Example name	Weight loss
Effect size	Risk difference
Analysis type	Subgroups analysis

Synopsis

This analysis includes 21 studies where patients were randomized to receive either a drug or placebo. Outcome was the proportion of patients meeting a criterion for success in losing weight. The effect size was the risk difference, i.e. the difference in success rates between the two groups.

Some studies compared Orlistat vs. placebo while others compared Sibutramine vs. placebo. The primary goal of the meta-analysis was to compare subgroups of studies, i.e. to see if the risk difference is higher (or lower) in studies that used Orlistat as compared with studies that used Sibutramine.

We use this example to show

- How to enter data for a moderator
- How to compare subgroups
- How to choose a method computing T^2 in the presence of subgroups
- How to understand the statistics for a mixed-effect analysis

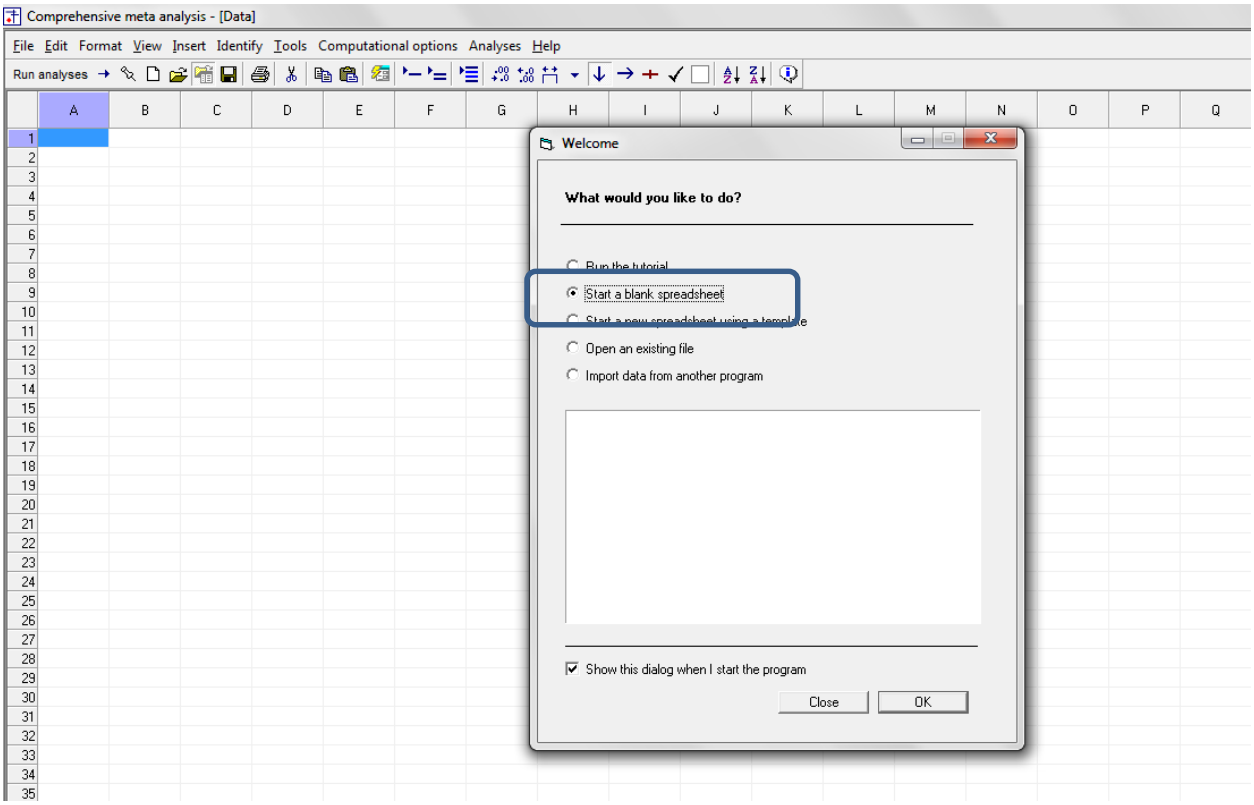
To open a CMA file > Download and Save file | Start CMA | Open file from within CMA

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

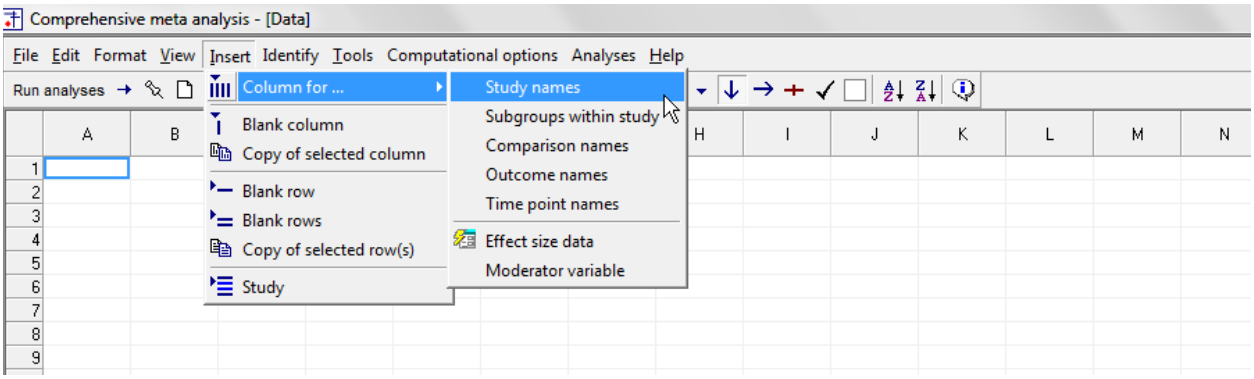
Download this PDF
Download data in Excel
Download trial of CMA

Start the program

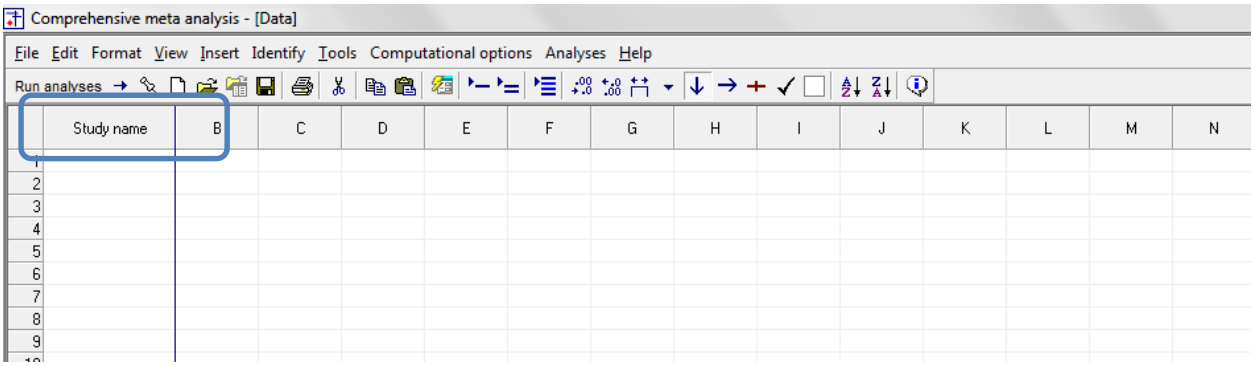
- Select the option [Start a blank spreadsheet]
- Click [Ok]



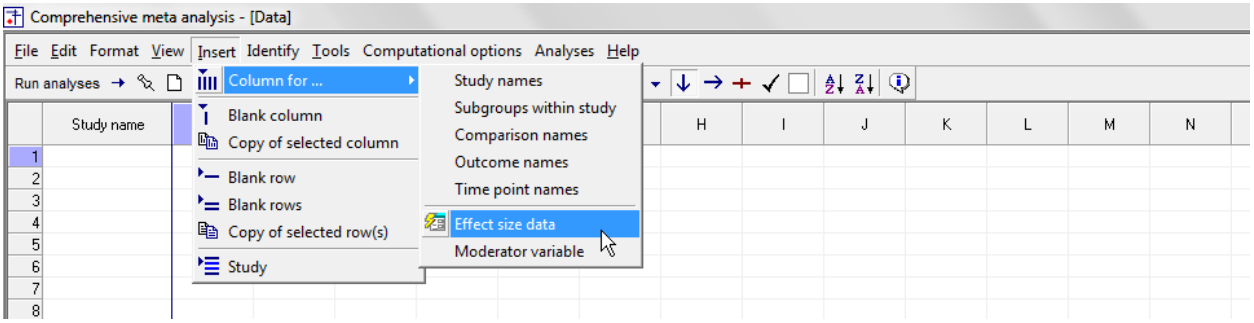
Click Insert > Column for > Study names



The screen should look like this

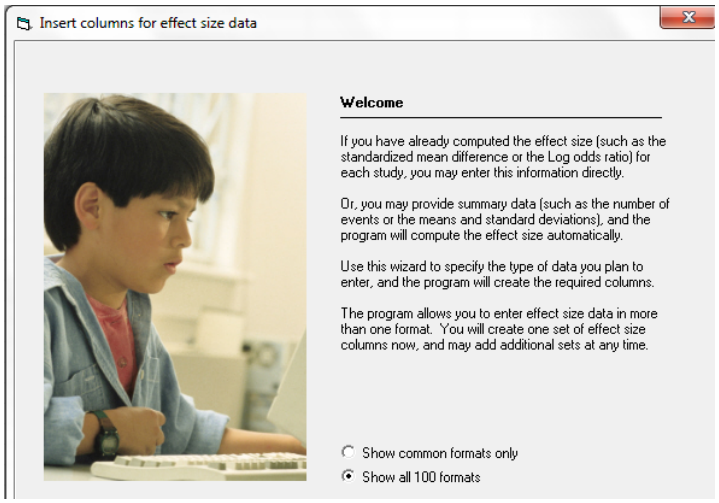


Click Insert > Column for > Effect size data

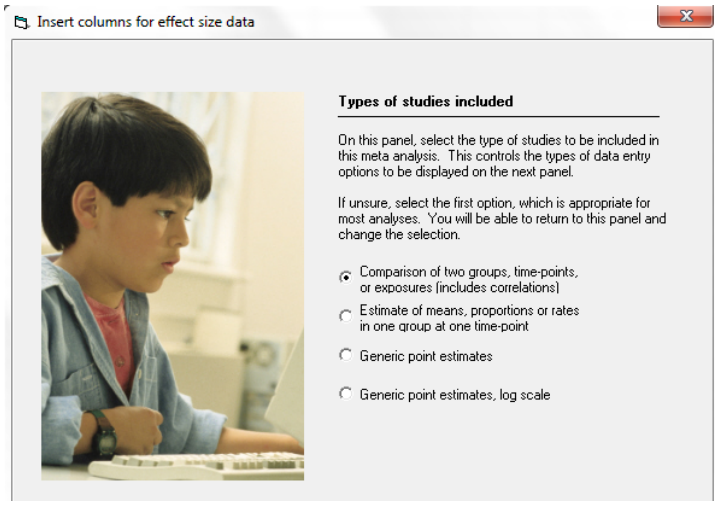


The program displays this wizard

Select [Show all 100 formats]
Click [Next]

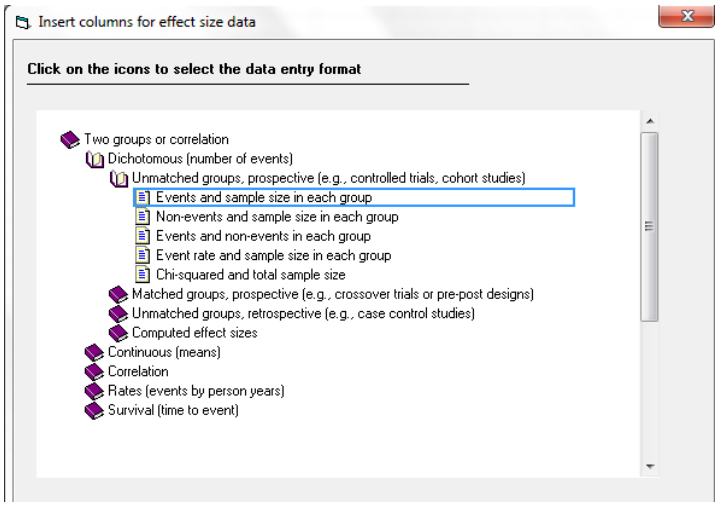


Select [Comparison of two groups…]
Click [Next]



Drill down to

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

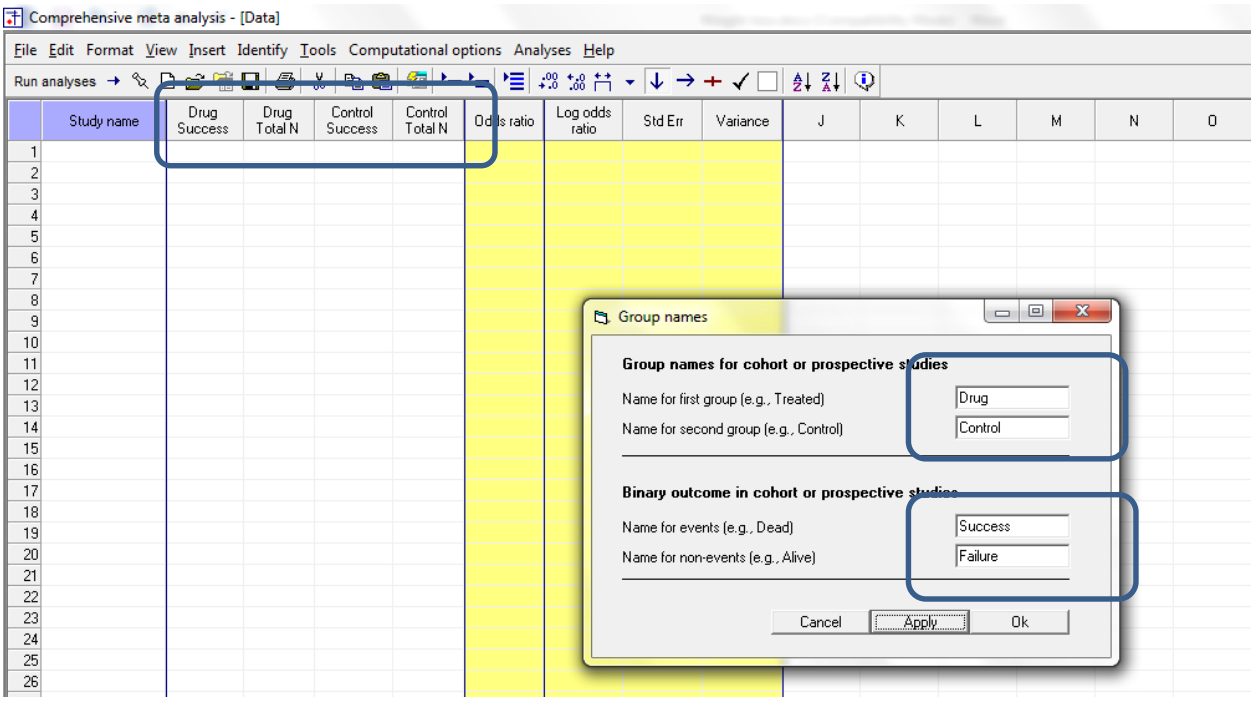


The program displays this wizard

Enter the following labels into the wizard

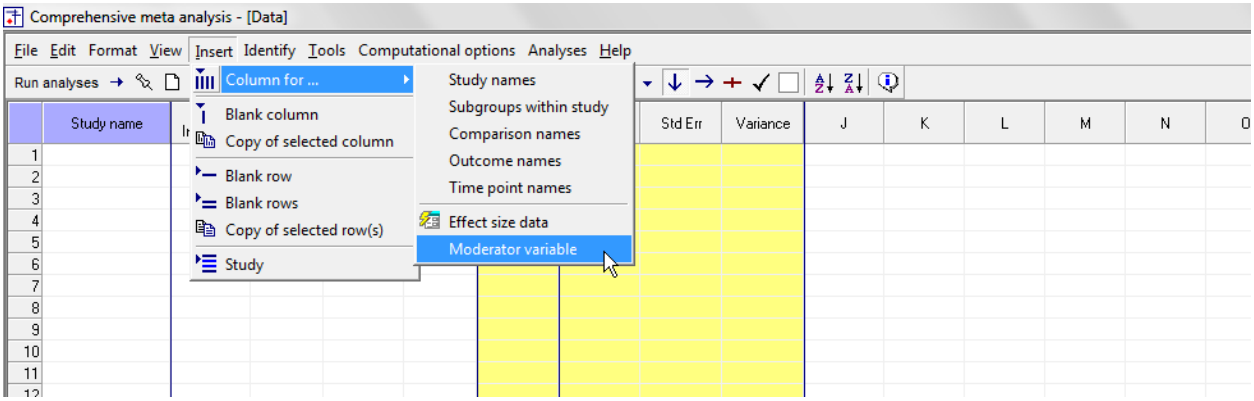
- First group > Drug
- Second group > Control
- Name for events > Success
- Name for non-events > Failure

