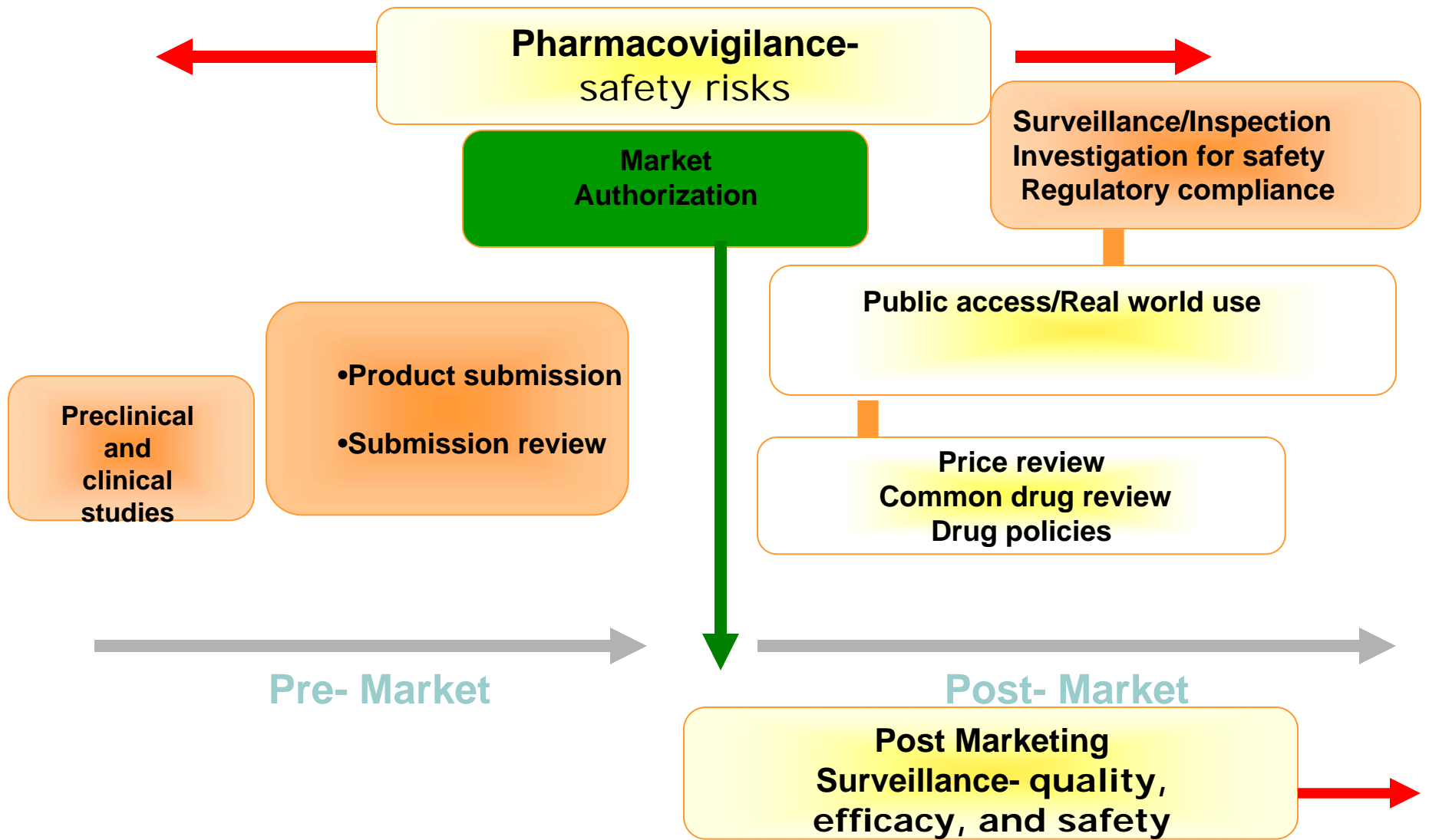


PHARMACOVIGILANCE OF ANTIMALARIAL TREATMENT IN AFRICA: IS IT POSSIBLE?

