

The potential role for mass drug administration in malaria elimination

Trials have shown that malaria transmission can be controlled by drugs. Professor William R Brieger discusses the key issues — and pitfalls — of such a strategy

As malaria control interventions are scaled up and sustained, and malaria transmission levels decline and prevalence falls, an increasing number of countries are starting to see elimination on the horizon. To help achieve this, countries are exploring strategies involving widespread distribution of antimalarial drugs, primarily artemisinin-combination therapies (ACTs), to asymptomatic individuals. Three approaches include mass drug administration (MDA) and mass screening, treatment (MSaT) and focal MDA or screening and treatment (FMAD/FSAT).¹

According to the US Centres for Disease Control and Prevention (CDC), 'MDA is the treatment of the entire population in a geographic area with a curative dose of an antimalarial drug without first testing for infection and regardless of the presence of symptoms'.² Herein we will review the basic elements for organising MDA, the precautions needed for pregnant women and the special circumstances such as health emergencies, where MDA may be valuable.

Elements of MDA

The World Health Organization stresses that...

MDA is conducted in a coordinated manner, so that the drug is taken at approximately the same time by the whole population at risk, often at repeated intervals. The objectives of MDA can be to reduce or interrupt transmission, to rapidly reduce malaria morbidity and mortality, or to prevent relapses and resulting malaria transmission.

Similar to challenges with other MDA programmes, for example, the elimination of lymphatic filariasis,³ coverage must be high, meaning that efforts can be jeopardised when a large portion of the population is mobile, absent or refuses treatment.

The additional challenge of regular repeated treatments depends on local epidemiology and reinfection rates. Again this is similar to the Seasonal Malaria Chemoprevention (SCM) programme that targets children in the West African Sahel with monthly treatments for three to four months during the high malaria transmission season.⁴ In short, one does not embark on malaria MDA lightly.

PATH reports that mass drug administration is a promising strategy for accelerating towards malaria

elimination in certain transmission settings.⁵ Their work in the Zambia supported study showed that MDA targeting the whole population with dihydroartemisinin-piperazine (DHAP), when added to the standard of package (enhanced case management, insecticide-treated bed nets (ITNs), indoor residual spraying, and robust surveillance including rapid reporting and case investigation) resulted in rapid and substantial reductions in infection prevalence in high- and low-transmission areas.

PATH compared these results for more focused test and treat in Senegal and Ethiopia and found that MDA was more effective. PATH's MDA in Zambia achieved high coverage and was backed with strong surveillance.

Some of the elements of successful MDAs as outlined by Newby and colleagues⁶ include:

- achieving at least 80% or even 90% coverage of the target population.
- with drug administration.
- directly observed treatment.
- strong community engagement.
- high coverage with concomitant vector control interventions such as nets and indoor spray.

While MDA can play an important role in the reduction of prevalence and transmission, especially in settings where malaria elimination is being targeted, there are some additional concerns. First is the fact that pregnant women usually comprise around 5% of the population in malaria endemic areas. Their safety must be considered in conducting MDA. Secondly, there are emergency situations, such as the recent Ebola outbreak, where MDA may be a major means of protecting the population from malaria.

MDA and pregnant women

For pregnant women, the antimalarial antibodies that have provided some level of protection in moderate to high malaria transmission settings are reduced as



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malaria transmission declines. Current evidence shows that as transmission levels decline, the consequences from *Plasmodium falciparum* malaria are even greater for pregnant women. As countries enter pre-elimination stage and move towards eventual elimination, it will be important to address the needs of pregnant women given their increased vulnerability.⁷

Animal studies have suggested potential embryo toxicity and teratogenic effects of artemisinin drugs in the first trimester of pregnancy. Given the limited human data, ACTs are currently contraindicated in first trimester, except in



A group of health workers and a crowd of men, women, and children sit together in Sinafala village, Zambia. Photo credit: Gabe Biencyzki/PATH

How do population-wide drug-based strategies for malaria elimination work?



