Measurement bias

Measurment bias

- Definition of Bias:

Systematic difference between observed result and the truth

Measurement bias

- Systematic error arising from inaccurate measurements (or classification) of subjects or study variables. (Last)
- Occurs when individual measurements or classifications of disease or exposure are inaccurate (i.e. they do not measure correctly what they are supposed to measure). (Beaglehole)
- If patients in one group stand a better chance of having their outcomes detected than those in another group. (Fletcher)

Measurement bias:

- Example: analysis of Hb by different methods (cyanmethemoglobin and Sahli's) in cases and controls.

- Example: biochemical analysis of the two groups from two different laboratories, which give consistently different results

Measurement / (Misclassification)

- Exposure misclassification occurs when exposed subjects are incorrectly classified as unexposed, or vice versa

- Disease misclassification occurs when diseased subjects are incorrectly classified as non-diseased, or vice versa

  - (Norell)

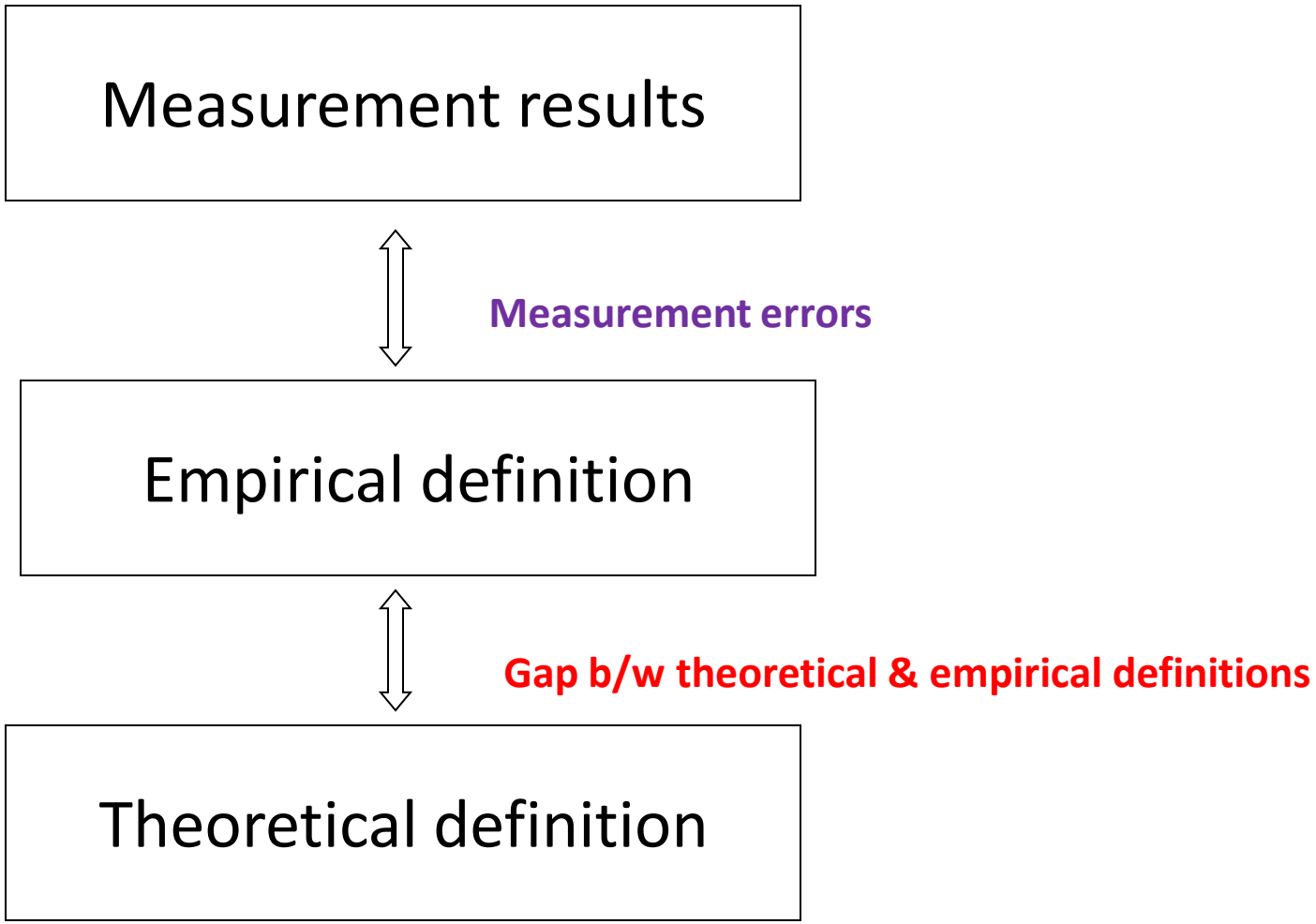
Causes of Misclassification

1. Measurement gap: gap between the measured and the true value of a variable

- Observer / interviewer bias
- Recall bias
- Reporting bias

2. Gap b/w the theoretical and empirical definition of exposure / disease

Sources of misclassification



Example… 'gap b/w definitions'

Theoretical definition

- Exposure: passive smoking – inhalation of tobacco smoke from other people's smoking
- Disease: Myocardial infarction – necrosis of the heart muscle tissue

Empirical definition

- Exposure: passive smoking – time spent with smokers (having smokers as room-mates)
- Disease: Myocardial infarction – certain diagnostic criteria (chest pain, enzyme levels, signs on ECG)

Exposure misclassification –differential

- *Differential misclassification* – **Errors in measurement are one way only**
  - **Example**: *Measurement bias* – **instrumentation may be inaccurate, such as using only one size blood pressure cuff to take measurements on both adults and children**

