

2nd New Challenges, New Tools in Vector Control Workstream

Feedback & Planning Workstream Activities

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New Tools and New Challenges for Vector Control

Presentations:

- Updates on expanding the vector control toolbox
 - **Allison Tatarsky & Yasmin Williams**
- Everything you need to know about residual malaria transmission in 10 minutes
 - **April Monroe**
- *Anopheles* species identification: an old and continuing challenge
 - **Basil Brooke/Maureen Coetzee**
- Ivermectin for malaria elimination: 2016, a year of exponential growth
 - **Carlos Chaccour**
- Progress on a Randomised Controlled Trial for evaluation of Eave Tubes
 - **Matt Thomas**
- Updates on Spatial Repellents for Malaria Elimination
 - **Neil Lobo**

“Updates on expanding the vector control toolbox”

- Allison Tatarsky & Yasmin Williams

Summary:

- A desk review and modelling based approach was applied to understand gaps in vector control (beyond ITNS and IRS) in order to identify potential solutions and to accelerate progress to elimination. The five workstreams were:
- Geospatial modelling to determine the extent of residual transmission. This was done in partnership with the MAP project, to identify areas where transmission does persist despite high coverage of nets.
- A Systematic Literature Review to determine the evidence that exists to date and what gaps remain. The review looked into 21 vector control tools (excluding ITNs and IRS) and trials showing epidemiological outcomes, or entomological outcomes. Out of 17,912 abstracts, 155 studies were eligible for inclusion. Only 7 of 21 vector control tools have gone through a Phase III evaluation.
- A technical review of aerial application to establish the potential for aerial spraying for *Anopheles* control.

“Updates on expanding the vector control toolbox”

- Allison Tatarsky & Yasmin Williams

- **The outcome is an ongoing development of a shortlist of “ready” tools with potential for impact:**
 - Environmental Management
 - Larviciding
 - Mosquito-proofed housing
- **Transmission modelling to identify the optimal combinations of tools. The Vector Control Optimisation Model simulates the addition of a new VCT into the local setting. Modular Analysis and Simulation for human Health is a model that takes into account environmental heterogeneities**
- **Case study series to help identify the enabling factors for the implementation of new tools. Case studies were taken from the US, Australia, and malaria endemic countries. Best practice showed; entomological and operational capacity; entomological intelligence linked with spatial, epidemiological**
- **These tools are needed immediately while R&D of other less researched tools is carried out.**
- **The RBM VCWG New Tool New Challenges workstream was asked to consider moving beyond the traditional research models to develop a learning-by-doing approach for emerging vector control tools.**
- **Summaries available on website: <http://www.shrinkingthemap.org/what-we-do/vector-control>**

“Updates on expanding the vector control toolbox”

- Allison Tatarsky & Yasmin Williams

Discussion:

- It was queried why the mapping component concentrated on SSA which has stable transmission and where elimination is not currently achievable. SSA was used for the mapping component as this area has the best available data. But the rest of the project was location agnostic. Exploring across different setting is a good research priority.
- An explanation of “learning by doing” was requested. A suggestion was made to set up an intervention trial, maybe with a control, but with a major emphasis on data collection and M&E. This allows methods and interventions to be adapted as needed, but lacks rigor as compared to RCTs. It may allow more rapid movement forward when facing elimination targets.

Everything you need to know about RMT in 10 minutes

- April Monroe

Summary:

- Residual Malaria Transmission (RMT) occurs where high ITN uptake and IRS are being carried out, but malaria transmission is continuing. RMT studies are taking place in Africa (Ethiopia, Kenya, Tanzania, Ghana, Cameroon, Burkina Faso), SE Asia (Vietnam and Thailand), Americas (Brazil and Peru) and the Western Pacific (Papua New Guinea).
- An outline of the Special Programme for Research and Training in Tropical Diseases (TDR) was given, which aims to quantify and characterise RMT across settings.
- Three more studies funded by PMI were outlined, in Zanzibar, Ghana and Ethiopia. All these groups are using different strategies to assess human behaviour, entomological and epidemiological outcomes.
- Other RMT activities include geospatial modelling and mapping and an entomological surveillance framework. RMT has been discussed at the Mekong outdoor malaria network workshop (Nov 2016), and a TDR investigators dissemination workshop is planned for Sept 2017 in Tanzania.
- The VCWG were asked to consider the following opportunities: a dedicated forum to share results and discuss methods across groups, setting and funders, re-establishment of outdoor transmission networks in other regions, consensus building around best practiced, standardised methods/tools for use across settings.

