Download

- http://www.palmx.org/samplesize/samplesize-2009.pdf

HOW TO CALCULATE YOUR OWN SAMPLE SIZE

or

Please don’t disturb us in JKM anymore…

The Magic Number

- How many subjects do I need to obtain a significant result for my study?
- In medical research, the sample size has to be "just large enough".
- If too small, it's a waste of time doing the study since no conclusive results are likely to be obtained.

What happens if the sample size is too small?

Data of a clinical trial on 30 patients on comparison of pain control between two modes of treatment.

Type of treatment * Pain (2 hrs post-op) Crosstabulation

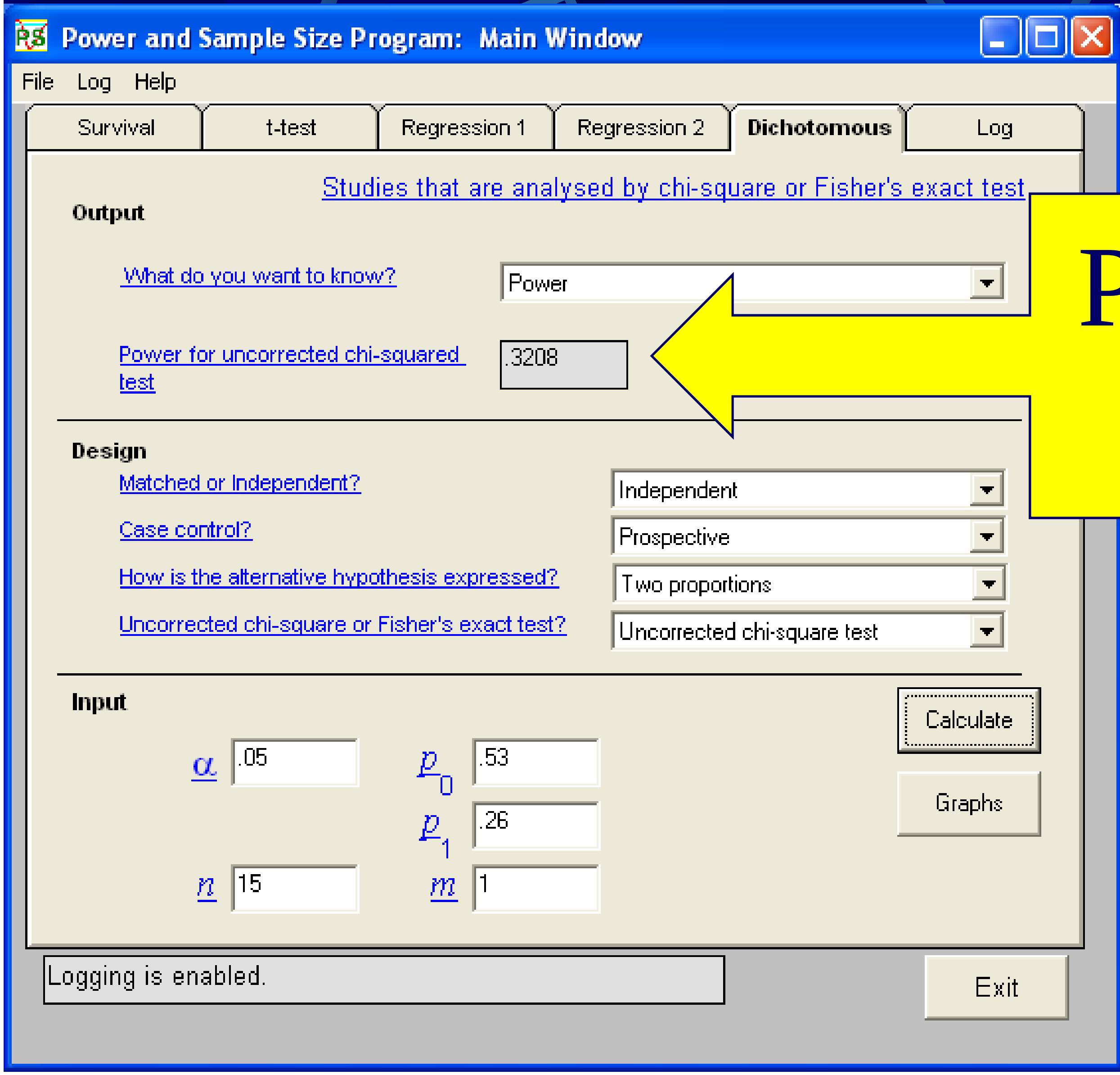
			Pain (2 hrs post-op)		
			No pain	In pain	Total
Type of treatment	Pethidine	Count	8	7	15
		% within Type of treatment	53.3%	46.7%	100.0%
	Cocktail	Count	4	11	15
		% within Type of treatment	26.7%	73.3%	100.0%
Total		Count	12	18	30
		% within Type of treatment	40.0%	60.0%	100.0%

Chi-square =2.222, p=0.136

p = 0.136. p bigger than 0.05. No significant difference and the null hypothesis was not rejected.

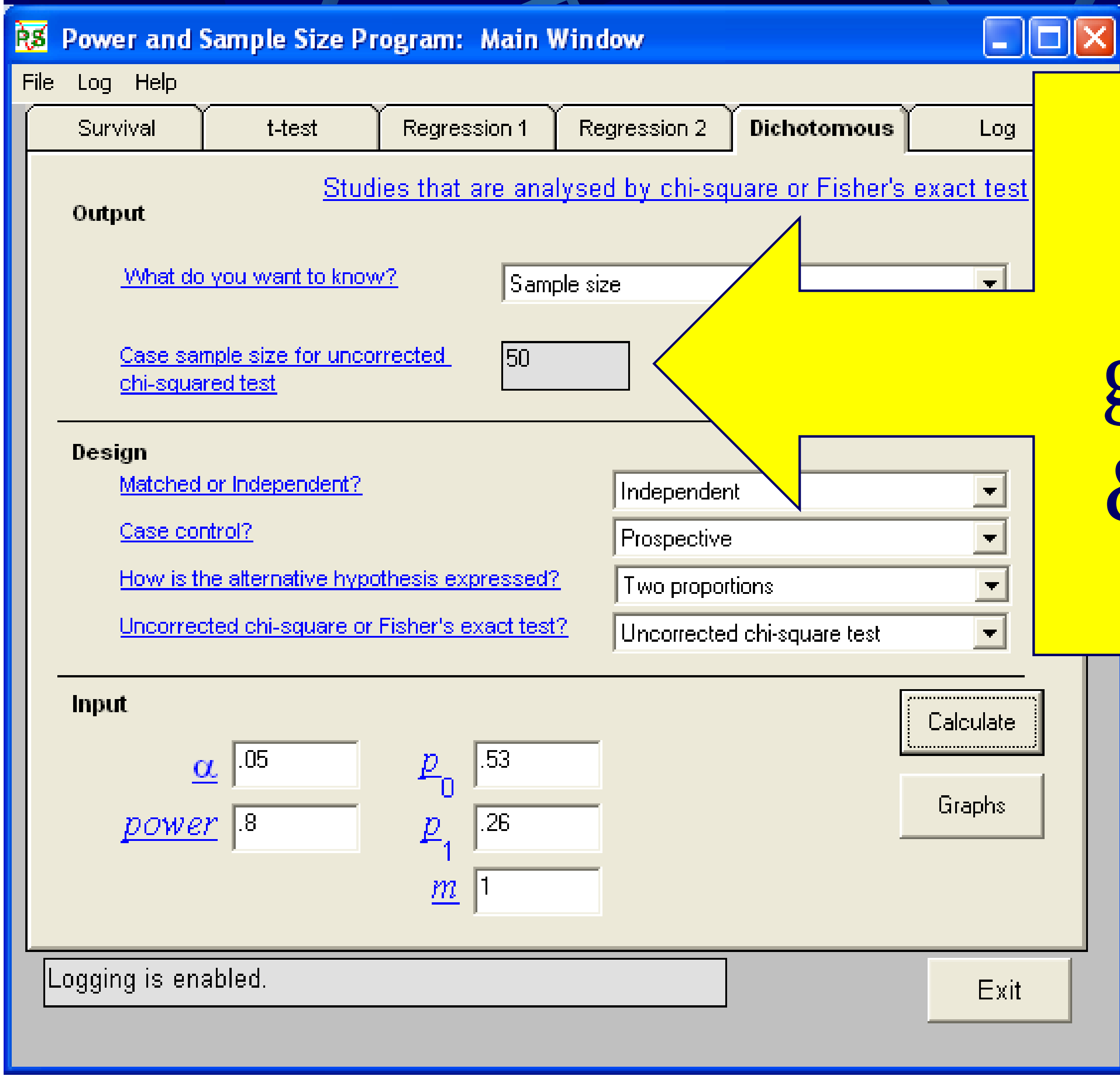
There was a large difference between the rates (53.3% vs 26.7%) but the result was not significant.

Not significant since power of the study is less than 80%.



Power is only 32%!

For power of the study of 80%, sample size required is;



Sample size reqd. 50 per group. For case & control, total 100!

Inadequate sample size

Data of a clinical … on 30 patients on comparison … n control between two modes of t…

…2 hrs post-o…

				…al
Type of treatme…				15
			…%	100.0%
	Cockt…		11	15
				100.0%
Total				30

What would happen if we increase the sample size from 30 to 90?

Chi-squa…

p = 0.136. p bigger tha… …o significant difference and the nu… …esis was not rejected.

There was a large difference between the rates (53.3% vs 26.7%) but the result was not significant.

By increasing the sample size…….

Data of a clinical trial on 90 (instead of 30!) patients on comparison of pain control between two modes of treatment.

Type of treatment * Pain (2 hrs post-op) Crosstabulation

			Pain (2 hrs post-op)		
			No pain	In pain	Total
Type of treatment	Pethidine	Count	24	21	45
		% within Type of treatment	53.3%	46.7%	100.0%
	Cocktail	Count	12	33	45
		% within Type of treatment	26.7%	73.3%	100.0%
Total		Count	36	54	90
		% within Type of treatment	40.0%	60.0%	100.0%

Chi-square =6.667, p=0.01

Now p = 0.01. p smaller than 0.05. There was significant difference and the null hypothesis was rejected.

The difference between the rates (53.3% vs 26.7%) are the same but the result was significant with the larger sample size.

Conclusion

- Same difference of rate but only significant with larger sample size (n=90 instead of 30).
- Therefore the sample size has to be “just large enough”.
- If too small, it’s a waste of time doing the study since no conclusive results are likely to be obtained.

Why do we calculate the required sample size?

- Cost of the study based on the sample size required – more sample, higher cost
- Estimate the length of the study i.e if sample needed is 120 patients and each year only 40 patients available, need at least 3 years to complete.
- Feasible or not? Whether within the constraints of time allocated (i.e. 1 year) and budget available (i.e. RM5000).

Why do you calculate it?

- So that your research proposal is approved by the ethical committee.
- ;-)

What is power?

- It is the probability of finding an effect given that one truly exists

p = probability of observing this data given that H_0 true

Power (denoted **1-β**) = probability of finding p<alpha given that H_0 false

- and thus to be reasonably sure that no such benefit exists, if it is not found in the trial.

Power and alpha

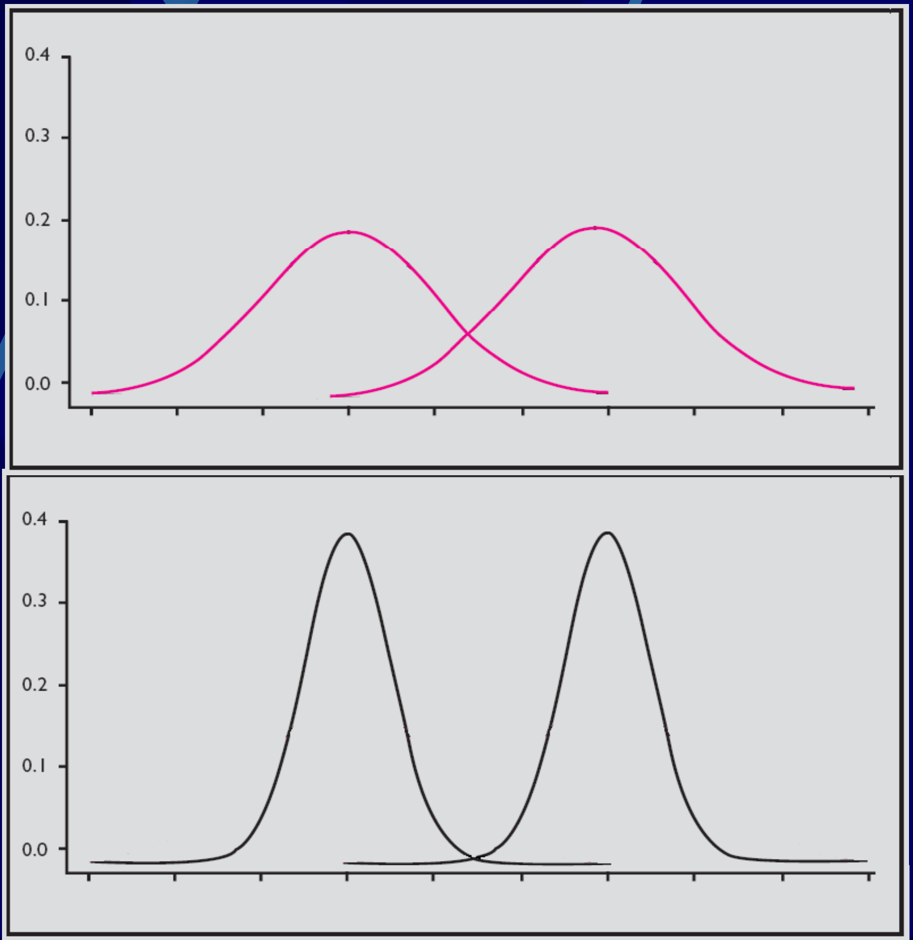
Experimental result		Real world: H_0 True	Real world: H_0 False
	H_0 Not Rejected	True negative Probability = **1- α**	Type II error (‘miss’) Probability = **β**
	H_0 Rejected	Type I error (‘false alarm’) Probability = **α**	True positive (‘hit’) Probability = **1-β**

INTRODUCTION

- The greater the power of study, the more sure we can be, but greater power requires a larger sample.
- It is common to require a power of between 80% and 90%.
- Power of 80% for detecting effect difference
- Power of 90% for proving equal effect (equivocal studies)

Power is affected by sample size

- An increase in sample size increases the power of the test.
- This is because as sample size increases, the standard error of the mean decreases, thus reducing the overlap between the null and alternative hypotheses.



INTRODUCTION

- Sample size calculations are based on the quantity known as the **effect size**.
- The smaller the **effect size**, the larger the required size of the sample.
- For example, if treated group improved 10x better than the control group, the sample size required is only 242.
- But if the treated group improved only 5x better than the control group, the sample size required is 664.

Effect Size

- ‘Effect Size’ is simply a way of quantifying the difference between two groups.
- For example, if one group has had an ‘experimental’ treatment and the other has not (the ‘control’), then the Effect Size is a measure of the effectiveness of the treatment.

