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Measures of Association

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Definition

- A measure of association quantifies the relationship between exposure and disease among the two groups.
  a) Exposure is used loosely to mean any way to stratify a group of people into two categories.
- Examples of measures of association:
  a) **Risk** ratio (relative risk)
  b) **Rate** ratio
  c) Odds ratio

https://www.cdc.gov/csels/dsepd/ss1978/lesson3/section5.html

Design * Measures of association

- Measures of association and study design often go together
  a) Need to understand the design to understand which measure of association we will use.
- Key questions about design
  a) Did the study measure prevalence or incidence?
  b) Does the study have a denominator?
  c) Are we interested in relative or absolute risk?
  d) How common is the disease in the study?

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Measures of Association

- Absolute Risk
- Relative **Risk** (aka risk ratio)
- **Rate** Ratio
- Odds Ratio

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Measures of Association

- **Absolute Risk**
  a) Defined as the incidence of a disease in a population
  b) Can show magnitude of risk in a specific group of people with a specific exposure, but does not include consideration of the risk of disease to people who were not exposed.

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Measures of Association

- **Risk Ratio**
  a) A risk ratio (RR), also called relative risk, compares the risk of a health event (disease, injury, risk factor, or death) among one group with the risk among another group.
- **Rate Ratio**
  a) A rate ratio compares the incidence rates, person-time rates, or mortality rates of two groups. As with the risk ratio, the two groups are typically differentiated by demographic factors or by exposure to a suspected causative agent.

Measures of Association

- **Odds Ratio (OR)**

  a) The OR represents the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2938757/

Risk Ratio and Rate Ratio

$$\text{Risk Ratio} = \frac{\text{Risk in exposed}}{\text{Risk in nonexposed}}$$

If RR = 1 Risk in exposed equal to risk in non-exposed (no association)

If RR > 1 Risk in exposed greater than risk in non-exposed (positive association; possibly causal)

If RR < 1 Risk in exposed less than risk in non-exposed (negative association; possibly protective)

Connection with study design

- Can only calculate Risk Ratio and Rate Ratio in studies with a denominator (e.g., cohort studies)
- Odds Ratio
  a) The odds ratio is the measure of association used in case-control studies (no denominator)
  b) Good estimate of the relative risk when disease is uncommon.

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Relative Risk in Cohort Studies

	Disease Develops	Disease Does Not Develop	Totals	Incidence Rates of Disease
Exposed	a	b	$a+b$	$\frac{a}{a+b}$
Nonexposed	c	d	$c+d$	$\frac{c}{c+d}$

Incidence in exposed

Incidence in nonexposed

$$\text{Relative Risk} = \frac{\textit{Incidence in exposed}}{\textit{Incidence in nonexposed}} = \frac{\left(\frac{a}{a+b}\right)}{\left(\frac{c}{c+d}\right)}$$

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Cohort Study of Smoking & Coronary Heart Disease (CHD)

	Disease Develops	Disease Does Not Develop	Totals	Incidence per 1,000 per year
Exposed	a 84	b 2916	$a + b$ 3,000	$\left(\frac{a}{a+b}\right)$*1000 =**28**
Nonexposed	c 87	d 4913	$c + d$ 5,000	$\left(\frac{c}{c+d}\right)$*1000=**17.4**

$$\text{Relative Risk} = \frac{\textit{Incidence in exposed}}{\textit{Incidence in nonexposed}} = \frac{\left(\frac{a}{a+b}\right)}{\left(\frac{c}{c+d}\right)} = \frac{28}{17.4} = 1.61$$

The Odds Ratio (Relative Odds)

In order to calculate a relative risk we need to know the incidence of disease in exposed and nonexposed individuals. This can be determined in a cohort study. In a case-control study however, we do not have this information because we start with diseased and non-diseased persons. Therefore, we cannot calculate relative risk directly in a case-control study. ***The odds ratio is the measure of association used in case-control studies*****.** Under many conditions, the odds ratio can provide a very good estimate of the relative risk.

