

Power for Subgroup Analysis

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Learning Objectives

Define subgroup analysis.

Demonstrate how to conduct power and sample size calculations for subgroup analysis.

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Subgroups may be defined by a variety of characteristics

Examples include race, ethnicity, and gender.

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Researchers are often interested in evaluating hypotheses within different groups

A **subgroup analysis** is a planned analysis that can help researchers understand whether effects differ between subgroups (subgroup by effect interaction or subgroup heterogeneity).

The process is often described as assessing heterogeneity of treatment effects in randomized trials.

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Researchers are often interested in evaluating hypotheses within different groups

Subgroup analysis can allow estimation of effects within each subgroup.

Subgroup analysis is often important in the study of disparities.

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Studies often have multiple subgroups

Example: A study with both genders and three age groups results in a study with six subgroups.

Age	Gender	
	Male	Female
10-39	Males, ages 10-39	Females, ages 10-39
40-49	Males, ages 40-49	Females, ages 40-49
50+	Males, ages 50+	Females, ages 50+

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Case control study example

Epidemiologist interested in a rare cancer may choose to recruit, for example, three control participants for every cancer case. In turn, gender is an important control variable. The result is four groups with size ratios 3:3:1:1.

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We will discuss two ways of conducting subgroup analyses

1. Traditional
2. Non-traditional

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TRADITIONAL APPROACH

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The traditional approach to subgroup analysis requires splitting data into separate sets for analysis

After stratifying data by subgroup, the traditional approach requires a separate hypothesis test within each stratum.

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The traditional approach for subgroup analysis has drawbacks

Stratifying the sample size results in small sample size in each individual stratum.

With the traditional approach, the variance estimate comes from each stratum; unbiased but more uncertainty.

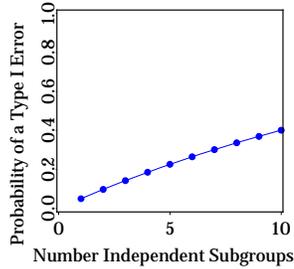
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In studies with multiple subgroups, conducting a hypothesis test in each one can inflate Type I error rate

Type I error is considered **inflated** when the true error rate is higher than the planned rate.

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The chance of having at least one Type I error increases with the number of subgroups



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A Bonferroni correction (alpha splitting) divides the Type I error by the number of groups. It applies to any kind of grouping.

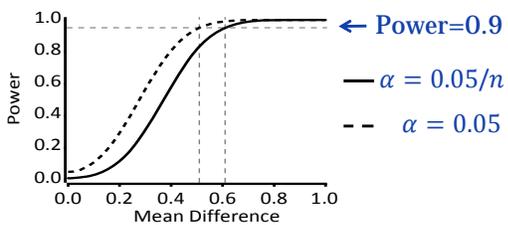
$$\alpha_{\text{original}} = 0.05$$

$$\alpha_{\text{corrected}} = \frac{0.05}{n}$$

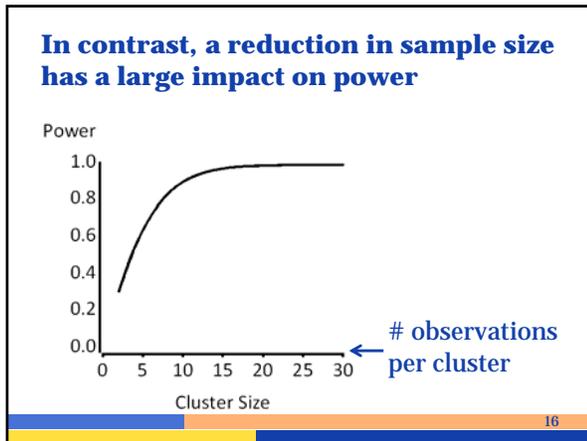
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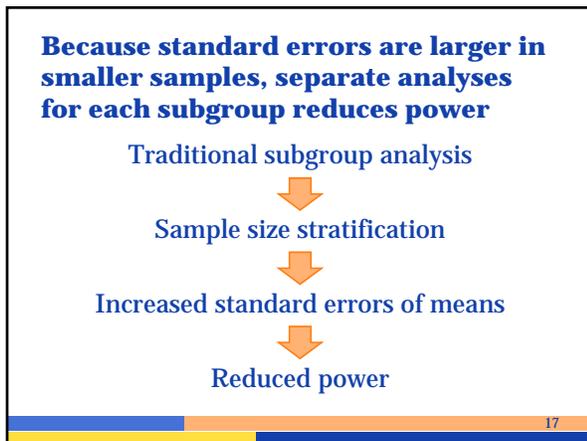
A Bonferroni correction (alpha splitting) reduces Type I error, and has a small impact on the difference detectable when the number of splits is small

Example: n=5 subgroups



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NON-TRADITIONAL APPROACH

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The non-traditional approach to subgroup data analysis does not stratify by subgroup

The non-traditional approach to subgroup analysis provides greater power than the traditional approach.

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The non-traditional approach yields more power by pooling the degrees of freedom across subgroups

Recall, larger samples have smaller standard errors.

Smaller standard errors give greater power.

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We will now briefly describe a data analysis method

Although aligned power analysis requires a basic understanding of the planned data analysis methodology, data analysis is not a focus of this course.

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Procedure for non-traditional subgroup analysis

1. Rather than stratify the data, fit a model using subgroup definition variables as predictors (between-ISU factors).
2. If X is the effect of interest, add subgroup and subgroup by X interaction effects to the model.
3. Test the subgroup by X interaction.

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Procedure for non-traditional subgroup analysis

4. If the interaction is significant, report interaction effect and estimates within subgroups.
5. Otherwise, test the subgroup and X effects.
6. Report tests and estimates.

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The non-traditional approach controls experiment-wise Type I error by testing in all subgroups at once

The single interaction test looks at all differences between subgroups at once.

The single main effect of subgroup test looks at all subgroup differences at once.

Alpha-splitting is only needed for any stepdown tests.

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Power is increased by the non-traditional (pooled analysis) approach

More power for a diffuse effect, which has two or more small effects, due to adding the effects together

More power for a concentrated effect, which has one large difference, due to increases error degrees of freedom

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REVIEW OF LEARNING OBJECTIVES

What is subgroup analysis?

A subgroup analysis is a planned analysis that allows investigators to test for heterogeneity of effects across subgroups (subgroup by effect interaction), estimate effects within each subgroup, and search for disparities.

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