# Mixed Model Power Analysis By Example: Using Free Web-Based Power Software

#### Deborah H. Glueck, Ph.D. and Aarti Munjal, Ph.D

Department of Biostatistics and Bioinformatics, Colorado School of Public Health, University of Colorado Denver

#### Co-authors

- $\Box$  Dr. S. M. Kreidler, DPT, MS<sup>1</sup>
- $\Box$  Dr. K. E. Muller, PhD<sup>2</sup>
- $\Box \quad Dr. Y. Guo, PhD^2$
- $\Box$  Dr. A. E. Barón, PhD<sup>1</sup>
- $\square$  Ms. U. R. Sakhadeo<sup>1</sup>

<sup>1</sup> Department of Biostatistics and Bioinformatics, Colorado School of Public Health, University of Colorado Denver.

<sup>2</sup> Health Outcomes and Policy, College of Medicine, University of Florida.

### Contributors

□ Ms. Brandy Ringham<sup>1</sup>

#### $\Box$ M. M. Maldonado-Molina, PhD, MS<sup>2</sup>

<sup>1</sup> Department of Biostatistics and Bioinformatics, Colorado School of Public Health, University of Colorado Denver.

<sup>2</sup> Health Outcomes and Policy, Institute for Child Health Policy, University of Florida.

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# Session Outline

Introduction Dr. Deb Glueck	1:45 – 1:50
Foundations of Power and Sample Size for the General Linear Mixed Model Dr. Deb Glueck	1:50 – 2:20
Break and Questions	2:20 - 2:30
Mixed Model Power Analysis By Example: Using Free Web-Based Power Software Dr. Aarti Munjal	2:30 - 3:10
Wrapping it Up: Writing the Grant Dr. Deb Glueck	3:10 - 3:20
Discussion: Question and Answer	3:20 - 3:30

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#### The Sample Size Problem

- □ Every study requires an accurate sample size calculation.
- If sample size is too large, participants are exposed to unnecessary risk.
- □ If sample size is too small, the study may have insufficient power.
- □ It is important to match power and sample size analysis to data analysis.
- Repeated measures and multilevel features make power and sample size analysis more challenging.
- □ Not all studies have a dedicated statistician to assist with design.

#### Power for the Linear Mixed Model

- □ No general power methods exist for mixed models.
- Extensive power methods exist for the general linear multivariate model.
- □ Can we use existing results in the linear mixed model?
- **u** How would we implement the methods in day-to-day practice?

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# Foundations of Power and Sample Size

#### Agenda

- □ Introduce two real world examples.
- □ Identify important design features related to power.
- Review power and sample size methods for the general linear multivariate model.
- □ Apply the methods to "reversible" mixed models.

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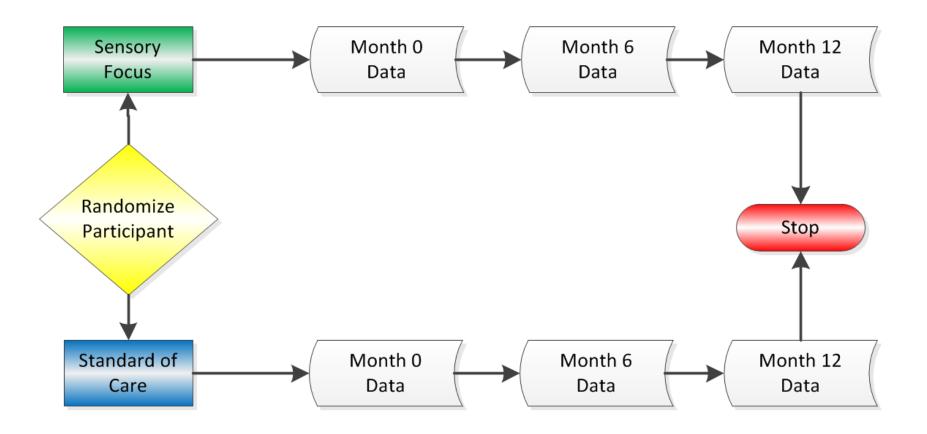
### Two Real World Examples

- Memory of Pain Trial: Sample size for proposed repeated measures study comparing a sensory focus intervention against placebo with regard to long-term memory of dental pain (Logan et al., 1995).
- Project Northland Chicago (PNC) Trial: Power for a proposed longitudinal, community-randomized trial testing an intervention for the prevention of alcohol use in adolescents (Komro et al., 2007).

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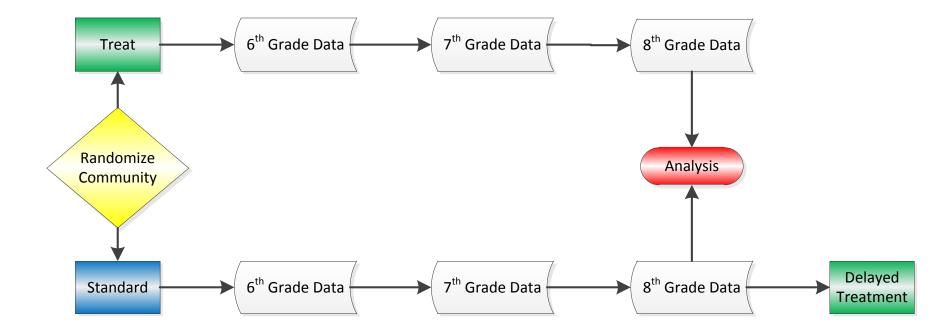
### Study Design: Memory of Pain Trial



### Two Real World Examples

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### Study Design: The PNC Trial



# Foundations of Power and Sample Size

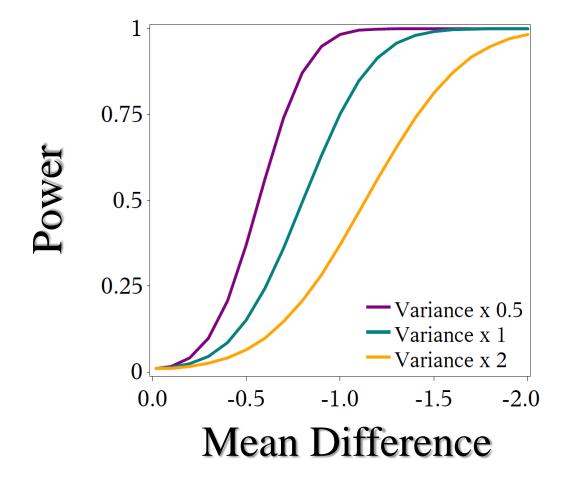
#### Agenda

□ Introduce two real world examples.

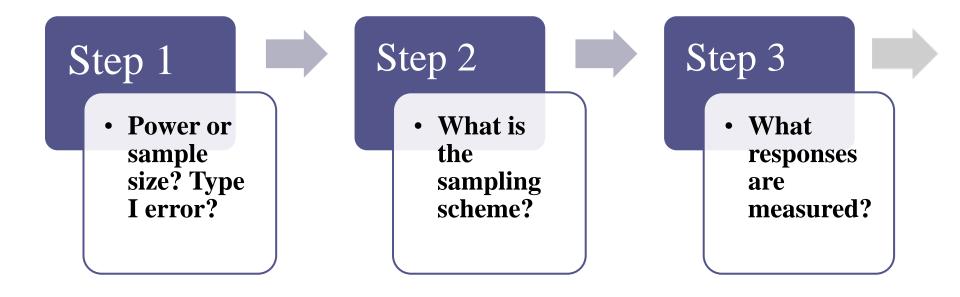
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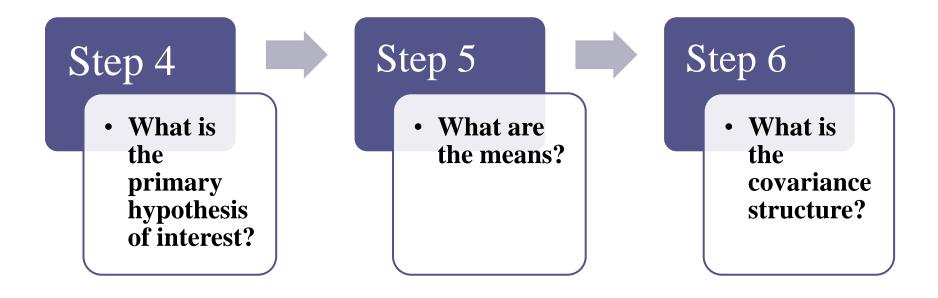
# What features of the design affect power?



### Checklist for Power and Sample Size Analysis



### Checklist for Power and Sample Size Analysis



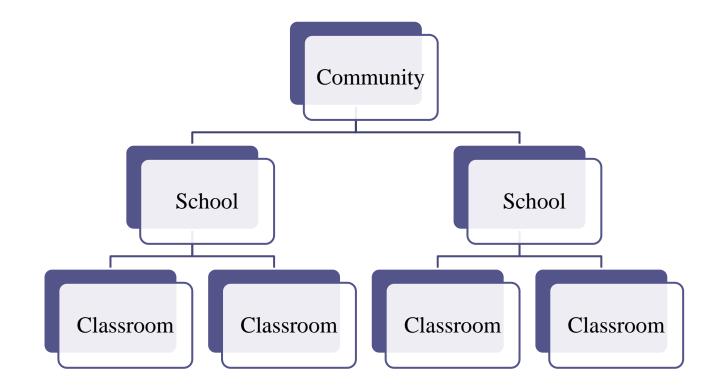
### Step 1: What is the study design goal?

