



# Pregnancy Exposure Registries in Resource Limited Settings

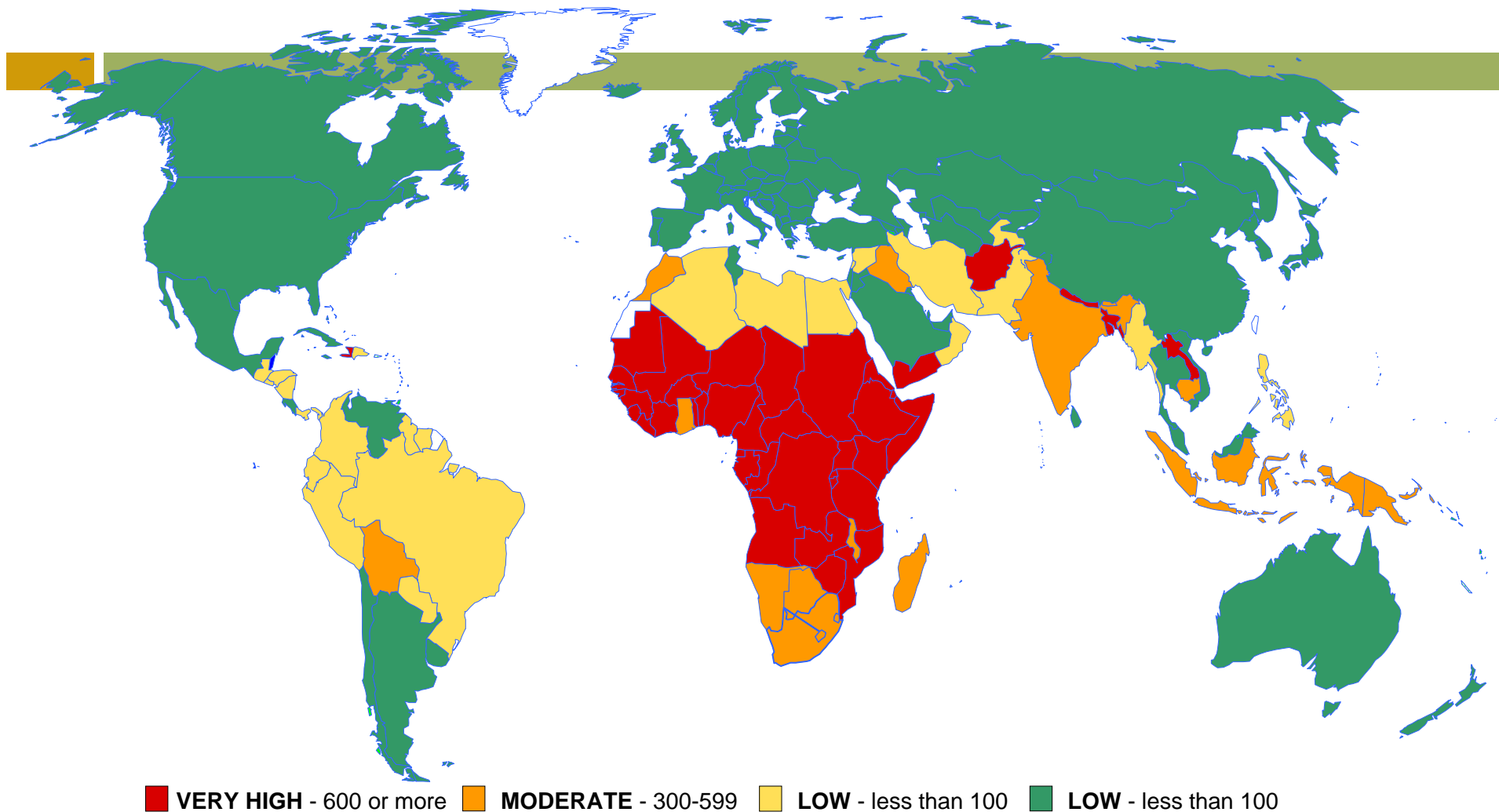
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# MDGs 4 and 5 (maternal and infant mortality)

