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TREATMENT OF ASYMPTOMATIC CARRIERS OF *PLASMODIUM FALCIPARUM* MALARIA WITH ARTEMETHER-LUMEFANTRINE TO REDUCE DISEASE TRANSMISSION: A MODELING AND SIMULATION STUDY

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Asymptomatic carriers (AC) of *Plasmodium falciparum* serve as a reservoir for malaria transmission. Identification and treatment of AC within a region should reduce the reservoir and thus transmission intensity in that area. Using computer simulation, the factors that influence the impact of this intervention, i.e. community screening campaigns (CSC) followed by artemether-lumefantrine (AL) treatment on disease transmission were explored. The model of Okell et al (2008) was modified with malaria vector seasonality added and components modified to represent screening and treatment of AC with AL. The age grouping, relative distribution of age in a region, and degree of heterogeneity in disease transmission were maintained. The impact of the number of CSC and their timing on malaria transmission throughout a period of 1 year was explored. A sensitivity analysis to determine factors with the greatest impact was done. The simulation showed the intervention reduces transmission in a region with marked seasonal transmission (6 months) of moderate intensity (EIR<100). Three CSCs scheduled in close succession (monthly intervals) at the start of the dry season had the greatest impact. Adding an extra CSC did not bring improvement. In areas with low transmission intensity (EIR<10) the reduction was sustained for years after a single intervention while gradually tapering off with return to initial setting. Repeated intervention at least every other year allowed to sustain the effect. The simulation results show that screening and treatment of asymptomatic carriers with AL in a region reduces malaria transmission significantly. Transmission intensity has the greatest impact on the magnitude and duration of malaria reduction. When combined with other strategies (LLINs, RDT, Prompt diagnosis & treatment, IRS), the effect of this intervention can persist for many years, and it may become a tool to accelerate the reduction transmission intensity to pre-elimination level. The modeling supports the evaluation of this approach in a prospective clinical trial in an area with marked seasonality.

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PROTECTIVE EFFECTS OF WHO-RECOMMENDED LLINS AGAINST *ANOPHELES DARLINGI* IN THE FIELD

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The Andean Malaria Program has adopted Long Lasting Insecticide Net (LLIN) distribution as an important strategy to prevent and control malaria in high risk areas of malaria transmission in the Amazon Region. The nets that have been distributed to date include Interceptor®, PermaNet 2.0®, and Olyset®. Respectively, these exploit the pyrethroids alpha-cypermethrin, deltamethrin and permethrin. All published studies on the field efficacy of these compounds when incorporated into LLINs refer only to African (An. gambiae s.l.) and Asian (An. culicifacies and An. fluviatilis) malaria vectors. Only a single comparative study between these compounds applied to bed nets has been completed (also in Africa). It is therefore essential to characterize the relative efficacy of these LLINs against An. darlingi, the most common and efficient malaria vector in the Amazon basin. This was done using a set of experimental huts sited close to the Amazon town of Iquitos, Peru. Using huts with open eaves and exit traps in the windows we examined 1) the lethal effects of the three LLINs on mosquitoes, 2) their impacts on mosquito exit and entry behavior, and 3) the protection that holed nets afforded their human occupants. We also examined the protection that nets gave to humans that were in the same house as the nets, but not under the nets.

Highly significant differences between the LLINs were noted, with some nets exerting far greater lethal effects, and some far greater repellent and irritant effects than others. An. darlingi is an early biting mosquito, which exhibits its peak in biting behavior before people have retired under their bed nets. These differences between the three LLINs therefore have profound implications for the patterns of protection that they give to humans against An darlingi.

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INNOVATIVE TOOL TO EVALUATE MALARIA RISK: TOWARD THE DEVELOPMENT OF A BIOMARKER OF INFECTING BITE?

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Malaria causative agent, i.e. Plasmodium parasite, is transmitted to human during the blood meal of the Anopheles mosquito. During blood feeding, the vector injects parasite and saliva into the vertebrate host skin. This saliva contains bioactive components which induced an immune response in the vertebrate host. Our team has previously developed a serological biomarker to assess the human exposure to mosquito bite. This tool is based on the evaluation of human antibody response against mosquito salivary proteins. Here we investigate whether a salivary antigen could be specific of the infecting bite and constitute a biomarker of the risk of disease. To assess this question, we have compared the human antibody response against salivary extracts infected or not by P. *falciparum*. Experimental infections of An. gambiae by P. *falciparum* were carried out and salivary glands were dissected 14 days post-infection. The infective status of each salivary gland was confirmed by PCR. Then two-dimensional western-blots were realized with different pools of infected vs non infected sera. These pools were constituted with sera from Senegalese 1-2 y.o. children leaving in deeply exposed village to Anopheles and presenting or not a high parasitemia.

The results of 2D-blots showed that immunogenic proteins around 70kDa are detected in both infected and non infected vector. Mass spectrometry analyses identified these proteins as the 5'nucleotidase and Apyrase, proteins which inhibiting platelet aggregation. Furthermore one immunogenic protein from infected salivary glands extracts was detected only with sera from infected children by P. *falciparum*. Mass spectrometry analysis on this protein is underway. These results indicated that human immune system could discriminate between an infective bite and a non infective bite. This work opens the way to design epidemiological tools to evaluate the risk of malaria in area of (re) emergence, but also have strong implications for the vector control and monitoring.

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