Example name	Tamiflu Symptom relief
Effect size Analysis type Level	Mean difference (Hours to relief) Basic 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 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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Click Insert > Column for > Effect size data

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The program displays this wizard

Select [Comparison of two groups...]

Select [Show all 100 formats] Click [Next]



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)
- 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

Click [Next]

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



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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

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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

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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		
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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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	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					
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Click here

Click here

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"

Enter "Auto	o" for	each	study						Click	here						
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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	0.386	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
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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

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	Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Effect direction	Std dif mear	fin ns	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	-(AI	Sort A 7			.092	0.008
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4	WV15707	154.000	166.500	17	93.600	134.400	9	Auto	0	Āŧ	Sort Z-A	.403	0.162		
5	WV15730	107.600	104.600	31	171.000	177.100	27	Auto	-(Column pro	.263	0.069		
6	WV15812/872	193.700	152.300	199	203.900	146.300	202	Auto	-(containin pro	perces			0.010
7	WV15819/876/978	185.000	145.600	358	192.400	145.200	375	Auto	-(Data entry a	ssistant		.074	0.005
8	WV16277	138.700	138.400	226	143.700	125.400	225	Auto	-0	Σ	Formulas			.094	0.009
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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"
- Click [Ok]

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	Study name	Tamiflu Mean	Tamiflu Std-Dev	Tamiflu Sample size	Placbo Mean	Placbo Std-Dev	Placbo Sample size	Std diff in		Std Err	Variance
1	M76001	140.600	125.200	933	165.500	156.500	4	c), encersize marces	2	0.057	0.003
2	WV15670	129.000	114.600	240	144.500	118.000	2	Use the following as the primary index	3	0.092	0.008
3	WV15671	102.400	89.900	204	125.300	98.900	2		2	0.100	0.010
4	WV15707	154.000	166.500	17	93.600	134.400		Difference in means	▼ 4	0.403	0.162
5	WV15730	107.600	104.600	31	171.000	177.100			8	0.263	0.069
6	WV15812/872	193.700	152.300	199	203.900	146.300	2	Display columns for these indices	8	0.100	0.010
7	WV15819/876/978	185.000	145.600	358	192.400	145.200	3		1	0.074	0.005
8	WV16277	138.700	138.400	226	143.700	125.400	2	Odds ratio	<u>▲</u> 8	0.094	0.009
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	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	0.032	0.008	-10.000	10.673	113.30Z	
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	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	
E	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	
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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. The authors of this analysis chose to keep them separate, and so we will use that option as well.

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1 M76001	140.60	0 125.200		Varia	nce for He	daes's a		73	Auto	-0.182	0.057	0.003	-24.900	7.706	59.384	
2 WV15670	129.00	0 114.600		240	199.000	110.000		235	Auto	-0.133	0.092	0.008	-15.500	10.673	113.902	
3 WV15671	102.40	0 89.900		204	125.300	98.900		200	Auto	-0.242	0.100	0.010	-22.900	9.400	88.357	
4 WV15707	154.00	0 166.500		17	93.600	134.400		9	Auto	0.374	0.403	0.162	60.400	64.528	4163.844	
5 WV15730	107.60	0 104.600		31	171.000	177.100		27	Auto	-0.438	0.263	0.069	-63.400	37.620	1415.240	
6 WV15812/872	193.70	0 152.300		199	203.900	146.300		202	Auto	-0.068	0.100	0.010	-10.200	14.913	222.384	
7 WV15819/876	/978 185.00	0 145.600		358	192.400	145.200		375	Auto	-0.051	0.074	0.005	-7.400	10.743	115.423	
8 WV16277	138.70	0 138.400		226	143.700	125.400		225	Auto	-0.038	0.094	0.009	-5.000	12.438	154.712	
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Click Computational options < Variance for mean difference

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

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	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	E Op	tions for comp	uting treatment e	ffects		2	60.400	64.528	4163.844		
5	WV15730	107.600	104.600	31	171.000					1000		53.400	37.620	1415.240		
6	WV15812/872	193.700	152.300	199	203.900							10.200	14.913	222.384		
7	WV15819/876/978	185.000	145.600	358	192.400	Varia	nce for raw n	nean difference i	n independe	nt groups		-7.400	10.743	115.423		
8	WV16277	138.700	138.400	226	143.700							-5.000	12.438	154.712		
9						When	n a studv include	s data for two indep	endent aroups	, the user may	,					
10						elect	to enter the SD I	or each of the group	os separately. I	n this case th	e					
11						progra	am can pool the (antian 20	variance in the two	groups (option	1) or not pool						
12						them	(option 2).									
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14						mean	differences. It k	ias no impact on ani	alyses of stand	ardized mean						
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[🚔	Open Opening screen w	Ctrl+0	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	
	opening screen w	12010	125.200	933	165.500	156.500	473	Auto	-0.182	0.057	0.003	-24.900	8.281	68.581	
[Import		114.600	240	144.500	118.000	235	Auto	-0.133	0.092	0.008	-15.500	10.676	113.973	
	Save	Ctrl+S	89.900	204	125.300	98.900	200	Auto	-0.242	0.100	0.010	-22.900	9.409	88.524	
	Save As		166.500	17	93.600	134.400	9	Auto	0.374	0.403	0.162	60.400	60.314	3637.761	
	Surc <u>H</u> Sin	-	104.600	31	171.000	177.100	27	Auto	-0.438	0.263	0.069	-63.400	38.918	1514.585	
6	Print	Ctrl+P	152.300	199	203.900	146.300	202	Auto	-0.068	0.100	0.010	-10.200	14.917	222.518	
l m	Print setup		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	
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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

