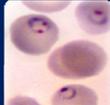




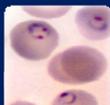
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of new antimalarials in the field:
challenges and opportunities

Malaria symposium, ASTMH 2009
Marriott, Washington DC, USA
Friday, November 20, 2009



Post Licensure Monitoring and Evaluation of Antimalaria Drug Effectiveness and Safety

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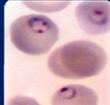
Acknowledgment

- Dr. Ambrose Talisuna – MMV, Uganda
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- Dr. Francois Bompert – Sanofi Aventis, Fr
- Dr. Steven Smits, NASF, Holland



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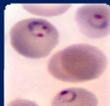


Pharmacovigilance

"the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other possible drug related problem"

World Health Organization, The importance of pharmacovigilance: safety monitoring of medicinal products, Geneva 2002

PV is an Ethical Concern:
Drugs must be beneficial and cause no harm



PHARMACOVIGILANCE IN CONTEXT

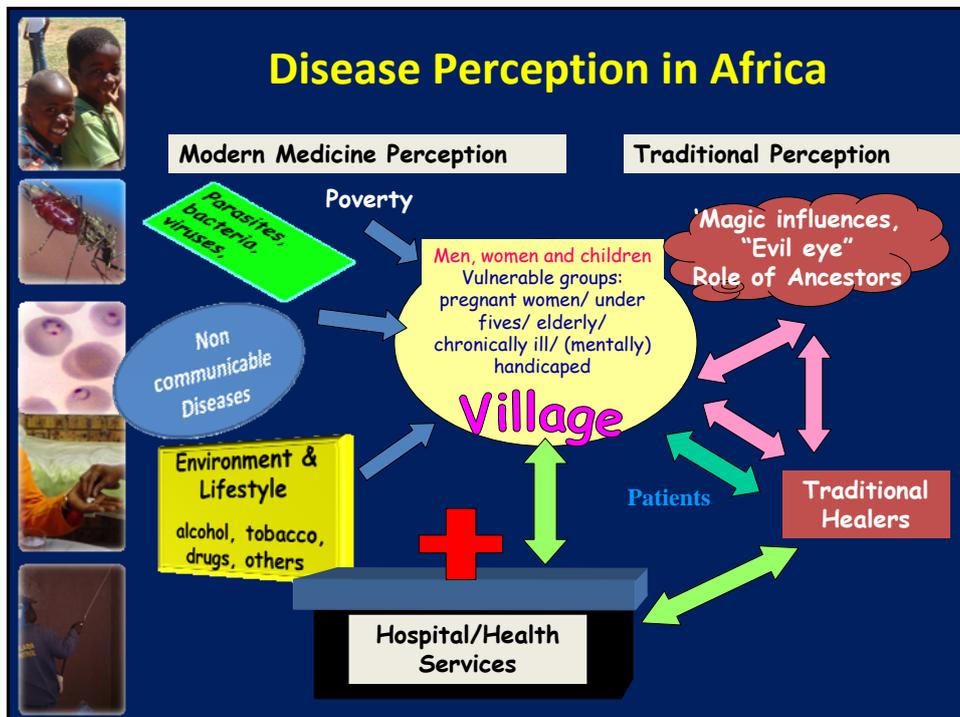
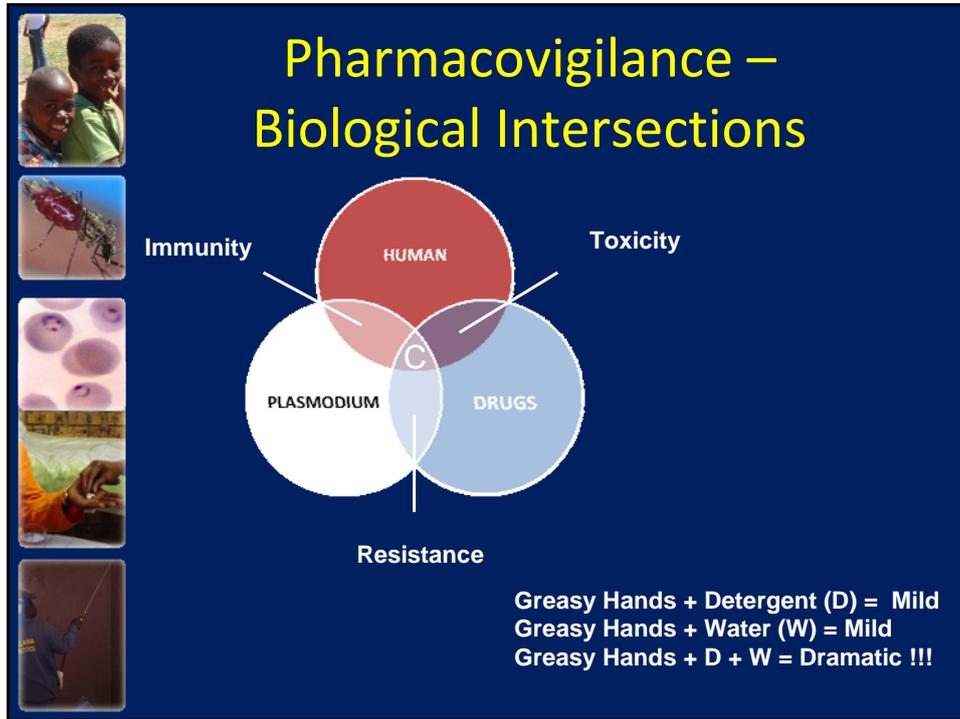