□ Are you solving for power or sample size?

- ➤ If power, what is the available sample size?
- ➤ If sample size, what is the desired power?
- □ What is the desired Type I Error rate?

Step 2: What is the sampling scheme?

#### □ Identify the independent sampling unit



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Step 2: What is the sampling scheme?

□ Identify predictors for each independent sampling unit.

One-sample



Two-sample

Multi-sample

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### Step 2: Other sampling scheme details

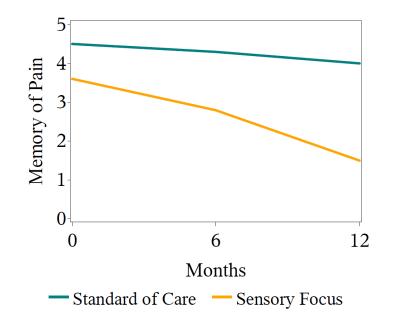
□ Are the group sizes equal or unequal?

□ Are all predictors known as part of the study design?

Step 3: What responses are measured?

□ What are the outcome variables?

□ How often is each outcome variable measured?



#### Step 4: What is the primary hypothesis of interest?

- Does the investigator wish to test a main effect, a trend, an interaction, or compare against a known mean?
- □ What between participant factors are included in the hypothesis?
- □ What within participant factors are included in the hypothesis?

### Step 5: What are the means?

- □ In power analysis, we have not yet observed the experiment, so we do not know the means.
- Reasonable choices for means can be obtained from the literature or pilot data.
- □ Means should present a "clinically meaningful" difference.

### Step 6: What is the covariance structure?

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□ Identify the sources of correlation

➤ Clustering

➢ Repeated measures

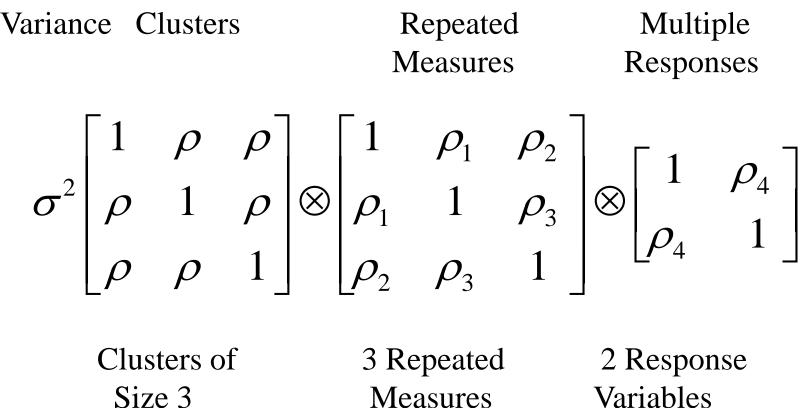
> Multiple outcome variables

#### Step 6: What is the covariance structure?

□ Select a covariance structure for each "source" of correlation

- ➢ Unstructured
- ≻ AR(1)
- Linear Exponent AR(1) (LEAR) (Simpson et al. 2010)

# Step 6: Build the Full Covariance Structure



Variables

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# Foundations of Power and Sample Size

#### Agenda

- □ Introduce two real world examples.
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 Review power and sample size methods for the general linear multivariate model.

□ Apply the methods to "reversible" mixed models.

### Power and Sample Size for the General Linear Multivariate Model

# □ The general linear multivariate model (GLMM)

 $Y = X B_{(N \times p)} B + E_{(N \times p)} B_{(q \times p)} + E_{(N \times p)}$ 

□ The general linear hypothesis

 $\Theta = CBU$ 

 $H_0: \boldsymbol{\Theta} = \boldsymbol{\Theta}_0$ 

### Power and Sample Size for the General Linear Multivariate Model

- Power and sample size theory developed over the past 30 years by Dr. Keith Muller and colleagues.
- □ No uniformly most powerful test.
- □ Under the null hypothesis: central F distributions.
- □ Under the alternative: non-central F distributions.

# Power for Fixed Designs

- Specify the Type I error rate, design matrix, contrast matrices, choices for means and covariance, null hypothesis matrix, and the test.
- □ Obtain critical value from a central F distribution.
- □ Calculate the non-centrality parameter.
- □ Calculate power using a non-central F distribution.

# Power for Designs with a Gaussian Covariate

□ Specify input matrices, the test, plus the following:

- Covariance of the outcomes.
- Covariance of the Gaussian covariate.
- Covariance between the outcomes and the covariate.
- □ Obtain critical value from central F distribution.
- Determine noncentrality parameter using either unconditional or quantile method.
- □ Calculate power using a non-central F distribution.

# Foundations of Power and Sample Size

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## The Linear Mixed Model

- □ Described by Laird and Ware (1982).
- Commonly used to analyze data from multilevel and longitudinal designs.
- □ Includes fixed effects for the mean.
- □ Includes random effects defining variability.

$$oldsymbol{y}_i = oldsymbol{X}_ioldsymbol{eta}_i + oldsymbol{Z}_ioldsymbol{d}_i + oldsymbol{e}_i \ = oldsymbol{X}_ioldsymbol{eta}_{+i} \ = ext{fixed} + ext{random} \ oldsymbol{eta}_{+i} \ oldsymbol{ ext{fixed}}_i + ext{random} \ oldsymbol{eta}_{+i} \ oldsymbol{ ext{E}}(oldsymbol{y}_i) \ oldsymbol{ ext{T}}(oldsymbol{y}_i) \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{V}}(oldsymbol{y}_i) \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{T}}(oldsymbol{ ext{J}}_i) \ oldsymbol{ ext{T}}(oldsymbol{ ext{J}}_i) \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{T}}(oldsymbol{y}_i) \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{T}}(oldsymbol{ ext{J}}_i) \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{T}}(oldsymbol{ ext{T}}_i) \ oldsymbol{ ext{T}}(oldsymbol{ ext{J}}_i) \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{model}}_i \ oldsymbol{ ext{T}}(oldsymbol{ ext{T}}_i) \ oldsymbol{ ext{model}}_i \ oldsy$$

## Possible Hypothesis Tests for the Mixed Model

- A) Power for testing fixed effects (means).
- B) Power for testing random effects (covariance).
- C) Power for testing fixed and random effects.

General and accurate power and sample size methodology is not available.

There are, however, good methods for most of class A.

## Reversible Mixed Models

- Some mixed models and hypotheses can be transformed into an equivalent general linear multivariate model.
- □ We refer to such models and hypotheses as "reversible".
- Once an equivalent general linear model is obtained, existing power and sample size methods may be applied.

## Criteria for "Reversibility"

- □ Homoscedastic covariance.
- Applies the Wald test of fixed effects with Kenward-Roger denominator degrees of freedom.

## Criteria for "Reversibility"

- □ Balanced design within independent sampling unit
  - □ No repeated covariates
  - □ Saturated with regard to between-within effects
  - □ No missing or mistimed data
  - □ Treatment assignment constant over time
  - □ Factorial design, including time by treatment interaction

## Important Equivalence

### Under reversibility conditions,

#### **Reversible Mixed Model**

Wald test with Kenward-Roger denominator degrees of freedom

#### General Linear Multivariate Model

#### = | Hotelling-Lawley Trace test

## Model Equivalence

□ Two equivalent representations for the regression equation for subject *i*:

$$Y'_i = (X_{Mi} \otimes I_p) \operatorname{vec}(B') + E'_i$$
 Stacked Multivariate Model

$$\Leftrightarrow$$

$$m{y}_i = m{X}_{mi} m{eta} + m{e}_{+i}$$
 Population Average Mixed Model

where  $X_{Mi} \otimes I_p = X_{mi}$  and  $\operatorname{vec}(B') = \beta$ 

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## **Missing Data Adjustments**

- Some useful crude approximations (Catellier and Muller, 2000):
  - Complete data power is an upper bound.
  - Power for N = (100% % missing) x # ISUs appears conservative, requires assuming data are Missing at Random.

□ Work is in progress to identify better approximations.

# Summary

Under widely applicable restrictions a mixed model can be expressed as a General Linear Multivariate Model for which accurate power and sample size analysis is available. 45

- □ Answers to a series of simple questions can completely specify the inputs to a power analysis.
- □ Convenient adjustments appear to suffice for simple missing data patterns.
- □ Free software is now available to implement the methods.

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## Mixed Model Power Analysis By Example

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- □ Motivate the need for GLIMMPSE.
- □ Introduce the GLIMMPSE software.
- □ Present GLIMMPSE validation results.
- □ Example 1: The Memory of Pain trial.
- □ Example 2: The Project Northland Chicago (PNC) trial.

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## Motivate GLIMMPSE

- Power and sample size calculation is critical for ethical study design.
- □ Known results are underutilized.
- Our goal: provide a user-friendly tool for calculating power and sample size.

## Mixed Model Power Analysis By Example

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## What is GLIMMPSE?

## GLIMMPSE is a user-friendly online tool for calculating power and sample size for multilevel and longitudinal studies.

http://glimmpse.samplesizeshop.org/

## GLIMMPSE Team

### □ Software Development:

- Sarah Kreidler, Tech Lead
- > Aarti Munjal, Senior Software Engineer
- > Uttara Sakhadeo, Software Engineer

### □ Manual Preparation:

- Zacchary Coker-Dukowitz
- > Brandy Ringham
- > Yi Guo

## Why a Web-based Interface?

#### □ Free

### □ Requires no programming expertise.

□ Built with industry standard Java technology.

