Sample Size Determination

Example

Wish to design a study on placebo effect on blood pressure reduction. BP to be measured before and 4 weeks after the subjects have been on placebo.

How many subjects are needed?

1. One-Sample Problem: Mean

Problem: Wish to determine optimal sample size to test the hypothesis:

$$H_o : \mu = \mu_o$$

Against the alternative

$$H_1 : \mu = \mu_1$$

- The intended detectable difference: $\Delta = (\mu_1 - \mu_o) > 0$
- The Type I error probability $= \alpha$
- The Type II error probability $= \beta$

Consider first the case $X_1, \cdots, X_n$, i.i.d. $N(\mu, \sigma^2)$, where σ^2 is known.

Then a test statistic for the above is:

$$Z = \frac{\sqrt{n}(\bar{X} - \mu)}{\sigma}$$

Using the relations

$$P[Z > Z_\alpha \mid H_o] = \alpha$$

and

Type II error prob = β

we have

$$\Phi[Z_\alpha + \frac{\sqrt{n}\Delta}{\sigma}] = \beta$$

giving

$$Z_\alpha + \frac{\sqrt{n}\Delta}{\sigma} = -Z_\beta$$

or

$$n = \frac{(Z_\alpha + Z_\beta)^2\sigma^2}{\Delta^2}$$

Remarks:

- n increases with σ
- n decreases as Δ increases
- Need to balance between α and β
- When σ unknown, need to use non-central t-distribution
- For two-sided test, use $Z_{\alpha/2}$

Example 2

Suppose an investigator wishes to determine the sample size required to compare two anti-hypertension drugs under the following assumptions. It is known that the clinically meaningful detectable difference with respect to diastolic blood pressure is at least 4 mmHg; and from historical data the common standard deviation $\sigma = 10$ *mmHg. Further, it is desired to use a two-sided test of level* $\alpha = 0.05$ *and power of 80%.*

2. Two-Sample Problem: Comparing Two Means

Let $X_1, \cdots, X_n$ be i.d.d., $N(\mu_1, \sigma_1^2)$ and $Y_1, \cdots, Y_m$ be i.d.d., $N(\mu_2, \sigma_2^2)$.
Assume $\sigma_1 = \sigma_2$ and $n = m$.

$$H_o : \mu_1 = \mu_2$$

vs

$$H_1 : \mu_1 - \mu_2 = \delta > 0$$

When σ^2, the common variance, is known, a test statistic for $H_o : \Delta = 0$ is

$$Z = \frac{\sqrt{n}(\bar{X} - \bar{Y})}{\sqrt{2}\sigma}$$

$$n = \frac{2(Z_\alpha + Z_\beta)^2 \sigma^2}{\Delta^2}$$

- For two-sided test, use $Z_{\alpha/2}$

When $n_2 = rn_1$ (i.e., unequal sample sizes).

Can show that

$$n_1 = \frac{\sigma^2(1 + 1/r)(Z_\alpha + Z_\beta)^2}{\Delta^2}$$

HWK Problem 1.

Suppose a $100(1-\alpha)\%$ confidence interval for Δ is to have length L. We can show that

$$L = 2Z_{\alpha/2}\sqrt{(\sigma_1^2 + \sigma_2^2)/n}$$

which implies

$$n = 4Z_{\alpha/2}^2(\sigma_1^2 + \sigma_2^2)/L^2$$

Example 3

A clinical trial is to be designed to compare two antibiotics (a new drug vs a standard therapy) for the treatment of bronchitis. It is known that the response rate for patients taking the standard therapy is 80%. It is suspected that the new therapy may be effective for at least 90% of the patients.

3. Sample Size for Proportions

Let X be distributed as $bin(n, p_1)$ and Y as $bin(n, p_2)$, such that X and Y are independent.

