Selected Scientific Publications (between 1 August and 31 October 2023)

ITNs

Effects of next-generation, dual-active-ingredient, long-lasting insecticidal net deployment on insecticide resistance in malaria vectors in Tanzania: an analysis of a 3-year, cluster-randomised controlled trial

Lancet Planetary Health August 2023

We aimed to measure phenotypic and genotypic insecticide-resistance profiles among wild Anopheles collected over 3 years to assess the longitudinal effects of dual-active-ingredient LLINs on insecticide resistance.

Interpretation: Our phenotypic data supports trial epidemiological findings; chlorfenapyr PY-LLINs provided superior protection from malaria across multiple transmission seasons, with few effects on insecticide-resistance selection. Rapid pyrethroid-resistance intensification in the piperonyl butoxide PY-LLIN group and pre-existing tolerance of pyriproxyfen in vector populations might explain the poorer performance of these two interventions regarding malaria outcomes. Further work is required to elucidate the potential mechanisms driving cross-resistance between pyrethroids and novel active ingredients to better inform the design of pre-emptive resistance-management strategies.

Effectiveness of piperonyl butoxide and pyrethroid-treated long-lasting insecticidal nets (LLINs) versus pyrethroid-only LLINs with and without indoor residual spray against malaria infection: third year results of a cluster, randomised controlled, two-by-two factorial design trial in Tanzania

Malaria Journal 3 Oct 2023

This study looks at the third year of rollout of nets treated with a pyrethroid and a synergist, piperonyl butoxide (PBO) in Muleba district, Tanzania to inform whether policy guidelines need to be updated.
At 28 and 33 months, study net usage among household participants was only 47% and 31%, respectively.

Despite low usage of PBO- Pyrethroid LLIN, a small impact of those nets on malaria infection prevalence was still observed in the 3rd year with the most protection offered to children still using them. To maximize impact, it is essential that net re-distribution cycles are aligned with this LLIN lifespan to maintain maximum coverage.

IRS

Community evaluation of VECTRON™ T500, a broflanilide insecticide, for indoor residual spraying for malaria vector control in central Benin; a two arm non-inferiority cluster randomised trial

Sci Rep 19 October 2023

We performed a two-arm non-inferiority community randomised evaluation of VECTRON™ T500, compared to Fludora® Fusion against pyrethroid-resistant *Anopheles gambiae* s.l. in an area of high coverage with pyrethroid-only nets in the Za-Kpota District of central Benin.
Using a non-inferiority margin of 50%, vector density indicated by the human biting rate (bites/person/night) was non-inferior in the VECTRON™ T500 arm compared to the Fludora® Fusion arm both indoors and outdoors. Sporozoite rates and entomological inoculation rates did not differ significantly between study arms. Cone bioassay mortality with both VECTRON™ T500 and Fludora® Fusion was 100% for 24 months post-IRS application on both cement and mud treated house walls with both susceptible and pyrethroid-resistant strains of *An. gambiae* s.l. VECTRON™ T500 was non-inferior to Fludora® Fusion in reducing the risk of malaria transmission by pyrethroid resistant vectors when applied for IRS in communities in central Benin.

Passive spatial emanators

Efficacy of the spatial repellent product Mosquito Shield™ against wild pyrethroid-resistant Anopheles arabiensis in south-eastern Tanzania

Malaria Journal 30 August 2023

The purpose of this study was to assess the efficacy of Mosquito Shield™ deployed in experimental huts against wild, free-flying, pyrethroid-resistant *Anopheles arabiensis* mosquitoes in Tanzania over 1 month. Landing inhibition was estimated to be 70% and blood-feeding inhibition was estimated to be 69%.
This study demonstrated that Mosquito Shield™ was efficacious against a wild pyrethroid-resistant strain of *An. arabiensis* mosquitoes in Tanzania for up to 1 month and could be used as a complementary or stand-alone tool where gaps in protection offered by core malaria vector control tools exist.

Deltamethrin and transfluthrin select for distinct transcriptomic responses in the malaria vector Anopheles gambiae

Malaria Journal 4 Sept 2023

In this study, a controlled selection was used to compare the dynamics of resistance between transfluthrin and the widely used pyrethroid deltamethrin in the mosquito *Anopheles gambiae*. Then, the associated molecular mechanisms were investigated using target-site mutation genotyping and RNA-seq.
A rapid increase in resistance to deltamethrin and transfluthrin was observed throughout the selection process in each selected line in association with an increased frequency of the L1014F *kdr* mutation.
This study confirms that recurrent exposure of adult mosquitoes to pyrethroids in a public health context can rapidly select for various resistance mechanisms. In particular, it indicates that in addition to target site mutations, the polyfluorinated pyrethroid transfluthrin can select for a broad metabolic response, which includes some P450s previously associated to resistance to classical pyrethroids. This unexpected finding highlights the need for an in-depth study on the adaptive response of mosquitoes to newly introduced active ingredients in order to effectively guide and support decision-making programmes in malaria control.

