Biostatistical Concepts and Examples

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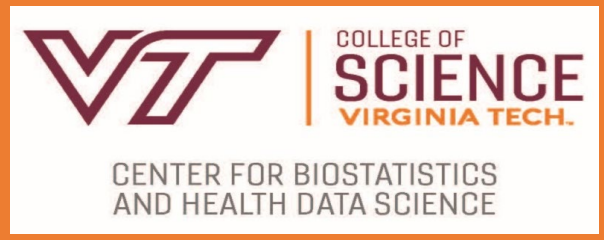
Learning Objectives

- Recognize fundamental topics in biostatistics including null/alternative hypothesis, alpha, beta, power, effect size, p-value, relative risk, and odds ratio.

- Identify the statistical tests associated with normal or non-normal distributed data.

Statistical Support Resources



HART

- **Director:** Mattie Tenzer
  - **Manager**: Mariana Salamoun

- Employed by Carilion Clinic
- **Email:** hart@carilionclinic.org
- **Website:** carilionclinic.org/health-analytics-research-team
- **Step-by-Step Guided Carilion Research Process:** https://redcap.link/MyProjectPath

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CBHDS

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- Located in Riverside 4 on Virginia Tech's Health and Sciences Technology campus

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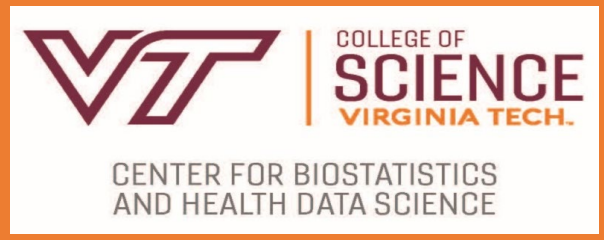
Statistical Support Offered



HART

- 20 team members providing end-to-end support
- Mix of grant funded / institution supported
- 250+ combined years in healthcare/research
- 165+ combined years at Carilion Clinic
- 83% diversity (non-white (33%), female (72%), veteran (5%))
- Full support for Research Informatics, Biostatistics, Data Science, Epidemiology, Research Design, data extraction and research navigation services
- Carilion component of NIH CTSA iTHRIV iBERDI group
- Innovation Department support (app development)
- Virtual Office Hours: Tuesday 10 am – Noon (*Copy Link from Here*)

hart@carilionclinic.org

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HART

End-to-End Research Support

https://redcap.link/MyProjectPath

Design

- Study design support
- Biostatistical consultation
  - Data discussion
    - Extract, Chart Review and/or Survey Data
  - Power Analysis
  - Feasibility – TriNetX
- Survey consultation
- Epic Research Access & Clinical Trial Support

Data

- Data extracts
  - Epic
  - TriNetX reidentification
  - Registries
- Data exploration, organization, and manipulation
- Data Management and Surveys (REDCap)
  - Survey Creation, Distribution & Support
- Secure Cloud-Based Data Storage (SPARC)

Analysis

- Data analysis support
  - Statistical Presentations
  - Guide and complete qualitative or quantitative analysis
  - Data Analysis in R-Studio, SAS Studio, Python, NVIVO
  - Data Science Methodologies
- Presentation of Findings
  - Poster, Manuscript, etc.
    - Images/Graphs
    - Methods/Results

