Measurement of Outcomes in PEY

THE OUTCOME MEASURES INCLUDE THE STUDIES ON

- Functional status (level of functioning, Supervision required, ability to work)
- Symptom status (days free of pain / an event)
- Patient satisfaction with various aspects of care (delivery of care, effects on daily activities or life satisfaction) and
- QOL studies

- The therapeutic outcomes may be classified as cure,improvement,no change or deterioration
- On the other hand they can also be classified as success or failure
- Morbidity & Mortality are the most commonly used measures of out come.

Morbidity is measured as the number of cases of disease or events that occur per unit of population (per 100), unit of time (per year) or both Ex:(events/100/year)

Other measures of morbidity are,

The number of hospitalizations resulting from drug use or prevented by drug use or days of hospitalization (or days avoided) and deaths due to or prevented by the use of drugs

THE MEASUREMENT OF OUTCOMES IN PEY CAN BE DONE BY THREE APPROACHES

- Outcome measures
- Drug use measures
- Diagnosis and therapy surveys

Out come measures

The occurrence of pharmacoepidemiological outcomes is commonly expressed by measurements such as,

- ✓ *Prevalence*
- ✓ *Cumulative incidence*
- ✓ *Incidence rate*

Prevalence

- It is concerned with the disease status
- *"It is the proportion of people affected with a disease or exposed to a particular drug in a population at a given time"*
- It is usually determined by surveying the population of interest
- Prevalence varies between 0-1, it can also be expressed as a percentage

Mathematically, Prevalence = a/b

a- number of population with disease at a given time

b- total number of population at a given time

Ex. In the year 2003, among 7.8 lac population of Mysore city, 1.2 lac suffered from chikungunya.

What is the prevalence of Chikungunya in Mysore in the year 2003?

P= 0.15 or 15%

Incidence:

"*It is a measure of the risk of developing some new condition with in a specified period of time*."

It is better expressed as a proportion or as a rate.

Cumulative incidence (incidence proportion):

It is the number of new cases with in a specified time period divided by the size of the population initially at risk

Ex. if a population initially contains 1,000 non-diseased persons and 28 develop a condition over two years of observation, the incidence proportion is 28 cases per 1,000 persons, i.e. 2.8%.

Incidence rate:

It is the number of *new cases per unit of person-time* at risk.

It describes the probability of a new case occuring during a given time interval.

