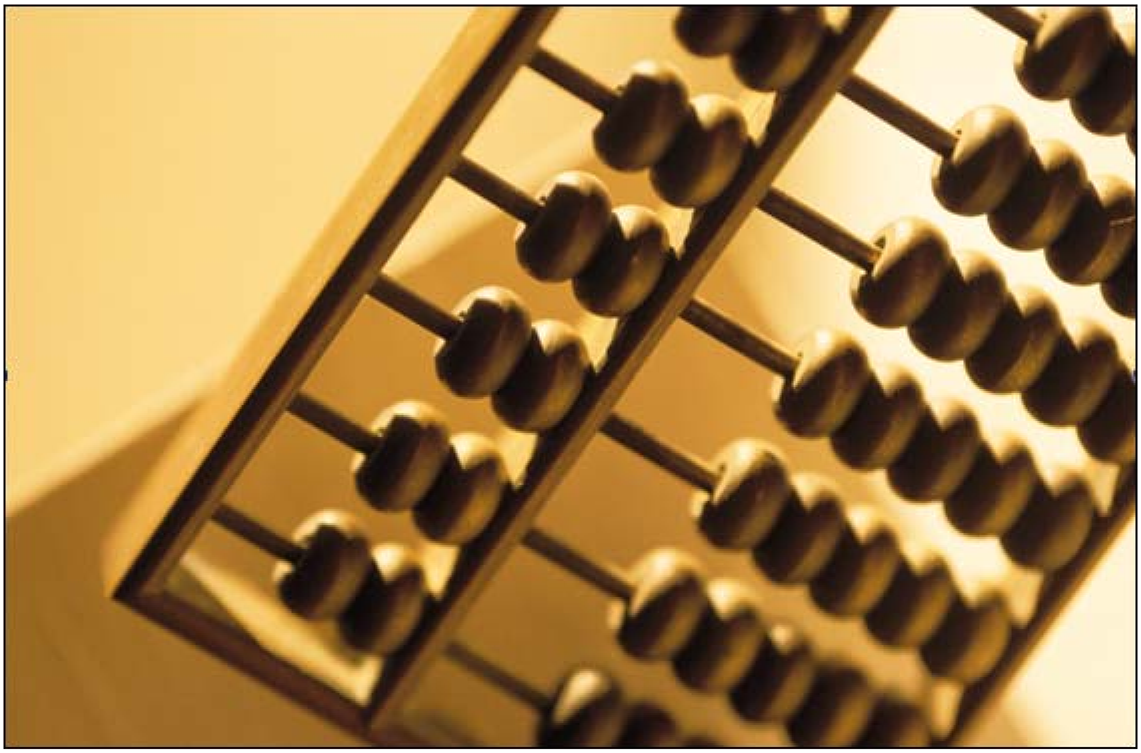
Comprehensive Meta Analysis Version 2.0

This manual will continue to be revised to reflect changes in the program. It will also be expanded to include chapters covering conceptual topics. Upgrades to the program and manual will be available on our download site.



Comprehensive Meta Analysis
Version 2

Developed by

Michael Borenstein
Larry Hedges
Julian Higgins
Hannah Rothstein

Advisory group

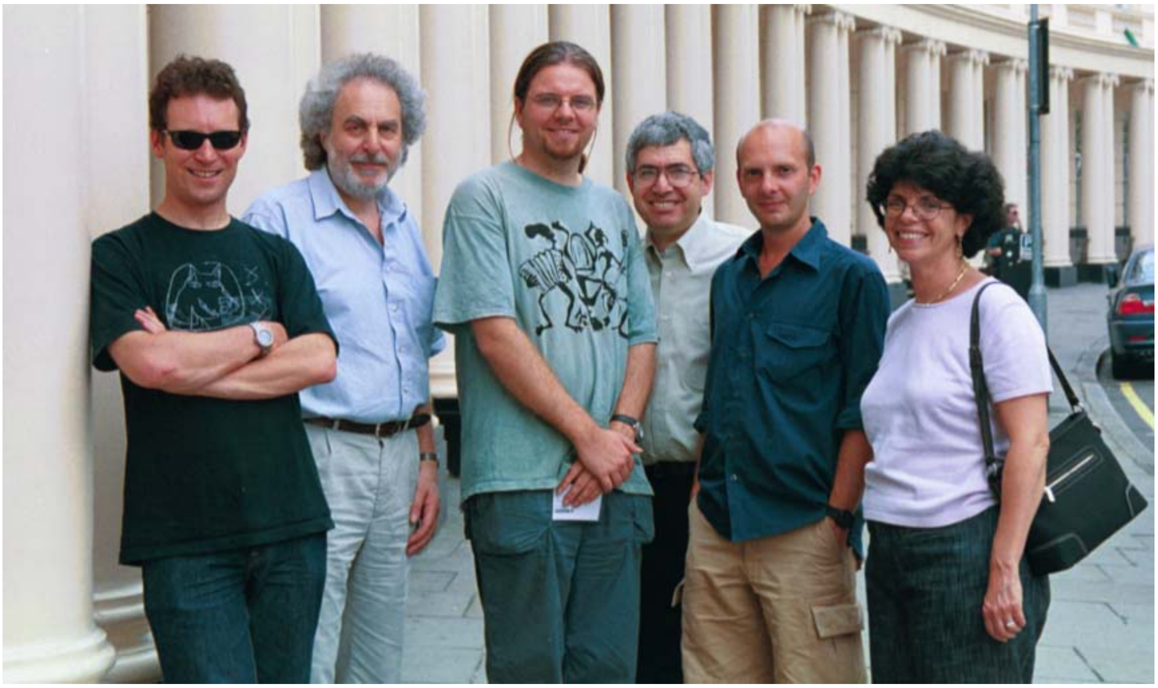
Doug Altman
Betsy Becker
Jesse Berlin
Harris Cooper
Despina Contopoulos-Ioannidis
Kay Dickersin
Sue Duval
Matthias Egger
Kim Goodwin
Wayne Greenwood
Julian Higgins
John Ioannidis
Spyros Konstantopoulos
Mark Lipsey
Michael McDaniel
Fred Oswald
Terri Pigott
Stephen Senn
Will Shadish
Jonathan Sterne
Alex Sutton
Steven Tarlow
Thomas Trikalinos
Jeff Valentine
John Vevea
Vish Viswesvaran
David Wilson

