

of the patients that were tested have only basic primary education. The malaria species endemic was *Plasmodium falciparum*. In the year 2005 the total number of malaria positive was 17%. A total of 83% patients were negative. The total of positive and negatives were 1860. In the year 2006 the total malaria positives were 242 (16%) out of 1509 (84%), in these two years there was no significant increase in malaria patients with time. In the year 2007 there were 217 (15%) malaria positives and 1488 (85%) malaria negatives. There were 200 (12%) malaria positives in 2008 and 1653 (88%) negative. Despite the increase in the number of patients tested in 2008 there were no significant increase in positivity in those two years. The same can be concluded of the year 2009. In conclusion, the malaria data in the five years confirms that the occurrence of malaria in Nairobi is low. Though only 1218(15%) out of 8157 (85%) had malaria, the positives are clinically significant, but cannot be referred to qualify Nairobi as a malaria zone. It is therefore prudent for the healthcare system to take more action to educate the public when travelling to use preventive measures and adhere to treatment when sick with malaria.

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INDIVIDUAL HETEROGENEITY AND THE POTENTIAL REBOUND EFFECT OF MALARIA INTERVENTION STRATEGIES

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Most trials designed to test the effectiveness of a malaria prevention method, such as insecticide-treated nets (ITNs) or insecticide-treated curtains (ITCs), randomize newborns or clusters of newborns to one or more treatment groups. These trials are then analyzed following the intention-to-treat framework. It is hypothesized that infants using malaria prevention methods early in life do not have the opportunity to build adequate immunity to malaria, thus causing higher mortality rates in these infants later in life. This is often referred to as a "rebound" in mortality. We focus on the situation in which the all-cause mortality rates of two groups of randomized infants (e.g., ITNs and no nets) are of interest. We assume that ITNs are given to the group with no nets at the end of year one and that all children, including those initially assigned to the ITN group, are followed for another year. Mortality rates for the two groups are compared for year one and again for year two to assess the treatment effectiveness. If a rebound effect exists, then the children who were initially randomized to the ITN group should have a higher mortality rate in the second year of life than the children initially randomized to the non-ITN group. Biological variation between individuals can account for a large portion of the variability seen in medical and public health studies and can distort observed effects (Aalen, 1998). We demonstrate with randomly generated data that a potential rebound effect can be caused by individual heterogeneity, as treatment groups followed from the end of year one are no longer randomized. We also use data from a randomized, controlled trial conducted in Burkina Faso (Diallo et al., 2004) to illustrate the relationship between individual heterogeneity and the rebound effect. This study found a mortality rate ratio of 1.16 in children aged 24-59 months when comparing original treatment groups after all study participants had been allocated ITCs, and we show that this effect could have arisen from individual heterogeneity alone.

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SIMULATING MALARIA TRANSMISSION DYNAMICS IN THE PILOT SITES OF THE COLOMBIAN INTEGRATED NATIONAL ADAPTATION PLAN: STEPS FORWARD OF THE INTEGRATED SURVEILLANCE AND CONTROL SYSTEM

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Changes in climatic conditions are likely to alter malaria incidence and spatial distribution in Colombia. As part of the Integrated National Adaptation Plan, the Colombian Institute of Health is working on the implementation of a proactive, collaborative, multidisciplinary, integrated surveillance and control system (ISCS). The aim of this initiative is to improve risk assessments of malaria transmission in order to facilitate effective allocation of health resources and more cost-effective preventive responses. One of its key components is an Early Warning System Framework, in which we are proposing several dynamical and statistical models. Dynamical models, in particular, are being used to integrate climatic variables with non-climatic factors in order to simulate malaria transmission dynamics. Twelve process-based models were studied and included in a single multi-model ensemble. Five tools were initially applied in the pilot sites where the ISCS is being implemented. Activities included the characterization of local eco-epidemiological settings and numerical simulations. Characteristics such as general profile (population at risk, natural resources, economic activities), climatic conditions (climatology, long-term trends), entomology (primary and secondary vectors, breeding sites, feeding frequencies, preferences), malaria situation (annual cycles of malaria incidence, stability conditions), and non-climatic factors (including control campaigns) were analyzed to assess local conditions. Simulations included retrospective experiments (base scenarios, changes in initial conditions, local settings, sensitivity analyses, and uncertainties) of at least 8-year simulation periods, as well as short-, medium- and long-term future changing scenarios. Complementary activities included the study of local spatial patterns of vectorial capacity, descriptions of the vulnerability of populations at risk, and a conceptual framework for the analysis of non-climatic drivers. Outreach activities included the design of interactive and online platforms as well as the documentation of our experiences. Dynamical models have improved our understanding of malaria complexity, allowed us to estimate previous malaria outbreaks in the selected pilot sites, and helped us to investigate decision-making processes. All these activities constitute steps forward in the implementation of the Colombian ISCS.

