www.epilepsy.va.gov/Statistics

Statistics in Evidence Based Medicine (2014)

Lecture 1: Understanding Relative Risks and Odds Ratios

Rizwana Rehman, PhD
Regional Statistician
Southeast Epilepsy Center of Excellence
Durham VA Medical Center, Durham NC
Rizwana.Rehman@va.gov
(919)286-0411 ext: 5024

Epilepsy Center of Excellence
SOUTHEAST

Course outline

Understanding logistic regression in five lectures

Difference between relative risk and odds ratio, marginal and conditional odds ratios, terminology and interpretation of logistic regression, matched data analysis

Suggested Book: Logistic Regression A Self-Learning Text by Kleinbaum & Klein

Third Edition Springer

Today's Lecture

- Definitions
  - Odds Ratios and Relative Risk
- Uses in Study Designs
  - Interpretation and appropriate use
  - Examples

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?

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 (probabilities)

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.

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?

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

Division of risks gives us Relative Risk (RR)

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)

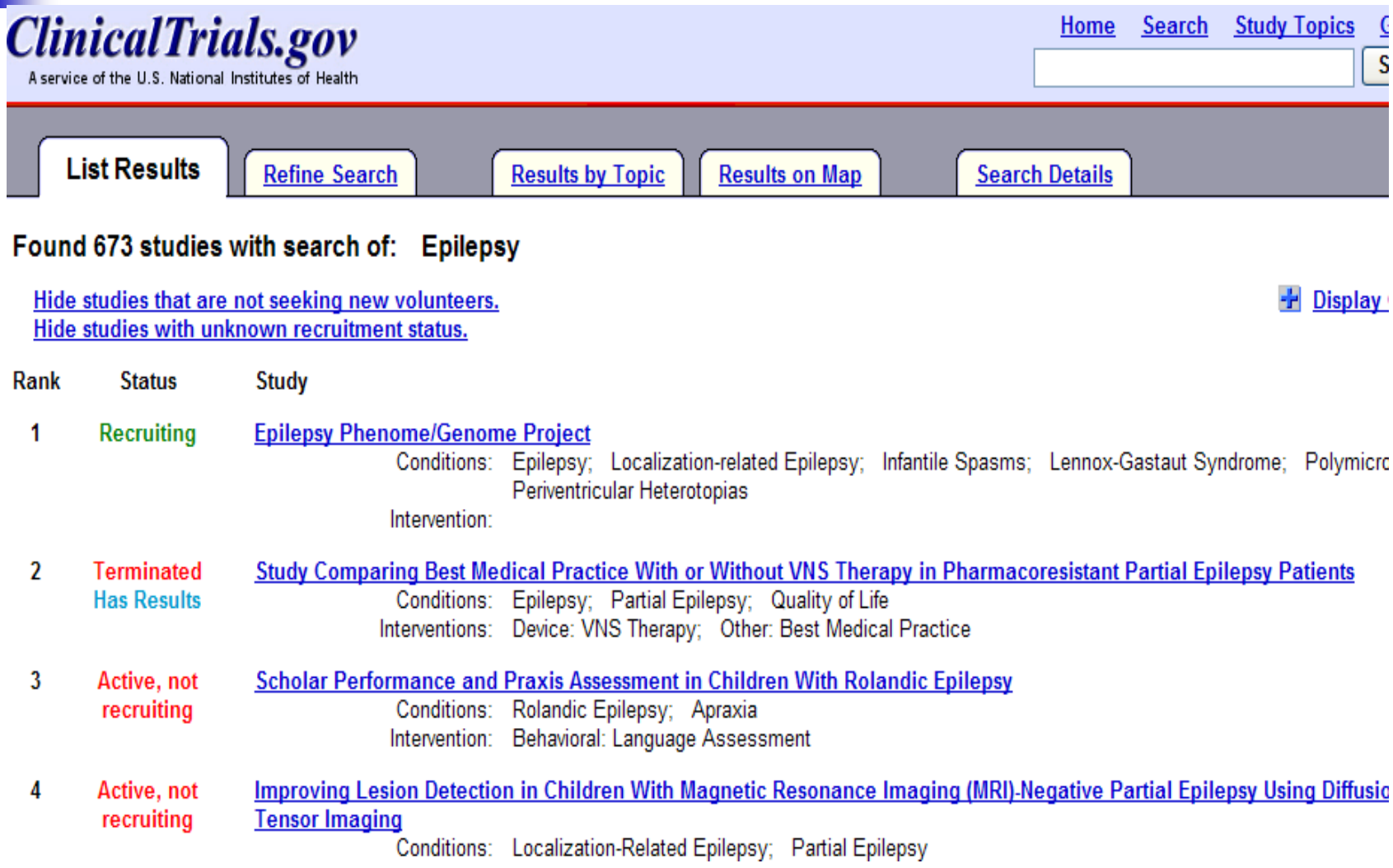
Use of Relative Risk in Study Designs

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

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

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

Absolute Risk Difference vs. Relative Risk Reduction

- Absolute Risk Difference provides number needed to treat (NNT), so may be more helpful.

$$NNT = 1/ARD$$

- If RRR is reported, multiply this with risk in control group (p_2) to get ARD.

$$RRR = ARD/p_2 \Longrightarrow ARD = RRR \times p_2$$

Prospective 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

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

< Previous Article | Next Article >

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 Broiled 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 broiled fish at all

Risk factor absent = Eating broiled 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 never eat fish are 1.75 times more likely to have stroke than those who eat fish almost daily.

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.

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

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

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
- For a 2×2 table divide the counts of occurrence of an event by counts of non occurrence of an event

Odds can lie between zero and infinity

Odds are ratios of proportions

Relationship between odds and probability

- To calculate the odds (o) from Probability (p)

$$\text{Odds}=\frac{p}{1-p}$$