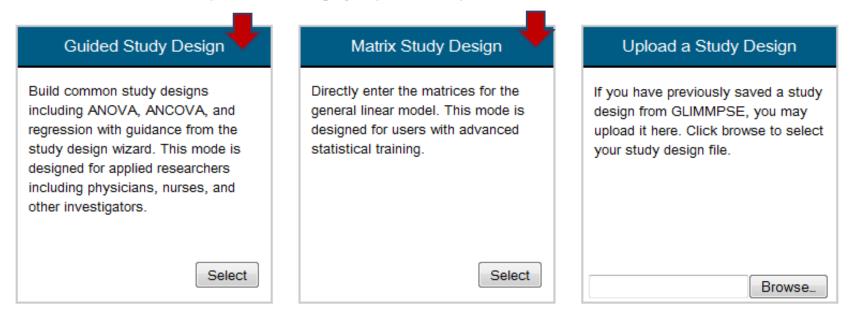
## **GLIMMPSE** Salient Features

- □ Web-based
- □ Free and open-source
- □ Designed with an intuitive wizard input style
- □ Able to produce power curves
- □ Able to export power results
- □ Able to save study designs for later use

# **Two Interaction Modes**

#### Start Your Study Design

Welcome to GLIMMPSE. The GLIMMPSE software calculates powerand sample size for study designs with normally distributed outcomes. Select one of the options below to begin your power or sample size calculation.



# Supported Study Designs

□ Cross-sectional studies

Longitudinal designs

□ Multilevel designs

□ Designs with a baseline covariate

## **Related Publications**

### □ GLMM with fixed predictors

- > Muller and Peterson, 1984
- > Muller and Barton, 1989
- ➢ Muller *et al.*, 1992
- ➢ Muller *et al.*, 2007
- □ GLMM with fixed predictors and a Gaussian covariate
  - Glueck and Muller, 2003

## **Current GLIMMPSE Limitations**

- □ Binary or count data
- □ Adjustments for missing data
- □ Sample size based on confidence interval width
- □ Very high dimensional, low sample size designs
- □ Certain classes of mixed models

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# Validation

### □ Validated against published results and simulation.

### □ Full validation results are available online.

http://samplesizeshop.org/documentation/glimmpsevalidation-results/

# Validation Results

- □ 6 decimal accuracy against published results.
- □ 2 decimal accuracy against simulation.
- □ Worst case error in 1<sup>st</sup> decimal for complex multivariate designs.

## Mixed Model Power Analysis By Example

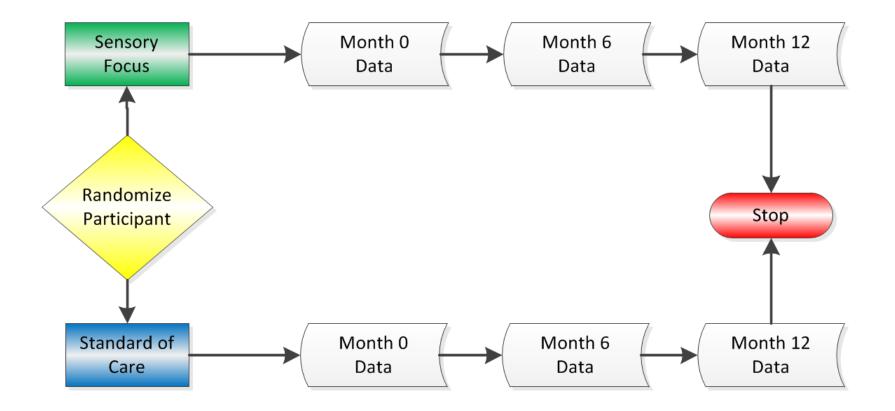
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## Memory of Pain Trial Study Design



1. Solving for:

Sample size

- 2. Desired power:
- 3. Type I error rate:

1. Solving for:

Sample size

2. Desired power:

0.90

3. Type I error rate:

1. Solving for:

Sample size

- 2. Desired power:
- 3. Type I error rate:

0.90

0.01

4. Outcome:

memory of pain

5. Predictor:

6. Hypothesis:

4. Outcome:

memory of pain

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5. Predictor:

treatment group

6. Hypothesis:

4. Outcome:

memory of pain

5. Predictor:

treatment group

6. Hypothesis:

time by treatment interaction

# Sample Size Calculation

#### Start Your Study Design

Select one of the options below to begin your power or sample size estimate.

Select

#### Guided Study Design

Build common study designs including ANOVA, ANCOVA, and regression with guidance from the study design wizard. This mode is designed for more applied researchers including physicians, nurses, and other principal investigators.

#### Matrix Study Design

Directly enter the matrices for the general linear model. This mode is designed for users with advanced statistical training.

Select

#### Upload a Study Design

If you have previously saved a study design from GLIMMPSE, you may upload it here. Click browse to select your study design file.

Browse...

# **GLIMMPSE** Solving For



#### Would you like to solve for power or sample size?

To begin your calculation, please indicate whether you would like to solve for power or total sample size.

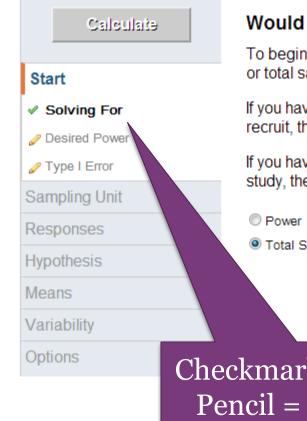
If you have a rough idea of the number of research participants you will be able to recruit, then solving for power may be more beneficial.

If you have fewer restrictions on recruitment and would like to ensure a well-powered study, then solving for sample size is likely to be more useful.

Power

Total Sample Size

# **GLIMMPSE** Solving For



#### Would you like to solve for power or sample size?

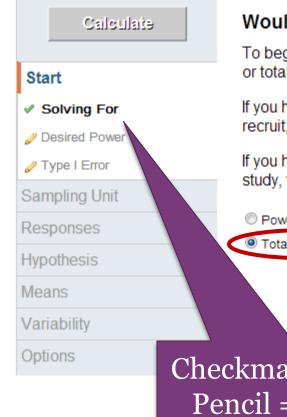
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Total Sample Size
 Checkmark = complete
 Pencil = incomplete

## **GLIMMPSE** Solving For

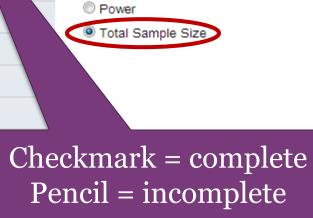


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### **GLIMMPSE** Desired Power

#### **Power Values**

Enter the desired power values in the list box below. Power values are numbers between 0 and 1. Higher values correspond to a greater likelihood of rejecting the null hypothesis. Common values are 0.8 or 0.9, although 0.9 or higher is usually preferred.

Type each value into the list box and click "Add". To remove an item, highlight the value and click the "Delete" button.

Power Values:	Add Delete	
0.9		*
		Ŧ

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# GLIMMPSE Type I Error Rate

#### Type I Error

A Type I error occurs when a scientist declares a difference when none is actually present. The Type I error rate is the probability of a Type I error occurring, and is often referred to as  $\alpha$ . Type I error rates range from 0 to 1. The most commonly used values are 0.01, 0.05, and 0.1.

Enter each Type I error value into the text box and click "Add". You may enter up to 5 values. To remove a value, select the value in the list box and click the "Delete" button.

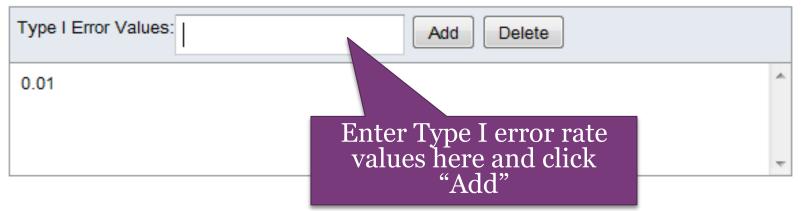
Type I Error Values:	Add Delete
0.01	*
	-

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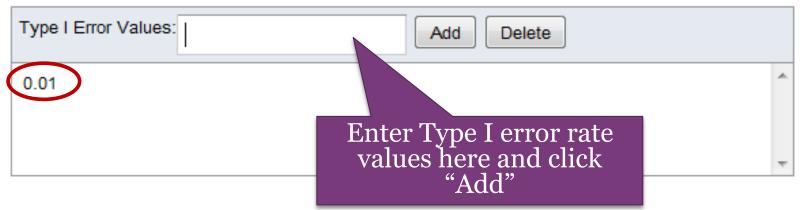


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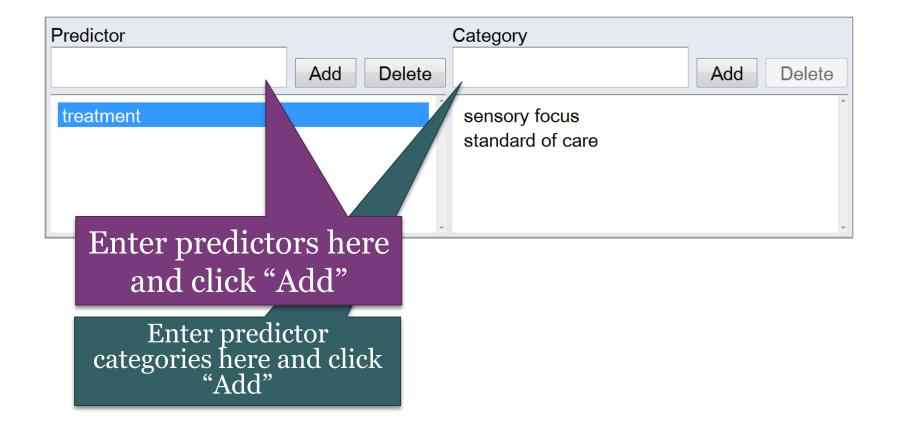
## **GLIMMPSE** Predictors

Predictor	1		Category	
	Add	Delete		Add Delete
treatment			sensory focus standard of care	

## **GLIMMPSE** Predictors

Predictor	_	Category	
	Add Delete		Add Delete
treatment		sensory focus standard of care	*
Enter predict and click "			

### **GLIMMPSE** Predictors



### GLIMMPSE Outcome

#### **Response Variables**

Enter the response variables in the table below. For example, in a study investigating cholesterol-lowering medication, the response variable could be HDL, LDL, and total cholesterol.

