Global Malaria Programme



Third meeting of the Vector Control Technical Expert Group (VCTEG)

Meeting report, 15–17 March 2015, Geneva, Switzerland



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BACKGROUND

The Technical Expert Group on Malaria Vector Control (VCTEG) is tasked with reviewing and providing guidance and making draft recommendations to the Malaria Policy Advisory Committee on the implementation of malaria vector control including issues related to programme management. The VCTEG is constituted by and reports to the MPAC.

The responsibilities of the TEG on malaria vector control are to:

- Review and recommend to MPAC on the predicted effectiveness and appropriate mix of vector control interventions for particular situations – including the adoption of new forms of vector control following recognition of "proof of principle" from the Vector Control Advisory Group (VCAG)¹;
- Formulate and propose to MPAC evidence-based norms, standards and guidelines for the implementation and management of malaria vector control;
- Address policy issues related to building capacity for entomological monitoring and optimization of vector control investments; and
- Identify gaps in evidence and suggest specific areas of priority research to improve management and implementation of malaria vector control.

The third meeting of the VCTEG was convened on 17 – 19 March 2015 at WHO Headquarters in Geneva, Switzerland.

OBJECTIVES

The specific objectives of the meeting were to:

- Review technical paper on Better targeting "graduation" of malaria vector control interventions: Background to topic and literature review.' for MPAC consideration
- Review Modelling background and assumptions description of OpenMalaria and scenario assumptions preliminary results and final simulation set.
- Review Simulation results and recommendations including Monte Carlo simulations
- Review 'Deployment of combination nets: the evidence'
- Identify new areas for policy guidance for VCTEG and MPAC consideration

OPENING REMARKS

Dr Pedro Alonso, Director of the WHO Global Malaria Programme, opened the meeting. He acknowledged the contributions of the group in compiling and reviewing technical overviews on challenges facing vector control, and providing policy recommendations and technical guidance for further reducing the burden of malaria. An update on the status of the Global Technical Strategy for Malaria: 2016-2030, GMP strategic refresh and proposed adjustment to improve GMP policy making was provided. The group was informed that GMP strategic refresh emphasize the need to strengthen entomology and vector control capacity for malaria control. Such capacity is also essential during elimination and when program transition from malaria control to vector borne diseases control.

¹ A group managed jointly by the Global Malaria Programme (GMP) and the department of Neglected Tropical Diseases (NTD)

Pedro indicated that, currently MPAC act as a validating body from all technical committees so as to provide advice to WHO on policies formulation. Adjustment on policy setting process aim to ensure GMP (WHO Secretariat), in consultation with chairs of various technical committees, act as clearing house for MPAC and repositioning MPAC as an advisor on most critical topics. This changes reinforce the importance of Technical Expert Groups TEG and ERGs on tasks to provide technical recommendations on critical topics to MPAC and when necessary provide specific advice directly to GMP for policy consideration by WHO. This implies TEG will therefore be required to take some function of MPAC to make bold policy advice to WHO. In addition WHO secretariat will play a role of linking various TEGs and ERGs when it involved making decision on converging strategic advice for policy recommendation.

Dr Melanie Renshaw, the chairperson of the VCTEG, reminded the meeting of the responsibilities and process of the meeting and gave an overview of the agenda. She indicated that the meeting would be reviewing technical papers prepared by members, technical advisors and resource persons to generate guidance and recommendations for policy decision by WHO. All meeting participants were requested to introduce themselves.

Dr Abraham Mnzava, coordinator GMP Vector Control Unit, read DOI as per requirement of WHO legal unit. Declared interest did not preclude anyone from participating in decision making.

Also introduce the objectives and expected outcomes of the meeting. Abraham introduced key topics for discussion and decision. This include confusion on definition of universal coverage and interpretation at program level, the request for advice by Member States on when to withdraw vector control and the evidence needed to guide deployment of PBO nets. Abraham informed the meeting on the following: 1) Recent update of VCAG to MPAC particularly the review of intervention targeting resistance and advice to GMP to provide guideline on where such tools can be deployed. To deliver on this task will require establishment of an expert group to review existing data and provide advice on deployment of resistance targeting interventions; 2) Update of GPIRM to MPAC lead to advice for full situation analysis and development of global response plan as well as provide technical recommendations to what countries should do to implement GPRIM. Draft response document will be centre for discussion and TEG is expected to provide suggestions for further development; 3) Brief highlight on changes in policy setting whereby MPAC will make decision on major issues while TEG will provide technical advice to GMP as well as MPAC for policy recommendation.

