# Choosing a Proper Statistical Method – Part II

Yuda Chongpison, PhD, MS, MBA
Research Affairs, Faculty of Medicine
Chulalongkorn University

# STUDY DESIGNS

# Study Designs

- From Exercise I, what would be the design of this study?
  - "*to compare cardiorespiratory and cerebrovascular functions between Karen women wearing brass neck coils and those without neck coils.*"
- Can it be experimental?

# Study Designs

- Experimental design: randomized controlled trial (RCT), cross-over RCT
- Non-experimental  design: cohort, case-control, cross-sectional studies

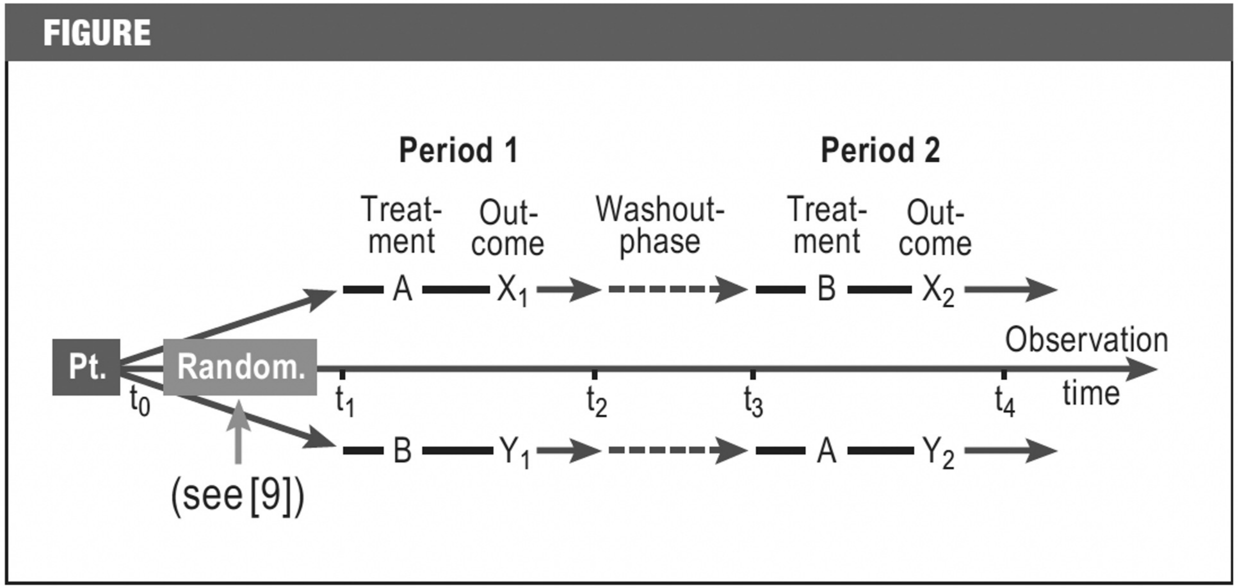
# Randomized Controlled Trial (RCT)

**Randomize Individuals**

→ **EXPOSED/ Active Rx Statin** → **Cholesterol Levels (***ldl − c level***)**

→ **UNEXPOSED/Control Dietary Control** → **Cholesterol Levels (***ldl − c level***)**

