Example name Systolic BP

Effect size Mean difference Analysis type Basic Level Basic

Synopsis

This analysis includes four studies where persons who donated a kidney were compared with persons in a control group. Outcome was the Systolic Blood Pressure. Effect size was the difference in mean Systolic Blood Pressure.

We use this example to show

- How to enter data for means in two independent groups
- How to get a sense of the weight assigned to each study
- How weights are affected by the statistical model
- How to interpret statistics for effect size
- How to interpret statistics for heterogeneity

To open a CMA file > Download and Save file | Start CMA | Open file from within CMA

Download CMA file for computers that use a period to indicate decimals Download CMA file for computers that use a comma to indicate decimals

Download this PDF Download data in Excel Download trial of CMA

Start the program

- Select the option [Start a blank spreadsheet]
- Click [Ok]

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Click Insert > Column for > Study names

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The program displays this wizard

Select [Show all 100 formats] Click [Next]



Select [Comparison of two groups...] Click [Next]



Types of studies included

On this panel, select the type of studies to be included in this meta analysis. This controls the types of data entry options to be displayed on the next panel.

If unsure, select the first option, which is appropriate for most analyses. You will be able to return to this panel and change the selection.

- Comparison of two groups, time-points, or exposures (includes correlations)
- C Estimate of means, proportions or rates in one group at one time-point
- C Generic point estimates

C Generic point estimates, log scale

Drill down to

Continuous (means) Unmatched groups, post-data only Mean, SD and sample size in each group



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— 4 —

The program displays this wizard

Enter the following labels into the wizard

- First group > Donor
- Second group > Control

Click [Ok] and the program will copy the names into the grid

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There are three options at this point

- Enter the data directly into CMA
- - or Open the CMA data file "Systolic BP after kidney donation.cma"
- - or Copy the data from Excel "Systolic BP after kidney donation.xls"

Here, we'll show how to copy the data from Excel

- Switch to Excel and open the file
- Highlight the rows and columns as shown (Columns A to G), and press CTRL-C to copy to clipboard

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4	Talselth, 1986	140	23	32	132	29	32			
5	Williams, 1886	136	25	38	129	16	16			
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- Switch to CMA
- Click in cell Study-name 1
- Press [CTRL-V] to paste the data
- The screen should look like this

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After checking that the data has been copied correctly, we can delete Row 1

- Click anywhere in Row 1
- Select Edit > Delete row, and confirm

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We need to enter a value for "Effect Direction"

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2 Undurraga, 1998	125.000	18.000	30	118.000	13.000	30	Auto	0.446	0.261	0.068	0.440	0.258	0.067	7.000	4.054	16.433
3 Talselth, 1986	140.000	23.000	32	132.000	29.000	32	Auto	0.306	0.251	0.063	0.302	0.248	0.062	8.000	6.543	42.813
4 Williams, 1886	136.000	25.000	38	129.000	16.000	16	Auto	0.307	0.299	0.090	0.303	0.295	0.087	7.000	6.786	46.056
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The program displays three effect sizes -d, g, and raw mean difference

- We want to hide the indices d and g
- We want to set the raw mean difference as the primary index

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- Right-click in any yellow column
- Click "Customize computed effect size display"

In the wizard,

- Select "Difference in means" in the drop-down box
- Un-check "Std diff in means"
- Un-check "Hedges's g"

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Note that the file name is now in the header.

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- [Save As...] will allow you to save the file with a new name

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2	Undurraga, 1998	125.000	18.000	30	118.000	13.000	30	Auto	7.000	4.054	16.433				
3	Talselth, 1986	140.000	23.000	32	132.000	29.000	32	Auto	8.000	6.543	42.813				
4	Williams, 1886	136.000	25.000	38	129.000	16.000	16	Auto	7.000	6.786	46.056				
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There are two options for computing the variance of the mean difference. We can pool the estimates from the two groups, or keep them separate. We will pool them.

Click Computational options > Variance for mean difference

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- Check the option "Assume a common variance"
- Click Ok

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7 Variance for raw mean difference in independent groups. 10 When a study includes data for two independent groups, the user may elect to enter the SD for each of the groups separately. In this case the program can pool the variance in the two groups (option 1) or not pool them (option 2). 11 This option affects the variance (and weights) used in an analysis of raw mean differences. It has no impact on analyses of standardized mean differences. It h	6	5							L. Options for c	omputing tre	atment effe	ects		×		
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By convention we've put the Experimental group (Donor) in the first columns and the control group in the next two columns.

The program will compute the mean difference as Experimental minus Control. Thus, a positive difference means that the donors had a higher BP.

(The column labeled Direction allows you to control this process. "Auto" means that the program will assign a "+" if the first group was higher and a "-" if the second group was higher.

It's always a good idea to check at least one study and make sure that we have the direction right. For this purpose we'll use the first study (Nalarian). The mean BP was 134 for Donor and 130 for Control. The Difference in means is positive (+4.000) which means that the donor group had a higher mean.

