Revolutionizing Vector Control for Malaria Elimination

Using mathematical models to optimize vector control

Key Messages

- Given the expanding vector control toolbox, programs need evidence to determine the optimal combination of vector control tools (VCTs)
- Especially in the absence of empirical evidence, models provide a virtual test ground through which programs and researchers can explore the expected impact of combinations of VCTs in a range of eco-epidemiological settings
- Two mathematical transmission models are presented to explore impact of combined VCTs:
  - **VCOM**: A population-based Vector Control Optimization Model based on the basic mosquito life and feeding cycles, and
  - **MASH**: An individual-based model incorporating spatial effects and heterogeneities to examine interventions targeting mosquitoes in complex environmental settings
- Both modeling platforms will be made accessible to the malaria community for future research and for programmatic decision-making

Maximizing the Impact of Vector Control Tools

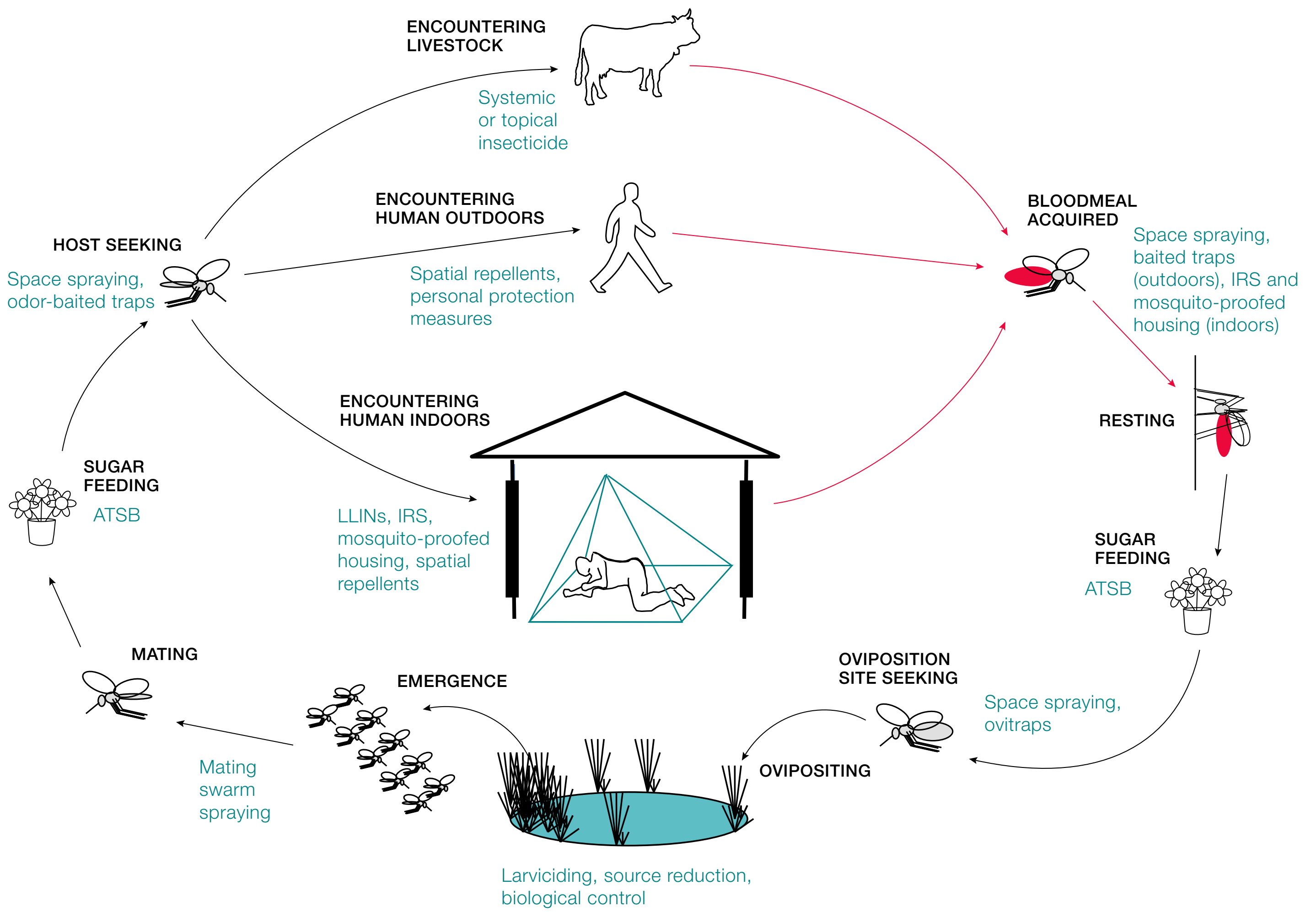
Despite successes in reducing malaria transmission by insecticide-treated nets (ITNs) and indoor residual spraying (IRS), the protective effect of ITNs and IRS is limited by the fact that they target mosquitoes solely indoors, while mosquito vectors of malaria increasingly feed upon humans outdoors and also feed upon non-human hosts such as cattle. Novel and underutilized VCTs are emerging that target mosquitoes both indoors and outdoors and at different stages of their life and feeding cycle.[1] Trials have been conducted to assess the effectiveness of some of these interventions at suppressing mosquito populations in isolation; however, it is increasingly recognized that vector control efforts aimed at malaria elimination will require a carefully chosen combination of interventions to achieve this goal.[2] While it is costly and onerous to conduct field trials of multiple combinations of interventions in multiple settings, models can be used to gain initial insights into combination interventions of interest by exploring their synergies in a quantitative way within the context of our understanding of the mosquito life cycle.