Note that repeated measurement information will be addressed on the next screen.

Response Variables:	Add Delete
memory of pain	*
	~

### GLIMMPSE Outcome

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Response Variables:	Add Delete	
memory of pain		*
		Ŧ
	Enter outcomes here	
	and click "Add"	

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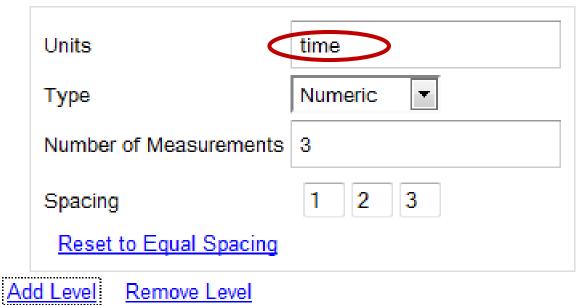
## **GLIMMPSE** Repeated Measures

#### Remove Repeated Measures

	Units	time
	Туре	Numeric 💌
	Number of Measurements	3
	Spacing	1 2 3
	Reset to Equal Spacing	
١d	d Level Remove Level	

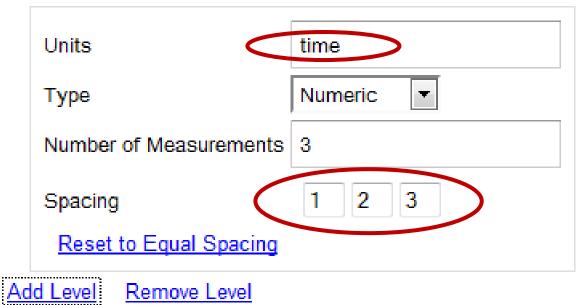
### **GLIMMPSE** Repeated Measures

#### Remove Repeated Measures



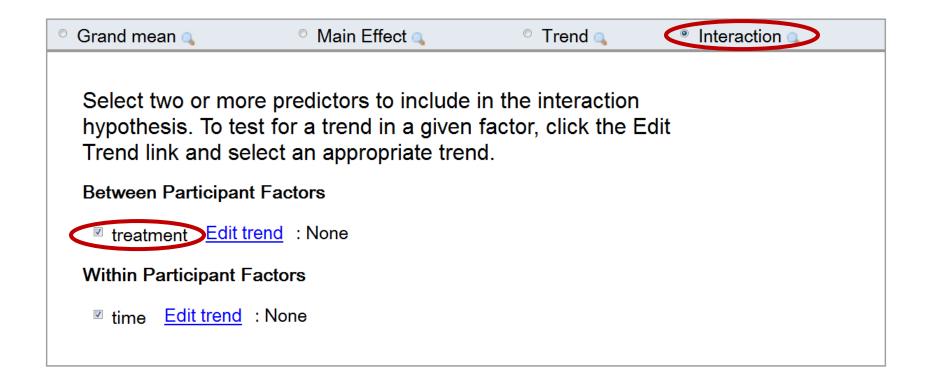
### **GLIMMPSE** Repeated Measures

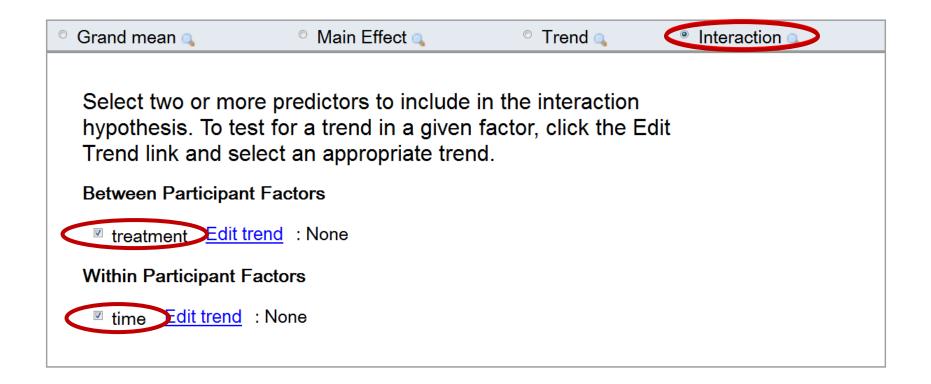
#### Remove Repeated Measures



$^{\circ}$ Grand mean 🔍	° Main Effect 🔍	Trend	Interaction
Select two or more predictors to include in the interaction hypothesis. To test for a trend in a given factor, click the Edit Trend link and select an appropriate trend.			
Between Participant Factors			
<sup>III</sup> treatment <u>Edit trend</u> : None			
Within Participant Factors			
<sup>III</sup> time <u>Edit trend</u> : None			

$^{\circ}$ Grand mean 🔍	° Main Effect 👞	Trend	Interaction			
	Select two or more predictors to include in the interaction					
hypothesis. To test for a trend in a given factor, click the Edit Trend link and select an appropriate trend.						
Between Participant Factors						
<sup>III</sup> treatment <u>Edit trend</u> : None						
Within Participant Factors						
<sup></sup> time <u>Edit trend</u>	: None					





#### GLIMMPSE Means Specifying a Mean Difference

treatment	memory of pain
sensory focus	-1.2
standard of care	0

Select the time (location, etc.) from the list(s) below. This will allow you to edit the means at the selected time (location, etc.).



#### GLIMMPSE Means Specifying a Mean Difference

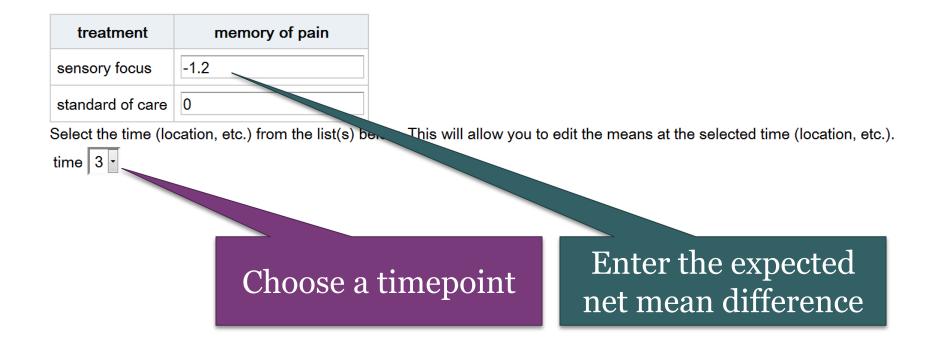
treatment	memory of pain
sensory focus	-1.2
standard of care	0

Select the time (location, etc.) from the list(s) below. This will allow you to edit the means at the selected time (location, etc.).



#### Choose a timepoint

#### GLIMMPSE Means Specifying a Mean Difference



#### GLIMMPSE Variability Entering Standard Deviation of the Outcome

time	Responses	

Enter the standard deviation you expect to observe for each response. Note that GLIMMPSE currently assumes that the standard deviation is constant across repeated measurements.

#### GLIMMPSE Variability Specifying Correlations



Enter the standard deviation you expect to observe for each response. Note that GLIMMPSE currently assumes that the standard deviation is constant across repeated measurements.

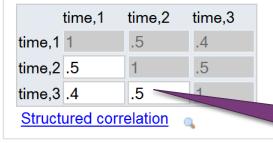
memory of pain 0.98

Enter standard deviation of the outcome variable

#### GLIMMPSE Variability Specifying Correlations



Enter the correlations you expect to observe among the repeated measurements.



Enter correlations between repeated measures

# GLIMMPSE Hypothesis Test

#### **Statistical Tests**

Select the statistical tests to include in your calculations. For study designs with a single outcome, power is the same regardless of the test selected.

