Is n=3 enough? How to approach sample size and power calculations

Jessica Minnier, PhD

Knight Cancer Institute Biostatistics Shared Resource

Oregon Health & Science University

AACR, March 30, 2019

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Outline

- Why calculate sample size?
- What are the important components?
- Examples
- Software

Goals of sample size and power calculations

- Design a study that will have enough information about underlying population to reject a hypothesis with high confidence.
- Calculate the number of sampling units (e.g. people, animals) you need to estimate statistics with a certain level of precision.

Design your study

Step 1: State your research hypothesis

- Define your:
  - Population
  - Outcome variables/measurements
  - Predictor variables (i.e. treatment, age, genetic mutation)
- Be specific!
- Example: Among *women* (population you sample from), the *BRCA1* mutation (predictor) is associated with an increased risk of developing *breast cancer* (outcome).
- Question: How many women do we need to sample/study to determine that BRCA1 is associated with breast cancer?

Your hypothesis and design inform your analysis method.

Step 2: Choose your analysis and test(s)

- You can't calculate sample size without knowing which test and model you will use.
- How will you measure your outcome? Continuous? Categorical? Binary (yes/no)?
  - choose outcomes with high sensitivity and low measurement error
- How many groups/experimental conditions/predictors?
  - the more you have the more samples you will need
- What test? t-test? Linear regression? Random effects model? Chi-square test?

Calculate sample size based on analysis method you will use.

Calculate power and sample size

Need to know (/tell your statistician!):

- Overall design (outcome, endpoint, hypothesis)
- Size/magnitude of effect of interest
  - What do you *hope* to detect
- Variability of measurements
  - Precision of your measurement, biological variability within population
- Level of type I error (significance level, \(\alpha\))
- Level of power
- Other design details (number of groups, clustering, repeated measures)

Components of Sample Size

Need to know 3 of the 4 to determine the 4th:

Measure	Definition
Effect Size	Magnitude of difference or assocation; i.e. (difference in means)/(population standard deviation) = $\frac{\mu_1 - \mu_0}{\sigma}$ = Δ
Sample Size	N
Type I Error / Significance level	α = probability of rejecting null hypothesis when it is true
Power	1 - β = 1 - Type II error = probability of rejecting null hypothesis when it is false

Components of Sample Size

Need to know 3 of the 4 to determine the 4th:

Do We Know?	Measure	Definition
??	Effect Size	Magnitude of difference or assocation; i.e. (difference in means)/(population standard deviation) = \(\frac{\mu_1 - \mu_0}{\sigma}\) = \(\Delta\)
??	Sample Size	N
0.05, 0.01	Type I Error / Significance level	\(\alpha\) = probability of rejecting null hypothesis when it is true
0.9, 0.8	Power	1 - \(\beta\) = 1 - Type II error = probability of rejecting null hypothesis when it is false

What is effect size?

- Summarizes the outcome of interest
- Magnitude of difference or assocation
- Specification depends on study design and statistical model/test

Examples:

- Difference in treatment and control mean outcomes, relative to variance (standard deviation)
- Correlation coefficient of two biomarkers
- Risk ratio of breast cancer comparing BRCA carriers to non-carriers
- Magnitude of regression coefficient

Effect size must be

- pre-specified
- based on what is meaningful biologically or clinically (not statistical significance)
- based on pilot data or literature review if available

Simple example

Outcome = Continuous measurement

Predictor = Treatment yes/no (treatment vs control group)