Different Types of Effect Sizes:

- Standardised Mean Difference
  - Comparing group research
    - Either treatment groups
    - Or naturally occurring groups
  - inherently continuous construct (continuous outcome–mean)
- Odds-Ratio
  - Comparing group research
    - Either treatment groups
    - Or naturally occurring groups
  - inherently dichotomous construct (categorical outcome-rate)
- Correlation Coefficient
  - association between variables research

Different Types of Effect Sizes:

- Proportion
  - Measures of central tendency research
    - HIV/AIDS prevalence rates
    - Proportion of homeless persons found to be alcohol abusers
- Standardised Gain Score
  - gain or change between two measurement points on the same variable
    - reading speed before and after a reading improvement class

Effect size formula

$$Effect\_size = \frac{\mu_0 - \mu_1}{\sigma}$$

- **where σ is standard deviation of population of dependent (outcome) measure scores.**

Cohen's Effect Size (d)

- Cohen (1992) gives the following guidelines for the social sciences:
  - small effect size, 0.2;
  - medium, 0.5;
  - large, 0.8.

Factors governing power

Power, 1-β = probability of finding an effect, given that there actually is one

- So power will obviously be governed by
  - Effect size (stronger effect size, more power)
  - Number of subjects (more subjects, more power)
  - Choice of alpha (0.01 need more, 0.05 need less)
- Also (maybe less obviously)…
  - Sources of variability (i.e. sampling method)
  - Study design (case-control vs cohort vs clinical trial)
  - Choice of statistical test (chi^2 or t-test)

Calculating power & sample size

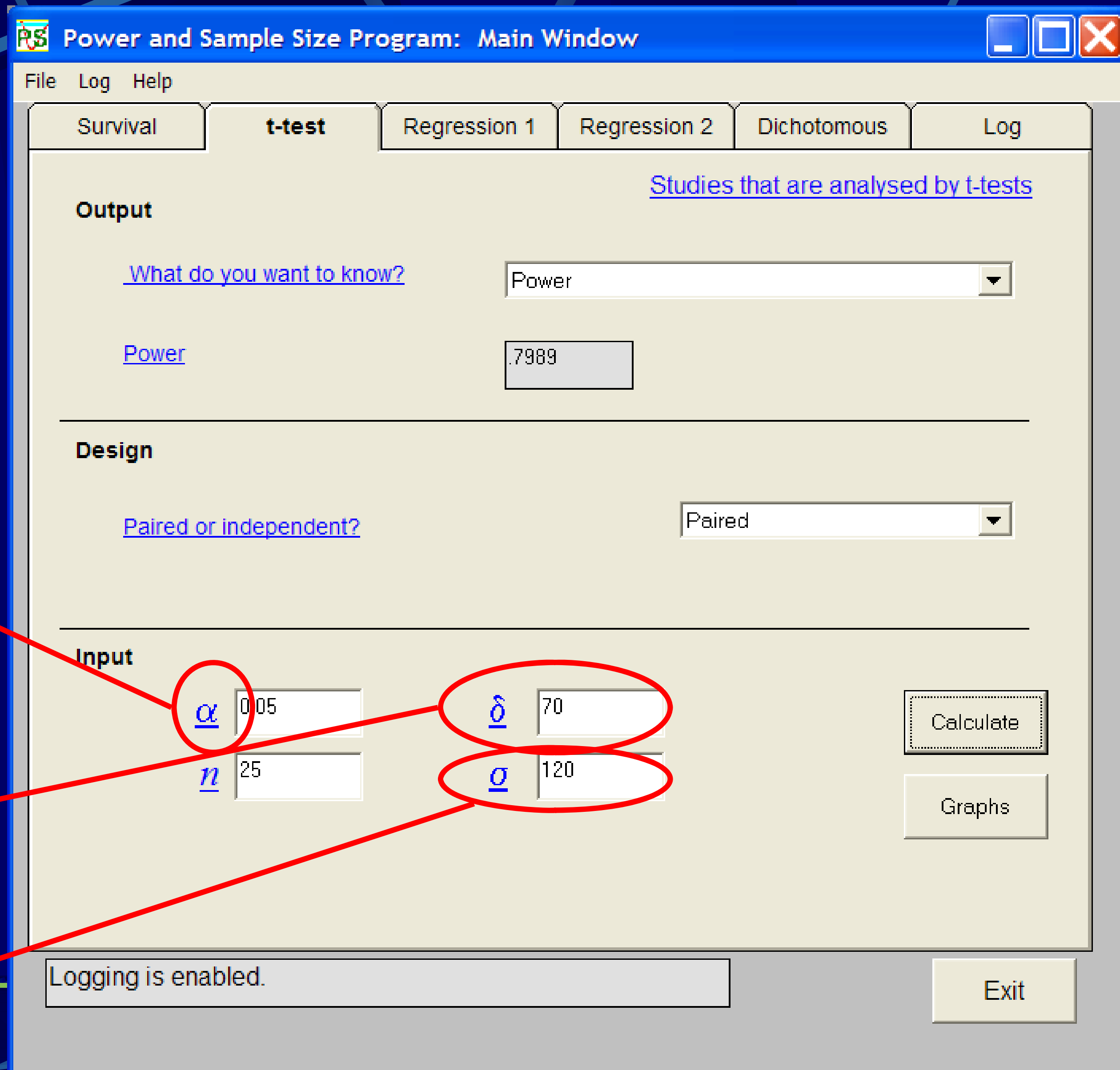
- As you've just seen, power is determined by
  - Effect Size
  - Number of subjects
  - Choice of alpha (usually 0.05)
- SPSS doesn't have the facility to calculate power/sample size but you can download a free program (PS2) to do so (given the above information) from

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

- Or you can use Statcalc (part of EpiInfo6) from

http://www.cdc.gov/epiinfo/Epi6/EI6dnjp.htm to calculate sample size

PS for Power/Sample Size calculations



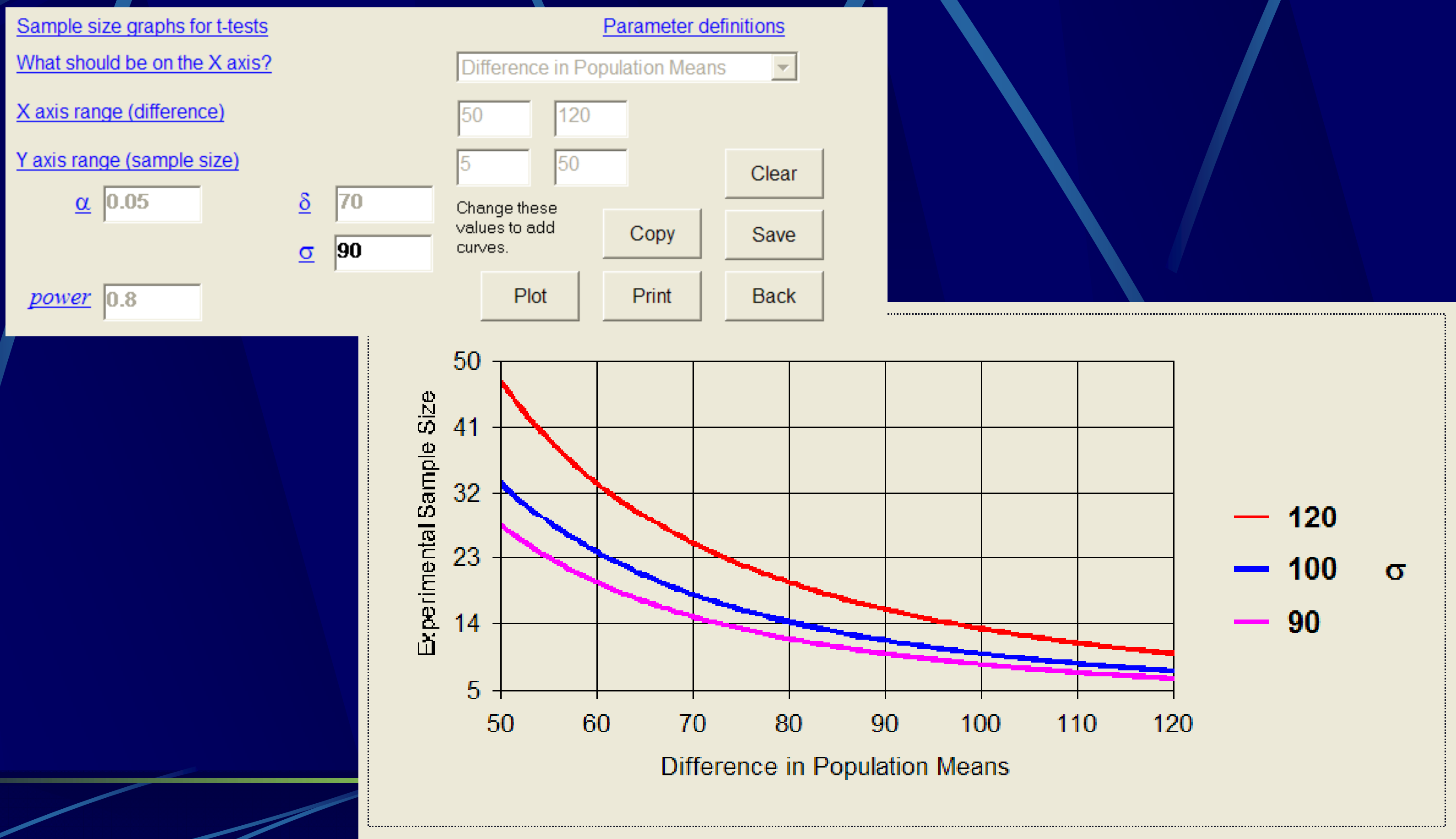
Any blue label leads to help

Delta means expected difference in scores

Expected standard deviation of the differences

PS for Power/Sample Size calculations

- Alternatively you can ask the program to calculate the sample size you need to give the *power* that you're looking for
- Also plots graphs for a range of powers etc…



PS2 can calculate sample size for

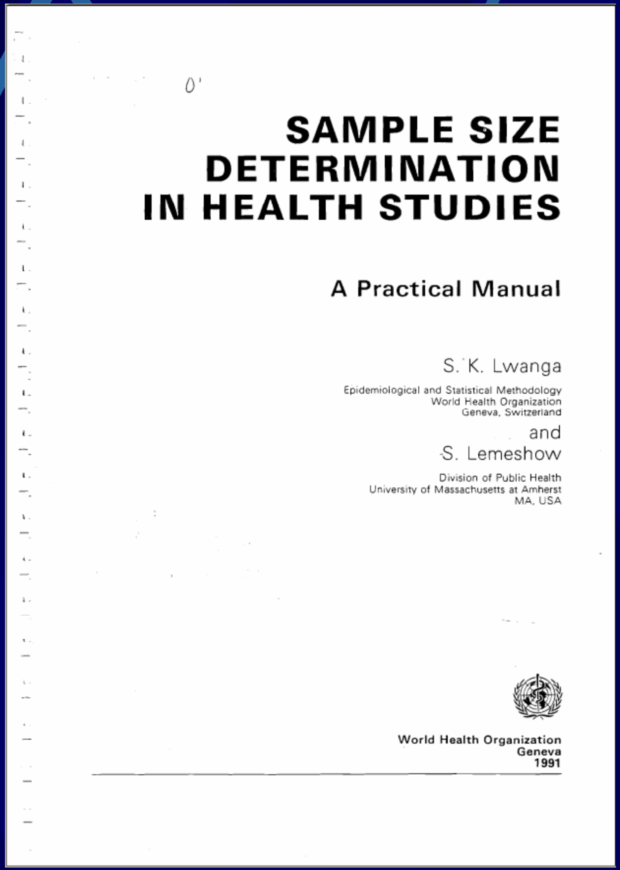
- Independent Case-Control Studies: Chi-square test, Fisher's exact test.
- Matched Case-Control Studies: McNemar's Test.
- Cohort Studies With Dichotomous Outcomes: Chi-square test, McNemar's test
- Continuous Response Measures in Two Groups: Paired and independent t tests.
- Linear Regression
- Survival Studies

StatCalc can calculate sample size

- Cross-Sectional – Prevalence Studies
- Cross-Sectional – Categorical Risk Factor & Outcome
- Cohort Studies With Dichotomous Outcomes: Categorical Risk Factor & Outcome
- Unmatched Case-Control Studies: Categorical Risk Factor & Outcome

Or refer to tables;

- Lwanga SK, Lemeshow S., 1991. Sample Size Determination in Health Studies: A Practical Manual. WHO.
- A pdf copy of the book is available.
- Only useful for prevalence studies.


SAMPLE SIZE
DETERMINATION
IN HEALTH STUDIES

A Practical Manual

S. K. Lwanga
Epidemiological and Statistical Methodology
World Health Organization
Geneva, Switzerland

and

S. Lemeshow
Division of Public Health
University of Massachusetts at Amherst
MA, USA

World Health Organization
Geneva
1991

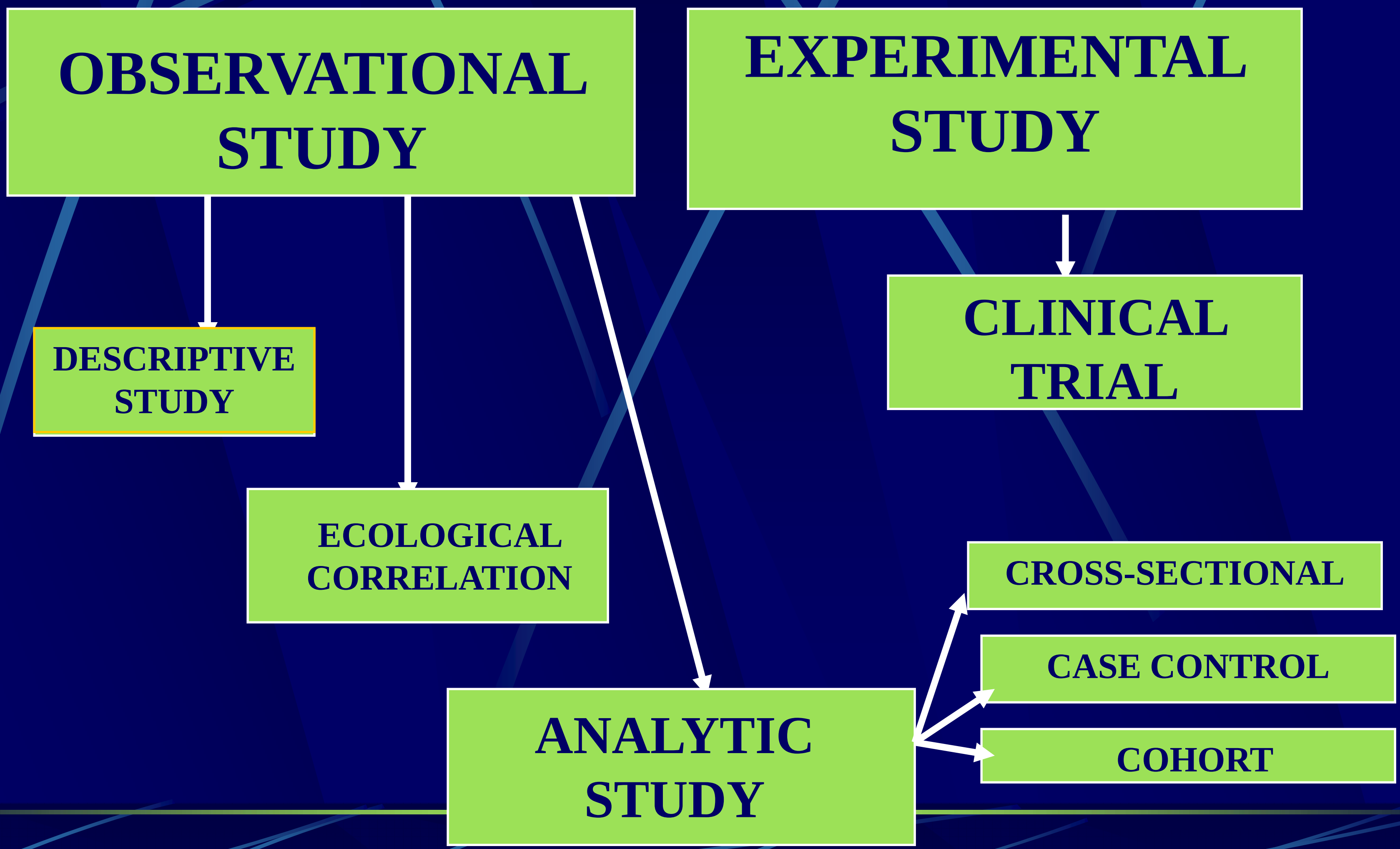
Other Sample Size Estimation Software

- License software
  - nQuery Advisor version 6.0.
- Free online calculator
  - http://www.changbioscience.com/stat/ssize.html
  - http://calculators.stat.ucla.edu/

Step One

Determine your research design and the outcome being measured

STUDY DESIGNS



Examples of Study Design

- Study the prevalence of obesity in HUKM - cross-sectional (prevalence)
- Comparing the rate of diabetes mellitus between Indians and non-Indians – cross-sectional (comparative)
- Comparing the rate of diabetes mellitus between those with cataract and those without cataract - case-control
- Measure the incidence and relative risk of diabetes mellitus between normal and overweight - cohort
- Comparing Fluoxetine against Sertraline for treating depression – clinical trial
- Measuring the sensitivity and specificity of a new serological test against the gold standard – diagnostic study

Step 2 – Go to the Respective Slides for that Design

- Cross Sectional Study (prevalence) – Go to 34
- Cross Sectional Study (comparative) – Go to 50
- Case Control – Go to 62
- Cohort – Go to 70
- Clinical Trial (qualitative outcome) – Go to 78
- Clinical Trial (continuous outcome) – Go to 90
- Diagnostic Study – Go to 101

Each design requires a different approach for sample size calculation

Calculate Your Own Sample Size

Cross-Sectional Study – Measuring Prevalence

Cross-Sectional

- What is the outcome being measured?
  - **Is it the prevalence of disease/risk factor?**
  - As[illegible] between the ma[illegible]ical risk factor [illegible]e ca[illegible] outcome?