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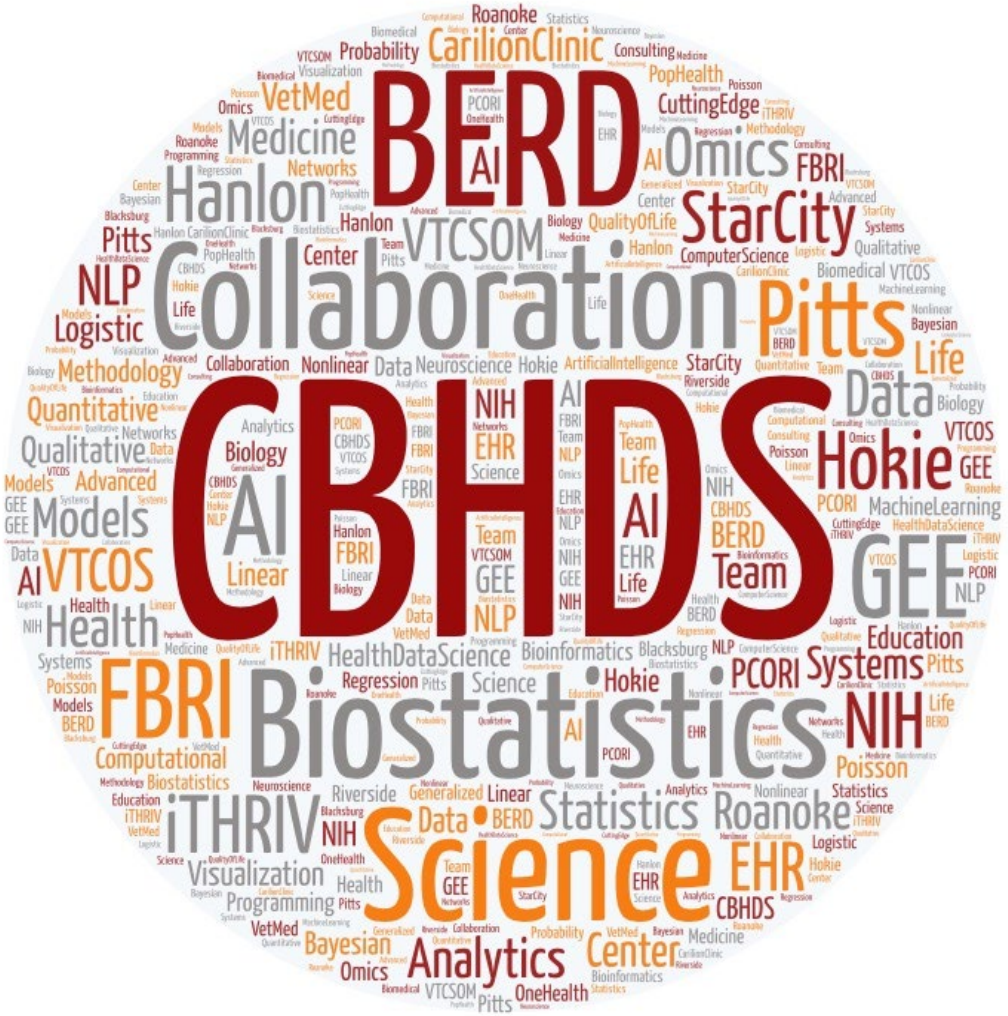

- Study Planning
- Research Support
- Publications and Presentations
- Community Building and Education

biostats@vt.edu

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Consulting & Collaboration

- Short-term consultants or long-term collaborators

- Short-term consulting: Zoom drop-in hours four days per week, funded by FLSI, VTCSOM, and our iTHRIV CTSA award
    - **Public hours:** Mondays 10am to 2pm, Wednesdays 3 to 7pm
    - **VTCSOM hours:** Tuesdays & Thursdays 2 to 4pm
    - To book an appointment and for more information, please visit: http://biostat.centers.vt.edu/zoomconsulting.html

- Longer-term collaborations: study design, through data acquisition, data analysis, interpretation, and dissemination of results

Long-Term Collaboration

Internal Projects with PIs - Grant or Departmental Funding

- **Collaborative research support within a team science model:** data analysis, data management, manuscript preparation and other requested tasks

Grant Life-Cycle Collaborations (as Co-I and/or Research Associate)

- **Proposal submission:** statistics analysis plan, specific aims, research strategy, help develop a statistics budget, provide documents for OSP pre-award, letters of support, other requested items
- **Multi-year project period:** ongoing analytical and data management support, weekly team meetings, continuation proposals and interim reports
- **Dissemination of research results:** manuscript preparation, abstracts, posters, oral presentations, travel to conferences

