Biostatistics A

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SCHOOL OF PHD PROGRAMMES
MAGNA GRAECIA UNIVERSITY

1. Introduzione
2. Esempi
   - recuperare informazioni descrittive

testi

Review

Statistics review 4: Sample size calculations

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Abstract

The present review introduces the notion of statistical power and the hazard of under-powered studies. The problem of how to calculate an ideal sample size is also discussed within the context of factors that affect power, and specific methods for the calculation of sample size are presented for two common scenarios, along with extensions to the simplest case.

Keywords statistical power, sample size

Previous reviews in this series introduced confidence intervals and *P* values. Both of these have been shown to depend strongly on the size of the study sample in question, with larger samples generally resulting in narrower confidence intervals and smaller *P* values. The question of how large a study should ideally be is therefore an important one, but it is all too often neglected in practice. The present review provides some simple guidelines on how best to choose an appropriate sample size.

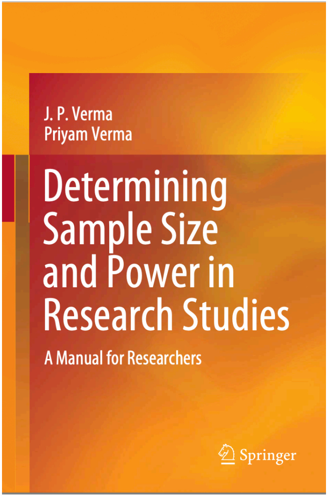
Research studies are conducted with many different aims in mind. A study may be conducted to establish the difference, or conversely the similarity, between two groups defined in terms of a particular risk factor or treatment regimen. Alternatively, it may be conducted to estimate some quantity, for example the prevalence of disease, in a specified population with a given degree of precision. Regardless of the motivation for the study, it is essential that it be of an appropriate size to achieve its aims. The most common aim is probably that of determining some difference between two groups, and it is this scenario that will be used as the basis for the remainder of the present review. However, the ideas underlying the methods described are equally applicable to all settings.

Power

The difference between two groups in a study will usually be explored in terms of an estimate of effect, appropriate confidence interval and *P* value. The confidence interval indicates the likely range of values for the true effect in the population, while the *P* value determines how likely it is that the observed effect in the sample is due to chance. A related quantity is the statistical power of the study. Put simply, this is the probability of correctly identifying a difference between the two groups in the study sample when one genuinely exists in the populations from which the samples were drawn.

The ideal study for the researcher is one in which the power is high. This means that the study has a high chance of detecting a difference between groups if one exists; consequently, if the study demonstrates no difference between groups the researcher can be reasonably confident in concluding that none exists in reality. The power of a study depends on several factors (see below), but as a general rule higher power is achieved by increasing the sample size.

It is important to be aware of this because all too often studies are reported that are simply too small to have adequate power to detect the hypothesized effect. In other words, even when a difference exists in reality it may be that too few study subjects have been recruited. The result of this is that *P* values are higher and confidence intervals wider than would be the case in a larger study, and the erroneous conclusion may be drawn that there is no difference between the groups. This phenomenon is well summed up in the phrase, 'absence of evidence is not evidence of absence'. In other words, an apparently null result that shows no difference between groups may simply be due to lack of statistical power, making it extremely unlikely that a true difference will be correctly identified.



Review

Statistics review 4: Sample size

Elise Whitley[1] and Jonathan Ball[2]

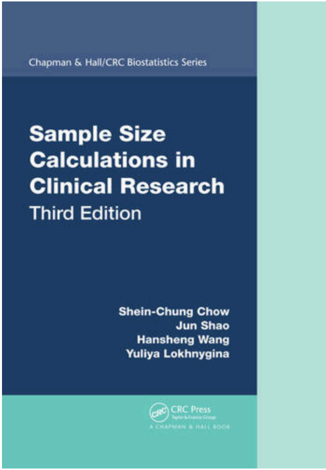
https://www.biomedcentral.com/collections/CC-Medical