Prevalence in Cross-Sectional

- Do a literature review to estimate the prevalence being studied.
- Determine the absolute precision required i.e. 5 percentage points (usually between 3 to 5).
- Calculate using (Kish L. 1965)

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

- or refer to a table in S.K. Lwanga, S. Lemeshaw 1991, Sample Size Determination in Health Studies, pg 25
- Or use StatCalc from EpiInfo6.

Example – Prevalence of Obesity in HUKM

- Confidence interval = 1 - α = 95%;
  $Z_{1-\alpha} = Z_{0.95} = 1.96$
  (from normal distribution table).
- Prevalence = P = 20%
- Absolute precision required = 5 percentage points,
  (if the calculated prevalence of the study 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
- $n = 1.96^2 \times (0.2(1-0.2)/0.05^2) = 245.84$

Refer to Table

- Refer to the table in S.K. Lwanga, S. Lemeshaw 1991, Sample Size Determination in Health Studies pg 25.
- With a Prevalence (P) of 20%, precision of 0.05, the table indicates that the sample size required is 246.

Table 1. Estimating a population proportion with specified absolute precision

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

(*a*) Confidence level 95%

d \ P	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50	0.55	0.60	0.65	0.70	0.75	0.80	0.85	0.90	0.95
0.01	1825	3457	4898	6147	7203	8067	8740	9220	9508	9604	9508	9220	8740	8067	7203	6147	4898	3457	1825
0.02	456	864	1225	1537	1801	2017	2185	2305	2377	2401	2377	2305	2185	2017	1801	1537	1225	864	456
0.03	203	384	544	683	800	896	971	1024	1056	1067	1056	1024	971	896	800	683	544	384	203
0.04	114	216	306	384	450	504	546	576	594	600	594	576	546	504	450	384	306	216	114
0.05	73	138	196	246	288	323	350	369	380	384	380	369	350	323	288	246	196	138	73
0.06	51	96	136	171	200	224	243	256	264	267	264	256	243	224	200	171	136	96	51
0.07	37	71	100	125	147	165	178	188	194	196	194	188	178	165	147	125	100	71	37
0.08	29	54	77	96	113	126	137	144	149	150	149	144	137	126	113	96	77	54	29
0.09	23	43	60	76	89	100	108	114	117	119	117	114	108	100	89	76	60	43	23
0.10	18	35	49	61	72	81	87	92	95	96	95	92	87	81	72	61	49	35	18
0.11	15	29	40	51	60	67	72	76	79	79	79	76	72	67	60	51	40	29	15
0.12	13	24	34	43	50	56	61	64	66	67	66	64	61	56	50	43	34	24	13
0.13	11	20	29	36	43	48	52	55	56	57	56	55	52	48	43	36	29	20	11
0.14	9	18	25	31	37	41	45	47	49	49	49	47	45	41	37	31	25	18	9
0.15	8	15	22	27	32	36	39	41	42	43	42	41	39	36	32	27	22	15	8
0.20	5	9	12	15	18	20	22	23	24	24	24	23	22	20	18	15	12	9	5
0.25	*	6	8	10	12	13	14	15	15	15	15	15	14	13	12	10	8	6	*

*Sample size less than 5.

Alternative to table

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

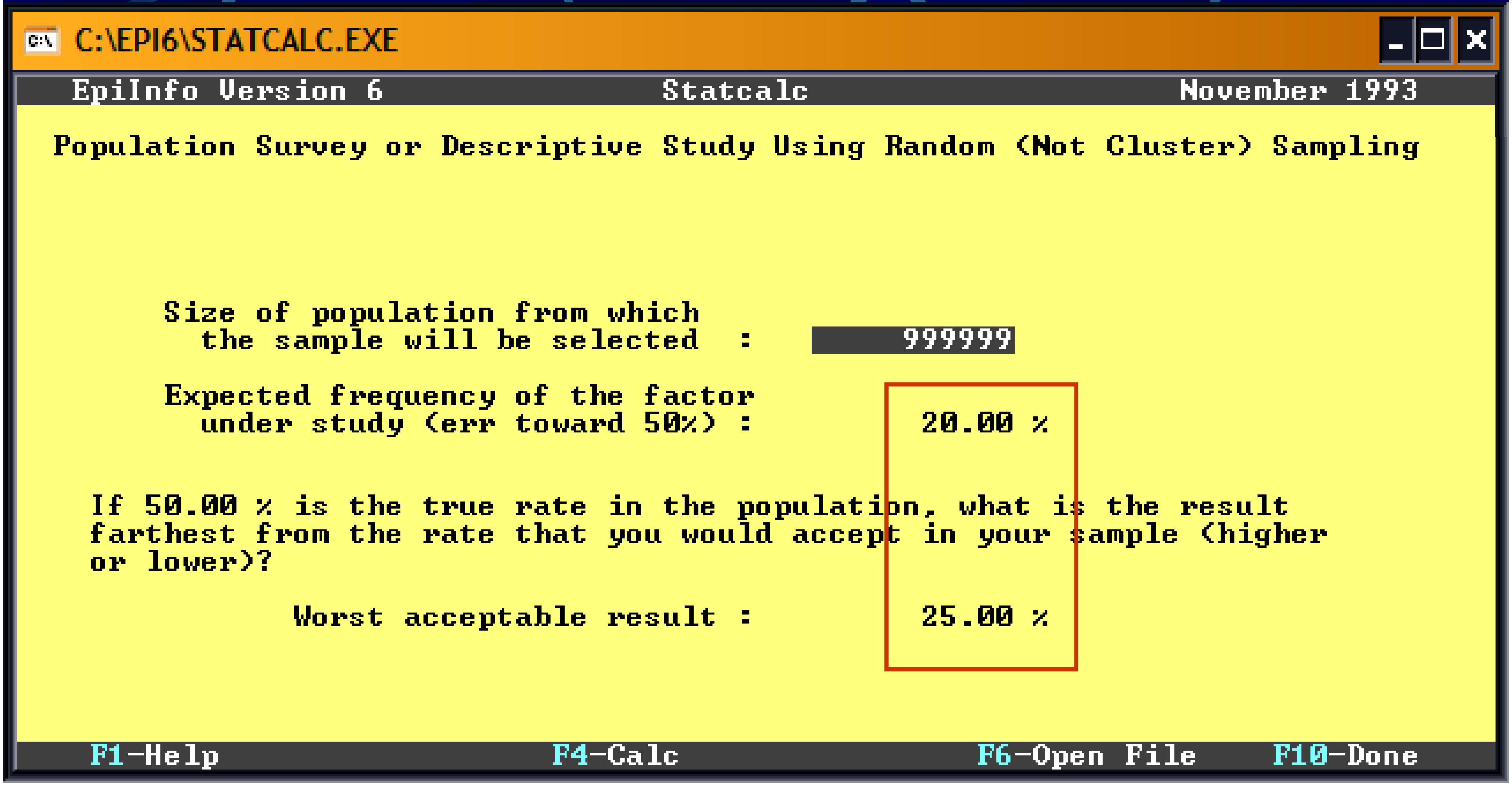
$n = (Z_{1-\alpha})2(P(1-P)/d^2)$ Confidence level 95%

Prevalence (P) ©drtamil@medic.ukm.my

Level of Accuracy (d)	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50	0.55	0.60	0.65	0.70	0.75	0.80	0.85	0.90	0.95
0.01	1825	3457	4898	6147	7203	8067	8740	9220	9508	9604	9508	9220	8740	8067	7203	6147	4898	3457	1825
0.02	456	864	1225	1537	1801	2017	2185	2305	2377	2401	2377	2305	2185	2017	1801	1537	1225	864	456
0.03	203	384	544	683	800	896	971	1024	1056	1067	1056	1024	971	896	800	683	544	384	203
0.04	114	216	306	384	450	504	546	576	594	600	594	576	546	504	450	384	306	216	114
0.05	73	138	196	246	288	323	350	369	380	384	380	369	350	323	288	246	196	138	73
0.06	51	96	136	171	200	224	243	256	264	267	264	256	243	224	200	171	136	96	51
0.07	37	71	100	125	147	165	178	188	194	196	194	188	178	165	147	125	100	71	37
0.08	29	54	77	96	113	126	137	144	149	150	149	144	137	126	113	96	77	54	29
0.09	23	43	60	76	89	100	108	114	117	119	117	114	108	100	89	76	60	43	23
0.10	18	35	49	61	72	81	87	92	95	96	95	92	87	81	72	61	49	35	18
0.11	15	29	40	51	60	67	72	76	79	79	79	76	72	67	60	51	40	29	15
0.12	13	24	34	43	50	56	61	64	66	67	66	64	61	56	50	43	34	24	13
0.13	11	20	29	36	43	48	52	55	56	57	56	55	52	48	43	36	29	20	11
0.14	9	18	25	31	37	41	45	47	49	49	49	47	45	41	37	31	25	18	9
0.15	8	15	22	27	32	36	39	41	42	43	42	41	39	36	32	27	22	15	8
0.16	7	14	19	24	28	32	34	36	37	38	37	36	34	32	28	24	19	14	7
0.17	6	12	17	21	25	28	30	32	33	33	33	32	30	28	25	21	17	12	6
0.18	6	11	15	19	22	25	27	28	29	30	29	28	27	25	22	19	15	11	6
0.19	5	10	14	17	20	22	24	26	26	27	26	26	24	22	20	17	14	10	5
0.20	5	9	12	15	18	20	22	23	24	24	24	23	22	20	18	15	12	9	5
0.21	4	8	11	14	16	18	20	21	22	22	22	21	20	18	16	14	11	8	4
0.22	4	7	10	13	15	17	18	19	20	20	20	19	18	17	15	13	10	7	4
0.23	3	7	9	12	14	15	17	17	18	18	18	17	17	15	14	12	9	7	3
0.24	3	6	9	11	13	14	15	16	17	17	17	16	15	14	13	11	9	6	3
0.25	3	6	8	10	12	13	14	15	15	15	15	15	14	13	12	10	8	6	3
0.26	3	5	7	9	11	12	13	14	14	14	14	14	13	12	11	9	7	5	3
0.27	3	5	7	8	10	11	12	13	13	13	13	13	12	11	10	8	7	5	3
0.28	2	4	6	8	9	10	11	12	12	12	12	12	11	10	9	8	6	4	2
0.29	2	4	6	7	9	10	10	11	11	11	11	11	10	10	9	7	6	4	2
0.30	2	4	5	7	8	9	10	10	11	11	11	10	10	9	8	7	5	4	2

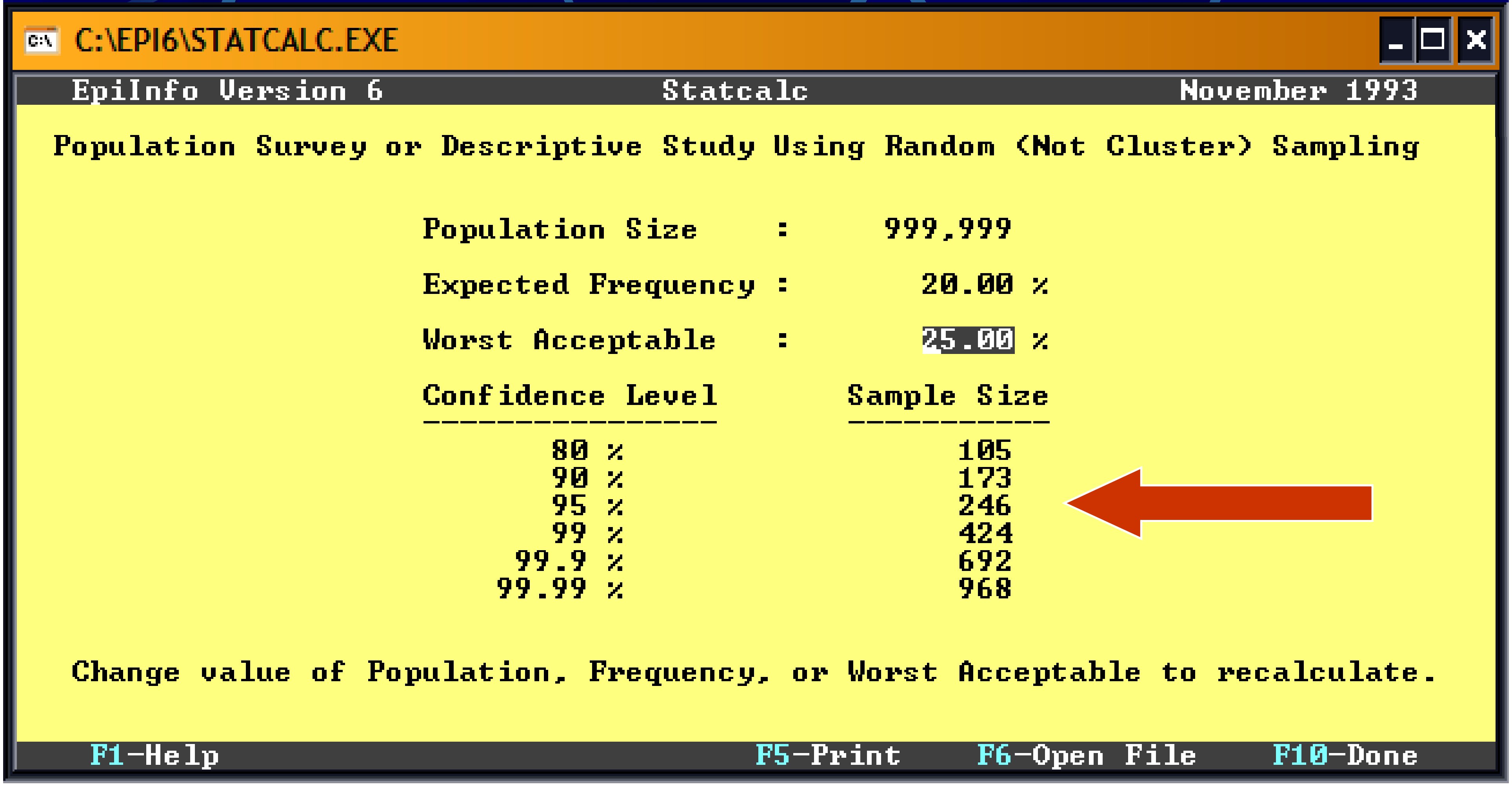
Or use StatCalc (Step 1)

- P = 20% = 0.2 in this example
- D = 5% = 0.05 therefore the true value of the prevalence lies between 15-25%. So worse acceptable result is either 15% or 25%
- Press F4 to calculate.