This project was funded by the National Institutes of Health

Group meetings to develop the program

July 2002. Left to right (Seated) Vish Viswesvaran, Will Shadish, Hannah Rothstein, Michael Borenstein, Fred Oswald, Terri Pigott. (Standing) Spyros Konstantopoulos, David Wilson, Alex Sutton, Jonathan Sterne, Harris Cooper, Sue Duval, Jesse Berlin, Larry Hedges, Mike McDaniel, Jack Vevea

August, 2003. Left to right (Seated) David Wilson, Betsy Becker, Julian Higgins, Will Shadish, Hannah Rothstein, Michael Borenstein, Mike McDaniel, Steven Tarlow. (Standing) Spyros Konstantopoulos, Larry Hedges, Harris Cooper, John Ioannidis, Despina Contopoulos-Ioannidis, Jack Vevea, Sue Duval, Mark Lipsey, Alex Sutton, Terri Pigott, Fred Oswald, Wayne Greenwood, Thomas Trikalinos.



August, 2004 Left to right: Jonathan Sterne, Doug Altman, Alex Sutton, Michael Borenstein, Julian Higgins, Hannah Rothstein

Introduction

The program installation will create a shortcut labeled Comprehensive Meta Analysis V2 on your desktop and also under “All programs” on the Windows Start menu.

It will also install several data files for use with this guide. These files will be installed in “Demo Files”, beneath the program directory, which (by default) will be C:\Program Files\Comprehensive Meta Analysis Version 2. Within “Demo Files”, select files from the language directory appropriate for your computer’s language settings.

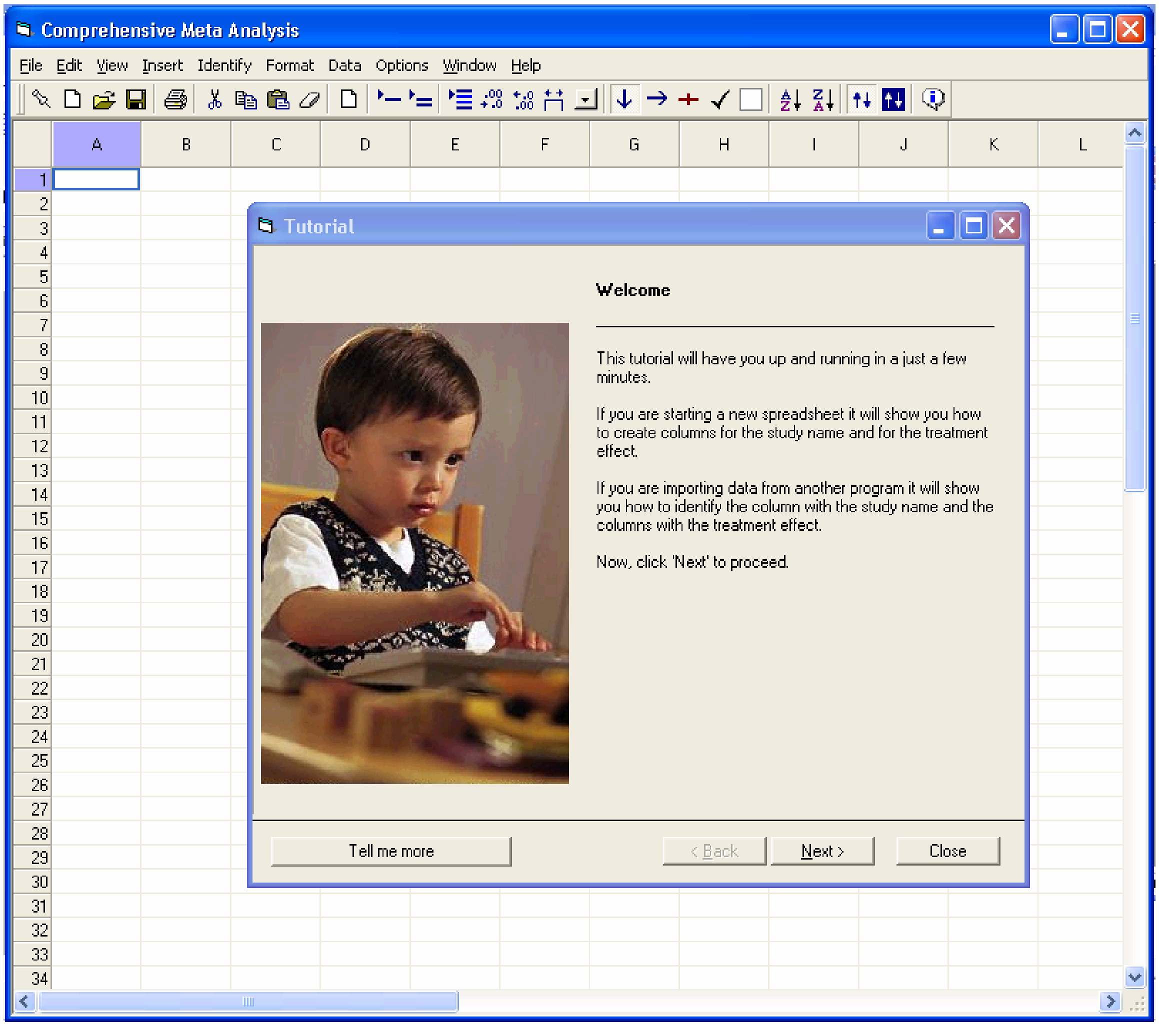
To uninstall the program use the Windows Control panel, select “Add or Remove Programs”, and remove “Comprehensive Meta Analysis Version 2”

This document includes the following sections.

Section 1. Basic data entry and analysis

This section shows how to set up a spreadsheet for data entry and run the basic analyses.