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- Pillai-Bartlett Trace
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- Univariate Approach to Repeated Measures with Box Correction
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- Univariate Approach to Repeated Measures, uncorrected

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- Univariate Approach to Repeated Measures, uncorrected

# **GLIMMPSE** Calculate Button

### Calculate

#### **Power Results**

Power	Total Sample Size	Target Power	Test	Type I Error Rate	Means Scale Factor	Variability Scale Fac
0.901	44	0.900	HLT	0.01	1	1
0.925	26	0.900	HLT	0.01	1	0.5
0.905	84	0.900	HLT	0.01	1	2
4				111		>

Save to CSV View Matrices

#### **Power Results**

Power	Total Sample Size	Target Power	Test	Type I Error Rate	Means Scale Factor	Variability Scale Fac
0.901	44	0.900	HLT	0.01	1	1
0.925	26	0.900	HLT	0.01	1	0.5
0.905	84	0.900	HLT	0.01	1	2
4						•

Save to CSV View Matrix

Total sample size to achieve at least 90% power

#### **Power Results**

Power	Total Sample Size	Target Power	Test	Type I Error Rate	Means Scale Factor	Variability Scale Fac	
0.901	44	0.900	HLT	0.01	1	1	
0.925	26	0.900	HLT	0.01	1	0.5	
0.905	84	0.900	HLT	0.01	1	2	
Save to CSV View Matrices Scale variance to ½ and 2 times to see how it affects sample size Total sample size to achieve at least 90% power							

105

#### **Power Results**

Power	Total Sample Size	Target Power	Test	Type I Error Rate	Means Scale Factor	Variability Scale Fac		
0.901	44	0.900	HLT	0.01	1	1		
0.925	26	0.900	HLT	0.01	1	0.5		
0.905	84	0.900	HLT	0.01	1	2		
Save to CSV View Matrices Scale variance to ½ and 2 times to see how it affects sample size Total sample size to achieve at least 90% power								

## Sample Size Calculation Summary

We plan a <u>repeated measures ANOVA</u> using the <u>Hotelling-</u> <u>Lawley Trace</u> to test for a <u>time by treatment interaction</u>. Based on previous studies, we predict measures of pain recall will have a variance of 0.96. The correlation in pain recall between baseline and 6 months will be <u>0.5</u>. Based on clinical experience, we predict that the correlation will decrease slowly over time. Thus, we anticipate a correlation of 0.4 between pain recall measures at baseline and 12 months. For a desired power of <u>0.90</u> and a Type I error rate of 0.01, we need to enroll 44 participants to detect a mean difference of 1.2.

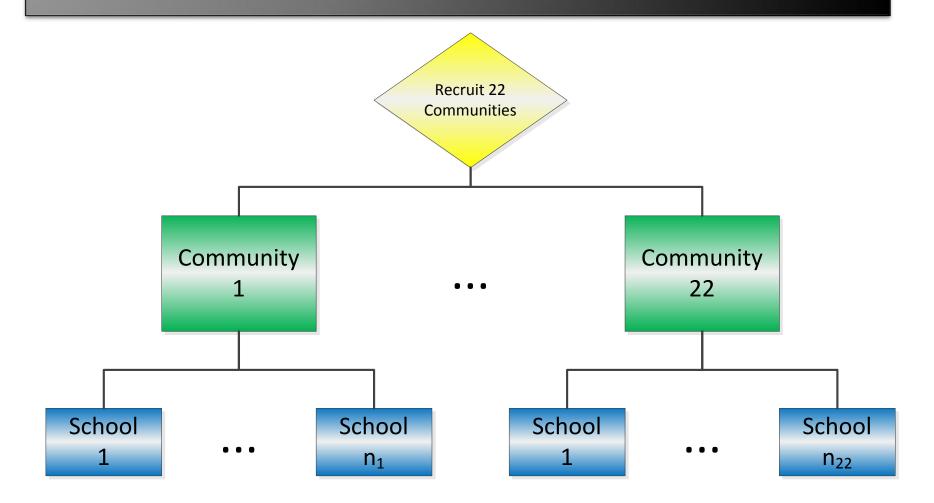
#### Mixed Model Power Analysis By Example

#### Agenda

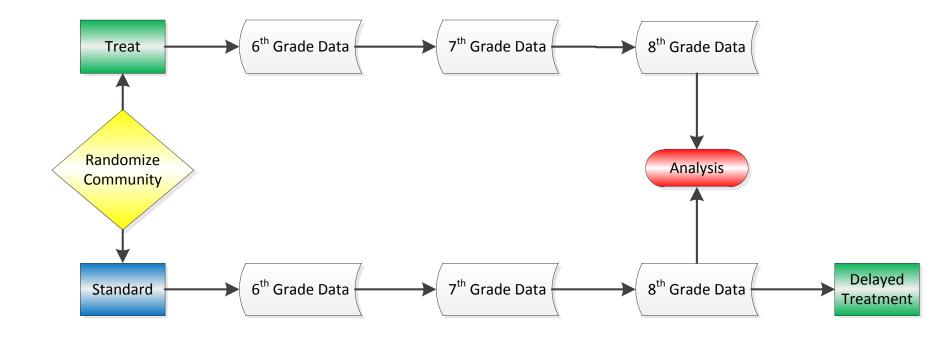
- □ Motivate the need for GLIMMPSE
- □ Introduce the GLIMMPSE software
- □ Present GLIMMPSE validation results
- □ Example 1: The Memory of Pain trial

#### **Characterization** Example 2: The Project Northland Chicago (PNC) trial

### The PNC Trial: Cluster Randomized Design



### The PNC Trial: Cluster Randomized Design



1. Solving for:

Power

- 2. Type I error rate:
- 3. Clustering

- 1. Solving for:
- 2. Type I error rate:
- 3. Clustering

Power

0.05

- 1. Solving for:
- 2. Type I error rate:
- 3. Clustering:

Power

0.05

By Community

114

2

- 4. Treatment Groups:
- 5. Covariates:
- 6. Communities:

115

2

None

4. Treatment Groups:

5. Covariates:

6. Communities:

- 4. Treatment Groups:
- 5. Covariates:
- 6. Communities:

None

2

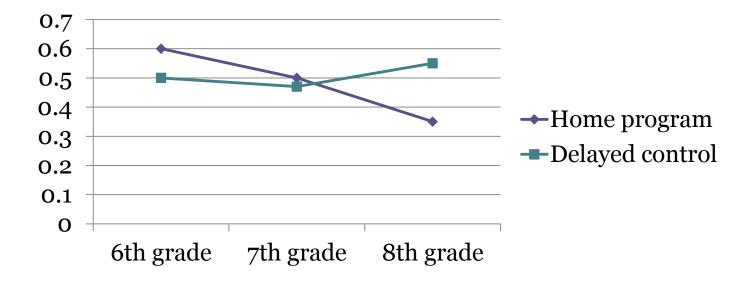
2, 3, ..., 10

### PNC Trial: What are the responses?

- □ What responses are measured?
  - Response variable: alcohol behavior scale.
- □ How often are the responses measured?
  - > 3 repeated measures in  $6^{\text{th}}$ ,  $7^{\text{th}}$ , and  $8^{\text{th}}$  grade.

# PNC Trial: What is the primary hypothesis of interest?

#### Time trend by treatment interaction



### PNC Trial: What are the means?

- We wish to detect a reduction in alcohol use in the treatment group in 8<sup>th</sup> grade
- □ A reduction of 0.25 on the alcohol behavior scale is considered clinically meaningful.

### PNC Trial: What is the variance structure?

### • Correlation due to clustering and repeated measures

- Cluster size: 10
- Standard deviation of alcohol behavior scale: 0.3
- □ Patterns of variability
  - > Clustering
    - Compound symmetry
    - ✤ Inter-class correlation: 0.01
  - Repeated Measures:
    - Correlation 1 year apart: 0.3
    - Decay rate: 0.3

### Power with GLIMMPSE

#### Start Your Study Design

Select one of the options below to begin your power or sample size estimate.

#### Guided Study Design

Build common study designs including ANOVA, ANCOVA, and regression with guidance from the study design wizard. This mode is designed for more applied researchers including physicians, nurses, and other principal investigators.

Select

#### Matrix Study Design

Directly enter the matrices for the general linear model. This mode is designed for users with advanced statistical training.

#### Upload a Study Design

If you have previously saved a study design from GLIMMPSE, you may upload it here. Click browse to select your study design file.

#### Select Guided Mode

Browse...

## **GLIMMPSE** Solving For

#### Would you like to solve for power or sample size?

To begin your calculation, please indicate whether you would like to solve for power or total sample size. 122

If you have a rough idea of the number of research participants you will be able to recruit, then solving for power may be more beneficial.

If you have fewer restrictions on recruitment and would like to ensure a well-powered study, then solving for sample size is likely to be more useful.



## GLIMMPSE Type I Error Rate

#### Type I Error

A Type I error occurs when a scientist declares a difference when none is actually present. The Type I error rate is the probability of a Type I error occurring, and is often referred to as  $\alpha$ . Type I error rates range from 0 to 1. The most commonly used values are 0.01, 0.05, and 0.1.

Enter each Type I error value into the text box and click "Add". You may enter up to 5 values. To remove a value, select the value in the list box and click the "Delete" button.

