Mass drug administration for malaria
A practical field manual

Malaria Policy Advisory Committee (MPAC) Meeting
22-24 March 2017, World Health Organization, Geneva, Switzerland
Background on MDA for malaria

• Over the past decade, mass drug administration (MDA) and other approaches to mass screening and treatment have received increasing interest in the context of malaria elimination and in emergency situations such as the Ebola epidemic in West Africa.

• Mass drug administration (MDA) has played a crucial role in the control and elimination of certain prevalent neglected tropical diseases (NTD’s) such as lymphatic filariasis, soil transmitted helminthiasis, onchocerciasis, trachoma and schistosomiasis.
WHO recommendations on MDA

Based on WHO ERG held in April 2015 and MPAC advice in September 2015

http://www.who.int/malaria/publications/atoz/role-of-mda-for-malaria.pdf?ua=1
Based on a recent evidence review, the WHO Malaria Policy Advisory Committee made the following recommendations on the role of MDA, mass screening and treatment and focal screening and treatment for malaria:

1. **Use of MDA for the elimination of** *P. falciparum* **malaria** can be considered in areas approaching interruption of transmission where there is good access to treatment, effective implementation of vector control and surveillance, and a minimal risk of re-introduction of infection.

2. **Given the threat of multidrug resistance and the WHO call for malaria elimination in the Greater Mekong subregion (GMS),** MDA may be considered as a component of accelerated malaria elimination efforts in areas of the GMS with good access to treatment, vector control and surveillance.
Malaria reported cases in Anjouan, Comores

- T3 policy
- Enforcement T3
- MDA Artequick
- LLIN distribution

Graph showing trends in malaria cases with specific interventions and dates.
3. Use of time-limited MDA to rapidly reduce malaria morbidity and mortality may be considered for epidemic control as part of the initial response, along with the urgent introduction of other interventions.

4. Use of time-limited MDA to reduce malaria morbidity and mortality may be considered in complex emergencies, during exceptional circumstances when the health system is overwhelmed and unable to serve the affected communities.

5. In the absence of sufficient evidence, WHO does not recommend the use of MDA in situations other than for areas approaching elimination, epidemics, and complex emergencies, as specified above (see 1-4).

6. Mass primaquine prophylactic treatment, requiring pre-seasonal MDA with daily administration of primaquine for two weeks without G6PD testing, is not recommended for the interruption of vivax transmission.
7. Mass screening and treatment and focal screening and treatment for malaria are not recommended as interventions to interrupt malaria transmission.

8. Medicines used for MDA must be of proven efficacy in the implementation area and preferably have a long half-life. WHO recommends that a medicine different from that used for first line treatment be used for MDA. Programs should include monitoring of efficacy, safety and the potential emergence of resistance to the antimalarial medicines deployed for MDA.

9. WHO supports the need for more research on the optimum methods of implementing MDA programmes, promoting community participation and compliance with treatment, and evaluating their effectiveness. Modelling can help guide the optimum method of administering MDA in different epidemiological circumstances and predict its likely impact.
• Definition/Clarity is required
• Checklist for countries
  • Analyze if it works – operational feasibility
  • Determine % *Plasmodium falciparum* in areas with mixed infections (threshold ?)
  • Population mobility
  • Not for the whole country, but for specific areas/foci/communities
• High coverage expected (total eligible population)
• National treatment guidelines
  • Inclusion of MDA, with indication of medicines to be used for MDA
  • Different chapters for epidemics containment and for malaria elimination (?)
• *P. vivax?*
  • Impact of MDA on *P. vivax*
  • Use of MDA with CQ for *P. vivax* - Primaquine after G6PD testing
Questions on MDA from the programs: planning

- Data availability
- Availability of funds
- Availability of medicines (buffer stock)
- Timing of operations in relation to the malaria season ... to be defined
- Use to control malaria epidemics
  - how to define epidemic thresholds
- Target population
  - Eligible population: exclude pregnant women or pregnancy testing?
- Health systems preparedness in detecting & managing ADRs and rumors
- Dosage for children with complex drug regimens – e.g. DHA-piperaquine
- Detailed (minimal essential) guidelines and SOPs
Questions on MDA from the programs: communication

