Study Design and Biostatistics for the Bedside Healthcare Professional.

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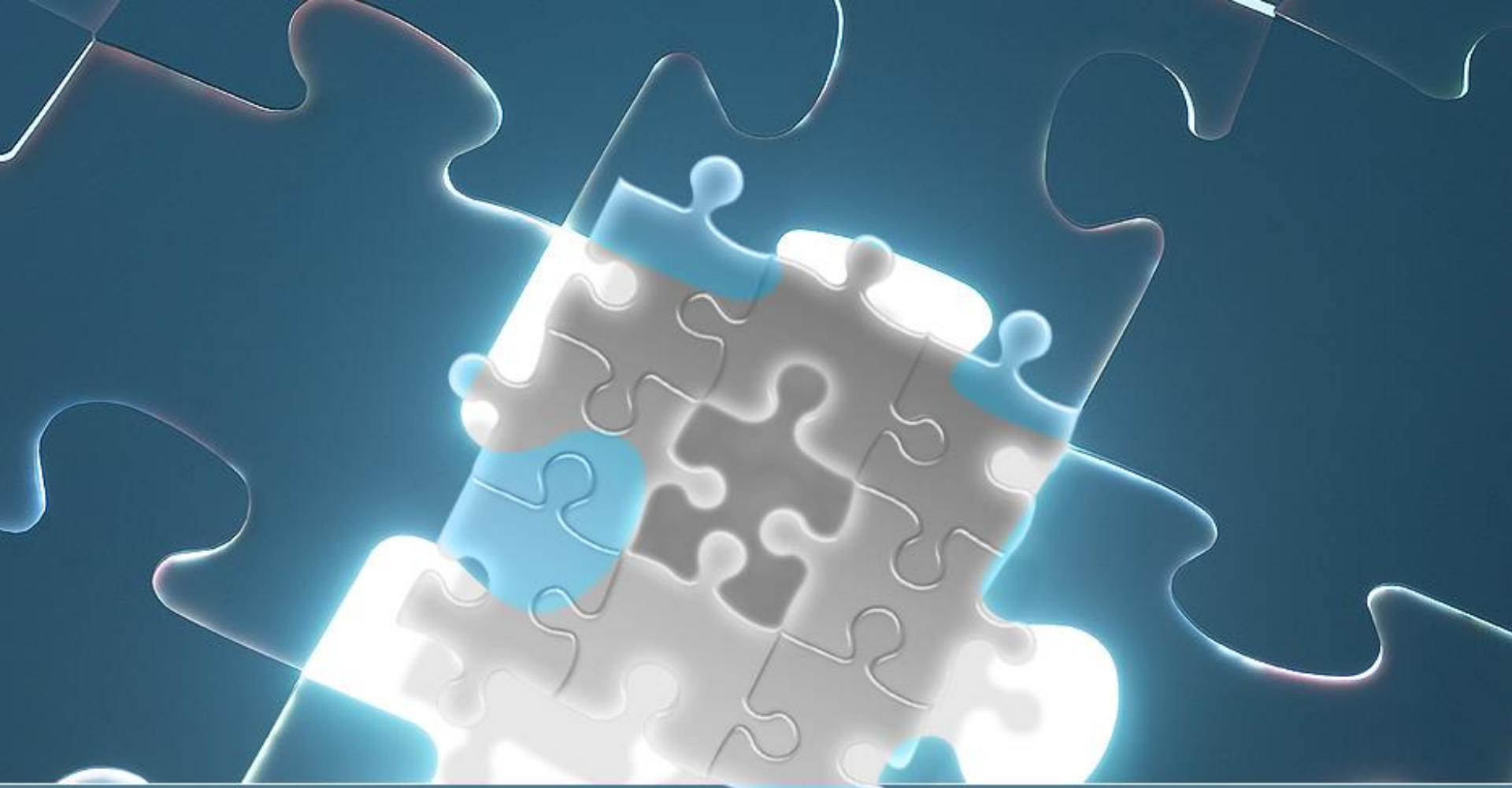

Study Design and Biostatistics for the Bedside Healthcare Professional

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Words of Wisdom

- *"[Biostatistics are] a whole lot of nothing!" (Gerard Dallal, 2000)*
- *"100% of all disasters are failures of design, not analysis." (Ron Marks, 1994)*
- *"Statistics is backwards!" (Gerard Dallal, 2000)*

Hypothesis Testing

- Begin with a Null and Alternative hypothesis
- Set the alpha level
- Perform the appropriate statistical test
- Calculate the p-value from the test statistic
- Decide if results are likely due to chance alone (not statistically significant) or unlikely due to chance alone (statistically significant)

