Example name	Tamiflu Hospitalized
Effect size	Risk ratio
Analysis type	Basic
Level	Basic

Synopsis

The US government has spent 1.4 billion dollars to stockpile Tamiflu, in anticipation of a possible flu pandemic. Cochrane recently published a 500+ page report that evaluates Tamiflu's utility in a wide number of areas. Tamiflu was shown to be effective for some outcomes but not for others. This analysis that follows is taken from that report, and focuses on Tamiflu's ability to reduce the risk of hospitalization.

This analysis includes seven studies where patients were randomized to receive either Tamiflu or placebo. Outcome was the proportion of patients hospitalized in each group. The effect size is the risk ratio.

We use this example to show

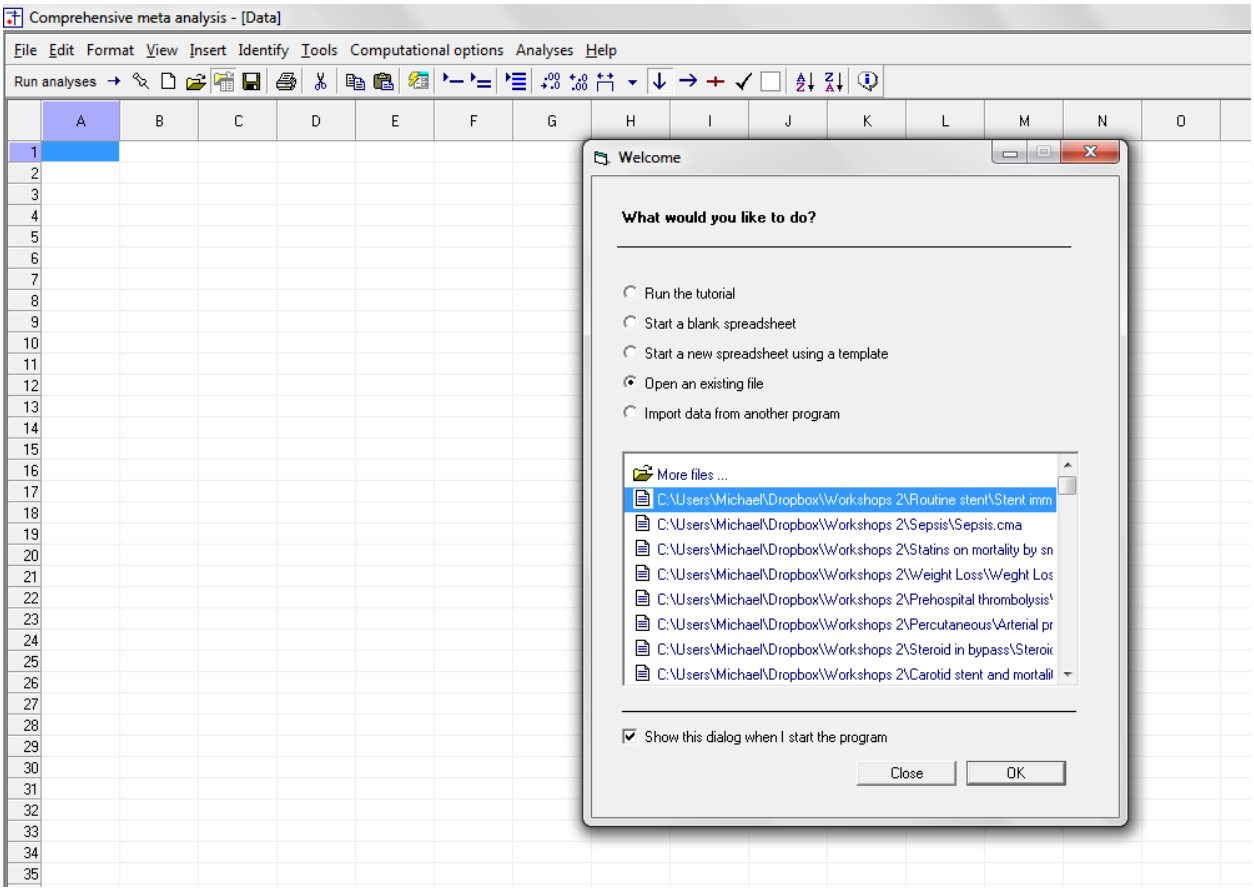
- How to enter data from 2x2 tables
- How to perform a simple analysis
- How to interpret statistics for effect size
- How to interpret statistics for heterogeneity
- How to create a high-resolution plot

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

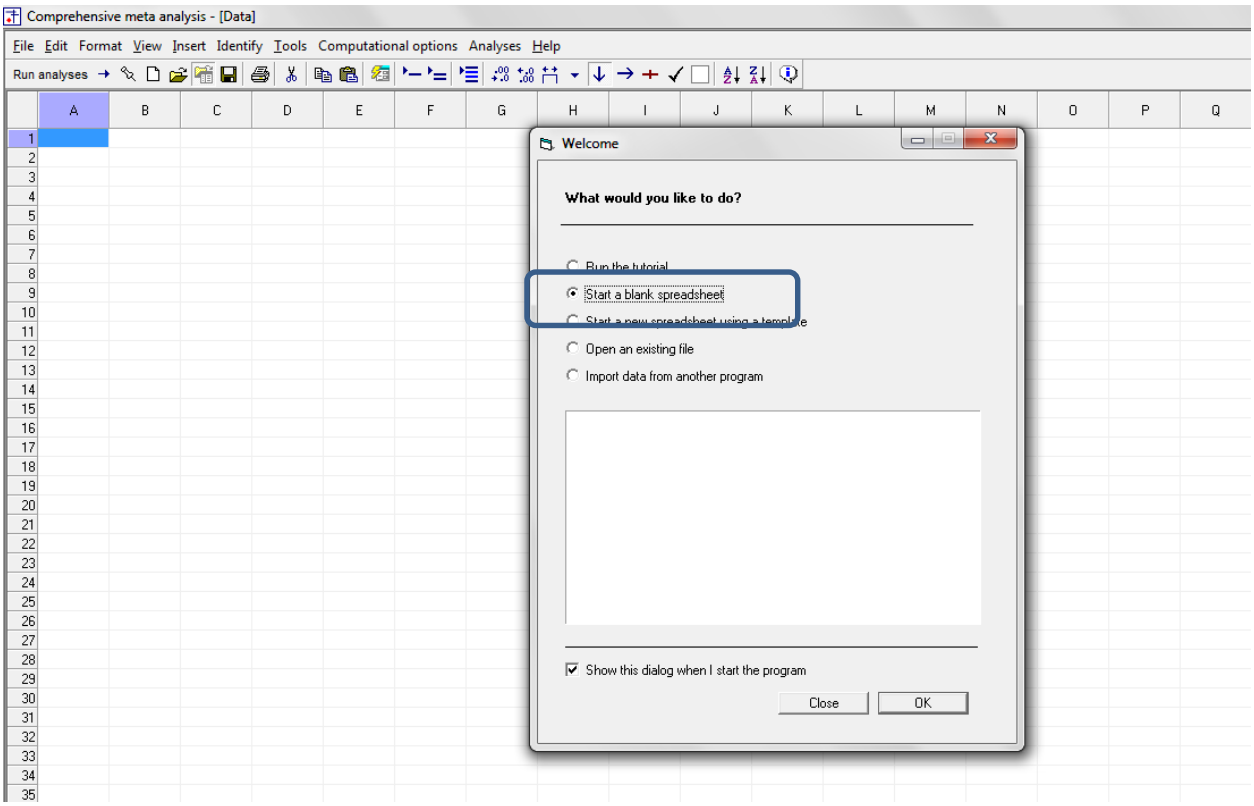
Download CMA file for computers that use a period to indicate decimals
Download CMA file for computers that use a comma to indicate decimals

