Sample size calculation

Research Week 2014
Health Cluster UKM

Introduction

- This is an abbreviated set of slides on how to calculate sample size.
- It will focus on those with
  - Measuring prevalence/incidence for outcome
  - Qualitative outcome (i.e. Dead vs Alive)
  - Continuous outcome (i.e. drop of BP in mm Hg)

  for commonly used study designs in PPUKM.
- Those who want the complete set of slides for calculating sample size, please refer to next page;

Sample Size Calculation on Slideshare

1. Why do we need to calculate sample size?
2. Tools to calculate sample size
3. Calculate sample size for prevalence studies
4. Calculate sample size for cross-sectional studies
5. Calculate sample size for case-control studies
6. Calculate sample size for cohort studies
7. Calculate sample size for clinical trials
8. Calculate sample size for clinical trials (continuous outcome)
9. Calculate sample size for diagnostic study
10. eBook

Measuring prevalence

Calculate sample size

Prevalence

- If the objective of your study is to measure the **prevalence** of the outcome of interest, then you will be conducting a **cross-sectional study**. So you will only **take a sample** of your population. The number of sample selected depends on the **expected prevalence** rate.
- To estimate the expected prevalence rate, you will need to **do a literature review**, hopefully similar to your own population.

Prevalence – Sample size

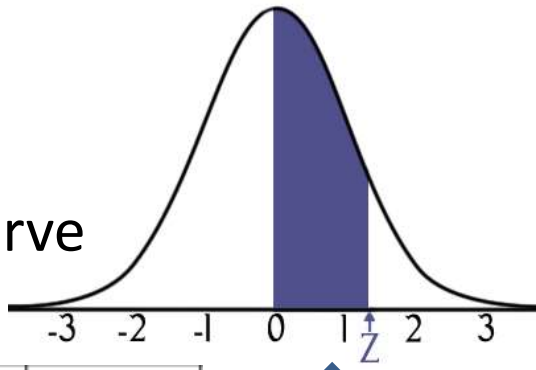
- Do a literature review to estimate the prevalence for the outcome of interest being studied.
- Determine the absolute precision required i.e. 5% (usually between 3% to 5%).
- Calculate manually using (Kish L. 1965)

$$n = (Z_{1-\alpha})^2(P(1-P)/D^2)$$

- Or use the attached Excel file.

Example – To determine Prevalence of Obesity

- Confidence interval = 1 - α = 95%;
  $Z_{1-\alpha} = Z_{0.95} = 1.96$ (value is fixed at 1.96)
  (from normal distribution table, area under curve =0.475x2=0.95 when z=1.96).



z	0.00	0.01	0.02	0.03	0.04	0.05	0.06
1.6	0.445	0.446	0.447	0.448	0.450	0.451	0.452
1.7	0.455	0.456	0.457	0.458	0.459	0.460	0.461
1.8	0.464	0.465	0.466	0.466	0.467	0.468	0.469
1.9	0.471	0.472	0.473	0.473	0.474	0.474	0.475

- Prevalence = P = 20%
- Absolute precision required = 5 percentage points,
  (means that if the calculated prevalence of obesity is 20%, then the true value of the prevalence lies between 15-25%).

Calculate Manually

- $n = (Z_{1-\alpha})^2(P(1-P)/D^2)$ where
- $Z_{1-\alpha} = Z_{0.95} = 1.96$ (from normal distribution table. This value of 1.96 is standard for CI of 95%).
- P = 20% = 0.2 in this example
- D = 5% = 0.05 in this example
- $n = 1.96^2 \times (0.2(1-0.2)/0.05^2) = 245.84$
- So the sample size required is 246.

Alternative to calculation

http://www.palmx.org/samplesize/Calc_Samplesize.xls

$$n = (Z_{1-\alpha})2(P(1-P)/d^2)$$

Prevalence (P)

Level of Accuracy (d)	0.05	0.10	0.15	0.20
0.01	1825	3457	4898	6147
0.02	456	864	1225	1537
0.03	203	384	544	683
0.04	114	216	306	384
0.05	73	138	196	246

Reminder

- If the prevalence for the outcome of interest is **less than 5%,** you should not be doing a cross-sectional study, instead you should be doing a **case-control study**.
- If your supervisor still insists that you do x-sectional study, then **the level of precision should be half of the prevalence**; i.e. prevalence of HIV among STD patients is 4% therefore accuracy (d) must be set at 2%. Therefore the required sample size would be 369, not 59.