Hypothesis Testing

- Uniform way to look at the results of the study.
- Null hypothesis H_O: There is no difference
- Alternative hypothesis H_A: There is a difference
- Since H_O and H_A are opposites we can just talk about H_O
- We talk about H_O by saying we 'accept' or 'reject' it
  - Accept means no difference or association
  - Reject means there is a difference or association

Setting it Up

- Sample Size
  - How many subjects are needed to truly answer the research question?
  - Is the study feasible?
  - How do we calculate it?
    - Hypothesis based
    - Confidence interval based

Sample Size Considerations

- Two fundamental concepts
  - Large differences between groups (if really there) are easier to find and take fewer subjects
  - Large variability in the variables you are studying make finding a difference harder and take more subjects

What I Need to Know to Compute Sample Size:

- A variance and mean assessment of the variable in question.
  - Can use old studies
  - Literature
  - Pilot study
- The Effect Size: What difference does the researcher consider significant?
- What p-value(s) the researcher wishes to use.

Effect Size

- Assume you are working in a diabetes program and the mean HgbA1c is 8.5, what does the effect size need to be to lower your patient population below risk?
- If the risk level is 7.5 then:
- 1-(7.5/8.5)=0.12 or 12 percent effect size is needed.

Power of a Statistical Test

- Power is the probability of rejecting the null hypothesis when the null hypothesis is false (1-ß).
- This is the correct decision. When the real world agrees with the statistics.
- Remember the table...

Power Analysis

- Each statistical procedure has its own formula for power determination.
- Effect Size - Difficult concept to teach because it is not determined by the statistician, but rather the clinician.
  - What do you consider meaningful?
- Must understand the difference between:
  - Clinical Significance
  - Statistical Significance

Significance

- Clinical - Change in a variable that has a physical advantage or disadvantage associated with it, i.e., an increase in risk of disease.
- Statistical - Mathematical change in a variable that achieves a probability threshold not due to chance alone.

Probability and Confidence

- "p values"-probability a particular outcome would have arisen by chance
- $p<0.05$ (1 in 20 chance)-statistically sig.
- $p<0.01$ (1 in 100 chance)- highly s.s.
- non-significant p value means no difference between groups or insufficient subject number-can't tell which

Step 1

- Descriptive Stats
  - Mean, Standard Deviation, Outliers
  - Summarize important features of numerical data
  - Identify errors
  - Characterized subjects
  - Assess assumptions for statistical tests

Step 2

- Analytical/Inferential Statistics
  - Looking at associations among two or more variables
  - Estimate pattern and strength of associations
  - Test hypotheses

How Do You Know
(some rules)

- The data that you have needs to be of the same quality as other studies
  - Collected at the same statistical level
  - Not viewed as secondary data
  - Needs reliability and validity indicators
  - Best if all the data reside in one system that is linkable

Statistical Tests

- Mathematical formulas that produce p-values that allow investigators to assess the likelihood that chance accounts for the results observed in the study.
- There are many different statistical tests.