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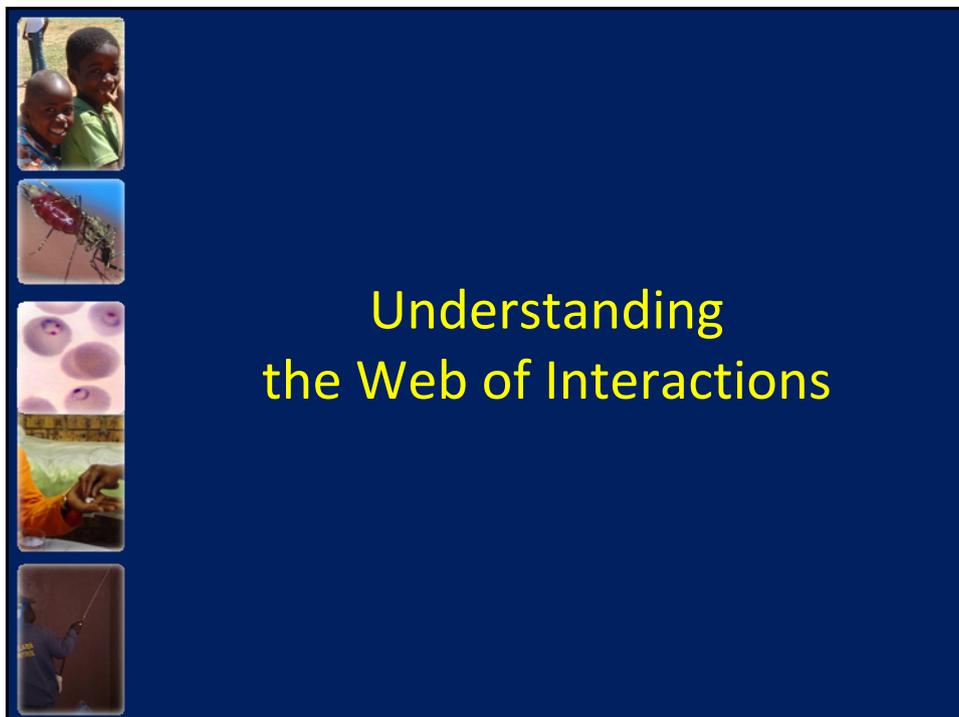
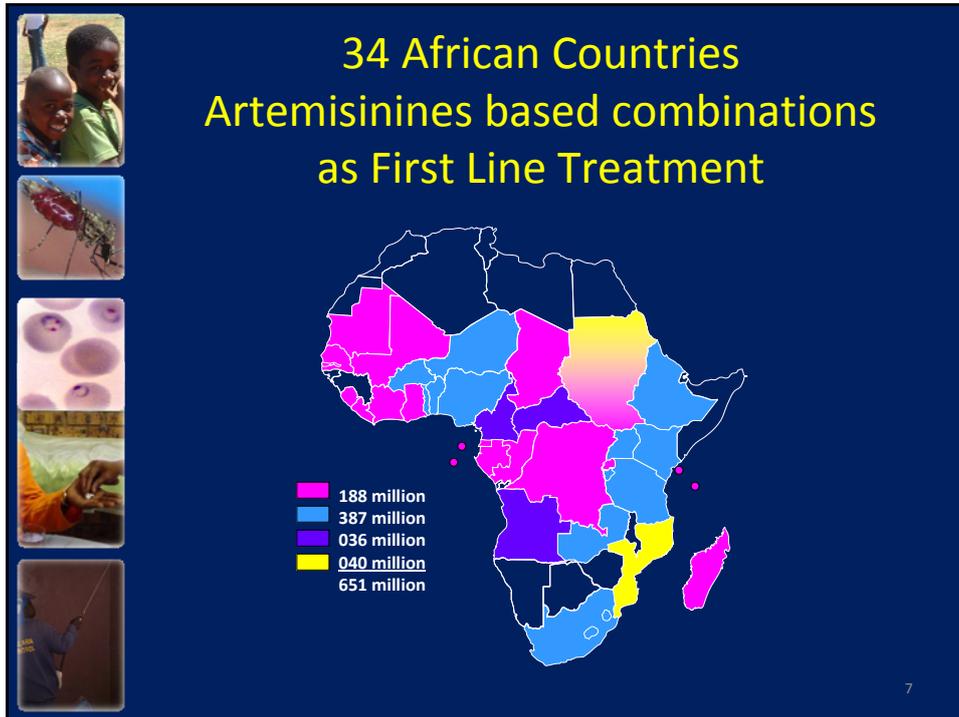
DNDi
Drugs for Neglected Diseases initiative





