Seasonal malaria chemoprevention in practice

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Transforming the malaria landscape in the Sahel: Seasonal malaria chemoprevention
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The recommendation for SMC

WHO recommends

• Seasonal Malaria Chemoprevention (SMC) is recommended in areas of highly seasonal malaria transmission across the Sahel sub-region. A complete treatment course of amodiaquine plus sulfadoxine-pyrimethamine (AQ+SP) should be given to children aged between 3 and 59 months at monthly intervals, beginning at the start of the transmission season, to a maximum of four doses during the malaria transmission season (provided both drugs retain sufficient antimalarial efficacy).

• The age-based recommended dosing schedule is:
  Infants < 12 months old: AQ – half (½) of a 153mg tablet given once daily for three days and a single dose of SP - half of a 500/25mg tablet.
  Children 12 – 59 months: AQ – a full tablet of 153 mg given once daily for three days and a single dose of SP - a full tablet of 500/25mg.

  The single dose of SP is given only on the first day together with the 1st dose of AQ.

• Target areas for implementation are areas where:
  o Malaria transmission and the majority of clinical malaria cases occur during a short period of about four months.
  o the clinical attack rate of malaria is greater than 0.1 attack per transmission season in the target age group, and
  o AQ+SP remains efficacious (>90% efficacy).

• SMC Contraindications:
  SMC should not be given to:
  o A child with severe acute illness or unable to take oral medication
  o An HIV-positive child receiving co-trimoxazole.
  o A child who has received a dose of either AQ or SP drug during the past month.
  o A child who is allergic to either drug (AQ or SP).
SMC in practice
Some important scientific and practical questions

- Can financial support be sustained?
- Can a high level of coverage be achieved?
- Can the efficacy seen in the initial trials be sustained?
- Is SP+AQ safe when given on a mass scale?
- Will resistance to SP and AQ develop?
- Can SMC be combined successfully with other interventions?
- Will ‘rebound’ malaria occur when SMC is stopped?
- When should SMC be stopped?
## Coverage

<table>
<thead>
<tr>
<th></th>
<th>Average Administrative Coverage</th>
<th>Coverage as per household surveys</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>At least 1 cycle</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>104.7%</td>
<td>95.8%</td>
</tr>
<tr>
<td>Chad</td>
<td>96.5%</td>
<td>96.0%</td>
</tr>
<tr>
<td>Mali</td>
<td>85.0%</td>
<td>87.2%</td>
</tr>
<tr>
<td>Nigeria</td>
<td>99.4%</td>
<td>77.3%</td>
</tr>
<tr>
<td>The Gambia</td>
<td>84.9%</td>
<td>93.7%</td>
</tr>
</tbody>
</table>

A high level of reported coverage but

- Issues with population data (underestimated)
- Some children are not reached all of the times (mobility, migration)
- Potential “cycle fatigue” – perception of achieved protection
- Methodological issues (recall bias)
Efficacy in Senegal

A ‘herd effect’?

Efficacy in Senegal

A ‘herd effect’?
## Safety

No drug related SAE in 780,000 treatments in Senegal  
(Ndiaye et al. submitted)

<table>
<thead>
<tr>
<th>Country</th>
<th>Children reached</th>
<th>Reported SAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burkina Faso</td>
<td>702,379</td>
<td>1</td>
</tr>
<tr>
<td>Chad</td>
<td>272,381</td>
<td>1</td>
</tr>
<tr>
<td>Gambia</td>
<td>76,922</td>
<td>1</td>
</tr>
<tr>
<td>Guinea</td>
<td>210,448</td>
<td>3</td>
</tr>
<tr>
<td>Mali</td>
<td>660,440</td>
<td>1</td>
</tr>
<tr>
<td>Niger</td>
<td>477,495</td>
<td>2</td>
</tr>
<tr>
<td>Nigeria</td>
<td>827,790</td>
<td>0</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>3,227,855</strong></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>
The emergence of drug resistance

Charles Darwin
The emergence of drug resistance
What has happened?

