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WHO IS AT RISK OF CHOLERA IN AFRICA? QUANTIFYING POTENTIAL VACCINE DEMAND AND IMPACT POLICY-RELEVANT SPATIAL LEVELS

Sean M. Moore[1], Andrew S. Azman[2], Heather S. McKay[2], Justin Lessler[2]

[1]University of Notre Dame, Notre Dame, IN, United States, [2]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States

Africa is subject to high-mortality cholera epidemics and areas of persistent incidence. Oral cholera vaccine (OCV) is becoming an important tool for cholera control as increased production has led to a growing interest in proactively vaccinating populations at high risk for infection. However, despite increases in OCV availability, the number of OCV doses available (~10 million in 2017) is too low to conduct large, generalized campaigns in at-risk countries. To prioritize the use of current supplies and quantify future production needs it is important to identify populations living at high risk of cholera infection who would derive the most benefit from prophylactic OCV use. Using cholera incidence reports from 2010-2016 over multiple spatial scales, we map the incidence of cholera in 20x20 km grid scales throughout Africa. To provide risk estimates at a policy-relevant scale, we identify districts (2nd ISO administrative level) with a significant at-risk subpopulation that comprises either ≥10% of a district's population or is ≥100,000 people. Based on these criteria, 69.2 (95% CrI: 49.8-89.2) million people live in high-risk districts in Africa based on an annual incidence threshold of ≥1 per 1,000, and an additional 141.5 (95% CrI: 106.7-184.0) million people live in moderate-risk districts with incidence between 1 per 1,000 and 1 per 10,000. Assuming only direct vaccine protection at levels consistent with a recent meta-analysis, vaccinating everyone living in moderate- and high-risk areas could directly prevent more than 582,000 (95% CrI: 339,000-1,044,000) cases over a five-year period, but would require 421.5 (95% CrI: 313.0-546.4) million doses, more than 50x the global annual production of OCVs in 2016. However, if districts are sequentially prioritized by incidence rate, 50% of these cases could be prevented with only 12% of the OCV doses (50.7 million doses, 95% CrI: 49.0-54.2 million), and 95% could be prevented with only 51% of the required doses (214.5 million doses, 95% CrI: 205.1-232.6 million).

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MALARIA TRANSMISSION AT THREE SENTINEL SITES IN WESTERN KENYA FROM 2002 TO 2016: THE RESURGENCE AND CAUSALITY ANALYSIS

Guofa Zhou[1], Guiyun Yan[1], Andew K. Githeko[2], Harrysone E. Atieli[2]

[1]University of California Irvine, Irvine, CA, United States, [2]Kenya Medical Research Institute, Kisumu, Kenya

The long-lasting insecticidal nets (LLINs), indoor residual spraying of insecticide (IRS) and artemisinin-based combination therapy (ACT) have been scaled up in Africa to control and eliminate malaria in the past decade. These intervention measures have led to overall significant declines in malaria burden. However, several studies have also documented little change in some sites in Africa. High-quality evidence for malaria burden changes and especially the mechanisms underlying these changes are often lacking. We conducted a long-term evaluation of malaria transmission dynamics in three sentinel sites with varying transmission intensity in western Kenya. The 15-year longitudinal monthly observational study found that in two highland sites, currently indoor resting vector density has resurged to the level of 2004-2005, the period before the LLIN mass distribution. Parasite prevalence remained unchanged at two sites since 2009 and bounced back to the level of 2005 at one site. We investigated the potential causes of the resurgence, including LLIN coverage rate, vector insecticide resistance, vector species composition shift, insecticidal decay effect of the LLINs, and climatic anomaly. Generalized additive model was used to determine the relative contributions of different factors through a stepwise feeding procedure. The results indicated that indoor resting *Anopheles gambiae* s.l. density was mainly affected by long-term trend and annual variability of climate regardless of study sites, whereas density and proportion of indoor resting An. funestus were correlated with resistance level and climatic factors. Parasite prevalence were strongly correlated with insecticide resistance, An. funestus indoor resting density, LLIN killing ability and climatic factors. The results suggested that insecticide resistance and shift of vector species became key factors affecting malaria control in this highly endemic area of Africa.

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HIGH *PLASMODIUM FALCIPARUM* OOCYST LOADS IN NATURALLY INFECTED MOSQUITOES IN AFRICA

Anais Bompard[1], Dari F. Da[2], Serge Yerbanga[2], Isabelle Morlais[1], Thierry Lefèvre[1], Thomas S. Churcher[3], Anna Cohuet[1]

[1]Institut de Recherche pour le Développement, Montpellier, France, [2]Institut de Recherche en Sciences de la Santé, Bobo-Dioulasso, Burkina Faso, [3]MRC Centre for Outbreak Analysis and Modelling, Infectious Disease Epidemiology, Imperial College, London, United Kingdom

The population dynamics of human-to-mosquito malaria transmission in the field has important implications for the genetics, epidemiology and control of malaria. The number of *Plasmodium falciparum* oocysts in naturally infected mosquitoes in the wild is poorly understood, though past work indicates that most mosquitoes have only one or two oocysts. The per bite mosquito force of infection (the mean number of oocysts gained from an infectious bite) is also unclear despite the force of infection influencing factors such as the efficacy of novel transmission blocking interventions currently under development. Here a yearlong analysis of malaria transmission in three sites in Burkina Faso and Cameroon is reported. Naturally fed mosquitoes were caught inside houses and dissected to assess the prevalence and intensity of oocysts and sporozoites 3 and 7 days after collection. Cross-sectional surveys of the resident human population were carried out to determine the prevalence and intensity of sexual and asexual parasites. Results show that oocysts intensity in naturally infected mosquitoes is substantially higher than previous estimates. In the rainy season infected mosquitoes had on average 9-18 oocysts per mosquitoes 3 days after collection, with one mosquito harboring 786 oocysts. Multivariate analysis indicated that village, season and bednet use in the local population to be associated with the prevalence and intensity of oocysts and the sporozoite rate. A dynamical mathematical model of transmission was used to estimate the per-bite transmission probability, the proportion of superinfections and average parasite exposure per bite for each location. The implications of high parasite exposure on biology of transmission and the development and use of transmission blocking interventions in the field are discussed.

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IMPACT OF PYRETHROID EXPOSURE ON RESISTANT MOSQUITO FITNESS

Alida Kropf[1], Behi Kouadio Fodjo[2], Marius Zoh Gonze[2], Bassirou Bonfoh[2], **Chouaibou Mouhamadou**[2]

[1]MIE, Bouake, Côte D'Ivoire, [2]CSRS, Abidjan, Côte D'Ivoire

The use of insecticides is the current backbone of vector control. But, it is widely believed that the current raise and spread of insecticides resistance in mosquito population could compromise its efficacy as exposures to LLINs or IRS are no longer able to kill their target. However very little is known about the long-term effect of insecticide exposure on resistant mosquito. We here hypothesize that mosquitoes that have survived insecticide exposure will have a reduced fitness, which may be express in a shorter lifespan, reduced blood-feeding success or reduced egg output. We tested this hypothesis in an experimental design where we measured different life history traits on 2 groups of resistant mosquitoes. One group was exposed repeatedly to insecticides before being allowed to have a