INTRODUCTION TO CLINICAL RESEARCH Summer 2010

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OBJECTIVES

- Discuss framework of clinical research
  - Development of hypothesis, research question, methods, analysis
- Development of project within residency - advantages and disadvantages
- Prepare for ILP
- Achieve competency in practice based learning

PROCESS OF RESEARCH

- Phase I (pre-operational)
  - Period of creativity
  - Laying the groundwork
  - Asking the right question
- Phase II (operational)
  - IRB application and presentation (with mentor)
  - Initiation of study plan

PROCESS OF RESEARCH

- Phase III
  - Data analysis
  - Presentation – Resident Research Day, Local and National Meetings
  - Manuscript

PHASE I

- Try to develop hypothesis and research question
- Literature review
  - National Library of Medicine/pubmed
  - *"has it been done before?"*
- Determine methods and statistics
  - Sample size – are there enough patients?
  - Independent and dependent variables
  - Confounding variables
  - Any unusual problems/costs related to your project?

PHASE II

- Repetitive presentation and development of ideas with peers and faculty
- Finalize methods, analysis, sample size
- Submit IRB application
- Pilot instrument/survey
- Prepare data collection forms
- Enroll subjects

PHASE III

- Data entry and cleaning (statistical package: SPSS, sysstat, SAS)
- Data analysis
- Prepare abstract
- Present of project
- Prepare of manuscript

RESEARCH PROJECT: *Practical Considerations*

- "Do-able" in 3 years?
- Funding required?
- Research assistant required?
- Interesting question?
- Do I have enough passion to spend the time necessary to complete project?

INSTITUTIONAL REVIEW BOARD

- IRB approval required prior to contact with medical records or study subjects
  - Approval also required for abstract submission, presentation, and publication
- Protection of study subjects
- Importance of consent form – English and Spanish
- May take several months for approval

RESEARCH PROJECT: *Potential Topics*

- Case study and review of the literature
- Survey
- Cross-sectional study
- Case-control study
- Retrospective chart review
- Prospective study

TIMELINE

- **Year 1 (July 2010-June 2011**):
  - July-December: determine question and methods; complete literature search (National Library of Medicine, etc) and faculty/colleague critique
  - January: submit application to IRB (with faculty mentor)
  - January-July: initiate project
- **Year 2 (July 2011-June 2012):**
  - July-July: collect data, analyze data

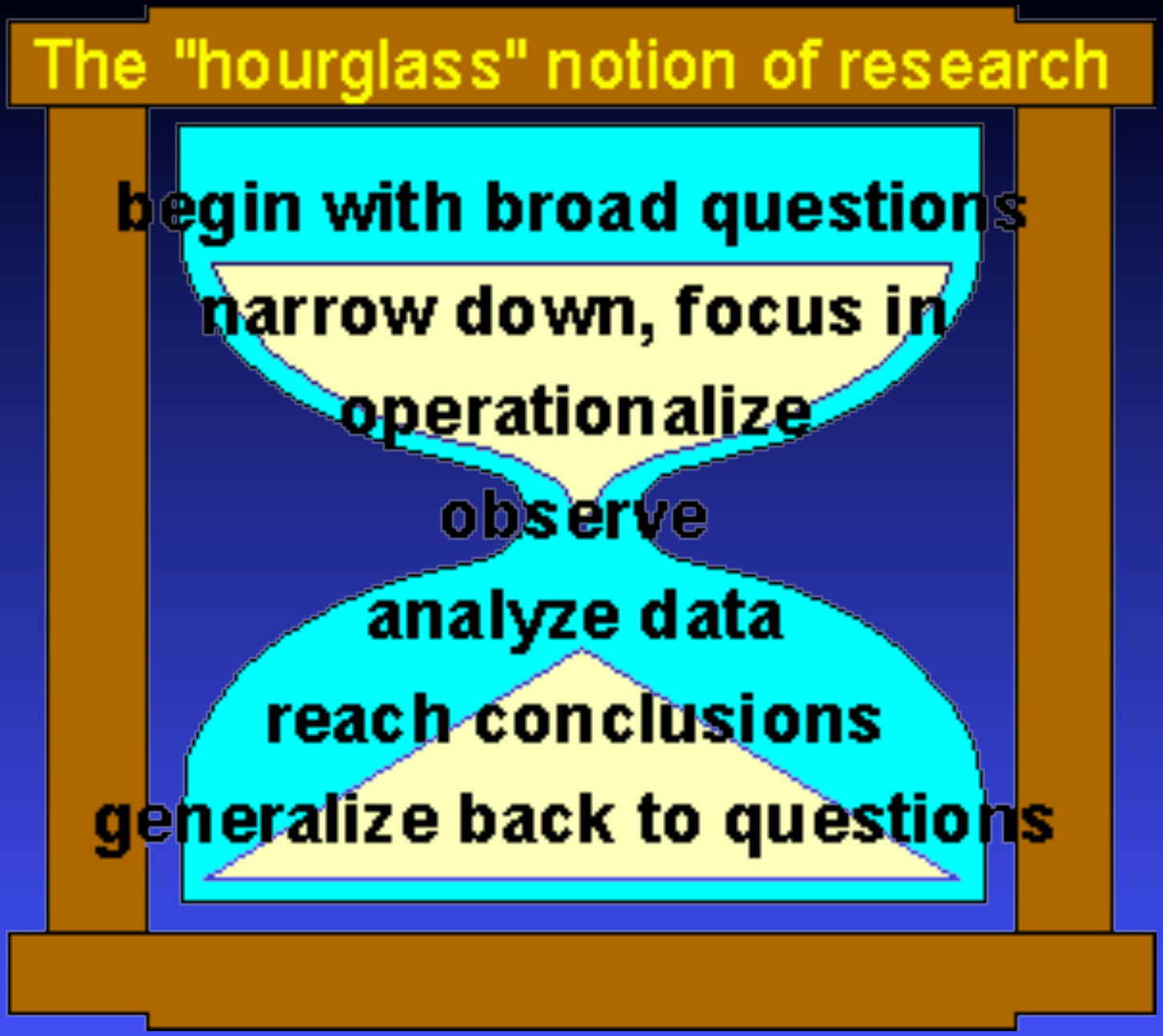
TIMELINE

- **Year 3 (July 2012-June 2013):**
  - July-December: prepare abstract for Spring 2013 presentation
  - May: prepare poster for SBH Resident Research Day
  - June: presentation at Grand Rounds

LITERATURE SEARCH

- St. Barnabas Hospital Library
- National Library of Medicine
  - Pubmed
- Google
- Topic, author
- Read/critique all pertinent articles
  - Similar ideas in the literature?
  - Methodology problems?
  - Can you do it better?
- If journal not available, order through PMID number

HOW DO I START?


