INTRODUCTION TO SAMPLE SIZE CALCULATIONS

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Objectives

- 1) Understand the concepts of sample size, power, effect size, and types of error
- 2) Understand the tradeoffs between these different parameters

Sample Size & Power

Why estimate sample size?

Purpose

- Justify the cost and scope of the proposed research
- Define your assumptions about the expected effect size and the minimum relevant effect size
- Anticipate challenges (e.g., loss to follow-up)
- *Make sure your research is not doomed to fail (be underpowered to draw conclusions)*

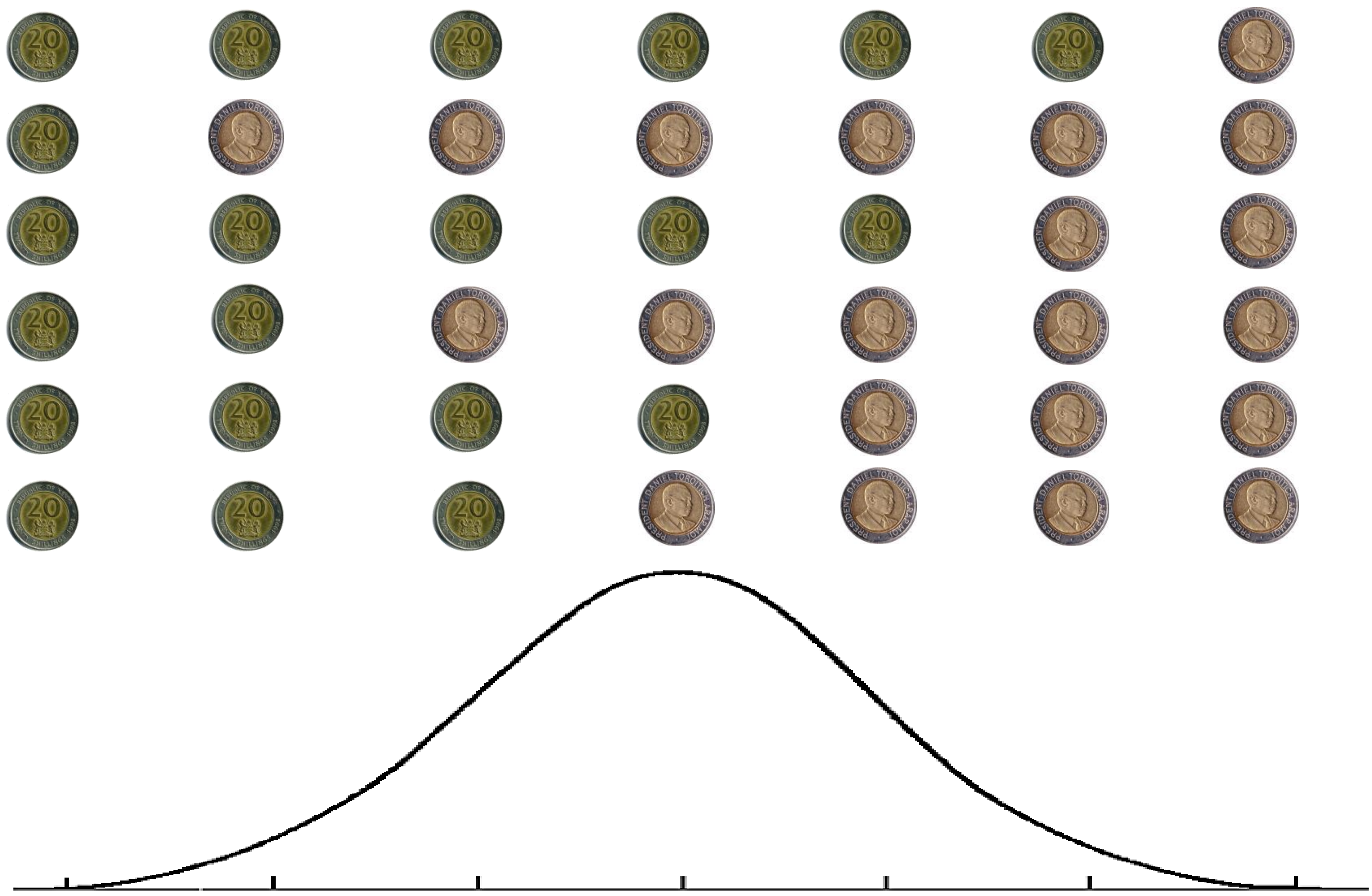
Example: Unbalanced Coin

- Flip a coin 4 times
  - 3 heads, 1 tail
  - Do you believe it is an unbalanced coin?
- Flip a coin 40 times
  - 30 heads, 10 tails
  - Now do you believe it is an unbalanced coin?
- Flip a coin 400 times
  - 300 heads, 100 tails
  - Are you convinced this is an unbalanced coin?

