Forum for Collaborative HIV Research

Monitoring HIV Treatment Associated Toxicities

A WHO-Forum Collaboration

2nd International Workshop on HIV Treatment, Pathogenesis and Prevention Research

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Acknowledgments

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  - Charlie Gilks
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- Forum for Collaborative HIV Research
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  - Ben Cheng
  - Abby Wilkes
  - Kimberly Johnson

Why is monitoring of toxicities needed in resource limited settings?

Compared to developed world:

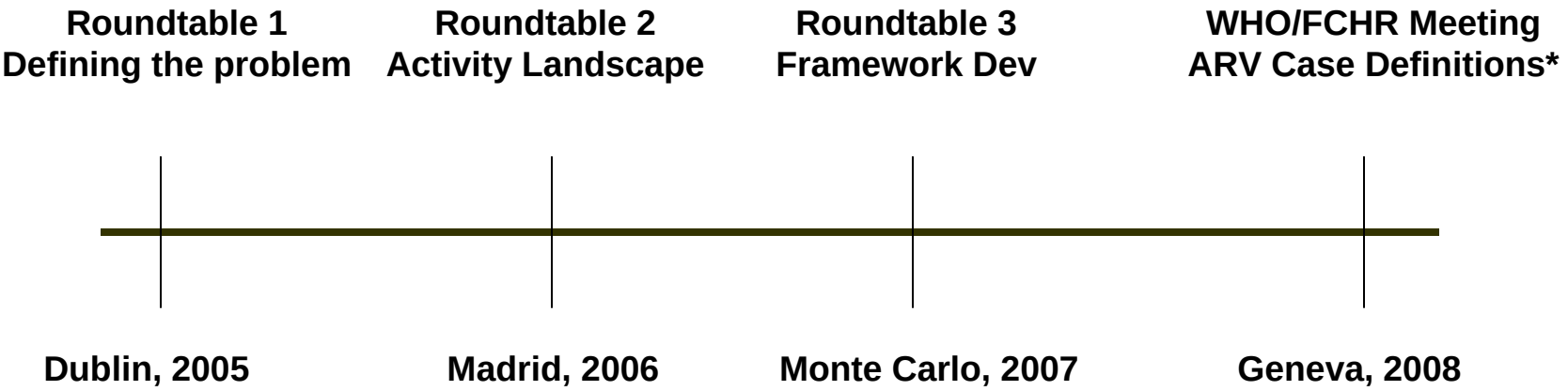
- **Rapid scale-up of antiretroviral treatment**
  - Limited expertise, experience among clinicians and patients
- **Difference in populations**
  - Race
  - More women and children, pregnancy
  - Presenting with advanced disease
  - High level of co-morbidities and co-infections
  - Nutritional status
  - Use of traditional medicines
- **Difference in drugs**
  - Standardized first line, 2nd line
  - FDC's, generics
  - Treatment of co-infections

Policy Information Gap

- Data on ARV toxicity is needed for
  - Development, review and revision of global, regional and national treatment guidelines
  - Program planning (supply of 1st and 2nd line drugs)
  - Program evaluation
  - Feedback to clinicians and patients
  - Regulatory considerations

FCHR Monitoring Toxicities Working Group & WHO Meetings

enhancing & facilitating HIV research



*with support from the Bill & Melinda Gates Foundation

http://www.hivforum.org/projects/LTM.htm
http://www.hivforum.org/projects/PV.html

