# How to Work with a Statistician

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# Overview

- Understand what statisticians can (and cannot) do for you
- Know your responsibilities as a researcher
- Highlight some “do’s” and “don’ts”
- Resources available through the CTSC
- Example consultations

# Why and when to work with a statistician?

- **Planning the study**
  - Study design, randomization, sample size
  - Proposal preparation
- **Conducting the study**
  - Interim analyses, DSMB
- **Evaluating the results**
  - Conducting statistical analyses
- **Reporting the results**
  - Interpreting the results
  - Manuscript preparation

# The Research Process

# "Gee, I wonder if..."

# Planning Stage Involvement

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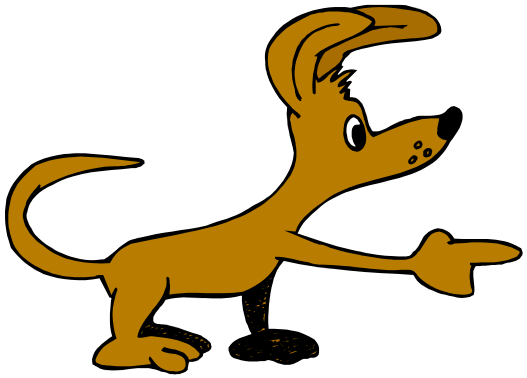


**Statistics can't fix a poorly designed study!**

# Planning Stage Activities

## RESEARCHER

- Develop specific aims
- Identify endpoints
- Formulate testable hypotheses
- Develop study protocol
- Identify confounding factors, potential biases

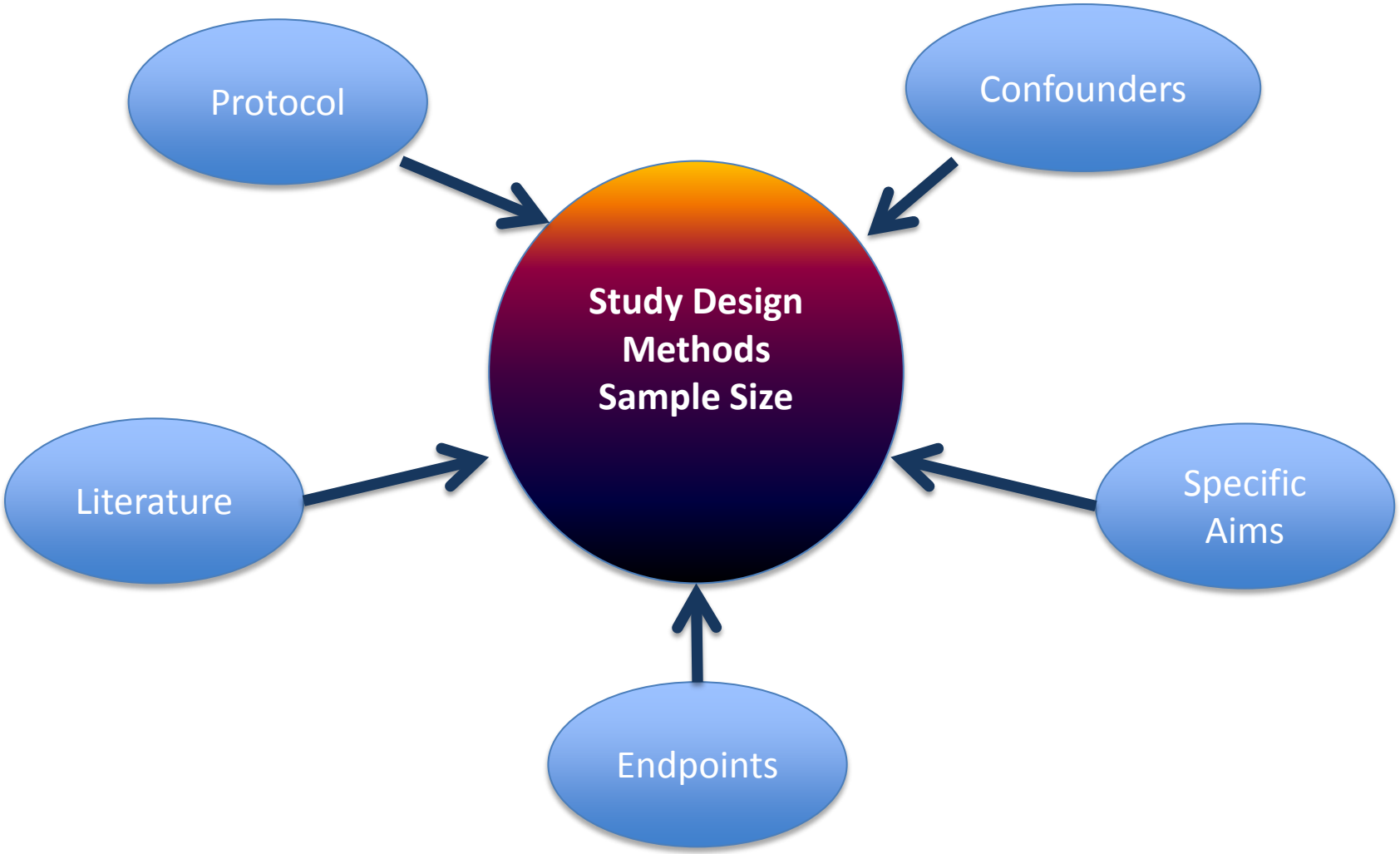
## STATISTICIAN

- Formulate testable hypotheses
- Study design, randomization, matching
- Sample size needs
- Statistical analysis plan
- Identify confounding factors, potential biases