ITEMS REVIEWED AND ARISING RECOMMENDATIONS

When can malaria control and elimination program safely reduce vector control efforts?

This work originated following requests from countries on practical consideration for graduation or scaling back, and eventual withdrawal of vector control interventions while minimising the risk of resurgence. In order to provide answer to this question, VCTEG review is presented into 3 sub-headings as follows:

Better targeting "graduation" of malaria vector control interventions: Background to topic and literature review, description of OpenMalaria and scenario assumptions: preliminary results and final simulation set

A background document by Joshua Yukich attempt to answer the question when it is safe for malaria control and elimination programs to scale back vector control was the subject of review by VCTEG.

There are several reasons to consider scale back of vector control, these include, 1) high cost of maintaining universal coverage of interventions; 2) when transmission and burden reductions is maintained, even in the absence, or reduction, of vector control, 3) in response to changes in epidemiology of malaria following decades of intervention and 4) consultations during Global Technical Strategy development made clear the need for guidance to countries. To the contrary, scale back of vector control might have cost implication such as 1) investment to support transition from a

malaria control to control of vector borne diseases and 2) enhance surveillance which is important for detection of malaria outbreak or resurgence.

Methodology involved included literature review to look at evidence on scaling back vector control and resurgence as well as model scenario to identify key factors and indicator to monitor success of scaling back vector control and risk of resurgence. There are many observation studies demonstrating positive and negative consequence of vector scale back, and no trials but one underway on IRS targeting in South Africa. A review by Cohen et al² associated causes of malaria resurgence with weakening of the control program, largely due to reduction in the level of vector control effort or outright vector control withdrawal. Also withdrawal of vector control can lead to resurgence of other vector borne diseases. Caribbean, for example, maintained elimination for decades but there have been event of malaria importation during mining operations. Vector control brought about elimination and high insecticide resistance but now there is treatment of cases and space spray for outbreak (emerging cases) control.

Monte Carlo simulation was used to identify indicators to monitor vector withdrawal and risk of resurgence. Key indicators were EIR, infection importation rate (IIR) as tracked in surveillance, human (annual) blood examination (H-A-BER). Based on preliminary results of simulation, draft recommendations were made on what should be considered in view of scaling back control.

Discussions: The meeting highlighted the need for using common definition of key terms such as API or SPR as thresholds of malaria transmission required to stratify different level of transmission, clear description of target areas for scaling back vector control, consideration for changing or adding new parameters on the modelling approach, clarity on definition of risk of resurgence, requirement of entomological surveillance, programmatic consideration and cost implication of scaling back vector control. It was agreed the definition of resurgence should capture an event of public health importance instead of using thresholds of probability. Model validation should include EIR and case management data for high and low transmission settings, acquired and inert immunity which is important indication for receptivity of a population, and consideration for both long and short term climate changes which can influence malaria transmission. This goes hand in hand assuming spatial heterogeneity / patchiness of malaria and variation in levels of receptivity.

VCTEG felt that greater emphasis was needed to give clear message on the risk of scaling back vector control in high malaria burden and the risk of resurgence, need to include case studies with example of programs which have successfully scale back vector control and sustained elimination. The group stressed that the aim of this work is to give practical information useful to programs particularly:

- Clear message on risk of graduation VC in high malaria burden and risk of resurgence
- Modelling backed up with real life experience case studies is useful to inform recommendation
- Vector control as a tool for both insecticide and drug resistance and implication on graduation.
- Economic development and reduction in transmission as well as drawing attention to secondary vector.
- Consequence of scale back of vector control are many this include: 1) Program resisting to scale back from routine control activities due to political and economic implication, for example vector control commodities are associated with large sum of money; 2) programmatic and cost implication of managing these changes.

² J. COHEN, D. SMITH, C. COTTER, A. WARD, G. YAMEY, O. SABOT, AND B. MOONEN, "Malaria resurgence: a systematic review and assessment of its causes", Malaria Journal 11(1), 122 (2012).

- Stages necessary to move program from universal control to elimination. Clear description of activities undertaken during transition stages, with clear indication on when to scale down universal coverage and start targeting control.
- Acknowledgement that scaling back VC is a challenging undertaking with operational and cost implications, which require more thinking to determine when withdrawal is strategic and cost effective, and identification of thresholds which are likely to be analysed case by case. Considerable efforts are needed to guide vector control scale back to avoid situation where high transmission countries embark in scaling back control effort which might eventually increase the risk of malaria, and a summary of VC scale back case studies will be useful.
- All issues around cost effectiveness and feasibility for vector control withdrawal should be explored, this include: re-planning, prioritisation and budget which might affect availability of supplies needed to sustain case management, surveillance and targeting. Actual vector control targeting is a complex and difficult to implement programmatically.