$$\textbf{Odds of an Event} = \frac{\textbf{Probability of an event occurring}}{\textbf{Probability of an event not occurring}} = \frac{P}{1-P}$$

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Odds Ratio

Odds Ratio in a COHORT STUDY

	Develop Disease	Do Not Develop Disease
Exposed	a	b
Not Exposed	c	d

ODDS RATIO

= Odds that an exposed person develops disease / Odds that a non-exposed person develops disease

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

Odds Ratio in a CASE-CONTROL STUDY

	Cases (With Disease)	Controls (Without Disease)
History of Exposure	a	b
No History of Exposure	c	d

ODDS RATIO

= Odds that a case was exposed / Odds that a control was exposed

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

Interpreting the Odds Ratio

Same interpretation as Relative Risk.

If OR = 1 Exposure is not related to disease

If OR > 1 Exposure is positively related to disease

If OR < 1 Exposure is negatively related to the disease

Measures of Impact

- Attributable Risk
- Population Attributable Risk

https://www.sciencedirect.com/topics/medicine-and-dentistry/attributable-risk

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Measures of Impact

- **Attributable Risk**

  a) Attributable risk (AR) is the portion of disease rate in the exposed group attributable to the exposure factor in the epidemiological context, or the portion of beneficial outcome rate attributable to a treatment.

- **Population Attributable Risk**

  a) Population Attributable risk (PAR) is the portion of disease rate in the population (both exposed and unexposed groups) attributable to the exposure factor in the epidemiological context, or the portion of beneficial outcome rate attributable to a treatment.

https://www.sciencedirect.com/topics/medicine-and-dentistry/attributable-risk

In the real world

- Extremely rare to see 2x2 tables in epi or public health papers
- Calculates are done using regression
  a) We get measures of uncertainty
  b) We can simultaneously adjust for confounding
- STROBE Guidelines can help you figure out study quality
  a) https://www.strobe-statement.org/
- Many other guidelines for other designs through Equator Network
  a) https://www.equator-network.org/

Paper work through

- Jun Eun S. Trends in mortality from road traffic injuries in South Korea, 1983–2017: Joinpoint regression and age-period-cohort analyses. Accident Analysis & Prevention. Volume 134, January 2020, 105325. https://doi.org/10.1016/j.aap.2019.105325

- Questions
  a) What is the study design?
  b) What measures of association are used?
  c) Interpret the findings in 2-3 sentences using your own words?
  d) Could you calculate an odds ratio using data from this paper?

Paper work through

- Rothman L, Howard A, Buliung R, Macarthur C, Richmond SA, Macpherson A. School environments and social risk factors for child pedestrian-motor vehicle collisions: A case-control study. Accid Anal Prev. 2017 Jan;98:252-258. https://pubmed.ncbi.nlm.nih.gov/27770691/
- Questions
  a) What is the study design?
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  c) Interpret the findings in 2-3 sentences using your own words?
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Scenarios

- Tuberculosis Example Slides 18-22
- Smoking Ban Example Slides 23-27
- COVID-19 Example Slides 28-32
- Alcohol Example Slides 33-47

Thanks to Dr. Maureen Anderson and Dr. Tasha Epp who shared these scenarios!

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Scenario 1

- An outbreak of Tuberculosis has been identified in a prison.
- You have been dispatched to investigate.
- There appears to be more inmates sick in the East Wing compared to the West Wing of the prison
- You must provide decision-makers epidemiological information on the extent of the outbreak, including quantitative measures to assess the risk of infection to inmates in the prison population.
- How would you approach this problem?

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Scenario 1: Worked example

During a tuberculosis outbreak at a prison in South Carolina, 28 of 157 inmates situated in the East Wing developed tuberculosis, as compared to 4 of 137 inmates situated in the West wing.

Measures of association:

1. Risk or attack rate for each group – cannot rely on counts eg) that it "seems" more folks sick in the East Wing. Need to take the population at risk into account.