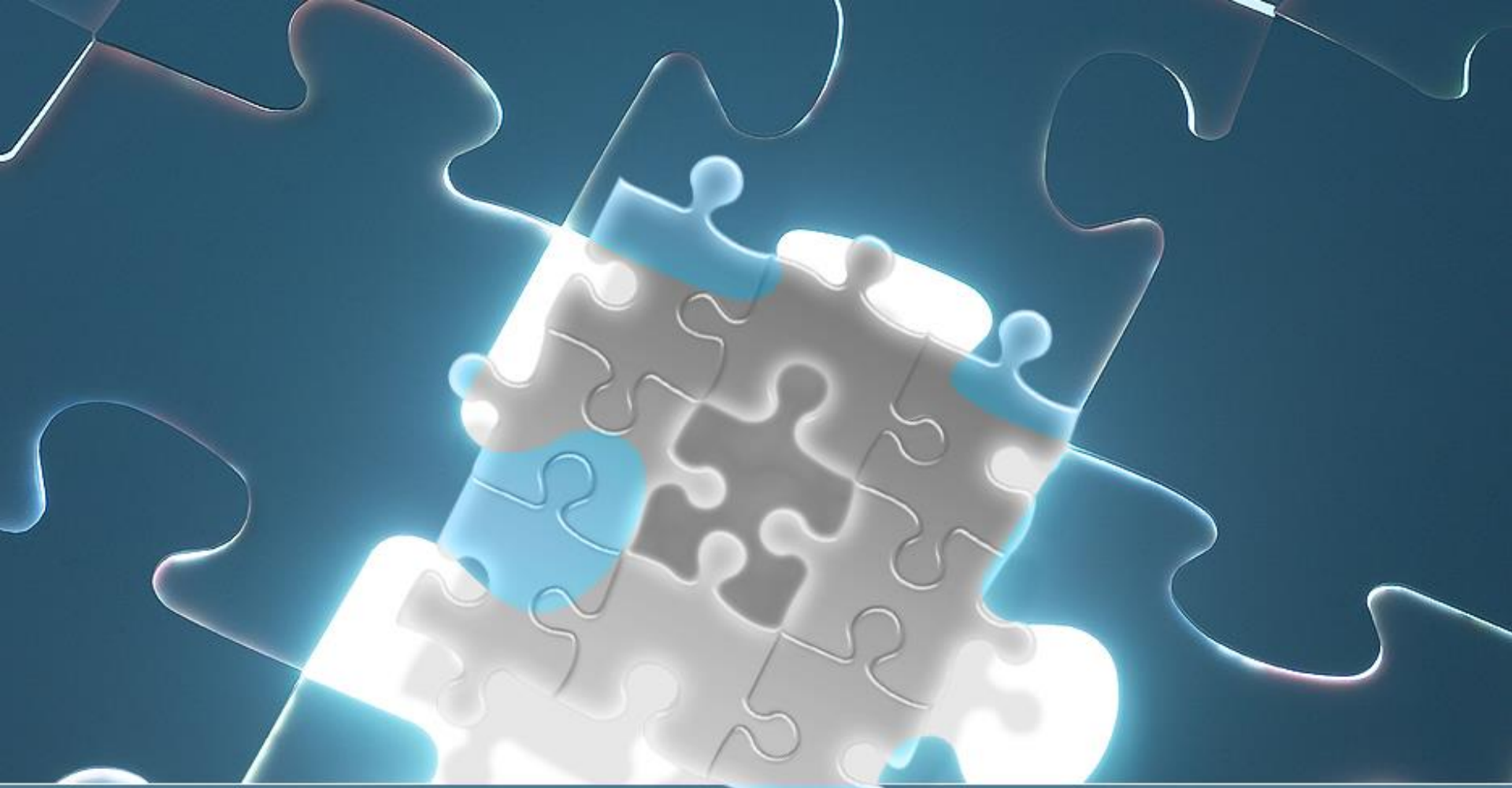
Which Statistical Test Do You Choose?

- This answer depends on:
  - The type of data
    - Continuous, Ordinal, or Nominal
  - The distribution of the data
    - Normally distributed, skewed
  - The type of study design
    - Means, proportions, number of groups, etc.

General Formula

- All statistical tests follow this general formula:

$$\text{Test Statistic} = \frac{\text{Observed val} - \text{Expected val}}{\text{Standard Error}}$$