Test: two sample T-test, equal variance

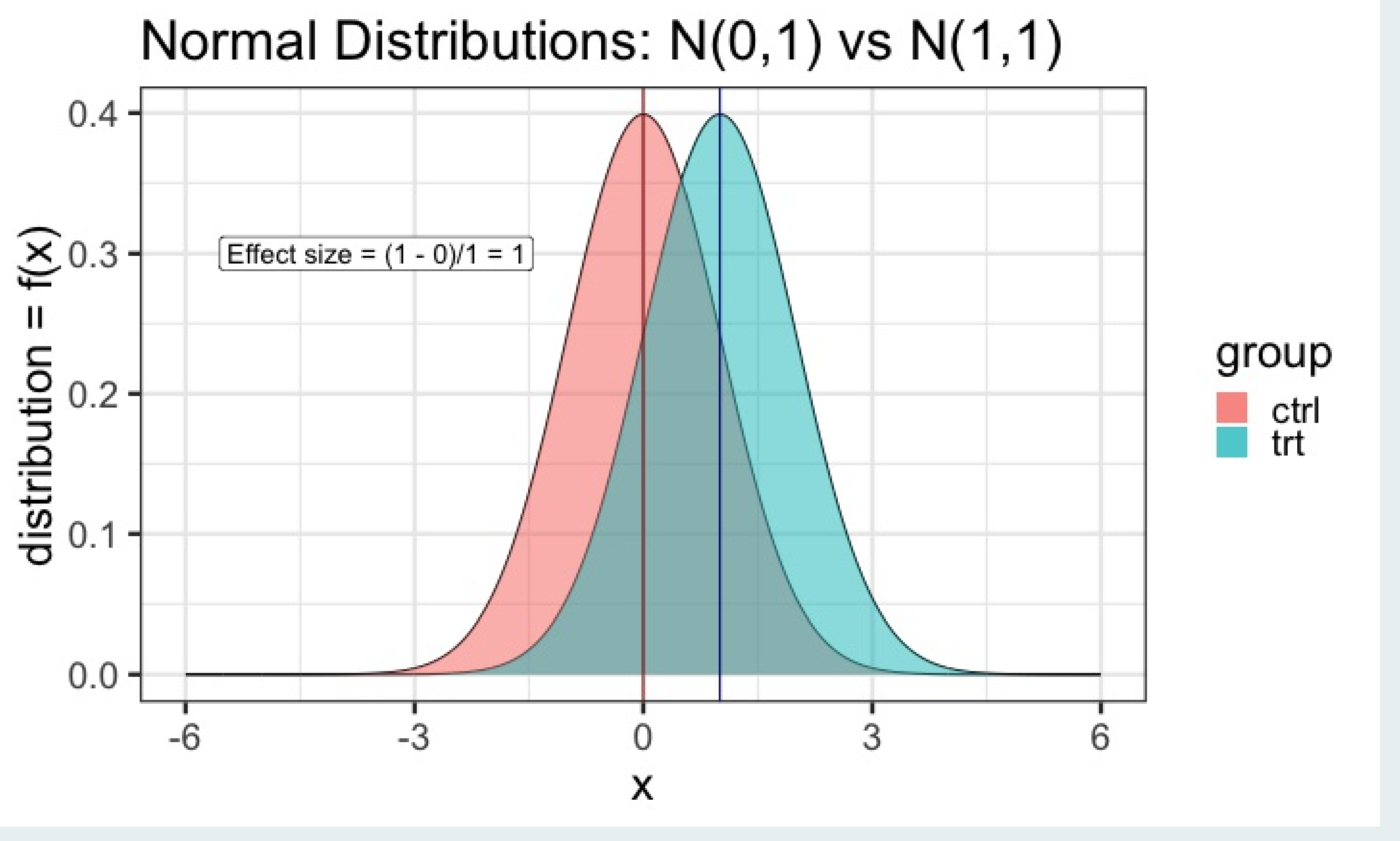
Effect Size: difference in means divided by standard deviation of population $\frac{\mu_{trt} - \mu_{ctrl}}{\sigma}$