Example: Unbalanced Coin

With a larger sample size, we become more sure that the difference we **observe** is a **true** difference and not due to **chance**

Example: Unbalanced Coin



Example: Unbalanced Coin

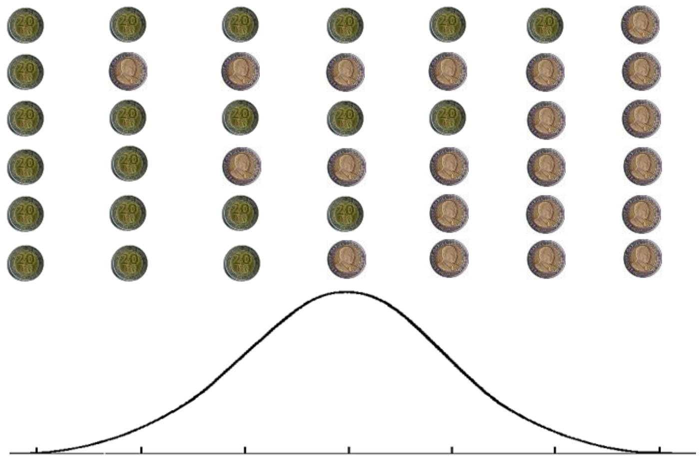
The coin is either truly balanced or unbalanced

This is the TRUTH

When we flip the coin a certain number of times we'll either conclude that the coin is balanced or unbalanced

