Study Design II: Case-Control Studies

Stephen McCurdy, M.D., M.P.H.

Department of Public Health Sciences

U.C. Davis School of Medicine

CASE-CONTROL STUDIES

Life's a journey. . .

The "study base" is a population of individuals, each carrying the burden of personal and group risk factors.

(Rothman and Greenland, Modern Epidemiology, 1998)

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A cohort study design follows the study base through time and observes whether persons with a given risk factor are more likely to *develop new disease* than are those without the risk factor.

We look at the relative risk in the exposed compared to unexposed.

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In a case-control study, we wait for people to develop the disease. We then look at the level of the risk factor in a group of case subjects compared to a group of healthy, or control, subjects.

If the level of the putative risk factor is higher in the cases, it implies an association between risk factor and disease.

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Objectives

Review case-control design

- -Utility
- -Odds ratio as outcome measure
- -Strengths
- -Limitations

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General Approach:

- > Define Research Question
- > Identify Case Population
- > Identify Control Population
- > Measure Variables

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Basic Idea:

Cases – Should represent all cases in the population

Controls – Should represent all persons without disease in the population

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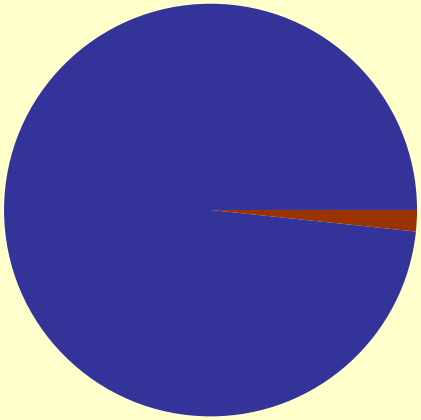
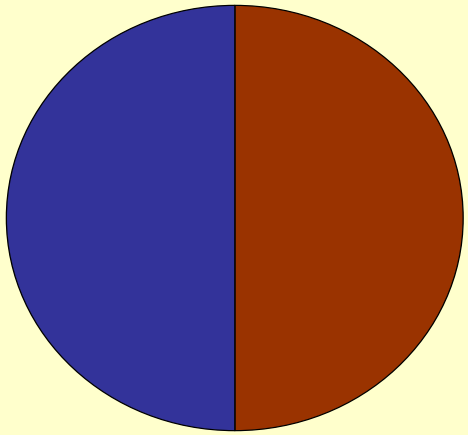
Population



- Lung Cancer Cases
- Healthy

Sample



- Lung Cancer Cases
- Control

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The Big Question

Is the Risk Factor more common in the cases than in the controls?

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Sources of Cases and Controls

Population-Based

- **Cases – from Registry (fed by population)**
- **Controls – from General Population**

Hospital-Based

- **Cases - selected group that made it to hospital**
- **Controls – as above**

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Temporality

Retrospective: At beginning of study, "Look back in time" to select all case and control subjects

Prospective: At beginning of study, "Look forward in time" to catch new cases as they are diagnosed.

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	(+)	(-)
	Case	Control
RF (+)	50	20
RF (-)	50	80

BASIC IDEA

Is the risk factor more common among cases than controls?

100 100

RF PREVALENCE FOR CASES **50/100=50%**

RF PREVALENCE FOR CONTROLS **20/100=20%**

PREVALENCE RATIO = **50% / 20% = 2.5**

CASE-CONTROL STUDIES

	(+)	(-)
	Case	Control
RF (+)	50	20
RF (-)	50	80

BASIC IDEA

Is the risk factor more common among cases than controls?

ODDS FOR CASES **50:50 = 1**

ODDS FOR CONTROLS **20:80 = 0.25**

ODDS RATIO = **50:50/20:80 = 1/0.25 = 4**

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Exp \ Disease	(+)	(-)
(+)	a	b
(-)	c	d

$$\text{Relative Risk} = \frac{a/(a+b)}{c/(c+d)}$$

For rare diseases, a is small compared to b, and c is small compared to d. So. . . . .

$$\text{Relative Risk} = \frac{a/(a+b)}{c/(c+d)} \approx \frac{a/b}{c/d} = \frac{a/c}{b/d} = \text{Odds Ratio}$$

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Bottom line:

Only cohort studies (including clinical trials) can yield incidence and relative risk.

The odds ratio, (e.g., from a case-control study) will always be greater than the relative risk. For rare diseases, the odds ratio will be close to the relative risk.

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Strengths:

- Efficient, cost-effective for rare outcomes

Weaknesses:

- ? Sequence of events ?
- Only one outcome
- Does not yield incidence or relative risk (although in some cases these can be inferred using external information)
- **BIAS**

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BIAS!

Selection

&

Information

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Selection Bias:

Cases may not represent population with disease

Controls may not represent population without disease

E.g. : Misdiagnosis

SES

Health Status

Risk Factors of Interest

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Information Bias

Measurement Different for Cases and Controls

E.g. : Recall bias

Observer bias

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Fighting Information Bias

> Use data collected before outcome occurred

> Standardized, objective variables

> Blind subjects, observers

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Fighting Bias

> Sample cases and controls in the same way (biases “cancel out”)

> Matching

> Multiple control groups

> Population-based sample

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Savitz, et al. EMF and childhood cancer. Am J Epidemiol 1990; 131:763

Introduction:

Exposures to electromagnetic radiation may be associated with increased risk for certain rare childhood tumors.

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Method: Population-based
Prospective case-control

Cases: All incident cases of childhood (<15 yo) cancer in Denver registry, 1976-1983

Controls: Random-digit dialing match on sex, age ± 3y

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Results

Electric Blanket	Brain Cancer: Case	Brain Cancer: Control
(+)	11	31
(-)	34	175

Case Odds:

11/34 = 0.32

Control Odds:

31/175 = 0.18

Odds Ratio:

0.32/0.18 = 1.8

(95% CI = 0.9 – 4.0)

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Other Points:

-Income was an important confounder; adjustment increased the odds ratio (from 1.8 to 2.5)

-Association strongest for

-First trimester use

-Early cancers

-Dose-Response effect was present

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