

# Lecture 5: Measures of Association

## Risk Ratios and Odds Ratios

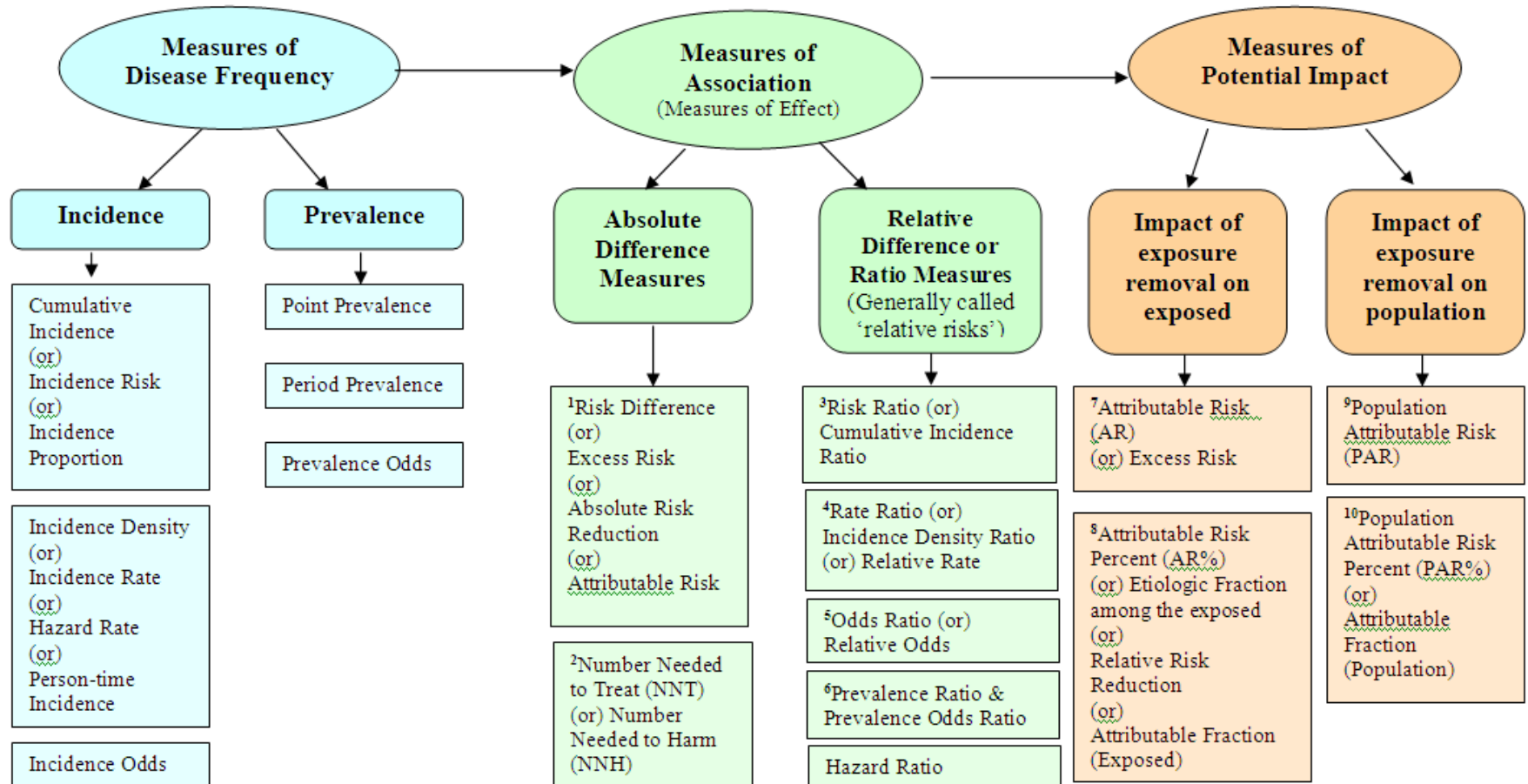
Lecture prepared by Dr. Hailey Banack, PhD

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**Banack, Hailey R. (2021). *Measures of Association*. [Lecture]. [www.haileybanack.com](http://www.haileybanack.com)**

# Overview of Measurement in Epidemiology



# Review

## RISK

- Incidence proportion
- Range: 0,1
- Probability that an individual will develop a disease during a specific period
- More assumptions
  - Steady state, follow-up
- Cannot handle losses to follow-up, attrition, competing risks

## RATE

- Incidence density
- Range: 0,  $\infty$
- Describes how rapidly new events occur in a specific population
- Fewer assumptions
- Can handle losses to follow-up, attrition, competing risks

# The big picture



Aim to quantify the association between groups by comparing the groups

# Review:

## Comparing Populations

When comparing the crude mortality rates from two populations, the difference could be due to:

- True differences in stratum-specific death rates
- Differences in population composition (distribution of characteristics)

Comparing crude rates is often inappropriate because of the differences in population composition (e.g., Alaska vs. Arizona)

# Two types of standardization

**Direct standardization:** rates that would have been observed in your population of interest if it had exactly the same distribution as the standard population with respect to the variable(s) for which the adjustment or standardization was carried out

**Indirect standardization:** the number of expected deaths in your population of interest had they died at the same rate as the general population

# Life Tables I

| (1)          | (A)                     | (2)                                | (3)  | (4)                                 | (5)                                      | (6)                            | (7)                            |
|--------------|-------------------------|------------------------------------|--|-------------------------------------|--|--------------------------------|--------------------------------|
| Age interval | ${}_n m_x$              | ${}_n q_x$                         | $l_x$                                      | ${}_n d_x$                          | ${}_n L_x$                               | $T_x$                          | $e_x^0$                        |
|              | Age-specific death rate | % who die in the interval          | # individuals at risk at start of interval | # deaths during interval            | # person years in age interval           | Cumulative sum of person years | Life expectancy                |
| X to X+n     | observed                | $= 1 - e^{-\text{interval} * m_x}$ | $= l_{x-n} * (1 - {}_n q_{x-n})$           | $= l_x * {}_n q_x$<br>$= (3) * (2)$ | $= {}_n d_x / {}_n m_x$<br>$= (4) / (A)$ | $= \sum {}_n L_x$              | $= T_x / l_x$<br>$= (6) / (3)$ |

# Note about age intervals

For age interval 1-4:

$$n = 4$$

Age-specific death rate ( ${}_4m_1$ ) = 0.00701

$${}_4q_1 = 1 - e^{-4 \cdot 0.00701} = 0.027651$$

$$4-1=3$$

But, we count the entire 4th year in the interval (the interval ends at the end of the 4<sup>th</sup> year)

So  $n=4$

Keep this in mind for your assignment!



