites for mosquito vectors; the obstruction of natural water drainage is also associated with increased leptospirosis, as waterlogging forces rodents to leave their burrows and saturated agricultural fields become contaminated with urine, exposing farm workers to infection (Dubey et al., 2021). Logging roads designed to bring timber workers deeper into forest environments can increase likelihood of human contact with novel pathogens, and allow hunting activities to take place from any location along these rapidly expanding networks rather than within a radius of a settlement (Laurance et al., 2006); logging practices have been linked to elevated bushmeat demand, the hunting and consumption of which are associated with blood-borne and ingestion pathways of zoonotic spillover (Karesh and Noble, 2009, Poulsen et al., 2009). Roads also importantly facilitate increased movement of people, goods, livestock, and wildlife including invasive species and animals captured for the international wildlife trade, which can lead to establishment of diseases in new areas. Dengue is thought to have been transported to some areas through the international trade of used tyres harbouring infected *Aedes* species (Bennett et al., 2019). In Morocco, foci of anthroponotic cutaneous leishmaniasis are aligned geographically and temporally with the construction of road networks (Kahime et al., 2014). Areas of forest converted for agricultural use are often irrigated; the

creation of novel freshwater habitats have been associated with increases in mosquito-borne and water-borne diseases. Risk of Japanese encephalitis virus (JEV), a mosquito-borne disease maintained zoonotically in wild birds, is elevated in irrigated areas (especially where pigs are kept as livestock and provide a domestic animal reservoir) (Pearce et al., 2018); this has been attributed to the proliferation of the primary vector *Culex tritaeniorhynchus* in habitat created by irrigation (Keiser et al., 2005b).

Different types of land cover change can be associated with different risks. For example: clear cutting of forest has a greater impact on biodiversity and the physical environmental conditions of a landscape, while individual exposure risk may be greater in selective logging due to more time spent in the forest environment (Wilcox and Ellis, 2006); in rice-farming areas of the Philippines, *S. japonicum* is more prevalent in males of working age than other demographics (Tarafder et al., 2006); miners are at high risk from malaria, likely a combination of the high population mobility and minimal infrastructure of small-scale mining camps (Douine et al., 2020); wildlife pathogens can infect livestock, and animal agriculture is associated with enhanced risk of zoonotic spillover and the potential for pathogen mixing and emergence (Jones et al., 2013). The effects of deforestation on disease emergence are not uniform, are highly dependent on how settlers and workers in frontier areas interact with and further alter their environments and are subject to change over time.

3. Distribution and burden of *Plasmodium knowlesi*

One of the critical limitations to understanding the role of these ecological changes on *P. knowlesi* transmission is data on the distribution of *P. knowlesi* infections in humans. While infection with *P. knowlesi* can cause severe and fatal disease in people, there are frequent asymptomatic infections and diagnostic limitations (William et al., 2011, Rajahram et al., 2012, Barber et al., 2013a, Daneshvar et al.,

2009, Grigg et al., 2016). Designing effective control programmes requires detailed information on the spatial epidemiology of *P. knowlesi* as well as an understanding of how environmental changes are likely to impact this distribution. Within this section, we review the spatial distribution of clinical and community-based *P. knowlesi* infections and associated reporting biases and describe reports of other simian malaria species.

3.1 Spatial distribution of reported *P. knowlesi* incidence

Molecular studies indicate *P. knowlesi* is not a newly emergent malaria species and likely predates human settlement in Southeast Asia (Lee et al., 2011). *P. knowlesi* was first described in macaques in the 1930s and the first naturally acquired human case was reported in 1965 in peninsular Malaysia (Chin et al., 1965, Knowles and Das Gupta, 1932). Subsequent epidemiological investigations of people residing within the area where this individual was infected did not identify any additional *P. knowlesi* cases in people, although *P. knowlesi* was detected in two out of the four long-tailed macaques screened (Warren et al., 1970). No further natural infections were reported until 2004, when the application of molecular diagnostic tools identified a large focus of *P. knowlesi* infections in the Kapit division of Sarawak in Malaysian Borneo (Singh et al., 2004). Retrospective studies have since detected *P. knowlesi* infections from archival blood films collected in the mid-1990s in Malaysia and Thailand, suggesting that previous human infections were misdiagnosed as other species by microscopy (Lee et al., 2009a, Jongwutiwes et al., 2011).

Since 2004, human *P. knowlesi* infections have been reported from a number of Southeast Asian countries (Moyes et al., 2014, Shearer et al., 2016b). While sporadic cases have been reported from countries including the Philippines, Thailand, Vietnam, Cambodia, Laos, Myanmar, Singapore, Brunei,

India, Indonesia and China, *P. knowlesi* is now the most common cause of human malaria in Malaysia (Luchavez et al., 2008, Putaporntip et al., 2009, Sermwittayawong et al., 2012, Jongwutiwes et al., 2004, Van den Eede et al., 2009, Khim et al., 2011, Jiang et al., 2010, Lee et al., 2009c, Zhou et al., 2014, Cox-Singh et al., 2008, Barber et al., 2012, William et al., 2014, William et al., 2013, Ninan et al., 2012, Tyagi et al., 2013, Figtree et al., 2010, Iwagami et al., 2018) (Figure 1). In the Malaysian state of Sabah, despite an overall decrease in malaria notifications following successful malaria control measures, the percentage of suspected *P. knowlesi* notifications increased from 2% (59/2741) of all malaria notifications in 2004 to 62% (996/1606) of reported malaria cases in 2013 (William et al., 2013, William et al., 2014). Similar trends have been reported in the neighbouring state of Sarawak, where suspected *P. knowlesi* accounted for the majority of reported malaria cases over the previous decade (Singh and Daneshvar, 2010). While Malaysia has reported no indigenous malaria cases since 2018 and is currently under review for malaria elimination, increasing numbers of *P. knowlesi* cases continue to be reported, including over 4100 confirmed human infections with *P. knowlesi* in 2018 (Chin et al., 2020b).

[Insert Figure 1 here]

However, the true burden of *P. knowlesi* remains poorly understood due to frequent misidentification as other human malaria species by microscopy and the limited availability of *P. knowlesi*- specific molecular diagnostic capabilities. *P. knowlesi* appears microscopically similar to the human malaria species *P. malariae* but also can be misdiagnosed as *P. falciparum* and *P. vivax* (Singh and Daneshvar, 2013, Barber et al., 2013c, Lee et al., 2009b). Rapid diagnostic tests (RDTs) developed for other malaria species are also insufficiently sensitive to detect *P. knowlesi* and can lead to misdiagnosis as other species (Barber et al., 2013b, Foster et al., 2014, Grigg et al., 2014). While it is difficult to determine whether there is a genuine increase in human cases rather than improved detection, evidence of a significant increase in

numbers and proportions of *P. knowlesi* malaria suggests transmission of *P. knowlesi* is rising in areas of Malaysia (William et al., 2013, William et al., 2014, Yusof et al., 2014, Joveen-Neoh et al., 2011).

3.2 Community-level spatial distribution of exposure and infection

Despite increasing amounts of data available for symptomatic *P. knowlesi* cases presenting at hospital facilities, there remain substantial knowledge gaps on patterns of infection and exposure in the community. The development and implementation of molecular diagnostic tools such as PCR has greatly contributed to the increasing detection of human *P. knowlesi* infection throughout Southeast Asia (Anstey and Grigg, 2019). Previous studies in Malaysia suggested that *P. knowlesi* infections were likely to be misdiagnosed as *P. malariae* by routine microscopy reading due to their similar morphological features (Singh et al., 2004, Kantele and Jokiranta, 2011, Lee et al., 2009b). In Indonesia, *P. knowlesi* has been universally misdiagnosed by microscopy, with no notifications of *P. knowlesi* made using standard national malaria reporting systems. However, a study in Indonesia identified an asymptomatic *P. knowlesi* case through a reactive case detection programme and *P. knowlesi* has been reported from specific research studies, confirming the presence of *P. knowlesi* in Indonesia (Herdiana et al., 2016). The burden of *P. knowlesi* cannot be revealed in the absence of sensitive and specific diagnostic tools such as PCR. Molecular detection methods will also be vital to accurately demonstrate elimination of human-only malaria species in countries approaching this goal, given current malaria rapid diagnostic tests also lack specificity to differentiate *P. knowlesi* (Singh and Daneshvar, 2013, Grigg et al., 2014). In addition, understanding the true prevalence of zoonotic *Plasmodium* species requires sensitive detection of submicroscopic and/or asymptomatic infections, now increasingly reported to be present from molecular surveys conducted in Malaysia (Fornace et al., 2015, Siner et al., 2017), Indonesia (Lubis et al., 2017), Cambodia (Imwong et al., 2018) and Myanmar (Ghinai et al., 2017). Population-based cross-

sectional surveys are required to understand the prevalence of these infections in different settings and understand spatial patterns of disease infection.

The distribution of community-level exposure can also be assessed by prevalence of antibodies to species-specific malaria antibodies, reflecting previous exposure to malaria (Bousema et al., 2010, Corran et al., 2007, Wilson et al., 2007). Age-specific prevalence of these antibodies can be used to calculate seroconversion rates and evaluate changes in transmission over time; this measure has been shown to be closely correlated with other indicators of malaria transmission intensity such as parasite prevalence or entomological inoculation rates (Drakeley et al., 2005). Serological indices of exposure also have increased utility in low transmission settings where the probability of detecting infections is very low (Bousema et al., 2010, Cook et al., 2010). While numerous antigens have been described for *P. falciparum* and *P. vivax*, species-specific antigens for *P. knowlesi* have only relatively recently been developed (Herman et al., 2018). This *P. knowlesi*-specific panel of novel recombinant antigens has allowed surveillance of selected endemic communities and has demonstrated that exposure to *P. knowlesi* is more widespread in women and children as well as male agricultural workers in Malaysia than previously thought and has also allowed evaluation of differences in spatial patterns of zoonotic versus non-zoonotic malaria (Fornace et al., 2019b, Fornace et al., 2018a). Integrating both serological and molecular diagnostic tools is the most promising approach to characterise community-level *P. knowlesi* risks and to identify how environmental changes are shaping these risks.

3.3. Reporting bias and surveillance for *P. knowlesi*

Since the identification of a large number of *P. knowlesi* cases in Sarawak, Malaysia in 2004, research and surveillance efforts for *P. knowlesi* have been concentrated in Malaysia. Of 26 research projects on

P. knowlesi identified between 2004 and 2021, 14 projects focused on Malaysia and another 10 projects focused solely on laboratory studies conducted in the United States, United Kingdom or Australia (MESA Track, 2021). This is broadly reflected in the published literature as well, with the number and amount of research publications addressing *P. knowlesi* dramatically increasing after 2004 (Figure 2). Similarly, the identification of human infections with *P. knowlesi* has been predominantly concentrated within Malaysia despite identification of cases across Southeast Asia. This is a product of both the increased focus of research studies within Malaysia as well as changes to policies for malaria diagnosis and surveillance within Malaysia, particularly around the use of molecular methods (Table 2).

[Insert Figure 2 here]

[Insert Table 2 here]

Diagnostic limitations are one of the key barriers to understanding the burden of *P. knowlesi* across Southeast Asia. WHO recommends countries confirm *P. knowlesi* infections by PCR and standardize case definition and investigation procedures but this is not routinely applied across all settings (World Health Organisation Regional Office for Western Pacific, 2017). Malaria has been a notifiable disease in Malaysia since 1988 and updated to include *P. knowlesi* specifically in 2010. (Figure 3) As of 2017, malaria was routinely diagnosed in Malaysia by microscopy. Cases diagnosed as *P. falciparum*, *P. vivax* and *P. ovale* were quality controlled with all cases diagnosed as *P. malariae* or *P. knowlesi* confirmed by PCR. Within Sabah, Malaysia, a *P. knowlesi* foci, all human malaria cases were screened with molecular methods (World Health Organisation Regional Office for Western Pacific, 2017). With a move towards

malaria elimination and the substantial decrease in non-zoonotic species, increased effort has been focused on diagnosing *P. knowlesi* in Malaysia (Chin et al., 2020b).

[Insert Figure 3 here]

Despite increasing data on *P. knowlesi* from Malaysia, there are notably fewer *P. knowlesi* reports from neighbouring Indonesia. All species of *Plasmodium* have been reported in Indonesia, with increasing number of human cases of *P. knowlesi* malaria being reported by several studies in the province of South Kalimantan (Sulistyaningsih et al., 2010), Central Kalimantan (Setiadi et al., 2016), North Sumatera (Lubis et al., 2017), and in Aceh (Herdiana et al., 2016, Herdiana et al., 2018b). The limited evidence of *P. knowlesi* infection in Indonesia was partly due to limited diagnosis capacity of the existing malaria surveillance and control programme (Sulistyaningsih et al., 2010, Coutrier et al., 2018). Although most of the current evidence of *P. knowlesi* infections in Indonesia came from studies in the island of Kalimantan and Sumatera, a geospatial modelling study has also estimated several other areas in Java and Sulawesi islands as areas with moderate to high risk of *P. knowlesi* malaria (Shearer et al., 2016b). These areas were identified as priority areas for surveillance based on regions with sparse data and high estimated risk. As evidence of *P. knowlesi* risk becomes more prominent, the Indonesian national malaria control programme has developed a molecular surveillance approach for *P. knowlesi* malaria that will be piloted in several areas in Kalimantan, Sumatera, and in Java island [personal communication with a member of national malaria committee]. Whilst there are ongoing cross-sectional surveys to assess molecular and seroprevalence of *P. knowlesi* in Kalimantan and North Sumatera, to better understand the extent of *P. knowlesi* transmission in Indonesia, similar works in other areas such as in Java and Sulawesi island are needed.

To date, reports of naturally acquired *P. knowlesi* are limited to Asia. Isolated cases of human *P. knowlesi* infections have been reported in Europe, North America, Japan, Australia and New Zealand but all reported individuals had histories of travel to Southeast Asia (Kantele et al., 2008, Bronner et al., 2009, Ta et al., 2010, Berry et al., 2011, Hoosen and Shaw, 2011, Bart et al., 2013, Tanizaki et al., 2013, Cordina et al., 2014, Seilmaier et al., 2014, Mackroth et al., 2016, Ozbilgin et al., 2016, De Canale et al., 2017, Takaya et al., 2018, Nowak et al., 2019, Roe et al., 2020). There have been no published *P. knowlesi* reports in travellers or other individuals in Africa or South America, potentially due to diagnosis as other malaria species in endemic regions. Although other simian malarias are reported in these regions, *P. knowlesi* distribution currently only extends to Southeast Asia and India. Within these regions, substantial spatial heterogeneities in reported disease burden remain, raising key questions about the mechanisms underlying these differences in *P. knowlesi* transmission.

3.4 Emergence of other zoonotic simian malarias in Southeast Asia

Although *P. knowlesi* is the most widely reported zoonotic malaria species globally, other simian malaria species can cause human infections. *P. cynomolgi*, a simian malaria parasite widely distributed in macaques in Southeast Asia, was first shown to be transmissible to people accidentally in laboratory studies conducted in the United States in 1960 (Eyles et al., 1960). Subsequent studies in experimentally infected human volunteers with *P. cynomolgi* demonstrated potential for non-zoonotic transmission through mosquito vectors (Schmidt et al., 1961, Contacos et al., 1962). Further studies also demonstrated the potential for human infection with the simian malaria *P. inui* in laboratory settings (Coatney et al., 1966). Recently, natural asymptomatic *P. inui* infections have been identified in people in Malaysia, although the extent and the public health importance of these infections remains unknown (in press).

Despite this early experimental evidence of zoonotic potential, the first naturally acquired human infection with *P. cynomolgi* was only identified in 2011. An adult residing in a malaria-free area of peninsular Malaysia reported to a clinic with symptomatic malaria molecularly identified as *P. cynomolgi* (Ta et al., 2014). Subsequently, asymptomatic infections with *P. cynomolgi* have been identified in Malaysian Borneo and Cambodia (Grignard et al., 2019, Imwong et al., 2019). A retrospective review of blood samples from symptomatic malaria patients in Sarawak, Malaysia additionally identified 6 *P. cynomolgi*/*P. knowlesi* co-infections (Raja et al., 2020). These isolated studies and the high prevalence of *P. cynomolgi* detected in both macaques and mosquito vectors suggest transmission of *P. cynomolgi* to people is almost certainly occurring more frequently than detected. There remains little evidence that *P. cynomolgi* currently causes significant public health impacts; however, monitoring transmission of other simian malarias is a priority for malaria surveillance in this region.

4. Landscape impacts on *P. knowlesi* disease dynamics

Land use changes, and associated ecological and social changes, have been proposed as the main drivers of the apparent emergence of human *P. knowlesi* and may impact risks of other simian malaria species (Cox-Singh and Singh, 2008, Lee et al., 2011). While many of the mechanisms through which land use change influences *P. knowlesi* transmission are less well characterised than for other diseases, deforestation and other landscape changes are known to impact the distribution, behaviour and susceptibility of human, macaque and mosquito populations. Southeast Asia is one of the most rapidly changing environments on the planet and has been identified as a global hotspot of disease emergence (Allen et al., 2017). Within this section, we review the drivers and extent of environmental change in

Southeast Asia, identifying links between landscape change and *P. knowlesi* risks and describe evidence of how landscape change impacts human populations, wildlife reservoirs and vector dynamics.

4.1 Environmental change in Southeast Asia

Southeast Asia contains around 15% of the world's tropical forest, encompassing a range of important and diverse habitats, including montane and lowland rainforests, dry deciduous forests, swamp forests and mangroves (Stibig et al., 2014). At least 4 of the globe's 25 most important biodiversity hotspots can be found in the region, home to endemic species found nowhere else (Sodhi et al., 2010). Tropical forests are also important carbon sinks, mitigating greenhouse gas emissions and providing a crucial buffer against climate change (De Deyn et al., 2008).

However, this region has experienced one of the highest rates of deforestation globally, losing an average of 1.6 million hectares of forest per year between 1990 and 2010 (Figure 4) (Stibig et al., 2014). Between 1990 and 2020, the region's forest cover declined by 376,000km², with rates differing between constituent countries (FAO, 2020) (Table 3). A substantial proportion of deforestation has occurred within protected conservation areas and led to predictions that up to 85% of the region's biodiversity could be lost by 2100 (Sodhi et al., 2010). Commodity-driven deforestation is the cause of over 75% of forest loss in Southeast Asia since 2000, with smaller losses attributable to smallholder shifting agricultural practices and forestry (Curtis et al., 2018). These forest losses are a major source of anthropogenic carbon emissions and are the focus of on-going national and international climate change initiatives (Estoque et al., 2019).

[Insert Table 3 here]

Within Southeast Asia, there are substantial heterogeneities in land use change, drivers and policy responses. Malaysia and Indonesia have been named as global hotspots of forest loss and degradation due the rapid conversion of land for industrial oil palm plantations and other agricultural activities (Bryan et al., 2013, Gaveau et al., 2016, Danylo et al., 2021). While both industrial and smallholder agricultural practices contribute to deforestation, industrial plantations have been associated with over three times the amount of forest conversion and are a main driver of loss in old growth forests (Gaveau et al., 2021). Increases in land used for industrial oil palm plantations are driven by global increases in crude palm oil prices, primarily due to the expanding markets for biofuels (Li et al., 2020). In 2011, Indonesia enacted a moratorium prohibiting conversion of primary forests and peat lands to tree plantations as part of a strategy to reduce emissions from deforestation (Busch et al., 2015). Malaysia has introduced similar restrictions on forest conversion and corporate commitments to reduce deforestation and promote sustainable palm oil development now cover the majority of industrial production in Malaysia and Indonesia (Weisse and Goldman, 2021). Although spikes in deforestation occurred in 2015 following widespread droughts and fires, rates of primary forest loss have consistently decreased in Malaysia and Indonesia from 2017- 2020 following these policy changes (Weisse and Goldman, 2021).

In mainland Southeast Asia, commodity production has also driven forest loss. Between 1998 and 2018, over 50% of lowland forest cover was lost in Vietnam, Thailand, Cambodia, Laos, Peninsular Malaysia and Myanmar. This included a 50% loss of lowland forests within protected areas (Namkhan et al., 2021). Notably, Cambodia has lost over 1.1 million hectares of primary forest and over 24% of the country's tree cover since 2002 (Hansen et al., 2013). In contrast to Malaysia and Indonesia, expansion of rubber plantations is the primary driver of Cambodian forest conversion, with forest loss highly

correlated with global rubber prices (Grogan et al., 2019). Within the Greater Mekong basin, small-scale shifting agriculture and local timber use have transformed areas into a patchwork of fragmented forests and cropland (Namkhan et al., 2021, Curtis et al., 2018). Swidden farming practices, in which land is cultivated for a short fertile period and then abandoned, are also an important driver of deforestation, especially in Northern Vietnam (Weisse and Goldman, 2021). Deliberate slash-and-burn agriculture and the draining of peat-swamps for farming are also associated with drought and wildfires that exacerbate direct deforestation effects (Page and Hooijer, 2016, Sloan et al., 2017). The majority (90%) of lowland forests within mainland Southeast Asia have been identified as severely threatened and vulnerable to deforestation (Namkhan et al., 2021). Further increases in deforestation and losses of biodiversity are predicted within this area following extensive infrastructure development for the Belt and Road Initiative (Ng et al., 2020).

Logging is also a lucrative industry in Southeast Asia and accounts for 19% of forest loss; its dipterocarp forests are one of the globe's most important sources of tropical hardwood (Kettle, 2009). Clear cutting operations fell all trees in an area, thereby completely deforesting it. Selective and reduced-impact logging extract only high-value trees, leaving most of the forest intact, and may involve additional measures to minimise forest degradation. For example, pre-harvest assessments and identification of crop trees ahead of time allow for carefully planned road and skid trail construction so as to minimise the number and destructive effects of these routes, while lianas and vines connecting tree crowns of non-target trees to crop trees and directional felling prevent non-target trees being pulled down or weakened (Putz et al., 2008). While licensed selective timber extraction is less ecologically disruptive, Southeast Asia (especially Indonesia) sees high rates of illegal logging usually employing more destructive measures (Weisse and Goldman, 2021).