The "hourglass" notion of research
begin with broad questions
narrow down, focus in
operationalize
observe
analyze data
reach conclusions
generalize back to questions

OUTLINE OF STUDY PROTOCOL

Research question (objective of the study, must be focused)	What question(s) does the study address?
Significance (review prior research and state its problems; proposed research may help resolve problems)	Why is the research question important?
Design (time frame and epidemiologic approach)	What is the structure of the study?
Subjects (selection and sampling)	Who are the subjects and how will they be selected?
Variables (independent, dependant, confounding)	What measurements will be made?
Statistical issues (hypotheses, sample size, approach to analysis)	How large is the study; what is the analysis?

STUDY OUTLINE

TITLE	
RESEARCH QUESTION/ HYPOTHESIS	
SIGNIFICANCE (REVIEW OF LITERATURE)	
DESIGN	
SUBJECTS-ENTRY CRITERIA	
SUBJECTS-RECRUITMENT	
VARIABLES – PREDICTOR (INDEPENDENT)	
VARIABLES – OUTCOME (DEPENDENT)	
SAMPLE SIZE, POWER, α,ß, STATISTICAL STRATEGY	

ASKING THE RIGHT QUESTION
(Eng, 2004)

- State the question in writing
- Question should be important, novel, answerable and provide useful information
- Question should be significant – ask colleagues if it is
  - Interesting
  - Novel
  - Ethical
  - Relevant

CHOOSING THE RIGHT PROJECT

- What makes a research project outstanding?
  - **Logical flow of ideas**
    - Hypothesis/aim -> methods -> analysis -> conclusion based on data -> impact of study *(?new way of thinking about subject?)*
  - Every detail reviewed – can it be improved?

PICKING A RESEARCH PROJECT

(Kahn, 1994)

- Anticipate results before the study
- Choose area on the basis of interest of the outcome to the scientific community
- Look for "underoccupied niche" with potential
- Attend lectures and read papers outside of your area of interest
- Build on a theme

POTENTIAL PROBLEMS AND SOLUTIONS

Potential Problems	Solutions
Research question too broad	Specify smaller set of variables, narrow the question
Not enough subjects	Expand inclusion criteria, modify exclusion criteria, add other sources for subjects, lengthen entry time into study
Methods beyond investigator's skills	Collaborate with other colleagues, review literature
Too expensive	Consider less costly study designs, fewer subjects, measurements, follow-up visits
Not interesting or vague	Modify question, specify outcome, independent and dependent variables

PRACTICAL ISSUES

- Are questionnaire and/or instruments **sensitive** enough to detect differences in major outcome variables?
- Too many subjects lost to follow-up?
  - Collect as much demographic information when subjects enter study including close relative
- Do you have and/or need a lot of time and funding?
- Should you consider a pilot study first?

PRACTICAL ISSUES

- If considering a retrospective design, watch out for selection bias (e.g. asthma treatment at a community v. non-community hospital)
- Collect information on those who declined to participate or "dropped out"
- Define "positive, negative, no change" in "Study Notebook"

SAMPLE SIZE

SAMPLE SIZE
(Maggard , 2003)

- Identified articles in 3 major surgical journals from 1999-2002 (*Annals of Surgery, Archives of Surgery, Surgery)*
- **Question asked**: Was there 80% power to detect treatment group differences – large (50%) and small (20%), one-sided, α=.05
- If underpowered, how many more patients needed?

SAMPLE SIZE

- 127 RCT identified; 48 (38%) reported sample size calculations
- 86 (68%) reported positive treatment effect
- 41 (32%) found negative treatment effect
- 63 (50%) of studies appropriately powered to detect 50% effect change
- 24 (19%) had power to detect 19% difference
- Of underpowered studies: >50% needed to increase sample size 10 X

HOW ARE THESE RELATED?

HYPOTHESIS

↓

SAMPLE SIZE

↓

POWER

NULL HYPOTHESIS

- There is no association between the independent and dependant variables
- Assuming no association, statistical tests estimate the probability that an association is due to chance ($p<.05$, 1/20)
- If there IS an association ($p<.05$, $p<.01$), we reject the null hypothesis

RELATIONSHIP

- The **hypothesis** determines the type of study
  - Risk of Reyes syndrome and aspirin
  - Drug A v Drug B and asthma
- Avoidance of type I and II errors needs to be assured by adequate **sample size** so study is adequately **powered** to show a difference

α and P VALUE

- Significance level = α (Type I error)
- Question: What is the association of watching TV and developing asthma?
  - Set α to .05
  - 5% is maximum chance of incorrectly inferring TV and asthma *are related when they are not related*
  - If P value < α, null hypothesis rejected – conclusion: TV is related to asthma
  - If P value > α, null hypothesis accepted – conclusion: TV not related to asthma

β and POWER

- β : probability of Type II error
- Type II error: incorrectly assuming no difference exists between 2 groups
  - Drug A is the same as Drug B in the treatment of acute asthma
- Small differences require large sample sizes

POWER PROBLEMS

- Low Power
  - Too little data
  - Meaningful effect size difficult to determine
- High Power
  - Too much data
  - Trivial effect sizes detected

TYPE I ERROR

- Type I (false positive)
  - Investigator rejects the null hypothesis when there is actually is no difference in the population
- Effect size: size of association detectable in population sample of clinical importance

TYPE II ERROR

- Type II (false negative)
  - Investigator fails to reject the null hypothesis and concludes there is no difference when there actually may be a difference
  - Sample size too small to detect difference in comparison groups