Download this PDF
Download data in Excel
Download trial of CMA

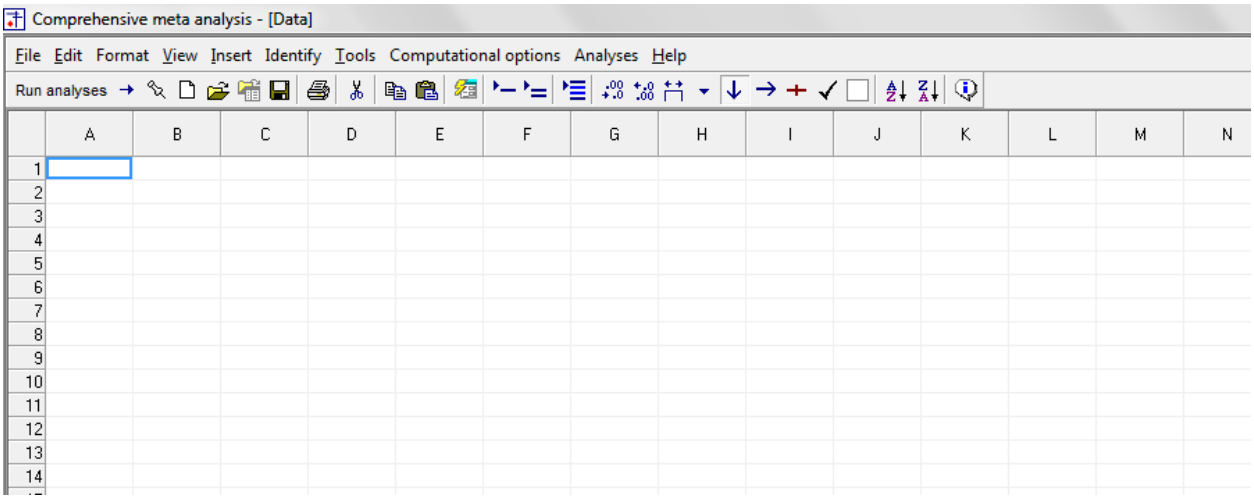
Start the program



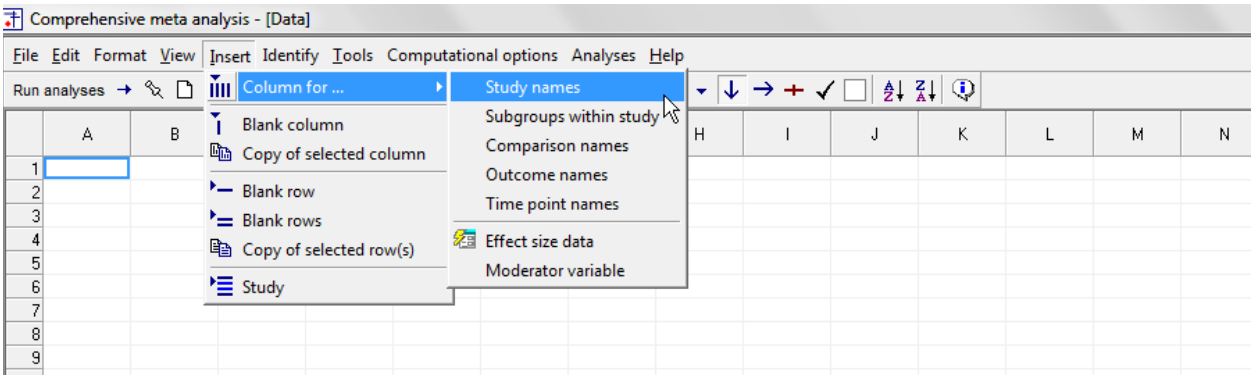
- Select the option [Start a blank spreadsheet]
- Click [Ok]



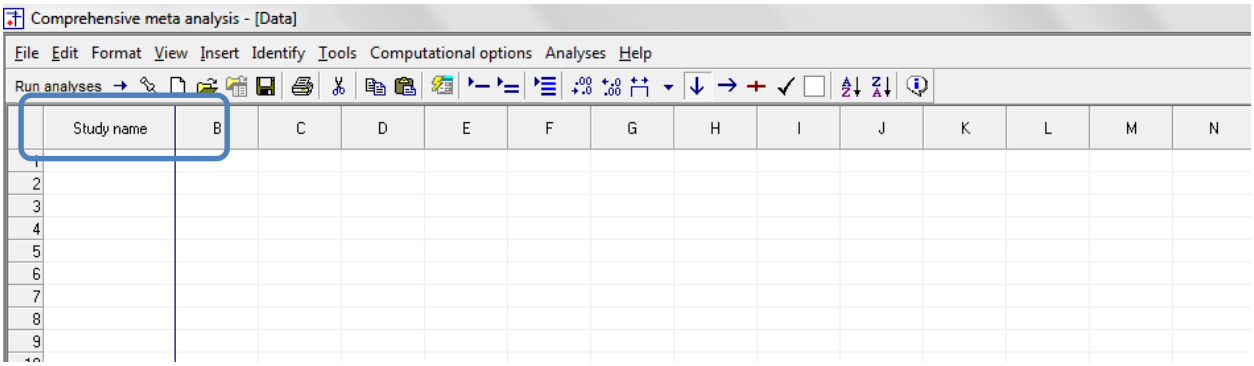
The screen should look like this



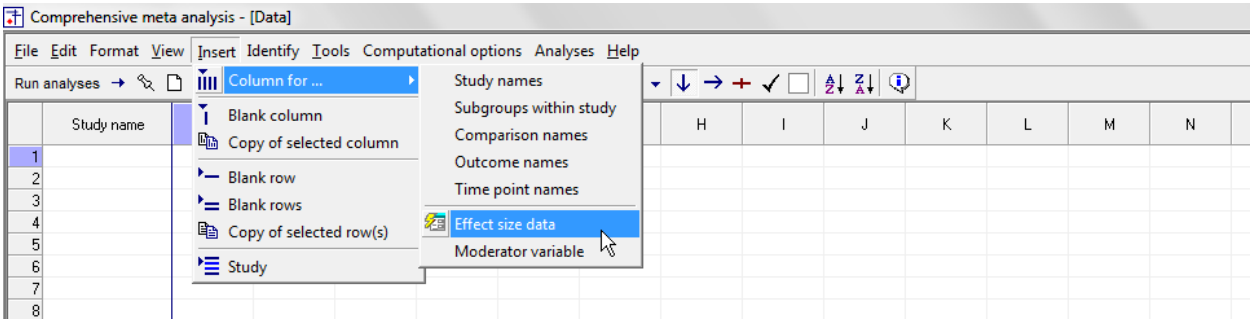
Click Insert > Column for > Study names



The screen should look like this

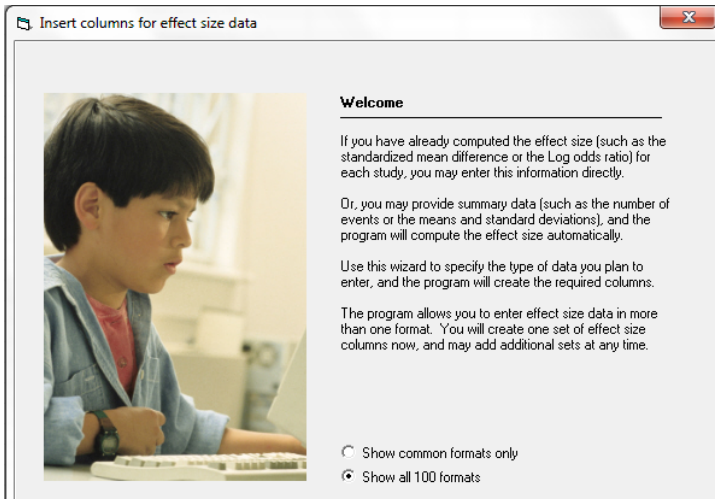


Click Insert > Column for > Effect size data

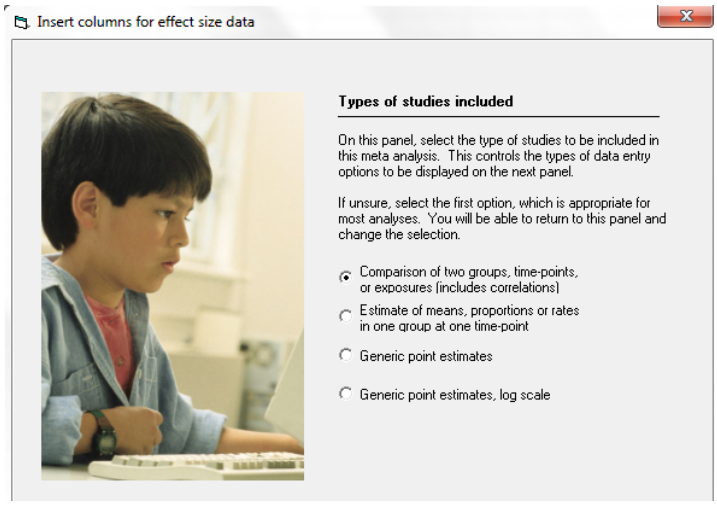


The program displays this wizard

Select [Show all 100 formats]
Click [Next]