Modelling background and assumptions - description of OpenMalaria and scenario assumptions - preliminary results and final simulation set

Technical document developed by Nakul Chitnis describe scenario assumptions to model planning scale back of interventions. OpenMalaria, a simulation platform, consisting of models of malaria epidemiology and immunology was used to predict malaria specific outcomes after withdrawing of interventions calculated under various assumptions. Simulation results were then analysed using logistic regression in order to derive predicted probabilities of resurgence under various scenarios defined by baseline EIR, case management coverage, vector control coverage and other parameters. Precision and bias associated with metrics to measure the important parameters necessary to determine if a situation meets the criteria for safe vector control graduate were examined using Monte Carlo simulation. It on the basis of this background information that VCTEG discussed and raised several points which should be considered in the model assumptions:

- Since number of imported infection is modelled as Poisson and actual detection rate is modelled as binomial (logistic), the concern was raised on what will happen to model prediction when case detection is low.
- Given the possibility that H(A)BET will include cases resulting from repeated testing of same people and how this is handled in the modelling.
- Consideration to include the following parameters in the model: 1) vectorial capacity, 2) stratification by age group to include infant parasite rate, 3) likelihood of effective treatment, 4) different forms of targeting e.g. geographic versus targeting vulnerable groups or migrant populations, 5) Inclusion of focal vector control as opposed to geographical targeting in the long term
- Model validation using prevalence data from both high and low transmission settings, as well as vector species from Asia and South, and animal settings with zoophilic vectors.

Simulation results and recommendations - including Monte Carlo simulations: Nakul Chitnis present preliminary simulation results on the pitfalls and potential for the safe graduation or relaxation of universal coverage of vector control intervention before and after local elimination of malaria transmission. Simulation provide answers to the question *'is it possible (or advisable), after successful vector control has been achieved and malaria disease burden reductions realized, to "graduate" from universally applied vector control measures to more focal approaches, or can transmission and burden reductions be maintained, even in the absence of vector control?*

A simulation model of malaria epidemiology and immunology was used to predict malaria specific outcomes after withdrawing vector control interventions under various assumptions. These results were then analysed using logistic regression to derive predicted probabilities of resurgence under

various scenarios defined by baseline entomological inoculation rate, case management coverage, vector control coverage and several other parameters. The Monte Carlo simulation was used to examine the precision and bias associated with metrics to measure the important system parameters necessary to determine if a situation meets the criteria for safe vector control scaling back.

Preliminary results presented indicate that, in absence of changes in malaria receptivity, there are few scenarios under which vector control can be reduced without strong expectation of resurgence. These, potentially safe, scenarios are characterized by low historic EIRs, successful control with vector control reaching elimination or near elimination, and effective surveillance systems with high coverage and effective treatment.

Based on this review, VCTEG made a number of suggestions for consideration before full scale model simulation is completed.

- Consideration that historical EIR can be estimated from a combination of parasite rate and net coverage.
- Current model assumes low levels of MSAT but this is an unlikely to be done in practice and therefore should be removed.
- Geographical targeting to be emphasised, this can be done in mid-term.
- Regression model should report in odds ratios and not logit coefficients.

Conclusions: Review of historical evidence and preliminary results of mathematical simulations based on a number of scenarios to determine the impact of 'scale-back' of malaria vector control indicate that for the vast majority of scenarios, the probability of malaria resurgence is high. The authors will revise model input based on feedback provided and new prediction generated, and results of final simulation will be circulated to the VCTEG for further comments.

Conversely, WHO received considerable requests from countries and donors on guidance on when to scale back vector control. This is prompted by observations in some settings where epidemiology of malaria changed after years of effective vector control and expectation that it might be possible to scale-back intervention in certain areas. As consequence, VCTEG drafted an interim guide to support countries deciding when it is safe to scale back interventions. A draft guidance is provided at section 3.1 of this report.

Deployment of combination nets, the evidence

Recently VCAG reviewed evidence on Pyrethroid + PBO LLIN, the first in class of a new paradigm resistance targeting product, and concluded that such net has public health value in areas with substantive pyrethroid resistance. Responding to VCAG recommendation on LLIN addressing insecticide resistance as a new paradigm, countries have requested an operational guideline on where to deploy such nets. Due to complexity of resistance there is need to guide program on areas where

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