Class 2 Outline

1. Sample Size : Two Samples (Equal sample sizes)
   - Continuous Outcome or Binary Outcome
2. Sample Size : Two Samples (Unequal sample sizes)
   - Continuous Outcome or Binary Outcome
3. Choices of α and β
4. Relationship between Sample Size, Statistical Power and Other Factors
5. Sample Size and Statistical Significance
6. Goals of Sample Size Calculation
7. Summary

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1. Sample Size for Two Groups for Hypothesis Test: Equal Sample Sizes

- Assuming equal sample sizes $n_1=n_2=n$

Population Value	Estimator	Sample Size
$\mu_1 - \mu_2$	$\bar{X}_1 - \bar{X}_2$	$n_1 = n_2 = \frac{(z_{\alpha/2} + z_\beta)^2(\sigma_1^2 + \sigma_2^2)}{\Delta^2}$
$p_1 - p_2$	$\hat{p}_1 - \hat{p}_2$	$n_1 = n_2 = \frac{\left(z_{\alpha/2}\sqrt{2\overline{pq}} + z_\beta\sqrt{p_1q_1 + p_2q_2}\right)^2}{\Delta^2}$

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1.1 Example: Sample Sizes for Test of Difference in Two Population Means

- Determine the sample sizes required to detect a difference of 5 mm in mean blood pressure between individuals receiving placebo and those receiving drug with a significance level of 0.05 and power of 0.80
- Assume $\sigma_1 = \sigma_2$ = 15 mm in each group.
- We are interested in testing:

  H_o: $\mu_1 - \mu_2 = 0$

  H_a: $\mu_1 - \mu_2 = 5$
- We would need 142 individuals in each group

$$n = \frac{(z_{\alpha/2} + z_\beta)^2(\sigma_1^{\ 2} + \sigma_2^{\ 2})}{\Delta^2} = \frac{(1.96 + 0.84)^2(15^2 + 15^2)}{5^2} = 141.1$$

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1.2 Example: Sample Sizes for Test of Difference in Two Means: Using Stata

```
. sampsi 0 5, sd1(15) sd2(15) a(0.05) p(.8)

Estimated sample size for two-sample comparison of means

Test Ho: m1 = m2, where m1 is the mean in population 1
              and m2 is the mean in population 2
Assumptions:
        alpha =   0.0500  (two-sided)
        power =   0.8000
           m1 =        0
           m2 =        5
          sd1 =       15
          sd2 =       15
        n2/n1 =     1.00

Estimated required sample sizes:
           n1 =      142
           n2 =      142
```

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1.3a Example: Sample Size for Test of Difference in Two Population Proportions

- A trial of a new treatment is being planned. The success rate of the standard treatment (to be used as a control) is 0.25. If the new treatment increases the success rate to 0.35, how many patients should be included in each group in order to detect this improvement?

- Assume a significance level of 0.05 and power of 0.80

- We are interested in testing:
  H_o: $p_1 - p_2 = 0$
  H_a: $p_1 - p_2 = 0.10$ (under assumption that $p_2=0.25$)

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1.3b Example: Sample Sizes for Test of Difference in Two Population Proportions

- We assume $p_1=0.35$, $p_2=0.25$, and $\Delta= p_1 - p_2=0.10$

- Calculate $\overline{p} = \frac{p_1 + p_2}{2} = \frac{0.35+0.25}{2} = 0.30$

- We would need approximately 329 patients in each group

$$n_1 = n_2 = \frac{\left(z_{\alpha/2}\sqrt{2\overline{pq}} + z_\beta\sqrt{p_1q_1 + p_2q_2}\right)^2}{\Delta^2}$$

$$n_1 = n_2 = \frac{\left(1.96\sqrt{2(0.30)(.70)} + 0.84\sqrt{(0.35)(0.65)+(0.25)(0.75)}\right)^2}{(0.10)^2}$$

$$n_1 = n_2 = 328.1$$

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1.4 Example: Sample Sizes for Test of Difference in Two Proportions: Using Stata

. sampsi 0.35 0.25, a(0.05) p(.8)

Estimated sample size for two-sample comparison of proportions

Test Ho: p1 = p2, where p1 is the proportion in population 1
and p2 is the proportion in population 2

Assumptions:

```
      alpha =   0.0500  (two-sided)
      power =   0.8000
         p1 =   0.3500
         p2 =   0.2500
      n2/n1 =   1.00
```

Estimated required sample sizes:

```
         n1 =     349
         n2 =     349
```

Note: the calculated sample size in Stata is higher because it uses a "correction for continuity"

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2. Sample Size for Two Groups for Hypothesis Test: Unequal Sample Sizes

- Assuming unequal sample sizes $n_2=\lambda n_1$

Population Value	Estimator	Sample Size
$\mu_1 - \mu_2$	$\overline{X}_1 - \overline{X}_2$	$n_1 = \dfrac{(z_{\alpha/2}+z_\beta)^2(\sigma_1^{\ 2}+\sigma_2^{\ 2}/\lambda)}{\Delta^2}$ $n_2 = \lambda n_1$
$p_1 - p_2$	$\hat{p}_1 - \hat{p}_2$	$n_1 = \dfrac{\left(z_{\alpha/2}\sqrt{\overline{p}\overline{q}(\lambda+1)/\lambda} + z_\beta\sqrt{p_1q_1+p_2q_2/\lambda}\right)^2}{\Delta^2}$ $n_2 = \lambda n_1$