# Additional Assignment Notes

## Q.5

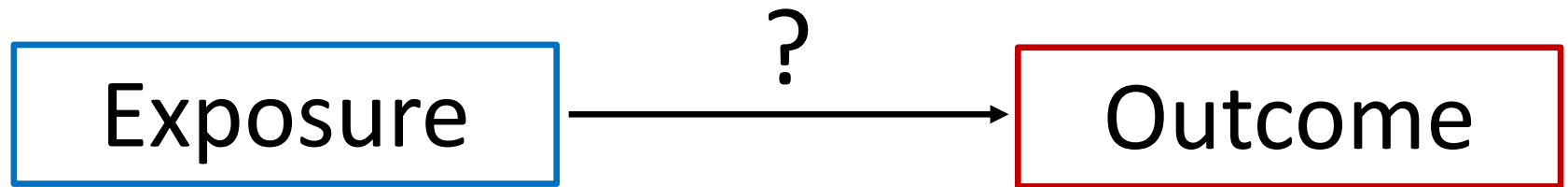
- **“The data describe a hypothetical population of 100,000 people from birth to age 85”**
  - Mortality rate presented as deaths per 100,000
  - E.g., 4.7 per 100,000
- Solving this requires combination of skills from different lectures (not just the life table content)

# Additional Life Table Calculations

| Interval | $l_x$<br># At Risk | $D_x$<br>Deaths in<br>Interval | $Q_x$<br>Mortality<br>Risk | Survival<br>Probability<br>$=1-Q_x$ | $P_t$<br>Cumulative<br>Survival<br>Probability |
|----------|--------------------|--------------------------------|----------------------------|-------------------------------------|--|
| 1        | 200                | 20                             | 0.1                        | 0.9                                 | 1.0  |
| 2        | 180                | 30                             | 0.17                       | 0.83                                | 0.9  |
| 3        | 150                | 40                             | 0.27                       | 0.73                                | 0.747  |

$$=0.9*1.0$$
$$=0.83*0.9$$

# Common objective in epidemiology



The BIG question: how do we estimate the “?”

# Excess Risk

- Comparing the risk of disease in exposed populations to the risk of disease in unexposed populations
- Usually the interest how of epidemiologic investigations
  - How much does exposure to factor \_\_\_\_ increase risk of outcome \_\_\_\_\_ compared to those who were not exposed

# Risk Factors

- Factors that increase or decrease your risk of disease
  - Harmful risk factor increases risk of disease
  - Protective risk factor decreases your risk

| Individual-level characteristics   | Environmental Factors  |
|--|--|
| <ul style="list-style-type: none"><li>• Age</li><li>• Sex</li><li>• Race/ethnicity</li><li>• Occupation</li><li>• Genetics</li><li>• Marital status</li><li>• Family History</li></ul> | <ul style="list-style-type: none"><li>• Climate</li><li>• Pollution</li><li>• Neighbourhood characteristics</li><li>• Water</li><li>• Radiation</li><li>• Viruses/bacteria</li><li>• Second-hand smoke</li></ul> |

# Environmental Risk Factor

## Flint water crisis

- In 2014, the water source in Flint, Michigan was changed from Lake Huron to the Flint river
- This water source had extremely high levels of lead, a neurotoxic chemical
- Flint River also had received raw sewage from the city's waste treatment plant, agricultural and urban runoff, and toxics from leaching landfills
- Water from Flint river also associated with an outbreak of Legionnaires' disease, caused by Legionella bacteria

# Video on Flint water crisis

<https://www.youtube.com/watch?v=NUSiLOWkrlw&t=4s>



# Risk factor \* health disparities

*“Compared to nationwide averages, Flint families are on the wrong side of every disparity: in life expectancy, infant mortality, asthma, you name it. Flint is a struggling deindustrialized urban center that has seen decades of crisis—disinvestment, unemployment, racism, illiteracy, depopulation, violence, and crumbling schools. Navy SEALs and other special ops medics train in Flint because the city is the country’s best analogue to a remote, war-torn corner of the world .... A kid born in Flint will live fifteen years less than a kid born in a neighboring suburb. Fifteen years less. Imagine what fifteen years of life means. In a country riven by inequalities, Flint might be the place where the divide is most striking.” – Dr. Mona Hanna Attisha*

- Children in Flint were already at a higher risk for lead exposure because of living conditions (older houses, lead paint) and poor nutrition
- Social determinants of health are non-medical factors that affect a person’s overall health and health outcomes
- The water crisis demonstrates that social determinants of health interact with our individual-level exposures to influence health outcomes



# Modifiable vs. Non-Modifiable

- There is an important distinction between risk factors that you can change (modifiable risk factors) compared with those that you cannot (non-modifiable risk factors)
- Examples of non-modifiable risk factors include age, biological sex, genetics, and family history of disease
- Examples of modifiable risk factors include occupation, marital status, and some environmental factors

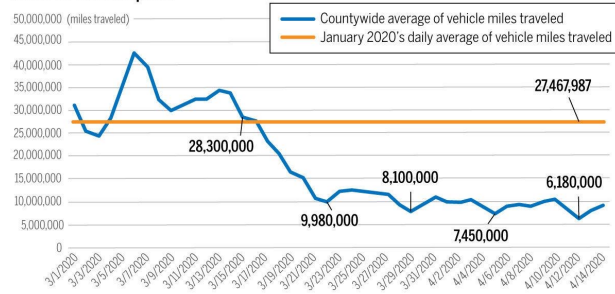
# “Modifiable”

- In theory, environmental factors are modifiable, because they *can* be changed but it can be very challenging

## Virus lockdown means less traffic, better air quality

The closures of many businesses, social services and cultural attractions recommended by Tucson Mayor Regina Romero in mid-March due to the coronavirus, followed by more closures ordered by Gov. Doug Ducey, have slashed vehicle traffic and improved air quality.

### COVID-19 traffic impacts

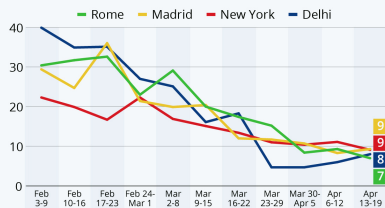


4/23/20 SOURCE: StreetLight Data Inc.

ARIZONA DAILY STAR

## COVID-19 Improves Air Quality in Just Three Months

Weekly average concentration of NO<sub>2</sub> in the air in selected cities (Feb-Apr 2020)\*

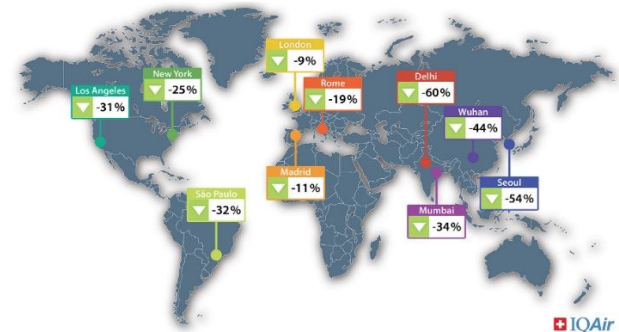


Central locations  
\* 95 percent of NO<sub>2</sub> in the air is caused by fossil fuel combustion  
Source: World Air Quality Index (WAQI)



statista

## Percent reduction in PM2.5 levels from 2020 lockdown period to the same period in 2019



IQAir

# Race vs. Racism

- Race/ethnicity is a non-modifiable risk factor for disease
- But is racism?
  - Optimistically & theoretically → Yes.
  - Realistically & practically → Maybe? Hopefully?



