TEACHING: ESTIMATION OF MINIMUM SAMPLE SIZE AND THE IMPACT OF EFFECT SIZE AND ALTERING THE TYPE - I & II ERRORS ON IT, IN CLINICAL RESEARCH

K. R. Sundaram and Amrutha Jose
Department of Biostatistics, Amrita Institute of Medical Sciences & Research Centre, India
krsundaram@aims.amrita.edu

In any research study, one of the most important questions asked for at the time of planning the study is 'what should be the sample size in my study'. Estimation of minimum sample size depends upon- design of the study, whether it is an estimation problem or a hypothesis testing problem, the type of variable(s) to be studied, type-I & II errors acceptable and rough estimates of the parameters to be studied. In this presentation estimation of sample size for a clinical trial, comparing the efficacy of two different drugs, in case of categorical variables and the effect of altering the type I & II errors and the effect size have been discussed with examples. The results showed that the sample size increases when the type-I or / and II errors are decreased. Symmetric nature of sample size on either side with respect to the effect size has also been explained.

BACKGROUND

In any research study, one of the most important questions asked for at the time of planning the study is 'what should be the sample size in my study'. Many students / researchers think that the figure on sample size can be got just by asking for it. Sample size is not a magic figure and it is also not a universal figure. It depends upon many factors - design of the study, whether it is an estimation problem or a hypothesis testing problem, the type of variable(s) to be studied (measurable or categorical), type - I & II errors acceptable and rough estimates of the parameters to be studied. Too large a sample size and too small a sample size are not recommended for many reasons. Too large a sample size, apart from resulting in unnecessary increase in the budget, may make a small difference in the parameter values between the groups statistically significant which may not be clinically significant. Similarly too small a sample size may not make a clinically important difference in the parameter values between the groups statistically significant. The pertinent question, then, is what should be the ideal / optimum / minimum sample size for any given study based on the information required for estimation of sample size.

For any research study there could be budget and time constraints. We would like to have our estimates for a pre-fixed Confidence Coefficient (1 - type I error) and allowable error which are determined based on the time & budget at the disposal of the investigator. Similarly we would like to test the statistical significance of the research hypothesis for a pre-fixed Confidence Coefficient and Power (1 - type II error) of the test which are determined based on the time & budget at the disposal of the investigator. Also whether the test is one-tailed or two-tailed affects the sample size. Besides these factors the effect size (obtained from the previous studies or from a pilot study) which is the difference in the proportions of positive effect between the test group and the comparative control (placebo) group also determines the minimum sample size. Demonstration of the determination of minimum sample size for the above mentioned parameters based on hypothetical data has been done in this presentation.

OBJECTIVES

- To study the effect of increasing the Confidence coefficient and Power of the test in the estimation of minimum sample size.
- To study the effect of testing one-sided hypothesis compared to two-sided hypothesis on the sample size.
- To study the effect of the magnitude of the differences in the proportions of the variable, say, positive response between two populations, say, test group and control (placebo) group on the sample size.

In C. Reading (Ed.), *Data and context in statistics education: Towards an evidence-based society. Proceedings of the Eighth International Conference on Teaching Statistics (ICOTS8, July, 2010), Ljubljana, Slovenia*. Voorburg, The Netherlands: International Statistical Institute. www.stat.auckland.ac.nz/~iase/publications.php [© 2010 ISI/IASE]

KNOWLEDGE REQUIRED

Concept of Standard Error, Type I & II errors, Confidence Coefficient & Power of the test Normal curve and One and Two - sided (tailed) tests (Bland, 2000; Alvan, 2001; Armitage et. al., 2002; Sundaram et. al., 2009). It is assumed that all the participants / readers have the necessary knowledge on the above indicated statistical concepts.