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

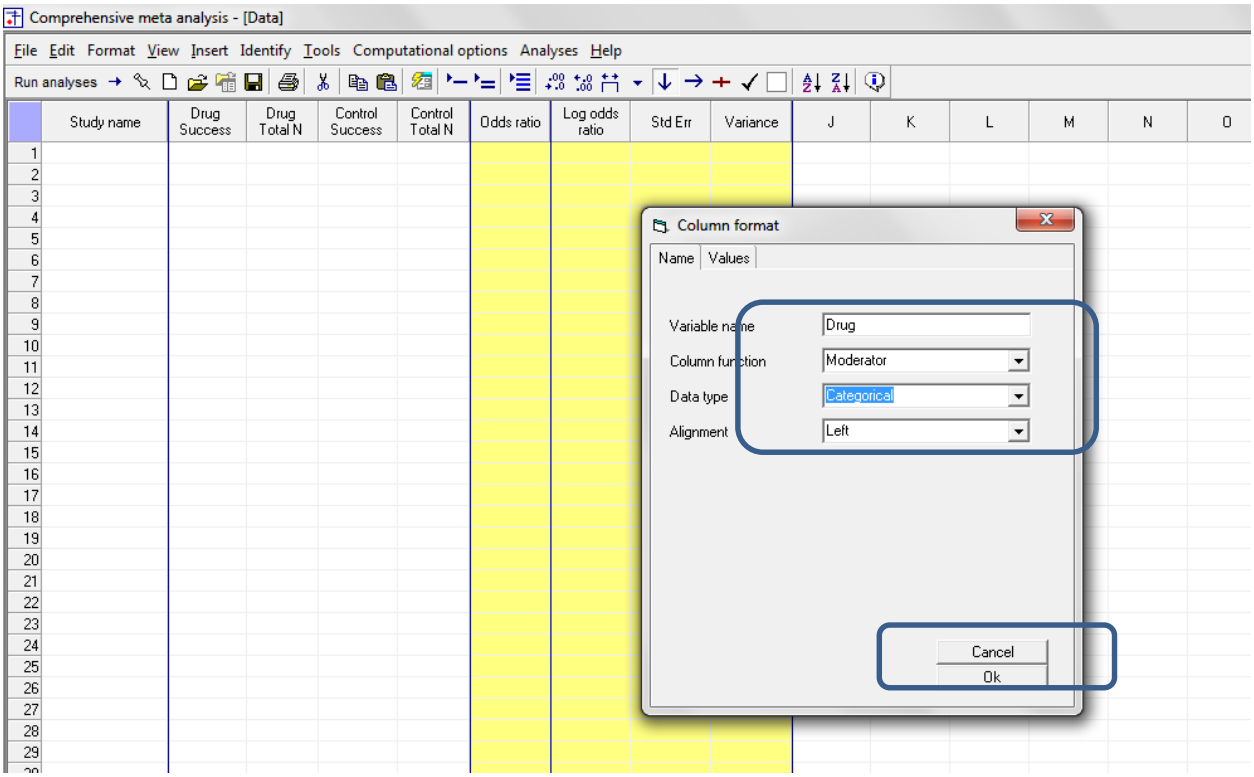


We also need to add a column for the moderator, Drug

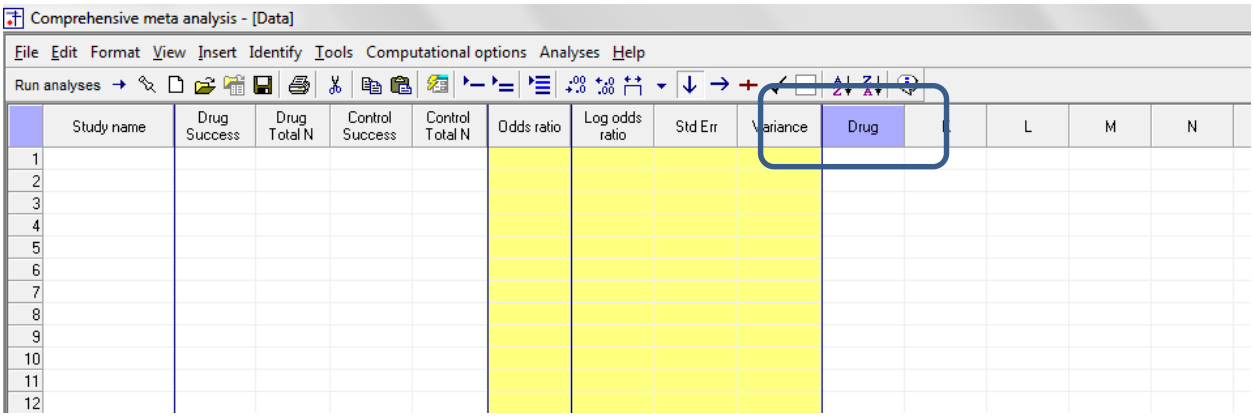
Click Insert > Column for > Moderator variable



- Name the moderator > Drug
- Set the data type to Categorical
- Click Ok

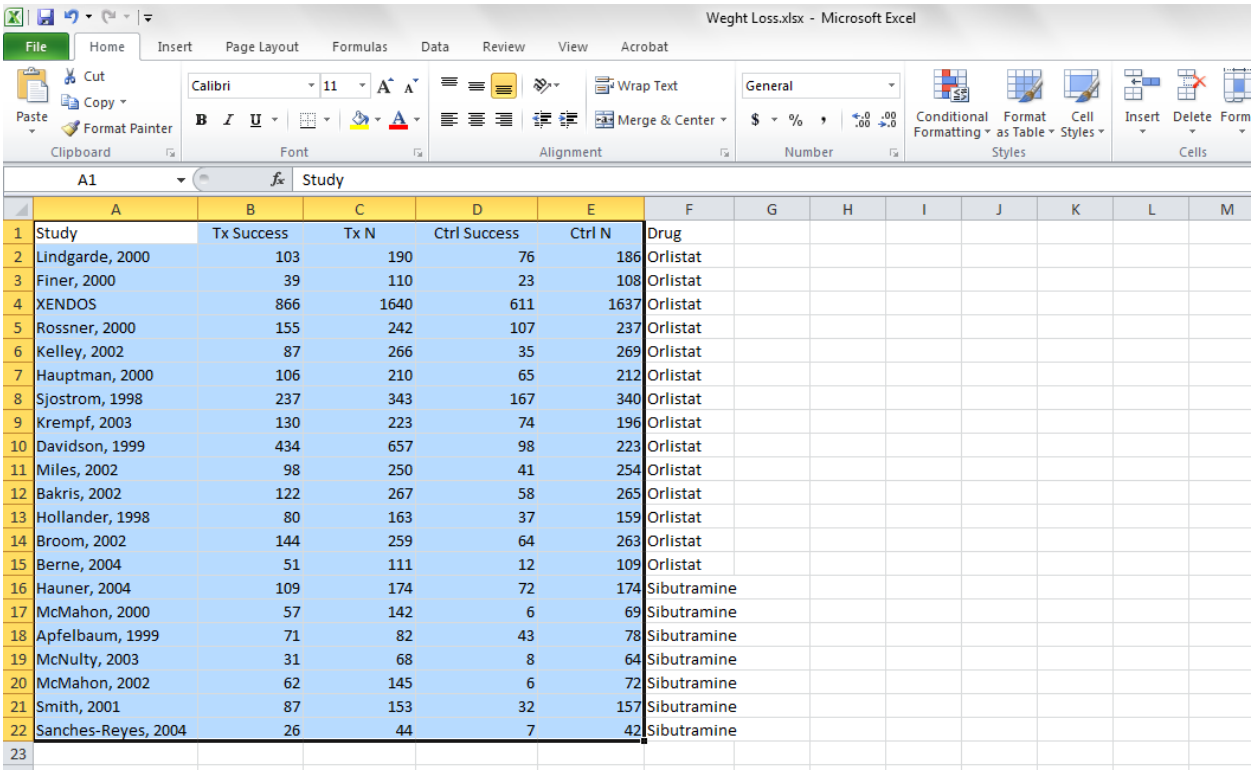


The screen should look like this



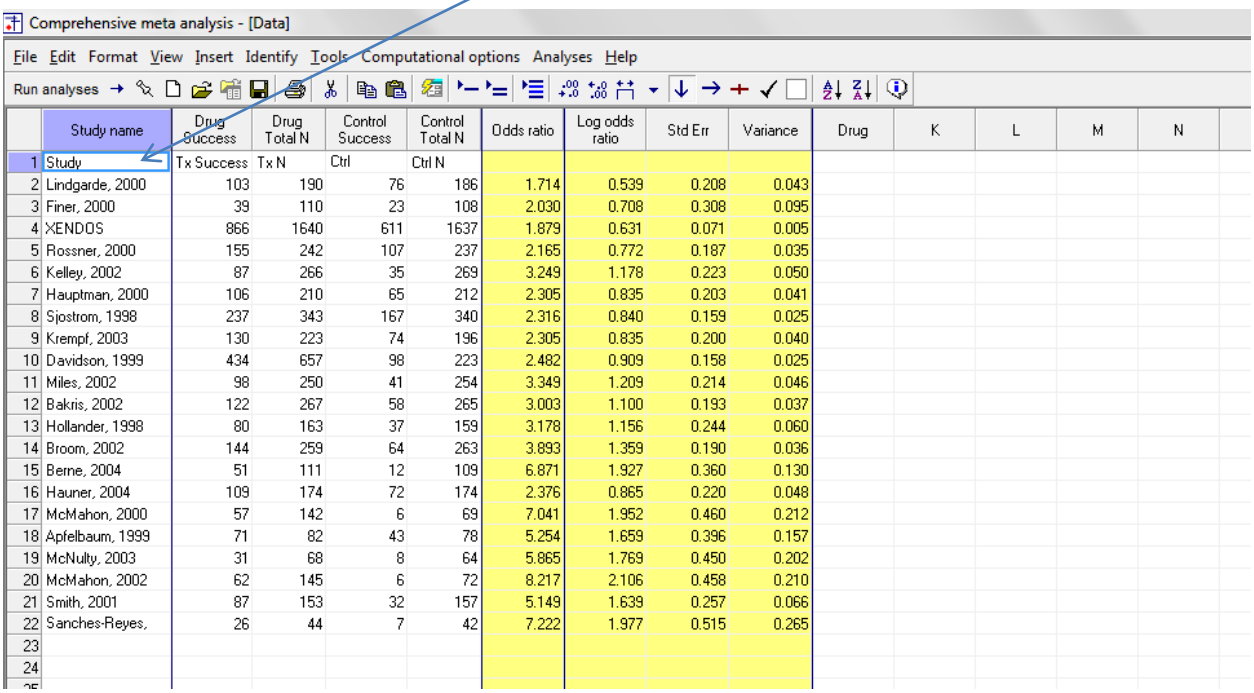
Rather than enter the data directly into CMA we will copy the data from Excel

- Switch to Excel and open the file “Weight loss”
- Highlight the rows and columns as shown (Columns A to E only), and press CTRL-C to copy to clipboard



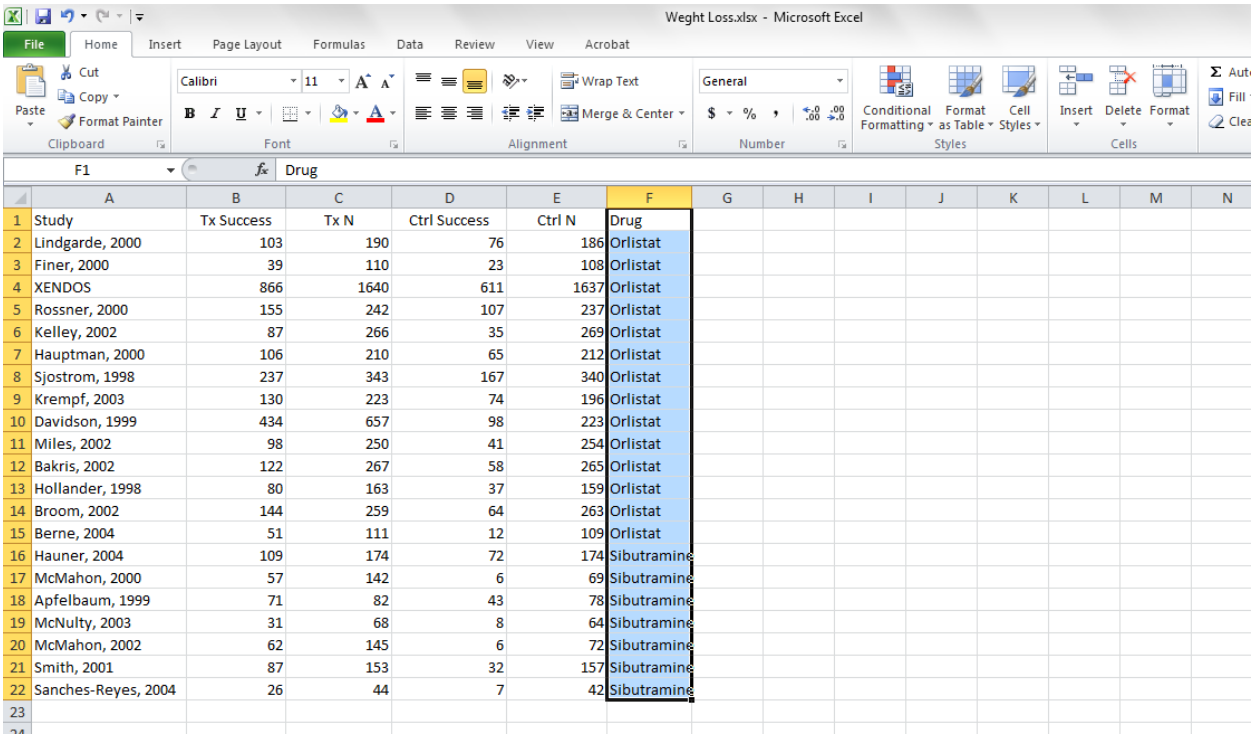
	A	B	C	D	E	F	G	H	I	J	K	L	M
1	Study	Tx Success	Tx N	Ctrl Success	Ctrl N	Drug							
2	Lindgarde, 2000	103	190	76	186	Orlistat							
3	Finer, 2000	39	110	23	108	Orlistat							
4	XENDOS	866	1640	611	1637	Orlistat							
5	Rossner, 2000	155	242	107	237	Orlistat							
6	Kelley, 2002	87	266	35	269	Orlistat							
7	Hauptman, 2000	106	210	65	212	Orlistat							
8	Sjostrom, 1998	237	343	167	340	Orlistat							
9	Krempf, 2003	130	223	74	196	Orlistat							
10	Davidson, 1999	434	657	98	223	Orlistat							
11	Miles, 2002	98	250	41	254	Orlistat							
12	Bakris, 2002	122	267	58	265	Orlistat							
13	Hollander, 1998	80	163	37	159	Orlistat							
14	Broom, 2002	144	259	64	263	Orlistat							
15	Berne, 2004	51	111	12	109	Orlistat							
16	Hauner, 2004	109	174	72	174	Sibutramine							
17	McMahon, 2000	57	142	6	69	Sibutramine							
18	Apfelbaum, 1999	71	82	43	78	Sibutramine							
19	McNulty, 2003	31	68	8	64	Sibutramine							
20	McMahon, 2002	62	145	6	72	Sibutramine							
21	Smith, 2001	87	153	32	157	Sibutramine							
22	Sanches-Reyes, 2004	26	44	7	42	Sibutramine							
23													

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



	Study name	Drug Success	Drug Total N	Control Success	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Drug	K	L	M	N
1	Study	Tx Success	Tx N	Ctrl	Ctrl N									
2	Lindgarde, 2000	103	190	76	186	1.714	0.539	0.208	0.043					
3	Finer, 2000	39	110	23	108	2.030	0.708	0.308	0.095					
4	XENDOS	866	1640	611	1637	1.879	0.631	0.071	0.005					
5	Rossner, 2000	155	242	107	237	2.165	0.772	0.187	0.035					
6	Kelley, 2002	87	266	35	269	3.249	1.178	0.223	0.050					
7	Hauptman, 2000	106	210	65	212	2.305	0.835	0.203	0.041					
8	Sjostrom, 1998	237	343	167	340	2.316	0.840	0.159	0.025					
9	Krempf, 2003	130	223	74	196	2.305	0.835	0.200	0.040					
10	Davidson, 1999	434	657	98	223	2.482	0.909	0.158	0.025					
11	Miles, 2002	98	250	41	254	3.349	1.209	0.214	0.046					
12	Bakris, 2002	122	267	58	265	3.003	1.100	0.193	0.037					
13	Hollander, 1998	80	163	37	159	3.178	1.156	0.244	0.060					
14	Broom, 2002	144	259	64	263	3.893	1.359	0.190	0.036					
15	Berne, 2004	51	111	12	109	6.871	1.927	0.360	0.130					
16	Hauner, 2004	109	174	72	174	2.376	0.865	0.220	0.048					
17	McMahon, 2000	57	142	6	69	7.041	1.952	0.460	0.212					
18	Apfelbaum, 1999	71	82	43	78	5.254	1.659	0.396	0.157					
19	McNulty, 2003	31	68	8	64	5.865	1.769	0.450	0.202					
20	McMahon, 2002	62	145	6	72	8.217	2.106	0.458	0.210					
21	Smith, 2001	87	153	32	157	5.149	1.639	0.257	0.066					
22	Sanches-Reyes,	26	44	7	42	7.222	1.977	0.515	0.265					
23														
24														

- Switch to Excel
- Highlight the Dose column as shown and click [CTRL-C]