# Before Meeting with a Statistician

- Clearly define your specific aims
- Identify measureable endpoints for each aim
- Know how you will collect the data
- Consider confounders and potential biases
- Review relevant literature

# Why are these important?



# Specific Aim 1: Determine if new treatment is better than standard care.

- **What constitutes *better?***
- **What measureable parameter reflects *better*?**
  - Survival, number of events, mean value?
- **What testable hypothesis addresses the specific aim?**
  - $H_0$: Mean cholesterol under new treatment does not differ from standard care
  - $H_a$: Mean cholesterol under new treatment differs from standard care

# How do I test my hypothesis?

- **Type of study**
  - Prospective or retrospective
- **Definition of cases and controls**
  - Exclusion and inclusion criteria
- **Matching/stratification procedures**
- **Randomization**
  - Subject selection, block randomization
- **Sample size requirements**

# How many subjects do I need?

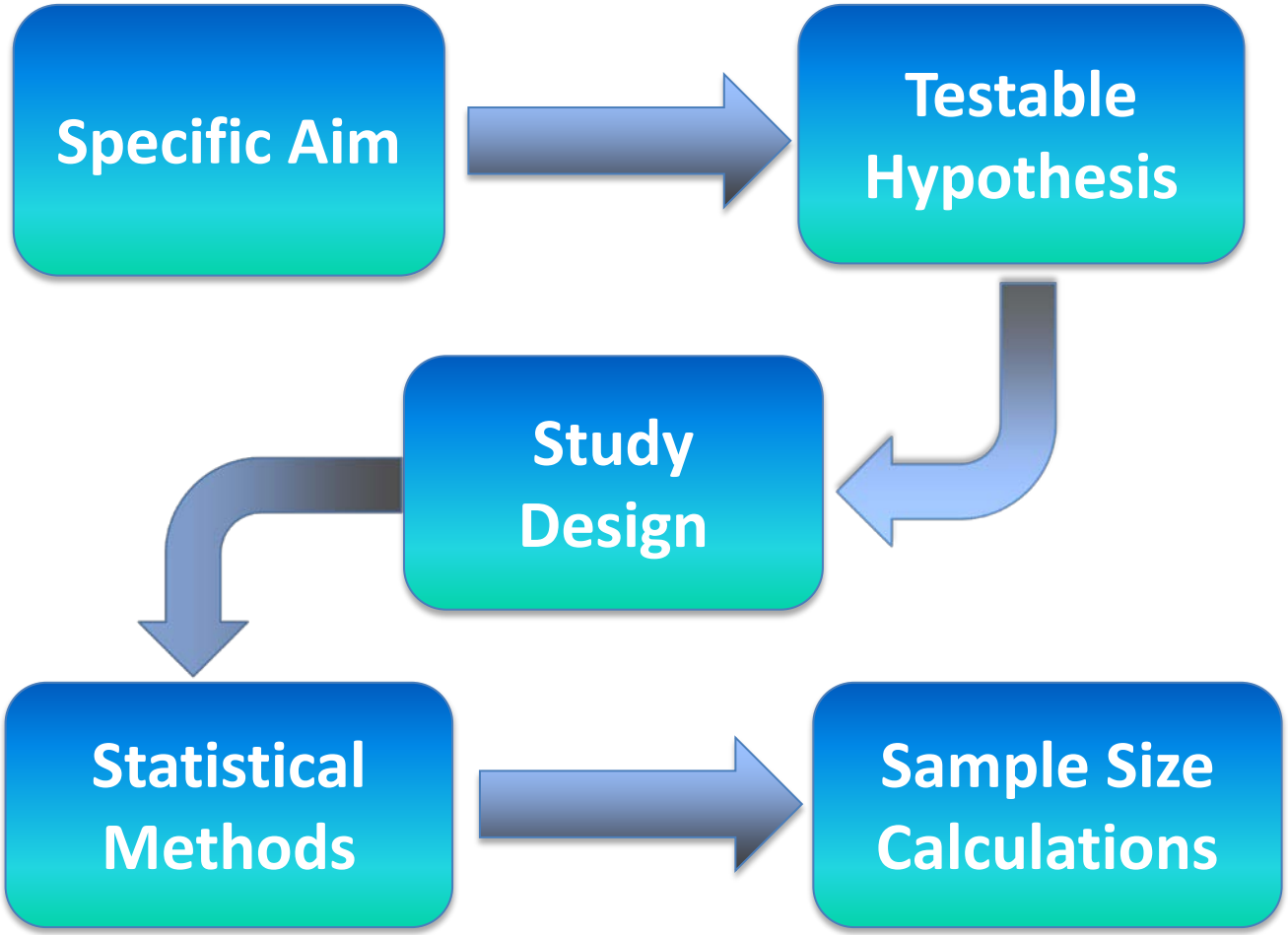
- Too few – insufficient power to detect differences
- Too many – unnecessary costs
- Statisticians need input from researchers to determine sample size requirements.

