

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

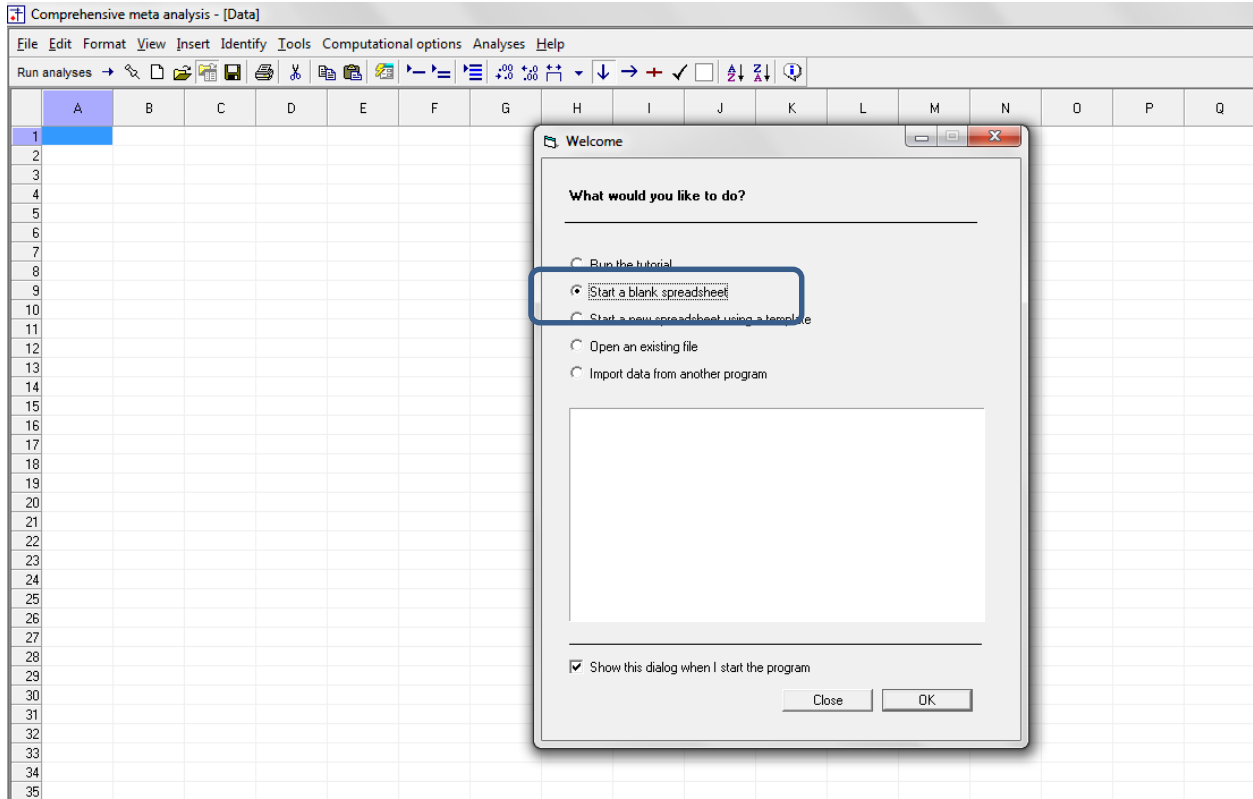
To open a CMA file > [Download and Save file](#) | [Start CMA](#) | [Open file from within CMA](#)

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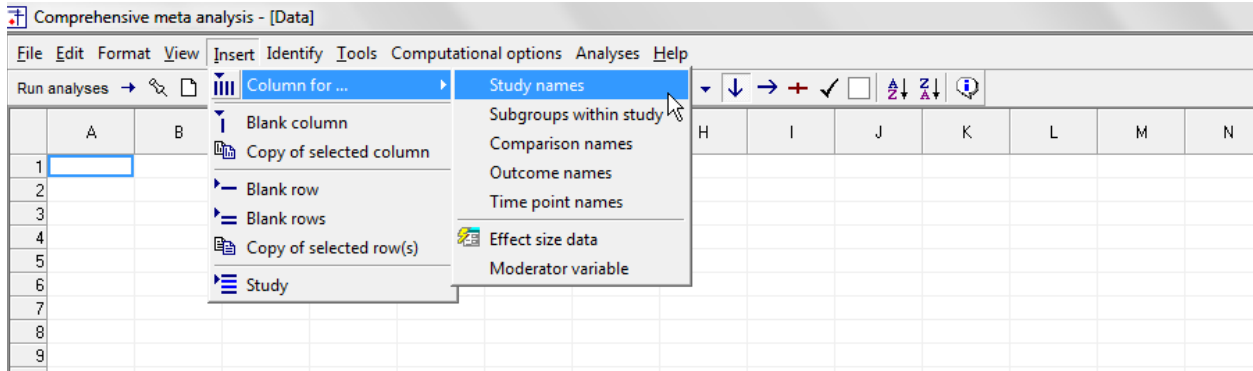
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Start the program