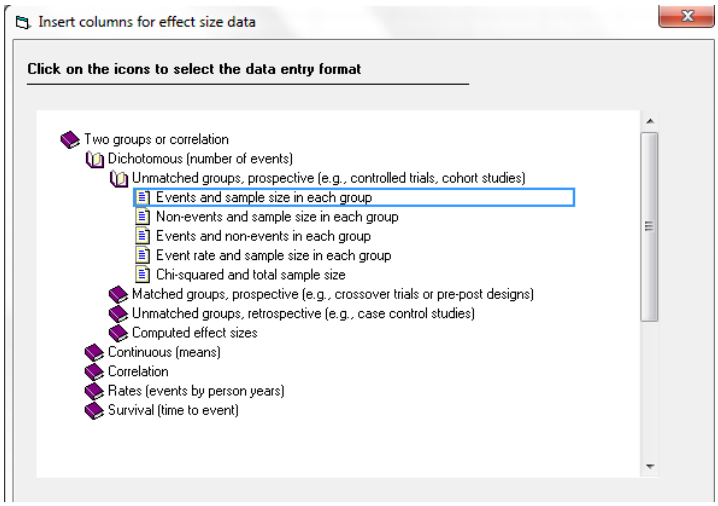


Select [Comparison of two groups…]
Click [Next]



Drill down to

Dichotomous (number of events)
Unmatched groups, prospective …
Events and sample size in each group

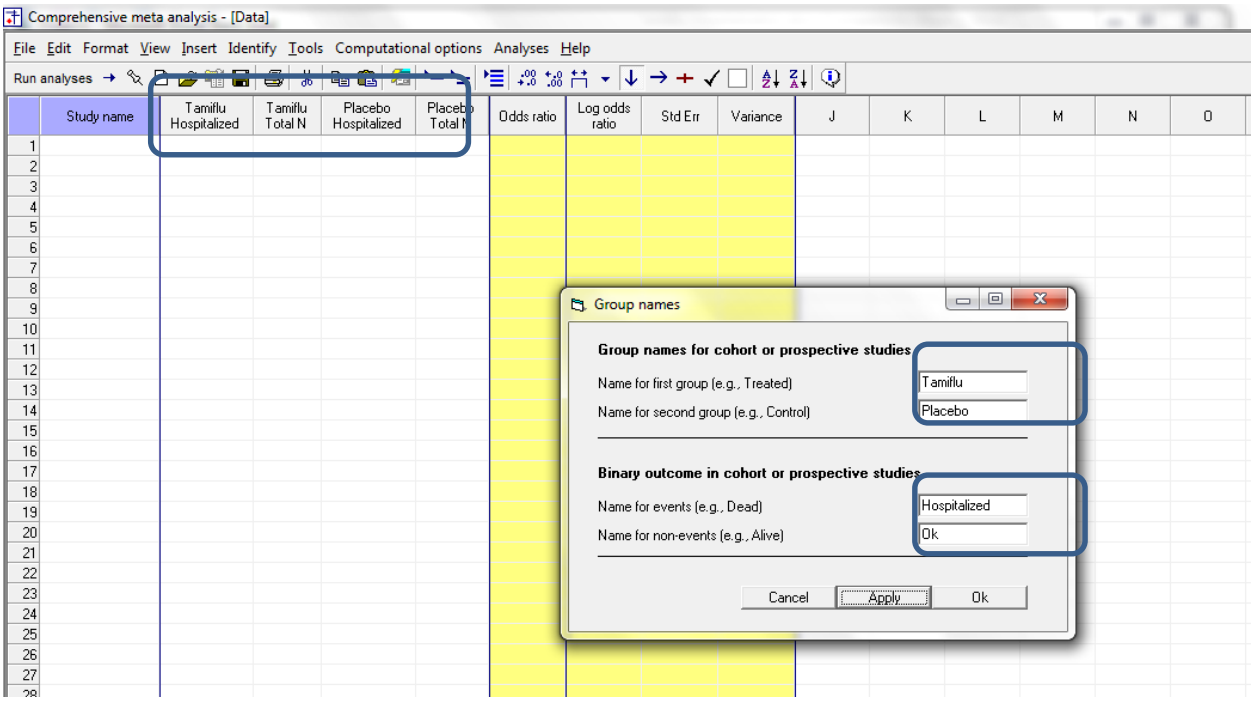


The program displays this wizard

Enter the following labels into the wizard

- First group > Tamiflu
- Second group > Placebo
- Name for events > Hospitalized
- Name for non-events > Ok

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

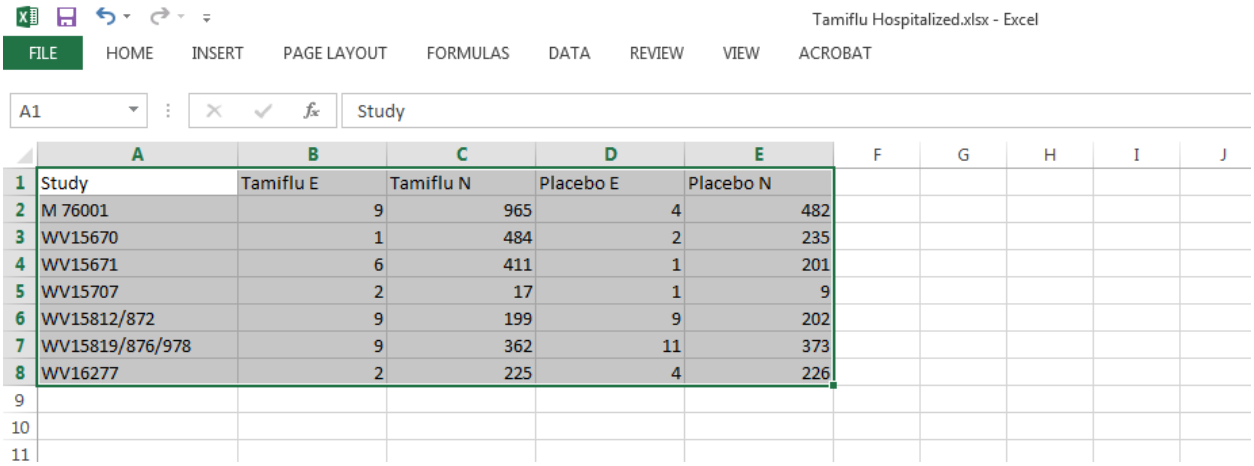


There are three options at this point

- Enter the data directly into CMA
- – or – Open the CMA data file
- – or – Copy the data from Excel

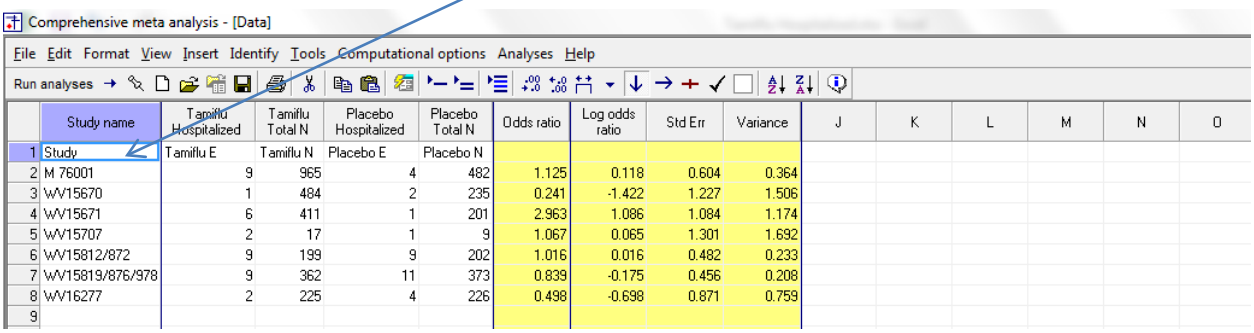
Here, we'll show how to copy the data from Excel

- Switch to Excel and open the file "Tamiflu Hospitalized.xls"
- Highlight the rows and columns as shown (Columns A to E only), and press CTRL-C to copy to clipboard