# Cross-Over RCT




**Design of a crossover trial:** Pt., patient; Random., randomization

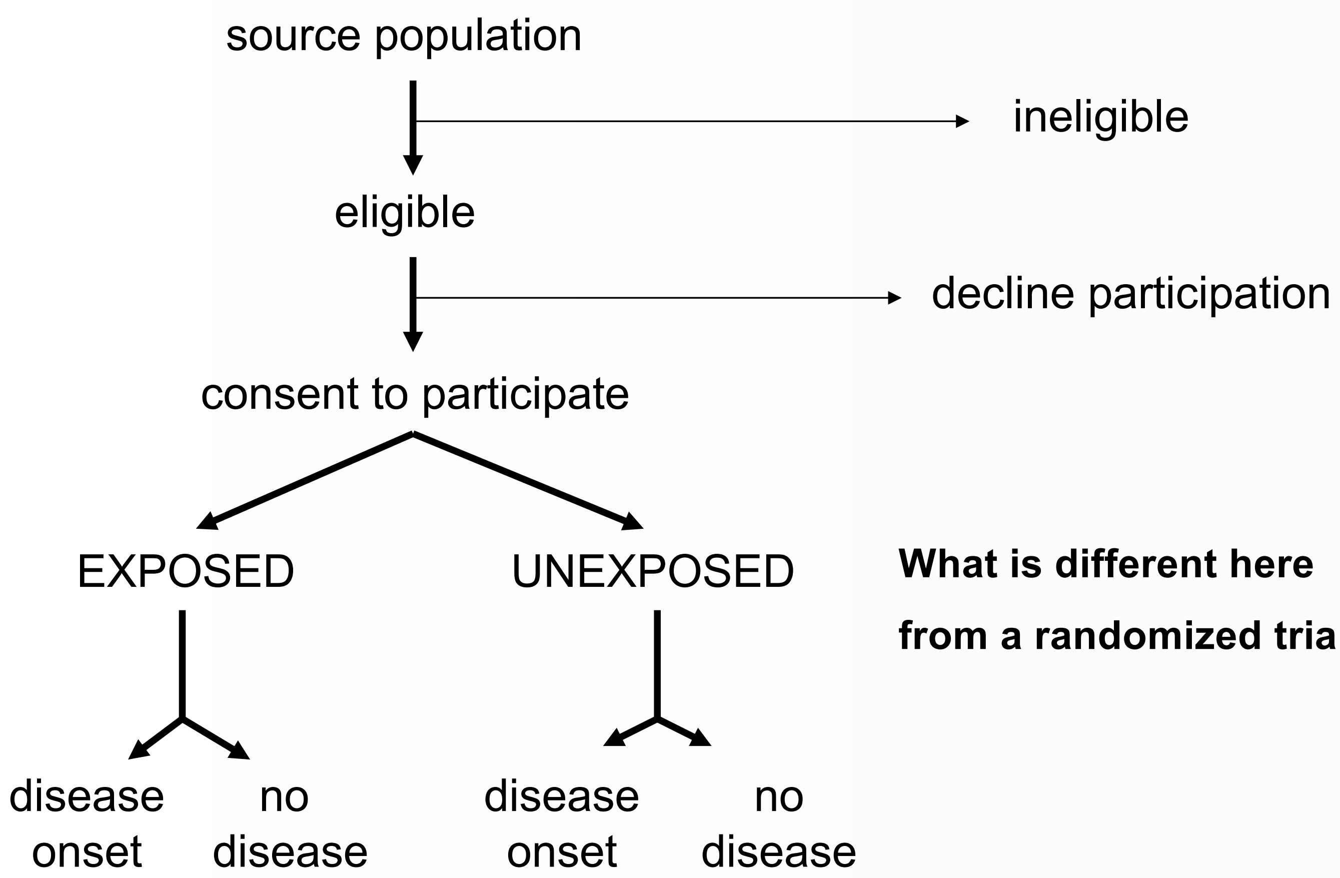
- Carry-over effect
- Treatment effect

Welleck & Blettner 2012; 109(15): 276–81. DOI: 10.3238/arztebl.2012.0276

# Non-Randomized Studies

- Cohort study
- Case-control study
- Cross-sectional study

# Schematic of a Cohort Study




**What is different here from a randomized trial?**

# Case-Control Study Design

Were exposed | Were not exposed

Have the disease

**CASES**

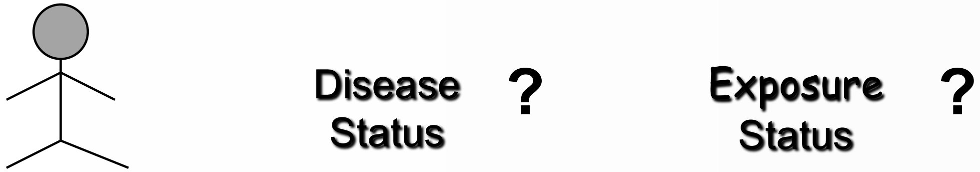
Were exposed | Were not exposed

Do not have the disease

**CONTROLS**

Basic Design: Select cases and controls without knowledge of their exposure status,
Measure exposure status in cases and controls