StatCalc (Step 2)

- Using 95% confidence level, the sample size required is 246, the same value as manual calculation & the table.



Formula for Sample Size of A Prevalence Study

- It is the same since all calculations uses the same formula.

C:\EPI6\EPI6.EXE

Chapter 32 – Statistics – p. 393

Sample Size Calculations in STATCALC

The sample size calculations for proportions in a descriptive study or survey use the following method:

Sample size=size of sample randomly selected from the population
Population=size of population which the sample is to represent
P=true proportion of factor in the population (guess)
D=(Maximum) difference between sample mean and population mean
Z=area under normal curve corresponding to the desired confidence level.

Confidence	Z
.90	1.645
.95	1.960
.99	2.575
.999	3.29

The formula is:

Samplesize=n/(1+(n/population))

in which: n=Z*Z(P(1-P)/D*D)

Esc-Topics 10-Quit

SS Calculation for a Known Population

- What if the required sample size is larger than the population being studied?
- i.e. study on stress among staff at Pusat Kesihatan Rembau. Expected rate of stress is 50% therefore at 5% precision, the required sample size is 384. But the number of staff is only 30!

SS Calculation for a Known Population

- Krejcie & Morgan
  - Krejcie, R.V. & Morgan, D.W. (1970). Determining sample size for research activities. *Educational & Psychological Measurement*, 30, 607-610.

$$S = \frac{X^2 NP(1-P)}{d^2 (N-1) + X^2 P(1-P)}$$

  - S = required sample size
    N = the given population size
    P = prevalence
    d = the degree of accuracy
    X^2 = 3.841 for the .95 confidence level

Table - Krejcie, R.V. & Morgan, D.W. (1970).

Required Sample Size†

Population Size	Confidence = 95%				Confidence = 99%			
	Margin of Error				Margin of Error			
	5.0%	3.5%	2.5%	1.0%	5.0%	3.5%	2.5%	1.0%
10	10	10	10	10	10	10	10	10
20	19	20	20	20	19	20	20	20
30	28	29	29	30	29	29	30	30
50	44	47	48	50	47	48	49	50
75	63	69	72	74	67	71	73	75
100	80	89	94	99	87	93	96	99
150	108	126	137	148	122	135	142	149
200	132	160	177	196	154	174	186	198
250	152	190	215	244	182	211	229	246
300	169	217	251	291	207	246	270	295
400	196	265	318	384	250	309	348	391
500	217	306	377	475	285	365	421	485
600	234	340	432	565	315	416	490	579
700	248	370	481	653	341	462	554	672
800	260	396	526	739	363	503	615	763
1,000	278	440	606	906	399	575	727	943
1,200	291	474	674	1067	427	636	827	1119
1,500	306	515	759	1297	460	712	959	1376
2,000	322	563	869	1655	498	808	1141	1785
2,500	333	597	952	1984	524	879	1288	2173
3,500	346	641	1068	2565	558	977	1510	2890
5,000	357	678	1176	3288	586	1066	1734	3842
7,500	365	710	1275	4211	610	1147	1960	5165
10,000	370	727	1332	4899	622	1193	2098	6239
25,000	378	760	1448	6939	646	1285	2399	9972
50,000	381	772	1491	8056	655	1318	2520	12455
75,000	382	776	1506	8514	658	1330	2563	13583
100,000	383	778	1513	8762	659	1336	2585	14227
250,000	384	782	1527	9248	662	1347	2626	15555
500,000	384	783	1532	9423	663	1350	2640	16055
1,000,000	384	783	1534	9512	663	1352	2647	16317
2,500,000	384	784	1536	9567	663	1353	2651	16478
10,000,000	384	784	1536	9594	663	1354	2653	16560
100,000,000	384	784	1537	9603	663	1354	2654	16584
300,000,000	384	784	1537	9603	663	1354	2654	16586

- Assumption of the table; prevalence = 50%. So need only 28 out of 30 for the study on stress, not 384.
- If population > 250,000, sample size equal to Kish's formula.

250,000	384
500,000	384
1,000,000	384
2,500,000	384
10,000,000	384
100,000,000	384
300,000,000	384

Kish, L (1960) = Krejcie, R.V. & Morgan, D.W. (1970) ?

Kish, L (1960)

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

$S = n/(1+(n/\text{population}))$

$(Z_{1-\alpha})^2 = X^2 = 3.841$

Population = N

P = P

$D^2 = d^2 = 0.0025$ (for 5%)

We usually use only 1st half of the formula!

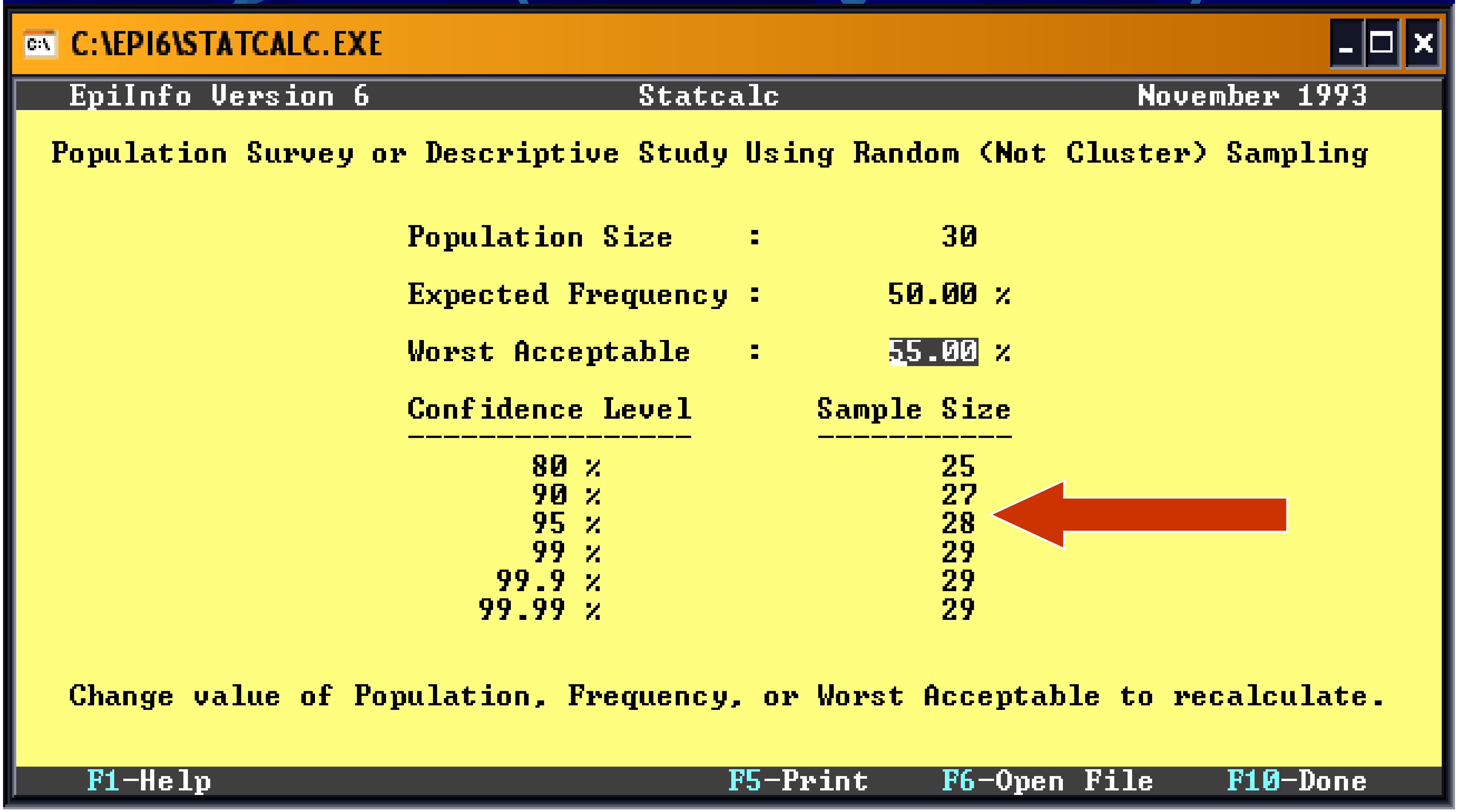
Krejcie, R.V. & Morgan, D.W. (1970)

$$S = \frac{X^2 NP(1-P)}{d^2(N-1) + X^2 P(1-P)}$$

So we can use STATCALC to calculate sample size for a known population!

StatCalc

- Using 95% confidence level, the sample size required is 28, the same value as in the table.



Calculate Your Own Sample Size

Comparative Cross-Sectional Study – Proving Association Between Risk & Outcome

Comparative Cross-Sectional

- What is the outcome being measured?
  - Is it the pr[illegible] risk factor?
  - **Association between the major risk factor being studied and the outcome?**

Cross-Sectional: Risk & Outcome

- If you want to show an association between a risk factor and outcome in a cross-sectional study, then the sample size calculation is different.
- For example you want to prove that Indians (ethnicity = risk) are at higher risk of having diabetes mellitus (outcome) compared to other races in your country, using a cross-sectional study.

Example – Indians are of higher risk for DM

From literature review, identify the rate of disease and proportion of those with the risk factor.

- Proportion of sample from unexposed (Others) population = 85%
- Proportion of sample from exposed (Indians) population = 15%
- P1=true proportion of DM in unexposed (Others) population = 8%
- P2=true proportion of DM in exposed (Indians) population =14%

From Literature Review: Indians & Diabetes M.

Sample ratio

- Indians (15%)
  - Disease + (14%)
  - Disease - (86%)
- Others (85%)
  - Disease + (8%)
  - Disease - (92%)

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

$1-\beta$ = Power = 0.8

r = n2/n1 = ratio of cases to controls

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

$\bar{Q} = 1-\bar{P}$.

$n_1 = m$

$n_2 = rm$

From table A.2 in Fleiss;

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

Calculate Manually

$P_1 = 0.08$ $P_2 = 0.14$ $r = 15/85$

$P = (0.08 + (15/85 \times 0.14))/(1 + 15/85) = 0.089$

$Q = 1 - P = 0.911$

$$m' = \frac{[1.96\sqrt{(15/85+1)x0.089x0.911} - (-0.842)\sqrt{(15/85x0.08x0.92)+(0.14x0.86)}]^2}{15/85 \times (0.14 - 0.08)^2}$$

$$= \frac{0.8333}{0.0006} = 1311.6976$$

$$m = \frac{1311.6976}{4} \times \left(1+\sqrt{1+\frac{(2x(15/85+1)}{(1311.6976x15/85x0.06)}}\right)^2 = 1420.64$$

$m = n_1 = 1421$ $n_2 = r \times m = 15/85 \times 1421 = 251$ $n_1 + n_2 = 1672$

Or use StatCalc

Tables (2 x 2, 2 x n)
Sample size & power
Ch

Population survey
Cohort or cross-sectional
Unmatched case-control

- n1 = 1422
- n2 = 251
- Total sample size required is 1673

C:\EPI6\STATCALC.EXE

EpiInfo Version 6 Statcalc November 1993

Unmatched Cohort and Cross-Sectional Studies (Exposed and Nonexposed)

Probability that if the two SAMPLES differ this reflects a true difference in the two POPULATIONS (Confidence level or 1-α) : 95.00 %

Probability that if the two POPULATIONS differ, the two SAMPLES will show a "significant" difference (Power or 1-β) : 80.00 %

Ratio (Number of Unexposed : Number of Exposed) : 85 : 15

Expected frequency of disease in unexposed group : 8.00 %

Please fill in the closest value to be detected for ONE of the following:

Risk ratio (RR) or relative risk--closest to 1.00 : 1.75
Odds ratio (OR)--closest to 1.00 : 1.87
Percent disease among exposed--closest to % for unexposed : 14.00 %

C:\EPI6\STATCALC.EXE

EpiInfo Version 6 Statcalc November 1993

Unmatched Cohort and Cross-Sectional Studies (Exposed and Nonexposed)
Sample Sizes for 8.00 % Disease in Unexposed Group

Conf.	Power	Unex:Exp	Disease in Exposed	Risk Ratio	Odds Ratio	Sample Size Unexp.	Sample Size Exposed	Sample Size Total
95.00 %	80.00 %	85:15	14.00 %	1.75	1.87	1,422	251	1,673
90.00 %	"	"				1,156	204	1,360
95.00 %	"	"				1,422	251	1,673
99.00 %	"	"				2,023	357	2,380
99.90 %	"	"				2,867	506	3,373
95.00 %	80.00 %	"				1,422	251	1,673
"	90.00 %	"				1,921	339	2,260
"	95.00 %	"				2,397	423	2,820
"	99.00 %	"				3,440	607	4,047
"	80.00 %	1:1				458	458	916
"	"	2:1				666	333	999
"	"	3:1				873	291	1,164
"	"	4:1				1,076	269	1,345
"	"	5:1				1,285	257	1,542
"	"	6:1				1,488	248	1,736

Change values for inputs as desired, then press F4 to recalculate.

F1-Help F5-Print F6-Open File F10-Done

StatCalc = Manual

- Sample size calculated manually is similar to the sample size generated by StatCalc.
- Since both methods use Fleiss JL (1981) unequal sample size formula as shown in the next slide.

