

Example name	Tamiflu Symptom relief
Effect size	Mean difference (Hours to relief)
Analysis type	Basic
Level	Basic
Reference	Cochrane Figure 4

Synopsis

We have a series of studies that evaluated the effect of Tamiflu on duration of flu symptoms. Each study compared Tamiflu vs. Placebo and reported the mean difference in time to relief. If the Drug yielded a shorter time to relief, the mean difference will be negative.

Since all studies used the same outcome (hours to relief) we can use either Raw Mean Difference or Standardized mean difference as the outcome. We do both, to show where they are similar and where they differ.

We show

- How to enter data for means and standard deviation in two independent groups
- How to run a fixed-effect and a random-effects analysis
- How to get a visual sense of the dispersion
- How to see the weight assigned to each study
- How to understand the statistics for the summary effect and the dispersion
- The correspondence between the raw mean difference and the standardized mean difference
- How to create a high-resolution plot

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](#)

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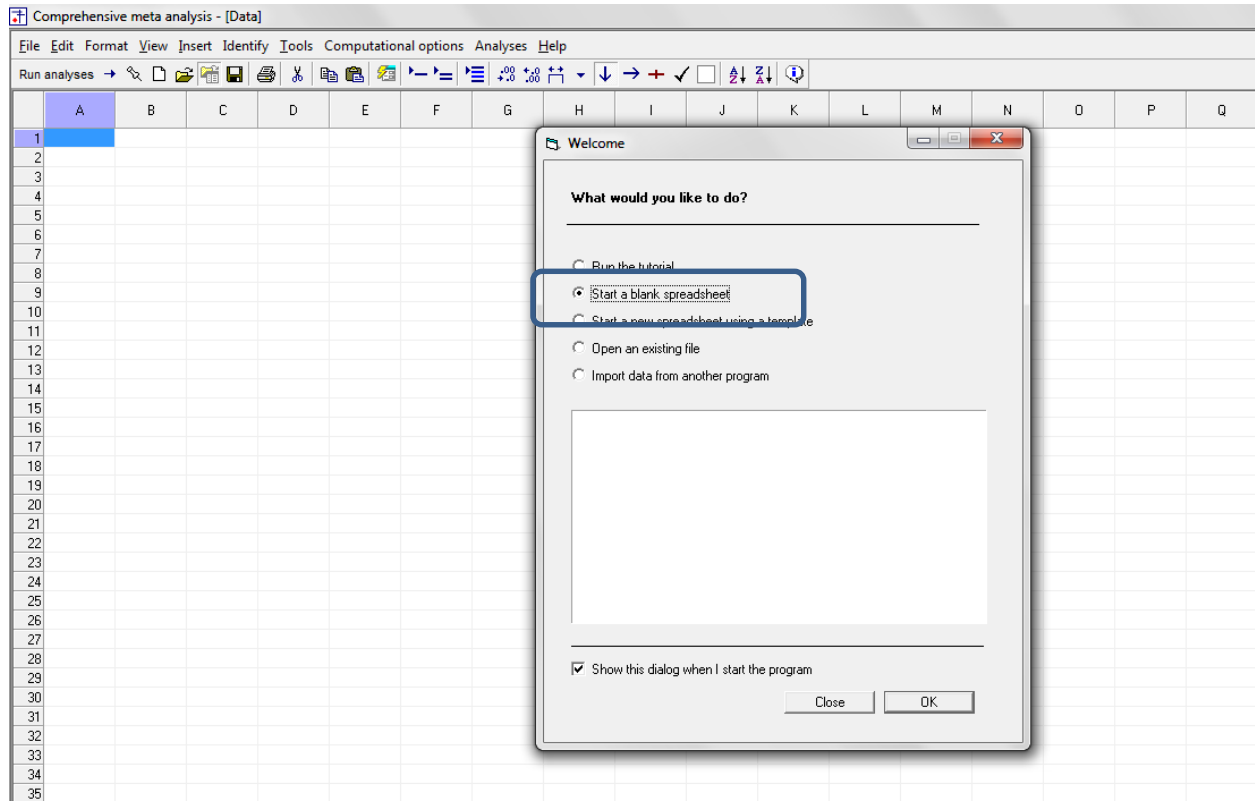
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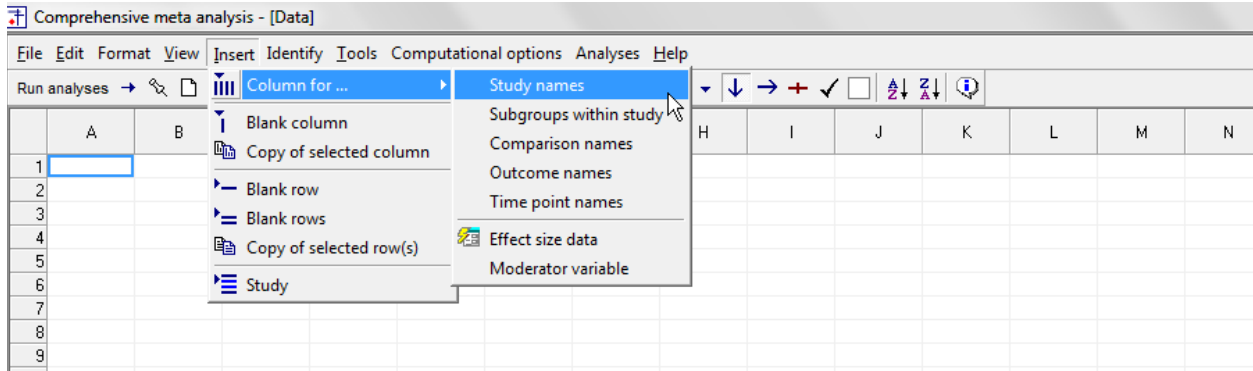
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Start the program

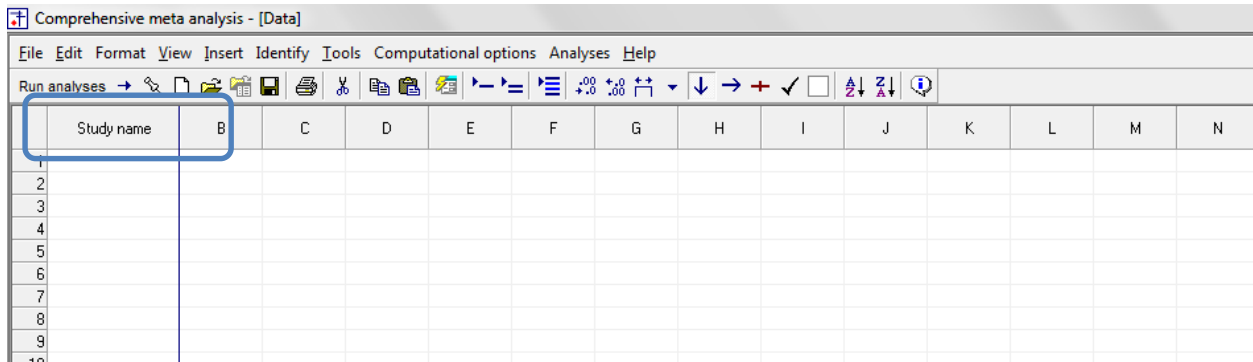
- Select the option [Start a blank spreadsheet]
- Click [OK]



