

EVALUATION OF EVIDENCE

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Session objectives

- Discuss the **sources of error**
- Explain **criteria** for establishing causation

References

- Bonita R, et al. Basic Epidemiology. WHO, 2006.
- Rothman K, et al. Modern Epidemiology, 3rded, 2008.

Evaluation of evidence

- In public health, evidence is useful for
 - Policy making and program planning
 - Service provision
 - Teaching and research
- In order to use evidence, one has to evaluate its relevance and validity

Relevance of evidence

- Relevance: applicability for intended use
- Appraisal
 - Identify focus of study (disease burden, health risks, health needs, cost-effective interventions) and
 - Evaluate appropriateness of the information considering
 - It relevance for purpose,
 - relevance to context and
 - timeliness

Validity of evidence

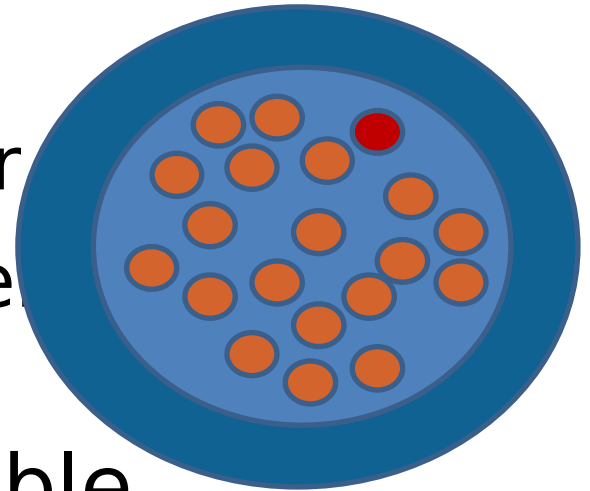
- Validity: acceptability of findings
- Appraisal
 - Evaluate credibility
 - Evaluate methodological quality in reducing various sources of error

Sources of Error

- “Beasts of epidemiology”
 - Sampling error/random error/chance
 - Bias/systematic error/deviation from plan
 - Confounding
 - Interaction?

Sampling error

- Results from taking sample to infer about population
- Refers to lack of precision or
- How to minimize sampling error
 - Increasing the sample size
- Sampling error is inevitable
 - Therefore, measure and indicate level of precision and power
 - Using p-value/CI and $1 - \beta$

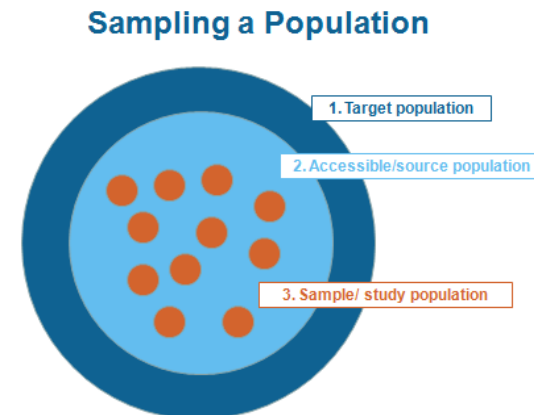


Bias

- more dangerous and more difficult to measure
- refers to lack in validity
- Types
 - Selection bias
 - Non-participation (Non-response or loss-to-follow-up)
 - Information or observation bias

Selection bias

- Results from non-representative sample selection
 - Using non-random methods of selection
- There are several types



Selection bias: Types

- Institution based researches – hospitals, occupation groups
 - Diagnostic bias; Occupation groups (Healthy worker effect)
- Self-selection bias – volunteer bias
- Survival bias, temporal bias
- Solution – population-based studies with random selection

Non-participation

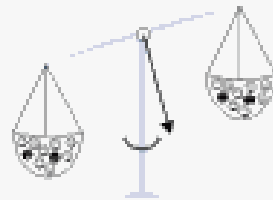
- Results from non-response or loss-to-follow-up (LTF)
- Commonest known source of bias
- Non-response could imply rejection or unavailability
- LTF – major problem in cohort studies



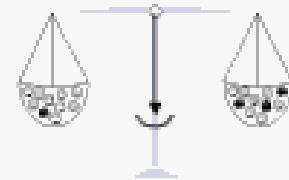
Non-participation bias

- Non-participation leads to serious bias
 - if non-participants are different from participants
 - When significant

Figure 4.1



(a) Error is unequal in one of these groups leading to a false interpretation of the pattern of disease
- falsely detecting differences



(b) Error is unequal in one of these groups leading to a false interpretation of the pattern of disease
- here failure to detect differences