METHODS

Formula:

$$n = \frac{2 \times \left(Z_{1-\alpha/2} + Z_{1-\beta}\right)^2 \times p \times q}{(p_1 - p_2)^2} \qquad \text{(Two - sided test)}$$

$$\text{where } p = \frac{(p_1 + p_2)}{2}.$$

TABLE ON Z - VALUES

Significance level (α) and Power (1- β) values for sample size calculation:

		Z -Values	
		Two - sided test ($Z_{1-\alpha/2}$)	One - sided test ($Z_{1-\alpha}$)
Significance Level	0.01	2.576	2.326
	0.05	1.960	1.645
	0.10	1.645	1.282
		$Z_{1-\beta}$	
Power	0.80	0.842	
	0.90	1.282	
	0.95	1.645	
	0.99	2.326	

RESULTS

Table 1 gives the minimum sample size estimated for increasing Confidence Coefficients (95%, 99% & 99.5%) and Power (80%, 90% & 95%) for the effect size - 0.05 ($p_1 = 0.05$ & $p_2 = 0.10$) and ($p_1 = 0.90$ & $p_2 = 0.95$), the two extreme values of p_1 and p_2.

Table 1. Sample size for different Confidence Coefficients & Power values for the two extreme combination of Proportions

Confidence Coefficient (%)	Power (%)	Proportions $p_1 = 0.05$ & $p_2 = 0.10$		Proportions $p_1 = 0.90$ & $p_2 = 0.95$	
		2 - sided	1 - sided	2 - sided	1 - sided
95	80	**435**	**342**	**435**	**342**
	90	**581**	**474**	**581**	**474**
	95	**718**	**598**	**718**	**598**
99	80	**648**	**557**	**648**	**557**
	90	**825**	**722**	**825**	**722**
	95	**987**	**874**	**987**	**874**
99.5	80	**946**	**856**	**946**	**856**
	90	**1157**	**1058**	**1157**	**1058**
	95	**1348**	**1240**	**1348**	**1240**

It could be seen from Table 1 and Figures 1 (a) and 1 (b) that minimum sample size increases when the Confidence Coefficient & Power increase. Also, sample size required, for a given Confidence Coefficient & Power, is less for a one-sided test compared to two-sided test.

If the direction of the test is known sample required for a given Confidence Coefficient & Power, is less compared to when the direction of the test is not known. The results also showed that sample size is the same for the effect size (p_1 - p_2) at the lower & upper extremes.

Figure 1(a). Sample Size for different Confidence Coefficients & Power values for two extreme combination of Proportions for two-sided tests

Figure 1(b). Sample Size for different Confidence Coefficients & Power values for two extreme combination of Proportions for one-sided tests

Table 2 gives the minimum sample size estimate for 95% confidence coefficient and 80% power for different effect sizes for different combinations from lower proportions to upper proportions (Table 2 (a) for effect size 0.05, Table 2 (b) for 0.10, Table 2 (c) for 0.20, Table 2 (d) for 0.30, Table 2 (e) for 0.40 and Table 2 (f) for effect size 0.50).

The results showed that for all the effect sizes, the sample size was lower at the two extremes of the proportion of the two groups and was increasing for the corresponding increase in p_1 and p_2 from the lower side and for the corresponding decrease from the upper side resulting symmetry of sample size on either sides (upper and lower), showing symmetric nature of the sample size for the same effect size with different combinations.

Table 2(a). Sample size for Effect size = 0.05 for different combination of Proportions with 95% Confidence Coefficient & 80% Power

Proportions	p_1	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50
	p_2	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50	0.55
Sample size		**435**	**686**	**906**	**1094**	**1251**	**1377**	**1471**	**1534**	**1565**	**1565**

0.55	0.60	0.65	0.70	0.75	0.80	0.85	0.90
0.60	0.65	0.70	0.75	0.80	0.85	0.90	0.95
1534	**1471**	**1377**	**1251**	**1094**	**906**	**686**	**435**