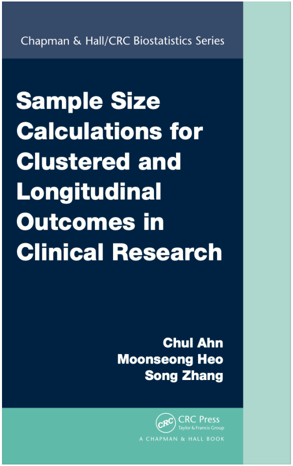
Determining Sample Size and Power in Research Studies

J J.P. Verma

https://www.academia.edu

testi


Chapman & Hall/CRC Biostatistics Series
Sample Size Calculations in Clinical Research
Third Edition
Shein-Chung Chow
Jun Shao
Hansheng Wang
Yuliya Lokhnygina
CRC Press


Chapman & Hall/CRC Biostatistics Series
Sample Size Calculations for Clustered and Longitudinal Outcomes in Clinical Research
Chul Ahn
Moonseong Heo
Song Zhang
CRC Press
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A CHAPMAN & HALL BOOK

Chapter 2: Understanding Statistical Inference

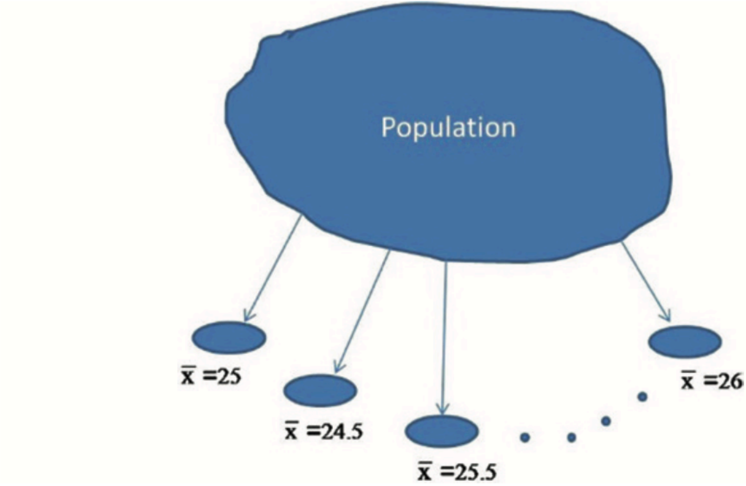


Fig. 2.1 Drawing all possible samples of the same size from the population

Chapter 2: Understanding Statistical Inference

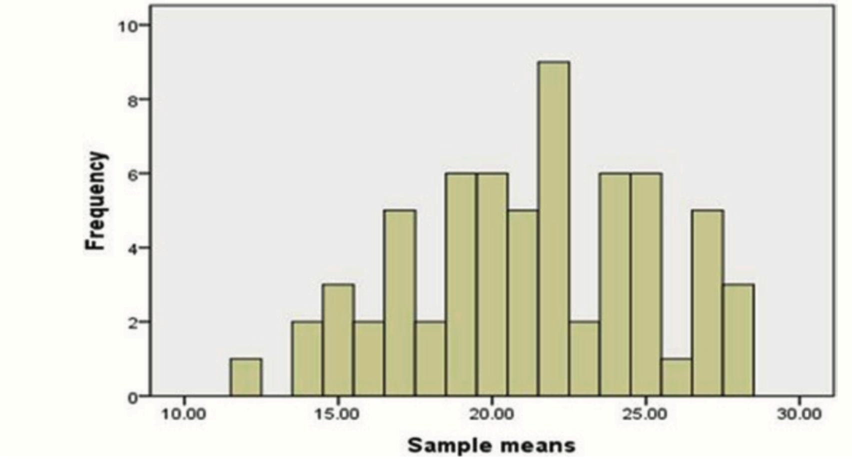


Fig. 2.3 Histogram of the sample means

Chapter 2: Understanding Statistical Inference

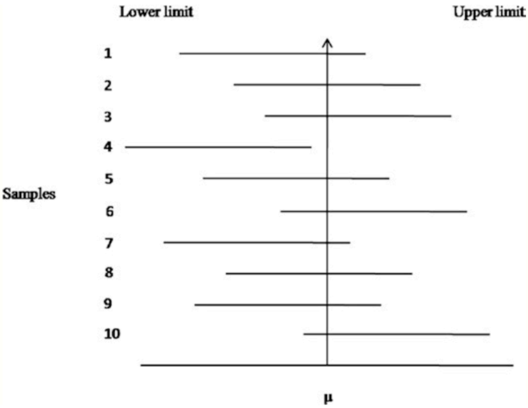
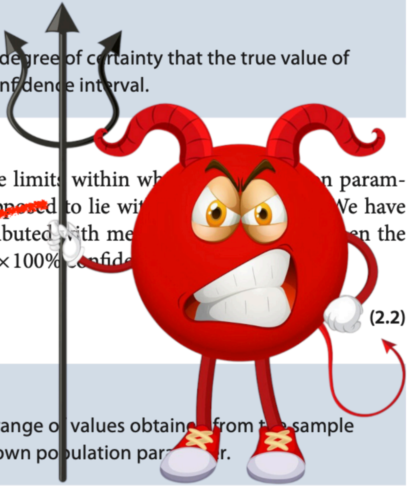


Fig. 2.7 Confidence intervals constructed on the basis of the sample for estimating population mean

Chapter 2: Understanding Statistical Inference

Definition

Confidence level can be defined as the degree of certainty that the true value of population parameter lies within the confidence interval.



Confidence Interval

Confidence interval can be defined as the limits within wh [illegible] n parameters such as mean or proportion are supposed to lie wi [illegible] We have seen that if a variable x is normally distributed with me [illegible] en the confidence interval of mean with $(1-\alpha)\times 100\%$ confide [illegible]

$$\bar{x} - Z_{\alpha/2}\frac{\sigma}{\sqrt{n}} \quad \text{to} \quad \bar{x} + Z_{\alpha/2}\frac{\sigma}{\sqrt{n}} \qquad \textbf{(2.2)}$$