# Biologist talks to Statistician video

https://www.youtube.com/watch?v=Hz1fyhVOjr4

Please consult a statistician early!

# Sample size determination comes at the end of a series of steps.



# How is sample size determined?

**Depends on:**

- **Specific aim – primary hypothesis of the study**
- **Study design**
  - These two influence the statistical test.
- **Effect size to be detected**
- **Variability of the response variable**
  - Researchers need to provide this information

# Example: New medication study

- **Test: $H_o$: $\mu_{new} = \mu_{old}$ vs. $H_a$: $\mu_{new} \neq \mu_{old}$**
- **Design: Randomized into each arm**
- **Statistical method: *t*-test**

$$n = \frac{\left(Z_{\alpha/2} + Z_{\beta}\right)^2 \sigma^2}{\Delta^2}$$

- **$\sigma^2$ = variance; $\Delta$ = effect size to detect**

Researchers need to provide this information.

- Published results
- Pilot data
- Clinically meaningful change

# Sample size calculations may not be straight-forward

- **More complex designs require more complex calculations**
- **Examples:**
  - Longitudinal studies
  - Cross-over studies
  - Correlation of outcomes
- **Sometimes simulations are required**

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**THERE IS NO MAGIC NUMBER.**

# Proposal Content

**Proposal sections involving statistics**

- **Sample size justification**
- **Statistical analysis plan**
  - Statistical methods for each aim

**For clinical trials,**

- **Interim analyses/Early stopping rules**

**Engage a statistician to write or at least review these sections.**

# Common statistical problems in proposals

- Sample size justification absent or insufficiently justified
- Lack of statistical analysis plan for all aims, including secondary aims
- Inappropriate statistical analysis methods

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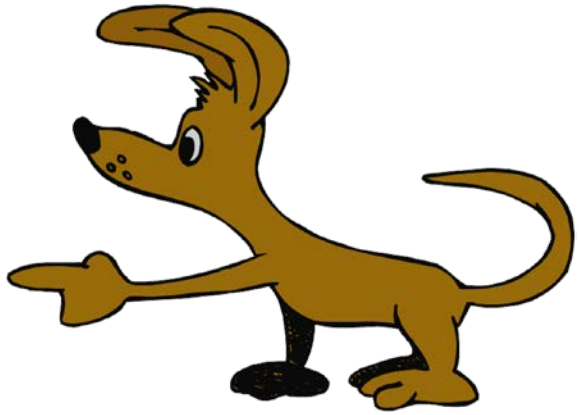
- Lack of statistical analysis plan for all aims, including secondary aims
- Inappropriate statistical analysis methods

**These issues can doom a proposal.**



# Data Collection and Compilation

www.ucdmc.ucdavis.edu/ctsc/redcap/

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## Clinical and Translational Science Center

Health System > Clinical and Translational Science Center > REDCap

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- Application for Resource Use (AFRU)
- Investigators
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- Community Engagement and Research
- CTSC Clinical Research Center (CCRC)
- Pilot Translational and Clinical Studies
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- Research Education, Training, and Career Development
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Application for Resource Use

### REDCap (Research Electronic Data Capture)

View dates for upcoming REDCap training and drop-in worshops at the CTSC Event Calendar

#### What is REDCap?

**REDCap** (Research Electronic Data Capture) is a secure web application for building and managing online databases for research.

Launch REDCap

REDCap™

Click here to go to REDCap Survey

Using REDCap's stream-lined process for rapidly developing projects, you may create and design projects by constructing a 'data dictionary' template file in Microsoft Excel, which can be later uploaded into REDCap. REDCap provides audit trails for tracking data manipulation and user activity, as well as automated export procedures for seamless data downloads to Excel, PDF, and common statistical packages (SPSS, SAS, Stata, R). Also included are a built-in project calendar, a scheduling module, ad hoc reporting tools, and advanced features, such as branching logic, file uploading, and calculated fields.

#### How do I get access to REDCap?

**You will only have to request access once. Access to individual projects is determined by the User Permissions Matrix submitted for each project.**

1. Submit a Lotus Notes Online Access Request, instructions are on the How to request access page
2. Send (fax, inter-office mail, or scan and email) the signed REDCap End User Agreement to the CTSC informatics staff responsible for your project

#### How do I begin using REDCap?

The CTSC Biomedical Informatics Program has developed a six-step process to create a database. We encourage researchers to begin working with biostatisticians early.

**To get started, please complete the CTSC Application for Resource Use.**

**Six-step process to create a REDCap Database (hover over each box for details)**

1. Introductory Meeting
2. Create Data Dictionary
3. Data Review Meeting
4. Create Database
5. Final Review
6. Begin Entering Data!