COMMON ERRORS

- Sample size estimates subjects to be followed not subjects enrolled (*beware of dropouts and problems in enrollment*)
- Don't estimate sample size late in the study

SAMPLE SIZE NUTS AND BOLTS

(Browner et al, 2001)

- State the null hypothesis and a one or two sided alternative hypothesis
- Select one of the following tests based on the independent and dependant variables in the hypothesis
  - chi-square
  - t-test
  - correlation coefficient
- Choose an effect size
- Set α and β
- Use appropriate table or formula to estimate sample size

STATISTICAL TESTS USED IN ESTIMATING SAMPLE SIZE

(Browner, 2001)

	Outcome Variable	
Predictor Variable	Dichotomous	Continuous
Dichotomous	Chi-Square	T-Test
Continuous	T-Test	Correlation coefficient

SAMPLE SIZE USING T-TEST

- Hypothesis: albuterol is more efficacious compared with ipratropium in the treatment of acute asthma
- Literature: Mean±SD for FEV_1 in treated patients was 2.0±1.0
- Method: RCT testing effect on FEV_1 to detect a 10% difference between 2 treatment groups
- $\alpha = .05$, $\beta = .80$

SAMPLE SIZE USING T-TEST

- *Null hypothesis:* Mean FEV_1 similar in both treatment groups
- *Effect size:* 10% x 2.0 liters = 0.2 liters
- SD of FEV_1 = 1.0 liter
- Calculation of Sample Size
  - $N = (z_\alpha) \times (s)^2 / (d)^2$
    - $Z_\alpha = 1.96$
    - S^2 = variance
    - D^2 = difference to be detected
  - Sample Size Tables
  - Sample Size (per group) = $16 / (E/S)^2$
    - $16 / (0.2)^2 = 400$ per group

SAMPLE SIZE USING CHI-SQUARE

- Hypothesis: does bronchiolitis predict asthma in children?
- Literature: children who have don't have bronchiolitis have a 20% chance of developing asthma by age 5
- Method: how many children with and without bronchiolitis need to be studied to determine the whether the rate is atleast 30% in children with bronchiolitis
- $\alpha = .05$, $\beta = .80$

SAMPLE SIZE USING CHI-SQUARE

- *Null hypothesis:* rate of asthma in children with and without bronchiolitis is the same in both groups
- *Incidence in non asthmatic children:* 20% (p1)
- *Incidence in non asthmatic children:* 30% (p2)
- Calculation of Sample Size
  - Sample Size Tables for comparing 2 proportions = 313 per group

The Emergency Department Utility of Simplify D-dimer™ to Exclude Pulmonary Embolism in Patients With Pleuritic Chest Pain

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Study objective: Pleuritic chest pain is a common presenting complaint in the emergency department (ED) and a symptom of pulmonary embolism. Patients with pleuritic chest pain would benefit from a simple and rapid way of screening for pulmonary embolism. The aim of this study is to assess the utility of Simplify D-dimer™ as a rule-out tool for pulmonary embolism in ED patients with pleuritic chest pain.

Methods: This was a prospective diagnostic study in a large city-center ED. Four hundred twenty-five patients with pleuritic chest pain were prospectively recruited between February 2002 and June 2003. Simplify D-dimer™ testing was performed on each patient in the ED. All patients followed an independent reference standard diagnostic algorithm for pulmonary embolism. Each patient was followed up clinically for 3 months.

Results: The calculated sensitivity of Simplify D-dimer™ for pulmonary embolism was 81.8% (95% confidence interval [CI] 61.4% to 92.7%), and specificity was 74.2% (95% CI 69.6% to 78.4%). The negative predictive value was 98.6% (95% CI 96.6% to 99.6%), positive predictive value 15.0% (95% CI 9.1% to 22.7%), negative likelihood ratio 0.25 (95% CI 0.10 to 0.52) and positive likelihood ratio 3.17 (95% CI 2.30 to 3.97). The study cohort pretest probability was 5.3%. A negative Simplify result reduced the posttest probability to 1.3% (95% CI 0.5% to 3.4%).

Conclusion: The Simplify D-dimer™ is not sufficiently sensitive to exclude the diagnosis of pulmonary embolism in all patients presenting to the ED with pleuritic chest pain. [Ann Emerg Med. 2005;46:305-310.]

ED UTILITY OF SIMPLIFY D-DIMER TO EXCLUDE PULMONARY EMBOLISM IN PATIENTS WITH PLEURITIC CHEST PAIN

- Hypothesis
  - Is “Simplify D-dimer” efficacious as a rule out tool for patients in the ED with chest pain with a possible pulmonary embolism
- Design
  - Prospective diagnostic study of patients with pleuritic chest pain and the efficacy of “Simplify D-dimer
- Subjects
  - Patients with pleuritic chest pain admitted to the ED

ED UTILITY OF SIMPLIFY D-DIMER TO EXCLUDE PULMONARY EMBOLISM IN PATIENTS WITH PLEURITIC CHEST PAIN

- Variables – Independent
  - Simplify D-dimer test results
- Variables – Dependant
  - Presence or absence of pulmonary embolism
- Sample Size, Statistics
  - Study cohort of 400 patients and prevalence of 10% could demonstrate 95% sensitivity with 95% CI of 83-99%
  - If prevalence was 5%, could demonstrate 95% sensitivity with 95% CI: 76-99%

Neonatal MRI to Predict Neurodevelopmental Outcomes in Preterm Infants

Lianne J. Woodward, Ph.D., Peter J. Anderson, Ph.D., Nicola C. Austin, M.D., Kelly Howard, B.Sc., and Terrie E. Inder, M.D.

ABSTRACT

BACKGROUND

Very preterm infants are at high risk for adverse neurodevelopmental outcomes. Magnetic resonance imaging (MRI) has been proposed as a means of predicting neurodevelopmental outcomes in this population.

METHODS

We studied 167 very preterm infants (gestational age at birth, 30 weeks or less) to assess the associations between qualitatively defined white-matter and gray-matter abnormalities on MRI at term equivalent (gestational age of 40 weeks) and the risks of severe cognitive delay, severe psychomotor delay, cerebral palsy, and neurosensory (hearing or visual) impairment at 2 years of age (corrected for prematurity).