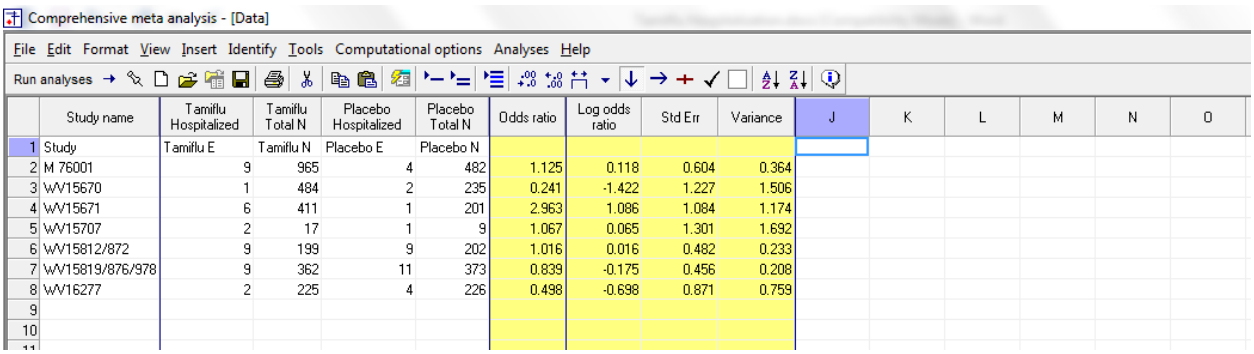
	A	B	C	D	E	F	G	H	I	J
1	Study	Tamiflu E	Tamiflu N	Placebo E	Placebo N					
2	M 76001	9	965	4	482					
3	WV15670	1	484	2	235					
4	WV15671	6	411	1	201					
5	WV15707	2	17	1	9					
6	WV15812/872	9	199	9	202					
7	WV15819/876/978	9	362	11	373					
8	WV16277	2	225	4	226					
9										
10										
11										

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



	Study name	Tamiflu Hospitalized	Tamiflu Total N	Placebo Hospitalized	Placebo Total N	Odds ratio	Log odds ratio	Std Err	Variance	J	K	L	M	N	O
1	Study	Tamiflu E	Tamiflu N	Placebo E	Placebo N										
2	M 76001	9	965	4	482	1.125	0.118	0.604	0.364						
3	WV15670	1	484	2	235	0.241	-1.422	1.227	1.506						
4	WV15671	6	411	1	201	2.963	1.086	1.084	1.174						
5	WV15707	2	17	1	9	1.067	0.065	1.301	1.692						
6	WV15812/872	9	199	9	202	1.016	0.016	0.482	0.233						
7	WV15819/876/978	9	362	11	373	0.839	-0.175	0.456	0.208						
8	WV16277	2	225	4	226	0.498	-0.698	0.871	0.759						
9															

At this point we should check that the data has been copied correctly



	Study name	Tamiflu Hospitalized	Tamiflu Total N	Placebo Hospitalized	Placebo Total N	Odds ratio	Log odds ratio	Std Err	Variance
1	Study	Tamiflu E	Tamiflu N	Placebo E	Placebo N				
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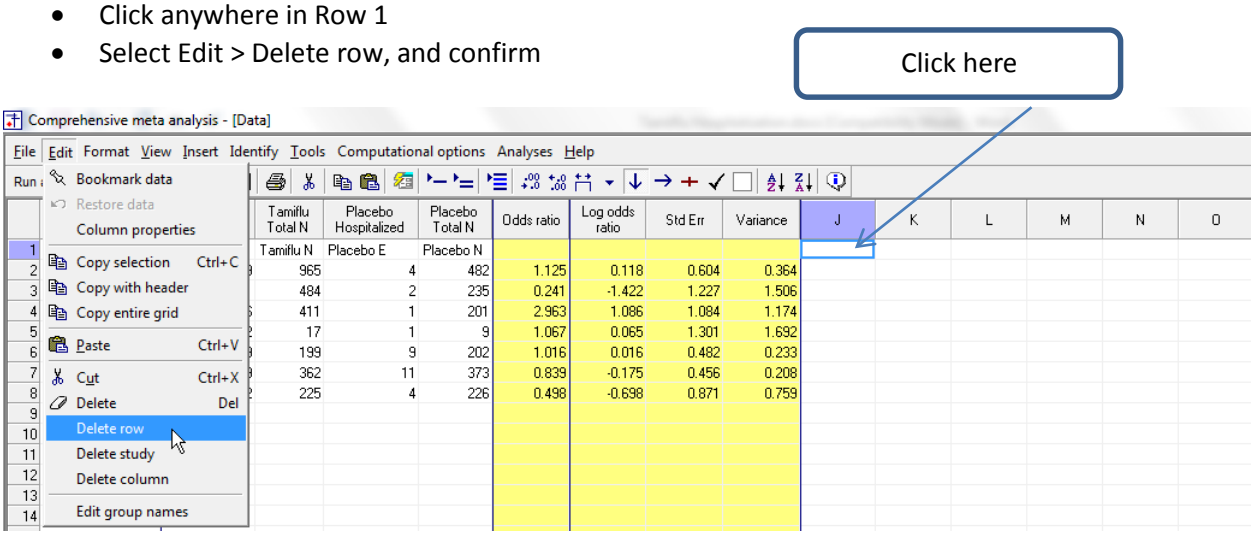
6	WV15812/872	9	199	9	202	1.016	0.016	0.482	0.233
7	WV15819/876/978	9	362	11	373	0.839	-0.175	0.456	0.208
8	WV16277	2	225	4	226	0.498	-0.698	0.871	0.759
9									
10									