Figure 7.4

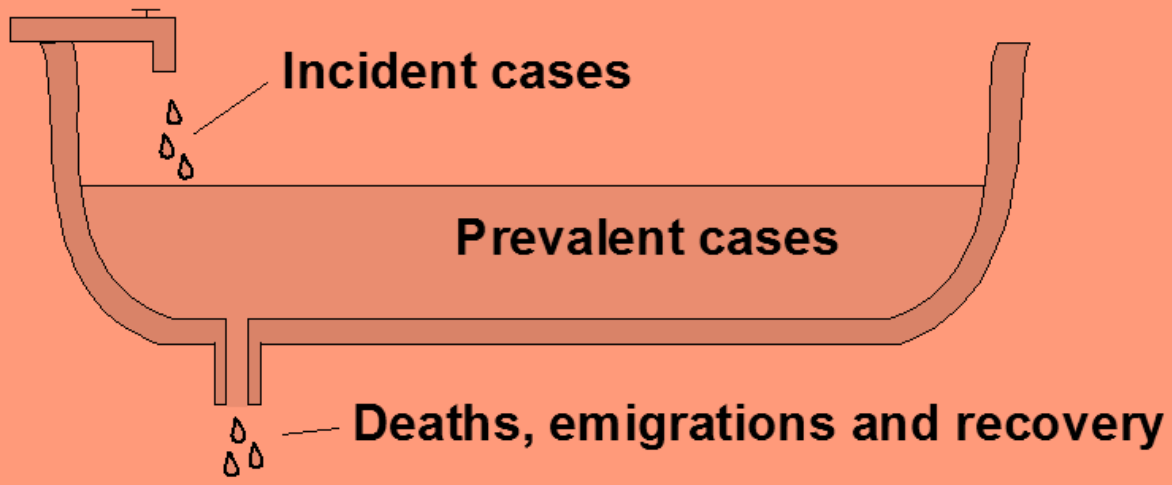
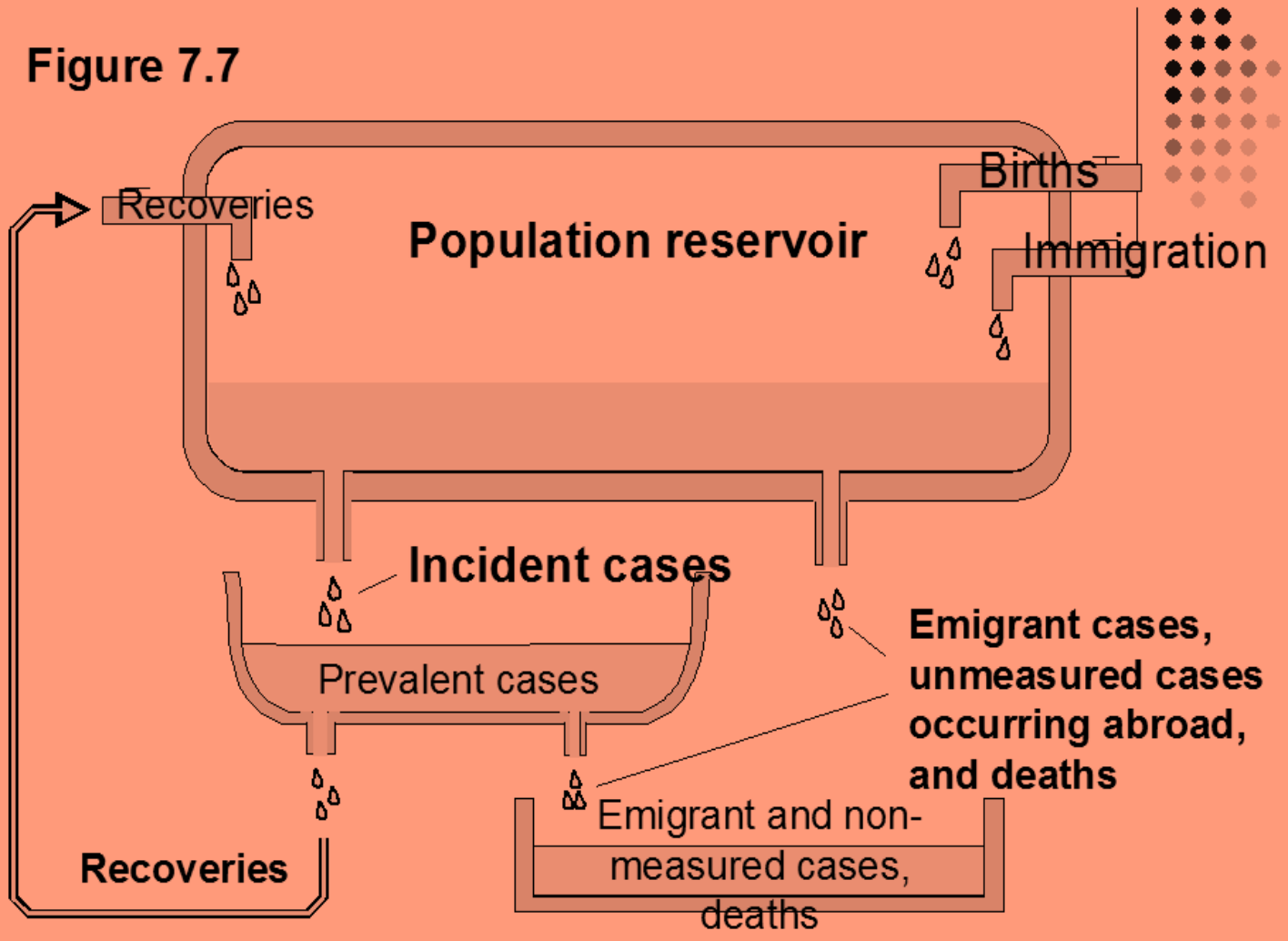

Incident cases
Prevalent cases
Deaths, emigrations and recovery

Figure 7.7


Recoveries
Population reservoir
Births
Immigration
Incident cases
Prevalent cases
Emigrant cases, unmeasured cases occurring abroad, and deaths
Recoveries
Emigrant and non-measured cases, deaths

What is person-time?