Type I Error Values:	Add Delete
0.05	*
	-

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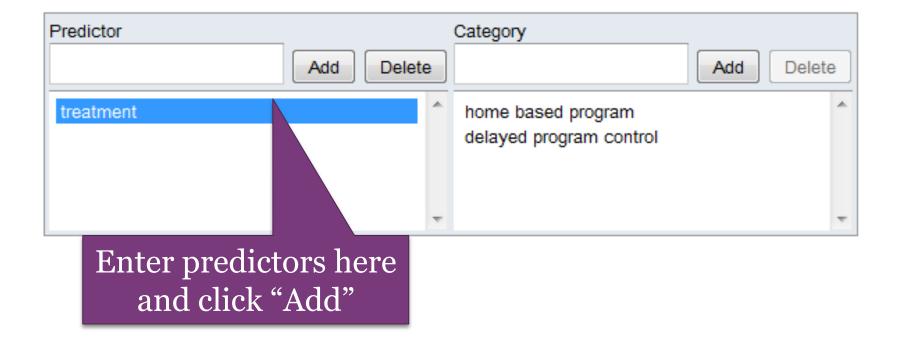
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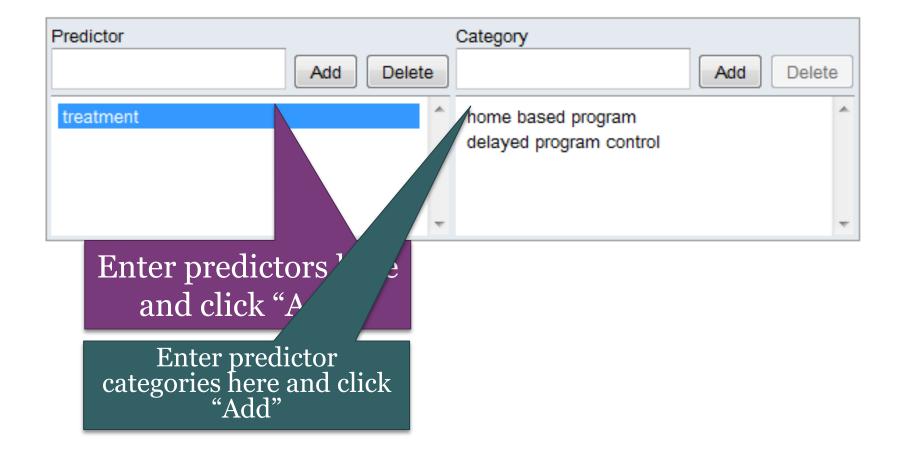
## **GLIMMPSE** Predictors

Predictor	Category		
Add Delete	Add Delete		
treatment	home based program delayed program control		
	r – – – – – – – – – – – – – – – – – – –		

### **GLIMMPSE** Predictors



### **GLIMMPSE** Predictors



### GLIMMPSE Clustering

#### Clustering

In a clustered design, the independent sampling unit is a cluster, such as a community, school, or classroom. Observations within a cluster are correlated. The labels for observations within a cluster must be exchangeable. For example, child "id" within classroom can be reassigned arbitrarily. In contrast, observations across time cannot be reassigned and should not be considered clustered observations. Clustering, or repeated measures, or a combination, creates a multilevel design. The common correlation between any pair of cluster members is termed the intraclass correlation or intracluster correlation.

To include clustering in the study, click "Add clustering" and follow the prompts. Use the "Remove clustering" button to remove clustering information.

Add clustering

### GLIMMPSE Clustering

#### Remove clustering

Cluster label community
Number of observations or sub-clusters
within each cluster of this type 10

Intra-cluster correlation

0.01

Add subgroup Remove subgroup

### GLIMMPSE Sample Size

#### Size of the Smallest Group

Enter the number of independent sampling units (participants, clusters) in the smallest group in the study. If your group sizes are equal, the value is the same for all groups. You may enter multiple values for the smallest group size in order to consider a range or total sample sizes.

Enter one or more sample sizes in the text box below and click "Add". To remove a sample size from the list, highlight it and click the "Delete" button.

Size of the Smallest Group:	Add Delete
2	A
3	=
4	
5	-

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Enter the number of independent sampling units (participants, clusters) in the smallest group in the study. If your group sizes are equal, the value is the same for all groups. You may enter multiple values for the smallest group size in order to consider a range or total sample sizes.

132

Enter one or more sample sizes in the text box below and click "Add". To remove a sample size from the list, highlight it and click the "Delete" button.



### GLIMMPSE Outcome

#### **Response Variables**

Enter the response variables in the table below. For example, in a study investigating cholesterol-lowering medication, the response variable could be HDL, LDL, and total cholesterol.

Note that repeated measurement information will be addressed on the next screen.

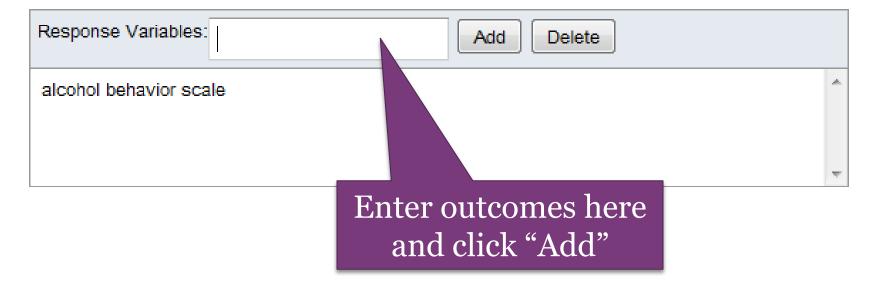
Response Variables:	Add Delete
alcohol behavior scale	*
	*

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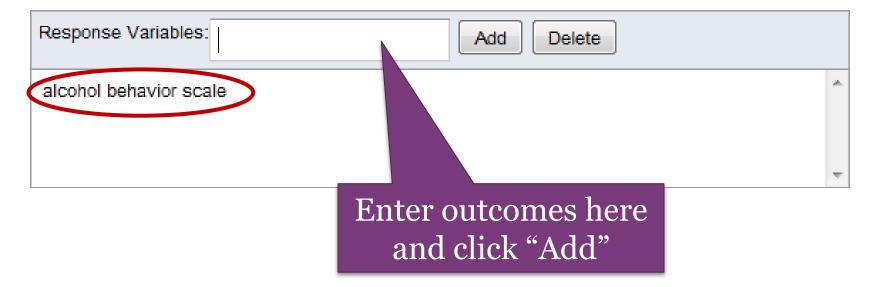


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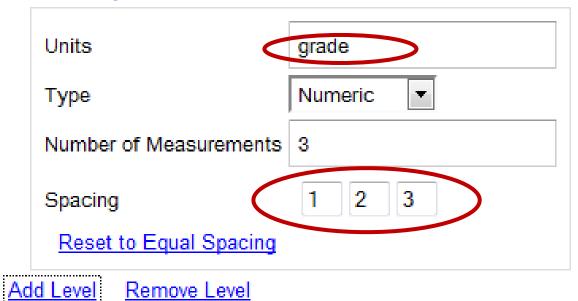
### **GLIMMPSE** Repeated Measures

#### Remove Repeated Measures

	Units	grade
	Туре	Numeric 💌
	Number of Measurements	3
	Spacing	1 2 3
	Reset to Equal Spacing	
Ad	d Level Remove Level	

### **GLIMMPSE** Repeated Measures

#### Remove Repeated Measures

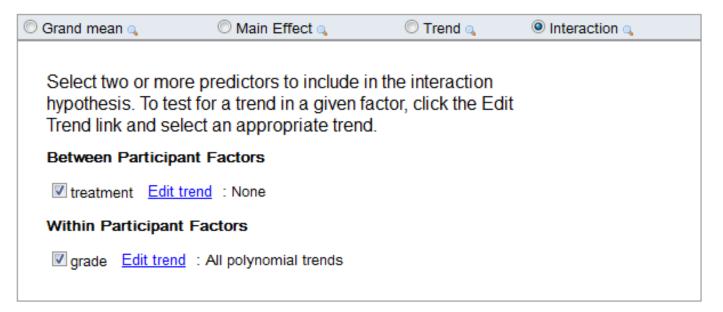


## GLIMMPSE Hypothesis

#### Hypotheses

The options below show the hypotheses which are available for the current study design. Select the hypothesis which most closely resembles your primary study hypothesis. This hypothesis will be used to determine power for your study.

To specify a hypothesis, select the radio button matching the type of hypothesis you wish to test, and then enter the requested details. Note that trends within an interaction hypothesis may be specified by selecting the "Interaction" button. For more information about the type of hypothesis, click the magnifying glass icon.

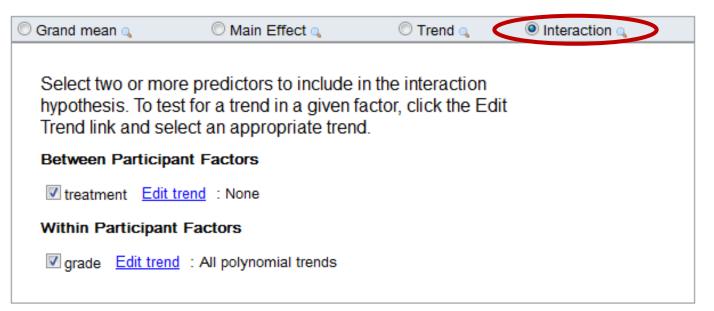


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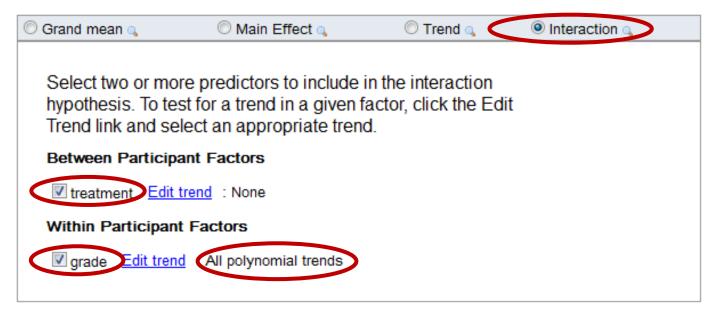


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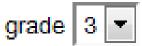
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### **GLIMMPSE** Means Specifying a Mean Difference

treatment	alcohol behavior scale		
home based program	-0.25		
delayed program control	0		

Select the time (location, etc.) from the list(s) below. This will etc.).





