JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

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Sample Size and Power Estimation

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Sample size and Power

"When statisticians are not making their lives producing confidence intervals and p-values, they are often producing power calculations"

Newson, 2001

”In planning of a sample survey, a stage is always reached at which a decision must be made about the size of the sample. The decision is important. **Too large** a sample implies a waste of resources, and **too small** a sample diminishes the utility of the results.“

Cochran, 1977

Sample size estimation: Why?

- Provides validity of the clinical trials/intervention studies – in fact any research study, even presidential election polls
- Assures that the intended study will have a desired power for correctly detecting a (clinically meaningful) difference of the study entity under study if such a difference truly exists

Sample size estimation

- ONLY two objectives:
  - Measure with a precision:
    - Precision analysis
  - Assure that the difference is correctly detected
    - Power analysis

First objective: measure with a precision

- Whenever we propose to estimate population parameters, such as, population mean, proportion, or total, we need to estimate with a specified level of precision
- **We like to specify a sample size that is sufficiently large to ensure a high probability that errors of estimation can be limited within desired limits**

Stated mathematically:

- we want a sample size to ensure that we can estimate a value , say, ***p*** from a sample which corresponds to the population parameter, ***P***.

- Since we may not guarantee that p will be exact to ***P***, we allow some error

- Error is limited to certain extent, that is this error should not exceed some specified limit, say ***d***.

- We may express this as:

  p - P = $\pm$ ***d***,

  i.e., the difference between the estimated p and true ***P*** is not greater than ***d*** (allowable error: margin-of-error)

- But do we have any confidence that we can get a ***p***, that is not far away from the error of $\pm$***d***?

- In other words, we want some confidence limits, say 95%, to our error estimate d.

  That is ***1-*** α = 95%

It is a common practice: α-error = 5%

In probability terms, that is,

$$prob\ \{-d \le p - P \le d\} \ge 1 - \alpha$$

In English, we want our estimated proportion *p* to vary between *p-d* to *p+d*, and we like to place our confidence that this will occur with a *1-*α probability.

From our basic statistical course, we know that we can construct a confidence interval for p by:

$$p \pm z_{1-\alpha/2} * se(p)$$

where z_α *denotes a value on the abscissa of a standard normal distribution (from an assumption that the sample elements are normally distributed) and se(p) =* σ_p is the standard error.

$$p \pm d = p \pm z_{1-\alpha/2}\sigma_p$$

Hence, we relate p ± d in probabilities such that:

$$d = Z_{1-\alpha/2}\sigma$$

$$= Z_{1-\alpha/2}\sqrt{\frac{p(1-p)}{n}}$$

If we square both sides,

$$d = Z_{1-\alpha/2}\sigma$$
$$= Z_{1-\alpha/2}\sqrt{\frac{p(1-p)}{n}}$$

$$d^2 = Z^2_{1-\alpha/2} \frac{p(1-p)}{n}$$

$$n = \frac{Z^2_{1-\alpha/2}}{d^2} p(1-p)$$

$$n = \frac{Z^2_{1-\alpha/2} p(1-p)}{d^2}$$

For the above example:

$$n = \frac{(1.96)^2 * 0.4 * 0.6}{(.10)\wedge 2} = 92.2 \approx 93$$

Note that, the sample size requirement is highest when p=0.5. It is a common practice to take p=0.5 when no information is available about p for a conservative estimation of sample size.