These changes in forest cover have occurred in parallel to wider population and climatic changes. An overall increase in temperature as well as increases in temperature extremes have been observed across Southeast Asia over the past century. These have been accompanied with increased variability of precipitation and resulting challenges in water scarcity and food insecurity (Hijioka et al., 2014). These changes are likely to interact with wider landscape and demographic changes to pose substantial challenges to sustainable development and public health. Consistent with global trends, populations in Southeast Asia have become increasingly urbanised. Across Southeast Asia, the proportion of populations living in urban areas increased from 15.6% in 1950 to over 50% in 2020, with 66% of the population projected to live in cities by 2050 (United Nations Department of Economic and Social Affairs Population Division, 2018). Despite rapidly growing urban centres, increasing urbanization has mainly corresponded to increased population density and less than 1% of deforestation is due to urban expansion (Curtis et al., 2018).

[Insert Figure 4 here]

4.2 Impacts of environmental change on distribution of *P. knowlesi*

Since the first identification of a large number of human *P. knowlesi* cases in forest and plantation workers, the recent increases in *P. knowlesi* incidence have widely been attributed to deforestation and land use change. Mathematical models of simulated data were first used quantitatively to examine the role of land use change in *P. knowlesi* transmission. Imai et. al used multi-host transmission models to assess the role of mixing between human and macaque populations in different ecological settings and demonstrate how deforestation may drive transmission by bringing these populations in closer

proximity (Imai et al., 2014). Using empirical data, statistical associations between deforestation and human *P. knowlesi* incidence were first confirmed in Northern Sabah, Malaysia. Analysing hospital-based reports adjusted for diagnostic uncertainty and remotely sensed data on land cover, village-level *P. knowlesi* incidence was positively associated with both forest cover and historical forest loss (Fornace et al., 2016a). Subsequent studies in the same region identified strong associations between forest cover, fragmentation and deforestation with household level *P. knowlesi* risks. These factors were most predictive at different spatial scales, highlighting the complex role of land cover in transmission of multi-host vector-borne diseases (Brock et al., 2019).

At regional levels, spatial modelling studies identified similar associations between different forest types, deforestation and *P. knowlesi* presence across Southeast Asia (Shearer et al., 2016a). These patterns were consistent with the distribution of the main *P. knowlesi* reservoirs and vectors across Southeast Asia (Moyes et al., 2016). Further mapping studies have demonstrated human infection risks are associated with specific agricultural practices in addition to deforestation. A cross-sectional survey across four districts in Northern Sabah, Malaysia identified positive associations between recent exposure to *P. knowlesi* (as measured by serology) and proportions and configuration of irrigated farming, pulpwood and oil palm plantations. This study additionally showed protective effects of intact, old-growth forests (Fornace et al., 2019b). A study examining reported incidence of symptomatic *P. knowlesi* cases in this region similarly identified associations between oil palm plantations and forest fragments (Sato et al., 2019). Although not specifically assessing the role of land cover, another study found significant spatial and temporal heterogeneity in reported cases in Peninsular Malaysia (Phang et al., 2020). Elsewhere in Southeast Asia, *P. knowlesi* infections have been detected during malaria surveys but at a frequency insufficient for analysis of environmental risk factors (e.g. (Shimizu et al., 2020)).

4.3 Human populations, movement and occupational risks

Landscape changes bring humans into closer contact with disease reservoirs and vectors as new areas are settled and agricultural and forest activities are undertaken. Individual human movement patterns influence the exposure to disease vectors and wildlife reservoirs within different environments (Hausermann et al., 2012, Stoddard et al., 2009). These movements occur on different spatial and temporal scales, from long term migrations to daily movements in areas surrounding households (Pindolia et al., 2014, Pindolia et al., 2012). Regional migration can lead to immunologically naïve individuals moving to areas of disease transmission or introduce infected individuals to areas previously free from disease (Wesolowski et al., 2012). On a local scale, deforestation has been associated with higher levels of human activities in forest areas and increased exposure to anopheline malaria vectors (Barbieri et al., 2005, de Castro et al., 2006). Other forest-related occupational activities, such as logging, rubber tapping and mining, have also been linked to higher malaria risks (Basurko et al., 2013, Hahn et al., 2014, Wai et al., 2014, Satitvipawee et al., 2012).

In Kapit, Sarawak, the majority (83%; 93/107) of molecularly confirmed *P. knowlesi* patients reported some type of forest exposure (Daneshvar et al., 2009). Similarly, a study of patients from a referral hospital in Sabah found that most *P. knowlesi* cases (92%, 119/130) had spent time in a forest or plantation the previous month (Barber et al., 2013a). However, reports from a district hospital in the largely deforested area of Kudat in Northwest Sabah describe a wide age distribution of *P. knowlesi* cases (0.7 to 89 years) and lack of association with forest activities (Barber et al., 2012). A subsequent case control study conducted within Kudat and Kota Marudu districts found a similarly wide age distribution (3 – 85 years), with 9% of cases occurring in children under the age of 15 (Grigg et al., 2017).

This study also identified plantation work, forest activities and sleeping outside overnight as associated with increased *P. knowlesi* risk, however, a minority of cases, including children, had no reported farm or forest activities, suggesting the possibility of peri-domestic transmission. The protective effects of indoor residual spraying (IRS) and associations between risk and vegetation surrounding the household provide additional evidence for transmission around the household. Community-based studies similarly found high proportions of women and children with evidence of asymptomatic infections and exposure to *P. knowlesi* and raises questions on the role and importance of peri-domestic transmission (Fornace et al., 2019b, Fornace et al., 2018a, Fornace et al., 2016b).

The increasing availability of technology offers new opportunities to characterise human movement patterns and behaviours. While mobile phone records can be used to track long-range human migration and movement patterns, GPS trackers and other devices allow fine-scale examination of how people use landscapes (Pindolia et al., 2012). A large-scale GPS tracking study in Northern Sabah, Malaysia identified substantial heterogeneities in routine individual space use patterns not strongly correlated with demographic characteristics or reported occupational activities. By integrating movement data with spatiotemporal models of mosquito biting and infection rates, this study demonstrated over 90% of infectious bites with *P. knowlesi* were likely to occur in areas close to households at forest edges despite higher biting rates in interior forested areas (Fornace et al., 2019a). Along the Thai-Myanmar border, entomological and human movement data were similarly integrated to identify likely areas of exposure, using repeated transect walks to estimate human population density. Results demonstrated the importance of farm huts and temporary dwellings in malaria transmission, notably identifying behaviour changes, including the reduced use of insecticide treated bed nets, within these forested areas (Edwards et al., 2019). An anthropological study in Cambodia also identified high variability in human

behaviour and use of vector control methods within these different environments (Gryseels et al., 2015).

These behavioural patterns are likely also to impact access to healthcare and corresponding immunity and susceptibility to infections. In addition to changing the physical environment, deforestation and other land use changes transform socio-economic and demographic practices (Fornace et al., 2021). Frontier communities involved in forestry or plantation activities often have reduced access to health systems; these dynamics may change over time as communities become more established and implement public health measures in response to outbreaks (Baeza et al., 2017). Individuals living within endemic areas are additionally more likely to acquire clinical immunity to malaria over time. In a frontier settlement in the Amazon, malaria risks were strongly associated with land clearing and agricultural activities; however, risks of clinical malaria sharply decreased after continued residence in this area (da Silva-Nunes et al., 2008). These infections are also much less likely to be detected by passive surveillance systems. In the Philippines, residence near intact forests was associated with decreased detection at health clinics, increased malaria infection risks detected by molecular methods and decreased risks of clinical malaria (Fornace et al., 2020). While the role of immunity to *P. knowlesi* through previous exposure or exposure to other malaria species is largely unknown, landscape change is likely to alter the susceptibility of human populations to *P. knowlesi* infections through both biological and social mechanisms.

4.4 Simian host ecology and infection rates

Changing habitats are likely to have similar effects on the distribution and density of the simian hosts (Table 4). The main natural hosts of *P. knowlesi* are long-tailed macaques (*Macaca fascicularis*) and pig-

tailed macaques (*Macaca nemestrina*) (Coatney et al., 1971). A report in peninsular Malaysia identified a banded leaf monkey (*Presbytis melalophos*) infected by *P. knowlesi* (Eyles et al., 1962) and a study in Thailand reported an infection of the parasite in dusky leaf monkey (*Semnopithecus obscurus*) (Putaporntip et al., 2010). A recent study by Fungfuang et al. (2020), first documented natural infections of stump-tailed macaques (*Macaca arctoides*) with *P. knowlesi* (Fungfuang et al., 2020). Other primate species identified as susceptible to *P. knowlesi* infection in laboratory studies include *Callithrix jacchus*, *Cebus* spp., *Cercocebus fuliginosus*, *Cercopithecus cephus*, *Cynocephalus papio*, *Hoolock hoolock*, *Macaca radiata*, *Macaca arctoides*, *Papio doguera*, *Papio jubilaeus*, *Papio papio*, *Presbytis cristatus*, *Saimiri sciureus* and *Semnopithecus entellus* (Coatney et al., 1971). Of these potential reservoirs, macaques are ecologically diverse and are the most widely distributed genus of nonhuman primates. Some macaques are prone to various infectious agents including viruses and parasites, and therefore could be the causes of emerging or re-emerging zoonotic diseases in humans (Wolfe et al., 1998). In particular, long-tailed macaques have substantial interfaces with humans, primarily with local populations but also with tourists visiting macaque habitats. This interface can lead to mutual disease transmission.

[Insert Table 4 here]

Previous studies have indicated a relatively high proportion of macaques are infected with *P. knowlesi* and genetic studies of human infections have identified two distinct parasite populations associated with long-tailed and pig-tailed macaque reservoir species (Lee et al., 2011, Divis et al., 2015). While the possibility of human to human transmission of *P. knowlesi* has been demonstrated experimentally, the high parasite diversity found within macaques suggests transmission remains primarily zoonotic (Assefa et al., 2015, Divis et al., 2015, Chin et al., 1968). Little data exist about the prevalence or infectiousness in macaque hosts. Identification of infections in macaques is limited by the same

diagnostic challenges as in human samples, further complicated by the difficulty of obtaining macaque blood samples or isolating *Plasmodium* from faecal samples (Stark and Salgado-Lynn, 2014, Siregar et al., 2015). Collecting additional data on macaque populations is challenged by both logistical difficulties in catching, sampling and detecting macaques as well as strict ethical guidelines on the sampling of non-human primates, both from local and international guidelines (e.g. CITES, the Convention on International Trade in Endangered Species of Wild Fauna and Flora). Although little is known about the pathology of *P. knowlesi* infections in macaques, the identification of large proportions of macaque populations as infected suggests that infections are likely to be long term (Lee et al., 2011). Available evidence suggests most monkey species are asymptomatic when infected with *P. knowlesi* and have low parasitaemia levels, with the notable exception of rhesus macaques (*M. mulatta*) in which *P. knowlesi* infections are typically fatal (Baird, 2009, Vadivelan and Dutta, 2014).

Substantial gaps remain in the understanding of infection dynamics within wild primates and how these are likely to respond to habitat changes. *P. knowlesi* transmission and prevalence can be affected by ecosystem changes by changing the ecology (abundance and behaviour) of reservoir hosts or by compromising immune function through stress (Keesing et al., 2010). These changes are likely to lead to geographical differences in the prevalence of malaria parasites in macaque species. Within the major *P. knowlesi* transmission focus of Sabah, Malaysia, human cases of *P. knowlesi* are mainly reported from the interior mountainous and more densely forested districts that lie along the Crocker range, which stretches along the southwest-northeast axis of Sabah from Tenom to Ranau. On the contrary, incidence in the more cultivated low-lying districts along the West and East coast has remained relatively low (William et al., 2014). The spatial distribution of *P. knowlesi* cases across Sabah is consistent with forest or forest-edge exposure being a likely risk factor for human infection and spillover occurring in forest edges or farms where both humans and macaques are present (Cox-Singh and Singh, 2008, Imai et al.,

2014). Studies of pig-tailed and long-tailed macaques within similar environments in Sarawak, Borneo identified a high proportion were infected with *Plasmodium species*, including 78% with *P. knowlesi* (Lee et al., 2011). In Thailand, a study demonstrated that malaria was prevalent in macaques living in mangrove forests, but no malaria infections were found in macaques living in urban areas (Seethamchai et al., 2008). Similarly, studies by Vythilingam *et al.* (2008) and Gamalo *et al.* (2019) also found no parasites in long-tailed macaques living in urban areas, however, monkeys caught in forested areas were infected with simian malaria parasites (Vythilingam et al., 2008, Gamalo et al., 2019).

These patterns of macaque infection and distribution may be changing due to increasing human encroachment into forests, high rates of construction and development, and the presence of secondary rainforests in the locality of urban and suburban residences which offer suitable habitats for monkeys that can harbour various species of simian malaria parasites (Braima et al., 2013). Deforestation converts primary forest to anthropogenic land uses and also fragments forest into smaller patches creating boundaries between small, disconnected islands of forest (Cushman et al., 2017, Taubert et al., 2018). Wildlife populations and individual primate species respond differently to the physical and biotic changes that arise as a result of disturbance of forest edge margins (Laurance et al., 2018). This habitat disturbance can influence primate disease transmission by altering ranging patterns, increasing density or crowding within forest patches or weakening immunity through exposure to other pathogens e.g. (Young et al., 2013, Nunn et al., 2014, Nunn et al., 2003, Kowalewski et al., 2011, Gillespie and Chapman, 2006, Mborra et al., 2009). Macaques are also frequently found in close contact to human settlements and in highly disturbed environments, where loss of natural habitat may lead to increased dependence on anthropogenic food sources and closer contact with people (Fooden, 1995, Moyes et al., 2016, Young et al., 2013). Deforestation may cause macaques to use the remaining forest patches, spend more time on the ground and change their ranging behaviour and microhabitat use (Chapman et al., 2005,

Chapman et al., 2006, Riley, 2008, Singh et al., 2001). Macaques may also go out to human settlements to raid crops or forage around houses, bringing them in contact with humans (Hambali et al., 2012).

Within Sabah, Malaysia, a case study report of a GPS-collared macaque troop suggests that macaque ranging behaviour is disturbed by deforestation events, with macaques moving in close proximity to houses where symptomatic human *P. knowlesi* cases were detected (Stark et al., (submitted)). Within this same geographic area, phylogenetic analysis provided further evidence of common *P. knowlesi* isolates between macaques, human cases and *An. balabacensis* mosquitoes in this region (Chua et al., 2017). A study by Brock et al. (2019) demonstrated that landscape fragmentation caused by deforestation influences *P. knowlesi* spillover into humans regionally, with the most predictive spatial scale of fragmentation influence on *P. knowlesi* transmission within 4 and 5 km of households. As macaques move distances up to 5 km in response to fragmentation, therefore, they may respond to deforestation on this emergent scale (Stark et al., 2019).

The transmission dynamics of *P. knowlesi* are almost certainly altered due to deforestation and changes in macaque populations and behaviour (Cox-Singh and Singh, 2008). Although Southeast Asian macaques harbour many parasites species, little is known about their distribution and epidemiology (Amir et al., 2020). It is critical to gather more information on the distribution and abundance of macaques as well as vectors of the parasite and assess how these may be influenced by rapidly changing landscapes over time. This information is essential to inform models of *P. knowlesi* transmission to target transmission hotspots and identify strategies for prevention and treatment.

4.5 Mosquito ecology, infection and bionomics

Physical changes in the environment, such as changes in vegetation, microclimate and soil, can affect the species composition and abundance of vector populations (Yasuoka and Levins, 2007). For example, deforestation has been shown to create environmental conditions favourable for larval breeding sites of malaria vectors (Vittor et al., 2009). Within Southeast Asia, agriculture such as rubber plantations and rice paddies have been associated with increased anopheline densities as well as increases in malaria incidence (Yasuoka and Levins, 2007). In some cases, deforestation has been reported to cause initial depletion of forest dwelling vectors followed by colonisation of the area by more efficient vector species and overall increases in malaria transmission (Guerra et al., 2006, Durnez et al., 2013). Deforestation may also alter the importance of sylvatic and peri-domestic transmission cycles, as seen in yellow fever dynamics (Valentine et al., 2019).

Entomological dynamics of *P. knowlesi* are undoubtedly complex, with numerous vectors implicated in sylvatic and zoonotic transmission. The main *P. knowlesi* vectors are members of the *Anopheles leucosphyrus* group of mosquitoes; *P. knowlesi* sporozoites and oocysts have been identified in *An. latens*, *An. cracens*, *An. balabacensis*, *An. dirus* and *An. introlatus* (Wong et al., 2015a, Vythilingam et al., 2006, Sallum et al., 2005, Chinh et al., 2019). The geographical distribution of the *Leucosphyrus* group of mosquitoes extends across Southeast Asia, with these species commonly reported to be associated with forest environments (Moyes et al., 2016). Molecular evidence additionally identified *P. knowlesi* within members of the *Barbirostris* and *Umbrosus* groups and the *Sundaicus* complex; although the presence of oocysts and sporozoites has not been confirmed within these groups. Further studies are needed to determine the role of mosquitoes outside the *Leucosphyrus* group in *P. knowlesi* transmission.

Previous studies on the main vectors of *P. knowlesi*, the primarily exophagic *Anopheles leucosphyrus* group of mosquitoes, found relatively high biting rates in both farm and forest edge areas

(Vythilingam et al., 2008, Tan et al., 2008). Entomological studies in Kapit, Sarawak have incriminated *An. latens* as the main vector of *P. knowlesi* in this area and observed this species is both attracted to macaques in the canopy and humans on the ground (Tan et al., 2008, Vythilingam et al., 2006). Studies within Sabah have implicated *An. balabacensis* as the primary vector of *P. knowlesi* in Northwest Sabah; this species was also historically the main vector of human malaria species within the region and has been experimentally shown to be able to transmit *P. knowlesi* (Wong et al., 2015b, Hii, 1985, Collins et al., 1967). Notably, the peak biting times of *An. balabacensis* and other mosquitoes from the Leucosphyrus group are in the early evening (6-10pm) when people are unlikely to be using bed nets (Wong et al., 2015a, De Ang et al., 2021). Other possible vectors have been reported biting during the day time (7-11am) which poses substantial challenges for vector control and prevention (De Ang et al., 2021).

Deforestation is likely to be impacting the distribution of *P. knowlesi* vectors. A study of mosquito ecology across a forest disturbance gradient in Sabah found abundance of *An. balabacensis* was higher in previously logged forests compared with primary forests. This vector was present at both ground and canopy levels, suggesting the potential for this mosquito to transmit *P. knowlesi* between canopy-dwelling primates and people at ground level (Brant et al., 2016). Additional investigations of anopheline mosquito densities within villages reporting *knowlesi* cases found higher densities of *An. balabacensis* in environments around cases households and identified vectors infected with simian malaras in peridomestic settings (Manin et al., 2016). Other studies have found higher *An. balabacensis* biting rates at both forest edges and farm or plantation areas (Brown et al., 2020, Hawkes et al., 2019). Despite this association with forest edges, the role of fragmentation in *P. knowlesi* vector ecology remains largely unknown; while fragmentation was not associated with increased *An. balabacensis* biting rates, fragmentation was associated with changes in vector composition and increases in density of secondary

vectors in Sabah (Hawkes et al., 2019). *An. balabacensis* have reported breeding in shallow, muddy pools in farms and at forest edges, raising the question of whether fragmentation may be creating new breeding sites (Rohani et al., 2019). Key questions remain on how landscape changes will impact adult vector distributions, larval ecology and biting preferences. However, together, these data indicate that changing land use patterns are affecting the distribution and behaviour of mosquito vectors and that conversion of previously intact forests to agricultural land may increase the abundance of these vectors.

5. Transmission dynamics and potential for human to human transmission

While data anecdotally support the theory that transmission remains primarily zoonotic and driven by increased spatial overlap between people, macaques and mosquitoes in response to land use change, the possibility of human to human transmission cannot be ruled out. Zoonotic diseases have a number of barriers to overcome before they can cause human infections. Factors contributing to these include ecological drivers, pathogen characteristics and human factors. *P. knowlesi* has already overcome a significant number of these, causing multiple large-scale outbreaks in Malaysia.

For non-zoonotic transmission to occur, and indeed drive the increase in human cases, a number of conditions need to be met. Firstly, human-host interactions have to be close enough to cause the initial spillover event into human populations. Once this has occurred, infection has to take hold of a human host, invading red blood cells and replicating enough to produce a significant infectious dose for a mosquito to consume. Inside the mosquito, parasites have to complete their life-cycle for the next mosquito bite to become infectious to humans. Humans have to live in enough proximity to each other and within the mosquito range for the next mosquito bite to become infectious to humans.

Ecological and epidemiological studies have shown that macaque and human populations live in enough close proximity with enough strength of interactions for repeated spillover events to take place. Indeed, sighting macaques in peri-domestic environments has been identified as a risk factor for *P. knowlesi* (Moyes et al., 2016, Shearer et al., 2016b). Experimental studies have shown that *P. knowlesi* can be transmitted from infected individuals to other people via suitable mosquito vectors, such as *An. balabacensis* (Chin et al., 1968). Parasite invasion of human red blood cells has been seen in laboratory experiments, with multiple proteins involved in different pathways (Moon et al., 2016, Tyagi et al., 2015). It has also been shown that *P. knowlesi* parasites can be maintained in laboratory settings using exclusively human blood, proving parasites are able to produce multiple generations without the need to infect macaques (Moon et al., 2013). Although experimental, this shows that there is biological plausibility for sustained human transmission to take place. Mathematical modelling studies have also identified specific scenarios under which this could be occurring (Imai et al., 2014, Brock et al., 2016). Although they concluded that sustained non-zoonotic transmission is unlikely to be occurring, conditions can be met for this to take place. Furthermore, there is evidence that this could have already occurred. Epidemiological studies have identified spatio-temporal clusters which are suggestive of sustained human to human transmission (Herdiana et al., 2018a).