Two New Models Predict the Impact of Vector Control Tools on Malaria Transmission

The Vector Control Optimization Model (VCOM) is a computational tool to predict the impact of combined vector control interventions at the mosquito population level

VCOM is one of two models the Malaria Elimination Initiative (MEI) at the University of California, San Francisco Global Health Group in partnership with the University of California, Berkeley, and Ifakara Health Institute, Tanzania, has developed to assess the impact of combinations of interventions on mosquito population dynamics. VCOM describes mosquitoes as a collective population and follows their development from eggs to larvae to pupae and then on to adults of both sexes. Of special relevance to malaria transmission, VCOM also models the mosquito feeding cycle, in which adult female mosquitoes blood-feed on humans indoors and outdoors and on animals and then lay eggs at breeding sites before returning for another round of blood-feeding (only female mosquitoes

Figure 1. Mosquito life and feeding cycle (in black) with interventions (in teal) targeting each stage as implemented in the VCOM model



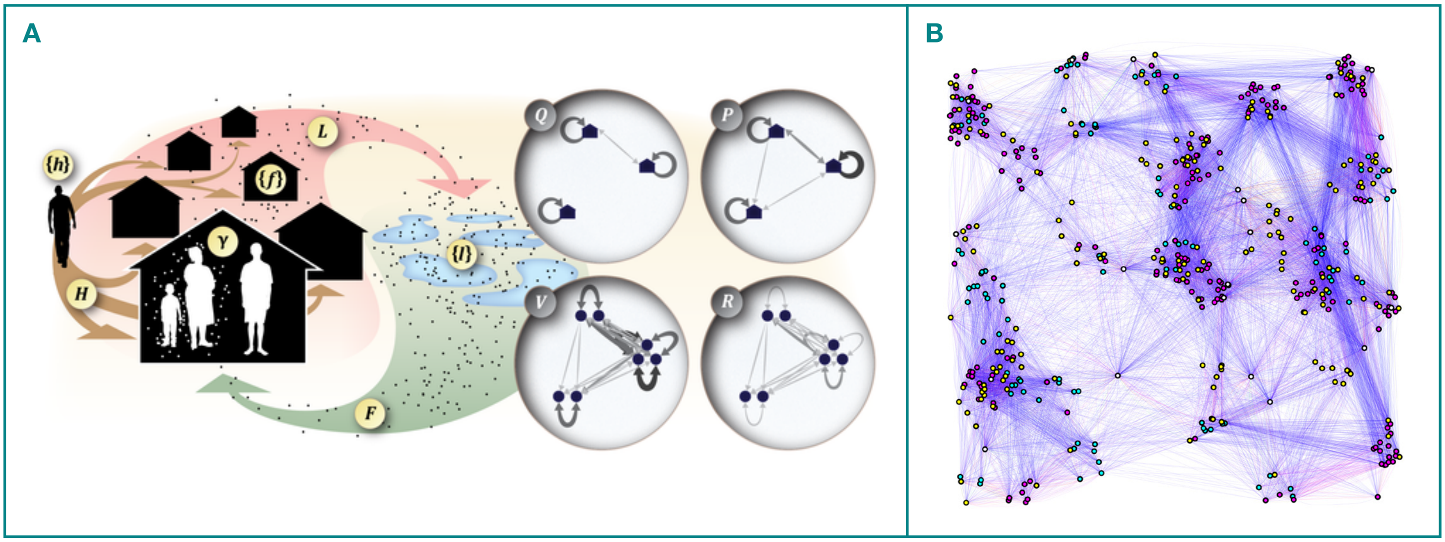
require blood meals since the blood is necessary for reproduction). Interventions are modeled at all stages of the life and feeding cycle—e.g. larviciding (ground and aerial) of immature mosquitoes, insecticide spraying of male mating swarms, attractive toxic sugar baits (ATSB), attract-and-kill mechanisms not based on sugar, space spraying targeting outdoor adult mosquitoes, and insecticide treatment of cattle (topical and systemic) targeting adult female mosquitoes feeding on animals (Figure 1).

Modular Analysis and Simulation for human Health (MASH) is an individual-based simulation tool capable of modeling combined vector control interventions incorporating the heterogeneities inherent in ecosystems

MASH is the second model the MEI is developing, in partnership with the Institute for Health Metrics and Evaluation at the University of Washington, to assess the impact of combinations of interventions on mosquito population dynamics. MASH is a spatial, individual-based simulation model that can address the impact of heterogeneities that exist in nature on intervention efficacy.