

chosen in batches of size  $b > 1$ , allowing new batch,  $\{x(kb+1), \dots, x(k+1)b\}$ , to depend on data obtained at locations  $x_1, \dots, x_{kb}$ . Batch sampling can't be more efficient theoretically than singleton, but is more realistic in practice. Using simulated data, we have evaluated batch sampling designs and assessed their efficiency relative to their singleton adaptive and non-adaptive counterparts by comparing their average prediction variance. We will present simulation results and describe an application to a multi-year rolling cross-sectional Malaria Indicator Survey that is being conducted within a 5-year malaria transmission reduction project in communities living around Majete Game Reserve, Malawi. Aims of this application are to: describe local variation in malaria infection in children below 5 years; identify hotspots that could guide more targeted disease control efforts; and investigate association of prevalence with environmental and social risk-factors, using a combination of survey data and publicly available, remotely sensed climate and environmental information.

## 286

### THE GEOGRAPHY OF IMPORTED MALARIA TO NON-ENDEMIC COUNTRIES

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Despite over fifty countries having achieved malaria elimination over the past century, the disease remains a problem to many 'malaria-free' countries through cases imported from endemic regions each year. Imported cases to non-endemic countries remain difficult to diagnose, expensive to treat and can occasionally spark secondary local transmission, while the movement of malaria between endemic countries is driving the spread of drug resistance. Quantifying the international movements of malaria can aid in improving our understanding of these phenomena and facilitate the design of mitigation strategies, providing insights into the epidemiology of malaria in regions where reliable surveillance data are lacking. We describe the assembly of a database of all publicly-available nationally reported statistics on imported malaria over the past 15 years, covering over 50,000 individual cases, and assessments of the geographical variations seen were undertaken. Results highlight the clear geographical differences that exist between non-endemic countries and regions in terms of imported malaria case numbers, origins and species composition, as well as the variations in composition for the countries where cases originate. Infection movements are strongly skewed towards a small number of high traffic routes, with the geographical distribution of cases correlating strongly with existing data on transmission intensities. The mapping of communities of countries linked strongly by imported case movements reveals clear groupings that are a result of historical, language and travel ties. Finally, examination of the species composition of origin cases provides a unique insight into the distribution, prevalence and acquisition risk of each of the malaria parasites.

## 287

### RISK FACTORS ASSOCIATED WITH OCCURRENCE OF PLACENTA MALARIA IN A POPULATION OF PARTURIENTS IN ABEOKUTA OGUN STATE, NIGERIA

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Placental malaria has long been acknowledged as a complication of malaria in pregnancy and has been associated with poor pregnancy outcome in malaria endemic areas. This study was conducted to determine the risk factors associated with occurrence of placenta malaria in a population of parturients in Abeokuta Ogun State. Maternal and placenta blood and relevant maternal demographic information were obtained from 211 parturients. Chi-square tests and regression model were computed to measure risk using SPSS version 16.0. Overall, 40.1% (86 of 211) of

the parturients had malaria at delivery, with 19.0% (40 of 211) having placenta malaria. Age range 18-22 years (OR= 4.4, 95% CI = (1.1 - 17.4),  $p = 0.046$ ), primigravidae (OR= 2.1, 95% CI = (0.9 - 5.1),  $p = 0.028$ ) and living in a congested apartment (OR= 1.6, 95% CI = (0.4 - 6.0),  $p = 0.029$ ) as a significant risk factor for placenta malaria. Non usage of Intermittent Preventive Treatment (IPT) (OR= 2.6, 95% CI = (1.2 - 5.4),  $p = 0.018$ ), Long Lasting Insecticidal Nets (LLINs) (OR= 2.7, 95% CI = (1.3 - 5.5),  $p = 0.005$ ) were also risk factors for placenta malaria. In Abeokuta, approximately one of every five parturients had placenta malaria at delivery, with 55% having parasite densities between (501-5000 parasites/ $\mu$ l of blood). Proper use of LLIN and IPT for pregnant women is hereby recommended.