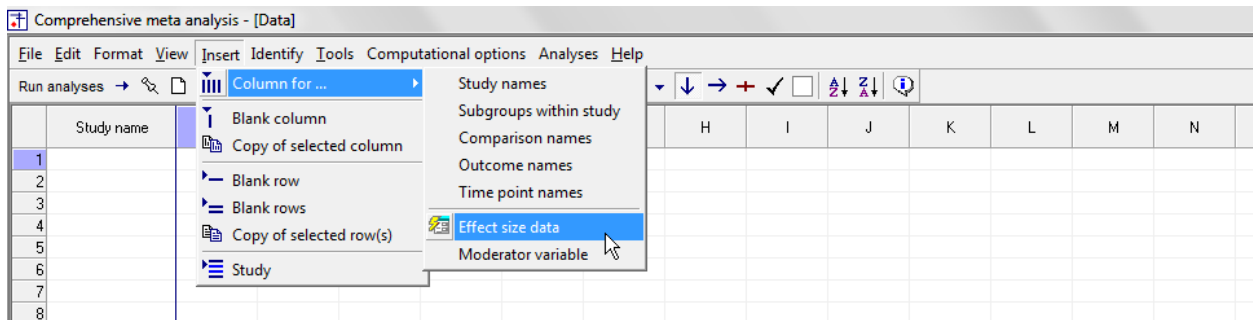
Click Insert > Column for > Study names



The screen should look like this

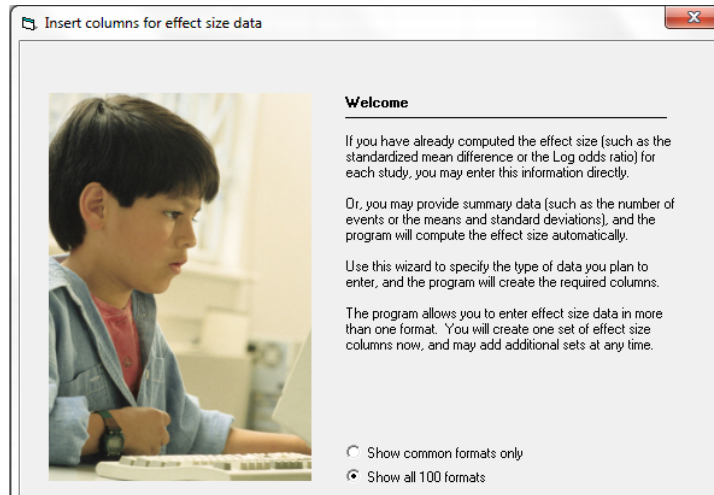


Click Insert > Column for > Effect size data

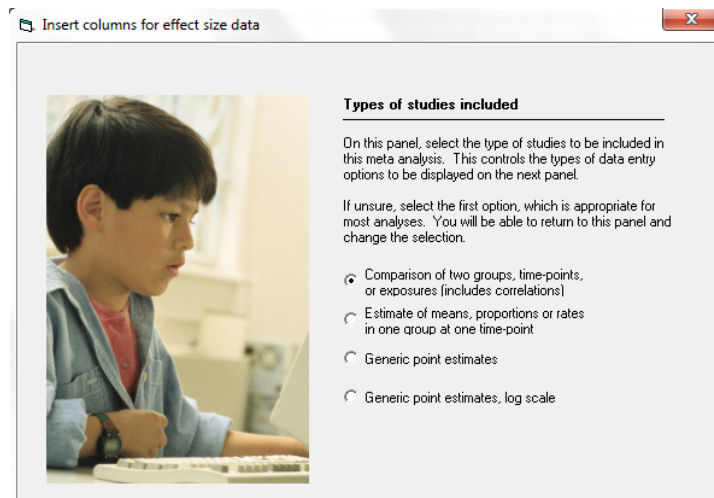


The program displays this wizard

Select [Show all 100 formats]
Click [Next]

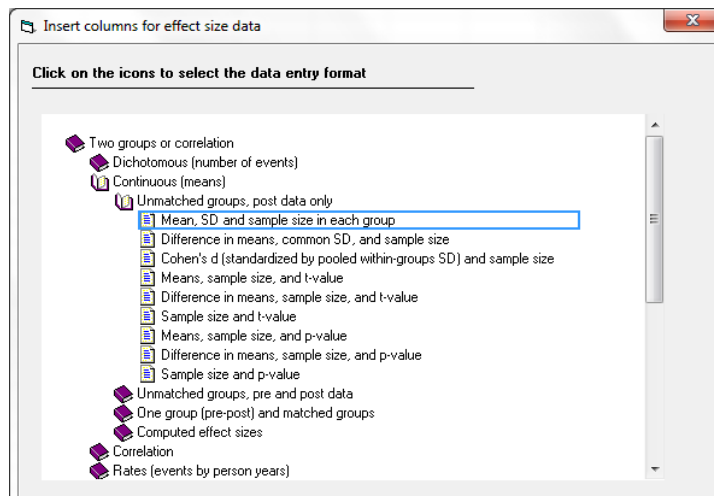


Select [Comparison of two groups...]
Click [Next]



Drill down to

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

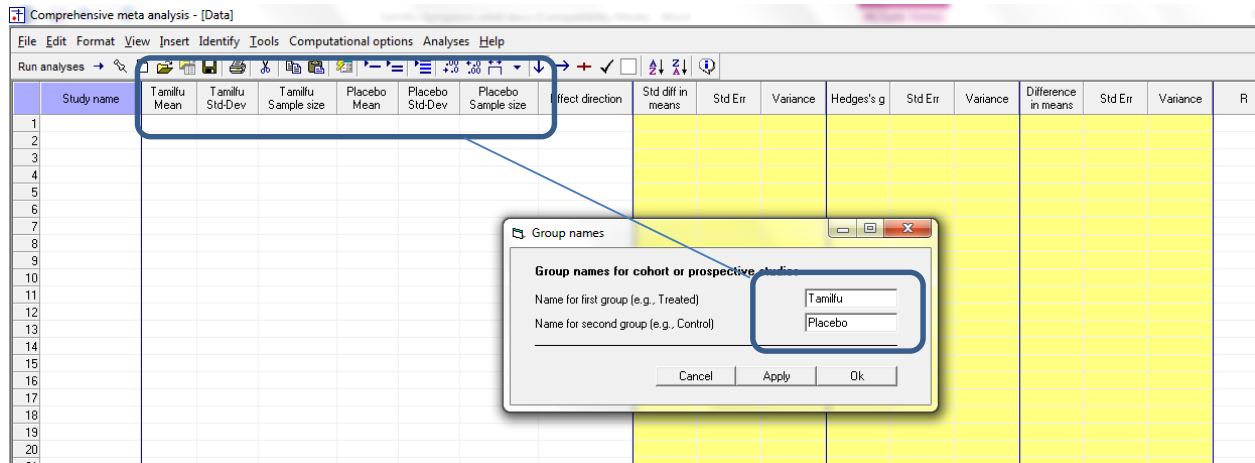


The program displays this wizard

Enter the following labels into the wizard

- First group > Tamiflu
- Second group > Placebo

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 “Tamiflu Symptom Relief.cma”
- – or – Copy the data from Excel “Tamiflu Symptom Relief.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