Calculate Your Own Sample Size Here!		
Expected Prevalence (P)	**0.04**	(Between 0.01 till 0.99)
Level of Accuracy (d)	**0.02**	(Usually between 0.03 till 0.05)
Sample Size Required	**369**	
Confidence level 95%		

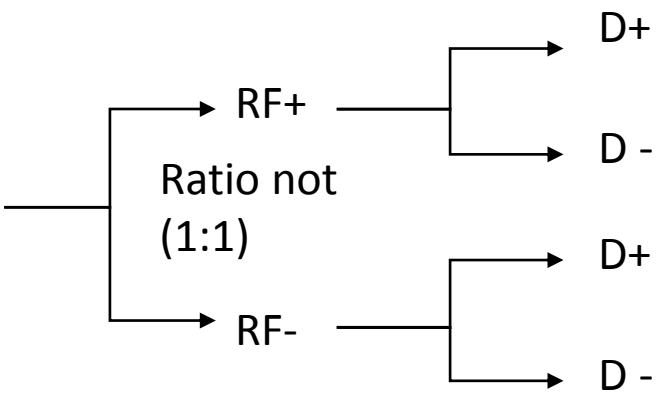
369 not 59!

Calculate Your Own Sample Size Here!		
Expected Prevalence (P)	**0.04**	(Between 0.01 till 0.99)
Level of Accuracy (d)	**0.05**	(Usually between 0.03 till 0.05)
Sample Size Required	**59**	
Confidence level 95%		

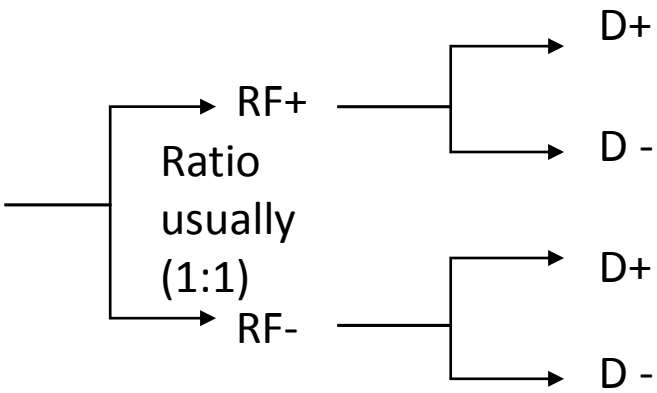
Dichotomous Qualitative Outcome

Calculate sample size

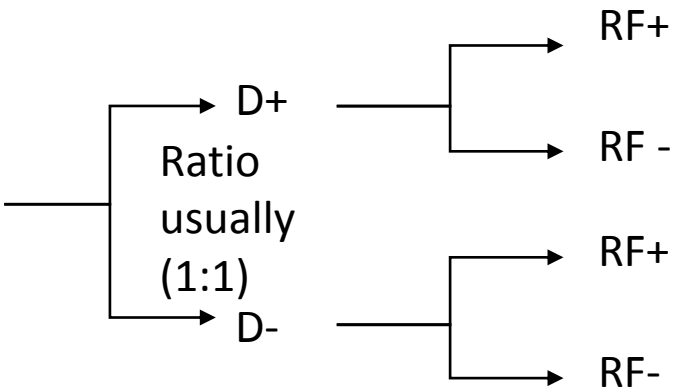
X-sectional vs cohort vs case control vs clinical trial