# Is racism a **non-modifiable** risk factor?

- There has been increasing attention to racism as a public health crisis

*APHA: "Racism is a system of structuring opportunity and assigning value based on the social interpretation of how one looks (which is what we call "race"), that unfairly disadvantages some individuals and communities, unfairly advantages other individuals and communities..." - Dr. Camara Phyllis Jones, MD, MPH, PhD*

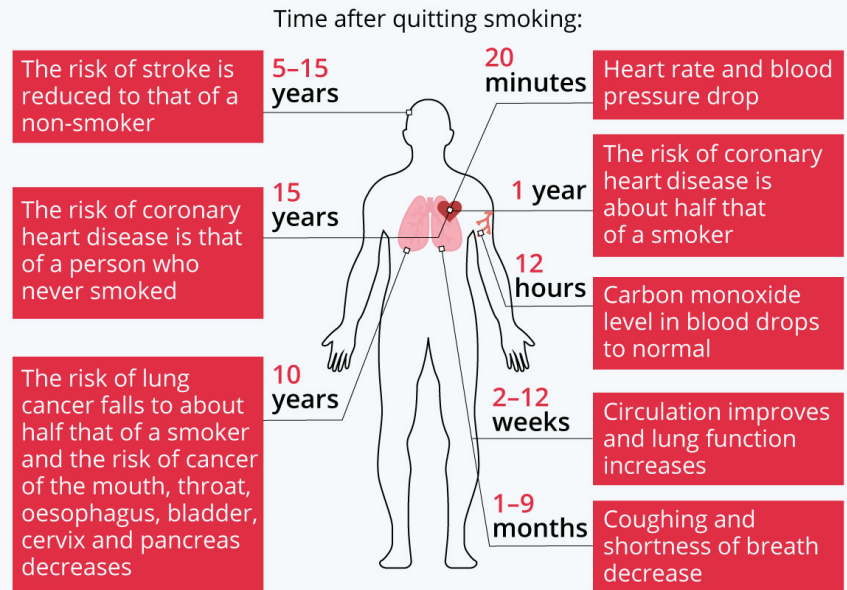
- Racism affects many individual level risk factors and social determinants of health: housing, education, access to healthcare, incarceration, and employment
- Framing racism as a public health issue will not solve the problem, but is a step in the right direction toward meaningful change

# Modifiable risk factors

- Many lifestyle characteristics are modifiable risk factors for disease, such as diet, physical activity, and smoking status
- Example: the effect of quitting smoking on health outcomes

## The Effects of Quitting Smoking

Health improvements that take place after quitting smoking, by time required



Source: World Health Organization







# Determining E-D association

- When assessing excess risk due to a particular risk factor, can calculate a ratio (a/b) or difference (a-b)

|                | (A)                 | (B)                         | (C)            | (D)                  |
|----------------|---------------------|-----------------------------|----------------|----------------------|
| Food           | <i>Ate (% Sick)</i> | <i>Did not eat (% Sick)</i> | <i>(A)/(B)</i> | <i>(A) - (B) (%)</i> |
| Egg salad      | 83                  | 30                          | 2.77           | 53                   |
| Macaroni       | 76                  | 67                          | 1.13           | 9                    |
| Cottage cheese | 71                  | 69                          | 1.03           | 2                    |
| Tuna salad     | 78                  | 50                          | 1.56           | 28                   |
| Ice cream      | 78                  | 64                          | 1.21           | 14                   |
| Other          | 72                  | 50                          | 1.44           | 22                   |

# Relative vs. Absolute Estimates

Measures of association can be relative (=ratio) or absolute (= difference)

Ratio = (Measure of disease<sub>exposed</sub>) / (Measure of disease<sub>unexposed</sub>)

Difference =(Measure of disease<sub>exposed</sub>) - (Measure of disease<sub>unexposed</sub>)



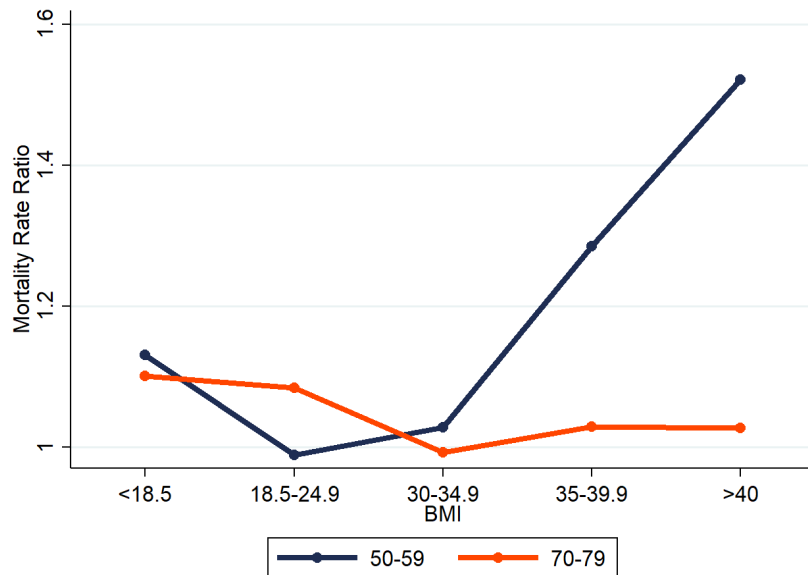
# Why does this matter?

|  | population |     |
|--|------------|-----|
|  | A          | B   |
| Incidence (%)                            |            |     |
| In exposed                               | 40         | 90  |
| In unexposed                             | 10         | 60  |
| <i>Difference</i> in incidence rates (%) | 30         | 30  |
| <i>Ratio</i> of incidence rates          | 4.0        | 1.5 |

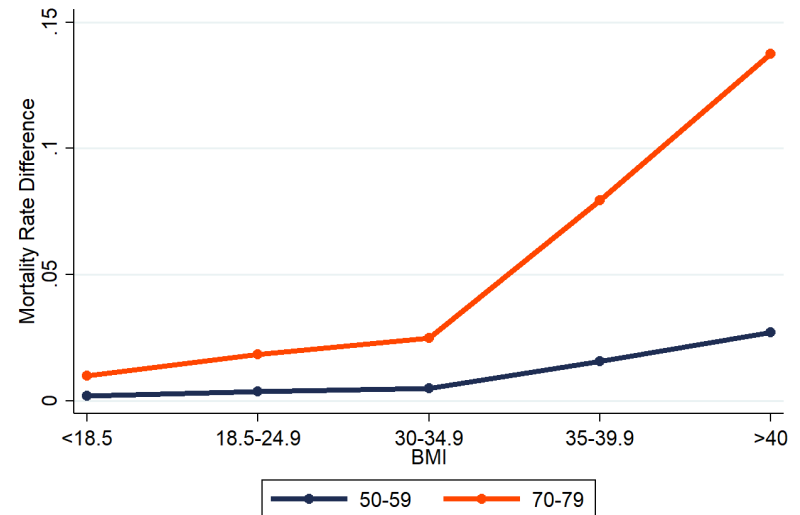
Using relative and absolute measures can lead to different conclusions

# Obesity and Aging

## Rate Ratio



## Rate Difference



Risk in the unexposed group increases with time → the same observed risk ratio corresponds with a larger change in absolute risk in older individuals than younger individuals

# The Problem with Ratios

Relative measures (ratios) can hide important information about the difference between comparison groups.

