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parasites. Early identification and comprehensive characterization of (potential) parasites in vectors or clinical samples would greatly improve patient treatment and rapid implementation of specific control measures. To address this need, we developed a rapid and cost-efficient screening technique to detect and identify both known and potential parasites present in human stool samples and vectors. We designed several sets of PCR primers, each targeting a different taxon of eukaryotic parasites and use massively-parallel sequencing to obtain the taxonomic information for any positive amplification. Our preliminary data demonstrates that this approach can efficiently recover and identify DNA from Apicomplexa, Platyhelminthes, Nematodes (Spirurida and Trichochephalida), Parabasalia, Kinetoplastida and Blastocystis parasites. This enables screening hundreds of samples simultaneously for all these taxa. Our assay can also easily be modified to provide, in a single sequencing run, information about the vector's species and the composition of its previous bloodmeals. We believe that this approach could complement the efforts of clinicians and entomologists to monitor the presence and spread of diseases and could lead to significant improvement in public health in a variety of settings.

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NOVEL VECTORS OF THE ZOONOTIC MALARIA PARASITE, PLASMODIUM KNOWLESI, IN TWO DISTRICTS OF SARAWAK, MALAYSIAN BORNEO

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The zoonotic malaria parasite, Plasmodium knowlesi, is the most common cause of human malaria in Sarawak, Malaysian Borneo. It accounted for over 80% of hospitalised malaria cases from 2014-2016. Previously identified vectors of the parasite in nature in Malaysia and Vietnam all belong to the Leucosphyrus Group. Only one study on vectors of P. knowlesi has been conducted in Sarawak that incriminated Anopheles latens as the vector in the Kapit District. This project was therefore undertaken to identify malaria vectors in other districts of Sarawak. Human landing catches were conducted in forested sites of the Betong and Lawas Districts. The salivary glands of anophelines were removed, DNA was extracted and screened with nested PCR assays for Plasmodium and species of Plasmodium. The sequences of the small sub-unit ribosomal RNA (SSUrRNA) genes of Plasmodium spp. and the internal transcribed spacer 2 (ITS2) and mitochondrial cytochrome c oxidase subunit 1 (CO1) sequences of the mosquitoes were derived from the *Plasmodium*-positive samples. Collectively, 238 anophelines and 2,127 culicines were caught. An. letifer (44.5%, n=173) and An. balabacensis (47.7%, n=65) were found to be the predominant anophelines in Betong and Lawas districts, respectively. By PCR, 15 anophelines were found to be infected with only P. knowlesi, while 8 others were infected with two or more simian Plasmodium species (P. coatneyi, P. cynomolgi, P. fieldi and P. inui). Phylogenetic analysis of the SSUrRNA genes confirmed the presence of P. knowlesi and other simian malaria parasites in 3 An. barbirostris, 6 An. balabacensis, 1 An. latens and 1 An. letifer. Phylogenies inferred from the ITS2 and CO1 sequences of An. balabacensis and An. barbirostris indicate that the former is genetically indistinguishable from An. balabacensis in Borneo while the latter is a sibling species of the Barbirostris Subgroup. In conclusion, new vectors of P. knowlesi were identified in Betong (An. barbirostris and An. balabacensis) and Lawas (An. latens and An. letifer), including 2 species (An. barbirostris and An. letifer) which do not belong to the Leucosphyrus Group.