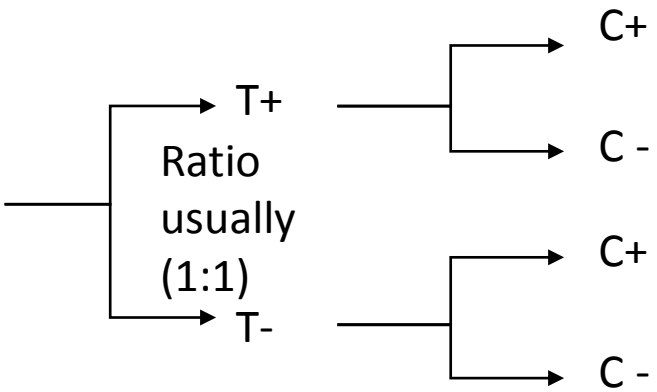
X-sectional



Cohort



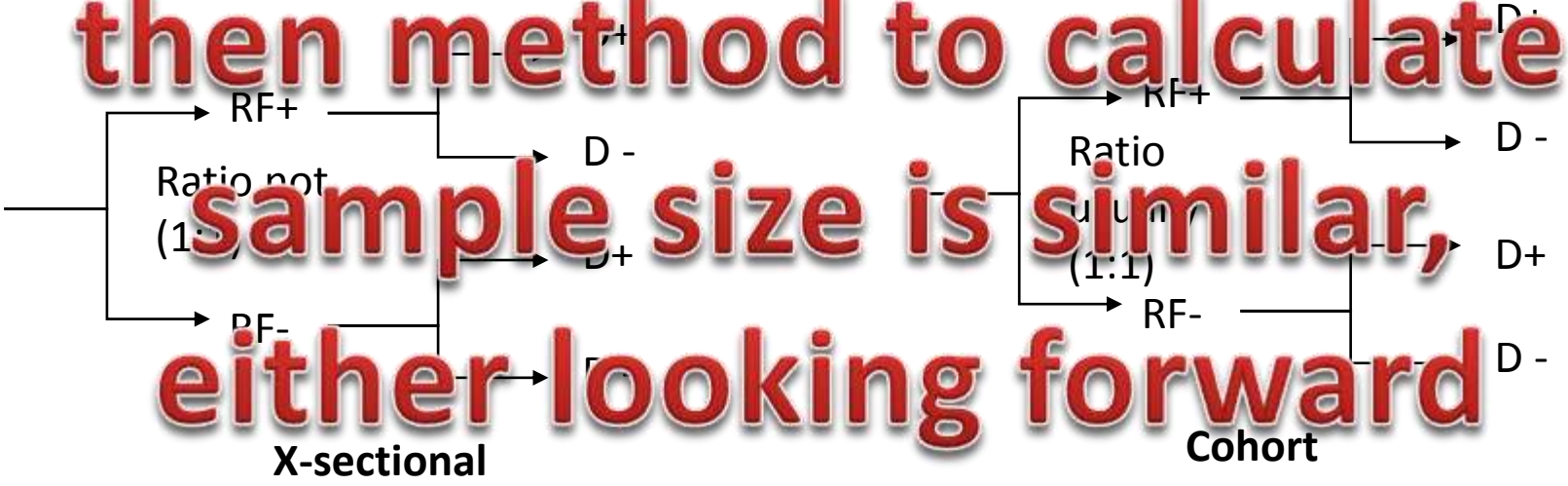
Case-Control



Clinical Trial

X-sectional vs cohort vs case control vs clinical trial

If dichotomous outcome, then method to calculate sample size is similar, either looking forward for the rate of disease or looking back for the rate of exposure.