Analysis of Continuous Data: Z and t Tests

One Sample Z Test

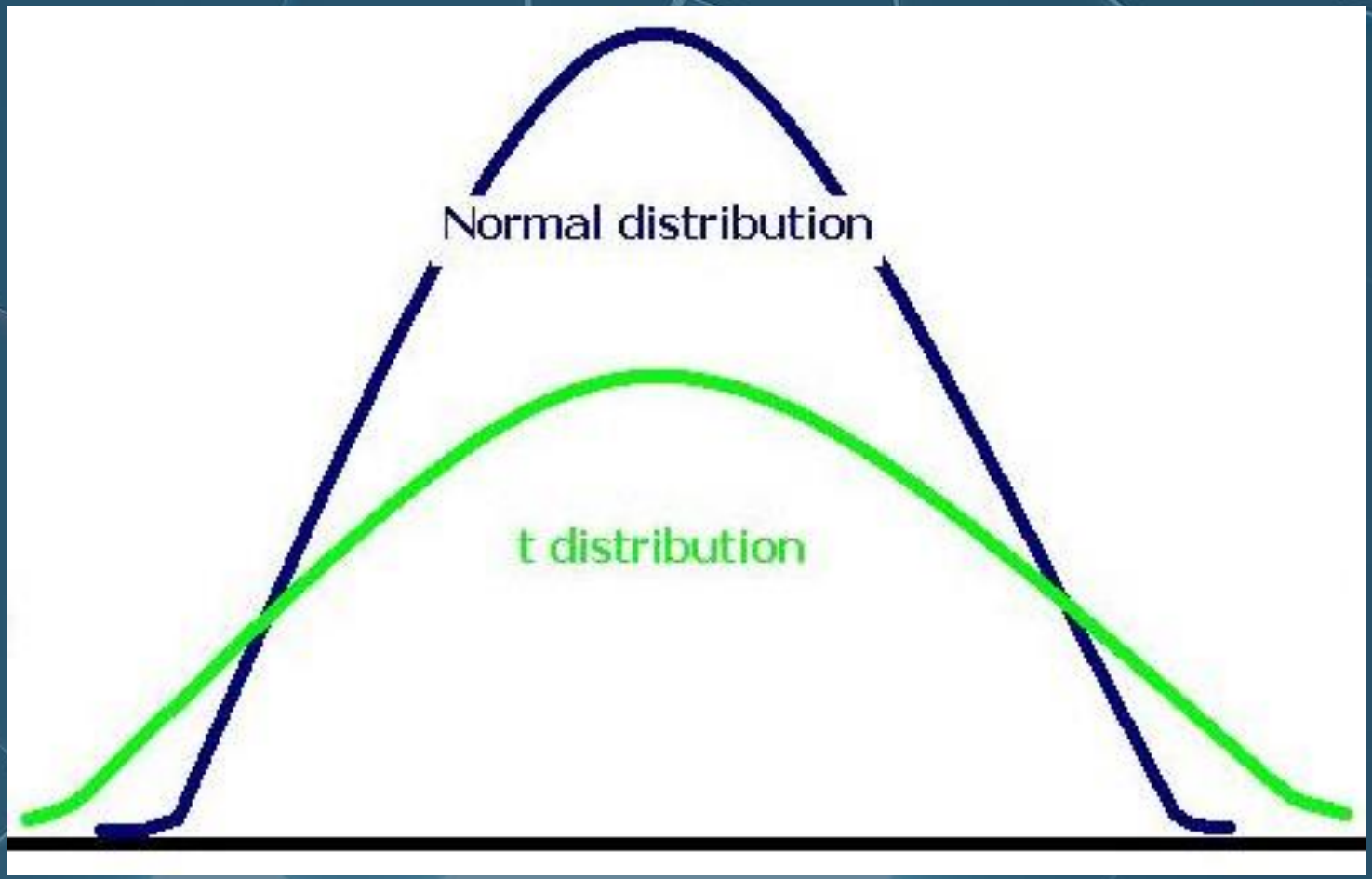
- Researchers are interested in whether the mean level of enzyme A in a certain population is different from 25. They measure levels of enzyme A in a sample of 10 individuals and find that the mean, $\bar{X} = 22$. Assume that the population has a known standard deviation, $\sigma = 6.7$
- H_0: $\mu = 25$ $\alpha = 0.05$

  H_A: $\mu \neq 25$
- Calculate test statistic: $Z = -1.41$
- Critical Value (from Z table): ± 1.96

t Tests

- Z test assumes population variance (or standard deviation) is known.
- When population standard deviation is unknown, but sample size is large (>30), then use sample standard deviation (s) to estimate population standard deviation and use normal distribution theory (Central Limit Theorem)
- If sample size is small and standard deviation is NOT known, use Student's t distribution theory.

Normal versus t Distribution



Properties of the t Distribution

- Family of distributions –different distribution for each sample value of n-1 (degrees of freedom)
- It has a mean of 0 and is symmetrical around the mean
- The t distribution approaches the normal distribution as n-1 approaches 30

One Sample t Test

- Example
  - Researchers are interested in whether the mean level enzyme B in a certain population is different from 120. They measure levels of enzyme B in a sample of 15 individuals and find that the mean =96 and the sample standard deviation is s=36.

Two Sample t Test

- Purpose is to compare the means of continuous variable in two independent samples.
- Example:
  - Researchers are interested in knowing whether people with diabetes have the same SBP as people without diabetes.

Paired t Test

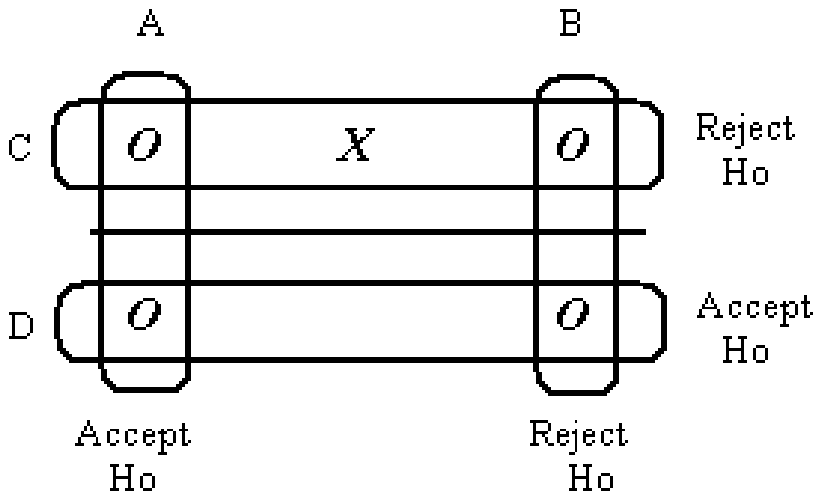
- Purpose is to compare means of two non-independent samples.
- Measurements on the same individuals before and after a treatment or intervention.
- Analysis performed on differences between individual pairs of observations.

