Sample size estimation

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Why Sample Size Calculation?

Large Sample:

- Cost, Time and Personnel
- Unethical

Small Sample:

- Unable to detect clinically important results.

Clinical Significance:

If 25% reduction in mortality is clinically relevant, then why sample size calculation?.

The worry is that the difference in mortality, ie:25% could have occurred by chance alone.

In order to prove that the 25% reduction in mortality is statistically significant, one should study 200 patients in each arm.

Types of Problems in Medical Research:

Estimation: (Prevalence/Descriptive Study)

- Given proportion or Prevalence
- Given mean and standard deviation

Testing Hypothesis:(Cohort/Case Control/Clinical Trial)

- Given two proportion or incidence rates
- Given two group means and standard deviations

Types of Errors:

After any decision, questions remain to be answered.

1. What is the probability that difference shown, occurred due to chance?.

   p is less than 5 in a hundred ($p<.05$).

Types of Errors (Contd..):

2. What is the probability, that if a true difference of a stated magnitude existed, but the study would not have picked it up as statistically significant?.

This is beta or Type II error.

		Truth	
		$H_{0(\text{Hb same})}$	$H_{1(\text{Hb different})}$
Decision	Do not H_0	Right Decision	Type II Error
	Reject H_0	Type I Error	Right Decision

Estimation

Formulae

&

Problems

Descriptive study

A: when proportion is the parameter of our study

$$n = \frac{Z^2 * p * q}{d^2}$$

Where

Z= Standardized Normal deviate (Z value)

p = Proportion or Prevalence of interest.

q = 100 - p

d = Clinically expected variation.

Example:

From a pilot study it was reported that among headache patients 28% had vascular headache. It was decided to have 95% C.I and 10% variability in the estimated 28%.

How many patients are necessary to conduct the study.

P = 28%

q = 100-p=72%

Z_α= 1.96 for α at 0.05

d = 10% of 28% = 2.8

$$n = \frac{(1.96)^2 * 28 * 72}{(2.8)^2} = 987.8$$

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Prevalence of anaemia among adolescent girls in the urban slums of Vellore, south India

- **ABSTRACT** A community-based, cross-sectional study was conducted to determine the prevalence of anaemia among unmarried, adolescent south Indian girls in an urban slum setting. A total of 100 apparently healthy girls between the ages of 11 and 18 years were recruited. Their socioeconomic, dietary and anthropometric information was collected, and blood haemoglobin (Hb) was estimated. The prevalence of anaemia (Hb < 12 g%) was 29%. Most had mild anaemia; severe anaemia was not seen. Two-thirds of those with anaemia had low serum ferritin (<12 microg/L). Significant associations were observed between anaemia and low socioeconomic status, religion and reporting infrequent/non-consumption of meat (heme iron). Only meat consumption was related to haemoglobin by multiple regression analysis. Anaemia is a common problem among adolescent girls in this setting, though severe anaemia is rare. There is a need to improve their haemoglobin status through dietary modification along with preventive supplementation and nutrition education.

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A sample size of 235 would be sufficient to observe 29% prevalence of anemia (Ref: Chowdhary et al) with 20% precision and 95% confidence interval

z	p	q=1-p	precision	n	95% CI	
1.96	0.29	0.71	30%	100	0.20	0.39
1.96	0.29	0.71	20%	235	0.23	0.35
1.96	0.29	0.71	10%	941	0.26	0.32

Testing Hypothesis

Formulae

&

Problems

Analytical study

A: when proportion is the parameter of our study

Where

Z_α = Z value for α level

Z_β = Z value for β level

$$n = \frac{(Z_\alpha + Z_\beta)^2 \; p * q * 2}{d^2}$$

p = average percentage between two groups

q = 100 - p

d = Clinically meaningful difference between two groups

Example (Qualitative) :

	Mortality		
	Dead	**Alive**	**Total**
High Dose	**4 (16.7)**	**20**	**24**
Low Dose	**1 (4.2)**	**23**	**24**
Total	**5 (10.4)**	**43**	**48**

P = (16.7+4.2)/2=10.4%

q = 89.6%

Z_α= 1.96 for α at 0.05

Z_β = 1.282 for β at 0.10

$$n = \frac{(1.96+1.282)^2 * 10.4 * 89.6 * 2}{(12.5)^2} = 125$$

in each arm

B: when mean is the parameter of our study

$$n = \frac{(Z_\alpha + Z_\beta)^2 * S^2 * 2}{d^2}$$

Where

Z_α = Z value for α error

Z_β = Z value for β error

S = Common standard deviation between two groups

d = Clinically meaningful difference

Example: Duration of ICU study (in hours):

	Low Dose	High Dose
Mean	61.7	33.2
SD	93.8	89.1
n	23	20

$\alpha = 0.05 \qquad \beta = 0.10$

$$n = \frac{(1.96 + 1.282)^2 * 2 * 90^2}{28.5^2} = 210$$

$\alpha = 0.05 \qquad \beta = 0.20$

$$n = \frac{(1.96 + 0.842)^2 * 2 * 90^2}{28.5^2} = 157$$

Cluster design

- The sample size obtained from a simple sample size calculation needs to be multiplied by a design effect
- Design effect, $D = 1 + (m + 1)\rho$
- Where m is the cluster size and ρ is the intracluster correlation co-efficient

- Eg: if D=1.3 for the previous example
- n=157*1.3=204
- If cluster size is 20, then number of clusters=10.2≅11

Type I (Alpha) Error

p	Z_{α}
0.05	1.96
0.01	2.57
0.001	3.29

Type II (Beta) Error

p	Z_{β}
0.10	1.282
0.15	1.037
0.20	0.842

Non Significant Study

A study was done to evaluate the scope of community health workers (CHWs), in independently treating major psychiatric illness. Seventy psychiatric patients from 10 villages were identified and the diagnosis confirmed by a senior psychiatrist, using established criteria. The patients were than assigned randomly to one of 2 groups - the first group to be treated by a CHW and the second group to be treated by a fully qualified psychiatrist. The CHWs, who had been given 6 weeks training in drug prescribing etc. were free to manipulate dosages and drugs. After 2 months, an independent psychiatrist unware of the purpose and details of the study, was asked to evaluate the condition of all patients.

		Patient condition	
		Optimal	Suboptimal
Group	CHW	14 (40%)	21
	PSY.	22 (62.8%)	13

A chi-square test was done to asses the difference between the two groups and it was seen that there was no statistically significant difference. An evaluation of side effects also showed no significant difference between the two groups. The study concluded that psychiatrists were no better than CHWs in treating psychoses.

- Should be done before embarking on a study
- Determines the number of subjects that should be studied or observations that should be made
- Data on the research question being asked is vital!
- Literature search
- Pilot data

Issues:

- Need to differentiate between Prevalence and Testing Hypothesis studies.

- Different formulae for Case Control studies and
- Survival Analysis.

- Incorporate drop out rates.

- Cluster designs should inflate the size based on
- Design effect.

https://www.youtube.com/watch?v=PbODigCZqL8

http://powerandsamplesize.com/Calculators/

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