2. Relative Risk

Data Source: *McLaughlin SI, Spradling P, Drociuk D, Ridzon R, Pozsik CJ, Onorato I. Extensive transmission of Mycobacterium tuberculosis among congregated, HIV-infected prison inmates in South Carolina, United States. Int J Tuberc Lung Dis 2003;7:665–672.*
Example Source*: https://www.cdc.gov/csels/dsepd/ss1978/lesson3/section5.html*

Calculate Risk of Tuberculosis

	Developed Tuberculosis	Did not Develop Tuberculosis	Total
East Wing	a	b	a + b
West Wing	c	d	c + d
Total	a + c	b + d	

Risk of Tuberculosis among Inmates in the East Wing (Attack Rate for exposed) **= a / a+b**

Risk of Tuberculosis among Inmates in the West Wing (Attack Rate for unexposed) **= c / c+d**

Relative Risk = $$\frac{\textit{Incidence in exposed}}{\textit{Incidence in nonexposed}} = \frac{\left(\frac{a}{a+b}\right)}{\left(\frac{c}{c+d}\right)}$$

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Calculate the RELATIVE risk

	Developed Tuberculosis	Did not Develop Tuberculosis	Total
East Wing	28	129	157
West Wing	4	133	137
Total	32	262	294

Risk of Tuberculosis among Inmates in the East Wing = 28 / 28+129 = 0.178 = 17.8%

Risk of Tuberculosis among Inmates in the West Wing = 4 / 4+133 = 0.029 = 2.9%

Relative Risk $= \dfrac{Incidence\ in\ exposed}{Incidence\ in\ nonexposed} = \dfrac{\left(\frac{a}{a+b}\right)}{\left(\frac{c}{c+d}\right)}$ **= 17.8 / 2.9 = 6.1**

Scenario 1: RR into plain language

The inmates who were situated in the East wing of the prison were **6.1 times as likely** as those who resided in the West wing to develop tuberculosis.

Data Source: *McLaughlin SI, Spradling P, Drociuk D, Ridzon R, Pozsik CJ, Onorato I. Extensive transmission of Mycobacterium tuberculosis among congregated, HIV-infected prison inmates in South Carolina, United States. Int J Tuberc Lung Dis 2003;7:665–672.*

Example source: *https://www.cdc.gov/csels/dsepd/ss1978/lesson3/section5.html*

Scenario 2

- A ban on indoor smoking in public places came into effect in provincial jurisdiction A on January 1 2015.
- You have been asked to assess how this ban may have impacted cardiovascular disease in the province.
- How would you approach this problem?

Scenario 2: Worked example

Public health officials compared emergency room visits for acute myocardial infarction for the year prior to the smoking ban (2014) and the year following (2016). Visits for MI per 1,000 patients per week in 2014 was 11.6; compared to 5.3 visits per 1,000 patients per week in 2016.

Calculate the incidence rate ratio.

Modified from example: https://www.cdc.gov/csels/dsepd/ss1978/lesson3/section5.html

Incidence Rate Ratio

Rate ratio =Rate for group of interest / Rate for comparison group

Rate ratio of 1.0 = equal rates in the two groups
Rate ratio > 1 = an increased risk for the group in the numerator
Rate ratio < 1.0 = a decreased risk for the group in the numerator.

Scenario 2: Example solution

Rate ratio = 11.6 ⁄ 5.3 = **2.2**

During 2014, patients visiting emergency room X in jurisdiction A were 2.2 times more likely to visit for acute myocardial infarction than were in 2016.

Plain language for policy-makers:
The incidence of heart attacks was 2.2 times higher prior to implementation of a province-wide smoking ban at indoor public places compared to after the ban.

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Can also calculate measures of impact!

Attributable Risk = **Incidence in exposed group** **—** **Incidence in nonexposed group**

$$\frac{11.6}{1000} - \frac{5.3}{1000} = \frac{\mathbf{6.3}}{\mathbf{1,000}}$$

Scenario 3

- Waning immunity to SARS-CoV-2 vaccination is a problem we still do not completely understand
- What measure of association is useful in understanding real-world protection from vaccines?
- How do you calculate it?
- Do you think the Omicron variant may elicit different measures of impact?
  - Why or why not?
  - How would you assess this?