# Cross-Sectional Design

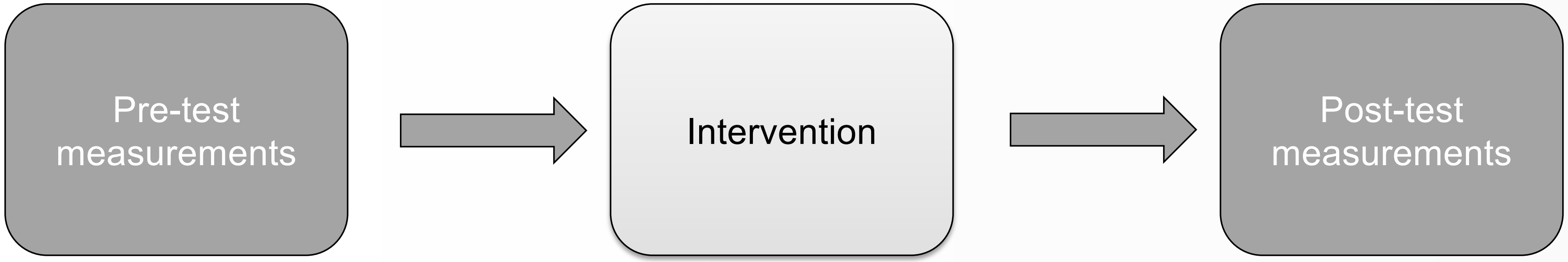



Investigators ascertain present (i.e., prevalent) DISEASE status and present (or past) EXPOSURE status simultaneously

# SINGLE VS REPEATED

# Single or repeated measure(s)

- Single measure: independent (not depend on other)
- Repeated measures: depend on previous measures
  - Quasi-experimental design: pre-test and post-test design



# Paired and unpaired data

**Paired data:**

- Left vs right eye (in same patient)
- BP before vs after drug (in the same patient)
- Married couples (husband vs wife)

**Unpaired data:**

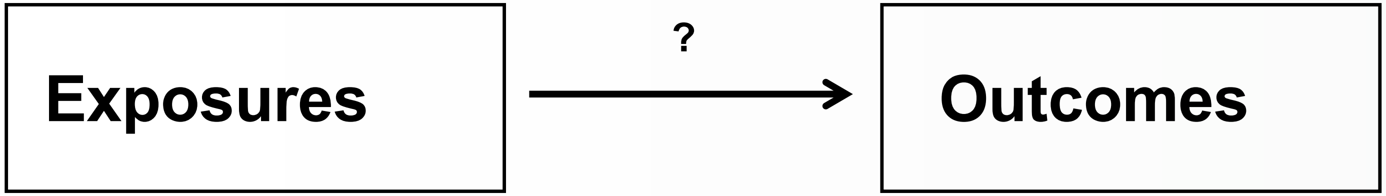
- Two randomized groups
- Male vs Female

# Why "pairedness" is important

- Paired data are not independent
  - Skin prick tests on your left and right arm could well be similar
  - Attitudes of a husband and wife about health may be similar
- The subject acts as their own baseline. Variation between patients is taken out of the 'mix' and only variation due to drug remains
- Considering the pair: increase the power of a test (ability to detect a true difference)

# Dependent Variable(s)

- In other words: outcome or response variables
- Number of outcomes
- Whether the outcomes are related or would be considered as a set