To better understand transmission, further research is needed to characterise fine-scale habitat preferences and densities of vectors and primate hosts. Currently available data are either too geographically limited to allow for extrapolation to other areas (e.g. (Stark et al., (submitted), Wong et al., 2015a)) or too broadly aggregated at larger spatial scales to examine effects of changing movement patterns or habitat selection in response to land use change (Moyes et al., 2016). More detailed data on the densities of these populations would additionally allow exploration of vector biting preferences based on host availability in different environments. Incorporating detailed spatial data on host, vector

and human populations would enable further insights into the mechanistic links between *P. knowlesi* incidence and land use change as well as quantification of the contribution of different populations to transmission and design of targeted control strategies.

6. Designing surveillance and control measures for changing environments

Despite increasing research on the role of landscape in *P. knowlesi* transmission, substantial knowledge gaps remain on *P. knowlesi* distribution regionally and how longer-term environmental changes are likely to shape human risks. One of the key barriers is lack of detailed information about spatial distributions of infections in the community due to detection bias from passive surveillance systems and diagnostic methods. Improving collection of spatial data on human infections enables detailed planning of control measures and can be integrated with environmental data to characterise these changing transmission patterns. Additionally, understanding the role of landscape in *P. knowlesi* transmission enables design of ecological interventions. As opposed to parasite-specific control strategies that focus on particular vector species or pathogens, wildlife and land management may provide a more general and sustainable strategy for controlling zoonotic malarias of current and future public health significance. Ecological interventions aim to prevent disease spillover by reducing pathogen flow between wildlife and human populations; this can include managing wildlife population sizes or pathogen prevalence, reducing contact between people, vectors and wildlife or targeted interventions to mitigate impacts of spillover (Sokolow et al., 2019). Within this section, we review potential surveillance and ecological control measures theoretically applicable to *P. knowlesi*.

6.1 Opportunities to improve surveillance for *P. knowlesi*

Heterogeneity of disease transmission occurs when a small proportion of the population is disproportionately affected and experiences the majority of the disease due to environmental, social or biological factors (Hay et al., 2013, Woolhouse et al., 1997). Capturing this heterogeneity is particularly critical for emerging diseases such as *P. knowlesi*, where the disease burdens are constantly shifting due to environmental change. To better target interventions, it is increasingly important to identify and target hotspots of transmission and understand the factors that may contribute to disease occurrence in these locations (Clements et al., 2013, Bannister-Tyrrell et al., 2017). However, assessment of transmission heterogeneity has been focused on national level estimates, mainly due to the availability of data. Previous studies reported that the detection of local level clusters of infection has an important role for improving understanding of the micro-epidemiological patterns of disease transmission, and to ensure that control strategies are tailored to the specific epidemiological characteristics in an area as much as is feasible (Bousema et al., 2012).

Adding data collection methods that enable surveillance to remotely capture spatial patterns of transmission at the micro epidemiological level are essential for strategic and operational planning of *P. knowlesi* surveillance and control programmes. Generally, the spatial analysis of disease transmission is based on address information automatically generated by geocoding software packages that can produce accurate spatial coordinate data for a large proportion of individuals (Carvalho and Nascimento, 2012, Dearwent et al., 2001). In circumstances where formal address data are unavailable, catchment areas of, for example, community pharmacies or general practitioners have been used for describing spatial patterns in disease occurrence (Sturrock et al., 2013, Han et al., 2013, Lash et al., 2012, Florentinus et al., 2006). However, this approach is likely to have less utility for resource-poor settings where formal address systems are commonly unavailable and where health-facility catchment areas are relatively large and poorly defined (Noor et al., 2009, Oduro et al., 2011, Stresman et al.,

2014). An alternative geolocation method utilising mobile technology-based participatory mapping approaches utilising high-resolution offline maps has been validated to effectively improve spatial data collection for malaria surveillance activities in Asia (Indonesia and the Philippines) (Fornace et al., 2018b). A similar approach has also been used to assess human mobility traceability in rural offline populations with contrasting malaria dynamics in the Peruvian Amazon (Carrasco-Escobar et al., 2019). This approach is also being used in ongoing studies aimed at determining the spatial epidemiology of *P. knowlesi* in North Sumatera and South Kalimantan, Indonesia.

In addition to improving the collection of spatial data, one of the critical barriers to determining the spatial distribution of *P. knowlesi* is capturing infections occurring in communities which may not be reported to health centres. Malaria surveillance has traditionally focused on passive case detection of symptomatic cases at health facilities (Barclay et al., 2012, Cotter et al., 2013). However, information generated by passive case detection may not necessarily reflect the true burden of disease in areas where *P. knowlesi* cases are rare, frequently misdiagnosed and disproportionately affect high-risk populations who may not utilise public health facilities (Cotter et al., 2013). In addition, studies suggest that passive surveillance will miss a large proportion of asymptomatic and sub-microscopic *P. knowlesi* infections present in the community (Imwong et al., 2018, Fornace et al., 2015). Many countries conduct countrywide community-based surveys such as malaria indicator surveys (MaIS) to supplement the health facility-based reporting on malaria burden. The MaIS are useful to obtain information on the current malaria burden across the country. However, due to logistical difficulties, the MaIS are typically conducted sporadically and become less efficient for assessing malaria burden when transmission levels are low as they require large numbers of samples to achieve sufficient statistical power (Rabinovich et al., 2017, Stresman et al., 2012).

Alternatively, convenience sampling strategies such as health facility-based surveys recruiting all attendees instead of just suspected malaria cases (e.g. (Surendra et al., 2020, Reyes et al., 2021, Oduro et al., 2011)) and school-based surveys (e.g. (Druetz et al., 2020, Stevenson et al., 2013)) could provide more robust and reliable data compared to routine passive case detection, and are more operationally feasible than the large community-based strategies such as MaIS. For example, a study across different malaria transmission settings in the Philippines illustrated the utility of health facility-based surveys to augment surveillance data to increase the probability of detecting *P. knowlesi*, *P. falciparum*, *P. vivax*, and *P. malariae* infections in the wider community (Reyes et al., 2021). The use of the convenience sampling of health facility attendees markedly increased detection probabilities and spatial coverage of surveillance, particularly in rural populations living in forested areas (Fornace et al., 2020). In addition, health facility-based surveys conducted in Indonesia were able to capture heterogeneity of *P. falciparum* and *P. vivax* malaria transmission and identify areas still receptive to malaria in an elimination setting (52). However, the bias of such convenience sampling strategies for *P. knowlesi* malaria surveillance is not well characterized and requires further study.

Improving spatial data on the distribution of *P. knowlesi* additionally offers opportunities to examine how landscape changes impact *P. knowlesi* distribution, ideally leading to the design of early warning systems or targeted surveillance. Earth Observation data, typically collected by satellite or aerial methods, enables integration of data on landscape factors with spatial data on the distribution of *P. knowlesi* cases (Fornace et al., 2021). The quantity, types of data and spatial and temporal resolutions of free and commercially available Earth Observation data are rapidly expanding (Wimberly et al., 2021). Analysis-ready products, such as near real-time deforestation alerts, make these datasets increasingly accessible to health programmes (Hansen et al., 2016). Malaysia is now exploring the use of land cover data through incorporation of metrics of recent deforestation and recent construction activities into

malaria foci investigations, in line with recent guidelines developed by the World Health Organization for defining malaria receptivity (World Health Organisation, 2019, Fornace et al., 2021). Increased data on relationships between land cover and *P. knowlesi* risks and developing sources of Earth Observation data offer new opportunities to develop environmentally targeted surveillance and control approaches for *P. knowlesi*.

6.2 Management of wildlife populations

In contrast to other human malaria species, there are fewer established control measures to reduce transmission of *P. knowlesi* following identification of high-risk areas. While vector control measures may limit human exposure to infectious bites, the zoonotic nature of *P. knowlesi* offers an opportunity to control transmission through management of macaque reservoir populations. In theory, this could include a variety of approaches ranging from population reduction, habitat segregation or even chemoprophylaxis directed at the macaque reservoir. To our knowledge, none of these approaches have been incorporated into *P. knowlesi* control strategies so far. Managing wildlife populations may offer opportunities to mitigate disruptions from environmental change on disease transmission by reducing the abundance or *P. knowlesi* prevalence in reservoirs. However, these interventions may have complex impacts on ecology, requiring further consideration and planning.

It has been speculated that reducing macaque population density via culling could be an effective means of reducing *P. knowlesi* spillover to humans, although ethical concerns and the unfeasible logistics prevent this strategy being adopted (Chin et al., 2020a). Ethics and logistic feasibility are sound arguments against macaque culling, but even in their absence the scientific case for such an approach is unclear. The expected impact of a culling programme would depend on the strength of the relationship between the macaque population size and human infection risk. This has not been empirically

estimated, but has been inferred through modification of standard, single-host models of malaria transmission incorporating human and macaque host population data (Yakob et al., 2018, Yakob et al., 2010). Here, transmission is predicted to be positively associated with the ratio of vector to macaque population density, with the expectation of macaque density-dependent transmission (Yakob et al., 2010, Yakob et al., 2018). However, other than the necessary requirement that macaques be locally available for transmission to occur, the contribution of macaque density to transmission is relatively small in comparison to the much larger effects of vector survival, feeding rates on macaques and humans respectively, and the parasite's extrinsic incubation period. Furthermore, as the effect of macaque density depends on corresponding vector density, there would be great uncertainty as to what level of macaque population reduction was required to prevent spillover in different ecological settings and seasons. Certainly, macaque culling in the absence of sustained vector control, including throughout the diverse forest and agricultural habitats where they occur, may be unlikely to have much impact.

In addition to these theoretical considerations, lessons can be learned from other zoonotic disease systems where wildlife culling has been employed for disease control. Worryingly, these provide several examples where culling either had no impact or increased transmission by changing aspects of the demographics and dispersal on the wildlife host population (Choisy and Rohani, 2006). Arguably the most poignant example is the controversial programme of badger culling implemented to reduce the transmission of bovine tuberculosis to livestock in the UK. Here, culling was not only found to be ineffective, but associated with increased infection risk in some settings because the repeated removal of badgers triggered inward migration of infected individuals from neighbouring areas (Bielby et al., 2014, Donnelly and Woodroffe, 2015). Similarly, the long-tailed and pig-tailed macaque reservoir hosts of *P. knowlesi* are territorial, with habitat where individuals or troops have been removed likely to be

recolonized (Fooden, 1995). Another zoonotic disease where culling has been extensively used as a control strategy is rabies. Rabies can be transmitted to humans by a variety of wildlife (ie.g foxes, bats) and domestic animals (dogs). Culling is often carried out in response to public concern when human cases occur, but review of evidence from large-scale culling programmes in Denmark, Indonesia and Korea found no impact on rabies incidence despite large reductions in dog population size. This was attributed to transmission being frequency rather than density-dependent, and/or that the degree of dog population reduction required to see any impact on human cases being beyond the feasibility of control programmes. Similarly, several countries in Latin America have carried out culling programmes for decades to control vampire bat-transmitted rabies. Despite these intensive efforts, transmission of bat rabies to livestock has persisted (Streicker et al., 2012). Again, this failure may be attributed to the unfeasibly high degree of wildlife population reduction required to see an impact on occasional spillover to livestock or human hosts. On the basis of theoretical and practical considerations, we argue that macaque culling is unlikely to be an effective strategy for *P. knowlesi* control.

Alternatively, the use of oral baits to distribute vaccines or drug treatments has been investigated and applied in a wide variety of wildlife populations (Cross et al., 2007, Abbott et al., 2012). Such programmes have been highly effective when used to control racoon-transmitted rabies in North America, and eliminate fox rabies in several European countries (Maki et al., 2017). Similar approaches have also been considered for control of Lyme disease in wildlife hosts (Bhattacharya et al., 2011).

Three key criteria have been defined for development of effective oral vaccines for wildlife: an efficacious immunogen, an appropriate delivery vehicle, and a species-specific bait (Cross et al., 2007).

As reviewed earlier, at present there are no vaccine candidates for *P. knowlesi* that could be adapted for use in wildlife programmes at present. However, oral baits could be considered for distribution of

chemoprophylaxis to macaques in areas of high *P. knowlesi* human incidence should appropriate formulations and delivery systems be available.

The control of zoonoses through distribution of chemoprophylaxis to wildlife is likely to be more demanding than vaccines due to the likely higher frequency of distribution required to sustain infection reduction in reservoir populations. However, such an approach is not without precedence. A notable example is the tapeworm *Echinococcus multilocularis* which infects foxes (Comte et al., 2013). Humans can be exposed to this helminth through its presence in fox droppings, with infection leading to potentially fatal alveolar echinococcus (AE). Following the successful eradication of rabies from European fox populations, there has been a large rise in urban fox populations and an associated rise in human AE cases in several countries. There is no effective vaccine against *E. multilocularis*, however, the parasite is susceptible to the anti-helminthic drug praziquantel (Comte et al., 2013). Large-scale programmes have been implemented in several European countries and Japan where anti-helminthics have been disseminated to foxes in areas of high human exposure. A recent systematic review and meta-analysis of results of these programmes indicates they are generally successful in reducing environmental contamination with *E. multilocularis* and thus human exposure, although may not be sufficient for complete eradication (Umhang et al., 2019). In these programmes, the treatment frequency of oral baits ranged from monthly to every six months. Given the focalized nature of *P. knowlesi* incidence in humans, this frequency of application could be feasible within hotspots of human cases. Such programmes could exploit the presumable lack of drug resistance in malaria parasites that primarily infect wildlife, by using cheap and readily available antimalarials like chloroquine for which other human malaria parasites have become resistant.

6.3 Land management strategies

Despite the clear relevance of deforestation and conversion of land for agriculture to *P. knowlesi* spillover, the specific nature of these impacts are complex due to the involvement of interlinked social, environmental and economic drivers of risk (Fornace et al., 2020.). Instead of a straightforward relationship between deforestation and human disease incidence, recent work suggests that risk is determined by a more complex range of factors related to land use, symmetry and fragmentation that act at different scales. Effective environmental management of *P. knowlesi* will require consideration of the combined impacts of these diverse land use factors arising at different scales, and how they could be exploited to develop strategies for minimizing risk of human infection risk. This will require thorough understanding of transmission ecology, and how landscapes can be manipulated to reduce overlap between humans and the macaque reservoir. This could involve for example, better planning of deforestation and agricultural activities to build in larger continuous blocks of protected forest areas that could retain macaque populations, and/or the creation of buffer zones and habitat corridors that minimize contact between macaques, human settlements and agricultural workers. Such habitat management strategies have not been incorporated into *P. knowlesi* control, but may be the only way to achieve targets for malaria elimination.

Land management strategies and environmental modification have a long history of successfully reducing risks of non-zoonotic malaria species (Fornace et al., 2021). Famously, this includes an extensive long-term land management policy in Italy after the first World War which led to draining of marsh areas and agricultural development aimed at reduction of vector breeding habitats (Gachelin and Opinel, 2011). A systematic review of environmental management for malaria control found these interventions were highly effective in reducing malaria morbidity and mortality (Keiser et al., 2005c). Increasingly, global policy initiatives have focused on identifying co-benefits between health and climate interventions, integrating health into wider climate change mitigation policies (Workman et al., 2018).

Climate mitigation strategies may already be having beneficial impacts in reducing *P. knowlesi* transmission, although it remains to be seen whether the recent changes in forest conservation policies in Malaysia and Indonesia aimed at reducing emissions will also lead to reductions in *P. knowlesi* burden (Weisse and Goldman, 2021). The recent COVID-19 pandemic has also led to renewed focus on landscape-based interventions to reduce pathogen spillover from wildlife; these interventions are essential for ensuring both human and ecosystem health (Reaser et al., 2021). While it remains unknown exactly how land management policies can reduce *P. knowlesi* risks, this is a priority for future research.

7. Conclusions and future research priorities

P. knowlesi exemplifies an emerging zoonotic disease driven by deforestation and other landscape changes. While substantial knowledge gaps exist on the true burden and distribution of *P. knowlesi*, increasing evidence illustrates how landscape impacts human, simian and mosquito populations and resulting *P. knowlesi* transmission between these populations. The identification of human *P. knowlesi* cases across Southeast Asia, particularly in areas where other human malaria species have been eliminated, highlights the urgent need to develop targeted control strategies for *P. knowlesi*. It is clear that for control of zoonotic malaria, much more innovative and intersectoral approaches are urgently needed to tackle the current public health problem of *P. knowlesi* now and emergence of other wildlife-dependent vector-borne diseases in the future.

Human exposure to zoonotic malaria is driven by a complex range of environmental, social and economic factors, acting across scales from individual, household, community up to landscape (Fornace et al., 2021). Correspondingly, effective control will require implementation of strategies acting at

different scales; ranging from provision of personal protection measures to high risk groups, vector control and targeted chemoprophylaxis of macaques in high transmission foci, and land use management. Here, malaria control programmes can learn much from the experiences of other zoonotic disease control approaches that have successfully applied such comprehensive One Health approaches. Close intersectoral collaboration between public health, wildlife biologists, ecologists, social scientists, land use planners, communities and government policy makers will be crucial for successful development and implementation of such approaches. Additionally, this must be underpinned by more effective surveillance systems with capacity to incorporate data on environmental factors and land use (Fornace et al., 2020.). Such cross-disciplinary surveillance and control approaches will require substantial capacity strengthening and training to establish core research units and expertise within control programmes. Investments in this type of capacity strengthening will reap great benefits by enhancing the response not only to simian malaria, but the wider range of forest and agricultural-associated zoonoses and vector-borne diseases that have the potential to emerge as a consequence of increasing rates of land use change and deforestation in endemic countries (Plowright et al., 2021).

7. References

- ABBOTT, R. C., OSORIO, J. E., BUNCK, C. M. & ROCKE, T. E. 2012. Sylvatic plague vaccine: a new tool for conservation of threatened and endangered species? *Ecohealth*, 9, 243-50.
- AFRANE, Y. A., ZHOU, G., LAWSON, B. W., GITHEKO, A. K. & YAN, G. 2006. Effects of microclimatic changes caused by deforestation on the survivorship and reproductive fitness of *Anopheles gambiae* in western Kenya highlands. *Am J Trop Med Hyg*, 74, 772-8.
- ALLEN, T., MURRAY, K. A., ZAMBRANA-TORRELIO, C., MORSE, S. S., RONDININI, C., DI MARCO, M., BREIT, N., OLIVAL, K. J. & DASZAK, P. 2017. Global hotspots and correlates of emerging zoonotic diseases. *Nat Commun*, 8, 1124.
- AMIR, A., SHAHARI, S., LIEW, J. W. K., DE SILVA, J. R., KHAN, M. B., LAI, M. Y., SNOUNOU, G., ABDULLAH, M. L., GANI, M., ROVIE-RYAN, J. J. & LAU, Y. L. 2020. Natural Plasmodium infection in wild macaques of three states in peninsular Malaysia. *Acta Trop*, 211, 105596.
- ANSTEY, N. M. & GRIGG, M. J. 2019. Zoonotic Malaria: The Better You Look, the More You Find. *J Infect Dis*, 219, 679-681.
- ASSEFA, S., LIM, C., PRESTON, M. D., DUFFY, C. W., NAIR, M. B., ADROUB, S. A., KADIR, K. A., GOLDBERG, J. M., NEAFSEY, D. E., DIVIS, P., CLARK, T. G., DURAISINGH, M. T., CONWAY, D. J., PAIN, A. & SINGH, B. 2015. Population genomic structure and adaptation in the zoonotic malaria parasite *Plasmodium knowlesi*. *Proc Natl Acad Sci U S A*, 112, 13027-32.
- BAEZA, A., SANTOS-VEGA, M., DOBSON, A. P. & PASCUAL, M. 2017. The rise and fall of malaria under land-use change in frontier regions. *Nat Ecol Evol*, 1, 108.
- BAIRD, J. K. 2009. Malaria zoonoses. *Travel Med Infect Dis*, 7, 269-77.
- BANNISTER-TYRRELL, M., VERDONCK, K., HAUSMANN-MUELA, S., GRYSEELS, C., MUELA RIBERA, J. & PEETERS GRIETENS, K. 2017. Defining micro-epidemiology for malaria elimination: systematic review and meta-analysis. *Malar J*, 16, 164.
- BARBER, B. E., RAJAHAM, G. S., GRIGG, M. J., WILLIAM, T. & ANSTEY, N. M. 2017. World Malaria Report: time to acknowledge *Plasmodium knowlesi* malaria. *Malaria Journal*, 16, 135.
- BARBER, B. E., WILLIAM, T., DHARARAJ, P., ANDERIOS, F., GRIGG, M. J., YEO, T. W. & ANSTEY, N. M. 2012. Epidemiology of *Plasmodium knowlesi* malaria in north-east Sabah, Malaysia: family clusters and wide age distribution. *Malar J*, 11, 401.
- BARBER, B. E., WILLIAM, T., GRIGG, M. J., MENON, J., AUBURN, S., MARFURT, J., ANSTEY, N. M. & YEO, T. W. 2013a. A prospective comparative study of *knowlesi*, *falciparum*, and *vivax* malaria in Sabah, Malaysia: high proportion with severe disease from *Plasmodium knowlesi* and *Plasmodium vivax* but no mortality with early referral and artesunate therapy. *Clin Infect Dis*, 56, 383-97.
- BARBER, B. E., WILLIAM, T., GRIGG, M. J., PIERA, K., YEO, T. W. & ANSTEY, N. M. 2013b. Evaluation of the sensitivity of a pLDH-based and an aldolase-based rapid diagnostic test for diagnosis of uncomplicated and severe malaria caused by PCR-confirmed *Plasmodium knowlesi*, *Plasmodium falciparum*, and *Plasmodium vivax*. *J Clin Microbiol*, 51, 1118-23.
- BARBER, B. E., WILLIAM, T., GRIGG, M. J., YEO, T. W. & ANSTEY, N. M. 2013c. Limitations of microscopy to differentiate *Plasmodium* species in a region co-endemic for *Plasmodium falciparum*, *Plasmodium vivax* and *Plasmodium knowlesi*. *Malar J*, 12, 8.
- BARBIERI, A. F., SAWYER, I. O. & SOARES-FILHO, B. S. 2005. Population and Land Use Effects on Malaria Prevalence in the Southern Brazilian Amazon. *Human Ecology*, 33, 847-874.
- BARCLAY, V. C., SMITH, R. A. & FINDEIS, J. L. 2012. Surveillance considerations for malaria elimination. *Malar J*, 11, 304.