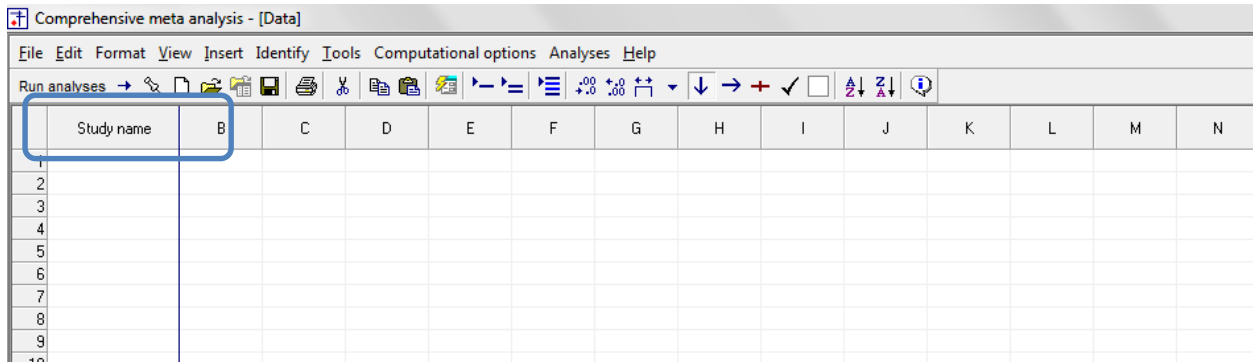
- Select the option [Start a blank spreadsheet]
- Click [OK]



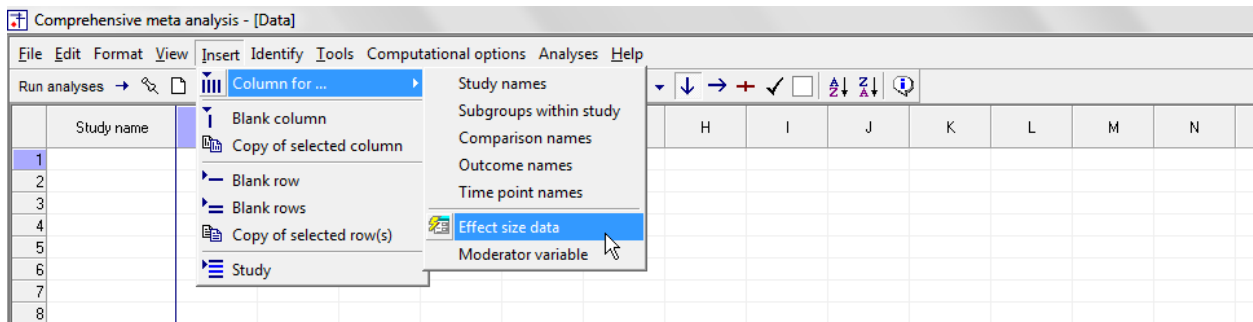
Click Insert > Column for > Study names



The screen should look like this

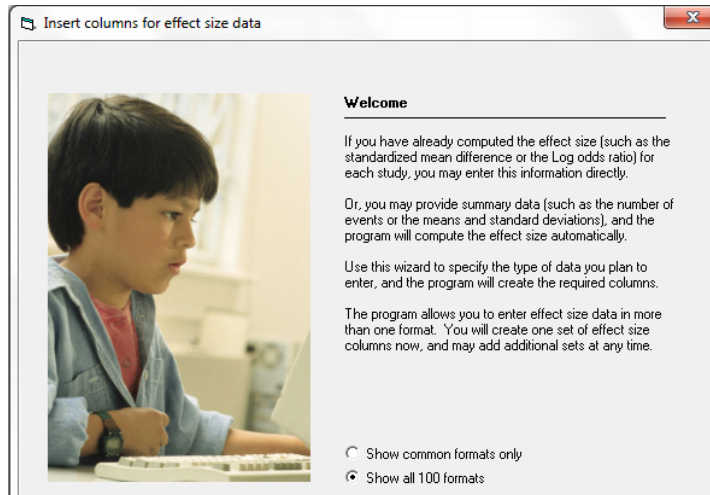


Click Insert > Column for > Effect size data

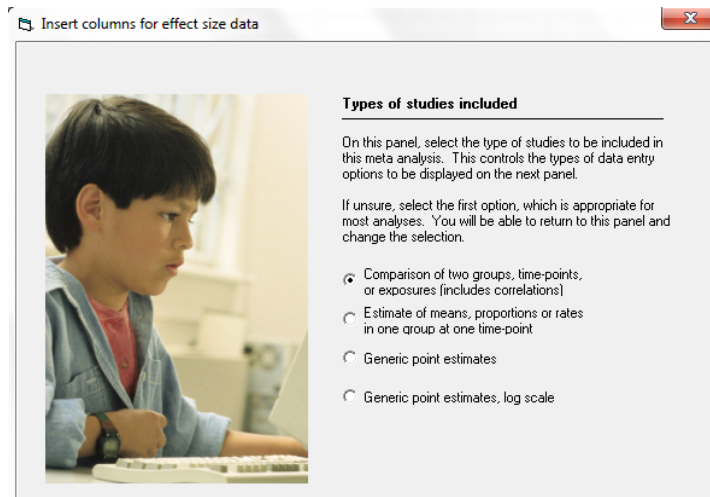


The program displays this wizard

Select [Show all 100 formats]  
Click [Next]