As an example, p = 0.5, d = 0. 05
(5% margin-of-error), and α-error = 0.05:

$$n = \frac{(1.96)^2 * 0.5 * 0.5}{(.05)\text{^}2} = 384.16 = 385 \approx 400$$

```
. di 1.96^2*.5*(1-.5)/(.05^2)
384.16
. di (invnorm(.05/2))^2*.5*(1-.5)/(.05^2)
384.14588
```

Stata

```
. sampsi .5 .55, p(.5) onesample

Estimated sample size for one-sample comparison of proportion
  to hypothesized value

Test Ho: p = 0.5000, where p is the proportion in the population

Assumptions:

         alpha =   0.0500  (two-sided)
         power =   0.5000
 alternative p =   0.5500

Estimated required sample size:

             n =      385
```

Sample Size Estimation for Relative Differences

If d is relative difference,

$$n = \frac{t^2 p(1-p)}{(d^* p)2}$$

$$= \frac{t^2 (1-p)}{d^2 p}$$

Consider that 10% change is relative to p=.40 in the above example.

Then, d = 0.4*0.10=0.04, that is, p varies between 0.36 to 0.44. Now,

$$\mathrm{n} = \frac{(1.96)^2 * 0.4 * 0.6}{(.10 * 0.4)\hat{}2} = 576.24 \approx 577$$

Note, *d* is very sensitive for sample size calculation.

Change the variance

Sample Size for Continuous Data

$$n = \frac{t^2 \sigma^2}{d^2}$$

Sources of variance information:

- Published studies
  - (Concerns: geographical, contextual, time issues – external validity)
- Previous studies
- Pilot studies

Study design and sample size

- Sample size estimation depends on the study design – as variance of an estimate depends on the study design
- The variance formula we just used is based on “simple random sampling” (SRS)
- In practice, SRS strategy is rarely used
- Be aware of the study design

Sample Size Under SRS Without Replacement

We know that under SRSWOR,

$$V(\bar{y}) = \frac{\sigma^2}{n} \frac{N-n}{N-1}$$

So, under SRSWOR:

$$d^2 = t_\alpha^2 \frac{p(1-p)}{n} \frac{N-n}{N-1}$$

$$n = \frac{NP(1-P)}{(N-1)D^2 + P(1-P)}$$

where,

$$D = d / t_\alpha$$

For continuous data,

$$n = \frac{N\sigma^2}{(N-1)D^2 + \sigma^2}$$

Alternative Specification (in two-stages):

This n, say n', is estimated under simple random sampling with replacement (SRSWR). When sampling is without replacement, we adjust the n by

$$n = \frac{n'}{1 + \frac{n'}{N}}$$

or,

$$n = \frac{1}{\frac{1}{n'} + \frac{1}{N}}$$

(n is adjusted for finite population correction factor, 1- n/N).

Example: For exercise study, 93 samples are needed.

Say, the population size is 200.

Under SRSWOR:

$$n = \frac{n'}{1 + \frac{n'}{N}}$$

$$n = \frac{93}{1 + \frac{93}{200}} = \frac{93}{1 + 0.465} = \frac{93}{1.465} = 63.48$$

$$n \approx 64$$

Smaller sample size is needed when population size is small, but opposite is not true

Derivation (alternative two-stage formula):

Remember the relationship between $\frac{S^2}{n'}....vs....\frac{N-n}{N}\frac{S^2}{n}$

$$=> \frac{1}{n'} = (1 - \frac{n}{N})\frac{1}{n}$$

$$=> \frac{1}{n'} = \frac{1}{N} - \frac{1}{n}$$

$$=> \frac{1}{n} = \frac{1}{n'} + \frac{1}{N}$$

$$=> \frac{1}{n} = \frac{1}{n'} + \frac{n'}{N}\frac{1}{n'}$$

$$=> \frac{1}{n} = \frac{1 + \frac{n'}{N}}{n'}$$

$$=> n = \frac{n'}{1 + n'/N}$$

Sample Size Based on Coefficient of Variation

- In the above, the sample size is derived from an *absolute* measure of variation, σ^2.
- Coefficient of variation (cv) is a *relative* measure, in which units of measurement is canceled by dividing with mean.
- Coefficient of variation is useful for comparison of variables.