www.hivforum.org

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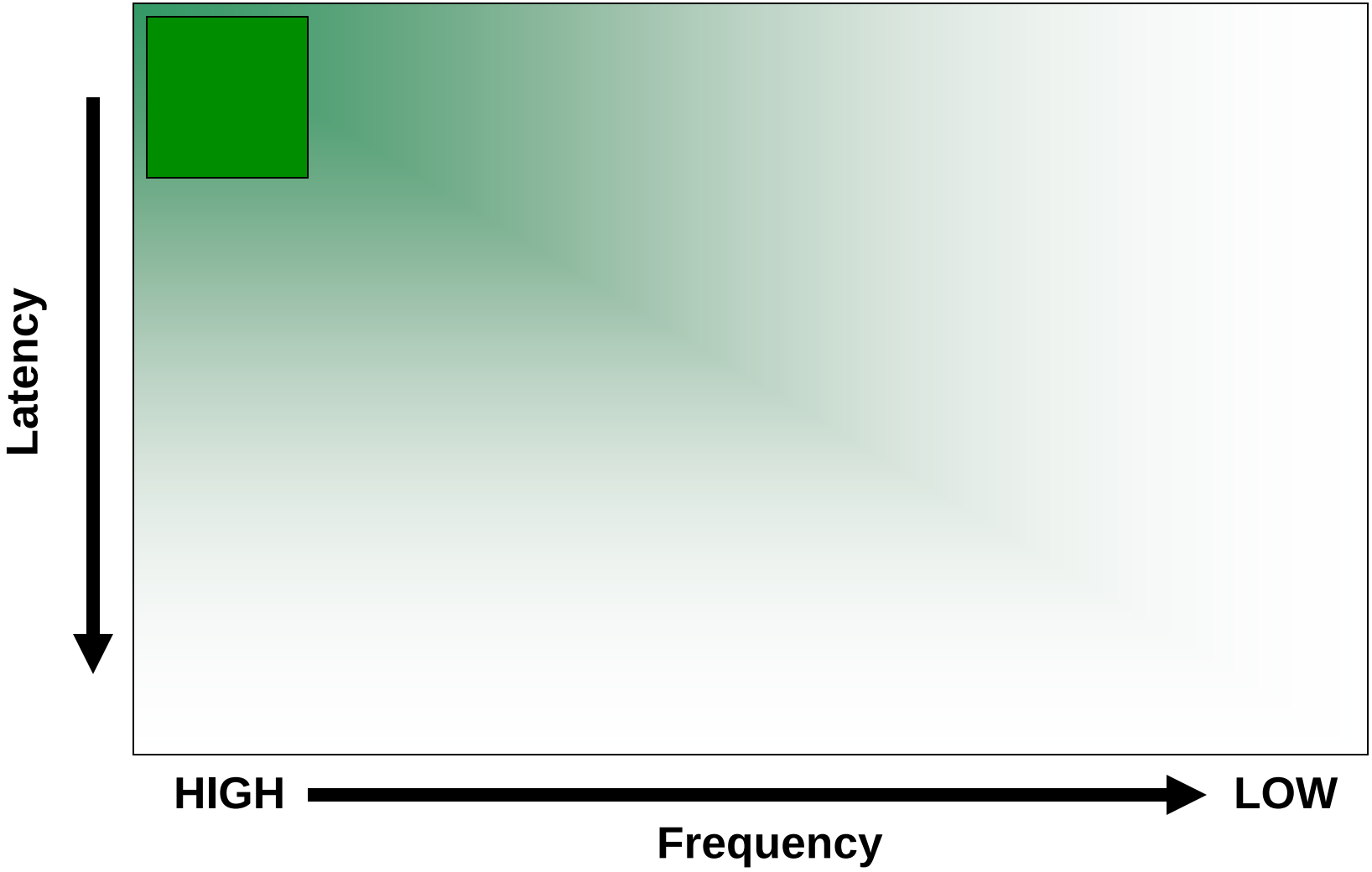
Adverse Event Field

Adapted from Evans and Waller, MCA 2002



Monitoring Toxicities & Pharmacovigilance

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Clinical Trials &/or Observational Cohorts:

- –Active, prospective reporting
- –Numerators, denominators
- –Lack of standardization of definitions, grading and data format
- –Multiple sponsors
- –Pharmacoepidemiology
  - ⊙causality

Pharmacovigilance:

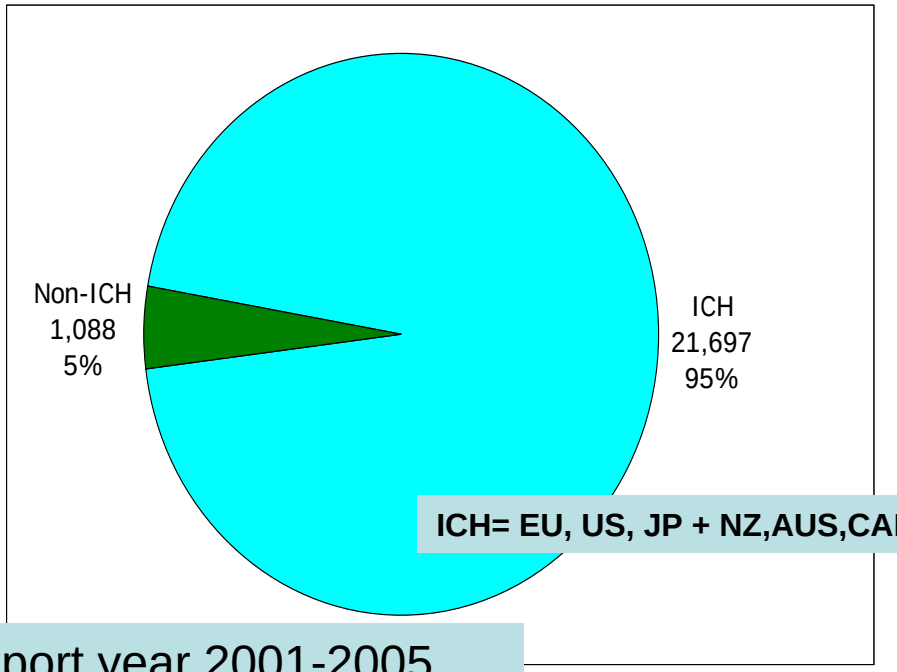
- –Passive reporting/under-reporting
- –Lack of numerators/denominators
- –Standardized definitions & protocols
- –MOH/Regulatory Agency based
- –Experience in data mining

New approach: take the best of both worlds into one system

Major Recommendations from Forum Roundtables

- Use sentinel-site based methodology for collecting toxicity data in a standardized format
- Make best use of currently ongoing observational cohort studies (Bakare presentation)
- Engage all stakeholders (including program sponsors and pharmaceutical industry) in the effort