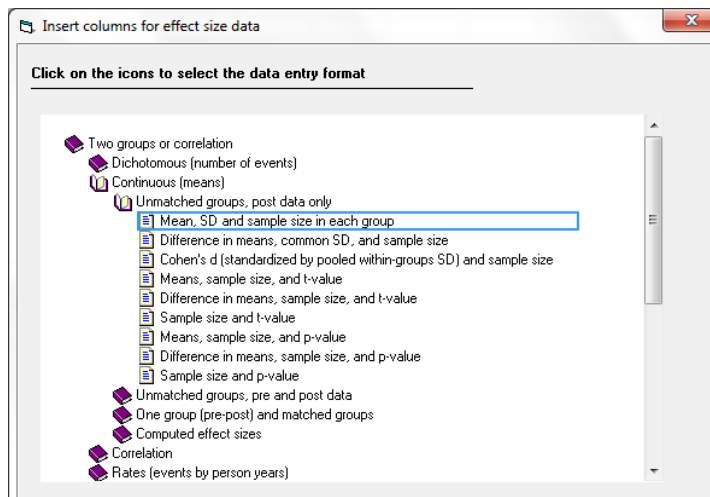


Select [Comparison of two groups...]  
Click [Next]



Drill down to

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

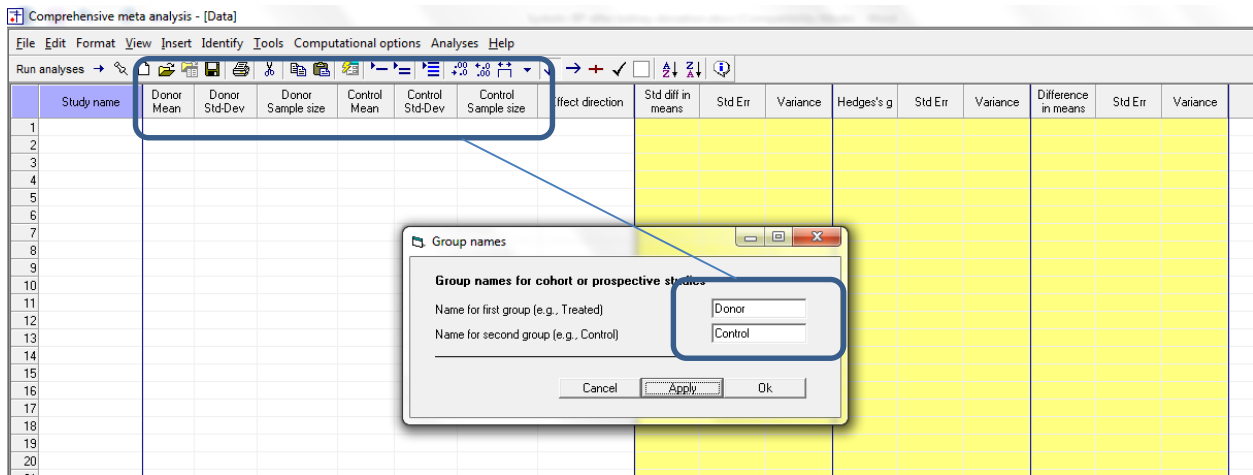


The program displays this wizard

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

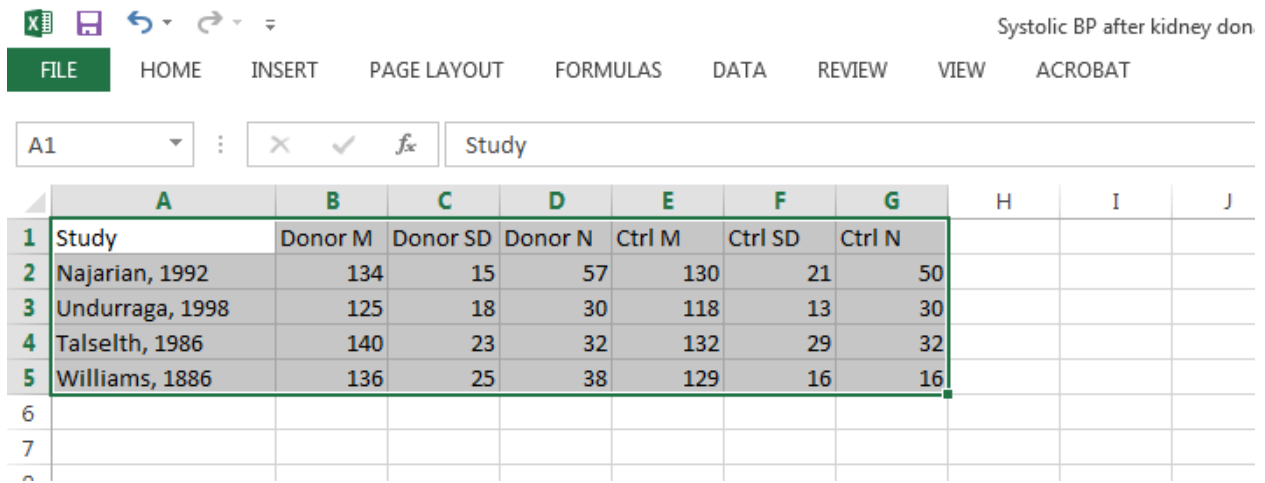


There are three options at this point

- 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



Systolic BP after kidney don

	A	B	C	D	E	F	G	H	I	J
1	Study	Donor M	Donor SD	Donor N	Ctrl M	Ctrl SD	Ctrl N			
2	Najarian, 1992	134	15	57	130	21	50			
3	Undurraga, 1998	125	18	30	118	13	30			
4	Talselth, 1986	140	23	32	132	29	32			
5	Williams, 1886	136	25	38	129	16	16			
6										
7										
8										

- Switch to CMA
- Click in cell Study-name 1
- Press [CTRL-V] to paste the data
- The screen should look like this

Click here

Comprehensive meta analysis - [Data]

