LIBR
Laureate Institute for Brain Research

THE UNIVERSITY of TULSA

K Club, Week 4

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Today's Topics

- Approach
- Action Items

K Application Sections

Research

- **Specific Aims** (1 page)
- **Research Strategy** (6 pages: **Significance, Innovation, Approach**)
- **Training in Responsible Conduct of Research** (1 page)
- **Project Summary / Abstract** (30 lines of text)
- **Project Narrative** (3 sentences)
- **Protection of Human Subjects from Research Risk**
- **Inclusion of Women and Minorities**
- **Inclusion of Individuals Across the Lifespan**
- **Inclusion Enrollment Report**
- **Budget + Budget Justification**
- **Bibliography + References Cited**

Career

- **Candidate Information and Goals for Career Development** (6 pages: **Candidate Background, Career Goals/Objectives, Career Development/Training Plan**)
- **Plans and Statements of Mentor and Co-Mentors** (6 pages)
- **NIH Biosketches** for you, Mentor, Co-Mentors (max 5 pages each)
- **Three Letters of Reference**
- **Letters of Support from Collaborators, Contributors and Consultants** (6 pages max)
- **Cover Letter**

Setting

- **Facilities and Other Resources**
- **Equipment**
- **Environment and Institutional Commitment to Candidate**
- **Resource Sharing Plan**

Research Strategy
(6 pages max)

Unlike **Specific Aims**, citations are required in this section

Significance → Expand on **Specific Aims**

Innovation → Explain the novelty of your theory, approach and/or methods

Approach → Explain study design, methods, and statistical analyses to accomplish each of your **Specific Aims**

Approach

- This should be the <u>longest section</u> in your **Research Strategy**
- Separate into K99 and R00 **Research Design** subsections, then within each, address:
  - **Overview**
  - **Participants**
  - **Assessments**
  - **Power Analysis for each Aim**
  - **Statistical Analysis for each Aim**
- **Potential Sources of Biological Variation**
- **Expected Outcomes**
- **Potential Problems and Alternative Strategies**
- **Timeline and Benchmarks for Success**
- **Future Directions**

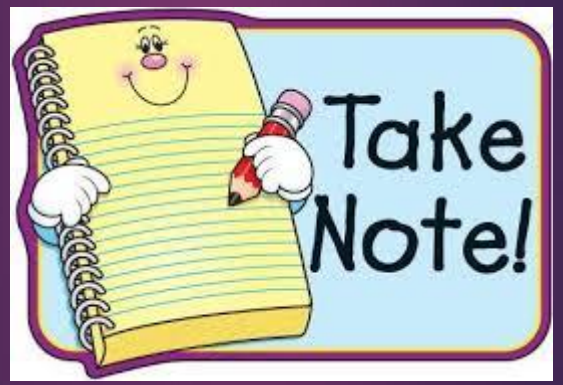
Overview

- Collecting new data or secondary data analysis?
- Is this a pilot study to test feasibility of a new task or intervention?
- Cross-sectional or longitudinal?
- Between-subjects, within-subjects, or both?
- If between-subjects, what groups or conditions?
- If within-subjects, what conditions and/or timepoints?
- If you have multiple timepoints/conditions and the procedure differs for each timepoint/condition, then say that here; in the **Assessments** section you can create subheadings to address each timepoint/condition

Participants

- How will they be recruited?
- If you have multiple groups, how will they be assigned or how will they be defined?
- How many per group? What is the age range?
- Inclusion/exclusion criteria and what assessments are needed to determine whether someone is eligible
- Will they be screened for eligibility via phone or in person?
- Will they be asked to give oral (during phone screening, if applicable) and written (in-person) consent to participate?