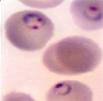
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PV Confounders

Category	Issues to consider
 <ul style="list-style-type: none">Urban/Rural	<ul style="list-style-type: none">My grand mother sees - pain & bitterness of the pill as part of therapy
 <ul style="list-style-type: none">Youth	<ul style="list-style-type: none">Raging hormones /self expression 14 – 25 yr olds and practices
 <ul style="list-style-type: none">Food Habits	<ul style="list-style-type: none">Free radicals scavengers & anti-oxidants, Zn and other immune booster foods, medicinal plants,
 <ul style="list-style-type: none">Genetics	<ul style="list-style-type: none">Fast/slow metabolisers Better responders/Fula group

Which Drugs for Whom ?

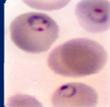
- Donation Drugs – quality?
- Street / Illegal Drugs
 - Expired drug dumpster from major pharmacies
 - Poor storage
 - Counterfeit from fake manufacturers
 - 2 500 people died from a substandard bbvaccine in Niger in 1995
 - 500 people vaccinated with a substandard vaccine in Douala in 2004
 - 20% of malaria incidence related death due to sub-standard anti-malarials



Provider Behaviour !



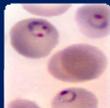
- Provider behaviour is important
- 40 % of practicing MDs got above half of the questions correct in a pre-test of Sanofi training of trainers in Ghana and Burundi
- Only 30% of fevers were malaria in CMR – over treatment ?
- 10% providers gave the right drug, right dose, for the right malaria condition in CMR
- The patient as self-provider was at 65% in CMR



The Appeal of « Alternative » Medicine



- Symptoms alleviation is perceived as being efficacious
- Cheap and proximity to source of drugs
- Less consultation waiting time
- No complication of further delays with diagnosis
- Payment can be in kind in rural settings

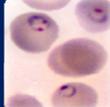




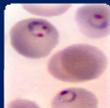
Repeated Dosing & Drug Interactions



- Many repeated episodes of malaria and treatment
- Automedication and prescribed drugs
- Prescribed drugs and medicinal plants
- Concomittant therapies and interactions
- Co-infections / Malaria and HIV



Detection and Assessment





Different Approaches

- Many small scale safety and efficacy studies and meta-analysis
- Cohort Event Monitoring,
 - Studies in Liberia (self expression age group)
 - Studies in Senegal and Uganda (repeated episodes)
 - Studies in Cote d'Ivoire (rare events -1/5000)
- ACT consortium PV initiative (quality & safety)
- WHO-MMV guidance notes for AMFm countries



Improving Spontaneous Reporting

- Spontaneous reporting-
 - mainstay of regulatory pharmacovigilance for several decades. **Tools may be adapted to meet current times – improved communication technology etc**
- *A practical handbook on the pharmacovigilance of antimalarial medicines* may not be enough
 - **needs intensive retraining of providers in detecting and communicating findings**
- Stimulated spontaneous reporting
 - is intended to improve the likelihood of identifying potential additional risks – **Establish patient registry; Simplified ADR reporting forms for private retailers; Active follow-up of a random subset of patients.**

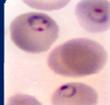




Set up More Control Cohort Events Monitoring



- Quick quality data by prospective follow-up (one week return) of a large population of individuals with documented exposure to the medicine/s in question.



