Using G6PD tests to enable the safe use of *P. vivax* malaria with primaquine on the Thai-Myanmar border: A cost-effectiveness analysis

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Aim

To evaluate the cost-effectiveness of using a screening strategy (14 day primaquine to those who test G6PD normal and weekly primaquine to those who test abnormal) as compared to:

1. Giving only chloroquine to everyone (Chloroquine strategy)
2. Giving primaquine to everyone without screening (Primaquine strategy)
Decision tree

- Weigh up the costs and disability-adjusted life-years (DALYs) averted for:
  - Recurrences
  - Haemolytic events
- Clinical trial data from North-western border of Thailand with Myanmar:
  - Chloroquine
  - Chloroquine + observed primaquine (0.5 mg/kg/day for 14 days)
- Assumes 100% adherence to primaquine regimen
- 1 year time horizon
Analysed males and females separately

- G6PD prevalence & risk varies
  - Severe deficiency: males & females with <30% G6PD activity
  - Moderate deficiency: females with 30-69% G6PD activity (heterozygotes)

- Primaquine is contraindicated in pregnancy
  - Pregnant women are not prescribed primaquine
  - Pregnancy test given to all women of childbearing age who don’t state that they are pregnant
Assumptions

- G6PD RDTs given at each episode
- Those who test G6PD abnormal will receive 8 weekly doses of primaquine
- Patients with severe deficiency never finish their primaquine course
  - Full cost of observed therapy
  - Recurrences equivalent to receiving chloroquine only
- Females with moderate deficiency will always finish primaquine course
Decisions

- Whether had at least one recurrence
- Whether had a haemolytic event requiring transfusion
- Whether they received that transfusion (mortality rate)
- Whether females were pregnant
- Whether received primaquine after G6PD test (sensitivity and specificity)
Key model parameters

• RDT sensitivity: 0.99 for severe deficiency and 0.44 for moderate deficiency [CareStart G6PD RDT - Bancone 2014]
• Cost of G6PD RDT = US$1.75
• Cost of supervised primaquine therapy = $1.67 per session
• Prevalence of G6PD deficiency: 0.14 in males, 0.05 in females (severe) and 0.16 females (moderate) [SMRU data]
• 2% of *P. vivax* cases are severe [Rahimi 2014]
• *P. vivax* mortality is 0.1% [Rahimi 2014]
Haemolysis Parameters

• Assumes that 11% of individuals with severe G6PD deficiency who receive primaquine will need a blood transfusion (1% for moderate deficiency) [Pamba 2012]

• 10% mortality for those who need a transfusion but do not receive it [assumption]
**Chloroquine strategy vs Screening strategy**

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th></th>
<th>Females</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Costs (US$)</td>
<td>DALYs</td>
<td>Costs (US$)</td>
<td>DALYs</td>
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<tr>
<td>Base case</td>
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<tr>
<td>Chloroquine strategy</td>
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<td>0.13</td>
<td>$38.5</td>
<td>0.14</td>
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<tr>
<td>Screening strategy</td>
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<td>0.01</td>
<td>$38.4</td>
<td>0.03</td>
</tr>
<tr>
<td>Incremental difference</td>
<td>$0.3 saved</td>
<td>0.12 averted</td>
<td>$0.1 saved</td>
<td>0.11 averted</td>
</tr>
</tbody>
</table>

**One way sensitivity analysis:**
- Screening strategy always averted more DALYs
- When *P. vivax* mortality was lowered to 0, the DALYs for screening strategy and chloroquine strategy were nearly equivalent
- Incremental costs were highest when
  - radical cure had a low impact on recurrences
  - costs were increased for supervised therapy, recurrences & G6PD RDT
Probabilistic sensitivity analysis
### Primaquine strategy vs Screening strategy

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<td><strong>Base case</strong></td>
<td><strong>Costs (US$)</strong></td>
<td><strong>DALYs</strong></td>
</tr>
<tr>
<td>Primaquine strategy</td>
<td>$45.3</td>
<td>0.10</td>
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<tr>
<td>Screening strategy</td>
<td>$38.2</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Incremental difference</strong></td>
<td>$7.1 saved</td>
<td>0.09 averted</td>
</tr>
</tbody>
</table>

**One way sensitivity analysis:**
- Screening strategy always averted more DALYs
- Screening strategy was always cost saving except for high G6PD RDT value ($10)
- Smaller impact on results than when comparing the screening and chloroquine strategies
Probabilistic sensitivity analysis

Males

Females

Probabilistic sensitivity analysis
Cohort analysis

• Males
  • 1 death per 668 treated with the primaquine strategy
  • 1 death per 66,816 treated with the screening strategy

• Females who aren’t pregnant
  • 1 death per 1,599 treated with the primaquine strategy
  • 1 death per 20,199 treated with the screening strategy
Conclusions

• Point of care RDTs for G6PD provide significant health benefits (around 1 month of disability-free life) by reducing recurrences while greatly reducing haemolytic risk in G6PD deficient patients

• Potential for cost savings or moderate cost increases with screening

• Results for other locations will vary due to differences in the epidemiology of *P. vivax* and G6PD deficiency

• Where blood transfusions are not accessible, risks may need to be weighed up more carefully, especially for heterozygous females
Any questions?