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



	Tamiflu Total N	Placebo Hospitalized	Placebo Total N	Odds ratio	Log odds ratio	Std Err	Variance
1	Tamiflu N	Placebo E	Placebo N				
2	965	4	482	1.125	0.118	0.604	0.364
3	484	2	235	0.241	-1.422	1.227	1.506
4	411	1	201	2.963	1.086	1.084	1.174
5	17	1	9	1.067	0.065	1.301	1.692
6	199	9	202	1.016	0.016	0.482	0.233
7	362	11	373	0.839	-0.175	0.456	0.208
8	225	4	226	0.498	-0.698	0.871	0.759
9							
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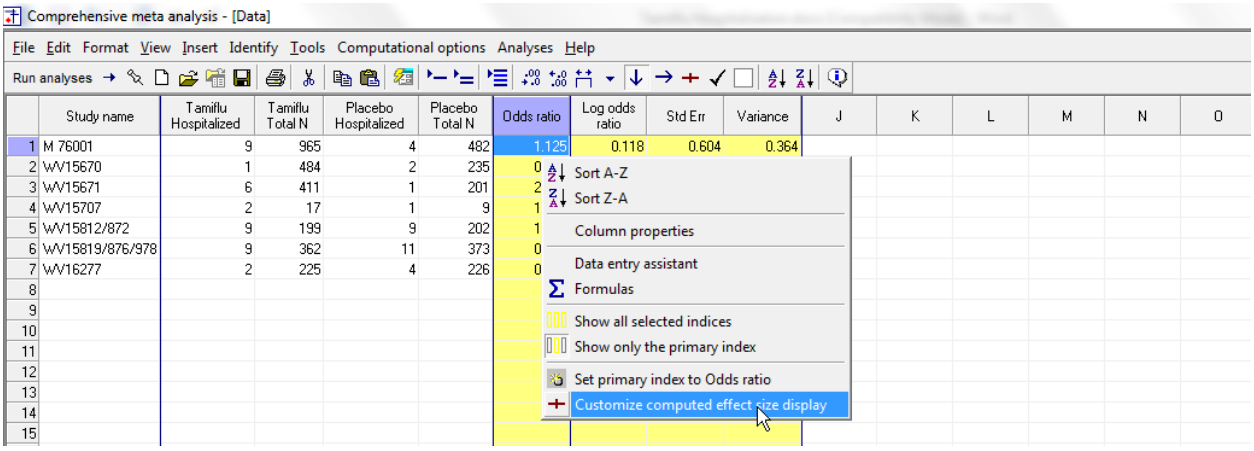
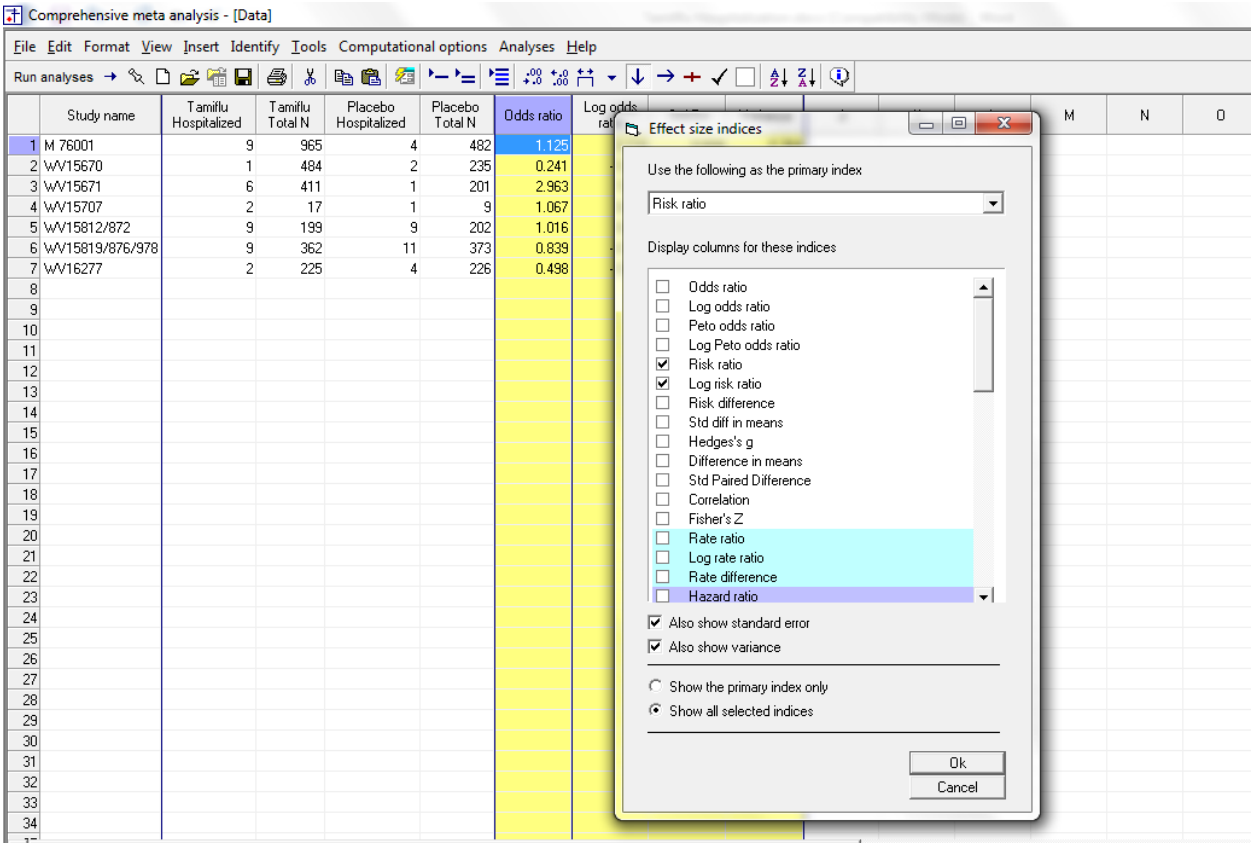
14							

By default, the program is displaying the odds ratio as the effect size

We want to switch to the risk ratio

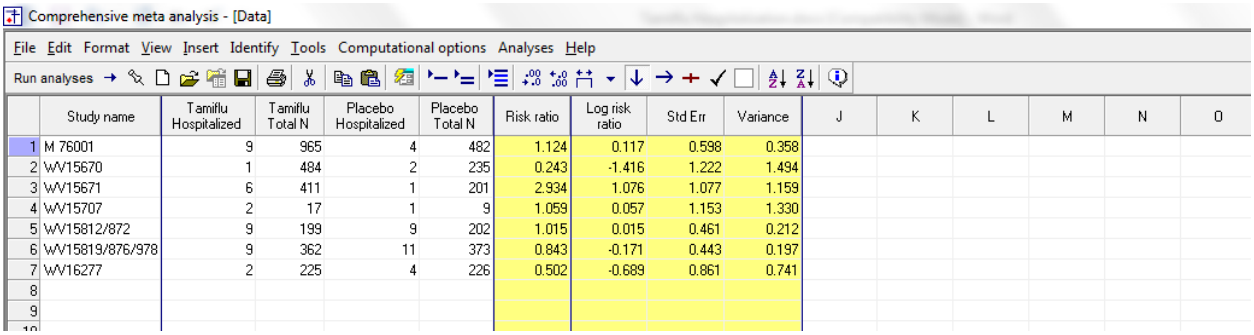


- Right-click on any of the yellow columns
- Click Customize computed effect size display



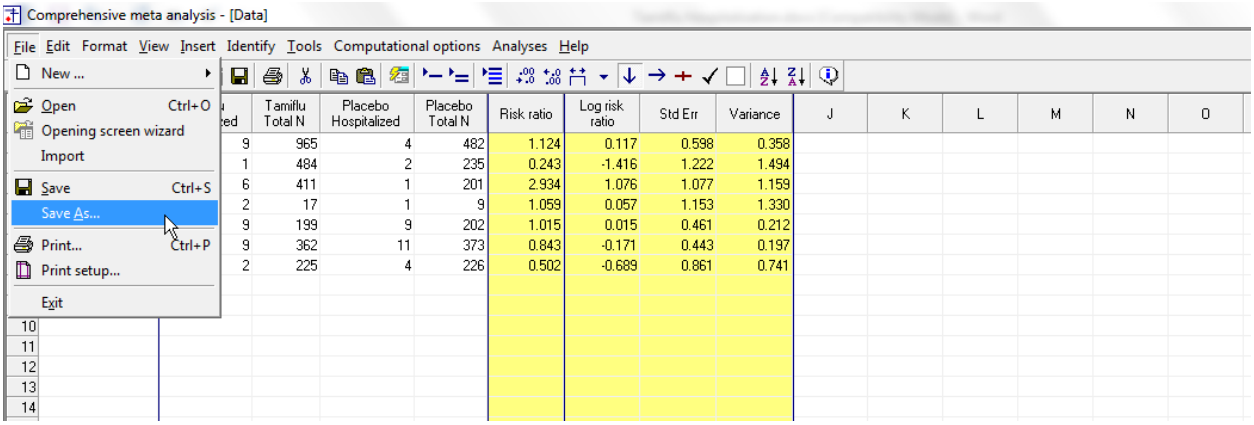
- Tick Risk ratio
- Tick Log risk ratio
- Select Risk Ratio in the drop-down box in the wizard
- De-select Odds ratio
- De-select log odds ratio
- Click Ok

The program now display the risk ratio rather than the odds ratio



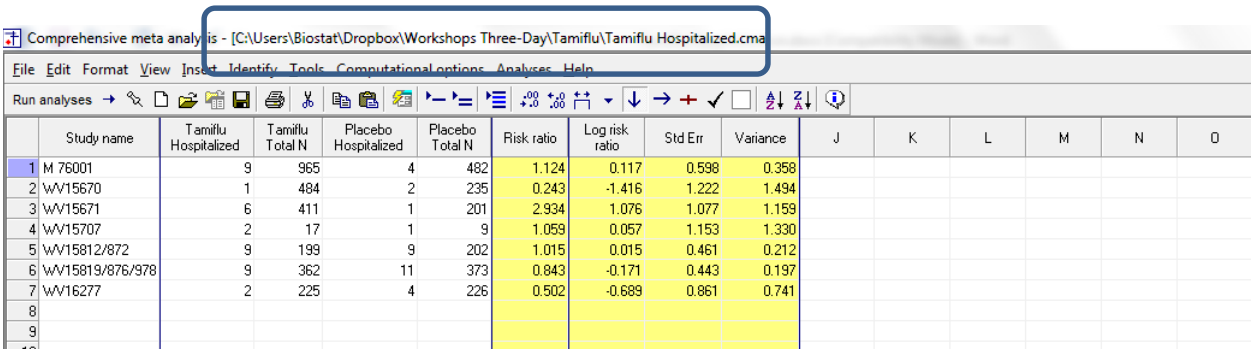
	Study name	Tamiflu Hospitalized	Tamiflu Total N	Placebo Hospitalized	Placebo Total N	Risk ratio	Log risk ratio	Std Err	Variance	J	K	L	M	N	O
1	M 76001	9	965	4	482	1.124	0.117	0.598	0.358						
2	WV15670	1	484	2	235	0.243	-1.416	1.222	1.494						
3	WV15671	6	411	1	201	2.934	1.076	1.077	1.159						
4	WV15707	2	17	1	9	1.059	0.057	1.153	1.330						
5	WV15812/872	9	199	9	202	1.015	0.015	0.461	0.212						
6	WV15819/876/978	9	362	11	373	0.843	-0.171	0.443	0.197						
7	WV16277	2	225	4	226	0.502	-0.689	0.861	0.741						
8															
9															