- Comparator drugs control and the before-and-after rates and outcomes of adverse events can be developed which can facilitate the detection of signals



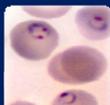
- Can characterize known reactions, detect drug interactions, potentially identify risk factors and identify deficiencies in rational drug use

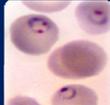


Needed! Improved Assessment Tools



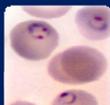
- Self reporting and physicals are not enough
- Biological markers of fatigue/physiological assessment of efforts
- Biological markers of neurotoxicity and audioxicity
- Presence of co-morbid infections - viral bacteria and others
- Presence of non-communicable illnesses





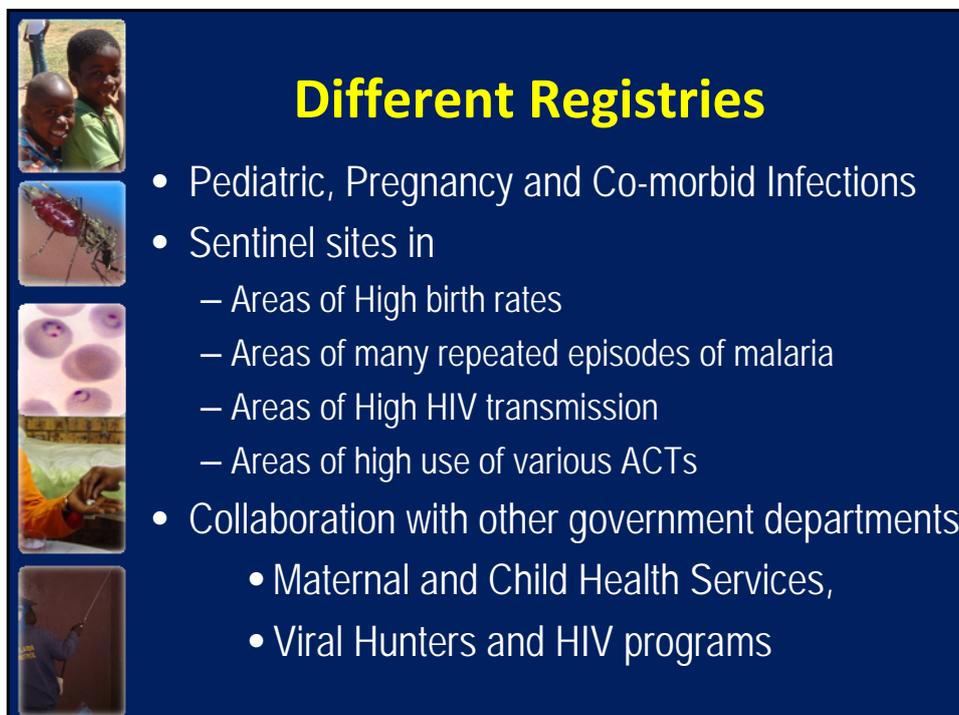
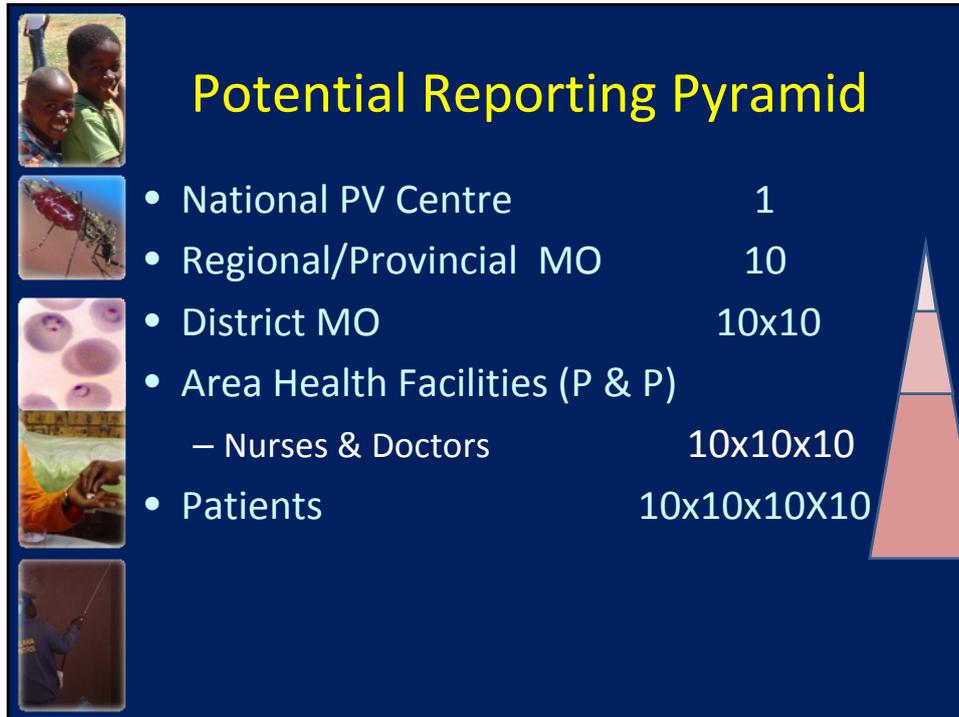
Causality Assessment?