Coefficient of variation is defined as,

$C_Y = \frac{S_y}{\bar{Y}}$, and is estimated by $c_y = \frac{s_y}{\bar{y}}$

Coefficient of variation (CV) of mean is

$$\boldsymbol{CV = \frac{SE}{\bar{y}} = \frac{s/\sqrt{n}}{\bar{y}} = \frac{s}{\bar{y}}\frac{1}{\sqrt{n}}}$$

So, $$n = \frac{1}{CV^2}\frac{s^2}{\bar{y}^2}$$

For proportion p,

$$n = \frac{1}{CV^2}\frac{p(1-p)}{p^2} = \frac{1}{CV^2}\frac{(1-p)}{p}$$

Caution about using coefficient of variation (CV)

- If mean of a variable is close to zero, *CV* estimate is large and unstable.

- Next, consider *CV* for binomial variables. For binary variables, the choice of P and Q=1-P does not affect P(1-P) estimate, but *CV* differs. So, the choice of P affects sample size when CV method is used.

Cost considerations for sample size

How many samples you may afford to interview, given then budget constraints?

$C(n)$ = cost of taking n samples

c_o = fixed cost

c_1 = cost for each sample interview

then,

$$C(n) = c_o + c_1 x\ n$$

Example:

C(n)=$10000 - your budget for survey implementation

c_o = $3000 - costs for interviewer training, questionnaire prints, etc

c_1 = $8.00 - cost for each sample interview

10000=3000+8*n

So, n=875

Objective 2: Issues of Power Calculation

POWER
The power of a test is the probability of rejecting the null hypothesis if it is incorrect.

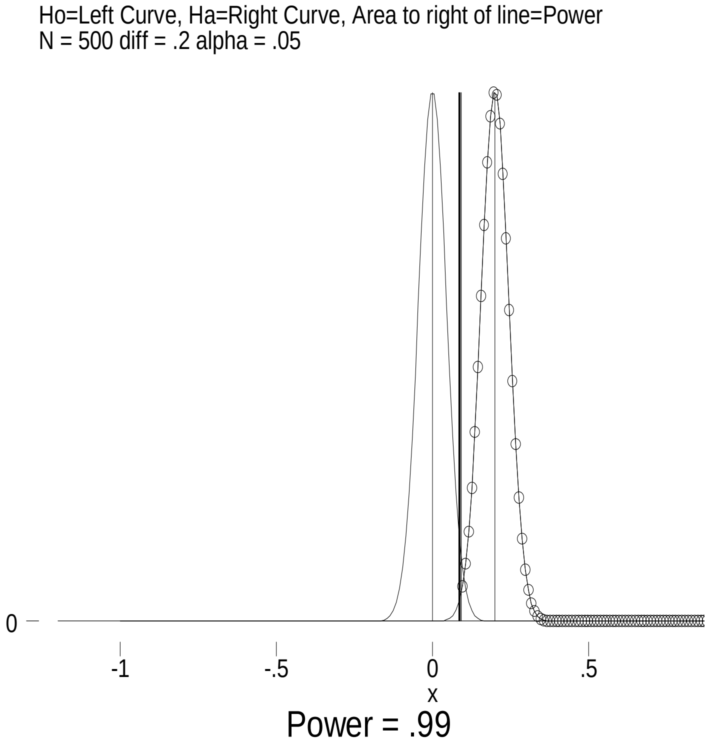
TRICKS to REMEMBER:
R, T: Reject the null hypothesis if it is true - Type I error (alpha error) { one stick in R, T}
A, F: Accept the null hypothesis if it is false - Type II error (beta error) {two sticks in A, F}
POWER: 1- type II error