	A	B	C	D	E	F
1	Study	Tx Success	Tx N	Ctrl Success	Ctrl N	Drug
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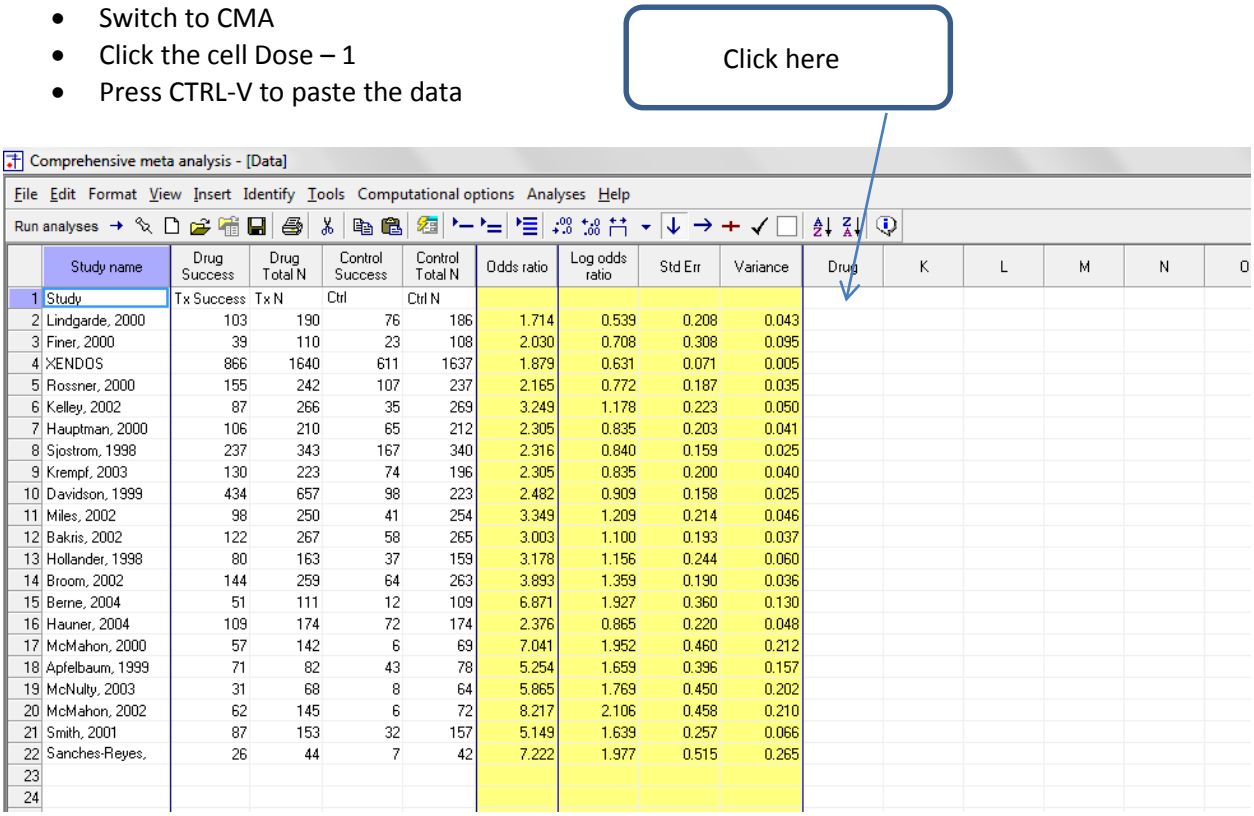
3	Finer, 2000	39	110	23	108	Orlistat
4	XENDOS	866	1640	611	1637	Orlistat
5	Rossner, 2000	155	242	107	237	Orlistat
6	Kelley, 2002	87	266	35	269	Orlistat
7	Hauptman, 2000	106	210	65	212	Orlistat
8	Sjostrom, 1998	237	343	167	340	Orlistat
9	Krempf, 2003	130	223	74	196	Orlistat
10	Davidson, 1999	434	657	98	223	Orlistat
11	Miles, 2002	98	250	41	254	Orlistat
12	Bakris, 2002	122	267	58	265	Orlistat
13	Hollander, 1998	80	163	37	159	Orlistat
14	Broom, 2002	144	259	64	263	Orlistat
15	Berne, 2004	51	111	12	109	Orlistat
16	Hauner, 2004	109	174	72	174	Sibutramine
17	McMahon, 2000	57	142	6	69	Sibutramine
18	Apfelbaum, 1999	71	82	43	78	Sibutramine
19	McNulty, 2003	31	68	8	64	Sibutramine
20	McMahon, 2002	62	145	6	72	Sibutramine
21	Smith, 2001	87	153	32	157	Sibutramine
22	Sanches-Reyes, 2004	26	44	7	42	Sibutramine
23						

- Switch to CMA
- Click the cell Dose – 1
- Press CTRL-V to paste the data



	Study name	Drug Success	Drug Total N	Control Success	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Drug
1	Study	Tx Success	Tx N	Ctrl	Ctrl N					
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4	XENDOS	866	1640	611	1637	1.879	0.631	0.071	0.005	
5	Rossner, 2000	155	242	107	237	2.165	0.772	0.187	0.035	
6	Kelley, 2002	87	266	35	269	3.249	1.178	0.223	0.050	
7	Hauptman, 2000	106	210	65	212	2.305	0.835	0.203	0.041	
8	Sjostrom, 1998	237	343	167	340	2.316	0.840	0.159	0.025	
9	Krempf, 2003	130	223	74	196	2.305	0.835	0.200	0.040	
10	Davidson, 1999	434	657	98	223	2.482	0.909	0.158	0.025	
11	Miles, 2002	98	250	41	254	3.349	1.209	0.214	0.046	
12	Bakris, 2002	122	267	58	265	3.003	1.100	0.193	0.037	
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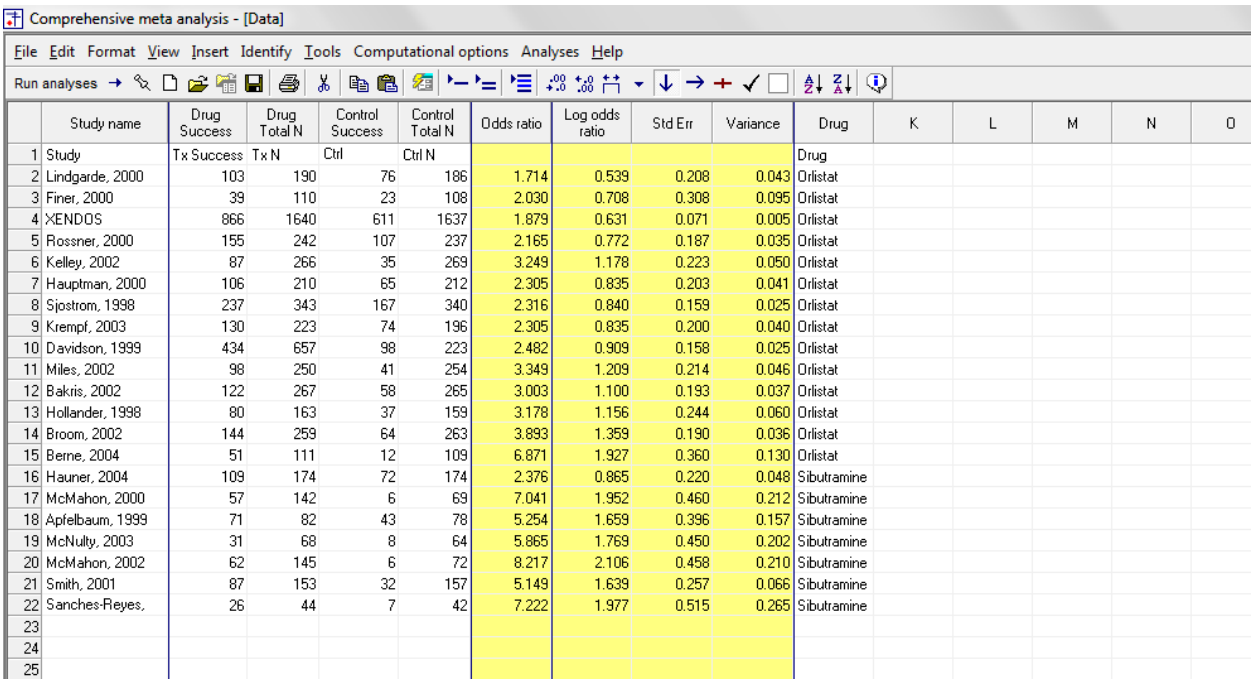
20	McMahon, 2002	62	145	6	72	8.217	2.106	0.458	0.210	
21	Smith, 2001	87	153	32	157	5.149	1.639	0.257	0.066	
22	Sanches-Reyes,	26	44	7	42	7.222	1.977	0.515	0.265	
23										
24										



	Study name	Drug Success	Drug Total N	Control Success	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Drug	K	L	M	N	O
1	Study	Tx Success	Tx N	Ctrl	Ctrl N					Drug					
2	Lindgarde, 2000	103	190	76	186	1.714	0.539	0.208	0.043	Orlistat					
3	Finer, 2000	39	110	23	108	2.030	0.708	0.308	0.095	Orlistat					
4	XENDOS	866	1640	611	1637	1.879	0.631	0.071	0.005	Orlistat					
5	Rossner, 2000	155	242	107	237	2.165	0.772	0.187	0.035	Orlistat					
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11	Miles, 2002	98	250	41	254	3.349	1.209	0.214	0.046	Orlistat					
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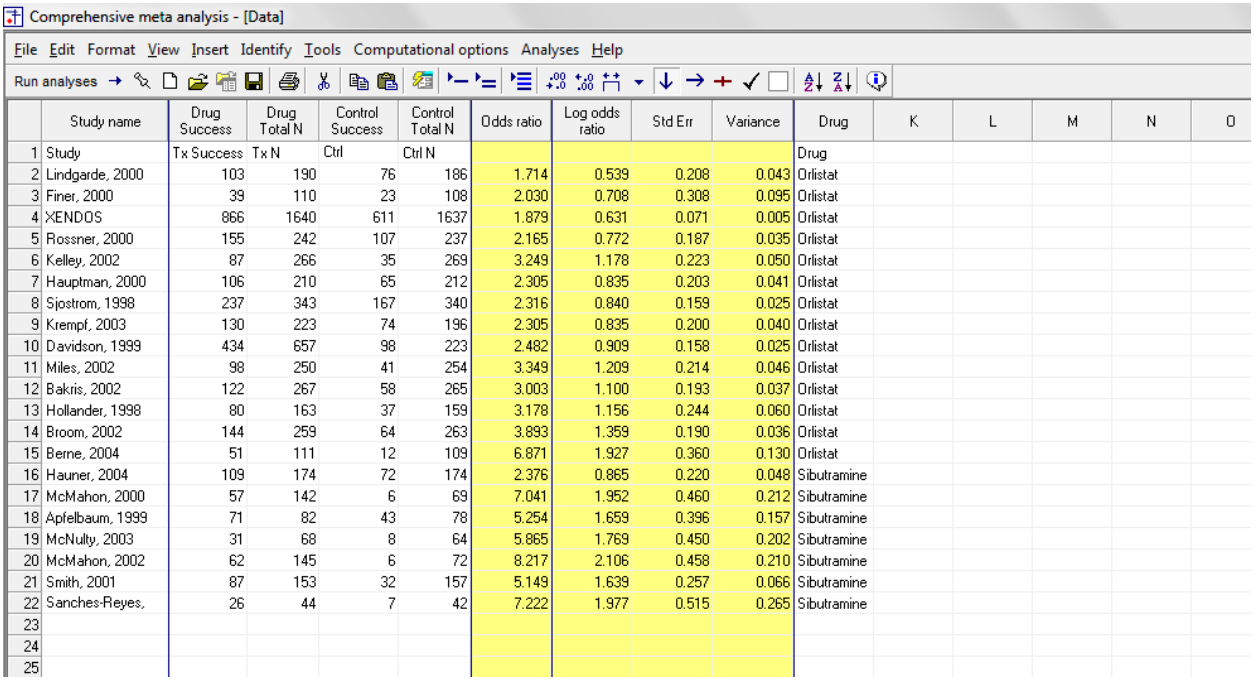
21	Smith, 2001	87	153	32	157	5.149	1.639	0.257	0.066	Sibutramine					
22	Sanches-Reyes,	26	44	7	42	7.222	1.977	0.515	0.265	Sibutramine					
23															
24															
25															

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

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



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3	Finer, 2000	39	110	23	108	2.030	0.708	0.308	0.095	Orlistat					
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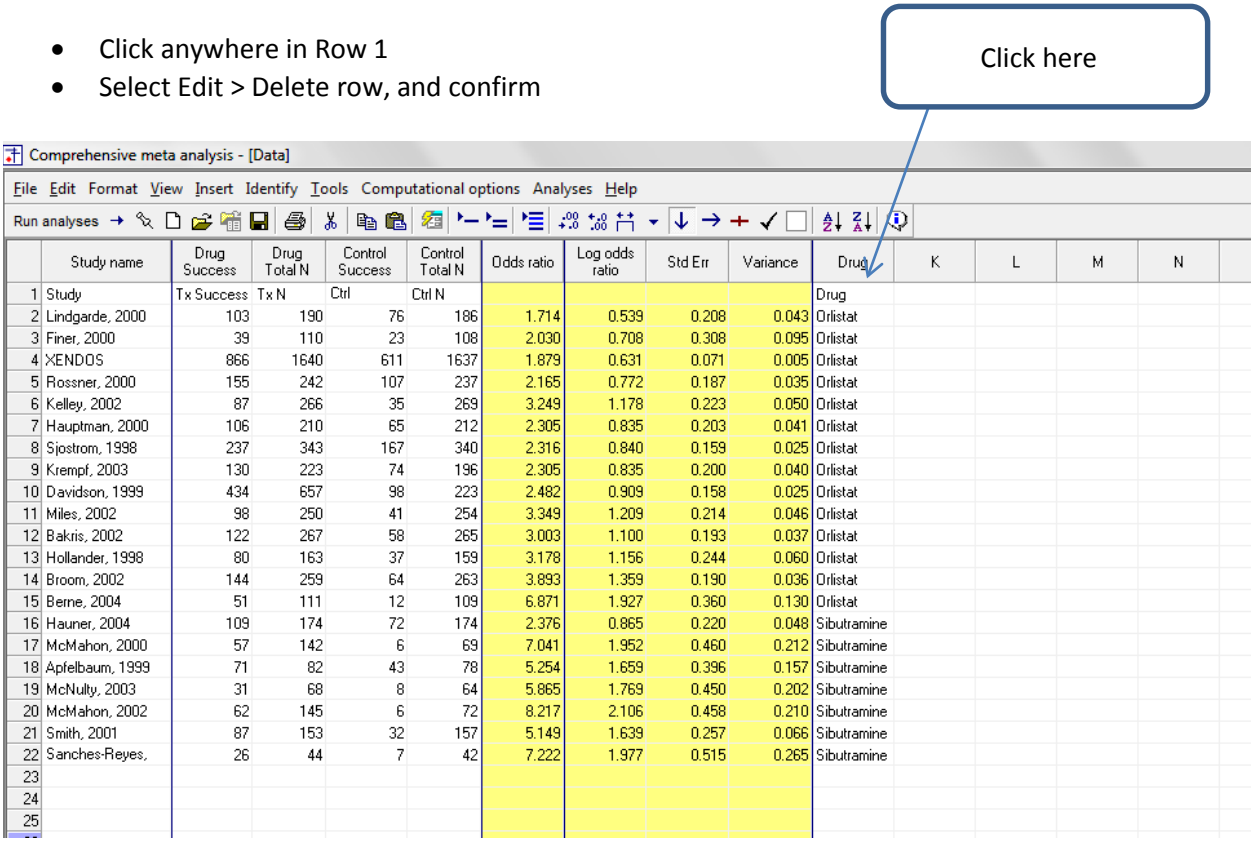
20	McMahon, 2002	62	145	6	72	8.217	2.106	0.458	0.210	Sibutramine					
21	Smith, 2001	87	153	32	157	5.149	1.639	0.257	0.066	Sibutramine					
22	Sanches-Reyes,	26	44	7	42	7.222	1.977	0.515	0.265	Sibutramine					
23															
24															
25															