DIFFERENTIAL EFFECTS OF TIRE LEACHATE ON AEDES MOSQUITOES MAY FACILITATE INVASION SUCCESS

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Discarded vehicle tire casings are an important habitat for the developmental stages of numerous vector mosquitoes. The rubber of the tire casings degrade under ultraviolet light and leaches numerous soluble metals (e.g., barium, cadmium, zinc) and organic substances (e.g., benzothiazole and its derivatives, polyaromatic hydrocarbons) that could affect any mosquito larvae inhabiting rainwater that collects within the tire casing. This study examined relationships between Zn, as a marker of tire leachate, and other environmental correlates on mosquito densities in discarded tires in the field and tested the effects of tire leachate concentration on the survival and development of newly hatched Aedes albopictus and Aedes triseriatus larvae in a controlled laboratory doseresponse experiment. Aedes albopictus and Ae. triseriatus co-occurred in over half (22/42, 52.4%) of tires in the field, and Ae. triseriatus was only collected without Ae. albopictus in one tire. Ae. triseriatus was more strongly negatively associated with zinc concentration than Ae. albopictus and another common mosquito, Cx. pipiens. Ae. albopictus was the most widespread species, being collected in 88.1% (37/42), and was correlated with detritus amount, while Ae. triseriatus (23/42, 54.8%) and Cx. pipiens (17/42, 40.5%) were less widespread and both were correlated with Ae. albopictus. In the laboratory experiment, Ae. albopioctus λ' and survival steeply declined to zero from 10,000 to 100,000 mg/L leachate. In contrast, Ae. triseriatus λ' and survival declined at the lower concentration of 100 mg/L leachate, and was zero at 500, 10,000, and 100,000 mg/L. These results suggest that the invasive Aedes albopictus has superior tolerance to tire leachate than the native Aedes triseriatus, and that this tolerance may contribute to its success and displacement of Ae. triseriatus in urban areas and resultant disease risk.

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INFLUENCE OF RUBBER AND PALM CULTIVATIONS ON HUMAN EXPOSURE TO *AEDES AEGYPTI* EVALUATED BY USING AN IMMUNO EPIDEMIOLOGICAL BIOMARKER

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In recent decades, numerous cases of arbovirus infections have been reported in Africa, mainly transmitted through infected Aedes aegypti bites. Their control is primarily based on anti-vector strategy and its efficient implementation requires an understanding of factors of risk of transmission linked to specific ecological settings. Environmental changes related to agricultural practices can impact upon arbovirus transmission, by influencing the vector species composition and their density which could, in turn, have an effect on the human-vector contact. The present study aims to assess the influence of oil palm and rubber plantations on a human exposure to Ae. aegypti bites, by using a new immunological tool which guantifies human IgG antibody (Ab) response to the Aedes Nterm-34kDa salivary peptide. Human IgG responses to the salivary peptide was assessed in 582 children living in different agro-ecosystem villages in Côte d'Ivoire: N'Zikro (rubber cultivation), Ehania-V5 (palm oil exploitation) and Ayébo (control village without plantations), in the dry and rainy seasons. In the dry season, specific IgG responses were significantly different between villages (P = 0.0089). The specific IgG level was significantly lower in Ayébo compared to Ehania-V5 (P = 0.0067) and N'Zikro (P = 0.0110). In contrast, specific IgG levels were similar between villages in the rainy season. As a consequence, specific IgG responses remained high in villages associated

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with intensive agricultural during both seasons whereas, in the control village, a significant increase of the specific IgG response was observed (P = 0.0017) in the rainy season compared to dry season. The present study indicated that rubber and oil palm plantations could maintain a high level of human exposure to *Ae aegypti* bites during both dry and rainy seasons. These agricultural activities could, therefore, represent a permanent factor of transmission risk of arboviruses.

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MAPPING GLOBAL VARIATION IN DENGUE TRANSMISSION INTENSITY AND ASSESSING THE IMPACT OF CONTROL STRATEGIES

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Reliable local estimates of the intensity of dengue transmission (as characterised by the reproduction number, R_{o} are required for evaluating the potential impact of control measures and informing public health policy. Published global dengue maps give estimates of the burden of disease but not of transmission intensity. Using age-stratified seroprevalence and incidence data, combined with a geostatistical machine-learning model based on environmental factors which drive suitability of Aedes aegypti's habitat, we have produced the first 1km resolution map of global dengue force of infection. Our force of infection predictions allowed us to also derive local estimates of the reproduction number and number of yearly dengue infections and cases. We predict high transmission rates in South America (Colombia, Venezuela and Brazil), Democratic Republic of Congo and south Asia (India, Indonesia and the Philippines). We estimated ~170 million infections annually, approximately half that of Bhatt et al. (2013). We also estimated an annual incidence of 80 million symptomatic infections. We then assessed the likely impact of two new control measures on dengue transmission intensity and disease burden: release of Wolbachia-infected mosquitoes, and introduction of childhood vaccination with the Sanofi dengue vaccine. The impact of both control measures varies as a function of local transmission intensity. Under the most pessimistic scenario examined, large scale release of Wolbachia might lead to a long-term reduction in dengue disease burden of 95%, rising to almost 100% reduction in more optimistic scenarios. We estimate that wide scale and near optimal use of the Sanofi dengue vaccine in line with WHO recommendations could reduce the global burden of dengue by approximately 20%. The high spatial resolution at which we have guantified dengue transmission intensity will help target and assess the potential impact of control measures.

