Basic epidemiology for the vaccinologist

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What is epidemiology?

- The study of the frequency, causes and distribution of disease and the control thereof.

- “Epidemiology is a slippery concept!” (Prof Jonny Myers; Dept Public Health, UCT; ca 1999)

Question

- Why should vaccinologists or budding vaccinologists pay any attention at all to epidemiology?

What I think…

- Can't measure it = can't manage it
  - Measurement sciences – epidemiology, statistics, information management, etc
- Can't measure it = can't prioritise and plan properly
- Can't measure it = can't impute causality, design interventions, understand mechanisms properly – ideas / hypothesis generation
- Good epidemiology underlies much research – both basic science and clinical.

Learning Objectives

At the end of this session, you should know:

- The definition of epidemiology
- The difference between incidence and prevalence.
- The different kinds of study design and what study design is used in clinical trials.
- How vaccine efficacy is calculated and interpreted.
- The difference between vaccine efficacy and vaccine effectiveness.

Incidence and prevalence

- Prevalence

The proportion of disease occurring at a point in time e.g. 100 out of a 1000 people are HIV positive in a survey done in October 2007

= 100/1000 *100 = 10% prevalence.

- Incidence

The number of NEW cases of disease in a population over a specified time period e.g. 1000 new TB cases in 2007 in a population of 100 000.

= 1000/100 000 *100 = 1% incidence in 2007.

Question

- Which is more important in vaccinology, incidence or prevalence and why?

Study designs

- Observational
  - Case series – A simple description of a series of cases of diease.
  - Cross-sectional study – a description of a defined group at a point in time – prevalence.
  - Case Control study – a group of cases is compared to a selected group of controls to determine causes.
  - Cohort study – defined group is followed up over time to determine incidence of disease (with the initial group possibly being classified by exposures)

Intervention studies - Clinical trials

- Studies where researchers administer an intervention e.g. drug, vaccine or educational intervention.
- Controlled
- Randomised
- Blinded – single, double, triple

Advantages and disadvantages of different study designs

- Cost
- Ability to study rare diseases/ outcomes.
- Time needed to do the study.
- Descriptive or analytic output needed.
- Prone to bias or not.

How is a vaccine efficacy study done?

- Phase III trial.
- Usually double blind, randomised and controlled.
- i.e. conditions are idealised.
- Strict inclusion and exclusion criteria
- Sample size determined based on expected incidence of disease in unvaccinated and estimated incidence in vaccinated.
- Usually for a limited period.

Vaccine effectiveness

- Evaluation of a vaccine under field conditions to determine operational feasibility.
- Other kinds of study designs used: before/ after, case control, long term cohort follow up, outbreak investigation.
- Be wary of biases and confounding.
- Usually not blinded nor randomised.
- May include whole populations.
- Long term follow up possible.
- Under field conditions so less controlled and less standardised.

Phase IV evaluation

- Post licensure.
- Efficacy in special risk groups.
- Surveillance for rare safety events.

Bias and confounding

- Bias is a factor which distorts the validity of an outcome measure of a study e.g. recall, selection, misclassification.
- Confounding is a special bias where a factor is associated with both the exposure and the disease outcome e.g. coffee may come up as a risk factor for lung cancer but this may be due to smoking being associated with coffee drinking and lung cancer.

Definition of vaccine efficacy/ effectiveness

The degree to which a vaccine reduces the number of cases due to a disease.

Traditionally VE =

Percentage (%) reduction in disease incidence attributable to vaccination (H Hohynek)

Measurement of vaccine efficacy

- VE = 1 - RR
- VE (%)

  $= \frac{(ARU - ARV)}{ARU} \times 100$
- [= (1 – $\frac{ARV}{ARU}$) x 100]

$RR = AR_V / AR_U$

AR_V = attack rate in vaccinated

AR_U = attack rate in unvaccinated

Calculating Vaccine efficacy - example

- Rate of disease in those who got placebo – 100 out of 1000.
- Rate of disease in those who got vaccine – 10 out of 1000.
- What is the vaccine efficacy?

