Roll Back Malaria Vector Control Working Group (RBM VCWG)
11th Annual Meeting, 3rd-5th February 2016
Moevenpick Hotel, Rue de Pré Bois, Geneva

1st New Challenges, New Tools in Vector Control Work Stream meeting
14.30-17.30, Thursday 4th February 2016
Moevenpick Hotel, Rue de Pré Bois, Geneva

Chairs: Fredros Okumu and Mike Reddy
Rapporteur: Lucy Tusting

Welcome and introduction – Mike Reddy, Bill and Melinda Gates Foundation, USA and Fredros Okumu, Ifakara Health Institute, Tanzania

This work stream will build on the previous *Outdoor/Residual Transmission* work stream activities which included establishing regional networks, developing guidelines for and estimating the importance of residual transmission and estimating malaria risk in specific populations. Moving forward, the key message is that universal coverage of long-lasting insecticide-treated nets (LLINs) (or indoor residual spraying (IRS)) remains an absolute priority and all other methods are supplementary to reducing malaria and achieving elimination. However, we need to generate local evidence on the magnitude of outdoor/residual transmission and industry and others are encouraged to develop new vector control tools to address residual transmission. We are also increasingly moving towards the evaluation of product classes, not individual products. The Vector Control Advisory Group (VCAG) was developed to review new paradigms.

The need for new tools to address residual/outdoor transmission is being addressed partly by the Bill and Melinda Gates Foundation (BMGF) Grand Challenges Exploration Round 14 (new approaches for addressing outdoor/residual malaria transmission) which funded nine Phase I projects. Promising technologies include spatial repellents, Attractive Toxic Sugar Baits (ATSBs) and gene drive. The previous work stream definition of residual transmission was 'that which persists after having achieved universal coverage with effective LLIN and or IRS interventions', but a new definition has been proposed as 'the complete set of transmission events that continue to occur in communities where primary interventions such as LLINs, IRS, case management and larviciding have already been widely implemented at high coverage, but where new *Plasmodium* infections still occur locally. Residual transmission therefore also refers to all new local malaria transmission events in non-naïve communities'. It is also important to measure residual transmission. The entomological inoculation rate continues to be the gold standard measure of transmission but may need to be rethought. It may also be possible to use environmental covariates to identify high-risk households. Additionally, there remains the challenge of maintaining and expanding entomological capacity.

Larval source management cannot be discounted from the work stream as many historical successes were achieved with this. It may be appropriate to modify the work stream name to encompass LSM.

Revolutionizing vector control for malaria elimination – Allison Tatarsky, University of California, San Francisco, USA

The project is situated in the context of ambitious new malaria elimination targets, the opportunity to learn from history, growing threats to current vector control interventions and gaps in the *Anopheles* control approach. Funded by the Parker Foundation, the project is responding to an opportunity to accelerate towards malaria elimination and eradication with innovative and aggressive vector control. The four project aims are to: (i) develop partnerships, (ii) elevate evidence, (iii) inform decision making in country and (iv) demonstrate impact of new tools on the ground. The five main activities within Phase I are: (i) a systematic review of the vector control toolbox, (ii) technical analysis of aerial programs and technologies, (iii) cross-country case studies on mosquito control programs, including delivery systems and tools, in Tanzania, the USA, Australia and Indonesia, (iv) geospatial modelling to improve our understanding of factors influencing transmission patterns in sub-Saharan Africa and modelling of the potential impact of different interventions and (v) a proposal for a Phase II demonstration project in multiple sites to focus on an approach to vector control using integrated delivery and tools, rather than a demonstration of individual tools. Building on recent work (Bhatt *et al.* 2015 *Nature*), estimates of residual transmission have identified areas of higher than and lower than expected transmission given LLIN and other intervention coverage.

Potential role of ivermectin and ivermectin-like compounds in malaria elimination – Carlos Chaccour, ISGlobal, Spain

Ivermectin is an endectocide with potential for mass drug administration to complement current vector control interventions. An overview of the mode of action and different possible implementation strategies and formulations was given. For endorsement and regulatory approval, efficacy (see preliminary data from Burkina Faso, Foy *et al.*, ASTMH 2015) and safety (total dose and spacing, current versus new formulation) data would be needed. Additionally, acceptability (by the population and other programmes), cost-effectiveness (current costs, procurement through the Global Fund) and feasibility (production needs, sustainability) evidence is needed for a policy recommendation. The next steps are to (i) generate evidence using the current formulation in different eco-epidemiological scenarios, (ii) start conversations for endorsement of the concept with the World Health Organization (WHO), VCAG and Malaria Policy Advisory Committee (MPAC), (iii) start conversations for regulatory approval (new indication), (iv) define what MPAC would need in order to give a recommendation and (v) start the pre-qualification process.