• Information about MDA,
  • Target communities, health workers, policy makers
  • Not as routine intervention, boost for elimination with other interventions

• Information about expected and unexpected side-effects

• Community acceptance
  • 30-50% not willing – don’t even start the MDA

• Manage rumors
  • Setting a system for communication in crisis
  • Active detection, management, media briefing and communication dissemination

• Community ownership and engagement
Questions from the programs: monitoring and evaluation

- Monitoring and Evaluation
  - Measure coverage (household members, dispensed drugs, adherence ...)
  - Role of molecular methods for parasite detection
  - Surveillance in elimination settings
  - Define indicators by settings – epidemics vs elimination

- When to stop? Emphasize MDA is time-bound
- Need effective pharmacovigilance as part of MDA
- Need for efficacy monitoring, using molecular markers of resistance
- Minimal reporting format
- ..........
Process for development of the MDA operational manual

- **Preparatory phase (before drafting committee meeting)**
  - *1st draft* developed by Dr Nanclares based on the MDA experience in Sierra Leone
  - Email review & inputs by 9 members of drafting committee (October – November)
  - *2nd draft* version developed to serve as basis of the drafting committee

- **Meeting**
  - Review by drafting committee in 4 thematic groups (22-23 November)
  - Collation of all inputs and development of *3rd draft* version by Rapporteur

- **Post-meeting**
  - Email review & inputs by drafting committee (December – January)
  - Collation of all inputs and development of **final version** by Rapporteur
  - Presentation and discussion at MPAC (March 2017)
Resource persons participating to the Drafting Committee

- Large-scale MDA with AS-AQ for malaria in Sierra Leone
- MDA with Art-PQP-PQ for malaria in Cambodia and Comoros
- MDA with DHA-PQP in Magude district, Southern Mozambique
- MDA with DHA-PQP in Southern Province of Zambia
- Research on MDA with DHA-PQP at Thai-Myanmar border
- Research on MDA with DHA-PQP in Viet Nam
- Research on MDA with DHA-PQP in Myanmar
- Community-based pharmacovigilance of ASAQ
- Programmatic experience with MDA for the control of NTD

MDA in the context of transmission reduction for malaria elimination
## List of contents of the field guide

1. Introduction, background, definitions, objectives, WHO recommendations
2. Organization and implementation of mass drug administration
   2.1 Design phase (macroplanning)
   2.2 Planning and preparation
   2.3 Implementation
3. Monitoring and evaluation
4. Reporting
5. Key steps in a mass drug administration for malaria

References
List of Annexes
Key steps in a MDA campaign for malaria

**Design phase (macro-planning)**
- Obtain commitment from policy-makers, and identify agencies to support the ministry of health
- Establish a task force or coordinating committee
- Conduct a context analysis
- Determine target population and geographical areas
- Determine antimalarial medicine to be used
- Estimate requirements, and order medicine
- Determine delivery strategy:
  - Door to door
  - Centralized
  - Mixed
- Determine period of intervention
- Establish number of rounds
- Establish a chronogram
- Estimate a budget

**Planning and preparation**
- Do micro-planning
- Ensure effective logistics
  - Procurement, storage and distribution
  - Transport
  - Accessibility
  - Distribution sites
  - Waste management
- Human resources
  - Identify requirements
  - Training
  - Salaries and per diem
- Community engagement and social mobilization
  - Define roles and responsibilities
  - Community assessment
  - Key messages
  - Engage mass media
  - Address rumours
  - Engage community

**Implementation**
- Stock management
- Distribution of antimalarial medicine
  - Supervision
- Data collection
- Coordination

**Monitoring and evaluation**
- Real-time monitoring
- Estimation of coverage
- Post-campaign survey
- Monitoring of consumption
- Pharmacovigilance
- Monitoring of drug resistance
- Evaluation of impact