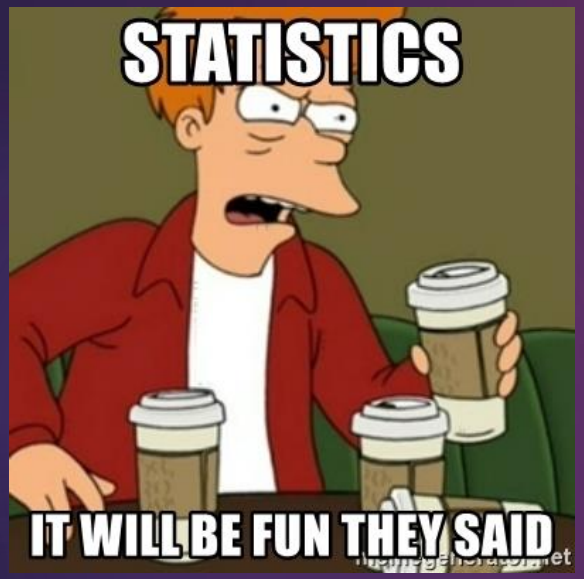
IMPORTANT TO NOTE

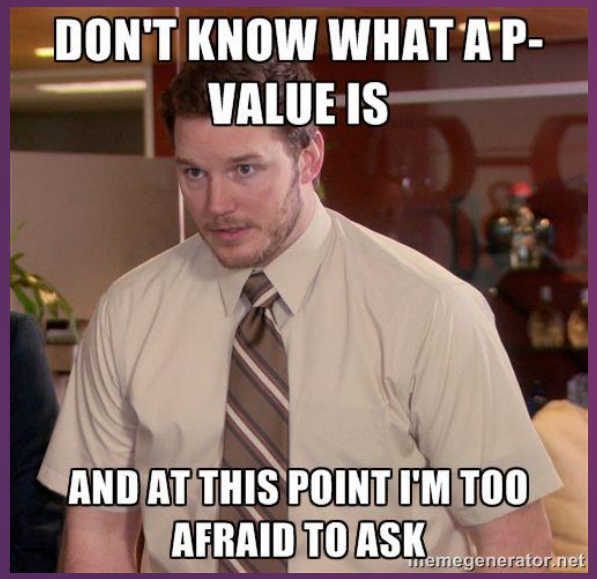


- We haven’t gone into creating your K99 and R00 budgets yet, but you need to start thinking about $$$ now
- K99 phase: $20K per year for research
  - You can’t collect a ton of new data here (especially when factoring subject payment) or pay for too much fMRI scan time
  - You also can’t buy a ton of new equipment or pay too much for any analysis services
  - Be mindful of this when designing your Approach
- R00 phase: $249K for everything (including research and salary)
  - This part of your application allows you to be more expansive in your Approach

Power Analysis for each Aim

- Let's do a little tutorial on Power now to refresh your memory from statistics….





For significance testing, you have:

- Null hypothesis (groups/conditions do not differ)
- Alternative hypothesis (groups/conditions differ)

Given any 3 of these (power, effect size, sample size, alpha) we can find the 4th!

- Sensitivity of a statistical test
- Probability that it correctly rejects the null hypothesis when it is FALSE

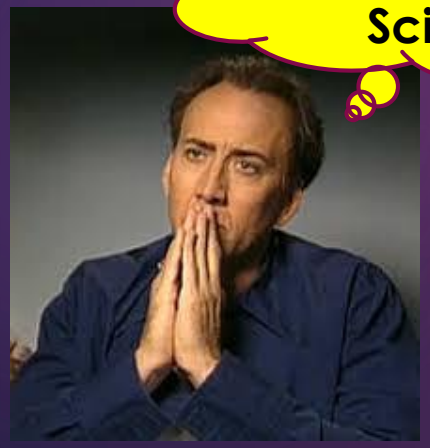
The larger the sample size, the lower the sampling error, making it easier to detect an effect

Study design (between vs. within) affects sample size

Larger magnitude effects are more easily detected than smaller ones!

The lower the p-level (alpha level), the less power you have to detect an effect

HYPOTHESIS TESTING OUTCOMES		Reality: The Null Hypothesis Is True	Reality: The Alternative Hypothesis is True
Research	The Null Hypothesis Is True	Accurate $1 - \alpha$	Type II Error β
Research	The Alternative Hypothesis is True	Type I Error α	Accurate $1 - \beta$



We have a MATCH!

1- alpha (typically set at p<.05) = 95 out of 100 times we retain the null when we should!

Typically this isn't what we were hoping would happen though: retaining the null hypothesis

HYPOTHESIS TESTING OUTCOMES		Reality	
		The Null Hypothesis Is True	The Alternative Hypothesis is True
Research	The Null Hypothesis Is True	Accurate $1 - \alpha$	Type II Error β
	The Alternative Hypothesis is True	Type I Error α	Accurate $1 - \beta$

We have a MATCH!

