



Denotes  
He-man



Denotes  
practical

# Power Simulation Ascertainment



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International Twin Workshop, Boulder, CO

**SHE-RA: PRINCESS OF POWER**  
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**FILMATION**  
GROUP W  
PRODUCTIONS

- What is power?
- What affects power?
- How do we calculate power?
- What is ascertainment?
- What happens with ascertained samples?
- What is simulation?
- Why do we simulate?
- How do we simulate?

**Slide of Questions**

- Definitions of power
- The probability that the test will reject the null hypothesis if the alternative hypothesis is true
- The chance the your statistical test will yield a significant result when the effect you are testing exists

**What is power?**

- Null Hypothesis
- Alternative Hypothesis
- Distribution of test statistics

**Key Concepts and Terms**

- Null Hypothesis
  - The baseline hypothesis, generally assumed to be the absence of the tested effect
- Alternative Hypothesis
  - The hypothesis for the presence of an effect
- Distribution of test statistics
  - The frequencies of the values of the tests statistics under the null and the alternative

**Key Concepts and Terms**

- We are going to simulate a normal distribution using R
- We can do this with a single line of code, but let's break it up

## Practical 1

- R has functions for many distributions
- Normal,  $\chi^2$ , gamma, beta (others)
- Let's start by looking at the random normal function: `rnorm()`

**Simulation functions**

Normal {stats}

R Documentation

## The Normal Distribution

### Description

Density, distribution function, quantile function and random generation for the normal distribution with mean equal to `mean` and standard deviation equal to `sd`.

### Usage

```
dnorm(x, mean = 0, sd = 1, log = FALSE)
pnorm(q, mean = 0, sd = 1, lower.tail = TRUE, log.p = FALSE)
qnorm(p, mean = 0, sd = 1, lower.tail = TRUE, log.p = FALSE)
rnorm(n, mean = 0, sd = 1)
```

### Arguments

<code>x, q</code>	vector of quantiles.
<code>p</code>	vector of probabilities.
<code>n</code>	number of observations. If <code>length(n) &gt; 1</code> , the length is taken to be the number required.
<code>mean</code>	vector of means.
<code>sd</code>	vector of standard deviations.

In R: `?rnorm`

# rnorm Documentation



- `rnorm(n, mean = 0, sd = 1)`



Function name



Number of Observations to simulate



Mean of distribution  
with default value



Standard deviation of distribution  
with default value

**rnorm syntax**

- This script will plot 4 samples from the normal distribution
- Look for changes in shape
- Thoughts?

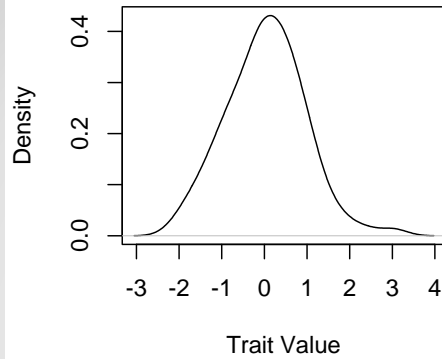


**R script: Norm\_dist\_sim.R**

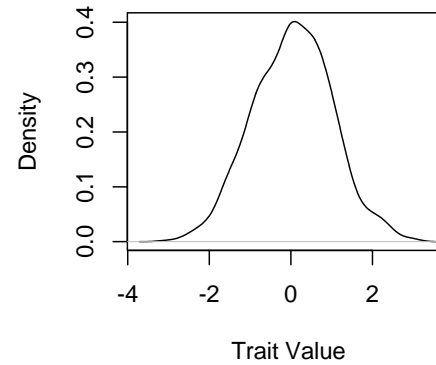
- You have to comment
- The presentation will not continue without audience participation
  - No this isn't a game of chicken

**What did we learn?**

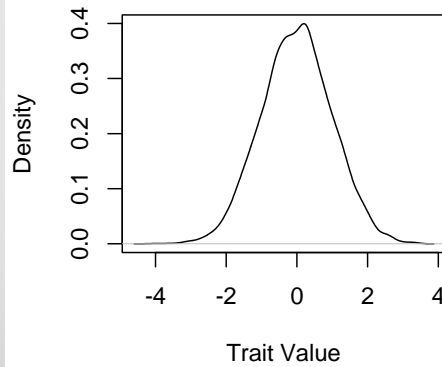
**100 observations**



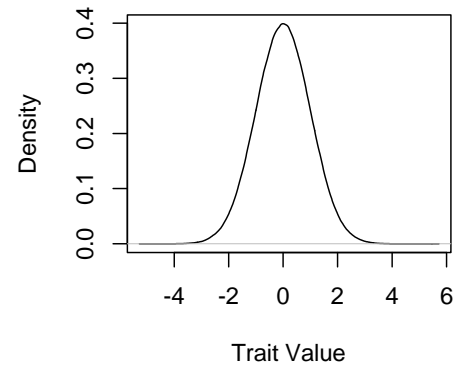
**1,000 observations**



**10,000 observations**



**1,000,000 observations**



**One I made earlier**

- Sampling variance
  - We saw that the 'normal' distribution from 100 observations looks stranger than for 1,000,000 observations
- Where else may this sampling variance happen?
- How certain are we that we have created a good distribution?

**Concepts**

- Rather than just simulating the normal distribution, let's simulate what our estimate of a mean looks like as a function of sample size
- We will run the R script `mean_estimate_sim.R`

**Mean estimation**

- This script will plot 4 samples from the normal distribution
- Look for changes in shape
- Thoughts?



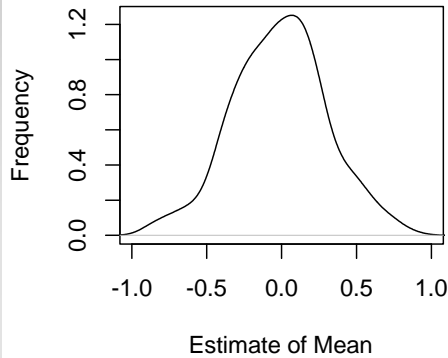
**R script: mean\_estimate\_sim.R**

- You have to comment
- The presentation will not continue without audience participation
  - No this isn't a game of chicken