## 288

### TRANSMISSION OF MALARIA AMONG INTRAVENOUS DRUG USERS IN THE UNITED STATES: A SHIFT FROM ENDOGENOUS TO EXOGENOUS CASES, 1929-1975

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Malaria remains a major health issue in developing countries. It is often overlooked in the industrial world unless there is a history of travel to a malarial zone. An especially overlooked issue, however, is malaria transmission between intravenous drug addicts. The sharing of needles among heroin users who are malaria-positive may well spark cases of this disease. Analysis of peer-reviewed literature in PubMed and PubMed Central from 1900 to 1975 was undertaken. The spread of malaria through shared equipment for injecting intravenous drugs was first reported in 1929 in Egypt. Since that time, several cases of induced malaria among heroin users have been identified. Beginning in the early 1930s, reports of malaria transmitted between IV drug users began to appear in the eastern United States, typically among individuals who reported no history of foreign travel. This trend continued until the late 1960s and early 1970s, the years of the Vietnam War, during which time cases were imported to California and New York after the Vietnam War. In each of these cases, transmission of the malaria parasite was due to sharing of needles among addicts. Usually, the index case had recently traveled to a malaria zone such as Southeast Asia and had contracted malaria. There has been a shift from domestic cases of malaria to imported cases during the latter part of the 20th century. Conclusions: Malaria among intravenous drug users remains an important, if not overlooked, public health issue. The number of heroin users is believed to be growing, and the potential for more cases of induced malaria remains high in the United States. Malaria among drug addicts remains a clinical problem of which physicians should be aware. The diagnosis of malaria should be considered in all intravenous drug users with fever and chills. This issue is hardly a new one and remains a potential public health issue in the early 21st century.

## 289

### IMPACT OF TARGETED MALARIA TREATMENT ON THE TRANSMISSION OF *PLASMODIUM FALCIPARUM* ALONG THE THAI-MYANMAR BORDER

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The emergence and spread of artemisinin resistance in *Plasmodium falciparum* (Pf) is challenging the efforts of malaria control and

elimination in South East Asia. The Shoklo Malaria Research Unit through the support of the Wellcome Trust and the Bill & Melinda Gates Foundation has implemented a pilot study in four villages along the Thai Myanmar border to assess whether Targeted Malaria Treatment (TMT) can eliminate the parasite reservoir and contain artemisinin-resistance. Entomological surveys using human landing catch technique were conducted in parallel to parasitological surveys to address the Pf-malaria transmission before and after intervention. One thousand two hundred and eighty two malaria vectors belonging to the Minimus, Maculatus and Dirus Groups were collected during baseline surveys (before TMT, during the rainy season). Bites of malaria vectors occur all night long but *An. maculatus* s.l. and *An. dirus* s.l. exhibit a peak in their biting behaviour during the early evening and a higher tendency to exophagy. An average of 267 bites of malaria vectors was received per person and per month (95% CI 226-309). Pf-sporozoitic index was 2.2 % (95% CI 0.0-4.4, n=1,782 mosquitoes inspected) and we estimated that each person received an average of 0.6 (95% CI 0.02-1.18) Pf-infective bites per month. Half of the transmission occurred outside the premise (2 on 4 infective bites) and half of the transmission occurred between 5:00 and 06:00 a.m. (2 on 4 infective bites). Data on the impact of TMT on Pf transmission will be presented during the meeting. In conclusion, malaria transmission in the studied area involves early feeding and exophagic vectors that could maintain residual transmission (i.e. transmission that is not controlled by full coverage of the population with long lasting insecticide-treated bed-nets) after TMT. Therefore the development and evaluation of vector control tools adapted to malaria transmission settings in South-East Asia are needed in order to act in synergy with TMT and achieve artemisinin-resistance containment.