Tamiflu Symptom relief.xlsx - Excel

FILE HOME INSERT PAGE LAYOUT FORMULAS DATA REVIEW VIEW ACROBAT

A1 : X ✓ fx Study

	A	B	C	D	E	F	G	H	I
1	Study	Tx Mean	Tx SD	Tx N	Pbo Mean	Pbo SD	Pbo N		
2	M76001	140.6	125.2	933	165.5	156.5	473		
3	WV15670	129	114.6	240	144.5	118	235		
4	WV15671	102.4	89.9	204	125.3	98.9	200		
5	WV15707	154	166.5	17	93.6	134.4	9		
6	WV15730	107.6	104.6	31	171	177.1	27		
7	WV15812/872	193.7	152.3	199	203.9	146.3	202		
8	WV15819/876/978	185	145.6	358	192.4	145.2	375		
9	WV16277	138.7	138.4	226	143.7	125.4	225		
10									
11									

Sheet1

READY AVERA

- 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 → [Icons]

Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges's g
1 Study	Tx Mean	Tx SD	Tx N	Pbo Mean	Pbo SD	Pbo N					
2 M76001	140.600	125.200	933	165.500	156.500	473					
3 WV15670	129.000	114.600	240	144.500	118.000	235					
4 WV15671	102.400	89.900	204	125.300	98.900	200					
5 WV15707	154.000	166.500	17	93.600	134.400	9					
6 WV15730	107.600	104.600	31	171.000	177.100	27					
7 WV15812/872	193.700	152.300	199	203.900	146.300	202					
8 WV15819/876/978	185.000	145.600	358	192.400	145.200	375					
9 WV16277	138.700	138.400	226	143.700	125.400	225					
10											
11											

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: [Icons]

	Tamiflu d-Dev	Tamiflu Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges's g
1	SD	Tx N	Pbo Mean	Pbo SD	Pbo N					
2	125.200	933	165.500	156.500	473					
3	114.600	240	144.500	118.000	235					
4	89.900	204	125.300	98.900	200					
5	166.500	17	93.600	134.400	9					
6	104.600	31	171.000	177.100	27					
7	152.300	199	203.900	146.300	202					
8	145.600	358	192.400	145.200	375					
9	138.400	226	143.700	125.400	225					
10										
11										
12										
13										
14										
15										
16										

We need to enter a value for “Effect Direction”

Enter “Auto” for each study

Click here

Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance
1 M76001	140.600	125.200	933	165.500	156.500	473	Auto	-0.182	0.057	0.003	-0.182	0.057	0.003	-24.900	7.706	59.384
2 wV15670	129.000	114.600	240	144.500	118.000	235	Auto	-0.133	0.092	0.008	-0.133	0.092	0.008	-15.500	10.673	113.902
3 wV15671	102.400	89.900	204	125.300	98.900	200	Auto	-0.242	0.100	0.010	-0.242	0.100	0.010	-22.900	9.400	88.357
4 wV15707	154.000	166.500	17	93.600	134.400	9	Auto	0.366	0.416	0.173	0.374	0.403	0.162	60.400	64.528	4163.844
5 wV15730	107.600	104.600	31	171.000	177.100	27	Auto	-0.444	0.266	0.071	-0.438	0.263	0.069	-63.400	37.620	1415.240
6 wV15812/872	193.700	152.300	199	203.900	146.300	202	Auto	-0.068	0.100	0.010	-0.068	0.100	0.010	-10.200	14.913	222.384
7 wV15819/876/978	185.000	145.600	358	192.400	145.200	375	Auto	-0.051	0.074	0.005	-0.051	0.074	0.005	-7.400	10.743	115.423
8 wV16277	138.700	138.400	226	143.700	125.400	225	Auto	-0.038	0.094	0.009	-0.038	0.094	0.009	-5.000	12.438	154.712

The program displays three effect sizes – *d*, *g*, and raw mean difference

- We want to hide the index *d*
- We want to set the raw mean difference as the primary index

Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges's g	Std Err	Variance
1 M76001	140.600	125.200	933	165.500	156.500	473	Auto	-0.182	0.057	0.003	-0.182	0.057	0.003
2 wV15670	129.000	114.600	240	144.500	118.000	235	Auto	-0.133	0.092	0.008	-0.133	0.092	0.008
3 wV15671	102.400	89.900	204	125.300	98.900	200	Auto	-0.242	0.100	0.010	-0.242	0.100	0.010
4 wV15707	154.000	166.500	17	93.600	134.400	9	Auto	0.366	0.416	0.173	0.374	0.403	0.162
5 wV15730	107.600	104.600	31	171.000	177.100	27	Auto	-0.444	0.266	0.071	-0.438	0.263	0.069
6 wV15812/872	193.700	152.300	199	203.900	146.300	202	Auto	-0.068	0.100	0.010	-0.068	0.100	0.010
7 wV15819/876/978	185.000	145.600	358	192.400	145.200	375	Auto	-0.051	0.074	0.005	-0.051	0.074	0.005
8 wV16277	138.700	138.400	226	143.700	125.400	225	Auto	-0.038	0.094	0.009	-0.038	0.094	0.009

- 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”
- Click [OK]

Effect size indices

Use the following as the primary index

Difference in means

Display columns for these indices

- 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

Also show standard error

Also show variance

Show the primary index only

Show all selected indices

Ok
Cancel

The screen should look like this

Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance
1 M76001	140.600	125.200	933	165.500	156.500	473	Auto	-0.182	0.057	0.003	-24.900	7.706	59.384
2 wV15670	129.000	114.600	240	144.500	118.000	235	Auto	-0.133	0.092	0.008	-19.300	10.673	113.502
3 wV15671	102.400	89.900	204	125.300	98.900	200	Auto	-0.242	0.100	0.010	-22.900	9.400	88.357
4 wV15707	154.000	166.500	17	93.600	134.400	9	Auto	0.374	0.403	0.162	60.400	64.528	4163.844
5 wV15730	107.600	104.600	31	171.000	177.100	27	Auto	-0.438	0.263	0.069	-63.400	37.620	1415.240
6 wV15812/872	193.700	152.300	199	203.900	146.300	202	Auto	-0.068	0.100	0.010	-10.200	14.913	222.384
7 wV15819/876/978	185.000	145.600	358	192.400	145.200	375	Auto	-0.051	0.074	0.005	-7.400	10.743	115.423
8 wV16277	138.700	138.400	226	143.700	125.400	225	Auto	-0.038	0.094	0.009	-5.000	12.438	154.712

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. The authors of this analysis chose to keep them separate, and so we will use that option as well.