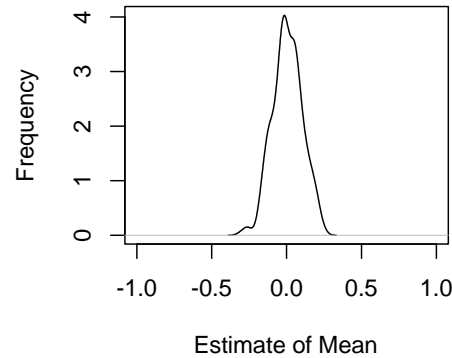
**What did we learn?**



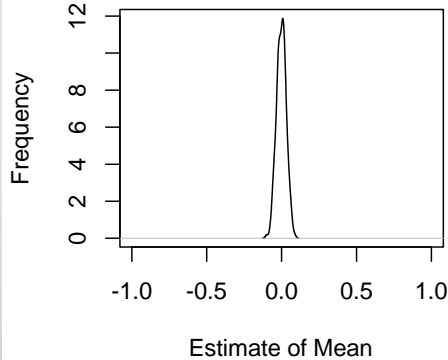
**10 sample size mean estimate**



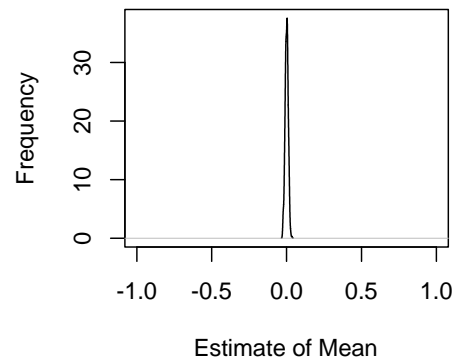
**100 sample size mean estimate**



**1,000 sample size mean estimate**



**10,000 sample size mean estimate**



**One I made earlier**

- We see an inverse relationship between sample size and the variance of the estimate
- This variability in the estimate can be calculated from theory
- $SE_x = s/\sqrt{n}$
- $SE_x$  is the standard error,  $s$  is the sample standard deviation, and  $n$  is the sample size

## Standard Error

# Existential Crisis!

What does this variability mean?  
Again—this is where you comment

The sampling variability in my estimate affects my ability to declare a parameter as significant (or significantly different)

**Key Concept 1**

The probability that the test will reject the null hypothesis if the alternative hypothesis is true

**Power definition again**

- Mean different from 0 hypotheses:
  - $h_0$  (null hypothesis) is  $\mu=0$
  - $h_a$  (alternative hypothesis) is  $\mu \neq 0$ 
    - Two-sided test, where  $\mu > 0$  or  $\mu < 0$  are one-sided
- Null hypothesis usually assumes no effect
- Alternative hypothesis is the idea being tested

## Hypothesis Testing

	Reject $H_0$	Fail to reject $H_0$
$H_0$ is true	$\alpha$	$1-\alpha$
$H_a$ is true	$1-\beta$	$\beta$

$\alpha$  = type 1 error rate

$\beta$  = type 2 error rate

$1-\beta$  = statistical power

## Possible scenarios

# Statistical Analysis

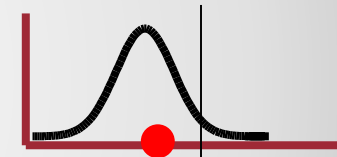
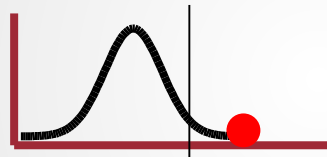
Rejection of  $H_0$

Non-rejection of  $H_0$

$H_0$  true

Type I error  
at rate  $\alpha$

Nonsignificant result  
( $1 - \alpha$ )

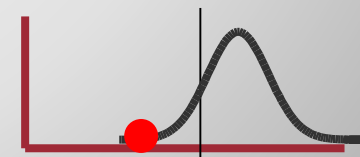
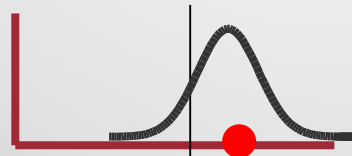


Truth

$H_A$  true

Significant result  
( $1 - \beta$ )

Type II error  
at rate  $\beta$





- The probability of rejection of the null hypothesis depends on:
  - The significance criterion ( $\alpha$ )
  - The sample size ( $N$ )
  - The effect size ( $\Delta$ )
- The probability of detecting a given effect size in a population from a sample size,  $N$ , using a significance criterion,  $\alpha$ .

