Mass Drug Administration: WHO policy update

Dr A. Bosman

AMAZON MALARIA INITIATIVE
AMAZON NETWORK FOR THE SURVEILLANCE OF ANTIMALARIAL DRUG RESISTANCE
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Outline of the presentation

- Objectives of MDA and general considerations
- Basis for recent WHO recommendations on MDA
  - Evidence Review Group (April 2015)
  - Grading evidence (June 2015)
  - Estimates from 4 modelling groups (July – August 2015)
  - Cost analysis of recent operational MDA (August 2015)
  - Review by WHO Malaria Policy Advisory Committee (September 2015)
Objectives of MDA

• The objective of MDA in the context of transmission reduction is to provide therapeutic concentrations of antimalarial drugs to as large a proportion of the population as possible in order to cure asymptomatic infections, to prevent re-infection during the period of post-treatment prophylaxis and, in some circumstances, to interrupt transmission.

• To impact on transmission, MDA requires high coverage of the target population which, in turn, demands a high level of community participation and engagement.
WHO considerations on MDA

- Mass drug administration rapidly reduces the prevalence and incidence of malaria in the short term. However, if malaria transmission is not interrupted or importation of malaria is not prevented, transmission eventually returns to its original level once MDA is terminated, unless the vectorial capacity is reduced and maintained at a very low level during the post MDA period.

The Garki project, 1980

Malaria Modelling Consortium, 2015
WHO considerations on MDA

- If malaria is not eliminated, mass drug administration may provide a significant selective pressure for the emergence of resistance, particularly in the case of *P. falciparum*. For this reason, mass drug administration should not be started unless there is a good chance that elimination is feasible in the area where MDA is being administered.
1. Meeting of WHO Evidence Review Group – April 2015
   http://www.who.int/malaria/mpac/mpac-sept2015-erg-mda-report.pdf?ua=1

2. GRADE Tables
   http://www.who.int/malaria/mpac/mpac-sept2015-erg-mda-grade-tables.pdf?ua=1

3. Consensus evidence from Malaria Modelling Consortium
   http://www.who.int/malaria/mpac/mpac-sept2015-consensus-modelling-mda.pdf?ua=1

4. Review of delivery costs of MDA for malaria

5. Review by the Malaria Policy Advisory Committee – Sept 2015
   http://www.who.int/entity/malaria/publications/atoz/role-of-mda-for-malaria.pdf
ERG was asked to address these questions:

Should MDA/MSAT/FSAT be recommended to interrupt transmission ....

1. ... and contain the spread of resistance in Thailand/ Cambodia?
2. ....in endemic island communities approaching elimination?
3. .... in low endemic non-island settings approaching elimination?

...and then in 4 working groups

Should MDA/MSAT/FSAT be recommended to reduce transmission ....

4. ... and reduce morbidity and mortality during malaria epidemics?
5. ... and reduce morbidity and mortality during exceptional circumstances when health services are overwhelmed (e.g. the Ebola outbreak)
6. ... and accelerate progress to elimination in areas with moderate or high transmission?
A recent systematic review of 32 studies assessed MDA in areas with different endemicity, with different medicines and dosages, different timings and number of rounds and concomitant implementation of vector control measures. 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\(^5\), including unpublished studies, identified 12 MDA studies demonstrating zero indigenous malaria cases in the population maintained over six months after the end of drug administration.

Over the last few years implementation research on MDA and FSAT have been conducted in Cambodia, and in other countries for which results are not yet in the public domain (MDA in Comoros, Sierra Leone, Thai-Myanmar border, Viet Nam, MPPT in DPRK and MSAT/FSAT in Cambodia, Indonesia, Kenya, Namibia, Swaziland, Thailand, Zambia and Zanzibar).