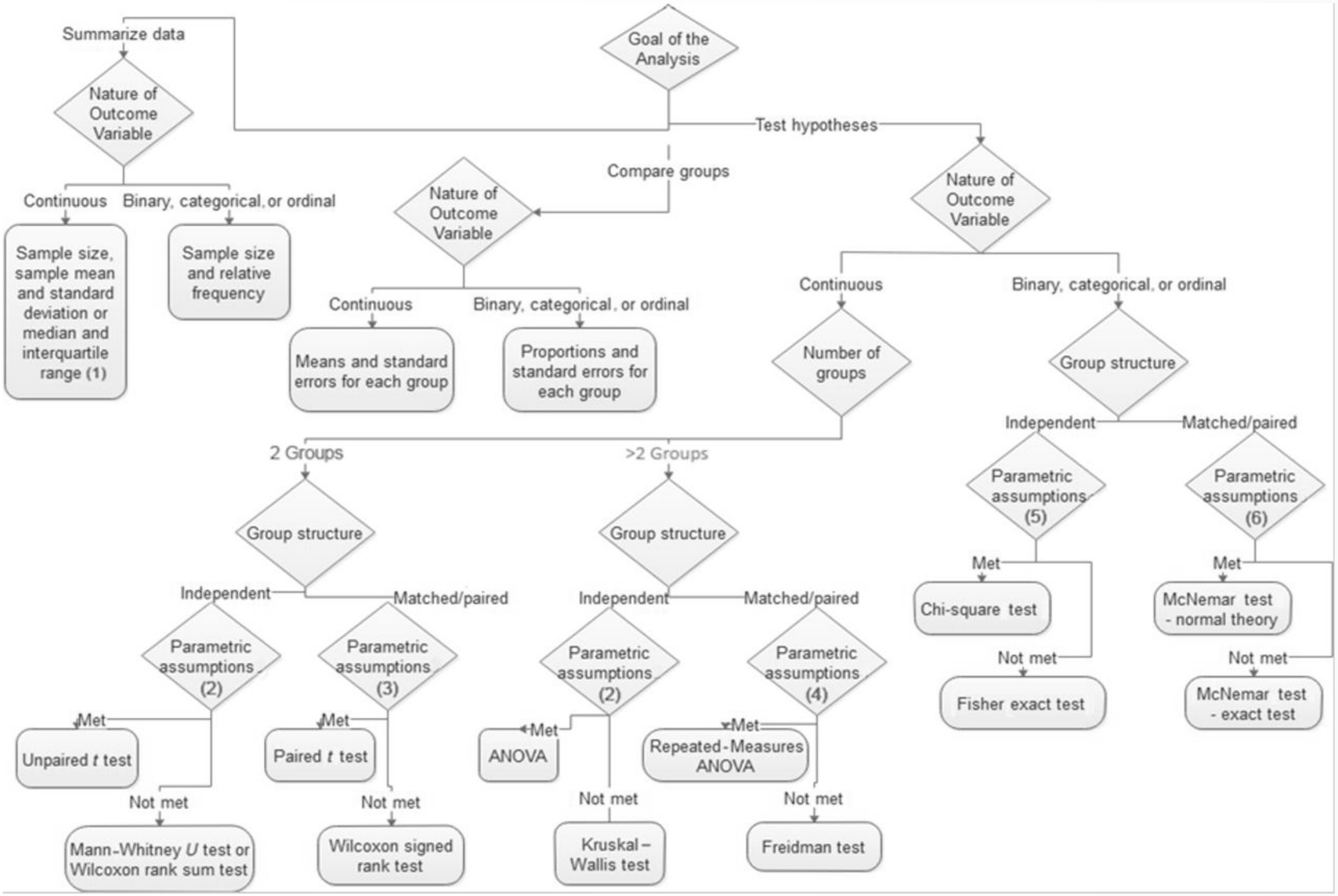


For one dependent variable

# CHOOSING A STATISTICAL METHOD

# Choosing a Statistical Test

- Purpose or question of the study
- Study design: independent vs dependent samples, longitudinal design, or pre- and post- design.
- A type of outcome measurement: continuous, categorical (binary, ordinal, or nominal), counts
- Number of explanatory variables




Lisa M. Sullivan et al. J Am Heart Assoc 2016;5:e004142

# Determining what statistical technique or test to do when:

- (1) mean and standard deviation if no extreme or outlying values are present;
- (2) independence of observations, normality or large samples, and homogeneity of variances;
- (3) independence of pairs, normality or large samples, and homogeneity of variances;
- (4) repeated measures in independent observations, normality or large samples, and homogeneity of variances;
- (5) independence of observations and expected count >5 in each cell;
- (6) repeated measures in independent observations.

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# REVIEW RESEARCH QUESTIONS

# Comparing means (two samples)

- We compare means when:
  - Dependent variable is continuous
  - Independent variable is categorical (ordinal or nominal)
- Examples:
  - Is systolic blood pressure (mmHg) dependent on treatment (placebo vs new drug)?
    - …..equivalently is SBP same for placebo and drug groups?
  - Is mental health score (range 0 to 100) dependent on being physically active (yes/no)?

# Comparing means (two + samples)

- ANOVA: To test for differences in a continuous variable between classes of categorical variables (factors) and their interactions
- Example: evaluate differences in systolic blood pressure between difference racial groups

$$H_0: \mu_{African} = \mu_{Asian} = \mu_{Caucasian}$$

# ANOVA Hypotheses

- Null hypothesis
  - $H_0$: $\mu_1 = \mu_2 = \ldots = \mu_k$
  - All group means are the same
- Alternative hypothesis
  - $H_0$: $\mu_1 = \mu_2 \neq \mu_3 = \ldots = \mu_k$
  - At least one group mean is different

