"What software would you recommend to give my presentation so much flash and sizzle that nobody notices that I have nothing to say?"
PILOT COHORT EVENT
MONITORING OF ACTS IN NIGERIA

C. K. SUKU
NATIONAL PHARMACOVIGILANCE CENTRE, NAFDAC, NIGERIA

ANTIRETROVIRAL PHARMACOVIGILANCE COURSE

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Outline

• Why we did CEM of ACTs in Nigeria
• What we looked for
• How we did it
• What we found
• Limitations of the Nigerian CEM
• Our Challenges
• Lessons from the Nigerian CEM experience
• Our next steps
• Conclusion
Acknowledgement

• Dr. Peter Bassi (Principal Investigator)
• NAFDAC
• NPC coordinator and staff
• WHO Geneva
• NMCP
• SFH
• YGC
• All sites, site coordinators and personnel
Why CEM of ACTs in Nigeria

CEM of ACTs became necessary due to

- **Endemic nature of malaria**
  - 63% of diseases in healthcare facilities
  - 25% of infant mortality
  - 30% of childhood mortality
  - 11% of maternal deaths

- **Reduced efficacy of previously used antimalarials (CQ, SP)**

- **Shift in malaria treatment policy from mono to combination therapy**

- **Change of status of ACTs from POM to OTC medicines**

- **Large scale deployment of ACTs for malaria treatment**

- **Inadequate safety data on ACTs in our population**

- **Inability of SR to adequately capture safety data**
What we looked for (I)

BROAD OBJECTIVE

• To evaluate safety in the use of ACTs among populations in Nigeria and develop the safety profile of ACTs used in Nigeria mainly AL and AA
What we looked for (II)

SPECIFIC OBJECTIVES

- Obtain information on adverse events in ACT users
- Establish causality relationship between observed adverse events and use of ACTs
- Identify risk factors among populations and provide evidence for intervention
- Document safety profile of AL and AA
Specific objectives cont’d

• Early characterization of
  – Adverse Events/ADR profile of ACTs
  – possible interactions (ACTs/other medicines; ACTs/herbal medicines; ACTs/concomitant diseases)

• Determine if ACTS are rationally prescribed, properly dispensed and correctly used

• Generate data for decision making

• Obtain cohort for future studies
How we did it (I)

Design
Prospective, longitudinal, observational study of adverse events in a cohort of 3000 patients treated with either AA or AL

Sites
6 sites spread across the 6 geopolitical zones of the country

Map of Nigeria showing location of the CEM sites
How we did it (II)

Data Collection

– Patient comes to clinic, s/he is seen by a nurse who records the vital signs then sends the patient to the doctor

– The doctor evaluates the patient for possible malaria (presumptive diagnosis), treats using one of the ACTs and informs the nurse to recruit the patient i.e. fill relevant sections of the questionnaire

– The patient is given a date to come back for follow-up visits then goes to the pharmacist to get prescribed medicines

– The nurse or study assistant ensures that patients come for follow-up visit or are followed-up by phone or home visit when necessary and as appropriate

– At follow-up the patient is seen by the doctor in order to get information on possible adverse events
How we did it (II)

Data analysis

– Filled questionnaires were collected during supervisory visits and sent to the NPC

– Statistical analyses were carried out using simple frequency distribution, percentages and Chi Square to study relationships

– Multinomial logistics regression was used to analyse associations of some risk factors e.g. age, dosage, gender, pregnancy, use of traditional medicines and presence of co-morbid conditions such as respiratory infection, epilepsy, diabetes, HIV, etc
What we found
### General statistics