- BARROS, F. S. & HONORIO, N. A. 2015. Deforestation and Malaria on the Amazon Frontier: Larval Clustering of *Anopheles darlingi* (Diptera: Culicidae) Determines Focal Distribution of Malaria. *Am J Trop Med Hyg*, 93, 939-53.
- BART, A., VAN HELLEMOND, J. J., VAN GENDEREN, P. J. & VAN GOOL, T. 2013. Plasmodium knowlesi infection imported to Germany, January 2013. *Euro Surveill*, 18.
- BASURKO, C., DEMATTEI, C., HAN-SZE, R., GRENIER, C., JOUBERT, M., NACHER, M. & CARME, B. 2013. Deforestation, agriculture and farm jobs: a good recipe for Plasmodium vivax in French Guiana. *Malar J*, 12, 90.
- BENNETT, K. L., GOMEZ MARTINEZ, C., ALMANZA, A., ROVIRA, J. R., MCMILLAN, W. O., ENRIQUEZ, V., BARRAZA, E., DIAZ, M., SANCHEZ-GALAN, J. E., WHITEMAN, A., GITTENS, R. A. & LOAIZA, J. R. 2019. High infestation of invasive Aedes mosquitoes in used tires along the local transport network of Panama. *Parasit Vectors*, 12, 264.
- BERRY, A., IRIART, X., WILHELM, N., VALENTIN, A., CASSAING, S., WITKOWSKI, B., BENOIT-VICAL, F., MENARD, S., OLAGNIER, D., FILLAUX, J., SIRE, S., LE COUSTUMIER, A. & MAGNAVAL, J. F. 2011. Imported Plasmodium knowlesi malaria in a French tourist returning from Thailand. *Am J Trop Med Hyg*, 84, 535-8.
- BHATTACHARYA, D., BENSACI, M., LUKER, K. E., LUKER, G., WISDOM, S., TELFORD, S. R. & HU, L. T. 2011. Development of a baited oral vaccine for use in reservoir-targeted strategies against Lyme disease. *Vaccine*, 29, 7818-25.
- BIELBY, J., DONNELLY, C. A., POPE, L. C., BURKE, T. & WOODROFFE, R. 2014. Badger responses to small-scale culling may compromise targeted control of bovine tuberculosis. *Proceedings of the National Academy of Sciences of the United States of America*, 111, 9193-9198.
- BLOOMFIELD, L. S. P., MCINTOSH, T. L. & LAMBIN, E. F. 2020. Habitat fragmentation, livelihood behaviours and contact between people and nonhuman primates in Africa. *Landscape Ecology*, 35, 985-1000.
- BOUNDENGA, L., OLOMO, B., ROUGERON, V., MOUELE, L. Y., MVE-ONDO, B., DELICAT-LOEMBET, L. M., MOUKODOUM, N. D., OKOUGA, A. P., ARNATHAU, C., ELGUERO, E., DURAND, P., LIEGEOIS, F., BOUE, V., MOTSCH, P., LE FLOHIC, G., NDOUNGOUE, A., PAUPY, C., BA, C. T., RENAUD, F. & PRUGNOLLE, F. 2015. Diversity of malaria parasites in great apes in Gabon. *Malar J*, 14, 111.
- BOUSEMA, T., GRIFFIN, J. T., SAUERWEIN, R. W., SMITH, D. L., CHURCHER, T. S., TAKKEN, W., GHANI, A., DRAKELEY, C. & GOSLING, R. 2012. Hitting hotspots: spatial targeting of malaria for control and elimination. *PLoS Med*, 9, e1001165.
- BOUSEMA, T., YOUSSEF, R. M., COOK, J., COX, J., ALEGANA, V. A., AMRAN, J., NOOR, A. M., SNOW, R. W. & DRAKELEY, C. 2010. Serologic markers for detecting malaria in areas of low endemicity, Somalia, 2008. *Emerg Infect Dis*, 16, 392-9.
- BRAIMA, K. A., SUM, J. S., GHAZALI, A. R., MUSLIMIN, M., JEFFERY, J., LEE, W. C., SHAKER, M. R., ELAMIN, A. E., JAMAIAH, I., LAU, Y. L., ROHELA, M., KAMARULZAMAN, A., SITAM, F., MOHD-NOH, R. & ABDUL-AZIZ, N. M. 2013. Is there a risk of suburban transmission of malaria in Selangor, Malaysia? *PLoS One*, 8, e77924.
- BRANT, H. L. 2011. *Changes in abundance, diversity and community composition of mosquitoes based on different land use in Sabah, Malaysia*. Master of Science, Imperial College London.
- BRANT, H. L., EWERS, R. M., VYTHILINGAM, I., DRAKELEY, C., BENEDICK, S. & MUMFORD, J. D. 2016. Vertical stratification of adult mosquitoes (Diptera: Culicidae) within a tropical rainforest in Sabah, Malaysia. *Malar J*, 15, 370.
- BRASIL, P., ZALIS, M. G., DE PINA-COSTA, A., SIQUEIRA, A. M., JUNIOR, C. B., SILVA, S., AREAS, A. L. L., PELAJO-MACHADO, M., DE ALVARENGA, D. A. M., DA SILVA SANTELLI, A. C. F., ALBUQUERQUE, H. G., CRAVO, P., SANTOS DE ABREU, F. V., PETERKA, C. L., ZANINI, G. M., SUAREZ MUTIS, M. C., PISSINATTI, A., LOURENCO-DE-OLIVEIRA, R., DE BRITO, C. F. A., DE FATIMA FERREIRA-DA-CRUZ,

- M., CULLETON, R. & DANIEL-RIBEIRO, C. T. 2017. Outbreak of human malaria caused by *Plasmodium simium* in the Atlantic Forest in Rio de Janeiro: a molecular epidemiological investigation. *Lancet Glob Health*, 5, e1038-e1046.
- BROCK, P. M., FORNACE, K. M., GRIGG, M. J., ANSTEY, N. M., WILLIAM, T., COX, J., DRAKELEY, C. J., FERGUSON, H. M. & KAO, R. R. 2019. Predictive analysis across spatial scales links zoonotic malaria to deforestation. *Proceedings of the Royal Society B*, 286.
- BROCK, P. M., FORNACE, K. M., PARMITER, M., COX, J., DRAKELEY, C. J., FERGUSON, H. M. & KAO, R. R. 2016. *Plasmodium knowlesi* transmission: integrating quantitative approaches from epidemiology and ecology to understand malaria as a zoonosis. *Parasitology*, 143, 389-400.
- BRONNER, U., DIVIS, P. C., FARNERT, A. & SINGH, B. 2009. Swedish traveller with *Plasmodium knowlesi* malaria after visiting Malaysian Borneo. *Malar J*, 8, 15.
- BROWN, R., CHUA, T. H., FORNACE, K., DRAKELEY, C., VYTHILINGAM, I. & FERGUSON, H. M. 2020. Human exposure to zoonotic malaria vectors in village, farm and forest habitats in Sabah, Malaysian Borneo. *PLoS Neglected Tropical Diseases [electronic resource]*, 14, e0008617.
- BRUUN, B. & AAGAARD-HANSEN, J. 2008. The social context of schistosomiasis and its control: an introduction and annotated bibliography. Geneva: World Health Organization.
- BRYAN, J. E., SHEARMAN, P. L., ASNER, G. P., KNAPP, D. E., AORO, G. & LOKES, B. 2013. Extreme differences in forest degradation in Borneo: comparing practices in Sarawak, Sabah, and Brunei. *PLoS One*, 8, e69679.
- BUSCH, J., FERRETTI-GALLON, K., ENGELMANN, J., WRIGHT, M., AUSTIN, K. G., STOLLE, F., TURUBANOVA, S., POTAPOV, P. V., MARGONO, B., HANSEN, M. C. & BACCINI, A. 2015. Reductions in emissions from deforestation from Indonesia's moratorium on new oil palm, timber, and logging concessions. *Proc Natl Acad Sci U S A*, 112, 1328-33.
- CARRASCO-ESCOBAR, G., CASTRO, M. C., BARBOZA, J. L., RUIZ-CABREJOS, J., LLANOS-CUENTAS, A., VINETZ, J. M. & GAMBOA, D. 2019. Use of open mobile mapping tool to assess human mobility traceability in rural offline populations with contrasting malaria dynamics. *PeerJ*, 7, e6298.
- CARVALHO, R. M. & NASCIMENTO, L. F. 2012. Spatial distribution of dengue in the city of Cruzeiro, Sao Paulo State, Brazil: use of geoprocessing tools. *Rev Inst Med Trop Sao Paulo*, 54, 261-6.
- CHAPMAN, C. A., GILLESPIE, T. R. & SPEIRS, M. L. 2005. Parasite prevalence and richness in sympatric colobines: effects of host density. *Am J Primatol*, 67, 259-66.
- CHAPMAN, C. A., SPEIRS, M. L., GILLESPIE, T. R., HOLLAND, T. & AUSTAD, K. M. 2006. Life on the edge: gastrointestinal parasites from the forest edge and interior primate groups. *Am J Primatol*, 68, 397-409.
- CHEN, J., FRANKLIN, J. F. & SPIES, T. A. 1995. Growing-Season Microclimatic Gradients from Clearcut Edges into Old-Growth Douglas-Fir Forests. *Ecological Applications*, 5, 74-86.
- CHEN, J., SAUNDERS, S. C., CROW, T. R., NAIMAN, R. J., BROSOFSKE, K. D., MROZ, G. D., BROOKSHIRE, B. L. & FRANKLIN, J. F. 1999. Microclimate in Forest Ecosystem and Landscape Ecology: Variations in local climate can be used to monitor and compare the effects of different management regimes. *Bioscience*, 49, 288-297.
- CHIN, A. Z., MALUDA, M. C. M., JELIP, J., JEFFREE, M. S. B., CULLETON, R. & AHMED, K. 2020a. Malaria elimination in Malaysia and the rising threat of *Plasmodium knowlesi*. *Journal of physiological anthropology*, 39, 36-36.
- CHIN, A. Z., MALUDA, M. C. M., JELIP, J., JEFFREE, M. S. B., CULLETON, R. & AHMED, K. 2020b. Malaria elimination in Malaysia and the rising threat of *Plasmodium knowlesi*. *J Physiol Anthropol*, 39, 36.
- CHIN, W., CONTACTOS, P. G., COATNEY, G. R. & KIMBALL, H. R. 1965. A Naturally Acquired Quotidian-Type Malaria in Man Transferable to Monkeys. *Science*, 149, 865.

- CHIN, W., CONTACOS, P. G., COLLINS, W. E., JETER, M. H. & ALPERT, E. 1968. Experimental mosquito-transmission of *Plasmodium knowlesi* to man and monkey. *Am J Trop Med Hyg*, 17, 355-8.
- CHINH, V. D., MASUDA, G., HUNG, V. V., TAKAGI, H., KAWAI, S., ANNOURA, T. & MAENO, Y. 2019. Prevalence of human and non-human primate *Plasmodium* parasites in anopheline mosquitoes: a cross-sectional epidemiological study in Southern Vietnam. *Tropical Medicine & Health*, 47, 9.
- CHOISY, M. & ROHANI, P. 2006. Harvesting can increase severity of wildlife disease epidemics. *Proc Biol Sci*, 273, 2025-34.
- CHUA, T. H., MANIN, B. O., DAIM, S., VYTHILINGAM, I. & DRAKELEY, C. 2017. Phylogenetic analysis of simian *Plasmodium* spp. infecting *Anopheles balabacensis* Baisas in Sabah, Malaysia. *PLoS Negl Trop Dis*, 11, e0005991.
- CLEMENTS, A. C., REID, H. L., KELLY, G. C. & HAY, S. I. 2013. Further shrinking the malaria map: how can geospatial science help to achieve malaria elimination? *Lancet Infect Dis*, 13, 709-18.
- COATNEY, G. R. 1963. Simian malaria. Its importance to worldwide eradication of malaria. *JAMA*, 184, 876-7.
- COATNEY, G. R., CHIN, W., CONTACOS, P. G. & KING, H. K. 1966. *Plasmodium inui*, a quartan-type malaria parasite of Old World monkeys transmissible to man. *Journal of Parasitology*, 52, 660-3.
- COATNEY, G. R., COLLINS, W. E., WARREN, M. & CONTACOS, P. G. 1971. *The primate malarias*, Atlanta, GA, The Division of Parasitic Diseases of the Centers for Disease Control and Prevention.
- COLLINGE, S. K. 1996. Ecological consequences of habitat fragmentation: implications for landscape architecture and planning. *Landscape and Urban Planning*, 36, 59-77.
- COLLINS, W. E., CONTACOS, P. G. & GUINN, E. G. 1967. Studies on the transmission of simian malarias. II. Transmission of the H strain of *Plasmodium knowlesi* by *Anopheles balabacensis* *balabacensis*. *J Parasitol*, 53, 841-4.
- COMTE, S., RATON, V., RAOUL, F., HEGGLIN, D., GIRAUDOUX, P., DEPLAZES, P., FAVIER, S., GOTTSCHKE, D., UMHANG, G., BOUE, F. & COMBES, B. 2013. Fox baiting against *Echinococcus multilocularis*: Contrasted achievements among two medium size cities. *Preventive Veterinary Medicine*, 111, 147-155.
- CONTACOS, P. G., ELDER, H. A. & COATNEY, G. R. 1962. MAN to MAN TRANSFER of TWO STRAINS of PLASMODIUM CYNOMOLGI by MOSQUITO BITE. *Md*, 186-193.
- COOK, J., REID, H., IAVRO, J., KUWAHATA, M., TALEO, G., CLEMENTS, A., MCCARTHY, J., VALLELY, A. & DRAKELEY, C. 2010. Using serological measures to monitor changes in malaria transmission in Vanuatu. *Malar J*, 9, 169.
- CORDINA, C. J., CULLETON, R., JONES, B. L., SMITH, C. C., MACCONNACHIE, A. A., COYNE, M. J. & ALEXANDER, C. L. 2014. *Plasmodium knowlesi*: clinical presentation and laboratory diagnosis of the first human case in a Scottish traveler. *J Travel Med*, 21, 357-60.
- CORRAN, P., COLEMAN, P., RILEY, E. & DRAKELEY, C. 2007. Serology: a robust indicator of malaria transmission intensity? *Trends Parasitol*, 23, 575-82.
- COTTER, C., STURROCK, H. J., HSIANG, M. S., LIU, J., PHILLIPS, A. A., HWANG, J., GUEYE, C. S., FULLMAN, N., GOSLING, R. D. & FEACHEM, R. G. 2013. The changing epidemiology of malaria elimination: new strategies for new challenges. *Lancet*, 382, 900-11.
- COUTO-LIMA, D., MADEC, Y., BERSOT, M. I., CAMPOS, S. S., MOTTA, M. A., SANTOS, F. B. D., VAZEILLE, M., VASCONCELOS, P., LOURENCO-DE-OLIVEIRA, R. & FAILLOUX, A. B. 2017. Potential risk of re-emergence of urban transmission of Yellow Fever virus in Brazil facilitated by competent *Aedes* populations. *Sci Rep*, 7, 4848.
- COUTRIER, F. N., TIRTA, Y. K., COTTER, C., ZARLINDA, I., GONZALEZ, I. J., SCHWARTZ, A., MANEH, C., MARFURT, J., MURPHY, M., HERDIANA, H., ANSTEY, N. M., GREENHOUSE, B., HSIANG, M. S. & NOVIYANTI, R. 2018. Laboratory challenges of *Plasmodium* species identification in Aceh

- Province, Indonesia, a malaria elimination setting with newly discovered *P. knowlesi*. *PLoS Negl Trop Dis*, 12, e0006924.
- COX-SINGH, J., DAVIS, T. M., LEE, K. S., SHAMSUL, S. S., MATUSOP, A., RATNAM, S., RAHMAN, H. A., CONWAY, D. J. & SINGH, B. 2008. Plasmodium knowlesi malaria in humans is widely distributed and potentially life threatening. *Clin Infect Dis*, 46, 165-71.
- COX-SINGH, J. & SINGH, B. 2008. Knowlesi malaria: newly emergent and of public health importance? *Trends Parasitol*, 24, 406-10.
- CROSS, M. L., BUDDLE, B. M. & ALDWELL, F. E. 2007. The potential of oral vaccines for disease control in wildlife species. *Vet J*, 174, 472-80.
- CROWL, T. A., CRIST, T. O., PARMENTER, R. R., BELOVSKY, G. & LUGO, A. E. 2008. The spread of invasive species and infectious disease as drivers of ecosystem change. *Frontiers in Ecology and the Environment*, 6, 238-246.
- CURTIS, P. G., SLAY, C. M., HARRIS, N. L., TYUKAVINA, A. & HANSEN, M. C. 2018. Classifying drivers of global forest loss. *Science*, 361, 1108-1111.
- CUSHMAN, S. A., MACDONALD, E. A., LANDGUTH, E. L., MALHI, Y. & MACDONALD, D. W. 2017. Multiple-scale prediction of forest loss risk across Borneo. *Landscape Ecology*, 32, 1581-1598.
- DA SILVA-NUNES, M., CODECO, C. T., MALAFRONTI, R. S., DA SILVA, N. S., JUNCANSEN, C., MUNIZ, P. T. & FERREIRA, M. U. 2008. Malaria on the Amazonian frontier: transmission dynamics, risk factors, spatial distribution, and prospects for control. *Am J Trop Med Hyg*, 79, 624-35.
- DANESHVAR, C., DAVIS, T. M., COX-SINGH, J., RAFA'EE, M. Z., ZAKARIA, S. K., DIVIS, P. C. & SINGH, B. 2009. Clinical and laboratory features of human Plasmodium knowlesi infection. *Clin Infect Dis*, 49, 852-60.
- DANYLO, O., PIRKER, J., LEMOINE, J., CECCHERINI, G., SEE, L., MCCALLUM, I., HADI, KRAXNER, F., ACHARD, F. & FRITZ, S. 2021. A map of the extent and year of detection of oil palm plantations in Indonesia, Malaysia and Thailand. *Scientific Data*, 8.
- DE ANDRADE, F. A., GOMES, M. N., UIEDA, W., BEGOT, A. L., RAMOS ODE, S. & FERNANDES, M. E. 2016. Geographical Analysis for Detecting High-Risk Areas for Bovine/Human Rabies Transmitted by the Common Hematophagous Bat in the Amazon Region, Brazil. *PLoS One*, 11, e0157332.
- DE ANG, J. X., YAMAN, K., KADIR, K. A., MATUSOP, A. & SINGH, B. 2021. New vectors that are early feeders for Plasmodium knowlesi and other simian malaria parasites in Sarawak, Malaysian Borneo. *Sci Rep*, 11, 7739.
- DE CANALE, E., SGARABOTTO, D., MARINI, G., MENEGOTTO, N., MASIERO, S., AKKOUCHE, W., BIASOLO, M. A., BARZON, L. & PALU, G. 2017. Plasmodium knowlesi malaria in a traveller returning from the Philippines to Italy, 2016. *New Microbiologica*, 40, 291-294.
- DE CASTRO, M. C., MONTE-MOR, R. L., SAWYER, D. O. & SINGER, B. H. 2006. Malaria risk on the Amazon frontier. *Proc Natl Acad Sci U S A*, 103, 2452-7.
- DE DEYN, G. B., CORNELISSEN, J. H. & BARDGETT, R. D. 2008. Plant functional traits and soil carbon sequestration in contrasting biomes. *Ecol Lett*, 11, 516-31.
- DEARWENT, S. M., JACOBS, R. R. & HALBERT, J. B. 2001. Locational uncertainty in georeferencing public health datasets. *J Expo Anal Environ Epidemiol*, 11, 329-34.
- DESJEUX, P. 2001. The increase in risk factors for leishmaniasis worldwide. *Trans R Soc Trop Med Hyg*, 95, 239-43.
- DESPOMMIER, D., ELLIS, B. R. & WILCOX, B. A. 2006. The role of ecotones in emerging infectious diseases. *Ecohealth*, 3, 281-289.
- DIVIS, P. C., SINGH, B., ANDERIOS, F., HISAM, S., MATUSOP, A., KOCKEN, C. H., ASSEFA, S. A., DUFFY, C. W. & CONWAY, D. J. 2015. Admixture in Humans of Two Divergent Plasmodium knowlesi Populations Associated with Different Macaque Host Species. *PLoS Pathog*, 11, e1004888.