### Mass drug administration in areas of high transmission

**Patient or population:** People living in malaria endemic areas  
**Settings:** Areas with high malaria transmission (≥ 40%)  
**Intervention:** Mass drug administration (any regimen)  
**Comparison:** No intervention (or baseline data in before-and-after studies)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of studies</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parasite prevalence</strong></td>
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</tr>
<tr>
<td>Study design: Cluster-RCT</td>
<td>1 month</td>
<td>RR 0.82 (0.67 to 1.01)</td>
<td>1 study</td>
<td>✫✫✫✫ low&lt;sup&gt;1-2,3&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>Assessed by: Microscopy</td>
<td>Control: 500 per 1000 (335 to 505)</td>
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<td></td>
<td>MDA: 410 per 1000 (335 to 505)</td>
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<td></td>
<td>4-6 months</td>
<td>RR 1.16 (0.93 to 1.44)</td>
<td>1 study</td>
<td>✫✫✫ moderate&lt;sup&gt;1,2,13&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>Control: 500 per 1000 (335 to 505)</td>
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<td>MDA: 580 per 1000 (465 to 720)</td>
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<td></td>
<td>4-6 months</td>
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<td>0 studies</td>
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<tr>
<td><strong>Parasite prevalence</strong></td>
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<tr>
<td>Study design: Non-randomized controlled trial</td>
<td>1 month</td>
<td>RR 0.17 (0.10 to 0.28)</td>
<td>3 studies</td>
<td>✫✫✫ moderate&lt;sup&gt;4,5,6,7&lt;/sup&gt;</td>
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<tr>
<td>Assessed by: Microscopy</td>
<td>Control: 500 per 1000 (50 to 140)</td>
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<td>MDA: 85 per 1000 (50 to 140)</td>
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<td></td>
<td>4-6 months</td>
<td>RR 1.07 (0.62 to 1.85)</td>
<td>1 study</td>
<td>✫✫✫✫ low&lt;sup&gt;2,3&lt;/sup&gt;</td>
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<td></td>
<td>Control: 100 per 1000 (62 to 185)</td>
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<td></td>
<td>MDA: 107 per 1000 (62 to 185)</td>
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<td></td>
<td>4-6 months</td>
<td>-</td>
<td>0 studies</td>
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<tr>
<td><strong>Gametocyte prevalence</strong></td>
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<tr>
<td>Study design: Cluster-RCT</td>
<td>1 month</td>
<td>RR 0.16 (0.08 to 0.30)</td>
<td>3 studies</td>
<td>✫✫✫ moderate&lt;sup&gt;4,5,6,7&lt;/sup&gt;</td>
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<tr>
<td>Assessed by: Microscopy</td>
<td>Control: 100 per 1000 (8 to 30)</td>
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<td></td>
<td>MDA: 16 per 1000 (8 to 30)</td>
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<td></td>
<td>4-6 months</td>
<td>-</td>
<td>0 studies</td>
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</tbody>
</table>

### Development of drug resistance

Several trials of MDA with pyrimethamine or proguanil monotherapy from the 1950s/60s reported the suspected development of resistance over the first 6 months of MDA.

### Adverse events

The drug related adverse events will depend on the MDA regimen used.  
Programmatic MDA also has the following risks which have not been quantified:  
- Inadvertently treating pregnant women in their first trimester,  
- Overdose or aspiration in children  
- Contributing to the development of resistance

The **assumed risk** for parasitaemia prevalence has been set at 50%. Gametocytamia prevalence was generally lower in the included studies and the **assumed risk** has therefore been set at 10%. The **assumed risk** for parasitaemia incidence is taken from the control group of the single trial. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

Cl: Confidence interval; RR: Risk ratio.
### Mass drug administration in areas of moderate transmission