Paired t Test

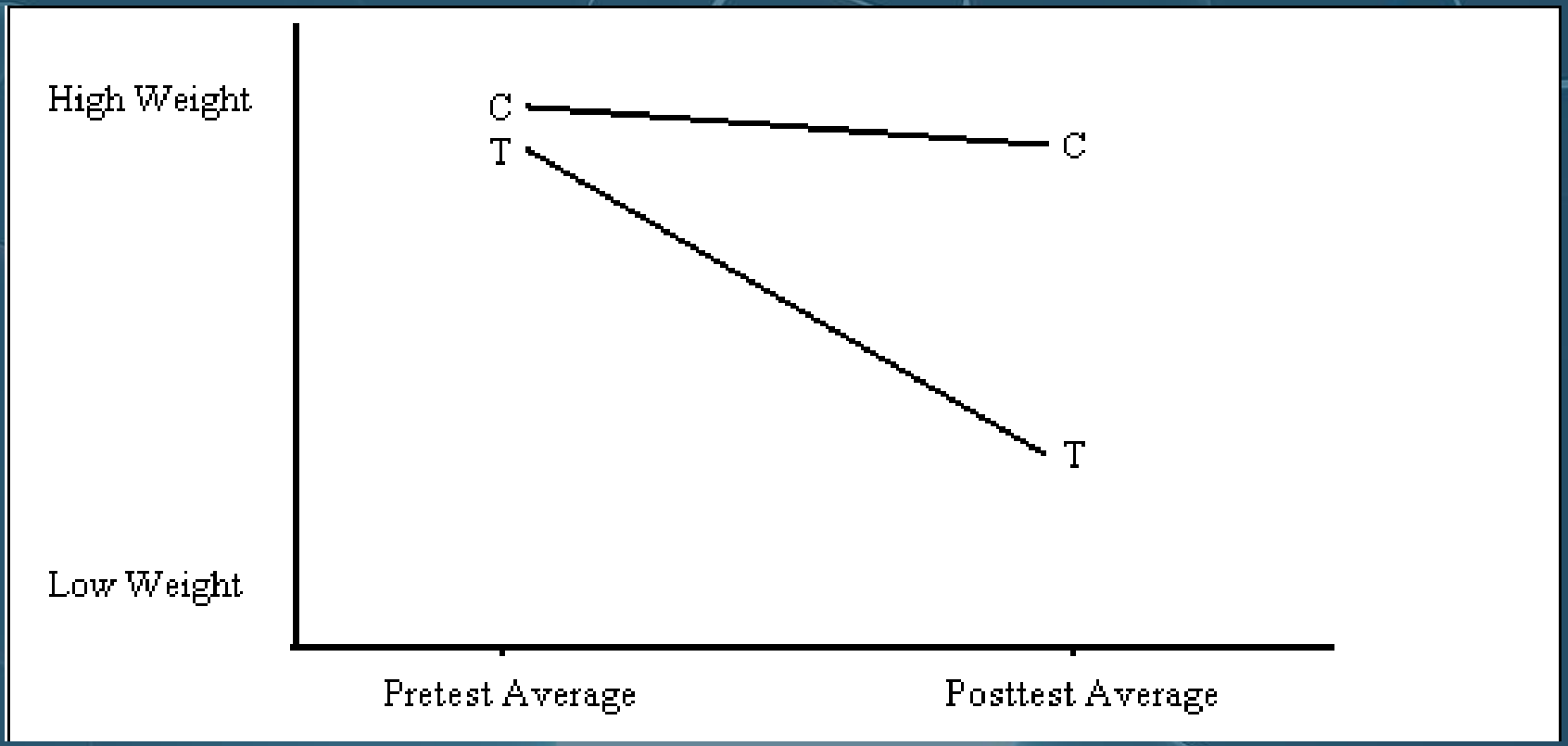
- Example
  - 12 subjects participated in a study on the effectiveness of a certain diet on serum cholesterol levels.