RESULTS

At two years of age, 17 percent of infants had severe cognitive delay, 10 percent had severe psychomotor delay, 10 percent had cerebral palsy, and 11 percent had neurosensory impairment. Moderate-to-severe cerebral white-matter abnormalities present in 21 percent of infants at term equivalent were predictive of the following adverse outcomes at two years of age: cognitive delay (odds ratio, 3.6; 95 percent confidence interval, 1.5 to 8.7), motor delay (odds ratio, 10.3; 95 percent confidence interval, 3.5 to 30.8), cerebral palsy (odds ratio, 9.6; 95 percent confidence interval, 3.2 to 28.3), and neurosensory impairment (odds ratio, 4.2; 95 percent confidence interval, 1.6 to 11.3). Gray-matter abnormalities (present in 49 percent of infants) were also associated, but less strongly, with cognitive delay, motor delay, and cerebral palsy. Moderate-to-severe white-matter abnormalities on MRI were significant predictors of severe motor delay and cerebral palsy after adjustment for other measures during the neonatal period, including findings on cranial ultrasonography.

CONCLUSIONS

Abnormal findings on MRI at term equivalent in very preterm infants strongly predict adverse neurodevelopmental outcomes at two years of age. These findings suggest a role for MRI at term equivalent in risk stratification for these infants.

N Engl J Med 2006;355:685-94.

MRI AS PREDICTOR OF NEURODEVELOPMENTAL OUTCOMES

- Hypothesis
  - MRI useful to predict neurodevelopmental outcomes
- Design
  - Prospective longitudinal study
- Subjects
  - 167 preterm infants (<30 weeks gestation)
  - At term equivalent all subjects had MRI
  - Comprehensive neurodevelopment assessment at 2 years

VOCABULARY

VARIABLES

- Dimensional
  - Age, scores, serum Na
- Categorical
  - Gender (male, female), age (0-10, ≥ 10-20, ≥20-30), ethnic (white, black, asian, hispanic)
- Independent – how does this variable affect outcome (under researcher's control)
- Dependant – outcome variables (not under researcher's control)

VARIABLE

CATEGORICAL (QUALITATIVE)

Nominal

Categories are mutually exclusive & unordered; gender, blood group

Ordinal

Categories are mutually exclusive & ordered; social class, disease stage

NUMERICAL (QUANTITATIVE)

Counts

Integer values; sick days per year, ED visits for asthma in 6 months

Measured (continuous)

Any value in a range of values; birthweight (kg), age (years), scores on a test

Campbell, 2007

Gender				
1 Female	1,689	73.0	7,995	68.0
2 Male	625	27.0	3,794	32.0
Age				
1 15–24	916	39.6	4,918	41.7
2 25–34	640	27.7	3,540	30.0
3 35–44	506	21.9	2,092	17.7
4 45–54	217	9.4	1,069	9.1
5 55–64	34	1.5	157	1.3
6 65+	1	.0	14	.12
Registration status				
1 Full-time	1,010	43.6	5,873	49.8
2 Part-time	1,304	56.4	5,917	50.2
Employment Status				
1 Part-time	609	26.3	3,683	31.2
2 Full-time	1,268	54.8	5,882	49.9
3 Not employed	437	18.9	2,224	18.9
Distance from campus				
1 On campus	23	1.0	176	1.5
2 < 30 minutes	852	36.8	5,006	42.5
3 30 minutes to 1 hour	510	22.0	2,633	22.3
4 1 hour to 2 hours	292	12.6	1,366	11.6
5 More than 2 hours	637	27.5	2,609	22.1
Modem type				
1 28.8	43	1.9	203	1.7
2 33.6	14	0.6	54	0.5
3 56	372	16.1	1,769	15.0
4 Cable Modem	948	41.0	4,980	42.2
5 LAN	193	8.3	926	7.9
6 DSL	333	14.4	1,631	13.8
7 ISDN	5	0.2	38	.3
8 Don't know	406	17.5	2,189	18.6
Why Online				
1 Conflict with personal schedule	820	35.4	4,887	41.6
2 Course not offered on campus/schedule conflict	412	17.8	2,000	17.0
3 Distance or lack of transportation	378	16.3	1,642	13.9
4 Family responsibilities	441	19.1	1,884	16.0
5 Interest in technology/internet	73	3.2	493	4.2
6 Other	190	8.2	884	7.5
Duration of course in days				
1 Less than 65	1,186	51.3		
2 More than 66	1,128	48.7		

Demographic	No. responses (n = 8)	Percentage (total = 100%)
Age in years	20–29 = 4 30–39 = 0 40–49 = 3 50–59 = 1	50 0 37.5 12.5
Gender	Male = 1 Female = 7	12.5 87.5
Type of employment	Enrolled nurse = 3 Direct care attendant = 1 Undergraduate nurse = 2 Health professional = 1 Nursing (not specified) = 1	37.5 12.5 25 12.5 12.5
Marital status	Married = 3 Single = 3 Divorced/separated = 2	37.5 37.5 25
Children/ dependents	Yes = 5 No = 3	62.5 37.5
Current residence	Metropolitan = 0 Rural/regional = 8 Remote = 0	0 100 0

	Group A	Group B	Group C	Group D	Group E
Number of patients	25	25	25	25	25
Mean age(years)	21.24±9.09	26.28±12.24	26.60±9.84	29.76±11.53	27.54± 10. 91
Mean weight(kg)	39.94±13.16	50.86±14.46	48.89±12.67	53.68±12.37	51.63± 15.01
Male	10	9	19	13	11
female	15	16	6	12	14
Mean duration of anesthesia(min.)	131.25±26.60	120.00±26.54	122.10±37.01	135.00±37.50	132.50± 24.49

EFFECT SIZE

- What is the magnitude of the association between independent and dependant variables?
  - Large: ***easy to detect***
  - Medium
  - Small: ***difficult to detect***
- Decide a priori what is important **clinically**
- Should be units of a response – not %
- Use effect size for the most important hypothesis for sample size planning

NUMBER NEEDED TO TREAT

- Usually seen in results of clinical trial investigating practical value of treatment
- Number of patients who would need to receive a specific type of treatment in order for 1 patient to benefit from the treatment (Sackett 1988)
- Calculated as 1/absolute risk reduction (ARR)