Example: “People who take Drug A are half as likely to die (RR=0.5) as people who take the placebo”

RR=0.5 could be consistent with

| Drug A           | Placebo          |
|------------------|------------------|
| 10% mortality    | 20% mortality    |
| 0.5% mortality   | 1% mortality     |
| 0.002% mortality | 0.004% mortality |

# What sounds more impressive?

“Effects presented in **relative terms** alone have been repeatedly shown to **seem more impressive** than the same effects presented in absolute terms in experimental studies of physicians, policy makers, and patients.”

## How effective are pap-smears as a screening test for cervical cancer?

- A study found that women over age 40 who had a pap test had a 33% reduction in death (RR = 0.67) from cervical cancer compared to people who were not tested
- However, the incidence of death in the pap group was 6 per 1,000 people, and the incidence of death in the no-pap group was 9 per 1,000.
- Which is a more exciting headline? “Pap smears save 3 lives per 1,000 women tested” or “Pap smears reduce cervical cancer mortality by 33%”

# Measures of Association

- How much does the **RISK** of outcome vary by level of exposure?
  - Risk difference
  - Risk ratio
- How much does the **RATE** of outcome occurrence vary by level of exposure?
  - Rate difference
  - Rate ratio

# 2x2 Tables for Counts

The most common way to calculate a measure of effect is to start with a 2x2 table:

|                     | <b>Disease +</b> | <b>Disease -</b> | <b>Row total</b> |
|---------------------|------------------|------------------|------------------|
| <b>Exposure +</b>   | a                | b                | a+b              |
| <b>Exposure -</b>   | c                | d                | c+d              |
| <b>Column total</b> | a+c              | b+d              | a+b+c+d          |

|                           | Disease + | Disease - | Row total<br>(Margins) |
|---------------------------|-----------|-----------|------------------------|
| Exposure +                | a         | b         | a+b                    |
| Exposure -                | c         | d         | c+d                    |
| Column total<br>(Margins) | a+c       | b+d       | a+b+c+d                |

*Risk Ratio:*

$$[a / (a + b)] / [c / (c + d)]$$

*Risk Difference:*

$$[a / (a + b)] - c / (c + d)$$

|                                   | <b>CHD +</b> | <b>CHD -</b> | <b>Row total<br/>(Margins)</b> |
|-----------------------------------|--------------|--------------|--------------------------------|
| <b>Smoking +</b>                  | 84           | 2916         | 3000                           |
| <b>Smoking -</b>                  | 87           | 4913         | 5000                           |
| <b>Column total<br/>(Margins)</b> | 171          | 7829         | 8000                           |

*Risk Ratio:* 
$$= [84 / (84 + 3000)] / [87 / (87 + 4913)]$$
  

$$= 1.61$$

*Risk Difference:* 
$$= [84 / (84 + 3000)] - [87 / (87 + 4913)]$$
  

$$= 10.6$$



# Interpretations

## **Risk difference:**

“Those exposed to  $X$  have [RD] higher/lower risk of  $Y$  compared to those not exposed to [or, exposed to a different level of]  $X$ .”

## **Risk ratio:**

“Those exposed to  $X$  have [RR] times the risk of  $Y$  compared to those not exposed to [or, exposed to a different level of]  $X$ .”

# Null value

- Null = no effect
- $H_0$ : no difference between groups

| Risk Ratio |   |
|------------|---|
| >1         | Risk in exposed greater than risk in unexposed                    |
| =1         | Risk in exposed equal to risk in unexposed (null; no association) |
| <1         | Risk in exposed less than risk in unexposed                       |

| Risk Difference |   |
|-----------------|---|
| >0              | Risk in exposed greater than risk in unexposed                    |
| =0              | Risk in exposed equal to risk in unexposed (null; no association) |
| <0              | Risk in exposed less than risk in unexposed                       |

# “Relative Risk”

*\*\*This is a very confusing term\*\**

- Most often used to refer to risk ratio
- Also sometimes used to refer to rate ratio
- Using correct and specific terminology is very important
- Please try not to use this term!

# 2x2 Tables for Person Time

|                           | Disease + | Disease - | Person Time   |
|---------------------------|-----------|-----------|---------------|
| Exposure +                | a         | --        | $PT_e$        |
| Exposure -                | c         | --        | $PT_0$        |
| Column total<br>(Margins) | a+c       | --        | $Pt_e + PT_0$ |

|                           | Disease + | Disease - | Person Time   |
|---------------------------|-----------|-----------|---------------|
| Exposure +                | a         | --        | $PT_e$        |
| Exposure -                | c         | --        | $PT_0$        |
| Column total<br>(Margins) | a+c       | --        | $PT_e + PT_0$ |

*Rate Ratio:*  $[a / PT_e] / [c / PT_0]$

*Rate Difference:*  $[a / PT_e] - [c / PT_0]$

# Comparing Measures of Association

| Measure         | Range                | No association |
|-----------------|----------------------|----------------|
| Risk difference | $[-1, +1]$           | 0              |
| Rate difference | $[-\infty, +\infty]$ | 0              |
| Risk ratio      | $[0, +\infty]$       | 1              |
| Rate ratio      | $[0, +\infty]$       | 1              |

- No association = null association = null effect

# Standardization

- Standardization is a general set of techniques that involves taking a weighted average of measures of occurrence (e.g., incidence) which can be used to calculate standardized measures of effect (e.g., standardized risk ratio or risk difference)
- Can use an external population as the standard distribution (2000 census) or an internal group as the standard distribution (exposed or unexposed group)

# Standardization examples

- We are given data representing 6 age-sex strata
  - Age categories 50 to 59 years, 60 to 69 years, and 70 to 74 years
  - Men and women

|       |       | Person time ( <b>T</b> ) | <b>N</b> at risk | Incidence | <b>I</b> ncidence rate | <b>R</b> isk |
|-------|-------|--------------------------|------------------|-----------|------------------------|--------------|
| Men   | 50-59 |                          |                  |           |                        |              |
|       | 60-69 |                          |                  |           |                        |              |
|       | 70-74 |                          |                  |           |                        |              |
| Women | 50-59 |                          |                  |           |                        |              |
|       | 60-69 |                          |                  |           |                        |              |
|       | 70-74 |                          |                  |           |                        |              |



# Standardized Rates

- Let  $T_1, T_2, \dots, T_6$  be the distribution of person-years in the six age–sex categories (the standard distribution)
- We are given the six age–sex specific incidence rates  $I_1, I_2, \dots, I_6$  corresponding to the age–sex specific strata

$$I_s = \frac{I_1 T_1 + \dots + I_6 T_6}{T_1 + \dots + T_6} = \frac{\sum_{k=1}^6 I_k T_k}{\sum_{k=1}^6 T_k}$$

Numerator of  $I_s$ : number of cases one would see in a population that had the person-time distribution  $T_1, T_2, \dots, T_6$  and these stratum-specific rates.