Wish to test

$$H_O : p_1 = p_2$$

vs.

$$H_1 : p_1 \neq p_2$$

- *Normal Approximation*
  Can show that
  $$n = \frac{\left[Z_{\alpha/2}\sqrt{2\bar{p}\bar{q}} + Z_\beta \sqrt{p_1 q_1 + p_2 q_2}\right]^2}{(p_2 - p_1)^2}$$
  where $\bar{p} = (p_1 + p_2)/2$, and $\bar{q} = 1 - \bar{p}$.

If test is with continuity correction:

$$n_c = \frac{n}{4}\left[1 + \sqrt{1 + \frac{4}{n \mid p_2 - p_1 \mid}}\right]^2$$

For unequal sample sizes, let $n_1 = r n_2$. Then

$$n_1 = \frac{\left[Z_{\alpha/2}\sqrt{(r+1)\bar{p}\bar{q}} + Z_{\beta}\sqrt{r p_1 q_1 + p_2 q_2}\right]^2}{r(p_2 - p_1)^2}$$

where

$$\bar{p} = \frac{p_1 + r p_2}{r + 1}$$

With continuity correction

$$n_{1,c} = \frac{n_1}{4}\left[1 + \sqrt{1 + \frac{2(r+1)}{n_1 \mid p_2 - p_1 \mid}}\right]^2$$

- *Arcsin transformation*

  Recall that $\hat{p} - p$ is approximately distributed as $N(0, pq/n)$, where $\hat{p} = X/n$, and X is $bin(n, p)$.

  Can show that $f(p) = 2\arcsin(\sqrt{p})$ is such that $f(\hat{p}) - f(p)$ is approximately $N(0, 1/n)$.

Now let $f(p_1) - f(p_2) = \Delta$.

Then

$$Z = \frac{f(\hat{p}_1) - f(\hat{p}_2) - \Delta}{\sqrt{2/n}}$$

$$n = \frac{(Z_{\alpha/2} + Z_\beta)^2}{\Delta^2}$$

General Considerations

1. Parameters of Interest:
   - Equality of Means
   - Proportions

2. Number of groups
   - One, two, > two

3. Analysis Methods
   - Test
   - Confidence interval

Implementation

R:

- Library(stats)
  - power.t.test(n = NULL, delta = NULL, sd = 1, sig.level = 0.05,
    power = NULL,
    type = c("two.sample", "one.sample", "paired"),
    alternative = c("two.sided", "one.sided"),
    strict = FALSE)
  - power.prop.test(n = NULL, p1 = NULL, p2 = NULL, sig.level = 0.05,
    power = NULL,
    alternative = c("two.sided", "one.sided"),
    strict = FALSE)

SAS: PROC POWER; PROC GLMPWER

Specialized Software:

- nQuery
- EAST

Examples

```
power.t.test(n = 20, delta = 1)
     Two-sample t test power calculation
              n = 20
          delta = 1
             sd = 1
      sig.level = 0.05
          power = 0.8689528
    alternative = two.sided
```

```
power.t.test(power = .90, delta = 1)
              n = 22
```

```
> power.t.test(power = .90, delta = 1, alt = "one.sided")

              n = 18
```

Two-sample comparison of proportions; power calculation

```
power.prop.test(n = 50, p1 = .50, p2 = .75)

     power = 0.7401659

power.prop.test(n = 70, p1 = .50, p2 = .75)

    power = 0.8715025

power.prop.test(n = 100, p1 = .50, p2 = .75)

    power = 0.9600175
```

```
> power.prop.test(p1 = .50, p2 = .75, power = .90)

          n = 76.70693
```

```
> power.prop.test(n = 50, p1 = .5, power = .90)

          p2 = 0.8026141
```

Problem Set 6

1) Verify the formula

When $n_2 = rn_1$ (i.e., unequal sample sizes).

Can show that

$$n_1 = \frac{\sigma^2(1 + 1/r)(Z_\alpha + Z_\beta)^2}{\Delta^2}$$

2) Reading Assignment pages 669-688 (The Statistical Sleuth: A Course in Methods of Data Analysis. Ramsey & Schafer)

3) Write a function in R to compute sample size and do the following:

a) Problem 12, p. 690
b) Problem 13, p. 690
c) Problem 14, p.691