Non-participation: Solutions

- Pre-testing
- Adding contingency samples
- Make diligent efforts
 - Revisits; Participation should be as convenient and painless as possible – mobile examination
- Evaluate non-respondents; Extreme analysis

Information bias

- Results from error in measurement
- Types by source
 - Observer/Interviewer bias
 - Interviewee bias, Recall bias
 - Invalid instrument/tool
- Solutions:
 - Standardization of procedures, intensive training, supervision and duplicate observation, use memory aids
 - Appropriate operational definition

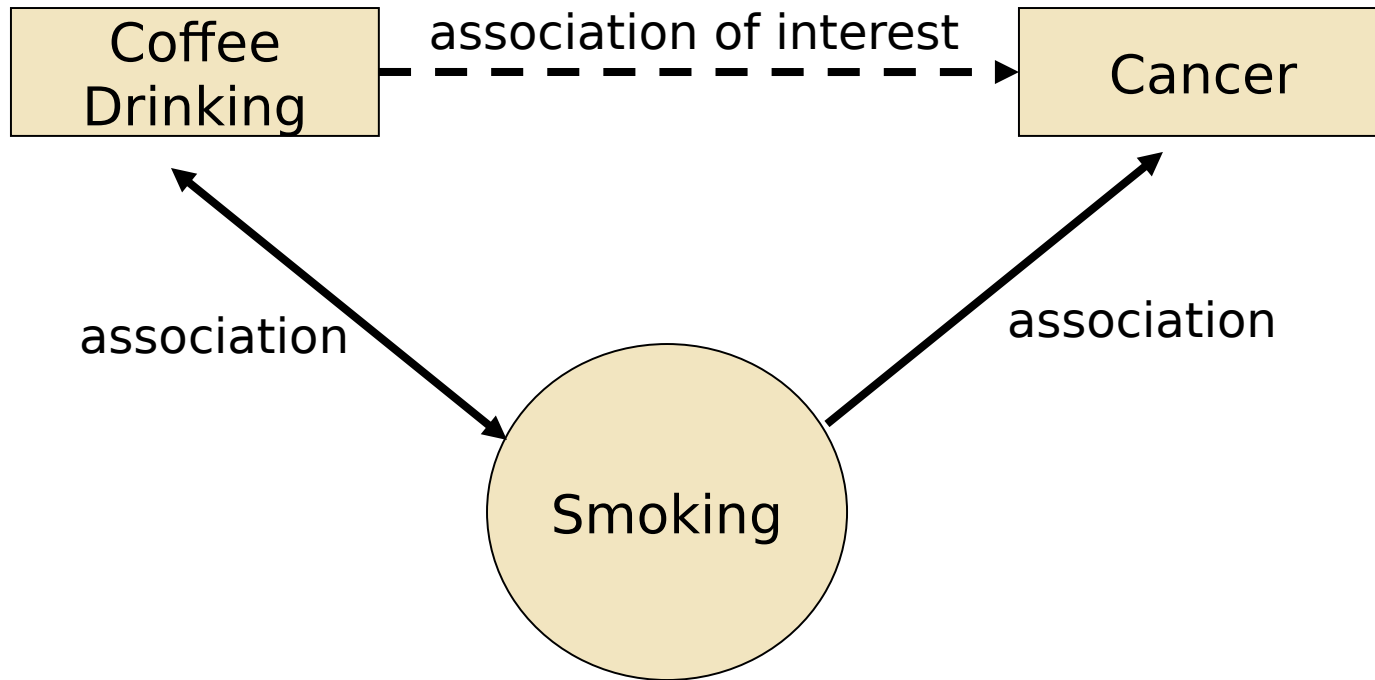
Confounding

- The distortion of the measure of effect of exposure on outcome
 - due its association with other factors that can influence the outcome
- Solution: prevent during design through restriction, matching or randomization or control by stratified analysis

Confounders

- Factors are labeled as confounders when
 - associated with the **exposure** and
 - Independently associated with the **disease**
- A confounder is not an **intermediate** variable or consequence of the disease

Illustration of confounder



Smoking can confound association between coffee and cancer

Interaction/Effect modification

- Varying measures of effect of exposure on outcome at **different levels** of other variable
- the **adjusted measure** can't adequately summarize the association
- E.g. Asbestos and cigarette smoking

Assessing Methodological Quality of Research

Assessing Methodological Validity

- To evaluate degree of error from different sources
- Key methods sections to be assessed
 - design
 - sampling
 - measurement
 - analysis
- What questions to ask in each section?

Is the design appropriate to research objective?

