CEM analyses
What are we trying to measure?

- First, the risks associated with each ARV regimen
  - Each regimen will be treated like a single drug

- Second, the risks associated with individual drugs
Approach

- **Keep it simple**
  - most of the important results can be revealed by simple measures

- **Keep it accurate**
  - clean, quality data
  - controlled at input
  - Example: variation in spelling
Small things 1

- Rates
  - What to do with drop-outs?
  - Choosing the denominator
    - total cohort includes drop-outs
      - demographics
    - total follow-up questionnaires returned
      - general rates eg rates of events; reactions & incidents
      - Sites / regions
  - Total per question answered
    - Rate per data element eg traditional meds, TB
Examples of rates

- **Overall reporting rate (response rate)**
  - Total cohort enrolled = 8432
  - Total follow-up forms received = 6998
  - Reporting rate = \( \frac{6998}{8432} = 83\% \)

- **Rates of events**
  - Total follow-up forms received = 6998
  - Total patients with oral candidiasis = 843
  - Rate of oral candidiasis = \( \frac{843}{6998} = 12\% \)
Examples of rates

- Rates per total question answered for use of traditional medicines
  - Total follow-up forms received = 6998
  - Total TM questions answered = 5432
  - Total answered ‘Yes’ = 3954
  - Rate of use of traditional medicines = 3954/5432 = 73%
Calculation of risk

- The rate of occurrence of an event in the exposed cohort is a measure of **absolute risk**

- **Attributable risk**: this is a measure of the increased risk associated with the medicine. It is calculated as follows:
  - rate in the exposed cohort minus
  - rate before exposure (in the control period)
Small things 4

- **Doses**
  - Analyses are done on the total daily dose
  - Total daily dose $\times$ weekly e.g.
    - 300mg 3 $\times$ weekly
    - Or 100mg 7 $\times$ weekly

- **Duration**
  - Duration in days
    - 1 m = 30 days
    - 1 y = 365 days
    - Between x & y - take mid-point
Data manipulation
Collation

- summary of reporting rates for males, females and totals;
- age/sex profiles of the cohort;
- patient numbers by region or site;
- event profiles by clinical category;
  - within a clinical category
  - reactions & incidents
Profile of Ages at First Prescription

![Chart showing age distribution for Celecoxib and Rofecoxib prescriptions.](chart.png)
## IMMP example – COX-2

<table>
<thead>
<tr>
<th>Age &amp; sex</th>
<th>Celecoxib</th>
<th>Rofecoxib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>63</td>
<td>58</td>
</tr>
<tr>
<td>Mode</td>
<td>59</td>
<td>53</td>
</tr>
<tr>
<td>&lt;40 years</td>
<td>6.9%</td>
<td>12.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Highly significant</td>
</tr>
<tr>
<td>70+ years</td>
<td>32.7%</td>
<td>25.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Highly significant</td>
</tr>
<tr>
<td>Women</td>
<td>61.6%</td>
<td>60.5%</td>
</tr>
<tr>
<td>Celecoxib dose mg/no./%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>6,622</td>
<td>8.1</td>
</tr>
<tr>
<td>200</td>
<td>65,591</td>
<td>80.5</td>
</tr>
<tr>
<td>300</td>
<td>274</td>
<td>0.3</td>
</tr>
<tr>
<td>400</td>
<td>8,927</td>
<td>11.0</td>
</tr>
<tr>
<td>600</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>800</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>
## Event profiles

<table>
<thead>
<tr>
<th>Category</th>
<th>Celecoxib</th>
<th>Rofecoxib</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circulatory</td>
<td>315 (17%)</td>
<td>214 (20%)</td>
<td>NS</td>
</tr>
<tr>
<td>Alimentary</td>
<td>302 (17%)</td>
<td>218 (20%)</td>
<td>0.8 (0.66, 0.97)</td>
</tr>
<tr>
<td>Died</td>
<td>293 (16%)</td>
<td>179 (16%)</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>160 (9%)</td>
<td>59 (5%)</td>
<td>1.7 (1.24-2.30)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>108 (6%)</td>
<td>54 (5%)</td>
<td></td>
</tr>
<tr>
<td>Psychiatric</td>
<td>88 (5%)</td>
<td>49 (5%)</td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>72 (4%)</td>
<td>46 (4%)</td>
<td></td>
</tr>
</tbody>
</table>
Events collation
Look Carefully
Understanding the dictionary
Examples

- Annex 8 events collation
- Annex 12 eye events with signal
- Annex 11 deaths
- Annex 13 concomitant medicines
Risk

- Risk calculation
- Relative risk (rate ratio)
  - Rate of A / rate of B = relative risk
  - Confidence intervals
- Risk factors eg age
  - RR
  - Multiple logistic regression
Risks of individual drugs

- Compare events before and after drug substitutions with the patients acting as their own controls eg
  - d4t(30)-3TC-NVP to d4t(30)-3TC-EFV
- Compare events between regimens where substitutions have taken place
- Use multiple logistic regression to test each drug as a risk factor for events of interest
- Large database needed for these analyses (pooled international data)
Life table (survival) analysis

- Helps to characterise a reaction
  - time to onset
  - spread of onset times
- Testing a possible signal
Statistical programmes

- **CemFlow**
  - automated outputs

- **MedCalc**
  - free for 25 sessions
Don’t be afraid!

of statistics