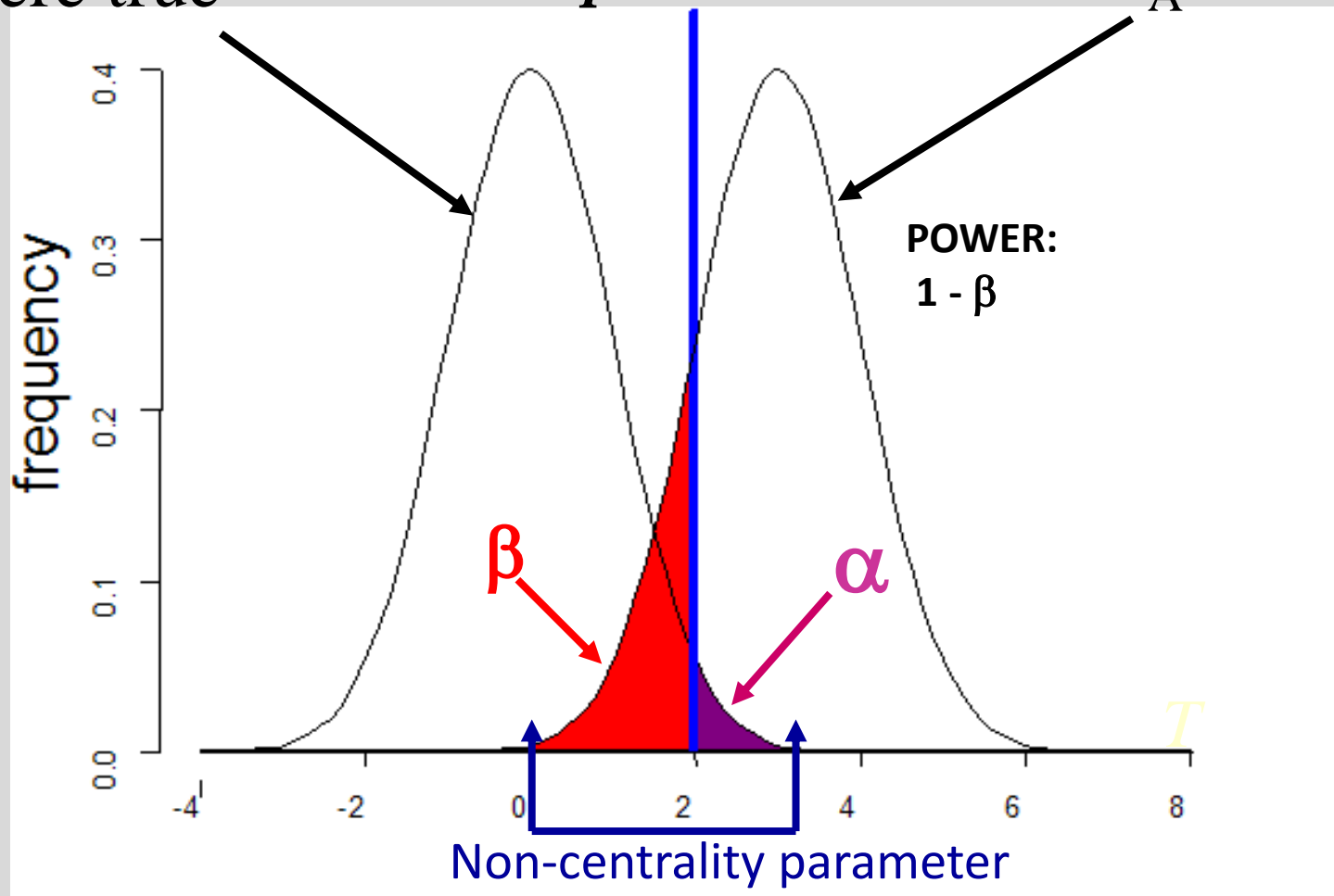
## Expanded Power Definition

# Standard Case

Sampling distribution if  $H_0$  were true

Sampling distribution if  $H_A$  were true

*alpha 0.05*

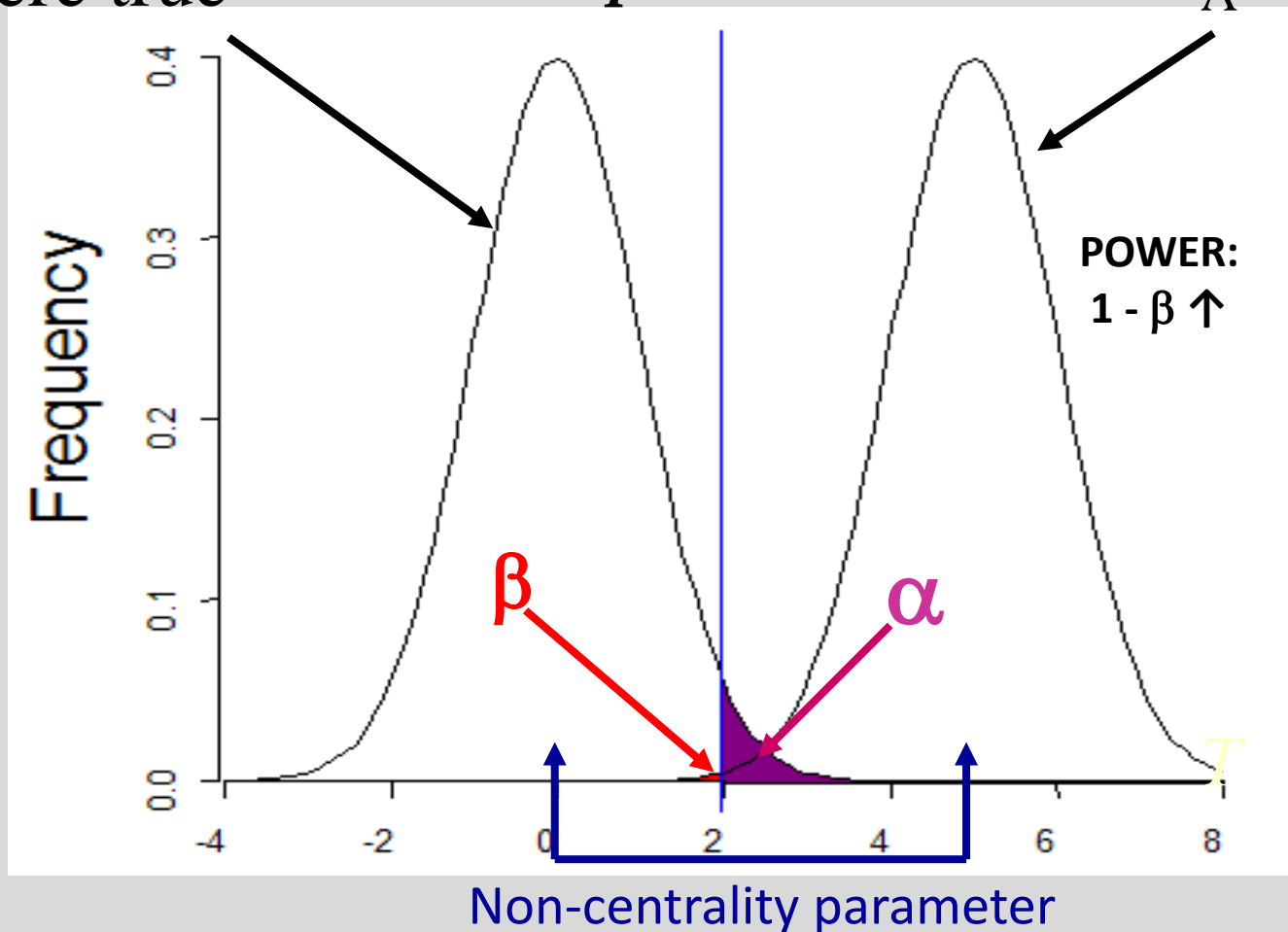


# Increased effect size

Sampling  
distribution if  
 $H_0$  were true

Sampling  
distribution if  
 $H_A$  were true

*alpha 0.05*

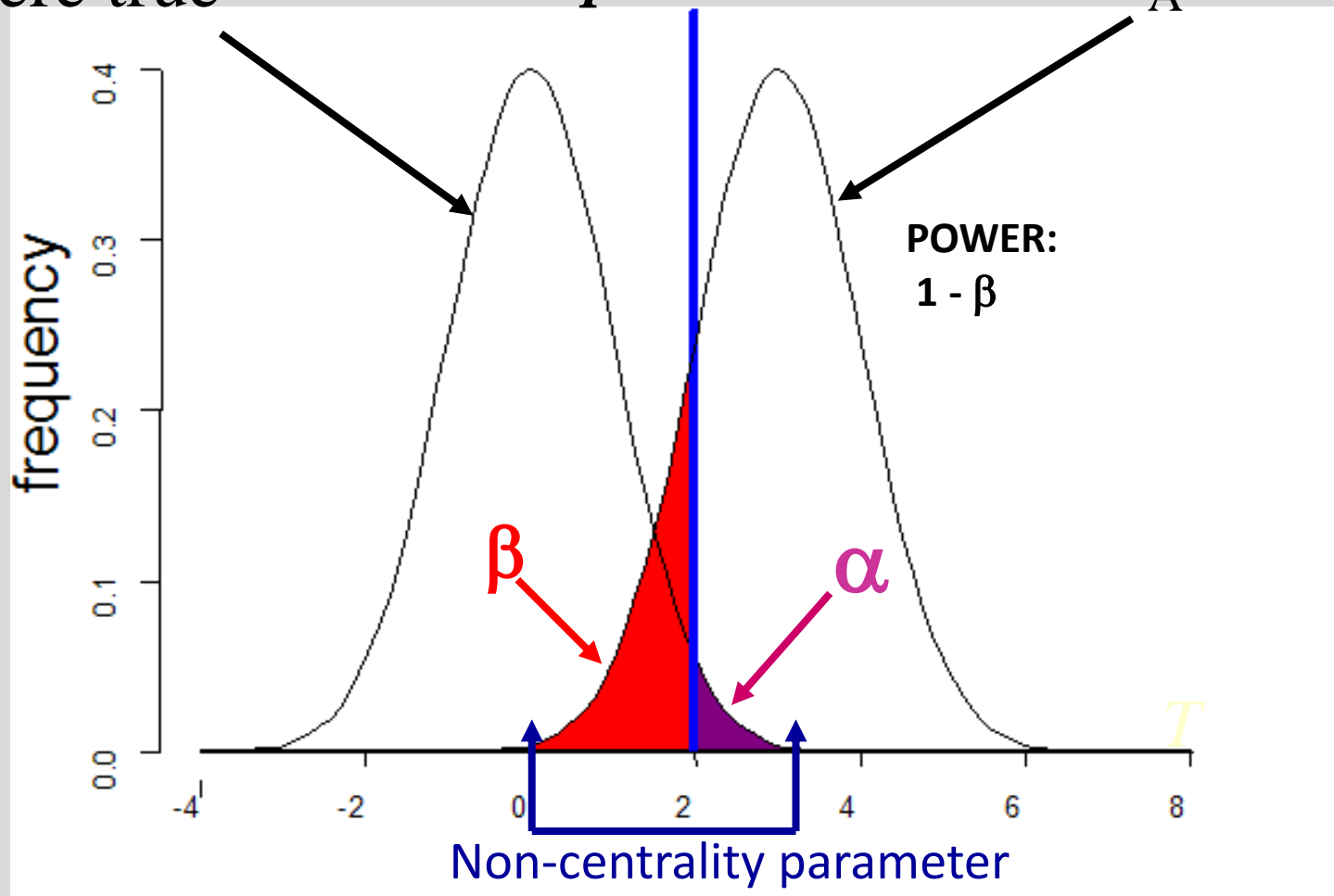


