Selecting the cohort

David Coulter
Simple

- Record all patients consecutively until you have 10,000 – 15,000
- But there’s more to think about
Numbers

- In general, 10,000 patients gives a 95% chance of identifying an event with an incidence of 1:3000 (uncommon-rare)
- Smaller numbers can still be very useful (eg IMMP & nifedipine)
- Greater numbers may be needed to test for any significant increase in incidence:
  - in sub-groups of interest eg tuberculosis
  - if the background incidence of an event of special interest is common
  - when comparing comparator drugs
Numbers

- At the same level of seriousness, common events are more important because they affect more people.
- A non-serious common reaction could be more important than a rare serious reaction.
- So, a 95% certainty of identifying an event at 1:1000 frequency (a smaller cohort) may be OK.
- Be aware of the limitations / strengths of your numbers.
Specific age groups

eg children

- The whole population of users will still need to be monitored to enable comparison of children with adults and determine any specific risks or risk factors for children.

- It may be necessary to continue monitoring children longer in order to get more numbers for higher statistical power.
Other sub-group analyses

eg malnutrition, concomitant drugs

- Larger numbers of these patients might be needed to detect differences with sufficient statistical power
- It all depends on the incidence
  - Common events no problem
  - Rare events need larger numbers
Approach

- Aim for 15,000
- Review data during monitoring (‘real time’ – interim analyses)
- This will provide a better idea of the problems needing evaluation and their incidence
- Reassess needs at intervals (every 3-6 months)
Choice of patients

- **Principles – aim for:**
  - Unselected
  - Consecutive or random
  - Typical of HIV/AIDS management in the country

- **Determinants of choice**
  - Expected numbers of cases
  - Time frame
  - Logistics of involvement in the clinics
Choice of patients

Timing / logistics

- Every day, all day would avoid biases
- If workload would be too great for every day, then:
  - All patients seen on specific days
  - Choose typical days
  - Maybe choose mornings (or afternoons)
- Discuss with clinic staff
- Run a pilot
- Try and be consistent across sites
Choice of patients

Health facility

- Which health facilities?
- Selection needs to be representative
  - Urban / rural
  - Hospitals / clinics
  - Geographically
  - Language areas (cultural differences)
- Selection needs to be in proportion to numbers of HIV/AIDS patients normally seen
  - eg if 40% of HIV/AIDS patients are urban, have 40% of cohort from urban sites
- Choose (sentinel) health facilities
  - Set target numbers for each
Choice of patients

- The study will be **dynamic** – new patients are added as you go along.
- The study must be **inceptional** – all patients must be monitored from the commencement of their treatment to exclude ‘drop-out’ bias.
‘Controls’

- Increase cost
- Control cohorts create an artificial situation
- The aim is a non-interventional study in normal clinical practice
- Comparison of different regimens
  - not always possible if numbers low
  - pooled international data increases power
- A good study of a single regimen
  - provides valuable data
  - has benchmark value
- ‘Self-controls’ are a helpful option
Planning

- Select health facilities
  - Hospitals
  - Clinics
- Make them representative as far as practical
  - urban / rural
- Set target numbers for each
- Determine what times monitoring will take place
Involve everyone