Measures of Association

UI-MEPI-J: Research Design and Methodology Workshop, May 10 - 12, 2016

Risk Ratio and Odds Ratio

- The **risk ratio** (or relative **risk**) is the **ratio** of the **risk** of an event in the two groups.
- odds **ratio** is the **ratio** of the odds of an event

```
                          ILL
     VANILLA    |     +      - | Total
     -----------+-------------+------
              + |    43     11 |    54
              - |     3     18 |    21
     -----------+-------------+------
          Total |    46     29 |    75

                    Single Table Analysis

Odds ratio                                                  23.45
Cornfield 95% confidence limits for OR  5.07 < OR < 125.19*

RISK RATIO(RR)(Outcome:ILL=+; Exposure:VANILLA=+)          5.57
95% confidence limits for RR                1.94 < RR <  16.03
            Ignore risk ratio if case control study

                         Chi-Squares   P-values
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Measures of Association

CDC. Oswego – An Outbreak of GI Illness Following a Church Supper., 1997 ed. 1940


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Measures of Association

CDC. Oswego – An Outbreak of GI Illness Following a Church Supper., 1997 ed. 1940

Measures of Association — Objectives

- Describe measures of association (e.g., *risk ratio, odds ratio)* and their use
- Identify which measure of association is most appropriate for each type of epidemiologic study
- Describe when an odds ratio approximates the risk ratio and when it does not

Risk

$$\frac{\text{\# new cases during a specified period}}{\text{size of population at start of period}}$$

= "Attack rate"
= Probability of getting disease
= Risk of disease
= Cumulative incidence
= Incidence proportion

Risk Calculations from NHANES Follow-up Study

- Deaths in diabetic men
  - 100 deaths
  - 189 men at start of follow-up period
  - Risk = 100/189 = 0.529 = 52.9%
- Deaths in nondiabetic men
  - 811 deaths
  - 3151 men at start of follow-up period
  - Risk = 811/3151 = 0.257 = 25.7%

Ref: Kleinman J, et al. Mortality among diabetics in a national sample. Am J Epidemiol 1988; 128:389-401.

Risk Calculations from Circumcision-HIV Study

- HIV seroconversion in circumcised men
  - 18 seroconversions
  - 908 men at start of follow-up period
  - Risk = 18 / 908 = 0.0198 = 1.98%
- HIV seroconversion in uncircumcised men
  - 154 seroconversions
  - 4608 men at start of follow-up period
  - Risk = 154 / 4608 = 0.0334 = 3.34%

Ref: Gray RH et al. Male circumcision and HIV acquisition and transmission: cohort studies in Rekai, Uganda. AIDS 2000; 14:2371–2381.

Example of Risk Calculation

- Ate vanilla ice cream
  43 ill / 54 ate vanilla ice cream
  Risk = 43 / 54 = 0.796 = 79.6%
- Did not eat vanilla ice cream
  3 ill / 21 did not eat vanilla ice cream
  Risk = 3 / 21 = 0.143 = 14.3%
- All study participants
  46 ill / 75 participants
  Risk = 46 / 75 = 0.613 = 61.3%

CDC. Oswego – An Outbreak of GI Illness Following a Church Supper., 1997 ed. 1940

Person-Time Rate – Example

Deaths in diabetic men
If all had been enrolled in 1971, and if none had died, and if all had been followed through 1984, then:

189 × 13 years of observation = 2457 PY f/u

But some were enrolled in 1972 - 1975, and 100 had died, and some were followed to 1982 or 1983. So, only 1414.7 actual PY of follow-up.

Rate = 100 / 1414.7 PY
= 70.7 deaths / 1,000 PY

Ref: Kleinman J, et al. Am J Epidemiol 1988; 128:389-401.

Person-time

- Person-time is an estimate of the actual time-at risk in years, months, or days that all persons contributed to a study.
- In certain studies people are followed for different lengths of time, as some will remain disease-free longer than others.

Person-time (contd.)