In resistance markers at the end of the drug administration

\[ \text{Parasite prevalence} = \text{Number of resistant parasites in the community} \]
Meeting the challenge of drug resistance

- Sustaining surveillance for the emergence of resistance to SP or amodiaquine after the ACCESS-SMC programme

- Development of new anti-malarials for prevention rather than treatment
  - Do not need to be rapid acting (cf. treatment)
  - Preferably single dose
  - Long acting (preferable providing at least a month’s protection)
Combination of SMC with other interventions
Potential candidates

• Nutritional surveillance and/or supplementation
• Vitamin A supplementation
• Mass drug administration for other infections – trachoma, NTDs (azithromycin trial)
• Vaccine catch-up campaigns
• Malaria vaccines
‘Rebound’ malaria definition

An increase in the incidence of malaria after a period of effective malaria control has been achieved (by any means) above what would have occurred if the intervention had not taken place.
Meeting the challenge of ‘rebound’

• Recognizing that this is likely to happen

• Enhancing malaria control in school-age children
  • e.g. enhancing ITN usage or improving treatment of malaria in schools
When to stop?
Cost effectiveness of SMC

(Cairns et al. Nature Communications 2012;3:881)
Questions for SMC when put into practice

- Can a high level of coverage be achieved? YES
- Can the efficacy seen in the initial trials be sustained? YES
- Is SP+AQ safe when given on a mass scale? YES
- Will resistance to SP and AQ develop? PROBABLY
- Can SMC be combined with other interventions? YES
- Will ‘rebound’ malaria occur when SMC is stopped? PROBABLY
- When should SMC be stopped? UNCERTAIN
Acknowledgements
Thank you

www.access-smc.org
### Efficacy in The Gambia

**Estimated effectiveness of SMC: reduction in inpatient cases during the months August-November**

<table>
<thead>
<tr>
<th></th>
<th>CRR</th>
<th>URR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2014</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expected cases &lt;5yrs</td>
<td>339</td>
<td>315</td>
<td>654</td>
</tr>
<tr>
<td>Observed cases &lt;5yrs</td>
<td>221</td>
<td>211</td>
<td>432</td>
</tr>
<tr>
<td>% reduction</td>
<td>35%</td>
<td>33%</td>
<td>34%</td>
</tr>
<tr>
<td><strong>2015</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expected cases &lt;5yrs</td>
<td>521</td>
<td>495</td>
<td>1086</td>
</tr>
<tr>
<td>Observed cases &lt;5yrs</td>
<td>229</td>
<td>141</td>
<td>370</td>
</tr>
<tr>
<td>% reduction</td>
<td>56%</td>
<td>72%</td>
<td>66%</td>
</tr>
</tbody>
</table>

*SMC was delivered over 3 months in 2014 and 4 months in 2015.
# Theoretical impact of SMC

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Incidence of malaria episodes per year</th>
<th>Change in incidence intervention/rebound</th>
<th>Cases prevented/ caused/ 100 children</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>1.0</td>
<td>↓ 50%</td>
<td>50</td>
</tr>
<tr>
<td>1-1.9</td>
<td>2.0</td>
<td>↓ 50%</td>
<td>100</td>
</tr>
<tr>
<td>2-2.9</td>
<td>2.0</td>
<td>↓ 50%</td>
<td>100</td>
</tr>
<tr>
<td>3-3.9</td>
<td>1.5</td>
<td>↓ 50%</td>
<td>75</td>
</tr>
<tr>
<td>4-4.9</td>
<td>1.0</td>
<td>↓ 50%</td>
<td>50</td>
</tr>
<tr>
<td>5-5.9</td>
<td>0.7</td>
<td>↑ 80%</td>
<td>56</td>
</tr>
<tr>
<td>6-6.9</td>
<td>0.5</td>
<td>↑ 20%</td>
<td>10</td>
</tr>
</tbody>
</table>

**Intervention**

**SAVING 361**

**Total** 375
Where should SMC be given?

- **Seasonality** - 60% rainfall in 3 months
- **Incidence** – > 0.2 episodes per child per year