Dr. Ambrose Talisuna, MBchB, Msc, PhD

Pharmacovigilance Vs. Post Marketing Surveillance



Activities essential to pharmacovigilance (WHO)

- Consideration of possible changes in the risks and benefits of therapy
- Communication -to health professionals and the population
- Evaluation of consequences of adverse drug events
- Taking regulatory action, if required

Rationale for PV of Antimalarial drugs in Africa

- Malaria transmission is high-Frequent treatments
- Many countries have adopted ACT- opportunity to assess safety on wide scale
- Little experience with ACTs in Africa outside clinical trials
- Presumptive treatment of fever in the informal sector is widespread
 - incorrect dosing, inappropriate treatment, drug interactions
- Administration of antimalarial treatments in patients with co-morbid illness is a concern

Challenges of PV in Africa

- AEs are often difficult to distinguish from common symptoms of malaria
- The maximum severity grading of an AE (WHO guidelines) is subjective
- Assigning a causal relationship is difficult-definitely unrelated-definitely related
 - Defining period of "reasonable temporal association": CT include partner drugs with long elimination half-lives.
- Determining if an event is unexpected-difficult for co administered drugs

Methods of pharmacovigilance (PV)

Two broad approaches

- Passive spontaneous reporting systems (UK's yellow card scheme- started in 1964, following Thalidomide tragedy of 1960s)
- Pharmaco-epidemiological methods (UK's prescription event monitoring (PEM))

Passive spontaneous post authorisation follow up

Potential challenges

- under-reporting
- difficulty of establishing a causal relationship between AEs and specific drugs

Initial focus

- Sentinel health facilities-district Hosp.
- Targeted populations-pregnant women and children <5
- Only SAEs or those deemed possible, probable or definitely related to drugs

Post licensure clinical trials (Phase IV trials)

- Comparison of multiple treatment groups-to test hypotheses that the risk of AEs varies with type of treatment
- **Critical issues:** Sample size estimation- Ideally be based on a primary safety outcome
- **Practical challenges:**
 - how to differentiate AEs from symptoms of malaria or other illnesses
 - how to establish the severity, relationship, and expectedness of AEs

Case control studies

- Suitable for rare AEs-pregnant mothers exposed to antimalarial treatments in the first trimester
- **Practical challenges:** Good antenatal and pregnancy registers-data on exposure to medicines in pregnancy –HMIS registers?
- **Initial focus:** Assessment of SAEs during the first year after delivery in cases and controls
 - At delivery
 - Time of routine vaccination
 - Any point of contact with the health care system

Active population-based post-authorization safety evaluation

Linked to other data platforms

- Targeted population at SS for monitoring antimalarial treatment-EANMAT, WANMAT1&2
- Linked to sample vital events registration- PMI, PEPFAR
- Linked to HBMF
 - Active PV could be conducted by drug distributors.
- Embedded within broader framework of M & E for malaria –MDGs!

Is pharmacovigilance of antimalarial treatment in Africa possible?