# Steps in conducting ANOVA

- Descriptive
- Overall F-test, if significant, report post-hoc results
- Post-hoc analysis

# Post Hoc Tests

- Bonferroni: most conservative
- Scheffe's test: likely to lead to Type II errors – except in situation that complex comparisons are being made
- Tukey's HSD test: for equal  sample sizes per group (can be adapted for unequal sample sized)
- When all pairs of means are being compared, Tukey's is the procedure of choice

# Non-parametric Equivalents for T-Test & ANOVA

| Parametric Tests | Non-parametric Tests |
| --- | --- |
| One sample t-test | Wlicoxon Single Sample T-test |
| Two independent samples t-test | Mann-Whitney U (Wilcoxon rank sum) Tests |
| Paired t-test | Wilcoxon Signed Rank Test |
| ANOVA | Kruskal-Wallis Test |

Dependent variable = outcome variable/values you want to compare
group variable = binary or categorical variables

# Increase risk of outcome

- Research question: which of these training modalities (high-intensity interval training or blood flow restriction) is more effective in reducing cardiovascular risk?
- What are the exposure and outcome variables?
- if the outcome variable is a binary such as having a condition and not having a condition, what would statistical test would you use?

# $\chi^2$ test of independence (two categorical variables)

- Perhaps the most widely used test for categorical variables
- This test used for *associations between two categorical variables*
- Fisher's exact test: used when assumption for $\chi^2$ test is not met
- McNemar's Chi-squared test: for dependent data (2x2)

Incidence and Prevalence

# MEASURE OF DISEASE FREQUENCY

# Incidence

- An “event”: the occurrence of any discrete phenomenon
  - heart attack, cancer, start smoking, quit drinking, failure of a light bulb
- Incident event: new (“first-ever”) event
- Incidence: the collection of incident events