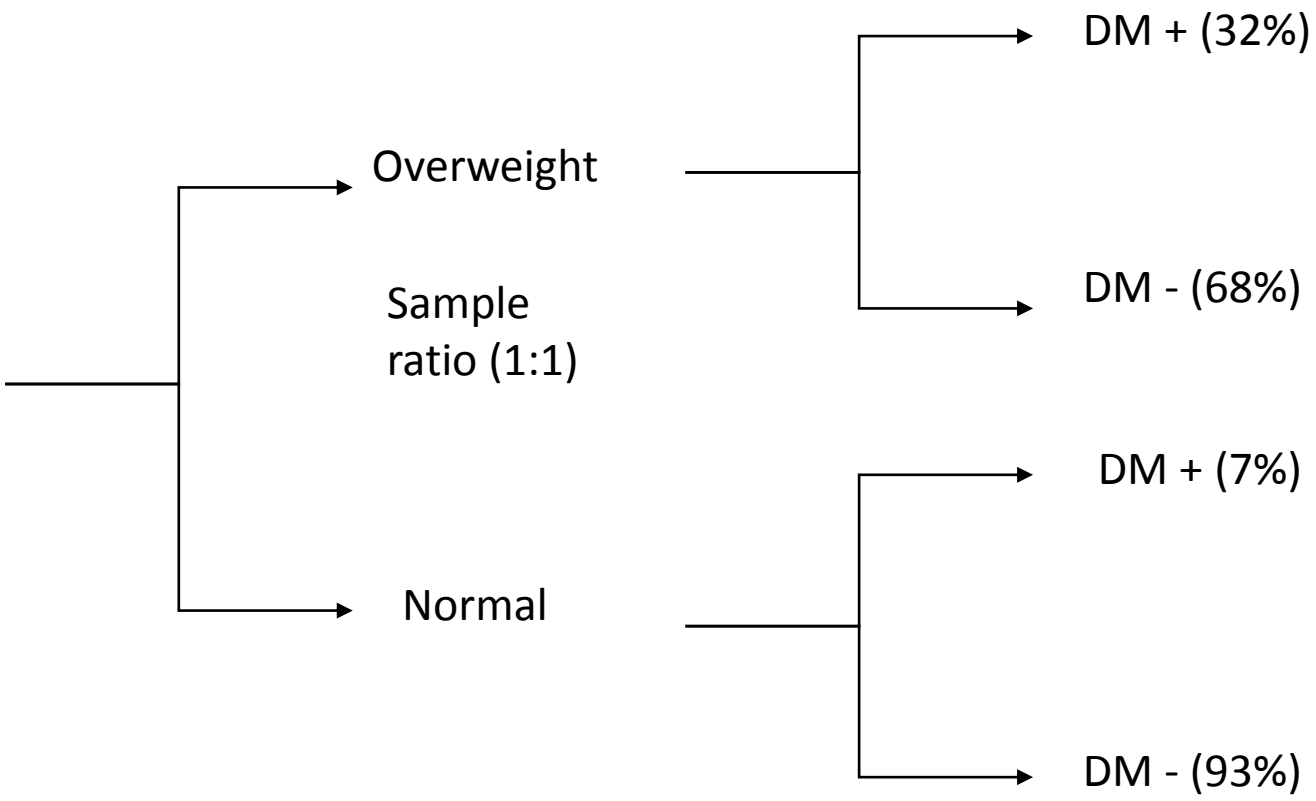


Example – overweight have higher risk of DM

From literature review, identify the rate of disease among those with & without the risk factor.

- Ratio of unexposed (Normal) vs exposed (Overweight); 1:1
- Equal ratio therefore equal proportion of sample from no-risk (Normal) and from at-risk (Overweight) population.
- P1=true proportion of DM in no-risk (Normal) population = 7%
- P2=true proportion of DM in at-risk (Overweight) population =32%
- (Rifas-Shiman SL et al, 2008.Diabetes and lipid screening among patients in primary care: A cohort study. BMC Health Services Research.)

From Literature Review: Obesity & Diabetes M.



Rifas-Shiman SL et al, 2008.Diabetes and lipid screening among patients in primary care: A cohort study. BMC Health Services Research.

Calculate Manually

Calculate using these formulas (Fleiss JL. 1981. pp. 44-45)

$$m' = \frac{\left[c_{\alpha/2}\sqrt{(r+1)\bar{P}\bar{Q}} - c_{1-\beta}\sqrt{rP_1Q_1 + P_2Q_2} \right]^2}{r(P_2 - P_1)^2}$$

$$m = \frac{m'}{4}\left[1 + \sqrt{1 + \frac{2(r+1)}{m'r|P_2 - P_1|}}\right]^2$$

$m=n_1$=size of sample from population 1 n_2=size of sample from population 2

P_1=proportion of **disease** in population 1 P_2=proportion of **disease** in population 2

α= "Significance" = 0.05 β=chance of not detecting a difference = 0.2

1-β = Power = 0.8 r = n2/n1 = ratio of cases to controls

$\bar{P} = (P_1+rP_2)/(r+1)$ Q = 1-P.