Everything you need to know about RMT in 10 minutes

- April Monroe

Discussion:

- An explanation of the RMT map presented (MAP Project; P. Gething PI) was requested. Red areas were those predicted to have high residual transmission, so would be areas where new tools other than LLINs and IRS are necessary. Blue areas have low RMT and represent areas where LLINs might still be useful. It was confirmed that insecticide resistance was included in the model as a driver of RMT. **The definition of “residual transmission” used in the model was queried. There has been some debate over the definition of RMT and it might be an issue worth discussing across the group. The working definition for the model is the same as WHO definition.**
- It was queried what indicators should be measured to detect RMT. It was stated that we need a platform to discuss best practice and to bring scientists together to discuss these issues.
- Request for future meeting to have more results from on the ground research. Evaluations of new tools, are required before recommending them to country programme managers. A bigger picture view of the research is needed allows a call for discussion of the work going on and comparison of methods.
- The large number of researchers in this area led to a query of whether there is duplication of work. But a lot of institutions are already collaborating, so effort is not necessarily being duplicated.

***Anopheles* species identification: an old and continuing challenge**

- Basil Brooke/Maureen Coetzee

Summary:

- Identification of the *An. funestus* and *An. gambiae* complex.
- Almost all anopheles have potential to act as vectors. As more incrimination studies are done, more species are emerging as minor vectors.
- So, when and where is molecular identification appropriate. There is a tendency in some labs to rely heavily on molecular identification of mosquito species.
- Collections from five African countries – non-vectors identified morphologically were put through molecular assays. Found very common to get mis-identification. So there should be sound morphological identification first, before molecular assays are used.
- MC is planning to update the keys (Gillies & Coetzee 1987) with high res photos and would appreciate feedback from users of the keys.

***Anopheles* species identification: an old and continuing challenge**

- Basil Brooke/Maureen Coetzee

Discussion:

- Morphological identification in SE Asia is planned through IP & PMI, including voucher specimens. It was suggested that research groups combine efforts and resources to improve basic skills.
- Query: Will any sequence data be included in the work? They will have to in the case of M & S forms at least. First step is to produce hard copy guide, next step to make this electronic to incorporate sequence data too.
- Query: When will the new keys be available? The current dichotomous keys are correct to use and the PCR are also correct to use. BUT what is important is to morphologically identify first, and then if necessary use PCR to separate for example *An. funestus* species complex.
- Query: Where there is little entomological training or expertise, what is proposed for keeping specimens in a state for morphological identification? That is one aspect of training courses, and also should be embedded in vector control programmes e.g. countries should build reference specimens collections.
- Proposed keys will be different to the existing IRD interactive key. Many people in the field are put off a large key if there are 12+ steps to get to an ID.
- Is there opportunity for simplified keys? Yes. But in low transmission settings, good taxonomic skills are required and there aren't really short cuts.

Ivermectin for malaria elimination: 2016, a year of exponential growth

- Carlos Chaccour

Summary:

- Three high-level assessments were made last year. A technical consultation with WHO to define key data that is missing before a policy recommendation can be made, and the development of a draft TPP. MPAC evaluated TPP (Sep 2016), which will be resubmitted in March 2017.
- MalERA refresh included endectocides in their publication from the Panel on Diagnostics, drugs, vaccines and vector control in malaria elimination and eradication.
- The MMV has included endectocides under TCP-6 as a new development in antimalarial target candidate and product profiles. More information is available on MESA track.
- The effect of ivermectin has been established on *Anopheles aquasalis*, *An. darlingi*, *An. dirus*, *An. minimus*, *An. sawadwongporni*, *An. campestris*.
- The IVERMAL trial has published partial results that show no adverse events following very large doses (9x higher than normal) and in combination with DHA-PIP. The effect on mosquito survival was longer than the drug itself lasts in the body, most likely due to metabolites. Measurable effect for 28 days on mosquito mortality.
- RIMDAMAL ivermectin intervention given to >5years, but 20% reduction in incidence of malaria seen in under 5s.
- IMSEA trial 16 volunteers, looked at safety of multiple drug regimens as well as mosquito mortality. The antimalarial effect of ivermectin extends to the parasite where it inhibits liver infection.