File Edit Format View Insert Identify Tools Computational options Analyses Help

Run analyses →

	Study name	Donor Mean	Donor Std-Dev	Donor Sample size	Control Mean	Control Std-Dev	Control Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges
1	Study	Donor M	Donor SD	Donor N	Ctrl M	Ctrl SD	Ctrl N					
2	Najarian, 1992	134.000	15.000	57	130.000	21.000	50					
3	Undurraga, 1998	125.000	18.000	30	118.000	13.000	30					
4	Talselth, 1986	140.000	23.000	32	132.000	29.000	32					
5	Williams, 1986	136.000	25.000	38	129.000	16.000	16					
6												
7												

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

Click here

Comprehensive meta analysis - [Data]

File Edit Format View Insert Identify Tools Computational options Analyses Help

Run: Bookmark data

Restore data

Column properties

	Donor Std-Dev	Donor Sample size	Control Mean	Control Std-Dev	Control Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges's g	Std Err
1	or SD	Donor N	Ctrl M	Ctrl SD	Ctrl N						
2	15.000	57	130.000	21.000	50						
3	18.000	30	118.000	13.000	30						
4	23.000	32	132.000	29.000	32						
5	25.000	38	129.000	16.000	16						
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17											

We need to enter a value for “Effect Direction”

Enter “Auto” for each study

Click here

Study name	Donor Mean	Donor Std-Dev	Donor Sample size	Control Mean	Control Std-Dev	Control Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance
1 Najarian, 1992	134.000	15.000	57	130.000	21.000	50	Auto	0.222	0.194	0.038	0.220	0.193	0.037	4.000	3.497	12.232
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

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

Study name	Donor Mean	Donor Std-Dev	Donor Sample size	Control Mean	Control Std-Dev	Control Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance
1 Najarian, 1992	134.000	15.000	57	130.000	21.000	50	Auto	0.222	0.194	0.038	0.220	0.193	0.037	4.0		
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	7.0		
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	8.0		
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	7.0		

- 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”

The screenshot shows the 'Comprehensive meta analysis - [Data]' window. The main data table is as follows:

Study name	Donor Mean	Donor Std-Dev	Donor Sample size	Control Mean	Control Std-Dev	Control Sample size	Effect direction	Difference in means	Std Err	Variance
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

An 'Effect size indices' dialog box is open on the right. It has a dropdown menu set to 'Difference in means'. Under 'Display columns for these indices', the following options are listed with checkboxes:

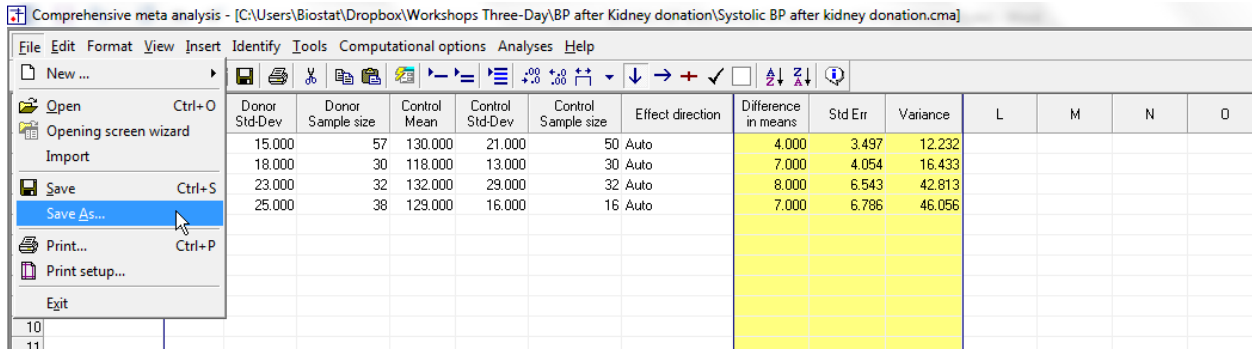
- Odds ratio
- Log odds ratio
- Peto odds ratio
- Log Peto odds ratio
- Risk ratio
- Log risk ratio
- Risk difference
- Std diff in means
- Hedges's g
- Difference in means
- Std Paired Difference
- Correlation
- Fisher's Z
- Rate ratio
- Log rate ratio
- Rate difference
- Hazard ratio

At the bottom of the dialog, there are three radio buttons: 'Also show standard error' (checked), 'Also show variance' (checked), and 'Show the primary index only' (unchecked). The 'Show all selected indices' radio button is selected. 'Ok' and 'Cancel' buttons are at the bottom right.

The screen should look like this

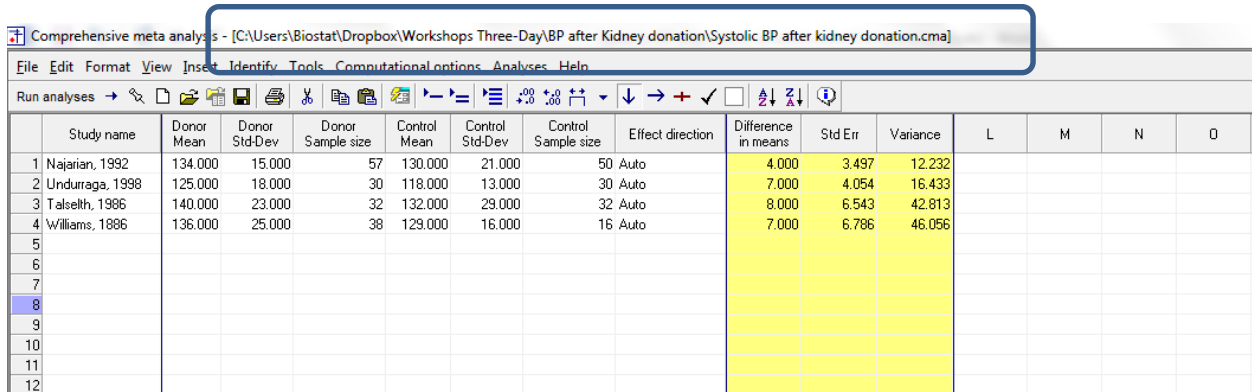
The screenshot shows the 'Comprehensive meta analysis - [Data]' window with the same data table as above. The 'Effect size indices' dialog box is no longer visible. The 'Difference in means' column is highlighted in yellow, and the 'Std Err' and 'Variance' columns are also highlighted in yellow. The 'Effect direction' column is highlighted in blue. The 'L', 'M', 'N', and 'O' columns are visible to the right of the data table.