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



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8	Sjostrom, 1998	237	343	167	340	2.316	0.840	0.159	0.025	Orlistat				
9	Krempf, 2003	130	223	74	196	2.305	0.835	0.200	0.040	Orlistat				
10	Davidson, 1999	434	657	98	223	2.482	0.909	0.158	0.025	Orlistat				
11	Miles, 2002	98	250	41	254	3.349	1.209	0.214	0.046	Orlistat				
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17	McMahon, 2000	57	142	6	69	7.041	1.952	0.460	0.212	Sibutramine				
18	Apfelbaum, 1999	71	82	43	78	5.254	1.659	0.396	0.157	Sibutramine				
19	McNulty, 2003	31	68	8	64	5.865	1.769	0.450	0.202	Sibutramine				
20	McMahon, 2002	62	145	6	72	8.217	2.106	0.458	0.210	Sibutramine				
21	Smith, 2001	87	153	32	157	5.149	1.639	0.257	0.066	Sibutramine				
22	Sanches-Reyes,	26	44	7	42	7.222	1.977	0.515	0.265	Sibutramine				
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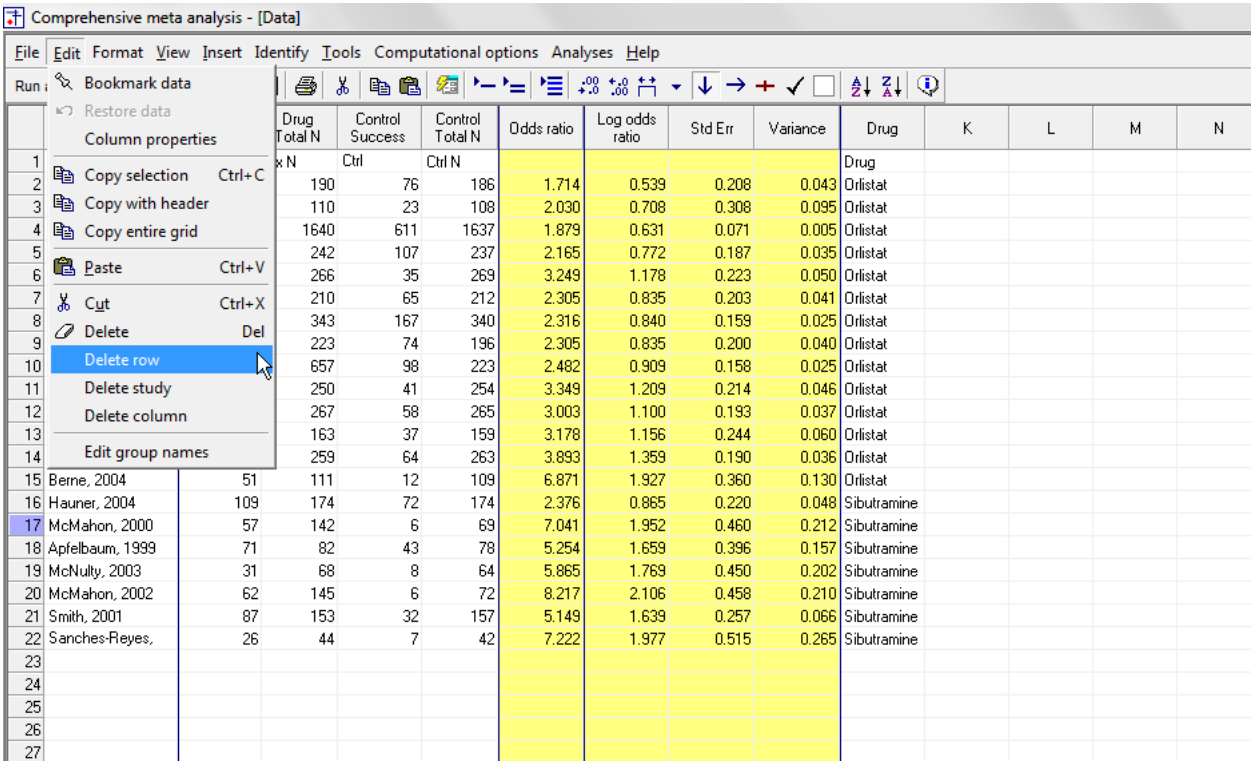
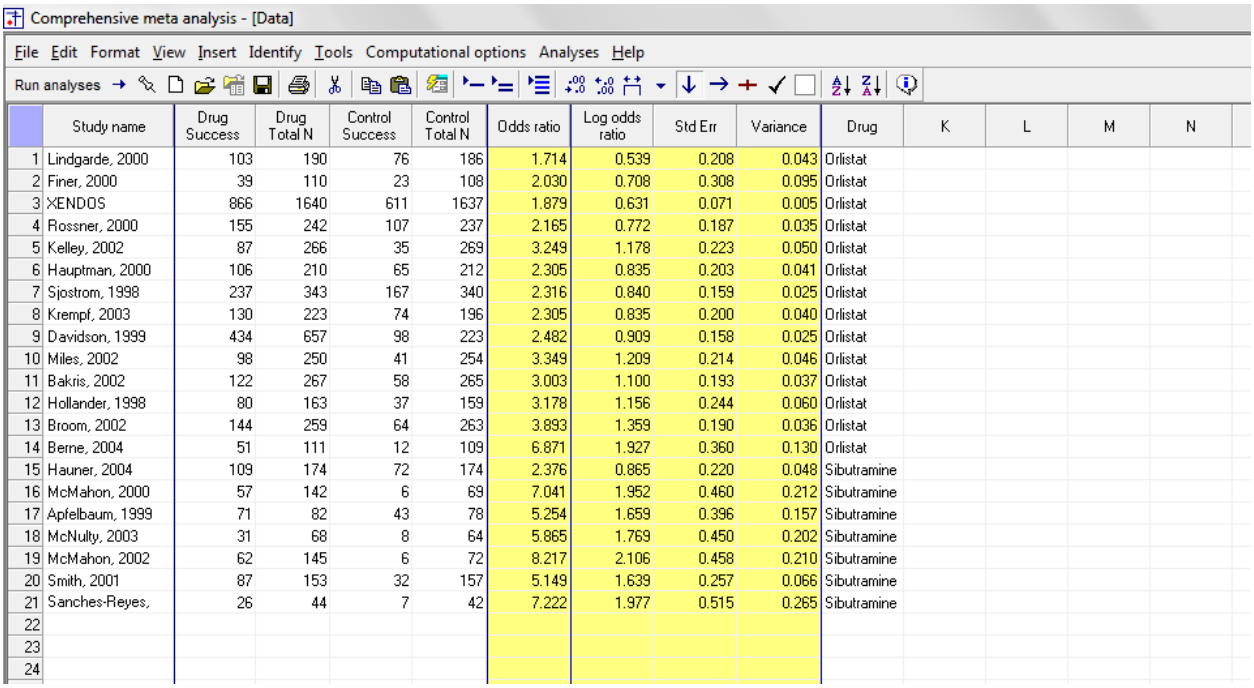


The screen should look like this



	Study name	Drug Success	Drug Total N	Control Success	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Drug	K	L	M	N
1	Lindgarde, 2000	103	190	76	186	1.714	0.539	0.208	0.043	Orlistat				
2	Finer, 2000	39	110	23	108	2.030	0.708	0.308	0.095	Orlistat				
3	XENDOS	866	1640	611	1637	1.879	0.631	0.071	0.005	Orlistat				
4	Rossner, 2000	155	242	107	237	2.165	0.772	0.187	0.035	Orlistat				
5	Kelley, 2002	87	266	35	269	3.249	1.178	0.223	0.050	Orlistat				
6	Hauptman, 2000	106	210	65	212	2.305	0.835	0.203	0.041	Orlistat				
7	Sjostrom, 1998	237	343	167	340	2.316	0.840	0.159	0.025	Orlistat				
8	Krempf, 2003	130	223	74	196	2.305	0.835	0.200	0.040	Orlistat				
9	Davidson, 1999	434	657	98	223	2.482	0.909	0.158	0.025	Orlistat				
10	Miles, 2002	98	250	41	254	3.349	1.209	0.214	0.046	Orlistat				
11	Bakris, 2002	122	267	58	265	3.003	1.100	0.193	0.037	Orlistat				
12	Hollander, 1998	80	163	37	159	3.178	1.156	0.244	0.060	Orlistat				
13	Broom, 2002	144	259	64	263	3.893	1.359	0.190	0.036	Orlistat				
14	Berne, 2004	51	111	12	109	6.871	1.927	0.360	0.130	Orlistat				
15	Hauner, 2004	109	174	72	174	2.376	0.865	0.220	0.048	Sibutramine				
16	McMahon, 2000	57	142	6	69	7.041	1.952	0.460	0.212	Sibutramine				
17	Apfelbaum, 1999	71	82	43	78	5.254	1.659	0.396	0.157	Sibutramine				
18	McNulty, 2003	31	68	8	64	5.865	1.769	0.450	0.202	Sibutramine				
19	McMahon, 2002	62	145	6	72	8.217	2.106	0.458	0.210	Sibutramine				
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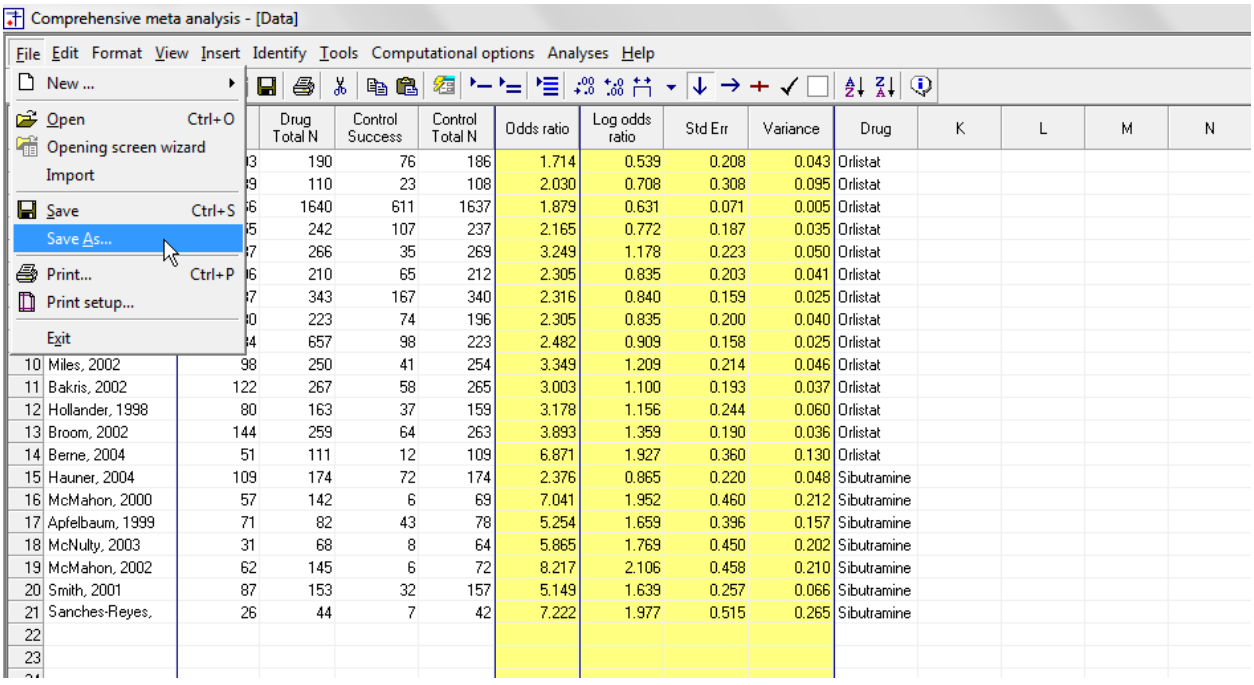
Click File > Save As and save the file



	Study name	Drug Total N	Control Success	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Drug	K	L	M	N
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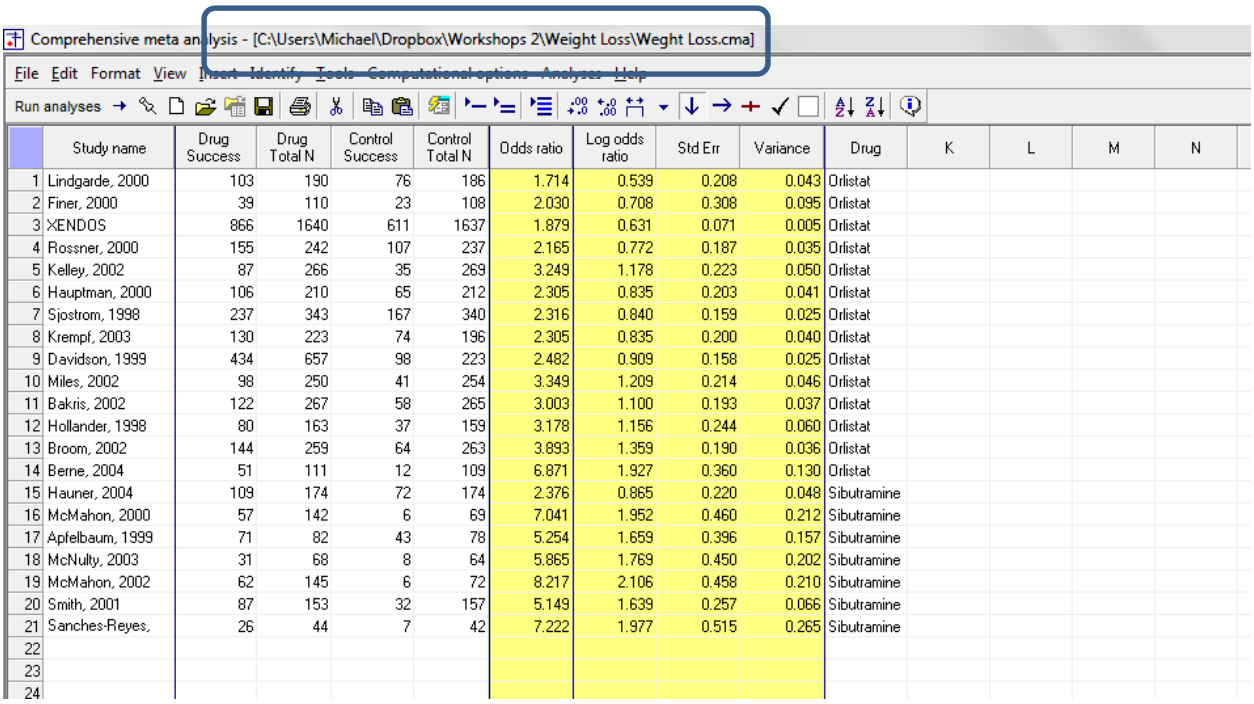
Note that the file name is now in the header.

- [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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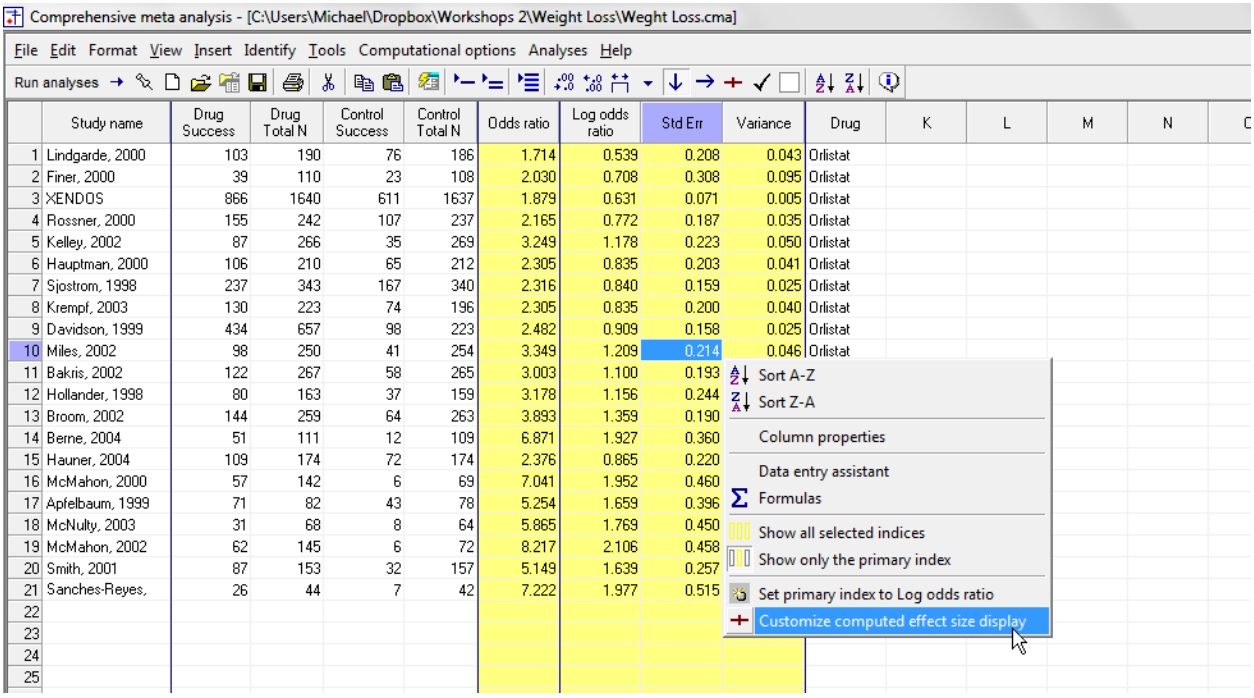
The program is displaying the odds ratio for each study. We want to use the risk difference.

Right-click anywhere in the yellow columns



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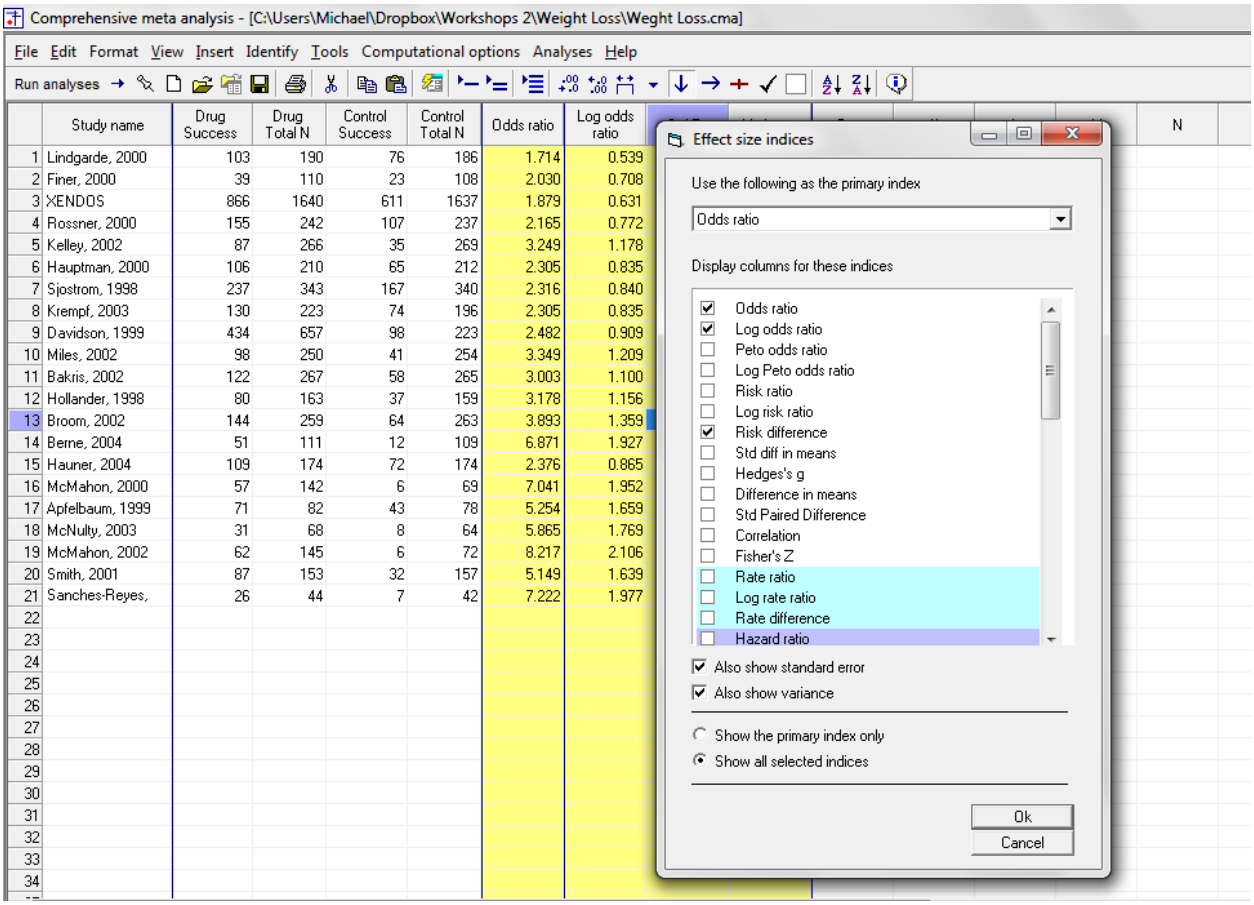
Select Customize computed effect size display