Null Hypothesis: Difference in means = 0

Alternative Hypothesis: Difference in means $\neq$ 0

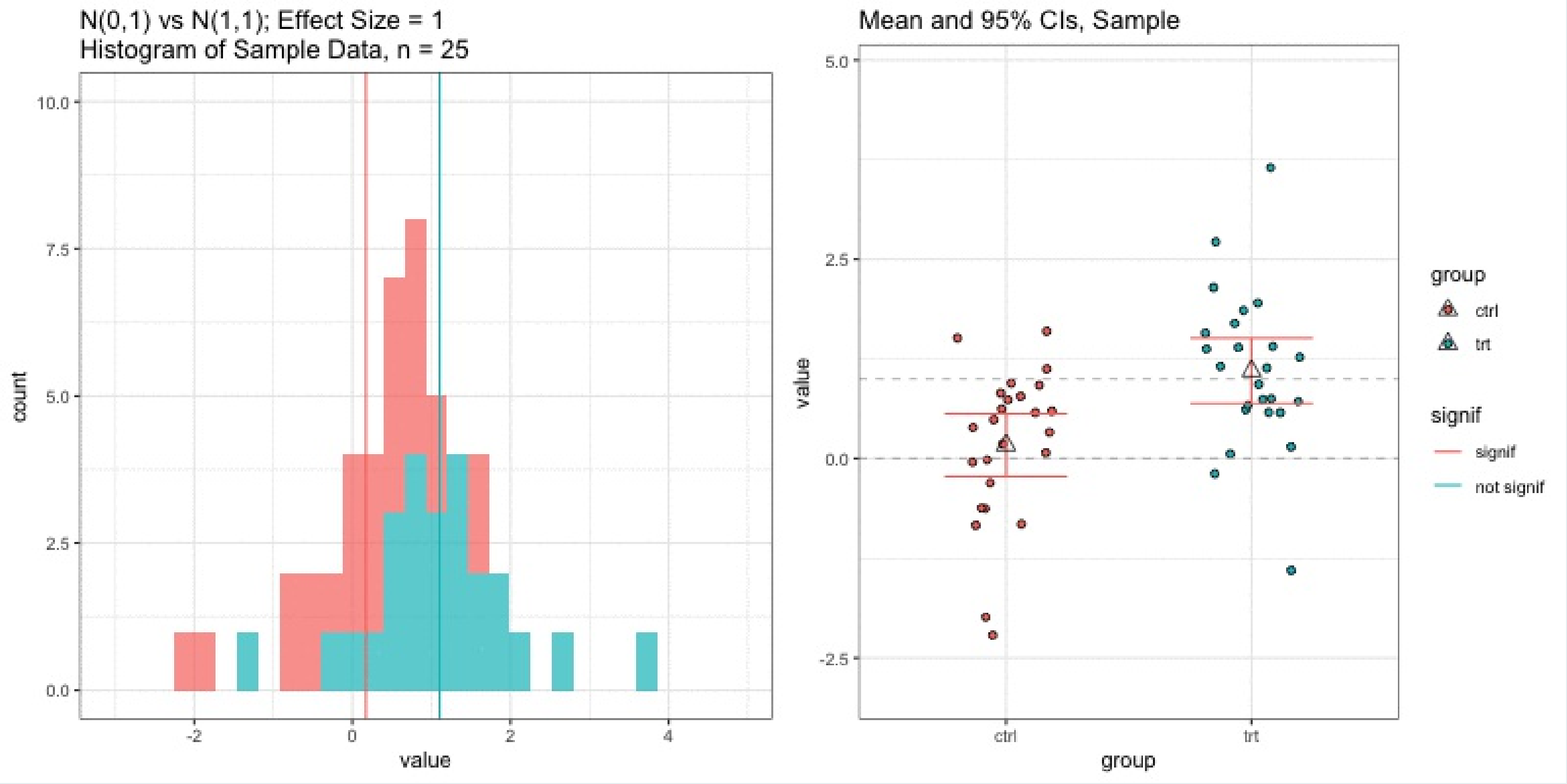
"Given a desired effect size (difference in means relative to the variance), what sample size gives us enough information to reject the null hypothesis with power 90%?"

