Example name	Statins by gender
Effect size	Risk ratio
Analysis type	Subgroups within study
Level	Intermediate
Reference	Cheung Figure 6

Synopsis

The goal of this review was to assess the impact of statins on stroke and mortality, and to see if the impact differed by subgroups. The analysis that follows looks at the impact of statins on major coronary events.

This analysis includes seven studies where patients were randomized to receive either a statins or a placebo. Outcome was the proportion of patients in each group suffering a major coronary event, and the effect size was the risk ratio.

Within each study patients were classified as being male or female. We ran an analysis to see if the impact of statins was greater (or smaller) for males vs. females.

We use this example to show

- How to enter data for independent subgroups within studies
- How to use study as the unit of analysis
- How to use subgroup as the unit of analysis
- How to compare the effect in different subgroups

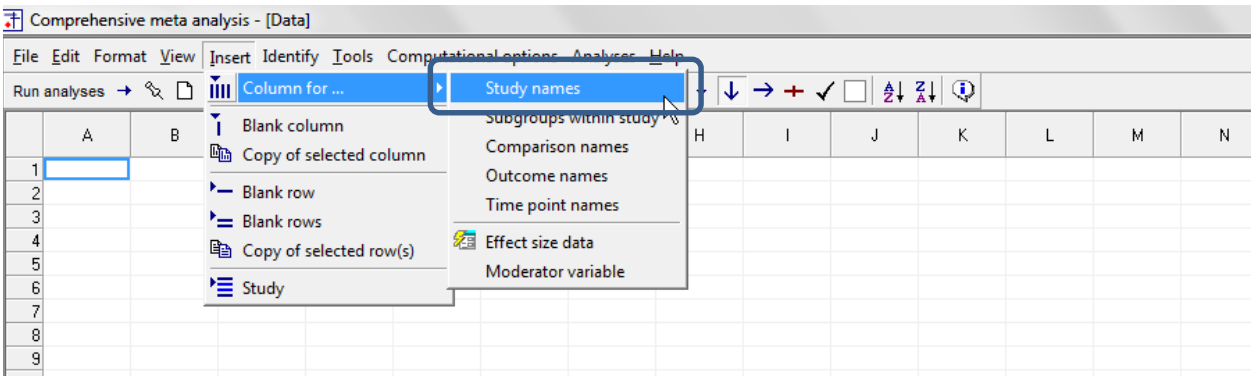
To open a CMA file > Download and Save file | Start CMA | Open file from within CMA

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

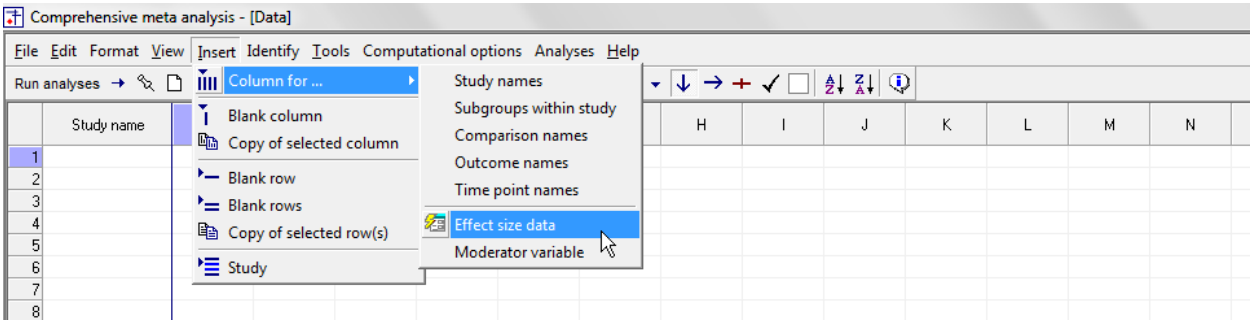
Download this PDF
Download data in Excel
Download trial of CMA

Start the program

- Select the option [Start a blank spreadsheet]
- Click [Ok]
- Click Insert > Column for > Study names

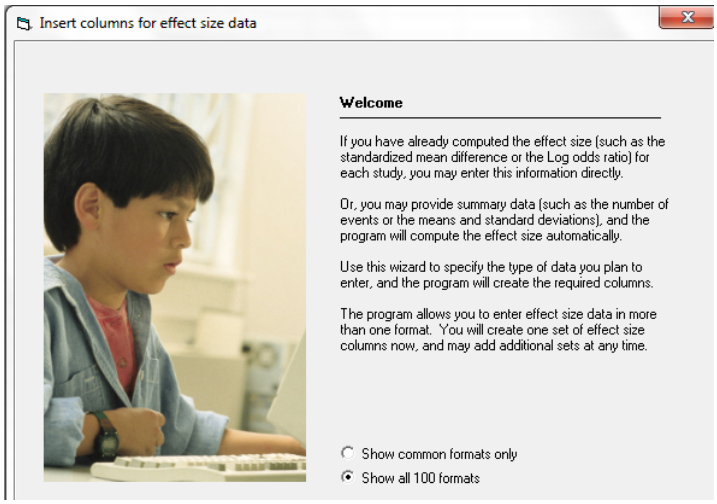


Click Insert > Column for > Effect size data

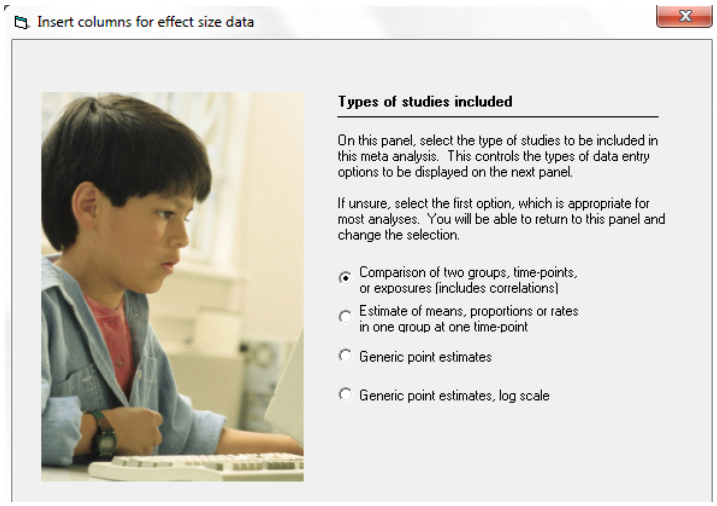


The program displays this wizard

Select [Show all 100 formats]
Click [Next]

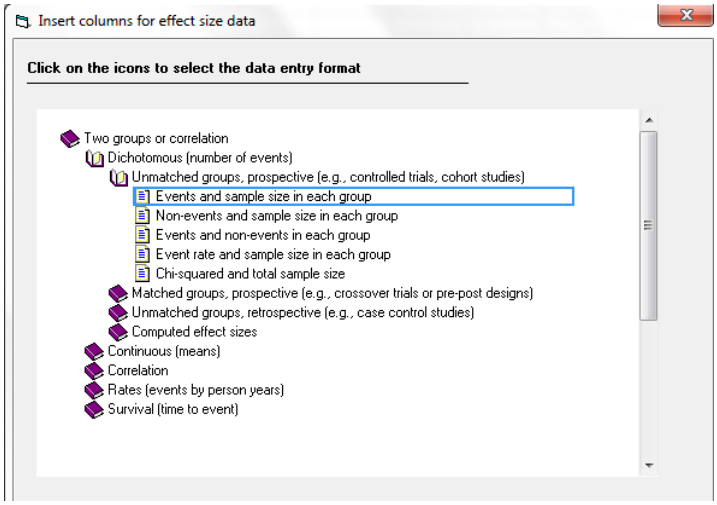


Select [Comparison of two groups…]
Click [Next]



Drill down to

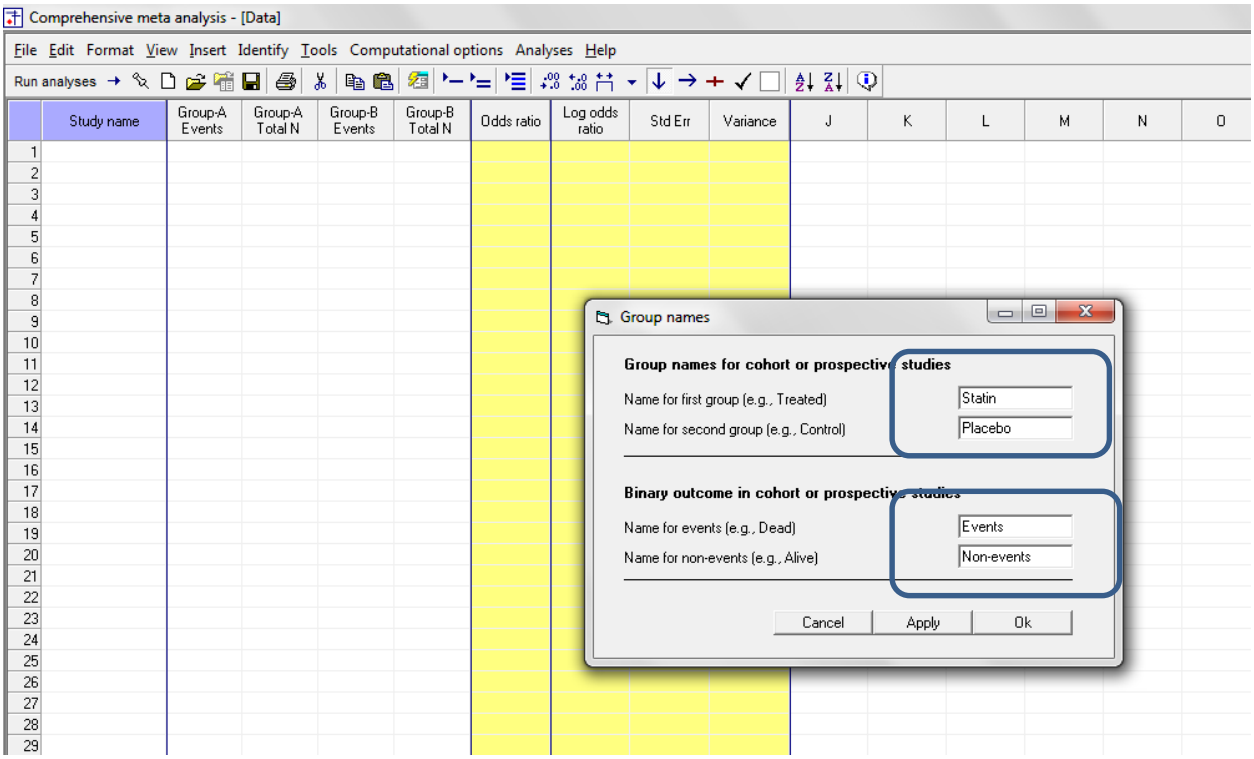
Dichotomous (number of events)
Unmatched groups, prospective …
Events and sample size in each group



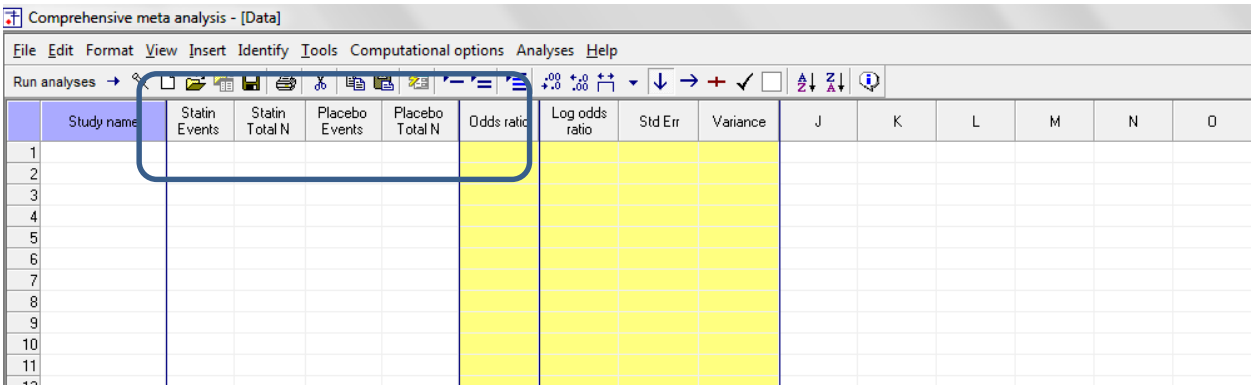
Enter the following labels into the wizard