Check the box for Risk difference



	Study name	Drug Success	Drug Total N	Control Success	Control Total N	Odds ratio	Log odds ratio	N
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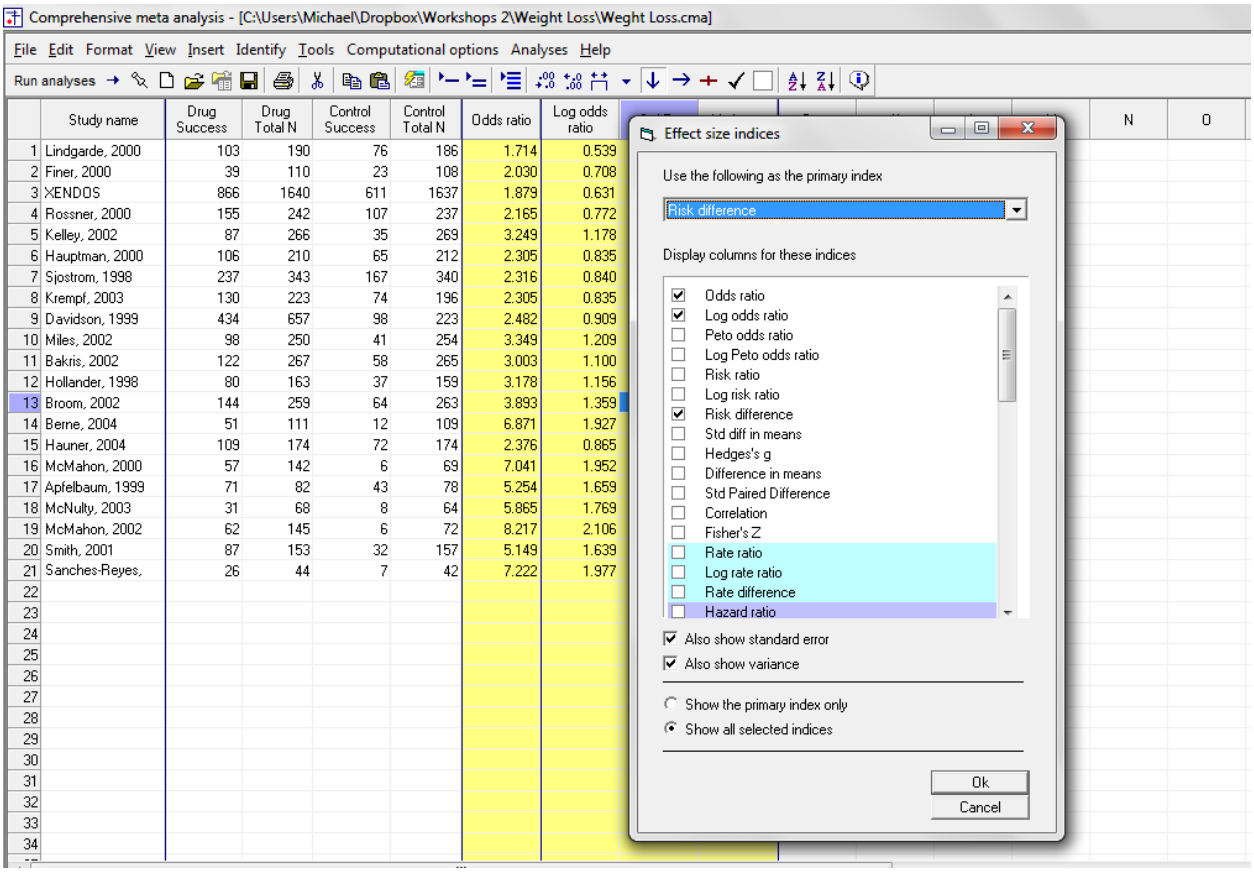
Set the primary index to risk difference



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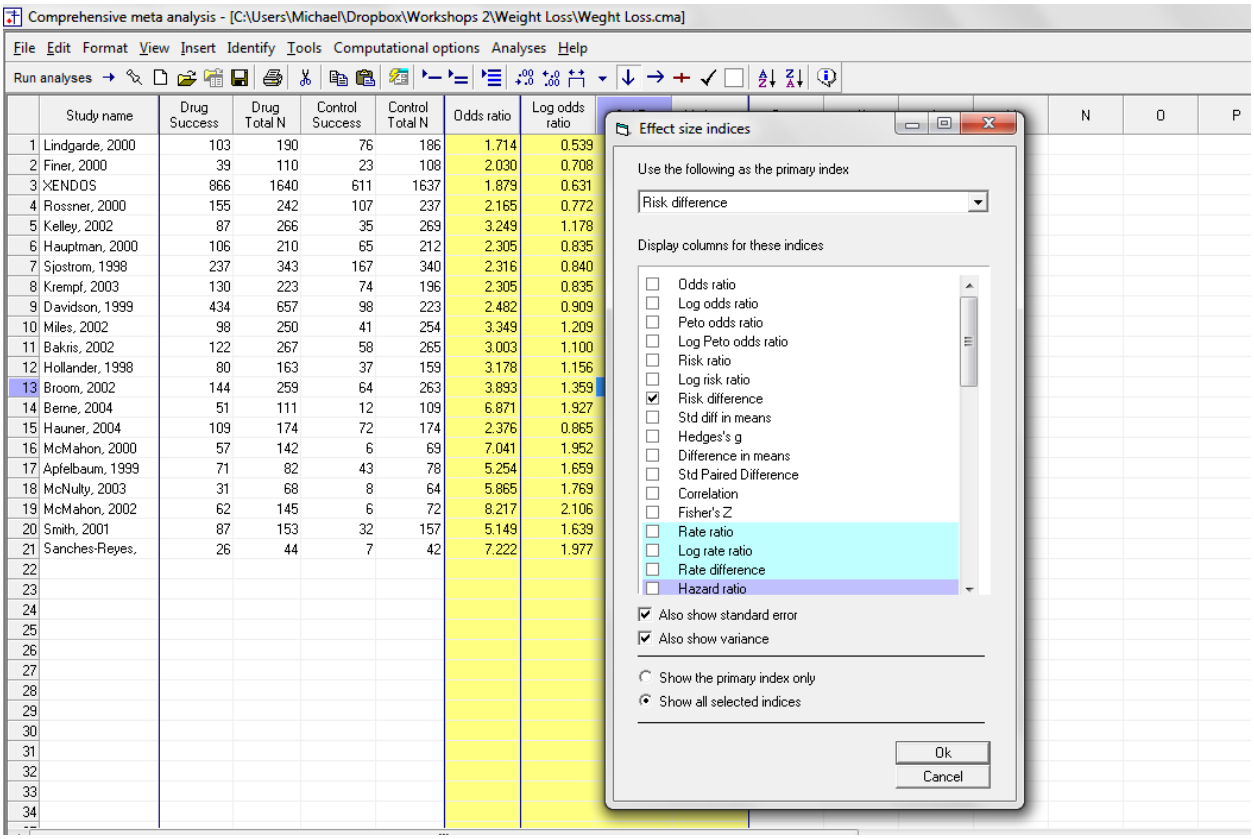
Un-check the boxes for odds ratio and log odds ratio



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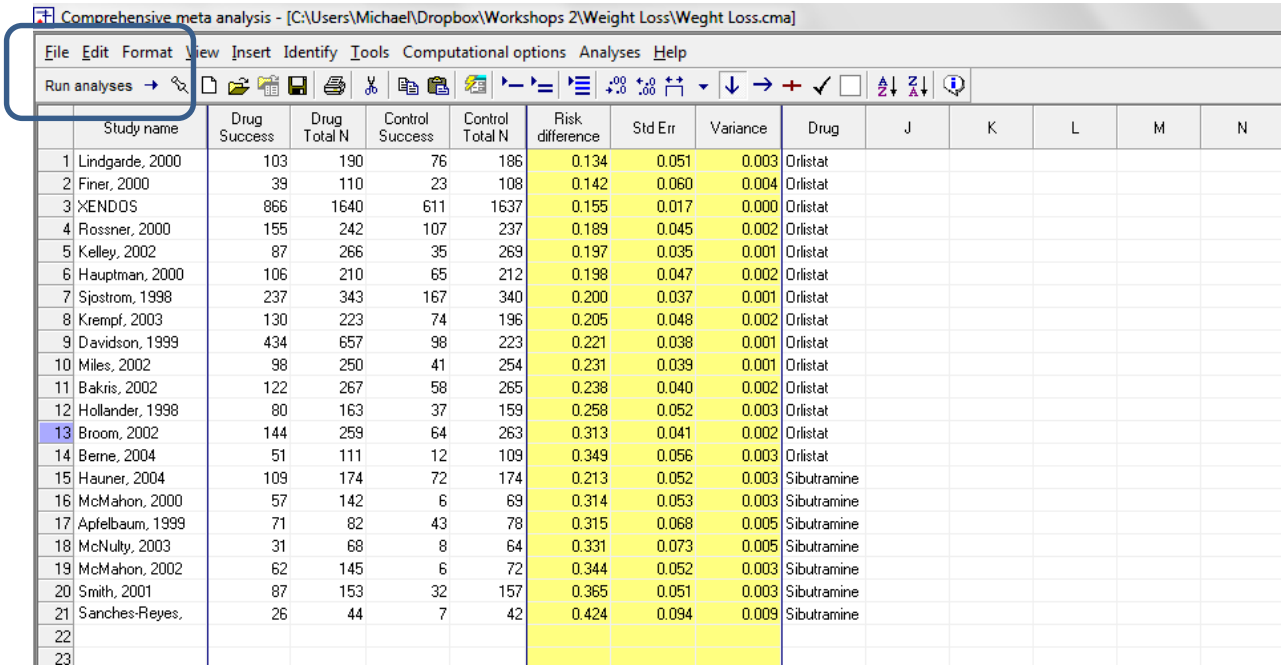
21	Sanches-Reyes,	26	44	7	42	7.222	1.977

- Check the box for Also show standard error
- Check the box for Also show variance
- Click Ok

The screen should look like this

- To run the analysis, click [Run analysis]



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1	Lindgarde, 2000	103	190	76	186	0.134	0.051	0.003	Orlistat					
2	Finer, 2000	39	110	23	108	0.142	0.060	0.004	Orlistat					
3	XENDOS	866	1640	611	1637	0.155	0.017	0.000	Orlistat					
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6	Hauptman, 2000	106	210	65	212	0.198	0.047	0.002	Orlistat					
7	Sjostrom, 1998	237	343	167	340	0.200	0.037	0.001	Orlistat					
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19	McMahon, 2002	62	145	6	72	0.344	0.052	0.003	Sibutramine					
20	Smith, 2001	87	153	32	157	0.365	0.051	0.003	Sibutramine					
21	Sanches-Reyes,	26	44	7	42	0.424	0.094	0.009	Sibutramine					
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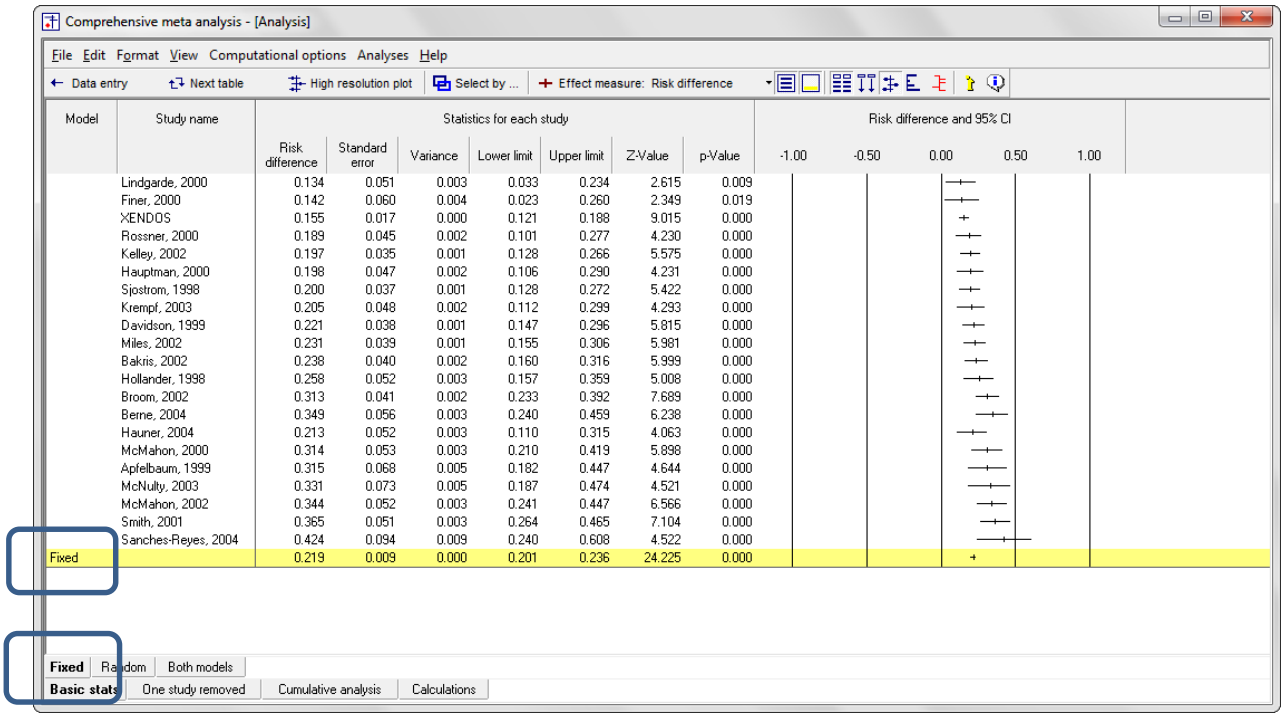
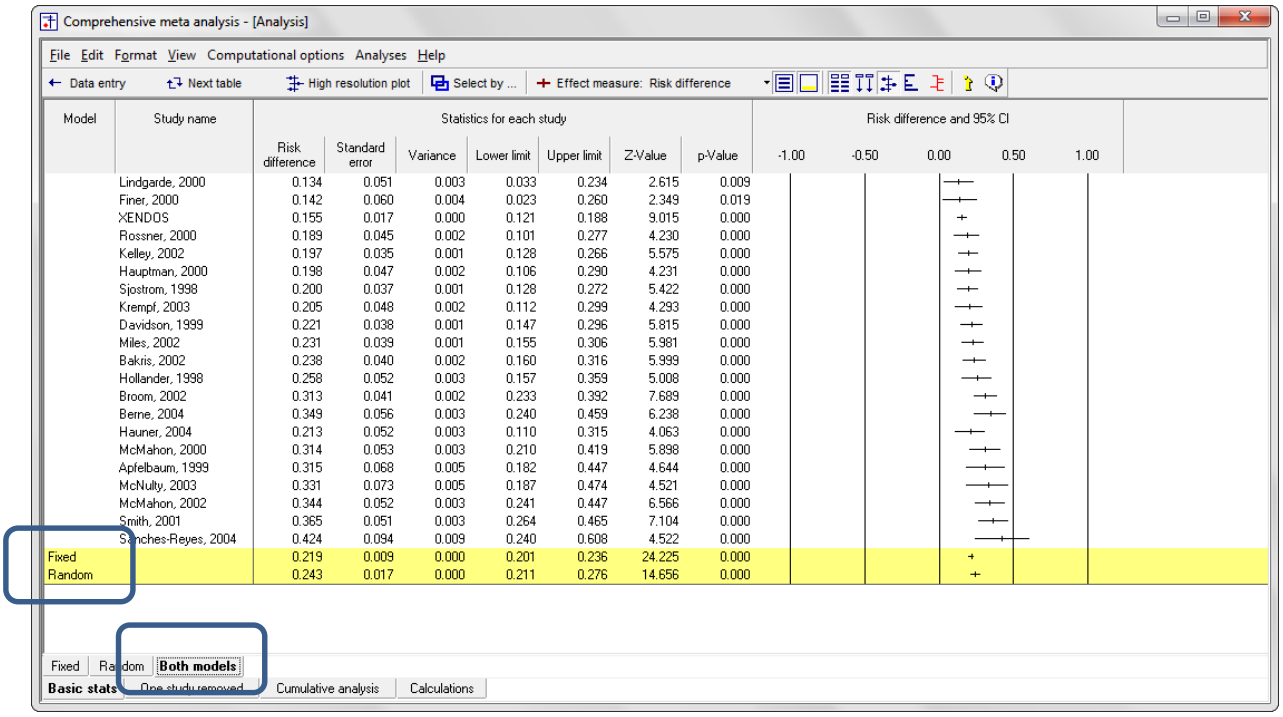
This is the basic analysis screen

Initially, the program displays the fixed-effect analysis. This is indicated by the tab at the bottom and the label in the plot.



Click [Both models]

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



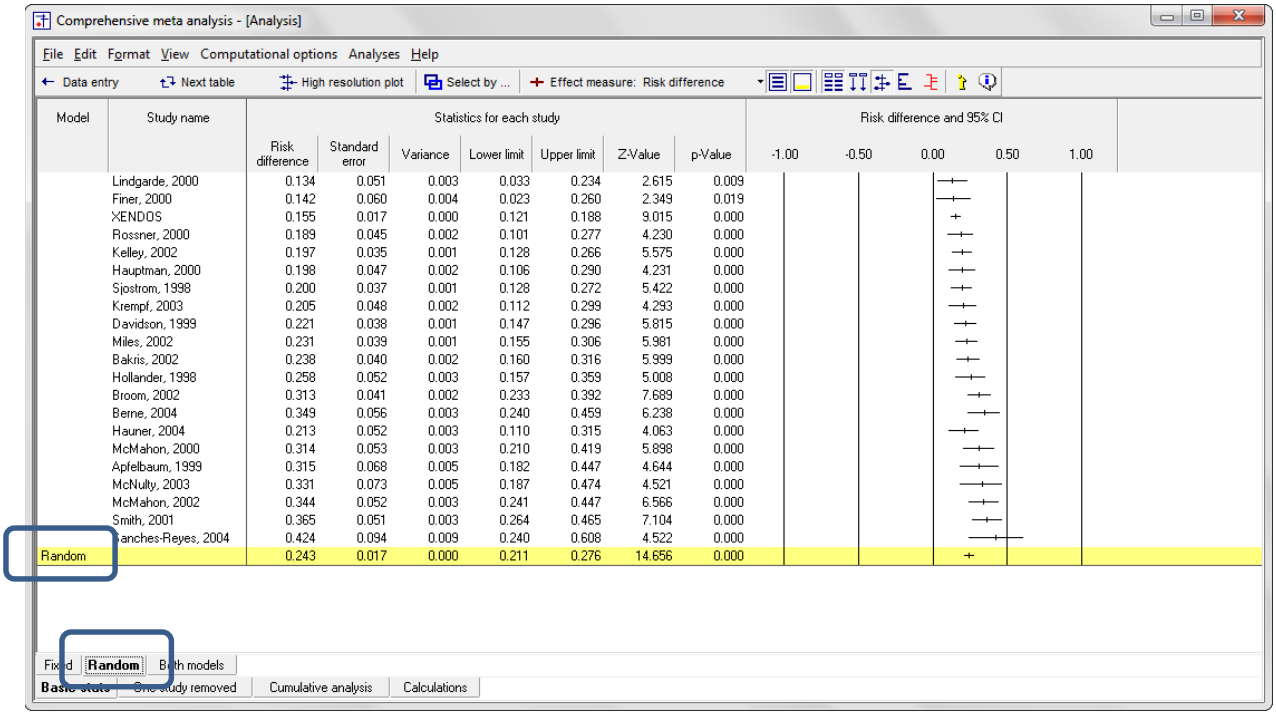
The fact that the two results differ tells us that the RE weights are different from the FE weights. This means that T^2, the estimate of between-study variance in true effects is not zero.