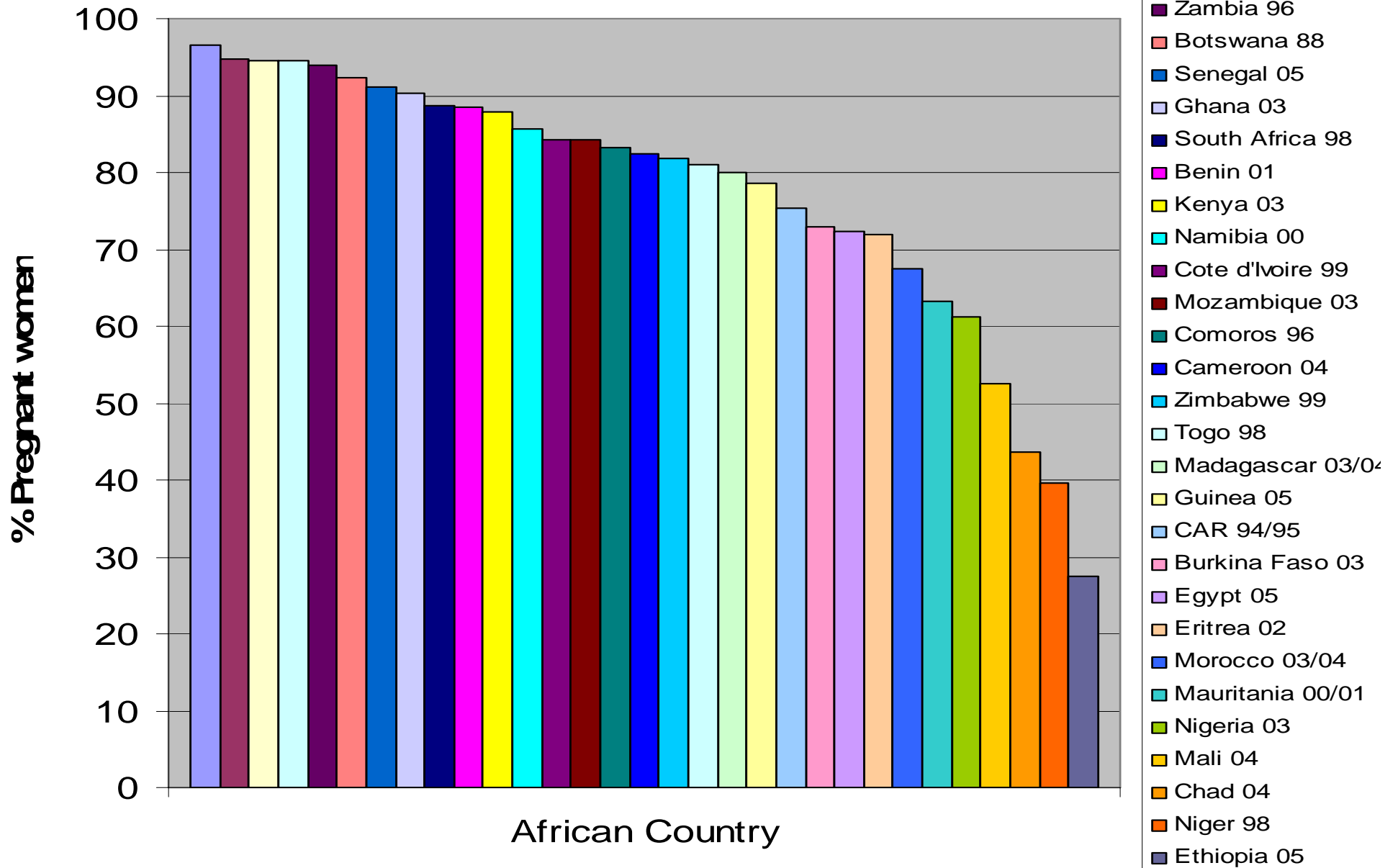
## Challenges

- High maternal and neonatal mortality ratios
- Annual decline in MMR <1% from 1990 globally
- 68,000 of maternal deaths from unsafe abortion
- 63% of births attended by a skilled health professional globally
- wide variations between regions & within countries.
- + 7 million babies are stillborn or die within the first 4 weeks of life per year
- Low IPTp & PMTCT coverage - the inadequate integration of vertical malaria, HIV & MCH services