Click File > Save As and save the file



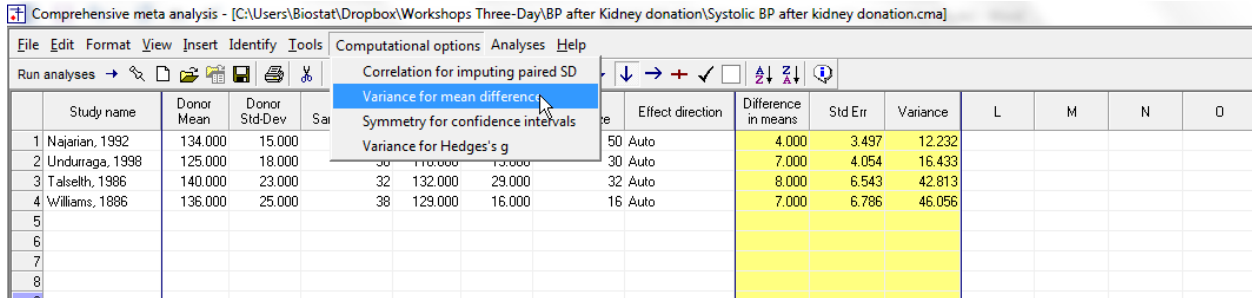
Note that the file name is now in the header.

- [Save] will over-write the prior version of this file without warning
- [Save As...] will allow you to save the file with a new name

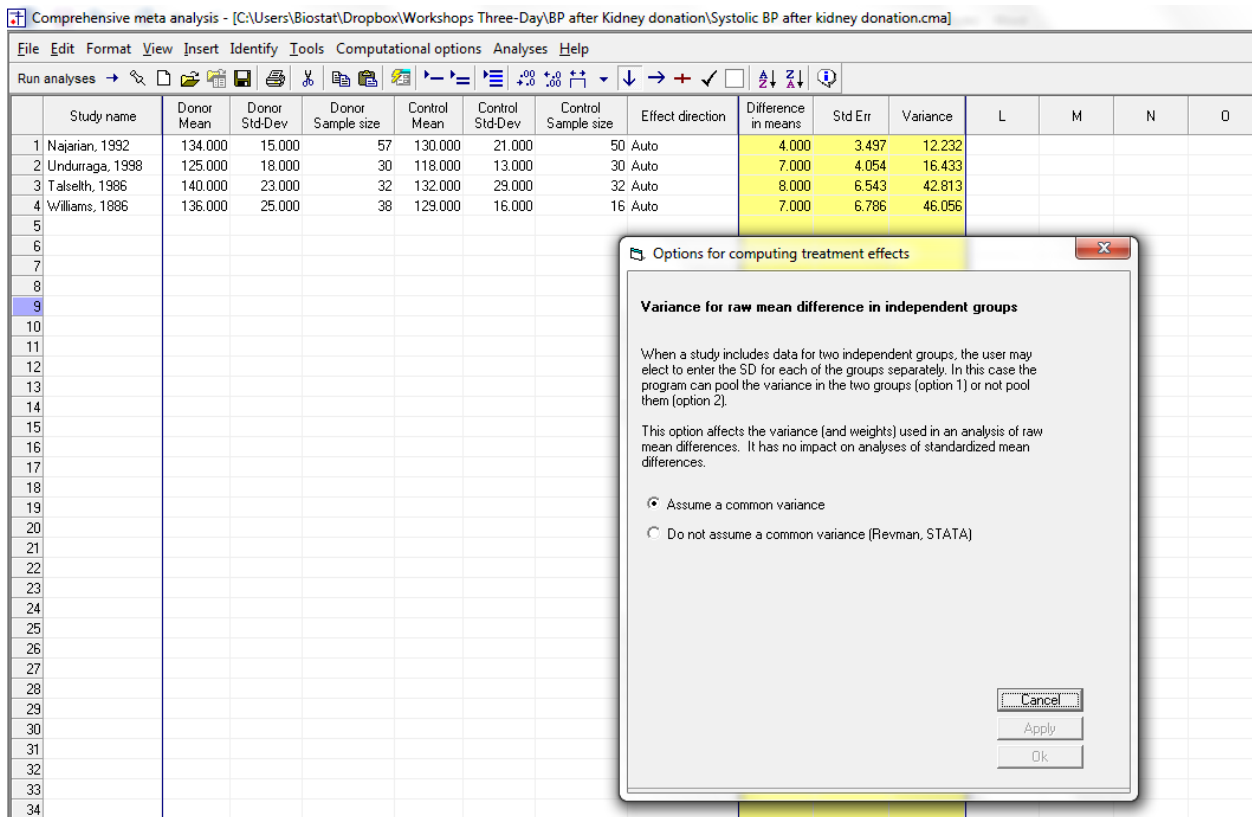


There are two options for computing the variance of the mean difference. We can pool the estimates from the two groups, or keep them separate. We will pool them.