"*It is an estimate of the actual time-at-risk in years, months or days that all persons contributed to study.*"

In certain studies people are followed for different lengths of time as some will remain disease-free longer than others.

A subject is eligible to contribute person-time to the study only so long as that person remains disease-free and therefore, still at risk of developing the disease of interest.

By knowing the number of new cases of disease and the person-time-at-risk contributed to the study, an investigator can calculate incidence rate

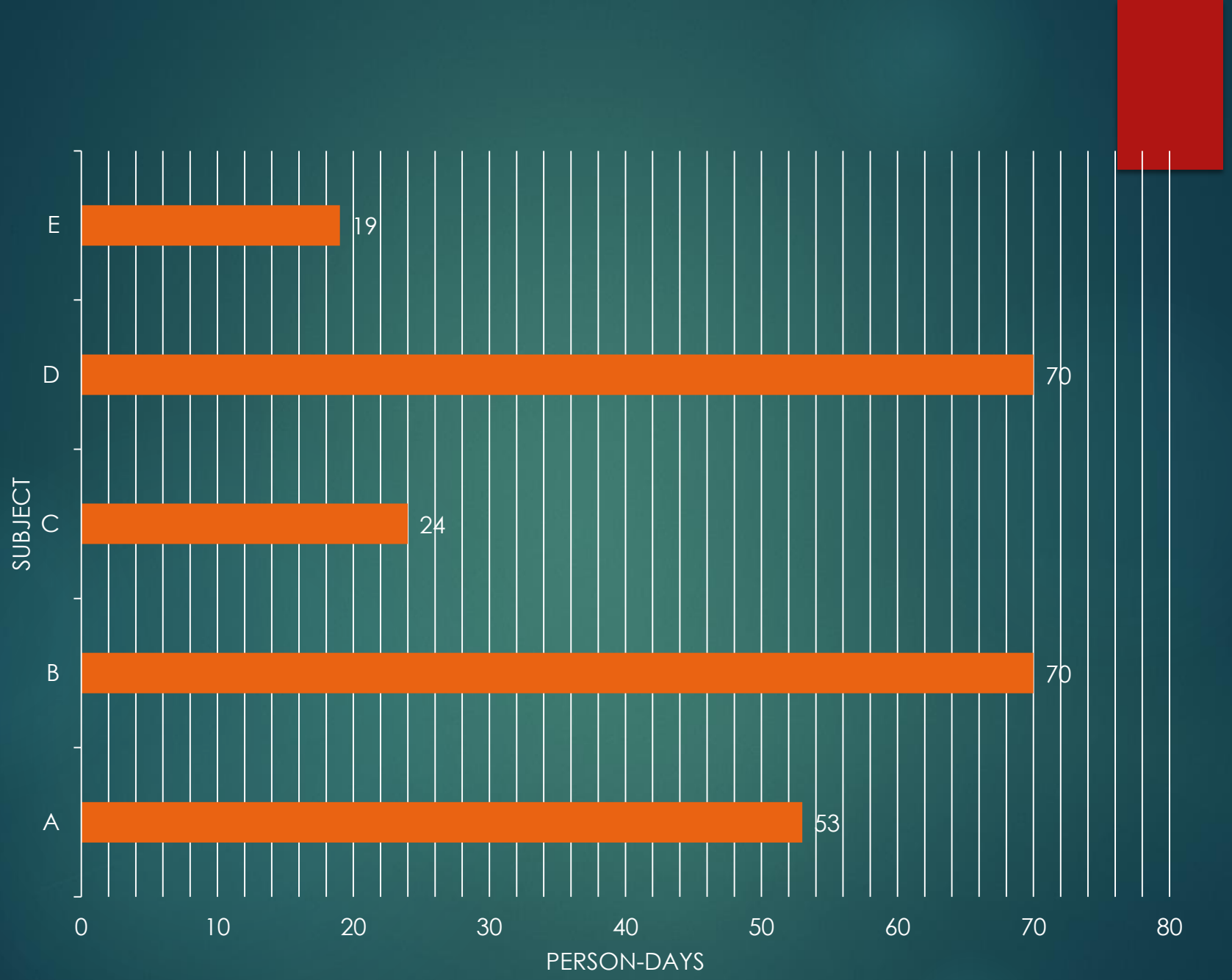
IR= the no. of new cases of disease during a period of time/the person-time-at-risk

