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Interpretation of observational studies
- inherently less convincing than a RCT

Why are there observational studies?
- randomization is impossible, unethical or impractical

Why are observational studies of clinical interest?

How to evaluate an observational study
confounding - interaction - bias

Ratio: The value obtained by dividing one quantity by another; the numerator and denominator may be separate and distinct quantities, neither being included in the other, such as a sex ratio (number of women / number of men).

Proportion: A ratio in which the numerator in is included in the denominator; a proportion is always between 0 and 1.

Rate: A measure of the frequency of the occurrence a phenomenon. Typically, the number of events in a specified period of time divided by persons at risk during that time period, per population unit. All rates are ratios; some are proportions.

Risk: The accumulated effect of a rate operating during a specified period of time; such as the lifetime risk of cancer. This is a proportion and will always fall between 0 and 100 percent.

Incidence: The number of **new** cases of a disease that occur during a specified period of time in a population at risk for developing the disease.
Cumulative incidence - for a fixed population
Incidence rate (incidence density) - for a dynamic cohort

Prevalence: The number of affected persons present in the population at a specific time divided by the number of persons. This is a proportion , not a rate, as there is no time dimension.

What is the relationship between incidence and prevalence?
Why are incident cases preferable for etiologic studies?

CONFOUNDING

A **confounder** is a variable that can cause or prevent the outcome of interest, is not an intermediate variable, and is associated with the factor under investigation. Unless it is possible to adjust for confounding variables, their effects cannot be distinguished from those of factor(s) being studied.
Ex. hepatocellular carcinoma, HBV, HCV

X is a confounder of the E - D association if the following are true:
1. X is a known risk factor for D
2. X is associated with E but is not a result of E
X and E should be associated in both cases and controls

+Confounding effects can create a spurious association
+Confounding effects can mask a real association

Confounding is not the product of a faulty study design or execution. The confounding is present in the study population.

Confounder's association with disease may be either cause-and-effect or may be the result of the confounder's association with a third factor, not the exposure, which is causal.

Ex. Alzheimer's , ERT, education

In practice, any extraneous risk factor, which itself is not a consequence of exposure, may be regarded as a confounder if its control appreciably alters the estimate of an exposure's effect.

INTERACTION (EFFECT MODIFICATION)

When the incidence rate of disease in the presence of two or more risk factors differs from the ***incidence rate expected*** to result from their individual effects.

- Biological vs. statistical
- Biological interpretation - finding should be replicated
- ex. Thrombotic stroke and OC

When interaction is suspected, the purpose of the analysis is not to remove the effects of interaction; the purpose is to detect the interaction.

What is the expected incidence rate?

Additive and Multiplicative models

BIAS

Deviations of results or inferences from the truth. Any trend in the collection, analysis, interpretation, publication, or review of data that can lead to conclusions that are systematically different from the truth. An error in design or conduct (unrelated to a partisan viewpoint)

Particular to case-control studies:

SELECTION BIAS - the relationship between exposure and disease is different for those who participate and those who would be theoretically eligible to participate but do not.

- Cases are not representative
  - case definition - misclassification bias
  - incidence-prevalence bias (Neyman's)
  - volunteer bias
  - admission bias (Berkson's)
- Controls are not representative

Controls should be persons who, had they developed the disease of interest, would have been part of the case series.

The major potential bias in a c-c study

community vs. hospital/clinic

Potential problems for both case-control and cohort studies:

INFORMATION BIAS - a flaw in measuring exposure or outcome data which results in different quality (accuracy) of information between comparison groups

recall

proxy

differential misclassification

interviewer bias

non-response bias