Malaria in Pregnancy (MiP) Consortium

Feiko ter Kuile

on behalf of the MiP Consortium
## Evolution of the MiP Consortium

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tr>
<td>2003</td>
<td>Recognition within the malaria research community that malaria in pregnancy was being neglected.</td>
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<td>2004</td>
<td>Recognition that coordinated approach is required. Informal discussions among scientists interested in MIP</td>
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<td></td>
<td>2 Meetings funded by EDCTP &amp; GMP</td>
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<td>2005</td>
<td>‘Start up proposal’ funded by the BMGF</td>
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<td>2006</td>
<td>Further network grant EDCTP</td>
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<td>Multi-donor meeting: Presentation to potential donors</td>
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<td>2007</td>
<td>Submission of a full proposal to the BMGF (April 2007) Submission of a full proposal to the EU (April 2007)</td>
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<td>2007?</td>
<td>Submission of a full proposal to EDCTP</td>
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• Membership (expanding)
  – Africa  4 → 12 research institutes (8 TBD)
  – Europe 5 → 8 Academic/research institutes
  – Asia  3 countries (India/Thailand/PNG)
  – Americas 3 countries [TBD]
  – USA  5 (CDC and 4 Academic Institutions)
  – Australia 1 University of Melbourne

• Secretariat in LSTM, Liverpool
MIP Consortium Members Europe
Research institutions with MiP research capacity and expression of interest

Initial MIP Working group 2005-7

Potential Expansion 2008

LSTM (Liverpool)
LSHTM (London)
Uo Oxford

IRD
PATH
Epicentre
FRANCE

AMC
Amsterdam

Uo Copenhagen
DBL
CMP

ITM
Antwerp

Uo Tampere
Uo Tübingen
Uo Berlin

Uo Malta
MIP Consortium Members Africa
Research institutions with MiP research capacity and expression of interest
MiP Consortium
Activities Startup period 2005-2007

1. Establish online MiP Library
   - A registry of MiP studies (trial registry)
   - Bibliography of published and unpublished research

2. Develop a research strategy

3. Produce full proposal for consideration by donors
The Malaria in Pregnancy Library

The Malaria in Pregnancy (MiP) Library is a regularly updated, comprehensive bibliographic database of published and unpublished literature relating to malaria in pregnancy, including a trial registry of planned and ongoing trials, for use by scientists, policy makers, funding agencies, industry and other interested parties. The MiP Library meets the demand for a current and international resource on malaria in pregnancy and is a product of an international collaboration between scientists working on MiP (the Malaria in Pregnancy Working Group).

Accessing the Malaria in Pregnancy Library

The Malaria in Pregnancy Library is available free of charge via the Internet from Update Software Ltd.

Contents

The MiP Library has been designed to be the most comprehensive database on malaria in pregnancy available. As such a diverse range of sources have been searched to bring together all literature concerning malaria in pregnancy. The database thus includes:

- Published and unpublished literature, dating from 1945 to the present day, with no restriction on languages
- Published literature includes journal articles, books, reports, PhD theses, governmental policy documents and a range of other non-conventional published literature
- Unpublished literature covers ongoing clinical trials, ongoing clinical studies, ongoing PhDs, unpublished PhDs, aborted research and any other non-conventional unpublished literature on the topic
MiP Consortium
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MiP Consortium Activities
Startup period 2005-2007

Malaria in Pregnancy

Review Literature

Identify Gaps

Research Priorities

Research Strategy

Lancet Infectious Diseases
Volume 7 Feb 2007
Evolution of the Research Strategy

33 Scientists: 7 working groups → 7 papers

1. Epidemiology and burden of disease
2. Pathogenesis and immunity
3. Case management
4. Preventive strategies
5. Pharmacokinetics and Pharmacovigilance
6. Public health issues
7. Economics
8. Summary Paper
Research Strategy planning meeting
Multi-donor meeting June 2006 London

Objective: Formulate research strategy and discuss funding options/process with donors

<table>
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<tr>
<th>Funding agents</th>
<th>Other</th>
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<tr>
<td>BM Gates Foundation</td>
<td>MMV</td>
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<td>EDCTP</td>
<td>WHO</td>
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<td>EU (FP7)</td>
<td>Researchers</td>
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<td>Wellcome Trust</td>
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<td>NIH</td>
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<td>DFID</td>
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Priorities within priorities

- Next drugs for treatment (Pf and Pv)
- Next drugs for prevention (Pf and Pv)
- Optimal combinations of preventive interventions in different epidemiological settings
- Improved delivery of existing recommendations to achieve high coverage
Added Value of Consortium Based Approach
Multi-donor meeting June 2006 London

• Research
  – Comprehensive research portfolio, avoids gaps/overlap
  – systematic approaches and standardized methods
  – Multi-centre approach: speed, power, quality, representative
    • Enhances Impact
    • Maximizes ability to deliver within a 5 year timeframe
  – Agreements:
    • Share results in timely manner
    • Contribute to centralized safety database

• Capacity Development

• Communication: Single platform
  – Joins expertise from diverse areas for generating research data for policy guidance
  – Advocacy for MIP (one voice)
  – Sharing data, Information, quality controlled reagents, liability

• Resource Centre
  – valuable source of all published and unpublished literature.
  – information on local or regional policy and coverage of interventions
  – Technical support to other organizations (e.g. RBM, WHO, MMV, etc)
Added Value of Consortium Based Approach
Potential for large sample sizes

• **Safety**
  – Levels of reassurance risk and benefits of antimalarials in pregnancy that have previously not been possible.