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



	Study name	Tamiflu Hospitalized	Tamiflu Total N	Placebo Hospitalized	Placebo Total N	Risk ratio	Log risk ratio	Std Err	Variance	J	K	L	M	N	O
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2	WV15670	1	484	2	235	0.243	-1.416	1.222	1.494						
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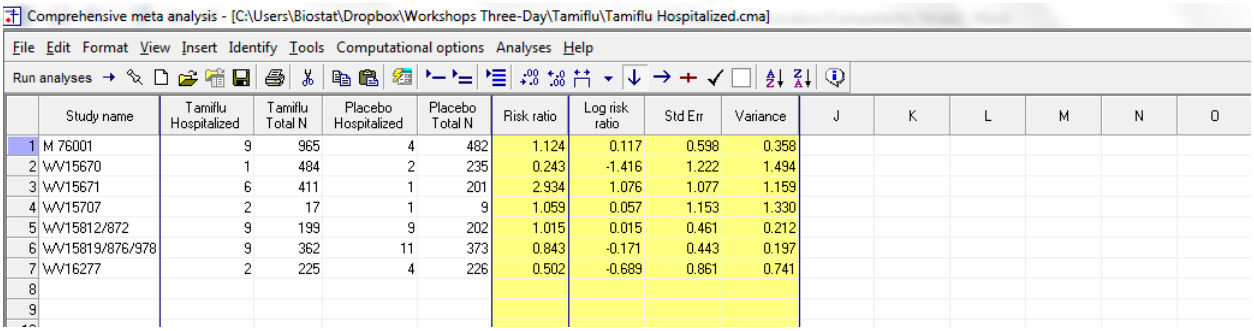
6	WV15819/876/978	9	362	11	373	0.843	-0.171	0.443	0.197						
7	WV16277	2	225	4	226	0.502	-0.689	0.861	0.741						
8															
9															

By convention we've put the treated group (Tamiflu) in the first two columns and the control (placebo) in the second two columns. Also by convention, we've defined "Event" as the presence of the outcome (Hospitalized).

When we follow these conventions, and the outcome is a bad event (as it is here) if the treated group does better than the control, the risk ratio will be less than 1.

Therefore, in the present case, a risk ratio less than 1 indicates that Tamiflu was associated with a decreased risk of hospitalization.

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 last study, where the risk ratio is relatively large, and the distinction between groups should be clear.



	Study name	Tamiflu Hospitalized	Tamiflu Total N	Placebo Hospitalized	Placebo Total N	Risk ratio	Log risk ratio	Std Err	Variance	J	K	L	M	N	O
1	M 76001	9	965	4	482	1.124	0.117	0.598	0.358						
2	WV15670	1	484	2	235	0.243	-1.416	1.222	1.494						
3	WV15671	6	411	1	201	2.934	1.076	1.077	1.159						
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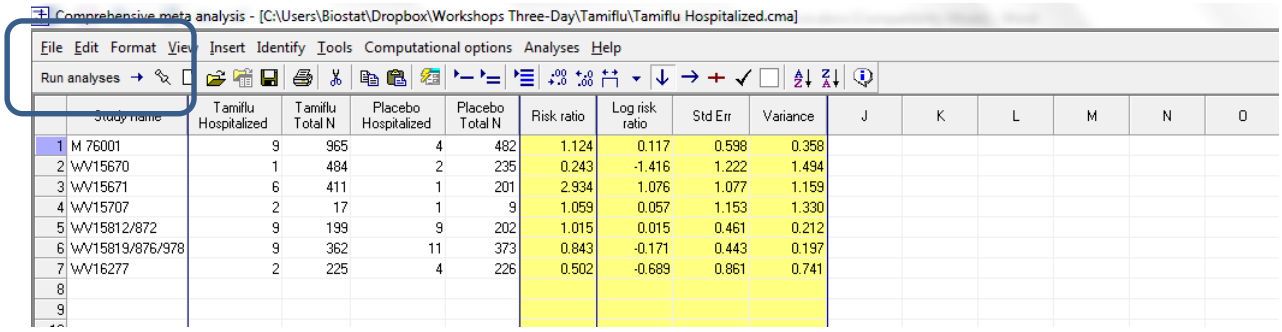
6	WV15819/876/978	9	362	11	373	0.843	-0.171	0.443	0.197						
7	WV16277	2	225	4	226	0.502	-0.689	0.861	0.741						
8															
9															

Both groups have approximately the same number of patients (about 225) but the number of hospitalizations is higher in the Placebo group than in the Tamiflu group (4 vs. 2). The risk ratio is less than 1 (0.502), which means that patients treated with Tamiflu were less likely to be hospitalized.

- To run the analysis, click [Run analysis]



	Study name	Tamiflu Hospitalized	Tamiflu Total N	Placebo Hospitalized	Placebo Total N	Risk ratio	Log risk ratio	Std Err	Variance	J	K	L	M	N	O
1	M 76001	9	965	4	482	1.124	0.117	0.598	0.358						
2	WV15670	1	484	2	235	0.243	-1.416	1.222	1.494						
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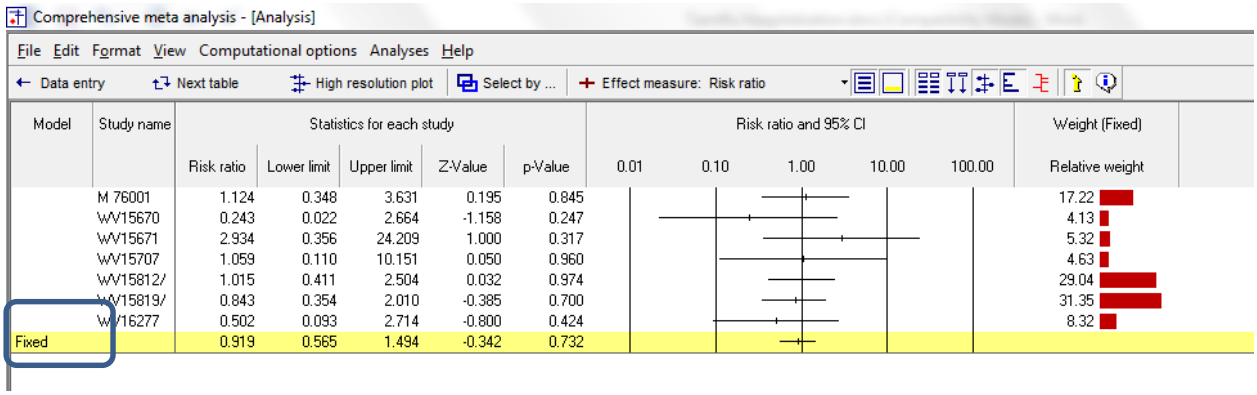
7	WV16277	2	225	4	226	0.502	-0.689	0.861	0.741						
8															
9															

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.



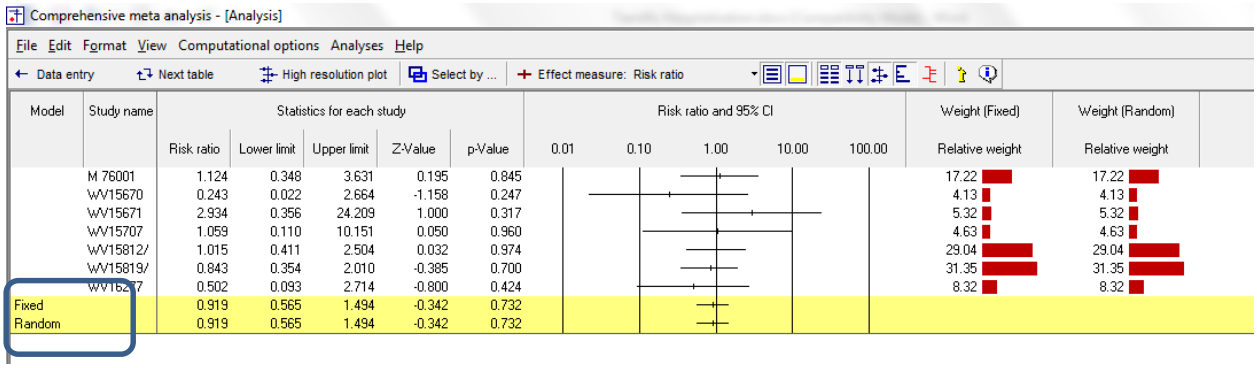
Four of the studies have risk ratios very close to 1.0, which means that the treatment was unrelated to outcome. Two studies show an advantage for Tamiflu and one study shows an advantage for placebo, but none of these is statistically significant.