[3] It is known that heterogeneity in malaria transmission exists at multiple levels—mosquitoes bite humans at different rates, some mosquito species prefer to feed on livestock rather than humans, and there is spatial heterogeneity in the distribution of people, houses, mosquito breeding sites, livestock, and sugar sources. The MASH simulation environment is able to assess the impact of combinations of interventions in the context of these heterogeneities (Figure 2).

Figure 2. Depiction of spatial heterogeneities in the MASH model,[3] essential for realistic modeling of mosquito and malaria control

A: This figure is an abstract visual representation of the model structure; mosquitoes and humans both move between various sites on a landscape. Networks show the various emergent dynamics of pathogen transmission that arise from spatial characteristics and behaviors of hosts and vectors. B: Circles represent habitat types that mosquitoes visit (pink: oviposition sites, cyan: human residences/blood-feeding sites, white: mating sites, yellow: sugar sources). Lines connecting these represent the probability that mosquitoes move from one site to another (red: higher probability, blue: smaller probability).



Interventions Targeting a Range of Resources in the Mosquito Life and Feeding Cycle are Required

The modeling frameworks will be useful for predicting the impact of combinations of VCTs on local malaria transmission in a range of settings. The models are capable of exploring a range of ecologies with differing transmission intensities, vector species and relative densities of non-human hosts. Sample results from VCOM are shown in Figure 3 for a population of *An. gambiae* (panel A) and *An. arabiensis* (panel B) mosquitoes in areas with moderate transmission (i.e., a baseline entomological inoculation rate (EIR) of 50 infective bites per person per year). In this scenario, to reduce EIR to an extent required for local malaria elimination,[4] additional VCTs to ITNs are required. Exploring combinations of interventions in addition to ITNs at 50% coverage, the VCOM modeling framework indicates that adding interventions not requiring human participation (e.g., larviciding, endoc-ticide-treated cattle, and attractive toxic sugar baits (ATSB), all at 80% coverage) may achieve malaria elimination for the two vector species studied in areas with moderate transmission and potentially in areas with low and high transmissions.