$n_1 = m$ $n_2 = rm$

From table A.2 in Fleiss;

- If 1- α is 0.95 then $c_{\alpha/2}$ is 1.960
- If 1- β is 0.80 then $c_{1\text{-beta}}$ is -0.842

Calculate Manually

$P_1 = 0.07 \qquad P_2 = 0.32 \qquad r = 1/1$

$P = (0.07 + (1 \times 0.32))/(1 + 1) = 0.195$

$Q = 1 - P = 0.805$

$$m' = \frac{[1.96\sqrt{(1+1)x0.195x0.805} - (-0.842)\sqrt{(1x0.07x0.93)+(0.32x0.68)}]^2}{1 \times (0.32 - 0.07)^2}$$

$$= \frac{2.3898}{0.0625} = 38.2369$$

$$m = \frac{38.2369}{4} \times \left[1 + \sqrt{1 + \frac{(2x(1+1)}{(38.2369x1x0.25)}}\right]^2 = 45.8882$$

$m = n_1 = 46 \qquad n_2 = r \times m = 1 \times 46 = 46 \qquad n_1 + n_2 = 92$

Alternative to calculation

http://www.palmx.org/samplesize/Calc_Samplesize.xls

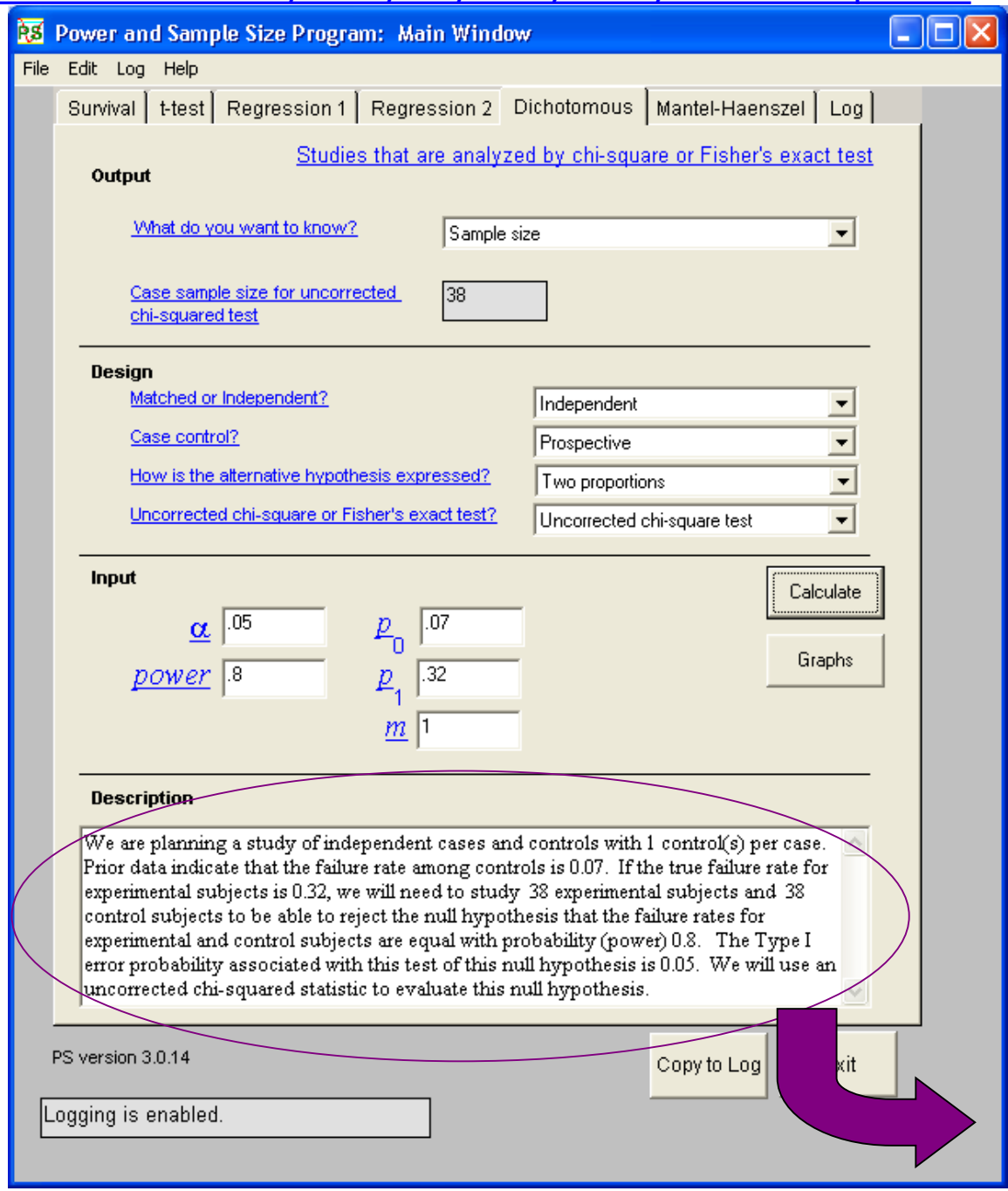
Calculate Your Own Sample Size Here!		
Smaller Proportion of Success (P_1)	**0.07**	(Between 0.01 till 0.99)
Larger Minus Smaller Proportion of Success (P2-P1))	**0.25**	(Between 0.01 till 0.99)
Sample Size Required For Cases Only	**46**	
Confidence level 95%, Power 80%		
Ratio of cases to controls = 1		