Source: WHO, UNICEF, UNFPA, *Maternal Mortality: Estimates developed by WHO, UNICEF, UNFPA.*



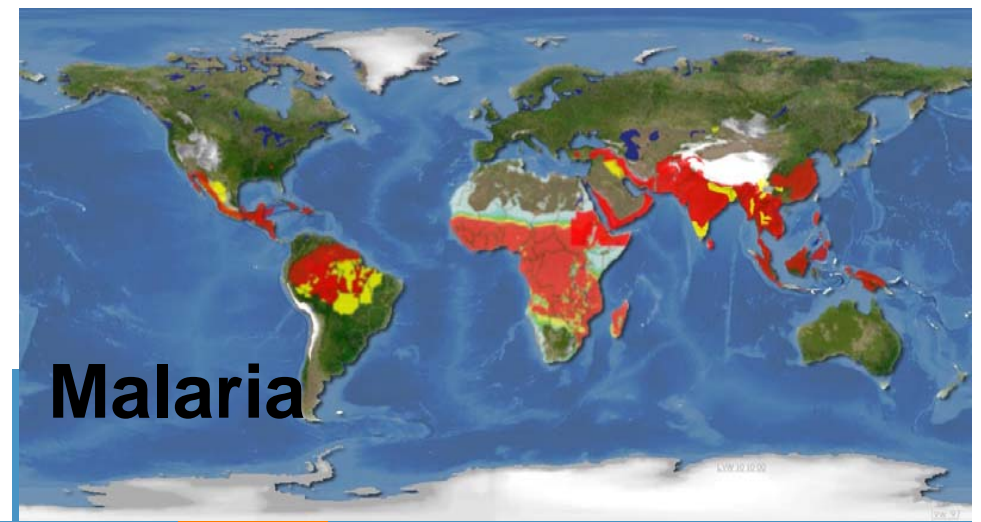
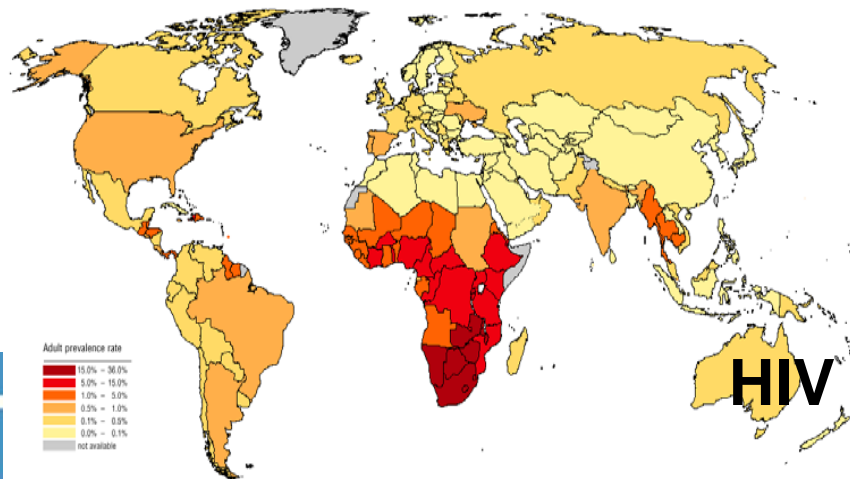
## Antenatal Care At Least 1 Visit birth in 3 yrs preceeding the DHS survey- updated Oct. 07