The tutorial



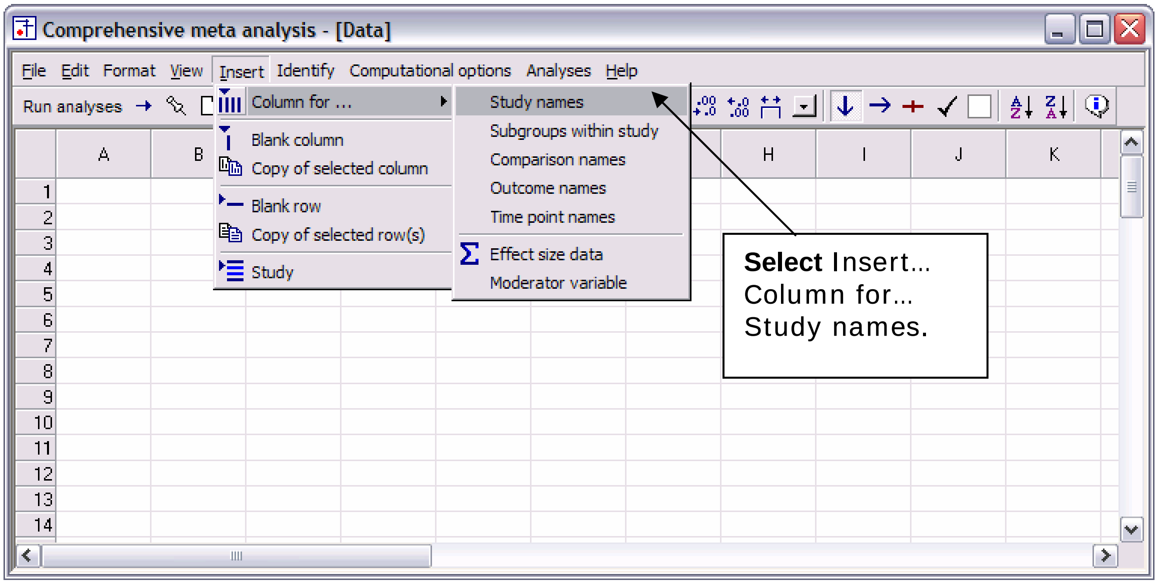
The program includes a tutorial which may be opened from the **Help** menu. The tutorial covers the same material that is explained on the following pages.

Overview

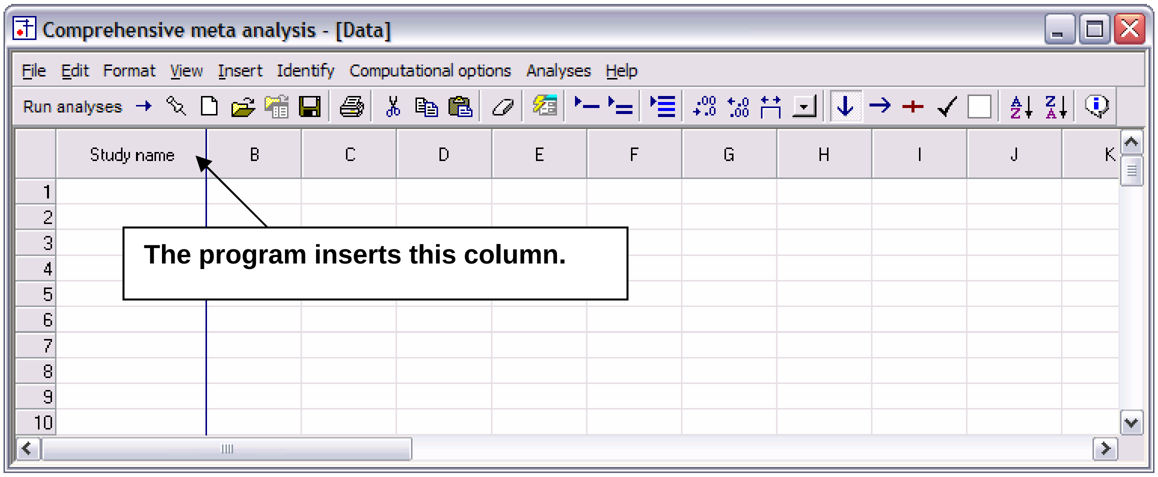
The program uses a spreadsheet for data entry, but requires the user to identify specific columns to hold the study names and the effect size data. This process is explained here.

Create a column for Study Names

Select **Insert… Column for… Study names.**

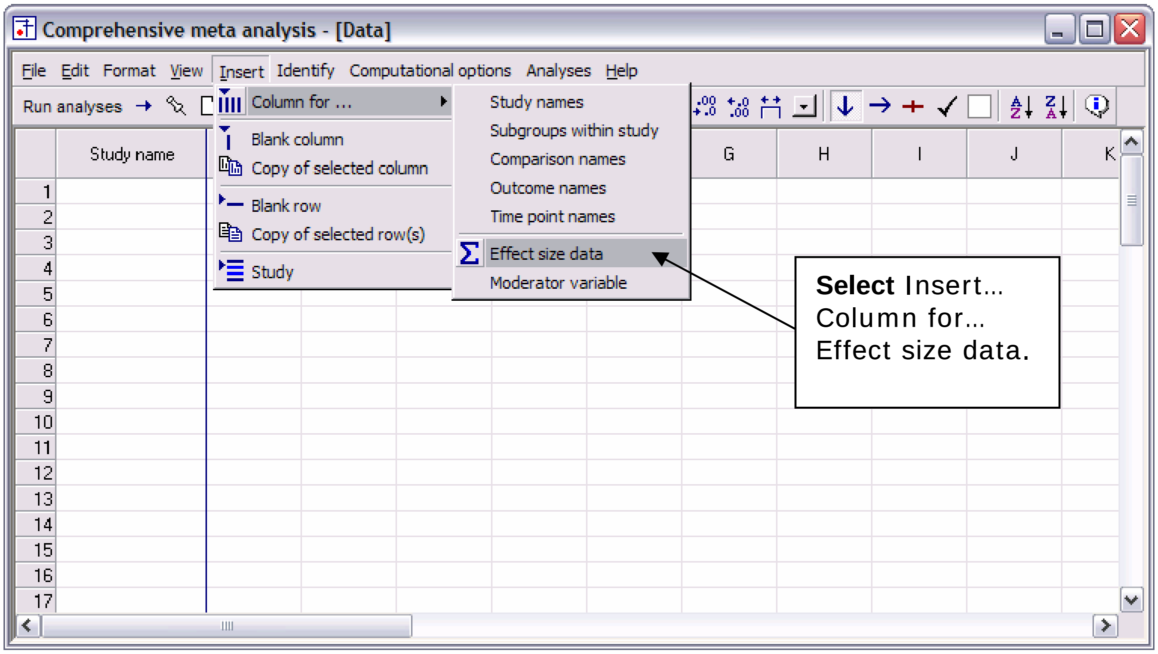


The program will insert a column for study names as shown below.