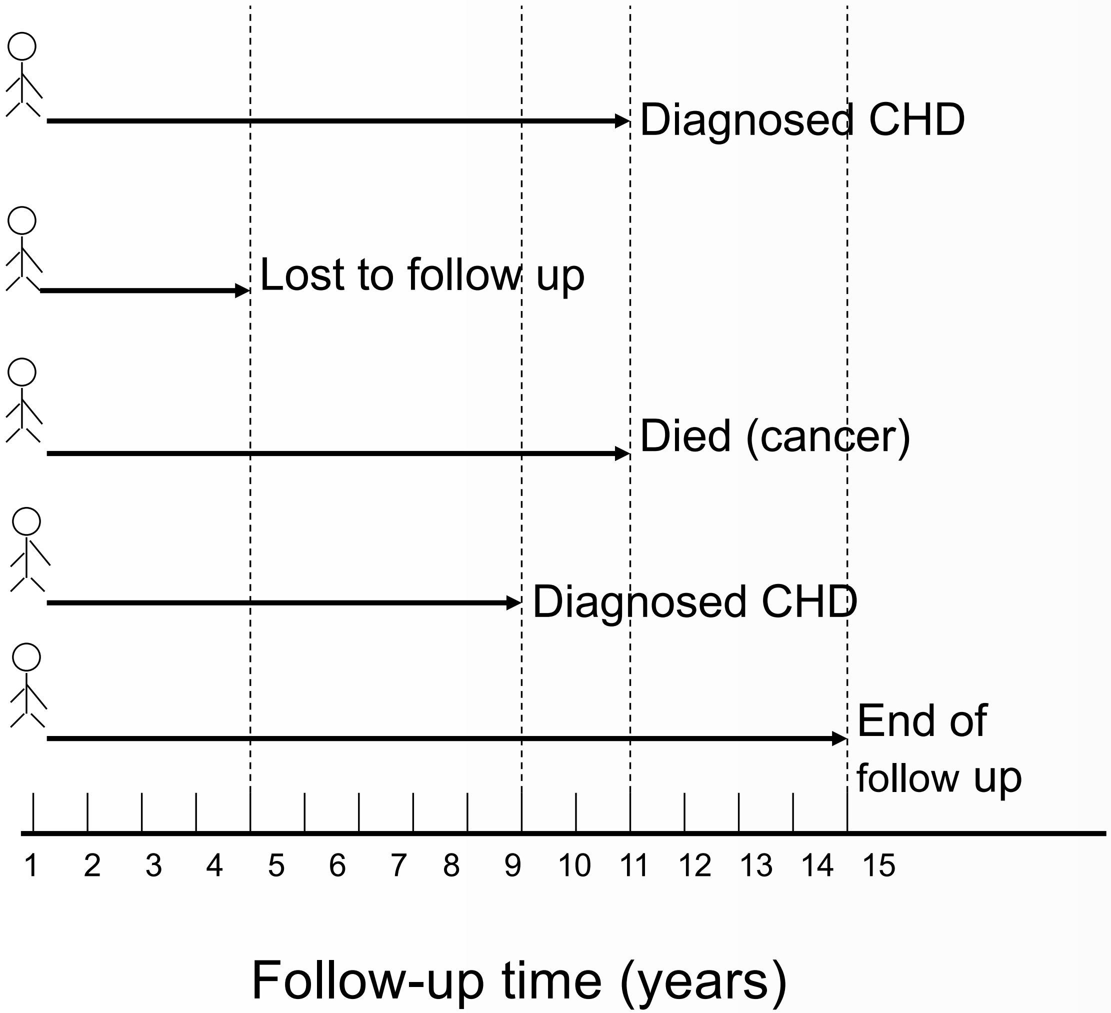
# Measures: Incidence Proportion

- Count of incident cases
- Incidence proportion/Cumulative incidence

$$\frac{\textbf{Count of incident events during a specific time period}}{\textbf{People at-risk of incident event during that period of time}}$$

- Example: cumulative incidence of new AIDS cases reported in Massachusetts in 2004 - 9.2 per 100,000 during 2004

## If people at risk are observed for different periods of time




Time at risk
11 years

4 years

11 years

9 years

15 years

Total = 50 person-years

# Measure: Incidence Rate

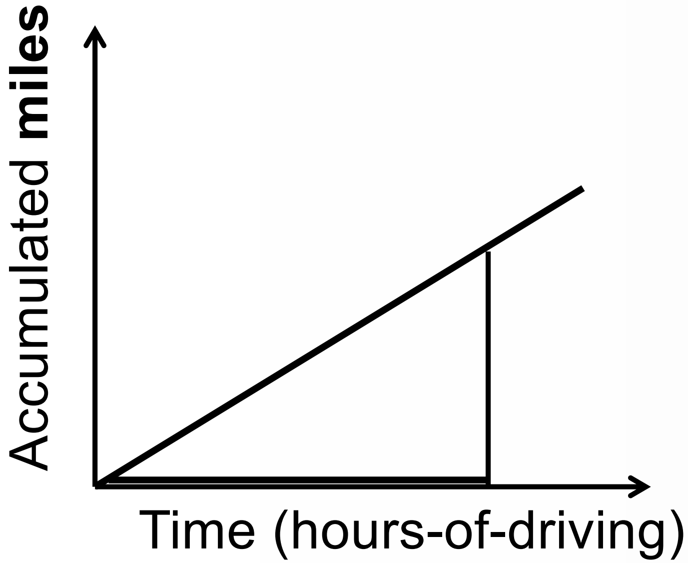
- Incidence rate/incidence density

$$\frac{\textbf{Count of incident events}}{\textbf{Person-time at-risk of incident event}}$$

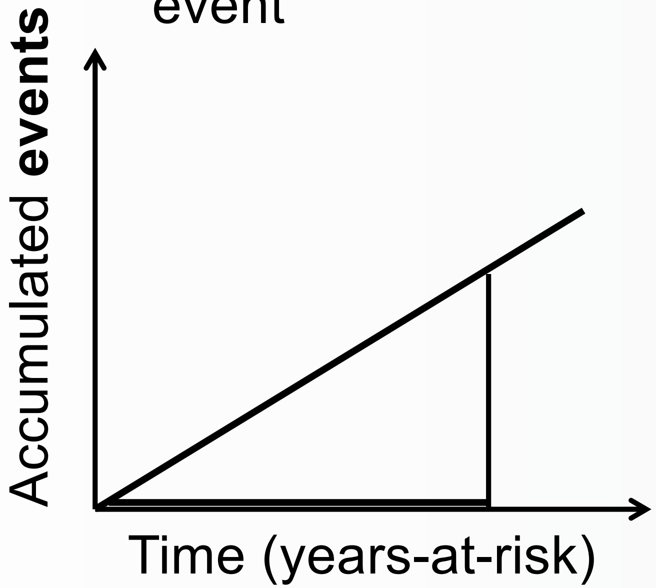
  – Time at-risk varies from person to person
  – Each person contributes time at-risk to the denominator
- Example: incidence rate of coronary artery disease among women using hormone replacement therapy was 55.2/100,000 person-years