Regional distribution of ARV reports

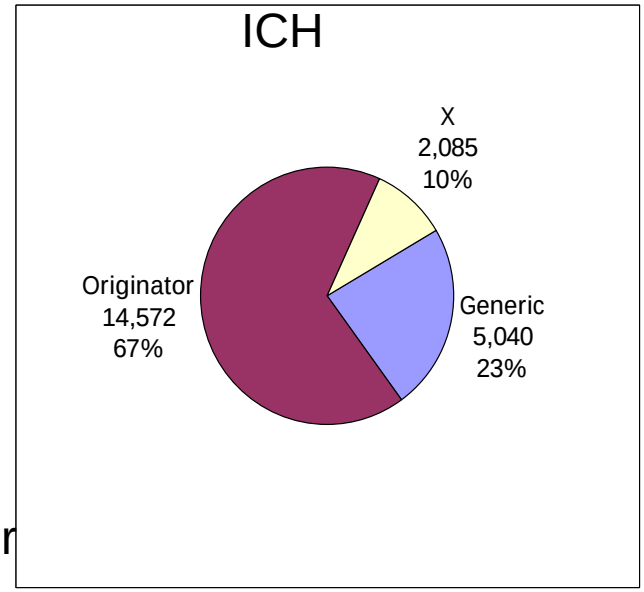


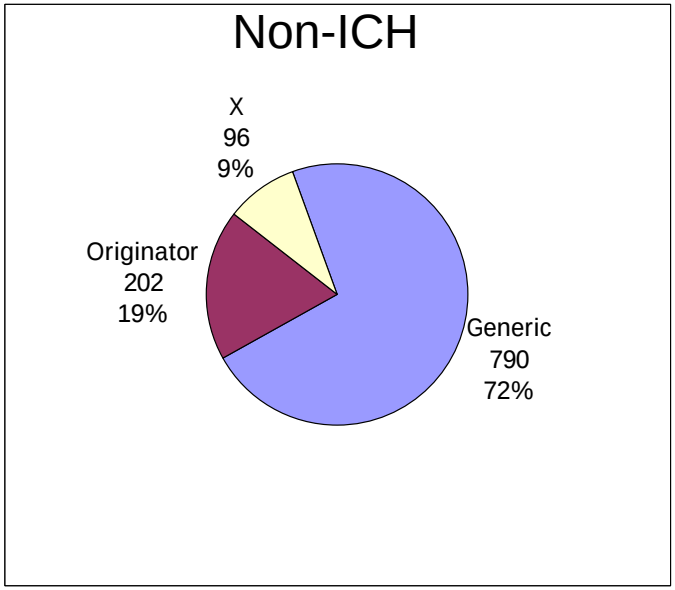
ICH= EU, US, JP + NZ,AUS,CAN

Report year 2001-2005

The WHO Collaborating Centre for International Drug Monitoring

ARV reports by product category





Marie Lindquist
Uppsala Monitoring Center

Heterogeneity of Reports

- Regional differences observed in Uppsala Monitoring Center*:
  - 900/1138 reaction terms in ICH countries only
  - 8/1138 in non-ICH countries only
  - Skin and GI reactions most common in non-ICH countries
- FCHR literature survey of treatment limiting toxicities**
  - South America: gastrointestinal & hematologic toxicities, neuropathy
  - Southeast Asia: lipodystrophy, rash, hepatitis
  - Africa: neuropathy, neutropenia, lipodystrophy

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*http://www.hivforum.org/uploads/PV/Lindquist.pdf
**http://www.hivforum.org/uploads/PV/background_doc.pdf