Misclassification Bias (cont.)

True Classification

	Cases	Controls	Total
Exposed	100	50	150
Nonexposed	50	50	100
	150	100	250

OR = ad/bc = 2.0; RR = a/(a+b)/c/(c+d) = 1.3

Differential misclassification - Overestimate exposure for 10 cases, inflate rates

	Cases	Controls	Total
Exposed	110	50	160
Nonexposed	40	50	90
	150	100	250

OR = ad/bc = 2.8; RR = a/(a+b)/c/(c+d) = 1.6

Misclassification Bias (cont.)

True Classification

	Cases	Controls	Total
Exposed	**100**	**50**	**150**
Nonexposed	**50**	**50**	**100**
	150	**100**	**250**

OR = ad/bc = 2.0; RR = a/(a+b)/c/(c+d) = 1.3

Differential misclassification - Underestimate exposure for 10 cases, deflate rates

	Cases	Controls	Total
Exposed	**90**	**50**	**140**
Nonexposed	**60**	**50**	**110**
	150	**100**	**250**

OR = ad/bc = 1.5; RR = a/(a+b)/c/(c+d) = 1.2

Misclassification Bias (cont.)

True Classification

	Cases	Controls	Total
Exposed	**100**	**50**	**150**
Nonexposed	**50**	**50**	**100**
	150	**100**	**250**

OR = ad/bc = 2.0; RR = a/(a+b)/c/(c+d) = 1.3

Differential misclassification - Underestimate exposure for 10 controls, inflate rates

	Cases	Controls	Total
Exposed	**100**	**40**	**140**
Nonexposed	**50**	**60**	**110**
	150	**100**	**250**

OR = ad/bc = 3.0; RR = a/(a+b)/c/(c+d) = 1.6

Misclassification Bias (cont.)

True Classification

	Cases	Controls	Total
Exposed	**100**	**50**	**150**
Nonexposed	**50**	**50**	**100**
	150	**100**	**250**

OR = ad/bc = 2.0; RR = a/(a+b)/c/(c+d) = 1.3

Differential misclassification - Overestimate exposure for 10 controls, deflate rates

	Cases	Controls	Total
Exposed	**100**	**60**	**160**
Nonexposed	**50**	**40**	**90**
	150	**100**	**250**

OR = ad/bc = 1.3; RR = a/(a+b)/c/(c+d) = 1.1

Exposure misclassification – Non-differential

- Misclassification does not differ between cases and non-cases
- Generally leads to dilution of effect, i.e. bias towards RR=1 (no association

- ***Nondifferential (random) misclassification*** **– errors in assignment of group happens in more than one direction**
  - **This will dilute the study findings -**
  - ***BIAS TOWARD THE NULL***

Misclassification Bias (cont.)