The denominator for IR (person-time) is a more exact expression of the *population at risk during the period of time* when the change from non-disease to disease is being measured

The denominator for IR changes as persons *originally at risk develop disease* during the observation period and are removed from the denominator

Calculating person-time

An investigator is conducting a study of the incidence of second MI. He follows 5 subjects from baseline (after first MI) for up to 10 weeks


E
D
C
B
A
SUBJECT
19
70
24
70
53
0
10
20
30
40
50
60
70
80
PERSON-DAYS

As we know, person-time is the sum of total time contributed by all subjects (days each subject remained as non-case from baseline)

Subject A: 53 days

Subject B: 70 days

Subject C: 24 days

Subject D: 70 days

Subject E: 19 days

Total person-days = 236 person-days

Now, 236 p-d becomes denominator in measuring IR

The total no. Of subjects becoming cases (A,C,E) is the numerator

Therefore,

The IR of second.MI is 3/ 236 p-d = 0.0127 cases per person-day

(1.27 cases/ 100 person-days or 12.7 cases/1000 person-days)

Person-days, can be converted into any interval appropriate to the disease being studied.

Second MI may be expressed in cases per person-year by:

0.0127 cases/p-d) X (365 p-d/1 p-y)

= 4.6 cases/p-y

Drug use measures

- Monetary units
- Numbers of prescription
- Units of drug dispensed
- Defined daily doses
- Prescribed daily doses
- Medication adherence measurement

Monetary units

Drug use has been *measured in monetary units* to quantify the amounts being consumed by population

It can indicate the burden on a society from drug use

Monetary units are convenient & can be converted to a common unit, which then allows for comparison

The disadvantage is *quantities of drugs actually consumed are not known & prices may vary widely*

Number of prescriptions

It has been used in research due to the availability & ease

The disadvantage is, *quantities dispensed vary greatly as duration of treatment*

Ex: Treatment with antibiotics, provide a fairly good estimate of the no. Of people exposed & of the no. Of treatment episodes

Units of drug dispensed

Units of drug dispensed like tablets, vials is easy to obtain & can be used to compare usage trends within population

The disadvantage is that *no information is available on the quantities actually taken by the patient*

Hence difficult to determine the actual no. Of patients exposed to the drug

Defined daily doses

"*It is the estimated avg. Maintenance dose per day of a drug when used in its major indication.*"

It is normally expressed as Drug Usage= Items issued* Amount of drug per item/ DDD

It is helpful in describing & comparing patterns of DU & provides denominator data for estimation of ADR rates.

Advantage is its usefulness for working with readily available drug statistics

It allows comparisons b/n drugs in the same therapeutic class

Disadvantage is problems arises when doses vary widely like with antibiotics or if the drug has more than 1 major indication

Ex: ASA

low dose- avoid cardiac events

moderate dose-pain management

high dose- for inflammatory conditions

Prescribed daily doses

"It is the average daily dose of a drug that has actually been prescribed"

Calculated from representative sample of prescriptions

Disadvantage is that *it does not indicate no. of population exposed to drug*

However, it provides estimate of no of person-days of exposure

Medication adherence measurements.