The confidence interval is wider for random-effects than for fixed-effects. This will always be the case when T^2 is not zero.

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

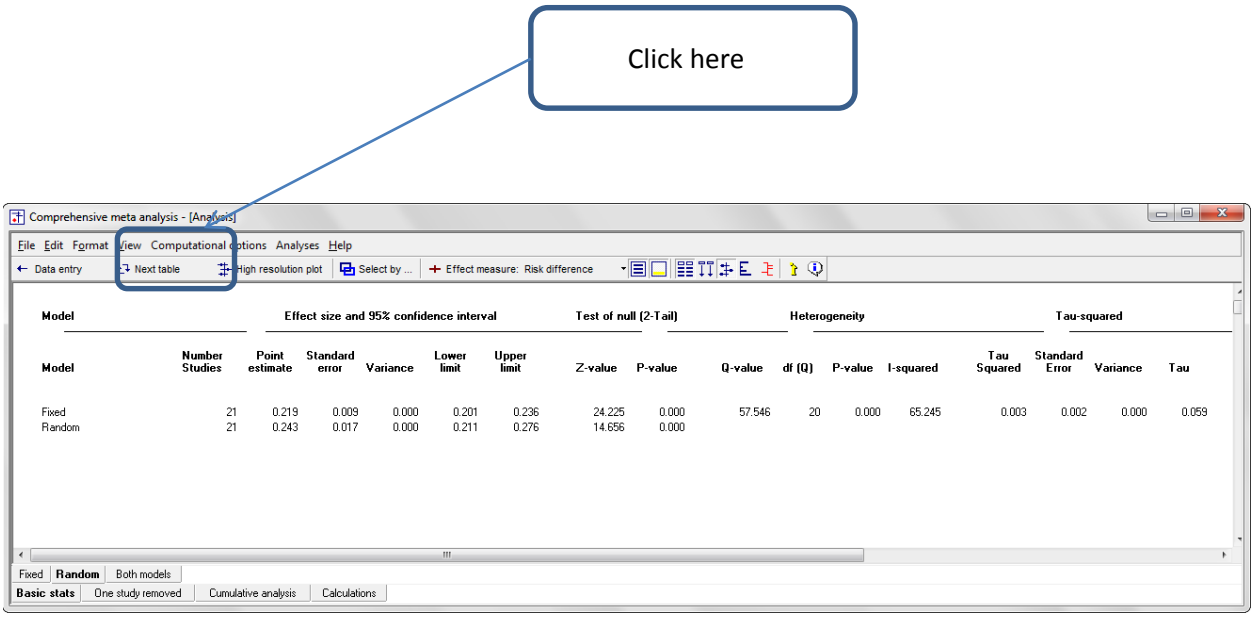
The plot now displays the random-effects analysis alone.



A quick view of the plot suggests the following

- All of the studies suggest an advantage for treatment over placebo
- The observed effect size ranges over a wide area. The dispersion appears to be more than we would expect based on the precision of each study.
- The summary effect is 0.243. On average, the success rate on drug was 24 percentage points higher than the success rate on placebo. The CI is 0.211 to 0.276, which tells us that the mean effect is clearly in the clinically important range.
- The summary effect has a Z-value 14.656 and a *p*-value of < 0.001. Thus we can reject the null hypotheses that the true risk difference is 0.0.
- To have a closer look at this variance we turn to the next table.

Click [Next table]



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

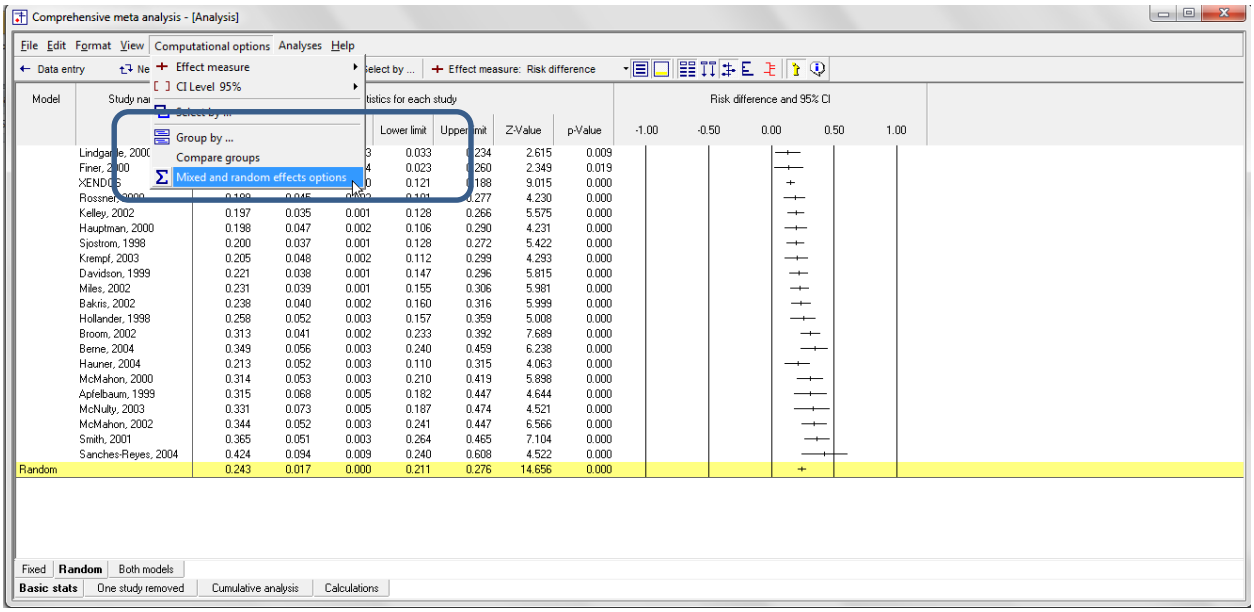
- Under the random-effects model the risk difference is 0.243 with a 95% confidence interval of 0.211 to 0.276. The test of the null (that the true risk difference is 0.0) yields a Z-value of 14.656 and a corresponding p-value of < 0.001.
- The statistics at the upper right relate to the dispersion of effect sizes across studies.
- The Q-value is 57.546 with df=20 and p < 0.001. *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 20). Here, Q exceeds that value, and so the estimate of T2 for the sample will be greater than zero. Additionally, Q exceeds that value by a large enough margin, so that we can find that T2 exceeds zero not only in the sample, but also for the population. Concretely, p < 0.001, and we reject the null hypothesis that all studies in the universe from which the sample was drawn share the same true effect size.
- T^2 is the estimate of the between-study variance in true effects. This estimate is 0.003. *T* is the estimate of the between-study standard deviation in true effects. This estimate is 0.059.
- I2 reflects the proportion of true variance to observed variance. This estimate is 65%. This means that if each of the studies had a huge sample size (and therefore estimated the effect in its population with little error) the variance in observed effect sizes would shrink to about 65% of the current value.
- Click [Next table] to return to this screen

In this analysis we want to focus on the treatment effect as a function of Drug. Specifically, we're going to run the analysis separately (a) for studies that compared Orlistat vs. placebo and (b) for studies that compared Sibutramine vs. placebo.

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.

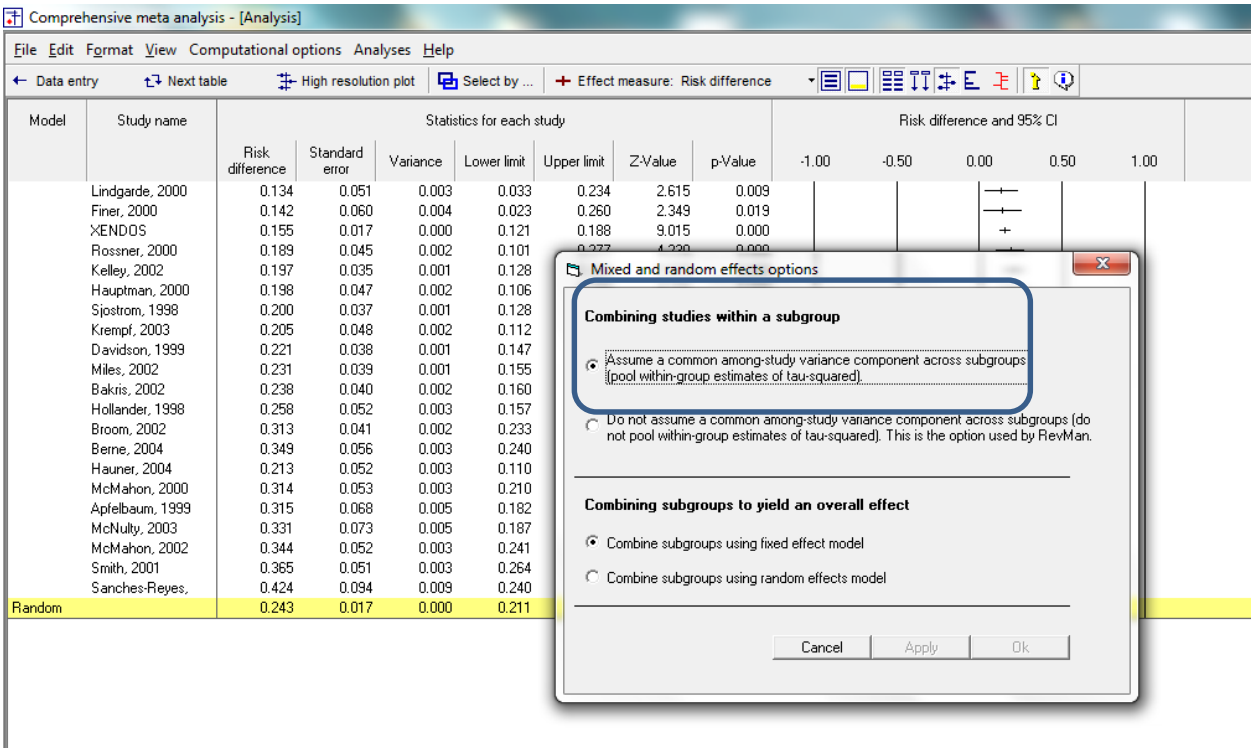
Our plan at the moment is to use a separate estimate for each subgroup. To select that option

Click Computational options > Mixed and random effects options



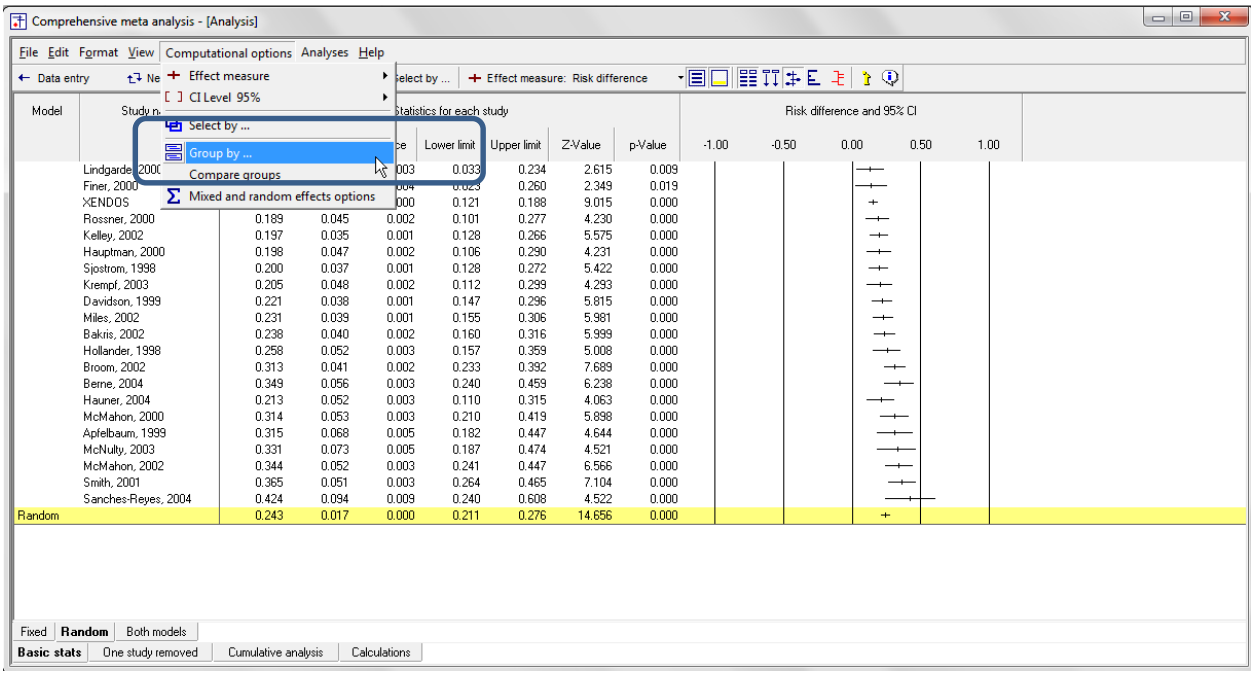
The program displays this wizard

- 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”



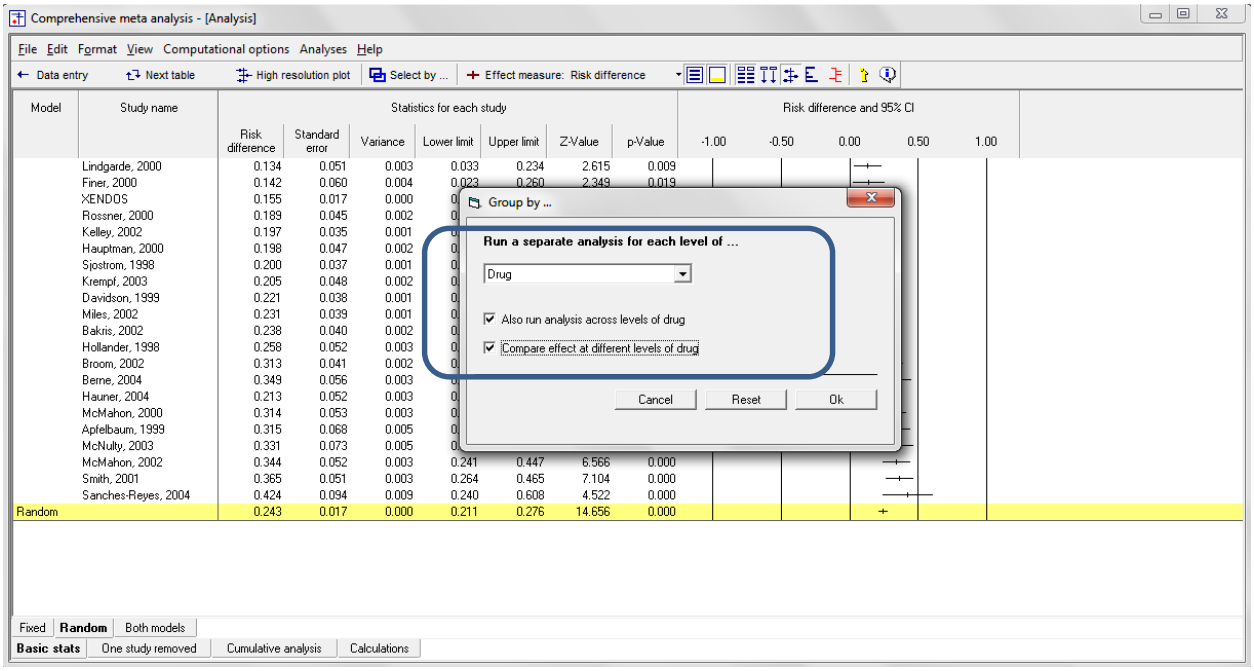
Now, we can tell the program to run the analysis by subgroups.