The denominator of  $I_s$  is the total person time in the population

$I_s$  is the rate one would see in a population with distribution  $T_1, T_2, \dots, T_6$  and specific rates  $I_1, I_2, \dots, I_6$ .

# Standardized Risks

- Now consider a set of stratum-specific incidence proportions  $R_1, R_2, \dots, R_6$
- And a standard distribution  $N_1, N_2, \dots, N_6$  of persons rather than person-time at risk

$$R_s = \frac{R_1 N_1 + \dots + R_6 N_6}{N_1 + \dots + N_6} = \frac{\sum_{k=1}^6 R_k N_k}{\sum_{k=1}^6 N_k}$$

# Standardization example: Risk

Standardized rate ratio

$$I_s = \frac{\sum_{k=1}^K T_k I_k}{\sum_{k=1}^K T_k}$$

Standardized Risk Ratio

$$IR_s = \frac{I_s}{I_s^*} = \frac{\sum T_k I_k}{\sum T_k I_k^*}$$

Standardized Risk Difference

$$ID_s = \sum T_k I_k - \sum T_k I_k^* = \sum T_k (I_k - I_k^*)$$

# Tolbutamide example

- Conducted a study to examine whether tolbutamide prevents complications of diabetes
- Want to examine age-specific estimates- risk of diabetes increases with age

Table 15-1 **Age-Specific Comparison of Deaths from All Causes for Tolbutamide and Placebo Treatment Groups, University Group Diabetes Program (1970)**

|                     | Stratum 1, Age <55 y |         | Stratum 2, Age 55 + y |         | Total (Crude) |         |
|---------------------|----------------------|---------|-----------------------|---------|---------------|---------|
|                     | Tolbutamide          | Placebo | Tolbutamide           | Placebo | Tolbutamide   | Placebo |
| <b>Dead</b>         | 8                    | 5       | 22                    | 16      | 30            | 21      |
| <b>Surviving</b>    | 98                   | 115     | 76                    | 69      | 174           | 184     |
| <b>Total</b>        | 106                  | 120     | 98                    | 85      | 204           | 205     |
| <b>Average risk</b> | 0.076                | 0.042   | 0.224                 | 0.188   | 0.147         | 0.102   |
| <b>RD</b>           | 0.034                |         | 0.036                 |         | 0.045         |         |
| <b>RR</b>           | 1.81                 |         | 1.19                  |         | 1.44          |         |

# Standardizing

- Can choose which strata to use as the standard (exposed, unexposed, total, external population)
- Using the total cohort as the standard:

Table 15-1 Age-Specific Comparison of Deaths from All Causes for Tolbutamide and Placebo Treatment Groups, University Group Diabetes Program (1970)

|                     | Stratum 1, Age <55 y |         | Stratum 2, Age 55 + y |         | Total (Crude) |         |
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| <b>RR</b>           | 1.81                 |         | 1.19                  |         | 1.44          |         |

$$\frac{226(0.076) + 183(0.224)}{226 + 183} - \frac{226(0.042) + 183(0.188)}{226 + 183} = 0.142 - 0.107 = 0.035$$

$$\frac{226(0.076) + 183(0.224)}{226 + 183} / \frac{226(0.042) + 183(0.188)}{226 + 183} = 0.142 / 0.107 = 1.33$$

# Standardizing: Exposed & Unexposed

- **Using the exposed population (Tolbutamide) as the standard:** To answer the question about the contrast between the effect measure in the exposed compared to the same effect measure in the unexposed had they been exposed.
- **Using the unexposed population (placebo) as the standard:** To answer the question about the contrast between the effect measures in the unexposed compared to the same effect measure in the exposed had they been unexposed

**Example:**

|             |              | Age |     | Total |
|-------------|--------------|-----|-----|-------|
|             |              | <55 | 55+ |       |
| Placebo     | 0            | 115 | 69  | 184   |
|             | 1            | 5   | 16  | 21    |
|             | <b>Total</b> | 120 | 85  | 205   |
| Tolbutamide | 0            | 98  | 76  | 174   |
|             | 1            | 8   | 22  | 30    |
|             | <b>Total</b> | 106 | 98  | 204   |

$$SRR = \frac{\sum_i w_i R_{1i}}{\sum_i w_i R_{0i}}$$

$$SRD = \frac{\sum_i w_i (R_{1i} - R_{0i})}{\sum_i w_i}$$

**Step 1. Calculate crude rates per strata**

$$R_{11} = \Pr(Y=1|X=1, Z=1) = 22/(76+22) = 0.22$$

$$R_{10} = \Pr(Y=1|X=1, Z=0) = 8/(98+8) = 0.08$$

$$R_{01} = \Pr(Y=0|X=0, Z=1) = 16/(69+16) = 0.19$$

$$R_{00} = \Pr(Y=0|X=0, Z=0) = 5/(115+5) = 0.04$$

**Step 2. Calculate weights per stratum**

$$\Pr(Z=1|X=1) = 98/204 = 0.48$$

$$\Pr(Z=0|X=1) = 106/204 = 0.52$$

**Step 3 and 4. Multiply crude rates by weights from standard population and calculate RD or RR**

$$SRR = [(0.52*0.08) + (0.48*0.22)] / [(0.52*0.04) + (0.48*0.19)] = 1.13$$

$$SRD = [(0.52*0.08) + (0.48*0.22)] - [(0.52*0.04) + (0.48*0.19)] = 0.0352$$



**Example:**

|             |              | Age |     | Total |
|-------------|--------------|-----|-----|-------|
|             |              | <55 | 55+ |       |
| Placebo     | 0            | 115 | 69  | 184   |
|             | 1            | 5   | 16  | 21    |
|             | <b>Total</b> | 120 | 85  | 205   |
| Tolbutamide | 0            | 98  | 76  | 174   |
|             | 1            | 8   | 22  | 30    |
|             | <b>Total</b> | 106 | 98  | 204   |

$$SRR = \frac{\sum_i w_i R_{1i}}{\sum_i w_i R_{0i}}$$

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**Step 1. Calculate crude rates per strata**

$$R_{11} = \Pr(Y=1|X=0, Z=1) = 16/(16+69) = 0.19$$

$$R_{10} = \Pr(Y=1|X=0, Z=0) = 5/(5+115) = 0.04$$

$$R_{01} = \Pr(Y=0|X=1, Z=1) = 22/(22+76) = 0.22$$

$$R_{00} = \Pr(Y=0|X=1, Z=0) = 8/(98+8) = 0.08$$

**Step 2. Calculate weights per stratum**

$$\Pr(Z=1|X=0) = 85/205 = 0.41$$

$$\Pr(Z=0|X=0) = 120/205 = 0.59$$

**Step 3 and 4. Multiply crude rates by weights from standard population and calculate RD or RR**

$$SRR = [(0.59*0.08) + (0.41*0.22)] / [(0.59*0.04) + (0.41*0.19)] = 1.34$$

$$SRD = [(0.59*0.08) + (0.41*0.22)] - [(0.59*0.04) + (0.41*0.19)] = 0.0359$$



# Odds

- The ratio of the probability of occurrence of an event to that of non-occurrence (Porta, 2008)