The sample size formula for comparison of two groups of equal or unequal size is taken from Fleiss (1), pp. 44-45, formulas 3.19 and 3.20, and table A.2 on p. 259. These formulas do not assume matching of the two populations, and they apply to univariate comparisons of the differences in proportions (rates) in the two populations.

```
m=size of sample from population 1
r*m=size of sample from population 2
P1=true proportion of factor in population 1
P2=true proportion of factor in population 2
alpha=chance of falsely declaring the two proportions to differ
      ("Significance")
beta=chance of not detecting a difference which is present (could be
     called "Lack of sensitivity")
1-beta=chance of detecting a real difference ("Power")
```

In the eq

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

$$m = \frac{m'}{4}\left[1 + \sqrt{1 + \frac{2(r+1)}{m'r|P_2 - P_1|}}\right]^2 \quad 3.29$$

These cor ... t takes considerable attention to detail ... how to look them up correctly

The formulas are:

```
m=mprime + (r+1)/(r*|P2-P1|)
```

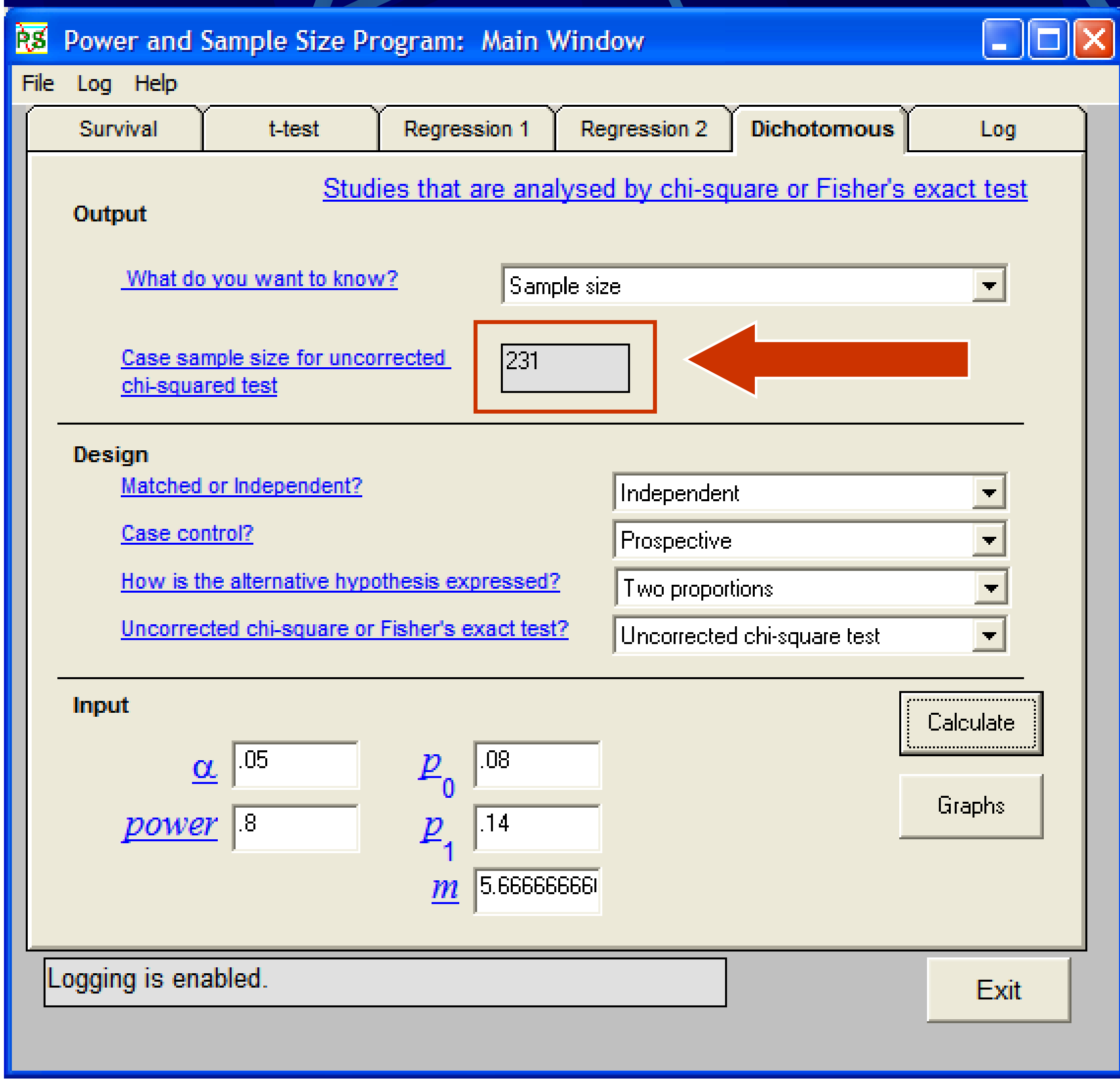
in which "|" denotes absolute value and:

```
mprime=(((c[alpha/2]*SQRT1)-(c[1-beta]*SQRT2))^2)/(r*((PR2-PR1)^2))
```

in which "[ ]" denotes a subscript and:

```
SQRT1=((r+1)*PB*QB)^0.5
SQRT2=((r*PR1*(1-PR1))+(PR2*(1-PR2)))^0.5
```

Or we can use PS2



- Based on this, the sample size for exposed is 231.
- So unexposed is 85/15*231= 1309
- Total 1540

PS2 ≠ StatCalc

- PS2 uses Schlesselman's method for independent case and control groups for studies that will be analysed using an uncorrected chi-square test
- PS2 uses Casagrande et al's method for independent studies that will be analysed using Yates Correction or Fisher's exact test.
- PS2 only uses the generalisation of Casagrande's method proposed by Fleiss for unequal case & control sample size. Even then the answers differ; 1673 vs 1540

Calculate Your Own Sample Size

Case-Control Study

Case-Control

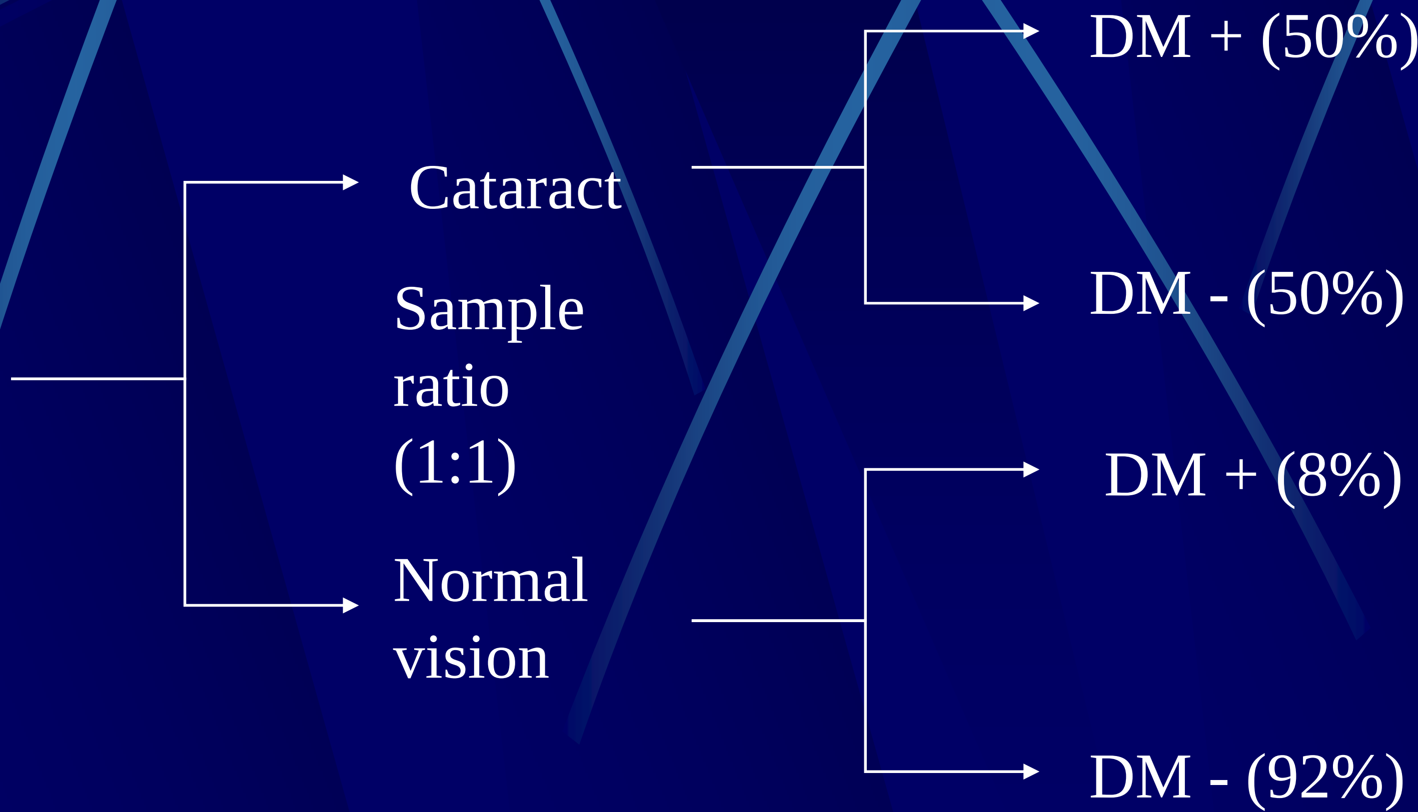
- In a case-control study, you identify the cases and controls. Then you compare the rate of exposure/risk factor between the case and control group.
- For example you want to prove that cataract patients (cases) have a higher rate of diabetes mellitus (risk factor) compared to patients with normal vision (controls).
- From literature review, identify the rate of exposure among the cases (i.e. 50%) and among the controls (i.e. 8%).
- Decide on the ratio; i.e. 1:1

Example – DM higher risk of cataract

From literature review, identify the rate of risk factor (DM) in cases and controls.

- Proportion of sample from controls (Normal) population = 50%
- Proportion of sample from cases (Cataract) population = 50%
- P1=true proportion of DM in controls (Normal) population = 8%
- P2=true proportion of DM in cases (Cataract) population =50%

From Literature Review: Cataract & Diabetes M.



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
P_1=proportion of **exposure** in population 1
α= "Significance" = 0.05
1-β = Power = 0.8
$\bar{P} = (P_1+rP_2)/(r+1)$
$n_1 = m$

n_2=size of sample from population 2
P_2=proportion of **exposure** in population 2
β=chance of not detecting a difference = 0.2
r = n2/n1 = ratio of cases to controls
$\bar{Q} = 1-\bar{P}$.
$n_2 = rm$

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

$P_1 = 0.08$ $P_2 = 0.5$ $r = 1/1$

$P = (0.08 + (1 \times 0.5))/(1 + 1) = 0.29$

$Q = 1 - P = 0.71$

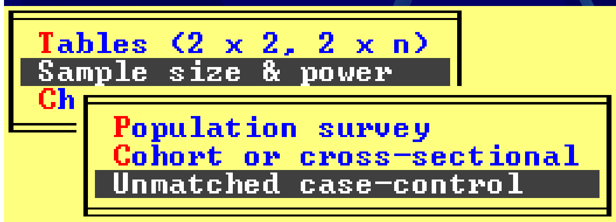
$$m' = \frac{[1.96\sqrt{(1+1)x0.29x0.71} - (-0.842)\sqrt{(1x0.08x0.92)+(0.5x0.5)}]^2}{1 \times (0.5 - 0.08)^2}$$

$$= \frac{3.0163}{0.1764} = 17.0991$$

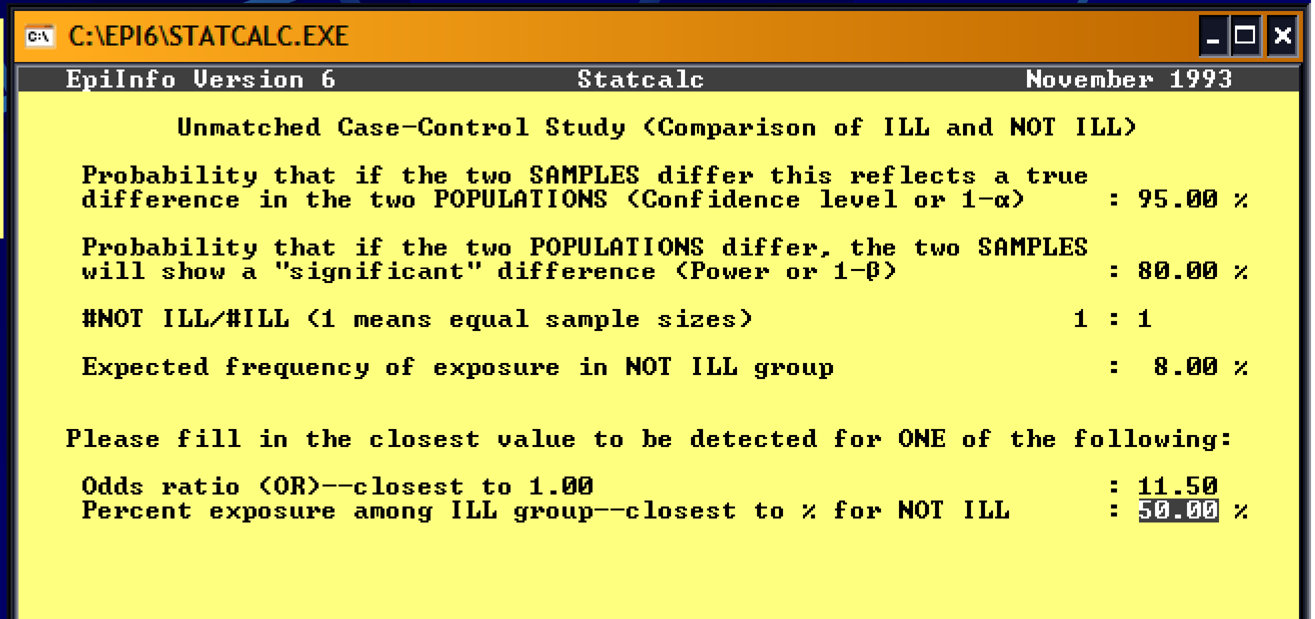
$$m = \frac{17.0991}{4} \times \left(1 + \sqrt{1 + \frac{(2x(1+1)}{(17.0991x1x0.42)}}\right)^2 = 21.5985$$

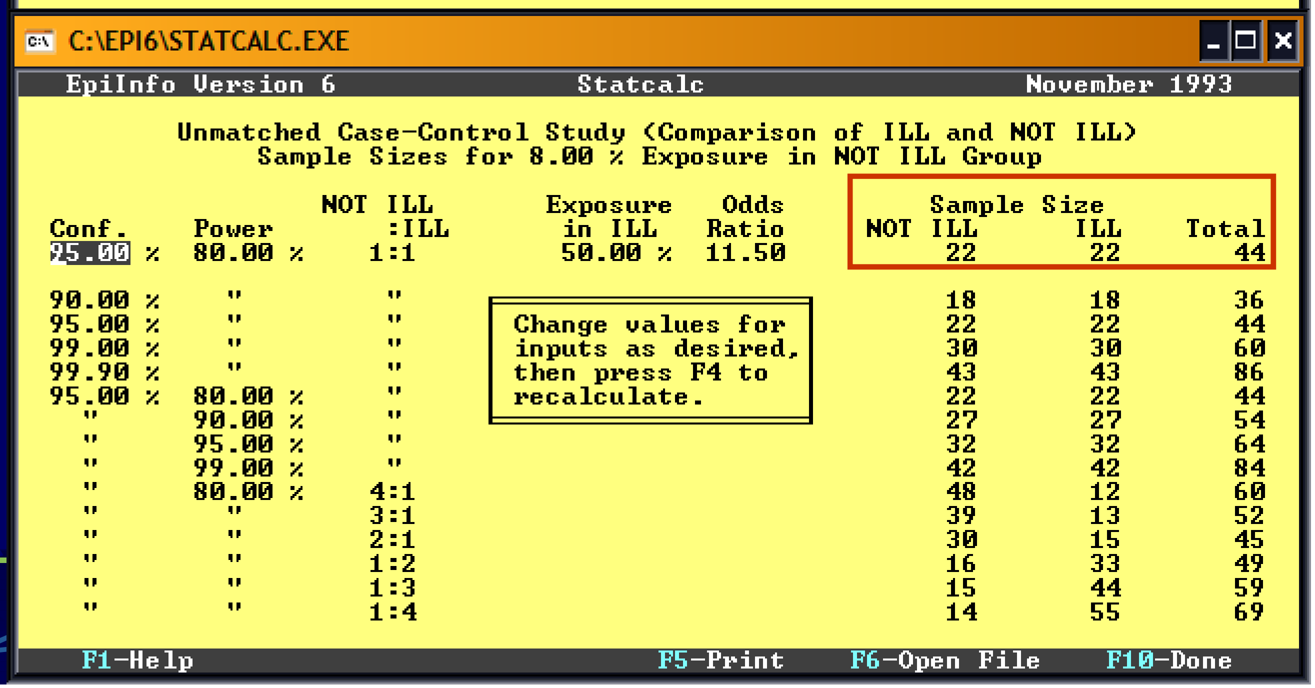
$m = n_1 = 22$ $n_2 = r \times m = 1 \times 22 = 22$ $n_1 + n_2 = 44$