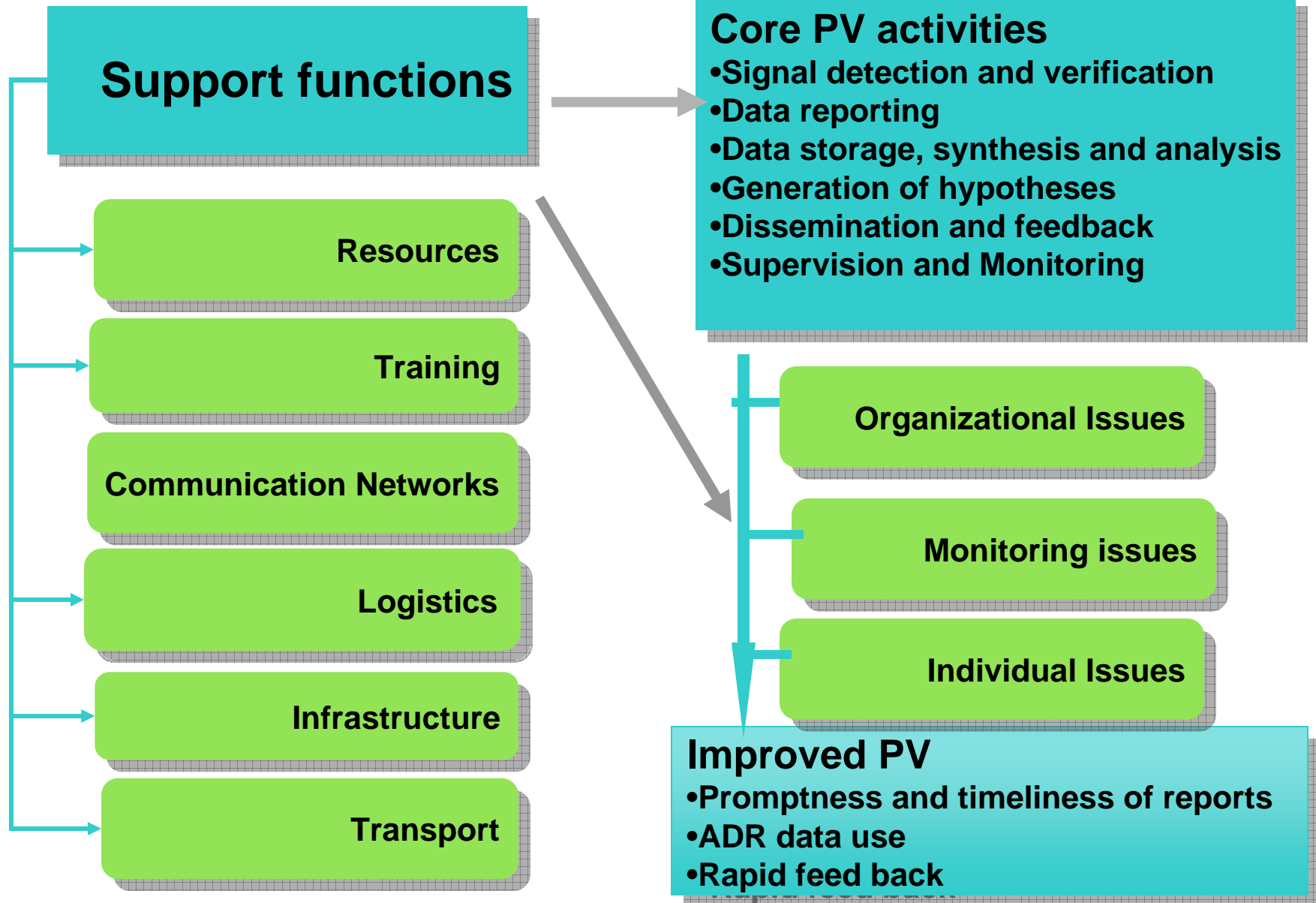
Yes but will be challenging!

- Conduct initial assessment
 - determine system to use for detection, evaluation of severity and determination relationship of AEs to drug

- Address Practical issues
 - How reporting will be done
 - By whom and to whom
 - Type of AEs to report (All AEs or SAEs?)

- We propose a conceptual model for strengthening PV at country level (McNabb et al, 200

Conceptual model for strengthening PV in Africa



Operational research needs

- A variety of methods for PV are available-t research is needed to identify the best mix of methods and the type of AE for each method
- Investigation of creative approaches for safety monitoring - incentive/motivation schemes for reporting AEs
- Identifying specific issues related to gender differences, informal providers, over the counter products and herbal medicinal products

Conclusion

- Rigorous and continuous QA and standardisation
- Harness present momentum to develop innovative proposals for PV
 - WHO's recent workshops on PV for Burundi, DRC, Mozambique, Zambia and Zanzibar
- Initial focus should be PV of Antimalarial drugs-later expansion to include all medicines

Acknowledgements

- Prof. Umberto D'Alessandro (ITM)
- Dr. Sarah Staedke (USCF)
- Ms. Juliet A. Okecho, Head of the Drug Information Department, Uganda National Drug Authority
- Task force for pharmacovigilance in the Zambian Ministry of Health and the Pharmacy and Poisons Board