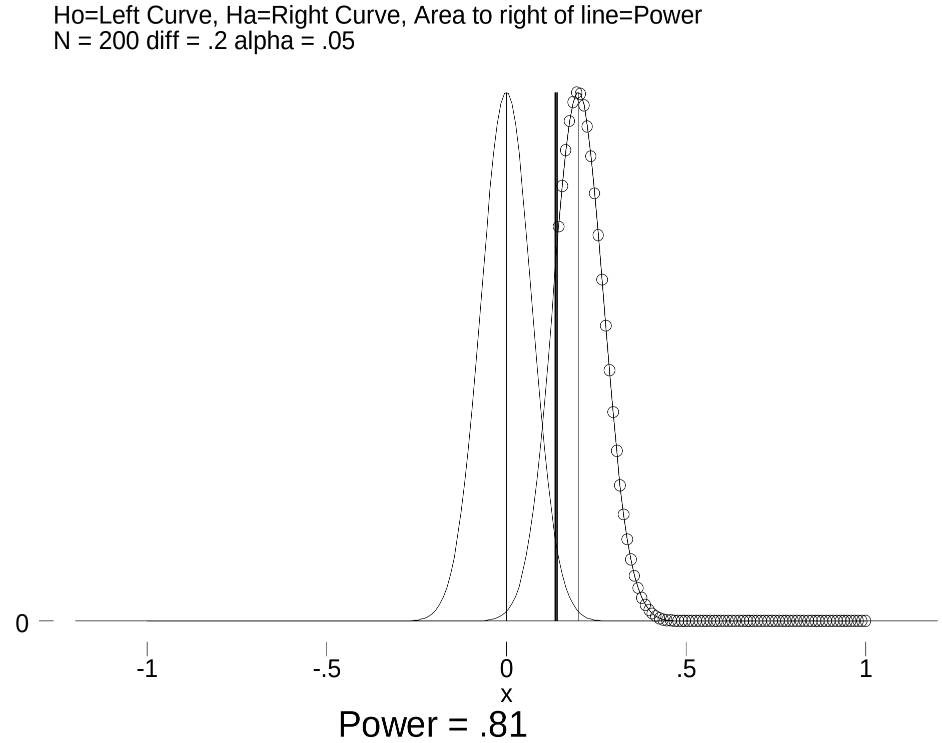
Power: Reject the null hypothesis if it is false.

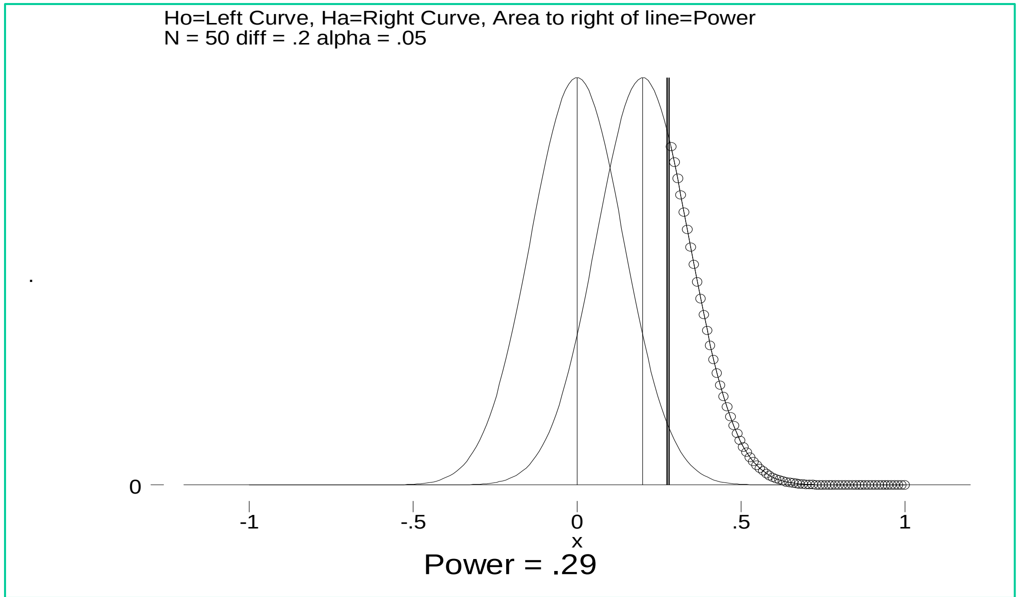
Another way:

False Positive (YES instead of NO) ?