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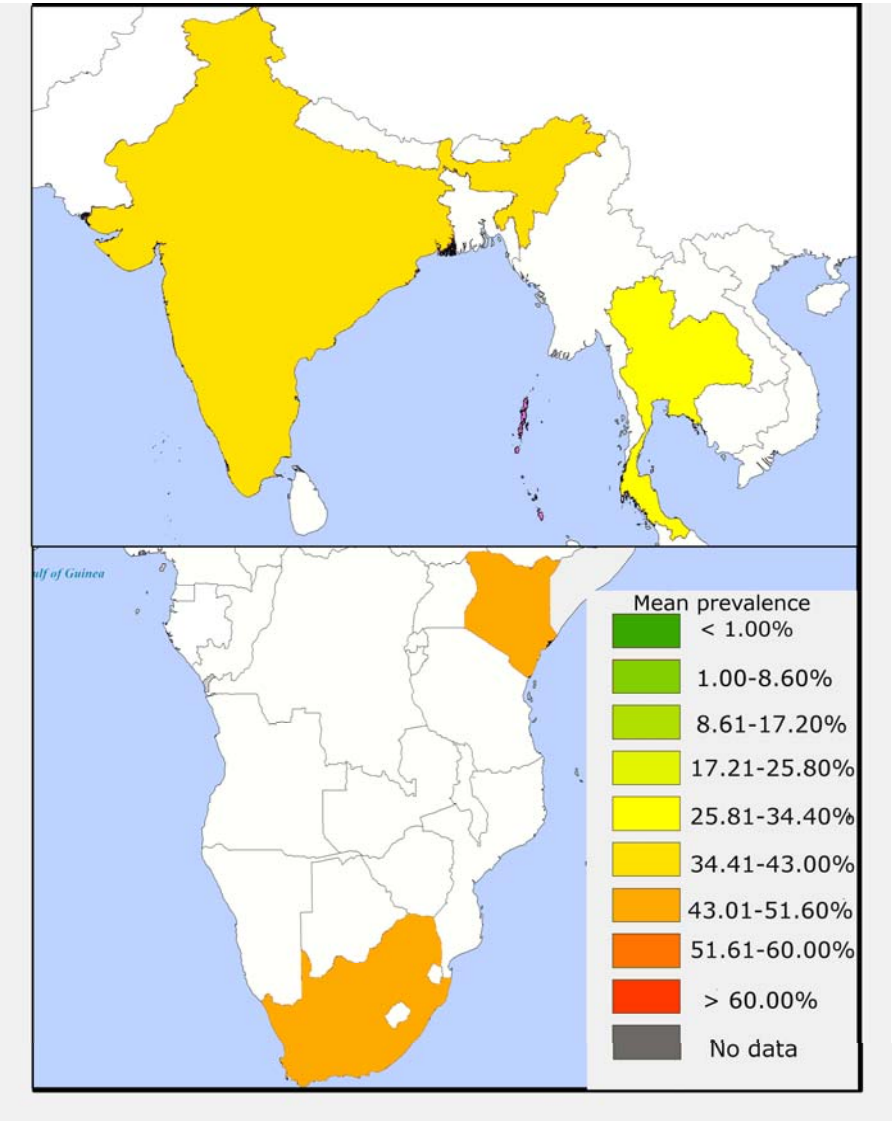
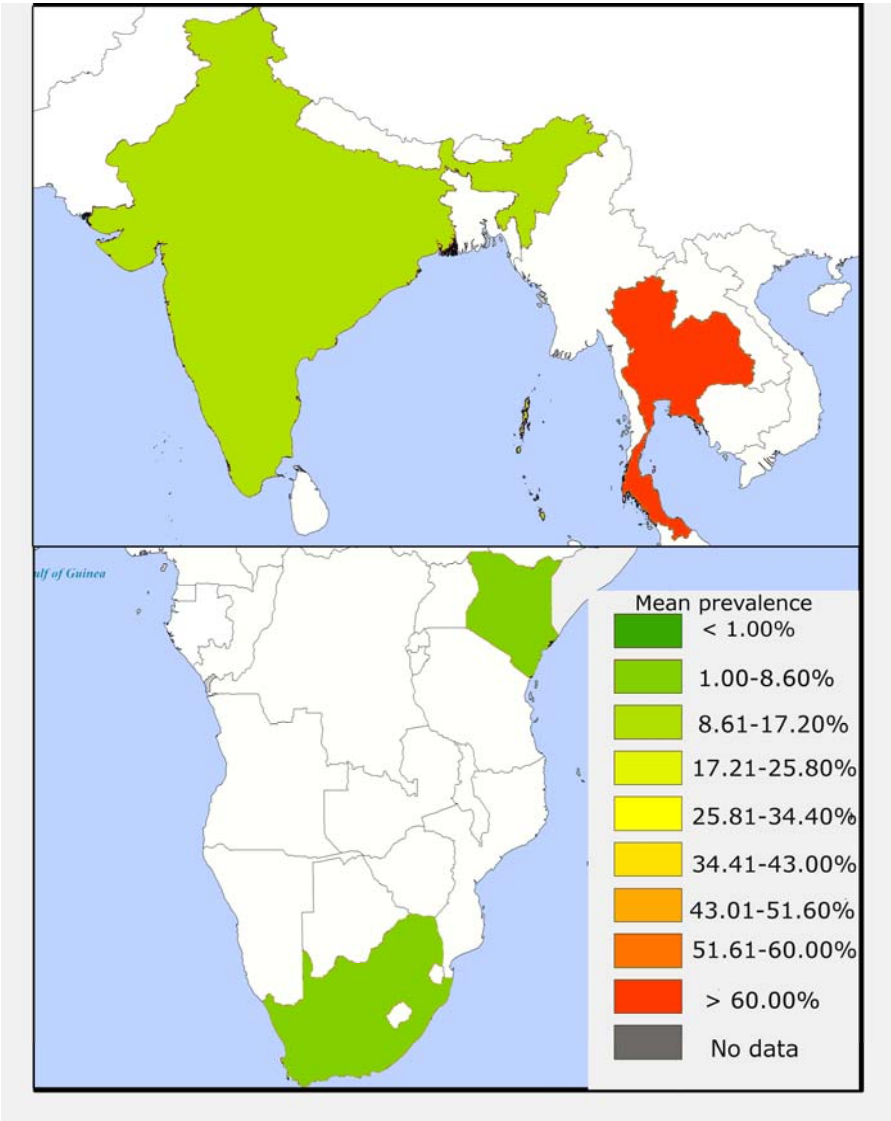
All reported ADRs in studies