# Rate

Velocity (speed)
of a car




Velocity (speed)
of the occurrence of an
event




Speed = Miles / Time

Rate = Events / person-time at risk

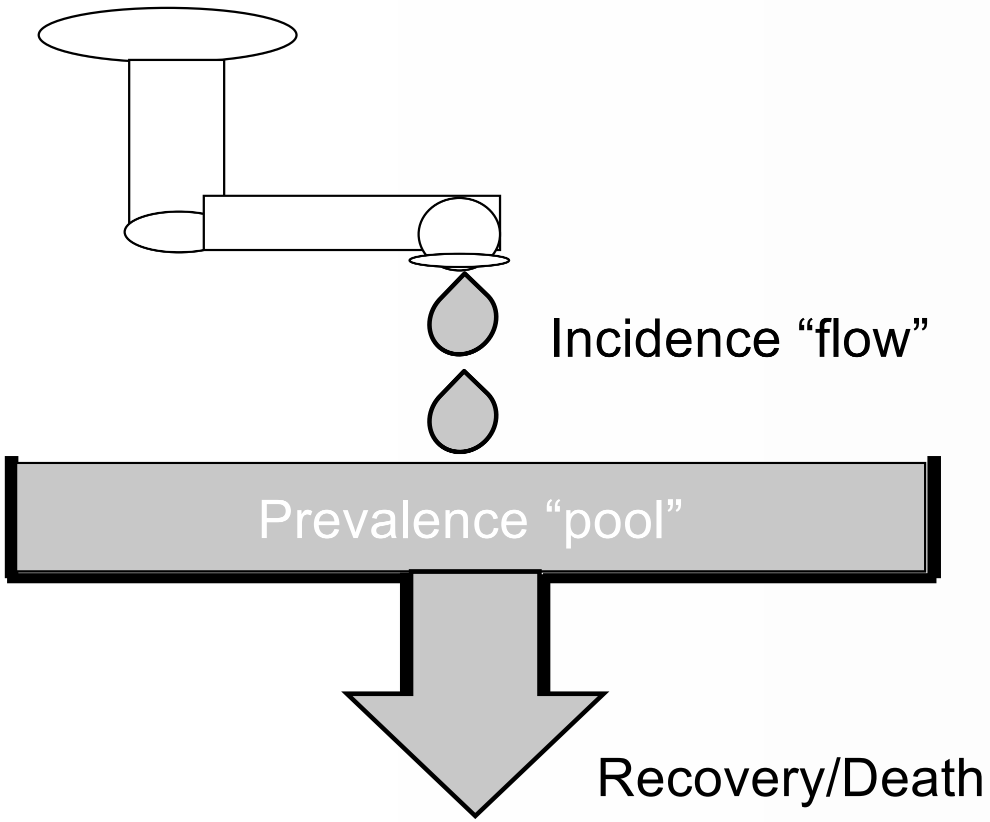
# Prevalence

- Prevalence: frequency of an existing event
- Count of prevalence cases
- Point prevalence: prevalence of the disease at a certain point in time

$$\frac{\textbf{Count of prevalence events at a point in time}}{\textbf{Number of persons in the population at that time}}$$

- Period prevalence: number of people have had the disease at any point during a certain time period. Time period: a month, a single calendar year, or 5-year period

# The prevalence “pool”




Prevalence = f(indicidence rate, duration of disease)

Adopted from Dr. Jim Neaton & Dr. Eyal Shahar

# Relationship between incidence and prevalence

- If the prevalence of a disease is constant and incidence and rate of cure or death are about the same, then the relationship is

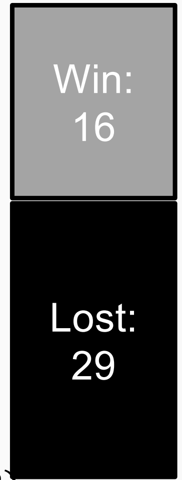
$$\frac{\boldsymbol{Prevalence}}{\mathbf{1}-\boldsymbol{Prevalence}} = \boldsymbol{Incidence\ Rate} \times \boldsymbol{Average\ Duration\ of\ Disease}$$

- P = proportion of the population with the disease
- 1- P = proportion of population without the disease