Types of Statistics

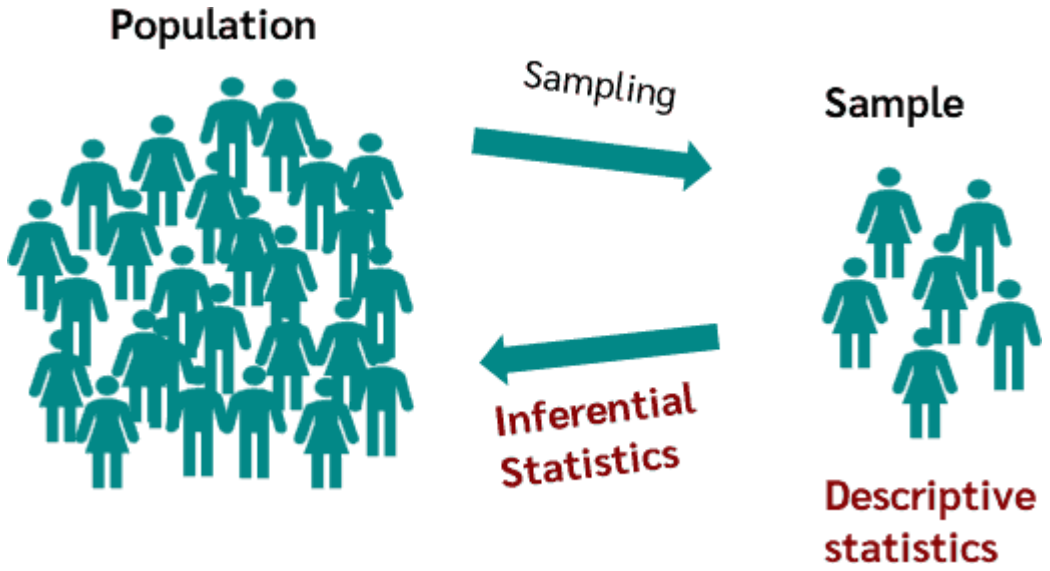
Types of Statistics

Quantitative

- **Descriptive Statistics** – Describes a set of data (mean, median, percentage, standard deviation, etc.)
- **Inferential Statistics** – Uses sample data to make conclusions about the population.

Qualitative

- Collects non-numerical data like observations, words, descriptions, etc.
- Focuses on the “why” and “how”
- Triangulation of data for outcomes



https://datatab.net/tutorial/descriptive-inferential-statistics

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Statistical Concepts Associated with Hypothesis Testing

Hypothesis Testing

Null hypothesis (H_0) – Impact of the intervention displays **NO Significant CHANGE** in outcome.

Alternative hypothesis (H_1) –Impact of the intervention displays **Significant CHANGE** in outcome.

Example: Studying the effects of new Drug X on reducing hypertension compared to the standard Drug A.

Null: Mean Systolic Blood Pressure of Patients on Drug A = Mean Systolic Blood Pressure of Patients on Drug X
Alternate: Mean Systolic Blood Pressure of Patients on Drug A ≠ Mean Systolic Blood Pressure of Patients on Drug X

Assume that H_0 is true; the decision we make is either to "reject" or "fail to reject" H_0

Alpha – Level of Significance

What does α=5% really mean?

- Addresses the role of chance.
- Amount of Type I error you are willing to take.
- Probability of rejecting null hypothesis when it is correct.
- 5 times out of 100 we will say there is an effect from our intervention, when there really was not.

One-Tailed Test (Left Tail)	Two-Tailed Test	One-Tailed Test (Right Tail)
$H_0 : \mu_X = \mu_0$ $H_1 : \mu_X < \mu_0$	$H_0 : \mu_X = \mu_0$ $H_1 : \mu_X \neq \mu_0$	$H_0 : \mu_X = \mu_0$ $H_1 : \mu_X > \mu_0$
		

https://www.sciencedirect.com/topics/mathematics/tail-test

One-Tailed Null: Mean SBP of Patients on Drug X ≥ Mean SBP of Patients on Drug A
One-Tailed Alternate: Mean SBP of Patients on Drug X < Mean SBP of Patients on Drug A

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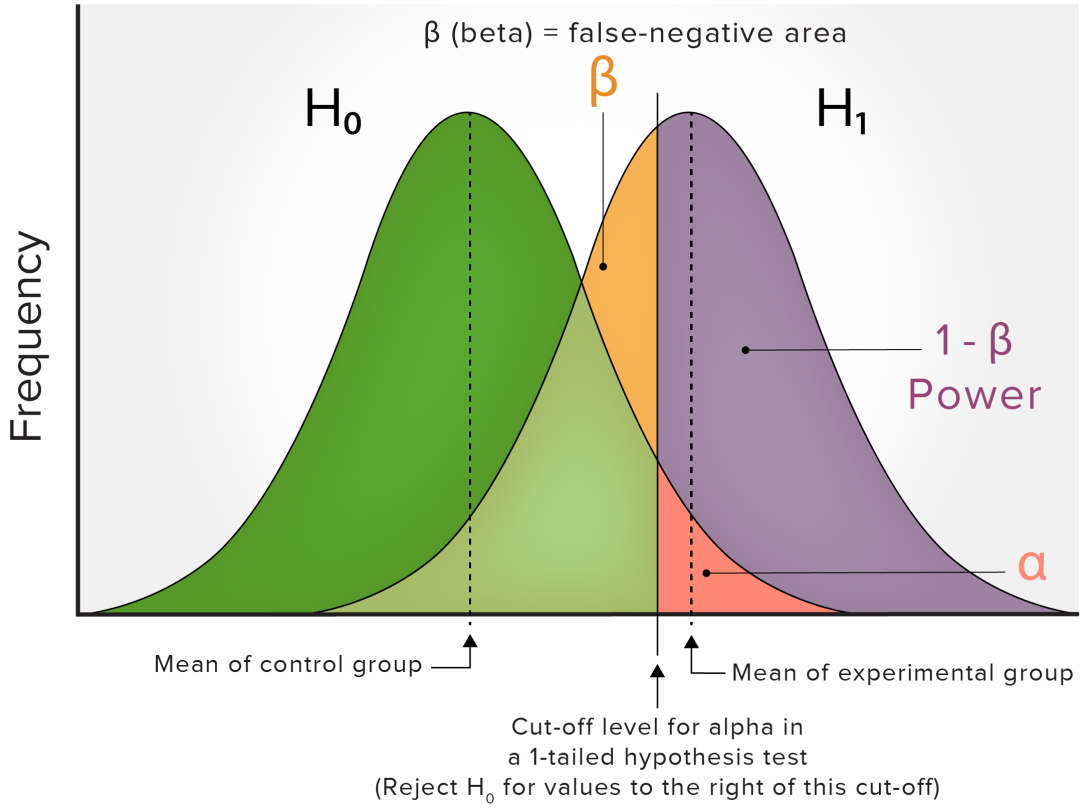
Beta and Power (1-Beta)