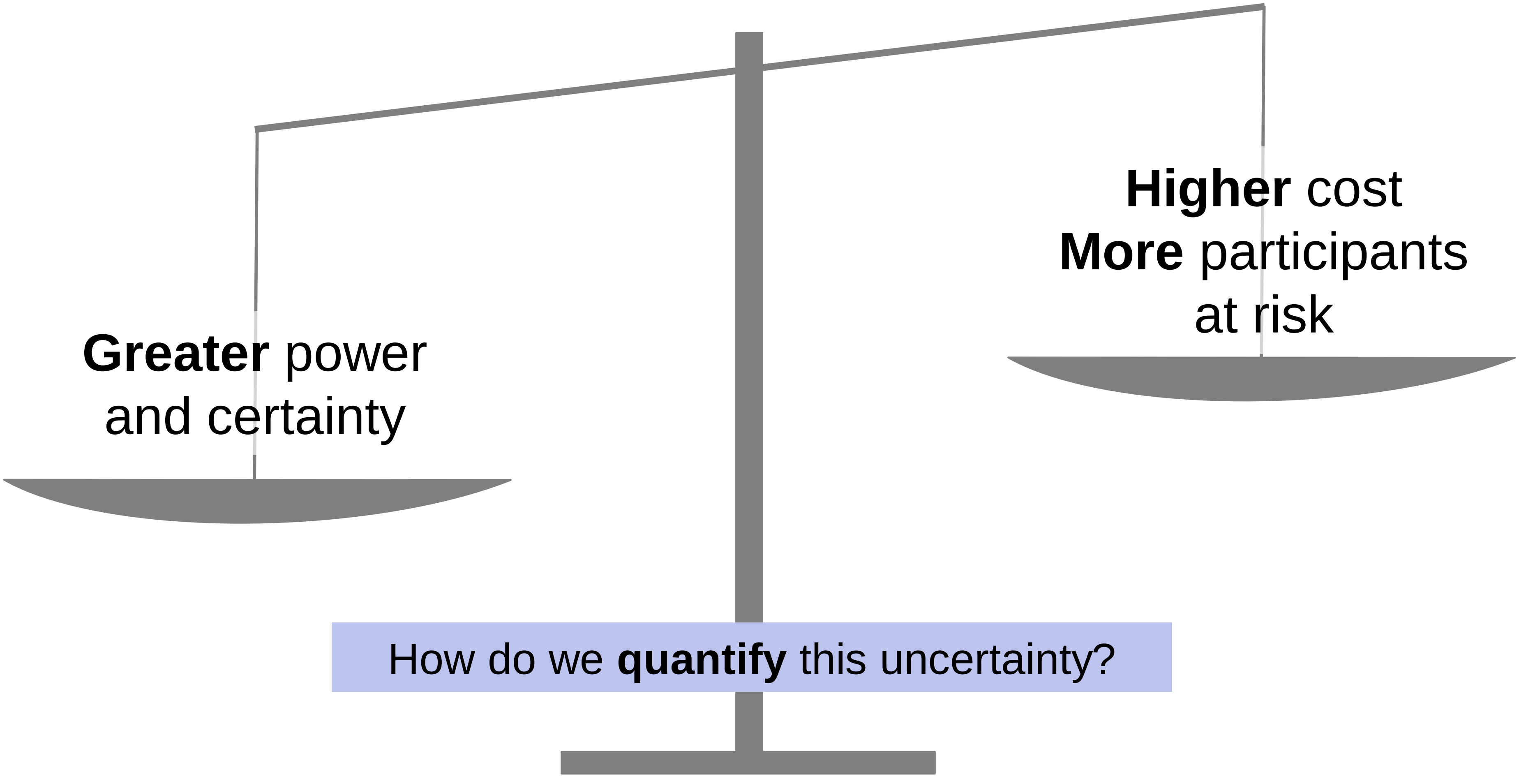
This is what we OBSERVE

Most of the times we'll conclude correctly (observed = truth), but sometimes we'll conclude incorrectly (observed ≠ truth) simply due to **chance**



How willing are we to risk making the **wrong** conclusion?

Increasing sample size has **tradeoffs**…



How do we **quantify** this uncertainty?

P-values

- p-value tells us what the probability is that we would see the observed difference due to **chance** EVEN IF there was truly **no** difference
  - *How likely is it that the coin toss would show 30 heads and 10 tails if it was truly a balanced coin?*
- p-value **decreases** with greater number of subjects

Does a p-value tell us how **strong** an **association** is?

Measures of association

- Calculated to explain *whether,* in *which direction* and *how strongly* an exposure is associated with an outcome
  - RR=1 means the exposure is ***not associated*** with the outcome
  - RR<1 means the exposure is ***negatively associated*** with the outcome and ***decreases*** risk
  - RR>1 means the exposure is ***positively associated*** with the outcome and ***increases*** risk

- RR = 0.8
  - "Subjects in the exposed group were 80% **as** likely / 20% **less** likely to have the outcome"

- RR = 1.5
  - "Subjects in the exposed group were 1.5 times **as** likely / 50% **more** likely to have the outcome."

P-value versus Effect Size

- My friend wants to improve her chances of getting pregnant; she can take one of two medications

- **Medication 1:** Increases her chance of getting pregnant by a factor of 1.1 and has a p-value of <0.0001
- **Medication 2:** Increases her chance of getting pregnant by a factor of 4.5 and has a p-value of 0.1
- **Which medication would you choose?**

What is Statistical Power?

- Power is a measure of our ability to convincingly **show** a difference when there **truly is** a difference
  - (REMEMBER: p-value is a measure of how often we would **observe** a difference when there **truly was no** difference)
- If I asked you to find out whether a coin was balanced but I only let you toss the coin 4 times, would you be able to make a convincing conclusion?
- **There is no point in doing a study unless we know that if there is a true difference, we will be able to show it**

Components of Statistical Power

Power is a function of four parameters

- Effect size
  - How **big** is the effect of your intervention?
- Sample size
  - How **many people** (or observations) do you have?
- Probability of false negative (β error)
  - (I – β) is **power**
- Probability of false positive (α error)

Components of Statistical Power

Power is a function of four parameters

- Effect size
  - How **unbalanced** is your coin?
  - What if it only showed heads 60% of the time? (6/10)
- Sample size
  - How **many times** do you need to flip your coin?
- Probability of false negative (β error)
  - How willing are you to conclude that the coin is **BALANCED** when it is truly **UNBALANCED**
- Probability of false positive (α error)
  - How willing are you to conclude that the coin is **UNBALANCED** when it is truly **BALANCED**?

Alpha and Beta?