- First group > Statin
- Second group > Control
- Name for events > Event
- Name for non-events > Ok

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



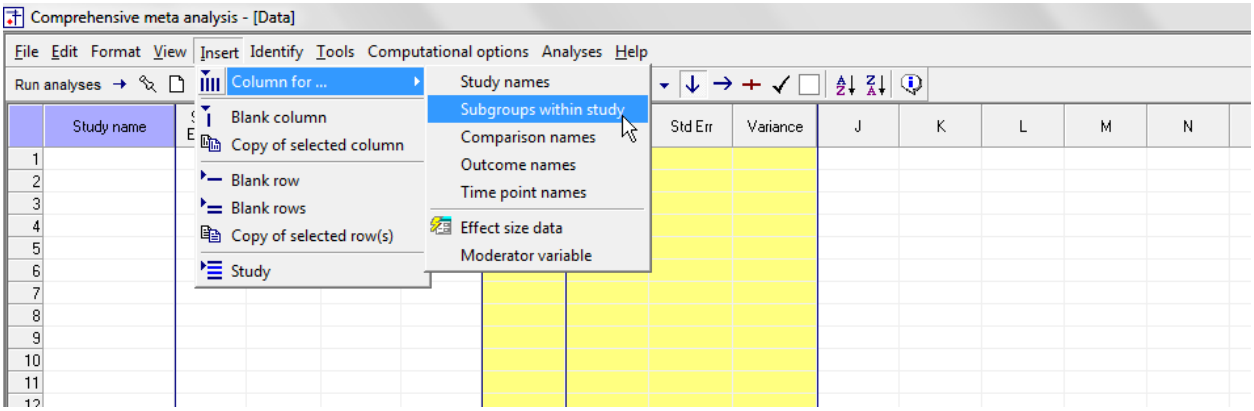
The screen should look like this



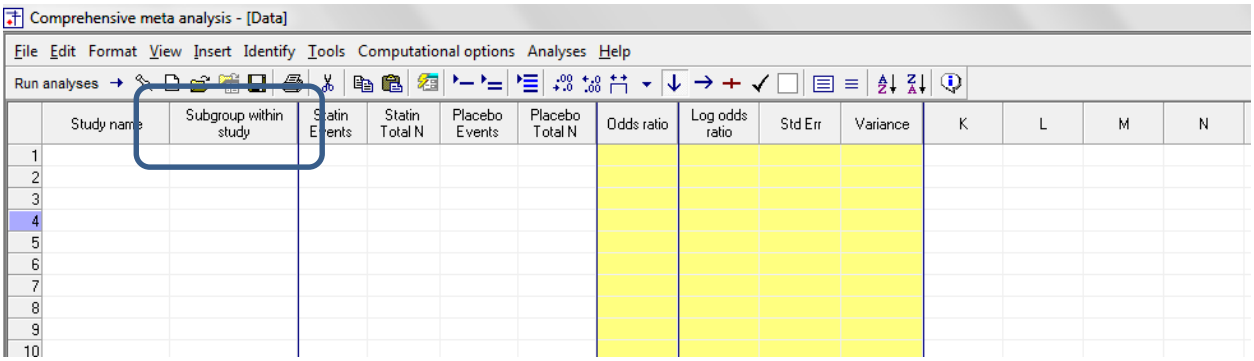
Every study will include data for two INDEPENDENT samples. That is, each person appears in one sample or the other, but not both.

The two samples are females and males. We will be using two rows for each study, and need a column that will identify the sample as non-smokers or smokers.

Click Insert > Column for > Subgroups within study

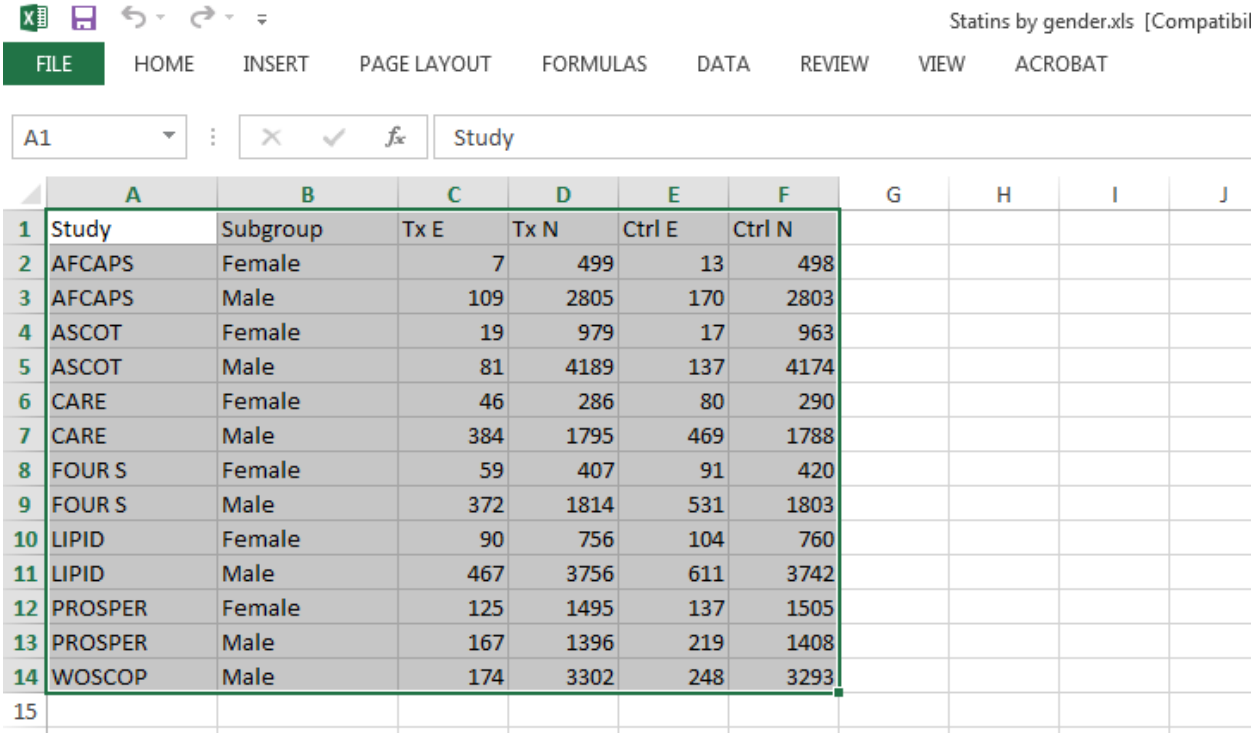


The screen should look like this



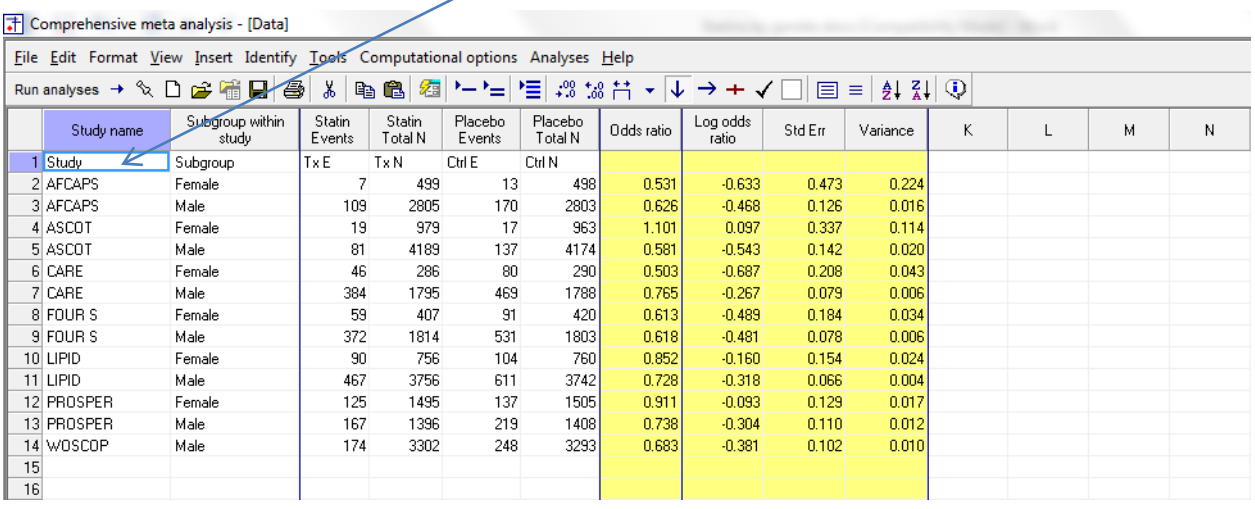
Rather than enter the data directly into CMA we will copy the data from Excel

- Switch to Excel and open the file “Statins by gender”
- Highlight the rows and columns as shown, and press CTRL-C to copy to clipboard



	A	B	C	D	E	F	G	H	I	J
1	Study	Subgroup	Tx E	Tx N	Ctrl E	Ctrl N				
2	AFCAPS	Female	7	499	13	498				
3	AFCAPS	Male	109	2805	170	2803				
4	ASCOT	Female	19	979	17	963				
5	ASCOT	Male	81	4189	137	4174				
6	CARE	Female	46	286	80	290				
7	CARE	Male	384	1795	469	1788				
8	FOUR S	Female	59	407	91	420				
9	FOUR S	Male	372	1814	531	1803				
10	LIPID	Female	90	756	104	760				
11	LIPID	Male	467	3756	611	3742				
12	PROSPER	Female	125	1495	137	1505				
13	PROSPER	Male	167	1396	219	1408				
14	WOSCOP	Male	174	3302	248	3293				
15										

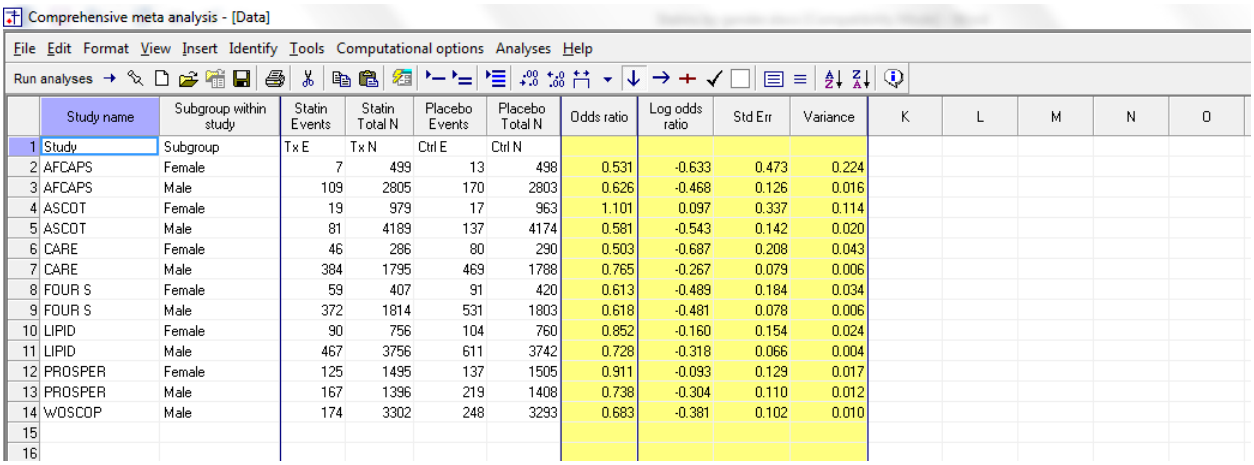
- Switch to CMA
- Click in cell Study-name 1
- Press [CTRL-V] to paste the data
- The screen should look like this