# Standard Case

Sampling distribution if  $H_0$  were true

Sampling distribution if  $H_A$  were true

*alpha 0.05*

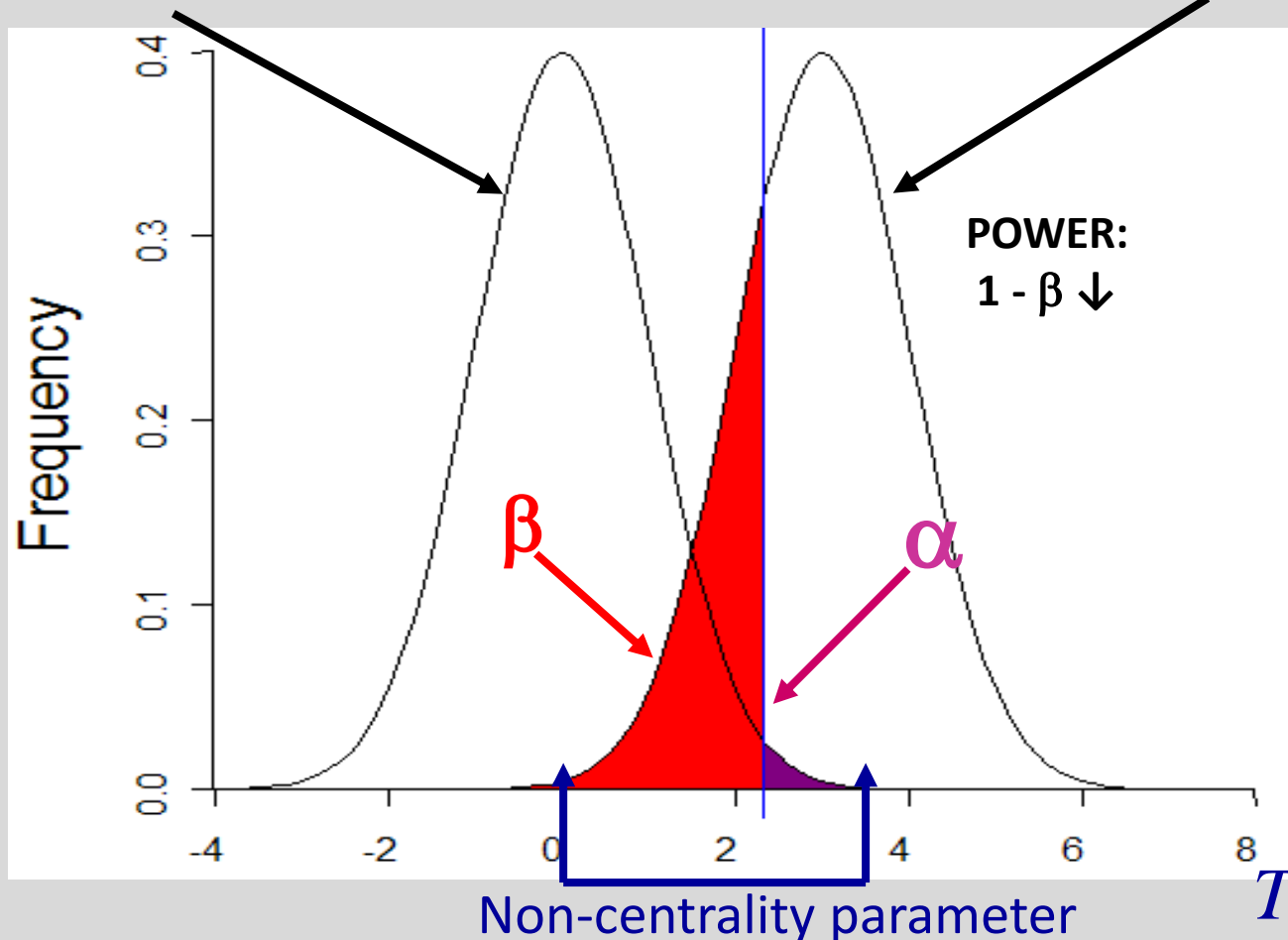


# More conservative $\alpha$

Sampling distribution if  $H_0$  were true

Sampling distribution if  $H_A$  were true

*alpha 0.01*

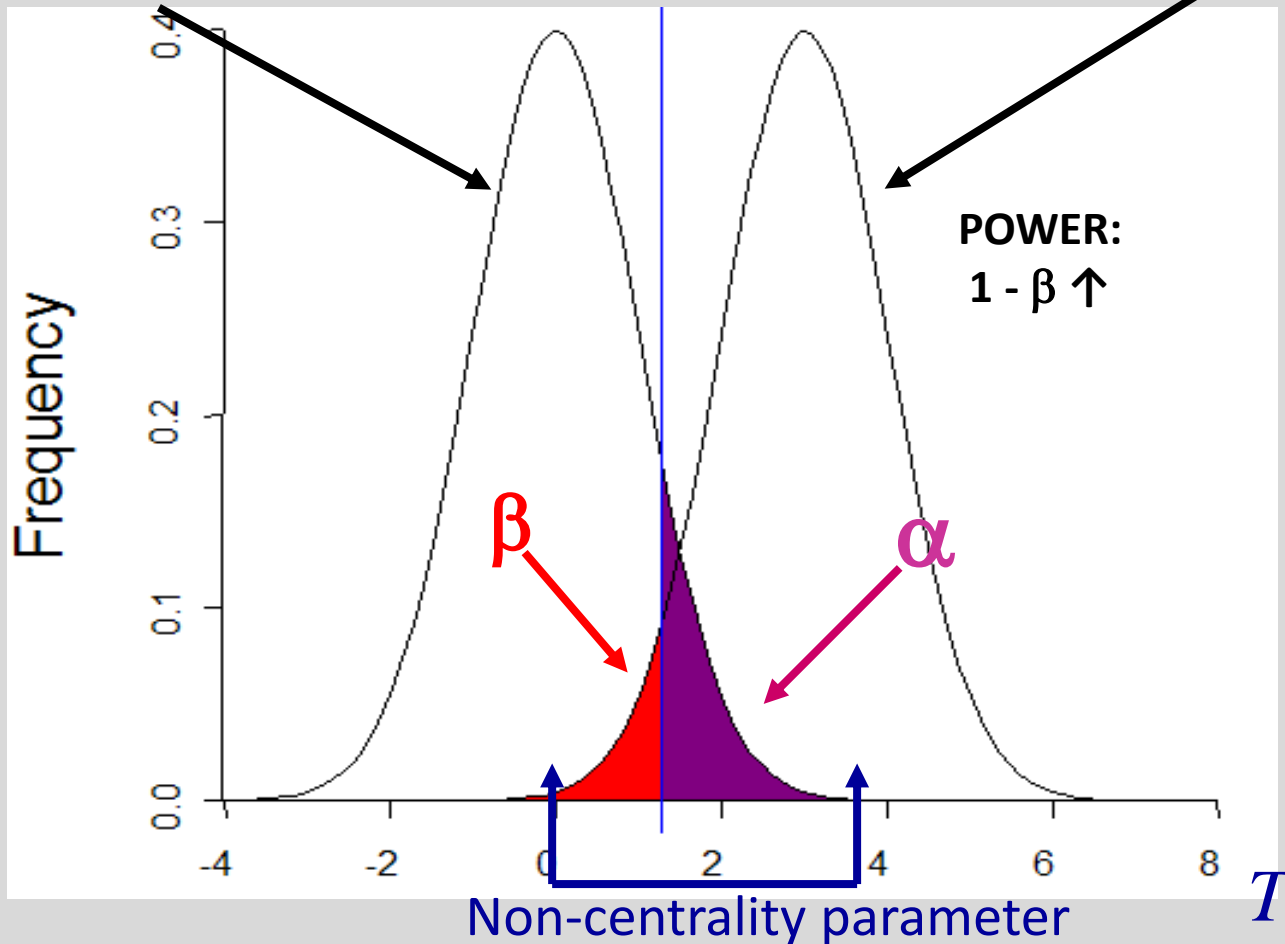