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MALARIA ASSOCIATED SYMPTOMS IN PREGNANT WOMEN: RESULTS OF A COHORT FOLLOW-UP IN BENIN

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Little is known on the symptoms of malaria infected pregnant women in stable endemic areas, as it is generally admitted they have acquired an immunity protecting them from acute clinical signs. By following-up

Beninese pregnant women, this study aims to evaluate the clinical burden of malaria in a highly endemic area. An ongoing prospective cohort of 1039 women followed monthly from their first antenatal visit (ANV) until delivery is conducted in three rural dispensaries since August 2008 in Benin. 570 women seen at ANVs, unscheduled visits and at delivery were analysed for the presence of symptoms. We used a multivariate logistic regression to determine the association between symptoms and malaria infection assessed by a positive rapid diagnostic test (RDT). During routine ANVs, headache was the only symptom associated with a higher risk of malaria (aOR=2.6; $p<0.001$) and was reported by 35% of infected women. On the occasion of unscheduled visits, fever (aOR=4.1; $p<0.001$), headache (aOR= 2.1; $p=0.01$) and shivering (aOR= 3.2; $p<0.001$) were significantly associated with a malaria infection and 82% of infected women presented at least one of these symptoms. We found an increasing proportion of positive RDTs in late pregnancy more than one month after the last intermittent preventive treatment dose (IPTp); moreover malaria infections during unscheduled visits occurred long after the last IPTp intake. In conclusion, the majority of pregnant women were symptomless during routine visits when infected with malaria in an endemic stable area. Only, during unscheduled visits a significant proportion of infected women were symptomatic. The prevention of malaria in pregnancy could be improved by using systematic RDTs to identify infected women consulting during non routine visits. The design of IPTp could also be optimized by reassessing the number of doses and time of administration of SP.

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NATIONWIDE PREVALENCE OF MALARIA IN CAMBODIA IN 2007: COMPARISON OF MICROSCOPY AND PCR

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In order to assess the current status of malaria in Cambodia and to compare it with the situation found in 2004, a nationwide malaria survey was conducted in November-December 2007, at the end of the rainy season, the time of peak malaria transmission. This was a stratified, multi-stage, cluster sampling survey. The country was divided into three domains based on expected malaria prevalence. The domain that included the provinces immediately around Phnom Penh was not surveyed, due to the very low prevalence found in previous surveys. The remaining provinces were divided into domains 1 and 2. Within each domain 38 clusters (villages) were selected; the clusters were stratified according to risk zones based on the distance from the village to the nearest forest (<250 m, 251-1000 m, 1-2 km, 2-5 km). Within each cluster 40 households were sampled, and from each household, 4 individuals provided malaria smears and filter paper blood spots for PCR-based diagnosis using the mitochondrial cytochrome b gene as a target. Based on microscopy, the overall estimated malaria prevalence and prevalences of *P. falciparum* and *P. vivax* infection in the sampled domains were 2.9% (95% CI, 1.8-4.6%), 1.6% (0.9-2.7%), and 0.9% (0.6-1.6%) respectively. The corresponding prevalences found in 2004 were 4.4% (2.8-6.8%), 2.9% (1.7-5.1%), and 1.3% (0.8-2.1%); this decline in prevalence, while appreciable, was not statistically significant. In order to determine the extent to which microscopy might underestimate the malaria prevalence, we performed PCR on 7707 samples; in these samples the malaria prevalences estimated by microscopy and PCR were 2.8% and 6.9%, respectively; 289 of 7162 microscopy negative samples (4.0%) were positive by PCR. The high prevalence of infection undetected by microscopy suggests that prevalence surveys based only on microscopy may significantly underestimate malaria prevalence. If these sub-microscopic infections contribute to transmission, then mass screening and treatment based on microscopy alone may miss a significant reservoir of infection.