Click Computational options < Variance for mean difference

Comprehensive meta analysis - [Data]

File Edit Format View Insert Identify Tools Computational options Analyses Help

Run analyses → [Icons]

Correlation for imputing paired SD
Variance for mean difference
 Symmetry for confidence intervals
 Variance for Hedges's g

	Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance
1	M76001	140.600	125.200	933	165.500	156.500	473	Auto	-0.182	0.057	0.003	-24.900	7.706	59.384
2	WV15670	129.000	114.600	240	144.500	118.000	235	Auto	-0.133	0.092	0.008	-15.500	10.673	113.902
3	WV15671	102.400	89.900	204	125.300	98.900	200	Auto	-0.242	0.100	0.010	-22.900	9.400	88.357
4	WV15707	154.000	166.500	17	93.600	134.400	9	Auto	0.374	0.403	0.162	60.400	64.528	4163.844
5	WV15730	107.600	104.600	31	171.000	177.100	27	Auto	-0.438	0.263	0.069	-63.400	37.620	1415.240
6	WV15812/872	193.700	152.300	199	203.900	146.300	202	Auto	-0.068	0.100	0.010	-10.200	14.913	222.384
7	WV15819/876/978	185.000	145.600	358	192.400	145.200	375	Auto	-0.051	0.074	0.005	-7.400	10.743	115.423
8	WV16277	138.700	138.400	226	143.700	125.400	225	Auto	-0.038	0.094	0.009	-5.000	12.438	154.712

- Check the option “Do not assume a common variance”
- Click Ok

Comprehensive meta analysis - [Data]

File Edit Format View Insert Identify Tools Computational options Analyses Help

Run analyses → [Icons]

	Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance	0
1	M76001	140.600	125.200	933	165.500	156.500	473	Auto	-0.182	0.057	0.003	-24.900	7.706	59.384	
2	WV15670	129.000	114.600	240	144.500	118.000	235	Auto	-0.133	0.092	0.008	-15.500	10.673	113.902	
3	WV15671	102.400	89.900	204	125.300	98.900	200	Auto	-0.242	0.100	0.010	-22.900	9.400	88.357	
4	WV15707	154.000	166.500	17	93.600	134.400	9	Auto	0.374	0.403	0.162	60.400	64.528	4163.844	
5	WV15730	107.600	104.600	31	171.000	177.100	27	Auto	-0.438	0.263	0.069	-63.400	37.620	1415.240	
6	WV15812/872	193.700	152.300	199	203.900	146.300	202	Auto	-0.068	0.100	0.010	-10.200	14.913	222.384	
7	WV15819/876/978	185.000	145.600	358	192.400	145.200	375	Auto	-0.051	0.074	0.005	-7.400	10.743	115.423	
8	WV16277	138.700	138.400	226	143.700	125.400	225	Auto	-0.038	0.094	0.009	-5.000	12.438	154.712	

Options for computing treatment effects

Variance for raw mean difference in independent groups

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).

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.

Assume a common variance

Do not assume a common variance (Revman, STATA)

Cancel Apply Ok

Click File > Save As and save the file

The screenshot shows the 'File' menu of the 'Comprehensive meta analysis' software. The 'Save As...' option is highlighted in blue. The background shows a data table with columns for Tamiflu and Placbo means, sample sizes, Hedges's g, and variance.

Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance
125.200	933	165.500	156.500	473	Auto	-0.182	0.057	0.003	-24.900	8.281	68.581
114.600	240	144.500	118.000	235	Auto	-0.133	0.092	0.008	-15.500	10.676	113.973
89.900	204	125.300	98.900	200	Auto	-0.242	0.100	0.010	-22.900	9.409	88.524
166.500	17	93.600	134.400	9	Auto	0.374	0.403	0.162	60.400	60.314	3637.761
104.600	31	171.000	177.100	27	Auto	-0.438	0.263	0.069	-63.400	38.918	1514.585
152.300	199	203.900	146.300	202	Auto	-0.068	0.100	0.010	-10.200	14.917	222.518
145.600	358	192.400	145.200	375	Auto	-0.051	0.074	0.005	-7.400	10.744	115.438
138.400	226	143.700	125.400	225	Auto	-0.038	0.094	0.009	-5.000	12.436	154.644

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

The screenshot shows the title bar of the software window, which now contains the file name: 'Comprehensive meta analysis - [C:\Users\Biostat\Dropbox\Workshops Three-Day\Tamiflu\Tamiflu Symptom relief.cma]'. The background shows a data table with columns for Study name, Tamiflu and Placbo means, sample sizes, Hedges's g, and variance.

Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance
1 M76001	140.600	125.200	933	165.500	156.500	473	Auto	-0.182	0.057	0.003	-24.900	8.281	68.581
2 wV15670	129.000	114.600	240	144.500	118.000	235	Auto	-0.133	0.092	0.008	-15.500	10.676	113.973
3 wV15671	102.400	89.900	204	125.300	98.900	200	Auto	-0.242	0.100	0.010	-22.900	9.409	88.524
4 wV15707	154.000	166.500	17	93.600	134.400	9	Auto	0.374	0.403	0.162	60.400	60.314	3637.761
5 wV15730	107.600	104.600	31	171.000	177.100	27	Auto	-0.438	0.263	0.069	-63.400	38.918	1514.585
6 wV15812/872	193.700	152.300	199	203.900	146.300	202	Auto	-0.068	0.100	0.010	-10.200	14.917	222.518
7 wV15819/876/978	185.000	145.600	358	192.400	145.200	375	Auto	-0.051	0.074	0.005	-7.400	10.744	115.438
8 wV16277	138.700	138.400	226	143.700	125.400	225	Auto	-0.038	0.094	0.009	-5.000	12.436	154.644

By convention we've put the Treated group (Tamiflu) in the first columns and the control group in the next columns.

The program will compute the mean difference as Treated minus Control. Thus, a negative difference means that the treated group responded in less time.

(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. In this example, studies will have a negative sign if the treated group had a lower value (which means they responded more quickly).

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. The mean time to response was 140.6 hours for Tamiflu and 165.5 hours for Control. The Difference in means is negative (-24.900 hours) which means that the treated group responded more quickly.

Comprehensive meta analysis - [C:\Users\Biostat\Dropbox\Workshops Three-Day\Tamiflu\Tamiflu Symptom relief.cma]

File Edit Format View Insert Identify Tools Computational options Analyses Help

Run analyses → 🔍 📄 📁 📂 📅 📆 📇 📈 📉 📊 📋 📌 📍 📎 📏 📐 📑 📒 📓 📔 📕 📖 📗 📘 📙 📚 📛 📜 📝 📞 📟 📠 📡 📢 📣 📤 📥 📦 📧 📨 📩 📪 📫 📬 📭 📮 📯 📰 📱 📲 📳 📴 📵 📶 📷 📸 📹 📺 📻 📼 📽 📾 📿 📠 📡 📢 📣 📤 📥 📦 📧 📨 📩 📪 📫 📬 📭 📮 📯 📰 📱 📲 📳 📴 📵 📶 📷 📸 📹 📺 📻 📼 📽 📾 📿

	Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance	0
1	M76001	140.600	125.200	933	165.500	156.500	473	Auto	-0.182	0.057	0.003	-24.900	8.281	68.581	
2	WV15670	129.000	114.600	240	144.500	118.000	235	Auto	-0.133	0.092	0.008	-15.500	10.676	113.973	
3	WV15671	102.400	89.900	204	125.300	98.900	200	Auto	-0.242	0.100	0.010	-22.900	9.409	88.524	
4	WV15707	154.000	166.500	17	93.600	134.400	9	Auto	0.374	0.403	0.162	60.400	60.314	3637.761	
5	WV15730	107.600	104.600	31	171.000	177.100	27	Auto	-0.438	0.263	0.069	-63.400	38.918	1514.585	
6	WV15812/872	193.700	152.300	199	203.900	146.300	202	Auto	-0.068	0.100	0.010	-10.200	14.917	222.518	
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8	WV16277	138.700	138.400	226	143.700	125.400	225	Auto	-0.038	0.094	0.009	-5.000	12.436	154.644	
9															
10															