1 minus beta (typically set at .20) = 80 out of 100 times we reject the null when we should!

YES! We typically want to be able to reject the null and go with the alternative!

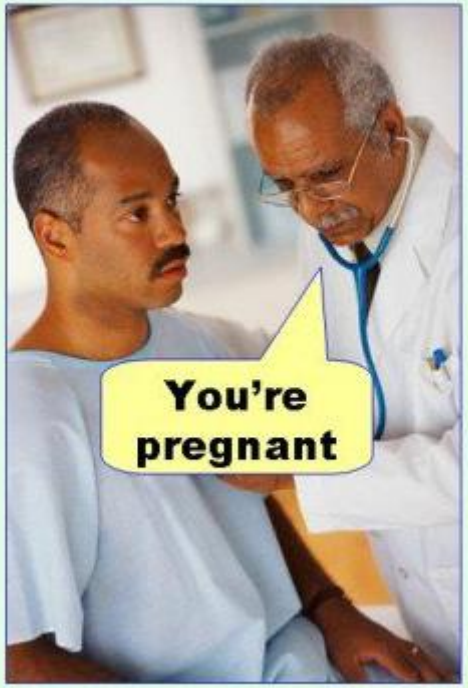
HYPOTHESIS TESTING OUTCOMES		Reality	
		The Null Hypothesis Is True	The Alternative Hypothesis is True
Research	The Null Hypothesis Is True	Accurate $1 - \alpha$ 	Type II Error β 
	The Alternative Hypothesis is True	Type I Error α 	Accurate $1 - \beta$ 

MISMATCH!

Alpha is typically $p < .05$

5 out of 100 times we reject the null when we shouldn't

Type I error
(false positive)

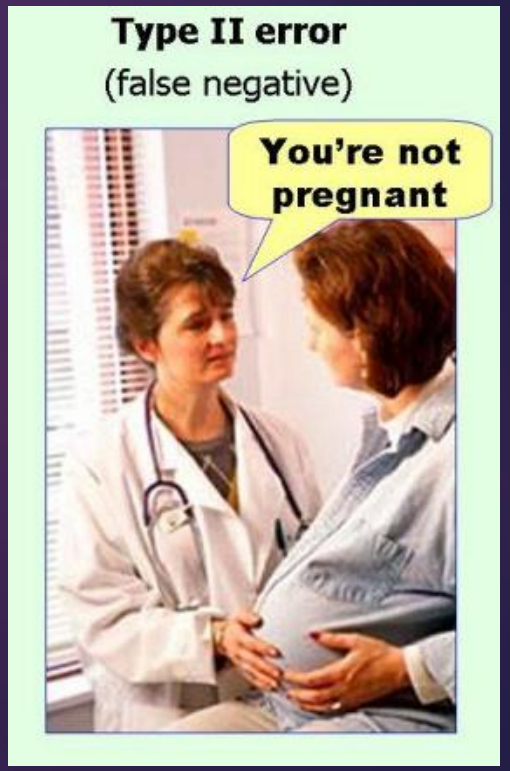


HYPOTHESIS TESTING OUTCOMES		Reality	
		The Null Hypothesis Is True	The Alternative Hypothesis is True
Research	The Null Hypothesis Is True	Accurate $1 - \alpha$	Type II Error β
	The Alternative Hypothesis is True	Type I Error α	Accurate $1 - \beta$

MISMATCH!

