اندازه نمونه در مطالعات تحلیلی

Sample Size in Analytical Studies

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Factors Determining Sample Size

- Number of **groups** and subgroups within the sample
- Value of **information** in the study
- **Accuracy** level required in results
- **Cost** of sample
- **Variability** of the population
- Sampling **Method**
- …….

Underlying Statistical Principles in Hypothsis Testing

- Type one error
- Type two error, power
- Effect size

Reality / Test Result Statistical Analysis show that:	H_0 is really true (Drug A and Drug B really have same effect)	H_0 is really false (Drug A and Drug B really have different effects)
Accept H_0 No difference is observed between Drug A and Drug B		**Type II error** β
Reject H_0 Significant difference is observed between Drug A and Drug B	**Type I error** α	**Power** **1-β**

Effect Size

- Effect size is the size of the association(or difference) that an investigator would like to be able to detect or that would be clinically important.
- Smallest difference worth detecting.
- Selecting appropriate effect size is the most **difficult** aspect of sample size planning

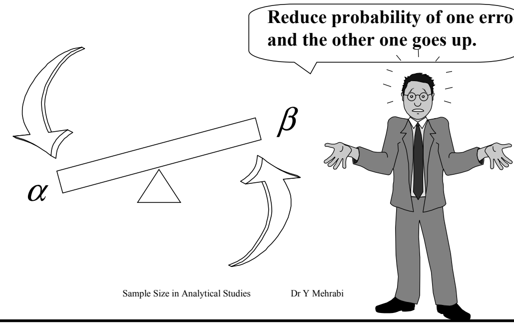
How to find the effect size

- Prior studies
- Choose the smallest effect size that is clinically meaningful.
- Do a small pilot.

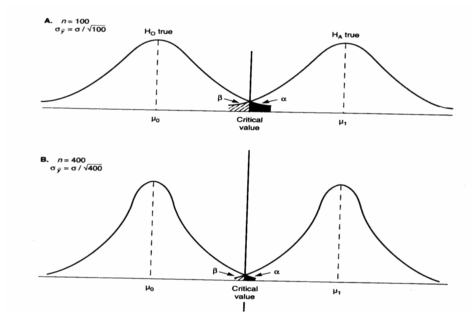
Power

- **1-Type two Error** 1- β
- The probability of rejecting the null hypothesis when it is actually false
- Usually power is set as 80% or 90% (power to find association if exists)

α & β Have an Inverse Relationship



Errors



Relation between α, β and n

Significance Level ↓ α

Power of Test ↑ 1-β → Sample Size ↑ n

Sample Size

for

Continuous Response Variables

Hypothesis testing for means of 2 independent groups (t-test)

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 \left(s_1^2 + s_2^2\right)}{\Delta^2}$$

برای هر گروه

$\Delta = Effect\ size$

s_1 = Sd of group 1

s_2 = Sd of group 2

Hypothesis testing for means of 2 independent groups (t-test)

$$n = \frac{2\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 s^2}{\Delta^2}$$ برای هر گروه

s = pooled standard deviation: $s^2 = \frac{s_1^2 + s_2^2}{2}$

α	1-α	β	1-β	$z_{1-\frac{\alpha}{2}}$	$z_{1-\beta}$	$\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^2$
0.05	0.95	0.1	0.90	1.96	1.28	10.5
0.05	0.95	0.2	0.80	1.96	0.84	7.84
0.01	0.99	0.1	0.90	2.57	1.28	14.82
0.01	0.99	0.2	0.80	2.57	0.84	11.6
.	.					.
.	.					.

مثال

مطالعه ای برای بررسی تاثیر کاهش نمک در رژیم غذایی، بر فشارخون افراد در دست طراحی است. بر اساس مطالعات قبلی انحراف معیار فشارخون در افراد با رژیم غذایی پرنمک ۱۲ و در افراد با رژیم غذایی کم نمک ۱۰/۳ میلی متر جیوه بوده است.

چه تعداد نمونه انتخاب کنیم تا بتوانیم با سطح اشتباه ۵ درصد و توان ۹۰ درصد حداقل اختلاف ۸ میلی مترجیوه بین میانگین دو گروه را معنی دار تلقی کنیم؟

پاسخ

α= 0.05 β=0.10 d=8

$$n = \frac{(1.96 + 1.28)^2 (12^2 + 10.3^2)}{8^2} = 41$$ در هر گروه

در مجموع تعداد **۸۲** نمونه لازم است

پاسخ (فرمول دوم)

α= 0.05 β=0.10 d=8

$$s^2 = \frac{s_1^2 + s_2^2}{2} = \frac{12^2 + 10.3^2}{2} = 125$$

$$n = \frac{2(1.96 + 1.28)^2 125}{8^2} = 41$$ در هر گروه

در مجموع تعداد **۸۲** نمونه لازم است

Hypothesis testing for paired sample means

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 s^2}{\Delta^2}$$ $\Delta = \textit{effect size}$

s = standard deviation of the differences

مثال

نتایج مطالعات نشان داده است که میانگین وزن مردانی که به تازگی بیماری قلبی آنها تشخیص داده شده است ۷۵ کیلوگرم بوده است. می خواهیم تاثیر نوعی تمرینات ورزشی را در کاهش وزن این گونه مردان آزمون کنیم.