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	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	C
1	I 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	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	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	
2	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	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	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	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	3 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	9														
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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\B	iostat\Dropbo	x\Worksho	ps Three-Da	ay\Tamiflu\Tar	niflu Symptom rel	ief.cma]	1	-				
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	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	
	B WV16277	138.700	138.400	226	143.700	125.400	225	Auto	-0.038	0.094	0.009	-5.000	12.436	154.644	
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•	To run the	analysis,	click	[Run analysis]
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Ч	_	Cludy 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															
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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 100

🕂 Compre	hensive meta analysi	is - [Analysis]					1000	-			-	_		
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Model	Study name			Stati	stics for each	study				Difference in mea	ns and 95% Cl			
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	-100.00	-50.00 0.0	0 50.00	100.00		
	M76001 WV15670	-24.900 -15.500	8.281 10.676	68.581 113.973	-41.131 -36.424	-8.669 5.424	-3.007 -1.452	0.003				5how/hi	de forest plot	1
	WV15671 WV15707 WV15730	-22.900 60.400 -63.400	9.409 60.314 38.918	88.524 3637.761 1514.585	-41.341 -57.813 -139.677	-4.459 178.613 12.877	-2.434 1.001 -1.629	0.015 0.317 0.103				Scale	•	Scale25 to + .25 Scale50 to + .50
	WV15812/872	-10.200	14.917	222.518	-39.437	19.037	-0.684	0.494			-			Scale -1 to +1
-	WV15613/6/6/3/6 WV16277	-5.000	12.436	154.644	-20.400	19.373	-0.665	0.431			_			Scale -2 to +2 Scale -4 to +4
Fixed		-16.759	4.256	18.113	-25.101	-8.418	-3.938	0.000						Scale -8 to +8 Customized

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.

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Model	Study name			Stati	stics for each	study				Difference	e in means a	nd 95% Cl		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			- 1			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
	www.sons./976/978	-7.400	10.744	115.438	-28.458	13.658	-0.689	0.491	1					15.69	15.69
	WV16277	-5.000	12.436	154.644	-29.373	19.373	-0.402	0.688	1					11.71	11.71
ixed		-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.

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Model	Study name			Stati	stics for each	study				Difference	in means an	id 95% Cl		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	
	M76001	-24.900	8.281	68.581	-41.131	-8.669	-3.007	0.003		+	- 1			26.41	
	WV15670	-15.500	10.676	113.973	-36.424	5.424	-1.452	0.147			-			15.89	
	WV15671	-22.900	9.409	88.524	-41.341	-4.459	-2.434	0.015			_			20.46	
	WV15707	60.400	60.314	3637.761	-57.813	178.613	1.001	0.317						0.50	
	WV15730	-63.400	38.918	1514.585	-139.677	12.877	-1.629	0.103						1.20	
	WV15812/872	-10.200	14.917	222.518	-39.437	19.037	-0.684	0.494						8.14	
	WV15819/876/978	-7.400	10.744	115.438	-28.458	13.658	-0.689	0.491						15.69	
	WV16277	-5.000	12.436	154.644	-29.373	19.373	-0.402	0.688						11.71	
Random		-16.759	4.256	18.113	-25.101	-8.418	-3.938	0.000		-	+				

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 Cl 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 <u>mean</u> 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 <u>varies</u> from study to study. This is an important clinical issue since we need to distinguish between various possibilities, such as

- a) Tamiflu consistently decreases the response time by 17 hours (with a mean of 17)
- b) 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.