What We Hope to See

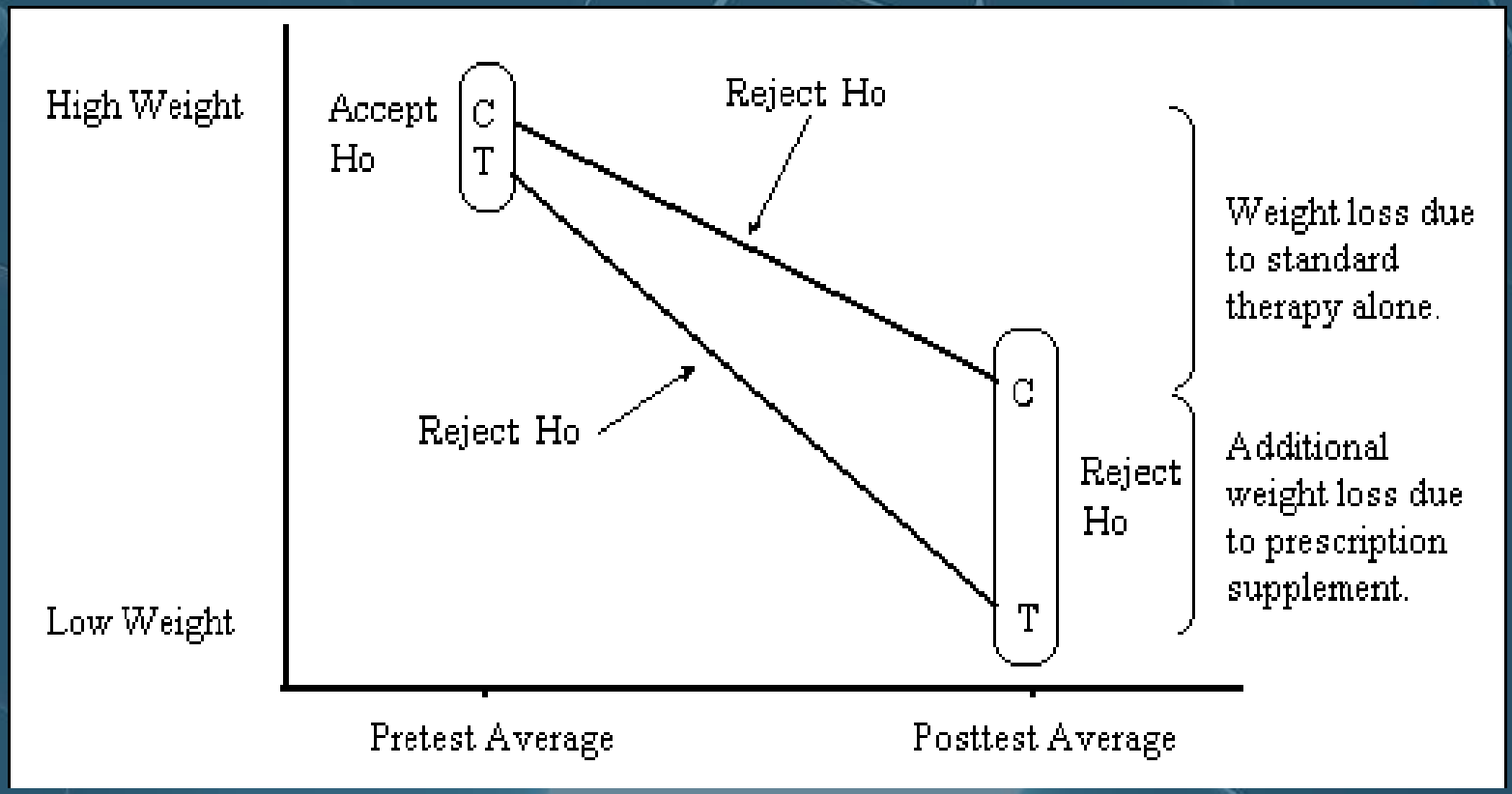
Theoretical testing for a NECG design.