تاثیر ورزش را زمانی معني دار تلقی خواهیم کرد که به طور متوسط وزن افراد را حداقل ده درصد (۷/۵ کیلوگرم) کاهش دهد. با در نظر گرفتن توان ۸۰ درصد و سطح اشتباه ۵ درصد چه تعداد نمونه انتخاب کنیم؟ انحراف معیار اختلافات را ۱۲ کیلوگرم در نظر بگیرید.

پاسخ

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

Sd=12 d=7.5 kg

$$n=\frac{(1.96+0.84)^2 12^2}{7.5^2}\cong 21$$

اگر توان آزمون ۹۰ درصد در نظر گرفته شود تعداد ۲۷ نفر لازم است

Non Response

- The sample size refers to the number of complete responses needed.
- Non response must be estimated and taken into account to arrive to the final size

Total Sample Size

If design is stratified and Tests/estimations will be done at each strata. *The sample size applies to each strata.*

Otherwise all within strata comparisons or estimations will have larger errors or confidence intervals

Randomization Methods

- Parallel Groups
- Matched Groups
  - **Individual Matching**
  - **Group Matching**

جدول ارقام تصادفی

01703	49894	57579	98505	85008	98681	56862	41860
87556	95669	39885	31669	31460	96413	84398	31562
84254	60541	73290	54685	80208	77044	14771	33378
12429	43566	32578	38935	75460	98133	18386	12417
63055	26768	63609	92424	50808	95416	12795	50787
18348	79628	05778	72095	90754	90430	00791	38023
19827	95727	02372	23485	54372	89732	67768	72151
30236	52309	99971	44890	28222	92140	40703	16888
32160	42795	04959	73840	99110	07527	73725	19291
14832	30334	18047	38712	32931	85481	15378	25011
21151	02668	44154	95153	63213	70014	67531	52581
89677	82090	42211	75118	36233	25131	13314	33063
67129	12388	41678	51286	80948	91599	52652	02519
27808	23807	25424	35877	96308	45847	88287	88419
24646	88222	66395	24060	98186	81741	08675	36931
10030	79086	89464	28282	89252	14777	02033	42852

Hypothesis testing for 2 independent proportions

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

$$\bar{p} = \frac{p_1 + p_2}{2}$$

Example

- In a pilot study, a sample of 50 adult subjects suffering from a certain disease were compared to a sample of 50 comparable control subjects who were free of disease.
- 30 of the subjects with the disease (60%) and 25 of the controls (50%) were involved in industries using a specific chemical.
- How many subjects should be studied in each of the two groups to have 90% power of detecting the true difference between the groups if the hypothesis tested at the 5% level?

Testing 2 prevalences Example

$p_1 = 0.60$ $p_2 = 0.50$ $\bar{p} = \frac{0.50 + .60}{2} = 0.55$

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

$$n = \frac{\left[1.96\sqrt{2\times 0.55\times(1-0.55)} + 1.28\sqrt{0.50(1-0.50)+0.60(1-0.60)}\right]^2}{(0.60-0.50)^2}$$

n = 518

For each group (1036 in total)

P1	P2	P_bar	$z_{1-\frac{\alpha}{2}}$	$z_{1-\beta}$	n
0.5	0.6	0.55	1.96	1.28	518
0.5	0.6	0.55	1.96	0.84	387
0.5	0.7	0.6	1.96	1.28	124
0.5	0.7	0.6	1.96	0.84	93
0.5	0.55	0.525	1.96	1.28	2092
0.5	0.55	0.525	1.96	0.84	1563

Testing 2 prevalences Example

•We want to test if the prevalences of a disease under two conditions are the same or not.

First we must decide which is the difference to detect. If the prevalence is estimated at 10% then a difference of 5% i.e. 15% can be considered 'significantly higher'.

• Second: we must decide on the errors rates,

alpha : we can easily choose 0.05 as everybody else.

beta : here we have a problem. If we are fairly sure that the prevalences will be different, then beta has almost no role in testing procedure and we can choose a standard value of 0.20.

But, if no difference, is a real possibility then we need a high probability at our cut point value of 5%, then beta = 0.05.

Testing 2 prevalences Example

Now we have

$$n = \frac{\left\{1.96\sqrt{2\times 0.125\times(1-0.125)} + 0.84\sqrt{0.10(1-0.10)+0.15(1-0.15)}\right\}^2}{(0.10-0.15)^2}$$

$$\bar{p} = \frac{0.10+0.15}{2} = 0.125$$

n = 424

with a beta = 0.05 we obtain :

n = 801

Almost double sample size in each group to be able to say that the difference is less than expected with only a 5 % margin of error. A 5 % margin of error is probably too narow, but it depends on the importance of the subject under study.