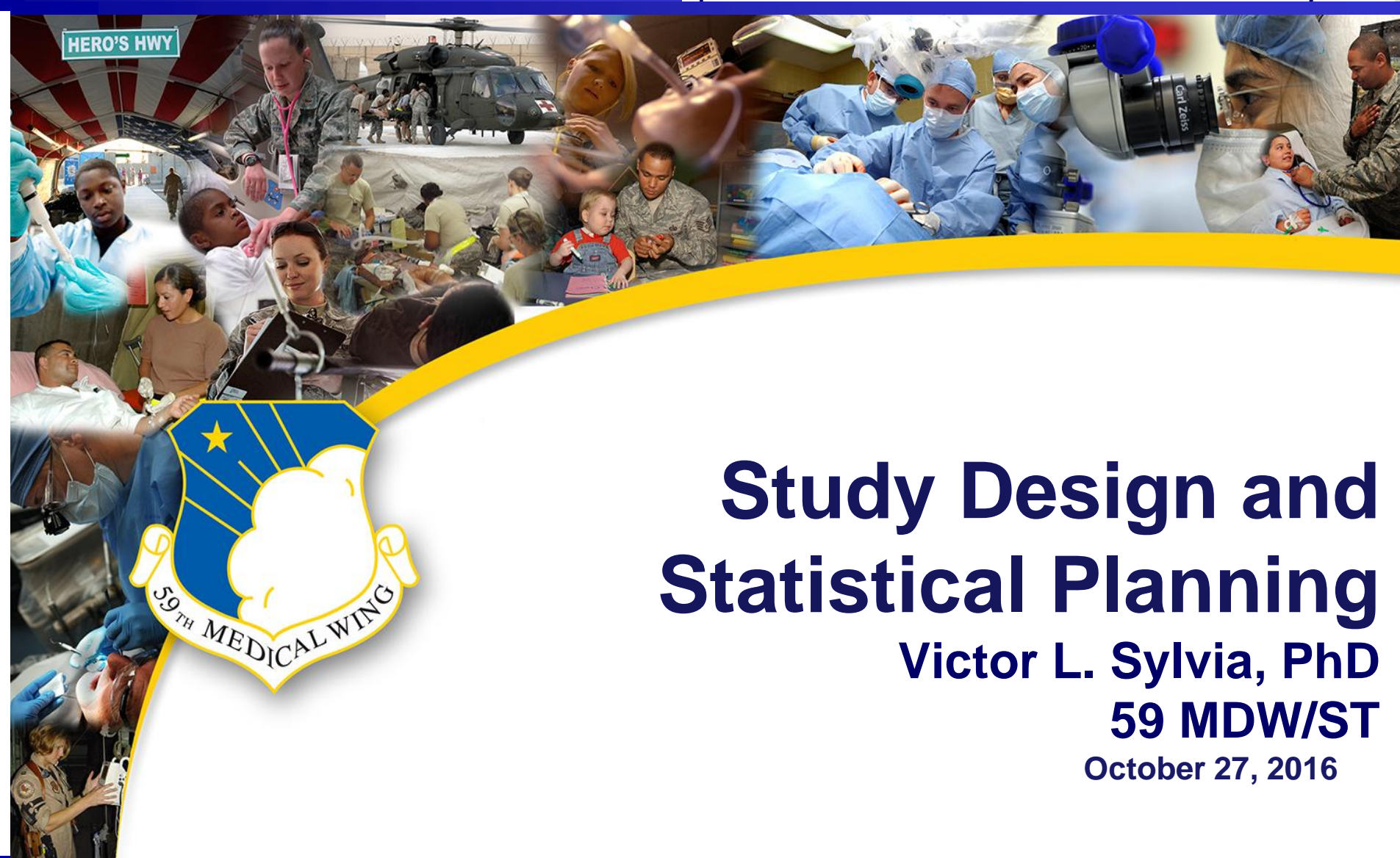




59th Medical Wing



Study Design and Statistical Planning

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59th Medical Wing



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or its Components"***

PEOPLE

MISSION

INNOVATION

IDEA 



Literature Search

Items to consider:

CRADA * **FDA Approval** * **Funding**
MTA, DUA, NDA, MOU, CRA, etc. NIH, OBA-RAC, IBC Review