# Malaria and HIV

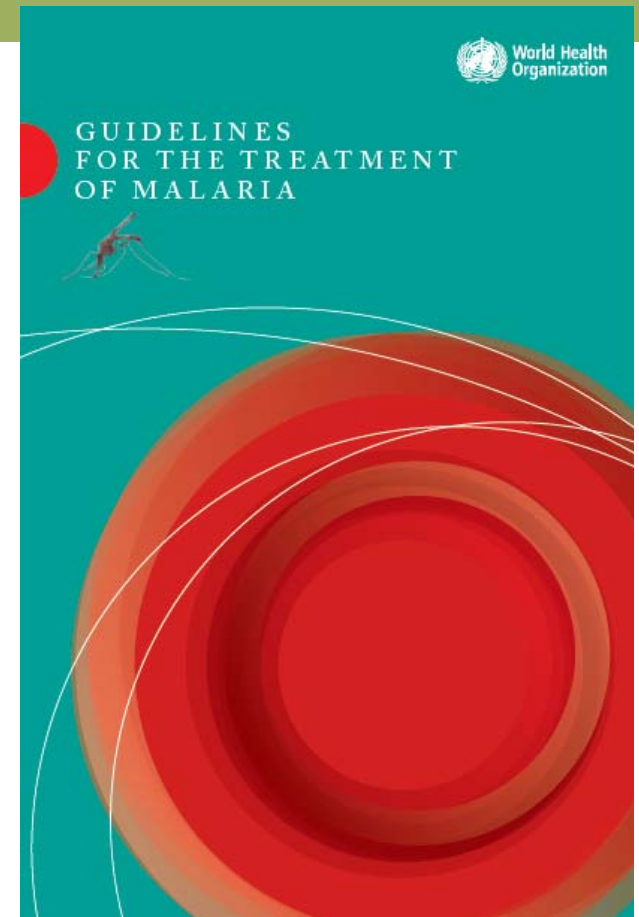
## Geographic overlap in sub-Saharan Africa

- 55% of HIV+ adults are reproductive aged women; 80% of the world's infected women
- 44% of 43 sub-Saharan African countries with malaria have HIV seroprevalence  $\geq 10\%$  among antenatal clinic attendees
- A small effect of malaria on HIV or vice-versa could have substantial population-level implications



# Policy Statement Unchanged on Artemisinin in Pregnancy

- **WHO Treatment Guidelines 2006 and 2009**
- ARTEMISININS should not be withheld if treatment is lifesaving
  - in severe malaria
- Recommended in 2<sup>nd</sup> or 3<sup>rd</sup> trimester for uncomplicated malaria and preferred to QN in severe malaria
- Only used in 1<sup>st</sup> trimester if it is the only effective treatment available
- **Need human evidence for policy**



# Rationale for a Pregnancy Register

- ❑ Lack of background data on birth defects in developing countries
- ❑ Large scale deployment of medicines – Malaria, HIV, leishmaniasis
- ❑ Limited capacity for assessing congenital anomalies
- ❑ Artemisinins –have potential for teratogenicity in >1 animal model (first trimester exp.)
- ❑ Malaria endemic areas have high prevalence of other diseases (HIV, TB, parasitic disease, malnutrition etc.) with exposure to other potentially teratogenic treatments
- ❑ Concerns about safety in pregnancy could undermine public confidence in life-saving therapies



# Pregnancy Register Protocol: A WHO interdepartmental activity, with expert advice

- ❑ MPS (Making Pregnancy Safer)
- ❑ TDR (Research & Training in Tropical Diseases)
- ❑ Global Malaria Programme
- ❑ Quality and Safety of Medicines
- ❑ Health system Strengthening
- ❑ HIV/AIDS Programme
- ❑ Tuberculosis Programme
- ❑ Neglected Tropical Diseases
- ❑ WHO country involvement



# Goal

- To promote the health of pregnant women and their children in resource poor settings
- By developing a pregnancy registry
- Provide evidence on safety of public health medicines used in pregnancy
- Malaria and HIV drug exposure as a pathfinder