Biological Assays

"Biological assays measure the concentration of a drug, its metabolites, or tracer compounds in the blood or urine of a patient."

- These measures are intrusive and often costly to administer.
- Patients who know that they will be tested may consciously take medication that they had been skipping so the tests will not detect individuals who have been no adherent.
- Drug or food interactions, physiological differences, dosing schedules, and the half-life of the drugs may influence the results
- Biological tracers that have known half lives and do not interfere with the medication may be used, but there are ethical concerns
- All of these methods have high costs for the assays that limit the feasibility of these techniques

Pill Counts

"Counting the number of pills remaining in a patient's supply and calculating the number of pills that the patient has taken since filling the prescription."

- It is the easiest method for calculating patient medication adherence.
- Some data indicate that this technique may underestimate adherence in older populations.
- Patterns of non-adherence are often difficult to discern with a simple count of pills on a certain date weeks to months after the prescription was filled.

Pill Counts….


Counting Pills
Quantity Poured
60
Drug Photo
Counting Pills
Quantity
30
Drug Photo

Weight of Topical Medications

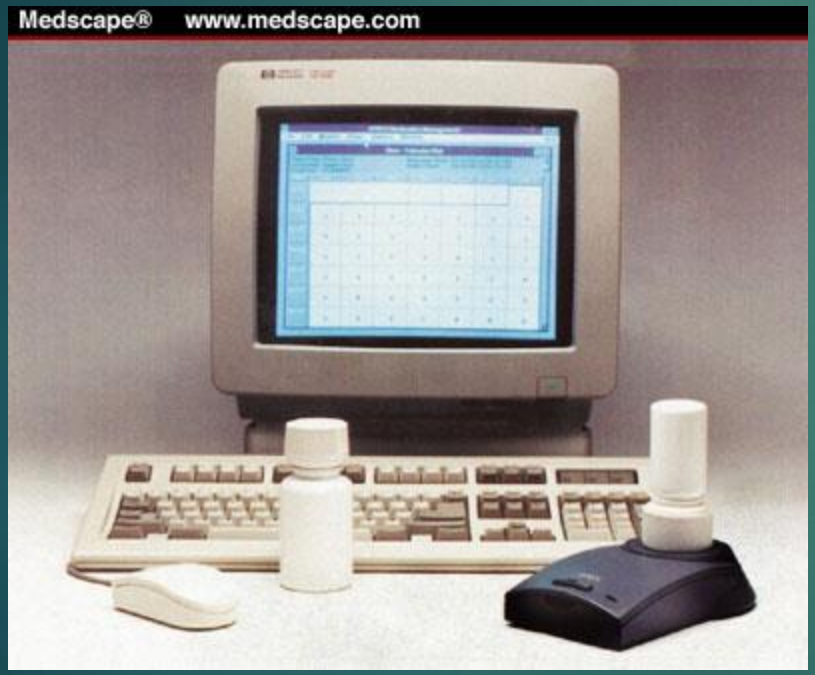
"The weight of a topical medication remaining in a tube is used as a measure of adherence. "

- When compared with patient log books of daily medication use, weight estimates of adherence were considerably lower than patient log estimates.
- In the clinical trials involving topical applications incorporate medication weights as the primary measure of adherence.
- In a comparison of methods to measure adherence, found that estimates calculated from medication logs and medication weights were consistently higher than those of electronic monitors

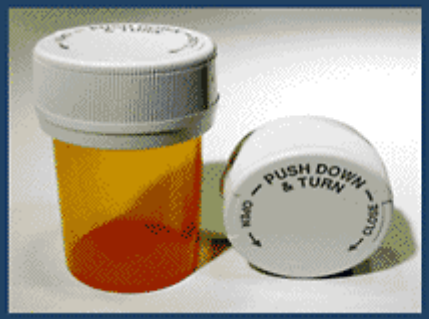
Electronic Monitoring

- The Medication Event Monitoring System (MEMS) manufactured by Aardex corporation
- Its allows the assessment of the number of pills missed during a period as well as adherence to a dosing schedule.
- The system electronically monitors when the pill bottle is opened, and the researcher can periodically download the information to a computer.
- The availability and cost of this system could limit the feasibility of its use.