## 290

### HIGH PREVALENCE OF FALCIPARUM MALARIA IN ASYMPTOMATIC INDIVIDUALS AND NO PFMDR1 AMPLIFICATION IDENTIFIED IN DEMOCRATIC REPUBLIC OF CONGO

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Malaria remains a major public health problem in Democratic Republic of Congo (DRC) with 14 million cases reported by the WHO malaria report in 2014. These figures only include patent malaria cases that were detectable by microscopy or by RDT. Asymptomatic malaria cases are known to be prevalent in endemic areas and are generally untreated, resulting in a significant source of gametocytes that may serve as reservoir of disease transmission. Considering that microscopy certainly underestimates the prevalence of *Plasmodium* infections within asymptomatic carriers and that PCR assays are currently recognized as the most sensitive methods for *Plasmodium* identification, this study was conducted to weigh the asymptomatic carriage in DRC by a molecular method. We additionally assessed the pfmdr1 gene amplification, that is related to many antimalarial drugs' resistance. Globally, almost half of the samples collected in the 6 provinces on the asymptomatic individuals (280/600; 46.6%) had *Plasmodium* infections and the most species identified was *P. falciparum* (97.8%) alone or combined with *P. malariae*. The lesser prevalence was found in Nord-Kivu province (22%) nearly at 1800 meter altitude. No pfmdr1 amplification > 2 copies was found. The high prevalence reported in our study should interpellate the bodies involved in

malaria control in DRC to take in account asymptomatic carriers in actions taken and consider asymptomatic malaria as a major hurdle for malaria elimination. This study was the first to assess pfmdr1 amplification in DRC.

## 291

### DOES STRESS PROVOKE *PLASMODIUM FALCIPARUM* RECRUDESCENCE?

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*Plasmodium falciparum*, unlike *P. vivax*, must maintain infection in the blood/bone marrow over many months/years in order to bridge periods between transmission periods. Asymptomatic parasitemia at very low concentrations is now known to be quite common due to molecular detection methods. Old tropical medicine texts commonly list many stressful events stated to provoke recrudescence of *falciparum* parasitemia such as fatigue, heat/chill, trauma/surgery, famine/war, transit between areas and other febrile illness. The older literature is reviewed to discover the factual basis of such varied reports since they have not been recently confirmed. Surgery / trauma studies have variably shown *falciparum* recrudescence in areas with high rates of infection and drug suppression. Travel particularly during times of war or famine has been noted to induce recrudescence likely contributing to complex public health emergencies. Provocative tests such as infections of epinephrine or endotoxin to aid diagnosis of cryptic infections could not be shown to induce *falciparum* recrudescence. It seems likely that human stress sometimes induces *falciparum* recrudescence of an otherwise asymptomatic infection. Reproducing such observations today has been radically altered as malaria chemotherapy has evolved from suppressive quinine to curative artemisinin combinations. Host stress provoked recrudescence may be part of *P. falciparum*'s survival strategy.

## 292

### HOST FACTORS IMPACTING UPON THE FUTURE USE OF PRIMAQUINE IN MALARIA-ENDEMIC SOUTHWESTERN UGANDA

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As malaria transmission continues to decline in southwestern Uganda, aggressive strategies, such as the addition of primaquine (PQ) to artemisinin-combination therapies (ACTs), are being considered. Despite the potential benefit of PQ in reducing transmission, concerns over its safety and efficacy have hampered its deployment. In particular, those with glucose-6-phosphate dehydrogenase (G6PD) deficiency are at a higher risk of hemolytic toxicity, and recent metabolic variants of CYP2D6 have the potential to impact upon PQ efficacy. To better assess the prevalence of host factors that may impact PQ use in southwestern Uganda, we conducted a stratified, two-stage cluster sampling cross sectional survey among 631 children under five years of age. Blood samples were collected to determine the following: (1) quantitative G6PD deficiency by spectrophotometric assay (Trinity Biotech®) and (2) qualitative G6PD deficiency assay by rapid diagnostic test (CareStart™ G6PD RDT). In addition, DNA was isolated to conduct (1) genotyping of the G6PD A- allele (RFLP analysis to detect the 202A/376G mutation), and (2) CYP2D6 genotyping to identify poor and ultrarapid metabolizers. Using the spectrophotometric assay as the gold-standard, the prevalence of mild G6PD deficiency (defined as 10-60% of normal activity) was 13.8% (95% CI: 11.1-16.5) as compared with 8.6% (95% CI: 6.4-10.8) by RDT. No children in our study were classified as being severely deficient (<10% enzyme activity). Of the 577/631 children with normal G6PD status by RDT, 37 were mildly deficient by quantitative assay. Of the 54 children found to be G6PD deficient by RDT, 4 were quantitatively normal. Performance