# Quantifiable Objectives

- ❑ Quantify baseline risk of major congenital malformations in malaria-endemic countries.
- ❑ Quantify risk of major congenital malformations associated with exposure to ACTs in 1<sup>st</sup> trimester of pregnancy.
- ❑ Identify other factors that may contribute to risk of major congenital anomalies and other adverse birth outcomes

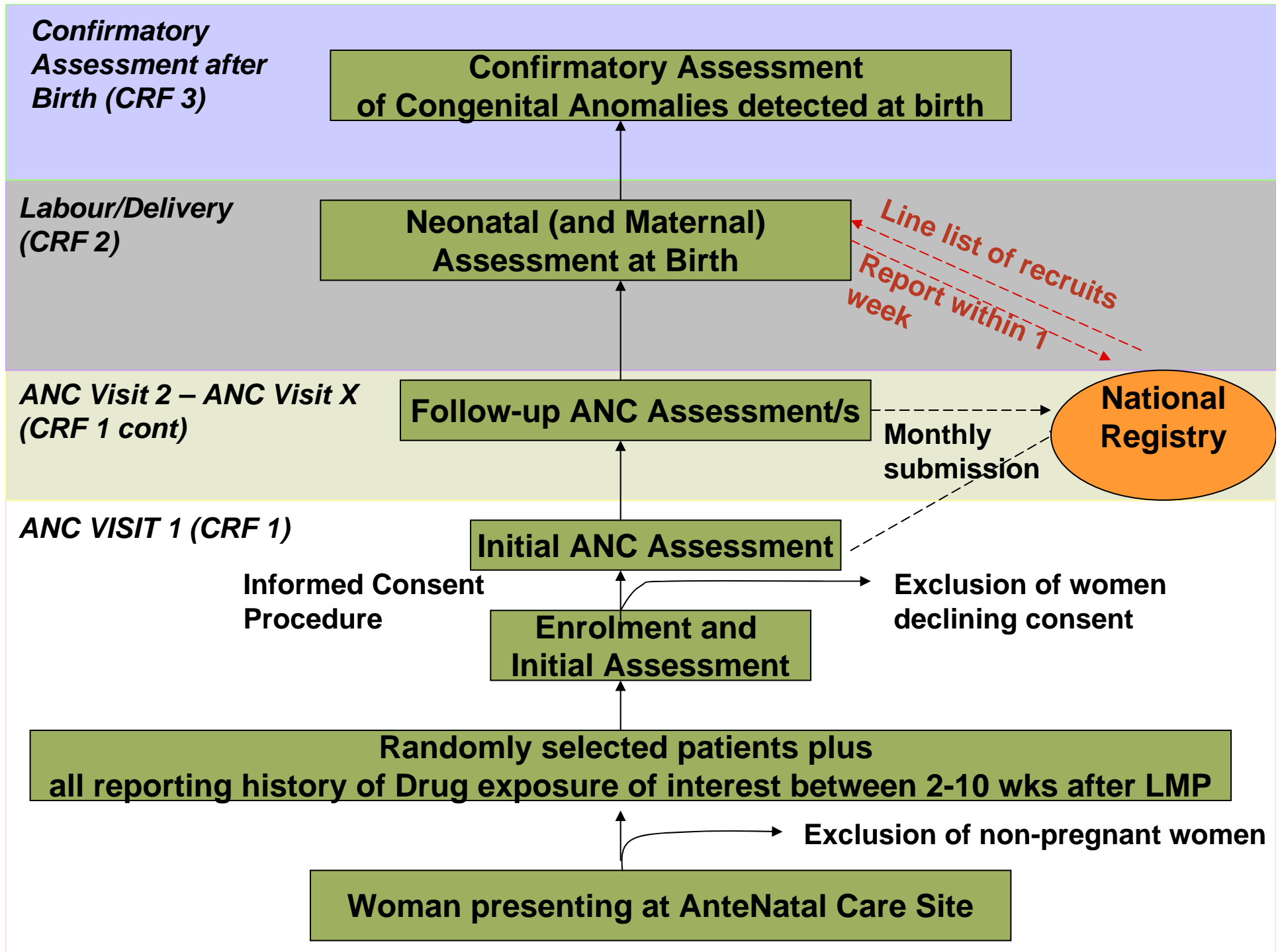
# Scoping Visits

- Seeking collaboration between
  - ▣ MOH: MCH, Malaria, HIV/AIDS, HMIS
  - ▣ Academia/research institutions incl. DSS sites
  - ▣ WHO & other relevant NGOs
  - ▣ Health facilities (PHC and referral facilities)
- Site visits to ANC clinics and referral hospitals
- Literature search for relevant publications from countries
- Assessment of treatment seeking and health indicators
- 1st Countries: Tanzania, Uganda, Ghana, Mozambique, Kenya
- Country owned data, pooled in a WHO repository

# Methods: General Principles

- ❑ Sentinel sites selected in areas of high malaria, HIV prevalence and other diseases
- ❑ Prospective observational cohort of randomly selected pregnant women. Enrollment as early as possible in pregnancy
- ❑ Generic study design enabling assessment of other drugs
- ❑ Active group: pregnant women with confirmed first, second or third trimester exposures to ACTs.
- ❑ Comparison groups:
  - Healthy pregnant women with no malaria and no exposure to ACTs during pregnancy
  - Pregnant women with malaria not exposed to ACTs
  - Women with no malaria being treated with other medication
- ❑ Primary outcome: major congenital anomalies at birth





# Pilot Study: Ghana, Kenya, Uganda, Tanzania, Mozambique

- Objectives
  - ▣ Assess feasibility of CRFs and all processes
  - ▣ Identify problems that are likely and consider local solutions to address these
  - ▣ Assess acceptability of registry by community and health staff
- Methods: qualitative studies, and quantitative analysis of data quality
- Feasibility assessment of data capture methods during pilot study (e.g. paper vs. hand-held device vs. desktop)