Ivermectin for malaria elimination: 2016, a year of exponential growth

- Carlos Chaccour

Summary (cont):

- There is research into formulations such as the Bellinger star-shaped pill that can release a drug over 2 weeks.
- Dosing is being reviewed as current weight based dosing hampers co-formulations. When used in a veterinary setting, although protective in the first instance, can reduce the efficacy of human-centred control measures and sustain R_0 above 1.
- Future work priorities should be focussed on the technical (gaps in pharmacokinetic knowledge and dosing; metabolites; other endectocides); study design (outcomes and size: what is required to assess this intervention properly) and regulatory and policy (a sponsor?)

Ivermectin for malaria elimination: 2016, a year of exponential growth

- Carlos Chaccour

Discussion:

- A query was raised as to why Merck was not supporting this work. They are donating a lot of drug for LF and onchocerciasis, but this kind of work may be out of their scope at present.
- As in SSA, most malaria is in children <5 years, what is safety profile in children? Treatment can be in adults to give protection to children. A safety assessment has just been submitted
- Does impact come from mortality or sterilising? Both together work to reduce malaria. Mortality effect is short-lived, and sterility is longer lasting.

Progress on a Randomised Controlled Trial for evaluation of Eave Tubes

- Matt Thomas

Summary:

- **Eave Tube Intervention:**
 - 1) Close eaves 2) screen windows and 3) Install “eave tubes” containing insecticide impregnated netting that allow odour plume >>> House becomes a lethal lure.
- **Housing usually already have metal roofs and closed eaves, but now have ventilation structures, often blocked up. Eave tubes can be targeted to take advantage of these ventilation structures.**
- **Current “Eave Tube” study is a Phase III trial measuring, epidemiological impact:**
 - 1 year set-up & 2 years of monitoring (40 villages) epidemiology (50 children active infection detection, parasite clearance and time to first infection monthly/2 weekly blood smears/PCR), entomology, physical environment, social science and economic analysis.
- **Baseline data: population & RDT +ve. Randomisation.**
- **Consent level often very high 80-90%, lower consent explore through social science.**
- **Despite high documented pyrethroid resistance – selected a pyrethroid - 10% beta cyfluthrin caused 100% mortality (possible due to physical transfer of powdered insecticide). No decline in efficacy after 5 months. (other non-pyrethroids investigated).**
- **Current Trial Status : installations complete, insert distributed in next couple of weeks, monitoring begins, Additional entomological studies to explain results whatever they may be.**

Progress on a Randomised Controlled Trial for evaluation of Eave Tubes

- Matt Thomas

Discussion

- Trial control is a new LLIN. Universal coverage achieved in villages, new LLINs are required for any trial. Effect size expected (based on semi-field studies in Ifakara TZ- LLINs and Eave tubes) powered to show an effect above and beyond the LLINs.
- Strong odour cue should attract a lot of mosquitoes, so surface area is not as important as how many mosquitoes are lured to the tube & make contact with netting.
- Safety of manufacture of inserts – closed system, with vacuum underneath. Also PPE
- How does pyrethroid work even though mosquitoes are resistant. The electrostatic charge on the netting binds the insecticide powder, the insects also have an electrostatic charge. Contact with electrostatic netting results in a transfer of an overwhelming dose of insecticide.
- By using a pyrethroid the selection pressure is huge – will roll out have monitoring of resistance and will future roll out include use of a non-pyrethroid. The initial plan was to use a non-pyrethroid, but the pyrethroid worked the best. The product profile is flexible – the insert can be changed frequently. Request to industry to bring forward a product

Progress on a Randomised Controlled Trial for evaluation of Eave Tubes

- Matt Thomas

Discussion (cont):

- Non-pyrethroid actives produced 100% mortality, but persistence did not last 3 months.
- Dust in the field – will that adhere to net and reduce efficacy. Nets are treated to saturation, so no new particles should adhere.
- Study area chosen for high insecticide resistance, nature of housing, and partners on the ground able to put trial into place.
- Time to installation of tubes = 1 minute. Installation of window screens is slower as windows are not standard size. Team of 10-15 people started in 1 village, budded off to three more village to train more and so on. With this team it take 1-2 week to treat a small village, and 3-4 weeks for a large village.
- Suggestion: Loss of efficacy over 5 months likely to be vapour pressure. Microencapsulation may help to overcome this. Towards the end of the project, different settings will be investigated by optimisation of the product – different actives & formulations.