Prisoner Example

		TRUTH	
		Guilty	Innocent
VERDICT	Prison	OK	**Problem**
	No prison	**Problem**	OK

Which is worse?

Problem A in RED or Problem B in GREEN?

Alpha and Beta?

Study Example

		TRUTH	
		Effect	No Effect
OBSERVED	Effect	OK	**Problem** (α error)
	No Effect	**Problem** (β error)	OK

Which is worse?

Problem A “alpha –Type I error” and Problem B “beta-Type II error”

Alpha usually 0.05 and beta usually 0.2 or 0.1

Willing to accept that 20% of the time we won’t be able to convincingly show that there is a difference, even when there **truly is** a difference; and 5% of the time we will conclude that there **is** a difference, even when there truly is **NO** difference.

What to solve for?

Power is a function of four parameters

- Effect size
- Sample size
- Power (1-β)
- Probability of false positive (α error)

Like in algebra, set 3 equal to real numbers and solve for the 4th

What to solve for?

I have…

- Effect size
- Power (1-β)
- Probability of false positive (α error)

What do I solve for?

- Sample size

What to solve for?

I have…

- Sample size
- Effect size
- Probability of false positive (α error)

What do I solve for?

- Power ($1-\beta$)

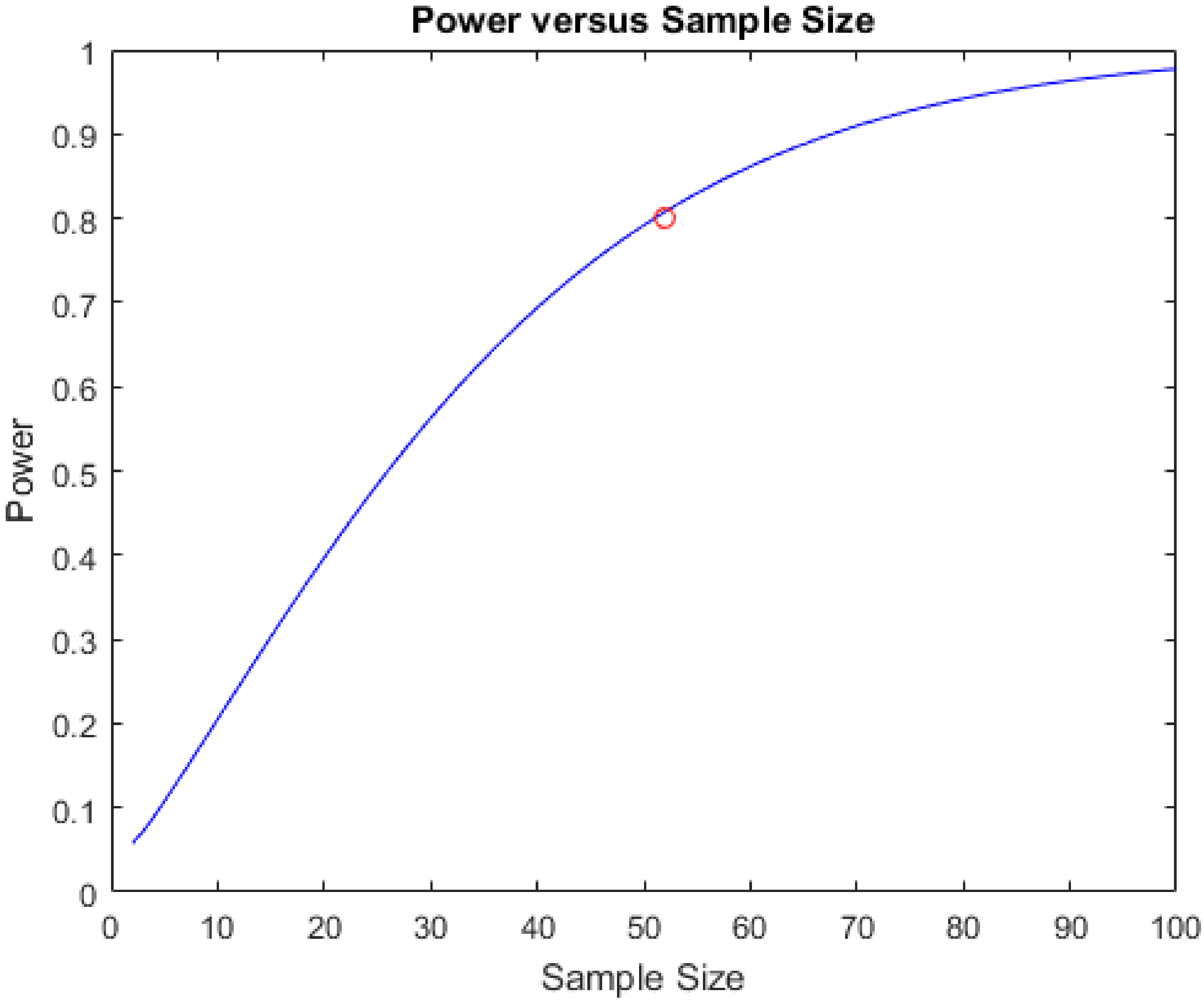
What to solve for?

