Matched Case-Control Study

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Learning Objectives

- Strategies to select cases and controls and to analyze data in pair-matched case-control studies.
- Identify strengths and limitations of case-control studies.

Case-Control Study

An epidemiological study in which a group of persons with the disease of interest (case group) and a group of persons similar to the case group but not having the disease (control group) are selected to compare the proportion of persons exposed to a risk factor of interest in order to elucidate the causal relationship of the risk factor of interest and the disease.

Interpretation of Odds Ratio - same as relative risk:

- OR = 1: exposure is not related to disease.
- OR > 1: a positive association (E is associated with increased risk of D).
- OR < 1: a negative association (E is associated with a lower risk of D).

What we need to know about a case-control study

From Table 2 of the AJE Paper (Costello et al)

1974 – 1989 Exposed to both agent vs. not exposed

Odds ratio =(74*113)/(39*93)=2.31

		1st Step: Select cases and controls	
2nd step:	Exposure	Diseased (Cases)	Non-diseased (controls)
Past Exp to both Pesticides	Yes	74	39
	No	93	113
	Total	167	152

The authors reported OR=2.14 (1.24, 3.68). Why different from 2.31 above?

They adjusted for age, sex, nonwhite race, education, and smoking status! Why?

Matching

- Select controls who are identical to cases on potential confounders

  – Pair match, frequency match

  – Better control for confounding, especially when the distributions of a confounder do not have much overlap between the cases and the source population (e.g., if cases of myocardial infarction tend to be older)

  – Matched controls represent the source population within each level of the matched variable

- Pair-matched data (Koepsell and Weiss, P 389)

	Controls	
Cases	Exposed	Non-exposed
Exposed	a	b
Non-exposed	c	d

  – Odds ratio = b/c

- 1:n matched data, see a biostatistics or advanced epidemiology textbook

- Pair-matched data: estrogens and endometrial carcinoma; matched on age at diagnosis (within 4 years) and year of diagnosis (within 2 years) (Hennekens and Buring, P 300)

	Controls		
Cases	Exposed	Non-exposed	Total
Exposed	39	113	152
Non-exposed	15	150	165
Total	54	263	317

  – Odds ratio = 113/15 = 7.5

- Unmatched analysis of pair-matched data: estrogens and endometrial carcinoma (Hennekens and Buring, P 302)

	Cases	Controls	Total
Exposed	152	54	206
Non-exposed	165	263	428
Total	317	317	634

  – Odds ratio = (152*263)/(54*165)= 4.5, biased towards null
  – The stronger the confounding, the stronger the bias.

- Pair-matched data: Tobacco use and acoustic neuroma (Bergenheim M, et al, AJE, 2012;175:1243-1251)
- Matched on age (within 5 years), sex, and place of residence
- 2 controls were attempted to be enrolled for 1 case
- Analysis: conditional logistic regression stratified by matched set with adjustment for potential confounders (Table 2 on P 1247)

- Strengths (compared to cohort studies)

  - Efficient

    Small sample size (rare disease)

    Less time (disease with long induction and latent period)

    Less expensive (small N, efficient for exposure that is expensive to measure)

- Limitations

  - Inefficient for rare exposure
  - Selection bias (Are cases representative? Do controls represent the source population?)
  - Challenge in measurement of exposure (measure exposure after the occurrence of disease)
  - Difficulty in determine temporality
  - Only one disease is studied
  - Incidence of disease cannot be studied, though OR is intended to estimate the relative risk (incidence ratio).

Summary of Observational Studies

- Cross-sectional Study
- Cohort Study
- Case-control study
  - Matched case-control study

Things to remember:

- Low response rate in cross-sectional study
- Low follow-up rate in cohort study
- Selection bias in case-control study
- Information (misclassification) bias in all studies
- Confounding bias in all studies
- Use the most appropriate analytical methods
- Work with your epidemiologists and biostatisticians **early**.