- DOBSON, A. 2004. Population dynamics of pathogens with multiple host species. *Am Nat*, 164 Suppl 5, S64-78.
- DONNELLY, C. A. & WOODROFFE, R. 2015. Badger-cull targets unlikely to reduce TB. *Nature*, 526, 640-640.
- DOUINE, M., LAMBERT, Y., MUSSET, L., HIWAT, H., BLUME, L. R., MARCHESINI, P., MORESCO, G. G., COX, H., SANCHEZ, J. F., VILLEGAS, L., DE SANTI, V. P., SANNA, A., VREDEN, S. & SUAREZ-MUTIS, M. 2020. Malaria in Gold Miners in the Guianas and the Amazon: Current Knowledge and Challenges. *Current Tropical Medicine Reports*, 7, 37-47.
- DRAKELEY, C. J., CORRAN, P. H., COLEMAN, P. G., TONGREN, J. E., MCDONALD, S. L., CARNEIRO, I., MALIMA, R., LUSINGU, J., MANJURANO, A., NKYA, W. M., LEMNGE, M. M., COX, J., REYBURN, H. & RILEY, E. M. 2005. Estimating medium- and long-term trends in malaria transmission by using serological markers of malaria exposure. *Proc Natl Acad Sci U S A*, 102, 5108-13.
- DRUETZ, T., STRESMAN, G., ASHTON, R. A., VAN DEN HOOGEN, L. L., JOSEPH, V., FAYETTE, C., MONESTIME, F., HAMRE, K. E., CHANG, M. A., LEMOINE, J. F., DRAKELEY, C. & EISELE, T. P. 2020. Programmatic options for monitoring malaria in elimination settings: easy access group surveys to investigate Plasmodium falciparum epidemiology in two regions with differing endemicity in Haiti. *BMC Med*, 18, 141.
- DUBEY, S., SINGH, R., GUPTA, B., PATEL, R., SONI, D., DHAKAD, B. M. S., REDDY, B. M., GUPTA, S. & SHARMA, N. 2021. Leptospira: An emerging zoonotic pathogen of climate change, global warming and unplanned urbanization: A review. *Journal of Entomology and Zoology Studies*, 9, 564-571.
- DUCHEYNE, E., MWEEMPWA, C., DE PUS, C., VERNIEUWE, H., DE DEKEN, R., HENDRICKX, G. & VAN DEN BOSSCHE, P. 2009. The impact of habitat fragmentation on tsetse abundance on the plateau of eastern Zambia. *Prev Vet Med*, 91, 11-8.
- DURNEZ, L., MAO, S., DENIS, L., ROELANTS, P., SOCHANATHA, T. & COOSEMANS, M. 2013. Outdoor malaria transmission in forested villages of Cambodia. *Malar J*, 12, 329.
- DUTTA, G. P., SINGH, P. P. & BANYAL, H. S. 1978. Macaca assamensis as a new host for experimental Plasmodium knowlesi infection. *Indian Journal of Medical Research*, 68, 923-6.
- EDWARDS, H. M., SRIWICHAJ, P., KIRABITTIR, K., PRACHUMSRI, J., CHAVEZ, I. F. & HII, J. 2019. Transmission risk beyond the village: entomological and human factors contributing to residual malaria transmission in an area approaching malaria elimination on the Thailand-Myanmar border. *Malar J*, 18, 221.
- ESTOQUE, R. C., Ooba, M., AVITABILE, V., HIJIOKA, Y., DASGUPTA, R., TOGAWA, T. & MURAYAMA, Y. 2019. The future of Southeast Asia's forests. *Nat Commun*, 10, 1829.
- EYLES, D. E., COATNEY, G. R. & GETZ, M. E. 1960. Vivax-type malaria parasite of macaques transmissible to man. *Science*, 131, 1812-3.
- EYLES, D. E., LAING, A. B. G., WARREN, M. W. & SANDOSHAM, A. A. 1962. Malaria parasites of Malayan leaf monkeys of the genus Presbytis. *Med J Malaya*, 17, 85-86.
- FAO 2020. Global Forest Resources Assessment 2020: Main Report. Rome: Food and Agriculture Organization of the United Nations.
- FEDDEMA, J. J., OLESON, K. W., BONAN, G. B., MEARN, L. O., BUJA, L. E., MEEHL, G. A. & WASHINGTON, W. M. 2005. The importance of land-cover change in simulating future climates. *Science*, 310, 1674-8.
- FERRARI, M. J., DJIBO, A., GRAIS, R. F., BHARTI, N., GRENFELL, B. T. & BJORNSTAD, O. N. 2010. Rural-urban gradient in seasonal forcing of measles transmission in Niger. *Proc Biol Sci*, 277, 2775-82.
- FERRARI, M. J., PERKINS, S. E., POMEROY, L. W. & BJORNSTAD, O. N. 2011. Pathogens, social networks, and the paradox of transmission scaling. *Interdiscip Perspect Infect Dis*, 2011, 267049.

- FIGTREE, M., LEE, R., BAIN, L., KENNEDY, T., MACKERTICH, S., URBAN, M., CHENG, Q. & HUDSON, B. J. 2010. Plasmodium knowlesi in human, Indonesian Borneo. *Emerg Infect Dis*, 16, 672-4.
- FLORENTINUS, S. R., SOUVEREIN, P. C., GRIENS, F. A., GROENEWEGEN, P. P., LEUFKENS, H. G. & HEERDINK, E. R. 2006. Linking community pharmacy dispensing data to prescribing data of general practitioners. *BMC Med Inform Decis Mak*, 6, 18.
- FOODEN, J. 1995. Systematic Review of Southeast Asian Longtail Macaques *Macaca fascicularis. Fieldiana*, 81.
- FORNACE, K. M., ABIDIN, T. R., ALEX, ER, N., BROCK, P., GRIGG, M. J., MURPHY, A., WILLIAM, T., MENON, J., DRAKELEY, C. J. & COX, J. 2016a. Association between Landscape Factors and Spatial Patterns of Plasmodium knowlesi Infections in Sabah, Malaysia. *Emerging Infectious Diseases*, 22, 201-8.
- FORNACE, K. M., ALEX, ER, N., ABIDIN, T. R., BROCK, P. M., CHUA, T. H., VYTHILINGAM, I., FERGUSON, H. M., MANIN, B. O., WONG, M. L., NG, S. H., COX, J. & DRAKELEY, C. 2019a. Local human movement patterns and land use impact exposure to zoonotic malaria in Malaysian Borneo. *eLife*, 8, 22.
- FORNACE, K. M., BROCK, P. M., ABIDIN, T. R., GRIGNARD, L., HERMAN, L. S., CHUA, T. H., DAIM, S., WILLIAM, T., PATTERSON, C. L. E. B., HALL, T., GRIGG, M. J., ANSTEY, N. M., TETTEH, K. K. A., COX, J. & DRAKELEY, C. J. 2019b. Environmental risk factors and exposure to the zoonotic malaria Plasmodium knowlesi across Northern Sabah, Malaysia: a cross-sectional survey. *Lancet Planet Health*, 3, E179-E186.
- FORNACE, K. M., DIAZ, A. V., LINES, J. & DRAKELEY, C. J. 2020. Achieving global malaria eradication in changing landscapes.
- FORNACE, K. M., DIAZ, A. V., LINES, J. & DRAKELEY, C. J. 2021. Achieving global malaria eradication in changing landscapes. *Malar J*, 20, 69.
- FORNACE, K. M., HERMAN, L. S., ABIDIN, T. R., CHUA, T. H., DAIM, S., LORENZO, P. J., GRIGNARD, L., NUIN, N. A., YING, L. T., GRIGG, M. J., WILLIAM, T., ESPINO, F., COX, J., TETTEH, K. K. A. & DRAKELEY, C. J. 2018a. Exposure and infection to Plasmodium knowlesi in case study communities in Northern Sabah, Malaysia and Palawan, The Philippines. *PLoS Negl Trop Dis*, 12, e0006432.
- FORNACE, K. M., NUIN, N. A., BETSON, M., GRIGG, M. J., WILLIAM, T., ANSTEY, N. M., YEO, T. W., COX, J., YING, L. T. & DRAKELEY, C. J. 2015. Asymptomatic and Submicroscopic Carriage of Plasmodium knowlesi Malaria in Household and Community Members of Clinical Cases in Sabah, Malaysia. *J Infect Dis*.
- FORNACE, K. M., NUIN, N. A., BETSON, M., GRIGG, M. J., WILLIAM, T., ANSTEY, N. M., YEO, T. W., COX, J., YING, L. T. & DRAKELEY, C. J. 2016b. Asymptomatic and Submicroscopic Carriage of Plasmodium knowlesi Malaria in Household and Community Members of Clinical Cases in Sabah, Malaysia. *J Infect Dis*, 213, 784-7.
- FORNACE, K. M., REYES, R. A., MACALINAO, M. L. M., BARENG, A. P. N., LUCHAVEZ, J. S., HAFALLA, J. C., ESPINO, F. E. & DRAKELEY, C. J. 2020. Disentangling fine-scale effects of environment on malaria detection and infection to design risk-based disease surveillance systems in changing landscapes. *medRxiv*.
- FORNACE, K. M., SURENDRA, H., ABIDIN, T. R., REYES, R., MACALINAO, M. L. M., STRESMAN, G., LUCHAVEZ, J., AHMAD, R. A., SUPARGIYONO, S., ESPINO, F., DRAKELEY, C. J. & COOK, J. 2018b. Use of mobile technology-based participatory mapping approaches to geolocate health facility attendees for disease surveillance in low resource settings. *Int J Health Geogr*, 17, 21.
- FOSTER, D., COX-SINGH, J., MOHAMAD, D. S., KRISHNA, S., CHIN, P. P. & SINGH, B. 2014. Evaluation of three rapid diagnostic tests for the detection of human infections with Plasmodium knowlesi. *Malar J*, 13, 60.

- FUNGFUANG, W., UDOM, C., TONGTHAINAN, D., KADIR, K. A. & SINGH, B. 2020. Malaria parasites in macaques in Thailand: stump-tailed macaques (*Macaca arctoides*) are new natural hosts for *Plasmodium knowlesi*, *Plasmodium inui*, *Plasmodium coatneyi* and *Plasmodium fieldi*. *Malar J*, 19, 350.
- GACHELIN, G. & OPINEL, A. 2011. Malaria epidemics in Europe after the First World War: the early stages of an international approach to the control of the disease. *História, Ciências, Saúde-Manguinhos*, 18, 431-470.
- GAMALO, L. E., DIMALIBOT, J., KADIR, K. A., SINGH, B. & PALLER, V. G. 2019. *Plasmodium knowlesi* and other malaria parasites in long-tailed macaques from the Philippines. *Malar J*, 18, 147.
- GAVEAU, D. L., LOCATELLI, B., SALIM, M. A., HUSNAYAEN, MANURUNG, T., DESCALS, A., ANGELSEN, A., MEIJAARD, E. & SHEIL, D. 2021. Slowing deforestation in Indonesia follows declining oil palm expansion and lower oil prices. *Research Square*.
- GAVEAU, D. L., SHEIL, D., HUSNAYAEN, SALIM, M. A., ARJASAKUSUMA, S., ANCRENAZ, M., PACHECO, P. & MEIJAARD, E. 2016. Rapid conversions and avoided deforestation: examining four decades of industrial plantation expansion in Borneo. *Sci Rep*, 6, 32017.
- GHINAI, I., COOK, J., HLA, T. T., HTET, H. M., HALL, T., LUBIS, I. N., GHINAI, R., HESKETH, T., NAUNG, Y., LWIN, M. M., LATT, T. S., HEYMANN, D. L., SUTHERLAND, C. J., DRAKELEY, C. & FIELD, N. 2017. Malaria epidemiology in central Myanmar: identification of a multi-species asymptomatic reservoir of infection. *Malar J*, 16, 16.
- GIBB, R., MOSES, L. M., REDDING, D. W. & JONES, K. E. 2017. Understanding the cryptic nature of Lassa fever in West Africa. *Pathog Glob Health*, 111, 276-288.
- GILES, J. R., EBY, P., PARRY, H., PEEL, A. J., PLOWRIGHT, R. K., WESTCOTT, D. A. & MCCALLUM, H. 2018. Environmental drivers of spatiotemporal foraging intensity in fruit bats and implications for Hendra virus ecology. *Sci Rep*, 8, 9555.
- GILLESPIE, T. R. & CHAPMAN, C. A. 2006. Prediction of parasite infection dynamics in primate metapopulations based on attributes of forest fragmentation. *Conserv Biol*, 20, 441-8.
- GOTTDENKER, N. L., STREICKER, D. G., FAUST, C. L. & CARROLL, C. R. 2014. Anthropogenic land use change and infectious diseases: a review of the evidence. *Ecohealth*, 11, 619-32.
- GRIGG, M. J., COX, J., WILLIAM, T., JELIP, J., FORNACE, K. M., BROCK, P. M., VON SEIDLEIN, L., BARBER, B. E., ANSTEY, N. M., YEO, T. W. & DRAKELEY, C. J. 2017. Individual-level factors associated with the risk of acquiring human *Plasmodium knowlesi* malaria in Malaysia: a case control study. *Lancet Planetary Health*, 1, e97-104.
- GRIGG, M. J., WILLIAM, T., BARBER, B. E., PARAMESWARAN, U., BIRD, E., PIERA, K., AZIZ, A., DHANARAJ, P., YEO, T. W. & ANSTEY, N. M. 2014. Combining parasite lactate dehydrogenase-based and histidine-rich protein 2-based rapid tests to improve specificity for diagnosis of malaria Due to *Plasmodium knowlesi* and other *Plasmodium* species in Sabah, Malaysia. *J Clin Microbiol*, 52, 2053-60.
- GRIGG, M. J., WILLIAM, T., MENON, J., DHANARAJ, P., BARBER, B. E., WILKES, C. S., VON SEIDLEIN, L., RAJAHRAM, G. S., PASAY, C., MCCARTHY, J. S., PRICE, R. N., ANSTEY, N. M. & YEO, T. W. 2016. Artesunate-mefloquine versus chloroquine for treatment of uncomplicated *Plasmodium knowlesi* malaria in Malaysia (ACT KNOW): an open-label, randomised controlled trial. *Lancet Infect Dis*, 16, 180-8.
- GRIGNARD, L., SHAH, S., CHUA, T. H., WILLIAM, T., DRAKELEY, C. J. & FORNACE, K. M. 2019. Natural Human Infections With *Plasmodium cynomolgi* and Other Malaria Species in an Elimination Setting in Sabah, Malaysia. *Journal of Infectious Diseases*, 220, 1946-1949.
- GROGAN, K., PFLUGMACHER, D., HOSTERT, P., MERTZ, O. & FENSHOLT, R. 2019. Unravelling the link between global rubber price and tropical deforestation in Cambodia. *Nat Plants*, 5, 47-53.

- GRYSEELS, C., DURNEZ, L., GERRETS, R., UK, S., SUON, S., SET, S., PHOEUK, P., SLUYDTS, V., HENG, S., SOCHANATHA, T., COOSEMANS, M. & PEETERS GRIETENS, K. 2015. Re-imagining malaria: heterogeneity of human and mosquito behaviour in relation to residual malaria transmission in Cambodia. *Malar J*, 14, 165.
- GUERRA, C. A., SNOW, R. W. & HAY, S. I. 2006. A global assessment of closed forests, deforestation and malaria risk. *Ann Trop Med Parasitol*, 100, 189-204.
- GUIMARAES, L. O., BAJAY, M. M., WUNDERLICH, G., BUENO, M. G., ROHE, F., CATAO-DIAS, J. L., NEVES, A., MALAFRONTA, R. S., CURADO, I. & KIRCHGATTER, K. 2012. The genetic diversity of *Plasmodium malariae* and *Plasmodium brasilianum* from human, simian and mosquito hosts in Brazil. *Acta Trop*, 124, 27-32.
- GUIVIER, E., GALAN, M., CHAVAL, Y., XUEREB, A., RIBAS SALVADOR, A., POULLE, M. L., VOUTILAINEN, L., HENTTONEN, H., CHARBONNEL, N. & COSSON, J. F. 2011. Landscape genetics highlights the role of bank vole metapopulation dynamics in the epidemiology of Puumala hantavirus. *Mol Ecol*, 20, 3569-83.
- HAHN, M. B., GANGNON, R. E., BARCELLOS, C., ASNER, G. P. & PATZ, J. A. 2014. Influence of deforestation, logging, and fire on malaria in the Brazilian Amazon. *PLoS One*, 9, e85725.
- HALLIDAY, F. W., ROHR, J. R. & LAINE, A. L. 2020. Biodiversity loss underlies the dilution effect of biodiversity. *Ecol Lett*, 23, 1611-1622.
- HALSEY, E. S. & MILLER, J. R. 2020. Maintenance of *Borrelia burgdorferi* among vertebrate hosts: a test of dilution effect mechanisms. *Ecosphere*, 11.
- HAMBALI, K. A., ISMAIL, A. H. & ZULKIFLI, S. Y. Z. 2012. Human-macaque conflict and pest behaviors of Long-tailed macaques (*Macaca fascicularis*) in Kuala Selangor Nature Park. *Tropical Natural History*, 12, 189-205.
- HAN, D., BONNER, M. R., NIE, J. & FREUDENHEIM, J. L. 2013. Assessing bias associated with geocoding of historical residence in epidemiology research. *Geospat Health*, 7, 369-74.
- HANSEN, M. C., KRYLOV, A., TYUKAVINA, A., POTAPOV, P. V., TURUBANOVA, S., ZUTTA, B., IFO, S., MARGONO, B. A., STOLLE, F. & MOORE, R. 2016. Humid tropical forest disturbance alerts using Landsat data. *Environmental Research Letters*, 11.
- HANSEN, M. C., POTAPOV, P. V., MOORE, R., HANCHER, M., TURUBANOVA, S. A., TYUKAVINA, A., THAU, D., STEHMAN, S. V., GOETZ, S. J., LOVELAND, T. R., KOMMAREDDY, A., EGOROV, A., CHINI, L., JUSTICE, C. O. & TOWNSHEND, J. R. 2013. High-resolution global maps of 21st-century forest cover change. *Science*, 342, 850-3.
- HANSEN, M. C., STEHMAN, S. V., POTAPOV, P. V., LOVELAND, T. R., TOWNSHEND, J. R., DEFRIES, R. S., PITTMAN, K. W., ARUNARWATI, B., STOLLE, F., STEININGER, M. K., CARROLL, M. & DIMICELI, C. 2008. Humid tropical forest clearing from 2000 to 2005 quantified by using multitemporal and multiresolution remotely sensed data. *Proc Natl Acad Sci U S A*, 105, 9439-44.
- HAUSERMANN, H., TSCHAKERT, P., SMITHWICK, E. A. H., FERRING, D., AMANKWAH, R., KLUTSE, E., HAGARTY, J. & KROMEL, K. 2012. Contours of risk: spatialising human behaviours to understand disease dynamics in changing landscapes. *Ecohealth*, 9, 251-255.
- HAWKES, F. M., MANIN, B. O., COOPER, A., DAIM, S., HOMATHEVI, R., JELIP, J., HUSIN, T. & CHUA, T. H. 2019. Vector compositions change across forested to deforested ecotones in emerging areas of zoonotic malaria transmission in Malaysia. *Scientific Reports*, 9.
- HAY, S. I., BATTLE, K. E., PIGOTT, D. M., SMITH, D. L., MOYES, C. L., BHATT, S., BROWNSTEIN, J. S., COLLIER, N., MYERS, M. F., GEORGE, D. B. & GETHING, P. W. 2013. Global mapping of infectious disease. *Philos Trans R Soc Lond B Biol Sci*, 368, 20120250.
- HERDIANA, H., COTTER, C., COUTRIER, F. N., ZARLINDA, I., ZELMAN, B. W., TIRTA, Y. K., GREENHOUSE, B., GOSLING, R. D., BAKER, P., WHITTAKER, M. & HSIANG, M. S. 2016. Malaria risk factor assessment using active and passive surveillance data from Aceh Besar, Indonesia, a low

- endemic, malaria elimination setting with *Plasmodium knowlesi*, *Plasmodium vivax*, and *Plasmodium falciparum*. *Malar J*, 15, 468.
- HERDIANA, H., IRNAWATI, I., COUTRIER, F. N., MUNTHE, A., MARDIATI, M., YUNIARTI, T., SARIWATI, E., SUMIWI, M. E., NOVIYANTI, R., PRONYK, P. & HAWLEY, W. A. 2018a. Two clusters of *Plasmodium knowlesi* cases in a malaria elimination area, Sabang Municipality, Aceh, Indonesia. *Malaria Journal*, 17, 186.
- HERDIANA, H., IRNAWATI, I., COUTRIER, F. N., MUNTHE, A., MARDIATI, M., YUNIARTI, T., SARIWATI, E., SUMIWI, M. E., NOVIYANTI, R., PRONYK, P. & HAWLEY, W. A. 2018b. Two clusters of *Plasmodium knowlesi* cases in a malaria elimination area, Sabang Municipality, Aceh, Indonesia. *Malar J*, 17, 186.
- HERMAN, L. S., FORNACE, K., PHELAN, J., GRIGG, M. J., ANSTEY, N. M., WILLIAM, T., MOON, R. W., BLACKMAN, M. J., DRAKELEY, C. J. & TETTEH, K. K. A. 2018. Identification and validation of a novel panel of *Plasmodium knowlesi* biomarkers of serological exposure. *PLoS Negl Trop Dis*, 12, e0006457.
- HERRERA-SILVEIRA, J. A. & RAMIREZ-RAMIREZ, J. 1996. Effects of natural phenolic material (tannin) on phytoplankton growth. *Limnology and Oceanography*, 41, 1018-1023.
- HIL, J. 1985. Anopheles malaria vector in Malaysia with reference to Sabah. In: HARINASUTA, R. (ed.) *Problems of malaria in endemic countries*. Tokyo: Southeast Asian Medical Information Centre.
- HIJIOKA, Y., LIN, E., PEREIRA, J. J., CORLETT, R. T., CUI, X., INSAROV, G. E., LASCO, R. D., LINDGREN, E. & SURJAN, A. 2014. Asia. In: BARROS, V. R., FIELD, C. B., DOKKEN, D. J., MASTRANDREA, M. D., MACH, K. J., BILIR, T. E., CHATTERJEE, M., EBI, K. L., ESTRADA, Y., GENOVA, R. C., GIRMA, B., KISSEL, E. S., LEVY, A. N., MACCRACKEN, S., MASTRANDREA, P. R. & WHITE, L. (eds.) *Climate Change 2014: Impacts, Adaptation and Vulnerability. Part B: Regional Aspects. Contribution of Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change*. Cambridge, UK and New York, USA: Cambridge University Press.
- HOUSEN, A. & SHAW, M. T. 2011. *Plasmodium knowlesi* in a traveller returning to New Zealand. *Travel Med Infect Dis*, 9, 144-8.
- IMAI, N., WHITE, M. T., GHANI, A. C. & DRAKELEY, C. J. 2014. Transmission and control of *Plasmodium knowlesi*: a mathematical modelling study. *PLoS Negl Trop Dis*, 8, e2978.
- IMWONG, M., MADMANEE, W., SUWANNASIN, K., KUNASOL, C., PETO, T. J., TRIPURA, R., VON SEIDLEIN, L., NGUON, C., DAVOEUNG, C., DAY, N. P. J., DONDORP, A. M. & WHITE, N. J. 2018. Asymptomatic Natural Human Infections With the Simian Malaria Parasites *Plasmodium cynomolgi* and *Plasmodium knowlesi*. *J Infect Dis*.
- IMWONG, M., MADMANEE, W., SUWANNASIN, K., KUNASOL, C., PETO, T. J., TRIPURA, R., VON SEIDLEIN, L., NGUON, C., DAVOEUNG, C., DAY, N. P. J., DONDORP, A. M. & WHITE, N. J. 2019. Asymptomatic Natural Human Infections With the Simian Malaria Parasites *Plasmodium cynomolgi* and *Plasmodium knowlesi*. *Journal of Infectious Diseases*, 219, 695-702.
- INADA, R., KITAJIMA, K., HARDIWINOTO, S. & KANZAKI, M. 2017. The effect of logging and strip cutting on forest floor light condition and following change. *Forests*, 8, 425.
- IWAGAMI, M., NAKATSU, M., KHATTIGNAVONG, P., SOUNDALA, P., LORPHACHAN, L., KEOMALAPHET, S., XANGSAYALATH, P., KAWAI, S., HONGVANTHONG, B., BREY, P. T. & KANO, S. 2018. First case of human infection with *Plasmodium knowlesi* in Laos. *PLoS Negl Trop Dis*, 12, e0006244.
- JACQUOT, M., ABRIAL, D., GASQUI, P., BORD, S., MARSOT, M., MASSEGLIA, S., PION, A., POUX, V., ZILLIOX, L., CHAPUIS, J. L., VOUREC'H, G. & BAILLY, X. 2016. Multiple independent transmission cycles of a tick-borne pathogen within a local host community. *Sci Rep*, 6, 31273.
- JIANG, N., CHANG, Q., SUN, X., LU, H., YIN, J., ZHANG, Z., WAHLGREN, M. & CHEN, Q. 2010. Co-infections with *Plasmodium knowlesi* and other malaria parasites, Myanmar. *Emerg Infect Dis*, 16, 1476-8.