Click Computational options > Variance for mean difference



- Check the option “Assume a common variance”
- Click Ok



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 (Najarian). 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.

	Study name	Donor Mean	Donor Std-Dev	Donor Sample size	Control Mean	Control Std-Dev	Control Sample size	Effect direction	Difference in means	Std Err	Variance	L	M	N	O
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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7															
8															
9															
10															
11															
12															

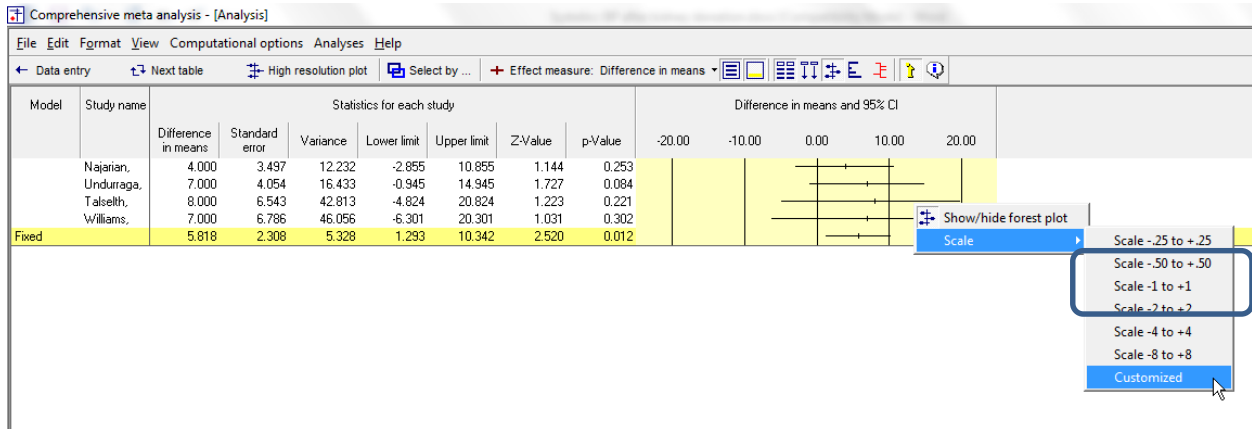
- To run the analysis, click [Run analysis]

	Study name	Donor Mean	Donor Std-Dev	Donor Sample size	Control Mean	Control Std-Dev	Control Sample size	Effect direction	Difference in means	Std Err	Variance	L	M	N	O
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				
5															
6															
7															
8															
9															
10															
11															
12															

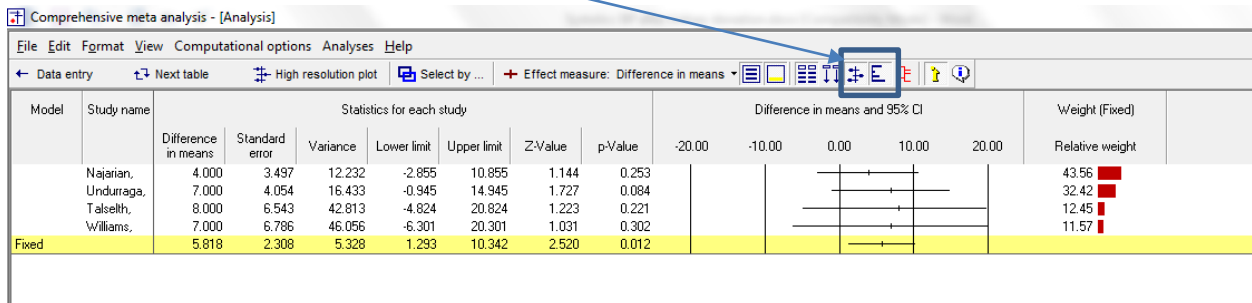
This is the basic analysis screen

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



Click the tool to show weights



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.

Click [Both models]

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

Model	Study name	Statistics for each study						Difference in means and 95% CI					Weight (Fixed)		Weight (Random)		
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	-20.00	-10.00	0.00	10.00	20.00	Relative weight	Relative weight	Relative weight	Relative weight
	Najarian,	4.000	3.497	12.232	-2.855	10.855	1.144	0.253						43.56	43.56	43.56	43.56
	Undurraga,	7.000	4.054	16.433	-0.945	14.945	1.727	0.084						32.42	32.42	32.42	32.42
	Talselht,	8.000	6.543	42.813	-4.824	20.824	1.223	0.221						12.45	12.45	12.45	12.45
	Williams,	7.000	6.786	46.056	-6.301	20.301	1.031	0.302						11.57	11.57	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.