Or Use StatCalc



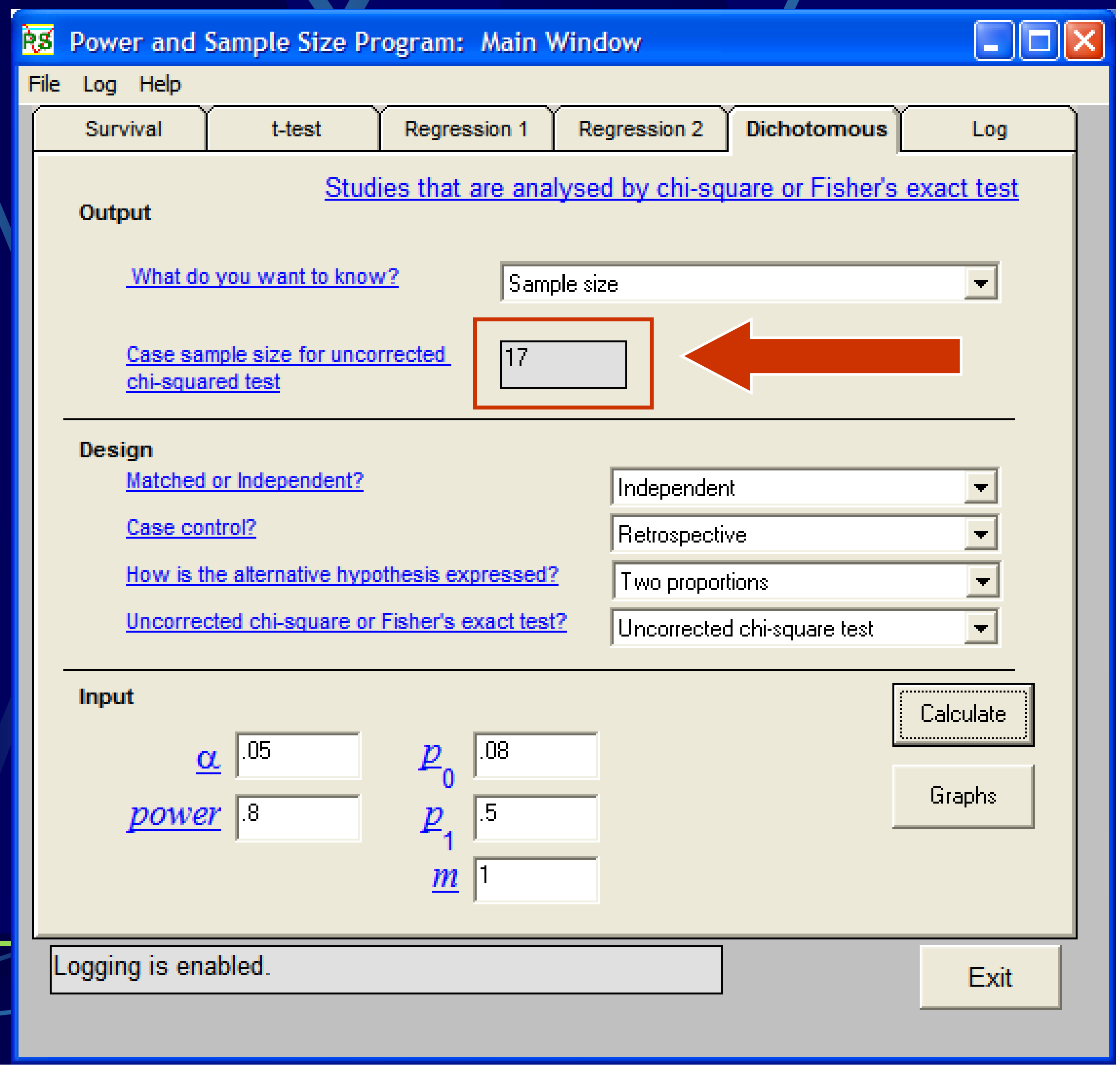
- So you need a sample size of only 22 cases and 22 controls.





Or use PS2

- Sample size for case is 17 and for control 17.
- Total 34
- StatCalc = 44 vs PS2 = 34 ……hmmm which would you prefer?



Calculate Your Own Sample Size

Cohort Study

Cohort

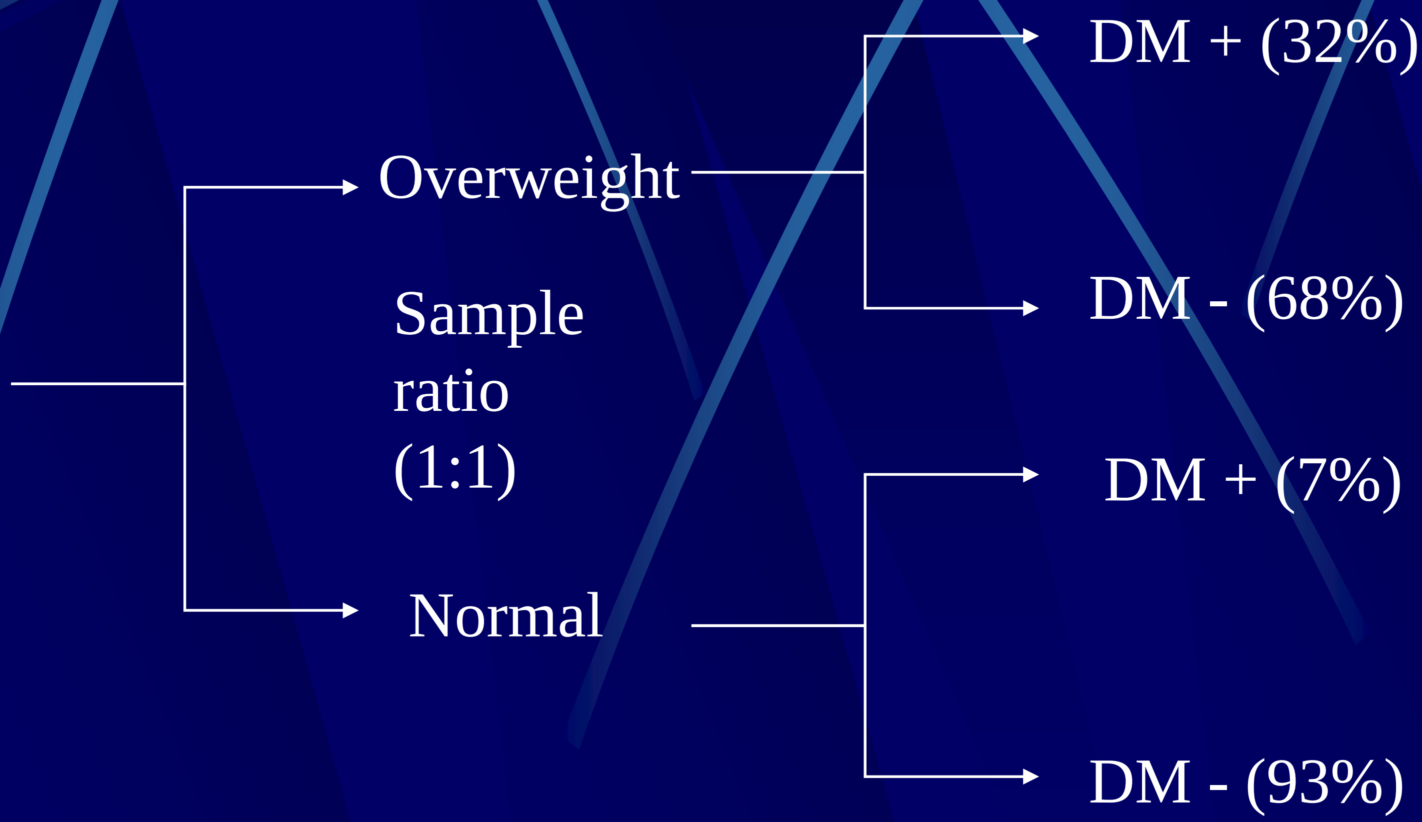
- In a cohort study, you identify those who are currently disease-free. Among them, you identify those with and without the exposure/risk factor. Then this cohort is followed up for a pre-determined amount of time to identify those who developed the disease and those who didn't.
- For example you want to prove that overweight adults have higher risk of diabetes mellitus compared to normal weight adults.

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 vs exposed; 1:1
- Proportion of sample from no-risk (Normal) population = 50%
- Proportion of sample from at-risk (Overweight) population = 50%
- P1=true proportion of DM in no-risk (Normal) population = 7%
- P2=true proportion of DM in at-risk (Overweight) population =32%

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

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

$\bar{Q} = 1-\bar{P}$.

$n_1 = m$

$n_2 = rm$

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

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

$P = (0.07 + (1 \text{ x } 0.32))/(1 + 1) = 0.195$

$Q = 1 - P = 0.805$

$$m' = \frac{[1.96\sqrt{(1+1)\text{x}0.195\text{x}0.805} - (-0.842)\sqrt{(1\text{x}0.07\text{x}0.93)+(0.32\text{x}0.68)}]^2}{1 \text{ x } (0.32 - 0.07)^2}$$

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

$$m = \frac{38.2369}{4} \text{ x } \left(1 + \sqrt{1 + \frac{(2\text{x}(1+1)}{(38.2369\text{x}1\text{x}0.25)}}\right)^2 = 45.8882$$

$m = n_1 = 46 \qquad n_2 = r \text{ x } m = 1 \text{ x } 46 = 46 \qquad n_1 + n_2 = 92$

Or Use StatCalc

Tables (2 x 2, 2 x n)
Sample size & power
Ch
Population survey
Cohort or cross-sectional
Unmatched case-control

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

C:\EPI6\STATCALC.EXE

EpiInfo Version 6 Statcalc November 1993

Unmatched Cohort and Cross-Sectional Studies (Exposed and Nonexposed)

Probability that if the two SAMPLES differ this reflects a true difference in the two POPULATIONS (Confidence level or 1-α) : 95.00 %

Probability that if the two POPULATIONS differ, the two SAMPLES will show a "significant" difference (Power or 1-β) : 80.00 %

Ratio (Number of Unexposed : Number of Exposed) : 1 : 1

Expected frequency of disease in unexposed group : 7.00 %

Please fill in the closest value to be detected for ONE of the following:

Risk ratio (RR) or relative risk--closest to 1.00 : 4.57
Odds ratio (OR)--closest to 1.00 : 6.25
Percent disease among exposed--closest to % for unexposed : 32.00 %

C:\EPI6\STATCALC.EXE

EpiInfo Version 6 Statcalc November 1993

Unmatched Cohort and Cross-Sectional Studies (Exposed and Nonexposed)
Sample Sizes for 7.00 % Disease in Unexposed Group

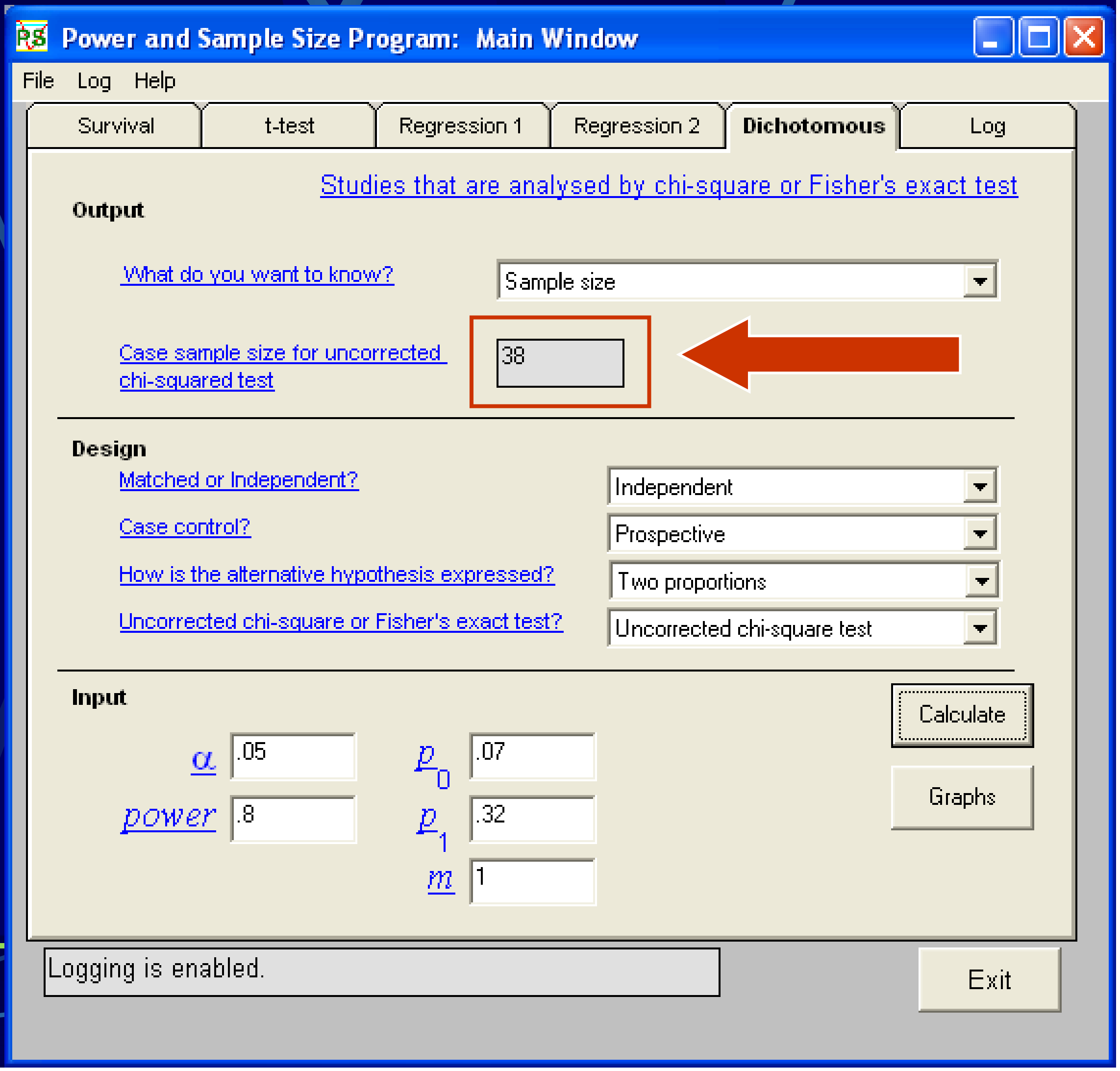
Conf.	Power	Unex:Exp	Disease in Exposed	Risk Ratio	Odds Ratio	Sample Size Unexp.	Sample Size Exposed	Total
95.00 %	80.00 %	1:1	32.00 %	4.57	6.25	46	46	92
90.00 %	"	"				38	38	76
95.00 %	"	"				46	46	92
99.00 %	"	"				65	65	130
99.90 %	"	"				92	92	184
95.00 %	80.00 %	"				46	46	92
"	90.00 %	"				58	58	116
"	95.00 %	"				70	70	140
"	99.00 %	"				95	95	190
"	80.00 %	4:1				100	25	125
"	"	3:1				81	27	108
"	"	2:1				64	32	96
"	"	1:2				36	72	108
"	"	1:3				32	97	129
"	"	1:4				30	121	151

Change values for inputs as desired, then press F4 to recalculate.