This graphic, from PATH's Malaria Learning Series publication *Population-Wide Drug-Based Strategies for Malaria Elimination*, illustrates the difference between several parasite clearance approaches evaluated for use in Southern Province, Zambia. Photo credit: PATH Malaria Control and Elimination Partnership in Africa (MACEPA)

documented cases of clinical malaria illness where quinine is unavailable. This poses a challenge in mass campaigns, as it requires the identification of women in early pregnancy who are not yet obviously pregnant. Screening including offering pregnancy tests and/or interview to ask a woman her pregnancy status directly may not work as many may not wish to reveal their pregnancy status.⁸

While only about 5% of the population is pregnant at any given time, and only one-third of those are in the first trimester, approximately 20% of the population is comprised of women of reproductive age who may be pregnant. Thus, the number of women who need to be screened for pregnancy is substantial

across countries. In addition to privacy issues, costs of screening processes are another barrier.⁷

Mozambique⁸ is learning whether MDA is a valuable component to malaria elimination in the low transmission areas in the southern part of the country. Over several rounds of MDA, Mozambique refined its pregnancy screening procedures over several rounds of MDA as seen in the slide above. Costs, confidentiality, convenience and efficiency entered into the equation, and saw a greater focus on communicating with women rather than testing. Lessons learned from MDA in Mozambique included:

- Screening for early pregnancy in the context of MDA is challenging, particularly among teenage girls

- where disclosing pregnancy can be problematic.
- Need to train field workers (preferably women) about the need to ensure confidentiality of pregnancy testing/results.
- Confidentiality is also crucial to ensure adherence to the pregnancy testing.
- Women not accepting pregnancy test must be warned on risks/benefits of ACTs in first trimester.
- Health authorities must understand that IPTp and MDA are not mutually exclusive.

MDA is a tool conceived primarily for countries and areas of countries as part of the pre-elimination strategy. It presents a variety of logistical challenges, but a major concern should also be the ethical issues of giving a potentially toxic drug to women in their first trimester. Alternative strategies to protect these women, including ITNs, must be explored.

MDA rationale in Sierra Leone during the Ebola outbreak

In Sierra Leone, MDA was seen as a lifesaving tool to prevent malaria deaths during the Ebola epidemic when taking blood samples for diagnosis was a major risk. The Ebola epidemic in Sierra Leone and its neighbours, Liberia and Guinea, devastated the health workforce, and the availability of any sort of malaria testing supplies was low. The country experienced a major drop in utilisation of clinic-based MCH services including those for malaria during the period.⁹

Sierra Leone used Artesunate-Amodiaquine (ASAQ) for its MDA in two rounds in eight districts with confirmed Ebola disease. Because of initial similarities in presenting symptoms between Ebola and malaria, people were often fearful of going to the health centre in case they were detained for Ebola care or were exposed to other patients who had Ebola.

Community MDA was one way to protect the population from malaria in this emergency situation.¹⁰ The rationale for the MDA was in part to prevent malaria episodes that could be confused with Ebola and risk nosocomial infections of non-Ebola febrile patients who might be confined with Ebola patients. In addition, the MDA could overcome the generally poor access to health services, improve relations with the community, and prevent people seeking malaria care in unsafe service points in the private sector.

The Ministry of Health and Sanitation reported that, 'Following the two rounds of MDA using ASAQ with moderate effective coverage, covering over 2.6 million people, the total number of cases suspected of malaria tested positive decreased significantly in the MDA targeted chiefdoms.'

Health system readiness

PATH⁵ again provides key guidance to determine if the 'health system capable of implementing a population wide drug-based strategy and achieving high coverage of the targeted population'. These considerations include:

- Sufficient numbers of motivated community health workers or other local health personnel to carry out the intervention.
- The targeted population is reasonably accessible.

- Infrastructure and means of transportation are adequate.
- Sufficient information about the target population (including household location, mobility, and community acceptance of the proposed interventions) to achieve high levels of population coverage.
- Surveillance systems are in place to allow detection and investigation of subsequent individual cases and foci.
- Is adequate funding available?
- The strategy cost-effective investment compared to other interventions in the particular setting.
- Intervention will result in long-term savings by eliminating or greatly diminishing the future malaria burden.

Added to these considerations, CDC² does caution that a single administration has little impact on malaria transmission rates over time and that indiscriminant use of medicines for MDA may promote drug resistance.

MDA can succeed in the right circumstances with adequate logistical, financial and management capacity. A country may start testing MDA approaches in areas with low transmission, and as other interventions such as nets, spraying and case management bring down transmission elsewhere, MDA can spread in the country. MDA is not a one-time-only intervention and should be integrated with strong surveillance systems, but with proper planning, integration and targeting, countries may find that MDA can be a valuable addition to the malaria elimination toolkit.

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CHRONOLAB SYSTEMS