NUMBER NEEDED TO TREAT
(Jekel 2001)

- In a study of hyperbaric oxygen therapy, leg ulcers were healed in 1/3 of patients resistant to other therapy
  - NNT = 1/ARR
  - ARR = 0.333
  - NNT = 1/0.333 = 3
- Results suggest that on average hyperbaric therapy would need to be given to 3 patients with resistant leg ulcers to benefit 1 patient

NUMBER NEEDED TO TREAT
(Campbell 2007)

- Use of antihypertensive drugs to prevent death, stroke, or MI
  - Over 1.5 years with diastolic 115-129mmHg; NNT = 3 *(need to treat 3 to benefit 1)*
  - Over 5.5 years with diastolic 90-109mmHg; NNT = 128 *(need to treat 128 to benefit 1)*

DIAGNOSTIC TESTS

	DISEASE +	DISEASE -
TEST +	A (TP)	B (FP)
TEST -	C (FN)	D (TN)

- Sensitivity: A/A+C
- Specificity: D/D+B
- PPV: A/A+B
- NPV: D/D+C

PREVALENCE/INCIDENCE

- **Prevalence**
  - Pre-existing + NEW cases in time period/ population at risk
  - Has all the cases NEW + old!
  - Prevalence=Incidence x duration
- **Incidence**
  - NEW cases in fixed time period/population at risk
  - NEW cases only!

RELATIVE RISK

- Incidence rate of disease in exposed group/incidence rate of disease in non-exposed group
  - RR=1, risk the same
  - RR<1, risk ↑ in not exposed group
  - RR>1, risk ↑ in exposed group
- Example: Among children with asthma, there is a 1.5 fold increase in mortality during the past 5 years

ODDS AND ODDS RATIO

- Similar to RR, but is used primarily in case control studies where no true incidence exists (need entire population)
  - OR=1, risk the same
  - OR<1, risk ↑ in not exposed group
  - OR>1, risk ↑ in exposed group

ODDS AND ODDS RATIO

RISK STATUS	DISEASE STATUS: PRESENT	DISEASE STATUS: ABSENT
PRESENT	A	B
ABSENT	C	D

-Risk of disease in exposed = a/a+b

-Odds of diseased in exposed = a/b; if a is small compared to b, then odds=risk

-**Odds Ratio = odds of exposure diseased/ odds of exposure in nondiseased**

OR = (a/c)/(b/d)

OR = ad/bc

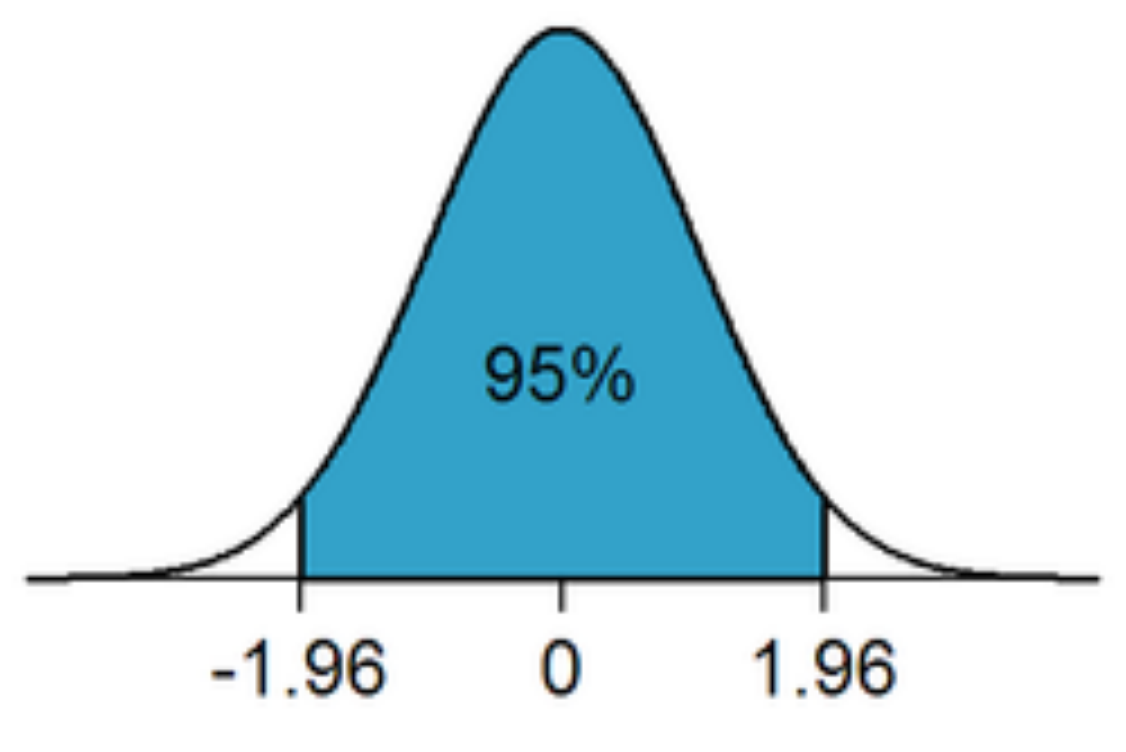
CONFIDENCE INTERVAL
(Jekel 2001)

- Standard deviation (SD) measures *variability* of indivdual observations
- Standard error (SE) measures the variability of means
- CI = range of values an investigator can be 95% confident that the true mean of the population falls
- 95% CI = mean ± 1.96(SE)

CONFIDENCE INTERVAL
(Jekel 2001)

- Step 1:
  - Number of observations of blood pressure values = 26
  - Mean = 113.2 mmHg; SD = 10.3 mmHg
- Step 2:
  - SE = SD/$\sqrt{N}$
  - SE = 10.3/5.1 = 2.02 mm Hg
- Step 3:
  - 95% CI = mean ± 1.96SE
  - 95% CI = 113.1±(1.96)(2.02)
  - 95% CI = 113.1±3.96 or 109.1, 117.1 mmHg

1.96



95% of the area under the *normal distribution* lies within 1.96 standard deviations of the mean