**Patient or population:** People living in malaria endemic areas  
**Settings:** Areas with moderate malaria transmission (6-39%)  
**Intervention:** Mass drug administration (any regimen)  
**Comparison:** No intervention (or baseline data in before-and-after studies)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of studies</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parasite prevalence</strong></td>
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<td></td>
<td>MDA probably substantially reduces the prevalence of parasitemia in the first few months after administration (moderate quality evidence)</td>
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<tr>
<td>Study design: Non-randomized controlled trial</td>
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<tr>
<td>Assessed by: Microscopy</td>
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<tr>
<td>&lt;1 month</td>
<td>Control: 10 per 1000 (3 to 5)</td>
<td>RR 0.03 (0.01 to 0.08)</td>
<td>3 studies</td>
<td>★★★★★ moderate1,2,3,4</td>
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<td></td>
<td>MDA: 5 per 1000 (3 to 15)</td>
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<tr>
<td>4-6 months</td>
<td>Control: 10 per 1000 (53 to 95)</td>
<td>RR 0.18 (0.10 to 0.33)</td>
<td>2 studies</td>
<td>★★★★★ low1,2,3,4</td>
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<tr>
<td></td>
<td>MDA: 70 per 1000 (53 to 95)</td>
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<td><strong>Gametocyte prevalence</strong></td>
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<td></td>
<td>There is insufficient evidence to know if, or for how long MDA reduces gametocyte prevalence in these settings</td>
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<tr>
<td>Study design: Non-randomized controlled trial</td>
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<tr>
<td>Assessed by: Microscopy</td>
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<tr>
<td>&lt;1 month</td>
<td>Control: 30 per 1000 (10 to 82)</td>
<td>RR 0.28 (0.1 to 0.82)</td>
<td>1 study</td>
<td>★★★★★ very low1,2,3,4</td>
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<td></td>
<td>MDA: 28 per 1000 (10 to 82)</td>
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<tr>
<td>4-6 months</td>
<td>Control: 52 per 1000 (24 to 111)</td>
<td>RR 0.52 (0.24 to 1.11)</td>
<td>1 study</td>
<td>★★★★★ very low1,2,3,4</td>
<td></td>
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<tr>
<td></td>
<td>MDA: 52 per 1000 (24 to 111)</td>
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<tr>
<td><strong>Development of drug resistance</strong></td>
<td>Several trials of MDA with pyrimethamine or proguanil monotherapy from the 1950s/60s reported the suspected development of resistance over the first 6 months of MDA.</td>
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</tbody>
</table>

**Adverse events**  
The drug related adverse events will depend on the MDA regimen used. Programmatic MDA also has the following risks which have not been quantified:  
- Inadvertently treating pregnant women in their first trimester,  
- Overdose or aspiration in children  
- Contributing to the development of resistance

---

The **assumed risk** for parasitaemia prevalence has been set at 25%. Gametocytæmia prevalence was generally lower in the included studies and the **assumed risk** has therefore been set at 10%. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk Ratio.

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1 No serious risk of bias: Although there were some differences in prevalence at baseline, these were much smaller in size than the large effects seen post-intervention.  
2 No serious indirectness: These three studies were conducted in Kenya in 1953 and 1954 (pyrimethamine administered every six months for three rounds), and in India in 1953 (amodiaquine administered every two weeks for five rounds). A fourth study from Nigeria in 1973 reported a similar reduction in prevalence during an ongoing MDA program. Although these studies are old, similar effects might be expected today with effective anti-malarials.  
3 No serious inconsistency: Consistent and large reductions were seen in these studies.  
4 Upgraded by 1 for large effect size: Very large effects were seen consistently across both controlled and uncontrolled studies.  
5 No serious indirectness: These two studies are both from Kenya in the 1950s, and both administer MDA as pyrimethamine alone. One study continued follow-up for > 6 months when an effect was still present.  
6 Downgraded by 1 for serious indirectness: This single trial in Kenya gave pyrimethamine every six months for three rounds. Different regimens may have different effects and primaquine, a drug with gametocytocidal properties, was not given. One further trial from Nigeria in the 1960s, which only reported on prevalence during an ongoing MDA programme, also administered MDA without primaquine.  
7 Downgraded by 1 for serious indirectness: This single trial found no substantial difference between groups at 4-6 months. Modern trials with different regimens may have different effects. This study did not administer primaquine as part of MDA.
Malaria reported cases in Anjouan, Comores

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

Global Malaria Programme

World Health Organization
## Mass drug administration in areas of low malaria prevalence