Weight Loss Example

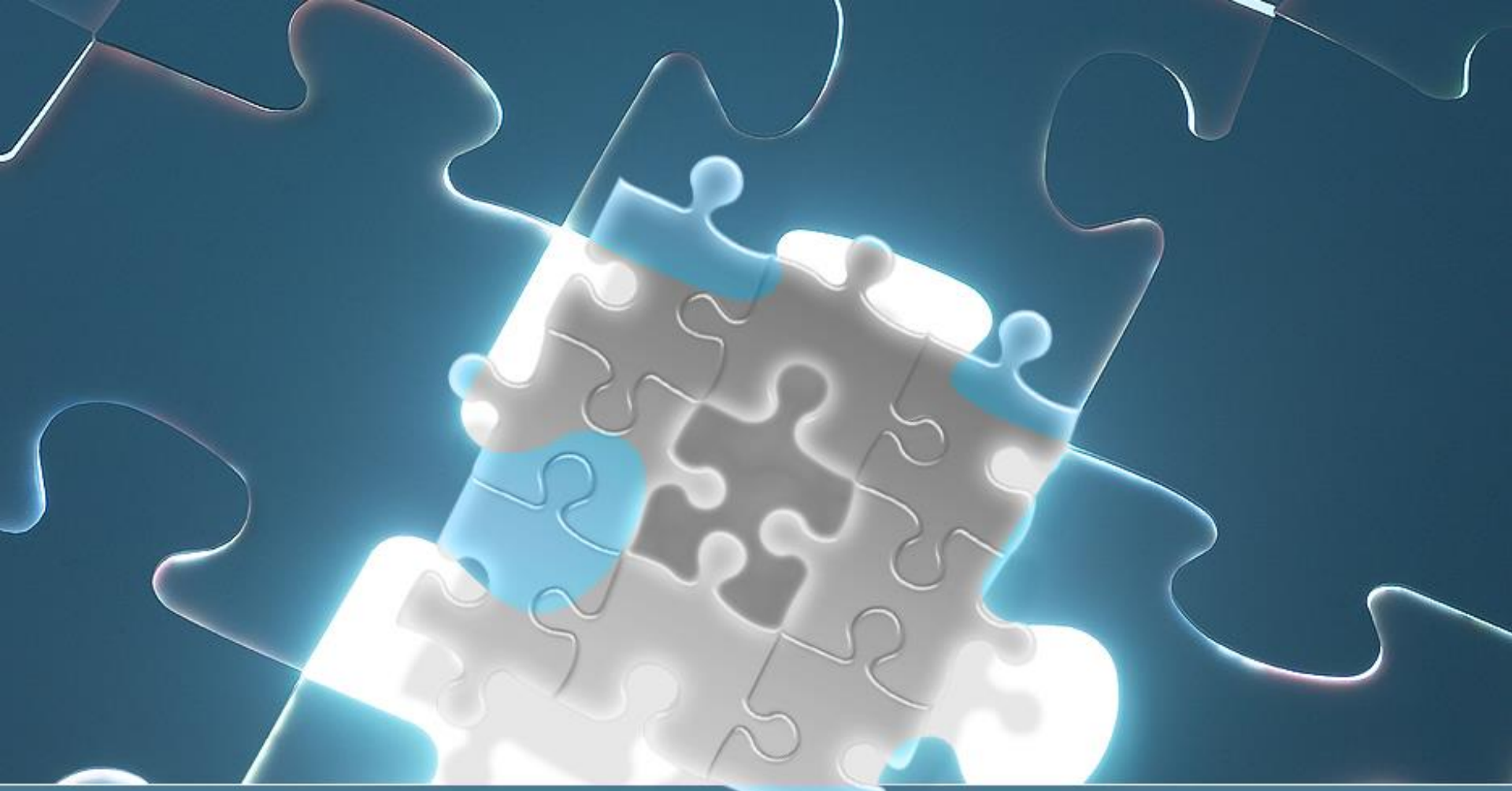


Effective Therapies



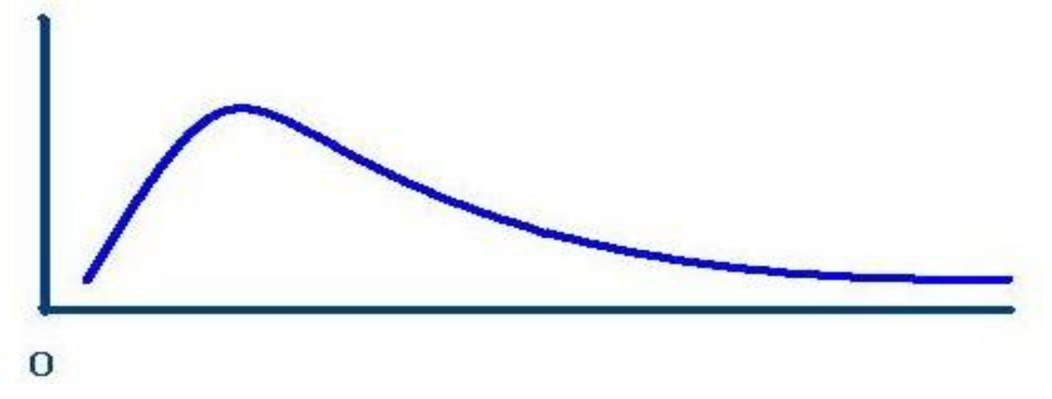
What if Your Data Do Not Meet Assumptions?

- Mathematically transform the data into a normal distribution (take the log or square root of values).
- Use a different class of tests called "non-parametric" tests. These tests are based on the ranking or ordering of data rather than their numerical values.