Click Computational options > Group by

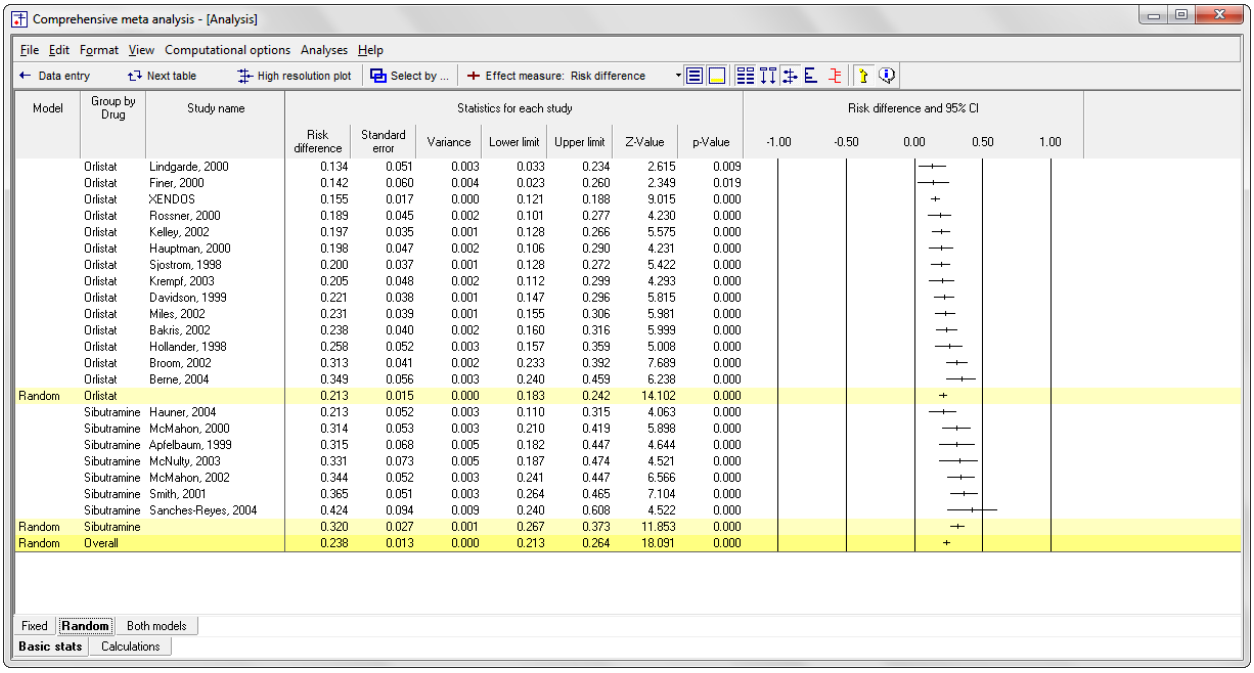


Lindgarde, 2000			0.003	0.033	0.234	2.615	0.009
Finer, 2000			0.004	0.023	0.260	2.349	0.019
XENDOS			0.000	0.121	0.188	9.015	0.000
Rossner, 2000	0.189	0.045	0.002	0.101	0.277	4.230	0.000
Kelley, 2002	0.197	0.035	0.001	0.128	0.266	5.575	0.000
Hauptman, 2000	0.198	0.047	0.002	0.106	0.290	4.231	0.000
Sjostrom, 1998	0.200	0.037	0.001	0.128	0.272	5.422	0.000
Krempf, 2003	0.205	0.048	0.002	0.112	0.299	4.293	0.000
Davidson, 1999	0.221	0.038	0.001	0.147	0.296	5.815	0.000
Miles, 2002	0.231	0.039	0.001	0.155	0.306	5.981	0.000
Bakris, 2002	0.238	0.040	0.002	0.160	0.316	5.999	0.000
Hollander, 1998	0.258	0.052	0.003	0.157	0.359	5.008	0.000
Broom, 2002	0.313	0.041	0.002	0.233	0.392	7.689	0.000
Berne, 2004	0.349	0.056	0.003	0.240	0.459	6.238	0.000
Hauner, 2004	0.213	0.052	0.003	0.110	0.315	4.063	0.000
McMahon, 2000	0.314	0.053	0.003	0.210	0.419	5.898	0.000
Apfelbaum, 1999	0.315	0.068	0.005	0.182	0.447	4.644	0.000
McNulty, 2003	0.331	0.073	0.005	0.187	0.474	4.521	0.000
McMahon, 2002	0.344	0.052	0.003	0.241	0.447	6.566	0.000
Smith, 2001	0.365	0.051	0.003	0.264	0.465	7.104	0.000
Sanches-Reyes, 2004	0.424	0.094	0.009	0.240	0.608	4.522	0.000
Random	0.243	0.017	0.000	0.211	0.276	14.656	0.000

- Select Drug
- Check the two boxes
- Click Ok


Comprehensive meta analysis - [Analysis]
File Edit Format View Computational options Analyses Help
Data entry
Next table
High resolution plot
Select by ...
Effect measure: Risk difference
Model
Study name
Statistics for each study
Risk difference
Standard error
Variance
Lower limit
Upper limit
Z-Value
p-Value
Risk difference and 95% CI
-1.00
-0.50
0.00
0.50
1.00
Lindgarde, 2000 0.134 0.051 0.003 0.033 0.234 2.615 0.009
Finer, 2000 0.142 0.060 0.004 0.023 0.260 2.349 0.019
XENDOS 0.155 0.017 0.000
Rossner, 2000 0.189 0.045 0.002
Kelley, 2002 0.197 0.035 0.001
Hauptman, 2000 0.198 0.047 0.002
Sjostrom, 1998 0.200 0.037 0.001
Krempf, 2003 0.205 0.048 0.002
Davidson, 1999 0.221 0.038 0.001
Miles, 2002 0.231 0.039 0.001
Bakris, 2002 0.238 0.040 0.002
Hollander, 1998 0.258 0.052 0.003
Broom, 2002 0.313 0.041 0.002
Berne, 2004 0.349 0.056 0.003
Hauner, 2004 0.213 0.052 0.003
McMahon, 2000 0.314 0.053 0.003
Apfelbaum, 1999 0.315 0.068 0.005
McNulty, 2003 0.331 0.073 0.005
McMahon, 2002 0.344 0.052 0.003 0.241 0.447 6.566 0.000
Smith, 2001 0.365 0.051 0.003 0.264 0.465 7.104 0.000
Sanches-Reyes, 2004 0.424 0.094 0.009 0.240 0.608 4.522 0.000
Random 0.243 0.017 0.000 0.211 0.276 14.656 0.000
Group by ...
Run a separate analysis for each level of ...
Drug
Also run analysis across levels of drug
Compare effect at different levels of drug
Cancel
Reset
Ok
Fixed
Random
Both models
Basic stats
One study removed
Cumulative analysis
Calculations

The screen should look like this



For the Orlistat studies the mean effect size is a risk difference of 0.213 with a confidence interval of 0.183 to 0.242, a Z-value of 14.102 and a corresponding p-value of < 0.001. It's clear that the drug is more effective than placebo, and that the impact is clinically as well as statistically significant.

For the Sibutramine studies the mean effect size is a risk difference of 0.320 with a confidence interval of 0.267 to 0.373, a Z-value of 11.853 and a corresponding p-value of < 0.001. It's clear that the drug is more effective than placebo, and that the impact is clinically as well as statistically significant.

For all studies together the mean effect size is a risk difference of 0.238 with a confidence interval of 0.213 to 0.264, a Z-value of 18.091 and a corresponding p-value of < 0.001. However, given that we had intended a priori to study the effect as a function of drug, this overall effect has limited meaning. In particular, the overall mean will depend on what proportion of the studies employed one drug rather than the other.

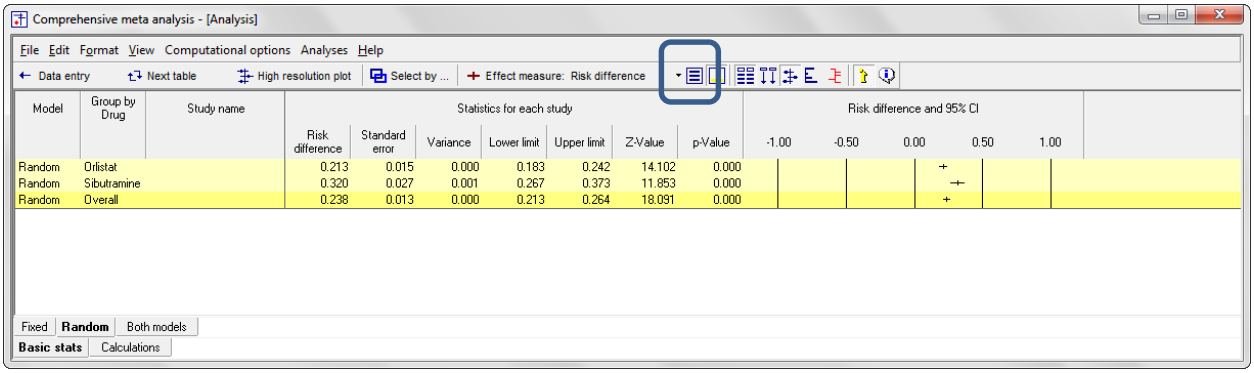
Therefore, we are better off focusing on the mean effect for each subgroup.

We want to know if the difference between the two effect sizes (0.213 vs. 0. 320) is statistically significant, and we'll run a test for this.

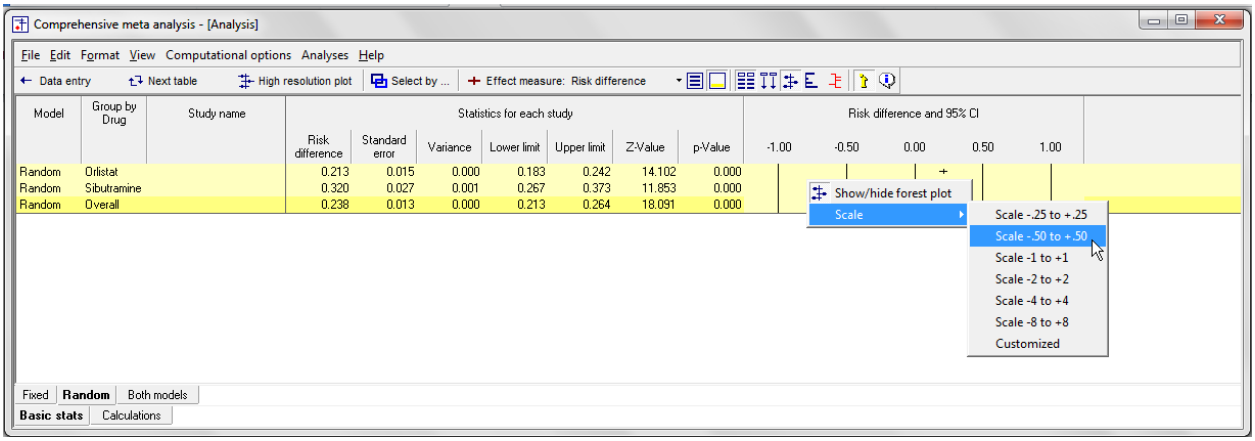
To get a better sense of what we're testing, click the "All studies" button. This will hide all of the individual studies and display the summary effects only as shown here.

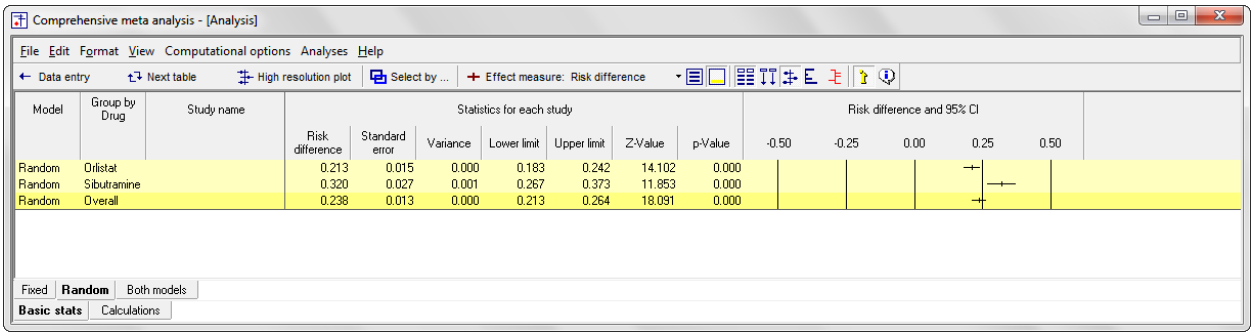
The test will compare the two mean effects relative to the precision of each effect. For two groups we can think of this as a Z-test for the ratio of the difference in means to the standard error of the difference.

Toggle the "All studies button" to display the studies again.



We can right-click on the plot and expand the scale to see this more clearly





Here, it seems clear that there is no overlap between the confidence intervals for the two subgroups. We would therefore expect that the test to compare the two means will yield a statistically significant p-value.

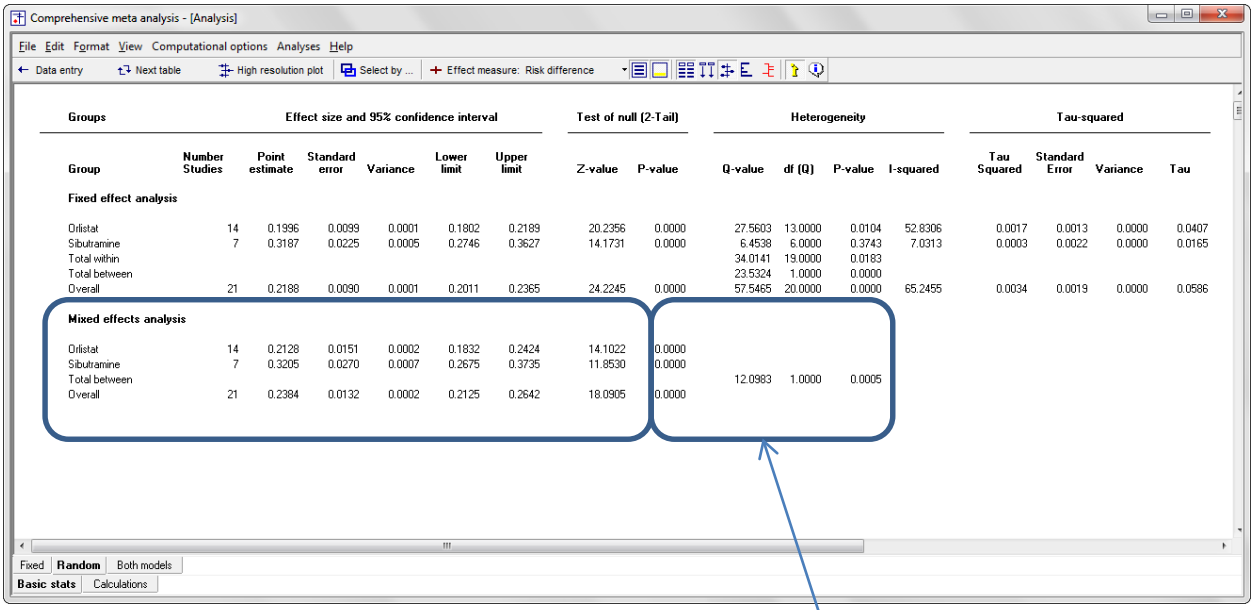
Click Next Table to see the results

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.

Click Format > Increase decimals



Groups		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Group	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed effect analysis																
Orlistat	14	0.1996	0.0099	0.0001	0.1802	0.2189	20.2356	0.0000	27.5603	13.0000	0.0104	52.8306	0.0017	0.0013	0.0000	0.0407
Sibutramine	7	0.3187	0.0225	0.0005	0.2746	0.3627	14.1731	0.0000	6.4538	6.0000	0.3743	7.0313	0.0003	0.0022	0.0000	0.0165
Total within									34.0141	19.0000	0.0183					
Total between									23.5324	1.0000	0.0000					
Overall	21	0.2188	0.0090	0.0001	0.2011	0.2365	24.2245	0.0000	57.5465	20.0000	0.0000	65.2455	0.0034	0.0019	0.0000	0.0586
Mixed effects analysis																
Orlistat	14	0.2128	0.0151	0.0002	0.1832	0.2424	14.1022	0.0000								
Sibutramine	7	0.3205	0.0270	0.0007	0.2675	0.3735	11.8530	0.0000								
Total between									12.0983	1.0000	0.0005					
Overall	21	0.2384	0.0132	0.0002	0.2125	0.2642	18.0905	0.0000								

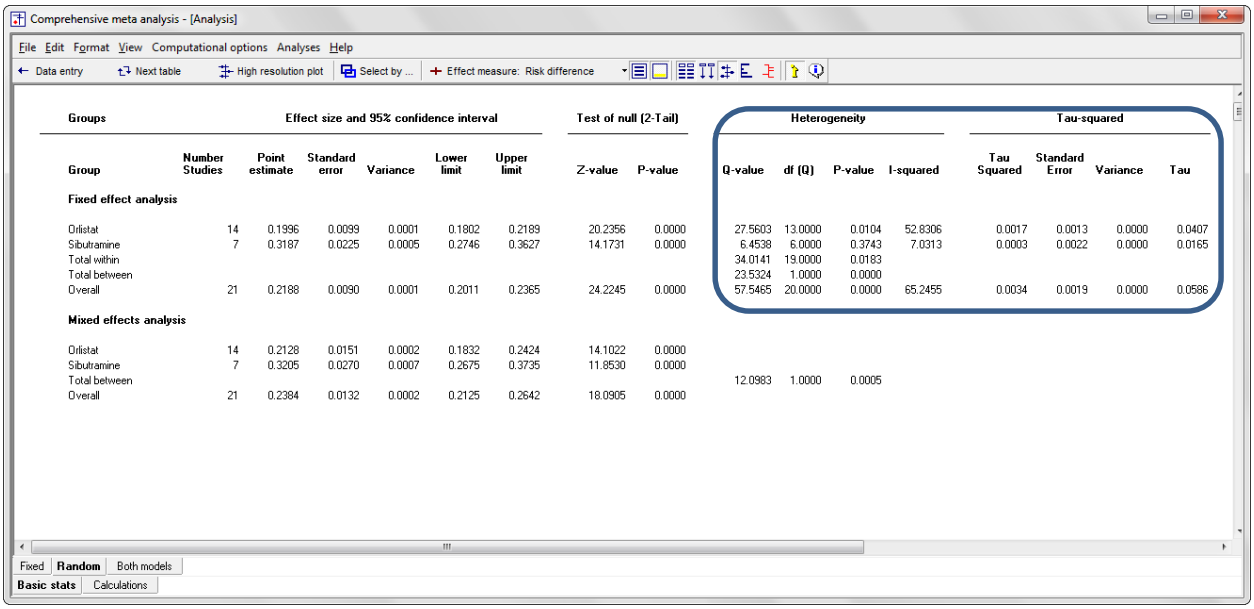
Toward the left of the screen the program displays the same numbers we saw a moment ago.

For the Orlistat studies the mean effect size is a risk difference of 0.213 with a confidence interval of 0.183 to 0.242, a Z-value of 14.102 and a corresponding p-value of < 0.001. It's clear that the drug is more effective than placebo, and that the impact is clinically as well as statistically significant.

