Basic Biostatistics

Section Two

A quick review

- Mean, Median and Mode are characteristics of a specific population
- Standard Deviation defines the spread around the mean in that specific population
- Variables of study are of specific types
  - This will determine which statistical test is applied

Distribution

- Normal Distribution Curves
  - The percent of a population encompassed by each standard deviation
  - Unimodal, Symmetric, and never reach zero or one (as a ratio)
- P values
  - The probability of that value or a greater (more extreme) given our population. (0.05 is usually considered appropriate in clinical medicine)

Inferential Statistics

- An analytic technique for drawing conclusions about the population from an appropriately collected sample.
  - This is an estimate but….Statistics tell us that the amount of imprecision is dependant on
    - Variability (standard deviation) AND
    - Sample size

Hypothesis

- Now ask a clinical question about our newly diagnosed diabetic patient:
  - Is Drug A better than Drug B in controlling Type II diabetes (yes or no)?
- To decide you must create a hypothesis, but in statistics it is called the Null Hypothesis.
  - The null states the there is no difference and you disprove it. (Don't ask)

Hypothesis

- Null Hypothesis
  - Labeled H_O
  - States that no difference exists
- Alternate Hypothesis
  - Labeled H_A
  - States that there is a difference

In our example, the Null Hypothesis is that there is no difference between Drug A and Drug B and our job is to disprove this hypothesis.

However it's a little more complex….

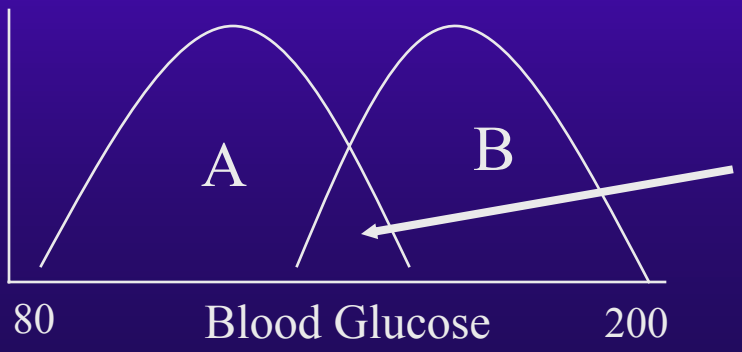
- H_O: Null Hypothesis
  - Drug A = Drug B
- H_A: Alternative Hypothesis
  - Drug A ≠ Drug B
    - Two sided hypothesis: either cause more lowering
  - Drug A > Drug B
    - One sided hypothesis: A only can cause more lowering so you would not want to test if B could lower more.
  - Drug A < Drug B
    - One sided hypothesis: same but opposite values as above

One versus Two sided hypothesis

- If you don't know which therapy or test will yield lower values you have a two sided hypothesis (our example)
- If you know that one must by biologic principles be lower then one sided hypothesis.
  - A trial of a cholesterol lowering drug versus placebo (It won't raise cholesterol, nor will placebo lower it)

One versus Two sided hypothesis

- This effects the p value
  - The overlap in the curves of the two therapies that you will allow before you call the curves significantly different changes.
    - If two sided 5% divided on two sides (2.5% each) 2 standard deviations from the mean
    - If one sided then 5% on one side 1.645 standard deviations from the mean



Overlap between the two populations doesn't exclude one from being statistically different from the other.

Patient

Back to our problem….

- So is Drug A better than Drug B?
  - Two sided test and p value to differentiate the groups with statistical significance
  - In clinical medicine 5% is the accepted rate where we are willing to say one is better even if it isn't (type I error)

In a study conducted:

- Patients treated with Drug A had a mean glucose of 92 and a standard deviation of 8 and patients treated with Drug B had a mean of 103 with a standard deviation of 12.
  - Drug A 92 ± 8
  - Drug B 103 ± 12

In conclusion

Using a Student's T test (don't worry about picking the test to use yet)

- P value of 0.03 from the T test table.
  - This is less than the accepted p= 0.05
  - Don't worry you won't need to do this yet.
- Statistically there is a 3% chance of finding a difference of this magnitude (difference in means) even if the two distributions really represent one (equivalent efficacy)
  - Let's begin to understand error and why so many clinical concepts in medicine are not as solid as we once believed….
  - Simply, a 3% chance that the difference in means (11) is not a reproducible value and the two drugs are the same.