- REDCap & REDCap Survey
  - REDCap
  - REDCap Survey
- Getting Started
  - CTSC Application for Resource Use
  - REDCap Project Level Agreement (PDF)
  - REDCap Text for IRB and Grant Submissions
  - Citing REDCap and the CTSC in Publications
  - Frequently Asked Questions
- Data Dictionary
  - How to Create the Data Dictionary (Video) (14 min)
  - Sample Data Dictionary (CSV)
  - User Permissions Matrix (Excel)
- Accessing REDCap
  - How to request access
  - REDCap End User Agreement (PDF)
  - UCDHS Confidentiality Agreement (PDF)
  - Create New UC Davis Kerberos Account
  - UC Davis Temporary Affiliate Form

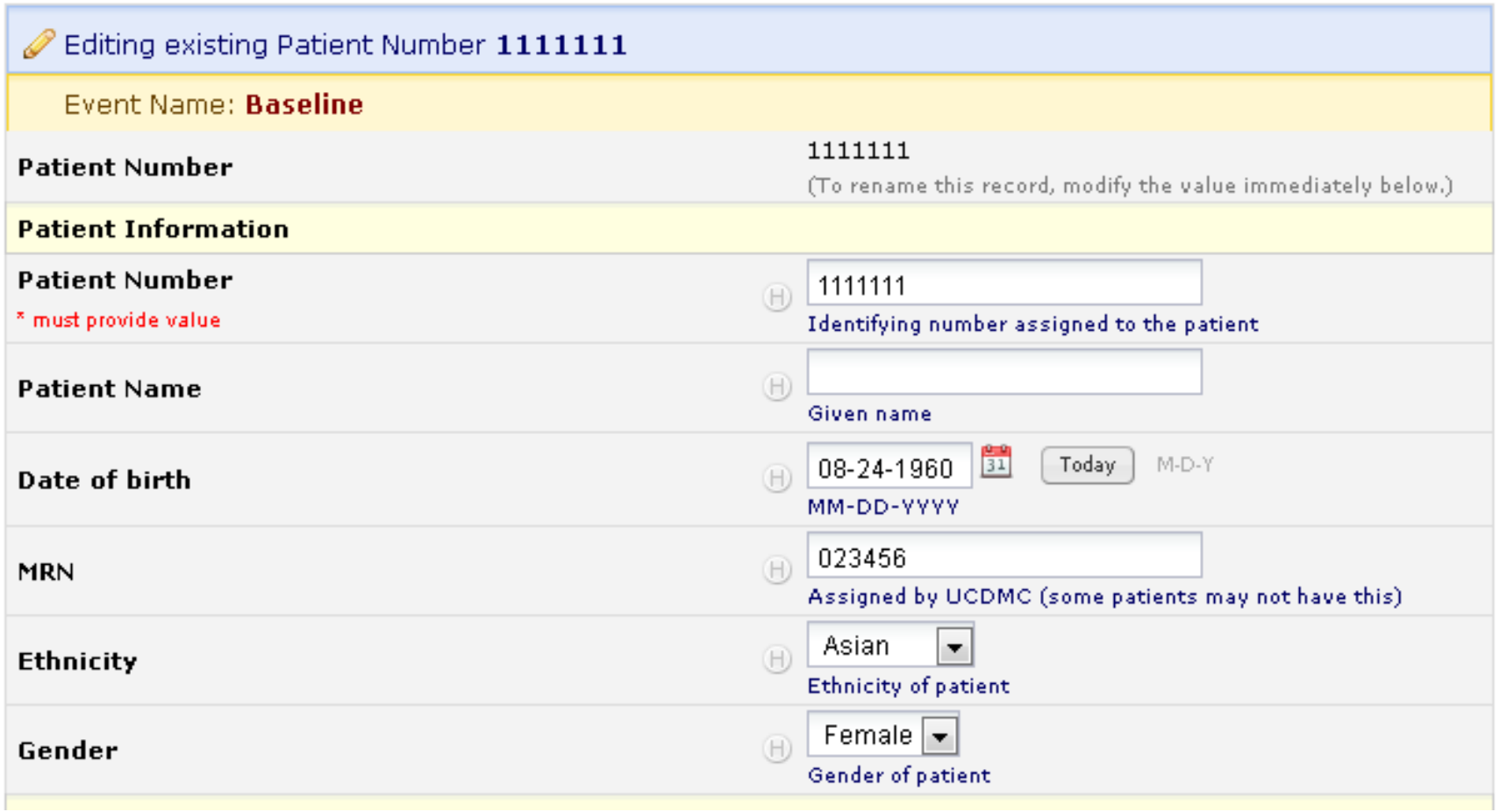
# Data Collection and Compilation

- **Valid results require**
  - Collection of accurate data
  - Clear and accurate data compilation
- **Create workable and documented data sets**
- **QA/QC procedures**
  - Validation during data entry
  - Periodically audit the data
  - Conduct internal validation of final data