- **Odds** = 
$$\frac{\text{Proportion with disease}}{\text{Proportion without disease}}$$

- **Odds** = 
$$\frac{P}{1-P}$$

# Common use of odds: gambling

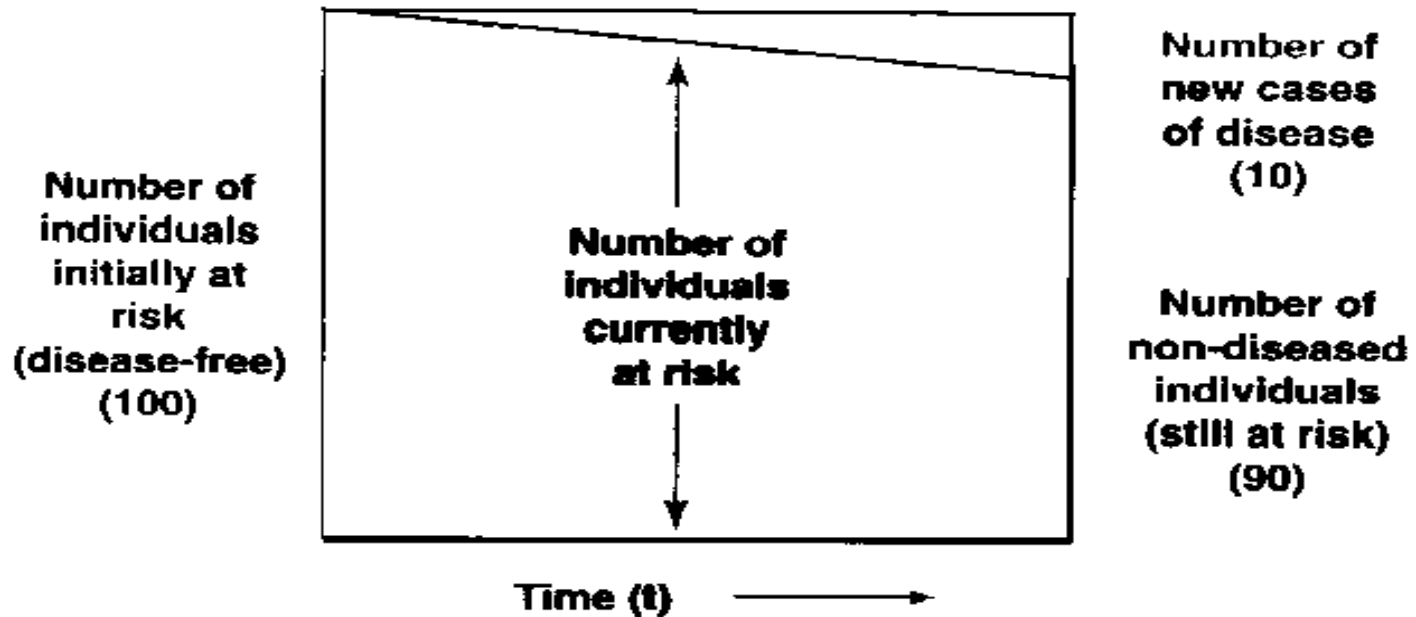
**Odds are commonly used when making a bet or gambling (e.g. odds of one team winning, odds of horse winning race)**

- LA Lakers have a 70% probability of winning the NBA championship (P) and a 30% probability of losing (1-P)
- What are the odds they will win?

$$\frac{P}{1-P} = \frac{70\%}{30\%} = 2.3$$

- Odds are not the same as probability --> probability of winning is 70%, odds of winning are 2.3

# Risk vs. Odds in Epidemiology



Thus, it is possible to calculate the risk and the odds of developing the disease during the study period as:

$$\text{Risk} = 10/100 = 0.10 = 10\%$$

$$\text{Odds of disease} = 10/90 = 0.11 = 11\%$$

# Risk vs. Odds

| CHARACTERISTIC                  | PROBABILITY   | ODDS   |
|---------------------------------|---|--|
| Ratio                           | $\frac{\text{occurrence}}{\text{whole}}$                          | $\frac{\text{occurrence}}{\text{nonoccurrence}}$           |
| Range                           | 0 to 1  | 0 to $\infty$  |
| Transformation to other measure | $\text{odds} = \frac{\text{probability}}{1 - \text{probability}}$ | $\text{probability} = \frac{\text{odds}}{1 + \text{odds}}$ |

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- **To go from Probability to Odds:**
  - Odds =  $P / (1 - P)$
  - E.g. If  $P = 0.20$ , Odds =  $0.20 / 0.80 = 0.25$
- **To go from Odds to Probability:**
  - Probability =  $\text{Odds} / (1 + \text{Odds})$
  - E.g. If Odds =  $0.25$ ,  $P = 0.25 / 1.25 = 0.20$

# Calculating Odds Ratios

|            | Disease + | Disease - |
|------------|-----------|-----------|
| Exposure + | a         | b         |
| Exposure - | c         | d         |

---

***Odds Ratio:***

$$[a * d] / [b * c]$$

---

$$OR = ad/bc$$

|             | Disease  | No Disease |
|-------------|----------|------------|
| Exposed     | <b>a</b> | <b>b</b>   |
| Not Exposed | <b>c</b> | <b>d</b>   |

**c** Odds Ratio (OR) = Cross Products Ratio =  $\frac{ad}{bc}$

# Interpreting Odds Ratios

OR= 1 = null association

OR  $\geq$  1 = exposure increases odds of disease (harmful)

OR  $\leq$  1 = exposure decreases odds of disease (protective)

*Often people will refer to risk when they're talking about odds. It's a very easy mistake to make! Sometimes it's true, but not always.*

*Helpful video for interpretation:*

[https://www.youtube.com/watch?v=5zPSD\\_e\\_N04](https://www.youtube.com/watch?v=5zPSD_e_N04)

# OR examples

|    | D+ | D- |
|----|----|----|
| E+ | 80 | 55 |
| E- | 20 | 45 |

$$= ad/bc = (80*45)/(20*55) = 3.3$$

|    | D+ | D- |
|----|----|----|
| E+ | 30 | 45 |
| E- | 70 | 55 |

$$= ad/bc = (30*55)/(45*70) = 0.52$$



# Odds Ratios and Risk Ratios

- If a disease/outcome is rare, the odds ratio will be approximately the same as the risk ratio
- If the probability of outcome is less than 10%, it is considered a rare outcome
- This is known as the **rare disease assumption**