I have…

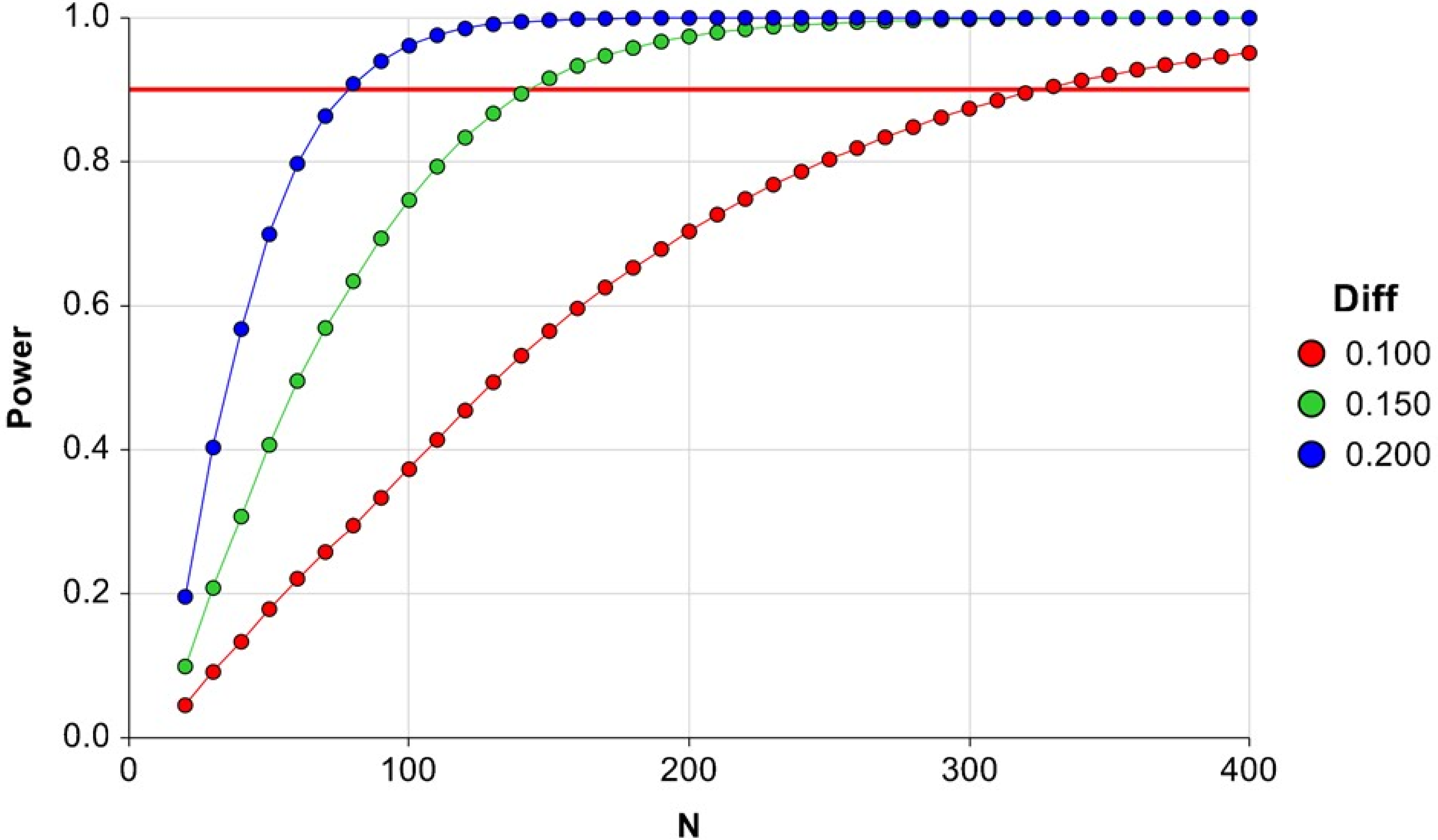
- Sample size
- Power (1-β)
- Probability of false positive (α error)

What do I solve for?

