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## **Research agenda related to control of malaria in pregnancy in the context of malaria elimination**

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Malaria in Pregnancy Consortium

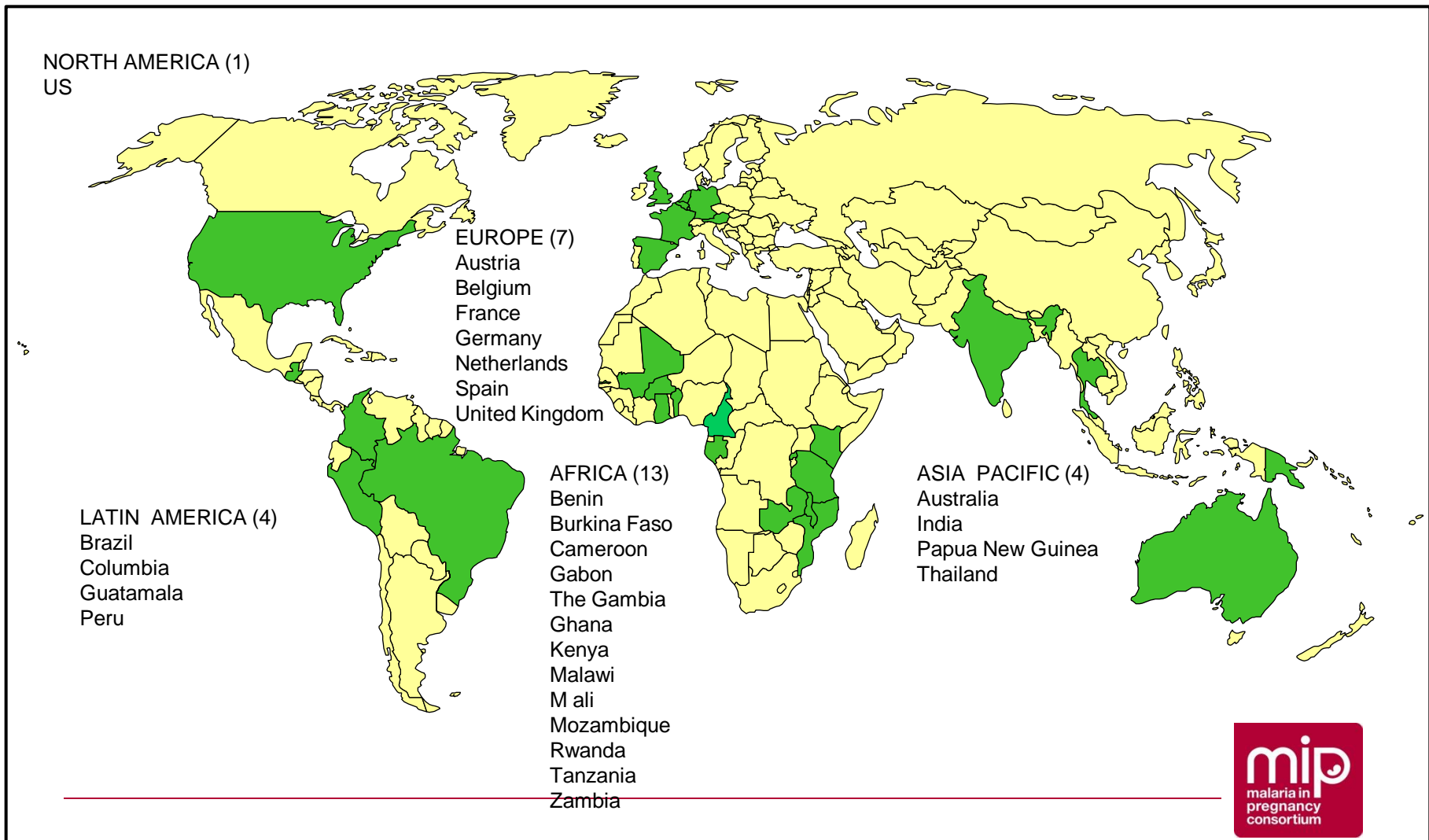
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# Outline

- Introduction to the Malaria in Pregnancy Consortium
- Background and rationale of the research agenda: changing epidemiology
- Implications of declining transmission: clinical features, optimal treatment and prevention strategies
- Malaria control by resultant transmission strata
- Research priorities and gaps in knowledge
- Monitoring
- Conclusion

# Malaria in Pregnancy Consortium

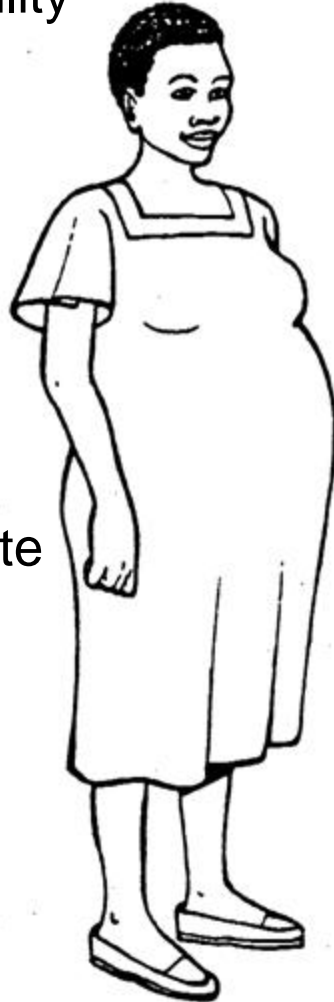
## 41 Institutions in 29 countries



# Impact of malaria in pregnancy

## Pregnancy

- Increases susceptibility
- More infections
- More severe



## Mother

- Asymptomatic to acute clinical illness / death
- Severe anaemia

## Effects depend on

- Malaria endemicity
- Maternal age
- Gravidity
- HIV status

## Foetus

- Miscarriage
- Stillbirth
- Low birth weight (2x)  
IUGR / Preterm

## Longer term effects

- Neonatal and post neonatal mortality
- Immune modulation (susceptibility)
- Infant anaemia
- Infant growth?
- neuro-cognitive development?