- **Beta – Probability of rejecting the alternative hypothesis when it is correct.**
  - Probability of Type II Error
- **Statistical power – the ability to detect an effect of the alternative hypothesis that actually exists.**
  - Probability that the test will correctly support the alternate hypothesis.
  - Power = 1 – β
  - If your results are significant, then you had enough power.
  - Increasing Power, decreases Beta or probability of Type II Error.



https://www.lecturio.com/concepts/statistical-power/

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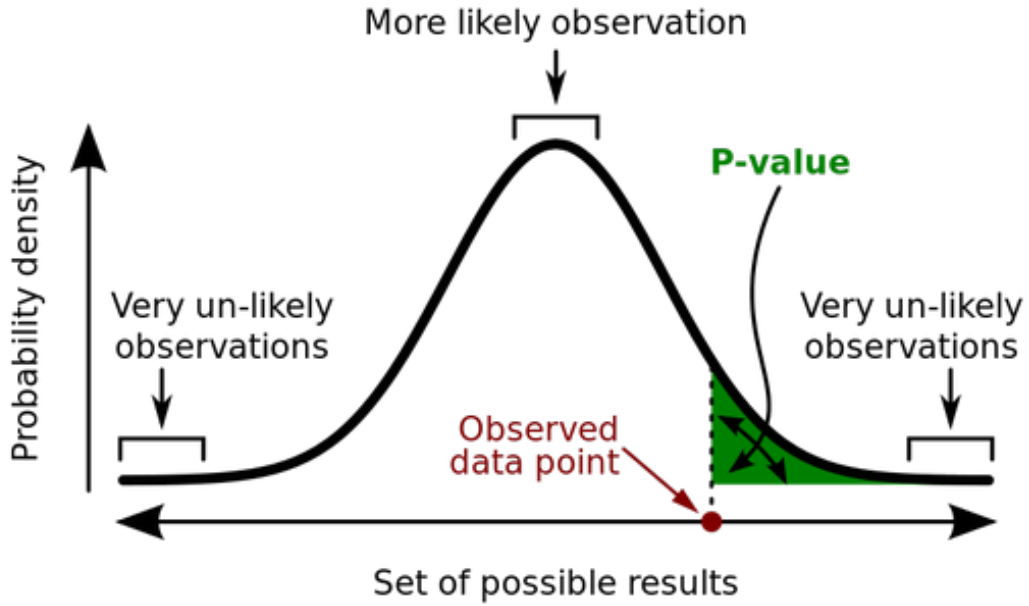
What is a p-value?

The probability of observing a point estimate as extreme as the calculated value, if the null hypothesis is true.