**Patient or population:** People living in malaria endemic areas  
**Settings:** Areas with low (≤5%) prevalence  
**Intervention:** Mass drug administration (any regimen)  
**Comparison:** Placebo or no intervention (or baseline data in before-and-after studies)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of studies</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parasite prevalence</strong></td>
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<td></td>
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</tr>
</tbody>
</table>
| Study design: Randomized controlled trial  
Assessed by: Microscopy  
1 month                          | 1 month                                | RR 0.27 (0.14 to 0.50)  | 1 RCT        | very low 1,2,3,4,5            | One cluster-RCT reported zero episodes of parasitaemia throughout five months follow-up in both the control and intervention arms |
| 6 months                        |                                        | RR 0.02 (0.0 to 0.12)   | 1 study      | very low 1,2,3,4,5            | One study from a small island, reported a sustained reduction in parasitemia for >12months following a single round of MDA with CQ.   |
| **Parasite prevalence**         |                                        |                          |               |                               |                                                                                                   |
| Study design: Uncontrolled before and after study  
Assessed by: Microscopy  
<1 month                          | 50 per 1000$^1$ (0.14 to 0.50)        | RR 0.27 (0.14 to 0.50)  | 1 study      | very low 1,2,3,4,5            |                                                                                                   |
| 12 months                       | 14 per 1000 (7 to 25)                  | RR 0.02 (0.0 to 0.12)   | 1 study      | very low 1,2,3,4,5            |                                                                                                   |
| **Parasite prevalence**         |                                        |                          |               |                               |                                                                                                   |
| Study design: qPCR               |                                        |                          |               |                               |                                                                                                   |
| **Gametocyte prevalence**       |                                        |                          |               |                               |                                                                                                   |
| **Development of resistance**   |                                        |                          |               |                               |                                                                                                   |
| Several trials of MDA with chloroquine or proguanil monotherapy from the 1950s/60s reported the suspected development of resistance over the first 6 months of MDA.   |
| **Adverse events**              |                                        |                          |               |                               |                                                                                                   |
| The drug related adverse events will depend on the MDA regimen used.  
Programmatic MDA also has the following risks which have not been quantified:  
Inadvertently treating pregnant women in their first trimester,  
Overdose or aspiration in children  
Contributing to the development of resistance |

The assumed risk has been set at 5%. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk Ratio.

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$^1$ For illustrative purposes the control group prevalence has been set at 5%.

$^2$ Downgrade by 1 for serious risk of bias: This single study is an uncontrolled before and after study, and so at very high risk of confounding.

$^3$ Downgraded by 1 for serious indirectness: This single study from a small island of Taiwan reported the effects of MDA administered as a single dose of chloroquine (12 mg/kg). Further trials are needed from a variety of settings to have confidence in this results.

$^4$ Compared to baseline data a large reduction in parasite prevalence was seen at 1 month and 12 months.
• Consensus advice from four malaria modelling groups to estimate the impact of MDA on prevalence in low transmission settings, and identify optimal strategies to implement MDA in different transmission settings

• Using malaria transmission models already extensively validated:
  • Fitted to MDA trial data
  • Predictions constantly tested

Sensitivity of MDA impact to changes from a baseline scenario:

1. Key operational variables analysis
   - Coverage, round interval, number of rounds, duration of program

2. Effects in different context
   - Endemicity, seasonal timing, population size, imported infections

3. Primaquine analysis
   - Analysis of low dose primaquine combined with ACTs in MDA

<table>
<thead>
<tr>
<th>Baseline scenario</th>
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<tbody>
<tr>
<td>Rounds per year</td>
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<tr>
<td>Effective coverage</td>
</tr>
<tr>
<td>Coverage correlation</td>
</tr>
<tr>
<td>Round interval</td>
</tr>
<tr>
<td>Programme duration</td>
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<tr>
<td>Drug choice</td>
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<tr>
<td>Endemicity</td>
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<tr>
<td>Population size</td>
</tr>
<tr>
<td>Seasonality</td>
</tr>
</tbody>
</table>

* Access to intervention x adherence x drug efficacy
**Key conclusions from modelling**

- MDA predicted to be effective
  - Suppression will be greater and last longer in low transmission settings

**Reaching unique individuals**
(maximising the number of people who receive least one treatment per year), from:

- Increasing coverage
- Targeting different people in different rounds
- More rounds
## Effect of other factors on MDA impact