So you'll need a sample size of 46 each for both groups. Total of 92.

http://biostat.mc.vanderbilt.edu/twiki/bin/view/Main/PowerSampleSize

Or use PS2

- So the sample size required for each group is 38. Total of 76
- Excel = 92 vs PS2 = 76
- Slight difference due to different formula used.



PS2

We are planning a study of independent cases and controls with 1 control(s) per case. Prior data indicate that the failure rate (DM) among controls (normal weight) is 0.07. If the true failure rate (DM) for experimental (overweight) subjects is 0.32, we will need to study 38 experimental (overweight) subjects and 38 control (normal weight) subjects to be able to reject the null hypothesis that the failure rates (DM) for experimental (overweight) and control (normal weight) subjects are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05. We will use an uncorrected chi-squared statistic to evaluate this null hypothesis.

Sample size calculation - Outcome is continuous data

Jones SR, Carley S & Harrison M.
An introduction to power and sample size estimation.
Emergency Medical Journal 2003;20;453-458. 2003

Example (two groups)

- If expected difference of BP between two treatment groups = 10 mmHg
- pop. standard deviation = 20 mm Hg
- (we usually get the above data based on literature review or from a pilot study).

Manual Calculation (2 groups)

$$n = 1 + 2C\left(\frac{s}{d}\right)^2$$

(Snedecor and Cochran 1989)

- s = standard deviation,
- d = the difference to be detected, and
- C = constant (refer to table below); if α=0.05 & 1-β=0.8, then C = 7.85.

	α	0.05	0.01
1-β	0.8	7.85	11.68
	0.9	10.51	14.88

Manual Calculation

- d = 10 mmHg
- s = 20 mm Hg

$n = 1 + 2 \times 7.85 (20/10)^2$

$= 63.8 = 64$

We will need 64 samples per treatment group. For two treatment groups, that will be a total of 128 samples.

Alternative to table

http://www.palmx.org/samplesize/Calc_Samplesize.xls

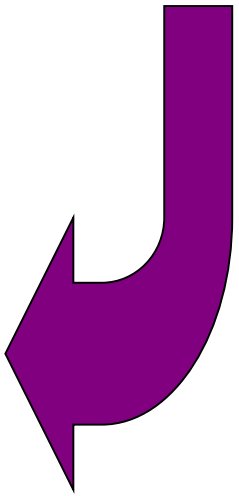
The standardised difference; 10 mm Hg/20 mm Hg = 0.5

$$Sdiff = \frac{\delta}{s.d}$$

δ = Clinically relevant difference

s.d = Standard deviation of the variable

Confidence level		99%		95%	
Power Level		0.90	0.80	0.90	0.80
Sdiff	0.10	2977	2337	2103	1571
	0.20	745	585	527	394
	0.30	332	261	235	175
	0.40	187	147	132	99
	0.50	120	94	85	64
	0.60	84	66	59	45
	0.70	62	49	44	33
	0.80	48	38	34	26
	0.90	38	30	27	20
	1.00	31	24	22	17
	1.10	26	20	18	14
	1.20	22	17	16	12
	1.30	19	15	13	10
	1.40	16	13	12	9
	1.50	14	11	10	8