- To run the analysis, click [Run analysis]

Comprehensive meta analysis - [C:\Users\Biostat\Dropbox\Workshops Three-Day\Tamiflu\Tamiflu Symptom relief.cma]

File Edit Format View Insert Identify Tools Computational options Analyses Help

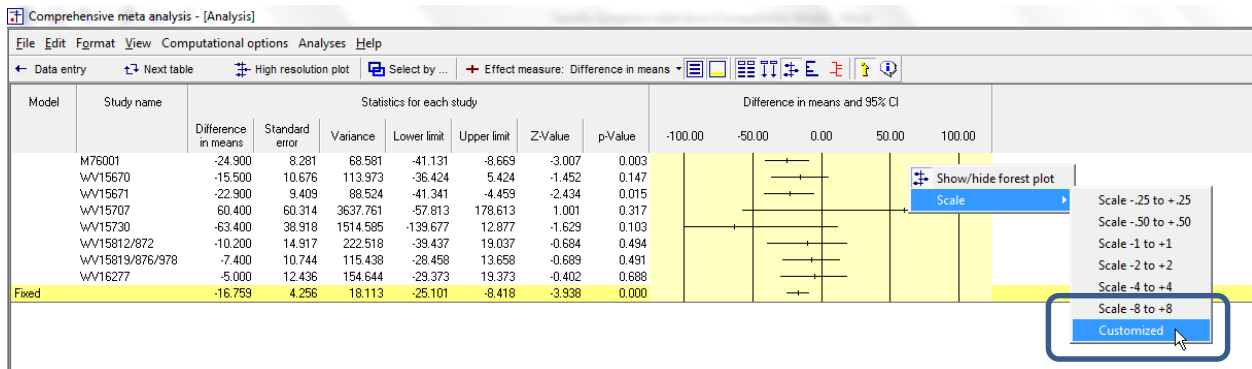
Run analyses → 🔍 📄 📁 📂 📅 📆 📇 📈 📉 📊 📋 📌 📍 📎 📏 📐 📑 📒 📓 📔 📕 📖 📗 📘 📙 📚 📛 📜 📝 📞 📟 📠 📡 📢 📣 📤 📥 📦 📧 📨 📩 📪 📫 📬 📭 📮 📯 📰 📱 📲 📳 📴 📵 📶 📷 📸 📹 📺 📻 📼 📽 📾 📿

	Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance	0
1	M76001	140.600	125.200	933	165.500	156.500	473	Auto	-0.182	0.057	0.003	-24.900	8.281	68.581	
2	WV15670	129.000	114.600	240	144.500	118.000	235	Auto	-0.133	0.092	0.008	-15.500	10.676	113.973	
3	WV15671	102.400	89.900	204	125.300	98.900	200	Auto	-0.242	0.100	0.010	-22.900	9.409	88.524	
4	WV15707	154.000	166.500	17	93.600	134.400	9	Auto	0.374	0.403	0.162	60.400	60.314	3637.761	
5	WV15730	107.600	104.600	31	171.000	177.100	27	Auto	-0.438	0.263	0.069	-63.400	38.918	1514.585	
6	WV15812/872	193.700	152.300	199	203.900	146.300	202	Auto	-0.068	0.100	0.010	-10.200	14.917	222.518	
7	WV15819/876/978	185.000	145.600	358	192.400	145.200	375	Auto	-0.051	0.074	0.005	-7.400	10.744	115.438	
8	WV16277	138.700	138.400	226	143.700	125.400	225	Auto	-0.038	0.094	0.009	-5.000	12.436	154.644	
9															
10															

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 100



Most studies have mean differences less than 0.0, which means that the Tamiflu group had symptom relief sooner than the control group.

There seems to be some variation in the observed effect sizes. However, the effect sizes (in particular the ones for the two extreme studies) are wide. The confidence interval for all studies overlaps the mean effect size.

The pooled effect is -16.759, which means that the mean Tamiflu group reported symptom relief about 17 hours sooner than the placebo group.

- Click [Both models]
- Click the tool to display weights

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	-100.00	-50.00	0.00	50.00	100.00	Relative weight	Relative weight
	M76001	-24.900	8.281	68.581	-41.131	-8.669	-3.007	0.003						26.41	26.41
	WV15670	-15.500	10.676	113.973	-36.424	5.424	-1.452	0.147						15.89	15.89
	WV15671	-22.900	9.409	88.524	-41.341	-4.459	-2.434	0.015						20.46	20.46
	WV15707	60.400	60.314	3637.761	-57.813	178.613	1.001	0.317						0.50	0.50
	WV15730	-63.400	38.918	1514.585	-139.677	12.877	-1.629	0.103						1.20	1.20
	WV15812/872	-10.200	14.917	222.518	-39.437	19.037	-0.684	0.494						8.14	8.14
	WV15812/876/978	-7.400	10.744	115.438	-28.458	13.658	-0.689	0.491						15.69	15.69
	WV16277	-5.000	12.436	154.644	-29.373	19.373	-0.402	0.688						11.71	11.71
Fixed		-16.759	4.256	18.113	-25.101	-8.418	-3.938	0.000							
Random		-16.759	4.256	18.113	-25.101	-8.418	-3.938	0.000							

Under the fixed-effect model the pooled mean difference is -16.759 with a confidence interval of -25.101 to -8.418 . Under the random-effects model these values are the same.

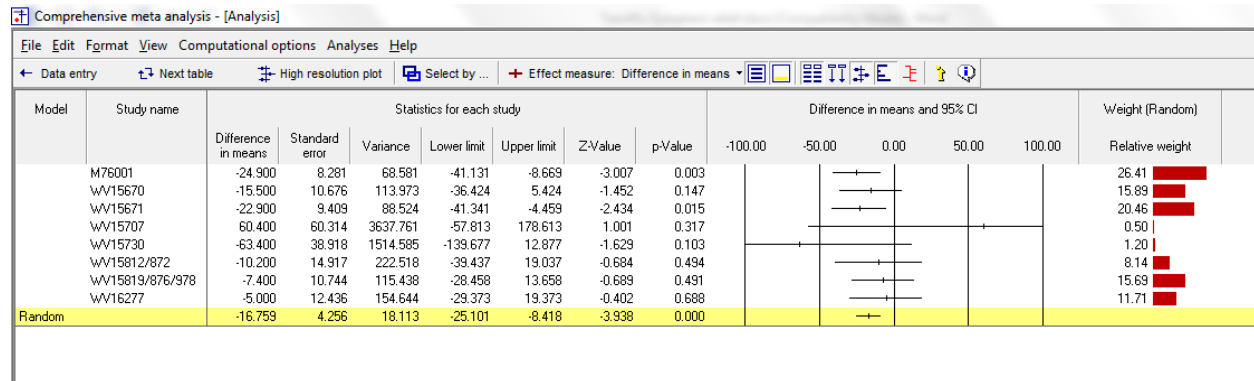
The fact that these values are identical under both models tells us that the weights assigned to each study must be identical under the two models, and (it follows) the between-study variance is estimated at zero.