Underlying data distributions



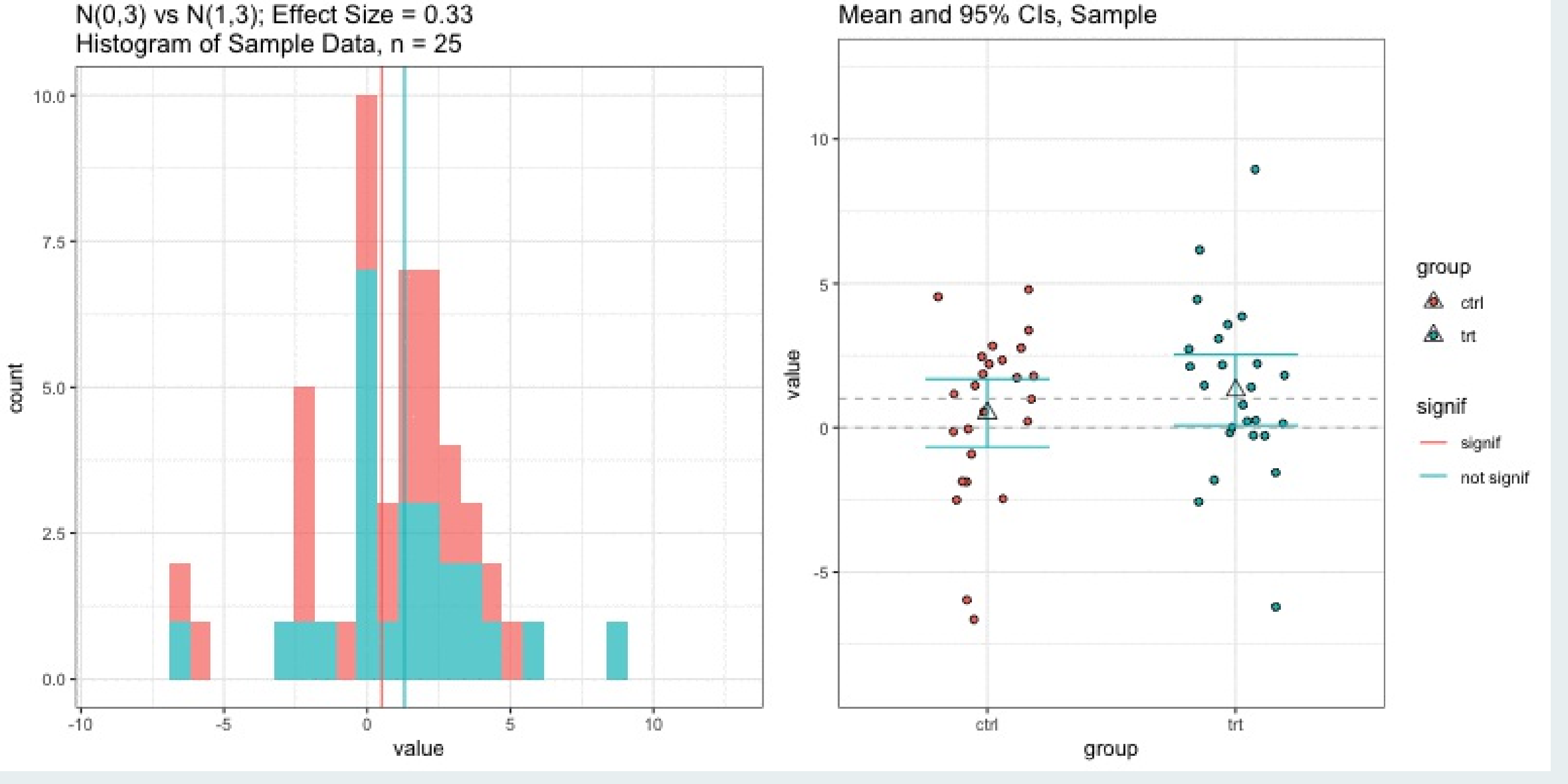
n=25, effect size = 1

Power = 0.93
(Significance based on two sample t-test for difference in means)



n=25, effect size = 0.33

Increase standard deviation from 1 to 3, divides effect size by 3
Power = 0.21



To detect an effect size of 0.33 with power = 0.9 and type I error = 0.05, what sample size would we need? n=194 in each group!

```
power.t.test(delta = 0.33, sd = 1, sig.level = 0.05, pow
```