https://nulib.github.io/moderndive_book/11-pvalues.html

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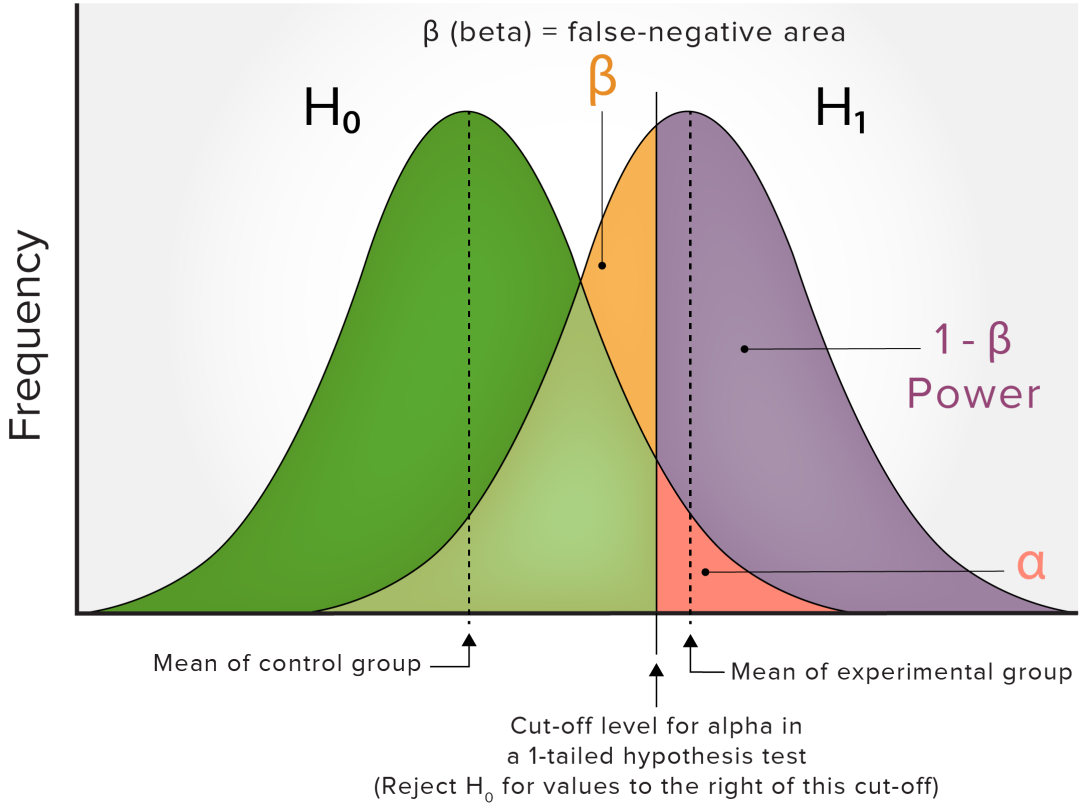
Type I and II Errors

Null:
Mean SPB Drug X =
Mean SBP Drug A

Alt:
Mean SPB Drug X ≠
Mean SBP Drug A

		TRUE STATE OF THE WORLD (a.k.a. REALITY)	
		Null Hyp. Is True: SBP is EQUAL Drug X and Drug A	**Alt Hyp. is True:** SBP is NOT EQUAL Drug X and Drug A
STUDY RESULT	Study Result is statistically significant (Reject Null Hyp.) **Alt Hyp. – Supported**	Type I error (**Prob = α**)	Alt Hyp Correct (**Prob = Power**)
	Study Result is NOT statistically significant (Fail to Reject Null) **Null Hyp – Supported**	Null Hyp Correct (**Prob = 1-α**)	Type II error (**Prob = β** or **1-Power**)



https://www.lecturio.com/concepts/statistical-power/

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How is Effect Size Related?

- Effect size measures the “distance” between the peaks of the two distributions.
- If the peaks are close together, then β is much larger. This means we need to increase the sample size to increase the power and decrease β.
- If the peaks are further apart, then β is smaller and power is larger. We could reduce sample size to something more feasible.

TABLE

Selected Effect Sizes and Their Interpretations Relevant to Nursing Education Research

		Interpretation of Effect Size[a]		
Primary Statistical Test	**Effect Size Statistic**	**Small**	**Medium**	**Large**
Chi-square	ϕ	.10	.30	.50
Pearson’s *r* correlation	*r*	.10	.20/.30	.30/.50
Linear regression	Cohen’s f^2	.01	.06	.14
Logistic regression	Odds ratio	1.44	2.47	4.25
t test	Cohen’s *d*	.20	.50	.80

[a] *Effect size guidelines are from Cohen (1988), except for those for r, which also depict the lower, more empirically derived guidelines from Gignac and Szodorai (2016).*