# Bad Scene!

| | A | B | C | D | E | F | G | H | I | J | K | L |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **Comparison of Drug A and Drug B** | | | | | | | | | | | |
| 2 | Drug A | Age of Patient | Patient | Height | Weight | 24hrhct | blood pressure | tumor | Race | Date | complications | |
| 3 | | | Gender | (inches) | (pound) | | | stage | | enrolled | | |
| 4 | | | | | | | | | | | | |
| 5 | 1 | 25 | Male | 61" | >350 | 38% | 120/80 | 2-3 | Hipanic | 1/15/99 | no | |
| 6 | 2 | 65+ | female | 5'8" | 161 | 32 | 140/90 | II | White | 2/05/1999 | yes | |
| 7 | 3 | ? | Male | 120cm | | 12 | >160/110 | IV | Black | Jan 98 | yes, pneumonia | |
| 8 | 4 | 31 | m | 5'6" | obse | 40 | 40 sys 105 dias | ? | African-Am | ? | | |
| 9 | 5 | 42 | f | >6 ft | normal | 39 | missing | =>2 | W | Feb 99 | | |
| 10 | 6 | 45 | f | 5.7 | 160 | 29 | 80/120 | NA | B | last fall | n | |
| 11 | 7 | unknown | ? | 6 | 145 | 35 | normal | 1 | W | 2/30/99 | n | |
| 12 | 8 | 55 | m | 72 | 161.45 | 12/39 | 120/95 | 4 | African-Am | 6-15-00 | y | |
| 13 | 9 | 6 months | f | 66 | 174 | 38 | 160/110 | 3 | Asian | 14/12/00 | y | |
| 14 | 10 | 21 | f | 5' | | | | | | | | |
| 15 | | | | | | | | | | | | |
| 16 | Drug B | | | | | | | | | | | |
| 17 | 1 | 55 | m | 61 | 145 | normal | 120/80 120/90 | IV | Native Am | 6/20/ | 3 | |
| 18 | 2 | 45 | f | 4"11 | 166 | ? | 135/95 | 2b | none | 7/14/99 | n | |
| 19 | 3 | 32 | male | 5'13" | 171 | 38 | 140/80 | not staged | NA | 8/30/99 | n | |
| 20 | 4 | 44 | na | 65 | ? | 40 | 120/80 | 2 | ? | 09/01/00 | n | |
| 21 | 5 | 66 | fem | 71 | 0 | 41 | 140/90 | 4 | w | Sep 14th | y, sepsis | |
| 22 | 6 | 71 | unknown | 172 | 199 | 38 | >160/110 | 3 | b | unknown | y, died | |
| 23 | 7 | 45 | m | ? | 204 | 32 | 40 sys 105 dias | 1 | b | 12/25/00 | n | |
| 24 | 8 | 34 | m | NA | 145 | 36 | 130 | 3 | w | July 97 | n | |
| 25 | 9 | 13 | m | 66 | 161 | 39 | 166/115 | 2a | w | 06/06/99 | n | |
| 26 | 10 | 66 | m | 68 | 176 | 41 | 1120/80 | 3 | w | 01/21/58 | n | |
| 27 | | | | | | | | | | | | |
| 28 | Average | 45 | | 65 | 155 | 38 | | | | | | |

# RedCAP is user-friendly alternative.



# Leverage informatics and biostatistics expertise

- **Medical informatics group can**
  - Create forms for data collection
  - Extract information from EMR
- **Use inter-disciplinary team to determine what information to collect and how**
  - Investigator, practitioners, biostatistician, informatics specialist
  - Ensures information is collected and compiled in a manner that facilitates analysis

# Data Do's and Don'ts

- **Use RedCAP where possible**
- **Assign unique ID to each subject and use consistently**
- **Remove all PHI prior submitting to statistician**
- **Unambiguously and consistently specify missing values**
  - Avoid using "0" or blanks for missing values
- **Avoid free text fields**