- Effect size



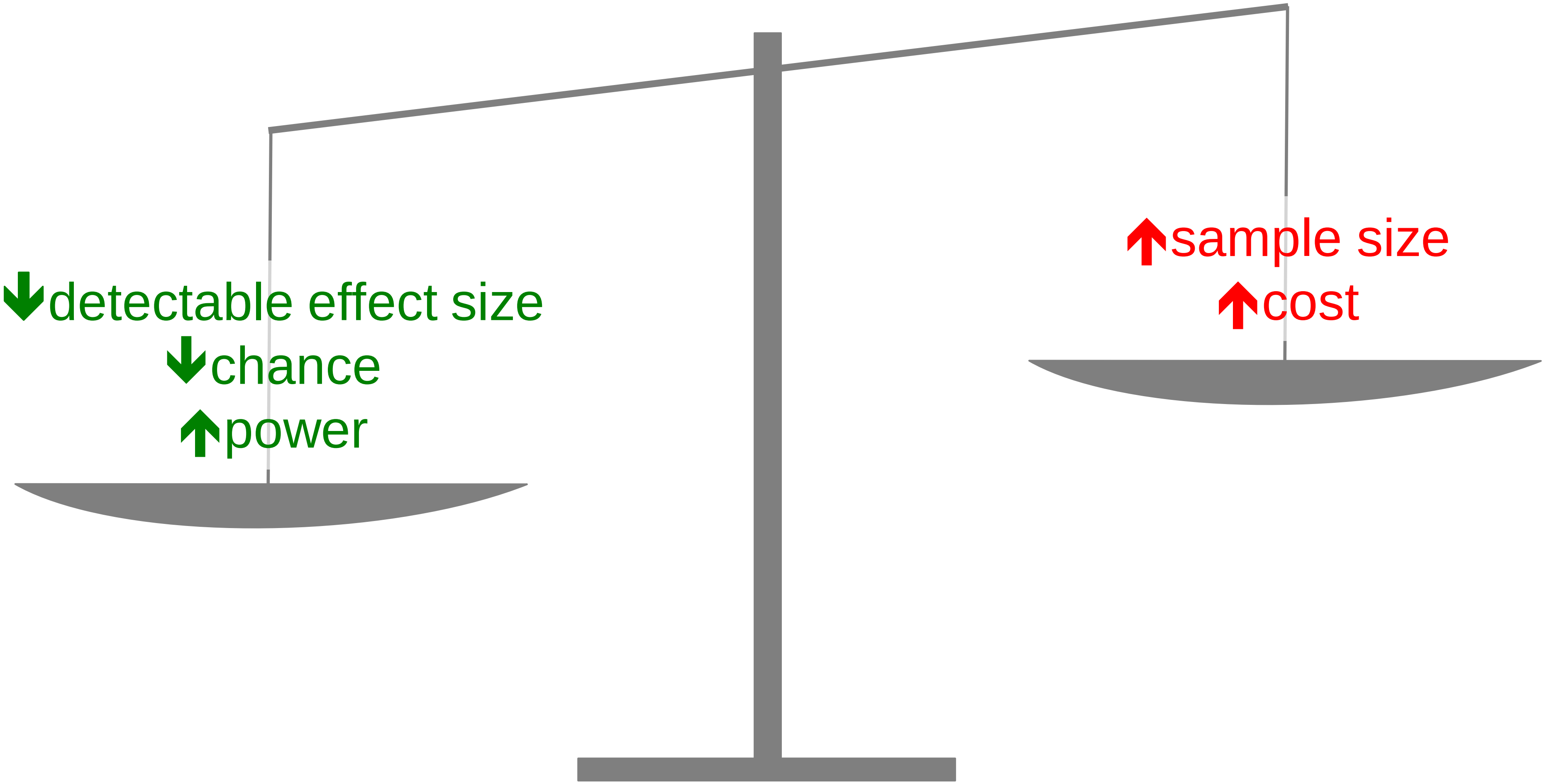
https://www.mathworks.com/help/stats/sampsizepwr.html?s_tid=gn_loc_drop



https://www.youtube.com/watch?v=Ly6uh_SnmJ4

How are these concepts connected?