	Study name	Subgroup within study	Statin Events	Statin Total N	Placebo Events	Placebo Total N	Odds ratio	Log odds ratio	Std Err	Variance	K	L	M	N
1	Study	Subgroup	Tx E	Tx N	Ctrl E	Ctrl N								
2	AFCAPS	Female	7	499	13	498	0.531	-0.633	0.473	0.224				
3	AFCAPS	Male	109	2805	170	2803	0.626	-0.468	0.126	0.016				
4	ASCOT	Female	19	979	17	963	1.101	0.097	0.337	0.114				
5	ASCOT	Male	81	4189	137	4174	0.581	-0.543	0.142	0.020				
6	CARE	Female	46	286	80	290	0.503	-0.687	0.208	0.043				
7	CARE	Male	384	1795	469	1788	0.765	-0.267	0.079	0.006				
8	FOUR S	Female	59	407	91	420	0.613	-0.489	0.184	0.034				
9	FOUR S	Male	372	1814	531	1803	0.618	-0.481	0.078	0.006				
10	LIPID	Female	90	756	104	760	0.852	-0.160	0.154	0.024				
11	LIPID	Male	467	3756	611	3742	0.728	-0.318	0.066	0.004				
12	PROSPER	Female	125	1495	137	1505	0.911	-0.093	0.129	0.017				
13	PROSPER	Male	167	1396	219	1408	0.738	-0.304	0.110	0.012				
14	WOSCOP	Male	174	3302	248	3293	0.683	-0.381	0.102	0.010				
15														
16														

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

The column that had been called “Tx E” is now “Statin Events”. Similarly, all columns have the intended labels



	Study name	Subgroup within study	Statin Events	Statin Total N	Placebo Events	Placebo Total N	Odds ratio	Log odds ratio	Std Err	Variance	K	L	M	N	O
1	Study	Subgroup	Tx E	Tx N	Ctrl E	Ctrl N									
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6	CARE	Female	46	286	80	290	0.503	-0.687	0.208	0.043					
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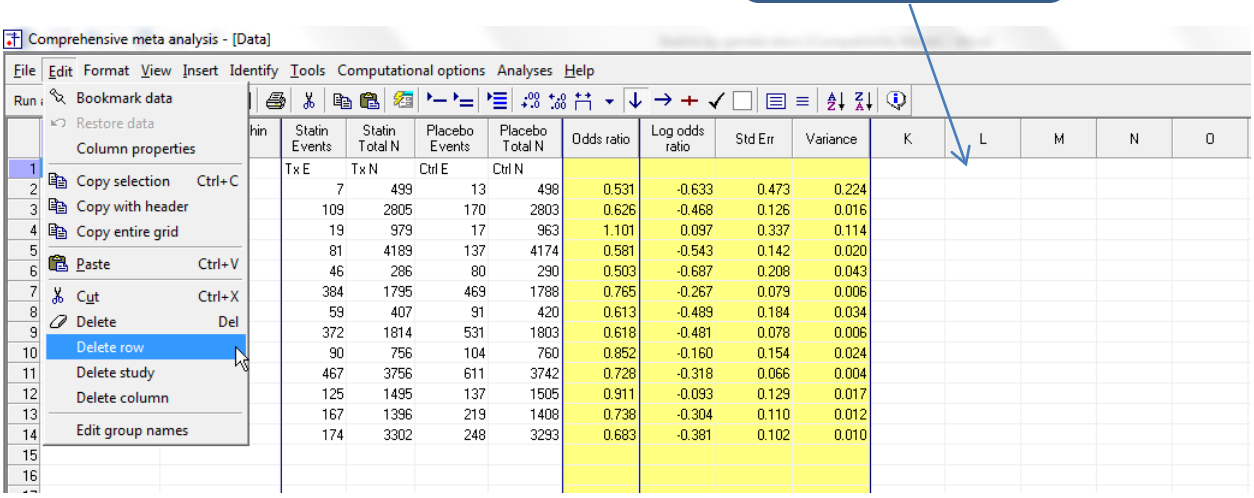
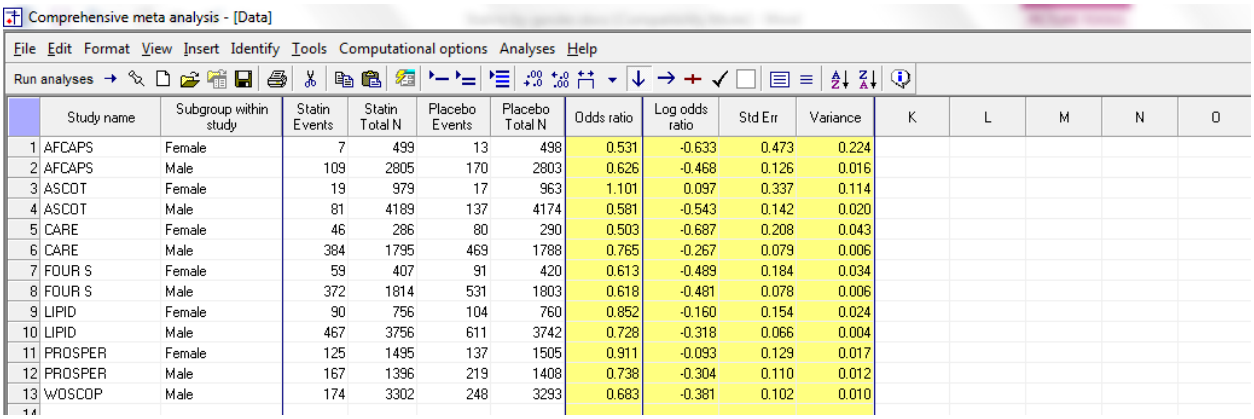
14	WOSCOP	Male	174	3302	248	3293	0.683	-0.381	0.102	0.010					
15															
16															

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



The screen should look like this



	Study name	Subgroup within study	Statin Events	Statin Total N	Placebo Events	Placebo Total N	Odds ratio	Log odds ratio	Std Err	Variance	K	L	M	N	O
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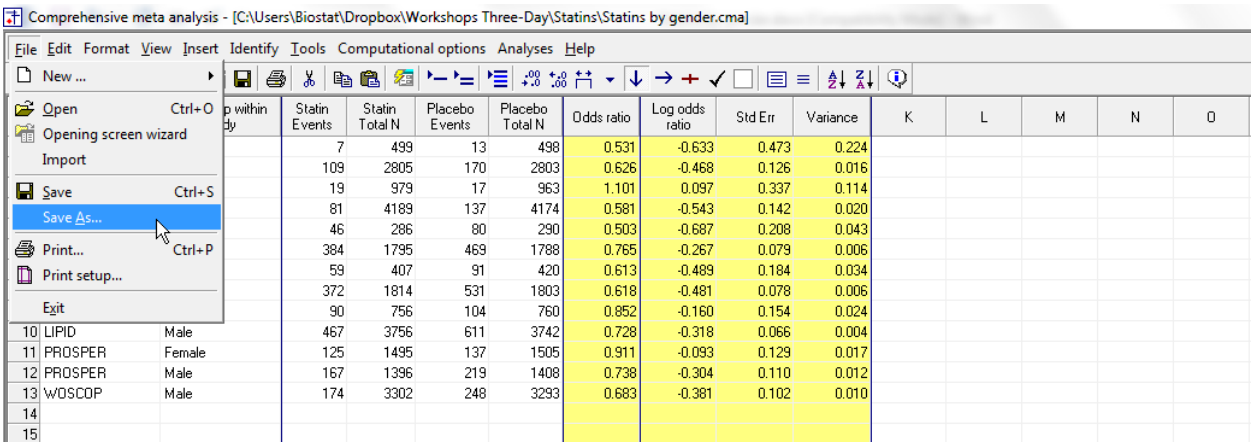
12	PROSPER	Male	167	1396	219	1408	0.738	-0.304	0.110	0.012					
13	WOSCOP	Male	174	3302	248	3293	0.683	-0.381	0.102	0.010					

Click File > Save As and save the file



	Study name	Subgroup within study	Statin Events	Statin Total N	Placebo Events	Placebo Total N	Odds ratio	Log odds ratio	Std Err	Variance	K	L	M	N	O
			7	499	13	498	0.531	-0.633	0.473	0.224					
			109	2805	170	2803	0.626	-0.468	0.126	0.016					
			19	979	17	963	1.101	0.097	0.337	0.114					
			81	4189	137	4174	0.581	-0.543	0.142	0.020					
			46	286	80	290	0.503	-0.687	0.208	0.043					
			384	1795	469	1788	0.765	-0.267	0.079	0.006					
			59	407	91	420	0.613	-0.489	0.184	0.034					
			372	1814	531	1803	0.618	-0.481	0.078	0.006					
			90	756	104	760	0.852	-0.160	0.154	0.024					
10	LIPID	Male	467	3756	611	3742	0.728	-0.318	0.066	0.004					
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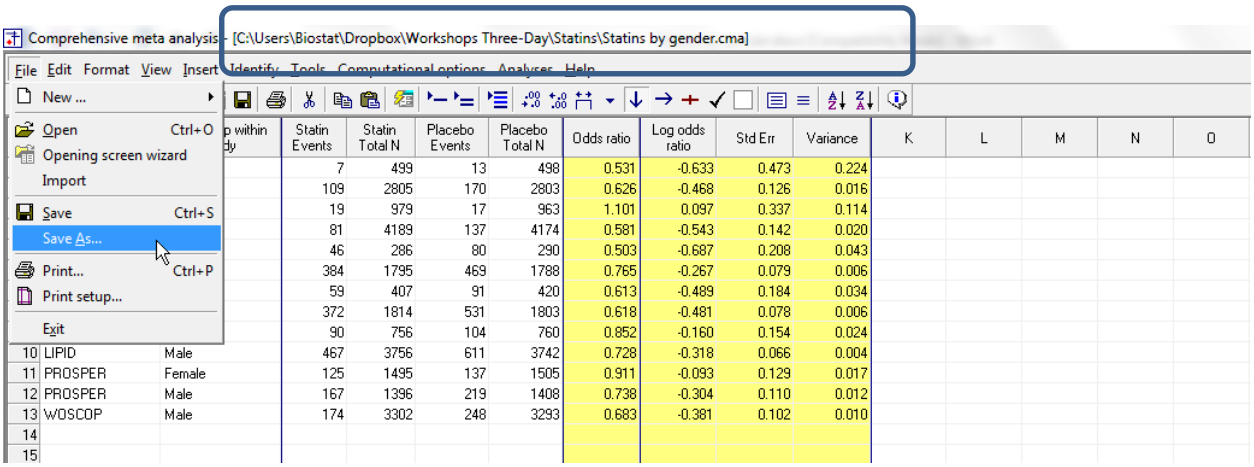
12	PROSPER	Male	167	1396	219	1408	0.738	-0.304	0.110	0.012					
13	WOSCOP	Male	174	3302	248	3293	0.683	-0.381	0.102	0.010					
14															
15															

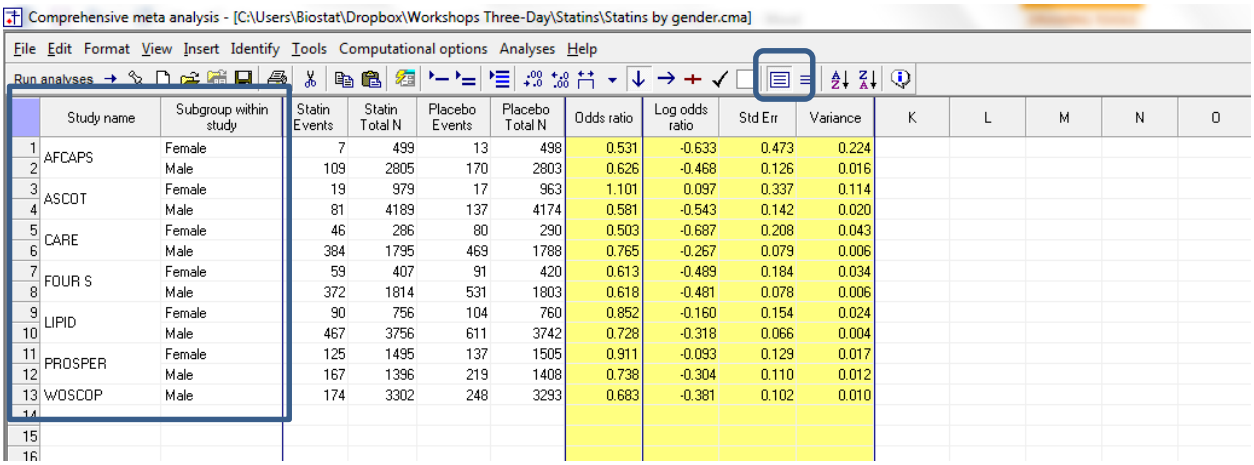
Note that the file name is now in the header.