F1-Help F5-Print F6-Open File F10-Done

Or use PS2

- So the sample size required for each group is 38. Total of 76
- StatCalc = 92 vs PS2 = 76



Calculate Your Own Sample Size

Clinical Trial Study

Clinical Trial

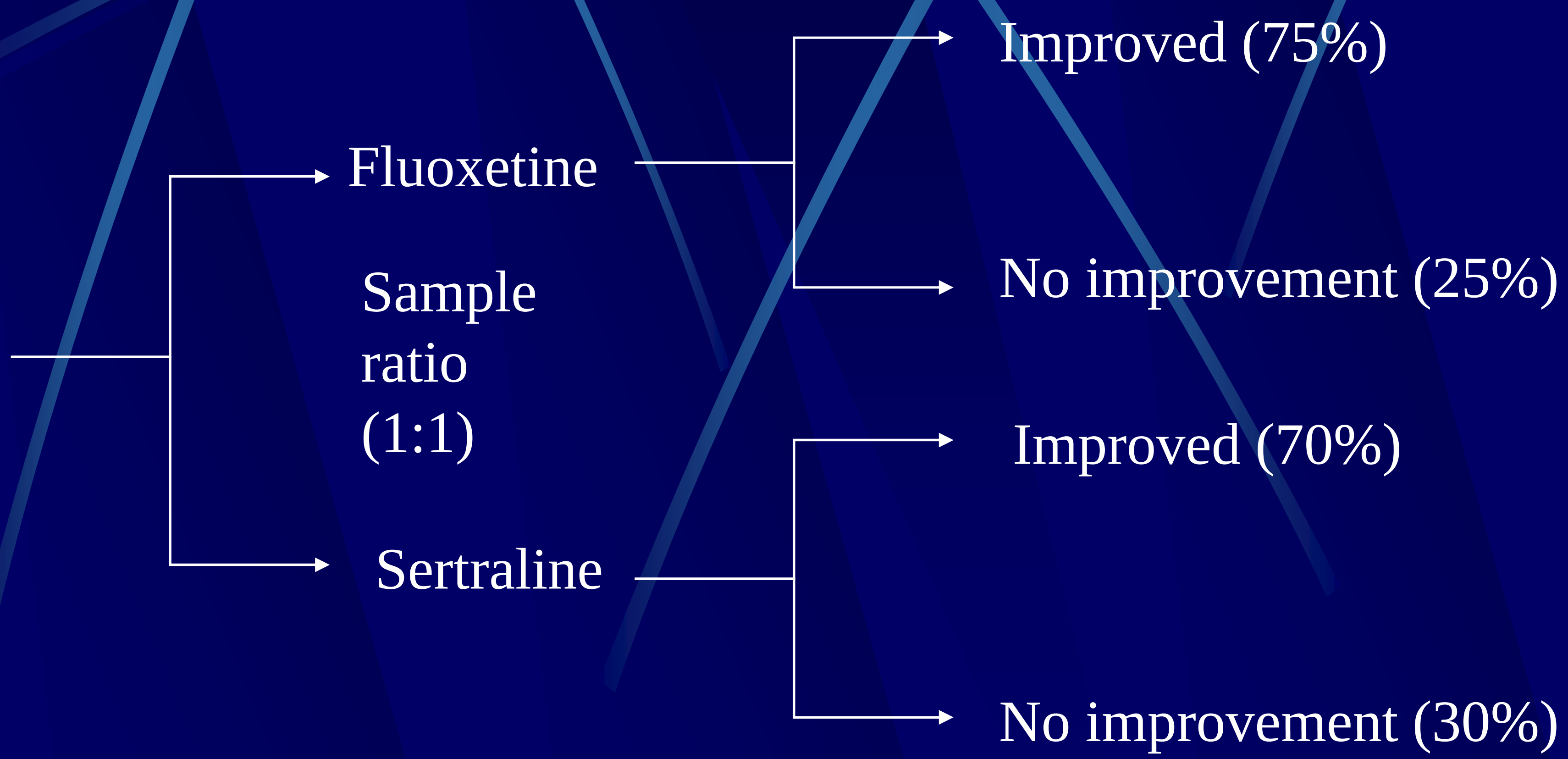
- Similar approach to cohort if the outcome is categorical.
- But it is easier to refer to available tables.
- For example comparing Fluoxetine against Sertraline for treating depression.
- From literature, 75% of Fluoxetine improved, 70% of Sertraline improved.

Example – treatment of depression

From literature review, identify the rate of improvement in the respective groups.

- Ratio of control vs treatment group; 1:1
- Proportion of sample from control (Fluoxetine) population = 50%
- Proportion of sample from treatment (Sertraline) population = 50%
- P1=true proportion of improvement in control (Fluoxetine) population = 75%
- P2=true proportion of improvement in treatment (Sertraline) population =70%

From Literature Review: treatment of depression



Refer to a Table

- The fastest way to calculate the sample size is to refer to a table. One such table is published in an article entitled "Clinical Trials in Cancer Research" in Environmental Health Perspectives Vol. 32, pp. 3148, 1979 by Edmund A. Gehan. It is available for download from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1637924
- Since the cure rate of 75% is not available in the table, we deduct 75% from 100%, giving us 25%. 0.25 is available in the table. The difference of cure rate is 0.05.

For table 3;

- Upper figure: α=0.05, power equals 0.8;
- middle figure: α=0.05, power equals 0.9;
- lower figure: α=0.01, power equals 0.95.

Table 3. Number of patients needed in an experimental and a control group for a given probability of obtaining a significant result (two-sided test).

Smaller proportion of success (P_1)	Number of patients for various larger minus smaller proportion of success ($P_2 - P_1$)[a]										
	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50	0.55
0.05	420	130	69	44	36	31	23	20	17	14	13
	570	175	93	59	42	37	31	24	21	18	16
	960	300	155	100	72	54	42	38	33	27	24
0.10	680	195	96	59	41	35	29	23	19	17	13
	910	260	130	79	54	40	36	29	24	20	17
	1550	440	220	135	92	68	52	41	38	32	26
0.15	910	250	120	71	48	39	31	25	20	17	15
	1220	330	160	95	64	46	40	31	26	22	18
	2060	560	270	160	110	78	59	47	41	35	29
0.20	1090	290	135	80	53	42	33	26	22	18	16
	1460	390	185	105	71	51	43	33	28	23	18
	2470	660	310	180	120	86	64	50	44	36	27
0.25	1250	330	150	88	57	44	35	28	22	18	16
	1680	440	200	115	77	56	45	36	29	23	18
	2840	740	340	200	130	95	68	52	45	36	29
0.30	1380	360	160	93	60	44	36	29	22	18	15
	1840	480	220	125	80	56	46	36	29	23	18
	3120	810	370	210	135	95	69	53	45	36	29
0.35	1470	380	170	96	61	44	36	28	22	17	13
	1970	500	225	130	82	57	46	36	28	22	17
	3340	850	380	215	140	96	69	52	44	35	26
0.40	1530	390	175	97	61	44	35	26	20	17	—
	2050	520	230	130	82	56	45	32	26	20	—
	3480	880	390	220	140	95	68	50	41	32	—

Alternative to table

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

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

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

Confidence level 95%, Power 80%

Ratio of cases to controls = 1

Larger Minus Smaller Proportion of Success (P_2-P_1)

Smaller Proportion of Success (P_1)	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50	0.55	0.60	0.65	0.70
0.01	249	106	66	47	36	29	23	20	17	15	13	11	10	9
0.02	307	120	72	50	38	30	24	20	17	15	13	11	10	9
0.03	364	134	77	53	39	31	25	21	18	15	13	11	10	9
0.04	419	147	83	56	41	32	26	21	18	15	13	12	10	9
0.05	474	159	88	58	43	33	27	22	18	16	14	12	10	9
0.06	526	172	93	61	44	34	27	22	19	16	14	12	10	9
0.07	578	184	98	64	46	35	28	23	19	16	14	12	10	9
0.08	628	196	103	66	47	36	29	23	19	16	14	12	11	9
0.09	677	207	108	69	49	37	29	24	20	17	14	12	11	9
0.10	725	219	112	71	50	38	30	24	20	17	14	12	11	9
0.11	772	229	117	74	52	39	30	25	20	17	14	12	11	9
0.12	817	240	121	76	53	40	31	25	20	17	15	12	11	9
0.13	861	250	125	78	54	40	31	25	21	17	15	13	11	9
0.14	903	260	130	80	55	41	32	26	21	17	15	13	11	9
0.15	945	270	133	82	57	42	32	26	21	18	15	13	11	9
0.16	985	279	137	84	58	43	33	26	21	18	15	13	11	9
0.17	1024	288	141	86	59	43	33	26	22	18	15	13	11	9
0.18	1062	296	144	88	60	44	34	27	22	18	15	13	11	9
0.19	1098	305	148	89	61	44	34	27	22	18	15	13	11	9
0.20	1133	313	151	91	62	45	34	27	22	18	15	13	11	9
0.21	1167	321	154	92	63	45	35	27	22	18	15	13	11	9
0.22	1200	328	157	94	63	46	35	27	22	18	15	13	11	9
0.23	1231	335	160	95	64	46	35	28	22	18	15	13	11	9
0.24	1262	342	162	97	65	47	35	28	22	18	15	13	11	9
0.25	1290	348	165	98	65	47	36	28	22	18	15	13	11	9
0.26	1318	354	167	99	66	47	36	28	22	18	15	13	11	9
0.27	1344	360	170	100	67	48	36	28	22	18	15	13	11	9
0.28	1370	366	172	101	67	48	36	28	22	18	15	12	10	9
0.29	1393	371	174	102	68	48	36	28	22	18	15	12	10	9
0.30	1416	376	175	103	68	48	36	28	22	18	15	12	10	9

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
P_1=proportion of **cure** in population 1
α= "Significance" = 0.05
$1-\beta$ = Power = 0.8
$\bar{P} = (P_1+rP_2)/(r+1)$
$n_1 = m$

n_2=size of sample from population 2
P_2=proportion of **cure** in population 2
β=chance of not detecting a difference = 0.2
r = n2/n1 = ratio of treatment grp to controls
$\bar{Q} = 1-\bar{P}$.
$n_2 = rm$

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-beta} is -0.842

Calculate Manually

$P_1 = 0.75$ $P_2 = 0.70$ $r = 1/1$

$P = (0.75 + (1 \text{ x } 0.70))/(1 + 1) = 0.725$

$Q = 1 - P = 0.275$

$$m' = \frac{[1.96\sqrt{(1+1)x0.725x0.275} - (-0.842)\sqrt{(1x0.75x0.25)+(0.70x0.30)}]^2}{1 \text{ x } (0.75 - 0.70)^2}$$

$$= \frac{3.1277}{0.0025} = 1251.0867$$

$$m = \frac{1251.09}{4} \text{ x } \left(1+\sqrt{1+\frac{(2x(1+1)}{(1251.09x1x0.05)}}\right)^2 = 1290.7769$$

$m = n_1 = 1291$ $n_2 = r \text{ x } m = 1 \text{ x } 46 = 1291$ $n_1 + n_2 = 2582$

Or Use StatCalc

Tables (2 x 2, 2 x n)
Sample size & power
Ch

Population survey
Cohort or cross-sectional
Unmatched case-control

- So you'll need a sample size of 1290 each for both groups. Total of 2580.

C:\EPI6\STATCALC.EXE

EpiInfo Version 6 Statcalc November 1993

Unmatched Cohort and Cross-Sectional Studies (Exposed and Nonexposed)

Probability that if the two SAMPLES differ this reflects a true difference in the two POPULATIONS (Confidence level or 1-α)	: 95.00 %
Probability that if the two POPULATIONS differ, the two SAMPLES will show a "significant" difference (Power or 1-β)	: 80.00 %
Ratio (Number of Unexposed : Number of Exposed) :	1 : 1
Expected frequency of disease in unexposed group	: 75.00 %

Please fill in the closest value to be detected for ONE of the following:

Risk ratio (RR) or relative risk--closest to 1.00	: 0.93
Odds ratio (OR)--closest to 1.00	: 0.78
Percent disease among exposed--closest to % for unexposed	: 70.00 %

F1-Help F4-Calc F6-Open File F10-Done

EpiInfo Version 6 Statcalc November 1993

Unmatched Cohort and Cross-Sectional Studies (Exposed and Nonexposed)
Sample Sizes for 75.00 % Disease in Unexposed Group

Conf.	Power	Unex:Exp	Disease in Exposed	Risk Ratio	Odds Ratio	Sample Size Unexp.	Sample Size Exposed	Total
95.00 %	80.00 %	1:1	70.00 %	0.93	0.78	1,290	1,290	2,580
90.00 %	"	"				1,025	1,025	2,050
95.00 %	"	"				1,290	1,290	2,580
99.00 %	"	"				1,901	1,901	3,802
99.90 %	"	"				2,762	2,762	5,524
95.00 %	80.00 %	"				1,290	1,290	2,580
"	90.00 %	"				1,714	1,714	3,428
"	95.00 %	"				2,110	2,110	4,220
"	99.00 %	"				2,965	2,965	5,930
"	80.00 %	4:1				3,180	795	3,975
"	"	3:1				2,550	850	3,400
"	"	2:1				1,920	960	2,880
"	"	1:2				974	1,949	2,923
"	"	1:3				869	2,607	3,476
"	"	1:4				816	3,265	4,081

Change values for inputs as desired, then press F4 to recalculate.

F1-Help F5-Print F6-Open File F10-Done

Or use PS2

- So the sample size required for each group is 1251. Total of 2502
- StatCalc = 2580 vs PS2 = 2502

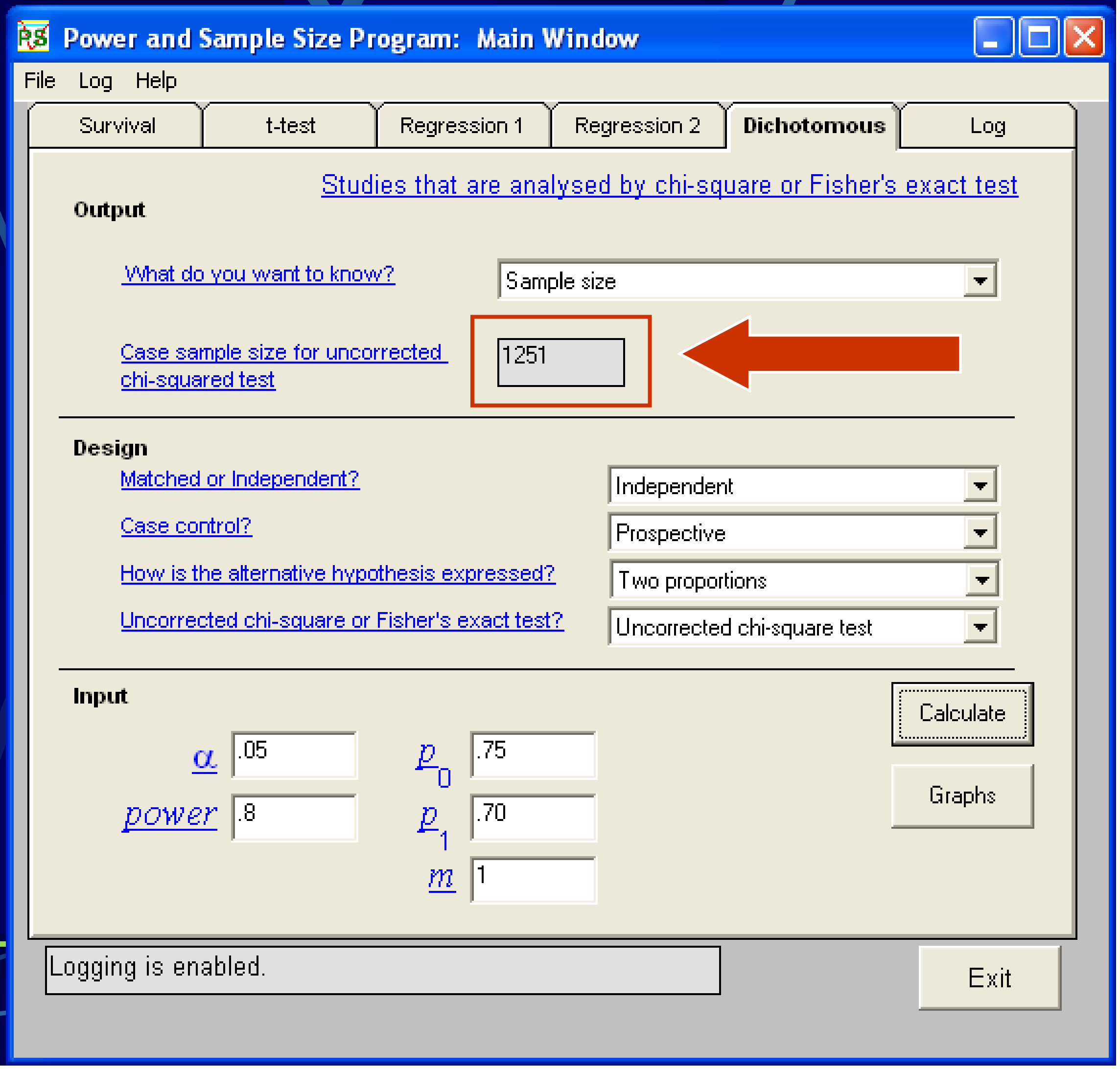


Table vs StatCalc vs PS2

- From table; 1250 from each group = 2500.
- From PS2; 1251 from each group = 2502
- From StatCalc; 1290 from each group = 2580.
- From manual calculation; 1291 from each group = 2582.
- So the sample size from the table is very similar to PS2's results.

