I. Biostatistics Refresher

A. Importance of Biostatistics
   i. Too much data coming out today
   ii. Researchers / biostatisticians are potentially "fudging" data to make things look better than they actually are
   iii. Up to practicing clinicians to look at the trials and see what they are really saying.

B. Fear of Statistics
   i. Everyone will have a fear of biostatistics
   ii. Those that are comfortable with statistics are usually conscious of subtleties

C. What we really need to know and do
   i. Statistics is not meant to be scary
   ii. Many times we pay too much attention statistical methods and not enough evaluating the validity / applicability of the study.
   iii. Poor statistical methods happen and can misrepresent data, but if we are aware of some stats basics, most can be avoided.

II. The Basics

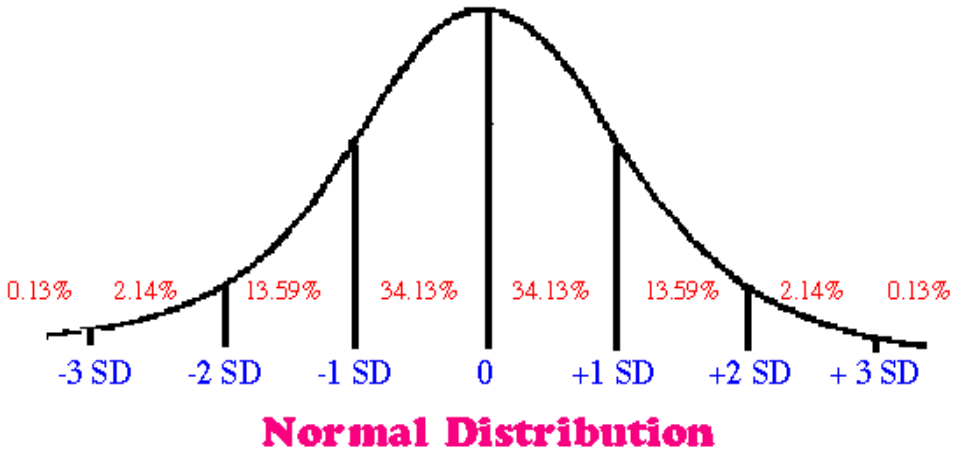
A. Mean, median, mode, standard deviation
   i. Mean: average
   ii. Median: place ALL data in order from highest to lowest; middle number
   iii. MODE: value occurring with the greatest frequency

B. Nominal, ordinal, continuous
   i. Nominal
      a. categories (yes/no, male/female, white/black/asian/indian, etc.)
      b. numbers assigned to categories to make classification easier
      c. numbers have NO value; do not indicate importance, severity, etc.

   ii. Ordinal
      a. number assignments have value (NYHA classes, Leichert scale)
      b. values represent a *meaningful* order (order of ranges)
      c. relationship/difference between numbers is not quantifiable

   iii. Continuous
      a. Interval
         a. the actual number/value (temp in Celsius / Fahrenheit)
         b. scales DO NOT have an absolute zero
      b. Ratio
         a. Same as interval data, but DOES have an absolute zero (i.e. temp in Kelvin, BP, HR, weight)
         b. Can truly quantify differences between two values of same measurement

C. Population, sample, normal distribution, standard deviation
   i. Population: Everyone (and their sister)
   ii. Sample: select group / defined group from the population
   iii. Normal distribution: representation of many naturally occurring phenomena
   iv. Standard deviation: indicates percentages/groups/areas above and below the mean
      a. Standard Error of the Mean (SEM)
      b. Z-score



D. Null & alternative hypothesis
   i. Null hypothesis: the opposite of the hypothesis proposed
      a. typically, the idea that a difference does not exist
      b. "fail to reject the null hypothesis"

   ii. Alternative hypothesis: The idea being researched and/or evaluated
      a. typically, the idea that a difference exists
      b. what researchers are testing for
         a. superiority
         b. inferiority
         c. equivalency

E. α (false positives, type I error), β (false negatives type II error), confidence interval, power
   i. α (false positives; typically 0.05): falsely reject the null hypothesis
      a. falsely accept the alternative
      b. make the statement your idea is true, when it is really false

   ii. β (false negatives): falsely accept the null hypothesis
      a. falsely reject the alternative
      b. make the statement your idea is false, when it is really true

   iii. Power (P; typically 0.80)
      a. ability of a test to detect if the null hypothesis is acceptable
      b. ability / probability to avoid type II error
      c. power = 1 – β

iv. Confidence interval (CI)
   a. % range from the normal distribution
   b. if the same study were conducted 100 times, the results should fall in this % range of normal distribution, that % of the time (i.e. 95% confidence interval means a study should / would produce similar results 95 out of 100 times)
   c. any value in a confidence interval has the same likelihood of occurring as any other value (i.e. a result of 1.3 with a 95% confidence interval of 0.6 to 2.0 means ANY VALUE from 0.6 to 2.0 has a chance of occurring 95% of the time)
   d. confidence interval = 1 – α

v. NOTE: if you are not able to reject the null hypothesis (accept the alternative), make sure to check that the study met its power (ability to detect a false negative)