Combining ITNs with ATSB and personal protection measures (e.g. insecticide-treated clothing) may achieve local malaria elimination for *An. gambiae*, but a fourth intervention, endectocide-treated cattle, is required for *An. arabiensis* based on these specified intervention coverage.

These Modeling Platforms Will Provide Increasingly Accurate Predictions

The VCOM and MASH modeling frameworks capture essential details of the interactions of mosquitoes with their hosts and the environment. This allows the synergies of a range of interventions to be captured and for the combined impact of various combinations of interventions to be predicted in a range of settings. These will be highly useful tools in the selection of interventions for vector control trials and operational research and in the design of trials themselves. The Graphical User Interface (GUI) will increase their accessibility and usefulness for policy makers, research scientists and national malaria control programs (NMCPs) (Figure 4).

The VCOM and MASH models will be highly useful tools in the design of vector control strategies and will provide increasingly accurate predictions and decision support as development continues.

- Using these modeling frameworks, the researchers and NMCPs will be able to develop a shortlist of VCTs to achieve malaria elimination in a range of eco-epidemiological settings.

- Making the modeling frameworks available and easy-to-use online will enhance the accessibility and usefulness of these tools.
- Researchers should work closely with NMCPs and other stakeholders and end users to ensure these tools provide useful results and can assist in informed decision making.
- As part of future research work, as new data becomes available for VCTs, these modeling frameworks will be refined, parameterized, and validated.
- In addition, cost data can be incorporated to enable cost-effectiveness analysis to be performed in a range of settings of interest to malaria control programs.

Figure 3: Sample VCOM results

Sample results indicate reductions in the entomological inoculation rate (EIR) from a baseline of 50 infective bites per person per year in areas where dominant malaria vectors are *Anopheles gambiae* (panel A) and *An. arabiensis* (panel B) due to a range of intervention combinations. In this example, modeled interventions include ITNs at 50%, ATSB, endectocide-treated cattle (ETC), larviciding (LAR), mosquito-proofed housing (HOU), and personal protection measures (PPM) such as insecticide-treated clothing. All additional interventions to ITNs are modeled at 80% coverage.