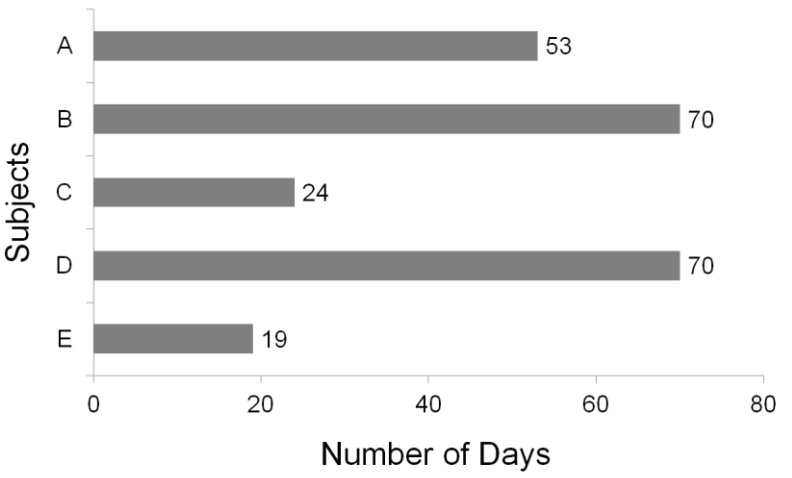
- A subject is eligible to contribute person-time to the study only so long as that person remains disease-free and, therefore, still at risk of developing the disease of interest.
- By knowing the number of new cases of disease and the person-time-at-risk contributed to the study, an investigator can calculate the incidence rate of the disease, or how quickly people are acquiring the disease.

Person-time (contd.)

Calculating person-time

- Suppose an investigator is conducting a study of the incidence of second myocardial infarction (MI).
- He therefore follows 5 subjects from baseline (first MI) for up to 10 weeks. The results are graphically displayed as follows:

Person-time (contd.)



Person-time (contd.)

- The graph shows how many days each subject remained in the study as a non-case (no second MI) from baseline.
- The unit for person-time in this study is person-days (p-d).

- **Time contributed by each subject:**

  Subject A: 53 days; Subject B: 70 days; Subject C: 24 days; Subject D: 70 days; Subject E: 19 days
- **Total person-days in the study**:

  53+70+24+70+19=**236** person-days

Odds

- Odds *in favor of* an event =

$$\frac{\text{probability that event will occur}}{\text{probability that event will NOT occur}}$$

- Odds of disease =

$$\frac{\text{probability of disease}}{1 - \text{probability of disease}}$$

or, more simply,

disease odds = # ill / # well

Example of an Odds Calculation

- *What are the ODDS of rolling a '3'?*
- Odds IN FAVOR OF rolling a 3 are:

$$\frac{\text{probability of a '3'}}{\text{probability of not '3'}}$$

= (1/6) / (5/6)
= 1 / 5, or 0.2:1

- Odds AGAINST rolling a 3 are 5:1.

Example — Odds of Outcome (Death)

- Deaths in diabetic men
  100 deaths, 189 men at start of follow-up period
  Probability of death = 100 / 189 = 0.529 = 52.9%
- Odds = probability of dying / probability of not dying
  = 0.529 / (1 - 0.529) = 0.529 / 0.471
  = 1.1:1
- Odds = # deaths / # survivors
  = 100 / 89
  = 1.1:1

Ref: Kleinman J, et al.
Am J Epidemiol 1988; 128:389-401.

"Every epidemiologic study
can be summarized
in a 2-by-2 table."

- H. Ory

Standard Two-by-Two Table (at CDC)

	Ill	Well	Total	Risk
Exposed	a	b	H_1	a / H_1
Unexposed	c	d	H_0	c / H_0
Total	V_1	V_0	T or N	

Basic Approach of Field Epidemiologists

- **C**ount cases
- **D**ivide number of cases by size of **population** to calculate **rates** (part of descriptive epidemiology)
- **C**ompare rates (part of analytic epidemiology)

Analytic Epidemiology Illustrated

Drank water?	Ill
Yes	43
No	3
Total	46

% Drank water 93%

Key to Analytic Epidemiology

Key = comparison group!

