Hypothesis Testing for Clinical Trials using JMP

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What is JMP?

• A computer program for statistics
  • A simple point-and-click system
    • Closer to SPSS, MiniTab
    • No coding, unlike SAS or R programs

• Can be used for data summary, data analysis, and visualization
What JMP can/cannot do for you

• **Pro:**
  • JMP can automatically save scripts to reproduce any data table or analysis in its current state
    • **Examples**
      • A set of analysis steps that should be followed routinely by your lab technicians
      • Fit the same model to new data every day, and the steps are always the same

• **Con:**
  • JMP cannot record scripts while you are working
    • Cannot use script-recording to observe how a sequence of interactive steps is performed
      • Lack of reproducibility, unlike R or SAS
Hypotheses tests

• Refers to the formal procedures used by statisticians to accept or reject statistical hypotheses.
  • A statistical hypothesis is an assumption about a population parameter

• \textbf{Null hypothesis }$H_0$ : A hypothesis which the researcher tries to disprove, reject or nullify.
  • Ex: A treatment has the same effectiveness as the placebo

• \textbf{Alternative hypothesis }$H_1$ : A hypothesis which the researcher tries to prove.
  • Ex: A treatment has the different effectiveness than the placebo
P-value

- The probability of obtaining a result equal or more extreme than actual observed results, if the null hypothesis is true
  - Compare this value to a significance level $\alpha$ (chosen before the study)
    - Reject null hypothesis if p-value < 0.05
    - Fail to reject null hypothesis if p-value $\geq$ 0.05
Type I and II errors

• Type I error – Rejecting the null hypothesis when the null is true
  • Ex: Effectiveness between two treatments are concluded different, but, in fact, they're not.
    • If the medications have the same effectiveness, the researcher may not consider this error too severe because the patients still benefit from the same level of effectiveness regardless of which medicine they take

• Type II error – Failing to reject the null hypothesis when the alternative is true
  • Ex: Effectiveness between two treatments are concluded the same, but, in fact, they're different.
    • This error is potentially life-threatening if the less-effective medication is sold to the public instead of the more effective one
      • We want these two instances to be small (can’t get both to be minimal simultaneously)
Two-sample t-test

- Used to determine if two independent population means are different
  - When to use it?
    - Ex: Treatment and placebo, male and females, etc.

- Groups are independent
  - Being in one group has no affect on the other group

- Null hypothesis: Means of the two groups are the same
- Alternative hypothesis: Means of the two groups are different

- More likely to reject the null hypothesis if:
  - Sample size increases
  - Smaller variability
  - Higher \( \alpha \) level
Two-sample t-test in JMP

1. Click on Analyze and then Fit Y by X
2. Click on “SBP” and then Y, Response
3. Click on “trt” and then X, Factor and then Okay
4. Click on red down arrow and then Means/ANOVA/Pooled
Two-sample z-test for proportions

- Used to determine if two independent population proportions are equal
- What do we do for binary data?
  - Pearson’s chi-squared test or relative risk can be used
    - Ex: Difference in proportions between smokers and nonsmokers who said “yes” in taxing cigarettes in latest survey
    - Some of your the papers test proportions using relative risk

- Null hypothesis: Proportions of the two groups are the same
- Alternative hypothesis: Proportions of the two groups are different
Two-sample z-test for proportions in JMP

1. Click on **Analyze** and then **Fit Y by X**
2. Click on “alive/death” and then **Y, Response**
3. Click on “trt” and then **X, Factor**
4. Click **Okay**
5. Click on **red down arrow** next to **Contingency** Analysis and then **two-sample test for proportions**
Survival Analysis

• Important to analyze survival data with special methods
  • The survival times usually have specialized non-normal distributions (no symmetric “bell” shaped curve)
  • Some of the data could be censored

• Survival functions are calculated using the nonparametric Kaplan-Meier method
  • One or more groups of either complete or right-censored data
  • Censoring is when you do not know the exact survival time
    • A condition in which the value of a measurement or observation is only partially known
      • Ex: Drug mortality rate and age of death
Censoring and Hypotheses

• Importance of censoring
  • Ignoring censored observations is an underestimation of the probability of survival beyond the fixed time-point
  • Results in potentially valuable information on survival being thrown away

• Null hypothesis: No difference in survival between treatment and placebo groups
• Alternative hypothesis: There is a difference in survival between treatment and placebo groups
Survival Analysis

- The elements of the survival function are:
  - Time indicating how long until the unit (or patient) either experienced the event or was censored
  - Censoring indicator that denotes whether an observation experienced the event or was censored
    - JMP uses 1 for censored and 0 for non-censored event
    - Explanatory variables (if a regression model is used.)

- Common terms used for reliability and survival data include lifetime, life, survival, failure-time, time-to-event, and duration
Survival Analysis in JMP

1. Click on **Analyze**, then **Reliability and Survival**, and then **Survival**
2. Click on “surv” and then **Y, Time to event**
3. Click on “trt” and then **Grouping**
4. Click on “censor” and then **Censor**
5. Click **Okay**
Comment on drop out and sample size

• In clinical trials, drop outs are an important consideration in survival analysis.
  • Cannot be ignored to avoid bias
  • Drop outs can affect survival curve results
Advice

• When planning any research study, consult a BCL consultant before data collection/analysis
• We are a full-time consulting laboratory at OCS
• This presentation will be put on the website
  • [http://www.biostatistics.vcu.edu/bcl/](http://www.biostatistics.vcu.edu/bcl/)
Questions?
Class activity

• Using patients that you accrued to, are the treatment and control groups different? If so, describe that difference.