- [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



- Click the Merge Rows icon

- The program will merge the study names for each study



	Study name	Subgroup within study	Statin Events	Statin Total N	Placebo Events	Placebo Total N	Odds ratio	Log odds ratio	Std Err	Variance
1	AFCAPS	Female	7	499	13	498	0.531	-0.633	0.473	0.224
2		Male	109	2805	170	2803	0.626	-0.468	0.126	0.016
3	ASCOT	Female	19	979	17	963	1.101	0.097	0.337	0.114
4		Male	81	4189	137	4174	0.581	-0.543	0.142	0.020
5	CARE	Female	46	286	80	290	0.503	-0.687	0.208	0.043
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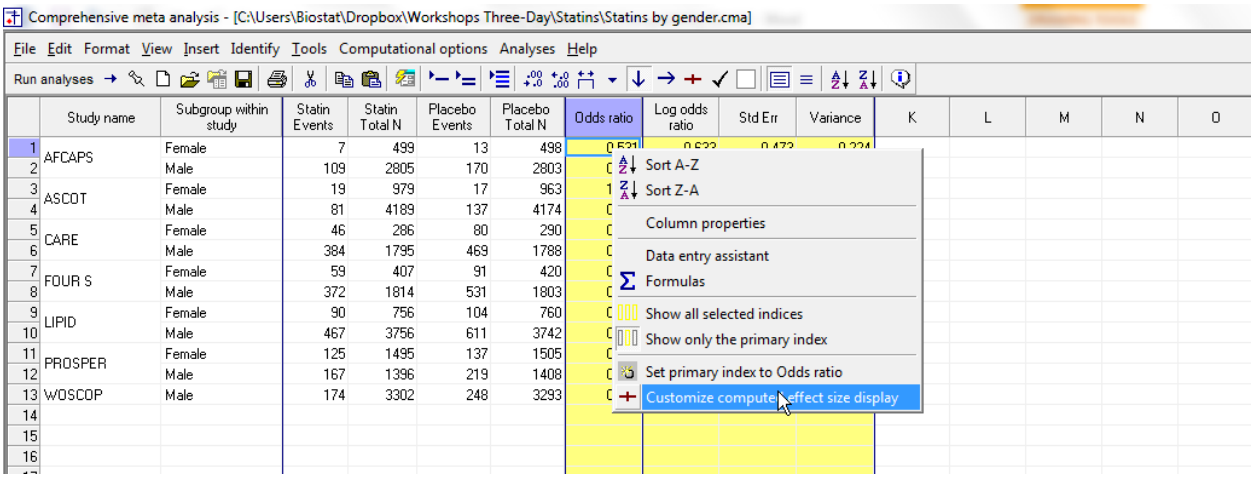
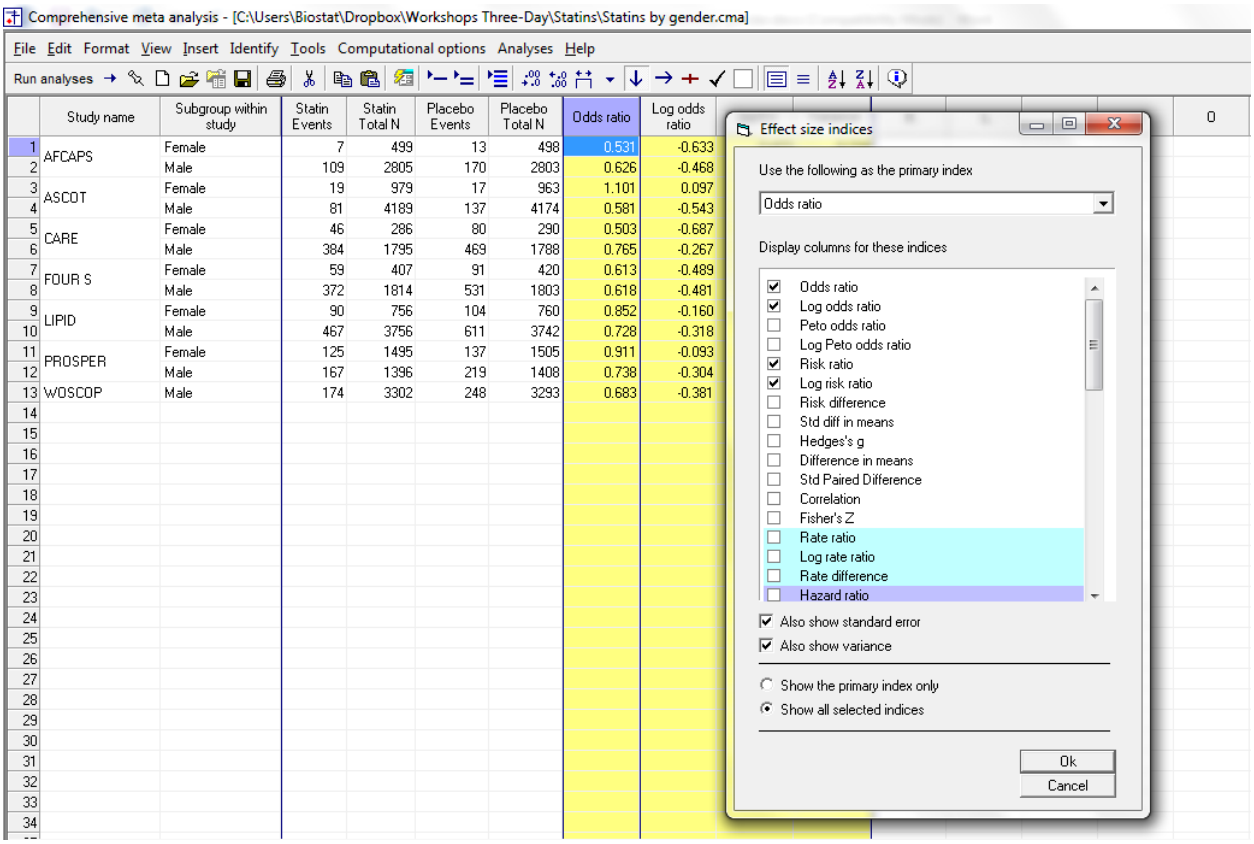
14										
15										
16										

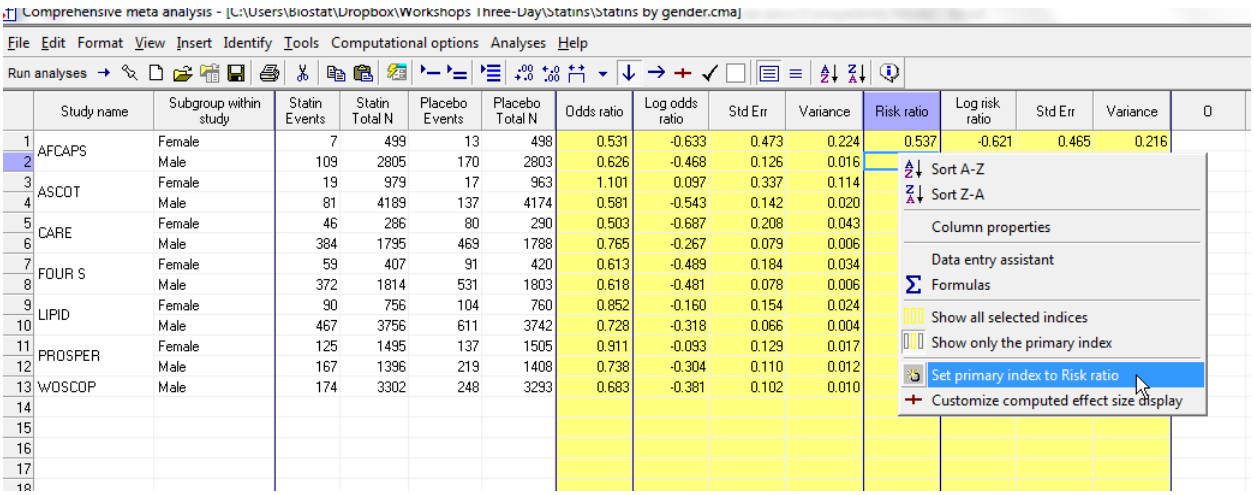
Right-click on the yellow columns and click [Customize computed effect size display]



Add Risk ratio and Log risk ratio to the display and click Ok



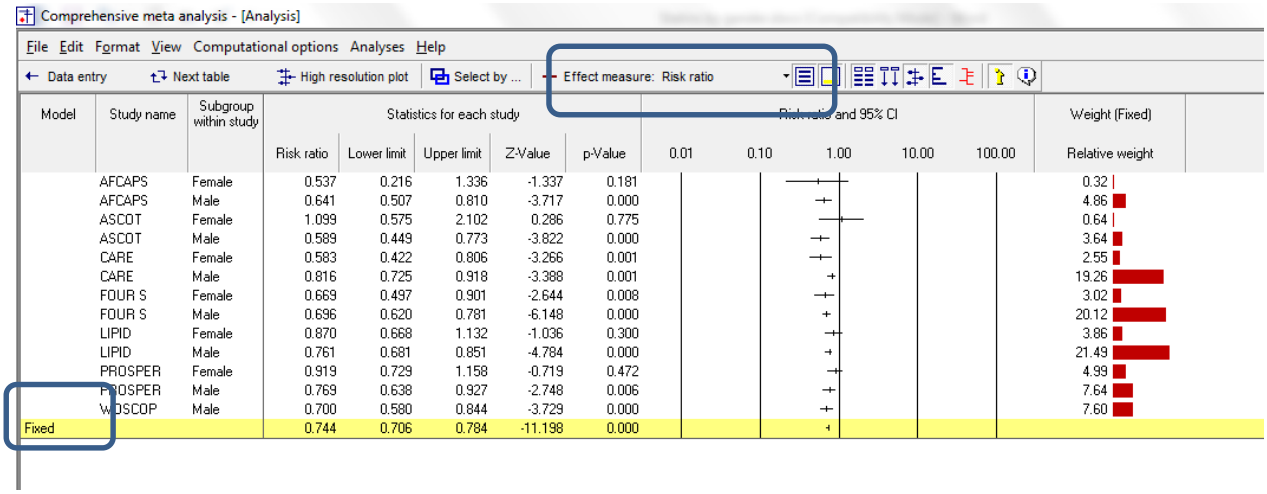
- Right-click on Risk ratio
- Click [Set primary index to Risk ratio]
- Click File > Save



Click [Run analysis]

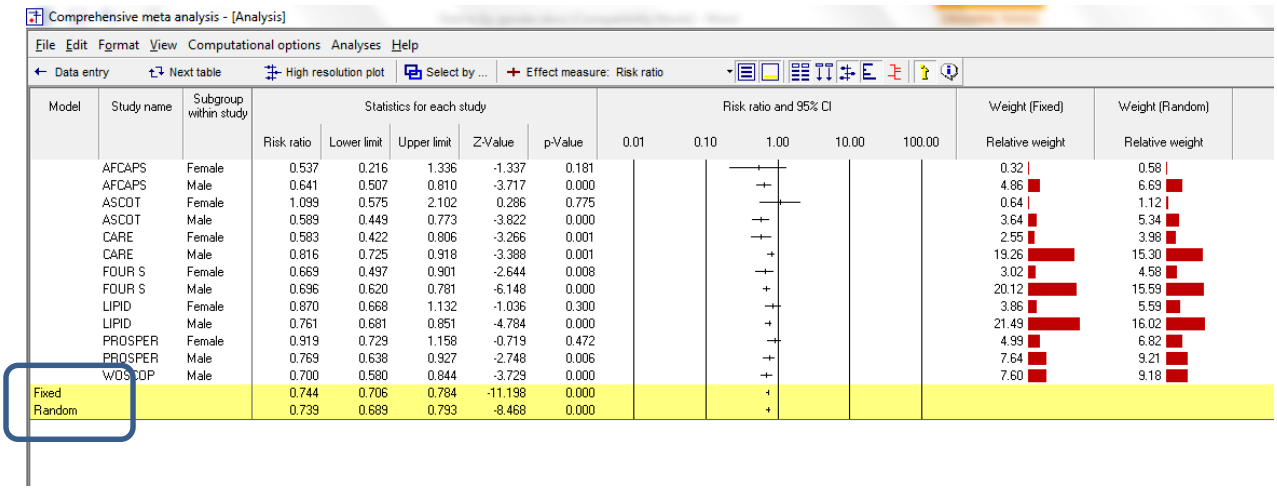
At this point we have the usual analysis, with a single set of studies. The two samples within each study are treated as two separate studies, since there is no overlap in the subjects.