False Negative (NO instead of YES) ?


Ho=Left Curve, Ha=Right Curve, Area to right of line=Power
N = 500 diff = .2 alpha = .05
0
-1
-.5
0
.5
x
Power = .99


Ho=Left Curve, Ha=Right Curve, Area to right of line=Power
N = 200 diff = .2 alpha = .05
0
-1
-.5
0
.5
1
x
Power = .81


Ho=Left Curve, Ha=Right Curve, Area to right of line=Power
N = 50 diff = .2 alpha = .05
0
-1
-.5
0
.5
1
x
Power = .29

We take power into consideration when we test hypotheses.

Example:

Consider following study questions:

1. What proportions of pregnant women received antenatal care?

There is no hypothesis.

b) Whether 80% of women received antenatal care?

There is a hypothesis:
To test that the estimated value is greater, less, or equal to a pre-specified value.

c) Do women in project (intervention) area more likely to utilize antenatal care, compared to control area?

There is a hypothesis:
To test that that P_1 is greater than P_2.

In terms of hypothesis:

Null hypothesis:	*Ho:P1=P2, i.e., P1-P2=0*
Alternative hypothesis:	*Ha:P1 > P2 (one-sided)*
	Ha:P1$\neq$P2 (two-sided) i.e., P1-P2 $\neq$ 0

Issues:

One-sided vs. two-sided tests.

One-sided: sample size will be smaller.
Two-side: sample size will be larger.

Always prefer "two-sided" - almost a mandatory in clinical trials.

Why? Uncertainty in knowledge (*a priori*).

How to incorporate "power" in sample size calculations?

1. Proportions:

$$n = \frac{(t_{\alpha} + t_{\beta})^2 \, \overline{p}(1 - \overline{p})}{d^2}$$

where $\overline{p}$ is $(p1 + p2)/2$

Note: **n for each group.**

Alternative:

$$n_1 = n_2 = \left[\frac{Z_{\alpha} + Z_{\beta}}{2\,arcsin\sqrt{p_1} - 2\,arcsin\sqrt{p_2}} \right]^2$$

Why?

Arcsin provides normal approximation to proportion quantities.

For continuous variables:

$$n = \frac{(Z_{1-\alpha/2} + Z_{\beta})^2 s^2}{d^2}$$

Values of $Z_{1-\alpha/2}$ and Z_{β} corresponding to specified values of significance level and power

	Values	Two-sided	One-sided
Level	1%	2.576	2.326
	5%	1.960	1.645
	10%	1.645	1.282
Power	80%	0.84	
	90%	1.282	
	95%	1.645	
	99%	2.326	

How to incorporate "power" in sample size calculations?

a) Proportions:

$$n = \frac{(z_{(1-\alpha/2)} + z_{1-\beta})^2 \, variance\ of\ difference[\mathrm{var}(p_1 - p_2)]}{(p_1 - p_2)^2}$$

How to estimate variance of difference?

$$\sigma^2_{(p_1-p_2)} = \sigma^2_d = \sigma^2_{p_1} + \sigma^2_{p_2} - 2\sigma_{p_1}\sigma_{p_2}$$

$$Under\ the\ assumption\ of\ independence, \mathrm{cov}(p1, p2) = \sigma_{p_1}\sigma_{p_2} = 0$$

$$If\ we\ also\ assume\ that\ \mathrm{var}(p1) = \mathrm{var}(p2) = \mathrm{var}(p),\ i.e.,\ have\ common\ variance$$

$$\sigma_d = \sigma^2_p + \sigma^2_p = 2\sigma^2_p$$

So,

$$n = \frac{(z_{(1-\alpha/2)} + z_{1-\beta})^2 \, variance \;\; of \;\; difference[v(p_1 - p_2)]}{(p_1 - p_2)^2}$$