# Background of the MiP Consortium research agenda

- Current malaria control strategies in moderate to high transmission areas
- Epidemiological features: semi-immunes and most infections asymptomatic; most infected prior to pregnancy or prior to 1<sup>st</sup> ANC visit; most deleterious effects in 1<sup>st</sup> and 2<sup>nd</sup> pregnancy
- Recommended control approaches: ITNs or IRS, IPTp, effective case management
- **Challenge:** Control approaches in low transmission settings remains unknown!

# Implications of transmission reduction

- Epidemiological basis for current strategies may no longer hold
- Need to adjust current intervention strategies while continuing ITNs or IRS as core community strategies
- IPTp may or may not be useful (not cost-effective)
- Future use of vaccines may not be cost-effective
- Diagnostics and monitoring increasingly important
- Creation of various transmission strata

## Transitional transmission strata & Control approaches

Intervention (in the context of ITNs/vector control)	Transmission
<b><i>IPTp</i></b> at regularly scheduled antenatal clinic visits as currently practiced.	<b>High/ Intermediate</b>
<p><b><i>Universal (Intermittent) screening strategies</i></b></p> <p>With lower transmission (reduced 10-fold ?), IPTp is replaced by use of diagnostics for universal screening regardless of symptoms – initially this may need to be done at regular intervals during pregnancy for all women.</p> <p>Acquired immunity is still relatively high as transmission reduction is recent; at later stage this could be restricted to a single screening event at booking followed by passive surveillance.</p>	<b>Low</b>
<p><b><i>Selective screening or passive case detection only</i></b></p> <p>At even lower levels of transmission, when acquired immunity in the population is very low and most infected persons including pregnant women will have symptoms with any infection, screening could be restricted to women with symptoms or a history of potential exposure, hot spots etc i.e. Selective screening.</p>	<b>Very low</b>
<p><b><i>Chemoprophylaxis /other</i></b></p> <p>Epidemics may also become more frequent and require a specific approach to malaria control in pregnancy</p>	<b>Epidemics</b>

# Challenges emerging due to change from high to low transmission

- Knowledge gaps: little research and less policy for MiP in medium-low transmission settings
- Focus of malaria control on transmission reduction, not on key target groups
- Implications for MiP unknown
- Appropriate interventions for MiP may change
- M&E remains important: burden reduction?
- Cost effectiveness increasingly relevant for policy
- Acceptability & 'Implementability' of new approaches

# Knowledge gaps & on-going research [1]

## Research questions 1

- Changing role of prevention (e.g. IPTp vs screening and treatment)
- Public Health implications: implementability, scale up, access
- When is it optimal to change interventions; use of modelling

## Research questions 2

- Use of pregnant women as 'easy access' sentinel groups (also ref. monitoring)
- Changing disease epidemiology
- Changing immunity

## Knowledge gaps & on-going research [2]

### Research question 3

- Which drug(s) for IPTp and effective treatment?

### Research question 4

- Improved diagnostics and diagnosis (also ref. monitoring)

### Research question 5

- Standardization and guidelines: Criteria or thresholds upon which to switch control strategies; guidelines to define high/moderate, low and very low transmission settings

# Monitoring: Changes in MiP indices with transmission reduction

Pregnant women as a sentinel group: high risk, self-present, large numbers; but need to examine how representative of general population

- Fall in prevalence and incidence of infection
- Decrease in malaria-attributable LBW/anaemia?
- Increase in severity of individual infections?

Role of diagnostics e.g. RDTs

Research to develop/validate M&E tools and indicators

# MIP Consortium On-going Treatment Trials (Fixed dose ACTs)

Africa

2010-2012

D'Alessandro et al  
Ghana, Burkina,  
Malawi, Zambia

Art-Lumefantrine  
AQ-AS  
MQ-AS  
DHA-PIP

India

2010-2012

Chandramohan et al  
3 sites

SP-Art  
MQ-Art

Brazil

2011-2012

Desai et al  
3 sites

Coartem  
MQ-ART

# IPTp new drugs: Ongoing clinical Trials

Mefloquine  
2012

15 mg/kg  
single / split dose  
Menendez et al

Kenya  
Mozambique  
Tanzania  
Gabon  
Benin

[Chloroquine-  
Azithromycin]  
2013?

Pfizer  
MMV  
LSHTN

5-6 Countries  
Africa

SP  
Azithromycin  
2012

Ivo Mueller et al

Papua New Guinea  
(High transmission)

# ISTp vs IPTp-SP Ongoing clinical Trials

## West Africa

Greenwood &  
Tagbor  
2013

Ghana  
The Gambia  
Burkina Faso  
Mali

## Malawi

Kalilani  
Ter Kuile  
2013

3 sites

## India

Chandramohan  
2013

2 sites

# Conclusions

- Transmission reduction will lead to changes in malaria epidemiology requiring changes in control strategies
- Need for identification of appropriate control strategies and thresholds for strategy switch over
- Identification of markers of malaria in pregnant women
- Develop and evaluate different diagnostic tools for detecting malaria in pregnancy and for monitoring/evaluation

# Acknowledgements

- Members of the working group of MiP Consortium for the development of the MiP control research agenda for reduced transmission setting
- Sponsors to the GHC Conference malaria panel

*Thank You*