- JONES, B. A., GRACE, D., KOCK, R., ALONSO, S., RUSHTON, J., SAID, M. Y., MCKEEVER, D., MUTUA, F., YOUNG, J., MCDERMOTT, J. & PFEIFFER, D. U. 2013. Zoonosis emergence linked to agricultural intensification and environmental change. *Proc Natl Acad Sci U S A*, 110, 8399-404.
- JONGWUTIWES, S., BUPPAN, P., KOSUVIN, R., SEETHAMCHAI, S., PATTANAWONG, U., SIRICHAISINTHOP, J. & PUTAPORNTIP, C. 2011. Plasmodium knowlesi Malaria in humans and macaques, Thailand. *Emerg Infect Dis*, 17, 1799-806.
- JONGWUTIWES, S., PUTAPORNTIP, C., IWASAKI, T., SATA, T. & KANBARA, H. 2004. Naturally acquired Plasmodium knowlesi malaria in human, Thailand. *Emerg Infect Dis*, 10, 2211-3.
- JOVEEN-NEOH, W. F., CHONG, K. L., WONG, C. M. & LAU, T. Y. 2011. Incidence of malaria in the interior division of sabah, malaysian borneo, based on nested PCR. *J Parasitol Res*, 2011, 104284.
- KAHIME, K., BOUSSAA, S., BOUNOUA, L., FOUAD, O., MESSOULI, M. & BOUMEZZOUGH, A. 2014. Leishmaniasis in Morocco: diseases and vectors. *Asian Pacific Journal of Tropical Disease*, 4, 273-276.
- KALINGA, A. & POST, R. J. 2011. An apparent halt to the decline of Simulium woodi in the Usambara foci of onchocerciasis in Tanzania. *Ann Trop Med Parasitol*, 105, 273-6.
- KANTELE, A. & JOKIRANTA, T. S. 2011. Review of cases with the emerging fifth human malaria parasite, Plasmodium knowlesi. *Clin Infect Dis*, 52, 1356-62.
- KANTELE, A., MARTI, H., FELGER, I., MULLER, D. & JOKIRANTA, T. S. 2008. Monkey malaria in a European traveler returning from Malaysia. *Emerg Infect Dis*, 14, 1434-6.
- KARESH, W. B. & NOBLE, E. 2009. The bushmeat trade: increased opportunities for transmission of zoonotic disease. *Mt Sinai J Med*, 76, 429-34.
- KEESING, F., BELDEN, L. K., DASZAK, P., DOBSON, A., HARVELL, C. D., HOLT, R. D., HUDSON, P., JOLLES, A., JONES, K. E., MITCHELL, C. E., MYERS, S. S., BOGICH, T. & OSTFELD, R. S. 2010. Impacts of biodiversity on the emergence and transmission of infectious diseases. *Nature*, 468, 647-52.
- KEISER, J., DE CASTRO, M. C., MALTESE, M. F., BOS, R., TANNER, M., SINGER, B. H. & UTZINGER, J. 2005a. Effect of irrigation and large dams on the burden of malaria on a global and regional scale. *Am J Trop Med Hyg*, 72, 392-406.
- KEISER, J., MALTESE, M. F., ERLANGER, T. E., BOS, R., TANNER, M., SINGER, B. H. & UTZINGER, J. 2005b. Effect of irrigated rice agriculture on Japanese encephalitis, including challenges and opportunities for integrated vector management. *Acta Trop*, 95, 40-57.
- KEISER, J., SINGER, B. H. & UTZINGER, J. 2005c. Reducing the burden of malaria in different eco-epidemiological settings with environmental management: a systematic review. *Lancet Infect Dis*, 5, 695-708.
- KETTLE, C. 2009. Ecological considerations for using dipterocarps for restoration of lowland rainforest in Southeast Asia. *Biodiversity and Conservation*, 19, 1137-1151.
- KHIM, N., SIV, S., KIM, S., MUELLER, T., FLEISCHMANN, E., SINGH, B., DIVIS, P. C., STEENKESTE, N., DUVAL, L., BOUCHIER, C., DUONG, S., ARIEY, F. & MENARD, D. 2011. Plasmodium knowlesi infection in humans, Cambodia, 2007-2010. *Emerg Infect Dis*, 17, 1900-2.
- KILPATRICK, A. M. & RANDOLPH, S. E. 2012. Drivers, dynamics, and control of emerging vector-borne zoonotic diseases. *Lancet*, 380, 1946-55.
- KNOWLES, R. & DAS GUPTA, B. M. 1932. A study of monkey-malaria and its experimental transmission to man. *Indian Medical Gazette*, 67, 301-320.
- KONDGEN, S., SCHENK, S., PAULI, G., BOESCH, C. & LEENDERTZ, F. H. 2010. Noninvasive monitoring of respiratory viruses in wild chimpanzees. *Ecohealth*, 7, 332-41.
- KOWALEWSKI, M. M., SALZER, J. S., DEUTSCH, J. C., RANO, M., KUHLENSCHMIDT, M. S. & GILLESPIE, T. R. 2011. Black and gold howler monkeys (Alouatta caraya) as sentinels of ecosystem health: patterns of zoonotic protozoa infection relative to degree of human-primate contact. *Am J Primatol*, 73, 75-83.

- KRAEMER, M. U. G., FARIA, N. R., REINER, R. C., JR., GOLDING, N., NIKOLAY, B., STASSE, S., JOHANSSON, M. A., SALJE, H., FAYE, O., WINT, G. R. W., NIEDRIG, M., SHEARER, F. M., HILL, S. C., THOMPSON, R. N., BISANZIO, D., TAVEIRA, N., NAX, H. H., PRADELSKI, B. S. R., NSOESIE, E. O., MURPHY, N. R., BOGOCH, II, KHAN, K., BROWNSTEIN, J. S., TATEM, A. J., DE OLIVEIRA, T., SMITH, D. L., SALL, A. A., PYBUS, O. G., HAY, S. I. & CAUCHEMEZ, S. 2017. Spread of yellow fever virus outbreak in Angola and the Democratic Republic of the Congo 2015-16: a modelling study. *Lancet Infect Dis*, 17, 330-338.
- KWEKA, E. J., KIMARO, E. E. & MUNGA, S. 2016. Effect of Deforestation and Land Use Changes on Mosquito Productivity and Development in Western Kenya Highlands: Implication for Malaria Risk. *Front Public Health*, 4, 238.
- LACROIX, C., JOLLES, A., SEABLOOM, E. W., POWER, A. G., MITCHELL, C. E. & BORER, E. T. 2014. Non-random biodiversity loss underlies predictable increases in viral disease prevalence. *J R Soc Interface*, 11, 20130947.
- LASH, R. R., CARROLL, D. S., HUGHES, C. M., NAKAZAWA, Y., KAREM, K., DAMON, I. K. & PETERSON, A. T. 2012. Effects of georeferencing effort on mapping monkeypox case distributions and transmission risk. *Int J Health Geogr*, 11, 23.
- LAURANCE, W. E., CROES, B. M., TCHIGNOUMBA, L., LAHM, S. A., ALONSO, A., LEE, M. E., CAMPBELL, P. & ONDZEANO, C. 2006. Impacts of roads and hunting on central African rainforest mammals. *Conserv Biol*, 20, 1251-61.
- LAURANCE, W. F., CAMARGO, J. L. C., FEARNSIDE, P. M., LOVEJOY, T. E., WILLIAMSON, G. B., MESQUITA, R. C. G., MEYER, C. F. J., BOBROWIEC, P. E. D. & LAURANCE, S. G. W. 2018. An Amazonian rainforest and its fragments as a laboratory of global change. *Biol Rev Camb Philos Soc*, 93, 223-247.
- LAURANCE, W. F. & YENSEN, E. 1991. Predicting the impacts of edge effects in fragmented habitats. *Biological Conservation*, 55, 77-92.
- LEE, K. S., COX-SINGH, J., BROOKE, G., MATUSOP, A. & SINGH, B. 2009a. Plasmodium knowlesi from archival blood films: further evidence that human infections are widely distributed and not newly emergent in Malaysian Borneo. *Int J Parasitol*, 39, 1125-8.
- LEE, K. S., COX-SINGH, J. & SINGH, B. 2009b. Morphological features and differential counts of Plasmodium knowlesi parasites in naturally acquired human infections. *Malar J*, 8, 73.
- LEE, K. S., DIVIS, P. C., ZAKARIA, S. K., MATUSOP, A., JULIN, R. A., CONWAY, D. J., COX-SINGH, J. & SINGH, B. 2011. Plasmodium knowlesi: reservoir hosts and tracking the emergence in humans and macaques. *PLoS Pathog*, 7, e1002015.
- LEE, Y. C., TANG, C. S., ANG, L. W., HAN, H. K., JAMES, L. & GOH, K. T. 2009c. Epidemiological characteristics of imported and locally-acquired malaria in Singapore. *Ann Acad Med Singapore*, 38, 840-9.
- LEONARDO, L. R., RIVERA, P. T., CRISOSTOMO, B. A., SAROL, J. N., BANTAYAN, N. C., TIU, W. U. & BERGQUIST, N. R. 2005. A study of the environmental determinants of malaria and schistosomiasis in the Philippines using Remote Sensing and Geographic Information Systems. *Parassitologia*, 47, 105-14.
- LI, W., FU, D., SU, F. & XIAO, Y. 2020. Spatial–Temporal Evolution and Analysis of the Driving Force of Oil Palm Patterns in Malaysia from 2000 to 2018. *ISPRS International Journal of Geo-Information*, 9, 280.
- LIU, W., LI, Y., LEARN, G. H., RUDICELL, R. S., ROBERTSON, J. D., KEELE, B. F., NDJANGO, J. B., SANZ, C. M., MORGAN, D. B., LOCATELLI, S., GONDER, M. K., KRANZUSCH, P. J., WALSH, P. D., DELAPORTE, E., MPOUDI-NGOLE, E., GEORGIEV, A. V., MULLER, M. N., SHAW, G. M., PEETERS, M., SHARP, P. M., RAYNER, J. C. & HAHN, B. H. 2010. Origin of the human malaria parasite Plasmodium falciparum in gorillas. *Nature*, 467, 420-5.

- LOAIZA, J. R., DUTARI, L. C., ROVIRA, J. R., SANJUR, O. I., LAPORTA, G. Z., PECOR, J., FOLEY, D. H., EASTWOOD, G., KRAMER, L. D., RADTKE, M. & PONGSIRI, M. 2017. Disturbance and mosquito diversity in the lowland tropical rainforest of central Panama. *Sci Rep*, 7, 7248.
- LOOI, L. M. & CHUA, K. B. 2007. Lessons from the Nipah virus outbreak in Malaysia. *Malays J Pathol*, 29, 63-7.
- LUBIS, I. N., WIJAYA, H., LUBIS, M., LUBIS, C. P., DIVIS, P. C., BESHIR, K. B. & SUTHERLAND, C. J. 2017. Contribution of Plasmodium knowlesi to multi-species human malaria infections in North Sumatera, Indonesia. *J Infect Dis*.
- LUCHAVEZ, J., ESPINO, F., CURAMENG, P., ESPINA, R., BELL, D., CHIODINI, P., NOLDER, D., SUTHERLAND, C., LEE, K. S. & SINGH, B. 2008. Human Infections with Plasmodium knowlesi, the Philippines. *Emerg Infect Dis*, 14, 811-3.
- LUIS, A. D., KUENZI, A. J. & MILLS, J. N. 2018. Species diversity concurrently dilutes and amplifies transmission in a zoonotic host-pathogen system through competing mechanisms. *Proc Natl Acad Sci U S A*, 115, 7979-7984.
- MACDONALD, A. J. & MORDECAI, E. A. 2019. Amazon deforestation drives malaria transmission, and malaria burden reduces forest clearing. *Proc Natl Acad Sci U S A*, 116, 22212-22218.
- MACKROTH, M. S., TAPPE, D., TANNICH, E., ADDO, M. & ROTHE, C. 2016. Rapid-Antigen Test Negative Malaria in a Traveler Returning From Thailand, Molecularly Diagnosed as Plasmodium knowlesi. *Open Forum Infect Dis*, 3, ofw039.
- MADSEN, H., COULIBALY, G. & FURU, P. 1987. Distribution of freshwater snails in the river Niger basin in Mali with special reference to the intermediate hosts of schistosomes. *Hydrobiologia*, 146, 77-88.
- MAKI, J., GUIOT, A. L., AUBERT, M., BROCHIER, B., CLIQUET, F., HANLON, C. A., KING, R., OERTLI, E. H., RUPPRECHT, C. E., SCHUMACHER, C., SLATE, D., YAKOBSON, B., WOHLERS, A. & LANKAU, E. W. 2017. Oral vaccination of wildlife using a vaccinia-rabies-glycoprotein recombinant virus vaccine (RABORAL V-RG (R)): a global review. *Veterinary Research*, 48, 26.
- MANIN, B. O., FERGUSON, H. M., VYTHILINGAM, I., FORNACE, K., WILLIAM, T., TORR, S. J., DRAKELEY, C. & CHUA, T. H. 2016. Investigating the Contribution of Peri-domestic Transmission to Risk of Zoonotic Malaria Infection in Humans. *PLoS Negl Trop Dis*, 10, e0005064.
- MBORA, D. N., WIECZKOWSKI, J. & MUNENE, E. 2009. Links between habitat degradation, and social group size, ranging, fecundity, and parasite prevalence in the Tana River mangabey (*Cercocebus galertus*). *Am J Phys Anthropol*, 140, 562-71.
- MCELWEE, P. 2009. Reforesting "bare hills" in Vietnam: social and environmental consequences of the 5 million hectare reforestation program. *Ambio*, 38, 325-33.
- MESA TRACK 2021. Plasmodium knowlesi. In: MESA ALLIANCE, I. (ed.). Barcelona, Spain.
- MOON, R. W., HALL, J., RANGKUTI, F., HO, Y. S., ALMOND, N., MITCHELL, G. H., PAIN, A., HOLDER, A. A. & BLACKMAN, M. J. 2013. Adaptation of the genetically tractable malaria pathogen Plasmodium knowlesi to continuous culture in human erythrocytes. *Proceedings of the National Academy of Sciences of the United States of America*, 110, 531-6.
- MOON, R. W., SHARAF, H., HASTINGS, C. H., HO, Y. S., NAIR, M. B., RCHIAD, Z., KNUEPFER, E., RAMAPRASAD, A., MOHRING, F., AMIR, A., YUSUF, N. A., HALL, J., ALMOND, N., LAU, Y. L., PAIN, A., BLACKMAN, M. J. & HOLDER, A. A. 2016. Normocyte-binding protein required for human erythrocyte invasion by the zoonotic malaria parasite Plasmodium knowlesi. *Proceedings of the National Academy of Sciences of the United States of America*, 113, 7231-6.
- MOYES, C. L., HENRY, A. J., GOLDING, N., HUANG, Z., SINGH, B., BAIRD, J. K., NEWTON, P. N., HUFFMAN, M., DUDA, K. A., DRAKELEY, C. J., ELYAZAR, I. R., ANSTEY, N. M., CHEN, Q., ZOMMERS, Z., BHATT, S., GETHING, P. W. & HAY, S. I. 2014. Defining the geographical range of the Plasmodium knowlesi reservoir. *PLoS Negl Trop Dis*, 8, e2780.

- MOYES, C. L., SHEARER, F. M., HUANG, Z., WIEBE, A., GIBSON, H. S., NIJMAN, V., MOHD-AZLAN, J., BRODIE, J. F., MALAIVIJITNOND, S., LINKIE, M., SAMEJIMA, H., O'BRIEN, T. G., TRAINOR, C. R., HAMADA, Y., GIORDANO, A. J., KINNAIRD, M. F., ELYAZAR, I. R., SINKA, M. E., VYTHILINGAM, I., BANGS, M. J., PIGOTT, D. M., WEISS, D. J., GOLDING, N. & HAY, S. I. 2016. Predicting the geographical distributions of the macaque hosts and mosquito vectors of *Plasmodium knowlesi* malaria in forested and non-forested areas. *Parasit Vectors*, 9, 242.
- MURO, A. I. & RAYBOULD, J. N. 1990. Population decline of *Simulium woodi* and reduced onchocerciasis transmission at Amani, Tanzania, in relation to deforestation. *Acta Leiden*, 59, 153-9.
- MWEEMPWA, C., MARCOTTY, T., DE PUS, C., PENZHORN, B. L., DICKO, A. H., BOUYER, J. & DE DEKEN, R. 2015. Impact of habitat fragmentation on tsetse populations and trypanosomosis risk in Eastern Zambia. *Parasit Vectors*, 8, 406.
- NAMKHAN, M., GALE, G. A., SAVINI, T. & TANTIPISANUH, N. 2021. Loss and vulnerability of lowland forests in mainland Southeast Asia. *Conserv Biol*, 35, 206-215.
- NG, L. S., CAMPOS-ARCEIZ, A., SLOAN, S., HUGHES, A. C., TIANG, D. C. F., LI, B. V. & LECHNER, A. M. 2020. The scale of biodiversity impacts of the Belt and Road Initiative in Southeast Asia. *Biological Conservation*, 248.
- NINAN, T., NALEES, K., NEWIN, M., SULTAN, Q., THAN, M. M., SHINDE, S., HABANA, A. V. F. & MOHD YUSOF, N. 2012. *Plasmodium knowlesi* malaria infection in human. *Brunei Int Med J*, 8, 358-361.
- NOOR, A. M., ALEGANA, V. A., GETHING, P. W. & SNOW, R. W. 2009. A spatial national health facility database for public health sector planning in Kenya in 2008. *Int J Health Geogr*, 8, 13.
- NORRIS, D. E. 2004. Mosquito-borne diseases as a consequence of land use change. *Ecohealth*, 1, 19-24.
- NOWAK, S. P., ZMORA, P., PIELOK, L., KUSZEL, L., KIERZEK, R., STEFANIAK, J. & PAUL, M. 2019. Case of *Plasmodium knowlesi* Malaria in Poland Linked to Travel in Southeast Asia. *Emerging Infectious Diseases*, 25, 1772-1773.
- NUNN, C. L., ALTIZER, S., JONES, K. E. & SECHREST, W. 2003. Comparative tests of parasite species richness in primates. *Am Nat*, 162, 597-614.
- NUNN, C. L., BREZINE, C., JOLLES, A. E. & EZENWA, V. O. 2014. Interactions between micro- and macroparasites predict microparasite species richness across primates. *Am Nat*, 183, 494-505.
- ODURO, A. R., BOJANG, K. A., CONWAY, D. J., CORRAH, T., GREENWOOD, B. M. & SCHELLENBERG, D. 2011. Health centre surveys as a potential tool for monitoring malaria epidemiology by area and over time. *PLoS One*, 6, e26305.
- OLIVERO, J., FA, J. E., REAL, R., MARQUEZ, A. L., FARFAN, M. A., VARGAS, J. M., GAVEAU, D., SALIM, M. A., PARK, D., SUTER, J., KING, S., LEENDERTZ, S. A., SHEIL, D. & NASI, R. 2017. Recent loss of closed forests is associated with Ebola virus disease outbreaks. *Sci Rep*, 7, 14291.
- OZBILGIN, A., CAVUS, I., YILDIRIM, A. & GUNDUZ, C. 2016. [The first monkey malaria in Turkey: a case of *Plasmodium knowlesi*]. *Mikrobiyol Bul*, 50, 484-90.
- PAGE, S. E. & HOOIJER, A. 2016. In the line of fire: the peatlands of Southeast Asia. *Philos Trans R Soc Lond B Biol Sci*, 371.
- PARRISH, C. R., HOLMES, E. C., MORENS, D. M., PARK, E. C., BURKE, D. S., CALISHER, C. H., LAUGHLIN, C. A., SAIF, L. J. & DASZAK, P. 2008. Cross-species virus transmission and the emergence of new epidemic diseases. *Microbiol Mol Biol Rev*, 72, 457-70.
- PEARCE, J. C., LEAROYD, T. P., LANGENDORF, B. J. & LOGAN, J. G. 2018. Japanese encephalitis: the vectors, ecology and potential for expansion. *J Travel Med*, 25, S16-S26.
- PHANG, W. K., HAMID, M. H. A., JELIP, J., MUDIN, R. N., CHUANG, T. W., LAU, Y. L. & FONG, M. Y. 2020. Spatial and Temporal Analysis of *Plasmodium knowlesi* Infection in Peninsular Malaysia, 2011 to 2018. *International Journal of Environmental Research & Public Health [Electronic Resource]*, 17, 11.