- To calculate the probability from Odds

$$\text{Probability}=\frac{o}{1+o}$$

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

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

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

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.

Example: Lung cancer among women in the US

In the US, the estimated annual probability that a women over the age of 35 dies of lung cancer equals 0.001304 for current smokers and 0.000121 for non smokers(*M Pagano and K. Gauvreau, principles of Biostatistics, 1993, p.134*).

a. Find and interpret the difference of proportions and the relative risk. Which measure is more informative for these data and why?

b. Find and interpret the odds ratio. Is odds ratio almost equal to relative risk? Why?

Example: Lung cancer among women in the US

In the US, the estimated annual probability that a women over the age of 35 dies of lung cancer equals 0.001304 for current smokers and 0.000121 for non smokers(*M Pagano and K. Gauvreau, principles of Biostatistics, 1993, p.134*).

ARD=0.001304-0.000121=0.001183

RR=0.001304/0.000121=10.777

RR is more informative than ARD

Example: Lung cancer among women in the US

In the US, the estimated annual probability that a women over the age of 35 dies of lung cancer equals 0.001304 for current smokers and 0.000121 for non smokers(*M Pagano and K. Gauvreau, principles of Biostatistics, 1993, p.134*).

$$\text{Odds Ratio} = \frac{0.001304/(1-0.001304)}{0.000121/(1-0.000121)} = 10.79$$

Odds Ratio ≈ Relative Risk

because both probabilities are very small

Misinterpretation of Odds Ratios

A research study estimated that under a certain condition, the probability that a subject would be referred for heart catheterization was 0.906 for whites and 0.847 for blacks. A press release about the study stated that the odds of referral for cardiac catheterization for blacks are 60% of the odds for whites. Explain how they obtained 60% (more accurately 57 %)

$$\frac{0.847/(1-0.847)}{0.906(1-0.906)} = \frac{0.847(1-0.906)}{0.906(1-0.847)} = 0.574$$

For details see New Engl. J. Med. 341: 279-283, 1999

Misinterpretation

An associated press story later described the study and said. **"Doctors were only 60% as likely to order cardiac catheterization for blacks as for whites".**

What is wrong with above interpretation? What is the correct percentage for this interpretation?

News story interpreted odds ratio as relative risk.

For correct interpretation

$$RR=\frac{0.847}{0.906}=93.488\%$$

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

www.epilepsy.va.gov/Statistics

Questions/Comments

Rizwana.Rehman@va.gov

(919) 286-0411 ext: 5024

Thank you for being patient !