Updates on Spatial Repellents for Malaria Elimination

- Neil Lobo

Summary:

- **Spatial repellents (SR)** = “bubble of personal protection”
- **Vector control “gaps” addressed by SR:**
 - Day time biting
 - Resistance
- **Previous Studies:** e.g. Sumba Is: coils = 32% reduction in biting >>> 52% reduction in incidence
- **Global Recommendation:** What is coverage required, how does efficacy vary with geography and bionomics; is there a diversion or a community wide effect; what is the effect against insecticide resistant vectos?
- **Newly funded project to generate an evidence base:** Indonesia and Peru. Missing diversion effect as this was planned in Kenya, and study sites with documented high resistance as there are no resistant populations in Indonesia.
- **Seven months of epi and ento data collection** – 12449 bloodspots, 19 HLCs, in Peru looking at seroconversion in around 1800 surveys. Blinded at present so no results to present.

Updates on Spatial Repellents for Malaria Elimination

- Neil Lobo

Discussion

- Query: Any data from African sites? No, but there is some prelim baseline data (Sarah Moore); If the study were to be performed in Africa, West Africa would have the highest KDR resistance
- Query: Study design for dengue: how do you cater for movement of individuals. Not catered for, as trial is house based, following sero-conversion.
- The dengue and malaria study design are completely different to deal with the different disease transmission dynamics (e.g. location of transmission may not be the home)
- Query: What type of emanation is being used? Answer: PASSIVE. Shield product from SC Johnson under evaluation. Active: Transfluthrin. Lasts 3 weeks, but they are being replaced every 2 weeks.
- Query: Is the spatial repellent evaluated in the presence/absence of currently recommended interventions (e.g. LLINs)? Baseline level – country level interventions already in place, so spatial repellent effect is over and above recommended interventions
- Query: Is indoor air concentration being monitored for transfluthrin. No - It would be helpful, to know with different levels of ventilation, especially as 2 weekly replacement is too frequent for a VC intervention.

Project/work plan:

Project 1: Re-examine the definition of Residual Transmission;

1. How should the definition of residual transmission take insecticide resistance into account?
2. Can the members to propose options?
3. Could we simply say persistent malaria?

#	Name of Activity	Timeline in 2017/2018	Actual Status	Responsible Project manager	Support required	Comments
1						
2						

Project/work plan:

Project 2: Joint meeting of partners working on residual malaria transmission to share findings from ongoing and recent projects from Africa and south-east Asia:

- 1. Establish consensus about methodologies for measuring residual transmission?**
- 2. Examine the value of parasite surveys in residual transmission measures;**
- 3. Develop a consensus on new tools that can be used in residual transmission settings;**
- 4. Develop a consensus on how to assess residual transmission in migratory communities as in SEA**

#	Name of Activity	Timeline in 2017/2018	Actual Status	Responsible Project manager	Support required	Comments
1						
2						

Project/work plan:

**Project 3: Identify examples of vector control tools that are amenable to learning and doing;
1. Share results where these are used (Example of MEI work from UCSF)**

#	Name of Activity	Timeline in 2017/2018	Actual Status	Responsible Project manager	Support required	Comments
1						
2						

Project/work plan:

Project 4: Update of current keys for mosquito identification in the Afro-tropical vectors

1. Planned work by Prof. Maureen Coetzee;
2. Contributions/sharing of experiences on mosquito taxonomy and identification;
3. Sharing of sequencing data and information on new species;
4. Improved capacity for taxonomy and vector identification.;

Niel Lobo & Seth Irish to assist

#	Name of Activity	Timeline in 2017/2018	Actual Status	Responsible Project manager	Support required	Comments
1						
2						

Project/work plan:

Project 6: Consolidation and sharing of lessons on the evaluation and use of new tools (e.g. spatial repellents; ivermectin; eave tubes) for control of malaria and non-malaria infections;

- 1. How would the design of these studies change when the target includes non malaria infections? (example in Dengue studies);**
- 2. What options are available for improved insecticide delivery (example of eave tubes)**
- 3. Can these improved delivery options be effective against insecticide resistant mosquitoes (data from the Eave Tubes Project; Data from other partners)**
- 4. What are the effects of spatial repellents on pyrethroid-resistant mosquitoes; data from field studies; evidence review from across sites?**
- 5. Which additional studies are needed to generate evidence for scale-up of ivermectin?**

#	Name of Activity	Timeline in 2017/2018	Actual Status	Responsible Project manager	Support required	Comments
1						
2						