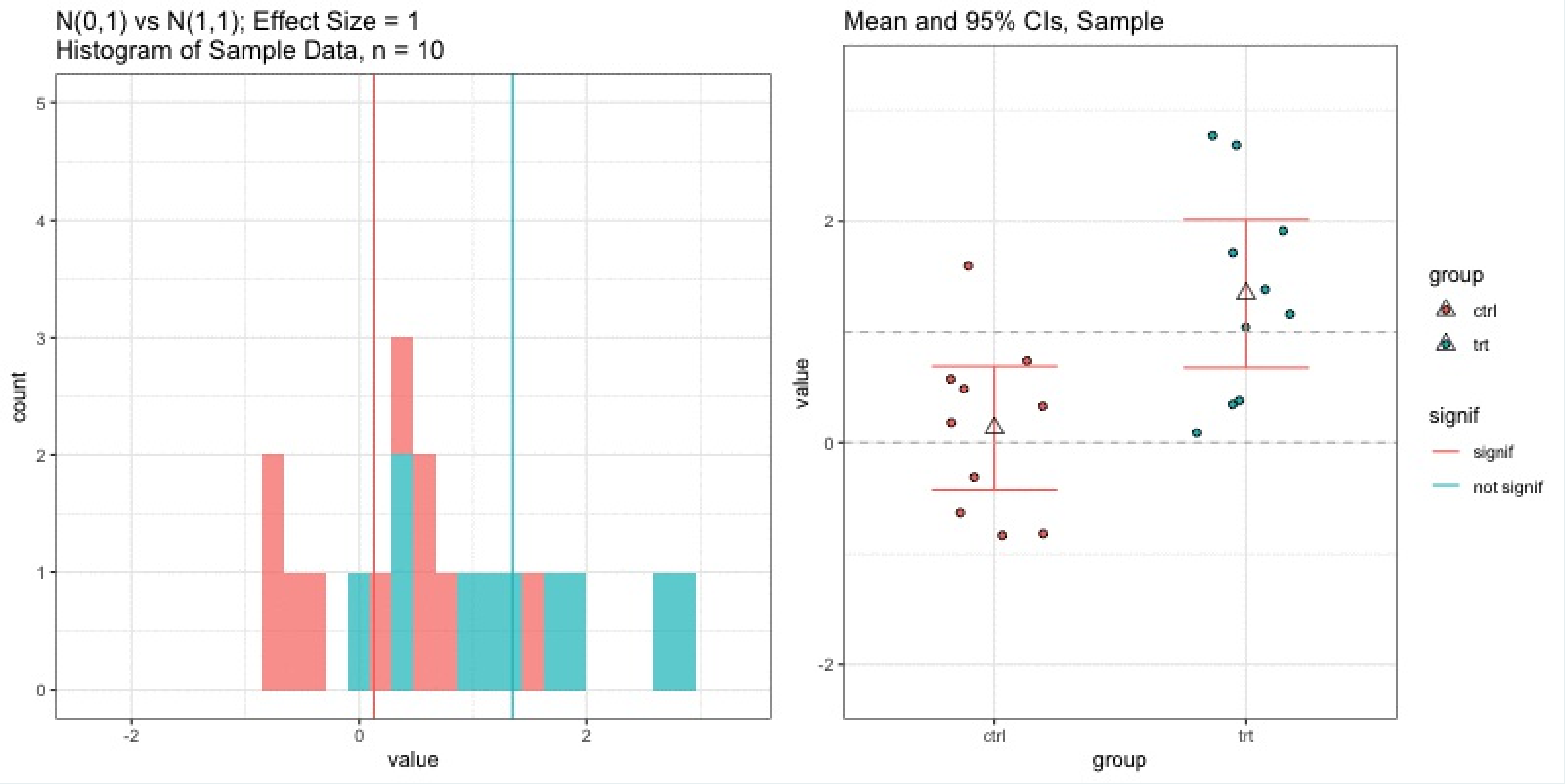
```
     Two-sample t test power calculation

              n = 193.9392
          delta = 0.33
             sd = 1
      sig.level = 0.05
          power = 0.9
    alternative = two.sided

NOTE: n is number in *each* group
```