There are **tradeoffs**…



Working with a statistician

- Statistician needs 3 of the 4 values:
  - Effect size
  - Sample size
  - Power ($1-\beta$)
  - Probability of false positive (α error)

Working with a statistician

- Statistician needs 3 of the 4 values:
  - Effect size – estimate from the literature or decide what effect size would be clinically meaningful
  - Sample size – may have a fixed number of participants or a limited budget
  - Power ($1-\beta$) – usually 80% (sometimes 90% in clinical studies)
  - Probability of false positive (α error) – usually 5%

Working with a statistician

- Example: I want to test whether initiating HIV-positive children on a more palatable ART regimen reduces the chances of virologic failure after 6 months of treatment
  - Sample size: UNKNOWN
  - Effect size: Unsure, but anything less than a 10% reduction in virologic failure would be clinically irrelevant. Current regimens have probability of failure of 30%
  - Power: 80%
  - Alpha: 5%

- Statistician will tell you how many people you would need to enroll to detect a difference as small as a 10% reduction in virologic failure from the baseline of 30% failure

Working with a statistician

- Example: I want to test whether viral loads of HIV-positive children who received an intensive ART adherence intervention are higher or lower than children who received standard of care adherence counseling. However, I only have funds to process a total of 50 samples
  - Sample size: 50 samples, 25 with the intervention, 25 SoC
  - Effect size: Unknown
  - Power: 80%
  - Alpha: 5%

- Statistician will tell you how much of a difference in viral load you would be able to detect with 50 samples

Calculating your own sample size

- Manual formulas or statistical software both valid options
- Most important to understand the **inputs** well
- Many statistical software options (non-exhaustive list)
  - Stata, SPSS, R: all flexible and powerful, require knowledge of coding
  - EpiInfo (StatCalc): free and user-friendly, also have web-based and mobile-based options
  - Power Sample Size (Vanderbilt University) is free and easy to use, does not require coding: *http://biostat.mc.vanderbilt.edu/wiki/Main/PowerSampleSize*

STATA Examples

```
.  power twoproportions 0.8 0.9, alpha (0.05) power (0.80)

Performing iteration ...

Estimated sample sizes for a two-sample proportions test
Pearson's chi-squared test
Ho: p2 = p1  versus  Ha: p2 != p1

Study parameters:

        alpha =    0.0500
        power =    0.8000
        delta =    0.1000  (difference)
           p1 =    0.8000
           p2 =    0.9000

Estimated sample sizes:

            N =       398
  N per group =       199

.
```

STATA Examples

```
.  power twoproportions 0.6 0.9, alpha (0.05) power (0.80)

Performing iteration ...

Estimated sample sizes for a two-sample proportions test
Pearson's chi-squared test
Ho: p2 = p1  versus  Ha: p2 != p1

Study parameters:

        alpha =    0.0500
        power =    0.8000
        delta =    0.3000  (difference)
           p1 =    0.6000
           p2 =    0.9000

Estimated sample sizes:

            N =        64
  N per group =        32

.
```

STATA Examples

```
.  power twomeans 2.5 2.75, alpha (0.05) power (0.80)

Performing iteration ...

Estimated sample sizes for a two-sample means test
t test assuming sd1 = sd2 = sd
Ho: m2 = m1  versus  Ha: m2 != m1

Study parameters:

        alpha =    0.0500
        power =    0.8000
        delta =    0.2500
           m1 =    2.5000
           m2 =    2.7500
           sd =    1.0000

Estimated sample sizes:

            N =       506
  N per group =       253

.
```

5-mintute activity break

Using YOUR study question, imagine you are either working with a biostatistician to do power calculations OR calculating your own sample size. Define 3 of the following 4 parameters and write a 1 sentence description of what the biostatistician or software will tell you.

- Effect size
- Power
- Sample size
- Alpha error

Summary

Statistical power and sample size

- Components of statistical power:
  - Effect size
  - Sample size
  - Power
  - Apha error

Questions?

Special thanks to:

Dr. Anjuli Wagner, MPH, PhD
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