Electronic Monitoring…



Medication Event Monitoring System (MEMS) TrackCap



- The MEMS TrackCap is a medication bottle cap containing microelectronics that record each time the bottle is opened and closed
- The TrackCap CR provides a means of measuring a patient's drug taking behavior

Pharmacy Records and Prescription Claims

This method can be used primarily for medications that are taken for chronic illnesses (such as hypertension)

These records provide only an indirect measure of drugs consumed

Patterns of over and under consumption for periods less than that between refills cannot be assessed

Patient Interviews

Studies have consistently shown that third-party assessments of medication adherence by healthcare providers tend to overestimate patients' adherence.

- Interviewing patients to assess their knowledge of the medications they have been prescribed and the dosing schedule provide little information as to whether the patient is adherent with the actual dosing schedule.
- Subjective assessments by interviewers can bias adherence estimates.
- This method is rarely used in medical research to assess adherence.

Direct questioning of patients to assess adherence can be an effective method

However, patients who claim adherence may be underreporting their non adherence to avoid caregiver disapproval

Other methods may need to be employed to detect these patients

Scaled Questionnaires:

Morisky et al. (1986) developed a *4-item scaled questionnaire to assess adherence with antihypertensive treatment.*

Li et al. (2005) developed *four instruments to measure antihypertensive medication adherence in a population of Chinese immigrants in the US*

The Hill-Bone Compliance to *High Blood Pressure Therapy Scale includes 14 items, 8 of which are directed at assessing medication taking behavior in hypertensive patients*

Not only is this method relatively simple and economically feasible to use, but it has the added advantage of soliciting information regarding situational factors that interfere with medication adherence

(e.g. forgetfulness, remembering to bring medications along when out of town)

The **Compliance-Questionnaire-Rheumatology (CQR) is a 19-item questionnaire that has been favorably compared with electronic medication event monitoring (de Klerk et al. 2003**). This instrument has good validity and reliability.

Table 1 The full compliance questionnaire for rheumatology (CQR19)

	Questions
Q1	If the rheumatologist tells me to take the medicines, I do so
Q2*	I take my anti-rheumatic medicines because I then have fewer problems
Q3*	I definitely don't dare to miss my anti-rheumatic medications
Q4	If I can help myself with alternative therapies, I prefer that to what my rheumatologist prescribes
Q5*	My medicines are always stored in the same place and that's why I don't forget them
Q6*	I take my medicines because I have complete confidence in my rheumatologist
Q7	The most important reason to take my anti-rheumatic medicines is that I can still do what I want to do
Q8	I don't like to take medicine. If I can do without them, I will
Q9	When I am on vacation, it sometimes happens that I don't take my medicines
Q10	I take my anti-rheumatic drugs, for otherwise what's the point of consulting a rheumatologist?
Q11	I don't expect miracles from my anti-rheumatic medicines
Q12	If you can't stand the medicines you might say: "throw it away, no matter what"
Q13	If I don't take my anti-rheumatic medicines regularly, the inflammation returns
Q14	If I don't take my anti-rheumatic medicines, my body warns me
Q15	My health goes above everything else and if I have to take medicines to keep well, I will
Q16	I use a dose organizer for my medications
Q17*	What the doctor tells me, I hang on to
Q18	If I don't take my anti-rheumatic medicines, I have more complaints
Q19	It happens every now and them, I go out for the weekend and then I don't take my medicines

Note: Items denoted with * have been retained in the final 5 item CQR5 questionnaire.