Analysis of Nominal Data: Chi-square Test

Chi square Distribution



- Not a symmetrical distribution
- Ranges from 0 to infinity –no negative values
- Skewed to the right
- Total area under the curve =1
- Family of distributions –different chi square distribution for each value of the degrees of freedom
- Degrees of freedom = (#rows-1) x (#columns -1)

Chi square Test

- Used when both exposure and outcome are nominal
- Can be 2 x 2 or larger tables
- Null hypothesis: No difference in proportions between groups

Chi square test

- Example:
  - In an air pollution study, a random sample 200 households were selected from each of 2 communities. A respondent in each household was asked whether or not anyone in the household was bothered by air pollution.
  - Data:

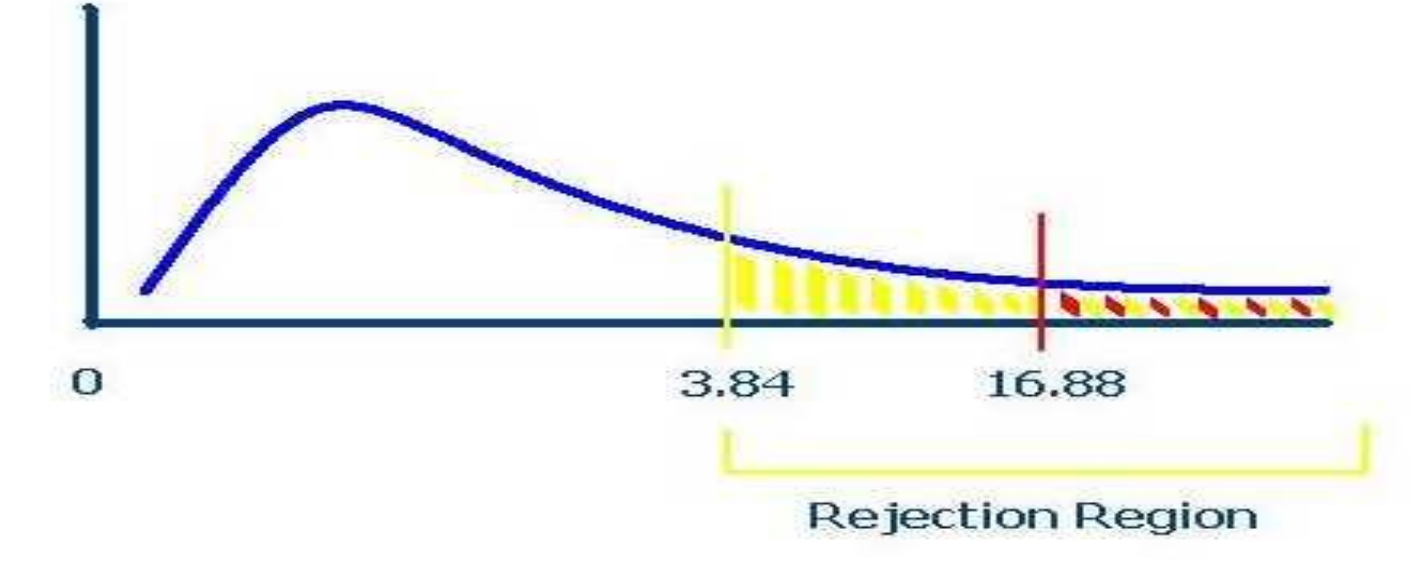
Bothered by air pollution	Community		Total
	A	B	
Yes	43	81	124
No	157	119	276
Total	200	200	400

Chi square Hypothesis

Bothered by air pollution	Community		Total
	A	B	
Yes	62 43	62 81	124
No	138 157	138 119	276
Total	200	200	400

- Expected = (row total x column total)/total population
  (124 x 200)/400 = 62 OR (124/400) x 200 = 62
- H_0: prop. bothered in Comm A = prop. bothered in Comm B.
- H_A: prop. bothered in Comm A ≠ prop. bothered in Comm B.
- α (alpha) =0.05

Chi square Results



- Critical value for Chi Square with 1 df =3.84
- 16.88 lies within the rejection region – reject the null hypothesis.
- $p<0.005$

Definitions

- Same statistical level (Nominal, Ordinal, Interval, Ratio)
- Secondary data (data collected for some other reason than what you need)
- Reliability and Validity (are you sure that coders/nurses/physicians see the same thing you do)
- Data that reside on one data system or, better yet, one data file are preferred.

Statistical Methods: What to Report

- Methods
  - Statistical procedure used
  - Significance level (Predetermined α level that will be considered statistically significant).
- Results
  - Sample size (n)
  - Means $\pm$ Standard Deviation
  - Observed significance level for each statistical test done
  - Confidence Interval for each mean

Have fun with stats!!!