https://journals.healio.com/doi/10.3928/01484834-20171020-02

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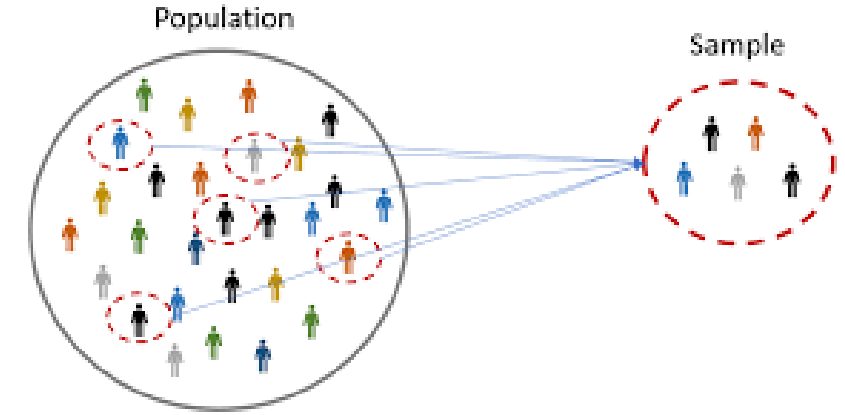
Power Analysis and Sample Size Estimations

Items needed for a Power Analysis:

- Research question or questions
- Desired significance level and power level
- Effect size of clinical relevance
  - What's the smallest change you *care* about from a clinical point of view?
- Variability
  - What range of measurements can we expect by chance?



Sample size is a balance of statistical and practical considerations.

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Poll Question #1

True or False: A study with low power is more likely to detect a small effect if it exists.

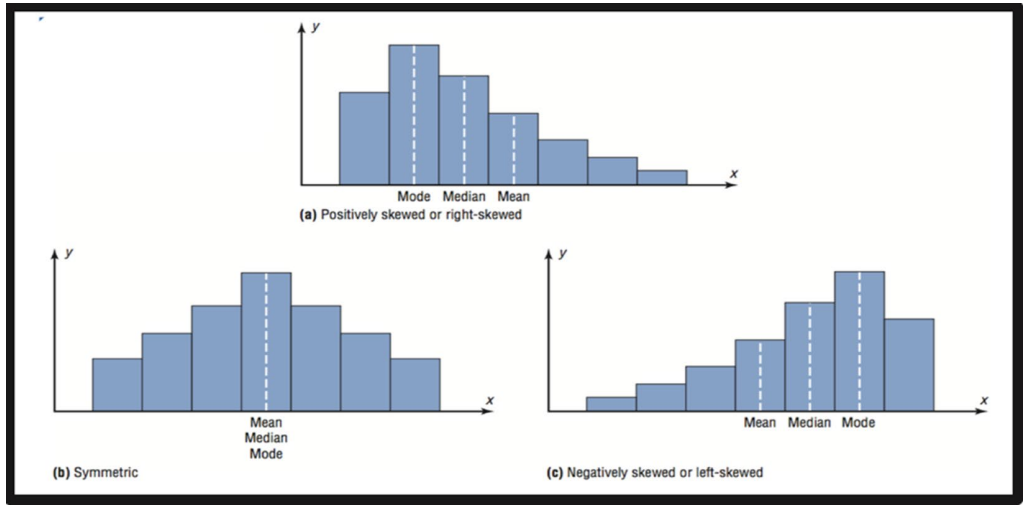
Answer: False (A study with low power is less likely to detect small effects, leading to a higher chance of a Type II error.)

Types of Statistical Tests

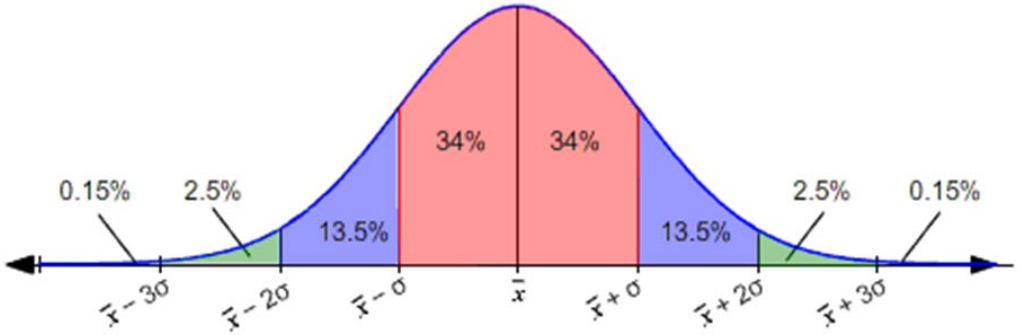
Continuous Data – Normal Distribution?