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.



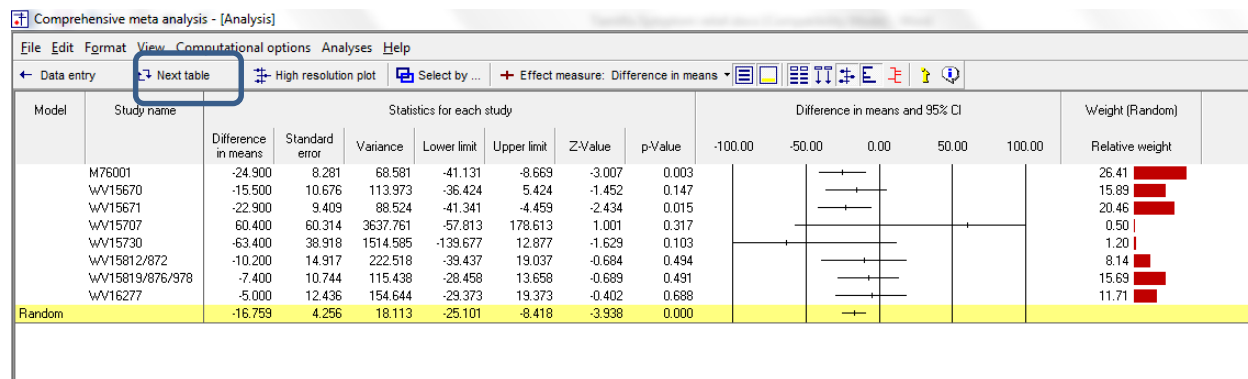
A quick view of the plot suggests the following

- The Tamiflu group responded more quickly than the placebo group in all studies but one
- The difference was statistically significant in two studies
- Putting aside the two studies with very wide confidence intervals, the observed effects ranged from 5 to 25 hours. It seems likely that most (or all) of this dispersion may be explained by random sampling error, and so it's not clear that the true effect sizes vary at all.
- The summary effect is -16.759 with a CI of -25.101 to -8.418 .
- The summary effect has a Z-value -3.938 a p -value of < 0.001 . Thus we can reject the null hypotheses that the true mean difference is 0.0.

Our studies were sampled from a universe of studies defined by the patient types, dosage, and other factors as outlined in the inclusion/exclusion criteria for the meta-analysis. The confidence interval tells us that the mean effect size in this universe of studies probably falls in range of -25.101 to -8.418 . 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

- Tamiflu consistently decreases the response time by 17 hours (with a mean of 17)
- Tamiflu decreases the response time by 0 hours in some studies, by 17 hours in others, and by 34 hours in others (with a mean of 17)

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.



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	8	-16.759	4.256	18.113	-25.101	-8.418	-3.938	0.000	6.325	7	0.502	0.000	0.000	82.850	6864.187	0.000
Random	8	-16.759	4.256	18.113	-25.101	-8.418	-3.938	0.000								

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 -16.759 with a CI of -25.101 to -8.418 , the Z-value for a test of the null is -3.938 and the p-value for a test of the null is < 0.001 .

The section labeled Heterogeneity shows a test of the null hypothesis that the true effect size is identical in all eight 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, 8 minus 1 equals 7).

The observed Q value is 6.325. This is less than we would expect if the null is true (7.0). 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.

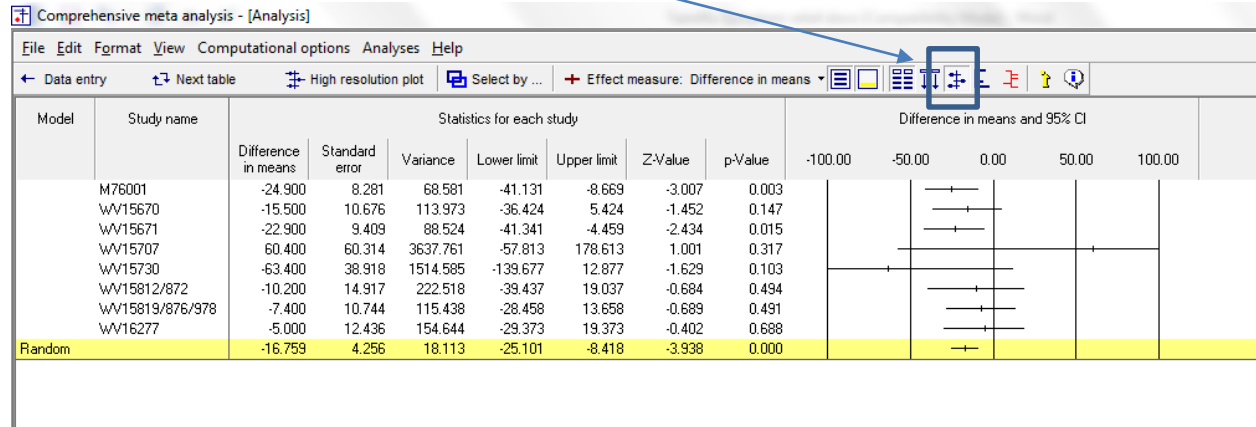
If the mean effect size is -16.759 , if the standard deviation of true effects is 0, then the true effect size for all studies is -16.759 .

This estimate also assumes that the mean of -16.759 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.

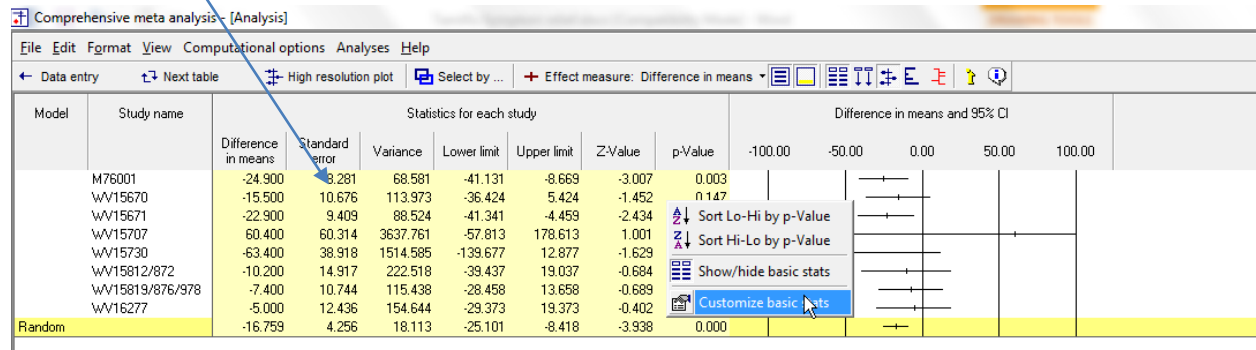
Click Next table

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



Comprehensive meta analysis - [Analysis]

File Edit Format View Computational options Analyses Help

Data entry Next table High resolution plot Select by ... Effect measure: Difference in means