### GLIMMPSE Means Specifying a Mean Difference

treatment	alcohol behavior scale		
home based program	-0.25		
delayed program control	0		

Select the time (location, etc.) from the list(s) below. This will etc.).

grade 3 -Choose a timepoint

### GLIMMPSE Means Specifying a Mean Difference

treatment	alcohol behavior scale	
home based program	-0.25	
delayed program control		

Select the time (location, etc.) from the list(s) below. This will

etc.).

grade 3

Choose a timepoint

Enter the expected net mean difference

#### GLIMMPSE Variability Entering Standard Deviation of the Outcome

grade Responses

#### Structured Correlation: The Linear Exponential Auto-Regressive Model (LEAR, Simpson et al., 2010)

The LEAR model describes correlation which monotonely decreases with distance between repeated measurements. The model has two correlation parameters, the base correlation and the decay rate. The base correlation describes the correlation between measurements taken 1 unit apart. The decay rate describes the rate of decrease in the base correlation as the distance or time between repeated measurements increases. Our experience with biological and behavioral data lead us to suggest using decay values between 0.05 and 0.5.

Base Correlation 🔍		0.3				
Decay Rate 🔍		0.3				
		grade,1	gra	ade,2	grade,3	
	grade,1	1.0	0.	3	0.209053	
	grade,2	0.3	1.	0	0.3	
	grade,3	0.209053	0.3	3	1.0	
Unstructured correla			<u>ation</u>	٩		

#### GLIMMPSE Variability Entering Standard Deviation of the Outcome

grade Responses

#### Structured Correa. (LEAR, Simpson et al.,

# Each tab represents a single "source" of correlation

#### Regressive Model

The LEAR model describes co

distance between repeated measurements. The model has two correlation parameters, the base correlation and the decay rate. The base correlation describes the correlation between measurements taken 1 unit apart. The decay rate describes the rate of decrease in the base correlation as the distance or time between repeated measurements increases. Our experience with biological and behavioral data lead us to suggest using decay values between 0.05 and 0.5.

Base Correlation 🔍			0.3	
Decay Rate 🔍		0.3		
	grade,1	gra	ade,2	grade,3
grade,1	1.0	0.	3	0.209053
grade,2	0.3	1.	0	0.3
grade,3	0.209053	0.3	3	1.0
Unstruc	tured cor	<u>ation</u>	٩	

# GLIMMPSE Variability

Entering the correlation across repeated measurements

grade Responses

#### Structured Corrector (LEAR, Simpson Co

The LEAR model describes co distance between repeated measure parameters, the base correlation describes the correlation between rate describes the rate of decre time between repeated measu and behavioral data lead us to

Base Correlation 🔍		0.3				
Decay Rate 🔍			0.3			
		grade,1	gra	ade,2	grade,3	
	grade,1	1.0	0.:	3	0.209053	
	grade,2	0.3	1.(	0	0.3	
	grade,3	0.209053	0.3	3	1.0	
Unstructured correlation				٩		

Each tab represents a single "source" of correlation

model has two correlation

Regressive Model

Select the "grade" tab to specify the correlation in alcohol use across grade levels

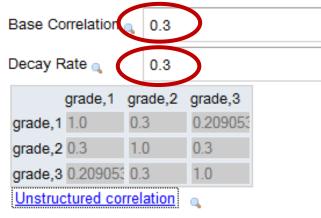
# GLIMMPSE Variability

Entering the correlation across repeated measurements

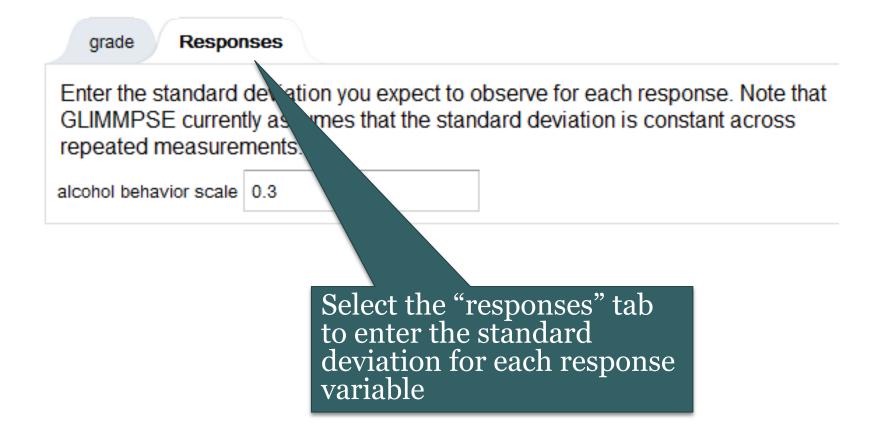
grade Responses

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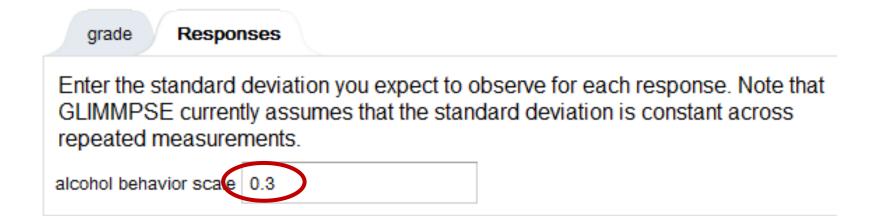
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# Entering Variability



### GLIMMPSE Variability Entering the standard deviation of the outcomes



# Checking a Range of Variability

#### Flexible Variability

On the previous screens, you entered standard deviations and correlations. GLIMMPSE has used these values to calculate a covariance matrix which describes the overall variability.

Changes in variability can dramatically affect power and sample size results. It is not possible to know the variability until the experiment is observed. To account for this uncertainty, it is common to calculate power or sample size for alternative values for variability.

By clicking the box below, GLIMMPSE will calculate power using the calculated covariance matrix, the covariance matrix divided by 2, and the covariance matrix multiplied by 2.

Yes, include power for the covariance matrix, the covariance matrix divided by 2, and the covariance matrix multiplied by 2.

# Selecting a Test

#### Statistical Tests

Select the statistical tests to include in your calculations. For study designs with a single outcome, power is the same regardless of the test selected.

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152

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  - Univariate Approach to Repeated Measures with Huynh-Feldt Correction
  - Univariate Approach to Repeated Measures, uncorrected

#### **Power Curve Options**

You may optionally create a power curve image for your results by unchecking this checkbox. Then select the values you would like to display on the power curve by selecting the appropriate options below.

•

I do not want to create a power curve.

1. Select the quantity to display on the horizontal axis of the power curve (the vertical axis will display the power value).

153

Total Sample Size

Add data series to the plot. Select values for each variable below. Click add to include sample size values matching these criteria as a data series on the plot. To remove a data series, highlight it in the list box and click "Remove data series".

Regression Coefficient Scale Factor	1
Variability Scale Factor	1
Statistical Test	Univariate Approach to Repeated Measures with Geisser-Greenhouse Correction
Type I Error	0.05 💌
Data Series Label	Power by Total N
Add Delete	
Power by Total N: T	est=Univariate Approach to Repeated Measures with Geisser-Greenhouse Correctic

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1. Select the quantity to display on the horizonta

Select the value displayed on the horizontal axis

Total Sample Size

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te power curve (th

Regression Coefficient Scale Factor	1 💌
Variability Scale Factor	
Statistical Test	Univariate Approach to Repeated Measures with Geisser-Greenhouse Correction
Type I Error	0.05 💌
Data Series Label	Power by Total N
Add Delete	
Power by Total N: T	est=Univariate Approach to Repeated Measures with Geisser-Greenhouse Correctic

#### **Power Curve Options**

checkbox. Then s selecting the app	elect the values you w ropriate options below			<u> </u>
Total Sample Size	to display on the honzon			
	the plot. Select values for	r each variable below. Click ad	ld to include sample size value	s matching
these criteria as a dat series".	ta series on the plot. To re	emove a data series, highlight	Then add oi	ne or more
Regression Coefficient Scale Factor	1		data series	to the plot
Variability Scale Factor	1			
Statistical Test	Univariate Approach to F	Repeated Measures with Geis:	ser-Greenhouse Correction 💌	
Type I Error	0.05 💌			
Data Series Label	Power by Total N			
Add Delete				
Power by Total N: T	est=Univariate Approach	to Repeated Measures with G	eisser-Greenhouse Correctic *	

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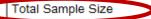
#### **Power Curve Options**

You may optionally create a power curve image for your results by unchecking this checkbox. Then select the values you would like to display on the power curve by selecting the appropriate options below.

•

I do not want to create a power curve.

1. Select the quantity to display on the horizontal axis of the power curve (the vertical axis will display the power value).



 Add data series to the plot. Select values for each variable below. Click add to include sample size values matching these criteria as a data series on the plot. To remove a data series, highlight it in the list box and click "Remove data series".