The effects seem to be reasonably consistent. The confidence interval for every study overlaps the mean.

The pooled effect is 0.919, which means that Tamiflu decreases the risk of being hospitalized by about 8%. However, the confidence interval is 0.565 to 1.494, and the p-value for a test of the null is 0.732.

Click [Both models]

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



Under the fixed-effect model the pooled effect size is 0.919 with a confidence interval of 0.565 to 1.494. Under the random-effects model the pooled effect size is 0.919 with a confidence interval of 0.565 to 1.494. While the two models yield identical results, the random-effects model is a better fit for the way the studies were sampled, and therefore that is the model we will use in the analysis.

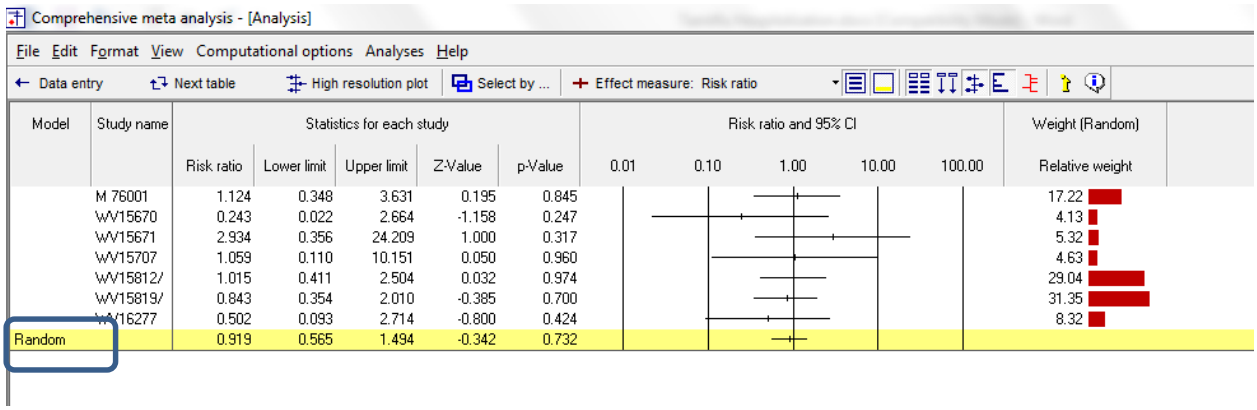
- The fixed-effect model would be appropriate if all the studies were virtual replicates of each other, which may or may not be the case here. The may have patients varied in some ways.

- The random-effects model would be appropriate if the studies vary in ways that may impact the effect size.

Under the circumstances the random-effects model will yield a more conservative estimate (the standard error will be as large or larger as compared with the fixed-effect model).

- Click Random on the tab at the bottom

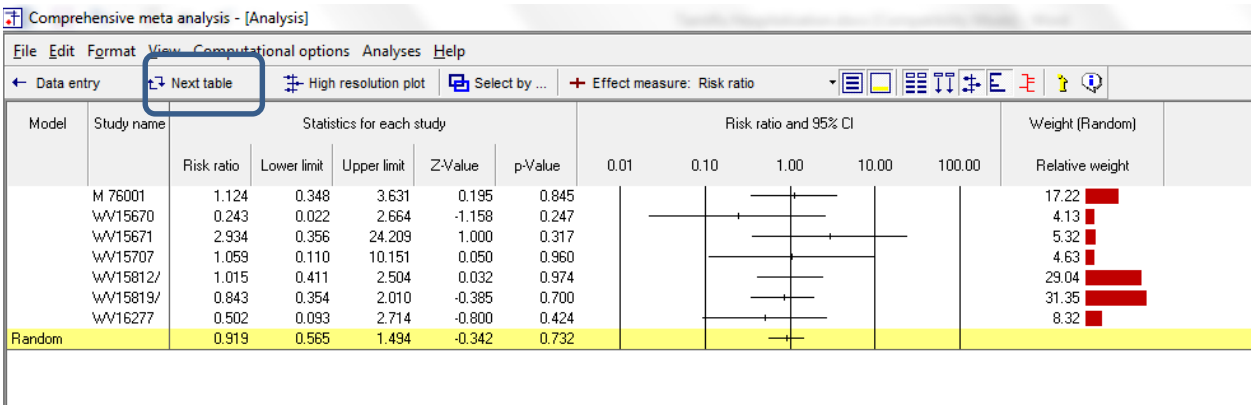
The plot now displays the random-effects analysis alone.

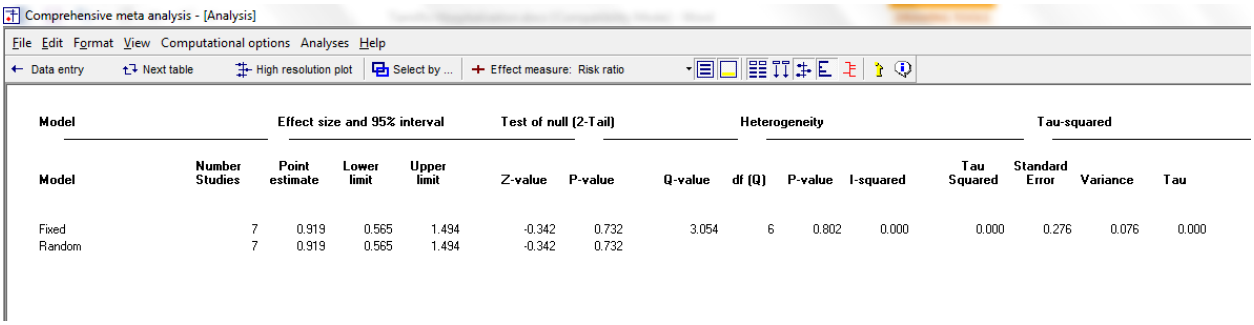


A quick view of the plot suggests the following

- Most of the studies show no real advantage for either group
- The observed effects are pretty consistent
- The summary effect is 0.919 with a CI of 0.565 to 1.494
- The summary effect has a Z-value −0.342 a *p*-value of < 0.732. Thus we cannot reject the null hypotheses that the true mean risk ratio is 1.0.