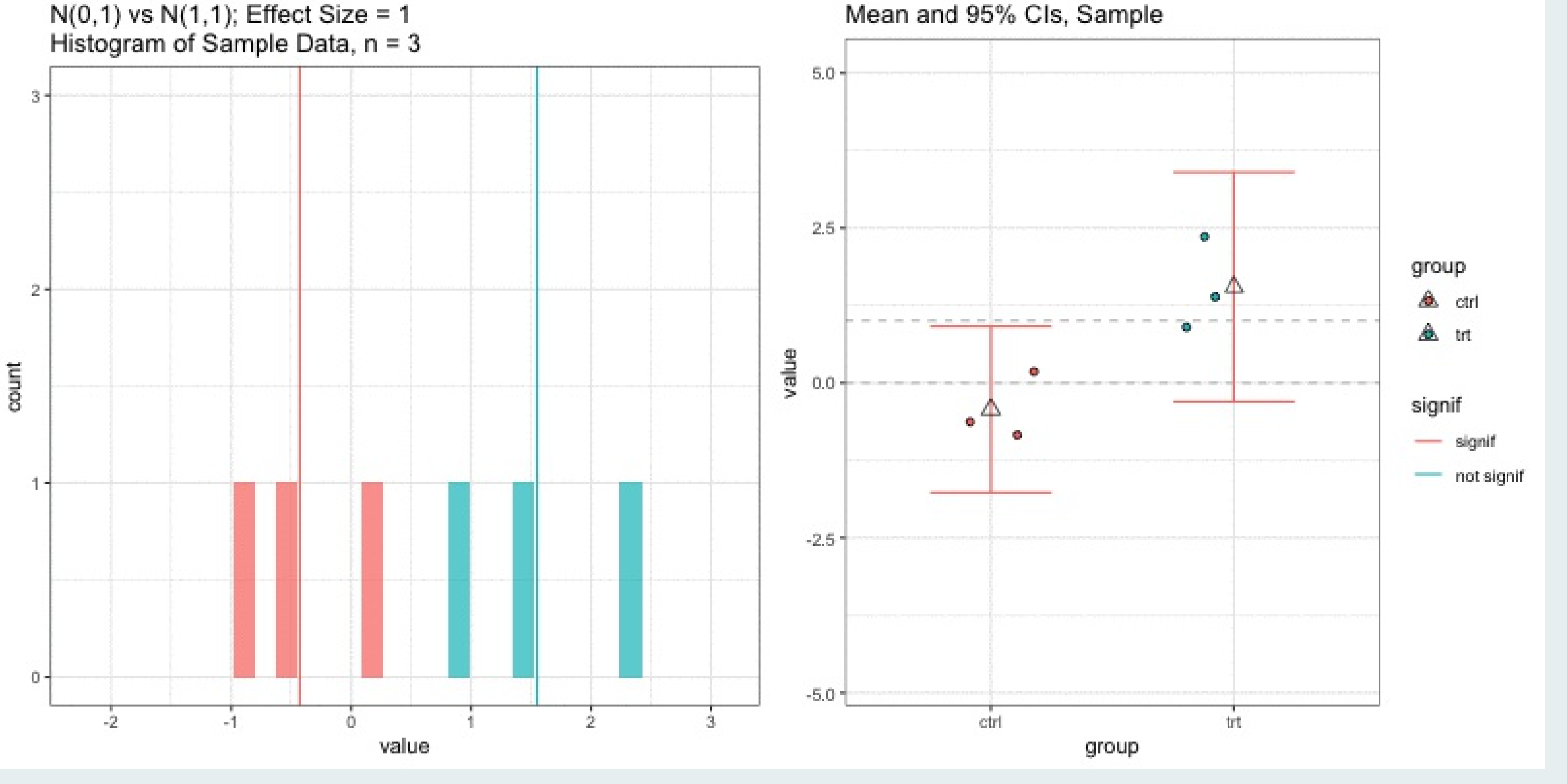
n=10, effect size = 1

Decrease sample size
Power = 0.56



n=3, effect size = 1

Decrease sample size even more
Power = 0.16



n = 3, power = 0.9, effect size = ?

In the **R** output below, the effect size is delta/sd = 3.59/1 = 3.59.

```
power.t.test(n=3, sd=1, sig.level=0.05, power=0.9)
```

```
     Two-sample t test power calculation

              n = 3
          delta = 3.589209
             sd = 1
      sig.level = 0.05
          power = 0.9
    alternative = two.sided

NOTE: n is number in *each* group
```

Other reasons to calculate sample size

Precision of statistics

- Sample sizes can also be calculated for a specific maxmimum width in confidence interval around an estimate
- i.e. we will estimate the proportion with a 95% confidence interval of width 0.1 such as [0.2, 0.3]

Prediction models

- Large sample sizes are needed for complex prediction models.
- Stability of prediction model accuracy measures depends on sample size.

Important to remember:

Sample size estimates are ESTIMATES.