Definition

A **confidence interval** is the estimated range of values obtained from the sample data which is likely to include the unknown population par [illegible] r.

Chapter 2: Understanding Statistical Inference

Researcher's decision		Actual state of H_0	
		H_0 *true*	H_0 *false*
	Reject H_0	Type I error (α) (False positive)	Correct decision $(1 - \beta)$
	Do not reject H_0	Correct decision	Type II error (β) (False negative)

1. L'errore di primo tipo (falso positivo, condannare l'innocente)
2. L'errore di secondo tipo (falso negativo, assolvere il colpevole)

Chapter 2: Understanding Statistical Inference

1. L'errore di primo tipo (falso positivo, condannare l'innocente)
2. L'errore di secondo tipo (falso negativo, assolvere il colpevole)

Definition
A Type I error can be defined as the probability of rejecting the null hypothesis when it is true. It is represented by α.

Definition
A Type II error is the probability of not rejecting the null hypothesis when it is false. It is represented by β.

Domanda cruciale

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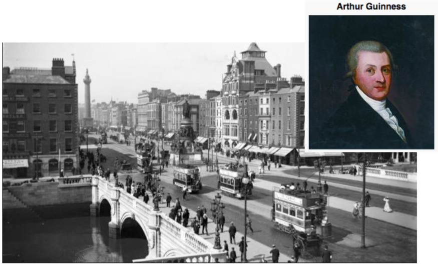
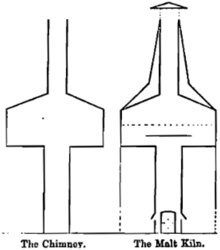
Quando facciamo un esperimento, uno studio clinico, siamo in grado di dire quanto valgono queste probabilità α e β ?





The Kiln Drying of Malt.

By H. M. Chubb.

Not Kiln-Dried	Kiln-Dried	Difference
1903	2009	+106
1935	1915	-20
1910	2011	+101
2496	2463	-33
2108	2180	+72
1961	1925	-36
2060	2122	+62
1444	1482	+38
1612	1542	-70
1316	1443	+127
1511	1535	+24

Tabella: One Sample T-Test

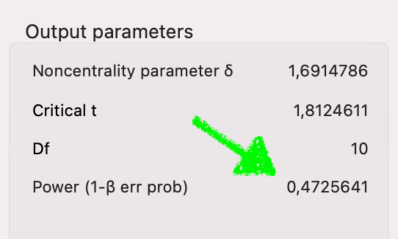
				95% CI for Mean Diff.	
t	df	p	Mean Diff.	Lower	Upper
1.690	10	0.122	33.727	−10.727	78.182