• **Efficacy: Methods of assessment**
  – Individuals: Optimal duration of follow-up and choice of endpoints (e.g. placental malaria versus birth weight).
  – Population: Tools to monitor and evaluate the impact of successful MiP control interventions (e.g. birth weight or anaemia charts).

• **Biological sample databank (support other initiatives)**
  – Rapid testing of new hypotheses on the pathogenesis of, and protection from, MiP.
  – Vaccine Development
    • MALVAC
    • Pregnancy Malaria Initiative
  – Genetics: Malaria Genomic Epidemiology Network (MalariaGEN)
MiP Consortium
Activities Startup period 2005-2007

1. Establish online MiP Library
   – A registry of MiP studies (trial registry)
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2. Develop a research strategy

3. Produce full proposal for consideration by donors
### MIP Consortium Funding Strategy

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<th>Trials</th>
<th>Lab</th>
<th>Burden</th>
<th>Drug safety register</th>
<th>Capacity building</th>
<th>Network</th>
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<td>Industry/MMV</td>
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16
Research Proposals

• BM Gates Foundation (April 2007: under consideration)
  – Liverpool School of Tropical Medicine on behalf of the Consortium

• EU FP7 (April 2007: under consideration)
  – *P. falciparum*: Burden, Immunology & Pathophysiology
    • Africa
    • Liverpool School of Tropical Medicine on behalf of 6 Consortium member institutions
  – *P. vivax*: Burden, Immunology & Pathophysiology
    • Asia and Latin America
    • University of Barcelona on behalf of 6 Consortium member institutions

• EDCTP (end 2007 / 2008?)
Research Agenda

Primary Objectives

- **Theme 1: Case management in Africa, Asia & L. America**
  - To identify at least 2 drug combinations that are safe, practical to use (3 day regimen or shorter) and highly effective for the treatment of uncomplicated falciparum and vivax MiP

- **Theme 2: Prevention Africa**
  - To optimize the existing regimen IPTp with SP in context of ITNs (Integrated approaches)
  - New drugs for IPTp: To identify at least 1 safe and effective alternative to sulfadoxine-pyrimethamine (SP)

- **Theme 3: Prevention Asia and Latin America**
  - To better define the malaria burden and to determine the optimal strategy for the control of malaria in pregnancy in areas with low falciparum and vivax malaria in Asia and Latin America.

- **Theme 4: Public Health Impact**
  - To determine optimal ways of scaling up use of control tools
Research Agenda - Con’t
Secondary Objectives

• **Drug Safety**
  – To determine the safety of antimalarials in all 3 trimesters by establishing a centralized trial safety database and AntiMalarials Pregnancy Exposure Registry (AMPER)

• **Pathogenesis and Immunity**
  – To determine the impact of interventions on the development of pregnancy specific malaria immunity in the mother and the development of immunity in the infant.

• **Capacity development**
  – Academic training (training of PIs: Phd, MSc)
  – Infrastructural site development
  – Training and Network Clinical trial coordinators and monitoring
MIP Consortium
Research Strategy

Research Themes

1. Treatment
   Africa, Asia, LA
2. Prevention
   Africa
3. Prevention
   Asia & Lat. America
4. Public Health
   Impact

Cross-Cutting activities
1. Pharmacokinetics; 2. Immunology & Pathogenesis; 3. Pharmacovigilance

Policy Working Group
Capacity Development WG
**Phasing, Milestones, and Timeline**

<table>
<thead>
<tr>
<th>MiP Project Milestones and Timeline</th>
<th>3m</th>
<th>1y</th>
<th>1.5</th>
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<td>Centralized drug safety registry (AMPER)</td>
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<td>Phase I: Treatment and prevention trials</td>
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**Treatment Africa**
- Asia & L. America

**Prevention Africa**
- Asia & L. America
Potential Contribution sought from EDCTP

• Support for Intervention trials in Africa
  – Pharmacokinetics
  – Treatment trials (ACTs)
  – Prevention trials (IPTp + ITNs)

• Support for Capacity Development
  – Infrastructural support
  – Individual fellowships (e.g. Phd, career development)
  – Workshops; e.g. GCP training, methodology (placental histology, ultrasound assessment of gestational age)

• Co-funding for the Network
  – Secretariat of Consortium
  – Drug safety registry
  – Member meetings
Projects

• Case-Management (3 Multicentre trials)
  • *Africa P. falciparum:* 4 combinations head to head (3 sites)
    – *PK Screen 6:* MQ-AS; AQ-AS; AL; DHA-PPQ; CDA; AQ-SP
  • *Asia and Latin America (PF and PV)*
    – MQ-AS; DHA-PPQ vs current policy (7 day QN-CL or AS-CL)

• Prevention: Africa (2 projects)
  • Optimizing existing regimen with IPTp-SP
    – Seasonal versus year-round IPTp in the context of ITNs
    – Dosing frequency in the context of ITNs
  • New drugs for IPT (MQ, (DHA-)PPQ, AZ+)

• Prevention Non-Africa (3 projects)
  • Stage I: Burden assessment and regimen finding studies
  • Stage II: Prevention trials (Passive CM, Active CM, IPTp)

• Pharmacovigilance: Trial data (2\textsuperscript{nd}/3\textsuperscript{rd} trim) and PER (1\textsuperscript{st} trim)

• Burden, Immunology and Pathogenesis

• Public Health Impact: Up-scaling; economics; anthropology
Anti-Malarial Pregnancy Exposure Register (AMPER)

- Global Centralized database on anti-malarial drug safety
- Data sources
  - from trials (2\textsuperscript{nd} and 3\textsuperscript{rd} trimester)
  - sentinel sites: 1\textsuperscript{st} trimester
- Regional offices; QA, monitoring, training & 1 global coordinating centre
- Training / Capacity development