Control = person without disease
(provides estimate of expected level of exposure)

Analytic Epidemiology Illustrated (2x2 Table)

Drank water?	Ill	Well	Total	% Ill
Yes	43	27	70	61%
No	3	2	5	60%
Total	46	29	75	61%
% Drank water	93%	93%		

Analytic Epidemiology Illustrated

Drank water?	Ill	Well	Total	% Ill
Yes	43	11	54	80%
No	3	18	21	14%
Total	46	29	75	61%
% Drank water	93%	38%		

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NHANES I Follow-up Study

	Dead	Alive	Total	% Dead
Diabetic	100	89	189	52.9%
Nondiabetic	811	2340	3151	25.7%
Total	911	2429	3340	27.3%

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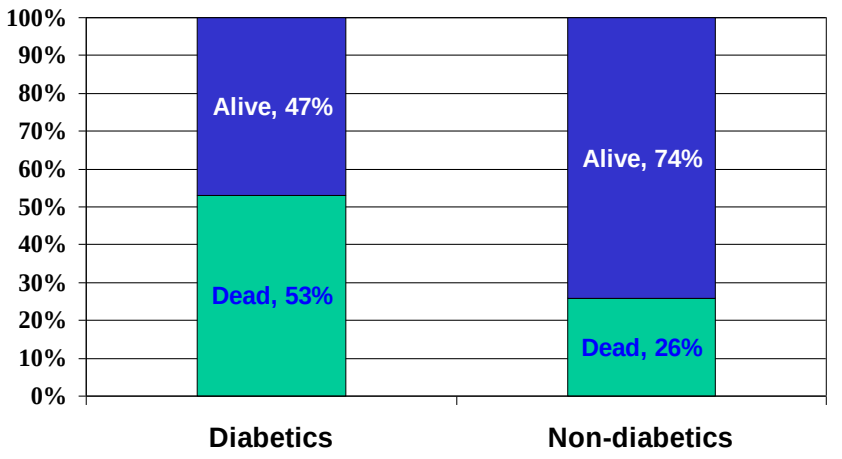
Ref: Kleinman J, et al.
Am J Epidemiol 1988; 128:389-401.

NHANES I Follow-up Study



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Measures of Association

Ref: Kleinman J, et al.
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Measures of Association

- Quantify the relationship between an "exposure" and outcome of interest
- Quantify the difference in occurrence of disease or death between two groups of people who differ on "exposure"
- Types of measures:
  - RATIOS: relative risk, rate ratio, odds ratio
  - DIFFERENCE: attributable risk
- Compare “observed” to “expected”

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Measures of Association

Risk Ratio / Relative Risk

$$\frac{\text{Risk in "exposed" group}}{\text{Risk in "unexposed" group}}$$

EXAMPLE:
Relative risk of death among diabetic men vs. nondiabetic men

$$RR = \frac{100/189}{811/3151} = \frac{0.529}{0.257} = 2.1$$

Ref: Kleinman J, et al.
Am J Epidemiol 1988; 128:389-401.

Template for Describing Risk Ratio

- The {exposed group} is {RR} times as likely to have {the outcome} as the {unexposed group}.

- Example:

  {Diabetic men} were {2.1} times as likely to {die during the follow-up period} as were {non-diabetic men}.

Outbreak of Gastroenteritis, Oswego

	D+	D-	Total	Risk
E+	43	11	54	79.6%
E-	3	18	21	14.3%
Total	46	29	75	61.3%

$$RR = \frac{43 / 54}{3 / 21} = 79.6 / 14.3 = \_\_\_\_\_$$

Outbreak of Gastroenteritis, Oswego

	D+	D-	Total	Risk
E+	43	11	54	79.6%
E-	3	18	21	14.3%
Total	46	29	75	61.3%

$$RR = \frac{43 / 54}{3 / 21} = 79.6 / 14.3 = \mathbf{5.6}$$

Study of Circumcision and HIV, Uganda

	HIV+	HIV−	Total	Risk
Circum+	18	890	908	1.98%
Circum−	154	4,454	4,608	3.34%
Total	172	5,344	5,516	3.12%

RR = 1.98 / 3.34 = _____

Interpretation:

Ref: Gray RH et al. AIDS 2000; 14:2371–2381.

Study of Circumcision and HIV, Uganda

	HIV+	HIV−	Total	Risk
Circum+	18	890	908	1.98%
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Total	172	5,344	5,516	3.12%

RR = 1.98 / 3.34 = **0.59**

Interpretation:

Ref: Gray RH et al. AIDS 2000; 14:2371–2381.

Study of Circumcision and HIV, Uganda

	HIV+	HIV−	Total	Risk
Circum+	18	890	908	1.98%
Circum−	154	4,454	4,608	3.34%
Total	172	5,344	5,516	3.12%

RR = 1.98 / 3.34 = **0.59**

Interpretation: **consistent with protective effect**

Ref: Gray RH et al. AIDS 2000; 14:2371–2381.