Odds, Probability, Risk

# MEASURE OF ASSOCIATIONS: DIFFERENCE, RATIOS

# Risk vs. Odds




**Risk or Chance**

$$Risk\ or\ Chance\ = \frac{occurence\ of\ an\ event\ of\ interest}{all\ possible\ outcomes}$$

**Odds**

$$Odds\ of\ an\ event = \frac{Probability\ of\ occurance\ of\ an\ event\ (P)}{Probablity\ of\ the\ event\ not\ occurring\ (1-P)}$$

Chance of winning a race
= 16/45 = 36%
= 36 per 100

Odds = 16/29 = 0.55
= 1: 1.18
= 5: 9

# Defining Odds

- The probability of having an attribute divided by the probability of not having that attribute
- The probability of winning (A)
  - Pr(A) = 16/45 = 0.36
- The probability of not winning (not A)
  - Pr(not A) = 29/45 = 0.64
- Odds of wining = 0.36/0.64 = 0.55

# Risk, Probability, Chance, Odds

| Risk (Probability) | Odds |
|---|---|
| Range: 0 to 1 | Range: 0 to +infinity |
| Pr(not A) = 1 – Pr (A) | Odds(not A) = 1/Odds(A) |
| 0.64 = 1 – 0.36 | 1.8/1 = 1/0.55 |

# Risk vs Odds (cont.)

| Risk (Chance) | Odds |
|---|---|
| 10% (1:10) | 1:9 |
| 25% (1:4) | 1:3 |
| 50% (1:2) | 1:1 |
| 75% (3:4) | 3:1 |

# Relative Risk (RR)

- Ratio of the risks $= \frac{Risk\ in\ exposed}{Risk\ in\ non{-}exposed}$

| | Interpreting relative risk (RR) of a disease | |
|---|---|---|
| RR = 1 | Risk in exposed equal to risk in non-exposed | No association |
| RR > 1 | Risk in exposed greater than risk in non-exposed | Positive association; possibly causal |
| RR < 1 | Risk in exposed less than risk in non-exposed | Negative association; possibly protective |

# Odds Ratio (OR)

- Odds = $\frac{P}{1-P}$
- Ratio of the odds
- $OR = \frac{\text{Odds that an exposed person develops disease}}{\text{Odds that a non-exposed person develop disease}}$
- Interpretations for odds ratio
  - OR = 1
  - OR > 1
  - OR < 1

# Hypothetical Cohort

- Evaluate whether smoking is associated with the development of coronary heart disease (CHD) over a 1-year period

| | **Developed CHD** | **CHD does not develop** | **Total** | **Incidence per 1,000 per year** |
|---|---|---|---|---|
| Smoker | 84 | 2916 | 3,000 | 28.0 |
| Nonsmokers | 87 | 4913 | 5,000 | 17.4 |

- Relative risk = 28.0/17.4 = 1.61

# Relationship between odds ratio and relative risk

| | Disease developed | No Disease developed | Total |
|---|---|---|---|
| Exposed | a | b | a+b |
| Not Exposed | c | d | c+d |
| Total | a+c | b+d | a+b+c+d |

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

*Odds ratio: a good approximation of the relative risk when the disease is rare*

# Example - Rare Disease

| | Disease developed | No Disease developed | Total |
|---|---|---|---|
| Exposed | 200 | 9,800 | 10,000 |
| Not Exposed | 100 | 9,900 | 10,000 |

- $Relative\ Risk = \frac{200/10{,}000}{100/10{,}000} = 2$
- $Odds\ Ratio = \frac{200 \times 9{,}900}{100 \times 9{,}800} = 2.02$

What would be the incidence of this disease?

# Example - Common Disease

| | Disease developed | No Disease developed | Total |
|---|---|---|---|
| Exposed | 50 | 50 | 100 |
| Not Exposed | 25 | 75 | 100 |

- $Relative\ Risk = \frac{50/100}{25/100} = 2$
- $Odds\ Ratio = \frac{50 \times 75}{25 \times 50} = 3$

Incidence of disease = ?

# Statistical vs Clinical Significance

**Statistical Significance**

- Tells us whether the effect is real or the association we observe could have happened just by chance

- NLR as a predictor of in-hospital mortality ($p < 0.001$)

**Clinical Significance**

- Observed effect that has an important clinical implication

- NLR as a predictor of in-hospital mortality: OR = 1.2 (95%CI 1.09, 1.35)

NLR = Neutrolphil count-to-differential lymphocyte count ratio

# Q & A