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Statistics in Evidence Based Medicine

Lecture 8: Analysis of study designs for binary outcomes (Proportions and Odds)

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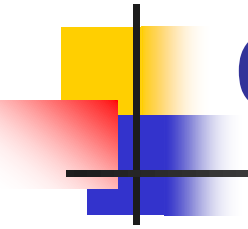

Overview

- Summary statistics for binary data
  - Clinical trials
  - Cohort study design
  - Case-control study design
  - Cross-sectional study design

- What summary statistics to use?

Binary Outcomes

A binary data takes only one of two values

Examples:

Alive or dead, Sick or Well, Exposed or Unexposed *etc*

We can find proportions for binary outcomes

Proportion (*p*)

A proportion represents a situation where the numerator and denominator both represent counts, and the numerator is a subset of the denominator.

A proportion always lies between 0 and 1

An Example of Proportions

Physicians' Health Study 1989

Aspirin for reduction of Myocardial Infarction

	MI Yes	MI No	Total
Aspirin Group	139	10,898	11,037
Placebo Group	239	10,795	11,034

Proportion of physicians who had an MI in aspirin group = 139/11,037

Proportion of physicians who had an MI in placebo group =239/11,034

Proportions are risks

How to compare risks between groups?

Absolute Risk Difference (ARD)

Risk of an MI in aspirin group p_1 = 139/11,037 = 0.0126

Risk of an MI in placebo group p_2= 239/11,034 = 0.0217

ARD=$|p_1-p_2|$=|0.0126 –0.0217|=0.0091

Interpretation per 10,000 persons:

The risk of MI in aspirin group was 126 per 10,000 people (0.0126×10,000) and risk of MI in placebo group was 217 (0.0217×10,000).

An extra 91(0.0091×10,000)people had an MI under placebo.

Number Needed to Treat (NNT)

How many persons would be treated with aspirin to save one more extra person from MI?

NNT=1/ARD=1/0.0091=109.89

110 persons needed to treat to save one more MI case

Determining Ratios of Risks

Risk of an MI in aspirin group p_1 = 139/11,037 = 0.0126

Risk of an MI in placebo group p_2= 239/11,034 = 0.0217

What if we divide the risks?

Risk of an MI in placebo group/Risk of an MI in aspirin group

= p_2 / p_1= 0.0217/0.0126=1.72

How to interpret the number 1.72?

Placebo group was 1.72 times more likely to have an MI than the aspirin group. Placebo group was at a 72% increased risk of MI than aspirin group.

Relative Risk (RR)

Risk of an MI in aspirin group p_1 = 139/11,037 = 0.0126

Risk of an MI in placebo group p_2 = 239/11,034 = 0.0217

What if we divide risks the other way?

Division of risks gives us Relative Risk (RR)

Risk of an MI in aspirin group/Risk of an MI in placebo group=0.581

How to interpret the number 0.581?

The Relative Risk of MI in aspirin group compared with placebo group is 0.581.

Relative Risk Reduction

When Relative Risk is less than 1

RRR=$(p_2 - p_1)/p_2$= ARD/p_2= 1 − RR

Relative Risk of MI with aspirin compared to placebo = 0.581

RRR=1 − 0.581=0.419

42% reduced risk of MI in aspirin group

compared with baseline group (placebo)

Clinical Trial

In a clinical trial an intervention such as new drug (treatment group) is compared with a placebo or standard therapy (control group) for an outcome (efficacy /safety) among humans.

Clinical Trials

Clinical Trial and Relative Risk

	Outcome Yes	Outcome No	Total
Treatment group	a	b	$a+b = N_1$
Control group	c	d	$c+d = N_2$
Total	$a+c = M_1$	$b+d = M_2$	$T = a+b+c+d$

Risk in treatment group $p_1 = a/N_1$

Risk in control group p_2 (baseline risk) = c/N_2

$$\text{Relative Risk} = \frac{p_1}{p_2} = \frac{a/N_1}{c/N_2}$$

Other Summary Statistics

- Risk Difference or Absolute Risk Difference
  ARD=$|p_1-p_2|$
- Number needed to treat NNT =1/ARD
  - Number needed to treat for harm NNTH= 1/ARD
- Relative Risk Reduction

$$RRR = (p_2 - p_1)/p_2 = ARD/p_2 = 1-RR$$

  - When RR<1
  - Often expressed as a percentage

Absolute Risk Difference vs. Relative Risk Reduction

- Absolute Risk Difference provides number needed to treat (NNT), so may be more helpful.
- If RRR is reported, multiply this with risk in control group (p_2) to get ARD.

$$\text{RRR} = \text{ARD}/p_2 \longrightarrow \text{ARD} = \text{RRR} \times p_2$$

Cohort study and Relative Risk

In a cohort study, a group without the disease is followed up to see who develops it, and disease incidence in persons with a characteristic (risk factor) is compared with incidence in persons without the characteristic (risk factor).