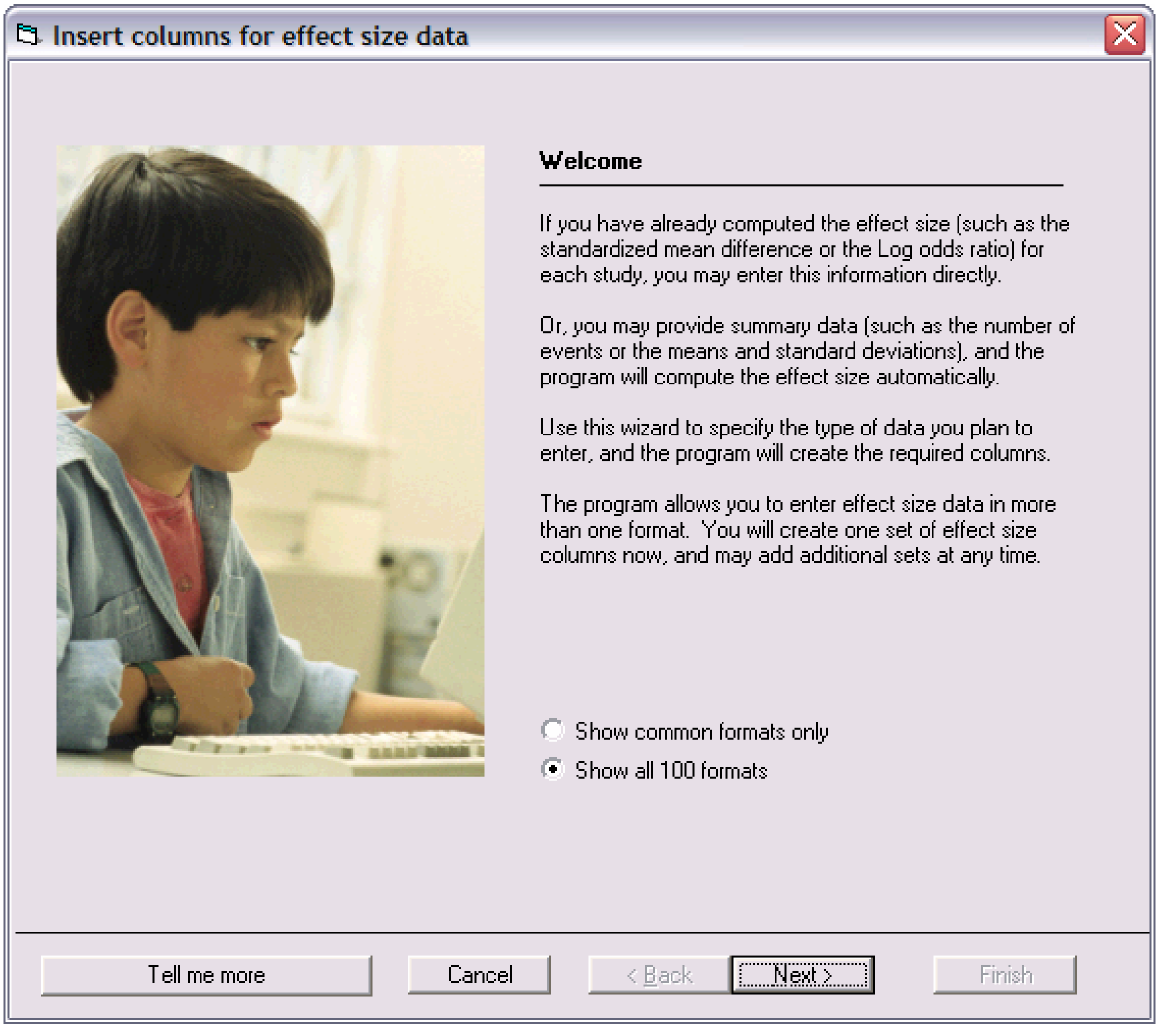
Create columns for effect size data

Select **Insert… Column for… Effect size data.**



This will launch a wizard that allows the user to select the desired format (or formats).

Effect size wizard (Screen 1)



The first screen in the wizard (above) offers an overview of the options for entering effect size data, as follows:

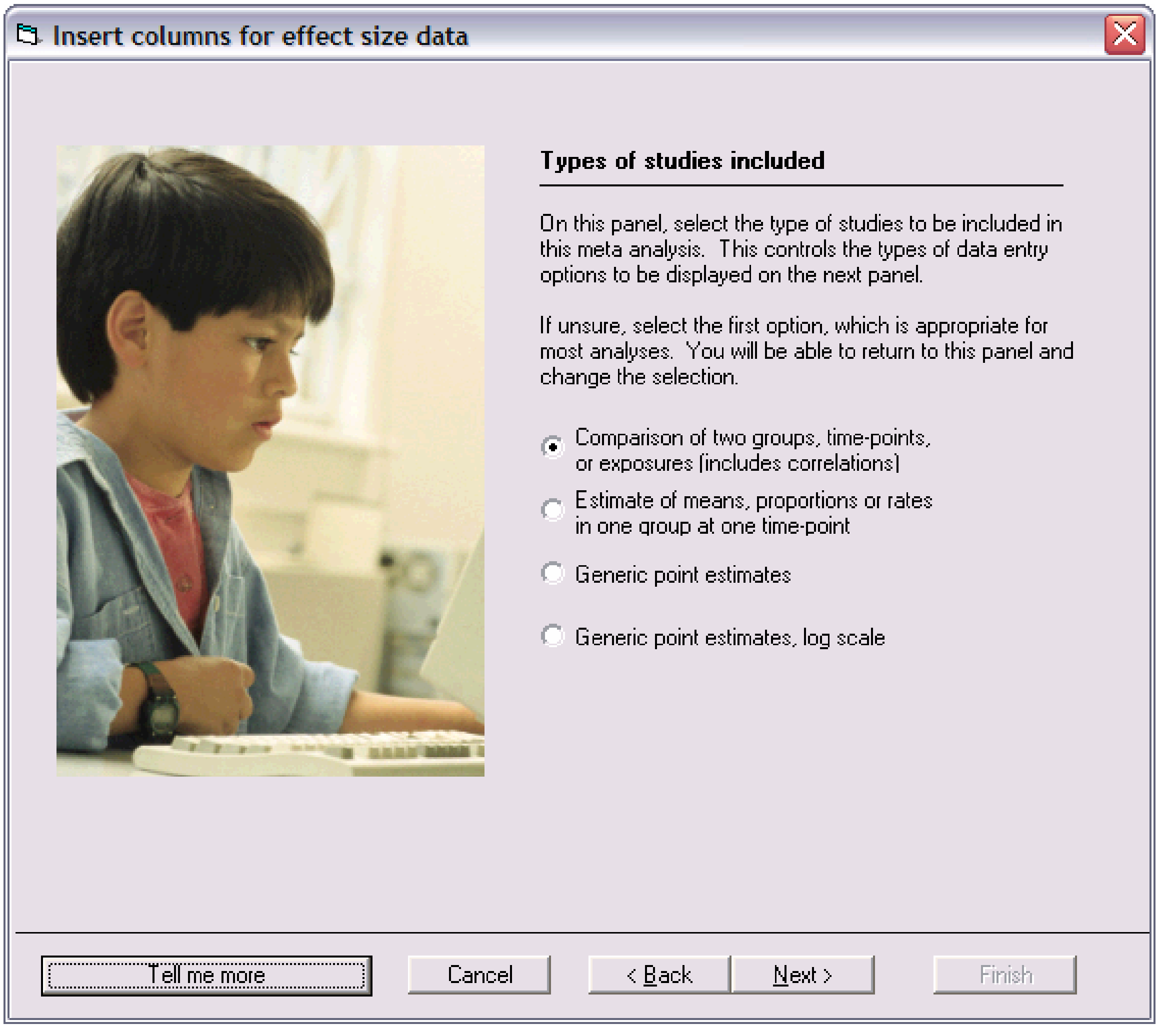
"If you have already computed the effect size (such as the standardized mean difference or the log odds ratio) for each study, you may enter this information directly.

"Or, you may provide summary data (such as the number of events or the means and standard deviations), and the program will compute the effect size automatically.

"Use this wizard to specify the type of data you plan to enter, and the program will create the required columns.

"The program allows you to enter effect size data in more than one format. You will create one set of effect size columns now, and may add additional sets at any time.

Effect size wizard (Screen 2)

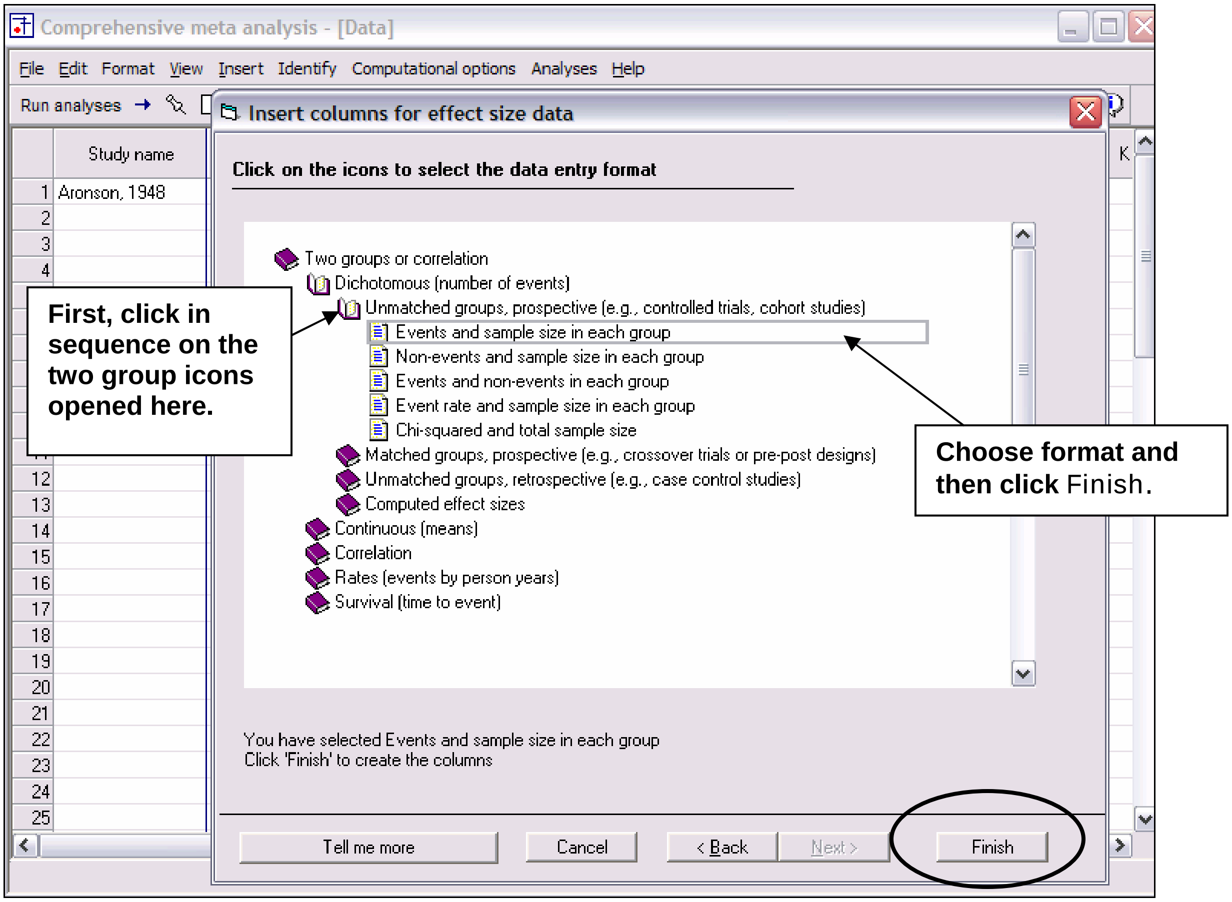


The second screen of the wizard is shown here, and allows the user to select the class of data entry types:

- Comparison of two groups, interventions, or exposures (includes correlations)
- Estimate of means, proportions, or rates in one group at one time-point
- Generic point estimates
- Generic point estimates, log scale

For the running example of the BCG data, select the first option.