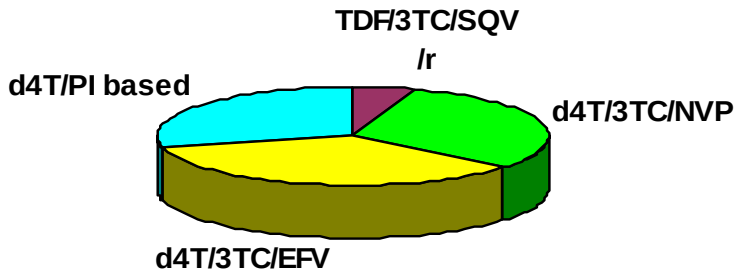
Reported lipodystrophy in studies



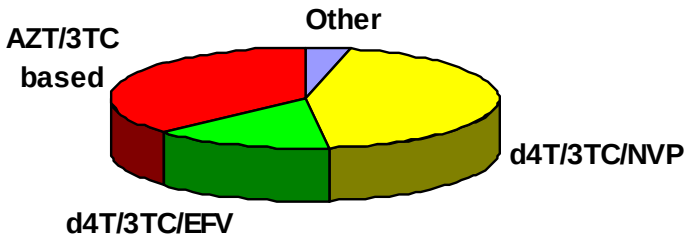
From K Johnson 2008: Survey of published studies in 4 countries (51 studies: >31,000 pts)

Adult Treatment Regimen Distribution Based on Published Studies

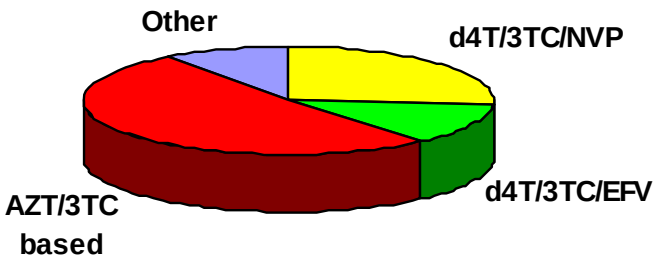
Thailand



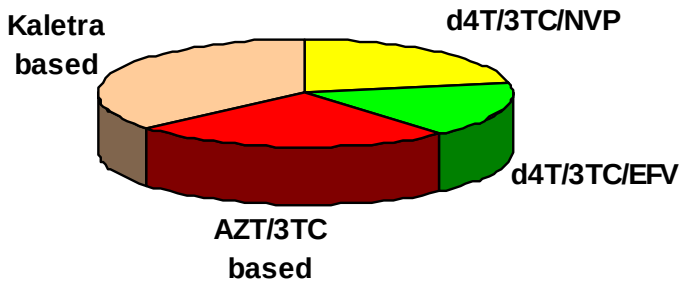
India



South Africa



Kenya



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From K Johnson, 2008

Regional Heterogeneity

- Several explanations possible:
  - True differences in populations
  - Differences in reporting frequencies
  - Differences in definitions used
  - Differences in regimen used
- The lack of a uniform reporting style for defining and grading AEs complicates extraction of data for comparison across sites, regions and populations

Discussion

- Toxicity monitoring/pharmacovigilance effort includes *all* stakeholders:
  - Bi and multi-lateral scale up programs
  - National MOH's and regulatory agencies
  - Pharmaceutical sector
    - Generic
    - Innovator
  - Clinicians and clinical researchers

Discussion - 2

- HIV treatment scale-up provides a unique opportunity to improve data gathering mechanisms for toxicity monitoring
  - Ultimately, this should extend beyond HIV/AIDS treatment
- Many opportunities exist for reducing the disease specific ‘silo approach’ and to energize the traditional pharmacovigilance approach