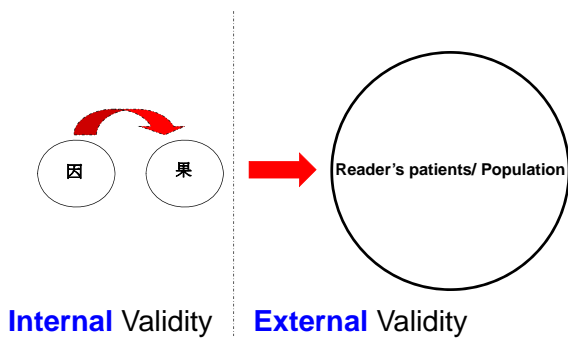**Bias and causal associations in observational research**
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1. Is the report **believable**?

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

Internal Validity   **External** Validity

（因 → 果 → Reader's patients/ Population）

Panel 1: **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?
In a case-control study, are cases and controls similar in all important respects except for the disease in question?

Is **information bias** present?
In a cohort study, is information about outcome obtained in the same way for those exposed and unexposed?
In a case-control study, is information about exposure gathered in the same way for cases and controls?

Is **confounding** present?
Could the results be accounted for by the presence of a factor—eg, age, smoking, sexual behaviour, diet—associated with both the exposure and the outcome but not directly involved in the causal pathway?

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?[11,12]
Is the difference statistically significant, and, if not, did the study have adequate power to find a clinically important difference?[13,14]

If the results still cannot be explained away, then (and only then) might the findings be real and worthy of note.

Selection Bias

- Membership bias

AMI

Non-joggers   Joggers

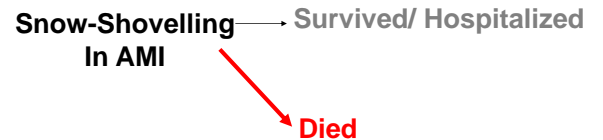? Other healthier lifestyles

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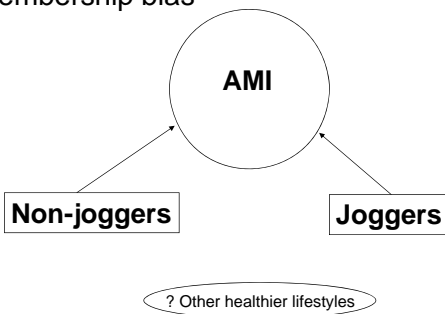
Selection Bias

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

Selection Bias

- Admission rate (Berkson) Bias
  - Exposure of interest ➜ ↑ Admission Rate
  - ↑ Odds ratio

Selection Bias

- Incidence-Prevalence (Neyman) Bias

Snow-Shovelling ——→ Survived/ Hospitalized
In AMI

Died

Selection Bias

- Unmasking (Dectection Signal) Bias
  - Exposure ➜ ↑ Outcome detection
  - (e.g. HRT ➜ symptomless endometrial cancer to bleed ➜↑ Odds ratio)

- Non-respondent Bias
  - ↓ return questionnaires in smokers

Information Bias

- Ascertainment
- Diagnostic suspicion
- Recall bias
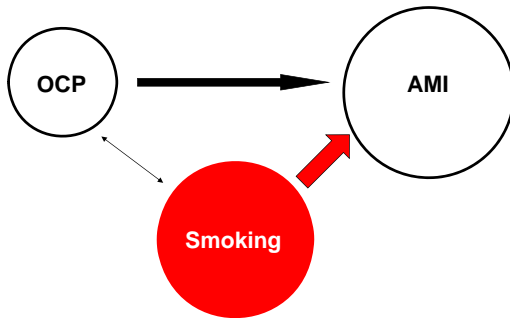
Information Bias

- Ascertainment
  - Information gathered in different ways
  - e.g. Exposure (bedside) ←→ Control (tel.)

- Diagnostic suspicion
  - ↑ intensive search for disease in exposed group

✸ **Double-blind**

Information Bias

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

Confounding

OCP → AMI

Smoking

How to Control Confounding?

- <u>Restriction</u>
  - Excludes confounding
  - ↑ Internal validity; ↓ External validity
- <u>Matching</u>
- <u>Multivariate technique</u>
- <u>Stratification</u>

Salpingitis

All women (n=2000)

Use of IUD	Yes	No	Total	Proportion with salpingitis
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)

Women with 1 sexual partner (n=1200)

Use of IUD	Yes	No	Total	Proportion with salpingitis
Yes	3	297	300	1·0%
No	9	891	900	1·0%

RR=$\frac{1·0\%}{1·0\%}$ =1·0

Women with >1 sexual partner (n=800)

Use of IUD	Yes	No	Total	Proportion with salpingitis
Yes	42	658	700	6·0%
No	6	94	100	6·0%

RR=$\frac{6·0\%}{6·0\%}$ =1·0

Panel 2: **Criteria for judgment of causal associations**[17,42,43]

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 randomised controlled trial been done?

Analogy
Is the association similar to others?