<table>
<thead>
<tr>
<th>Factor</th>
<th>Relative influence on impact</th>
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<tbody>
<tr>
<td><strong>Operational variables</strong></td>
<td></td>
</tr>
<tr>
<td>Increasing effective coverage</td>
<td>High</td>
</tr>
<tr>
<td>Decreasing coverage overlap</td>
<td>High</td>
</tr>
<tr>
<td>Increasing rounds per year</td>
<td>High (if they reach new individuals)</td>
</tr>
<tr>
<td>Decreasing interval between rounds</td>
<td>Low</td>
</tr>
<tr>
<td>Increasing duration of programme</td>
<td>Medium</td>
</tr>
<tr>
<td>Addition of primaquine</td>
<td>Low</td>
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<tr>
<td><strong>Different contexts</strong></td>
<td></td>
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<tr>
<td>Optimal seasonal timing of MDA</td>
<td>Medium</td>
</tr>
<tr>
<td>Decreasing starting transmission intensity</td>
<td>High</td>
</tr>
<tr>
<td>Increasing imported infections</td>
<td>Low</td>
</tr>
<tr>
<td>Decreasing population size</td>
<td>High</td>
</tr>
</tbody>
</table>
Limitations of the modelling analyses

• Models not fully harmonized
  • All show similar patterns, but vary in magnitude of predicted effect
  • Can be due to different assumptions, or different interpretations of the baseline
  • Full harmonization to understand these differences (like for RTS,S) takes longer

• Limited ability to predict transmission interruption
  • Assumptions about large well mixed populations are unrealistic close to elimination

Models can’t tell us everything, but their consensus provide important evidence
Consensus from modelling analysis

- MDA with long-lasting ACTs predicted to be effective
  - Percentage reduction in transmission will be greater and last longer in low transmission settings
  - Treating a large proportion of the population in a single year in at least one round is a key determinant of MDA effectiveness whether it is achieved through high coverage in a single round, or reaching new individuals by implementing additional rounds.
  - MDA will be more effective if conducted in the low transmission season and over longer time periods however the effect of the timing is small relative to other operational factors, if high coverage is achieved.
  - Varying the time interval between rounds from 4 to 6 weeks and the addition of primaquine to MDA with ACTs has little additional impact on transmission, even in the context of artemisinin resistance

Imperial College, London | Swiss TPH, Basel | IDM, Seattle | MORU, Bangkok
MDA cost analysis

• Cost data were collected for three experiences of using MDA for malaria, all using door-to-door MDA delivery. Two were implemented in island settings (Comoros and Vanuatu) and one in an emergency scenario (Sierra Leone).

• Cost data were available on:
  o drugs, personnel, transportation, supplies, equipment and utilities in Comoros;
  o drugs, local transportation and travel allowances, medical supplies and bednets in Vanuatu; and
  o drugs, other medical supplies, non-medical supplies, personnel, transport, utilities and other recurrent costs in Sierra Leone.

• Covered populations ranged between about 720 people in Vanuatu, 680 000 in Comoros and 3.05 million in Sierra Leone
## MDA cost (in 2015 US$)

<table>
<thead>
<tr>
<th>Context (year)</th>
<th>District or country</th>
<th>Drug</th>
<th>No of rounds (a)</th>
<th>No of people targeted per round (b)</th>
<th>No of people covered per round (d)= (b)×(c)</th>
<th>Total cost per round (e)</th>
<th>Total cost per targeted person-round (f)=(e)/(b)</th>
<th>Total cost per covered person-round (g)=(e)/(d)</th>
<th>Delivery cost per targeted person - round</th>
<th>Delivery cost per covered person – round</th>
</tr>
</thead>
<tbody>
<tr>
<td>Island (2007/14)</td>
<td>Comoros</td>
<td>Artequick, PQ</td>
<td>2</td>
<td>679,018</td>
<td>75.5%</td>
<td>515,109</td>
<td>$ 7.28 million</td>
<td>$ 10.72</td>
<td>$ 14.13</td>
<td>$ 8.38</td>
</tr>
<tr>
<td>Island (1991)</td>
<td>Vanuatu, Aneityum island</td>
<td>PQ,CQ, SP</td>
<td>9</td>
<td>718</td>
<td>100%</td>
<td>n/a</td>
<td>$ 5.95</td>
<td>$ 5.95</td>
<td>$ 4.73</td>
<td>$ 4.73</td>
</tr>
<tr>
<td>Emergency (2014/15)</td>
<td>Sierra Leone, 8 districts</td>
<td>ASAQ</td>
<td>2</td>
<td>3,043,438</td>
<td>92%</td>
<td>2,806,810</td>
<td>$ 3.32 million</td>
<td>$ 1.22</td>
<td>$ 1.31</td>
<td>$ 0.32 (min $ 0.29–max $ 0.39)</td>
</tr>
</tbody>
</table>