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1. Calculate the Risk of COVID among vaccinated and unvaccinated

	COVID case	Non-case	Total
Vaccinated	a	b	a + b
Unvaccinated	c	d	c + d
Total	a + c	b + d	

Risk of COVID among vaccinated = a / a+b
Risk of COVID among unvaccinated = c / c+d

2. Calculate the Relative Risk

	COVID case	Non-case	Total
Vaccinated	a	b	a + b
Unvaccinated	c	d	c + d
Total	a + c	b + d	

Relative Risk = $$\frac{\textit{Incidence in exposed}}{\textit{Incidence in nonexposed}} = \frac{\left(\frac{a}{a+b}\right)}{\left(\frac{c}{c+d}\right)}$$

3. Calculate the Vaccine Effectiveness

VE = % reduction in disease incidence in vaccinated group compared to unvaccinated group

$$= \frac{\textbf{(Risk among unvaccinated group) – (Risk among vaccinated group)}}{\textbf{Risk among unvaccinated group}}$$

*The numerator (risk among unvaccinated − risk among vaccinated) in this equation is sometimes referred to as the risk difference.

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Scenario 3: Worked example

	COVID case	Non-case	Total
Vaccinated	18	134	152
Unvaccinated	3	4	7
Total	21	138	159

Risk of COVID among vaccinated = 18/152 = 0.118 = 11.8%

Risk of COVID among unvaccinated = 3/7 = 0.429 = 42.9%

Relative Risk = 0.118 / 0.429 = 0.28

Vaccine Effectiveness = (42.9 – 11.8) / 42.9 = 31.1 / 42.9 = 72%
OR **VE = 1- RR = 1 – 0.28 = 72%**

Modified example from Data Source: *Tugwell BD, Lee LE, Gillette H, Lorber EM, Hedberg K, Cieslak PR. Chickenpox outbreak in a highly vaccinated school population. Pediatrics 2004 Mar;113(3 Pt 1):455–459. https://www.cdc.gov/csels/dsepd/ss1978/lesson3/section5.html*

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Scenario 4

- Understanding the population-level impact of interventions is a critical component of public health epidemiologists’ work
- You are interested in understanding the risk of breast cancer associated with a potentially modifiable risk factor such as alcohol consumption
- What measures of effect/impact would help you?
- How would you calculate them?

Scenario 4: Worked example

You decide to follow women who drink alcohol and those who do not - 3,000 drinkers and 5,000 nondrinkers were followed over a one-year time period. The findings at the end of the study showed that of those who drank alcohol, 84 developed breast cancer and 2,916 did not develop breast cancer. Of those who did not drink alcohol, 87 developed breast cancer and 4,913 did not develop breast cancer.

1) Calculate the incidence per 1,000 population among the exposed and the non-exposed.
2) Calculate the Relative Risk
3) Calculate the incidence of breast cancer in the exposed group (drink alcohol) that is attributable to the exposure (Attributable Risk)
4) Calculate the proportion of incidence attributable to exposure.
5) Calculate the Attributable Risk for the Total Population
6) Calculate the proportion of the incidence in the total population that is attributable to the exposure.

1. Calculate the Incidence per 1,000 population per year among the exposed and nonexposed.

	Develop breast cancer	Do Not Develop breast cancer	Total	Incidence per 1,000 per year
Drinks alcohol	a	b	a + b	$\frac{a}{a+b}$
Does not drink alcohol	c	d	c + d	$\frac{c}{c+d}$

	Develop CHD	Do Not Develop CHD	Total	Incidence per 1,000 per Year
Drinks alcohol	84	2,916	3,000	28
Does not drink alcohol	87	4,913	5,000	17.4

Incidence in 2014 = 84 / 3,000 = 28 per 1,000

Incidence in 2016 = 87 / 5,000 = 17.4 per 1,000

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2. Calculate the Relative Risk

	Disease Develops	Disease Does Not Develop	Totals	Incidence Rates of Disease
Exposed	a	b	$a+b$	$\frac{a}{a+b}$
Nonexposed	c	d	$c+d$	$\frac{c}{c+d}$