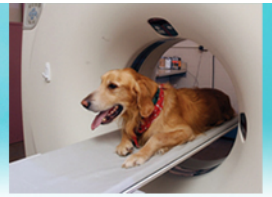
# Each data set needs a Code Book

**Guidelines for Data Set Documentation**
**http://biostats.ucdavis.edu/DatasetDocumentation.php**

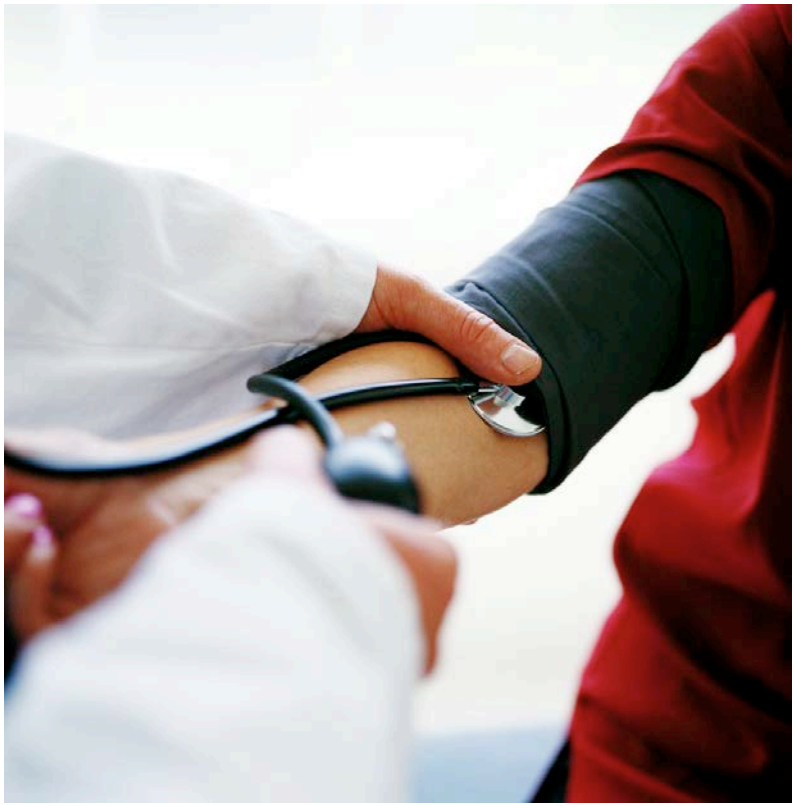
- **Name of the data file as it is stored on the computer**
- **Name of the code book's author, including contact information**
- **Date the code book was last updated.**
- **Number of records in the data file.**
  - List of variables, including for each variable
  - Variable name
  - Location of variable, length of field
  - Allowable range for data
  - Missing data codes
  - Interpretation of values if not obvious (e.g. 1-male, 2-female.)







# Go forth and collect data!



# Statistician activities during the study

- **Sometimes limited involvement by statistician**
- **Involvement can include**
  - Conducting interim analyses
  - Serving on DSMB
- **Some study designs entail periodic reassessments and statistician will necessarily be involved during the study**
  - Two-stage, adaptive or sequential trials

# Analysis and Reporting

**(P.S. This is the fun part.)**

# Analyzing the data

- **Conduct statistical analyses**
  - Data validation
  - Run statistical tests
- **Interpret the results**
- **Prepare tables and figures to illustrate findings**

# Working with a Statistician to Analyze your Data

## Range of support provided

One-time
Advice Only

Select methods
Conduct all analyses

# If statistician analyzes the data…

- **Remove PHI**
- **Provide "clean" data set**
- **Provide data dictionary**
- **Allow sufficient time for analysis**
  - Rule of Thumb is 4 to 6 weeks
- **Provide references from similar studies if available**
- **Iterative and interactive process**

# Incorrect method results in incorrect conclusions.


**Data with special statistical issues**

- **Correlated values**
  - Multiple measurements on same subject
  - Clustering of subjects (e.g., same hospital, same litter)
- **Longitudinal data**
  - Repeated measurements over time on same subject
- **Missing data and drop outs**
- **High-dimensionsal data**
  - microarrays, proteomics

# Report/Publication Preparation

- Craft statistical analysis section
- Contribute to results section
- Generate tables and figures

# Resources at UC Davis

- **Clinical and Translational Science Center**
  - Biostatistics Workshop: 12-1 on Tuesdays

    sltaylor@ucdavis.edu
  - Biostatistics Core
    - Assist with study design, grant writing, data analysis and interpretation
    - Application for Resource Use (AFRU) http://www.ucdmc.ucdavis.edu/ctsc/
- **Division of Biostatistics**

# Parting Tidbits

# What we can't do.

Fix a poorly designed study

Make something significant

P value < 0.05

Tell you what's important

# What we won't do.

Find a significant result, i.e., "data snooping"

Clean up your data


Troubleshoot your code

# Requests that Seriously Irritate Us

- **“My abstract is due Friday. Can you analyze my data by tomorrow?”**
- **“I have a really simple question. It’ll only take 15 minutes.”**
- **“My paper got rejected because of the statistics. Can you fix it?**
- **“I keep getting error messages with my code. Can you look at it?”**