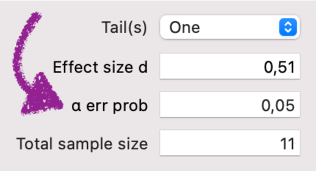
SPOILER: con G*Power si può

- basta considerare l'**effect size** (la d di Cohen)

$$d = \frac{m - \mu}{s}$$

t	p	Cohen's d
1.69	0.122	0.510





Domanda cruciale

Definition
A Type I error can be defined as the probability of rejecting the null hypothesis when it is true. It is represented by α.

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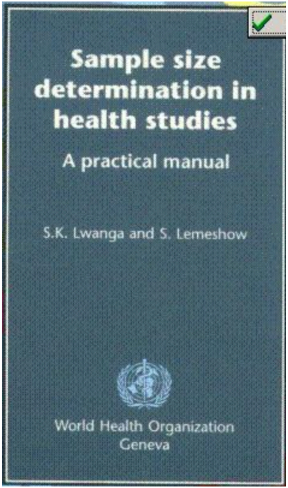
Nell'esperimento di Gossett, se **scegliamo** la probabilità $\alpha = 5\%$ allora $\beta = 53\%$ (poiché $1 - \beta = 47\%$)

$\beta = 0.53$? Vuol dire 'testa o croce'

Nell'esperimento di Gossett, se scegliamo la probabilità $\alpha = 5\%$ allora $\beta = 53\%$

It is important to be aware of this because all too often studies are reported that are simply too small to have adequate power to detect the hypothesized effect. In other words, even when a difference exists in reality it may be that too few study subjects have been recruited. The result of this is that *P* values are higher and confidence intervals wider than would be the case in a larger study, and the erroneous conclusion may be drawn that there is no difference between the groups. This phenomenon is well summed up in the phrase, 'absence of evidence is not evidence of absence'. In other words, an apparently null result that shows no difference between groups may simply be due to lack of statistical power, making it extremely unlikely that a true difference will be correctly identified.

Perché 80% ?


Sample size
determination in
health studies
A practical manual
S.K. Lwanga and S. Lemeshow
World Health Organization
Geneva

Perché 80% ?

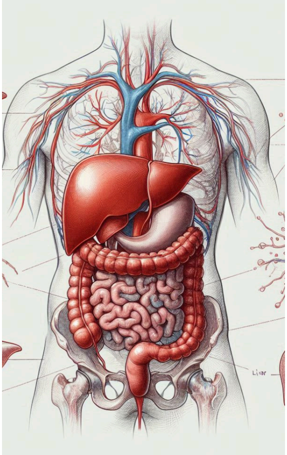
"Lehr's Equation" or the "Rule of 16":