Effect size wizard (Screen 3)

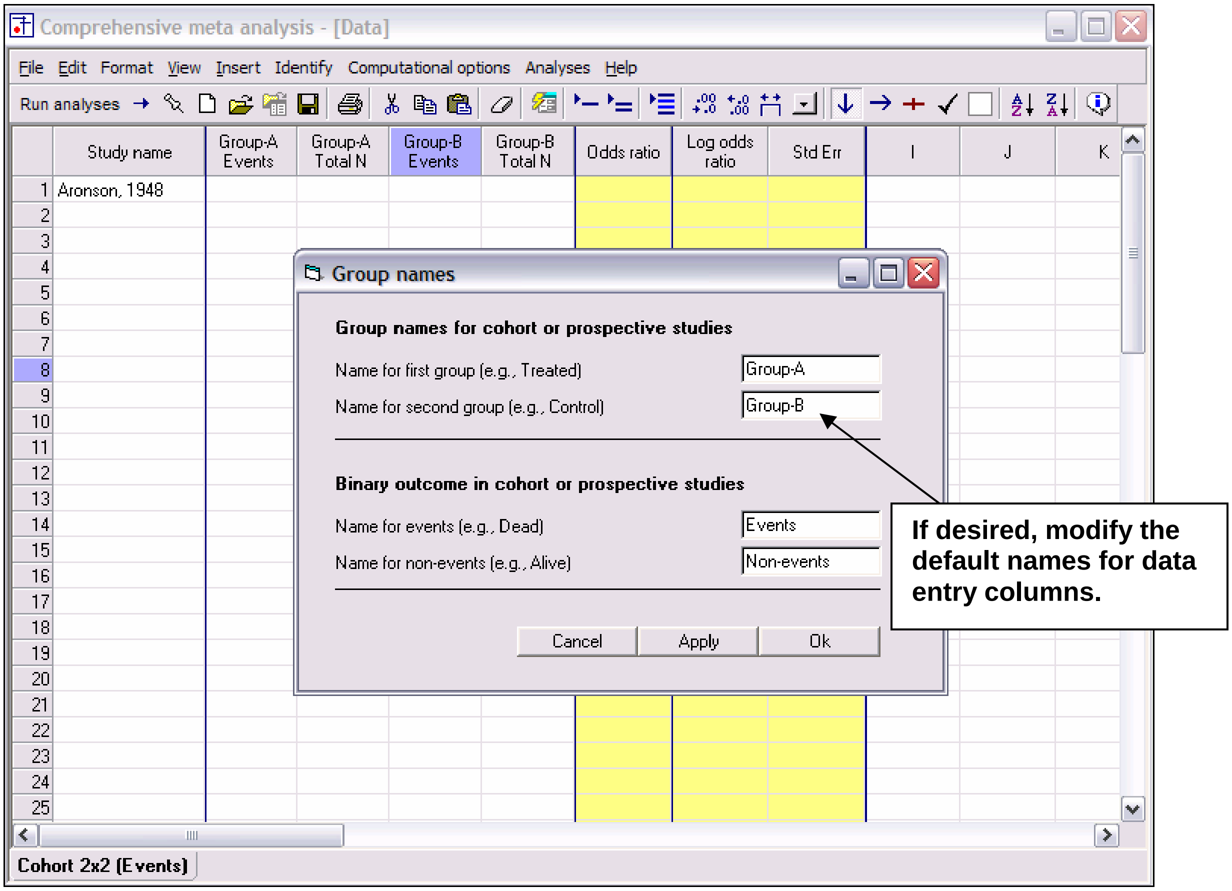


The third screen shows the list of formats arranged hierarchically. In the running example, drill down in the hierarchy to select the following.

- **Dichotomous (number of events)**
    - **Unmatched groups, prospective (e.g., controlled trials, cohort studies)**
        - **Events and sample size in each group**

At this point, the **Finish** button will be activated. Click on it to create the columns for data entry.