# What we love to do.

**Help investigators achieve goals**

**Collaborate to bring new insights**

**Contribute to societal improvements**

# Example Project #1

## Traumatic Brain Injury Outcomes

# How do TBI patient outcomes differ with Glasgow Coma Scores at admission?

- **What is your outcome?**

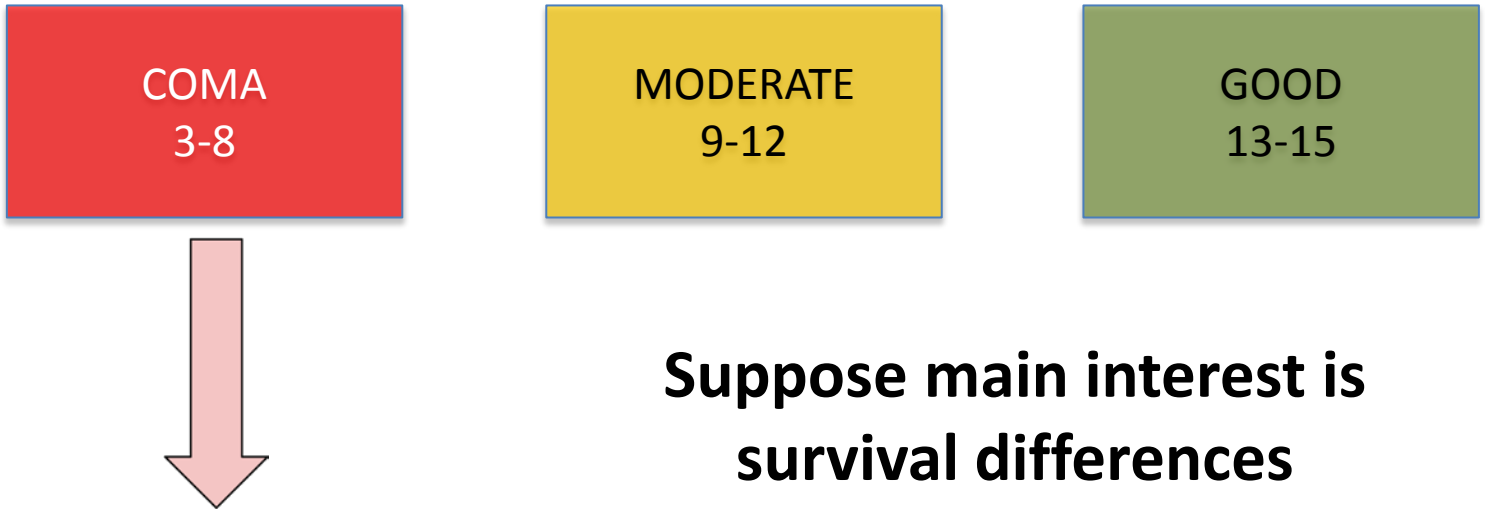
# How do TBI patient outcomes differ with Glasgow Coma Scores at admission?

- **What is your outcome?** **Survival**
- **Survival to when?**
  - **60-day?**
  - **30-day?**
  - **Discharge?**

# How do TBI patient outcomes differ with Glasgow Coma Scores at admission?

- What is your outcome? **Survival**
- Survival to when?
  - 60-day?
  - 30-day?
  - **Discharge**
- What specifically do we want to test?

# GCS Groups




**High mortality**

**Suppose main interest is survival differences between moderate and good GCS groups.**

# TBI Patient Outcomes Study Aim

**Specific Aim 1:**
**Determine if survival to discharge differs between patients with moderate (9-12) and good (13-15) Glasgow Coma Scores.**

**Endpoint:**
**Survival to discharge**

**Testable Hypothesis:**
$H_o: p_{mod} = p_{good}$ versus $H_a: p_{mod} \neq p_{good}$

**Statistical Test:**
**Two-sample Proportion Test**

# How do we test this hypothesis?

- **How about a prospective study?**
  - How could you do this?
  - Follow patients that come in with TBI and GCS of 9 or greater
- **What issues/questions arise with a prospective approach?**
  - How many patients necessary?
  - How long to recruit this number?
  - What are the confounders? Can we control for them?

# How do we test this hypothesis?

- **How about a retrospective study?**
  - How could you do this?
  - Extract EMR information for patients with TBI and a GCS of 9 or greater
- **What issues/questions arise with a retrospective approach?**
  - Do we have enough patients in the EMR?
  - What are the confounders? How can we account for them?

# Prospective vs. Retrospective

## Prospective

- Ensure ALL desired data collected
- Current information
- Randomization
- Matching or stratification

## Retrospective

- Large sample size
- Data available now
- Easier logistically
- Confounding factors

# Prospective vs. Retrospective

## Prospective

- Ensure ALL desired data collected
- Current information
- Randomization
- Matching or stratification

## Retrospective

- Large sample size
- Data available now
- Easier logistically
- Confounding factors

**For this particular study, a retrospective approach makes the most sense.**

# Sample Size Requirements

- **Prospective studies – how many to recruit**
- **Retrospective studies – do we have enough**
- **Information needs**
  - Survival of patients with moderate GCS
  - Difference in survival you want to detect

# Inclusion/Exclusion Criteria

## Include

- TBI with GCS 9+
- 16+ years old
- Arrival at Level 1 trauma center, including transfers

## Exclude

- No TBI or GCS < 9
- Under 16 years old
- Penetrating injury
- Burn injury
- Others?

# What are other potential confounding factors?

- Injury severity
- Age
- Gender
- Comorbidities

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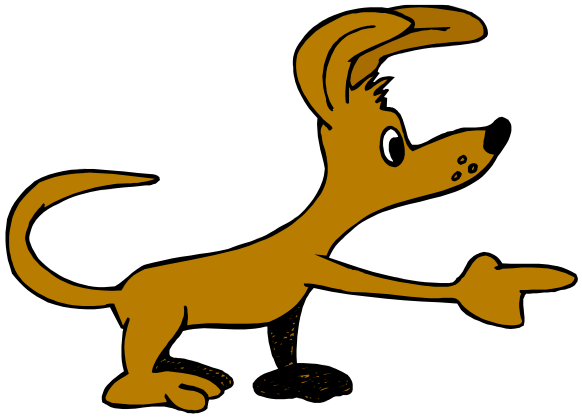

**Statistics can't help a woefully unbalanced study**

# Next Steps

- **Develop statistical analysis plan**
- **Work with Informatics and Biostatistics**
  - Identify data to extract from the EMR
  - Develop data dictionary and supporting data forms
- **Conduct data validation**
- **Statistically analyze the data**

# Example Project #2

## Toradol Use for Rib Fractures

# Does Toradol reduce the incidence of pneumonia in patients with rib factures?

- What is the endpoint of interest?
- Prospective or retrospective?