- PINDOLIA, D. K., GARCIA, A. J., HUANG, Z., FIK, T., SMITH, D. L. & TATEM, A. J. 2014. Quantifying cross-border movements and migrations for guiding the strategic planning of malaria control and elimination. *Malar J*, 13, 169.
- PINDOLIA, D. K., GARCIA, A. J., WESOLOWSKI, A., SMITH, D. L., BUCKEE, C. O., NOOR, A. M., SNOW, R. W. & TATEM, A. J. 2012. Human movement data for malaria control and elimination strategic planning. *Malar J*, 11.
- PLOWRIGHT, R. K., REASER, J. K., LOCKE, H., WOODLEY, S. J., PATZ, J. A., BECKER, D. J., OPPLER, G., HUDSON, P. J. & TABOR, G. M. 2021. Land use-induced spillover: a call to action to safeguard environmental, animal, and human health. *Lancet Planet Health*, 5, e237-e245.
- POULSEN, J. R., CLARK, C. J., MAVAH, G. & ELKAN, P. W. 2009. Bushmeat supply and consumption in a tropical logging concession in northern Congo. *Conserv Biol*, 23, 1597-608.
- PRIST, P. R., PS, D. A. & METZGER, J. P. 2017. Landscape, Climate and Hantavirus Cardiopulmonary Syndrome Outbreaks. *Ecohealth*, 14, 614-629.
- PUTAPORNTIP, C., HONGSRIMUANG, T., SEETHAMCHAI, S., KOBASA, T., LIMKITTIKUL, K., CUI, L. & JONGWUTIWES, S. 2009. Differential prevalence of Plasmodium infections and cryptic Plasmodium knowlesi malaria in humans in Thailand. *J Infect Dis*, 199, 1143-50.
- PUTAPORNTIP, C., JONGWUTIWES, S., THONGAREE, S., SEETHAMCHAI, S., GRYNBERG, P. & HUGHES, A. L. 2010. Ecology of malaria parasites infecting Southeast Asian macaques: evidence from cytochrome b sequences. *Mol Ecol*, 19, 3466-76.
- PUTZ, F. E., ZUIDEMA, P. A., PINARD, M. A., BOOT, R. G., SAYER, J. A., SHEIL, D., SIST, P., ELIAS & VANCLAY, J. K. 2008. Improved tropical forest management for carbon retention. *PLoS Biol*, 6, e166.
- QUESADA, B., ARNETH, A. & DE NOBLET-DUCOUDRE, N. 2017. Atmospheric, radiative, and hydrologic effects of future land use and land cover changes: A global and multimodel climate picture. *Journal of Geophysical Research: Atmospheres*, 122, 5113-5131.
- RABINOVICH, R. N., DRAKELEY, C., DJIMDE, A. A., HALL, B. F., HAY, S. I., HEMINGWAY, J., KASLOW, D. C., NOOR, A., OKUMU, F., STEKETEE, R., TANNER, M., WELLS, T. N. C., WHITTAKER, M. A., WINZELER, E. A., WIRTH, D. F., WHITFIELD, K. & ALONSO, P. L. 2017. malERA: An updated research agenda for malaria elimination and eradication. *PLoS Med*, 14, e1002456.
- RAJA, T. N., HU, T. H., KADIR, K. A., MOHAMAD, D. S. A., ROSLI, N., WONG, L. L., HII, K. C., SIMON DIVIS, P. C. & SINGH, B. 2020. Naturally Acquired Human Plasmodium cynomolgi and P. knowlesi Infections, Malaysian Borneo. *Emerging Infectious Diseases*, 26, 1801-1809.
- RAJAHRAM, G. S., BARBER, B. E., WILLIAM, T., MENON, J., ANSTEY, N. M. & YEO, T. W. 2012. Deaths due to Plasmodium knowlesi malaria in Sabah, Malaysia: association with reporting as Plasmodium malariae and delayed parenteral artesunate. *Malar J*, 11, 284.
- RANDOLPH, S. E. & DOBSON, A. D. 2012. Pangloss revisited: a critique of the dilution effect and the biodiversity-buffers-disease paradigm. *Parasitology*, 139, 847-63.
- REASER, J. K., WITT, A., TABOR, G. M., HUDSON, P. J. & PLOWRIGHT, R. K. 2021. Ecological countermeasures for preventing zoonotic disease outbreaks: when ecological restoration is a human health imperative. *Restoration Ecology*.
- REYES, R. A., FORNACE, K. M., MACALINAO, M. L. M., BONCAYAO, B. L., DE LA FUENTE, E. S., SABANAL, H. M., BARENG, A. P. N., MEDADO, I. A. P., MERCADO, E. S., BAQUILOD, M. S., LUCHAVEZ, J. S., HAFALLA, J. C. R., DRAKELEY, C. J. & ESPINO, F. E. J. 2021. Enhanced Health Facility Surveys to Support Malaria Control and Elimination across Different Transmission Settings in the Philippines. *Am J Trop Med Hyg*.
- RILEY, E. P. 2008. Ranging patterns and habitat use of Sulawesi Tonkean macaques (*Macaca tonkeana*) in a human-modified habitat. *Am J Primatol*, 70, 670-9.

- ROE, K., THANGARAJAN, A., LILLEY, K., DOWD, S. & SHANKS, D. 2020. Plasmodium knowlesi infection in an Australian soldier following jungle warfare training in Malaysia. *Journal of Military and Veterans Health*, 28, 53-56.
- ROHANI, A., WAN NAJDAH, W. M. A., MOHD HANIF, O., AIDIL AZAHARY, A. R., ZURAINEE, M., YU, K. X., JELIP, J., HUSIN, T. & LIM, L. H. 2019. Characterization of the larval breeding sites of Anopheles balabacensis (Baisas), in Kudat, Sabah, Malaysia. *Southeast Asian J Trop Med Public Health*, 49, 566-79.
- ROQUE, A. L., XAVIER, S. C., DA ROCHA, M. G., DUARTE, A. C., D'ANDREA, P. S. & JANSEN, A. M. 2008. Trypanosoma cruzi transmission cycle among wild and domestic mammals in three areas of orally transmitted Chagas disease outbreaks. *Am J Trop Med Hyg*, 79, 742-9.
- RUIZ CUENCA, P., KEY, S., DRAKELEY, C. J. & FORNACE, K. M. 2021. Evidence of human-mosquito-human transmission of the zoonotic malaria *Plasmodium knowlesi*: a systematic literature review. Geneva: World Health Organization.
- RULLI, M. C., SANTINI, M., HAYMAN, D. T. & D'ODORICO, P. 2017. The nexus between forest fragmentation in Africa and Ebola virus disease outbreaks. *Sci Rep*, 7, 41613.
- SAKKAS, H., BOZIDIS, P., FRANKS, A. & PAPADOPOULOU, C. 2018. Oropouche fever: a review. *Viruses*, 10.
- SALLUM, M. A. M., PEYTON, E. L. & WILKERSON, R. C. 2005. Six new species of the *Anopheles leucosphyrus* group, reinterpretation of *An. elegans* and vector implications. *Medical and Veterinary Entomology*, 19.
- SATITVIPAWEE, P., WONGKHANG, W., PATTANASIN, S., HOITHONG, P. & BHUMIRATANA, A. 2012. Predictors of malaria-association with rubber plantations in Thailand. *BMC Public Health*, 12, 1115.
- SATO, S., TOJO, B., HOSHI, T., MINSONG, L. I. F., KUGAN, O. K., GILOI, N., AHMED, K., JEFFREE, S. M., MOJI, K. & KITA, K. 2019. Recent Incidence of Human Malaria Caused by Plasmodium knowlesi in the Villages in Kudat Peninsula, Sabah, Malaysia: Mapping of The Infection Risk Using Remote Sensing Data. *International Journal of Environmental Research & Public Health [Electronic Resource]*, 16, 16.
- SCHMIDT, L. H., GREENL, R. & GENTHER, C. S. 1961. The transmission of Plasmodium cynomolgi to man. *Amer*, 679-688.
- SEETHAMCHAI, S., PUTAPORNTIP, C., MALAIVIJITNOND, S., CUI, L. & JONGWUTIWES, S. 2008. Malaria and Hepatocystis species in wild macaques, southern Thailand. *Am J Trop Med Hyg*, 78, 646-53.
- SEILMAIER, M., HARTMANN, W., BEISSNER, M., FENZL, T., HALLER, C., GUGGEMOS, W., HESSE, J., HARLE, A., BRETZEL, G., SACK, S., WENDTNER, C., LOSCHER, T. & BERENS-RIHA, N. 2014. Severe Plasmodium knowlesi infection with multi-organ failure imported to Germany from Thailand/Myanmar. *Malar J*, 13, 422.
- SERMWITTAYAWONG, N., SINGH, B., NISHIBUCHI, M., SAWANGJAROEN, N. & VUDDHAKUL, V. 2012. Human Plasmodium knowlesi infection in Ranong province, southwestern border of Thailand. *Malar J*, 11, 36.
- SETIADI, W., SUDOYO, H., TRIMARSANTO, H., SIHITE, B. A., SARAGIH, R. J., JULIAWATY, R., WANGSAMUDA, S., ASIH, P. B. & SYAFRUDDIN, D. 2016. A zoonotic human infection with simian malaria, Plasmodium knowlesi, in Central Kalimantan, Indonesia. *Malar J*, 15, 218.
- SHARP, P. M. & HAHN, B. H. 2011. Origins of HIV and the AIDS pandemic. *Cold Spring Harb Perspect Med*, 1, a006841.
- SHEARER, F. M., HUANG, Z., WEISS, D. J., WIEBE, A., GIBSON, H. S., BATTLE, K. E., PIGOTT, D. M., BRADY, O. J., PUTAPORNTIP, C., JONGWUTIWES, S., LAU, Y. L., MANSKE, M., AMATO, R., ELYAZAR, I. R., VYTHILINGAM, I., BHATT, S., GETHING, P. W., SINGH, B., GOLDING, N., HAY, S. I. & MOYES, C. L. 2016a. Estimating Geographical Variation in the Risk of Zoonotic Plasmodium knowlesi Infection

- in Countries Eliminating Malaria. *PLoS Neglected Tropical Diseases [electronic resource]*, 10, e0004915.
- SHEARER, F. M., HUANG, Z., WEISS, D. J., WIEBE, A., GIBSON, H. S., BATTLE, K. E., PIGOTT, D. M., BRADY, O. J., PUTAPORNTIP, C., JONGWUTIWES, S., LAU, Y. L., MANSKE, M., AMATO, R., ELYAZAR, I. R., VYTHILINGAM, I., BHATT, S., GETHING, P. W., SINGH, B., GOLDING, N., HAY, S. I. & MOYES, C. L. 2016b. Estimating Geographical Variation in the Risk of Zoonotic *Plasmodium knowlesi* Infection in Countries Eliminating Malaria. *PLoS Negl Trop Dis*, 10, e0004915.
- SHIMIZU, S., CHOTIRAT, S., DOKKULAB, N., HONGCHAD, I., KHOWSROY, K., KIATTIBUTR, K., MANEECHAI, N., MANOPWISEDJAROEN, K., PETCHVIJIT, P., PHUMCHUEA, K., RACHAPHAEW, N., SRIPPOOROTE, P., SUANSOMJIT, C., THONGYOD, W., KHAMSIWATCHARA, A., LAWPOOLSRI, S., HANBOONKUNUPAKARN, B., SATTABONGKOT, J. & NGUITRAGOOL, W. 2020. Malaria cross-sectional surveys identified asymptomatic infections of *Plasmodium falciparum*, *Plasmodium vivax* and *Plasmodium knowlesi* in Surat Thani, a southern province of Thailand. *International Journal of Infectious Diseases*, 96, 445-451.
- SINER, A., LIEW, S. T., KADIR, K. A., MOHAMAD, D. S. A., THOMAS, F. K., ZULKARNAEN, M. & SINGH, B. 2017. Absence of *Plasmodium inui* and *Plasmodium cynomolgi*, but detection of *Plasmodium knowlesi* and *Plasmodium vivax* infections in asymptomatic humans in the Betong division of Sarawak, Malaysian Borneo. *Malar J*, 16, 417.
- SINGH, B. & DANESHVAR, C. 2010. *Plasmodium knowlesi* malaria in Malaysia. *Med J Malaysia*, 65, 166-72.
- SINGH, B. & DANESHVAR, C. 2013. Human infections and detection of *Plasmodium knowlesi*. *Clin Microbiol Rev*, 26, 165-84.
- SINGH, B., KIM SUNG, L., MATUSOP, A., RADHAKRISHNAN, A., SHAMSUL, S. S., COX-SINGH, J., THOMAS, A. & CONWAY, D. J. 2004. A large focus of naturally acquired *Plasmodium knowlesi* infections in human beings. *Lancet*, 363, 1017-24.
- SINGH, M., KUMARA, H. N., KUMAR, M. A. & SHARMA, A. K. 2001. Behavioural responses of lion-tailed macaques (*Macaca silenus*) to a changing habitat in a tropical rain forest fragment in the Western Ghats, India. *Folia Primatol (Basel)*, 72, 278-91.
- SIREGAR, J. E., FAUST, C. L., MURDIYARSO, L. S., ROSMANAH, L., SAEPULOH, U., DOBSON, A. P. & ISKANDRIATI, D. 2015. Non-invasive surveillance for *Plasmodium* in reservoir macaque species. *Malar J*, 14, 404.
- SLOAN, S., LOCATELLI, B., WOOSTER, M. J. & GAVEAU, D. L. 2017. Fire activity in Borneo driven by industrial land conversion and drought during El Nino periods, 1982-2010. *Global Environmental Change*, 47, 95-109.
- SODHI, N. S., POSA, M. R. C., LEE, T. M., BICKFORD, D., KOH, L. P. & BROOK, B. W. 2010. The state and conservation of Southeast Asian biodiversity. *Biodiversity and Conservation*, 19, 317-328.
- SOKOLOW, S. H., NOVA, N., PEPIN, K. M., PEEL, A. J., PULLIAM, J. R. C., MANLOVE, K., CROSS, P. C., BECKER, D. J., PLOWRIGHT, R. K., MCCALLUM, H. & DE LEO, G. A. 2019. Ecological interventions to prevent and manage zoonotic pathogen spillover. *Philos Trans R Soc Lond B Biol Sci*, 374, 20180342.
- STARK, D. & SALGADO-LYNN, M. 2014. Interim Report on Primatology Component, MONKEYBAR project
- STARK, D. J., FORNACE, K. M., BROCK, P. M., ABIDIN, T. R., GILHOOLY, L., JALIUS, C., GOOSSENS, B., DRAKELEY, C. J. & SALGADO-LYNN, M. 2019. Long-Tailed Macaque Response to Deforestation in a *Plasmodium knowlesi*-Endemic Area. *Ecohealth*.
- STARK, D. J., FORNACE, K. M., BROCK, P. M., ABIDIN, T. R., GILHOOLY, L., JALIUS, C., GOOSSENS, B., DRAKELEY, C. J. & SALGADO-LYNN, M. (submitted). Response of a group of long-tailed macaques (*Macaca fascicularis*) to habitat clearing in Sabah, Malaysian Borneo: implications for *Plasmodium knowlesi* risk.

- STEVENSON, J. C., STRESMAN, G. H., GITONGA, C. W., GILLIG, J., OWAGA, C., MARUBE, E., ODONGO, W., OKOTH, A., CHINA, P., ORIANGO, R., BROOKER, S. J., BOUSEMA, T., DRAKELEY, C. & COX, J. 2013. Reliability of school surveys in estimating geographic variation in malaria transmission in the western Kenyan highlands. *PLoS One*, 8, e77641.
- STIBIG, H. J., ACHARD, F., CARBONI, S., RASI, R. & MIETTINEN, J. 2014. Change in tropical forest cover of Southeast Asia from 1990 to 2010. *Biogeosciences*, 11, 247-258.
- STODDARD, S. T., MORRISON, A. C., VAZQUEZ-PROKOPEC, G. M., PAZ SOLDAN, V., KOHEL, T. J., KITRON, U., ELDER, J. P. & SCOTT, T. W. 2009. The role of human movement in the transmission of vector-borne pathogens. *PLoS Negl Trop Dis*, 3, e481.
- STREICKER, D. G., RECUENCO, S., VALDERRAMA, W., GOMEZ BENAVIDES, J., VARGAS, I., PACHECO, V., CONDORI CONDORI, R. E., MONTGOMERY, J., RUPPRECHT, C. E., ROHANI, P. & ALTIZER, S. 2012. Ecological and anthropogenic drivers of rabies exposure in vampire bats: implications for transmission and control. *Proc Biol Sci*, 279, 3384-92.
- STRESMAN, G., KOBAYASHI, T., KAMANGA, A., THUMA, P. E., MHARAKURWA, S., MOSS, W. J. & SHIFF, C. 2012. Malaria research challenges in low prevalence settings. *Malar J*, 11, 353.
- STRESMAN, G. H., STEVENSON, J. C., OWAGA, C., MARUBE, E., ANYANGO, C., DRAKELEY, C., BOUSEMA, T. & COX, J. 2014. Validation of three geolocation strategies for health-facility attendees for research and public health surveillance in a rural setting in western Kenya. *Epidemiol Infect*, 142, 1978-89.
- STURROCK, H. J., HSIANG, M. S., COHEN, J. M., SMITH, D. L., GREENHOUSE, B., BOUSEMA, T. & GOSLING, R. D. 2013. Targeting asymptomatic malaria infections: active surveillance in control and elimination. *PLoS Med*, 10, e1001467.
- SULISTYANINGSIH, E., FITRI, L. E., LOSCHER, T. & BERENS-RIHA, N. 2010. Diagnostic difficulties with *Plasmodium knowlesi* infection in humans. *Emerg Infect Dis*, 16, 1033-4.
- SUNDARARAMAN, S. A., LIU, W., KEELE, B. F., LEARN, G. H., BITTINGER, K., MOUACHA, F., AHUKA-MUNDEKE, S., MANSKE, M., SHERRILL-MIX, S., LI, Y., MALENKE, J. A., DELAPORTE, E., LAURENT, C., MPOUDI NGOLE, E., KWIATKOWSKI, D. P., SHAW, G. M., RAYNER, J. C., PEETERS, M., SHARP, P. M., BUSHMAN, F. D. & HAHN, B. H. 2013. *Plasmodium falciparum*-like parasites infecting wild apes in southern Cameroon do not represent a recurrent source of human malaria. *Proc Natl Acad Sci U S A*, 110, 7020-5.
- SURENDRA, H., SUPARGIYONO, AHMAD, R. A., KUSUMASARI, R. A., RAHAYUJATI, T. B., DAMAYANTI, S. Y., TETTEH, K. K. A., CHITNIS, C., STRESMAN, G., COOK, J. & DRAKELEY, C. 2020. Using health facility-based serological surveillance to predict receptive areas at risk of malaria outbreaks in elimination areas. *BMC Med*, 18, 9.
- TA, T. H., HISAM, S., LANZA, M., JIRAM, A. I., ISMAIL, N. & RUBIO, J. M. 2014. First case of a naturally acquired human infection with *Plasmodium cynomolgi*. *Malaria Journal*, 13, 68.
- TA, T. T., SALAS, A., ALI-TAMMAM, M., MARTINEZ MDEL, C., LANZA, M., ARROYO, E. & RUBIO, J. M. 2010. First case of detection of *Plasmodium knowlesi* in Spain by Real Time PCR in a traveller from Southeast Asia. *Malar J*, 9, 219.
- TAKAYA, S., KUTSUNA, S., SUZUKI, T., KOMAKI-YASUDA, K., KANO, S. & OHMAGARI, N. 2018. Case Report: *Plasmodium knowlesi* Infection with Rhabdomyolysis in a Japanese Traveler to Palawan, the Philippines. *American Journal of Tropical Medicine & Hygiene*, 99, 967-969.
- TAN, C. H., VYTHILINGAM, I., MATUSOP, A., CHAN, S. T. & SINGH, B. 2008. Bionomics of *Anopheles latens* in Kapit, Sarawak, Malaysian Borneo in relation to the transmission of zoonotic simian malaria parasite *Plasmodium knowlesi*. *Malar J*, 7, 52.
- TANGENA, J. A., THAMMAVONG, P., WILSON, A. L., BREY, P. T. & LINDSAY, S. W. 2016. Risk and Control of Mosquito-Borne Diseases in Southeast Asian Rubber Plantations. *Trends Parasitol*, 32, 402-15.