The delivery cost per covered person per round varied greatly: $ 11.05 in Comoros, $ 4.73 for all nine rounds ($ 0.53 per round) in Vanuatu and $ 0.36 in Sierra Leone. NTD MDA = mean cost < than $ 0.50 per person treated, excluding drug costs.
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.
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.
New WHO recommendations on MDA (III)

7. Mass screening and treatment and focal screening and treatment for malaria are not recommended as interventions to interrupt malaria transmission *with the tests currently available*.

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.
Backup slides
Choice of drugs

- Efficacious drugs and an optimal regimen must be deployed.
- The drug of choice should be a long-acting ACT, preferably not the first-line antimalarial medicine used in that region.
- Pregnancy testing, active follow-up and inadvertent drug exposures may need to be considered, depending on the drug.
- Drugs should be selected so as to avoid increasing drug resistance, and drug resistance markers should be monitored.
- The addition of a single low dose (0.25 mg/kg) of PQ is recommended to reduce the transmissibility of *P. falciparum* gametocytes.
- Concurrent interventions need to be monitored in the target population before roll-out, to avoid interactions between drugs.
Coverage

- Obtaining high intervention coverage is crucial to success.
- Ideally, timing of MDA should be structured when people are at home and can be reached.
- Mobile, migrant and remote populations can be especially hard to target for multiday drug regimes.
- People may be unwilling to take drugs when they feel well and have not been tested.
- People of higher socioeconomic status and young men are generally less likely to comply with MDA.
- Imported cases and recrudescent infections can jeopardize impact.
Drug delivery methods

- Full therapeutic dosage should be used for all MDA.
- Completion of treatment is critical; therefore, DOT or a comparable delivery system should be used, to ensure high adherence.
- DOT could be performed by local health workers and volunteers to improve acceptability and drug uptake.
- House-to-house delivery of drugs is preferable to inviting people to participate in a central location. Any other approach that would guarantee high coverage without causing movement of the population may be acceptable.
- Community drug distributors need to be incorporated into other programmes after MDA.
- It is important to involve personnel from the existing health system.
Timing and rounds of MDA

- With the exception of an epidemic or complex emergency, it is preferable to implement MDA in the low-transmission season, before the start of the malaria-transmission season.
- At present, the evidence supports recommending three rounds of MDA at monthly intervals.
- Further research is required to determine whether two rounds would be sufficient in different situations, or even one round in foci elimination.
Logistics and other essential elements for success:

- Supply management, including ordering, customs clearance and stock distribution matched with timing of MDA.
- Active engagement of the population at community, district and national levels, including multisectoral collaboration, if relevant;
- Concomitant deployment of all relevant malaria interventions; in particular, vector control, prompt case management and surveillance;
- Capacity to achieve high coverage and, at about the same time, to ensure adherence to treatment in the target population, and to do this at repeated intervals in a coordinated manner.
Monitoring and Evaluation:

- Development of a post-intervention strategy to sustain the impact on malaria, should also include monitoring to capture potential resurgence;
- The impact of MDA should be measured by evaluating changes in reported malaria cases or malaria incidence. Depending on the objectives of MDA other monitoring methods may be added (e.g. surveys based on molecular tests to detect submicroscopic infections).
- Coverage of target population, adherence to treatment, acceptability (which could be measured in a random sample of the population) and concomitant interventions should also be recorded.
- Enhanced pharmacovigilance is recommended for detection and reporting of adverse events.
- Routine monitoring of MDA interventions should include monitoring of concomitant medication, adherence to treatment and medication errors.
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