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1	Najarian, 1992	134.000	15.000	57	130.000	21.000	50	Auto	4.000	3.497	12.232				
2	Undurraga, 1998	125.000	18.000	30	118.000	13.000	30	Auto	7.000	4.054	16.433				
3	Talselth, 1986	140.000	23.000	32	132.000	29.000	32	Auto	8.000	6.543	42.813				
4	Williams, 1886	136.000	25.000	38	129.000	16.000	16	Auto	7.000	6.786	46.056				
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• To run the analysis, click [Run analysis]

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	2 Undurraga, 1998	125.000	18.000	30	118.000	13.000	30	Auto	7.000	4.054	16.433				
	3 Talselth, 1986	140.000	23.000	32	132.000	29.000	32	Auto	8.000	6.543	42.813				
	4 Williams, 1886	136.000	25.000	38	129.000	16.000	16	Auto	7.000	6.786	46.056				
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This is the basic analysis screen

Initially, the program displays the fixed-effect analysis. This is indicated by the tab at the bottom and the label in the plot.

Right-click on the forest plot > Customized > Set the scale to 20

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		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	-20.00	-10.00	0.00	10.00	20.00		
	Najarian,	4.000	3.497	12.232	-2.855	10.855	1.144	0.253							
	Undurraga,	7.000	4.054	16.433	-0.945	14.945	1.727	0.084					-		
	Talselth,	8.000	6.543	42.813	-4.824	20.824	1.223	0.221					**		1
	Williams,	7.000	6.786	46.056	-6.301	20.301	1.031	0.302		- -			+ Show/h	ide forest plot	1
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Fixed		5.818	2.308	5.328	1.293	10.342	2.520	0.012				•			

All studies have mean differences over 0.0, which means that the donor group had a higher Systolic BP than the control.

The effects seem to be reasonably consistent. The confidence interval for all studies overlaps the mean effect size.

The pooled effect is 5.818, which means that the mean Systolic BP in the donor group was about 6 points higher than the control.

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Click [Both models]

The program displays results for both the fixed-effect and the random-effects analysis.

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Und	ndurraga,	7.000	4.054	16.433	-0.945	14.945	1.727	0.084			+		-	32.42	32.42 📕
Tak	ilselth,	8.000	6.543	42.813	-4.824	20.824	1.223	0.221						12.45	12.45
	inamo,	7.000	6.786	46.056	-6.301	20.301	1.031	0.302		-				11.57	11.57
Fixed		5.818	2.308	5.328	1.293	10.342	2.520	0.012							
Random		5.818	2.308	5.328	1.293	10.342	2.520	0.012				+			

Under the fixed-effect model the pooled mean difference is 5.818. Under the random-effects model the pooled mean difference is also 5.818.

This tells us that the any between-study variance in the observed effects is within the range we would expect based on sampling error. Our estimate of the between-study variance in true effects is zero. Therefore, the fixed-effect weights and random-effects weights are identical.

While both models yield the same result, we still need to say which model we are using.

- The fixed-effect model would be appropriate if all the studies were virtual replicates of each other. This is not the case, which is not the case here since the study populations varied in numerous (if unknown) ways.
- The random-effects model would be appropriate if the studies vary in ways that may impact the effect size. Therefore, we will use the random-effects model.

• Click Random on the tab at the bottom

The plot now displays the random-effects analysis alone.

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	Undurraga, 1998	7.000	4.054	16.433	-0.945	14.945	1.727	0.084				-		32.42	
	Villiams 1886	8.000 7.000	6,543	42.813	-4.824	20.824	1.223	0.221		_				12.45	
andom		5.818	2.308	5.328	1.293	10.342	2.520	0.012							

A quick view of the plot suggests the following

- The BP was always higher in the donor group than the control
- The observed effects are pretty consistent, in that the confidence intervals for all studies but one overlap the mean effect size.
- The summary effect is 5.818 with a Cl of 1.293 to 10.342.
- The summary effect has a Z-value 2.520 a *p*-value of 0.012. Thus we can reject the null hypotheses that the true mean difference is 0.0.
- At the same time, the magnitude of mean difference is relatively modest

The confidence interval tells us that the <u>mean</u> effect size falls in range of 1.293 to 10.342. It tells us nothing about how widely the true effect size varies from study to study. This is an important clinical issue since we need to distinguish between various possibilities, such as

- a) The mean BP is consistently about 6 points higher in the donor group
- b) The donor group sometimes has a mean BP 0 points higher, sometimes 6 points higher, sometimes 12 or more points higher

To address this we need not only the mean difference but also the standard deviation of the differences. For this we turn to the next screen.