Presentation to Committee

Protocol Approved

Documents for IRB/IACUC

- Progress Reports
- Adverse Event Report
 - Annual Report
 - Final Report

Research Presentations/Publications

Must have PA approval – Form 3039



Study and Experimental Design



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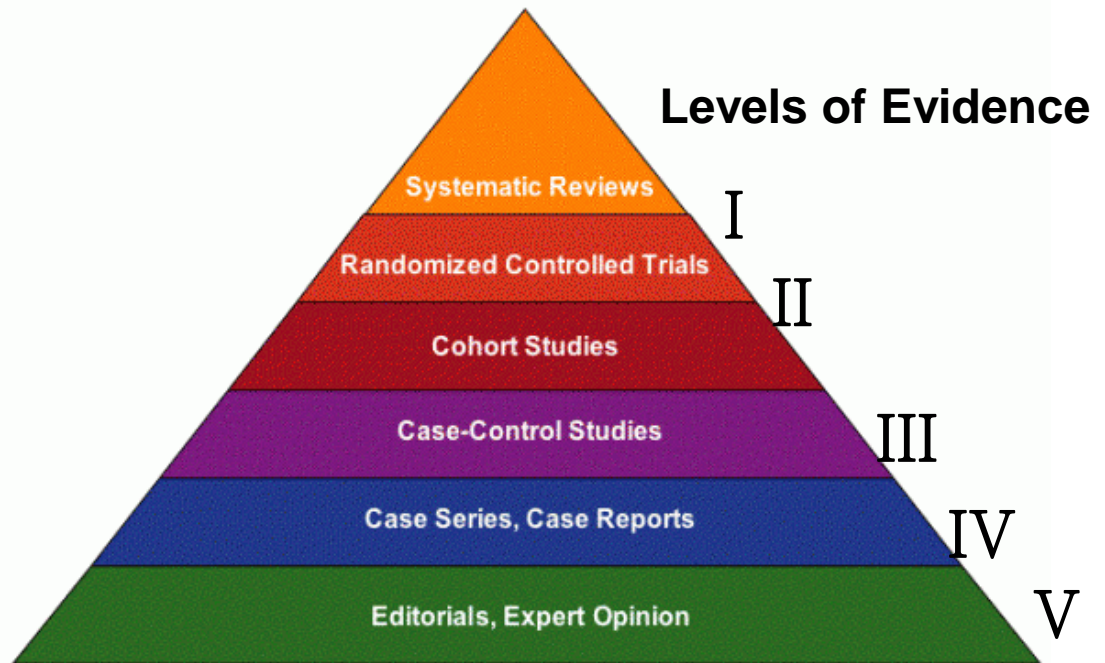
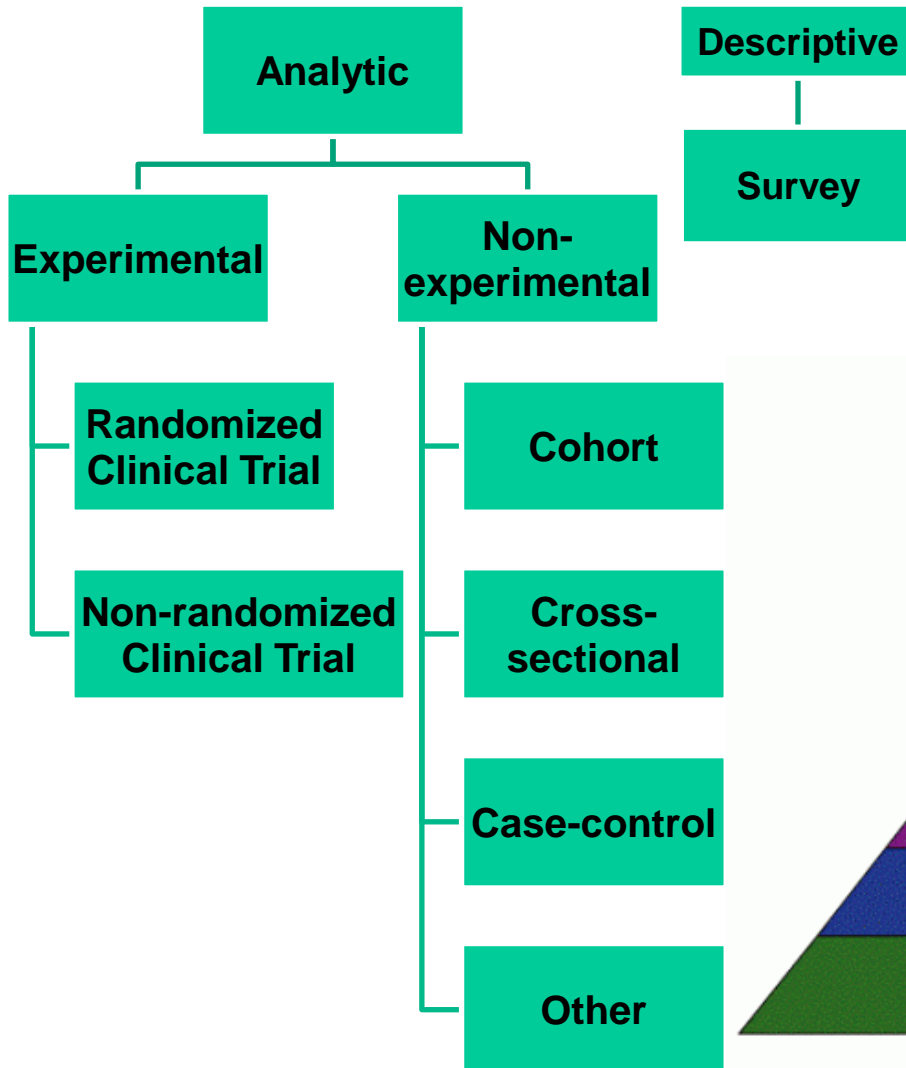
- Retrospective vs. Prospective
- Descriptive study, hypothesis generating, clearly defined study aims
- Best design to achieve your objectives