Data can deviate from normal distribution in two ways:

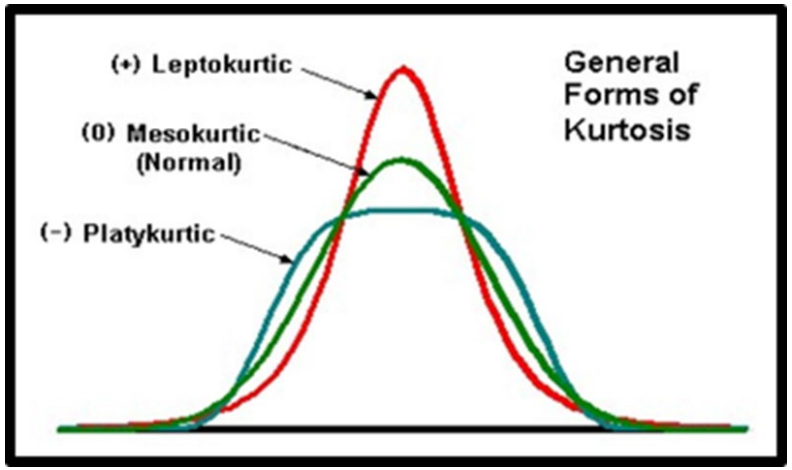
1. Skewness – affects the central tendency of the mean
2. Kurtosis – affects the standard deviations



https://statisticstechs.weebly.com/desciptive-statistics/category/c-properties-of-frequency-distribution



https://www.varsitytutors.com/hotmath/hotmath_help/topics/normal-distribution-of-data



https://statisticstechs.weebly.com/desciptive-statistics/category/c-properties-of-frequency-distribution

Analyzing Continuous Data with Categorical Groups

Normally Distributed

Mean (Std. Dev.)

- Two Groups
  - Independent Groups
    - Two-Sample T-Test
  - Dependent Groups
    - Paired T-Test
- Three or More Groups
  - Independent Groups
    - ANOVA
  - Dependent Groups
    - Repeated Measures ANOVA or linear mixed effects modeling

Non-Normally Distributed

Median (IQR)

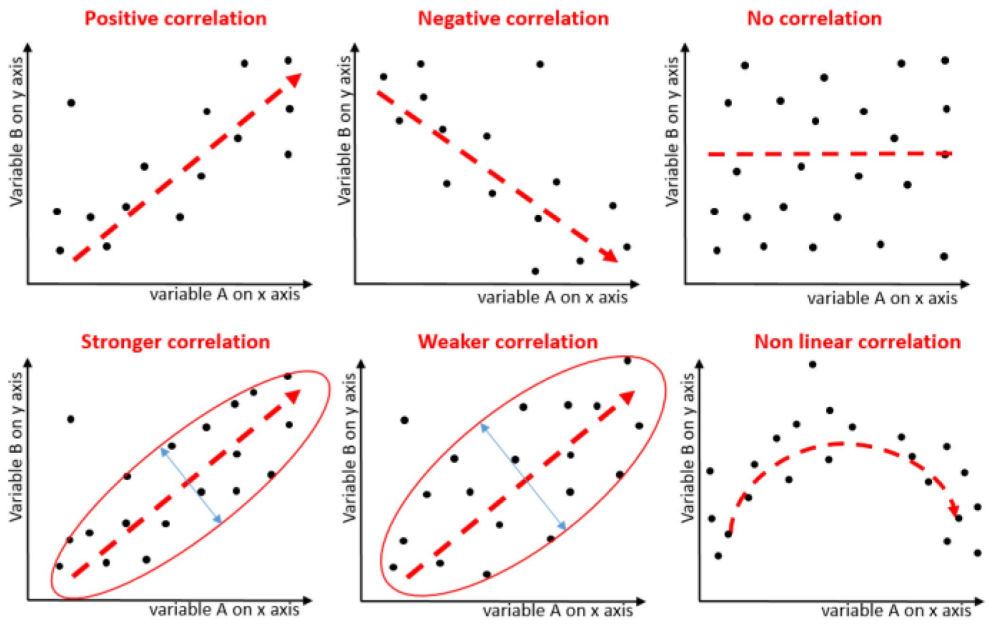
- Two Groups
  - Independent Groups
    - Wilcoxon Rank-Sum Test
  - Dependent Groups
    - Wilcoxon Signed-Rank Test
- Three or More Groups
  - Independent Groups
    - Kruskal-Wallis Test
  - Dependent Groups
    - Friedman Repeated Test or Generalized linear mixed effects modeling

Analyzing Two Continuous Variables – Correlation Analysis

- Normally Distributed Data
  - Pearson Product-Moment Correlation (r)
    - Measures the strength and direction of a linear relationship between two variables.

