P. vivax malaria
The consequences of not providing radical cure

Ric Price
Rise of Non Falciparum Malarious

Thailand: 1965-2001

Brazil: 1960-2009

Colombia: 1960-2008

Sattabongkot et al. Trends in Parasite 2004;

Source: Oliveira-Ferreira et al. Malaria J 9 (1), 2010

Rodriguez et al. Mem Inst Oswaldo Cruz, 2011
P. vivax

Thailand 1993-1996
Child cohort
Density of Infection

Number of Recurrences

Papua, Indonesia
The predominant morbidity and mortality of *P. vivax* is related to its propensity to recur.

Relapses

Drug Resistance

Reinfection
Poor Drugs
Poor Adherence…

MORE SEVERE ANAEMIA
Malaria’s indirect contribution to all-cause mortality in the Andaman Islands during the colonial era

G Dennis Shanks, Simon I Hay, David J Bradley

Andaman Islands Penal Colony 1872-1939

14,000 prisoners
All cause mortality 630 per 1000
"Falciparum kills you quickly, vivax kills you slowly"

"Death by a thousand cuts"
**P. vivax Relapses Drive Transmission**

Relapses have high rates of gametocyte carriage

High representation with *P. vivax* after *P. falciparum*

**Thailand**
Primaquine / Tafenoquine

- Contraindicated in pregnant women and infants
- Unsure of the optimal dose (15mg vs 30mg)
- Poor adherence of Pq
- Risk of severe haemolysis in G6PD deficiency
Primaquine Effectiveness

Unsupervised primaquine for the treatment of *Plasmodium vivax* malaria relapses in southern Papua: A hospital-based cohort study

### Pharmacy Records

- **n=46,221 High dose Pq**

### Risk of P. vivax Recurrence

- **No PQ**
- **Low dose**
- **High dose**

<table>
<thead>
<tr>
<th></th>
<th>AHR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.90</td>
<td>0.86-0.95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 to &lt;5yrs</td>
<td>0.85</td>
<td>0.79-0.90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5 to &lt;15yrs</td>
<td>0.98</td>
<td>0.86-1.12</td>
<td>0.764</td>
</tr>
<tr>
<td>&gt;=15yrs</td>
<td>0.99</td>
<td>0.91-1.08</td>
<td>0.876</td>
</tr>
<tr>
<td>2007</td>
<td>0.91</td>
<td>0.85-0.97</td>
<td>0.003</td>
</tr>
<tr>
<td>Outpatients</td>
<td>0.89</td>
<td>0.84-0.93</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Controlling for: Age, Gender, Admission status, Ethnicity, Year
Effectiveness vs Tolerability
The Long And The Short Of It….

Adherence Issues

Tafenoquine
Single Dose

Primaquine…
High Dose 7days
Low Dose 7days
High Dose 14days
Low Dose 14days
Weekly x8

Need for G6PD Testing
Conclusions

- *P. vivax* relapses are associated with significant morbidity, indirect mortality, sustained transmission

- **Radical Cure** is vital to achieve malaria elimination milestones
  - Novel regimens/drugs, G6PD diagnostics, improved adherence

- Targeted interventions to prevent recurrence in those at greatest risk

- Healthcare providers and policymakers are often scared to prescribe primaquine and don’t recognize the benefits
Acknowledgements

**Menzies Team**
Nicholas Douglas
Nicholas Anstey
Tsin Yeo
Jutta Marfurt
Sarah Auburn
Irene Handayani
Grennady Wirjanata
Rob Commons
Zuleima Pava
Damian Oyong
Steven Kho

**Timika Research Unit**
Rini Poespoprodjo
Enny Kenangalem
Lenny Burdam
Frans Thio
Daniel Lampah
Gjyse Pontororing
Ferryanto Chalfein
Pak Prayoga
Frans Wabisar
Ibu Natalie
Ibu Munik

**PHMC / ISOS**
Michael Bangs
Michael Stone
Pasi Penttinen
Ketut Gdeumana
Sam Koibur
Rosaline
Noah Wariker
Govert Waramori
Any many more...

**MORU**
Lorenz von Seidlein
Nick Day
Nick White

**Melbourne University**
Julie Simpson
Michael Malloy

**UGM**
Yati Soenarto
Yodi Mahendradhata

**Indonesian CDC**
Rita Kusriastuti
Ferdinand Laihad

**NIHRD**
Emiliana Tjitra
Hadjar Siswantoro
Muhammed Karyana
Armedy Hasugian

**Dinas Kesehatan**
Maurits Okesaray
Enny Kenangalem
Erens Meokbum
Rosemini

---

ICPVR, Manaus   13th June 2017