# Cohort Event Monitoring

(*Prescription Event Monitoring*)

# CEM –What is it?

- Monitoring events in a -
- Defined population of users (cohort)

- Prospective observational cohort study of a drug or combination

# Cohort event monitoring

- Intensive Medicines Monitoring Programme (IMMP), NZ, 1977
- Prescription Event Monitoring, DSRU, England, 1980
- J-PEM, Japan

*Pharmacovigilance, Mann & Andrews, Wiley, 2002*

# Expectations

- Earliest possible recognition of new ADRs, including interactions
- Characterize reactions -known and unexpected
- Risk estimate (including comparative)
- Identify risk factors eg

  Age Duration of therapy
  Gender Concomitant disease
  Dose Concomitant therapy

- Assess safety in children
- Assess safety in pregnancy & lactation

# Expectations

- Provide an evidence base for :
  - Comparative safety –choice of therapy
  - Effective risk management
  - Safer prescribing
  - Benefit / harm assessment
  - Regulatory changes
- Cohorts for study

# Expectations

- Detect inefficacy, which might be due to
  - Non-compliance
  - Faulty administration
  - Poor storage conditions
  - Out of date product
  - Poor quality product
  - Counterfeit product
  - Interactions

# Event monitoring

- Finney DJ 1965

"…a particular untoward happening experienced by a patient, undesirable either generally or in the context of his disease."

# Adverse Events

*Adverse event (experience)*

An AE is,

*"any untoward medical occurrence that may present during treatment with a medicine, but which does not necessarily have a causal relationship with this treatment".*

WHO

# Events

Any new clinical experience (favourable or unfavourable) that is worthy of a record in the patient's file, regardless of its severity and without judgement on its causality.

# Non-serious events

- May indicate serious problem
- May affect compliance
  - nausea
  - impotence
  - diarrhoea
- May be more important than serious reactions
- Recording all events is easier than being selective

# Why adverse events?
## To identify signals of new reactions

- If only known adverse reactions are reported, unexpected adverse reactions will not be identified
- It is important to identify signals, validate them, determine the incidence, understand their significance and identify the risk factors as soon as possible
- It is not logical to specify the types of events to be recorded. Unexpected reactions cannot be identified by recording only the known or expected.

# Methodology

- Establish cohort
- Record events
- Analyse events

# The cohort

- The cohort is established using the best source of usage data available
  - Dispensings (pharmacies or central records)
  - Patient records
    - Doctors
    - Clinics
    - Hospitals
    - Other
  - Programme records
    - Prospective
    - Inceptional
    - Dynamic

# Cohort size

- General aim 10,000 (IMMP 11,000)
- Greater numbers required to detect differences
  - if events naturally common
  - for sub-group analyses
- Smaller numbers still produce good data
  - fluoxetine <7000
- Signals can be identified / confirmed with much smaller numbers (<1000)
  - eg nifedipine & eye pain
- Frequency of 1/1000: 95% chance in 3000

# Event recording

## Real time or later

**Treatment centre / Clinic** : …….. **Contact person** : ……

**A. Patient :** Name : …… …….. Clinic Number ……

Contact details: …… …… ….

Date of birth : …./…./…. Gender: Male ? Female ?

**B. HIV/AIDS :** st age at current review ……..

**C. Medicines**

| ARV medicines | Daily d ose | Date begun | Date stopped |
|---|---|---|---|
| 1. | | | |
| 2. | | | |
| 3. | | | |
| 4. | | | |

Reason (s) for stopping ARV medicines
Poor compliance ? ; Lost to follow -up ? ; Death ? (give date & cause below in secti on E );
Suspected adverse reaction ? (describe in E ); Lack of effect ? ; Other ? (describe)
Comment on efficacy:

| **Other medicines** (in review period) | | | |
|---|---|---|---|
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |

**D. Laboratory tests** *(Blank row is for other tests)*

| Test | Date | Result | Test | Date | Result |
|---|---|---|---|---|---|
| CD4 count | | | Cholesterol | | |
| Viral load | | | Triglyceride | | |
| ALT | | | Glucose | | |
| FBC | | | | | |
| | | | | | |

**E. Any new events** or worsening problems over the period since last seen

| Date | Event(s) |
|---|---|
| | |
| | |
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| | |
| | |
| | |

*Continue on other side of form if neces sary*

**G. Has the patient become pregnant ?** Yes ? No ? If yes, complete pregnancy questionnaire

*PLEASE SEND THIS FORM TO ????*

# Analysis

- Collation and signal identification
- Rates and profiles
  - Comparisons by drug, age group, etc
  - By system organ class
  - Within system organ class
  - Individual events
- Multiple logistic regression
  - esp. for risk factors