- Non-Normally Distributed Data

  (like ordinal data)
  - Spearman Rank Correlation (rho: ρ)
  - Kendall Rank Correlation (tau: τ)



https://www.mdpi.com/1660-4601/15/12/2907

Analyzing Categorical Data

Chi-Square Test

N (%)

- Not as reliable with small data sets
- Expected Count must be ≥ 5 for each cell
- Determines whether two fields are statistically dependent on each other

$$Expected\ Count = \frac{(Row\ Total)\cdot(Column\ Total)}{(Grand\ Total)}$$

$$\chi^2 = \sum \frac{(Observed - Expected)^2}{Expected} = \sum \frac{(O-E)^2}{E},\ df = k - 1$$

Fisher's Exact Test

N (%)

- Works well with small data sets
- Expected Count is not needed or calculated
- Determines whether two fields are statistically dependent on each other

	Sample A	Sample B	Row Total
Category A	a	b	*a+b*
Category B	c	d	*c+d*
Column Total	*a+c*	*b+d*	*Grand Total: a+b+c+d*

Poll Question #2

True or False: When data are non-normally distributed, it is appropriate to report the mean and standard deviation.

Answer: False (For non-normally distributed data, the median and interquartile range (IQR) are more appropriate as they are not influenced by extreme values.)

Statistics Associated with Treatment Effect on Outcomes

Risk vs Odds

Risk – probability a specific event will happen out of all possibilities

Odds – ratio of the frequency of an event occurring to the frequency of the event not occurring

Risk of Rolling 6 on 1 die?

1/6

$$\text{Risk} = \frac{\#\ of\ people\ who\ have\ the\ outcome}{\#\ of\ people\ at\ risk}$$

Odds of Rolling 6 on 1 die?

1/5

$$\text{Odds} = \frac{\#\ of\ people\ who\ have\ the\ outcome}{\#\ of\ people\ who\ do\ not}$$

Relative Risk vs Odds Ratio

N=250	Death	No Death
Drug A	20	105
Placebo	24	101

Scenario: Patients enrolled in an RCT were either given Drug A or a placebo. Of the 250 patients in the study, 20 patients in the Drug A group (n=125) and 24 patients in the placebo group (n=125) die.

What is the risk of death in the Drug A group and the placebo group?

Drug A: $\frac{20}{125} = 16\%$ Placebo: $\frac{24}{125} = 19.2\%$

Relative Risk or Risk Ratio (RR) – ratio of the probability of an event occurring in the treatment group versus the probability of the event occurring in the control group.

$$\text{RR} = \frac{Risk\ of\ event\ in\ Treatment\ Group}{Risk\ of\ event\ in\ Control\ Group} = \frac{a/(a+b)}{c/(c+d)}$$

What is the relative risk of death? $\frac{16\%}{19.2\%} = 0.8333$

Interpretation: The risk of death in Drug A group is reduced by 1-0.8333 = 16.67% as compared to the placebo group.

What is the odds of death in the Drug A group and the placebo group?

Drug A: $\frac{20}{105} = 19.05\%$ Placebo: $\frac{24}{101} = 23.7\%$

Odds Ratio (OR) – ratio of the Odds of the event in the treatment group to the Odds of the event in a control group.

$$\text{OR} = \frac{Odds\ of\ event\ in\ Treatment\ Group}{Odds\ of\ event\ in\ Control\ Group} = \frac{a/b}{c/d} = \frac{ad}{bc}$$

What is the odds ratio of death? $\frac{19.05\%}{23.7\%} = 0.804$

Interpretation: Odds are 80.4 to 100 that death will occur in the Drug A group.

OR

The odds of death is reduced by 1-0.804 = 19.6% for those receiving Drug A as compared to placebo.

Number Needed to Treat/Harm

N=250	Death	No Death
Drug A	20	105
Placebo	24	101

Absolute Risk Reduction (ARR) is used when the risk is beneficial.

Absolute Risk Increase (ARI) is used when the risk is harmful.

Calculated the SAME

$$\mathbf{ARR} = |Risk\ of\ event\ in\ Treatment\ Group\ - Risk\ of\ event\ in\ Control\ Group| = \boldsymbol{ARI}$$

Number Needed to Treat (NNT) is used when the risk is beneficial.

Number Needed to Harm (NNH) is used when the risk is harmful.

NNT = $\frac{1}{ARR}$ **Calculated the SAME** NNH = $\frac{1}{ARI}$

Risk of Death in Drug A Group? $\frac{20}{125} = .16$

Risk of Death in Placebo Group? $\frac{24}{125} = .192$

Is the risk factor of death in the "treatment" or Drug A group beneficial or harmful?
Beneficial

ARR = |0.16 – 0.192| = 0.032

NNT = 1/0.032 = 31.25
Number needed to treat with Drug A to avoid 1 death.

Q & A

Thank you!

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