True Classification

	Cases	Controls	Total
Exposed	**100**	**50**	**150**
Nonexposed	**50**	**50**	**100**
	150	**100**	**250**

OR = ad/bc = 2.0; RR = a/(a+b)/c/(c+d) = 1.3

Nondifferential misclassification - Overestimate exposure in 10 cases, 10 controls – bias towards null

	Cases	Controls	Total
Exposed	**110**	**60**	**170**
Nonexposed	**40**	**40**	**80**
	150	**100**	**250**

OR = ad/bc = 1.8; RR = a/(a+b)/c/(c+d) = 1.3

Implications of Differential exposure misclassification

- An improvement in accuracy of exposure information (i.e. no misclassification among those who had breast cancer), actually reduced accuracy of results
- Non-differential misclassification is 'better' than differential misclassification
- So, epidemiologists are more concerned with **comparability of information** than with improving accuracy of information

Differential exposure misclassification

- Recall Bias: Systematic error due to differences in accuracy or completeness of recall to memory of past events or experience.

❖ Example: patients suffering from MI are more likely to recall and report 'lack of exercise' in the past than controls

Differential exposure misclassification

- Example: Mothers of children with birth defects are likely to remember drugs they took during pregnancy differently than mothers of normal children.
- Underreporting the past exposure: mothers of infants who died from SIDS may be inclined to under report their use of alcohol or recreational drugs during pregnancy.

Differential outcome misclassification

- Recall bias can also occur in retrospective cohort studies.

How? Example?

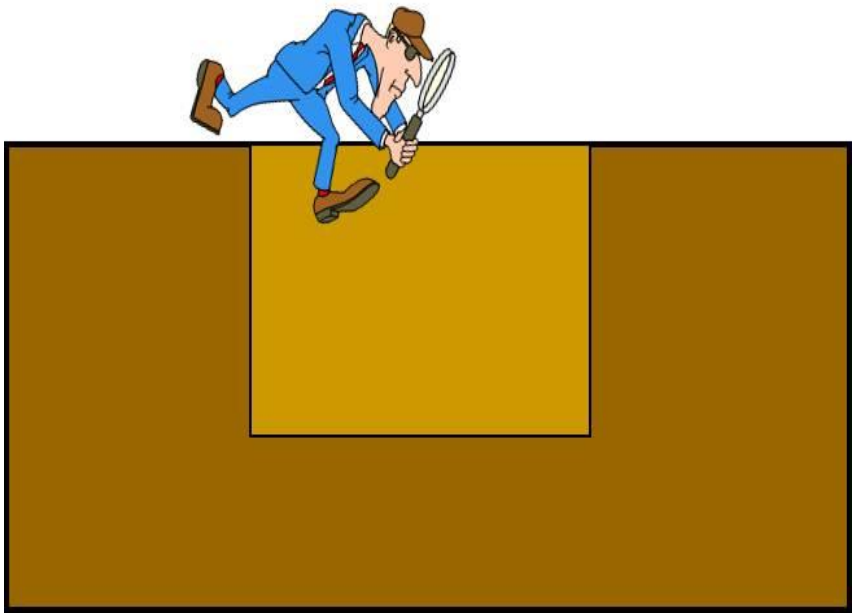
Differential outcome misclassification

- Example, those who have been exposed to a potentially harmful agent in the past may remember their subsequent outcomes with a different degree of completeness or accuracy.

Differential outcome misclassification

- Example: In the retrospective portion of the Ranch Hand Study which looked at effects of exposure to Agent Orange (dioxin). Pilots who had been exposed may have had a greater tendency to remember skin rashes that occurred during the year following exposure.

Differential exposure misclassification



Pitfall:

- **In a case-control study, if both cases and controls have more or less *equal difficulty* in remembering past exposures accurately, it is nondifferential, and it is a form of *nondifferential* misclassification.**

Differential exposure misclassification

Ways to Reduce Recall Bias

- Use a control group that has a different disease (that is unrelated to the disease under study).
- Use questionnaires that are carefully constructed in order to maximize accuracy and completeness. Ask specific questions.
- For socially sensitive questions, such as alcohol and drug use or sexual behaviors, use a self-administered questionnaire instead of an interviewer.
- If possible, assess past exposures from biomarkers or from pre-existing records.

Differential exposure misclassification

- Example: In the retrospective portion of the Ranch Hand Study which looked at effects of exposure to Agent Orange (dioxin). Pilots who had been exposed may have had a greater tendency to remember skin rashes that occurred during the year following exposure.