$$= \frac{(z_{(1-\alpha/2)} + z_{1-\beta})^2 \, 2 * \overline{p}\overline{q}}{(p_1 - p_2)^2} \;\; where \;\; \overline{p} = (p_1 + p_2)/2$$

under the assumption of common variance

The sample size formula for testing two proportions under independence without the assumption of common variance is then:

$$n_1 = n_2 = \frac{(z_{1-\alpha/2} + z_{1-\beta})^2 [p_1(1-p_1) + p_2(1-p_2)]}{(p_1 - p_2)^2}$$

Note that Fleiss (1981) suggested more precise formula:

$$n' = \frac{\left\{ z_{1-\alpha/2}\sqrt{2\overline{p}(1-\overline{p})} + z_{1-\beta}\sqrt{p_1(1-p_1) + p_2(1-p_2)} \right\}^2}{(p_1 - p_2)^2}$$

$$where,\ p = (p_1 + p_2)/2$$

When n_1 and n_2 is not equal and related by a ratio, say by r, the formula is:

$$n' = \frac{\left\{ z_{1-\alpha/2}\sqrt{(r+1)\overline{p}(1-\overline{p})} + z_{1-\beta}\sqrt{rp_1(1-p_1) + p_2(1-p_2)} \right\}^2}{r(p_1 - p_2)^2}$$

The final formula (using normal approximation with continuity correction [without the correction, the power is considered low than expected] with proportions) is:

$$n_1 = \frac{n'}{4}\left\{ 1 + \sqrt{1 + \frac{2(r+1)}{n'r\,|\,p_1 - p_2\,|}} \right\}^2$$

$$n_2 = rn_1$$

The STATA has implemented this formula in SAMPSI command.

Stata implementation

NO Hypothesis

. sampsi .5 .55, p(.5) onesample

Estimated required sample size:

n = 385

Study has a hypothesis, but comparing with a hypothesized value

. sampsi .5 .55, p(.8) onesample

Estimated sample size for one-sample comparison of proportion to hypothesized value

Estimated required sample size:

n = 783

Study has a hypothesis, and comparing between two groups

. sampsi .5 .55, p(.8)

Estimated sample size for two-sample comparison of proportions

n1 = 1605

n2 = 1605

```
. di 783/385
2.0337662

. di
(1.96+.84)^2/1.96^2
2.0408163
```

Stata implementation

. sampsi .5 .55, p(.8) <u>nocontinuity</u>

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 = 0.5000
p2 = 0.5500
n2/n1 = 1.00