<table>
<thead>
<tr>
<th>S/no</th>
<th>Data Element</th>
<th>#</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Total number of patients recruited</td>
<td>3010</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Total number that came for 1&lt;sup&gt;st&lt;/sup&gt; Follow-up Visit (FUV)</td>
<td>2904</td>
<td>96.5</td>
</tr>
<tr>
<td>3</td>
<td>Total number that came for 2&lt;sup&gt;nd&lt;/sup&gt; FUV only</td>
<td>59</td>
<td>2.0</td>
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<tr>
<td>4</td>
<td>Total number that came for both FUV</td>
<td>2936</td>
<td>97.5</td>
</tr>
<tr>
<td>5</td>
<td>Number lost to follow up</td>
<td>15</td>
<td>0.5</td>
</tr>
<tr>
<td>6</td>
<td>Response rate</td>
<td>2936</td>
<td>97.5%</td>
</tr>
</tbody>
</table>
## Distribution of cohort by sex and Health facility

<table>
<thead>
<tr>
<th>Health Facility</th>
<th>Sex</th>
<th></th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Not Indicated</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>ABUTH</td>
<td>239</td>
<td>276</td>
<td>0</td>
<td>515</td>
<td></td>
</tr>
<tr>
<td>UCH</td>
<td>180</td>
<td>337</td>
<td>11</td>
<td>528</td>
<td></td>
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<tr>
<td>NIPRD</td>
<td>242</td>
<td>236</td>
<td>5</td>
<td>483</td>
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<tr>
<td>UNTH</td>
<td>196</td>
<td>322</td>
<td>9</td>
<td>527</td>
<td></td>
</tr>
<tr>
<td>FMCG</td>
<td>246</td>
<td>260</td>
<td>17</td>
<td>523</td>
<td></td>
</tr>
<tr>
<td>UUTH</td>
<td>184</td>
<td>248</td>
<td>2</td>
<td>434</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1287</strong></td>
<td><strong>1679</strong></td>
<td><strong>44</strong></td>
<td><strong>3010</strong></td>
<td></td>
</tr>
</tbody>
</table>
### Overall distribution of cohort by sex

<table>
<thead>
<tr>
<th>Sex</th>
<th>M</th>
<th>F</th>
<th>Unkn</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1287</td>
<td>1679</td>
<td>44</td>
<td>3010</td>
</tr>
</tbody>
</table>

### Distribution of cohort by age group and sex

![Bar chart showing distribution by age group and sex](chart.png)
Pattern of symptoms at presentation

- Fever, 2231
- Headache, 1437
- Diarrhoea, 189
- Dizziness, 236
- Cough, 477
- Chills/Rigors, 224
- Bitter Taste, 552
- Loss of Appetite, 879
- Body Pain, 864
- Body Weakness, 605
- Vomiting, 356
- Nausea, 193
- Abdominal Pain, 429
- Catarrh, 75
Distribution of Co-Morbid Conditions
Frequency of New Events at 1\textsuperscript{st} Follow Up Visit (FUV)

- WEAKNESS, 424
- ABDPAIN, 135
- DIZZINESS, 180
- FEVER, 22
- HEAD ACHE, 50
- JOINT PAIN, 7
- NAUSEA, 32
- VOMITTING, 10
- BODY PAIN, 48
- BITTERNESS OF MOUTH, 4
- CHILLS/RIGOUR, 1
- DIARRHEA, 29
- LOSS OF APPETITE, 49
- WEAKNESS, 424
- ABDPAIN, 135
- DIZZINESS, 180
- FEVER, 22
- HEAD ACHE, 50
- JOINT PAIN, 7
- NAUSEA, 32
- VOMITTING, 10
- BODY PAIN, 48
- BITTERNESS OF MOUTH, 4
- CHILLS/RIGOUR, 1
- DIARRHEA, 29
- LOSS OF APPETITE, 49
Distribution of new events by drug use at 1\textsuperscript{st} FUV
Frequency of new events at 2\textsuperscript{nd} FUV

- dizziness, 55
- body weakness, 210
- body pain, 12
- pain, 19
- vomiting, 29
- Abdo pain, 1
- bitter taste, 1
- urine, 10
- urti, 10
- loss of appetite, 12
- palp/restless, 8
- nose bleeding, 1
- nausea, 10
- itching, 6
- headache, 19
- foaming, 1
- fever, 2
- diarrhoea, 7
- Fever/chills, 7
- dry mouth, 3
- burn sensation, 1
- sleepless, 23
- bitter taste, 4
- rash, 2
New and worsening (Persisting) events at 2nd FUV
Outcome of Adverse Events by drug use