**Reporting**
- Debrief and review intervention
- Write a final report
Executive summary

Planning and preparation phase

This phase involves planning the operational aspects of the framework defined at national level:

- Conduct **micro-planning at province or district level** according to the strategies defined by the national task force to guarantee an effective campaign by ensuring adequate distribution of supplies, training of staff, engagement of the community and proper management of resources. The micro-plan should include:
  - demographic information on the province or district eligible for MDA
  - information on the area (e.g. maps, infrastructure, location of health facilities, hard-to-reach areas)
  - timing of MDA in the district
  - delivery strategies
  - human resources (number required, number available) and training plan
  - logistical information
  - social mobilization and communications plan and
  - pharmacovigilance plan.
Planning and preparation phase (cont'd)

- Ensure effective logistics, taking into consideration:
  - procurement, storage and distribution of antimalarial medication
  - procurement, storage and distribution of other supplies necessary for MDA
  - transport
  - accessibility to the entire target population, including those in hard-to-reach areas
  - identification and preparation of distribution sites and
  - waste management.

- Plan human and financial resources:
  - number of teams required and composition
  - training and
  - adequate payment of salaries and per diem.
Human resource requirements

• **Door-to-door strategy:** The daily output depend on population density. In urban areas, one team can reach max 75–100 people per day (average of 15–20 households of five people, visits lasting 15–20 min per household). In rural areas, one team can reach max 50–75 people per day (10–15 households), considering time for transfer and communication to individual households.

• **Centralized, fixed-site strategy:** One team can distribute medicines to 400-500 people per day. As this strategy is likely to miss a higher proportion of the population than door-to-door distribution, special activities are required to mobilize and ensure the participation of the population.

• The daily output depends on whether MDA cards are issued or a registration book is completed, which is more time-consuming.

• Specific teams might be considered for distribution in schools, prisons, military camps and orphanages and perhaps for the main local companies, such as factories, mines and plantations.
Implementation phase

The implementation phase involves the actual distribution of antimalarial treatment and includes:

- **stock management**: preparation of distribution kits with all the necessary materials ahead of time at the distribution point or peripheral health facility at which supplies are prepositioned
- **distribution** of the antimalarial medicine itself, either door to door or at a centralized, fixed site
- **supervision, an essential component** to ensure the quality of the campaign: at peripheral, district, regional and national levels
- **data collection**: collection and reporting of information on the number of people who receive treatment at community level, adverse drug reactions (ADRs) and analysis and compilation of data at higher levels through a well-established pathway of flow of information and
- **coordination** of all actors to monitor activities, detect any difficulties or constraints, address them and react to unforeseen events.
Monitoring and evaluation

• intra-campaign monitoring system: a high-quality system for monitoring the campaign allows identification of constraints that require immediate action - can be done by monitors identified within the team or by independent monitors.

• estimate of distribution coverage: the proportion of the target population that has been reached by distribution.

• post-MDA survey: recommended, if feasible, after each round or at least at the end of the entire campaign to obtain more reliable information on coverage and to evaluate adherence to treatment, determine reasons for non-participation or non-adherence and evaluate the presentation of ADRs.

• monitoring consumption: daily monitoring of the number of treatments distributed and the number taken.
Monitoring and evaluation (cont'd)

- **pharmacovigilance**: a vital component of an MDA, which should be planned to ensure training, detection, reporting, management of follow-up of adverse events and to promote and monitor adherence by both passive and active surveillance. This component is also essential to obtain and maintain good understanding and compliance of the population.

- monitoring drug resistance: one of the main concerns with regard to MDA is the emergence and spread of drug resistance although there is no evidence that MDA of artemisinin-based combined therapy (ACT) at therapeutic doses is related to the emergence of resistance, monitoring of resistance should be an essential component of an MDA campaign.