Beta typically = .20

20 out of 100 times we retain the null when we shouldn't



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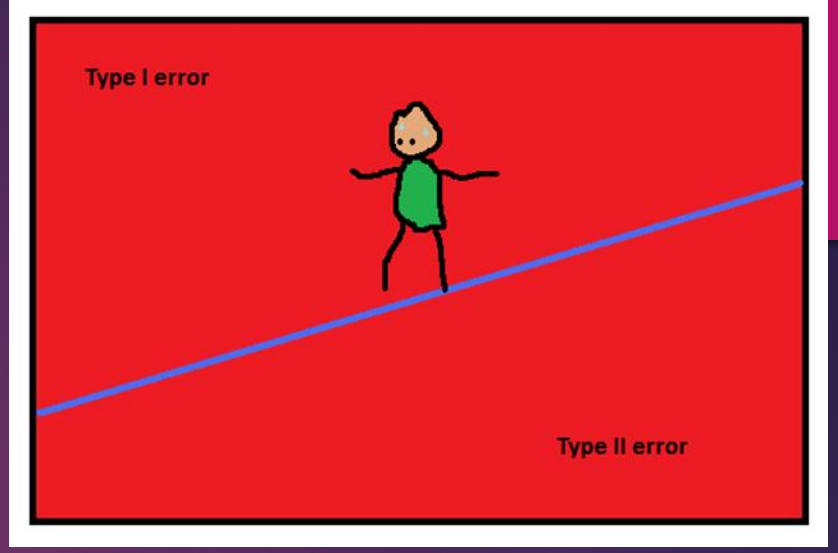
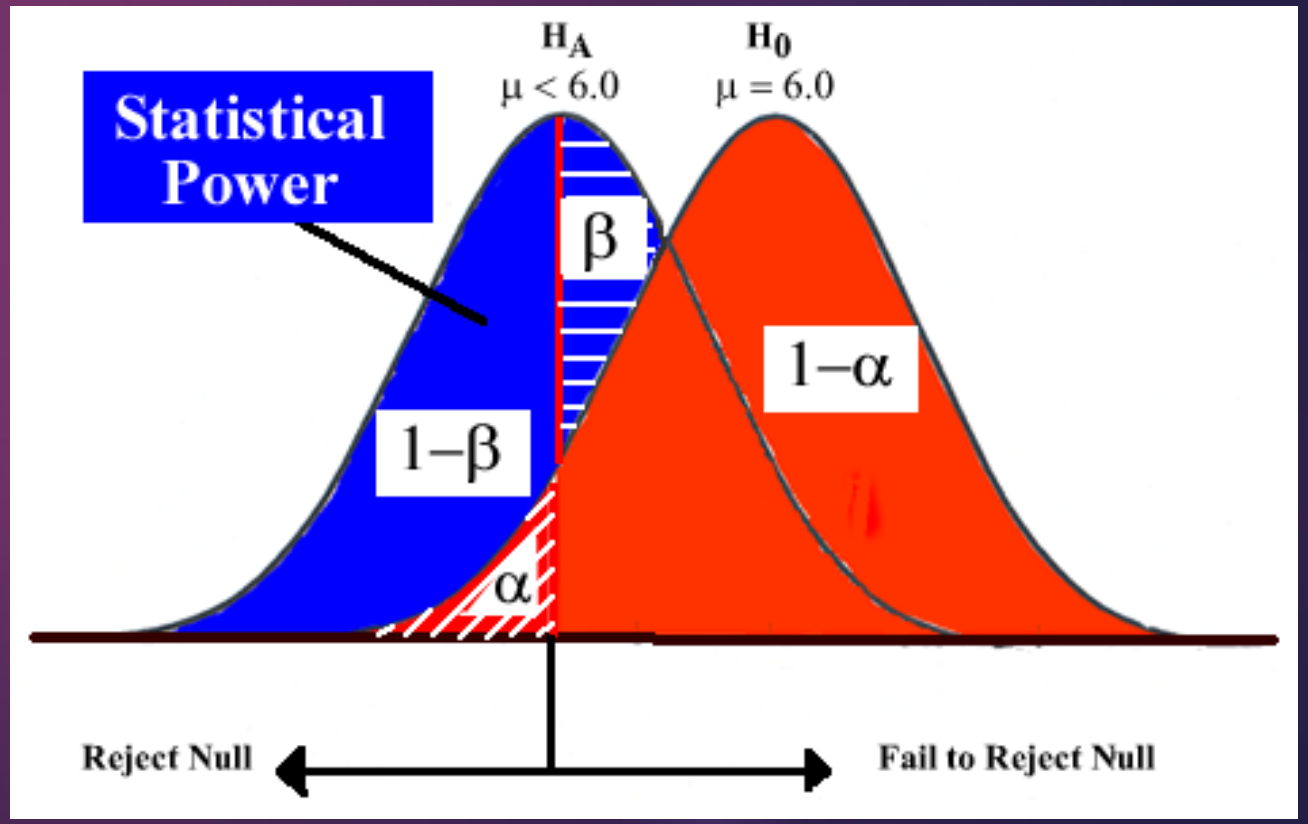