# Less conservative $\alpha$

Sampling distribution if  $H_0$  were true

Sampling distribution if  $H_A$  were true

*alpha 0.10*

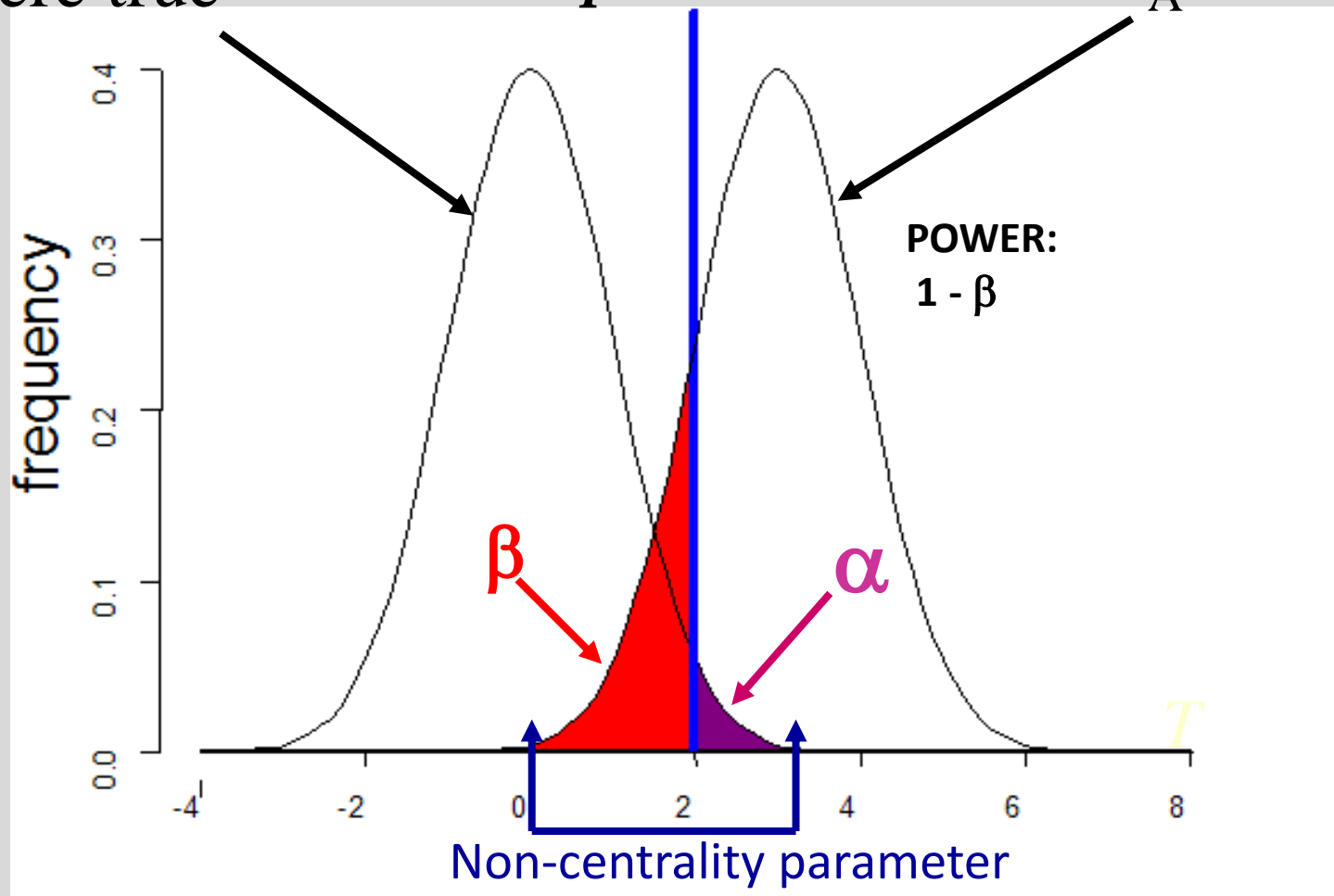


# Standard Case

Sampling distribution if  $H_0$  were true

Sampling distribution if  $H_A$  were true

*alpha 0.05*

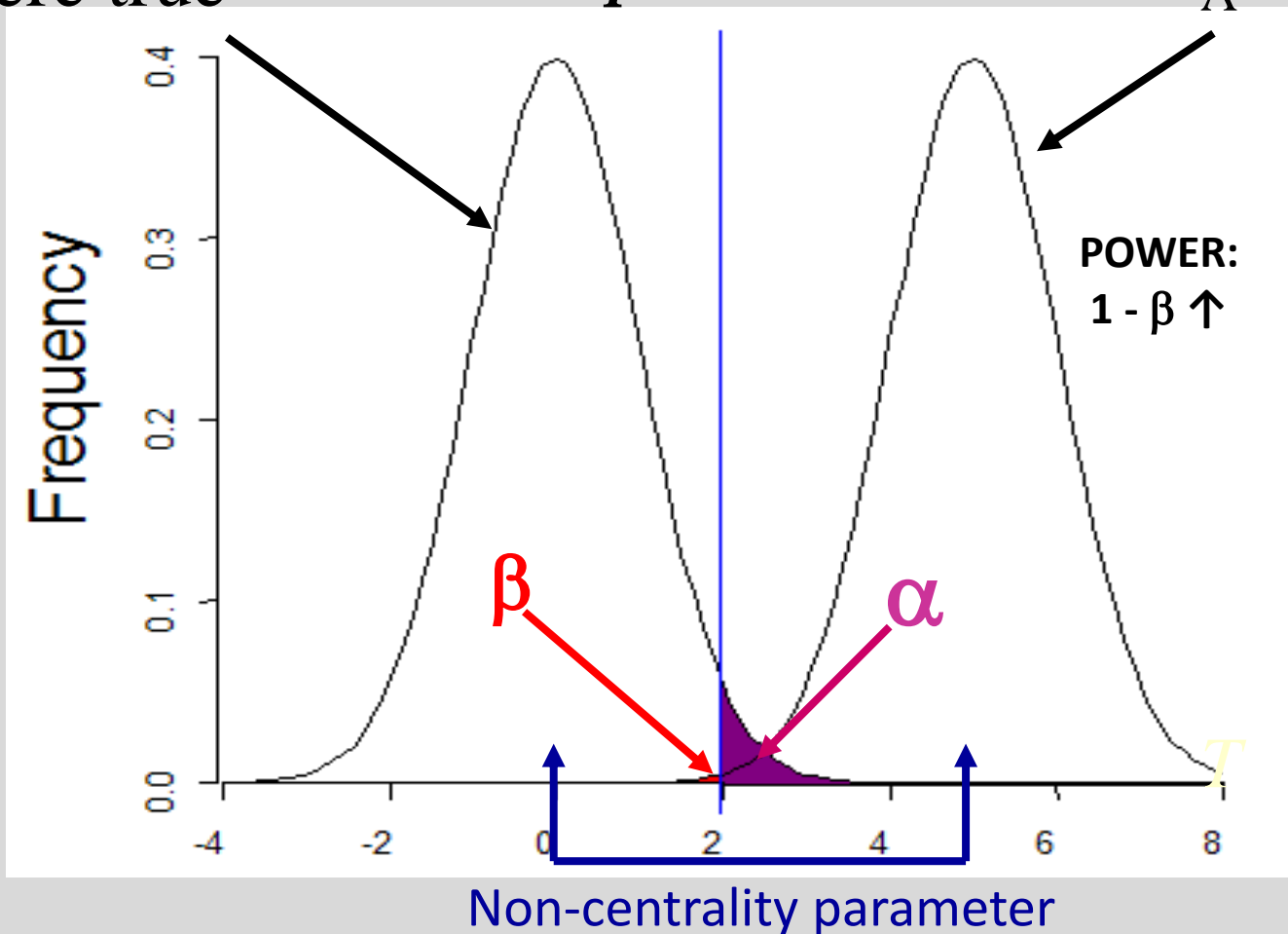


# Increased sample size

Sampling distribution if  $H_0$  were true