# Odds Ratio vs. Risk Ratio

Let's examine the risk of myocardial infarction (MI) among individuals with high BP compared to those with low BP:

|                                      | <b>Disease +<br/><i>MI</i></b> | <b>Disease –<br/><i>No-MI</i></b> | <b>Total</b> |
|--------------------------------------|--------------------------------|-----------------------------------|--------------|
| <b>Exposure +<br/><i>High BP</i></b> | 180                            | 9820                              | 10,000       |
| <b>Exposure –<br/><i>Low BP</i></b>  | 30                             | 9970                              | 10,000       |

# OR and RR

|                              | Disease +<br><i>MI</i> | Disease –<br><i>No-MI</i> | Total  |
|------------------------------|------------------------|---------------------------|--------|
| Exposure +<br><i>High BP</i> | 180                    | 9820                      | 10,000 |
| Exposure –<br><i>Low BP</i>  | 30                     | 9970                      | 10,000 |

$$RR = \frac{\frac{180}{10000}}{\frac{30}{10000}} = \frac{0.0180}{0.0030} = 6.00$$

$$OR = \frac{\frac{180}{9820}}{\frac{30}{9970}} = \frac{0.01833}{0.00301} = 6.09$$

The risk ratio and odds ratio are similar because heart attacks are a rare occurrence in the population:

$$((180+30) / 20000) = 1.05\%$$

# Odds Ratio vs. Risk Ratio

Let's examine the risk of a local skin reaction among individuals who receive a flu shot compared to those who receive a placebo injection:

|                                       | <b>Disease +<br/><i>Skin reaction</i></b> | <b>Disease –<br/><i>No reaction</i></b> | <b>Total</b> |
|---------------------------------------|---|---|--------------|
| <b>Exposure +<br/><i>Flu shot</i></b> | 650                                       | 1920                                    | 2570         |
| <b>Exposure –<br/><i>No shot</i></b>  | 170                                       | 2240                                    | 2410         |

# Skin Reaction

|                               | Disease +<br><i>Skin reaction</i> | Disease –<br><i>No reaction</i> | Total |
|-------------------------------|-----------------------------------|---------------------------------|-------|
| Exposure +<br><i>Flu shot</i> | 650                               | 1920                            | 2570  |
| Exposure –<br><i>No shot</i>  | 170                               | 2240                            | 2410  |

$$RR = \frac{\frac{650}{2570}}{\frac{170}{2410}} = \frac{0.2529}{0.0705} = 3.59$$

$$OR = \frac{\frac{650}{1920}}{\frac{170}{2240}} = \frac{0.3385}{0.0759} = 4.46$$

The risk ratio and odds ratio are not similar because skin reactions were not a rare occurrence in the population:

$$((650+170) / 4890) = 16.7\%$$

# THE EFFECT OF RACE AND SEX ON PHYSICIANS' RECOMMENDATIONS FOR CARDIAC CATHETERIZATION

KEVIN A. SCHULMAN, M.D., JESSE A. BERLIN, Sc.D., WILLIAM HARLESS, Ph.D., JON F. KERNER, Ph.D., SHYRL SISTRUNK, M.D., BERNARD J. GERSH, M.B., Ch.B., D.Phil., ROSS DUBÉ, CHRISTOPHER K. TALEGHANI, M.D., JENNIFER E. BURKE, M.A., M.S., SANKEY WILLIAMS, M.D., JOHN M. EISENBERG, M.D., AND JOSÉ J. ESCARCE, M.D., Ph.D.



**TABLE 1.** RATE OF REFERRAL FOR CARDIAC CATHETERIZATION, ODDS OF REFERRAL, ODDS RATIO, AND RISK RATIO ACCORDING TO SEX AND RACE.\*

| PATIENTS       | MEAN REFERRAL RATE<br>% | ODDS OF REFERRAL | ODDS RATIO (95% CI) | RISK RATIO (95% CI) |
|----------------|-------------------------|------------------|---------------------|---------------------|
| Four strata    |                         |                  |                     |                     |
| White men†     | 90.6                    | 9.6 to 1         | 1.0                 |                     |
| Black men      | 90.6                    | 9.6 to 1         | 1.0 (0.5–2.1)       |                     |
| White women    | 90.6                    | 9.6 to 1         | 1.0 (0.5–2.1)       |                     |
| Black women    | 78.8                    | 3.7 to 1         | 0.4 (0.2–0.7)       | 0.87 (0.80–0.95)    |
| Aggregate data |                         |                  |                     |                     |
| White†         | 90.6                    | 9.6 to 1         | 1.0                 |                     |
| Black          | 84.7                    | 5.5 to 1         | 0.6 (0.4–0.9)       | 0.93 (0.89–0.99)    |
| Men†           | 90.6                    | 9.6 to 1         | 1.0                 |                     |
| Women          | 84.7                    | 5.5 to 1         | 0.6 (0.4–0.9)       | 0.93 (0.89–0.99)    |
| Overall        | 87.7                    | 7.1 to 1         |                     |                     |

\*Referral rates for the four strata were inferred from aggregate rates and odds ratios reported by Schulman et al.<sup>1</sup> The odds of referral were calculated according to the following formula: referral rate ÷ (100% – referral rate). The risk ratio was calculated as the referral rate for the group in question divided by the referral rate for the reference group. CI denotes confidence interval.

†This was the reference group.

# Understanding the Results

- OR= 0.6
  - The odds that black patients would be referred for catheterization were 40 percent lower than the odds of referral for white patients
- Odds are odd and hard to understand
  - Usually people understand odds by equating it with risk
- BUT, when the outcome is common, odds  $\neq$  risk



# How common was the outcome?

- Very common
  - 84.7% of Black people and 90.6% of White people were referred for cardiac intervention/surgery
- Authors report an odds ratio of 0.6, but because the outcome is so common the risk ratio is 0.93
  - 40% lower odds of referral among black patients compared with white patients, but black people actually only had a 7% lower risk of being referred



# Why are odds so hard to understand?

- With risk, you're dividing the number of people who have an event divided by the total number of people in the population
- With odds you're expressing the number of those who experience the event divided by the number of those who do not
  - Range from 0 (event will never happen) to infinity (event will occur with absolute certainty).

# Point estimates & confidence intervals

- Point estimate: observed estimate of the E-D association from your data
- Confidence interval: range of values plausible values for the same E-D association
  - Upper and lower bounds – confidence limits
  - Used to indicate precision of the estimate, width of CI depends on the amount of variability
- Help evaluate the certainty of an estimate (risk, odds, rates)
  - Alternatively: How much uncertainty surrounds the estimate I have chosen to report?