For the Sibutramine studies the mean effect size is a risk difference of 0.320 with a confidence interval of 0.267 to 0.373, a Z-value of 11.853 and a corresponding p-value of < 0.001. It's clear that the drug is more effective than placebo, and that the impact is clinically as well as statistically significant.

The test to compare the two effect sizes (0.213 vs. 0.320) yields a Q-value of 12.098 with 1 df and a corresponding p-value of 0.001.

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.



Groups		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Group	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed effect analysis																
Orlistat	14	0.1996	0.0099	0.0001	0.1802	0.2189	20.2356	0.0000	27.5603	13.0000	0.0104	52.8306	0.0017	0.0013	0.0000	0.0407
Sibutramine	7	0.3187	0.0225	0.0005	0.2746	0.3627	14.1731	0.0000	6.4538	6.0000	0.3743	7.0313	0.0003	0.0022	0.0000	0.0165
Total within									34.0141	19.0000	0.0183					
Total between									23.5324	1.0000	0.0000					
Overall	21	0.2188	0.0090	0.0001	0.2011	0.2365	24.2245	0.0000	57.5465	20.0000	0.0000	65.2455	0.0034	0.0019	0.0000	0.0586
Mixed effects analysis																
Orlistat	14	0.2128	0.0151	0.0002	0.1832	0.2424	14.1022	0.0000								
Sibutramine	7	0.3205	0.0270	0.0007	0.2675	0.3735	11.8530	0.0000								
Total between									12.0983	1.0000	0.0005					
Overall	21	0.2384	0.0132	0.0002	0.2125	0.2642	18.0905	0.0000								

For the Orlistat studies the variance in effects yields a *Q*-value of 27.560 with 13 *df* and $p = 0.010$. T^2 is estimated at 0.002, *T* is 0.041, and I^2 is 52.831%

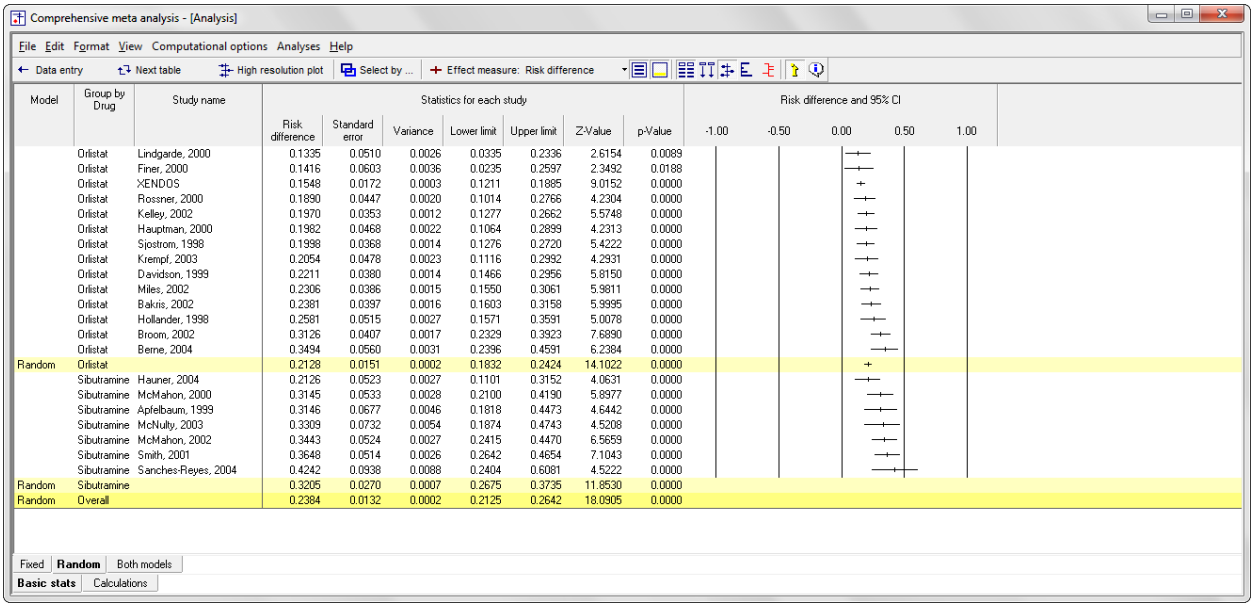
For the Sibutramine studies the variance in effects yields a *Q*-value of 6.454 with 6 *df* and p = 0.374. T^2 is estimated at 0.0003, *T* is 0.017, and I^2 is 7.031%

We can also perform an omnibus test by pooling the *Q* values and *df* across subgroups. The pooled *Q* is 34.014 with $df = 19$ and $p = 0.018$.

These tests are goodness-of-fit tests. They ask if the grouping (Orlistat vs. Sibutramine) explains all of the variance in true effect sizes, or if some true variance remains, even within subgroups. Here, there is evidence of true variance within subgroups.

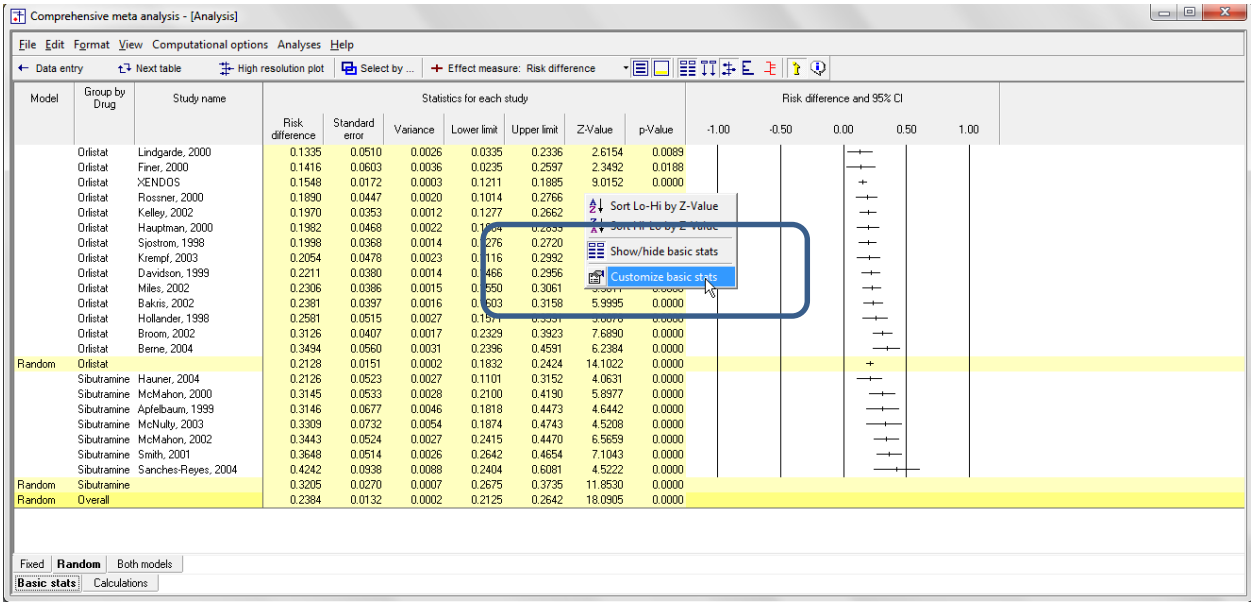
Note that the tests of homogeneity are displayed in the fixed-effect section, even though we're using the random-effects model within subgroups. This is because these tests always are always based on using within-study (fixed-effect) weights. That is, we pose the null (that T^2 is zero) and then see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

Click Next table to return to this screen.

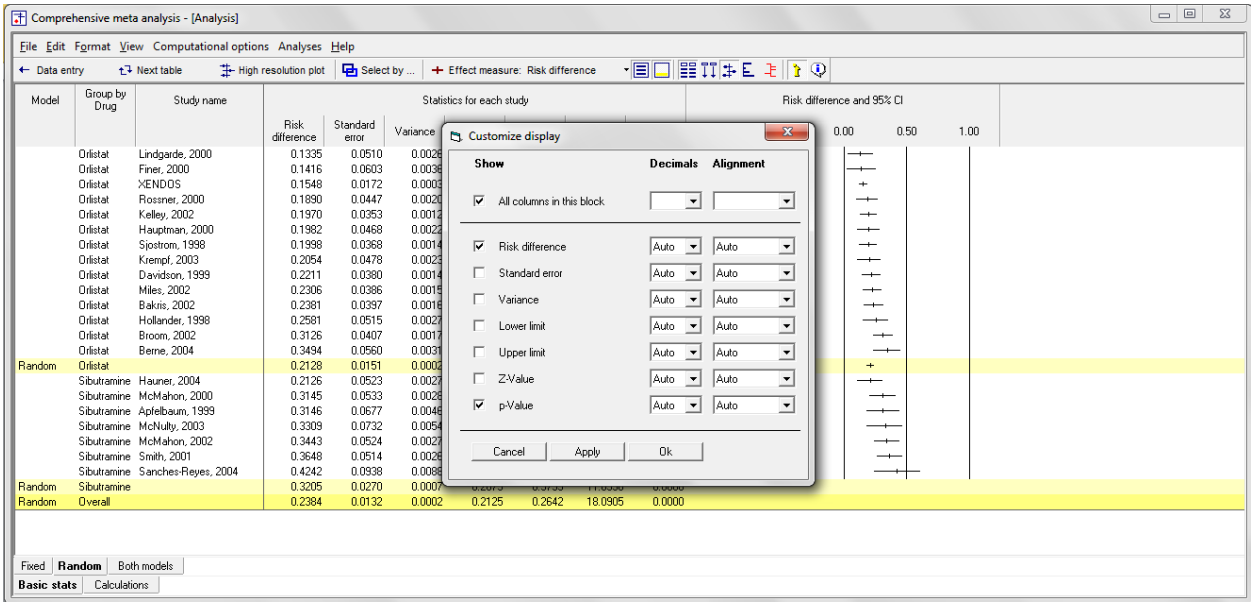


Next, we want to create a high-resolution plot

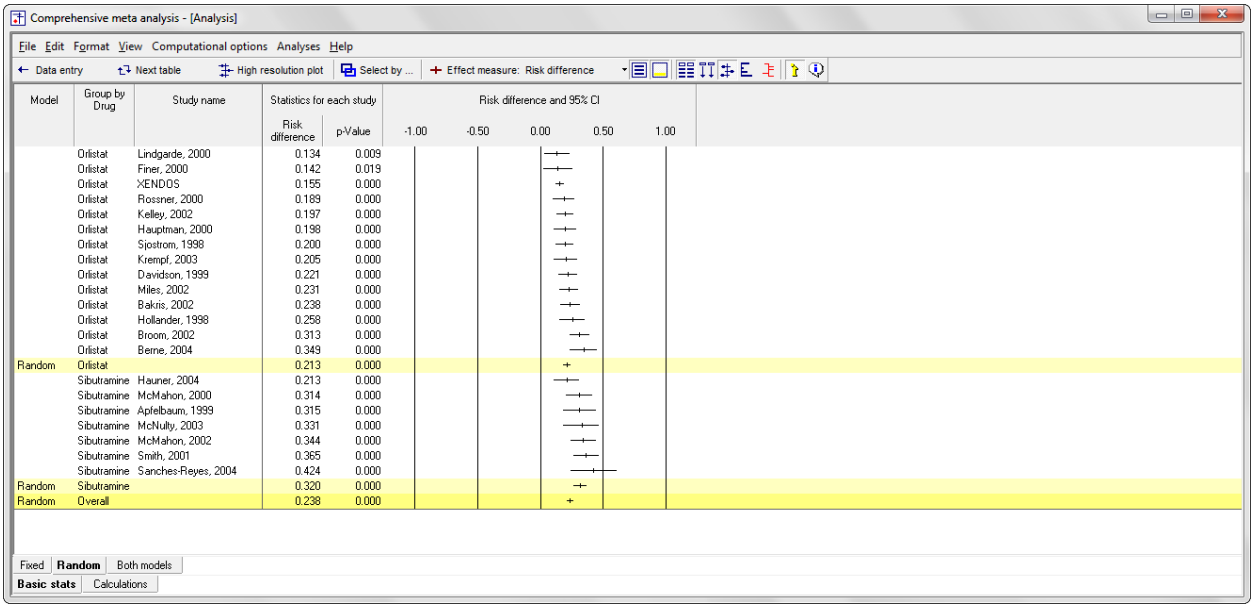
- Right-click on the statistics section
- Select Customize basic stats



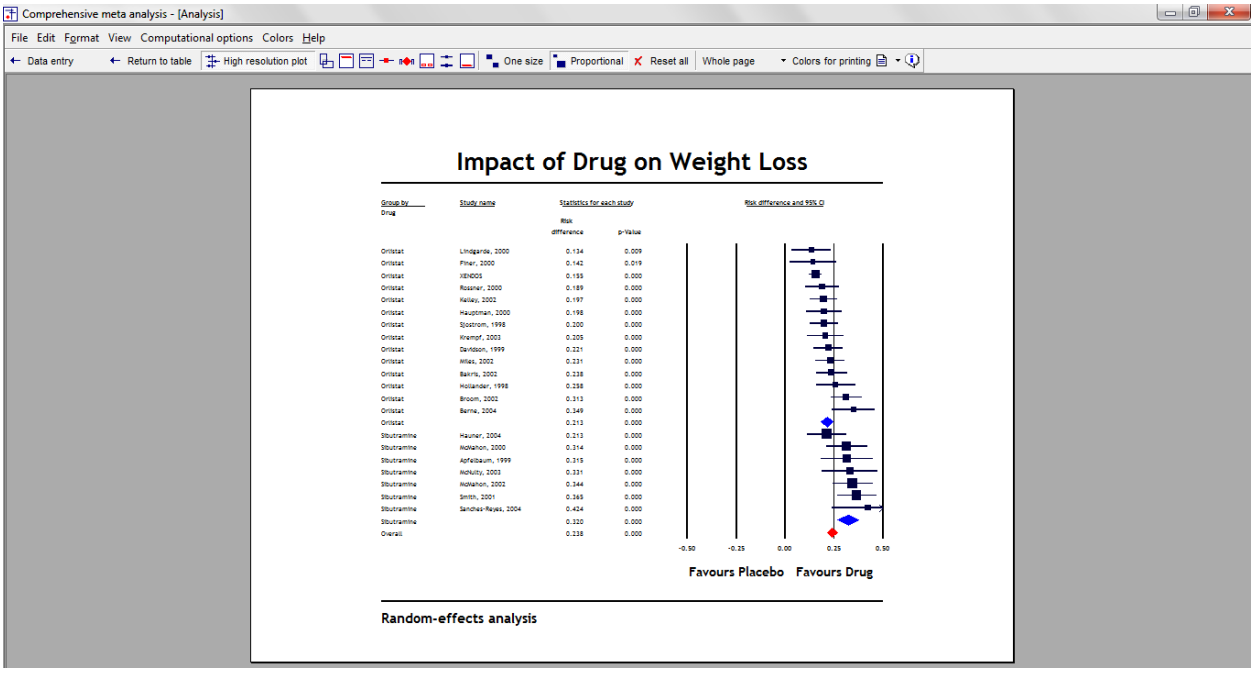
- Check the boxes for risk difference and p-value
- Uncheck all other boxes
- Click Ok



The screen should look like this



- Click High-Resolution plot
- Reset All
- The screen should look like this



It's always a good idea to double-check the labels, and ensure that the studies classified as "Favors Drug" did indeed have the higher lower event rate if the event is success, as it is here – or a lower event rate if the event is a bad outcome.

Now that we've established that the treatment effect varies by drug, we might want to run a completely separate analysis for the Orlistat studies and for the Sibutramine studies.

The basic idea would be Select by drug, and then to run the same kind of analysis that we normally use for a single set of studies.

Summary

This analysis includes 21 studies where patients were randomized to receive either a drug or placebo. Outcome was the proportion of patients meeting a criterion for success in losing weight. The effect size was the risk difference, i.e. the difference in success rates between the two groups.

Some studies compared Orlistat vs. placebo while others compared Sibutramine vs. placebo. The primary goal of the meta-analysis was to compare subgroups of studies, i.e. to see if the risk difference is higher (or lower) in studies that used Orlistat as compared with studies that used Sibutramine.

Are the drugs effective?

The mean risk difference is 0.243, which means that being assigned to a drug rather than a placebo resulted in a 24.3 point increase in the likelihood of success.

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 difference is 0.211 to 0.276, which tell us that the mean risk difference in the universe of studies could fall anywhere in this range. This range does not include a risk difference of zero, which tells us that the mean risk difference in the universe of studies is probably not zero.

Similarly, the *Z*-value for testing the null hypothesis (that the mean risk difference is zero) is 14.656, with a corresponding *p*-value is < 0.001. We can reject the null that the likelihood of success is the same in both groups, and conclude that the likelihood of success is higher in the drug group.

Is drug type (Orlistat vs. Sibutramine) related to the likelihood of success?

The mean effect for the Orlistat studies was 0.213 with a confidence interval of 0.183 to 0.252. The mean effect for the Sibutramine studies was 0.320 with a confidence interval of 0.268 to 0.374. The test for the difference between means yields a Q-value of 12.098 with 1 df and p=0.0005.

We reject the null that the mean true effect is identical in the two (in the universe from which the Orlistat studies were sampled and the universe from which the Sibutramine studies were sampled), and conclude that the effect is stronger in the Sibutramine studies.

In each study random-assignment was used to allocate patients to drug or placebo. Within a study we can assume that the patients in each condition are identical except for being given drug or placebo. Therefore, the main effect in each study (drug vs. placebo) can be attributed to the drug. Similarly, the main effect in the analysis (Drug vs. placebo across all studies) can be attributed to the drug.

By contrast, random-assignment was not used to allocate studies to Orlistat vs. Sibutramine. We cannot assume that the populations in the two subgroups of studies were identical in all respects except for the choice of drug. It's possible, for example, that one drug was favored at sites that had an older population while the other was favored at sites that had a younger population. Therefore, while we can report that one subgroup did better than the other, we cannot say definitively that this was due to the drug.