Sampling distribution if  $H_A$  were true

*alpha 0.05*



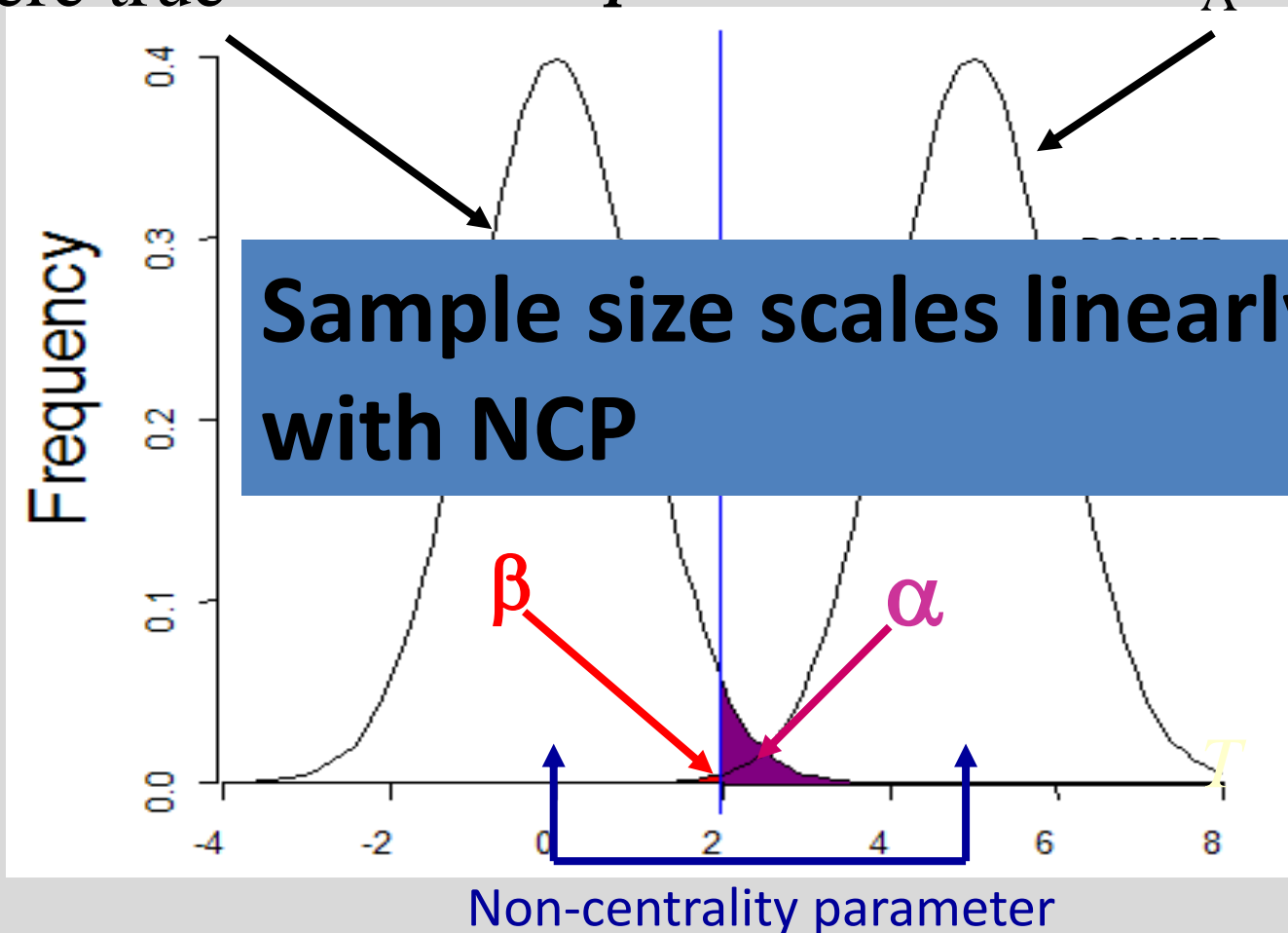


# Increased sample size

Sampling distribution if  $H_0$  were true

Sampling distribution if  $H_A$  were true

*alpha 0.05*



- Type of Data
  - Continuous > Ordinal > Binary
  - Do not turn “true” binary variables into continuous
- Multivariate analysis
- Remove confounders and biases
- MZ:DZ ratio