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- **What is the endpoint of interest?**
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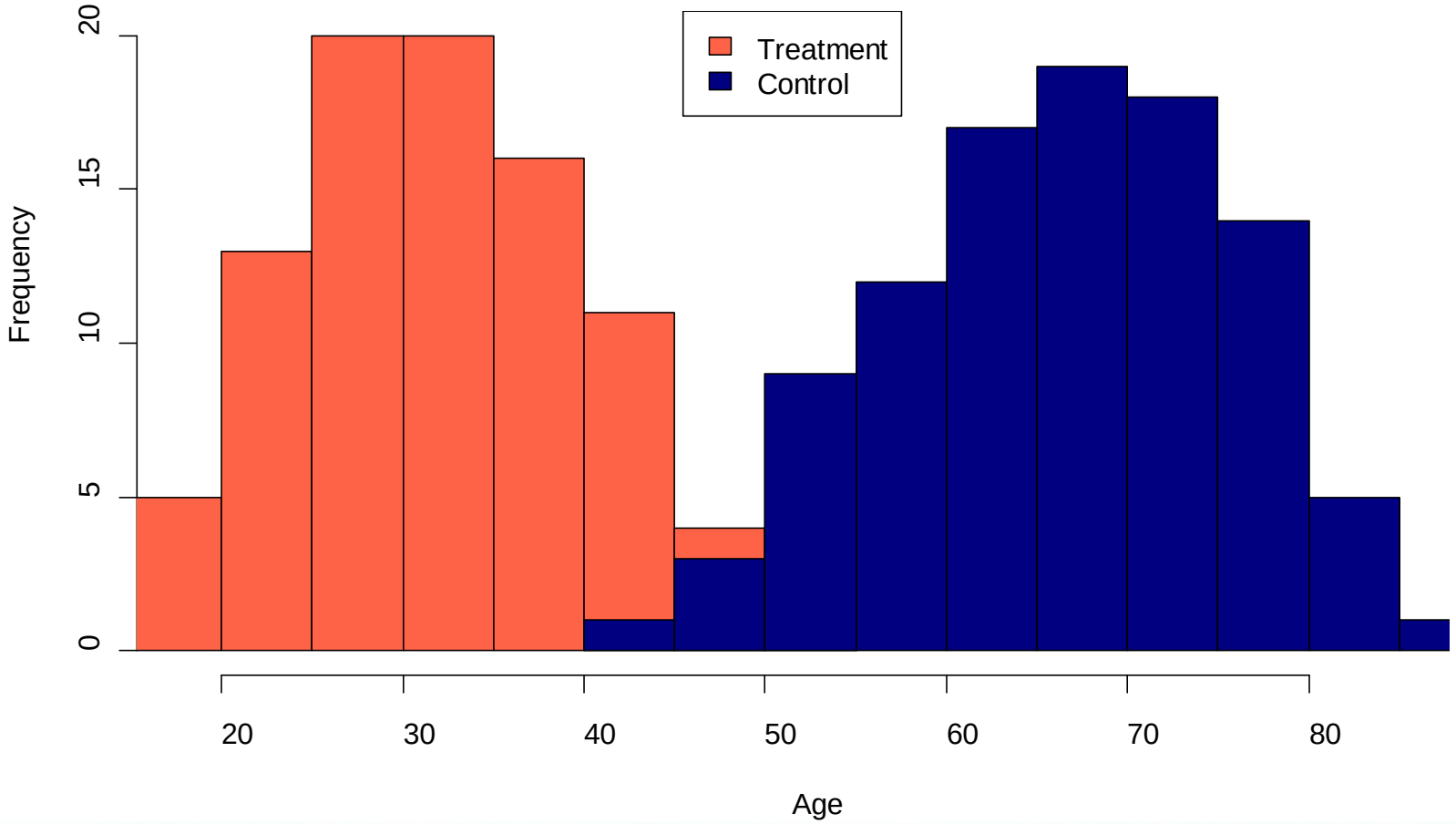
  - Prospective preferred (Why?)

# Does Toradol reduce the incidence of pneumonia in patients with rib factures?

- **What is the endpoint of interest?**
- **Prospective or retrospective?**
  - Prospective preferred (Why?)
- **What issues arise for a retrospective study?**
  - Comparability of groups
  - Age, injury severity, comorbidities

# What if the data look like this?



# Take Home Messages

- **Statistics matter**
  - Study design, sample size, appropriate analytical methods
- **Consult earlier rather than later**
  - Greatest value from consulting early
  - Can't fix a poorly designed study
- **View statisticians as collaborators**
  - Authorship, funding support