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Model	Study name			Stati	stics for each	study				Difference	in means ar	id 95% Cl		Weight (Random)
		Differenc in mean:	e Standard s error	Variance	Lower limit	Upper limit	Z-Value	p-Value	-100.00	-50.00	0.00	50.00	100.00	Relative weight
	M76001	-24.9	00 8.281	68.581	-41.131	-8.669	-3.007	0.003			-			26.41
	WV15670	-15.5	00 10.676	113.973	-36.424	5.424	-1.452	0.147			+-+			15.89
	WV15671	-22.9	00 9.409	88.524	-41.341	-4.459	-2.434	0.015		+				20.46
	WV15707	60.4	00 60.314	3637.761	-57.813	178.613	1.001	0.317						0.50
	WV15730	-63.4	00 38.918	1514.585	-139.677	12.877	-1.629	0.103			_			1.20
	WV15812/872	-10.2	00 14.917	222.518	-39.437	19.037	-0.684	0.494		—				8.14
	WV15819/876/978	-7.4	00 10.744	115.438	-28.458	13.658	-0.689	0.491						15.69
	WV16277	-5.0	00 12.436	154.644	-29.373	19.373	-0.402	0.688						11.71
landom		-16.7	59 4.256	18.113	-25.101	-8.418	-3.938	0.000			+			
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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	0.0
Devident		8	-16 759	4 256	18 11 3	-25 101	-8.418	-3.938	0.000								

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 -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.

Tamiflu symptom relief

 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 I2 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

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		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	-100.0	0 -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	-4.459	-2.434	0.015		-			
	WV15707	60.400	60.314	3637.761	-57.813	178.613	1.001	0.317					
	WV15730	-63.400	38.918	1514.585	-139.677	12.877	-1.629	0.103					
	WV15812/872	-10.200	14.917	222.518	-39.437	19.037	-0.684	0.494		-		-	
	WV15819/876/978	-7.400	10.744	115.438	-28.458	13.658	-0.689	0.491					
	WV16277	-5.000	12.436	154.644	-29.373	19.373	-0.402	0.688				-	
Random		-16.759	4.256	18.113	-25.101	-8.418	-3,938	0.000					

Right-click here and hide some of the statistics columns

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	WV16277	-5.000	12.436	154.644	-29.373	19.373	-0.402	Custo	omize basic 💦	ts _		-		
Random		-16.759	4.256	18.113	-25.101	-8.418	-3.938	0.000	, i i i i i i i i i i i i i i i i i i i					

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	M76001	-24.900	8.281	68.58	1 -41.131	-8.669	-3.007	0.003		+	-			
	WV15670	-15.500	10.676	113.97	3 -36.424	5.424	-1.452	0.147	_		++			
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• 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 deviaiton 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).

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	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	i 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)														
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The analysis of raw mean differences looked like this

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Model	Study name			Statis	tics for each	study			Ĺ	ifference in mea	ans and 95% Cl		Weight (Random)
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	-100.00 -50).00 0.0	0 50.00	100.00	D Relative weight
	M76001	-24.900	8.281	68.581	-41.131	-8.669	-3.007	0.003					26.41
	WV15670	-15.500	10.676	113.973	-36.424	5.424	-1.452	0.147		— 	-		15.89
	WV15671	-22.900	9.409	88.524	-41.341	-4.459	-2.434	0.015		—+—			20.46
	WV15707	60.400	60.314	3637.761	-57.813	178.613	1.001	0.317					0.50
	WV15730	-63.400	38.918	1514.585	-139.677	12.877	-1.629	0.103	+		-		1.20
	WV15812/	-10.200	14.917	222.518	-39.437	19.037	-0.684	0.494		— • 	_		8.14
	WV15819/	-7.400	10.744	115.438	-28.458	13.658	-0.689	0.491		+	-		15.69
	WV16277	-5.000	12.436	154.644	-29.373	19.373	-0.402	0.688		+	_		11.71
Random		-16.759	4.256	18.113	-25.101	-8.418	-3.938	0.000					
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We can use the drop-down box and switch Hedge's g. Now the analysis looks like this

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Model	Study name			Statis	tics for each :	study				Hedg	jes's g and 9	5% CI		Weight (Random)
		Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	-1.00	-0.50	0.00	0.50	1.00	Relative weight
	M76001	-0.182	0.057	0.003	-0.293	-0.072	-3.225	0.001		-	+			30.43
	WV15670	-0.133	0.092	0.008	-0.313	0.047	-1.451	0.147		-				13.04
	WV15671	-0.242	0.100	0.010	-0.437	-0.047	-2.427	0.015						11.17
	WV15707	0.374	0.403	0.162	-0.415	1.163	0.928	0.353		—				0.73
	WV15730	-0.438	0.263	0.069	-0.953	0.078	-1.665	0.096						1.71
	WV15812/	-0.068	0.100	0.010	-0.264	0.127	-0.684	0.494		-				11.17
	WV15819/	-0.051	0.074	0.005	-0.196	0.094	-0.689	0.491						19.30
	WV16277	-0.038	0.094	0.009	-0.222	0.146	-0.402	0.688						12.45
landom		-0.127	0.035	0.001	-0.194	-0.059	-3.673	0.000			+			

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 <u>mean</u> 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 l^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, l^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.