This is the basic analysis screen, showing a fixed-effect analysis.



Click [Both models]

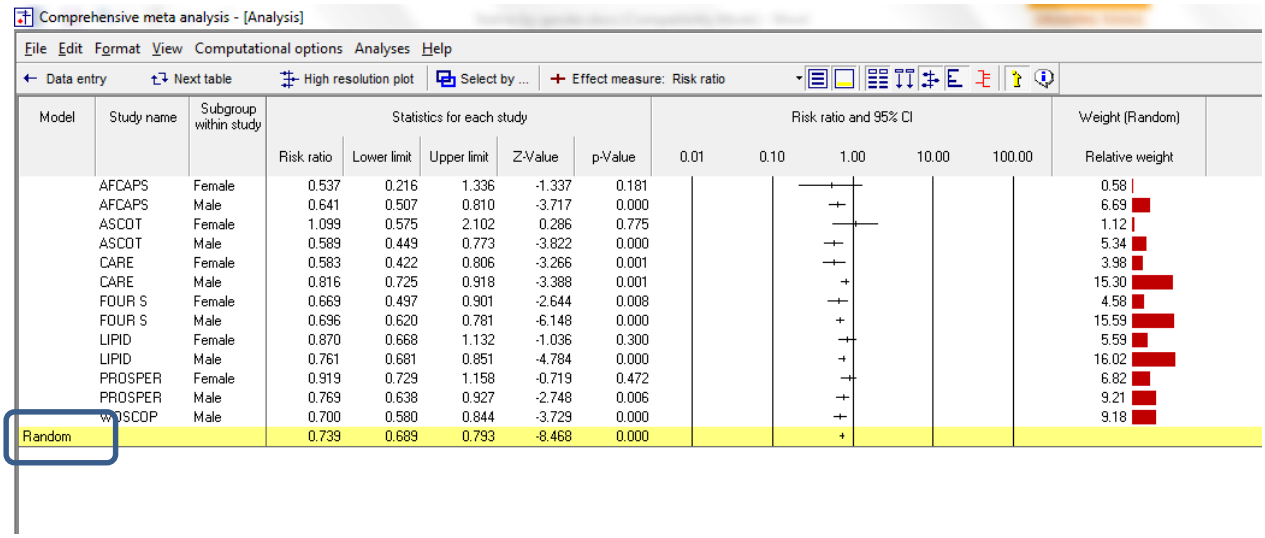
The program displays results for both the fixed-effect and the random-effects analysis.



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.

- Click Random on the tab at the bottom

The plot now displays the random-effects analysis alone.

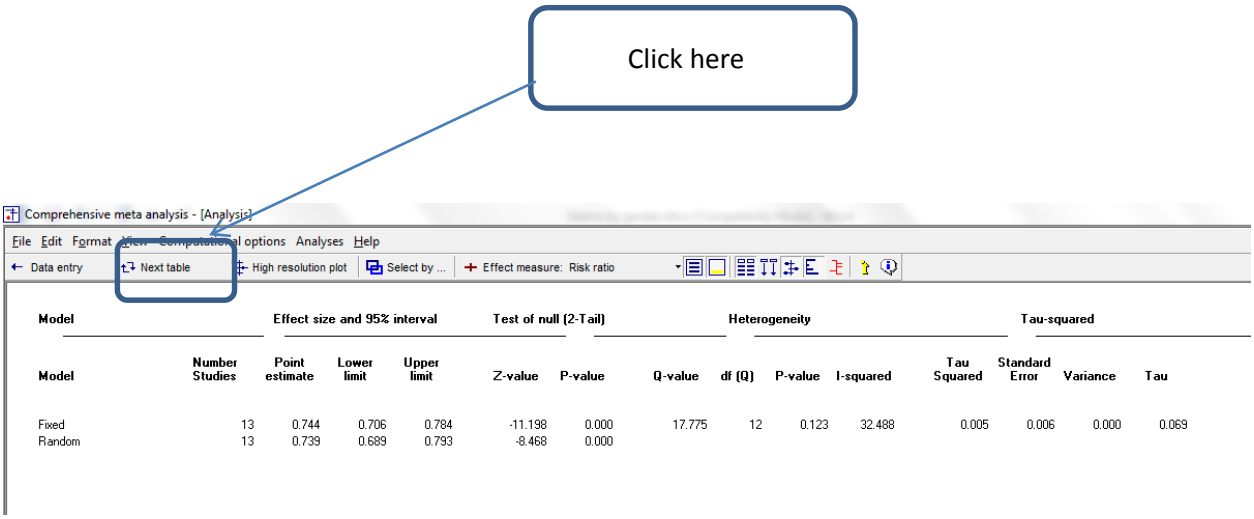


Model	Study name	Subgroup within study	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	Weight (Random)
	AFCAPS	Female	0.537	0.216	1.336	-1.337	0.181	0.58
	AFCAPS	Male	0.641	0.507	0.810	-3.717	0.000	6.69
	ASCOT	Female	1.099	0.575	2.102	0.286	0.775	1.12
	ASCOT	Male	0.589	0.449	0.773	-3.822	0.000	5.34
	CARE	Female	0.583	0.422	0.806	-3.266	0.001	3.98
	CARE	Male	0.816	0.725	0.918	-3.388	0.001	15.30
	FOUR S	Female	0.669	0.497	0.901	-2.644	0.008	4.58
	FOUR S	Male	0.696	0.620	0.781	-6.148	0.000	15.59
	LIPID	Female	0.870	0.668	1.132	-1.036	0.300	5.59
	LIPID	Male	0.761	0.681	0.851	-4.784	0.000	16.02
	PROSPER	Female	0.919	0.729	1.158	-0.719	0.472	6.82
	PROSPER	Male	0.769	0.638	0.927	-2.748	0.006	9.21
	WOSCOP	Male	0.700	0.580	0.844	-3.729	0.000	9.18
Random			0.739	0.689	0.793	-8.468	0.000	

A quick view of the plot suggests the following

- All of the studies suggest an advantage for statins over placebo
- The observed effect sizes fall within a relatively narrow range.
- The summary effect is 0.7389 with a CI of 0.689 to 0.793. Thus, the mean effect is in the clinically important range.
- The summary effect has a Z-value −8.468 and a *p*-value of < 0.001. Thus we can reject the null hypotheses that the true risk ratio is 1.0.

Click [Next table]



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

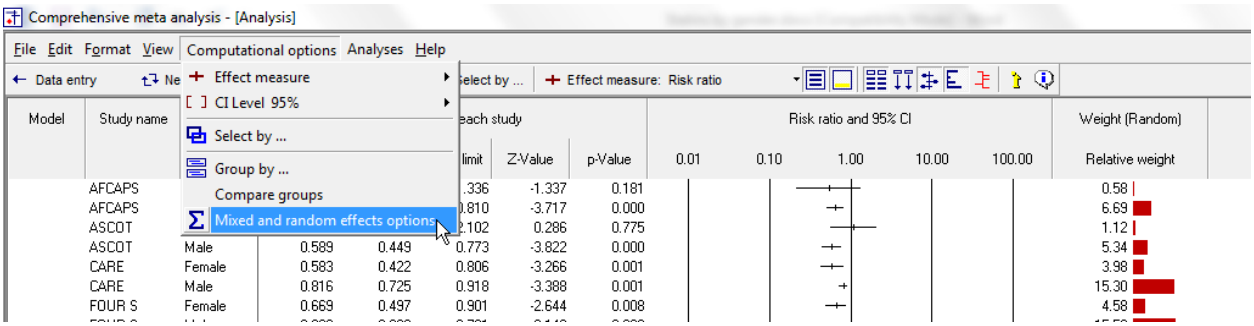
- Under the random-effects model the summary effect is 0.739 with a CI of 0.689 to 0.793. Thus, the mean effect is in the clinically important range.
- The summary effect has a Z-value −8.468 and a *p*-value of < 0.001. Thus we can reject the null hypotheses that the true risk ratio is 1.0.
- The statistics at the upper right relate to the dispersion of effect sizes across studies.
- The Q-value is 17.775 with df=12 and p=0.123. *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.
- T^2 is the estimate of the between-study variance in true effects. This estimate (in log units) is 0.005. *T* is the estimate of the between-study standard deviation in true effects. This estimate (in log units) is 0.069.
- I^2 reflects the proportion of true variance to observed variance. I^2 is 32.488, which means that about 32% of the variance on observed effects reflects variance in true effects. The remaining 68% is attributed to sampling error, and would probably disappear if the sample sizes were large enough.
- Click [Next table] to return to this screen

In this analysis we want to focus on the treatment effect as a function of smoking. Specifically, we're going to run the analysis separately (a) for females and (b) for males.

When we're dividing the studies into two subgroups, the between-studies variance (T^2) must be computed within subgroups. However, we have two options. We can then pool the separate estimates, and use the pooled value for all subgroups. Or, we can use a separate estimate for each subgroup.

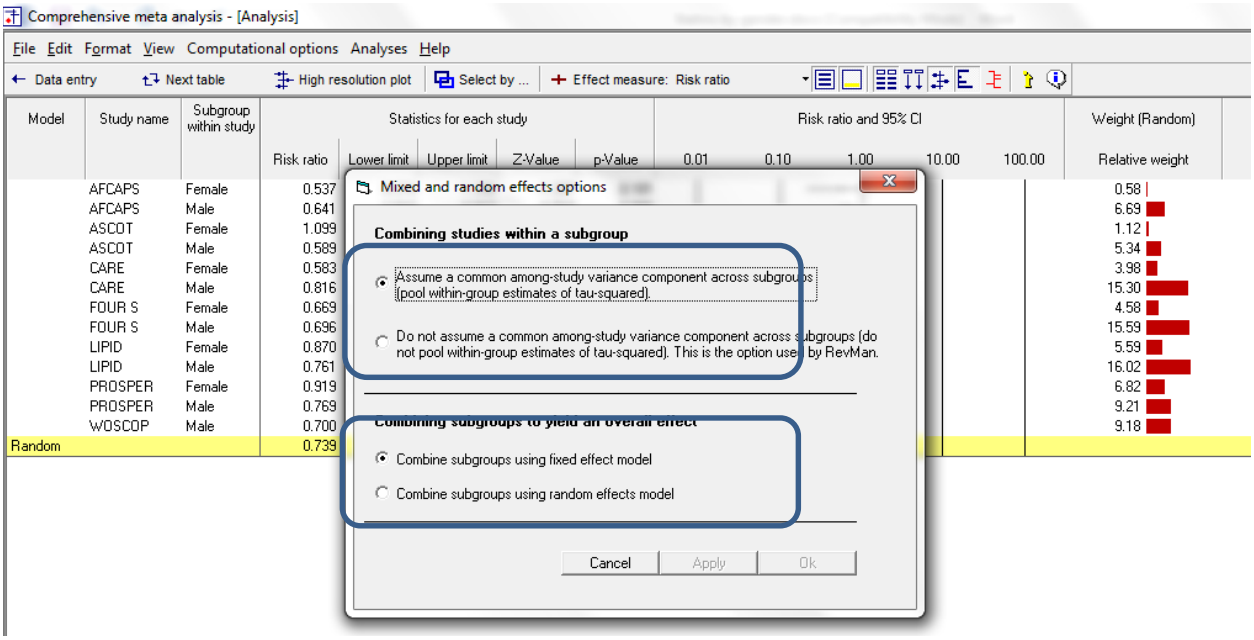
Our plan at the moment is to pool the two estimates. To select that option