Don’t be fooled….

- The statistics only state that Drug A and Drug B are different.
  - We reject the null hypothesis
  - Clinically we infer from the means that Drug B is better at lowering blood glucose, but we don’t know how much.
  - We can guess that it is the difference in the means, but this isn’t exact without further statistical testing. (Next lesson)
- Is this really correct? … What can go wrong?

The Error Table

Decision	H_O : False	H_A : True
Reject H_O	Power $(1 - \beta)$	Type I Error (α)
Accept H_O	Type II Error (β)	$1 - \alpha$

The Error Table

- Alpha Level: probability investigator is willing to accept of stating a difference exists, when no real difference exists (false positive)
- P value: actual probability of detecting a difference of the same magnitude or greater (as you found in your study) if the groups are actually the same.

So what's that p value really mean to me?

- If $p < 0.05$ and we reject the null hypothesis
  - The difference truly exists or…
  - Chance occurred at the difference is not real. (5%)
- If $p > 0.05$ and we accept the null hypothesis
  - No difference exists, or difference exists but we did not detect it;
    - Sample size adequate?
      - If yes, conclude no difference
      - If no, inconclusive results

When you're wrong….

- Type I error (alpha): probability of concluding a significant difference when none actually exists
- Type II error (beta): probability of concluding no significant difference when in fact it exists

OR

- Power: probability of detecting a difference when one actually exists (true positives)

1- Beta = Power

Sample size estimation

- Clinician: Is there enough in the sample to detect the difference?
- Statistician: How many (n) does it require to detect the magnitude of difference
  - Depends on the Alpha set (type I error rate) and the desired Power (1- type II error rate)

Relationships are tricky

- If sample size is set
  - If magnitude of difference you wish to detect is unchanged, as power increases, type II decreases and alpha (type I error) increases;
  - Similarly, if alpha decreases (type I error) power decreases (type II increases)
  - Type I and Type II error are inversely related
  - Type I and Power are directly related

More relationship troubles

- If power is increased or alpha decreased
  - Either the detectable difference increases or the sample size must increase
    - To be more sure about the conclusion (less chance of stating difference when none exists) then
      - More people (larger sample)
      - Larger difference between groups needed
- If the detectable difference is decreased
  - Either the sample size must increase or the power will decrease or the alpha must increase or a combination of both.
    - If you wish to detect a smaller difference you need either more people (sample size increase) or a larger chance of concluding incorrectly that a difference exists when it does not.

Statistical or Clinical Significance

- Does the difference in glucose control between the two drugs mean anything to a practicing physician?
- A difference can be detected that is meaningless in the care of patients
  - A good example is
    - Drug X lowers systolic blood pressure 2mm Hg more than Drug Y.
    - Drug G lowers cholesterol by 3 more points than Drug H

No Mathematics Necessary

- Clinical Significance is a value judgment by the appropriate clinician, not a statistician.
- Clinical Significance cannot exist without statistical significance but
- Statistical significance can exist alone
  - If the sample is large enough you can detect very small differences with good power and alpha levels. (*see that stuff was clinically relevant*)
    - One treatment is better than another
    - One screening tool is better than another
    - One agent causes more side effects than another
  - Bias in reporting can mislead physicians and the public
    - Direct to Consumer advertising
    - Wall Street Journal Health Section (the most read medical journal by non physicians)

So what did we learn?

- Inferential Statistics
  - The null hypothesis
  - What p means
    - One versus Two sided
    - Conclusions that can be drawn from a p value
- The types of errors and their relationships
- Statistical versus Clinical Significance