Larval control

Cost and quality of operational larviciding using drones and smartphone technology

Malaria Journal 27 Sept 2023

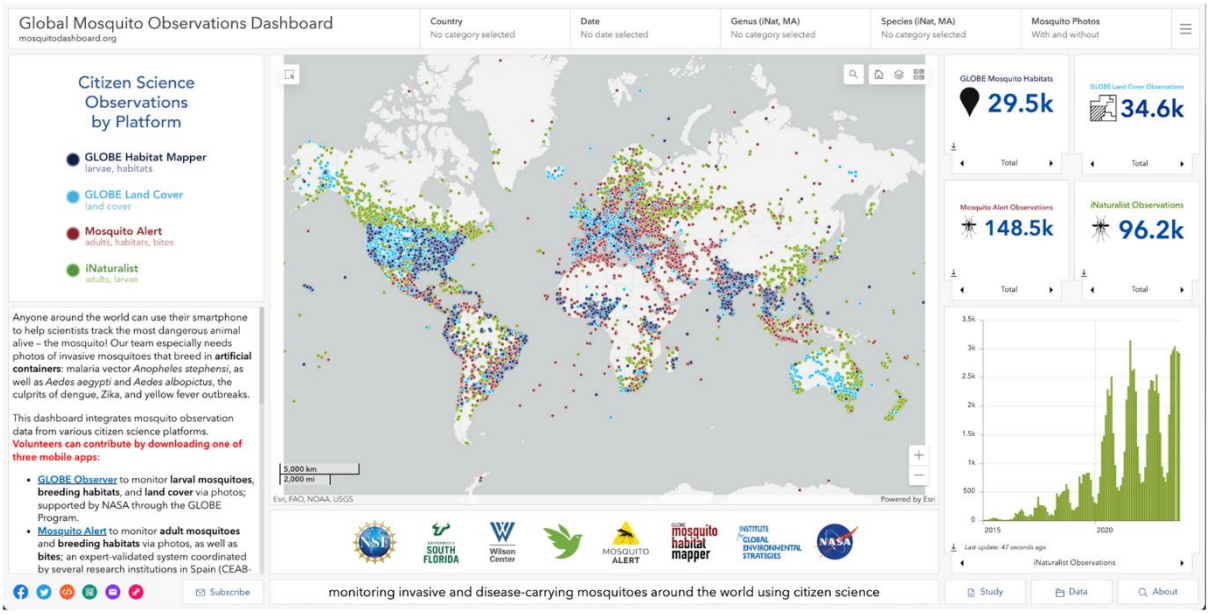
Previous studies have demonstrated the potential for drone imaging technology to map malaria vector breeding sites. However, key questions remain unanswered related to the use and cost of this technology within operational vector control.
Using Zanzibar (United Republic of Tanzania) as a demonstration site, a protocol was collaboratively designed that employs drones and smartphones for supporting operational LSM, termed the Spatial Intelligence System (SIS). SIS was evaluated over a four-month LSM programme by comparing key mapping accuracy indicators and relative costs (both mapping costs and intervention costs) against conventional ground-based methods. Additionally, malaria case incidence was compared between the SIS and conventional study areas, including an estimation of the incremental cost-effectiveness of switching from conventional to SIS larviciding.
The results demonstrate that the SIS approach is significantly more accurate than a conventional approach for mapping potential breeding sites: mean % correct per site: SIS = 60% (95% CI 32–88%, p = 0.02), conventional = 18% (95% CI − 3–39%). Whilst SIS cost more in the start-up phase, overall annualized costs were similar to the conventional approach, with a simulated cost per person protected per year of $3.69 ($0.32 to $15.12) for conventional and $3.94 ($0.342 to $16.27) for SIS larviciding. The main economic benefits were reduced labour costs associated with SIS in the pre-intervention baseline mapping of habitats. There was no difference in malaria case incidence between the three arms. Cost effectiveness analysis showed that SIS is likely to provide similar health benefits at similar costs compared to the conventional arm.