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MAPPING THE GLOBAL ESTIMATES OF DENGUE SEROPREVALENCE AND TRANSMISSION INTENSITY

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The first dengue vaccine (CYD-TDV) has been licensed for use in children >9 years of age in several countries. The World Health Organization recommends countries consider vaccination only in areas (national or subnational) with high endemicity corresponding to a seroprevalence of \geq 70% in the target age group. Vaccination is not recommended where seroprevalence is <50%. Given these recommendations and the observed safety signal of the vaccine in seronegative recipients, it is important to know the proportion of potential vaccine recipients who might be seronegative. We have previously published work showing that the force of infection can be inferred by fitting catalytic models to age-stratified

seroprevalence and incidence data, and that estimates derived from the two data types are largely comparable. In order to present available estimates and provide some guidance to countries considering introducing the vaccine, a web tool was developed . The web tool maps currently available estimates of dengue transmission intensity at subnational levels, derived from age-stratified data on dengue: i) seroprevalence and ii) incidence, as well as the expected seroprevalence for several countries. The uncertainty around each estimate is also presented. The interactive web tool allows the user to explore how the transmission intensity relates to the expected seroprevalence at the target vaccination age group, or the expected age at which e.g. 70% seroprevalence is reached. The target age group or target seroprevalence can also be determined by the user. Users are also able to export all the estimates visualised on the website. Since the map only presents estimates for regions where data are available, it can also help to identify countries, regions, and sub-regions lacking dengue data which may inform surveillance systems. Although there are limitations such as the spatial heterogeneity observed in dengue transmission even at very small scales, having a baseline estimate of transmission intensity and seroprevalence at subnational level will be an important consideration for vaccine programmes deciding where to deploy the vaccine and who to target.

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A MULTI-COUNTRY STUDY OF THE ECONOMIC BURDEN OF DENGUE FEVER IN SIX COUNTRIES OF DVI FIELD STUDIES: VIETNAM, THAILAND, COLOMBIA, CAMBODIA, BURKINA FASO AND KENYA

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Dengue is a major public health concern in the tropics and subtropics. With the first dengue vaccine licensed in several countries, it is critical to understand the economic burden of dengue fever to set health policy priorities for effective use of the vaccine. Dengue Vaccine Initiative (DVI) has conducted cost-of-illness studies in six countries: Vietnam, Thailand, Colombia, Cambodia, Burkina Faso, and Kenya. In order to capture all costs during the entire period of illness, patients were followed up on multiple interviews, after confirmation of dengue on rapid diagnostic tests on the first day of clinical visit, until the patients recovered from the current illness. Various cost items were collected such as direct medical and non-medical costs, indirect costs, and non-out-of-pocket costs. These cost components were presented as private, non-private, and societal perspectives. In addition, socio-economic factors affecting disease severity were also identified by adopting a logit model. We found that direct medical costs as patients' private expenditure were the highest in Vietnam and the lowest in Thailand where the universal healthcare system was implemented. The average direct medical costs in Burkina Faso (\$10) and Kenya (\$15) lied in between Vietnam and Thailand. In terms of direct non-medical costs, the two African countries were lower than the other four countries showing less than \$1 and \$3 in Burkina Faso and Kenya respectively. Among the first three countries, total cost per episode ranges from \$141 to \$385 for inpatient and from \$40 to \$158 outpatient, with Colombia having the highest and Thailand having the lowest. The percentage of the private economic burden of dengue fever was highest