- Identify focus/objective of study
- Assess
 - appropriateness of design in relation to objective
 - strength and limitations of design

Is the sample size adequate?

- Identify sample size determination method
- Assess
 - Adequacy of sample considering
 - appropriateness of assumptions
 - non-response

Is there selection bias?

- **Assess:**
 - Representativeness of samples considering the
 - Sampling technique
 - Inclusion and exclusion criteria
 - Character of non-respondents

Is there measurement error?

- Assess:
 - validity of
 - data collection formats
 - data collection instruments
 - data collection procedures
 - definition of variables

Is there confounding?

- **Assess:**
 - liability to confounding considering
 - techniques used to prevent confounding during design
 - control of confounders during analysis
 - presence of unmeasured confounders

Are statistical analysis appropriate?

- Assess
 - Appropriateness of analytic methods
 - Fulfillment of requirements for statistical tests

Critical appraisal assignment

- Focus on appraisal of methodological quality
 - In line with previous questions
- cohort study
- experimental study

More evidence

- Single research
 - Likely to be affected by sources of error
- Better evidence from
 - Systematic review
 - Meta-analysis
- Errors are difficult to completely rule out
 - Additional considerations are required to make causal inferences

Establishing Causation

- How to separate causal from non-causal associations in epidemiology?
 - Setting criteria
- Offered by Bradford Hill
 - Guides, not rules – support causal association
 - Strength, consistency, temporality, dose-response relationship, biologic plausibility, experimental evidence

Temporal relation

- Refers to the necessity that the cause **precedes** the effect in time
 - Which type of observational study is best for documenting time sequence?
- Such time sequence does not in itself establish causation
 - could be confounded
- Reverse time order does not rule out causal relationship

Strength of association

- Refers to magnitude of measure of association
- **Strong** association more likely to be causal
 - If due to confounder, its effect would be more stronger and it would have been evident
 - Weak associations could be causal
 - E.g. smoking and cardiovascular disease
 - Even strong associations might not be causal
 - E.g. – down syndrome Vs birth order is confounded by maternal age

Dose-response relationship

- Increase in outcome incidence with increase in exposure level
 - E.g. BP and IHD
- But some causes have all-or-none or non-linear effect
 - E.g. – DES and adenocarcinoma of vagina
- Dose-response relation could be due to confounding
 - E.g. gray hair Vs death by age

Consistency

- Refers to similar findings in **different** populations under different circumstances
 - Systematic review, Meta-analysis
- Serves to rule out the role of a factor that varies across studies
- Lack of consistency does not rule out causal association
 - Unknown unusual component cause might be needed

Biologic **Plausibility** (1)

- Coherence with current **scientific** knowledge on pathogenesis of the disease
 - E.g. 1- smoking and lung ca; substances in the cigarette smoke have been shown to cause histopathological changes in respiratory epithelium of animals
 - E.g. 2- presence of viral genome in liver cells supports association between Hepatitis B and liver cancer

Biologic Plausibility (2)

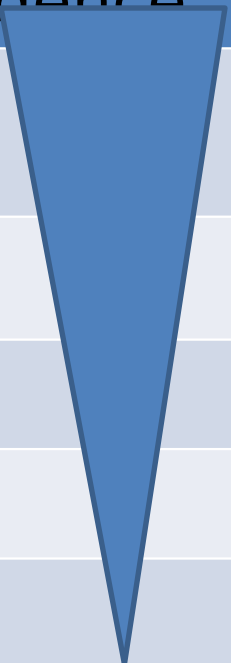
- However, biological plausibility is a relative concept, and seemingly implausible associations may eventually be shown to be causal
 - Lack of plausibility may simply reflect lack of scientific knowledge
- Doubts about the therapeutic effects of acupuncture and homeopathy may be partly attributable to the absence of information about a plausible biological mechanism

Reversibility

- When the **removal** of the factor results in a reduced disease risk
 - E.g. – cessation of smoking reduces risk of lung ca
- If the cause leads to rapid irreversible changes that subsequently produce disease whether or not there is continued exposure, then reversibility cannot be a condition for causality

Study **Design** - Hierarchy of Causation

Relative ability of different types of study to “prove” causation

Type of study	Strength of evidence
Systematic review and Meta-analysis	
Randomized controlled	
Cohort	
Case-control	
Cross-sectional	
Ecological	

Judging the evidence

- There are **no completely reliable** criteria
- Evidence is stronger when several criteria are met
- In causation uncertainty remains and judgement is made based on the available evidence
- **More weight** is given to
 - plausibility, consistency and the dose-response relationship
 - correct temporal relationship is essential