Click Computational options > Mixed and random effects options



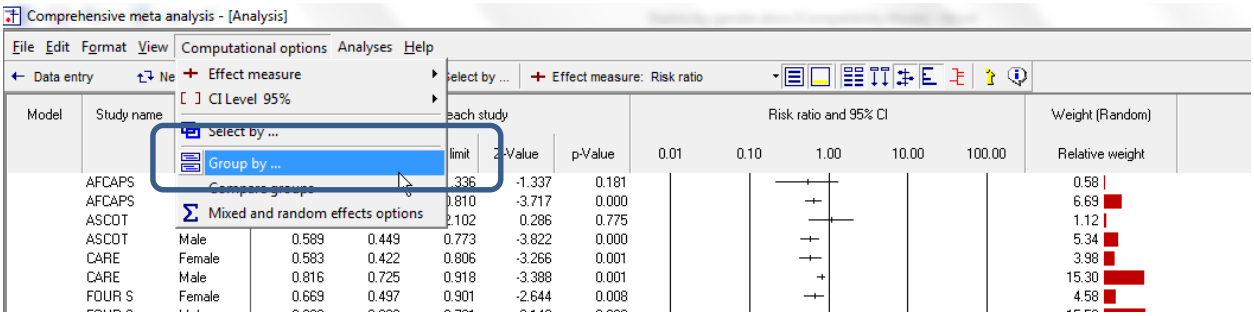
The program displays this wizard

- At the top select the first option, to "Assume a common among-study variance"
- At the bottom select the first option, to "Combine subgroups using a fixed-effect model"

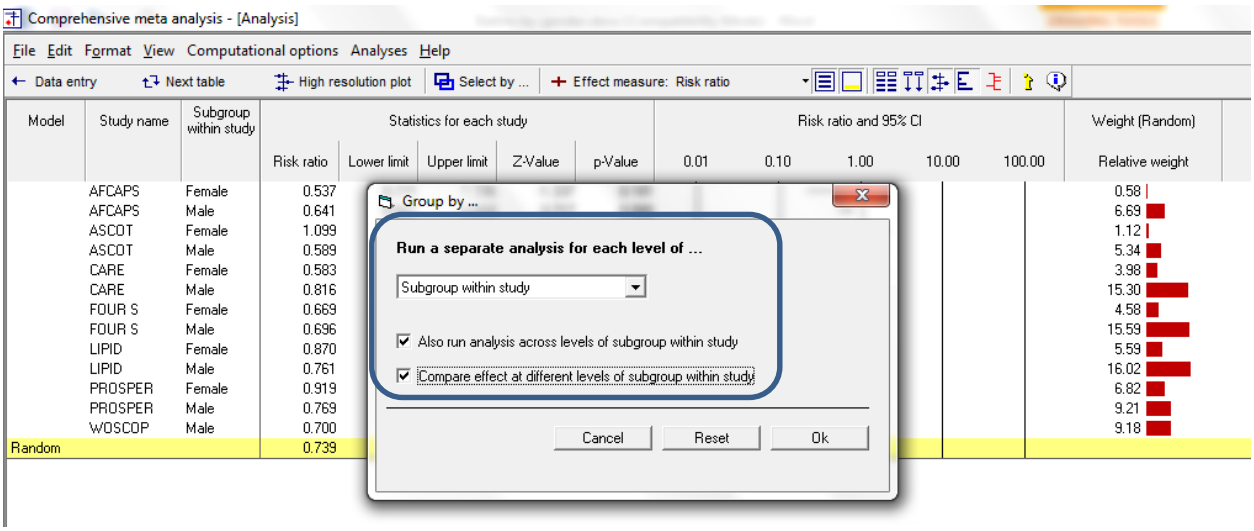


Now, we can tell the program to run the analysis by subgroups.

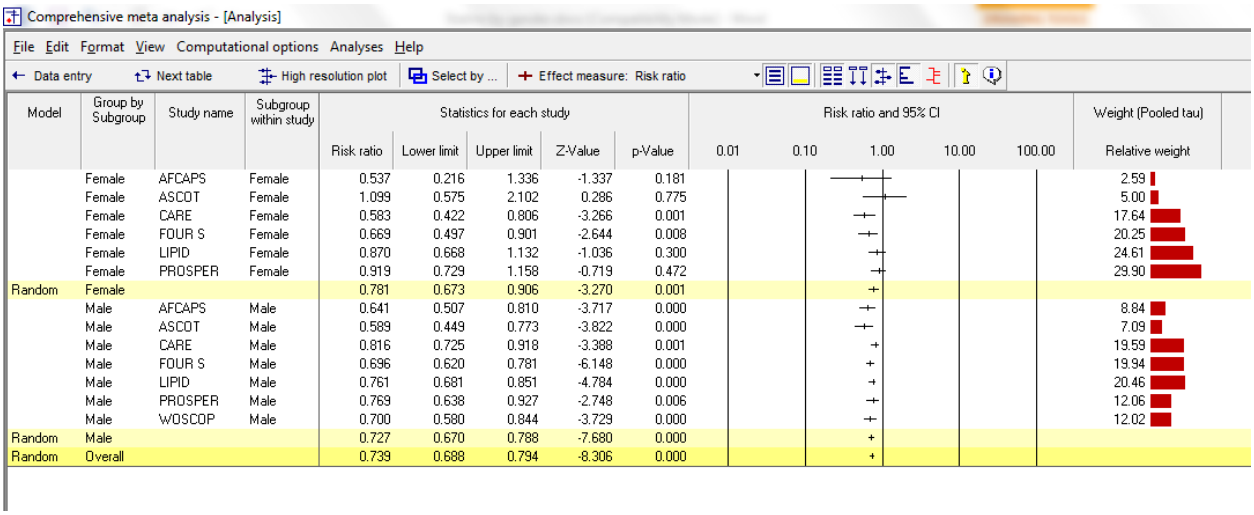
Click Computational options > Group by



- Select Subgroup within study
- Check the two boxes
- Click Ok



The screen should look like this



Model	Group by Subgroup	Study name	Subgroup within study	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
	Female	AFCAPS	Female	0.537	0.216	1.336	-1.337	0.181	2.59
	Female	ASCOT	Female	1.099	0.575	2.102	0.286	0.775	5.00
	Female	CARE	Female	0.583	0.422	0.806	-3.266	0.001	17.64
	Female	FOUR S	Female	0.669	0.497	0.901	-2.644	0.008	20.25
	Female	LIPID	Female	0.870	0.668	1.132	-1.036	0.300	24.61
	Female	PROSPER	Female	0.919	0.729	1.158	-0.719	0.472	29.90
Random	Female			0.781	0.673	0.906	-3.270	0.001	
	Male	AFCAPS	Male	0.641	0.507	0.810	-3.717	0.000	8.84
	Male	ASCOT	Male	0.589	0.449	0.773	-3.822	0.000	7.09
	Male	CARE	Male	0.816	0.725	0.918	-3.388	0.001	19.59
	Male	FOUR S	Male	0.696	0.620	0.781	-6.148	0.000	19.94
	Male	LIPID	Male	0.761	0.681	0.851	-4.784	0.000	20.46
	Male	PROSPER	Male	0.769	0.638	0.927	-2.748	0.006	12.06
	Male	WOSCOP	Male	0.700	0.580	0.844	-3.729	0.000	12.02
Random	Male			0.727	0.670	0.788	-7.680	0.000	
Random	Overall			0.739	0.688	0.794	-8.306	0.000	

Risk ratio and 95% CI: 0.01 0.10 1.00 10.00 100.00

Weight (Pooled tau)

For Females the mean effect size is a risk ratio of 0.781 with a confidence interval of 0.673 to 0.906, a Z-value of −3.270 and a corresponding p-value of < 0.001. It's clear that the statins are more effective than placebo, and that the impact is clinically as well as statistically significant.

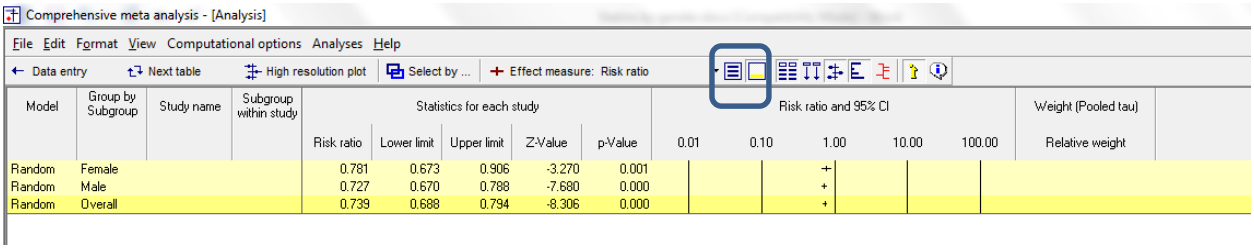
For Males the mean effect size is a risk ratio of 0.727 with a confidence interval of 0.670 to 0.798, a Z-value of −7.680 and a corresponding p-value of < 0.001. It's clear that the statins are more effective than placebo, and that the impact is clinically as well as statistically significant.

For all samples together the mean effect size is a risk ratio of 0.739 with a confidence interval of 0.688 to 0.794, a Z-value of −8.306 and a corresponding p-value of < 0.001.

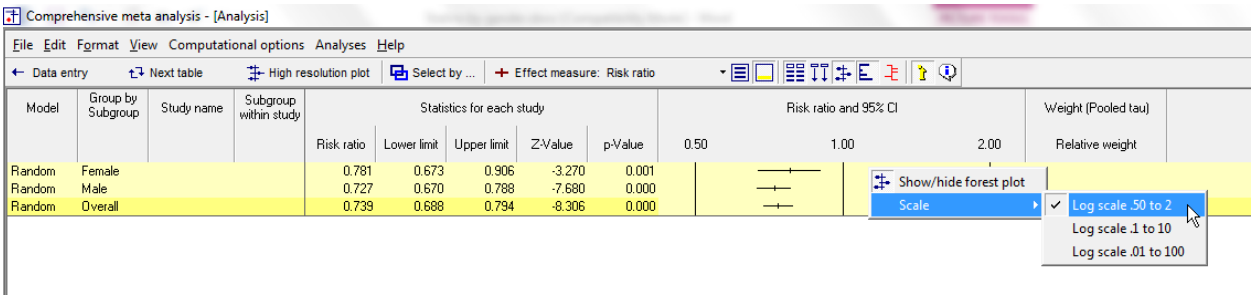
We want to know if the difference between the two effect sizes (0.781 vs. 0.727) is statistically significant, and we'll run a test for this.

To get a better sense of what we're testing, click the "All studies" button. This will hide all of the individual studies and display the summary effects only as shown here.

The test will compare the two mean effects relative to the precision of each effect. For two groups we can think of this as a Z-test for the ratio of the difference in means to the standard error of the difference.



Expand the scale for detail

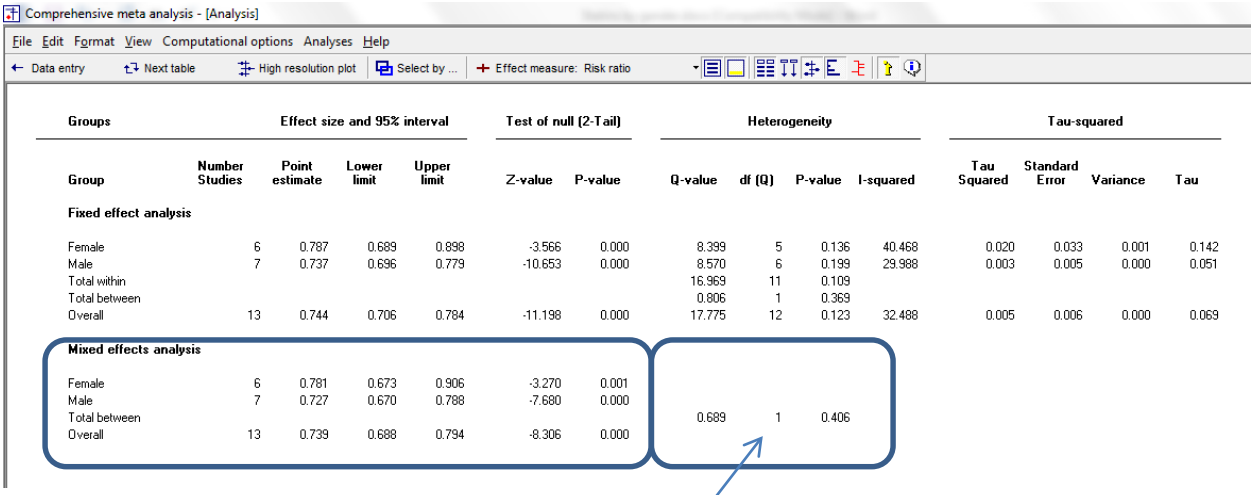


- Re-set the scale
- Toggle the "All studies button" to display the studies again.
- Click Next Table to see the results

The top section of the page (labeled Fixed-effect analysis) is for an analysis where we compute the summary effect in each group using FE weights, and then compare these values

The bottom section of the page (Mixed-effects analysis) is for an analysis where we compute the summary effect for each group using RE weights, and then compare these values.