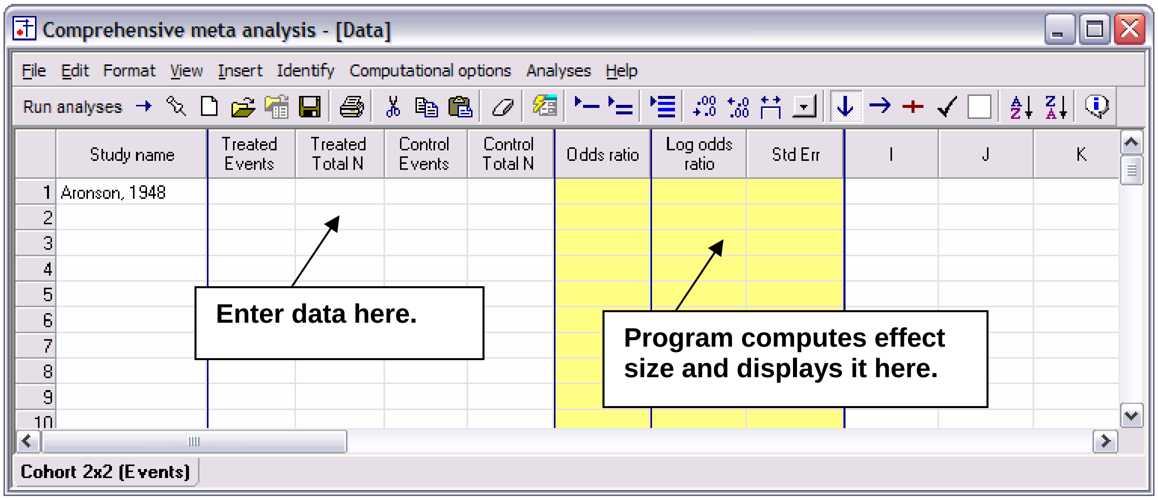
Modify data entry column names



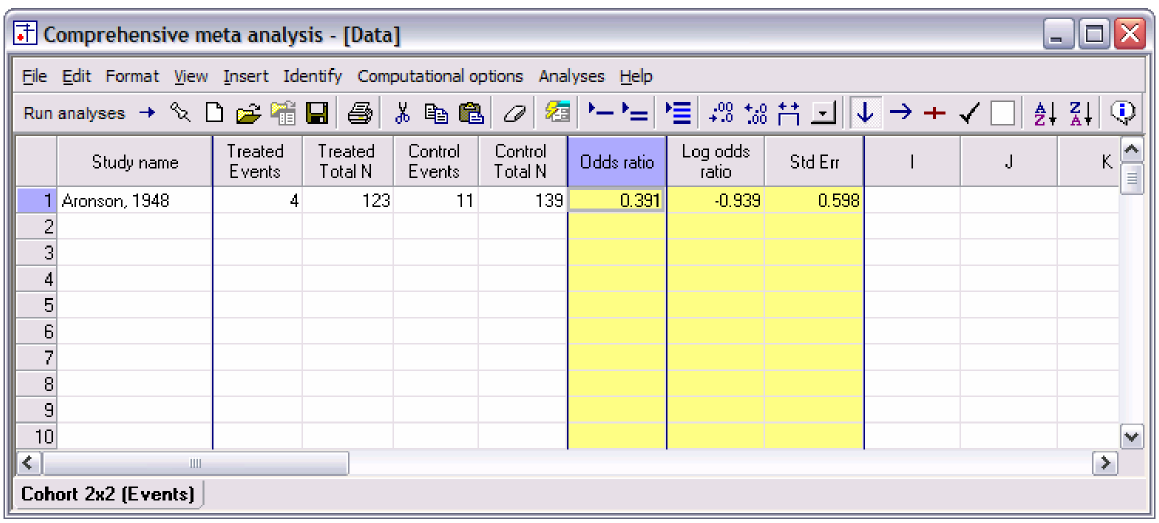
The wizard will close and the program will automatically offer this dialog for modifying effect size format column names. If, for example, you elect to substitute “Treated” for “Group-A” and “Control” for “Group-B”, you will create column names such as “Treated events” and “Control events”.

The modifications made here will be applied not only to the format selected, but also to columns in any related format (in this case, in formats of the “cohort or prospective studies” type). The dialog gives name override suggestions consistent with the format type but will accept any user-entered value.

Enter effect size data



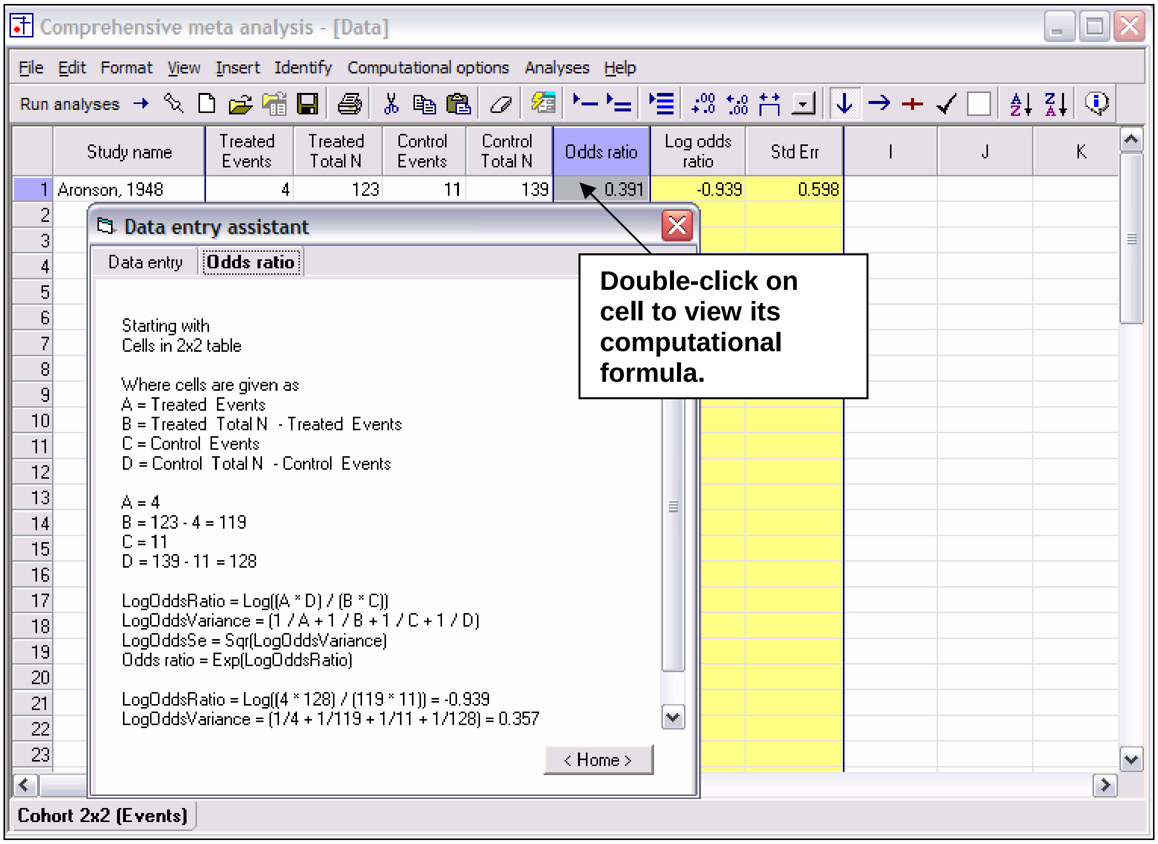
When the group names dialog closes, the spreadsheet looks like this. White columns are used for entering data. Yellow columns display the computed effect size. Note that the entry column names have been modified ("Treated" and "Control" in place of the defaults, "Group-A" and "Group-B").