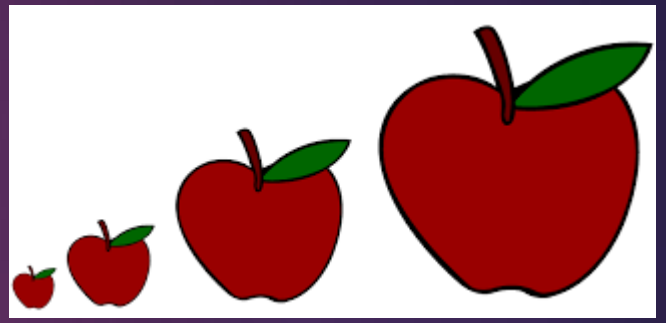
Typical Parameters

Power set at .80
β (prob. Type II error) set at .20
 (prob. Type I error) set at .05 or less



IMPORTANCE OF Effect size!

- Null significance hypothesis testing = reliability of effect (how often we expect it to happen: less than 5 out of 100 times under the null hypothesis, with p < .05 threshold)
- Effect size = magnitude of effect (how big it is)
- We can always reach statistical significance if there is a large enough sample size, unless the effect size is 0
- Even a large effect may not be statistically significant if the sample size is too small



Effect size: Interpretations

Difference between two variables' mean values is certain # of units

- Cohen's d
- Glass's delta
- Hedge's g
- Pearson's correlation r

Proportion of variance shared between two variables

- R-squared
- Eta-squared (η^2)
- Partial eta-squared ($\eta^2 p$)

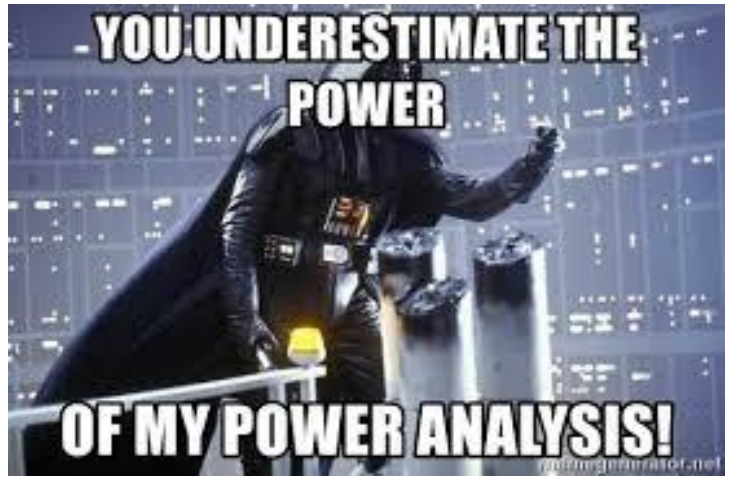
Power Analysis for each Aim

- The effect size you want to obtain will be based on previous literature that tested something similar!!!
  - Effect sizes reported in papers could be: eta-squared (η^2), partial eta-squared (η^2_p), Pearson's correlation (r), Cohen's d, Hedge's g, or R^2
  - Even if the paper did not report an effect size, you can calculate it if the paper reports the means and standard deviations per group

- Explain what software (e.g., G*Power, R) you used to figure out your sample size, given:
  - Alpha = .05
  - Power = .80
  - Effect size you want to get (e.g., Cohen's *d* = 0.5, which is a medium effect size)