Incidence in exposed

Incidence in nonexposed

$$\text{Relative Risk} = \frac{\textit{Incidence in exposed}}{\textit{Incidence in nonexposed}} = \frac{\left(\frac{a}{a+b}\right)}{\left(\frac{c}{c+d}\right)}$$

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$$\textbf{Relative Risk} = \frac{\textit{Incidence in exposed}}{\textit{Incidence in nonexposed}} = \frac{\left(\frac{a}{a+b}\right)}{\left(\frac{c}{c+d}\right)}$$

= 28 / 17.4 = 1.61

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3. Calculate the Incidence Attributable to Exposure (Attributable Risk or Risk Difference)

	Develop breast cancer	Do Not Develop breast cancer	Total	Incidence per 1,000 per Year
Drinks alcohol	84	2,916	3,000	28
Does not drink alcohol	87	4,913	5,000	17.4

Attributable Risk = Incidence in exposed group – Incidence in nonexposed group

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Attributable Risk = Incidence in exposed group − Incidence in nonexposed group

$$\frac{28}{1000} - \frac{17.4}{1000} = \frac{\mathbf{10.6}}{\mathbf{1,000}}$$

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4) Calculate the proportion of incidence attributable to exposure (Attributable Fraction (exposed)).

$$\frac{\text{Incidence in exposed group} - \text{Incidence in nonexposed group}}{\text{Incidence in exposed group}}$$

Proportion of Incidence Attributable to Exposure =

$$\frac{\text{Incidence in exposed group} \; - \; \text{Incidence in nonexposed group}}{\text{Incidence in exposed group}}$$

$$\frac{28-17.4}{28} = \frac{\mathbf{10.6}}{28} = 0.379 = \mathbf{37.9\%}$$

5) Calculate the Attributable Risk for the Total Population

Incidence in total population − Incidence in nonexposed group

To Calculate Attributable Risk for the Total Population we must know *Either* the incidence of breast cancer in the total population *OR* all three of the following:

1) **Incidence among drinkers (28 per 1,000)**
2) **Incidence among nondrinkers (17.4 per 1,000)**
3) **The proportion of the total population that drinks alcohol (let's say a previous study suggests that the proportion of individuals in this population that drink alcohol is 44%)**

The incidence in the population can be calculated as follows:

$$\begin{pmatrix}\textit{Incidence in} \\ \textit{Drinkers}\end{pmatrix}\begin{pmatrix}\%\ \textit{Drinkers} \\ \textit{in Population}\end{pmatrix} + \begin{pmatrix}\textit{Incidence} \\ \textit{in nondrinkers}\end{pmatrix}\begin{pmatrix}\%\ \textit{Nondrinkers in} \\ \textit{population}\end{pmatrix}$$

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$$\left(\frac{28}{1000}\right)(0.44) + \left(\frac{17.4}{1,000}\right)(0.56) = \frac{22.1}{1,000}$$

We can now use this value to complete the calculation:

Incidence in total population	-	Incidence in nonexposed group

$$\frac{22.1}{1000} - \frac{17.4}{1000} = \frac{\mathbf{4.7}}{\mathbf{1000}}$$

6) Calculate the Proportion of the incidence in the Total Population that is attributable to the exposure.

$$\frac{\textbf{Incidence in total population} - \textbf{Incidence in nonexposed group}}{\textbf{Incidence in total population}}$$

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Proportion of the incidence in the **total population** that is attributable to the exposure =

$$\frac{\textbf{Incidence in total population} - \textbf{Incidence in nonexposed group}}{\textbf{Incidence in total population}}$$

$$\frac{22.1 - 17.4}{22.1} = \mathbf{21.3\%}$$

This means that 21.3% of the incidence of breast cancer in this total population can be attributed to drinking. If one wanted to introduce a prevention program to eliminate alcohol consumption, the most that we could see is a 21.3% reduction in the incidence of breast cancer in the total population (which consists of both drinkers and nondrinkers).