Statistical Analysis: Risk Ratio or Relative Risk or Cumulative Incidence Ratio(RR, CIR)

Cohort Study

The Lancet, Volume 314, Issue 8140, Pages 458 - 461, 1 September 1979
doi:10.1016/S0140-6736(79)91505-8 Cite or Link Using DOI

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ANTICONVULSANT DRUGS AND CANCER A Cohort Study in Patients with Severe Epilepsy

SusanJ. White , AndréE.M. Mclean , Catherine Howland

Abstract

Over 2000 epileptic patients admitted to the Chalfont Centre for Epilepsy between 1931 and 1971 and taking anticonvulsants were followed up to the end of 1977. Mortality between 1951 and 1977 was greatly in excess of that in the general population of England and Wales in that period allowing for age and sex. Some of the excess was directly attributable to epilepsy, but there were also more deaths from suicide and circulatory, respiratory, and malignant disease than would be expected. Apart from the brain and central nervous system, no particular site had a significant excess of tumours. In particular, there were no liver tumours (and only one gallbladder carcinoma). This makes it unlikely that the liver tumours produced on feeding phenobarbitone

Cohort Study and Relative Risk

Exposure (Risk Factor)	Outcome (Disease)	Yes	No	Total
	Yes	a	b	$a+b=N_1$
	No	c	d	$c+d=N_2$
	Total	$a+c=M_1$	$b+d=M_2$	$T=a+b+c+d$

Risk of disease among exposed $p_E = a/N_1$

Risk of disease among unexposed p_{NE} (baseline risk) = c/N_2

$$\text{Relative Risk(RR)} = \frac{a/N_1}{c/N_2}$$

A Cohort Study
Eating Fish Reduces the Risk of Stroke

Intake of animal products and stroke mortality in the Hiroshima/Nagasaki Life Span Study

Sauvaget C, Nagano J, Allen N, et al. (2003)

International Journal of Epidemiology

Risk factor present = Not eating fish at all

Risk factor absent = Eating fish

Eating Fish Reduces the Risk of Stroke

	Stroke Yes	Stroke No	Total
Risk factor Yes (Don't eat fish)	82	1549	1631
Risk factor No (Eat fish)	23	779	802
Total	105	2328	2433

$$\text{Risk of stroke among exposed } p_E = \frac{82}{1631} = 0.0503$$

$$\text{Risk of stroke among unexposed } p_{NE} = \frac{23}{802} = 0.0287$$

$$RR = \frac{0.0503}{0.0287} = 1.75$$

Interpretation of Relative Risk

RR=1.75

Those who don't eat fish are 1.75 times more likely to have stroke than those who eat fish.

Case-Control Study

A case-control study is one in which “cases” (persons with disease) are identified, “controls” (similar to cases but disease free) are identified, and the two groups are compared with respect to prior exposure to risk factor.

We can’t compute Relative Risk directly in a case-control study. Instead we calculate Odds Ratio.

Case-Control Study

Epilepsia
The Journal of the International League Against Epilepsy

Read the president's paper on the future

Predictors of Intractable Epilepsy in Childhood: A Case-Control Study

Anne T. Berg[1,*], Susan R. Levy[2], Edward J. Novotny[2], Shlomo Shinnar[3]

Article first published online: 3 AUG 2005

DOI: 10.1111/j.1528-1157.1996.tb00507.x

Issue

Epilepsia

Volume 37, Issue 1, page 24–30, January 1996

Validity of Relative Risk in a Case-Control Study

	Case	Control	Total
Exposed	a	b	a+b
Not exposed	c	d	c+d
Total	a+c	b+d	a+b+c+d

$$\text{Relative Risk} = \frac{\text{Risk of disease among exposed}}{\text{Risk of disease among unexposed}} = \frac{a/a+b}{c/c+d}$$

What if we double controls?