New vector control tools and approaches

Global mosquito observations dashboard (GMOD): creating a user-friendly web interface fueled by citizen science to monitor invasive and vector mosquitoes

International Journal of Health Geographics 28 October 2023

To effectively combat this issue, there is a need for increased public awareness and mosquito control. However, traditional surveillance programs are time-consuming, expensive, and lack scalability. Fortunately, the widespread availability of mobile devices with high-resolution cameras presents a unique opportunity for mosquito surveillance. In response to this, the Global Mosquito Observations Dashboard (GMOD) was developed as a free, public platform to improve the detection and monitoring of invasive and vector mosquitoes through citizen science participation worldwide.
GMOD is an interactive web interface that collects and displays mosquito observation and habitat data supplied by four datastreams with data generated by citizen scientists worldwide. By providing information on the locations and times of observations, the platform enables the visualization of mosquito population trends and ranges. It also serves as an educational resource, encouraging collaboration and data sharing. The data acquired and displayed on GMOD is freely available in multiple formats and can be accessed from any device with an internet connection.
Since its launch less than a year ago, GMOD has already proven its value. It has successfully integrated and processed large volumes of real-time data (~ 300,000 observations), offering valuable and actionable insights into mosquito species prevalence, abundance, and potential distributions, as well as engaging citizens in community-based surveillance programs.
The future of citizen science holds great promise, and GMOD stands as an exciting initiative in this field.



Anopheles stephensi

Evidence for a role of Anopheles stephensi in the spread of drug and diagnosis-resistant malaria in Africa

Nature Medicine 26 Oct 2023

Anopheles stephensi, an Asian malaria vector, continues to expand across Africa. The vector is now firmly established in urban settings in the Horn of Africa. Its presence in areas where malaria resurged suggested a possible role in causing malaria outbreaks. Using a prospective case control design, we investigated the role of *An. stephensi* in transmission following a malaria outbreak in Dire Dawa, Ethiopia in April-July 2022. Screening contacts of malaria patients and febrile controls revealed spatial clustering of *P. falciparum* infections around malaria patients in strong association with *An. stephensi* presence in the household vicinity. *Plasmodium* sporozoites were detected in these mosquitoes. This outbreak involved clonal propagation of parasites with molecular signatures of artemisinin and diagnostic resistance. This study provides the strongest evidence to date for a role of A*n. stephensi* in driving an urban malaria outbreak in Africa, highlighting the major public health threat this fast-spreading mosquito poses.

Odds & Ends

What constitutes high-quality evidence for malaria vector control?

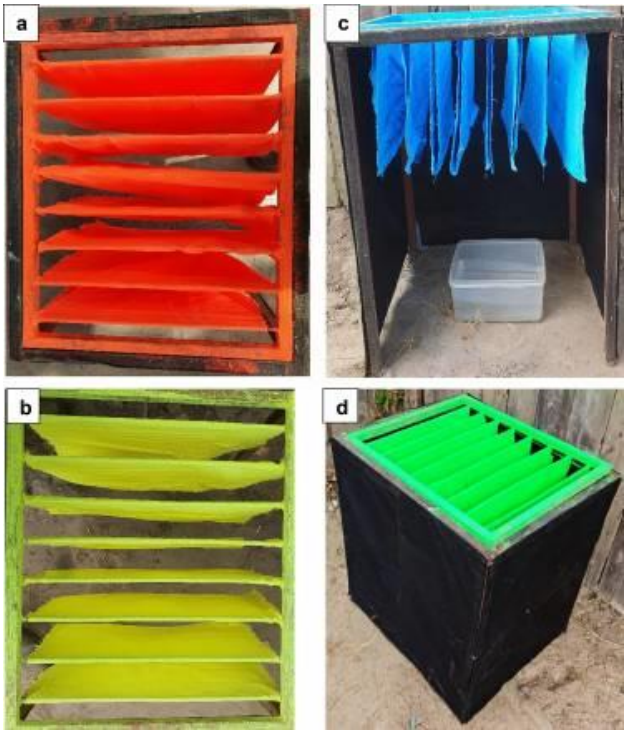
Lancet 2 Sept 2023

In this opinion piece, the authors suggest a more flexible approach in assessment of evidence in support, or not, of new medicines, vaccines, and surgical procedures should be considered. “Arguments for greater flexibility in evaluation of such interventions have greater force for those aimed at vectors of disease, but do not diminish the importance of well designed RCTs for evaluation of interventions, where appropriate.” They suggest, “making WHO guidance more inclusive of entomological outcomes and study designs other than RCTs—including historical evidence or implementation of novel test-negative designs—would allow countries to more easily access a range of innovative interventions, resulting in improved locally appropriate vector control, thereby accelerating malaria control and elimination globally and saving lives now.”

Life expectancy of Anopheles funestus is double that of Anopheles arabiensis in southeast Tanzania based on mark-release-recapture method

Sci Reports 22 September 2023

Anopheles arabiensis and *Anopheles funestus* sensu stricto mosquitoes are major East African malaria vectors. Understanding their dispersal and population structure is critical for developing effective malaria control tools. Three mark-release-recapture (MRR) experiments were conducted for 51 nights to assess daily survival and flight range of *An. arabiensis* and *An. funestus* mosquitoes in south-eastern, Tanzania. Probability of daily survival was 0.76 for *An. arabiensis* and 0.86 for *An. funestus* translating into average life expectancy of 3.6 days for *An. arabiensis* and 6.5 days for *An. funestus*. Dispersal distance was 654 m for *An. arabiensis* and 510 m for *An. funestus*. *An. funestus* life expectancy was substantially longer than that of *An. arabiensis*. The MRR method described here could be routinely utilized when evaluating the impact of new vector control tools on mosquito survival.



