Proposal for an Evidence Review Group on MDA, MSAT & FSAT*

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Short summary of current WHO recommendations

Mass drug administration (MDA – mass treatment of all, or a large section, of the population whether symptoms are present or not) has been implemented by malaria control programs in the past, as a way of controlling epidemics most often in conjunction with insecticide residual spraying. Based on the review of results of 19 MDA projects during the period 1932–1999 by von Seidelein and Greenwood, WHO concluded that there is little evidence that MDA is effective in reducing transmission although reduction in parasite prevalence and transient reduction in mortality and morbidity have been documented in some cases. Mass treatment of symptomatic febrile patients was recommended for epidemic and complex emergency situations, with active search for febrile patients to ensure that as many cases are treated.

This intervention has received renewed interest over the last decade in the context of malaria elimination initiatives and as part of artemisinin resistance containment efforts. In 2010 a WHO consultation reviewed the potential role of MDA in the context of artemisinin resistance in the Greater Mekong subregion based on evidence of impact of existing interventions, operational and modelling considerations. The consultation recommended immediate planning of a pilot MDA operation in western Cambodia or eastern Thailand and the collection of essential information on the safety and efficacy of the candidate drugs for MDA.

The consultation also reviewed the potential role of mass screening and treatment (MSAT – all the people in a broad geographic area are screened, regardless of whether they have symptoms of malaria). While MSAT generates important information on the epidemiology of malaria that can be useful for further containment efforts, this approach is resource-intensive and logistically challenging, especially in view of the lack of a field-ready, high-throughput, highly sensitive diagnostic test. The strategy, when applied in a defined geographical area is named focused screening and treatment (FSAT – screening all the people in a defined geographical area and providing treatment for those who test positive). While operationally more feasible than MSAT, this is not delivered in all villages simultaneously, and, therefore, it is unlikely to contribute significantly in elimination efforts. The contribution of MSAT and FSAT effective in reducing transmission needs to be confirmed.

Background and Rationale

A recent systematic review of MDA has been published including areas with different endemicity, various medicines and dosages, different timings and number of MDA rounds and concomitant

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implementation of vector control measures.\textsuperscript{4} The review concluded that MDA appears to quickly reduce malaria parasitaemia and several clinical outcomes, but more studies are required to assess its impact after 6 months, the barriers for community uptake and the potential contribution to the development of drug resistance. A subsequent review of the literature, including unpublished studies, identified 12 MDA studies with follow-up periods of greater than six months showing zero indigenous malaria cases in the target population maintained over six months after the end of drug administration.\textsuperscript{5} Over the last few years implementation research on MDA and FSAT have been conducted in Cambodia\textsuperscript{6,7}, and in other countries for which results are not yet in the public domain (e.g. FEMSE\textsuperscript{8} in Comoros, MDA in Zanzibar, MSAT in Zambia and MDA at Thai-Myanmar border).

There is continuous interest by national malaria control programmes on the potential role of MDA, MSAT and FAST for malaria elimination, and growing interest of the scientific community and major funders for potential role of MDA in combination with other interventions also in areas with moderate-to-high transmission.\textsuperscript{9} The availability of new evidence on impact and operational requirements in different epidemiological situations from unpublished studies provides an opportunity to extract lessons and define further guidance for policy makers and research groups which are investing in the evaluation of these interventions.

In view of the above and of the urgency of implementing cost-effective interventions for elimination of artemisinin-resistant falciparum malaria, WHO/GMP is proposing to the Malaria Policy Advisory Committee to establish and Evidence Review Group (ERG) on the role of MDA, MSAT and FSAT for malaria transmission reduction and elimination.

**Objectives of the Evidence Review Group**

The ERG could be held on 8-10 December 2014 with the following objectives:

a) review all available published and unpublished reports on the impact of MDA, MSAT and FSAT on malaria transmission, building on the most recent Cochrane Review;
b) review results of experiences/unpublished studies of large-scale implementation of MDA in Comoros, at the Thai-Myanmar border and Zanzibar, of MSAT in Zambia and other relevant initiatives;
c) evaluate the role of concomitant administration of low-dose primaquine (0.25 mg base/kg) as gametocytocide of *P. falciparum* together with the ACT deployed for MDA;
d) define the specific conditions of application of MDA, MSAT and FSAT to reduce malaria transmission in terms of endemicity, medicines and dosages, diagnostics, timings and number of MDA rounds, concomitant implementation of vector control measures and best strategies to ensure community uptake and pharmacovigilance;
e) identify research gaps and provide recommendations on data requirements, study methods and ethical considerations for research groups and policy makers interested in further evaluating the role of MDA, MSAT and FSAT in reducing malaria transmission.

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\textsuperscript{6} Song, et al., Rapid and effective malaria control in Cambodia through mass administration of artemisinin-piperquine. *Malaria Journal* 2010, 9:57

\textsuperscript{7} Hoyer et al., Focused Screening and Treatment (FSAT): A PCR-based strategy to detect malaria parasite carriers and contain drug resistant *P. falciparum*, Pailin, Cambodia. *PLOS ONE* 2012, e45797

\textsuperscript{8} Fast Elimination of Malaria by Eradicating Source (FEMSE)

\textsuperscript{9} http://www.irinnews.org/report/100365/kenya-to-pilot-community-wide-malaria-treatments
WHO/GMP secretariat is proposing that the ERG will be convened to develop draft recommendations on the impact of MDA, MSAT and FSAT on malaria transmission for review and endorsement by the MPAC in March 2015.

Proposed questions to be addressed by the Evidence Review Group

1. Is there evidence of impact on malaria transmission at six month and one year following implementation of MDA, MSAT and FSAT in endemic settings?

2. What are the key determinants of positive impact on malaria transmission at six month and one year following implementation of MDA, MSAT and FSAT?

3. What are the optimal conditions for application of MDA, MSAT and FSAT to reduce malaria transmission in terms of endemicity levels, combination of medicines and dosages, use of diagnostics, timings and number of MDA rounds, concomitant deployment of vector control interventions, IEC and pharmacovigilance?

4. What are the major limitations and challenges faced by multiple groups for the successful application of MDA, MSAT and FSAT to reduce malaria transmission?

5. What is the specific role of MDA, MSAT and FSAT in the advanced phase of malaria elimination?

6. What is the specific role of MDA, MSAT and FSAT for the elimination of artemisinin resistant falciparum malaria?

7. What are the key gaps in knowledge and what data need to be available for review to enable a wider deployment of MDA, MSAT and FSAT as part of initiatives aiming at malaria transmission reduction?

8. Which of methodological aspects and ethical requirements need to be considered by research groups and national ethical review boards for the preparation and assessment of studies on the durable impact of MDA, MSAT and FSAT on malaria transmission?

Suggested timetable

i. September 2014: identify ERG members and contact researcher(s) to present evidence to ERG

ii. October: compile and analyse recent literature (including grey literature)

iii. October-November: preparation of short reports of recent/ongoing studies

iv. End November: dissemination of pre-reads to ERG members

v. December: meeting of ERG

vi. January –February 2015: finalization of ERG meeting report

vii. End February: sharing ERG meeting report with MPAC members

viii. March 2015: present outcome of ERG review to MPAC

Declaration of Interests

All ERG members to complete a DoI form which will be evaluated by WHO Secretariat and the summary of the assessment included in the ERG report and published on the MPAC website for public record.