Click Next Table

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	Najarian, 1992	4.00	D 3.497	12.232	-2.855	10.855	1.144	0.253							43.56
	Undurraga, 1998	7.00	D 4.054	16.433	-0.945	14.945	1.727	0.084							32.42
	Talselth, 1986	8.00	D 6.543	42.813	-4.824	20.824	1.223	0.221			-				12.45
	Williams, 1886	7.00	D 6.786	46.056	-6.301	20.301	1.031	0.302							11.57
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The program displays this screen

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Fixed		4	\$ 5.818	2.308	5.328	1.293	10.342	2.520	0.012	0.497	3	0.920	0.000	0.000	19.300	372.507	0.000
Random		4	5.818	2.308	5.328	1.293	10.342	2.520	0.012								

The section labeled "Effect size and 95% confidence interval and the section labled "Test of null" address the <u>mean</u> effect size and the null hypothesis that the mean difference is zero. These are the same statistics we saw on the previous screen. The mean difference is 5.818 (1.293 to 10.342), the Z-value for a test of the null is 2.520 and the p-value for a test of the null is 0.012.

The section labeled Heterogeneity shows a test of the null hypothesis that the true effect size is identical in all four studies and that 100% of the variation in the observed effects is due to sampling error. Put another way, if every one of the studies had an infinite sample size (so that we knew the true effect size in that study exactly) the observed effects would all be identical to each other.

To test this hypothesis we compute Q, which is basically a weighted sum of squares (we compute the difference of every effect size from the mean effect size, square that difference, assign larger weights to more precise studies, and then sum these weighted values). If the null hypothesis is true (that all the variation in effects is due to sampling error), the expected value of Q is equal to the number of studies minus 1 (here, 4 minus 1 equals 3).

The observed Q value is 0.497. This is less than we would expect if the null is true (3.0). Therefore, we do not reject the null. We have no evidence that the true effect size varies from study to study.

Since the observed variance is actually less than we would expect by chance alone, our estimate of the true variance must be zero. This is expressed in several statistics.

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 l^2 is 0.0%. This tells us that about 0& of the variance that we see in the forest plot reflects difference in the true effect sizes, while the other 100% reflects sampling error. Put another way, if we were able to plot the true effects rather than the observed effects, the data points would align one directly above the other.

Importantly, l^2 is a proportion – it tells us what proportion of the observed variance is real (if our esimates are correct) but does not tell us how much variance there is. However, if l^2 is 0% then it follows that the absolute variance must also be 0.0.

- T^2 (shown as 0.000) is the estimate of variance in true effect sizes.
- *T* (shown 0.000) is the estimate of the standard deviaiton in true effect sizes.

We can use this to get a sense of how the true effects are distributed.

If the mean effect size is 5.818, if the standard deviation of true effects is 0, then the true effect size for all studies is 5.818.

This estimate also assumes that the mean of 5.818 is known. If we want to report the prediction interval (to say that 95% of all studies will have a mean difference in the range of A to B) then we need to take into account also the imprecision of the mean effect. At the moment, however, we're focusing on the dispersion of effects. And based on this sample we have no evidence that the effect size varies from study to study.

Click Next table

We want to create a high-resolution plot

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	Williams, 1886	7.000	6.786	46.056	-6.301	20.301	1.031	0.302		-				
Random		5.818	2.308	5.328	1.293	10.342	2.520	0.012						

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- Select "Random" rather than "Both" on the bottom tab
- Click Hi-Resolution plot
- Adjust the columns widths



Summary

This analysis includes four studies where persons who donated a kidney were compared with persons in a control group. Outcome was the Systolic Blood Pressure. Effect size was the difference in mean Systolic Blood Pressure.

Is kidney donation related to Systolic blood pressure?

The pooled difference in means is 5.818, which means that the systolic BP for persons who donated a kidney was (on average) 5.818 units higher than the systolic BP for persons who did not donate a kidney.

These studies were sampled from a universe of possible studies defined by certain inclusion/exclusion rules as outlined in the full paper. The confidence interval for the mean difference is 1.293 to 10.342, which tell us that the <u>mean</u> difference in the universe of studies could fall anywhere in this range. This range does not include a difference of zero, which tells us that the true difference is probably not zero.

Similarly, the Z-value for testing the null hypothesis (that the mean difference is zero) is 2.520, with a corresponding p-value is 0.012. We can reject the null that mean systolic BP is the same in both groups, and conclude that the mean systolic BP is higher in the donor group.

Does the effect size vary across studies?

The *observed* effect size varies somewhat from study to study, but a certain amount of variation is expected due to sampling error. We need to determine if the observed variation falls within the range that can be attributed to sampling error (in which case there is no evidence of variation in true effects), or if it exceeds that range.

The *Q*-statistic provides a test of the null hypothesis that all studies in the analysis share a common effect size. If all studies shared the same effect size, the expected value of *Q* would be equal to the degrees of freedom (the number of studies minus 1).

The *Q*-value is 0.497 with 3 degrees of freedom. Thus, the observed dispersion is less than the amount of dispersion we would expect to see based solely on sampling error. Our best estimate of the dispersion in true effects is zero, and it follows that we cannot reject the null hypothesis that the effect size is the same in all studies.

The l^2 statistic tells us what proportion of the observed variance reflects differences in true effect sizes rather than sampling error. This is zero.

 T^2 is the variance of true effect sizes (in log units). Here, T^2 is zero. *T* is the standard deviation of true effects (in log units). Here, *T* is zero.

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