- Recovered: 551 (AA), 139 (AL)
- Improved: 303 (AA), 64 (AL)
- Remain Unchanged: 110 (AA), 21 (AL)
- Life threatening: 2 (AA), 0 (AL)
- Prolong Hosp. stay: 1 (AA), 1 (AL)
Summary of results

- Most common Adverse Events (AEs) observed in the Cohort
  - General body weakness - 38/36% (AA/AL)
  - Dizziness - 16.2/1.4% (AA/AL)
  - Loss of appetite - 9.1/3.5% (AA/AL)
  - Abdominal Pain - 6.1/1.0% (AA/AL)

- Mean Duration of illness (events) - 3 days.
- Patients treated with AA had more AEs but had better outcome after AE
- 2 patients on AA had life threatening AEs
- 1 patient each on AA and AL experienced prolonged hospital stay
- Twitching/foaming also occurred with use of AA
LIMITATIONS

• Splitting of dose of AA by some physicians (b.d instead of o.d) may have affected observed AE profile of AA

• Incomplete filling of some sections of the questionnaire may affect interpretation of results e.g. how do you interpret an unfilled question?

• No data was collected on events experienced 7 days before treatment initiation thus making it difficult to make ‘control’ comparisons
Our challenges (I)

- Late arrival of some study materials
- Higher administrative cost due to large number of study personnel
- Overwhelming patient workload
- Inadequacy of funds
- Follow-up issues (incomplete or no traceable contact address)
How do you locate any patient here?
Lessons from the CEM Experience

Lesson 1

Seemingly simple study but many challenges – don’t take anything for granted

(All study materials must be available before commencement of study)
Lesson 2

The use of an incentive scheme (LLINs at completion of follow-up) encouraged patients to complete follow-up.

Involvement of practitioners created a sense of ownership in the pharmacovigilance programme for those who participated.
Issues we hope to clarify

Pre-testing of data collection tools and processes is a must in the pilot

How will it work for the scale-up?
Issues we hope to clarify

There have been comments that we were looking for too many things – For instance how can CEM detect interactions (drug-drug, drug-food, etc)
Discussions/conclusion

- Good response rate (97.5%) was recorded

- Adherence to study protocol was good (> 63%)

- Most sites reached their recruitment target of 500 patients at end of the study

- Observed AEs similar to ADR profile of ACTs reported in literature with few documented rare AE
Discussions/conclusion

• CEM was helpful in identifying AEs following use of ACTs
• Severe Adverse events were not common occurrence in the observed cohort
• A larger cohort will give more statistical power to findings and possibly help identify rare AEs.
Our immediate next steps

• Review all data collection tools (questionnaire, patient card, SOP) preparatory to scale-up

• Deploy CemFlow for data management and analysis including capacity building for optimum use (on going)

• Scale-up to a cohort of 7000 patients by 2010

• Source funding for scale-up (on going)
Update your algebra

**Equation 1**

Men = eat + sleep + earn money  
Donkeys = eat + sleep

Substituting,  
Men = Donkeys + earn money

Therefore,  
Men - earn money = Donkeys

**In other words,**

Men that don't earn money = Donkeys
Equation 2

Women = eat + sleep + spend money
Donkeys = eat + sleep

Substituting,
Women = Donkeys + spend money

Therefore,
Women - spend money = Donkeys

In other words,
Women that don't spend money = Donkeys
From Equations 1 and 2

Men that don't earn money = Women that don't spend = Donkeys.

Postulations

Postulate 1: Men earn money not to let women become Donkeys!
Postulate 2: Women spend money not to let men become Donkeys!

So,

Men + Women = Donkeys + earn money + Donkeys + spend money

Conclusion

Man + Woman = 2 Donkeys that should live happily together!
SO

WHY DO MEN AND WOMEN NOT ALWAYS LIVE HAPPILY EVER AFTER?
Thank you