- Development of an open access data management system

# To do this, first we have to.....

- ❑ Build capacity to assess, monitor birth outcomes especially for congenital malformations and other adverse pregnancy outcomes.
- ❑ Develop culture of drug safety awareness through (antenatal, postnatal) service delivery in selected sentinel sites in participating countries
- ❑ Contribute towards building capacity in participating countries to detect, assess and manage major congenital anomalies

# Management Challenges

- ❑ Consultation with national and local authorities, programmes, health staff and ethics committees
- ❑ Assess training and infrastructure needs at sites, development of training curricula
- ❑ Staff training & remuneration. Tasks shifting?
- ❑ Quality of birth examinations
- ❑ Appropriate informed consent procedures
- ❑ Maintaining constant communication and reporting from sites
- ❑ Ensuring appropriate follow-up, feedback and communication to sentinel sites and communities
- ❑ Data quality, electronic access to data
- ❑ Suitable model for involving pharmaceutical industry

# Current and Ongoing Activities

- ❑ Development of a Registry Co-ordinating team
- ❑ International Birth Defects Panel for the pilot study
- ❑ Concurrent pilot testing of data capture & management tools
- ❑ Training:
  - ❑ Development of SOPs
  - ❑ Surface exam training video
  - ❑ Registry training programme

# Why MPS is interested in this research?

## Possible outcomes of the PR:

- Strengthened ANC comprehensive services
  - in providing integrated service delivery
  - in improving quality of care and case management
- Increased country capacity on birth defects detection and management and on drugs safety in pregnancy (not only for ACTs or ARVs)
- Increased demand by the communities for quality services during pregnancy and child birth.

# Collaboration

- Pooling of data
  - ▣ Similar data quality
  - ▣ Reliable surface exams
  - ▣ Internal control group

- Official Call for contributions

<http://www.who.int/tdr/svc/grants/calls/call-contributions>