What if the 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

Continuous data (two independent groups)

- We need to specify the following;
  - Standard deviation of the variable (s.d)
  - Clinically relevant difference (δ)
  - The significant level (α) – 0.05
  - The power ($1 - \beta$) – 80%

Continuous data (two independent groups)

- The **standardised difference** is calculated as;

$$\frac{\delta}{s.d},$$

Example

- If difference between means = 10 mmHg
- & pop. standard deviation = 20 mm Hg
- Then standardised difference;

10 mm Hg/20 mm Hg = 0.5

Continuous data (two independent groups)

- We draw a straight line from the value for the standardized difference to the value of 0.80 on the scale for power.
- Read off the value for N on the line corresponding to $\alpha = 0.05$, which gives a total sample size of eg. 128, so we required 64 samples for each group.

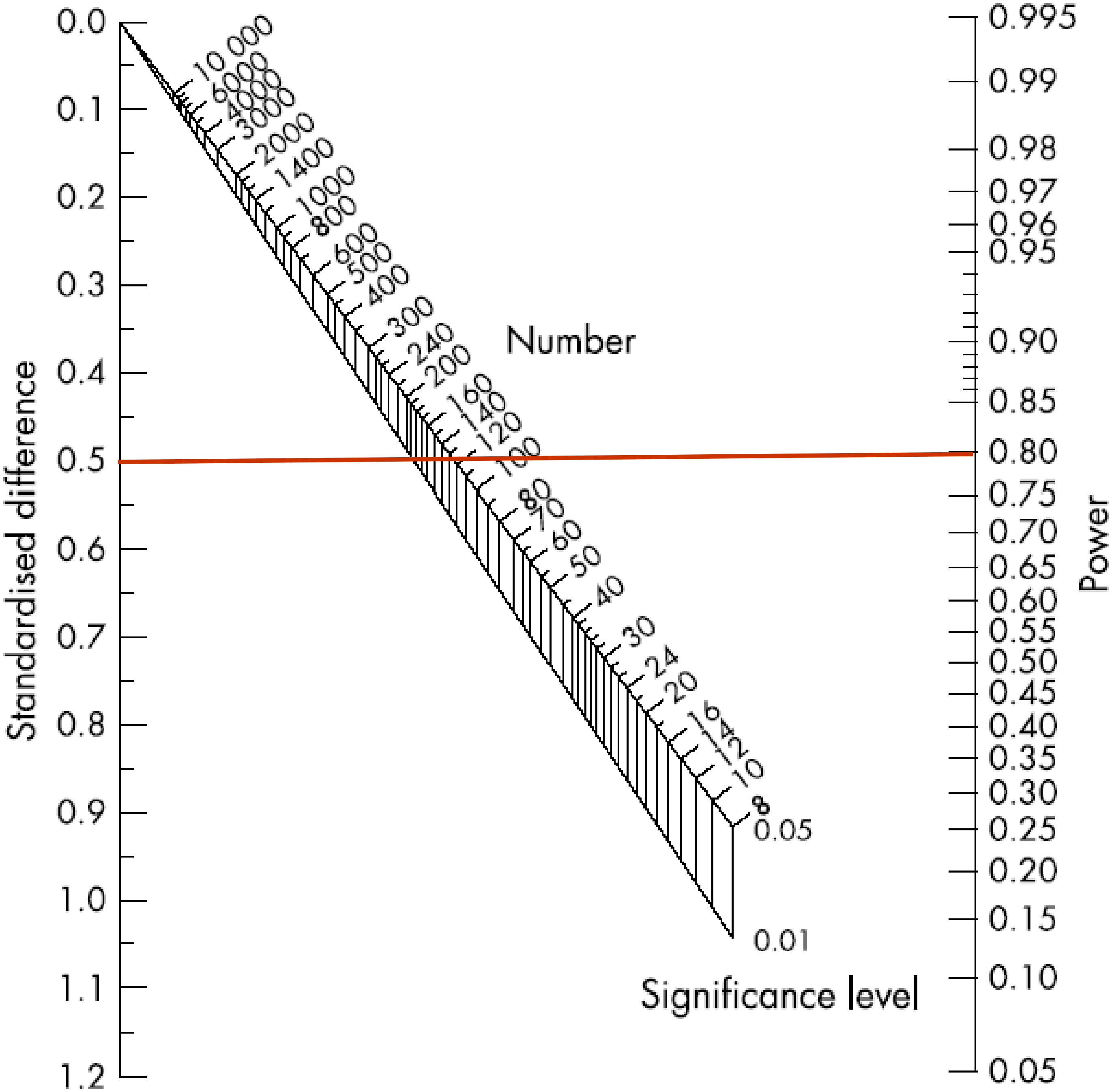


Figure 3 Nomogram for the calculation of sample size.

Or refer to a table

- Sdiff = 0.5, sample size = 64.
- So 2 groups = 128.

Table 3 How power changes with standardised difference

	Power level (pβ)			
Sdiff	0.99	0.95	0.90	0.80
0.10	3676	2600	2103	1571
0.20	920	651	527	394
0.30	410	290	235	176
0.40	231	164	133	100
0.50	148	105	86	64
0.60	104	74	60	45
0.70	76	54	44	33
0.80	59	42	34	26
0.90	47	34	27	21
1.00	38	27	22	17
1.10	32	23	19	14
1.20	27	20	16	12
1.30	23	17	14	11
1.40	20	15	12	9
1.50	18	13	11	8

Sdiff, standardised difference.

Alternative to table

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

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

δ = Clinically relevant difference

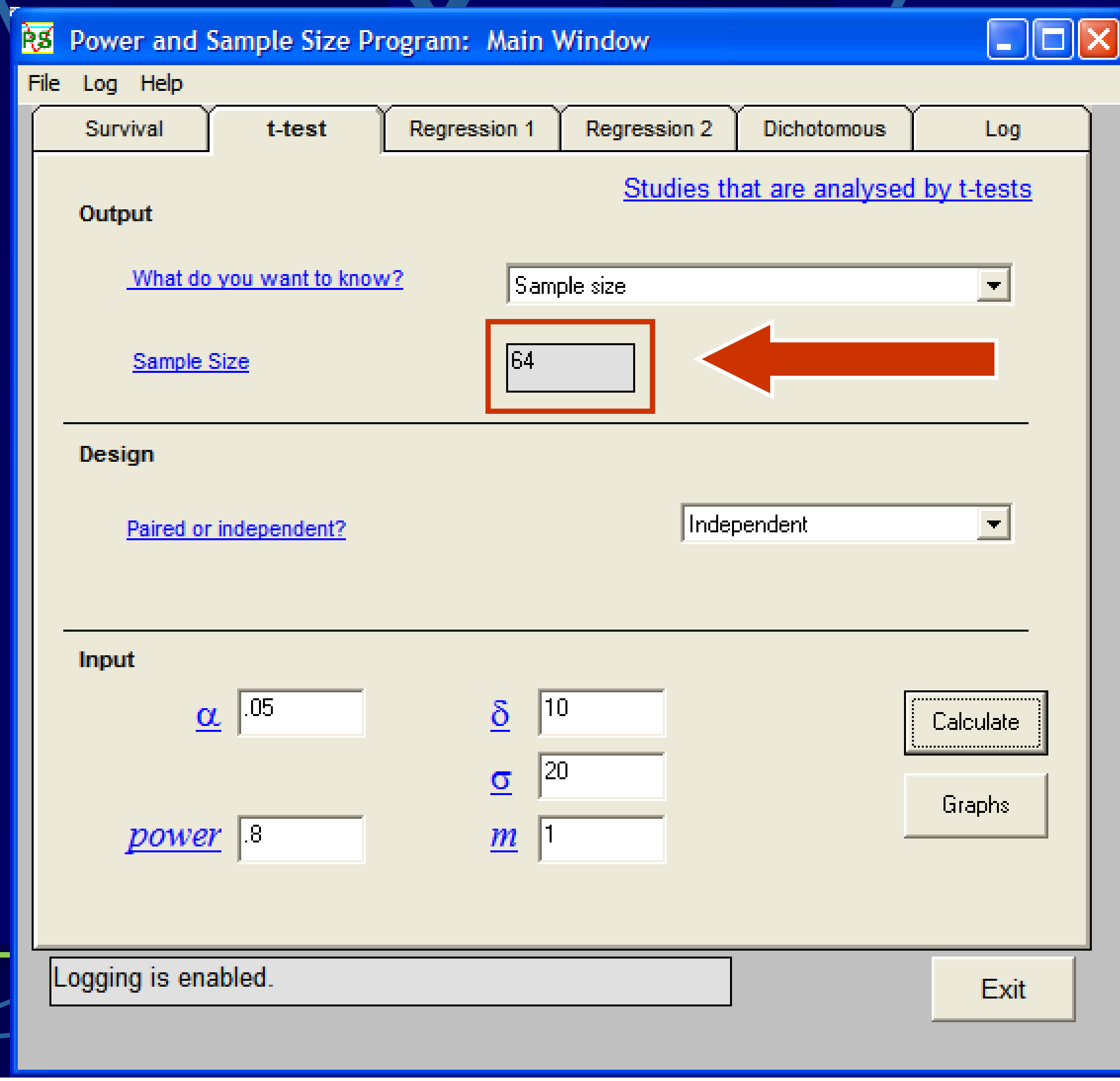
s.d = Standard deviation of the variable

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

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.



Manual Calculation

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

(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

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

$= 63.8 = 64$

This is similar to the table and PS2!

Calculate Your Own Sample Size

Diagnostic Study

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

Diagnostic Study

- Based upon literature review, identify the sensitivity & specificity of the diagnostic test being studied.
- Calculate the sample size based on the sensitivity using the following formula;

$$TP + FN = z^2 \times \frac{(SN(1 - SN))}{W^2}$$

$$N(sN) = \frac{TP + FN}{P}$$

Terms

- TP = True Positive
- FN = False Negative
- SN = Sensitivity
- z = Confidence Interval normal distribution value i.e. for 95%, z = 1.96
- P = prevalence of disease in the test population
- W = accuracy = 0.05

Example (SN=95%)

- SN = 95%
- z = 1.96
- P = 30%
- W = 0.05

Example (SN=95%)

$$TP + FN = z^2 \times \frac{(SN(1 - SN))}{W^2}$$

$$= 1.96^2 \times \frac{(0.95(1 - 0.95))}{0.05^2}$$

$$= 3.842 \times \frac{0.0475}{0.0025}$$

$$N(sN) = \frac{TP + FN}{P} \qquad = \frac{72.998}{0.3}$$

Diagnostic Study

- Calculate again the sample size based on the specificity using the following formula;

$$FP + TN = z^2 \times \frac{(SP\,(1 - SP))}{W^2}$$

$$N\,(sp) = \frac{FP + TN}{(1 - P)}$$

Example (SP=80%)

- SP = 80%
- z = 1.96
- P = 30%
- W = 0.05

Example (SP=80%)

$$FP + TN = z^2 \times \frac{(SP\,(1 - SP))}{W^2}$$

$$= 1.96^2 \times \frac{(0.80\,(1 - 0.80))}{0.05^2}$$

$$= 3.842 \times \frac{0.16}{0.0025}$$

$$N\,(sp) = \frac{FP + TN}{(1 - P)} \qquad = \frac{245.888}{(1 - 0.3)}$$

Diagnostic Study

- N for Sensitivity 95% = 243
- N for Specificity 80% = 351
- If interested in both sensitivity and specificity, then take the higher number (e.g. 351).

Conclusion

- You can calculate your own sample size.
- Tools are available and most of them are free.
- Decide what is your study design and choose the appropriate method to calculate the sample size.
- If despite following these notes fastidiously, your proposal is still rejected by the committee due to sample size, kindly SEE THEM, not us.

References (incl. for StatCalc)

- Fleiss JL. Statistical methods for rates and proportions. New York: John Wiley and Sons, 1981.
- Gehan EA. Clinical Trials in Cancer Research. Environmental Health Perspectives Vol. 32, pp. 3148, 1979.
- Jones SR, Carley S & Harrison M. An introduction to power and sample size estimation. Emergency Medical Journal 2003;20;453-458. 2003
- Kish L. Survey sampling. John Wiley & Sons, N.Y., 1965.
- Krejcie, R.V. & Morgan, D.W. (1970). Determining sample size for research activities. *Educational & Psychological Measurement*, 30, 607-610.
- Snedecor GW, Cochran WG. 1989. Statistical Methods. 8th Ed. Ames: Iowa State Press.

References (PS2)

- Dupont WD, Plummer WD, Jr: Power and Sample Size Calculations: A Review and Computer Program. Controlled Clinical Trials 11:116-128, 1990
- Dupont WD, Plummer WD, Jr: Power and Sample Size Calculations for Studies Involving Linear Regression. Controlled Clinical Trials 19:589-601, 1998
- Schoenfeld DA, Richter JR: Nomograms for calculating the number of patients needed for a clinical trial with survival as an endpoint. Biometrics 38:163-170, 1982
- Pearson ES, Hartley HO: Biometrika Tables for Statisticians Vol. I 3rd Ed. Cambridge: Cambridge University Press, 1970
- Schlesselman JJ: Case-Control Studies: Design, Conduct, Analysis. New York: Oxford University Press, 1982
- Casagrande JT, Pike MC, Smith PG: An improved approximate formula for calculating sample sizes for comparing two binomial distributions. Biometrics 34:483-486, 1978
- Dupont WD: Power calculations for matched case-control studies. Biometrics 44:1157-1168, 1988
- Fleiss JL. Statistical methods for rates and proportions. New York: John Wiley and Sons, 1981.

THANK YOU