Basic Biostatistics

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Statistics for Public Health Practice

Chapter 19
Stratified 2-by-2 Tables

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In Chapter 19:

- 19.1 Preventing Confounding
- 19.2 Simpson's Paradox
- 19.3 Mantel-Haenszel Methods
- 19.4 Interaction

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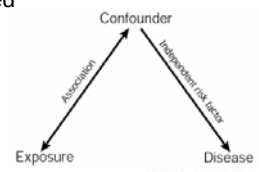
§19.1 Confounding

- **Confounding** ("to mix together") ≡ a distortion brought about by extraneous variables
- Properties of confounder:
  - Confounder is associated with the exposure
  - Confounder is an independent risk factor
  - Confounder is *not* in causal pathway



Mitigating Confounding

1. **Randomization** –balances group with respect to potential confounders (breaks the association with exposure)
2. **Restriction** – imposes uniformity in the study base; homogeneity with respect to potential confounder

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Mitigating confounding (cont.)

3. **Matching** – balances potential confounders; require special analytic techniques (e.g., §18.6)
4. **Regression models** – mathematically adjusts for confounding variables
5. **Stratification** – subdivides data into homogenous groups, then pools results

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§19.2 Simpson's Paradox

An extreme form of confounding in which in which the confounding variable reverses the direction the association

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Accident Evacuation
Crude Analysis

	Died	Survived	Total
Helicopter	64	136	200
Road	260	840	1100

Relative Risk, crude = (64/200) / (260/1100)
= .32 / .2364
= 1.35

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Accident Evacuation
Serious Accidents

	Died	Survived	Total
Helicopter	48	52	100
Road	60	40	100

Relative Risk, stratum 1 = (48 / 100) / (60 / 100)
= .48 / .60
= 0.80

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Accident Evacuation
Minor Accidents

	Died	Survived	Total
Helicopter	16	84	100
Road	200	800	1000

Relative Risk, stratum 2 = (16 / 100) / (200 / 1000)
= .16 / .20
= 0.80

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Accident Evacuation
Properties of Confounding

- Seriousness of accident (C) is associated with helicopter evacuation (E)
- Seriousness of accident (C) is an independent risk factor for death (D)
- Seriousness of accident (C) is *not* in the causal pathway between helicopter evacuation and death (the helicopter evaluation does not cause the accident to become more serious)

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Notation

- Subscript *k* indicates stratum number
- Strata-specific *RR* estimates: *RR*-hat$_k$

Table 19.4 Notation, stratum *k*

Group	Success	Failure	Total
Treatment	a_{1k}	b_{1k}	n_{1k}
Control	a_{2k}	b_{2k}	n_{2k}
Total	m_{1k}	m_{2k}	n_k

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Mantel-Haenszel
Summary Relative Risk

Combine strata-specific *RR*^s to derive a single **summary measure of effect** "adjusted" for the confounding factor

$$\hat{RR}_{\text{M-H}} = \frac{\sum \frac{a_{1k} n_{2k}}{n_k}}{\sum \frac{a_{2k} n_{1k}}{n_k}}$$

Calculate by computer

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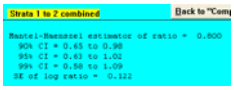
WinPEPI > Compare2 >A.

Input

Output



RR-hat$_{M\text{-}H}$ = 0.80 (95% CI for RR: 0.63 – 1.02)

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Mantel-Haenszel Test

Step A: H_0: no association (e.g., $RR_{M\text{-}H} = 1$)

Step B: WinPEPI > Compare2 > A. > Stratified

Step C:

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Mantel-Haenszel test:
  chi-square (DF = 1)   =  3.460   P = 0.063
  continuity-corrected  =  3.110   P = 0.078
```

Step D: P = .063 or P = .2078 (cont-corrected)
⇒ evidence against H_0 is marginally significant

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Other Mantel-Haenszel Summary Estimates

Mantel-Haenszel methods are available for odds ratio, rate ratios, and risk difference

Same principle apply (stratify & use M-H to summarize and tests

Covered in text, but not covered in this presentation

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19.4 Interaction

- Statistical interaction = heterogeneity in the effect measures, i.e., different effects within subgroups
- Do not use Mantel-Haenszel summary statistics when interaction exists ⇒ this would hide the non-uniform effects
- Assessment of interaction
  - Inspection!
  - Hypothesis test

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Inspection

Asbestos, Lung Cancer, Smoking

Case-control data

Table 19.7 Stratum 1 (Smokers).

	Lung CA+	Lung CA−
Asbestos +	75	20
Asbestos −	5	80

$$\widehat{OR}_1 = \frac{75 \cdot 80}{20 \cdot 5} = 60.00$$

Too heterogeneous to summarize with a single OR

Table 19.8 Stratum 2 (Nonsmokers).

	Lung CA+	Lung CA−
Asbestos +	5	18
Asbestos −	10	72

$$\widehat{OR}_2 = \frac{5 \cdot 72}{18 \cdot 10} = 2.00$$

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Test for Interaction

Overview

A. H_0: no interaction vs. H_a: interaction

B. Various chi-square interaction statistic exist (Text: ad hoc; WinPEPI: Rothman 1986 or Fleiss 1981)

C. Small P-value ⇒ good evidence against H_0 ⇒ conclude interaction

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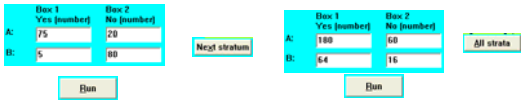
Test for Interaction
Asbestos Example

A. H_0:$OR_1 = OR_2$ (no interaction) versus
H_a:$OR_1 \neq OR_2$ (interaction)

B. WinPEPI > Compare2 > A. > Stratified ⇒

Input



OR-hat$_1$ = 60

OR-hat$_2$ = 2

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Test for Interaction
Asbestos Example

C. Output:

```
Heterogeneity of odds ratios:
  chi-sq (DF: 1) = 21.38    P = 0.000 [ 3.8E-6 ]
```

D. Conclude: Good evidence of interaction ⇒
avoid MH and other summary adjustments

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