CONFIDENCE INTERVAL

- If value corresponding to NO effect (eg RR=1) falls outside the 95% CI, then unlikely that results are significant at the .05 level
- IF CI barely includes value of no effect and is wide, significance may have been reached if the study had more power
- Advantage of CI: can see range of accepted values and compare with what is clinically significant

CONFIDENCE INTERVAL – Clinical Examples

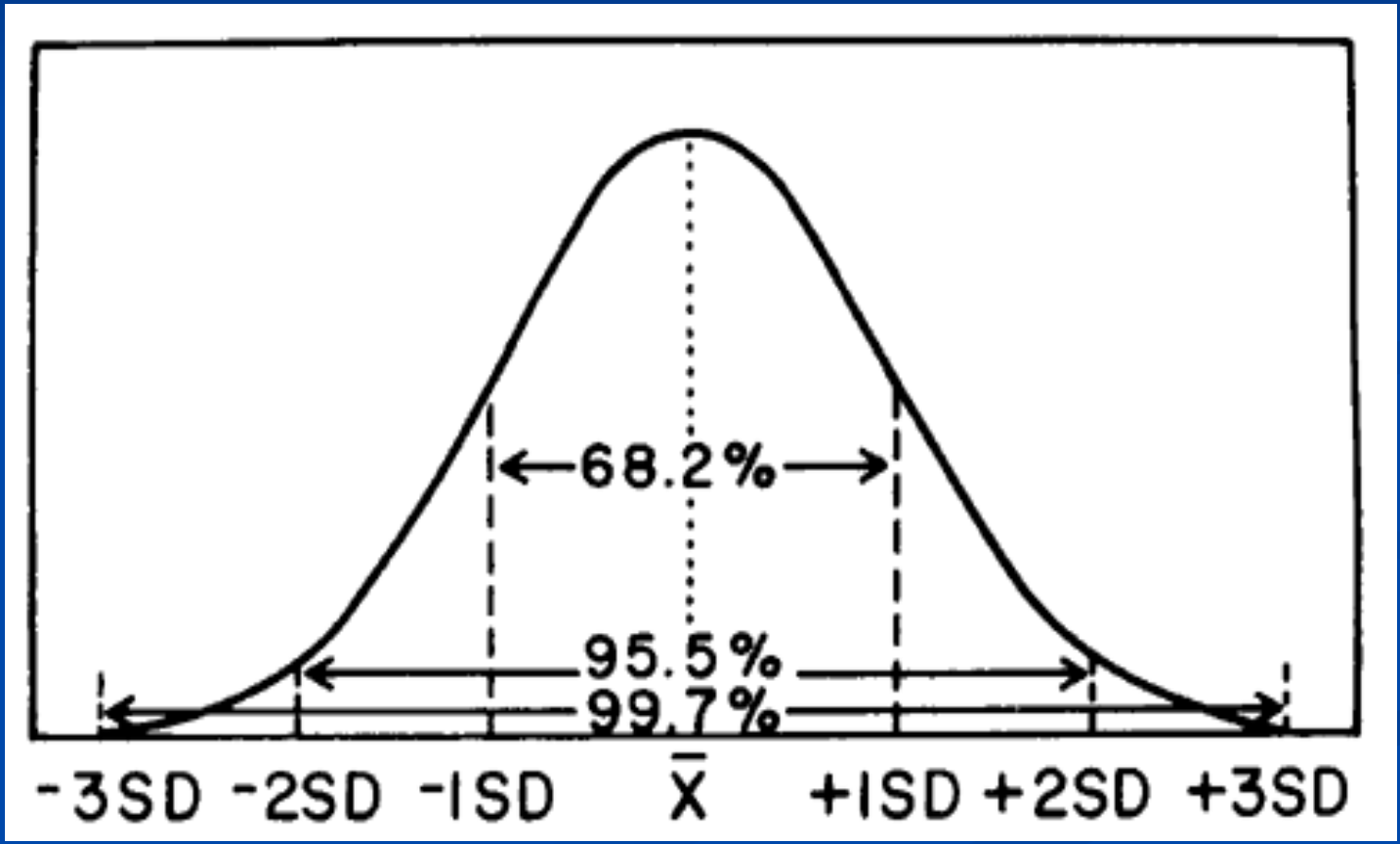
- Risk for intracranial bleed after serious head trauma is 8.22, 95% CI=6.25,10.21
  - Actual risk could be between 6.25-10.22
  - If risk was 1.0, this would indicate no risk between exposed and non exposed groups
- Sensitivity of clinical exam for splenectomy is 27% (95% CI 19-36%)

PARAMETRIC/NONPARAMETRIC

- Parametric Data
  - Data for which descriptive data are known (usually mean, SD)
  - Frequency distribution of data defined as "normal"
  - Examples of parametric tests
    - T- Test
    - Pearson Correlation Coefficient