We want to use the bottom section. The RE model is a better fit for the way the studies were sampled, and so this is the appropriate analysis.



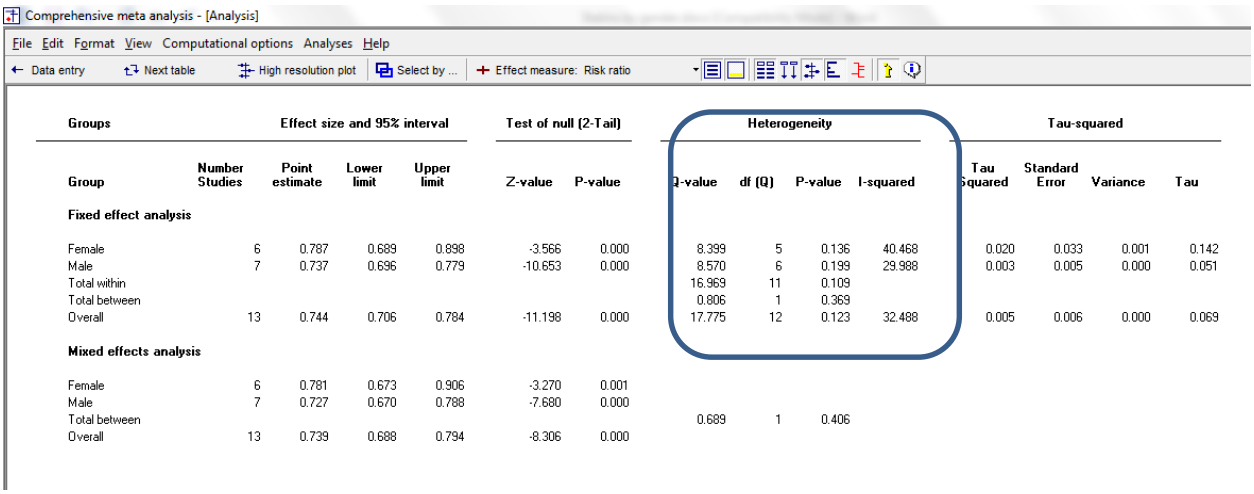
Groups		Effect size and 95% interval			Test of null (2-Tail)		Heterogeneity				Tau-squared			
Group	Number Studies	Point estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed effect analysis														
Female	6	0.787	0.689	0.898	-3.566	0.000	8.399	5	0.136	40.468	0.020	0.033	0.001	0.142
Male	7	0.737	0.696	0.779	-10.653	0.000	8.570	6	0.199	29.988	0.003	0.005	0.000	0.051
Total within							16.969	11	0.109					
Total between							0.806	1	0.369					
Overall	13	0.744	0.706	0.784	-11.198	0.000	17.775	12	0.123	32.488	0.005	0.006	0.000	0.069
Mixed effects analysis														
Female	6	0.781	0.673	0.906	-3.270	0.001								
Male	7	0.727	0.670	0.788	-7.680	0.000								
Total between							0.689	1	0.406					
Overall	13	0.739	0.688	0.794	-8.306	0.000								

Toward the left of the screen the program displays the same numbers we saw a moment ago.

For Females the mean effect size is a risk ratio of 0.781 with a confidence interval of 0.673 to 0.906, a Z-value of −3.270 and a corresponding p-value of < 0.001. It's clear that the statins are more effective than placebo, and that the impact is clinically as well as statistically significant.

For Males the mean effect size is a risk ratio of 0.727 with a confidence interval of 0.670 to 0.788, a Z-value of −7.680 and a corresponding p-value of < 0.001. It's clear that the statins are more effective than placebo, and that the impact is clinically as well as statistically significant.

The test to compare the two effect sizes (0.781 vs. 0.727) yields a Q-value of 0.689 with 1 df and a corresponding p-value of 0.406.



Groups		Effect size and 95% interval			Test of null (2-Tail)		Heterogeneity				Tau-squared			
Group	Number Studies	Point estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed effect analysis														
Female	6	0.787	0.689	0.898	-3.566	0.000	8.399	5	0.136	40.468	0.020	0.033	0.001	0.142
Male	7	0.737	0.696	0.779	-10.653	0.000	8.570	6	0.199	29.988	0.003	0.005	0.000	0.051
Total within							16.969	11	0.109					
Total between							0.806	1	0.369					
Overall	13	0.744	0.706	0.784	-11.198	0.000	17.775	12	0.123	32.488	0.005	0.006	0.000	0.069
Mixed effects analysis														
Female	6	0.781	0.673	0.906	-3.270	0.001								
Male	7	0.727	0.670	0.788	-7.680	0.000								
Total between							0.689	1	0.406					
Overall	13	0.739	0.688	0.794	-8.306	0.000								

Toward the right of the screen the program displays information about between-study heterogeneity. As was true for the single-group of studies, these statistics are based on FE weights and are therefore displayed in the top section, but they apply to the RE analysis as well.

For Females the variance in effects yields a Q-value of 8.399, with 5 df and p=0.136. Therefore, there is no evidence of dispersion in true effects among the studies that enrolled females.

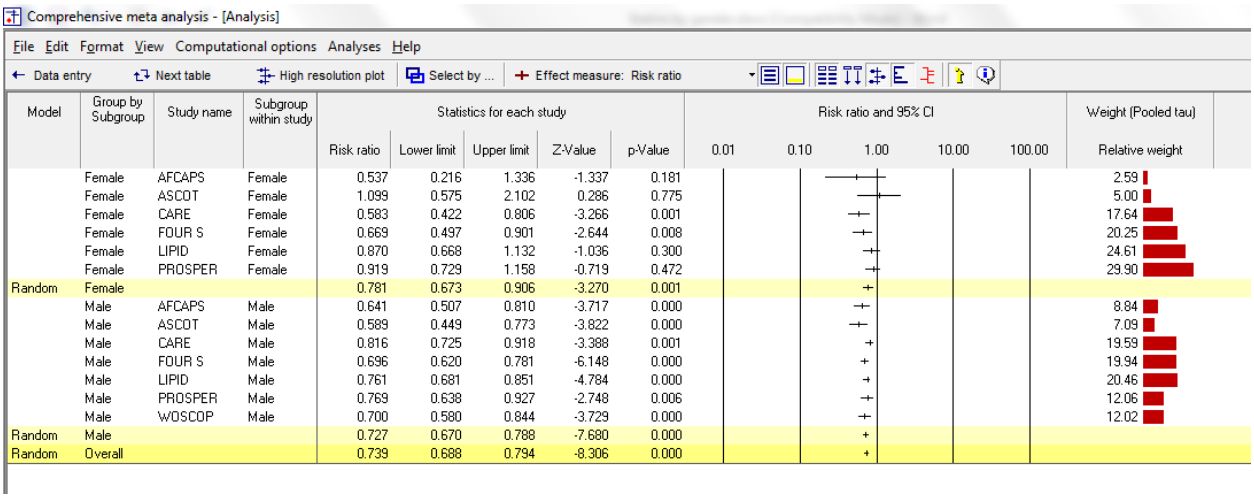
For Males the variance in effects yields a Q-value of 8.570 with 6 df and p=0.199. Therefore, there is no evidence of dispersion in true effects among the studies that enrolled males

We can also perform an omnibus test by pooling the Q values and df across subgroups. The pooled Q is 16.969 with 11 df and p=0.109. The conventional level for significance of heterogeneity is 0.10, and this is very close to that level.

These tests are goodness-of-fit tests. They ask if the grouping (Females vs. Males) explains all of the variance in true effect sizes, or if some true variance remains, even within subgroups. Here (based on the p-value of 0.109), there is evidence of true variance within subgroups.

Note that the tests of homogeneity are displayed in the fixed-effect section, even though we're using the random-effects model within subgroups. This is because these tests always are always based on using within-study (fixed-effect) weights. That is, we pose the null (that T^2 is zero) and then see is the variance is consistent with the null.

Click Next table to return to this screen.



Model	Group by Subgroup	Study name	Subgroup within study	Statistics for each study					Risk ratio and 95% CI					Weight (Pooled tau)
				Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00	Relative weight
	Female	AFCAPS	Female	0.537	0.216	1.336	-1.337	0.181						2.59
	Female	ASCOT	Female	1.099	0.575	2.102	0.286	0.775						5.00
	Female	CARE	Female	0.583	0.422	0.806	-3.266	0.001						17.64
	Female	FOUR S	Female	0.669	0.497	0.901	-2.644	0.008						20.25
	Female	LIPID	Female	0.870	0.668	1.132	-1.036	0.300						24.61
	Female	PROSPER	Female	0.919	0.729	1.158	-0.719	0.472						29.90
Random	Female			0.781	0.673	0.906	-3.270	0.001						
	Male	AFCAPS	Male	0.641	0.507	0.810	-3.717	0.000						8.84
	Male	ASCOT	Male	0.589	0.449	0.773	-3.822	0.000						7.09
	Male	CARE	Male	0.816	0.725	0.918	-3.388	0.001						19.59
	Male	FOUR S	Male	0.696	0.620	0.781	-6.148	0.000						19.94
	Male	LIPID	Male	0.761	0.681	0.851	-4.784	0.000						20.46
	Male	PROSPER	Male	0.769	0.638	0.927	-2.748	0.006						12.06
	Male	WOSCOP	Male	0.700	0.580	0.844	-3.729	0.000						12.02
Random	Male			0.727	0.670	0.788	-7.680	0.000						
Random	Overall			0.739	0.688	0.794	-8.306	0.000						

To this point, the analysis where each study provided data for two subgroups was identical to the analysis we would have performed if each row of data came from a different study.

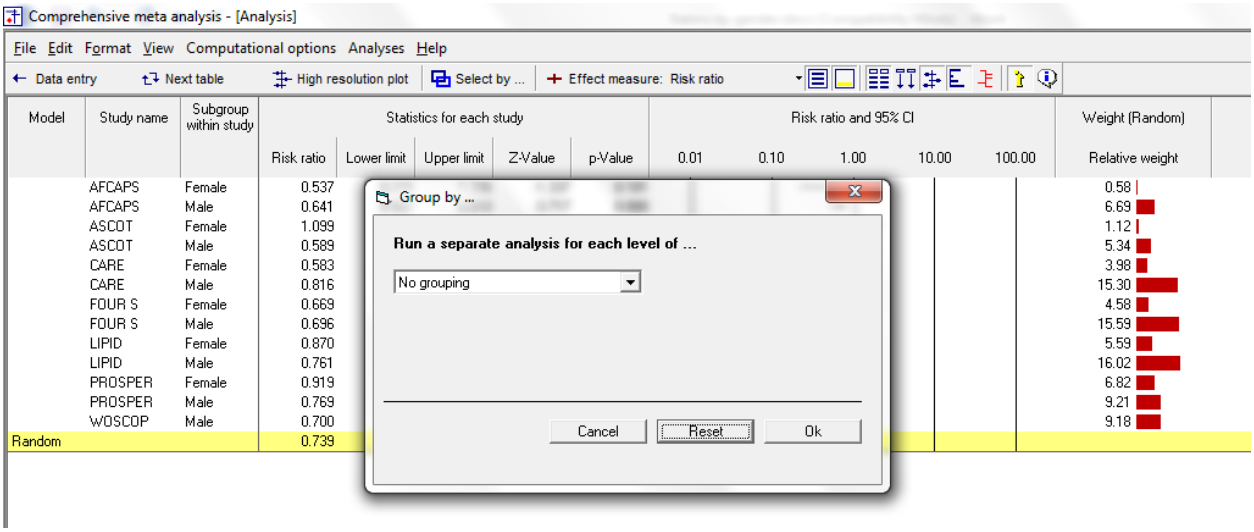
This is true for the overall analysis, and it's true for the analysis where we compared the treatment effect for Females vs. the treatment effect for Males.