Discussion

- It is important to consider the resistance profile of vectors before using ivermectin.
- Ivermectin may have an effect on *Chrysomya* spp. and reduce fly production in pit latrines.

Potential and cost-effectiveness of LSM – Silas Majambere, Innovative Vector Control Consortium, UK and Eve Worrall, Liverpool School of Tropical Medicine, UK

There is considerable evidence that Larval Source Management (LSM) works (Tusting *et al.* 2013 *Cochrane Database)* and it is recommended as a supplementary malaria control intervention in Africa, Asia and South America. A cost analysis of larviciding was done for Dar es Salaam, Tanzania; Vihiga, Kenya and Mbita, Kenya (Worrall and Fillinger 2011 *Malar J*). Cost per person protected ranged from US$1-3 per year. More recently a cost effectiveness analysis was done for the Urban Malaria Control Programme in Tanzania (Maheu-Giroux and Castro 2014 *Malar J*). In a scenario of relatively high endemicity (227 cases per 1000 per year) LSM cost US$16.50 per infection averted and in a lower endemic setting (122 cases per 1000 per year) LSM cost US$31.20 per infection

averted. This compares favourably with the cost-effectiveness of primary vector control interventions (White *et al.* 2011 *Malar J*) (although there are difficulties in comparing the two analyses). The number of countries reporting the use of LSM has increased from 27 in 2011 to 48 in 2014. To understand whether this is good from an economic point of view, it is important to understand how these programmes are being financed. There is an opportunity to gather evidence for/against LSM and to support LSM implementation. Domestic funding for LSM should be encouraged. The recommendations of the WHO LSM Operational Manual should be followed and industry engaged for long-lasting actives. There is considerable innovation in LSM today including improved and new spraying technologies and mapping technology.

Discussion

- Rather than discussing whether or not there is a role for LSM, it is important to move on and support LSM implementation as best possible. We have three proven interventions: LLINs, IRS and LSM and it is important to preserve LSM. An independent work stream is still needed. The definition of residual transmission of being that which persists after high effective coverage with LLINs, IRS and LSM has been achieved excludes LSM from this work stream.
- LSM is the sole intervention in many locations outside Africa including urban India, where it has been used since 1971 and today in 131 cities.
- It would be useful to give countries simple guidelines to follow to implement LSM; the Operational Manual is a long document.

Targeted spraying of mosquito swarms for malaria control – Abdoulaye Diabate, Institut de Recherche en Sciences de la Santé, Burkina Faso

New approaches to vector control can exploit alternative behaviours. Mating behaviour currently remains underexploited. It is known that male mating swarms are consistently found in the same location. Pilot work in Vallée du Kou, Burkina Faso has mapped the spatial distribution of swarms and there is clear evidence of clustering, the pattern of which is relatively the stable over time. It is not yet known why mosquitoes swarm in particular locations. Swarm collection has been conducted in Sudan, The Gambia and Mali which indicates that swarming behaviour is relatively consistent across different settings and that male swarming behaviour can be manipulated. Targeting swarms is being investigated as a potential means to reduce overall mosquito population density.

Discussion

It was queried whether elimination of one part of a swarm will cause it to re-form elsewhere. It seems that mosquitoes use visual cues and that swarms will return to the same location. It was queried whether targeting swarms could be applied to *Anopheles arabiensis.* Pilot data indicates that behaviour is relatively similar across species and that through the seasons, different species may inherit the same site.