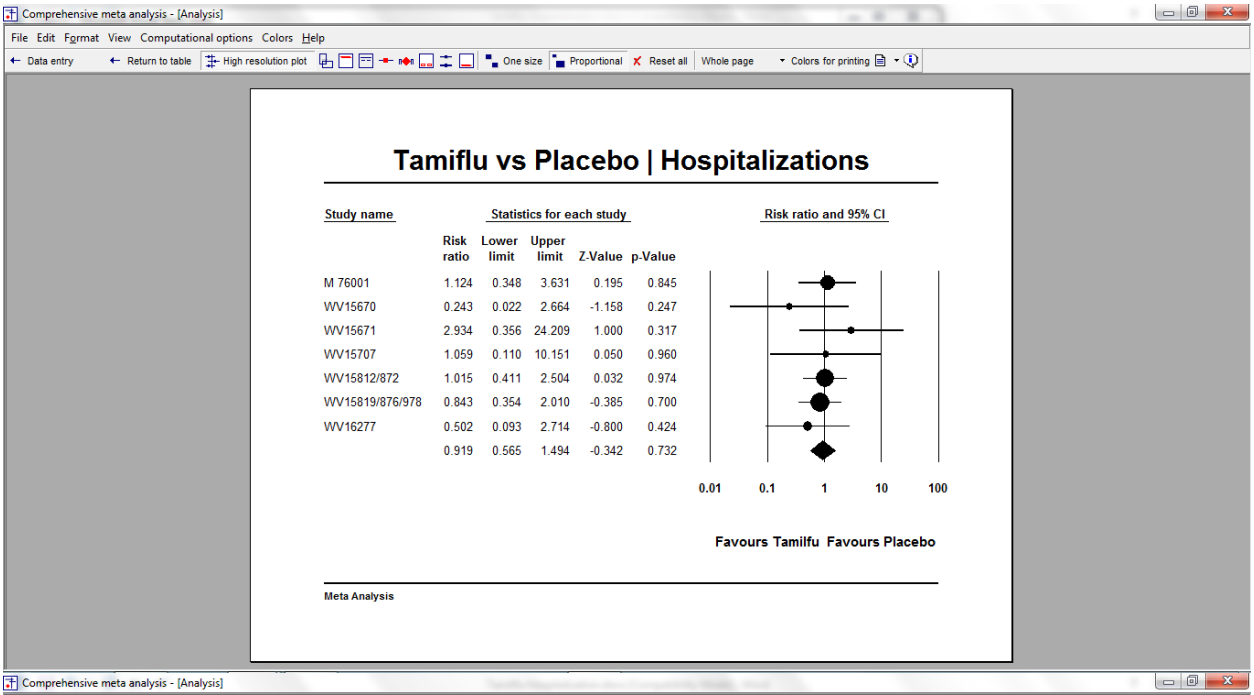
Click [Next table]





The statistics at the left duplicate those we saw on the prior screen.

- The summary effect is 0.919 with a CI of 0.565 to 1.494. The test of the null (that the true risk ratio is 1.0) yields a *Z*-value of −0.342 and a corresponding *p*-value of 0.732.
- The statistics at the upper right relate to the dispersion of effect sizes across studies. The Q-value is 3.054 with *df*=6 and *p*=0.802. *Q* reflects the distance of each study from the mean effect (weighted, squared, and summed over all studies). *Q* is always computed using FE weights (which is the reason it is displayed on the "Fixed" row, but applies to both FE and RE analyses.
- If all studies actually shared the same true effect size, the expected value of *Q* would be equal to df (which is 6). Here, *Q* is less than this value, and so there is no evidence of variance in true effects.
- I^2 is the proportion of the observed variance that reflects differences in true effects rather than sampling error. Since the variance in true effects is zero, I^2 must be zero.
- T^2 is the estimate of the between-study variance in true effects. *T* is the estimate of the between-study standard deviation in true effects. Since the variance in true effects is zero, both of these values must be zero. These value are both in log units.
- Click [Next table] to return to this screen


Comprehensive meta analysis - [Analysis]
File Edit Format View Computational options Colors Help
Data entry
Return to table
High resolution plot
One size
Proportional
Reset all
Whole page
Colors for printing
Tamiflu vs Placebo | Hospitalizations
Study name
Statistics for each study
Risk ratio and 95% CI
Risk ratio
Lower limit
Upper limit
Z-Value
p-Value
M 76001 1.124 0.348 3.631 0.195 0.845
WV15670 0.243 0.022 2.664 -1.158 0.247
WV15671 2.934 0.356 24.209 1.000 0.317
WV15707 1.059 0.110 10.151 0.050 0.960
WV15812/872 1.015 0.411 2.504 0.032 0.974
WV15819/876/978 0.843 0.354 2.010 -0.385 0.700
WV16277 0.502 0.093 2.714 -0.800 0.424
0.919 0.565 1.494 -0.342 0.732
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0.1
1
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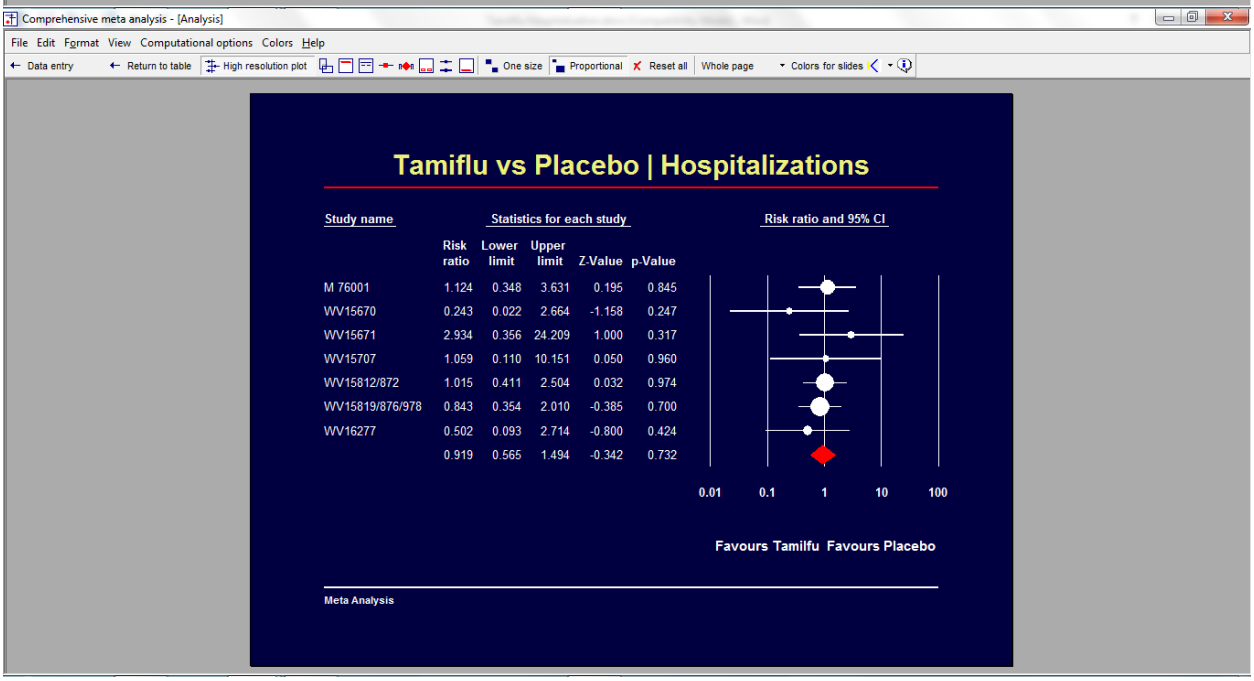
100
Favours Tamilfu
Favours Placebo
Meta Analysis


Comprehensive meta analysis - [Analysis]
File Edit Format View Computational options Colors Help
Data entry
Return to table
High resolution plot
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Tamiflu vs Placebo | Hospitalizations
Study name
Statistics for each study
Risk ratio and 95% CI
Risk ratio
Lower limit
Upper limit
Z-Value
p-Value
M 76001 1.124 0.348 3.631 0.195 0.845
WV15670 0.243 0.022 2.664 -1.158 0.247
WV15671 2.934 0.356 24.209 1.000 0.317
WV15707 1.059 0.110 10.151 0.050 0.960
WV15812/872 1.015 0.411 2.504 0.032 0.974
WV15819/876/978 0.843 0.354 2.010 -0.385 0.700
WV16277 0.502 0.093 2.714 -0.800 0.424
0.919 0.565 1.494 -0.342 0.732
0.01
0.1
1
10
100
Favours Tamilfu
Favours Placebo
Meta Analysis

Summary

Synopsis

This analysis includes seven studies where patients were randomized to receive either Tamiflu or placebo. Outcome was the proportion of patients hospitalized in each group. The effect size is the risk ratio.

Does Tamiflu affect the risk of hospitalization?

The mean risk ratio is 0.919, which means that being assigned to a Tamiflu rather than a placebo resulted in an 8% lower risk of being hospitalized. The 95% confidence interval for the risk ratio is 0.565 to 1.494. The Z-value for a test of the null is -0.342, with a corresponding *p*-value of 0.732.

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 risk ratio is 0.565 to 1.494, which tell us that the mean risk ratio in the universe of studies could fall anywhere in this range. This range includes a risk ratio of 1.0, which tells us that the mean risk ratio could be 1.0.

Similarly, the *Z*-value for testing the null hypothesis (that the mean risk ratio is 1.0) is -0.342, with a corresponding *p*-value of 0.732. We cannot reject the null that the risk of hospitalization is the same in both groups.

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 3.054 with 6 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 (in log units). Here, T^2 is zero. T is the standard deviation of true effects (in log units). Here, T is zero.