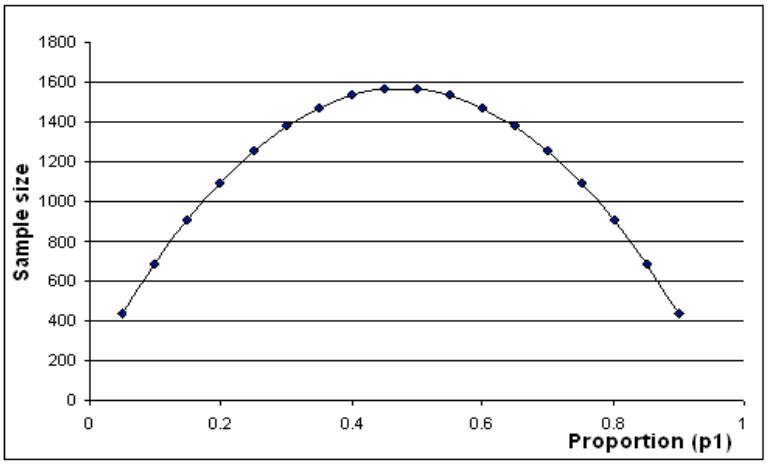

Figure 2. Sample size for Effect size=0.10 for different combination of Proportions with 95% Confidence Coefficients & 80% Power

Table 2(b). Sample size for Effect size = 0.10 for different combination of Proportions with 95% Confidence Coefficients & 80% Power

Proportions	p_1	0.05	0.15	0.25	0.35	0.45	0.55	0.65	0.75	0.85
	p_2	0.15	0.25	0.35	0.45	0.55	0.65	0.75	0.85	0.95
Sample size		**140**	**250**	**329**	**376**	**391**	**376**	**329**	**250**	**140**

Table 2(c). Sample size for Effect size = 0.20 for different combination of Proportions with 95% Confidence Coefficients & 80% Power

Proportions	p_1	0.05	0.15	0.25	0.35	0.45	0.55	0.65	0.75
	p_2	0.25	0.35	0.45	0.55	0.65	0.75	0.85	0.95
Sample size		**49**	**72**	**88**	**96**	**96**	**88**	**72**	**49**

Table 2(d). Sample size for Effect size = 0.30 for different combination of Proportions with 95% Confidence Coefficients & 80% Power

Proportions	p_1	0.05	0.15	0.25	0.35	0.45	0.55	0.65
	p_2	0.35	0.45	0.55	0.65	0.75	0.85	0.95
Sample size		**27**	**35**	**41**	**42**	**41**	**35**	**27**

Table 2(e). Sample size for Effect size = 0.40 for different combination of Proportions with 95% Confidence Coefficients & 80% Power

Proportions	p_1	0.05	0.15	0.25	0.35	0.45	0.55
	p_2	0.45	0.55	0.65	0.75	0.85	0.95
Sample size		**17**	**21**	**23**	**23**	**21**	**17**

Table 2(f). Sample size for Effect size = 0.50 for different combination of Proportions with 95% Confidence Coefficients & 80% Power

Proportions	p_1	0.05	0.15	0.25	0.35	0.45
	p_2	0.55	0.65	0.75	0.85	0.95
Sample size		**12**	**14**	**14**	**14**	**12**

DISCUSSION AND CONCLUSION

The aim of this paper is mainly for educating the students of Statistics and the research workers, the method of estimation of minimum sample size for different values of confidence coefficients and power of the test and for different effect sizes. The students and researchers will get clear idea of the impact of type I and type II errors and the direction of the test depending upon the effect size. Minimum sample size can be determined and finalized depending upon the time and budget available for the study by altering type I and type II errors and also depending upon the direction of the test (one-sided or two-sided).

REFERENCES

Bland, M. (2000). *An introduction to Medical Statistics*. Oxford University Press.

Alvan, R. F. (2001). *Principles of medical statistics*, CRC press.

Armitage, P., Berry, G., & Matthews, J. N. S. (2002). *Statistical Methods in Medical Research*. *4th Ed.*, Blackwell science.

Sundaram, K. R., Dwivedi, S. N., & Sreenivas V. (2009). *Medical Statistics: Principles & Methods*. New Delhi: BI Publications.