Broadening vector control targets for malaria elimination – Matt Thomas, Penn State University, USA

Data on seasonal malaria transmission patterns and vector densities from Orissa, India were presented. Genetic analyses of species complexes and blood meal analyses indicate a shift to a more zoophilic subspecies which helps to explain the loss of the classic malaria peak in November to

January. This species shift mirrors the shift from *An. gambiae* to *An. arabiensis* in parts of Africa. In Orissa today, transmission is thus dominated by *An. culicifacies and An. fluviatilis,* both predominantly zoophilic, with higher densities found in cattle sheds than human homes. Modelling of malaria transmission has explored the potential impact of using IRS in cattle sheds in addition to human homes. This indicates that the use of IRS or LLINs in domestic dwellings is not sufficient to reduce transmission below the elimination threshold, even at maximal coverage. Yet the extension of IRS to attack the zoophilic cycle could more transmission towards the tipping point. Funding from the National Institute of Allergy and Infectious Diseases as part of the International Center of Excellence for Malaria Research (ICEMR) program was acknowledged.

Attractive toxic sugar baits (ATSB): from basic science to product – a new paradigm for vector control – Günter Müller, Hebrew University, Israel

Both male and female mosquitoes require plant sugar feeding for survival. Location of sugar sources is guided by chemical attractants. The concept behind ATSBs is that once attracted, mosquitoes feed and are exposed to a low level dose of insecticide within the bait. Since ATSB competes directly with natural sugar sources, the quality of the attractant is crucial. Initially, non-attractive toxic sugar baits were applied to highly attractive flowers. While effective at controlling mosquitoes, this is not environmentally sustainable or scalable. Subsequently, extracts of highly attractive fruits and flowers was formulated with a toxin to spray on vegetation. Since these formulations can be washed away by rainfall, a long process of development has been undertaken to develop viable commercial products that fulfil various criteria. These criteria include: readily available ingredients for production, being able to be produced on industrial scale, being easily applied in different environments, having a high bait stability under severe environmental conditions, being potentially combinable with a variety of pesticides and having minimum impact on non-target organisms. Different products have been developed for *Aedes* and *Culex* in developed countries and vector control in Africa. Early trials in Mali demonstrate that 90% *Anopheles gambiae* population reduction could be achieved using both spray and bait stations. Ongoing field trials in southern Mali funded by IVCC and the BMGF Grand Challenges are testing commercially viable bait stations for indoor and outdoor control of *Anopheles.* Products for the US market targeting container-breeding *Aedes* have also been developed.

Discussion – All

The way forward:

- *Product/intervention development:* The IVCC published a framework for the rapid assessment of new vector control tools (VCTs) (Vontas *et al*. 2014 *Trends Parasitol*) and we should explore how the work stream can disseminate information to innovators on the pathways to approval. It is critical to have a route to market that is clear and concise, with recognised hurdles that can be anticipated. It would be helpful to document previous and ongoing experiences of product developers and to document the pathway to approval. The work stream should serve as a forum to develop enquiries on the I2I process.
- *Implementation of new VCTs:* We should be clear where and when new tools are appropriate. Position statements on new paradigms may be helpful. It would be good to consider costing, cost-effectiveness and how to finance new or supplementary interventions. An element of 'learning by doing' could be valuable and the work stream could guide countries in Phase IV evaluations.

- Consolidating evidence on new challenges and new tools should be a key objective.
- It is not only important to develop new tools but also new methods to measure transmission.

Day 3: Friday 5th February

Session 3: Feedback from the work stream meetings
Chairperson: Jacob Williams

1st New challenges, new tools in vector control work stream meeting – Fredros Okumu, Ifakara Health Institute, Tanzania and Mike Reddy, Bill and Melinda Gates Foundation, USA
The main conclusions from the meeting were that the work stream should: (i) help to consolidate evidence on new challenges, new tools and (ii) support countries by providing recommendations, and consensus statements on key issues. It was also proposed that LSM should stay as a separate work stream.

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Discussion – All

- I2I will have permanent staff funded by BMGF and hosted by IVCC from June 2016. These staff will organise the inputs from six work streams. The relationship between I2I and WHOPES was clarified: I2I is advisory and there is no obligation for WHO to take up its recommendations.

Larval Source Management:

- LSM is clearly supported by WHO and it is now up to NMCPs to implement it where useful and for programmes to be given adequate guidance on how this can be done.

New interventions:

- The process of getting new interventions or products approved and recommended is very lengthy. This work stream can help speed up the process by forwarding assessments to WHO (via MPAC) for consideration.
- If products do not get to the market there will be little incentive for future innovation.
- It is important to keep focusing on supporting NMCPs and to help programmes to do correct evaluation frameworks.

LSM as a separate work stream:

- The consensus from the work stream meeting was that LSM needs to be kept separate.
- The plenary voted in favour of having a separate LSM work stream.