Model	Study name	Statistics for each study						Difference in means and 95% CI					
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	-100.00	-50.00	0.00	50.00	100.00
	M76001	-24.900	8.281	68.581	-41.131	-8.669	-3.007	0.003					
	WV15670	-15.500	10.676	113.973	-36.424	5.424	-1.452	0.147					
	WV15671	-22.900	9.409	88.524	-41.341	-4.441							
	WV15707	60.400	60.314	3637.761	-57.813	178.613							
	WV15730	-63.400	38.918	1514.585	-139.677	12.877							
	WV15812/872	-10.200	14.917	222.518	-39.437	19.037							
	WV15819/876/978	-7.400	10.744	115.438	-28.458	13.658							
	WV16277	-5.000	12.436	154.644	-29.373	19.373							
Random		-16.759	4.256	18.113	-25.101	-8.441							

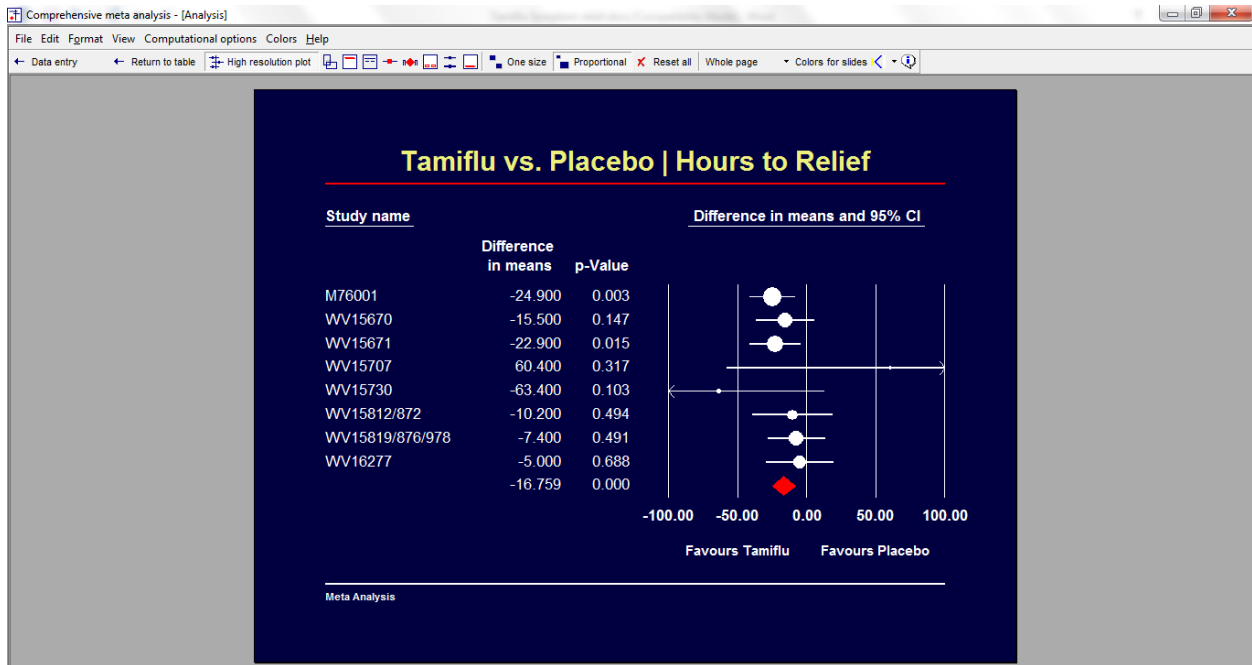
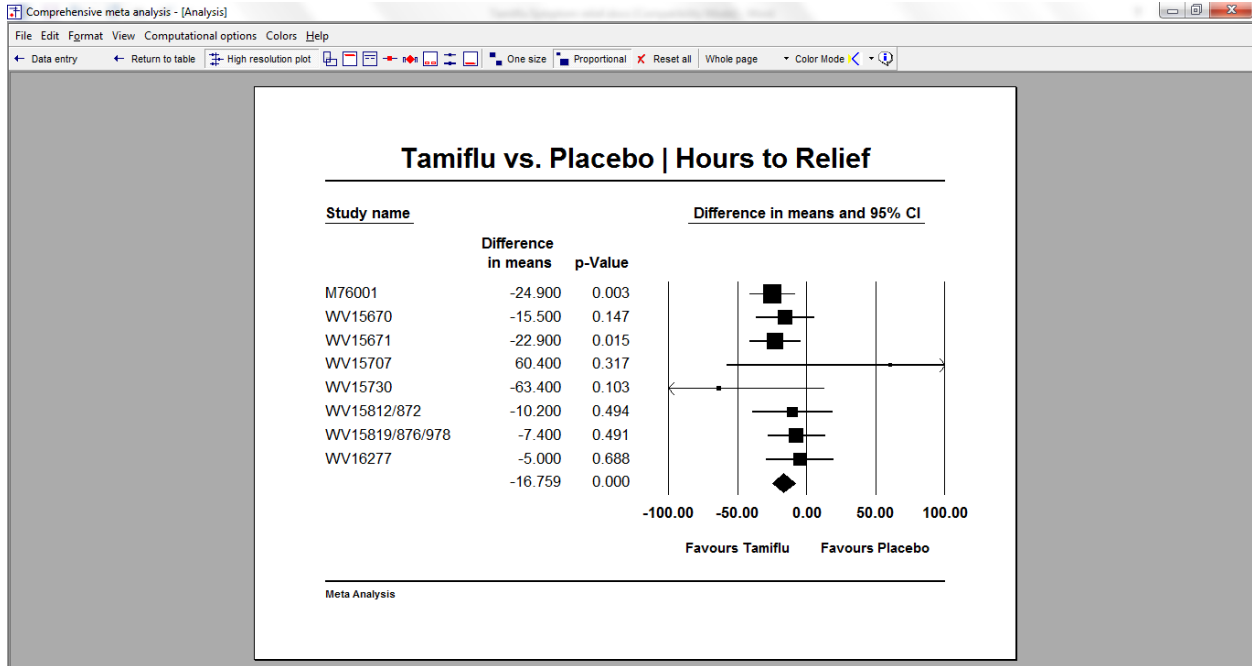
Customize display

Show	Decimals	Alignment
<input checked="" type="checkbox"/> All columns in this block		
<input checked="" type="checkbox"/> Difference in means	Auto	Auto
<input type="checkbox"/> Standard error	Auto	Auto
<input type="checkbox"/> Variance	Auto	Auto
<input type="checkbox"/> Lower limit	Auto	Auto
<input type="checkbox"/> Upper limit	Auto	Auto
<input type="checkbox"/> Z-Value	Auto	Auto
<input checked="" type="checkbox"/> p-Value	Auto	Auto

Cancel Apply Ok

- Select “Random” rather than “Both” on the bottom tab

- Click Hi-Resolution plot
- Adjust the columns widths



In this analyses the effect size was the mean difference, which was reported in hours. This is one of the cases where a raw mean difference is an appropriate effect size, because three conditions are met

- The outcome is in a metric that is meaningful and widely understood (hours)
- All studies employed the same outcome
- The standard deviation is roughly comparable across studies

Alternatively, we could have used the standardized mean difference. This takes the mean difference and puts it on a standardized scale

- A difference of 0.25 indicates that the mean on Group-A is 0.25 standard deviations above the mean of Group-B.
- A difference of 0.50 indicates that the mean on Group-A is 0.50 standard deviations above the mean of Group-B.
- A difference of 0.75 indicates that the mean on Group-A is 0.75 standard deviations above the mean of Group-B.