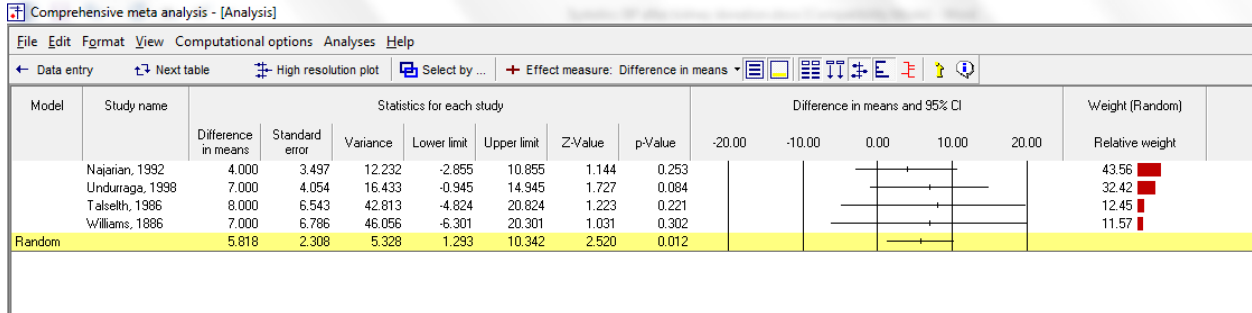
This tells us that the any between-study variance in the observed effects is within the range we would expect based on sampling error. Our estimate of the between-study variance in true effects is zero. Therefore, the fixed-effect weights and random-effects weights are identical.

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.



A quick view of the plot suggests the following

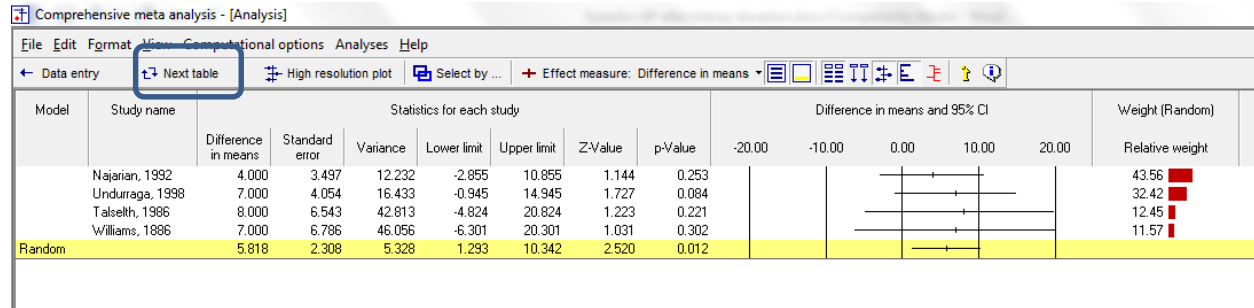
- The BP was always higher in the donor group than the control
- The observed effects are pretty consistent, in that the confidence intervals for all studies but one overlap the mean effect size.
- The summary effect is 5.818 with a CI of 1.293 to 10.342.
- The summary effect has a Z-value 2.520 a  $p$ -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 mean 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

- The mean BP is consistently about 6 points higher in the donor group
- 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



The program displays this screen

Model	Effect size and 95% confidence interval						Test of null (2-Tail)		Heterogeneity			Tau-squared				
	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
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 labeled “Test of null” address the mean 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.



$I^2$  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,  $I^2$  is a proportion – it tells us what proportion of the observed variance is real (if our estimates are correct) but does not tell us how much variance there is. However, if  $I^2$  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 deviation in true effect sizes.

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

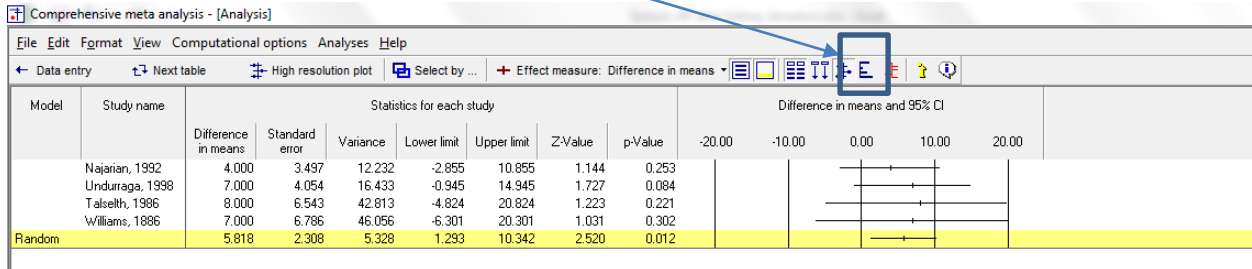
If the mean effect size is 5.818, if the standard deviation of true effects is 0, then the true effect size for all studies is 5.818.

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.