PARAMETRIC/NONPARAMETRIC

- **Parametric Data**

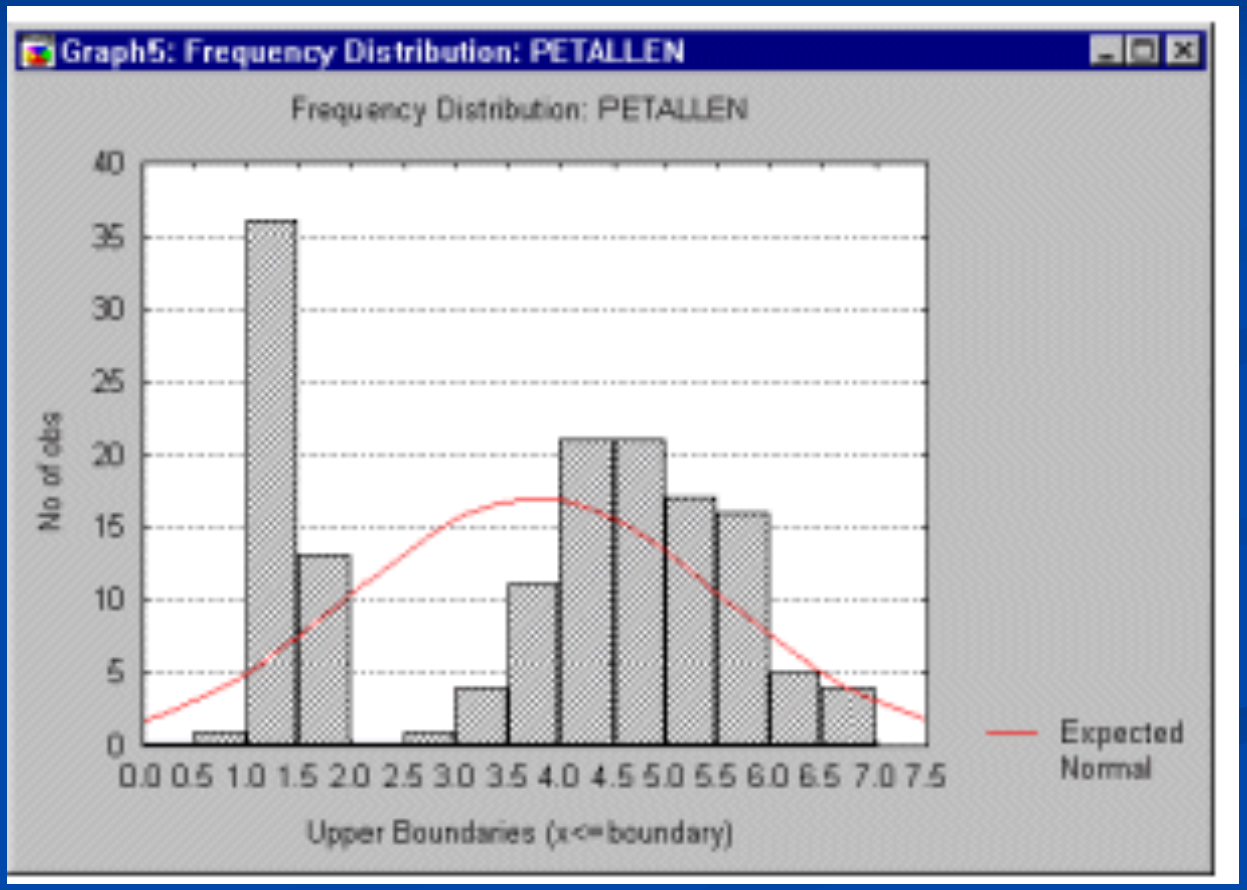


PARAMETRIC/NONPARAMETRIC

- Nonparametric Data
  - Data for which descriptive data cannot be obtained due to no measurement scale
  - No assumption regarding the underlying frequency of the data; only certainty is rank order
  - Examples of nonparametric tests
    - Sign test
    - Wilcoxon matched pairs test
    - Mann Whitney U Test

PARAMETRIC/NONPARAMETRIC

- **Nonparametric Data**



COMMONLY USED STATISTICAL TESTS

PARAMETRIC TEST	CORRESPONDING NONPARAMETRIC TEST	PURPOSE OF TEST
t test for independent samples	Mann-Whitney U test; Wilcoxon rank-sum test	Compares two independent samples
Paired *t* test	Wilcoxon matched pairs signed-rank test	Examines a set of differences
Pearson correlation coefficient	Spearman rank correlation coefficient	Assesses linear association between two variables
One way analysis of variance (*F* test)	Kruskal-Wallis analysis of variance by ranks	Compares three or more groups
Two way analysis of variance	Friedman Two way analysis of variance	Compares groups classified by two different factors

BIAS
(Altzema 2004)

- Selection Bias
  - Selection of subjects systematically distorted and may predetermine outcome
  - Example: *hospital study of diarrhea will overestimate severity of disease*
- Measurement/information Bias
  - Bias in classifying disease, exposure, or both
  - Example: *knowing too much about disease may influence exposure*

BIAS
(Altzema 2004)

- Confounding Variables
  - A factor that may influence the relationship between dependent and independent variables
  - Example: *Risk of morbidity from hypertension should control for age, gender, race, etc*
- Verification Bias
  - Patients with positive or negative test result preferentially selected for testing – other patients may have been missed for testing with milder form of the disease
  - Example: *Morbidity and childhood asthma*

STUDY DESIGNS

STUDY DESIGN	FEATURE	EXAMPLE
Descriptive Reports	Recognize new/ atypical characteristic of disease	Case report – first case(s) of pediatric lyme disease
Cohort	1 group followed over time	Infants followed for effects of smoke exposure for 2 years
Cross-Sectional	A group examined at 1 point in time	Psychometric testing in homeless vs. nonhomeless children
Case-Control	Two groups, based on outcome	Aspirin and Reyes Syndrome
Randomized Trial	Two groups, randomly created, blinded intervention	Effect of educational intervention on asthma morbidity

DESCRIPTIVE REPORTS

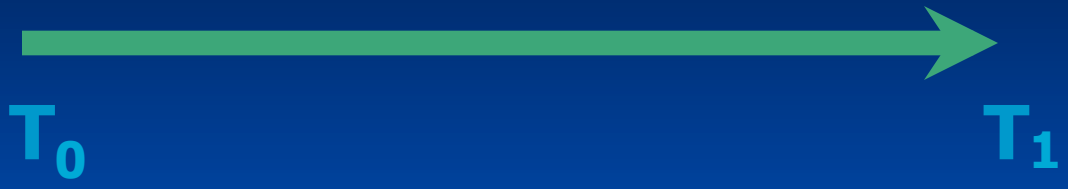
- Description of a new aspect or new disease
- No comparison group needed
- Description is usually a basic statistic summary or profile of the group of cases
  - Mean, SD, range, confidence intervals, correlation between variables

Ann Neurol. 2010 Jan 20;68(1):92-101. [Epub ahead of print]

Pediatric moyamoya disease: An analysis of 410 consecutive cases.