Study of Circumcision and HIV, Uganda

	HIV+	HIV−	Total	Risk
Circum−	154	4,454	4,608	3.34%
Circum+	18	890	908	1.98%
Total	172	5,344	5,516	3.12%

RR = 3.34 / 1.98 = _____

Interpretation:

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Study of Circumcision and HIV, Uganda

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Interpretation:

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Study of Circumcision and HIV, Uganda

	HIV+	HIV−	Total	Risk
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Circum+	18	890	908	1.98%
Total	172	5,344	5,516	3.12%

RR = 3.34 / 1.98 = 1.7

Interpretation: **lack of circumcision associated with increased risk of HIV**

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Ref: Gray RH et al. AIDS 2000; 14:2371–2381.

Questions about Risk Ratio

$$\frac{\text{Risk in "exposed" group}}{\text{Risk in "unexposed" group}}$$

- What does RR > 1 mean?
- What does RR = 1 mean?
- What does RR < 1 mean?

Comments about Risk Ratio

- The further away from 1, the stronger the association between exposure and disease
- Risk ratio is preferred measure of association for cohort studies
- Cannot calculate risk ratio from case-control study

Strength of Association (Outbreaks)

< 2.0	hard to believe / very weak association
2.0 – 3.9	weak – moderate association
≥ 4.0	probably believable unless study strongly biased / moderate – strong association

Rate Ratio for P-T Rates

$$\frac{\text{Person-time rate in "exposed" group}}{\text{Person-time rate in "unexposed" group}}$$

EXAMPLE:
Death rate ratio among diabetic men vs. nondiabetic men

$$RR = \frac{100/1414.7}{811/28{,}029.8} = \frac{70.7/1000}{28.9/1000} = 2.5$$

Ref: Kleinman J, et al. Am J Epidemiol 1988; 128:389-401.

Comments about Rate Ratio

- The further away from 1, the stronger the association between exposure and disease
- Can only calculate Rate Ratio from follow-up cohort study

Odds Ratio

- FORMULA 1 *("Disease Odds Ratio"):*

$$\frac{\text{Odds of disease/death in "exposed" group}}{\text{Odds of disease/death in "unexposed" group}}$$

- FORMULA 2 *("Exposure Odds Ratio"):*

$$\frac{\text{Odds of being "exposed" among cases}}{\text{Odds of being "exposed" among non-cases}}$$

Disease Odds Ratio

	Dead	Alive	Odds of Disease
Diabetic	100	89	100 / 89
Nondiabetic	811	2340	811 / 2340

Using formula 1,

$$OR = \frac{100 / 89}{811 / 2340} = \frac{100 \times 2340}{89 \times 811} = 3.2$$

Ref: Kleinman J, et al.
Am J Epidemiol 1988; 128:389-401.

Exposure Odds Ratio

	Dead	Alive
Diabetic	100	89
Nondiabetic	811	2340
Odds of Exposure	100 / 811	89 / 2340

Using formula 2,

$$OR = \frac{100 / 811}{89 / 2340} = \frac{100 \times 2340}{89 \times 811} = 3.2$$

Ref: Kleinman J, et al.
Am J Epidemiol 1988; 128:389-401.

Odds Ratio as Cross-Product Ratio

	Dead	Alive
Diabetic	100	89
Nondiabetic	811	2340

OR = ad / bc

$$OR = \frac{ad}{bc} = \frac{100 \times 2340}{89 \times 811} = 3.2$$

Ref: Kleinman J, et al.
Am J Epidemiol 1988; 128:389-401.

When Does the Odds Ratio Approximate the Risk Ratio?

	D+	D-	Total	Risk
E+	a	b	a+b	a/a+b
E−	c	d	c+d	c/c+d

$$RR = \frac{\frac{a}{a+b}}{\frac{c}{c+d}}$$

When Does the Odds Ratio Approximate the Risk Ratio?

	D+	D-	Total	Risk
E+	a	b	a+b	a/a+b
E−	c	d	c+d	c/c+d

$$RR = \frac{\frac{a}{a+b}}{\frac{c}{c+d}}$$

For a rare disease, a <<< b, so a+b ≈ b
c <<< d, so c+d ≈ d

When Does the Odds Ratio Approximate the Risk Ratio?

	D+	D-	Total	Risk
E+	a	b	a+b	a/a+b
E−	c	d	c+d	c/c+d

$$RR = \frac{\frac{a}{a+b}}{\frac{c}{c+d}} \approx \frac{\frac{a}{b}}{\frac{c}{d}}$$

For a rare disease, a <<< b, so a+b ≈ b
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When Does the Odds Ratio Approximate the Risk Ratio?