- Critical step in PV
- Very challenging
 - Particularly for anti malarials
- When to assess? Initial report? Upon review?
- Considerations
 - Timing of drug administration and events
 - Likelihood of other causes
 - Status of malaria
 - Evidence of other illnesses
 - Concomitant medications, herbal treatments
 - Expectedness of event
 - Response to withdrawal, re-challenge
 - Age group behaviours and
 - Unlikely, possibly, probably, definitely related



Harmonisation of Reporting Procedures across studies

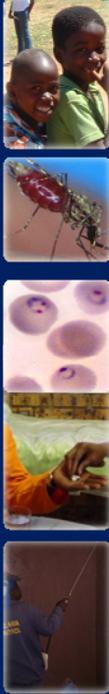
- What and How to measure!
- There is a handbook
 - *A practical handbook on the pharmacovigilance of antimalarial medicines* WHO, Geneva
- Standardisation of Operating Procedures
- Certification of PV Centres in good practices





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Improvements Towards Prevention



A Global Commitment with a Local Start

- Make the regular health system more appealing to people
- Better case management and rational drug use
- Good Practices
 - Pharmaceutical
 - Clinical and laboratory
 - Public Health
- Decrease the profit incentive of counterfeiters
- Find creative ways of beating them on their own game by implementing aggressive business approaches - available and cheap



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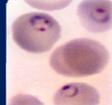


Set up Improved Communication Loops



- Step up reporting back to care givers to improve clinical practice and boost confidence

- Town hall meetings, cell phone calls, media, newsletters etc



- Vertical & Horizontal Communication Streams

- Other countries
- Uppsala Monitoring Centre
- Pharmaceutical manufacturers
- The WHO



- Maintaining a balanced information flow between the Active and the Passive systems



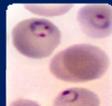
PV Systems Up Keep

- Source for sponsorship from non-traditional and new funders



- Strengthen PV center's resources

- **Infrastructure** - internet, phone, fax, copier, archiving system
- **Human Resources** - Expertise in clinical medicine, pharmacology, toxicology, epidemiology, as well as administration, data management etc.



- Strengthening the national drug regulatory authorities



- Be all inclusive:

- Ministries, Universities, Pharmaceutical Industries
- Public and Private (common initiative groups and missionary HCF)
- Integration with existing programs?

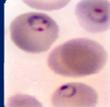




Training and Retraining



- Standardise treatment training kits for different levels
 - Advanced Module - Doctors and clinical officers
 - Basic module-Nurses and mid wives
 - Elementary module-Nursing Assistants
 - Simple module-Community groups and informal private sector



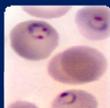
- Standardise the PV Elements of Review
 - Coding of events, drug names and terms (ADR, AE, SR, SE, etc), using standardized codes (WHO, MedDRA)
 - Determination of Relevance – Reduction of over-reporting
 - Assessment of quality of documentation
 - Causality assessment - Suspected relationship to medication



Advocacy



It is only when you and I, as scientists who understand the issues of pharmacovigilance as a moral obligation to our communities, are able to get out of our closets and talk to policy makers, donors and care givers, can we see the gains of advocacy for such a cause.



Wilfred Mbacham