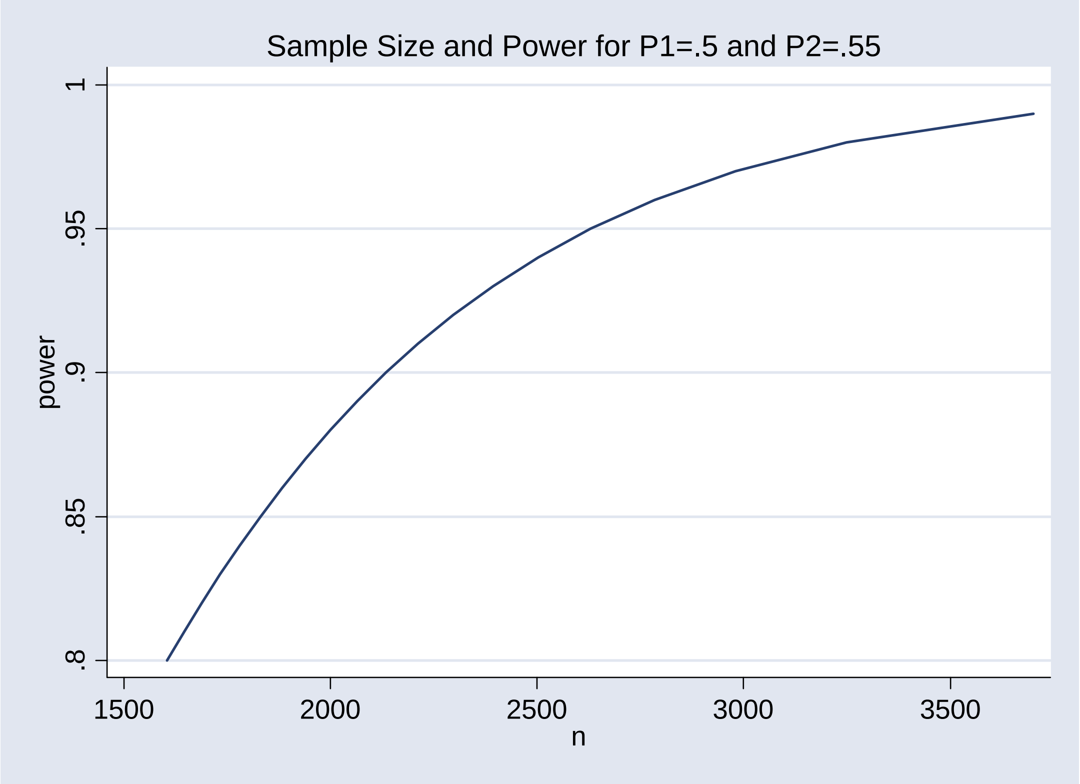
Estimated required sample sizes:

n1 = 1565
n2 = 1565

```
. di 783*2
1566

In each group,
sample size is
doubled
```

Power graph in Stata



```
*Calculate and plot sample size by power from .8 to .99

***************************************************************************
args p1 p2 type

clear
set obs 20
gen n=.
gen power=.
local i 0

while `i' <_N {
    local i = `i' +1

    local j=.79 +`i'/100

    quietly sampsi `p1' `p2', p(`j') `type'
    replace n=r(N_1) in `i'
    replace power=r(power) in `i'

    }

noisily list power n

graph twoway line power n, t1("Sample Size and Power for P1=`p1' and P2=`p2' `type'")
*****************************************************************************
```

Save the above commands as “do” file (e.g., sample_graph.do).

Execute the above file by:

run sample_graph

Sample size determination when expressed in "relative risk"

In epidemiological studies, often the hypothesis is expressed in
relative risk or odds ratio, e.g, H0:R=1.

A sample size formula given in Donner (1983) for Relative Risk (p. 202) is:

$$n = \left\{ Z_{\alpha}\sqrt{2\overline{P}_R(1-\overline{P}_R)} + Z_{\beta}\sqrt{P_c\left\{1+R-P_c(1+R^2)\right\}} \right\}^2 / [P_c(1-R)]^2$$

$$Where \quad \overline{P}_R = [P_c(1+R)]/2 \quad and \quad R = P_E / P_c$$

Nothing but the Fleiss' formula:

$$n' = \frac{\left\{ z_{1-\varepsilon}\sqrt{2\overline{p}(1-\overline{p})} + z_{1-\beta}\sqrt{p_E(1-p_E) + p_C(1-p_C)} \right\}^2}{(p_C - p_E)^2}$$

$$where,\ p = (p_E + p_C)/2$$

Note, $R = \frac{P_E}{P_C} = P_E = RP_C$

Solution: Replace all P_E with RP_C and apply Fleiss' formula

How Donner's formula was derived:

$P=(P_E+P_C)/2=(RP_C+P_C)/2=[P_C(R+1)]/2=[P_C(1+R)]/2$

$P_E(1-P_E)+P_C(1-P_C)=RP_C(1-RP_C)+P_C(1-P_C)$

$=RP_C-R^2P_C^2+P_C-P_C^2$

$=P_C(R-R^2P_C+1-P_C)$

$=P_C\ (1+R-P_C\ (1+R^2)$

and, $(P_C-P_E)^2=(P_C-RP_C)^2=[P_C(1-R)]^2$

Sample size for odds-ratio (OR) estimates:

$$OR = \frac{\dfrac{P_2}{1-P_2}}{\dfrac{P_1}{1-P_1}} = \frac{P_2 Q_1}{P_1 Q_2}$$

$$P_2 Q_1 = OR * P_1 Q_2 = OR * P_1 (1 - P_2) = OR * P_1 - OR * P_1 * P_2$$

$$P_2 (Q_1 + OR * P_1) = OR * P_1$$

$$P_2 = \frac{OR * P_1}{OR * P_1 + Q_1}$$

Convenient to do in two stages:

1. Estimate P_2 from odds-ratio (OR)
2. Apply "proportion method" (of Fleiss)

An example

Suppose we want to detect an OR of 2 using an ratio of 1:1 cases to controls in a population with expected exposure proportion in non-cases of 0.25 while requiring a α= 0.05 and power = 0.8.

How to estimate SS?

EpiTable calculates m1 = m2 = 165. (Total sample size = 330).

So, P1=.25,

P2= (2*.25)/(2*.25+.75) = 0.4

In Stata:

. sampsi .25 .40, p(.8)

Estimated required sample sizes:

n1 = 165

n2 = 165

SAMPLE SIZE determination for Logistic Regression Models

Consider a logistic regression,

$$\log\left(\frac{p}{1-p}\right) = logit(p) = \alpha + \beta x$$

We want to estimate sample size needed to achieve certain power for testing null hypothesis

Ho:β=0. Recall that null hypothesis testing depends on the **variance of β**. In logistic regression, the **effect size** is expressed as "log odds ratio" (η).

Hsieh(1989) suggested the following formula for one-sided test:

$$n = \left[z_\alpha + z_\beta \exp(-\eta^2/4)\right]^2 \left(1 + 2\hat{p}\delta\right)/(\hat{p}\eta^2)$$

where,

$$\delta = [1 + (1+\eta^2)\exp(5\eta^2/4)]/[1+\exp(-\eta^2/4)]$$

Say, you want to examine the **effect size** of **log odds ratio** of 1.5 = log(1.5)= .40546511 = ~0.41

See, the implementation of formula in STATA:

```
. clear
. set obs 1
obs was 0, now 1

. *Enter "odds-ratio"
. gen p=0.10
. gen or=1.5

. gen beta=log(or)

. di beta
.4054651
. gen delta= (1+(1+beta^2)*exp(5*beta^2/4))/(1+exp(-beta^2/4))
.
. di delta
1.2399909
.
. di " n = "  (1.645+1.282*exp(-
beta^2/4))^2*(1+2*p*delta)/(p*beta^2)
 n = 627.61987
```

So, **n = 628 = ~ 630**

Sample Size for Multiple logistic Regression

Multiple logistic regression requires larger n to detect effects. Let R denote the multiple correlation between the independent variable of interest, *X,* and the other covariates.

Then, sample size:

$n` = n/(1-R^2)$

Say, if R=0.25, then n` = 630/(1-0.25^2)= 672

Stata’s add-on programs for sample size estimation

- STPOWER: Survival studies
- Sampsi_reg: Linear regression
- Sampclus: Cluster sampling
- ART: randomized trials with survival time or binary outcome
- XSAMPSI: Cross-over trials
- Samplesize: Graphical results
- MVSAMPSI: multivariate regression

- STUDYSI: Comparative study with binary or time-to-event outcome
- SSKAPP: Kappa statistics measure of inter-rater aggrement
- CACLSI: log-rank/binomial test

Additional topics to be covered

- Sample allocation – stratified sampling
- Sample size corrected for design-effect(DEFF)
- Optimal sample size per cluster
- Sample size for clusters
- Sample size and power for pre-post surveys in program evaluation