	Case	Control	Total
Exposed	a	2b	a+2b
Not exposed	c	2d	c+2d
Total	a+c	2b+2d	a+2b+c+2d

$$\text{Relative Risk} = \frac{a/a+2b}{c/c+2d}$$

Odds (*o*)

The odds (*O*) of an event are the likelihood of an event occurring **divided** by the likelihood of event not occurring

Odds can lie between zero and infinity

Odds are ratios of proportions

Example of Odds

Male Lung Cancer & Smoking (Doll and Hill 1950)

	Lung cancer (Case)	Control
Smokers	647	622
Non-smokers	2	27

$$\text{Odds of smoking among Cases} = \frac{647}{2}$$

$$\text{Odds of smoking among Controls} = \frac{622}{27}$$

$$\text{Odds of lung cancer among Smokers} = \frac{647}{622}$$

$$\text{Odds of lung cancer among Non-smokers} = \frac{2}{27}$$

Comparing Groups With Respect to Smoking

Odds of smoking in cases =647:2 = 647/2

Odds of smoking in controls =622:27 = 622/27

We obtain Odds Ratio by division of odds

Odds of smoking in cases/ Odds of smoking in controls =

$$\text{Odds Ratio} = \frac{647/2}{622/27} = \frac{647 \times 27}{2 \times 622} = 14.04$$

The odds of smoking in lung cancer patients were 14 times the odds of smoking in controls

Comparing Groups With Respect to Lung Cancer

Odds of lung cancer in smokers =647:622 = 647/622

Odds of lung cancer in controls =2:27 = 2/27

What if we divide again? We obtain odds Ratio

Odds of lung cancer in smokers/ Odds of lung cancer in non-smokers =

$$\frac{647/622}{2/27} = \frac{647 \times 27}{2 \times 622} = 14.04$$

The odds of lung cancer in smokers were 14 times the odds of lung cancer in non-smokers

Odds Ratio for a Case-Control Study

	Case	Control	Total
Exposed	a	b	a+b
Not exposed	c	d	c+d
Total	a+c	b+d	a+b+c+d

odds of exposure in cases= a/c

odds of exposure in controls=b/d

$$\text{Odds Ratio} = \frac{a/c}{b/d} = \frac{ad}{bc}$$

Odds Ratio is symmetrical

Odds Ratio Approximates Relative Risk for a Rare Disease

	Case	Control	Total
Exposed	a	b	a+b
Not exposed	c	d	c+d
Total	a+c	b+d	a+b+c+d

When a disease is rare

$$\frac{a}{a+b} \cong \frac{a}{b} \;\&\; \frac{c}{c+d} \cong \frac{c}{d}$$

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

Other Uses of Odds Ratios

- Odds Ratios are used in all kind of studies
  - Odds Ratios have nice mathematical properties
  - Odds Ratios are results of Logistic regression. Logistic regression adjusts for confounding
- A common way to present results of a meta analysis

Cross-Sectional Study

In a cross-sectional study people are observed at a single point in time. We inquire what is happening right now? We can investigate prevalence of disease and exposure to risk factors.

Examples; Surveys, Registries reports etc

Cross-Sectional Study

J Vet Intern Med. 2002 May-Jun;16(3):262-8.

A cross-sectional study of epilepsy in Danish Labrador Retrievers: prevalence and selected risk factors.

Berendt M, Gredal H, Pedersen LG, Alban L, Alving J.

Department of Clinical Sciences, The Royal Veterinary and Agricultural University of Copenhagen, Denmark. meb@kvl.dk

Abstract

The purpose of this study was to investigate the prevalence and selected risk factors of epilepsy, the proportion of dogs with epilepsy in remission, and the types of seizures in Danish Labrador Retrievers. A prospective cross-sectional study of epilepsy was conducted in 1999-2000. The study was carried out in 2 phases in a reference population consisting of 29,602 individuals. In phase 1, 550 dogs were selected by random sampling stratified by year of birth. A telephone interview was used to identify dogs with possible epilepsy. In phase 2, dogs judged during phase 1 as possibly suffering from epilepsy were further subjected to physical and neurologic examination, CBC, blood chemistry, and a questionnaire on seizure phenomenology. Seventeen dogs were diagnosed with epilepsy, yielding a prevalence of 3.1% (95% CI 1.6-4.6%) in the

Analysis of a Cross-Sectional Study

Exposure (Risk Factor)	Outcome (Disease)	Yes	No	Total
	Yes	a	b	$a+b=N_1$
	No	c	d	$c+d=N_2$
	Total	$a+c=M_1$	$b+d=M_2$	$T=a+b+c+d$

$$\text{Prevalence of disease} = \frac{M_1}{T}$$

$$\text{Prevalence of Exposure} = \frac{N_1}{T}$$

$$\text{Odds Ratio} = \frac{ad}{bc}$$

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

What Summary Statistic to use?

- For prospective studies (clinical trials/cohort) quote Relative Risk.
- For case-control studies quote Odds Ratio.
- Odds Ratio approximates Relative Risk for a rare disease in case-control studies.
- For a cross-sectional study one has a choice between Odds Ratio and Relative Risk.

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Questions/Comments

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Thank you for being patient !