- TANIZAKI, R., UJIE, M., KATO, Y., IWAGAMI, M., HASHIMOTO, A., KUTSUNA, S., TAKESHITA, N., HAYAKAWA, K., KANAGAWA, S., KANO, S. & OHMAGARI, N. 2013. First case of Plasmodium knowlesi infection in a Japanese traveller returning from Malaysia. *Malar J*, 12, 128.
- TARAFDER, M. R., BALOLONG, E., JR., CARABIN, H., BELISLE, P., TALLO, V., JOSEPH, L., ALDAY, P., GONZALES, R. O., RILEY, S., OLVEDA, R. & MCGARVEY, S. T. 2006. A cross-sectional study of the prevalence of intensity of infection with Schistosoma japonicum in 50 irrigated and rain-fed villages in Samar Province, the Philippines. *BMC Public Health*, 6, 61.
- TAUBERT, F., FISCHER, R., GROENEVELD, J., LEHMANN, S., MULLER, M. S., RODIG, E., WIEGAND, T. & HUTH, A. 2018. Global patterns of tropical forest fragmentation. *Nature*, 554, 519-522.
- TCHOUASSI, D. P., TORTO, B., SANG, R., RIGINOS, C. & EZENWA, V. O. 2020. Large herbivore loss has complex effects on mosquito ecology and vector-borne disease risk. *Transbound Emerg Dis*.
- TUNO, N., OKEKA, W., MINAKAWA, N., TAKAGI, M. & YAN, G. 2005. Survivorship of Anopheles gambiae sensu stricto (Diptera: Culicidae) larvae in western Kenya highland forest. *J Med Entomol*, 42, 270-7.
- TUSTING, L. S., BOTTOMLEY, C., GIBSON, H., KLEINSCHMIDT, I., TATEM, A. J., LINDSAY, S. W. & GETHING, P. W. 2017. Housing Improvements and Malaria Risk in Sub-Saharan Africa: A Multi-Country Analysis of Survey Data. *PLoS Med*, 14, e1002234.
- TUSTING, L. S., IPPOLITO, M. M., WILLEY, B. A., KLEINSCHMIDT, I., DORSEY, G., GOSLING, R. D. & LINDSAY, S. W. 2015. The evidence for improving housing to reduce malaria: a systematic review and meta-analysis. *Malar J*, 14, 209.
- TUSTING, L. S., WILLEY, B., LUCAS, H., THOMPSON, J., KAFY, H. T., SMITH, R. & LINDSAY, S. W. 2013. Socioeconomic development as an intervention against malaria: a systematic review and meta-analysis. *Lancet*, 382, 963-72.
- TYAGI, K., GUPTA, D., SAINI, E., CHOUDHARY, S., JAMWAL, A., ALAM, M. S., ZEESHAN, M., TYAGI, R. K. & SHARMA, Y. D. 2015. Recognition of Human Erythrocyte Receptors by the Tryptophan-Rich Antigens of Monkey Malaria Parasite Plasmodium knowlesi. *PLoS ONE [Electronic Resource]*, 10, e0138691.
- TYAGI, R. K., DAS, M. K., SINGH, S. S. & SHARMA, Y. D. 2013. Discordance in drug resistance-associated mutation patterns in marker genes of Plasmodium falciparum and Plasmodium knowlesi during coinfections. *J Antimicrob Chemother*, 68, 1081-8.
- UMHANG, G., POSSENTI, A., COLAMESTA, V., D'AGUANNO, S., LA TORRE, G., BOUE, F. & CASULLI, A. 2019. A systematic review and meta-analysis on anthelmintic control programs for Echinococcus multilocularis in wild and domestic carnivores. *Food Waterborne Parasitol*, 15, e00042.
- UNITED NATIONS DEPARTMENT OF ECONOMIC AND SOCIAL AFFAIRS POPULATION DIVISION 2018. World Urbanization Prospects: The 2018 Revision. Geneva: United Nations.
- VADIVELAN, M. & DUTTA, T. 2014. Recent advances in the management of Plasmodium knowlesi infection. *Trop Parasitol*, 4, 31-4.
- VALENTINE, M. J., MURDOCK, C. C. & KELLY, P. J. 2019. Sylvatic cycles of arboviruses in non-human primates. *Parasit Vectors*, 12, 463.
- VAN DEN BOSSCHE, P., SHUMBA, W. & MAKHAMBERA, P. 2000. The distribution and epidemiology of bovine trypanosomosis in Malawi. *Vet Parasitol*, 88, 163-76.
- VAN DEN EEDE, P., VAN, H. N., VAN OVERMEIR, C., VYTHILINGAM, I., DUC, T. N., HUNG LE, X., MANH, H. N., ANNE, J., D'ALESSANDRO, U. & ERHART, A. 2009. Human Plasmodium knowlesi infections in young children in central Vietnam. *Malar J*, 8, 249.
- VITTOR, A. Y., PAN, W., GILMAN, R. H., TIELSCH, J., GLASS, G., SHIELDS, T., SANCHEZ-LOZANO, W., PINEDO, V. V., SALAS-COBOS, E., FLORES, S. & PATZ, J. A. 2009. Linking deforestation to malaria in the Amazon: characterization of the breeding habitat of the principal malaria vector, Anopheles darlingi. *Am J Trop Med Hyg*, 81, 5-12.

- VYTHILINGAM, I., NOORAZIAN, Y. M., HUAT, T. C., JIRAM, A. I., YUSRI, Y. M., AZAHARI, A. H., NORPARINA, I., NOORRAIN, A. & LOKMANHAKIM, S. 2008. Plasmodium knowlesi in humans, macaques and mosquitoes in peninsular Malaysia. *Parasit Vectors*, 1, 26.
- VYTHILINGAM, I., TAN, C. H., ASMAD, M., CHAN, S. T., LEE, K. S. & SINGH, B. 2006. Natural transmission of Plasmodium knowlesi to humans by Anopheles latens in Sarawak, Malaysia. *Trans R Soc Trop Med Hyg*, 100, 1087-8.
- WAI, K. T., KYAW, M. P., OO, T., ZAW, P., NYUNT, M. H., THIDA, M. & KYAW, T. T. 2014. Spatial distribution, work patterns, and perception towards malaria interventions among temporary mobile/migrant workers in artemisinin resistance containment zone. *BMC Public Health*, 14, 463.
- WALSH, J. F., MOLYNEUX, D. H. & BIRLEY, M. H. 1993. Deforestation: effects on vector-borne disease. *Parasitology*, 106 Suppl, S55-75.
- WARREN, M., CHEONG, W. H., FREDERICKS, H. K. & COATNEY, G. R. 1970. Cycles of jungle malaria in West Malaysia. *Am J Trop Med Hyg*, 19, 383-93.
- WEISSE, M. & GOLDMAN, E. D. 2021. *Primary rainforest destruction increased 12% from 2019 to 2020* [Online]. Washington DC: World Resources Institute. Available: https://research.wri.org/gfr/forest-pulse?utm_medium=globalforests&utm_source=email&utm_campaign=globalforestreview [Accessed].
- WESOLOWSKI, A., EAGLE, N., TATEM, A. J., SMITH, D. L., NOOR, A. M., SNOW, R. W. & BUCKEE, C. O. 2012. Quantifying the impact of human mobility on malaria. *Science*, 338, 267-70.
- WILCOVE, D. S., MCLELLAN, C. H. & DOBSON, A. P. 1986. Habitat fragmentation in the temperate zone. *Conservation Biology*, 6, 237-256.
- WILCOX, B. A. & ELLIS, B. 2006. Forests and emerging infectious diseases of humans. *UNASYLVA-FAO*, 57.
- WILKINSON, D. A., MARSHALL, J. C., FRENCH, N. P. & HAYMAN, D. T. S. 2018. Habitat fragmentation, biodiversity loss and the risk of novel infectious disease emergence. *J R Soc Interface*, 15.
- WILLIAM, T., JELIP, J., MENON, J., ANDERIOS, F., MOHAMMAD, R., AWANG MOHAMMAD, T. A., GRIGG, M. J., YEO, T. W., ANSTEY, N. M. & BARBER, B. E. 2014. Changing epidemiology of malaria in Sabah, Malaysia: increasing incidence of Plasmodium knowlesi. *Malar J*, 13, 390.
- WILLIAM, T., MENON, J., RAJAHRAM, G., CHAN, L., MA, G., DONALDSON, S., KHOO, S., FREDERICK, C., JELIP, J., ANSTEY, N. M. & YEO, T. W. 2011. Severe Plasmodium knowlesi malaria in a tertiary care hospital, Sabah, Malaysia. *Emerg Infect Dis*, 17, 1248-55.
- WILLIAM, T., RAHMAN, H. A., JELIP, J., IBRAHIM, M. Y., MENON, J., GRIGG, M. J., YEO, T. W., ANSTEY, N. M. & BARBER, B. E. 2013. Increasing incidence of Plasmodium knowlesi malaria following control of P. falciparum and P. vivax Malaria in Sabah, Malaysia. *PLoS Negl Trop Dis*, 7, e2026.
- WILSON, S., BOOTH, M., JONES, F. M., MWATHA, J. K., KIMANI, G., KARIUKI, H. C., VENNERSVALD, B. J., OUMA, J. H., MUCHIRI, E. & DUNNE, D. W. 2007. Age-adjusted Plasmodium falciparum antibody levels in school-aged children are a stable marker of microgeographical variations in exposure to Plasmodium infection. *BMC Infect Dis*, 7, 67.
- WIMBERLY, M. C., DE BEURS, K. M., LOBODA, T. V. & PAN, W. K. 2021. Satellite Observations and Malaria: New Opportunities for Research and Applications. *Trends Parasitol*, 37, 525-537.
- WOLFE, N. D., DASZAK, P., KILPATRICK, A. M. & BURKE, D. S. 2005. Bushmeat hunting, deforestation, and prediction of zoonoses emergence. *Emerg Infect Dis*, 11, 1822-7.
- WOLFE, N. D., ESCALANTE, A. A., KARESH, W. B., KILBOURN, A., SPIELMAN, A. & LAL, A. A. 1998. Wild primate populations in emerging infectious disease research: the missing link? *Emerg Infect Dis*, 4, 149-58.
- WONG, M. L., CHUA, T. H., LEONG, C. S., KHAW, L. T., FORNACE, K., WAN-SULAIMAN, W. Y., WILLIAM, T., DRAKELEY, C., FERGUSON, H. M. & VYTHILINGAM, I. 2015a. Seasonal and Spatial Dynamics of

- the Primary Vector of *Plasmodium knowlesi* within a Major Transmission Focus in Sabah, Malaysia. *PLoS Negl Trop Dis*, 9, e0004135.
- WONG, M. L., VYTHILINGAM, I., LEONG, S. C., CHUA, T. H., LOKE, T. K., FORNACE, K., YUSSOF, W., TORR, S., DRAKELEY, C. J. & FERGUSON, H. 2015b. Dynamics of *Anopheles balabacensis* on Banggi Island and Kudat, Sabah, Malaysia in relation to *Plasmodium knowlesi*.
- WOOLHOUSE, M. E., DYE, C., ETARD, J. F., SMITH, T., CHARLWOOD, J. D., GARNETT, G. P., HAGAN, P., HILL, J. L., NDHLOVU, P. D., QUINNELL, R. J., WATTS, C. H., CHANDIWANA, S. K. & ANDERSON, R. M. 1997. Heterogeneities in the transmission of infectious agents: implications for the design of control programs. *Proc Natl Acad Sci U S A*, 94, 338-42.
- WORKMAN, A., BLASHKI, G., BOWEN, K. J., KAROLY, D. J. & WISEMAN, J. 2018. The Political Economy of Health Co-Benefits: Embedding Health in the Climate Change Agenda. *Int J Environ Res Public Health*, 15.
- WORLD HEALTH ORGANISATION 2019. Meeting report of the WHO Evidence Review Group on assessment of malariogenic potential to inform elimination strategies and plans to prevent re-establishment of malaria. Geneva: World Health Organization.
- WORLD HEALTH ORGANISATION REGIONAL OFFICE FOR WESTERN PACIFIC 2017. Expert consultation on *Plasmodium knowlesi* malaria to guide malaria elimination strategies. Manila, Philippines: World Health Organization.
- YAKOB, L., BONSALL, M. B. & YAN, G. 2010. Modelling *knowlesi* malaria transmission in humans: vector preference and host competence. *Malar J*, 9, 329.
- YAKOB, L., LLOYD, A. L., KAO, R. R., FERGUSON, H. M., BROCK, P. M., DRAKELEY, C. & BONSALL, M. B. 2018. *Plasmodium knowlesi* invasion following spread by infected mosquitoes, macaques and humans. *Parasitology*, 145, 101-110.
- YASUOKA, J. & LEVINS, R. 2007. Impact of deforestation and agricultural development on anopheline ecology and malaria epidemiology. *Am J Trop Med Hyg*, 76, 450-60.
- YOUNG, H., GRIFFIN, R. H., WOOD, C. L. & NUNN, C. L. 2013. Does habitat disturbance increase infectious disease risk for primates? *Ecol Lett*, 16, 656-63.
- YUSOF, R., LAU, Y. L., MAHMUD, R., FONG, M. Y., JELIP, J., NGIAN, H. U., MUSTAKIM, S., HUSSIN, H. M., MARZUKI, N. & MOHD ALI, M. 2014. High proportion of *knowlesi* malaria in recent malaria cases in Malaysia. *Malar J*, 13, 168.
- ZHOU, X., HUANG, J. L., NJUABE, M. T., LI, S. G., CHEN, J. H. & ZHOU, X. N. 2014. A molecular survey of febrile cases in malaria-endemic areas along China-Myanmar border in Yunnan province, People's Republic of China. *Parasite*, 21, 27.

Tables

Table 1: Examples of effects of land use change on infectious disease risk

Environmental changes		References
Deforestation	Biodiversity loss caused by deforestation may be followed by colonization or domination by more efficient vectors and hosts of disease e.g. malaria, hantavirus, Chagas disease.	(Guerra et al., 2006, Roque et al., 2008, Durnez et al., 2013, Prist et al., 2017)
	Changes in vector habitat suitability are linked with forest disturbance, including for <i>Aedes</i> , <i>Culex</i> , and <i>Anopheles</i> mosquitoes.	(Brant, 2011, Loaiza et al., 2017)
	Changes in ecological structure and biodiversity can increase or decrease density and infection rates in hosts and vectors and availability of blood meals for vectors, influencing disease risks e.g. malaria, trypanosomiasis, Lyme disease, hantaviruses.	(Leonardo et al., 2005, Randolph and Dobson, 2012, Mweempwa et al., 2015, Halsey and Miller, 2020)
Agricultural expansion	Irrigation systems provide habitat for disease vectors and hosts including: anopheline & culicine mosquitoes incriminated in transmission of diseases such as malaria, Japanese encephalitis, and filiarisis, and intermediate snail hosts of schistosomiasis.	(Madsen et al., 1987, Keiser et al., 2005a, Leonardo et al., 2005)
	Rubber plantations associated with vector-borne diseases (including malaria, chikungunya, dengue, JEV, filiarisis), with increased density of mosquitoes & their breeding sites.	(Yasuoka and Levins, 2007, Tangena et al., 2016)
	Introduction of livestock to forest fringe areas increases opportunity for pathogen spillover from wild to domestic animals and farm workers e.g. transmission of rabies to cattle and humans by vampire bats in South America has been associated with proximity of large cattle herds to deforesting activities.	(Jones et al., 2013, de Andrade et al., 2016)
Socio-demographic changes		
Population at risk	Influx of susceptible populations into endemic areas in response to increased economic opportunity can increase	(Desjeux, 2001, Barbieri

	prevalence of diseases to which local people have gained some immunity e.g. malaria, leishmaniasis, Oropouche fever.	et al., 2005, Sakkas et al., 2018, Pindolia et al., 2014)
	Economic opportunities increase numbers and movement of migrant worker populations: in the Amazon and Southeast Asia this has been linked to malaria; seasonal fluctuations of urban-rural migration for agriculture drive measles outbreaks in Niger; schistosomiasis prevalence and spread in Tanzania.	(Bruun and Aagaard-Hansen, 2008, Hansen et al., 2008, Ferrari et al., 2010, Satitvipawee et al., 2012, Wai et al., 2014)
	Occupational changes, such as forestry, farming, and extraction activities bringing people into habitats where they are more likely to interact with vectors of diseases such as malaria and Yellow Fever, and wildlife disease hosts like non-human primates and rodents.	(Norris, 2004, de Castro et al., 2006, Basurko et al., 2013, Gibb et al., 2017, Bloomfield et al., 2020)
Socioeconomic status	Increased income following agricultural development leading to decrease in disease risks and improved health outcomes e.g. improved house structure mitigating malaria risk.	(Tusting et al., 2017, Tusting et al., 2015, Tusting et al., 2013)
Wildlife reservoirs		
Origin of disease	60% emerging infectious diseases thought to have zoonotic origin, with three quarters of these having wildlife origins. E.g. <i>P. falciparum</i> originated from non-human primates; bats have been implicated in emergence of multiple viruses affecting humans; HIV thought to have evolved from SIV infecting chimpanzees South Cameroon.	(Liu et al., 2010, Sharp and Hahn, 2011)
Spatial overlap with wildlife hosts	Increased contact between people and non-human primates hypothesised as main driver of human infections with: <i>P. knowlesi</i> and <i>P. cynomolgi</i> in Asia; <i>P. simium</i> and <i>P. brasilianum</i> in South America; thought to have a role in Ebola transmission in Africa.	(Imai et al., 2014, Guimaraes et al., 2012, Brasil et al., 2017, Olivero et al., 2017)

	Habitat loss driving fruit bats to feed from cultivated orchards and increasing contact with livestock and/or humans implicated in emergence & outbreaks of Nipah and Hendra viruses.	(Looi and Chua, 2007, Giles et al., 2018)
Maintenance of infections	Pathogens causing human disease can be maintained in wild animal populations e.g. human malaria species circulating in great apes and gorillas in West and Central Africa; wild chimpanzees in the Cote d'Ivoire harbour human metapneumovirus (HMPV) and human respiratory syncytial virus (HRSV).	(Kondgen et al., 2010, Sundararaman et al., 2013, Boundenga et al., 2015)

Table 2. Number of studies reporting cases of human *P. knowlesi* infections by country and period within published scientific literature (Ruiz Cuenca et al., 2021). Numbers in brackets represent total number of cases. Excludes routine surveillance data.

	<2000	2000-2004	2005-2009	2010-2014	2015-2020
Brunei	0	0	0	0	1 (73)
Cambodia	0	0	3 (4)	2 (2)	1 (6)
India	0	0	0	0	9 (19)
Indonesia	0	0	2 (2)	13 (414)	0
Laos	0	0	0	0	1 (1)
Malaysia	1 (1)	4 (120)	63 (1167)	42 (1699)	26 (1401)
Myanmar	0	0	4 (32)	2 (17)	1 (1)
Philippines	0	0	2 (4)	0	2 (2)
Singapore	0	0	3 (5)	0	0
Thailand	1 (1)	1 (1)	5 (13)	3 (3)	20 (34)
Vietnam	0	2 (5)	3 (32)	0	0
South-East Asia*	0	0	1 (1)	1 (1)	1 (1)

* Studies identifying human cases but unable to specify which country infection took place in

Table 3. Change in forest area in Southeast Asian countries between 1990-2020 (FAO, 2020). While most underwent net forest loss in this time period, some countries which saw significant deforestation prior to this time period have entered a reforestation phase; concentrated efforts towards restoring historical levels of forest cover in Vietnam have been implemented since the 1990s, for example (McElwee, 2009).

Country	Forest area (1000 ha)
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	1990	2020	Change	Cover change (%)
Myanmar	39,218.48	28,543.89	-10,674.59	-27.22
Cambodia	11,004.79	8,068.37	-2,936.42	-26.68
Indonesia	118,545.00	92,133.20	-26,411.80	-22.28
Brunei	413.00	380.00	-33.00	-7.99
the Philippines	7,778.81	7,188.59	-590.22	-7.59
Malaysia	20,618.50	19,114.04	-1,504.46	-7.30
Laos	17,843.00	16,595.50	-1,247.50	-6.99
Timor-Leste	963.10	921.10	-42.00	-4.36
Thailand	19,361.00	19,873.00	512.00	2.64
Singapore	14.83	15.57	0.74	4.99
Vietnam	9,375.96	14,643.09	5,267.13	56.18

Table 4. Hosts with confirmed evidence of *P. knowlesi* infections, separated into confirmed hosts, possible hosts (single case reports of infections in wild) and laboratory infections

Confirmed hosts			Possible hosts			Experimental infections		
Long-tailed macaque	<i>Macaca fascicularis</i>	(Coatney et al., 1971)	Stump-tailed macaque	<i>Macaca arctoides</i>	(Fungfung et al., 2020)	Common marmoset	<i>Callithrix jacchus</i>	(Coatney et al., 1971)
Pig-tailed macaque	<i>Macaca nemestrina</i>	(Coatney et al., 1971)	Banded leaf monkey	<i>Presbytis melalophos</i>	(Eyles et al., 1962)	White-eyed mangabey	<i>Cercocebus fuliginosus</i>	(Coatney et al., 1971)
			Dusky leaf monkey	<i>Semnopithecus obscurus</i>	(Putaporntip et al., 2010)	Moustached guenon	<i>Cercopithecus cephus</i>	(Coatney et al., 1971)
						Yellow baboon	<i>Cynocephalus papio</i>	(Coatney et al., 1971)
						Western hoolock gibbon	<i>Hoolock hoolock</i>	(Coatney et al., 1971)
						Bonnet macaque	<i>Macaca radiata</i>	(Coatney et al., 1971)
						Assam macaque	<i>Macaca assamensis</i>	(Dutta et al., 1978)
						Dog face baboon	<i>Papio doguera</i>	(Coatney et al., 1971)
						Baboon	<i>Papio jubilaeus</i>	(Coatney et al., 1971)

						Guinea baboon	<i>Papio papio</i>	(Coatney et al., 1971)
						Silvered leaf-monkey	<i>Presbytis cristatus</i>	(Coatney et al., 1971)
						Common squirrel monkey	<i>Saimiri sciureus</i>	(Coatney et al., 1971)
						Gray langur	<i>Semnopithecus entellus</i>	(Coatney et al., 1971)

Figure Captions

Figure 1: Reports of PCR confirmed *P. knowlesi* infections in people by country from 1996 – 2021 by published literature (Ruiz Cuenca et al., 2021)

Figure 2. Number of peer-reviewed papers on *P. knowlesi* retrieved in May 2021 from MEDLINE by year. Vertical dotted lines represent 2 key points in time, the first report of natural human infection with *P. knowlesi* and the identification of a *P. knowlesi* outbreak in Sarawak, Malaysian Borneo (Ruiz Cuenca et al., 2021)

Figure 3. Routinely collected malaria surveillance data of clinical malaria cases detected at health facilities from Malaysia (Chin et al., 2020b)

Figure 4. Forest loss from 2000 – 2019 in Southeast Asia (forest cover defined as greater than 50% canopy cover, obtained from (Hansen et al., 2013))