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SPATIO-TEMPORAL DISTRIBUTION OF MALARIA IN HAINAN PROVINCE, CHINA

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Hainan Province is one of the regions of the highest malaria incidence in China. Our study analyzed the distribution of malaria and the change of main epidemic areas from 1995 to 2008, to provide basis for the prevention and control of malaria in Hainan Province. The study was based on the data of each county/city between 1995 and 2008. Records of malaria cases were obtained from Hainan Center for Disease Control and Prevention and demographic data from Hainan statistical yearbook. Cluster analysis of time-space scanning was performed with the maximum cluster size of 25% of the population used SatScan 8.0. The temporal cluster analysis of 1995-2008 showed that 2003-2004 was the most likely cluster ($RR=1.86$, $P=0.001$). The space-time cluster analysis of 1995-2008 showed 7 counties/cities (San Ya, Bao Ting, Le Dong, Wu Zhishan, Ling Shui, Bai Sha and Qiong Zhong) in 2003-2004 was the most likely cluster ($Incidence=2671.0/100,000$, $RR=4.97$, $P=0.001$). The space-time cluster analysis of 1995-2002 showed 5 counties/cities (Bao Ting, San Ya, Wu Zhishan, Ling Shui and Qiong Zhong) in 1997-1998 was the most likely cluster ($Incidence=1852.8/100,000$, $RR=4.49$, $P=0.001$) and 3 counties/cities (Chang Jiang, Dong Fang and Bai Sha) in 2001-2002 the secondary one ($Incidence=1258.6/100,000$, $RR=3.25$, $P=0.001$). The space-time cluster analysis of 2005-2008 showed 5 counties/cities (Ling Shui, Bao Ting, Wan Ning, Qiong Zhong and Wu Zhishan) in 2005 was the most likely cluster ($Incidence=1193.7/100,000$, $RR=4.55$, $P=0.001$) and 4 counties/cities (Dong Fang, Chang Jiang Le Dong and Bai Sha) in 2006 the secondary one ($Incidence=1038.9/100,000$, $RR=3.30$, $P=0.001$). In conclusion, during 1995-2008, malaria incidence reached its peak in 2003-2004 and the southern Hainan Province was the main epidemic area. Although the average incidence decreased, the main epidemic area was expanded to the southeastern and southwestern Hainan Province gradually. Hence, future public health planning and resource allocation in Hainan Province should be focused on these areas.

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INSIGHT INTO ANTIGENIC DIVERSITY OF VAR2CSA-DBL5E DOMAIN FROM MULTIPLE PLASMODIUM FALCIPARUM PLACENTAL ISOLATES

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High levels of anti-VAR2CSA antibodies levels are associated with protection against pregnancy-associated malaria. VAR2CSA contains molecular signatures associated with parity in one of its domain, and variants preferentially infecting primigravidae are thought to be the most virulent. Therefore it is critical to identify sequence characteristics of this molecule that can interfere with immune response. Highly conserved domains of VAR2CSA such as DBL5e are likely to contain conserved epitopes, and therefore constitute attractive targets for vaccine development. Sequences of the VAR2CSA-DBL5e domain obtained from cDNA of 40 placental isolates were analysed by experimental and in silico tools. Competition ELISA assays on two DBL5e variants, using women plasma samples from two different areas and mice specific antisera, indicated that DBL5e possess conserved and cross-reactive B cell epitopes. Peptide ELISA identified conserved areas that are recognised by naturally acquired antibodies. Specific antibodies against these peptides