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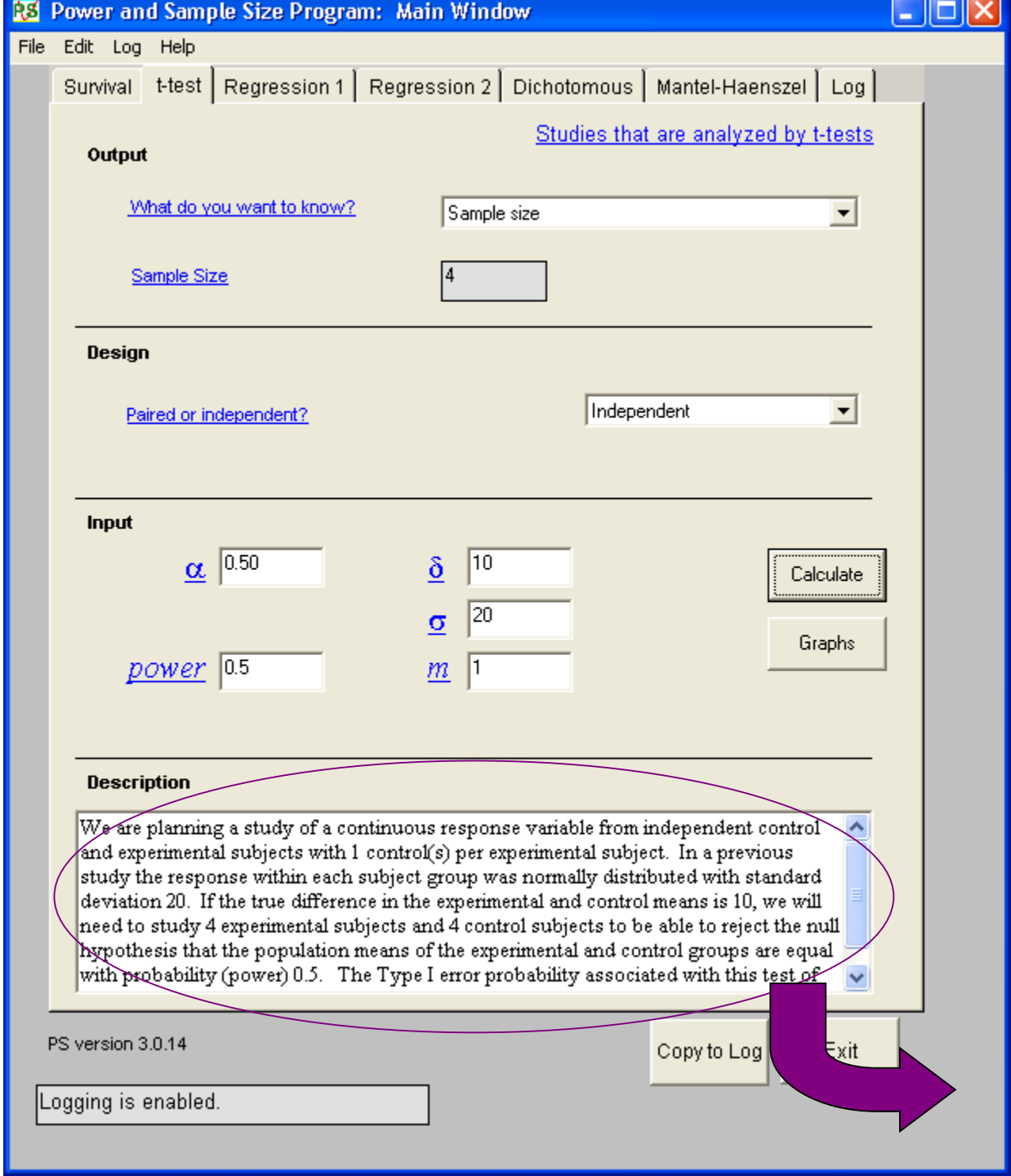
Azmi M.T. 2008. *Calculate Your Own Sample Size* . Kuala Lumpur: Penerbit SPF

Or you can use PS2

- We still end up with the same answer.