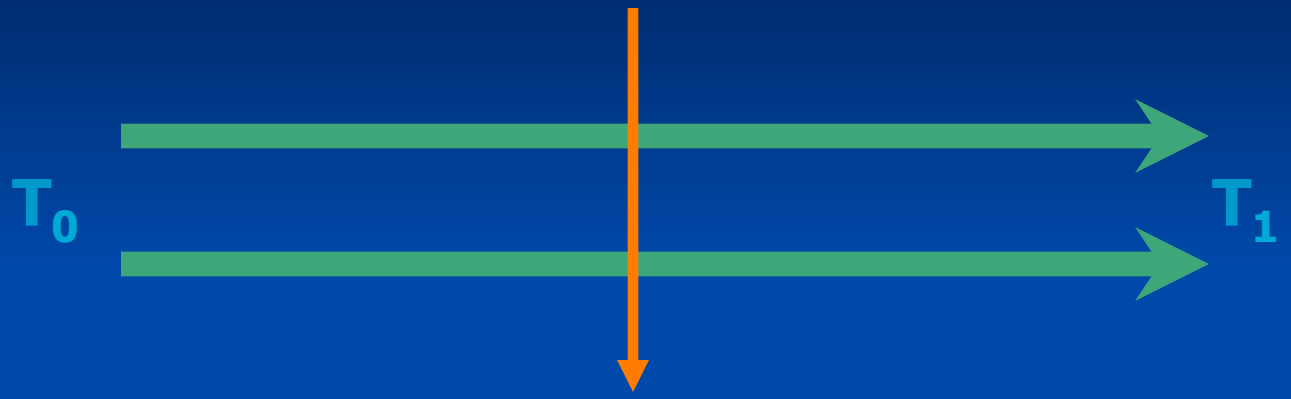
Kim SK, Cho BK, Phi JH, Lee JY, Chae JH, Kim KJ, Hwang YS, Kim IO, Lee DS, Lee J, Wang KC.
Division of Pediatric Neurosurgery, Seoul National University Children's Hospital, Seoul National University College of Medicine, Seoul, Republic of Korea

COHORT STUDY



- Population followed forward over time
- Baseline: acute pharyngitis
- Outcome: Prevention of rheumatic fever or glomerulonephritis
- Admission Criteria?: Evidence of ß-hemolytic streptococcus vs pharyngeal inflammation

CROSS SECTIONAL STUDY

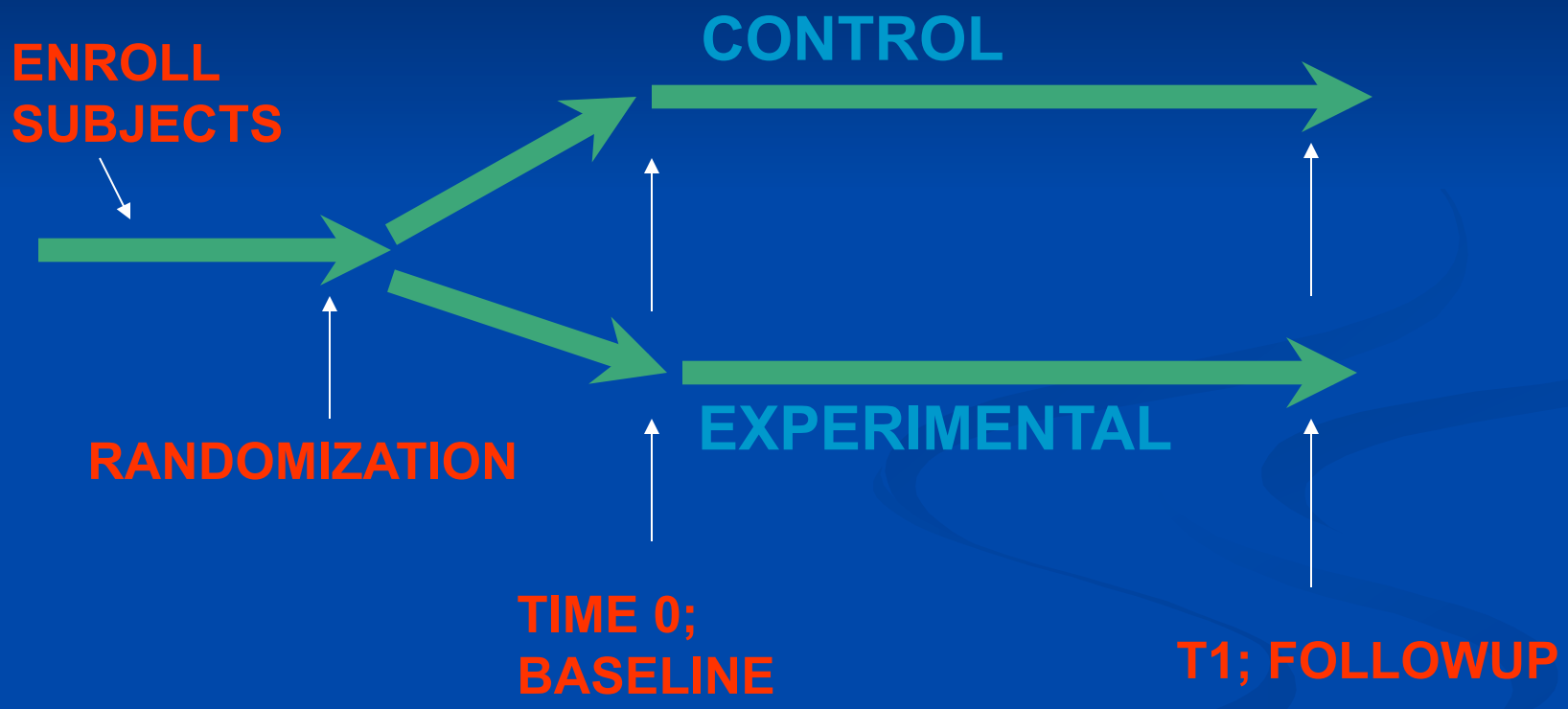


- Collect data on 2 groups at 1 point in time
- Compare group differences
- Cholesterol levels in athletes vs. non athletes at a midwest university

CASE CONTROL STUDY

- Risk factors in both cases and controls are compared for a condition – especially rare diseases
- Important methodology regarding choice of cases, controls

RANDOMIZED CONTROL TRIAL



SUMMARY

- Acquire knowledge of research process and initiate process now
- Acquire basic knowledge of epidemiology and research methods
- Achieve satisfaction in production/ completion of research project
- RE: ILP; establish method of criticism of what you do and what is in the literature

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