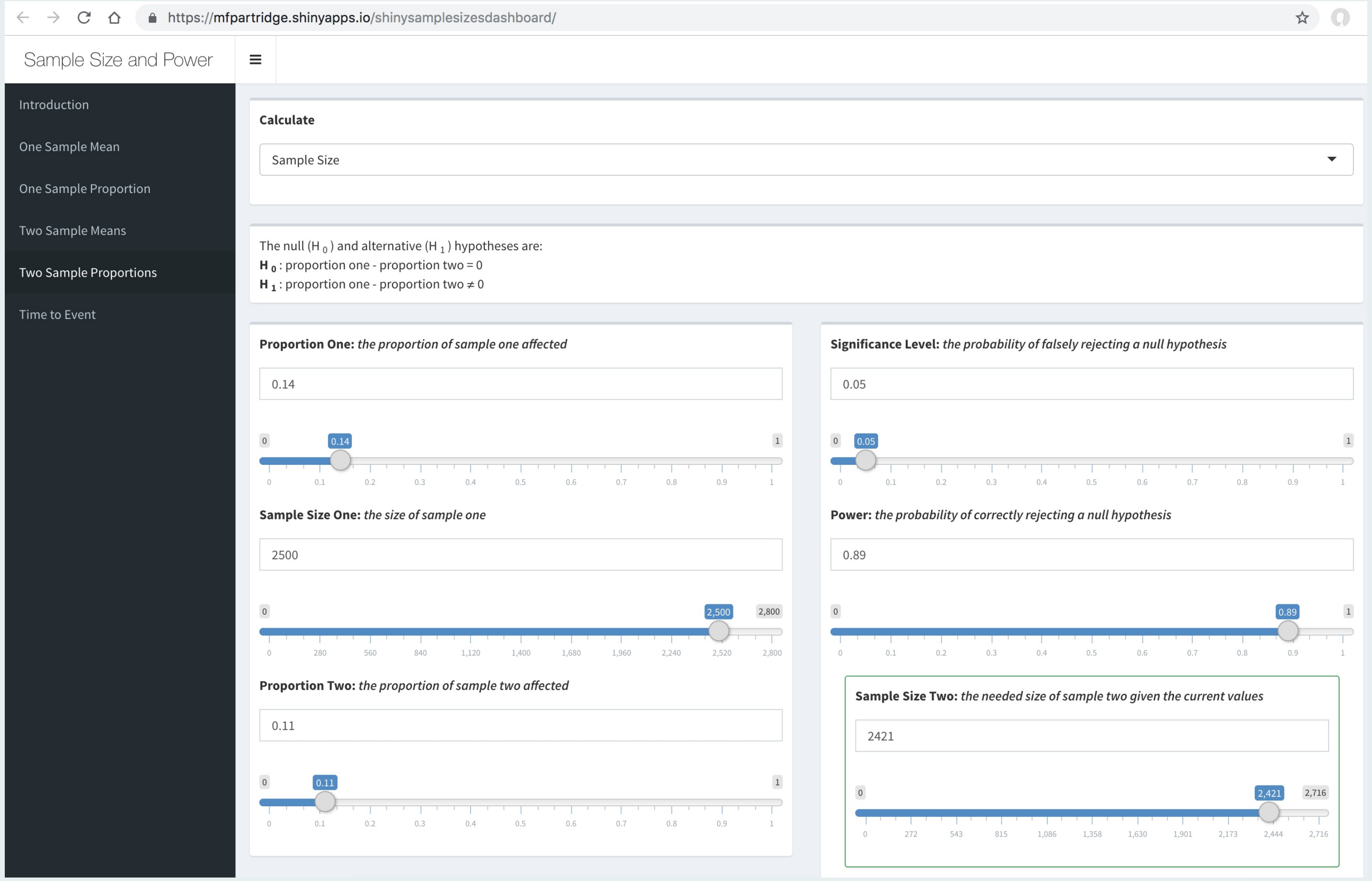
- based on assumptions that could be incorrect
- based on pilot data that could be a poor sample or too small
- the more you don't know, the more conservative you should be (inflate your n)
- good to provide multiple estimates for a variety of scenarios/effects

Free online software

G*power

(examples of how to use it:
http://www.ats.ucla.edu/stat/gpower/)

Shiny Dashboard for Sample Size and Power Calculations



Others

- TrialDesign.org
- GLIMMPSE
- CRAB Stat tools
- The Shiny CRT Calculator: Power and Sample size for Cluster Randomised Trials
- Cal Poly Stats Dept Apps
- Statistical software such as R, SAS, STATA

Take home message:

Do your research before you do your research!

Thank you!

Contact me: minnier-[at]-ohsu.edu, datapointier, jminnier

Slides available: bit.ly/aacr-power

Slide code available at: github.com/jminnier/talks-etc

References

- Some of this talk adapted from: David Yanez's Sample Size talk at OCTRI Research Forum (OHSU)
- Statistical Rules of Thumb, Chapter 2