PS2

- We are planning a study of a continuous response variable from independent control (placebo) and experimental (treatment) subjects with 1 control(s) per experimental subject. In a previous study the response within each subject group was normally distributed with standard deviation 20. If the true difference in the experimental and control means is 10 (mm Hg), we will need to study 64 experimental subjects and 64 control subjects to be able to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

Example for pre vs post

- If expected difference of BP before and after treatment = 10 mmHg
- pop. standard deviation = 20 mm Hg
- (we usually get the above data based on literature review or from a pilot study).

Manual Calculation (pre post)

$$n=2+C\left(\frac{s}{d}\right)^2$$

(Snedecor and Cochran 1989)

- s = standard deviation,
- d = the difference to be detected, and
- C = constant (refer to table below); if α=0.05 & 1-β=0.8, then C = 7.85.

	α	0.05	0.01
1-β	0.8	7.85	11.68
	0.9	10.51	14.88

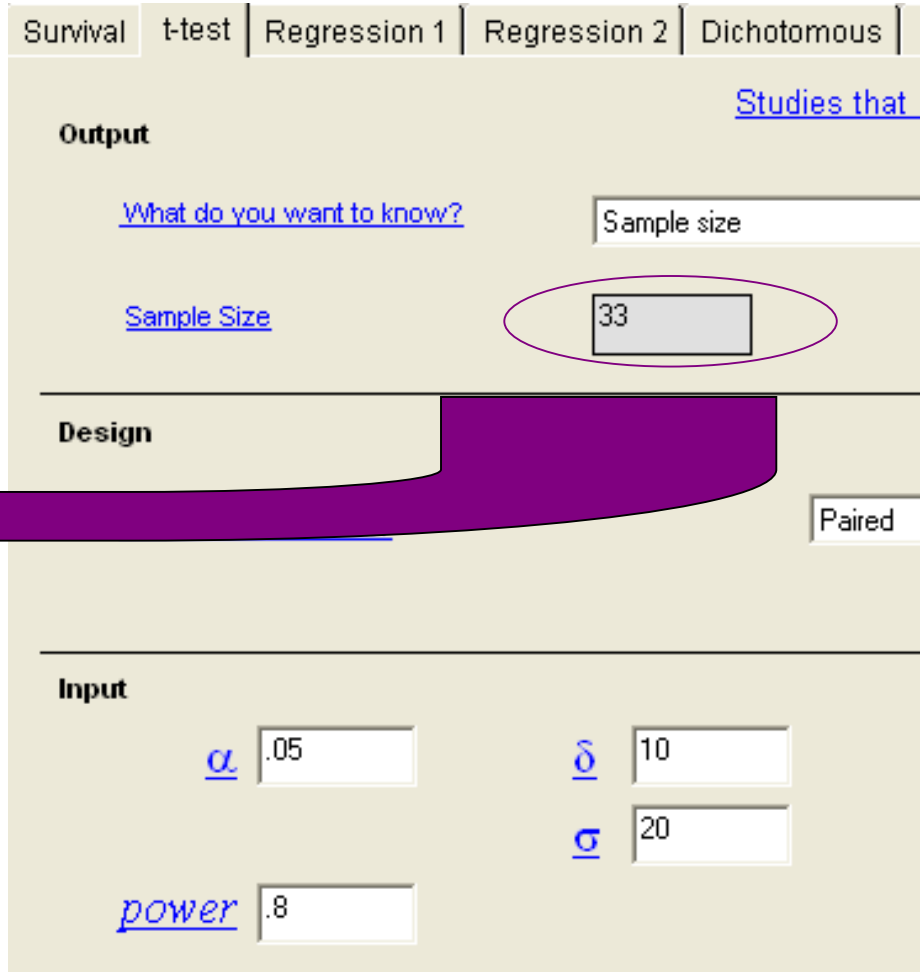
Manual Calculation

- d = 10 mmHg
- s = 20 mm Hg

$n = 1 + 7.85\ (20/10)^2$

$= 32.4 = 33$

This is similar as the answer in PS2!



Next

Exploring your data