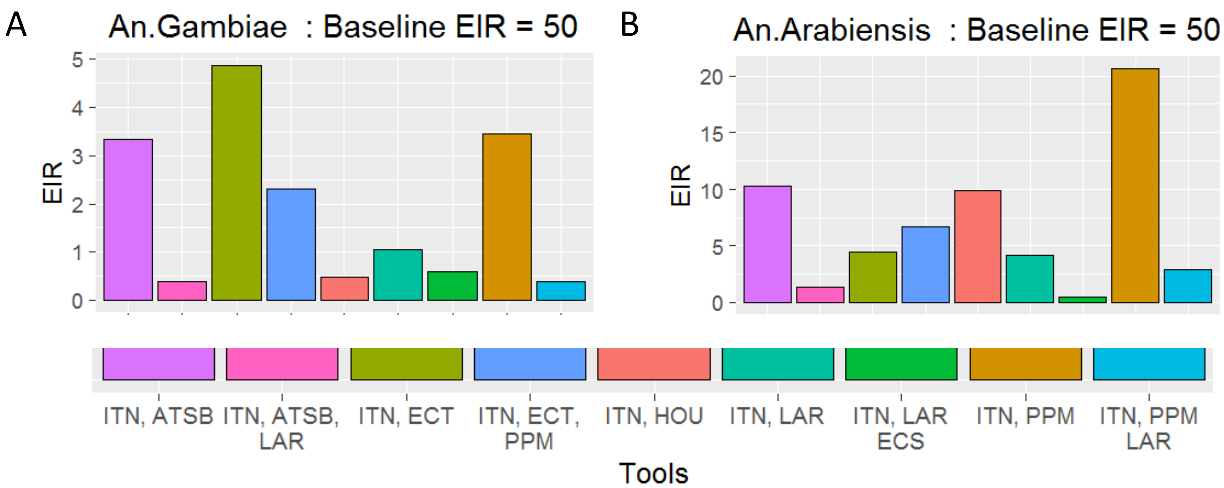
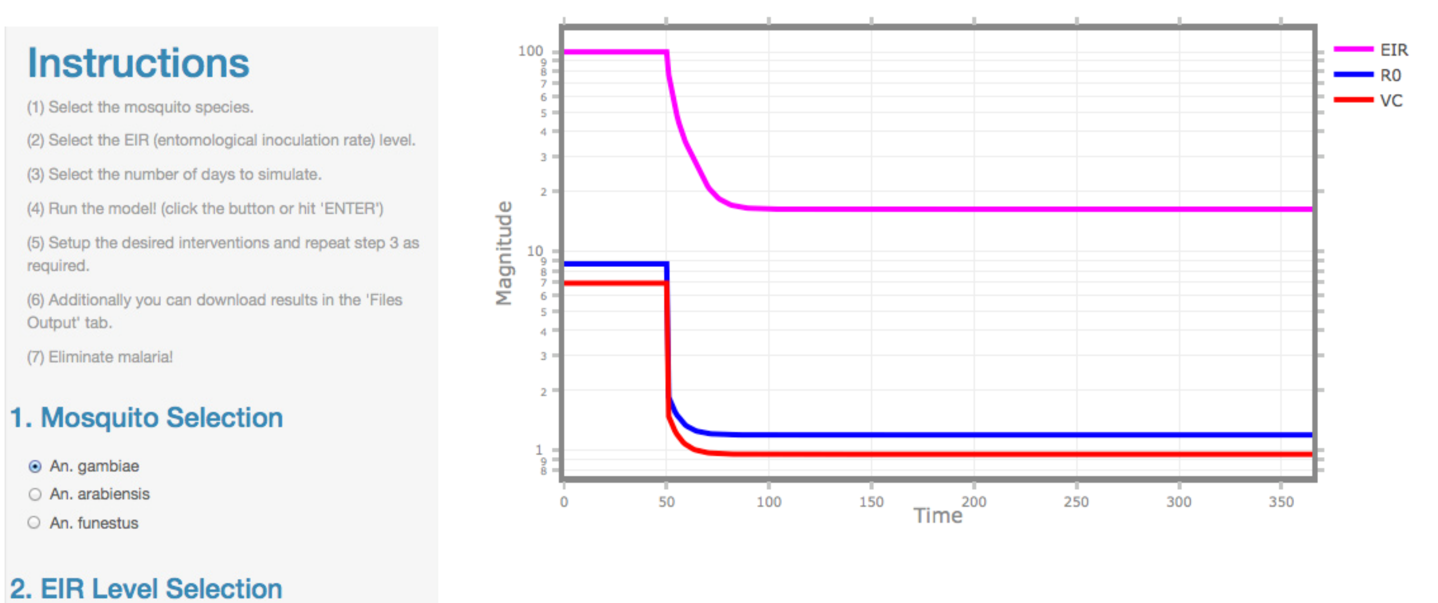


Figure 4. VCOM software Graphical User Interface

VCOM users can explore the impact of combination interventions using the easy-to-use GUI. Users are able to run simulations based on a given mosquito species, transmission setting, cattle-to-human ratio and choice of intervention(s). Advanced options are available to alter the parameter values of the mosquito ecology and intervention models as desired. GUI online: **http://chipdelmal.github.io/VCOM**



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The **Malaria Elimination Initiative (MEI)** at the University of California San Francisco (UCSF) Global Health Group believes a malaria-free world is possible within a generation. As a forward-thinking partner to malaria-eliminating countries and regions, the MEI generates evidence, develops new tools and approaches, disseminates experiences, and builds consensus to shrink the malaria map. With support from the MEI's highly-skilled team, countries around the world are actively working to eliminate malaria—a goal that nearly 30 countries will achieve by 2020.

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