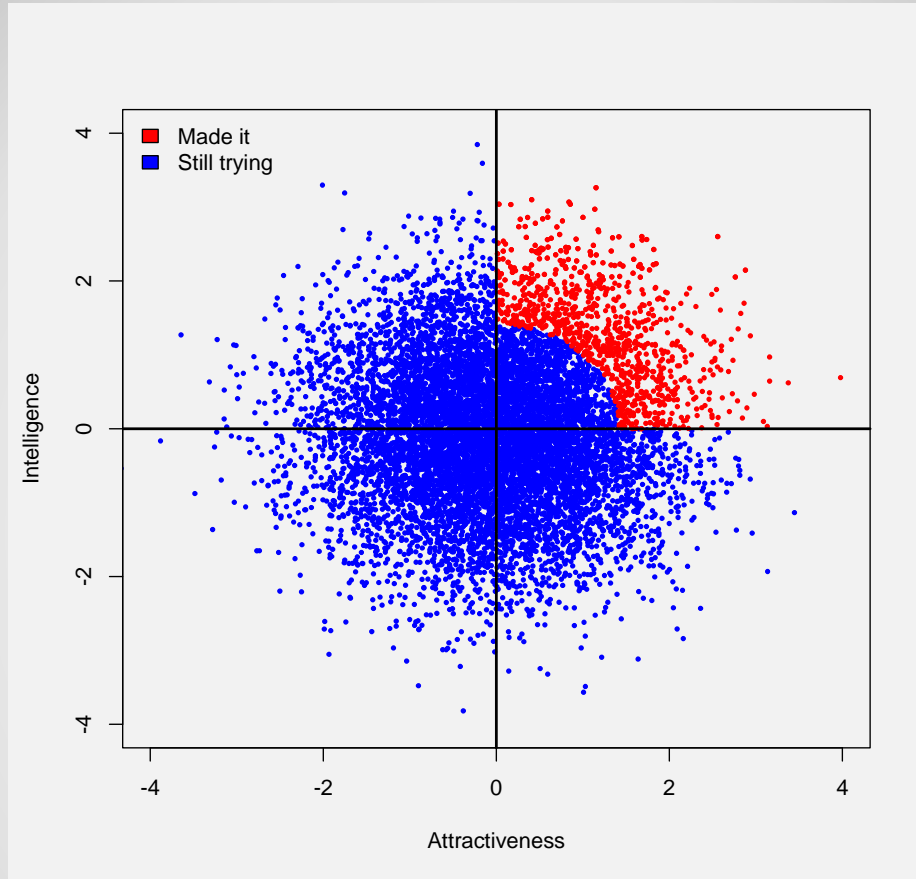
**Additional Factors**

- Larger effect sizes
  - Reduce heterogeneity
- Larger sample sizes
- Change significance threshold
  - False positives may become problematic