Actual Answer

Tested / Result Answer	+	-
+	Correct	Type II error
-	Type I error	Correct

III. Study Types

A. Case reports, case controls, cohorts
   i. Case report: identifies single to multiple (3-4) events that has been caused by an outside / unique situation (i.e. drug, diet, habit, etc.)
   ii. Case control: identifies an OUTCOME and then looks at subjects retrospectively (backwards) for commonalities
   iii. Cohort: identifies a population, typically with something in COMMON, and then follows them looking for an outcome (i.e. Framingham, Mass.)
   iv. Clinical trial: tests a hypothesis against a control
      a. design (crossover, independent groups)
      b. randomized (simple, blocked, stratified)
      c. blinding (single blind, double blind, triple blind)
      d. control (placebo, standard of care)
   v. Meta-analysis: compilation of clinical trials with similar design and measured outcomes to "simulate" a large clinical trial
   vi. Systematic Review: similar to meta-analysis, but with highly scrutinized methods
      a. hardest to perform
      b. highest reliability for interpreting evidence
      c. Cochrane Systematic Reviews / Analysis

IV. Reporting the Results

A. p-value
   i. the most popular statistical value
   ii. reports the probability of a result actually being true (sounds like an α)
   iii. most accepted as p-value < 0.05 being
   iv. as long as the p-value is less than what it is set to be, the results can be considered *statistically* significant
   v. NOTE: lower p-values do not indicate importance / magnitude of significance (i.e. p-value = 0.048 is NOT more significant that p-value = 0.0000001)

B. Odds ratio, relative risk, and relative risk reduction
   i. Odds ratio (OR): reported with case control studies
      a. Reports how many times more likely a sample population are to have been exposed to a variable, given their current status
      b. Value = 1.0; no relationship between outcome and variable exposure
      c. Value < 1.0; patient with outcome is *less* likely to have been exposed
      d. Value > 1.0; patient with outcome is *more* likely to have been exposed

$$OR = \frac{[\text{Group A \# exposed / Group A total}]}{[\text{Group B \# exposed / Group B total}]}$$

   ii. Relative Risk (RR): reported with cohort studies
      a. Reports how many times more likely a population is to experience an outcome, given presence (or absence) of a variable.
      b. Value = 1.0; no relationship between variable and outcome
      c. Value < 1.0; presence of variable makes the measured outcome *less* likely
      d. Value > 1.0; presence of variable makes the measured outcome *more* likely

$$RR = \frac{[\text{Group A \# event / Group A total}]}{[\text{Group B \# event / Group B total}]}$$

   iii. If a CI value (for either OR or RR) falls both below and above 1.0, the results cannot be considered significant because there is an equal chance of an outcome / variable and variable being *less* AND *more* likely related to the variable / outcome

iv. Relative Risk Reduction (RRR)
   a. % difference in chance of an outcome, given exposure to a variable
   b. RRR = zero; no relationship between variable and outcome
   c. RRR < zero; presence of variable makes the measured outcome *more* likely
   d. RRR > zero; presence of variable makes the measured outcome *less* likely

   e. RRR = 1 – RR

v. If a CI value (for RRR) is both above and below ZERO, the results cannot be considered significant because there is an equal chance of an outcome and variable being *less* AND *more* likely related.

vi. Absolute Relative Risk (ARR): absolute difference between chance of outcome, given variable exposure and NO outcome, given variable exposure.

$$ARR = \left| \frac{[\text{Group A \# event}]}{[\text{Group A total}]} - \frac{[\text{Group B \# event}]}{[\text{Group B total}]} \right|$$

C. Number need to treat, number needed to harm
   i. Number needed to treat: how many individuals from the control group would have to be exposed with the hypothesis to prevent / cause one outcome
      a. i.e. how many people with HTN and NOT taking aspirin need to be treated with aspirin to save one life

   ii. Number needed to harm: how many individuals from the control group need to be exposed to a variable to cause one adverse event
      a. i.e. how many people with HTN and not taking ASA need to be treated with ASA to cause a specific adverse event

$$NNT \text{ (or NNH)} = 1 / \left| \frac{[\text{Group A \# event}]}{[\text{Group A total}]} - \frac{[\text{Group B \# event}]}{[\text{Group B total}]} \right|$$

   iii. Typically, NNT and NNH < 50 are considered *clinically* significant
      a. NNT <50 is GOOD
      b. NNH <50 is BAD

V. Who Cares

A. Ask the following questions:
   i. Do the results make sense?

   ii. Do the results mean anything to my individual patient?

   iii. Do the results mean anything to my patient population (internal vs. external validity)?

VI. More information

A. Annals of Emergency Medicine Series: *Introduction to Biostatistics*
   i. Part 1: basic concepts. Ann Emerg Med 1990;86-89
   ii. Part 2: descriptive statistics. Ann Emerg Med 1990;309-315
   iii. Part 3: sensitivity, specificity, predictive value, and hypothesis testing. Ann Emerg Med 1990;591-7
   iv. Part 4: statistical inference techniques in hypothesis testing. Ann Emerg Med 1990;820-5
   v. Part 5: statistical inference techniques for hypothesis testing with nonparametric data. Ann Emerg Med 1990;1054-9
   vi. Part 6: correlation and regression. Ann Emerg Med 1990;1462-8

B. Cho, MK and L Bero. Instruments for assessing the quality of drug studies published in the medical literature. JAMA 1994;272(2):101-4

C. *High Yield Biostatistics*, 2nd ed. by Glasser, Anthony N. Lippincott Williams & Wilkins 2001.

D. *Studying a Study and Testing a Test*, 4th ed. By Riegelman, Richard K. Lippincott Williams & Wilkins 2000.

E. Glasser SP & Howard G. Clinical Trial Design Issues: At Least 10 Things You Should Look For in Clinical Trials. J. Clin. Pharmacol., Oct 2006; 46: 1106 - 1115