Let's see what the analysis would look like if we had used the standardized mean difference (g) rather than the mean difference.

We'll focus on the random-effects analysis

On the data-entry screen we entered the mean and standard deviation for each group in each study

The first study had a mean difference of 165.500 vs. 140.600, or -24.900. This is the value that we see in the column labeled “Mean Difference”, and is the effect size we used in the analysis.

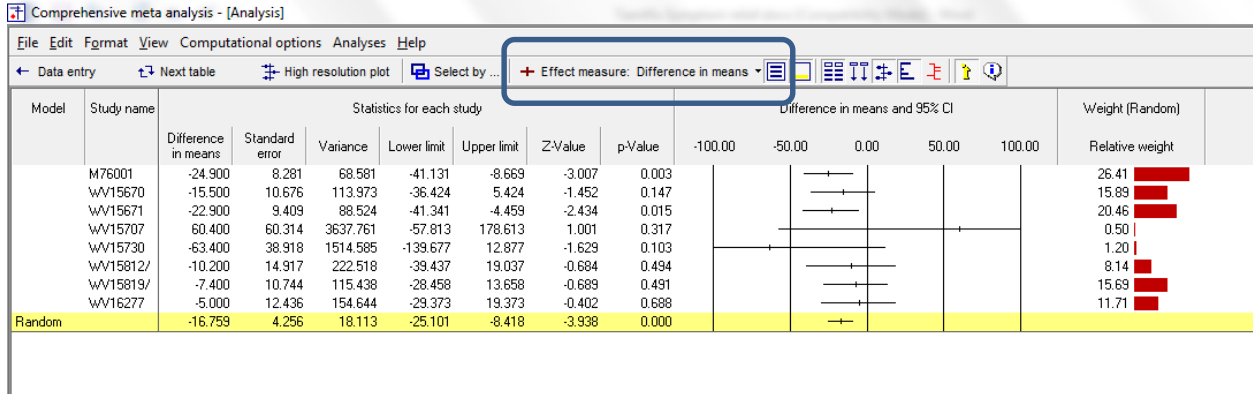
The standard deviation (computed within groups and pooled) is 116.294

The standardized mean difference is then $-24.900/116.294 = 0.182$. This is the value we see listed under Hedges’s g. (In fact, the formula yields Cohen’s d which we then multiply by a correction factor, but the correction is very small in this example).

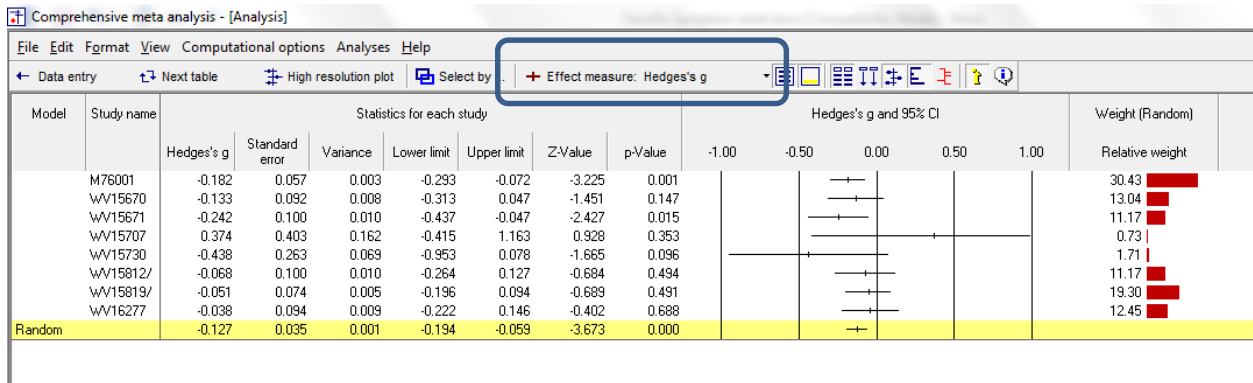
Comprehensive meta analysis - [C:\Users\Biostat\Dropbox\Workshops Three-Day\Tamiflu\Tamiflu Symptom relief.cma]

Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance
1 M76001	140.600	125.200	933	165.500	156.500	473	Auto	-0.182	0.057	0.003	-24.900	8.281	68.581
2 wv15670	129.000	114.600	240	144.500	118.000	235	Auto	-0.133	0.092	0.008	-15.500	10.676	113.973
3 wv15671	102.400	89.900	204	125.300	98.900	200	Auto	-0.242	0.100	0.010	-22.900	9.409	88.524
4 wv15707	154.000	166.500	17	93.600	134.400	9	Auto	0.374	0.403	0.162	60.400	60.314	3637.761
5 wv15730	107.600	104.600	31	171.000	177.100	27	Auto	-0.438	0.263	0.069	-63.400	38.918	1514.585
6 wv15812/872	193.700	152.300	199	203.900	146.300	202	Auto	-0.068	0.100	0.010	-10.200	14.917	222.518
7 wv15819/876/978	185.000	145.600	358	192.400	145.200	375	Auto	-0.051	0.074	0.005	-7.400	10.744	115.438
8 wv16277	138.700	138.400	226	143.700	125.400	225	Auto	-0.038	0.094	0.009	-5.000	12.436	154.644
9													
10													
11													

The analysis of raw mean differences looked like this



We can use the drop-down box and switch Hedge's g. Now the analysis looks like this



In the first analysis we reported a mean difference of 16.758 hours. In the second we report a mean difference of 0.127 standard deviations. The first gives us a sense of the actual time difference. The second gives us the sense that this is a fairly small effect inasmuch as the standard deviation of recovery times is about 8 times as large as the difference between groups.

In this example the weight assigned to each study is similar (but not identical) in the two analysis. This will generally be the case when the standard deviation is similar across studies.

Summary

The analysis is based on eight studies that evaluated the effect of Tamiflu on duration of flu symptoms. Each study compared Tamiflu vs. Placebo and reported the time to relief in symptoms. The effect size is the raw mean difference.

Does Tamiflu decrease the time to symptom relief?

The difference in means is -16.8 hours. On average, patients treated with Tamiflu reported symptom relief 16.8 hours sooner than patients treated with placebo.

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 difference in means is -25.101 to -8.418, which tell us that the mean raw 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 mean difference is probably not zero.

Similarly, the Z-value for testing the null hypothesis (that the mean difference is 0.0) is -3.938, with a corresponding *p*-value is < 0.001. We can reject the null that the drug has no impact on time to symptom relief.

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 6.325 with 7 degrees of freedom. Thus, the observed dispersion is actually less than we would expect by chance. It follows that there is no evidence that the true effect size varies from study to study.

The I^2 statistic tells us what proportion of the observed variance reflects differences in true effect sizes rather than sampling error. Since the variance in true effect sizes is zero, I^2 must be zero.

T^2 is the variance of true effect sizes. Here, T^2 is zero. T is the standard deviation of true effects. Here, T is zero.