

## Bias and causal associations in observational research

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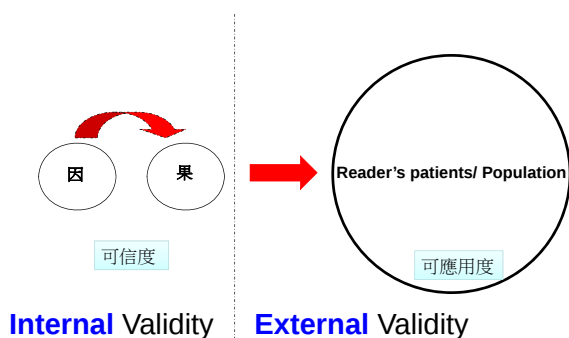
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1. Is the report **believable**?

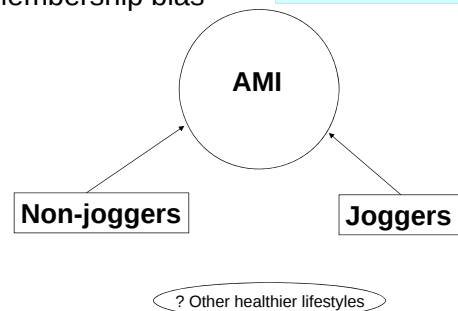
2. Is it **relevant** to my practice?



## Selection Bias

- Membership bias

Are the groups similar in all important respects?



## Selection Bias

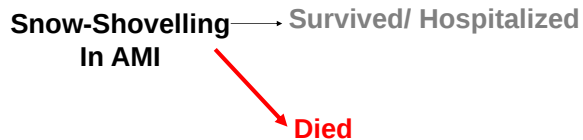
- Membership
- Admission-Rate
- Incidence-Prevalence
- Unmasking
- Non-respondent

## Selection Bias

- Admission rate (Berkson) Bias
  - Exposure of interest → ↑ Admission Rate
  - ↑ Odds ratio
  - Ex. IUD pt V.S Hormone therapy in salpingitis

## Selection Bias

- Incidence-Prevalence (Neyman) Bias



## Selection Bias

- Unmasking (Detection Signal) Bias
  - Exposure → ↑ Outcome detection
  - (e.g. HRT → symptomless endometrial cancer to bleed → ↑ Odds ratio)
- Non-respondent Bias
  - ↓ return questionnaires in smokers

volunteer bias

## Information Bias

Has information been gathered in the same way?

observation, classification or measurement bias

- Ascertainment
- Diagnostic suspicion
- Recall bias

## Information Bias

- Ascertainment
  - Information gathered in different ways
  - e.g. Exposure (bedside) ↔ Control (tel.)
- Diagnostic suspicion
  - ↑ intensive search for disease in exposed group
  - Ex: IV drug users → HIV; OCP → DVT

✱ Double-blind

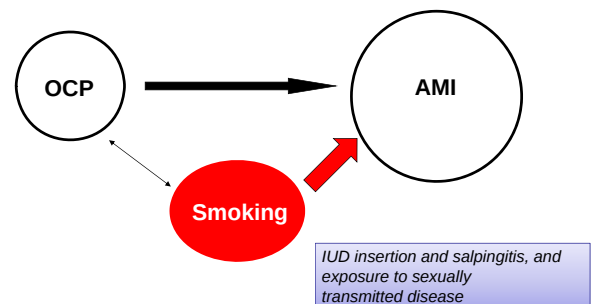
## Information Bias

- Recall bias
  - ↑ recall in cases (↑ motives)

non-differential misclassification

## Confounding

Is an extraneous factor blurring the effect?



## How to Control Confounding?

- Restriction
  - Excludes confounding
  - ↑ Internal validity; ↓ External validity
- Matching Problem: 干擾因子太多, match的項目無法被測量
- Multivariate technique simultaneously control for age, race, family history, parity
- Stratification

## Mantel-Haenszel procedure

|                    |                   | Salpingitis |     | Total | Proportion with salpingitis |
|--------------------|-------------------|-------------|-----|-------|-----------------------------|
|                    |                   | Yes         | No  |       |                             |
| All women (n=2000) | Use of IUD<br>Yes | 45          | 955 | 1000  | 4.5%                        |
|                    | No                | 15          | 985 | 1000  | 1.5%                        |

Crude RR =  $\frac{4.5\%}{1.5\%} = 3.0$  (95% CI 1.7–5.4)

|                                      |                   | Salpingitis |     | Total | Proportion with salpingitis |
|--------------------------------------|-------------------|-------------|-----|-------|-----------------------------|
|                                      |                   | Yes         | No  |       |                             |
| Women with 1 sexual partner (n=1200) | Use of IUD<br>Yes | 3           | 297 | 300   | 1.0%                        |
|                                      | No                | 9           | 891 | 900   | 1.0%                        |

RR =  $\frac{1.0\%}{1.0\%} = 1.0$

|                                      |                   | Salpingitis |     | Total | Proportion with salpingitis |
|--------------------------------------|-------------------|-------------|-----|-------|-----------------------------|
|                                      |                   | Yes         | No  |       |                             |
| Women with >1 sexual partner (n=800) | Use of IUD<br>Yes | 42          | 658 | 700   | 6.0%                        |
|                                      | No                | 6           | 94  | 100   | 6.0%                        |

RR =  $\frac{6.0\%}{6.0\%} = 1.0$

## What to look for in observational studies

- **Is selection bias present?**
  - In a cohort study, are participants in the exposed and unexposed groups similar in all important respects except for the exposure?
- **Is information bias present?**
  - In a cohort study, is information about outcome obtained in the same way for those exposed and unexposed?

## What to look for in observational studies

- **Is confounding present?**
- **If the results cannot be explained by these three biases, could they be the result of chance?**
  - What are the relative risk or odds ratio and 95% CI?
  - Is the difference statistically significant, and, if not, did the study have adequate power to find a clinically important difference?

## Criteria for judgment of causal associations

- **Temporal sequence**
  - Did exposure precede outcome?
- **Strength of association**
  - How strong is the effect, measured as relative risk or odds ratio?
- **Consistency of association**
  - Has effect been seen by others?
- **Biological gradient (dose-response relation)**
  - Does increased exposure result in more of the outcome?

- **Specificity of association**
  - Does exposure lead only to outcome?
- **Biological plausibility**
  - Does the association make sense?
- **Coherence with existing knowledge**
  - Is the association consistent with available evidence?
- **Experimental evidence**
  - Has a randomized controlled trial been done?
- **Analogy**
  - Is the association similar to others?

## 結論

1. 觀察到的關係
2. 此關係是否因選擇或資訊偏差所致？
3. 此關係是否因干擾因子所致？
4. 此關係是否因chance所致？
5. 此關係是否為因果關係？