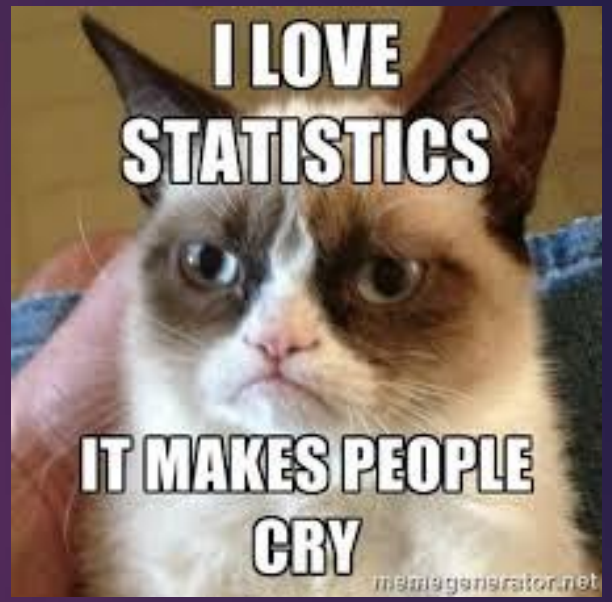
Power Analysis for each Aim

- This section is very important for your grant application!
- Ask your Primary Mentor/Mentorship Team for help
- LIBR IT has G*Power that can be installed on your computer
- There are G*Power manuals and tutorials online
- Here are some links to help you calculate power:
  - https://osf.io/ixgcd/
  - https://psyarxiv.com/vxfbh/



Statistical Analysis for each Aim

- What statistics program will you use to analyze your data?
- Restate each hypothesis
- Explain what test you will use to evaluate each hypothesis
  - Example: Mixed ANOVA with (1) group (depressed vs. control) as the between-subjects variable, (2) condition as the within-subjects variable (no win, small win, large win) and (3) striatum activation as the dependent variable
  - What the outcome of interest is (e.g., is it a group*condition interaction?)
- In addition to test statistics (e.g., if ANOVA, then F, degrees of freedom, and p values), what other statistics will you report?
  - Effect sizes (say what measure you will use, e.g., Cohen's *d*)
  - 95% confidence intervals
  - Explain when you will do post-hoc tests (e.g., overall ANOVA group*condition $p < .05$)
  - How will you correct for familywise error / multiple comparisons?



Potential Sources of Biological Variation

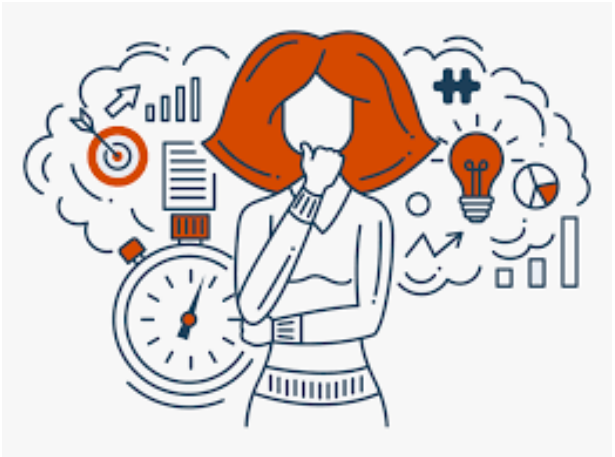
- Here is where you need to justify:
  - What age range you are using for your study
  - Whether or not you will have enough statistical power to compare your results between males and females (biological sex)
  - Whether or not you will have enough statistical power to compare your results between races/ethnicities, and if so, which ones
  - Any other biological differences that could be relevant to your study

Expected Outcomes

- The ideal scenario if everything works out as you hypothesized
- You can take this from **Specific Aims** and expand on it
- ~2 sentences explaining the payoff Reviewers can expect to get if they vote to recommend funding for your project
- There should be at least one expected outcome for each Aim and they should collectively relate to your overall grant objective outlined in **Specific Aims**

Potential Problems and Alternative Strategies

- Think of problems you might encounter with your study and steps you will take to overcome these problems
  - Examples:
    - Issues with recruitment (sites, Inclusion/Exclusion criteria)
    - Participant drop-out rates
    - Potential adverse/unexpected events
    - If you are testing feasibility of a task or intervention and it doesn't end up working, how will you use this knowledge to change your task or intervention?