Differential exposure misclassification

- Interviewer / observer bias: systematic error due to observer variation (failure of the observer to measure or identify a phenomenon correctly)

- systematic differences in soliciting, recording, or interpreting information on exposure (in a case-control study) or outcome (in retrospective and prospective cohort studies and in intervention studies [clinical trials]).

Differential exposure misclassification

- Example: in patients of thrombo-embolism, look for h/o OCP use more aggressively

Differential exposure misclassification

Ways to Reduce Interviewer Bias

- Use standardized questionnaires consisting of closed-end, easy to understand questions with appropriate response options.
- Train all interviewers to adhere to the question and answer format strictly, with the same degree of questioning for both cases and controls.
- Obtain data or verify data by examining pre-existing records (e.g., medical records or employment records) or assessing biomarkers.

Measurement bias in treatment effects

Hawthorne effect: effect (usually positive / beneficial) of being under study upon the persons being studied; their knowledge of being studied influences their behavior

Placebo effect: (usually, but not necessarily beneficial) expectation that regimen will have effect, i.e. the effect is due to the power of suggestion.

Control for bias

- **Be purposeful in the study design to minimize the chance for bias**
  - Example: use more than one control group
- **Define, a priori, who is a case or what constitutes exposure so that there is no overlap**
  - Define categories within groups clearly (age groups, aggregates of person years)
- **Set up strict guidelines for data collection**
  - Train observers or interviewers to obtain data in the same fashion
  - It is preferable to use more than one observer or interviewer, but not so many that they cannot be trained in an identical manner

Control for bias, cont,

- **Randomly allocate observers/interviewer data collection assignments**
- **Institute a masking process if appropriate**
  - Single masked study – subjects are unaware of whether they are in the experimental or control group
  - Double masked study – the subject and the observer are unaware of the subject's group allocation
  - Triple masked study – the subject, observer and data analyst are unaware of the subject's group allocation
- **Build in methods to minimize loss to follow-up**

Validity

- The degree to which a measurement or test measure what it is supposed to measure

Validity

- The degree to which a measurement or test measure what it is supposed to measure

❖ Content validity

❖ Criterion validity

Validity

- Content validity

Have you measured the concept thoroughly?

- Criterion validity

How close to the “truth” are you in your measurement?

Validity

❖Content validity

- Example: smoking

Need to ask:

- Amount
- Type
- Exposure to passive smoking

Validity

❖Content validity

- Other examples where content validity is important:

  - SES
  - Ethnicity
  - Quality of life
  - Physical activity

Validity

- Criterion validity
  - Sensitivity
  - Specificity

Validity

❖Criterion validity

- How well does a person's self-reported current smoking status reflect the "truth"?

Validity

- Criterion validity

- Sensitivity: 0.80=80%

	Truth		
test	**+**	**-**	**Total**
positive	**80**	10	90
negative	20	390	410
Total	**100**	400	500

Validity

- Criterion validity

- Specificity: 0.98=98%

	Truth		
test	**+**	**-**	**Total**
positive	80	10	90
negative	20	**390**	410
Total	100	**400**	500

Validity

- Criterion validity

- determination of pregnancy status

	Truth		
Preg test	**+**	**-**	**Total**
positive	95	80	175
negative	5	320	325
Total	100	400	500

Validity

- Criterion validity

- determination of pregnancy status

- **Sensitivity=0.95**
- **Specificity=0.80**

	Truth		
Preg test	**+**	**-**	**Total**
positive	95	80	175
negative	5	320	325
Total	100	400	500

Repeatability/Reliability

- Ability of a measure or test to produce the same result when used repeatedly in the same person

Repeatability

	Murmur		
	heard	**Not heard**	**Total**
Clinician A	10	90	100
Clinician B	10	90	100
Total	20	180	200

Repeatability

- % agreement: (1+81)/100= 82%

	Clinician A		
Clinician B	**heard**	**Not heard**	**Total**
heard	1	9	10
Not heard	9	81	90
Total	10	90	100

Reliability

❖ **Have you ever used the OCP?**

	First interview		
Second interview	**yes**	**no**	**Total**
yes			256
no			115
Total	252	119	371

Reliability

- Have you ever used the OCP?
- % disagreement : (37+41)/371=21%

	First interview		
Second interview	**yes**	**no**	**Total**
yes	215	**41**	256
no	**37**	78	115
Total	252	119	371