However, there is one additional option available in when we have subgroups within studies that is not available when each row of data comes from a different study. We have the option to take all the rows from each study and collapse them into a single row.

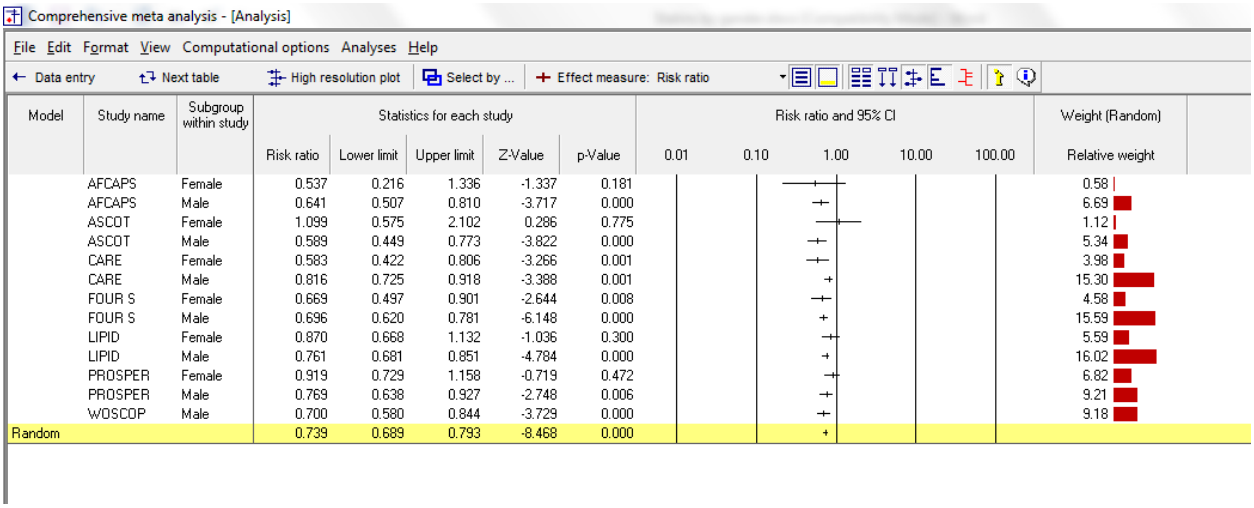
In the current example, we might decide that while the effect size is not identical for Females and for Males, the two effects are close enough that we want to combine the data. This might make sense, for example, if all studies had included both Females and Males, but some studies reported the data for each gender separately, while others reported the data only for the sample as a whole.

First, we need to turn off grouping. If we are going to collapse subgroups into a single group we obviously cannot group by gender.

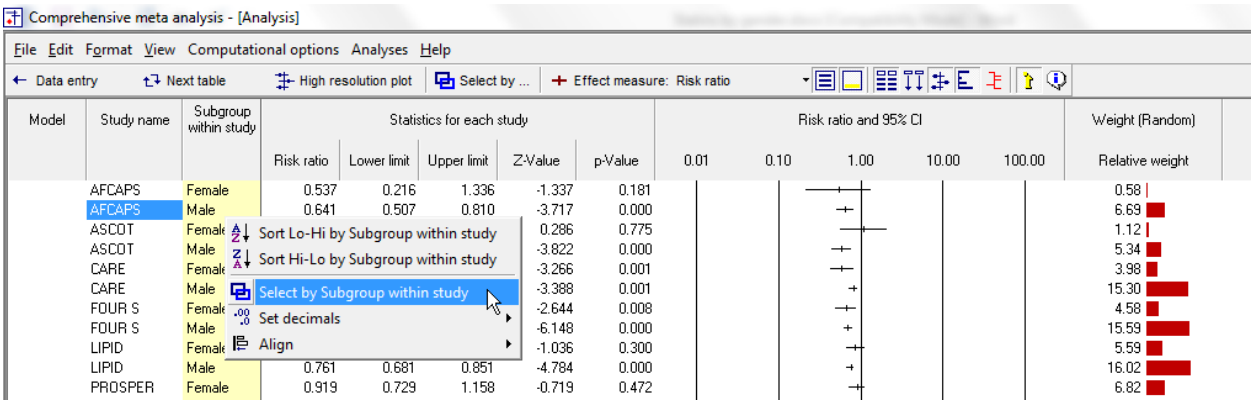
Click Computational options > Group by > Reset

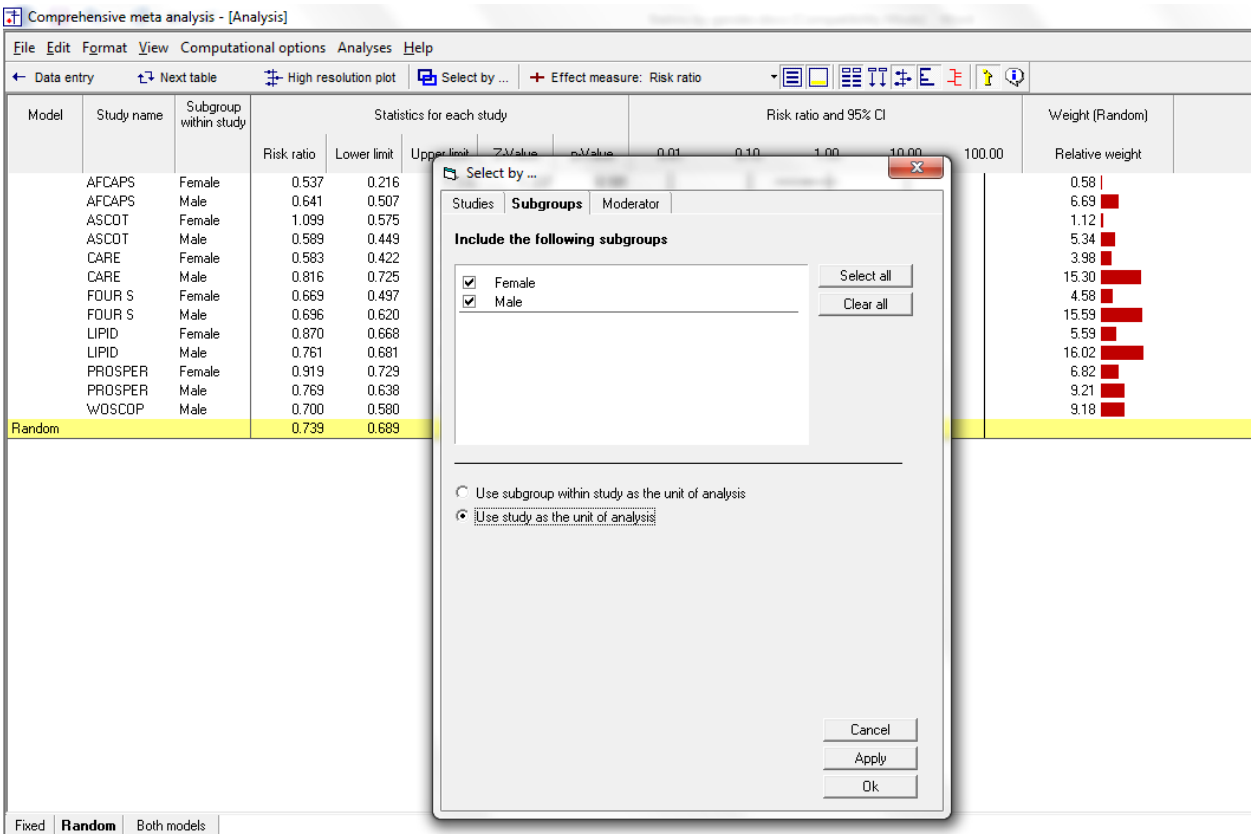


The screen should look like this



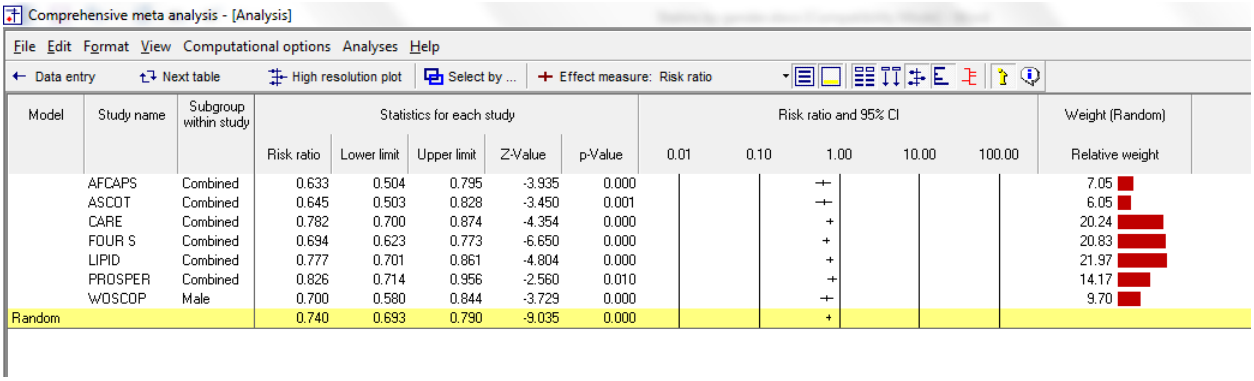
- Right-click on the column “Subgroup within study”
- Click Select by Subgroup within study





The two options here are “Use subgroup within study as the unit of analysis” and “Use study as the unit of analysis”

To this point we’ve been using the first option. Now, select the second option and click OK



Note the following

- We now have seven rows of data rather than thirteen
- The subgroup for most studies is listed as “Combined” since these studies had two subgroups, and the data displayed is for the two combined. The Subgroup for WOSCOP is listed as Male, since this study had a male subgroup only.
- The summary effect size is 0.740, which is very close to the one before (0.739). We wouldn’t expect them to be identical
- The confidence interval is 0.694 to 0.790. Again, this is very close to the one before (0.689 to 0.793). The reason that the CI width is approximately the same in both versions of the analysis is that the two samples (Female and Male) are independent of each other. As long as we treat them as independent in both versions of the analysis, the two versions may have similar precision (but see note below).
- The same applies to the Z-value and p-value. These are −9.035 with $p < 0.001$ in the new analysis. They had been −8.468 with $p < .001$ in the earlier analysis.

Note

Because the two subgroups are independent of each other, either approach to the analysis is based on the same amount of information and may yield estimates with similar precision. However, there are other factors that affect the precision of the estimate as well and these may differ in the two versions of the analysis. In particular, the estimates may differ substantially if the two approaches yield substantially different estimates of T^2.

This example focused on the case of independent subgroups within studies. This is very different from the case where the same sample provides data for more than one outcome, time-point, or comparison. In that case the samples are not independent and a very different analysis would be used.

Summary

This analysis includes seven studies where patients were randomized to receive either a statins or a placebo. Outcome was the proportion of patients in each group suffering a major coronary event, and the effect size was the risk ratio.

Within each study patients were classified as being females or males. We ran an analysis to see if the impact of statins was greater (or smaller) for either gender.

Do statins affect the risk of major cardiovascular events?

For this analysis we used subgroups within studies as the unit of analysis.

The mean risk ratio is 0.739, which means that statins decreased the risk of a major cardiovascular event by some 26%. The 95% confidence interval is 0.688 to 0.794. The Z-value for a test of the null (that statins have no impact on the event rate) is −8.306 with a corresponding p-value of < 0.001.

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 0.688 to 0.794, which tell us that the mean risk ratio in the universe of studies could fall anywhere in this range. This range does not include a risk ratio of 1.0, which tells us that the mean risk ratio is probably not 1.0.

Similarly, the *Z*-value for testing the null hypothesis (that the mean risk ratio is 1.0) is −8.306, with a corresponding *p*-value is < 0.001. We can reject the null that the risk of a major cardiovascular event is the same in both groups, and conclude that the risk is lower in the statin group.

Does the effect size vary by subgroup?

The mean risk ratio for females is 0.781. The mean risk ratio for smokers is 0.727. The test of the difference in risk between the two subgroups of studies yields a Q-value of 0.689 with df = 1 and p=0.406. Thus, there is no evidence that the impact of statins varies by gender.