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2.1 Revisiting Example 1.1

- What are the needed sample sizes if the sample size is twice as big for those receiving drug as those receiving placebo?
- In this case, we could write $n_2=\lambda\ n_1=2\ n_1$

$$n_1 = \frac{(1.96+.84)^2(15^2+15^2/2)}{5^2} = 106$$
$$n_2 = \lambda n_1 = 2(106) = 212$$

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2.2 Revisiting Example 1.1 Using Stata

```
sampsi 0 5, sd1(15) sd2(15) a(0.05) p(.8) r(2)

Estimated sample size for two-sample comparison of means

Test Ho: m1 = m2, where m1 is the mean in population 1
             and m2 is the mean in population 2
Assumptions:
      alpha =   0.0500  (two-sided)
      power =   0.8000
         m1 =        0
         m2 =        5
        sd1 =       15
        sd2 =       15
      n2/n1 =     2.00

Estimated required sample sizes:
         n1 =      106
         n2 =      212
```

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3. Common Choices of α and β for Sample Size Calculations

- The test may be one-sided or two-sided:
  - Often α is specified as 0.05 and Z_{α} = 1.645 and $Z_{\alpha/2}$ =1.96
- Power is one-sided and Z_{β} is always one-sided
  - Often power is specified as 0.80 and β=0.20 with Z_{β} = 0.84
  - If power is specified as 0.90 and β=0.10 with Z_{β} = 1.28

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4.1 Relationship between Sample Size and Other Factors

$$n_1 = n_2 = \frac{(z_{\alpha/2} + z_{\beta})^2 (\sigma_1^2 + \sigma_2^2)}{\Delta^2}$$

Factors influencing <u>sample size n</u>:

n ↑ as σ^2 ↑ ↑
n ↑ as α ↓
n ↑ as β ↓
n ↑ as $(1-\beta)$ ↑
n ↑ as Δ ↓
n ↓ as Δ ↑

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4.2 Relationship between Statistical Power and Other Factors

$$n_1 = n_2 = \frac{(z_{\alpha/2} + z_{\beta})^2(\sigma_1^{\ 2} + \sigma_2^{\ 2})}{\Delta^2}$$

Factors influencing power:

Power ↓ as α ↓

Power ↑ as Δ ↑

Power ↑ as n ↑

Power ↓ as σ^2 ↑

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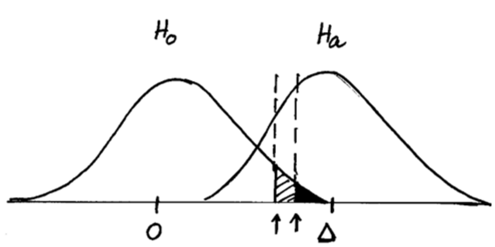
4.3a Visual Depiction: Change in α

- All other factors (n, Δ, σ)constant,
  when α↓,
  then β ↑ and (1-β) ↓



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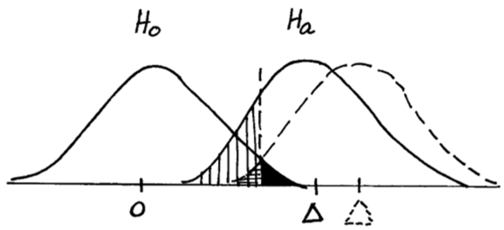
4.3b Visual Depiction: Change in Δ

- All other factors (n, α, σ)constant, when $\Delta \uparrow$, then $\beta \downarrow$ and (1-β) $\uparrow$



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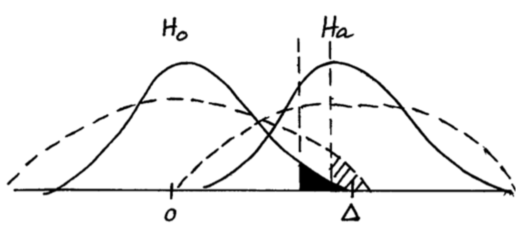
4.3c Visual Depiction: Change in σ

- All other factors (n, α, Δ)constant, when $\sigma \uparrow$ then $\beta \uparrow$ and (1-β) $\downarrow$



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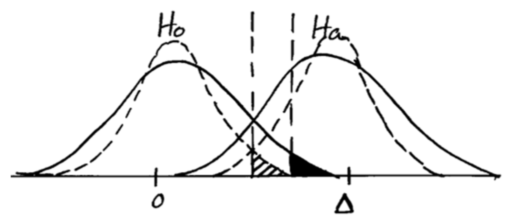
4.3d Visual Depiction: Change in n

- All other factors (σ , α, Δ)constant, when n↑, then β↓and (1-β) ↑



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5. Sample Size and "Statistical Significance"

- Large sample size can result in statistical significance when Δ is very small (not of practical, clinical or public health importance)
- Small sample size can result in a non-statistically significant finding even when Δ is large (of practical, clinical or public health importance)

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6.Goals of Sample Size Calculation

- Perform a study with large enough sample size and sufficient power to detect (through hypothesis testing) a meaningful difference Δ
- Sample size calculation should be informed by previous investigations (science, biology, medicine and health) when possible

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7a. Summary

- Sample size can be calculated for one or two groups for purposes of :
  - Precision (requires desired width of CI and specification of α)
  - Hypothesis testing (requires null hypothesis and specific alternative hypothesis [to calculate Δ] and specification of assumed α, β, variance)
- Sample sizes for two groups:
  - Equal samples sizes $n_1=n_2=n$
  - Unequal samples $n_1 \neq n_2$

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7b. Summary

- Sample size is derived from knowledge of the sampling distribution of the sample statistic of interest
- Sample size determination must go beyond calculating a single value
- Choice of sample size depends on a balance of reasonable assumptions, time, effort, and expense

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