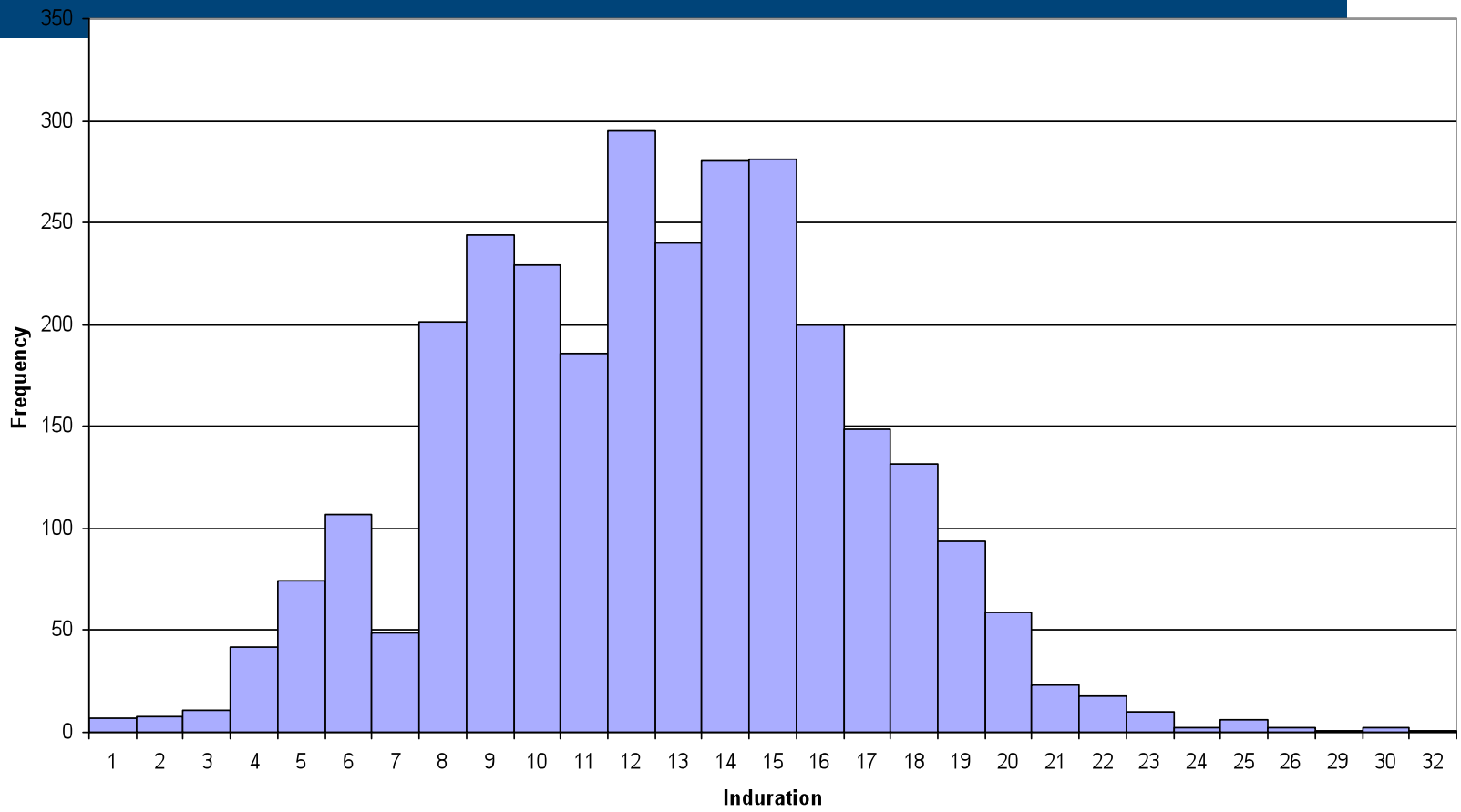
Calculation in our example

- $\frac{\text{(ARU - ARV)}}{\text{ARU}} \times 100$
- $\frac{100/1000 - 10/1000}{100/1000} \times 100 =$
- $\frac{0.1 - 0.01}{0.1} \times 100 = \frac{0.09}{0.1} \times 100$
- = 0.9 X 100 = 90%

Basic statistical measures

- Average measures: mean, median and mode
- Proportions (often expressed as percentages).
- Data classification process – categorical/ numerical (discrete or continuous).
- Statistical tests depend on type of data.
- Multivariate analyses

ACS TST distribution at baseline



Immunisation coverage

Data for 1999	
	District X
Primary course completed (birth, 6, 10, 14 weeks and 9 months	3,886
DPT 1st dose	4,389
Births 1999	3541
Population <1 in 1999	4060
% DPT 1	88.5
% births	109.7
% of population < 1 in 1999	95.7

Concluding summary

- Basic epidemiological measures are crucial to vaccinology.
- Vaccine efficacy is measured through randomised, controlled, blinded clinical trials.
- There are different study designs that can be used to determine vaccine effectiveness.