RR= 1.5 (95% CI: 1.0, 2.0)

# Conceptual definition of CIs

Over an infinite number of repetitions of the same study, the confidence interval will contain the true parameter 95% of the time

-This interpretation is based on sampling and probability theory and is not particularly helpful interpreting your study results

-Estimate of uncertainty in your results due to random error

# Interpreting Confidence Intervals

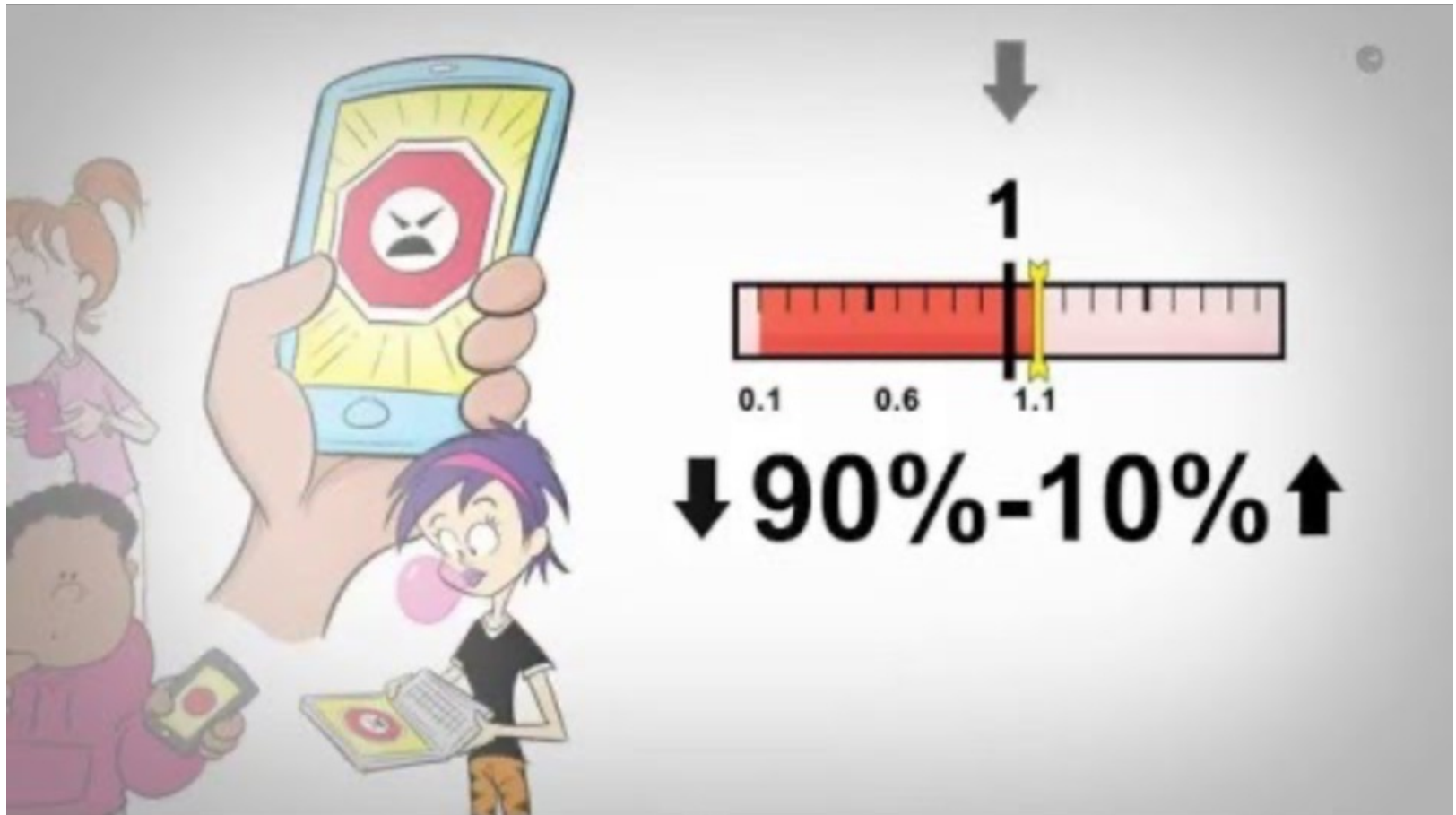
among cancer patients who received radiation, therapy tumor size decreased  $-.66\text{cm}$  (95% CI  $-0.46, -0.96$ ) compared with those who did not receive radiation therapy

**Correct Interpretation:** It is likely that the true mean difference between the two groups is somewhere between  $-0.46$  ( a reduction of  $.46\text{ cm}$ ) and  $-0.96$  (a reduction of  $.96\text{ cm}$ )

**Incorrect Interpretation:** We are 95% certain that the true effect is between  $-.46$  and  $-.96$

# Confidence Interval Video

<https://www.youtube.com/watch?v=v0FXSAdYCKQ>



# 95% CI example

BJOG. 2016 Jan 20. doi: 10.1111/1471-0528.13863. [Epub ahead of print]

## The effect of prenatal lifestyle intervention on weight retention 12 months postpartum: results of the Norwegian Fit for Delivery randomised controlled trial.

Sagedal LR<sup>1,2</sup>, Sanda B<sup>1,3</sup>, Øverby NC<sup>3</sup>, Bere E<sup>3</sup>, Torstveit MK<sup>3</sup>, Lohne-Seiler H<sup>3</sup>, Hillesund ER<sup>3</sup>, Pripp AH<sup>4</sup>, Henriksen T<sup>5</sup>, Vistad I<sup>1</sup>.

### + Author information

#### Abstract

**OBJECTIVE:** To examine the effect of a prenatal lifestyle intervention on postpartum weight retention (PPWR).

**DESIGN:** Randomised controlled trial.

**SETTING:** Healthcare clinics in southern Norway.

**POPULATION:** Healthy, nulliparous women with body mass index  $\geq 19$  kg/m<sup>2</sup>, age  $\geq 18$  years, and singleton pregnancy of  $\leq 20$  gestational weeks.

**METHODS:** Women were randomised to intervention (dietary counselling twice by phone and access to twice-weekly exercise groups during pregnancy) or control group (standard prenatal care). Intervention compliance was defined post-factum as attending dietary counselling and  $\geq 14$  exercise classes.

**MAIN OUTCOME MEASURES:** PPWR (weight measured postpartum minus self-reported pre-pregnancy weight) and the proportion of women returning to pre-pregnancy weight.

**RESULTS:** Of 606 women randomised, 591 were included in an intention-to-treat analysis of pregnancy outcomes and 391 (64.5%) were analysed 12 months postpartum. Mean PPWR was not significantly different between groups (0.66 kg for intervention versus 1.42 kg for control group, mean difference -0.77 kg, 95% CI -1.81, 0.28;  $P = 0.149$ ). An increased proportion of intervention participants achieved pre-pregnancy weight (53% versus 43%, OR 1.50, 95% CI 1.003, 1.471;  $P = 0.045$ ). However, the difference was not statistically significant when we adjusted for missing data (adjusted odds ratio (OR) 2.23,  $P = 0.067$ ) using logistic mixed-effects models analysis. Women compliant with intervention had significantly lower PPWR than control participants, also after adjusting for potential confounders (adjusted mean diff -1.54 kg, 95% CI -3.02, -0.05;  $P = 0.039$ ).

**CONCLUSIONS:** The Norwegian Fit for Delivery intervention had little effect on PPWR, although women who were compliant with the intervention demonstrated significantly lower PPWR at 12 months.