Concept of risk

Risks (defined as the probability of a new occurrence disease among individuals in an initially disease free population, over a defined period of time) can be compared by two ways, either ratios (relative comparison) or difference (absolute comparison)

A distinction should also be made between risk & harm

Risk refers to the probability of developing an outcome, regardless of severity

Harm is a more descriptive term & includes not only frequency of occurrence but also severity & duration

The ICH, distinguished serious (outcome of ADR) from severe (grading of the degree of any ADR) reactions

Ex: severe pruritus is not a serious ADR because serious denotes that a reaction is life-threatening

The CIOMS introduced scale of risk level terms,

Very common ≥ 1 in 10

Common < 1 in 10 but ≥ 1 in 100

Uncommon < 1 in 100 but ≥ 1 in 1000

Rare < 1 in 1000 but ≥ 1 in 10000

Very rare < 1 in 10000

WHO has developed categories of likelihood for causal associations of exposure-event relationships.

Certain

Probable

Possible

Unlikely

Conditional

unclassifiable

Measurement of risk

The risk of an ADR is expressed in many ways

- Attributable risk
- Relative risk
- Time-risk relationship
- Odds ratio

Attributable risk

Useful approach to express the magnitude of problems also called as the risk difference or excess risk

It is the difference b/n the risk in the exposed group & the baseline risk in unexposed population

Thus, it is the risk in excess of the baseline risk that may be attributed to exposure to the drug

i.e. AR= (a/b)-(c/d)

Ex: if 26 people among 1000 exposed (2.6%) and 36 out of 2000 not exposed (1.8%) developed rash

AR=2.6%-1.8%=0.8%

From AR it is possible to calculate NNT,

It determines the number of people who would have to be treated to produce 1 more case of the outcome

NNT=1/AR

Ex: NNT=1/0.8% = 1/0.008 = 125

i.e. You would need to treat 125 people to produce 1 additional case of rash

Relative risk (risk ratio)

It is the ratio of the risk rate in the exposed group to the risk rate in the non exposed group

Ex: the probability of developing lung cancer among smokers was 20% & among non smokers 1%

Risk factor	Disease status	
	Present	Absent
Smokers	A=20	B=80
Non smokers	C=1	D=99

$$RR = \frac{A/A+b}{C/C+D} = \frac{20/20+80}{1/1+99} = \frac{20/100}{1/100}$$

RR= 20

It means, smokers would be twenty times as likely as non-smokers to develop lung cancer

RR of 1 there is no difference in risk b/n the two groups

RR of < 1 the event is less likely to occur in the experimental group than in the control group

RR of > 1 the event is more likely to occur in the experimental group than in the control group.

Ex:

if RR is 0.5, means exposed person experience 50% reduction in risk

If RR is 0.2 it indicates 80% reduction in risk

Time-risk relationships

The ***risk varies with time in a number of different ways*** that are dependent on the drug &/or the type of ADR that it produces.

Hence while expressing risk of an event***, exposure time must always be considered*** & risk should ideally be expressed as a function of time.

There are several mechanisms for the different shapes of the time-risk curves.

Early adaptation of ***homeostatic mechanism*** may explain first dose or early symptoms

For immunological mechanism, it takes a certain amount of time for the immune system to become activated & to synthesize antibodies

For fibrotic lesions as well as cancers there is usually an induction time of months to years

Odds ratio

It is a way of comparing whether the probability of a certain event is the same for two groups.

It is expressed as the ratio of odds of exposure in diseased subjects to the odds of exposure in the non diseased.

	Case	Control
Exposed	A	B
Non exposed	C	D
Odds of exposure	A/C	B/D

An odds ratio of 1 implies that the event is equally likely in both groups

An odds ratio greater than one implies that the event is more likely in the first group

An odds ratio less than one implies that the event is less likely in the first group

The data in the table below is information about infant birth weights and mortality among white infants in New York City in 1974.

	Dead	alive
Low birth wt	618	4597
Normal birth wt	422	63,093
total	1040	71,690

The odds ratio for death in one year is

OR=618 X 63,093 / 422 X 4597

OR= 21.4

This odds ratio illustrates that mortality is far more likely in the low birth weight group.

Thank you