- evaluation of impact: through routine surveillance and parasitological surveys and

- reporting: after each round and at the end of the intervention, of the coverage achieved, challenges and difficulties faced and solutions found, lessons learnt, practices with good results, effective social mobilization activities, useful tools and the costs of the intervention.
List of Annexes

Annex 1. Standard distribution of populations in a developing country
Annex 3. Example of calculation of orders of antimalarial medicine
Annex 4. Example of a chronogram for MDA for malaria (distribution at 8 weeks)
Annex 5. Example of micro-planning used in urban Western Area, Sierra Leone
Annex 7. Example of radio spot on MDA for malaria used in Sierra Leone
Annex 8. Examples of discussion points on MDA for community meetings (adapted from Sierra Leone)
Annex 10. Example of laminated leaflet used by CHWs in Sierra Leone to explain treatment dosage
Examples of useful tools included in the Annexes

Household visit guide for drug dispensers (Zambia)

ASAQ dose chart for home visits (Sierra Leone)
<table>
<thead>
<tr>
<th>Annex</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.</td>
<td>Example of supervisors’ checklist used in Sierra Leone in 2014–2015</td>
</tr>
<tr>
<td>12.</td>
<td>Example of MDA card</td>
</tr>
<tr>
<td>13.</td>
<td>Example of tally sheet (adapted from that used in Sierra Leone 2014–2015)</td>
</tr>
<tr>
<td>14.</td>
<td>Example of a household registration form (adapted from the Zambia MDA handbook)</td>
</tr>
<tr>
<td>15.</td>
<td>Example of daily summary form used in Sierra Leone</td>
</tr>
<tr>
<td>16.</td>
<td>Example of database for distribution team supervisors (adapted from Sierra Leone)</td>
</tr>
<tr>
<td>17.</td>
<td>Example of standard template for reporting a suspected adverse drug reaction</td>
</tr>
<tr>
<td>18.</td>
<td>Example of questionnaire for post-MDA survey</td>
</tr>
<tr>
<td>19.</td>
<td>Example of pharmacovigilance preparedness checklist (used in Sierra Leone)</td>
</tr>
<tr>
<td>20.</td>
<td>Example of an MDA Pharmacovigilance training module</td>
</tr>
</tbody>
</table>
Change in QTc induced by antimalarials

ASAQ & DP

HV, AL
HV, DHA-PPQ
HV, other
mal, AL
mal, ASAAQ
mal, HL
mal, MQ
mal, DHA-PPQ
mal, PY-AS

HV = healthy volunteers, mal = patients with uncomplicated malaria.
Change in QTc induced by antimalarials

DP in healthy volunteers & DP in malaria patients

HV = healthy volunteers, mal = patients with uncomplicated malaria.

Global Malaria Programme
5. Is the risk of cardiotoxicity after exposure to piperaquine containing medicines higher than that of chloroquine?

• No. Review of pharmacovigilance, clinical and preclinical data, along with preliminary results of PK/PD modelling, provides no evidence of a significant difference in the risk of cardiotoxicity following exposure to the currently recommended doses of piperaquine, chloroquine or amodiaquine.

6. Is the risk of cardiotoxicity of piperaquine containing medicines higher in healthy volunteers compared to malaria patients?

• No. Review of pharmacovigilance and clinical data, along with preliminary results from PK/PD modelling, provides no evidence of a difference in the risk of cardiotoxicity of piperaquine-containing medicines in healthy volunteers compared to malaria patients.
WHO has recently reviewed the cardiotoxicity of antimalarial medicines. The full report of the Evidence Review Group meeting and the recommendations provided by the Malaria Policy Advisory Committee are available at the following URLs.....

This review has concluded that the cardiovascular risk associated with the antimalarial drugs piperaquine, amodiaquine, chloroquine is considered very low and these medicines can be used in mass drug administration for malaria.

As a precautionary principle DHA-PPQ, chloroquine or amodiaquine should not be given for MDA to individuals with a family history of sudden unexplained death consistent with cardiac arrhythmia. Concomitant intake of medicines which prolong the QT interval should be avoided (see http://crediblemeds.org).

Pharmacovigilance should be strengthened to track and investigate the risk factors associated with sudden unexplained deaths or any other adverse events associated with antimalarial drug use.
Discussion