A bioassay method validation framework for laboratory and semi-field tests used to evaluate vector control tools

Malaria Journal 28 Sept 2023

Vector control interventions play a fundamental role in the control and elimination of vector-borne diseases. The evaluation of vector control products relies on bioassays, laboratory and semi-field tests using live insects to assess the product's effectiveness. Bioassay method development requires a rigorous validation process to ensure that relevant methods are used to capture appropriate entomological endpoints which accurately and precisely describe likely efficacy against disease vectors as well as product characteristics within the manufacturing tolerance ranges for insecticide content specified by the World Health Organization. Currently, there are no standardized guidelines for bioassay method validation in vector control. This report presents a framework for bioassay validation that draws on accepted validation processes from the chemical and healthcare fields and which can be applied for evaluating bioassays and semi-field tests in vector control. The validation process has been categorized into four stages: preliminary development; feasibility experiments; internal validation, and external validation. A properly validated method combined with an appropriate experimental design and data analyses that account for both the variability of the method and the product is needed to generate reliable estimates of product efficacy to ensure that at-risk communities have timely access to safe and reliable vector control products.

Sub-lethal exposure to chlorfenapyr reduces the probability of developing Plasmodium falciparum parasites in surviving Anopheles mosquitoes

Parasites and Vectors 3 Oct 2023

To overcome pyrethroid resistance, Interceptor® G2 (IG2), a 'first-in-class' dual insecticidal net that combines alpha-cypermethrin with chlorfenapyr, was developed. Chlorfenapyr is a pro-insecticide, requiring bio-activation by oxidative metabolism within the insect's mitochondria, constituting a mode of action preventing cross-resistance to pyrethroids. Recent epidemiological trials conducted in Benin and Tanzania confirm IG2's public health value in areas with pyrethroid-resistant *Anopheles* mosquitoes. As chlorfenapyr might also interfere with the metabolic mechanism of the *Plasmodium* parasite, we hypothesised that chlorfenapyr may provide additional transmission-reducing effects even if a mosquito survives a sub-lethal dose.

We demonstrated that sub-lethal exposure of pyrethroid-resistant mosquitoes to chlorfenapyr substantially reduces the proportion of infected mosquitoes and the intensity of the *P. falciparum* infection. This will likely also contribute to the reduction of malaria in communities beyond the direct killing of mosquitoes.

WHO News and Publications

WHO recommends a second vaccine for malaria prevention

The addition of the R21/Matrix-M vaccine to complement the ongoing rollout of the first malaria vaccine, RTS,S/AS01, is expected to result in sufficient vaccine supply to benefit all children living in areas where malaria is a major public health problem.

Recent WHO publications of interest

18th VCAG Meeting Report
1 August 2023
This report details the proceedings and outcomes of the meeting, including advice provided to applicants working on interventions in the following intervention types: bait stations, spatial repellents, systemic endectocide treatment, and reduction of pathogen transmission induced by *Wolbachia*.

Webinars, websites and other resources

APMEN Webinar YouTube channel

APMEN hosts a *webinar series* to provide a platform for discussing a variety of topics of interest and sharing information related to malaria elimination. Recorded sessions are available on their YouTube channel. Recent and upcoming topics include:

- 17 August 2023 – ***Managing Vector Borne Diseases during Climate Emergencies in Pakistan***
- 22 August 2023 – ***Genetic Approach to Vector Control: How can Gene Drive Help Control Malaria and Other Diseases?***
- 20 September 2023 – ***Vector Control in Complex Situations***

Announcing AMCA's Best Practices for Integrated Mosquito Management Virtual Training Program

The American Mosquito Control Association's (AMCA) has launched a free virtual training program, titled "AMCA's Best Practices for Integrated Mosquito Management Virtual Training Program." This comprehensive program is designed to equip mosquito control professionals with the essential knowledge and skills needed to excel in the field of mosquito control and is available free to the public.

The online course is available ***here***

In the news and social media

Syngenta Submits New Insecticide SOVRENTA® to WHO VCP Pre-Qualification

Syngenta, is pleased to announce the submission of its new insecticide, SOVRENTA®, to the World Health Organization (WHO) Vector Control Product Pre-Qualification program. This novel insecticide will be used as an indoor residual spray for the control of mosquitoes that transmit malaria, a disease affecting millions of people worldwide.

SC Johnson Reaches Major Milestone with Breakthrough Mosquito Repellent Tool

20 September 2023

New field testing shows SC Johnson Guardian™, a spatial repellent made by SC Johnson, is demonstrating a game-changing efficacy of one year.