Study Design



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Study Design



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Study Design	Key Feature	Example
Experimental Design		
Randomized blinded trial	Two groups created by a random process, and a blinded intervention	The investigator randomly assigns women to receive hormone or identical placebo, then follows both treatment groups for several years to observe the incidence of heart attacks.
Observational Designs		
Cohort study	A group followed over time	The investigator examines a cohort of women yearly for several years, observing the incidence of heart attacks in hormone users and non-users.
Case-control study	Two groups, based on the outcome	The investigator examines a group of women with heart attacks (the “cases”) and compares them with a group of healthy women (the controls) asking about hormone use.
Cross-sectional study	A group examined at one point in time	The investigator examines the group of women once, observing the prevalence of a history of heart attacks in hormone users and non-users.



Sample Size Calculation



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- Also called “power analysis”.
- When designing a study, one needs to determine how large a study is needed.
- Power is the ability of a study to avoid a Type II error (claiming there is no difference between two samples when in fact there is).
- Sample size calculation yields the number of study subjects needed, given a certain desired power to detect a difference and a certain level of P value that will be considered significant.
 - Many studies are completed without proper estimate of appropriate study size.
 - This may lead to a “negative” study outcome in error.



Types of Data



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- Discrete data-limited number of choices
 - Binary: two choices (yes/no)
 - Dead or alive
 - Disease-free or not
 - Categorical: more than two choices, not ordered
 - Race
 - Age group
 - Ordinal: more than two choices, ordered
 - Stages of a cancer
 - Likert scale for response
 - E.G. strongly agree, agree, neither agree or disagree, etc.



Types of Data



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- Continuous data
 - Theoretically infinite possible values (within physiologic limits) , including fractional values
 - Height, age, weight
 - Can be interval
 - Interval between measures has meaning.
 - Ratio of two interval data points has no meaning
 - Temperature in Celsius, day of the year).
 - Can be ratio
 - Ratio of the measures has meaning
 - Weight, height