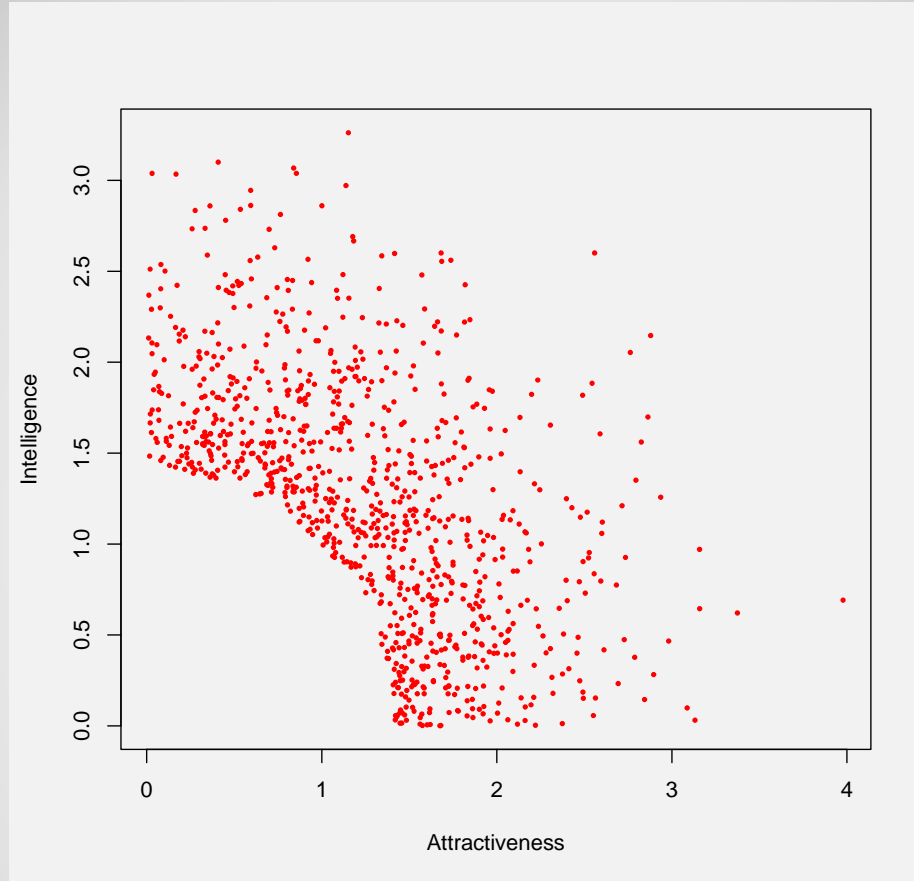
**Effects Recap**

# Ascertainment

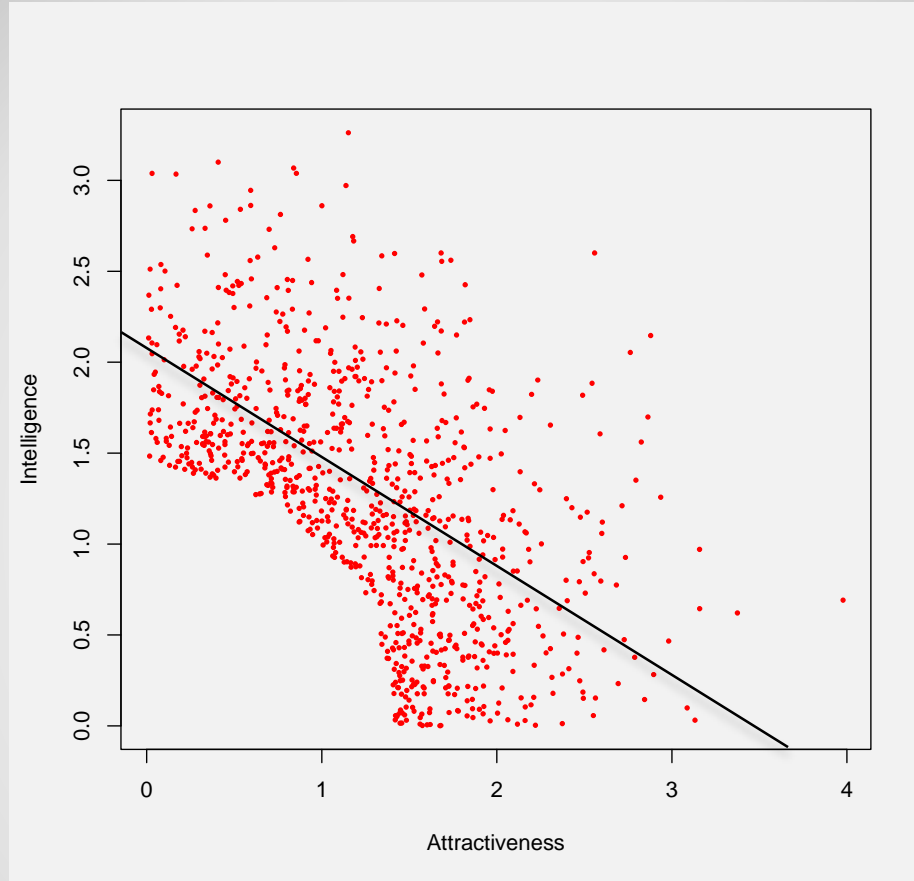
Why being picky can be good and bad



**Bivariate plot for actors in  
Hollywood**



**Bivariate plot for actors who  
"made it" in Hollywood**



**$P < 2e-16$**

**Bivariate plot for actors who  
"made it" in Hollywood**

- Again – you're meant to say something
- I'm waiting...

**What happened?**



- Bias in your parameter estimates
  - Bias is a difference between the “true value” and the estimated value
- Can apply across a range of scenarios
  - Bias estimates of means, variances, covariances, betas etc.

**Ascertainment**

- For testing means, ascertainment increases power
- For characterizing variance:covariance structure, ascertainment can lead to bias

**When might we want to ascertain?**

- For testing means, ascertainment increases power
- For characterizing variance:covariance structure, ascertainment can lead to bias

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## Mapping Mendelian Factors Underlying Quantitative Traits Using RFLP Linkage Maps

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Accepted for publication October 6, 1988

**When might we want to ascertain?**

# Now for something completely different

OK only 50% different from a genetics point of view

## 2. THE POWER OF DISCRIMINATING BETWEEN SIMPLE MODELS

### (i) Theory

If we have a set of observed mean squares  $O_i$ , their expected values calculated on the basis of the "true" model of variation  $F_i$  and the expected values calculated on the basis of a "false" model,  $E_i$ , then we wish, for each  $i$  to test the null hypothesis

$$H_0: \mathcal{E}(O_i) = E_i$$

If  $H_0$  is true and the degrees of freedom  $\nu_i$  are large then  $O_i \sim N(E_i, 2E_i^2/\nu_i)$  approximately. We assume  $H_0$  is to be tested by the statistic  $\frac{\nu_i(O_i - E_i)^2}{2E_i^2}$  which is approximately chi-square with one degree of freedom. The power function of this test is not known for all alternative hypotheses. Consequently we follow Mitra (1958) and consider the limiting power function of the test for large sample sizes and alternative models not too far from the hypothesised model. To express this idea suppose

$$H_1: \mathcal{E}(O_i) = F_i = E_i + \mu_i/\sqrt{\nu_i}$$

where  $\mu_i = \sqrt{\nu_i}(F_i - E_i)$  is the deviation between the two models. Given that  $\nu_i$  is large, then if  $H_0$  is true

$$O_i \sim N(E_i, 2E_i^2/\nu_i)$$

while if  $H_1$  is true then

$$O_i \sim N(F_i, 2F_i^2/\nu_i) \sim N(F_i, (2E_i^2/\nu_i)(1 + o(\nu_i^{-1/2}))).$$

where  $o(\nu_i^{-1/2})$  denotes a term of the order of  $\nu_i^{-1/2}$ .

Thus

$$\frac{\sqrt{\nu_i}(O_i - E_i)}{\sqrt{2E_i^2}} \sim N\left(\frac{\sqrt{\nu_i}(F_i - E_i)}{\sqrt{2E_i^2}}, 1 + o(\nu_i^{-1/2})\right)$$

and the asymptotic power function of

$$\frac{\nu_i(O_i - E_i)^2}{2E_i^2}$$

is non-central chi-square with non-centrality parameter  $\frac{\nu_i(F_i - E_i)^2}{2E_i^2}$  and one degree of freedom. In general, to test

# Power of Classical Twin Model

## 2. THE POWER OF DISCRIMINATING BETWEEN SIMPLE MODELS

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You can do this by hand

But machines can be much more fun

# Power of Classical Twin Model

Martin, Eaves, Kearsley, and Davies Power of the Twin Study, Heredity, 1978

**How can we determine  
our power to detect  
variance components?**

- We'll run through three different scripts
- `power_approximation.R`
  - This lays out a theoretical consideration for correlations
- `test_C_sim_2014.R`
  - Creates a function for running a simulated ACE model to drop C
- `run_C_sim_2014.R`
  - This will run the function from `test_C_sim.R`

**A trio of scripts**



- We'll walk through the script to explore the core statistical concepts we discussed earlier
- Most of the rest of this session will be done in R 😊.

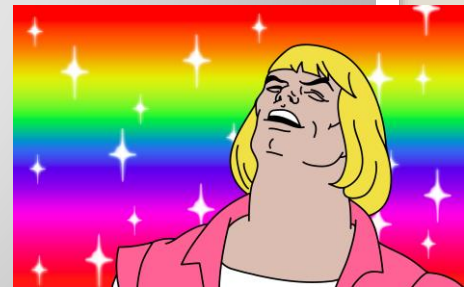


**power\_approximation.R**

- Just like we simulated estimates of means we can simulate chi squares from dropping C
- We get to play God [well more than usual]
  - We fix the means and variances as parameters to simulate
  - We fit the model ACE model
  - We drop C
  - We generate our alternative sampling distribution of statistics

**Simulation is king**

- This script does not produce anything, but rather creates a function
- I will walk through the script explaining the content
- We will make this function and then run the function once to see what happens
- Then we can generate a few more simulations (though I'm not super keen on the computation power of the machines)



**Script: test\_C\_sim\_2014.R**

- Now we understand what the function is doing, we can run it many times
- We are going to use sapply again
- This time we will sapply the new function we made
- In addition to generating our chis, we create an object of the chis to assess our power and see what our results look like



**Script: run\_C\_sim\_2014.R**

*"All models are wrong but some are useful"*  
--George Box

- Simulation is useful for refining intuition
- Helpful for grant writing
- Calibrates need for sample size
- Many factors affect power
  - Ascertainment
  - Measurement error
  - Many others

**Principles of Simulation**

- Simulation is super easy in R
- ClassicMx did not have such routines
- We can evaluate our power easily using R as well
- We can generate pictures of our power easily

**Why R is great**

- Genetic Power Calculator
  - Good for genetic studies with genotype data
  - Also includes a probability function calculator
  - <http://pngu.mgh.harvard.edu/~purcell/gpc/>
- Wiki has pretty good info on statistical power
  - [http://en.wikipedia.org/wiki/Statistical\\_power](http://en.wikipedia.org/wiki/Statistical_power)

**Additional Online Resources**

Visscher PM, Gordon S, Neale MC., Power of the classical twin design revisited: II detection of common environmental variance. *Twin Res Hum Genet.* 2008 Feb;11(1):48-54.

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## Citations for power in twin modeling