$$n_{group} = \frac{2(1.96 + 0.84)^2}{(\Delta)^2}$$

$$n_{group} = \frac{16}{(\Delta)^2}$$

PMID: 27688437

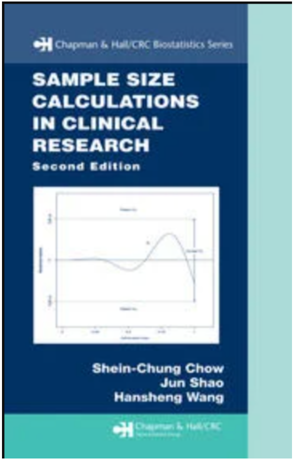
esempio: angiosarcoma



- 5 yrs survival rate: $\sim 10\%$
- studio preclinico: 2/6 ok
  - $\sim 30\%$

i test esatti per le proporzioni

il test binomiale: un solo campione



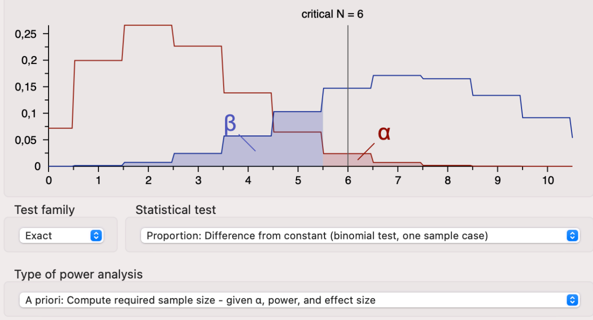
i test esatti per le proporzioni

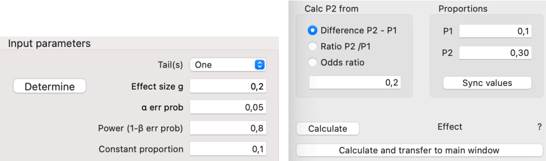
il test binomiale: un solo campione

5.1.3 An Example

Suppose the investigator is interested in conducting a trial to study the treatment effect of a test compound in curing patients with certain types of cancer. The responder is defined to be the subject who is completely cured by the study treatment. According to literature, the standard therapy available on the market can produce a cure rate of 10% ($p_0 = 10\%$). A pilot study of the test compound shows that the test compound may produce a cure rate of 30% ($p_1 = 30\%$). The objective of the planning trial is to confirm such a difference truly exists. It is desirable to have a sample size, which can produce 80% power at 5% level of significance. According to Table 5.1.1, the total sample size needed is given by 25. The null hypothesis should be rejected if there are at least 5 subjects who are classified as responders.

i test esatti per le proporzioni





recuperare informazioni descrittive

1. media: 49 anni
2. s.d.: 27.2 anni

mediana ?
quartili ?

oppure: mediana 44, primo quartile 41, terzo quartile 74.
Media? Deviazione standard?

recuperare informazioni descrittive / 1 of 2

Possiamo dedurre la media μ dalla mediana, dai quartili e dal range?

$$\mu \approx \frac{a+2m+b}{4} + \frac{a-2m+b}{4n} \approx \frac{a+2m+b}{4}$$

$$\mu \approx \frac{a+2Q_1+2m+2Q_3+b}{8}$$

$$\mu \approx \frac{Q_1+m+Q_3}{3}$$

recuperare informazioni descrittive / 2 of 2

Possiamo dedurre la deviazione standard σ dalla mediana, dai quartili e dal range?

$$\sigma \approx \frac{b-a}{\xi(n)}$$

$$\sigma \approx \frac{Q_3-Q_1}{\eta(n)}$$

$$\sigma \approx \frac{1}{2}\left(\frac{b-a}{\xi(n)}+\frac{Q_3-Q_1}{\eta(n)}\right)$$

Un esempio

- the Reference Data Set
  - dal 2003 al 2014, King's College London Dental Institute

- LL8Gf
  - Lower Left Third Molar
  - Stage G female
  - 18 years old
  - caucasian UK

Un esempio

https://www.dentalage.co.uk/rds-uk-caucasian/

$$n = 114$$

$$\mu \approx \frac{a + 2Q_1 + 2m + 2Q_3 + b}{8}$$

$$\frac{14.9 + 34.2 + 36.2 + 39.9 + 22.8}{8}$$

$$\mu \approx 18.5$$

0th%ile	0.5%ile	5%ile	10%ile
14.96	15.73	15.97	16.32
25%ile	**50%ile**	**75%ile**	**90%ile**
17.07	18.13	18.99	20.64
95%ile	**99.5%ile**	**100th%ile**	
21.35	21.91	22.78	

Un esempio

https://www.dentalage.co.uk/rds-uk-caucasian/

$$n = 114$$

$$\sigma \approx \frac{1}{2}\left(\frac{b-a}{\xi(n)} + \frac{Q_3 - Q_1}{\eta(n)}\right)$$

$$\frac{1}{2}\left(\frac{22.8-14.9}{4.55} + \frac{19.0-17.1}{1.35}\right)$$

$$\sigma \approx 1.6$$

0th%ile	0.5%ile	5%ile	10%ile
14.96	15.73	15.97	16.32

25%ile	50%ile	75%ile	90%ile
17.07	18.13	18.99	20.64

95%ile	99.5%ile	100th%ile
21.35	21.91	22.78

Un esempio

$$\mu \approx 18.5$$

$$\sigma \approx 1.6$$

TDS	n	mean	sd
LL8Gf	114	18.25	1.63