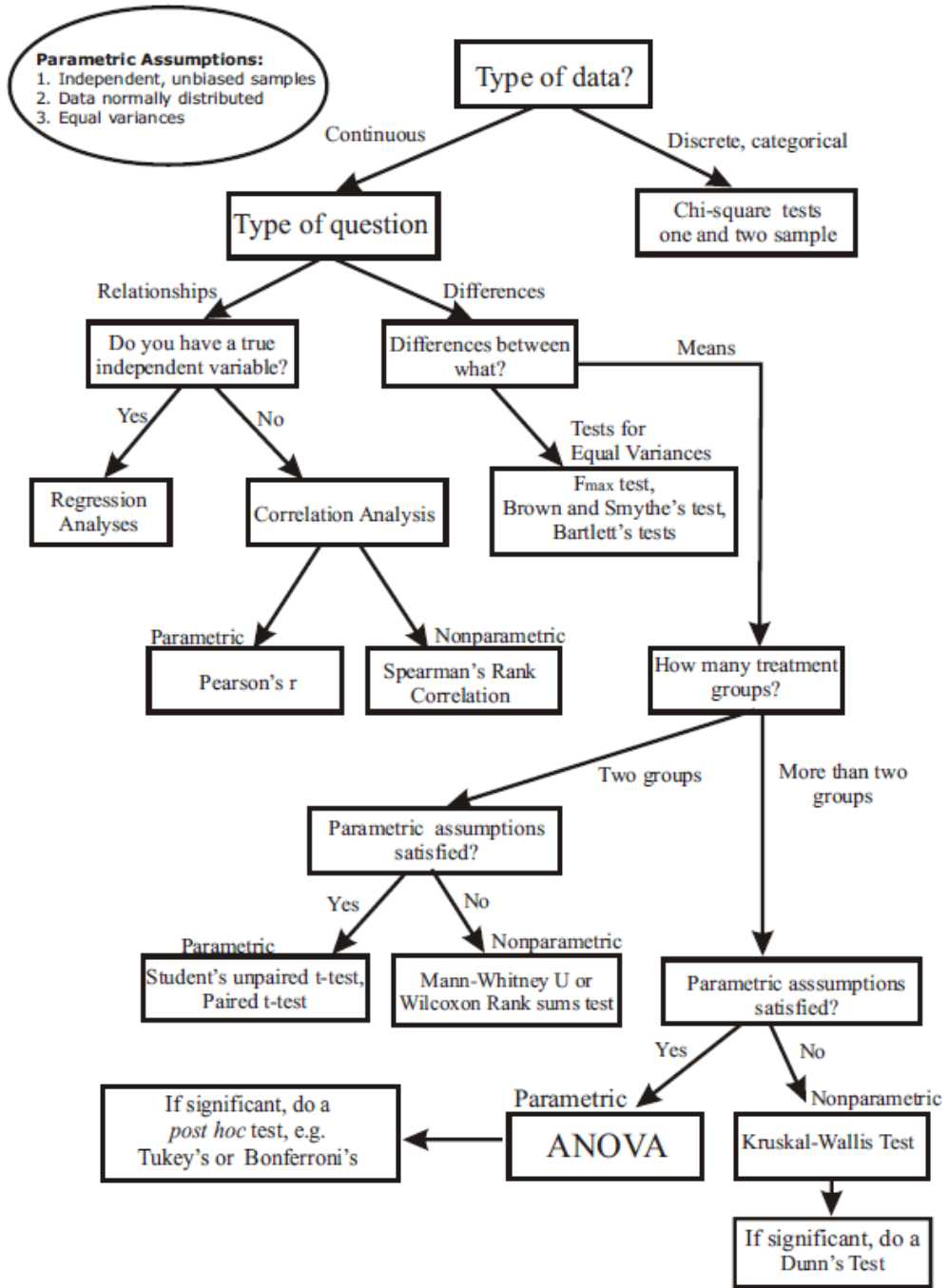
Types of Data



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- Why important?
 - The type of data defines the summary measures used:
 - Mean, Standard deviation for continuous data
 - Proportions for discrete data
 - Statistics used for analysis:
 - T-test for normally distributed continuous
 - Wilcoxon Rank Sum for non-normally distributed continuous

Flow Chart for Selecting Commonly Used Statistical Tests





P Values and Confidence Intervals



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- P values provide less information than confidence intervals.
 - A P value provides only a probability that estimate is due to chance
 - A P value could be statistically significant but of limited clinical significance.
 - A very large study might find that a difference of .1 on a VAS Scale of 0 to 10 is statistically significant but it may be of no clinical significance
 - A large study might find many “significant” findings during multivariable analyses.
 - “Tyranny of Power” - “a large study dooms you to statistical significance” – Dr. Roy W. Haas



Regression Analysis



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Types of regression

- Linear- uses continuous data to predict continuous data outcome
- Logistic- uses continuous data to predict probability of a dichotomous outcome
- Poisson regression- time between rare events
- Cox proportional hazards regression- survival analysis



Multiple Regression



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- Determining the association between two variables while controlling for the values of others
- Example: Uterine Fibroids
 - Both age and race impact the incidence of fibroids.
 - Multiple regression allows one to test the impact of age on the incidence while controlling for race (and other factors)



ANOVA



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- Used to determine if two or more samples are from the same population- the null hypothesis
 - If two samples, is the same as the T test
- If it appears they are not from same population, can't tell which sample is different
 - Would need to do pair-wise tests



Non-parametric Tests



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- Testing proportions
 - (Pearson's) Chi-Squared (χ^2) Test
 - Fisher's Exact Test
- Testing ordinal variables
 - Mann Whiney "U" Test
 - Kruskal-Wallis One-way ANOVA
- Testing Ordinal Paired Variables
 - Sign Test
 - Wilcoxon Rank Sum Test



Summary



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- Understanding basic statistical concepts is central to understanding the medical literature.
- Important to know when a statistical test should be used and how to interpret its results
- For further study “*Medical Statistics Made Easy*”
 - M. Harris and G. Taylor
 - <https://www.amazon.com/Medical-Statistics-Made-Easy-third/dp/1907904034>



Questions?



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Common Timeline Challenges



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- Contract Actions
 - Personnel
 - Direct costs/equipment
- Agreements
 - CRADA
 - MTA
 - MOU/MOA
 - ISSA
- Regulatory Requirements
 - IRB
 - IACUC
 - FDA - IND/510K
- Funding
 - Grant writing
 - Grant reviews/Funding delays
- Organizational
 - Accounting
 - Fiscal Year Rollover
- Career
 - PCA/PCS
 - Deployment