Timeline and Benchmarks for Success

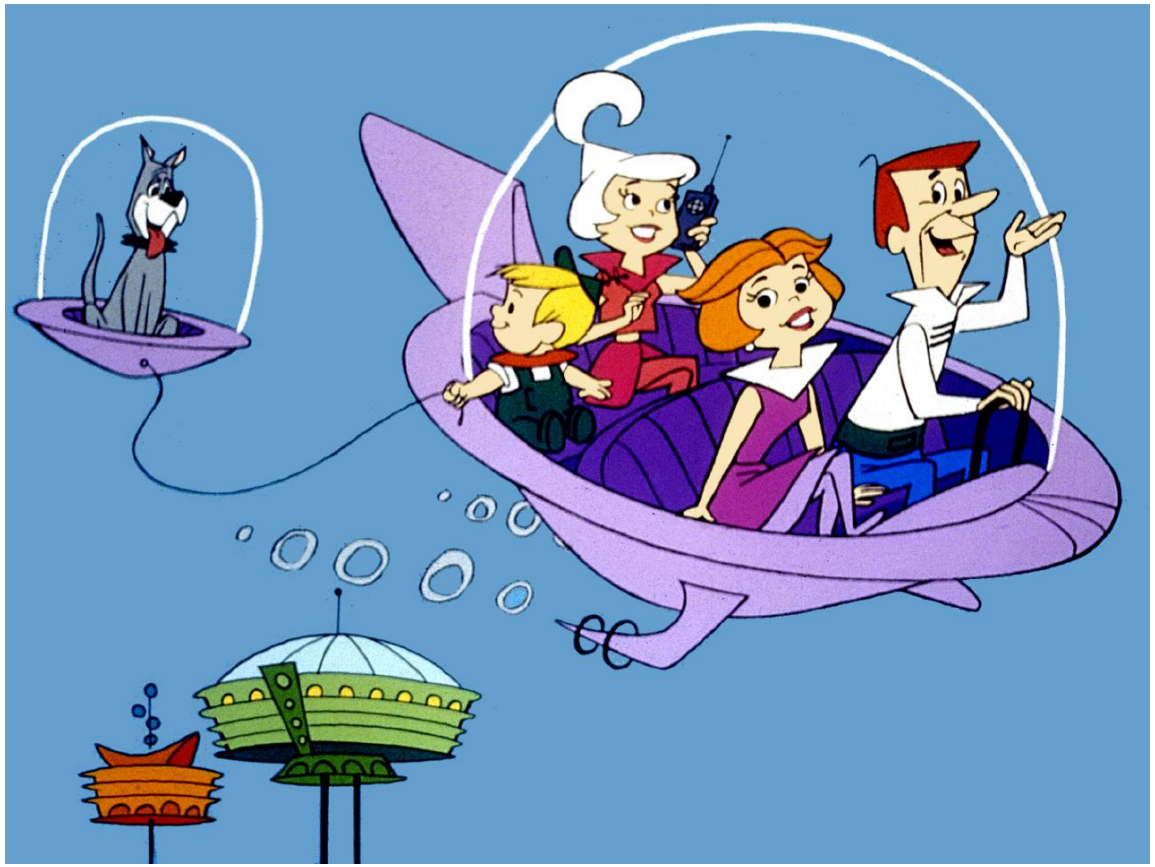
- Create a 5-year research timeline
- Outline # of subjects/month for recruitment (if collecting new data)
- If you have a longitudinal design, how many subjects completing those sessions per year
- When does data preprocessing/analysis happen
- If you are doing secondary data analysis for your entire K99/R00 project, you will need to be able to show why you need 5 years to analyze the data and write up the results

Study Timetable

Project activity	7/04–12/04	1/05–6/05	7/05–12/05	1/06–6/06	7/06–12/06	1/07–6/07	7/07–12/07	1/08–6/08	7/08–12/08	1/09–6/09
Study activity										
Interrater reliability/training	X	X	X	X	X					
Database setup	XX									
Patient enrollment	XX	XXX	XXX	XXX	XXX					
Data management	XX	XXX	XXX	XXX	XXX					
Data analysis, specific aim 1					XXX	XXX				
Manuscript preparation, aim 1						X	XX			
Data analysis, specific aim 2						XX	XXX	X		
Manuscript preparation, aim 2								XXX		
Data analysis, specific aim 3								XX	XXX	X
Manuscript preparation, aim 3									X	XXX

Future Directions

- Where are the outcomes of this project expected to lead?
- How will these outcomes separate your research from that of your **Primary Mentor**?



How am I going to fit this **Approach** section, the **Significance**, and **Innovation** into a SIX-page document?

- Right now, don't worry about the page limit
- Your Mentorship Team can help in cutting words later

Action Items

- Revise your **Significance** and **Innovation** sections based on **Primary Mentor** feedback
- Write a draft of your **Approach** and get feedback from your **Primary Mentor**