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E+	a	b	a+b	a/a+b
E−	c	d	c+d	c/c+d

$$RR = \frac{\frac{a}{a+b}}{\frac{c}{c+d}} \approx \frac{\frac{a}{b}}{\frac{c}{d}} = \frac{ad}{bc} = OR$$

For a rare disease, a <<< b, so a+b ≈ b
c <<< d, so c+d ≈ d

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Example of the "Rare Disease" Assumption

	D+	D-	Total	Risk
E+	90	499,950	500,040	0.00018
E−	10	499,950	499,960	0.00002

$$RR = \frac{90/\ 500{,}040}{10/\ 499{,}960} = \frac{0.00018}{0.00002} = 9.0$$

$$OR = \frac{ad}{bc} = \frac{(90)(499{,}950)}{(499{,}950)(10)} = 9.0$$

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Example of the "Rare Disease" Assumption

	D+	D-	Total	Risk
E+	90	50	140	0.643
E−	10	50	60	0.167

RR = $\frac{90/140}{10/60} = \frac{0.643}{0.167} = 3.9$

OR = $\frac{ad}{bc} = \frac{(90)(50)}{(50)(10)} = 9.0$

Example of the "Rare Disease" Assumption

	D+	D-	Total	Risk
E+	90	100	190	0.474
E−	10	100	110	0.091

RR = $\frac{90/190}{10/110} = \frac{0.474}{0.091} = 5.2$

OR = $\frac{ad}{bc} = \frac{(90)(100)}{(100)(10)} = 9.0$

Example of the "Rare Disease" Assumption?

	D+	D-	Total	Risk
E+	43	11	54	79.6%
E–	3	18	21	14.3%

RR = $\frac{43 / 54}{3 / 21}$ **= 5.6**

OR = $\frac{ad}{bc}$ **=** _____ **=**

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CDC. Oswego – An Outbreak of GI Illness Following a Church Supper., 1997 ed. 1940

Example of the "Rare Disease" Assumption?

	D+	D-	Total	Risk
E+	43	11	54	79.6%
E–	3	18	21	14.3%

RR = $\frac{43 / 54}{3 / 21}$ **= 5.6**

OR = $\frac{ad}{bc}$ **=** $\frac{43 \times 18}{11 \times 3}$ **=**

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Example of the "Rare Disease" Assumption?

	D+	D-	Total	Risk
E+	43	11	54	79.6%
E–	3	18	21	14.3%

$$RR = \frac{43 / 54}{3 / 21} = 5.6$$

$$OR = \frac{ad}{bc} = \frac{43 \times 18}{11 \times 3} = 23.5$$

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CDC. Oswego – An Outbreak of GI Illness Following a Church Supper., 1997 ed. 1940

Comments about Odds Ratio

- Preferred measure of association for case-control study (Risk Ratio, Rate Ratio cannot be calculated from case-control study)
- For simple analyses, should not be used if risk ratio can be calculated (use RR for cohort study)
- Approximates Risk Ratio when disease is rare
- Always further from 1.0 than risk ratio, especially if disease is NOT rare

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Summary of Measures of Association

NHANES Diabetes Follow-up Study

- Risk Ratio = 52.9% / 25.7% = 2.1
- Rate Ratio = 70.7 / 28.9 = 2.5
- Odds Ratio = 3.2

Oswego

- Risk Ratio = 79.6% / 14.3% = 5.6
- Odds Ratio = 23.5

Comparison Groups in Cohort and Case-Control Studies

	Cohort Study	Case-control Study
Index group ("Observed")	Exposed Group	Cases
Comparison group ("Expected")	Unexposed Group	Controls
Measure of occurrence	Attack Rate (Risk)	Odds of exposure
Measure of association	Risk ratio (Relative risk)	Odds ratio

Conclusion

- Measures of association (RR, OR) describe the strength of association between exposure and disease
- Use risk ratio for standard cohort study
- Use rate ratio for person-time cohort study
- Use odds ratio for case-control study
- Odds ratio only approximates risk ratio when disease is rare

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Measures of Association

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Author, References

Author

- Richard Dicker

References

- CDC. *Principles of Epidemiology in Public Health Practice, 3rd ed*. Atlanta: CDC, 2006
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