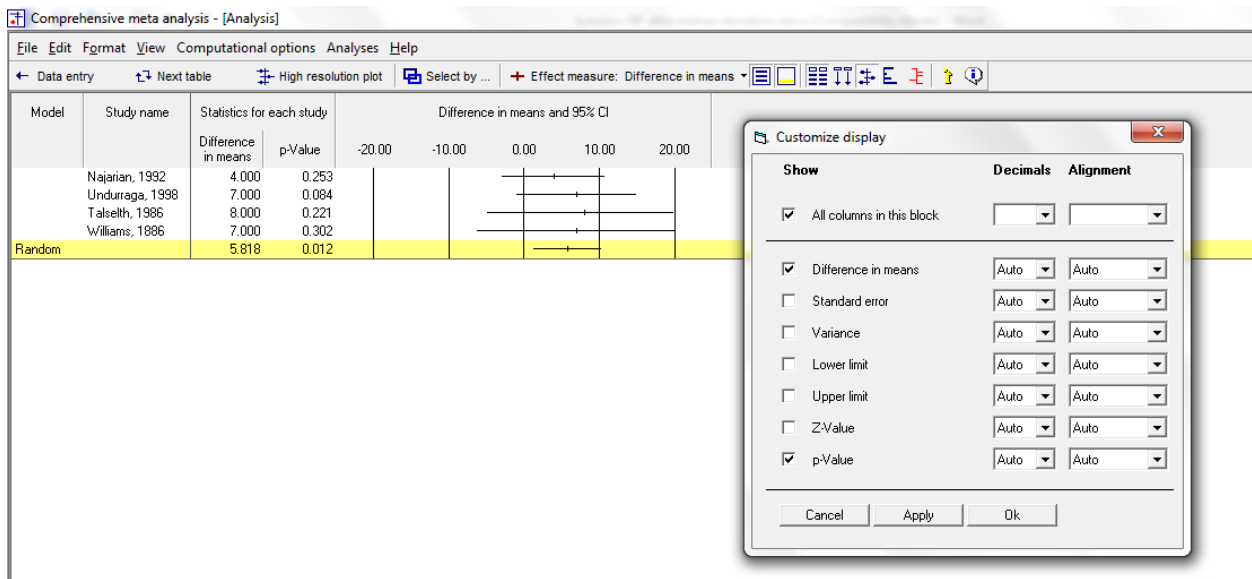
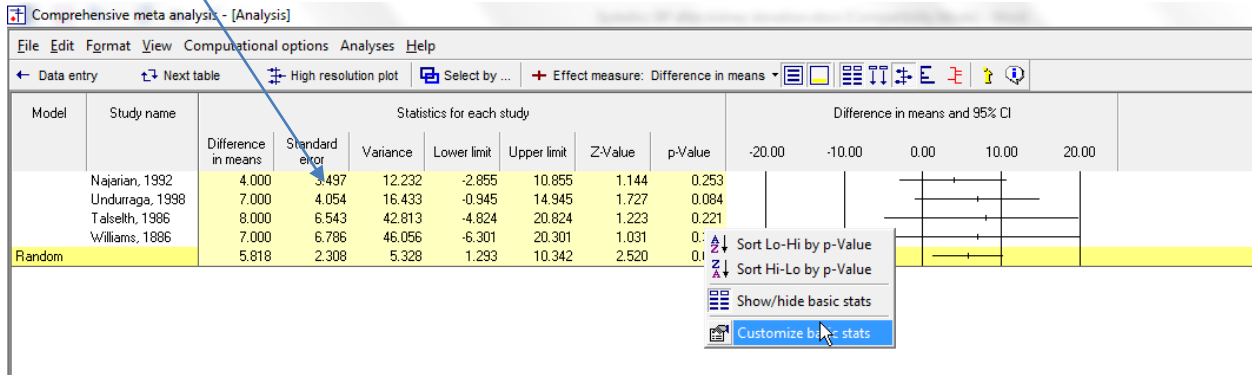
Click Next table

We want to create a high-resolution plot

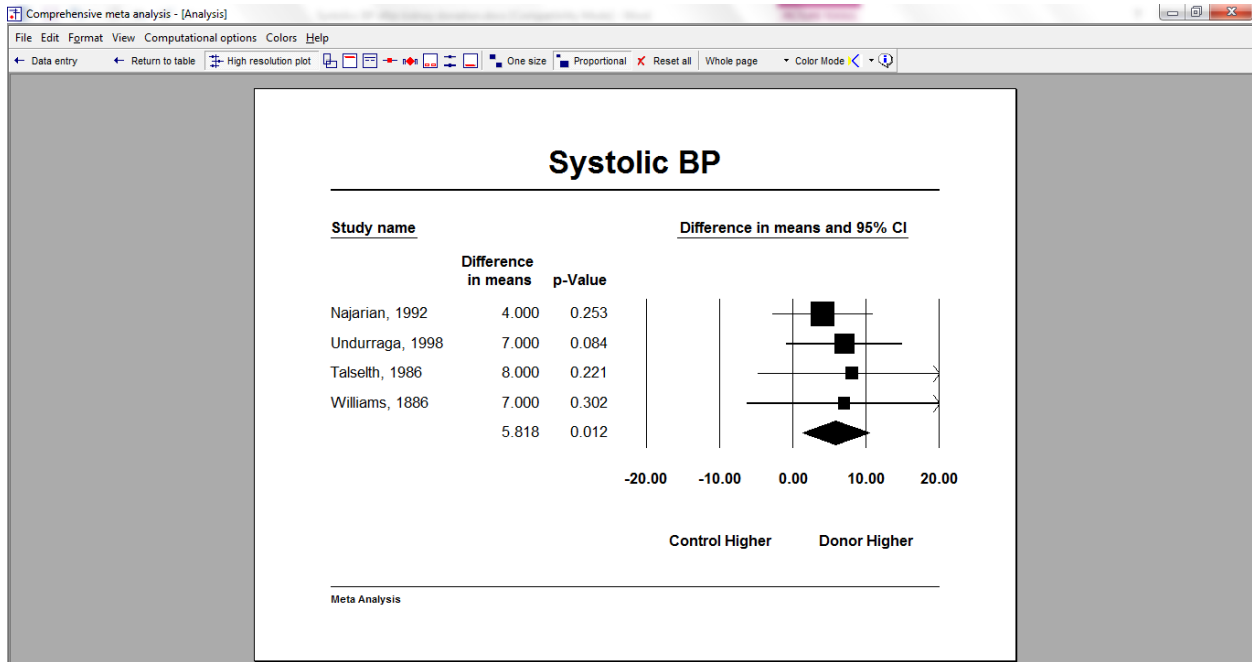
Click here to hide the column of weights



Right-click here and hide some of the statistics columns



- 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 mean 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  $I^2$  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.