Regression Coefficient Scale Factor	1	
Variability Scale Factor		
Statistical Test	Univariate Approach to Repeated Measures with Geisser-Greenhouse Correction	
Type I Error	0.05 💌	
Data Series Label	Power by Total N	
Add Delete		
Power by Total N: T	est=Univariate Approach to Repeated Measures with Geisser-Greenhouse Correctic	>

# Results

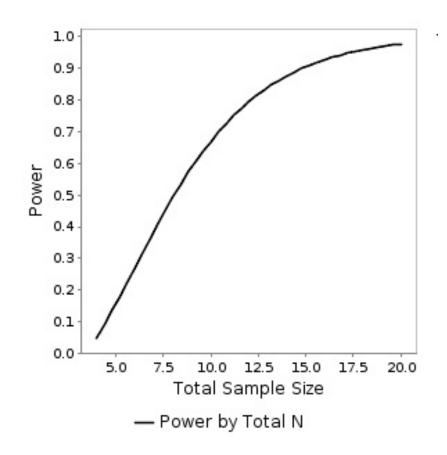
#### Power Results

Power	Total Sample Size	Test	Type I Error Rate	Means Scale Factor	Variability Scale Fact
0.206	6	HLT	0.05	1	1
0.485	8	HLT	0.05	1	1
0.722	10	HLT	0.05	1	1
0.867	12	HLT	0.05	1	1
0.942	14	HLT	0.05	1	1
0.976	16	HLT	0.05	1	1
0.991	18	HLT	0.05	1	1
0.997	20	HLT	0.05	1	1
4					

Save to CSV View Matrices

# Results

#### Power Curve



# Power Calculation Summary Draft

Ten communities were randomized to receive either the home based intervention or delayed intervention. Ten students were recruited from each community. The intracluster correlation within community was assumed to be 0.01. Correlation between repeated alcohol behavior scores within a student was assumed to be 0.3 for measures taken one year apart, with gradual decay over time. Power was calculated for a time by treatment interaction using the <u>Hotelling-Lawley trace test</u>. For a Type I error rate of 0.05, and an assumed standard deviation of 0.3 for alcohol behavior scores, the study had <u>97.7%</u> power to detect a difference of 0.25 in a time by treatment interaction.

# Summary

- Power and sample size calculations are a critical part of study design.
- □ Answers to basic questions about the study design can lead investigators to an appropriate sample size calculation.
- □ GLIMMPSE is a free, web-based tool to aid in calculating power or sample size for a variety of multilevel and longitudinal designs.

# Session Outline

Introduction Dr. Deb Glueck	1:45 – 1:50
Foundations of Power and Sample Size for the General Linear Mixed Model Dr. Deb Glueck	1:50 – 2:20
Break and Questions	2:20 - 2:30
Mixed Model Power Analysis By Example: Using Free Web-Based Power Software Dr. Aarti Munjal	2:30 - 3:10
Wrapping it Up: Writing the Grant Dr. Deb Glueck	3:10 - 3:20
Discussion: Question and Answer	3:20 - 3:30

### Outline Writing the Grant

- Aligning power analysis with data analysis
- Justifying the power analysis
- □ Accounting for uncertainty
- Handling missing data
- Demonstrating enrollment feasibility
- Planning for multiple aims

### Sample Size Calculation Summary

We plan a <u>repeated measures ANOVA</u> using the <u>Hotelling-Lawley Trace</u> to <u>test for a time by</u> <u>treatment interaction</u>.

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# Aligning Power Analysis with Data Analysis

- □ Type I error rate  $> \alpha = 0.01$
- Hypothesis test
   Wrong: power = treatment data analysis = time x treatment
   Right: power = time x treatment
  - data analysis = time x treatment

### Sample Size Calculation Summary

Based on previous studies, we predict memory of pain measures will have a standard deviation of 0.98 and the correlation between baseline and 6 months will be 0.5. Based on clinical experience, we believe the correlation will decrease slowly over time, for a correlation of 0.4 between pain recall measures at baseline and 12 months.

### Sample Size Calculation Summary

Based on previous studies, we predict memory of pain measures will have a <u>standard deviation of 0.98</u> and the correlation between baseline and 6 months will be 0.5. Based on clinical experience, we believe the correlation will decrease slowly over time, for a correlation of 0.4 between pain recall measures at baseline and 12 months.

# Justifying the Power Analysis

# □ Give all the values needed to recreate the power analysis.

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#### □ Provide appropriate citation.

### Sample Size Calculation Summary

For a desired power of 0.90 and a Type I error rate of 0.01, we estimated that we would need 44 participants to detect a mean difference of 1.2.

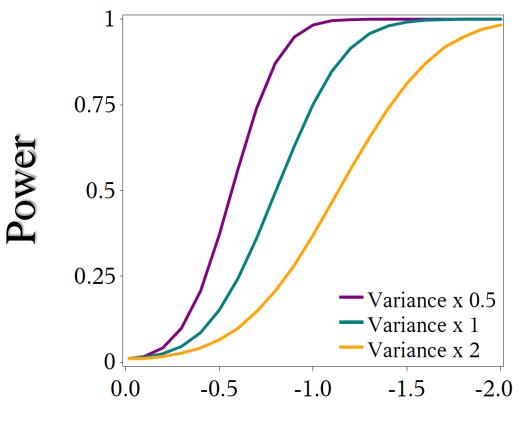
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### Sample Size Calculation Summary

For a <u>desired power of 0.90</u> and a <u>Type I error rate of 0.01</u>, we estimated that we would need <u>44 participants</u> to detect a <u>mean difference of 1.2</u>.

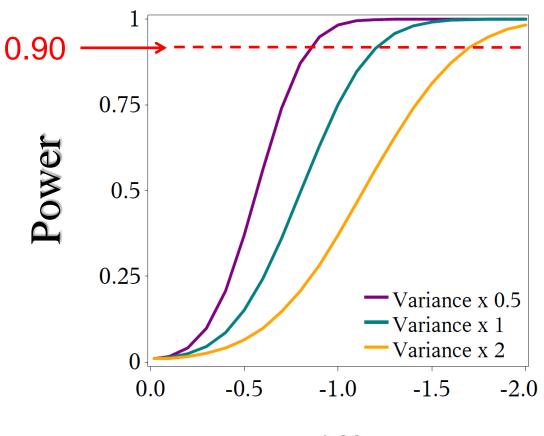
169

# Accounting for Uncertainty



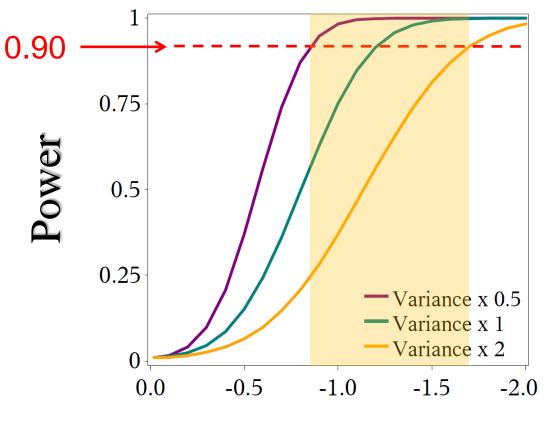
### Mean Difference

# Accounting for Uncertainty



Mean Difference

# Accounting for Uncertainty



Mean Difference

# Sample Size Calculation Summary Draft

We plan a <u>repeated measures ANOVA</u> using the <u>Hotelling</u>-Lawley Trace to test for a time by treatment interaction. Based on previous studies, we predict measures of pain recall will have a standard deviation of 0.98. The correlation in pain recall between baseline and 6 months will be 0.5. Based on clinical experience, we predict that the correlation will decrease slowly over time. Thus, we anticipate a correlation of 0.4 between pain recall measures at baseline and 12 months. For a desired power of 0.90and a Type I error rate of 0.01, we need to enroll 44 participants to detect a mean difference of 1.2.

# Handling Missing Data

- □ 25% loss to follow-up
- □ Inflate calculated sample size by 25%

# $44 \times 1.25 = 55$

# Handling Missing Data

- □ 25% loss to follow-up
- □ Inflate calculated sample size by 25%

# $44 \times 1.25 \approx 56$

### Sample Size Calculation Summary

Over 12 months, we expect 25% loss to follow up. We will inflate the sample size by 25% to account for the attrition, for a total enrollment goal of 56 participants, or 28 participants per treatment arm.

# Sample Size Calculation Summary

Over 12 months, we expect 25% loss to follow up. We will inflate the sample size by 25% to account for the attrition, for a total enrollment goal of <u>56 participants</u>, or 28 participants per treatment arm.

### Demonstrating Enrollment Feasibility

- □ Is the target population sufficiently large?
- □ Can recruitment be completed in the proposed time period?

# Planned Sample Size vs. Available Sample Size

- □ 30 patients per week with a high desire / low felt coping style
- □ 40% consent rate

Sample size needed 56

Sample size available

# Planned Sample Size vs. Available Sample Size

- □ 30 patients per week with a high desire / low felt coping style
- □ 40% consent rate



# Planned Sample Size vs. Available Sample Size

- □ 30 patients per week with a high desire / low felt coping style
- □ 40% consent rate



### Sample Size Calculation Summary

The clinic treats 30 patients per week with the high desire/low felt coping style. Based on recruitment experience for previous studies, we expect a 40% consent rate. At an effective enrollment of 12 participants per week, we will reach the enrollment goal of 56 participants in 5 weeks time.

### Sample Size Calculation Summary

The clinic treats <u>30 patients per week</u> with the high desire/low felt coping style. Based on recruitment experience for previous studies, we expect a <u>40%</u> consent rate. At an effective enrollment of 12 participants per week, we will reach the enrollment goal of <u>56 participants in 5 weeks time</u>.

# Planning for Multiple Aims

- □ Aims typically represent different hypotheses
- □ Maximum of the sample sizes calculated for each aim

# GLIMMPSE Lite

#### GLIMMPSE Lite for iPhone and Android



# Questions?



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