In the white columns enter the "Number of Events" and "Total N" for the treated group (4, 123) and the control group (11, 139).

The program automatically computes the odds ratio (0.391) as well as the log odds ratio and its standard error (-.939, .598) and displays these in the yellow columns.

View computational formulas

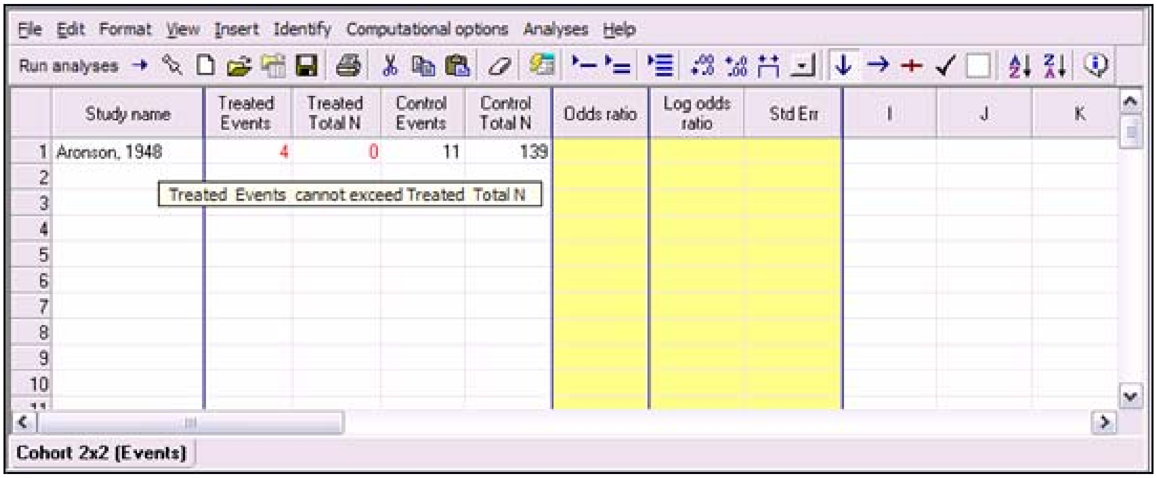


This dialog displays the formulas used to compute the effect size and, when pertinent, standard error, for a given cell's index. It also displays the formulas used to derive related indices. In this case it traces the computation of odds ratio as well as its related index, log odds ratio.

Note that actual numeric values are substituted for variable names at the bottom of the display, clarifying the steps which lead to the final results. (The formula views are currently implemented for most, but not all, effect size entry formats.)

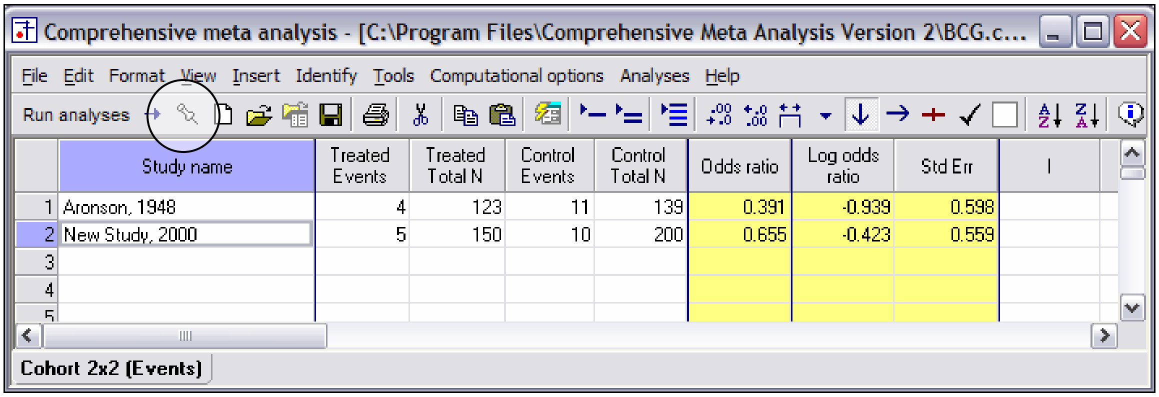
You can view the formula for any effect size index displayed on the spreadsheet by clicking on the appropriate tab at the top of this dialog. Here there is only one tab, **Odds ratio**. (Clicking on the **Data entry** tab offers a view of one row's values and an alternate mode of data entry.)

Diagnose data entry problems



When the data are not valid, the effect size results can't be computed. To diagnose the problem, simply move the mouse over any of the cells highlighted in red. The related problem description displays in a pop-up.

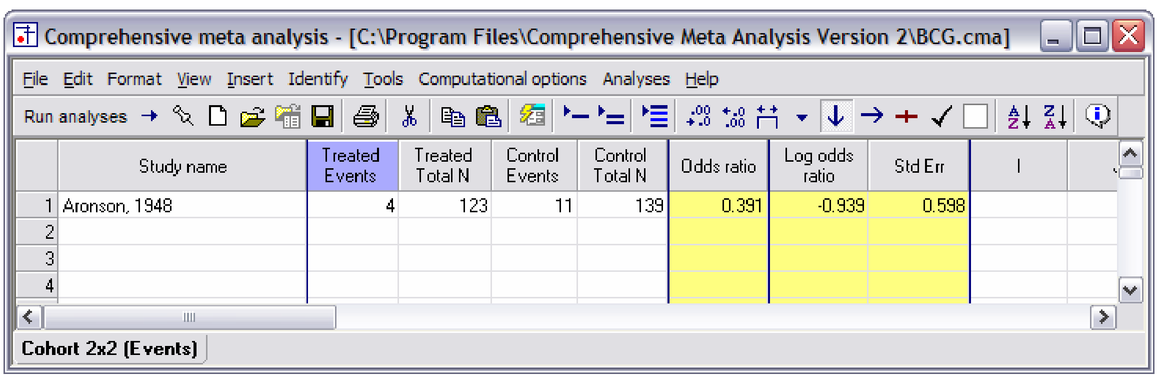
Bookmark entered data



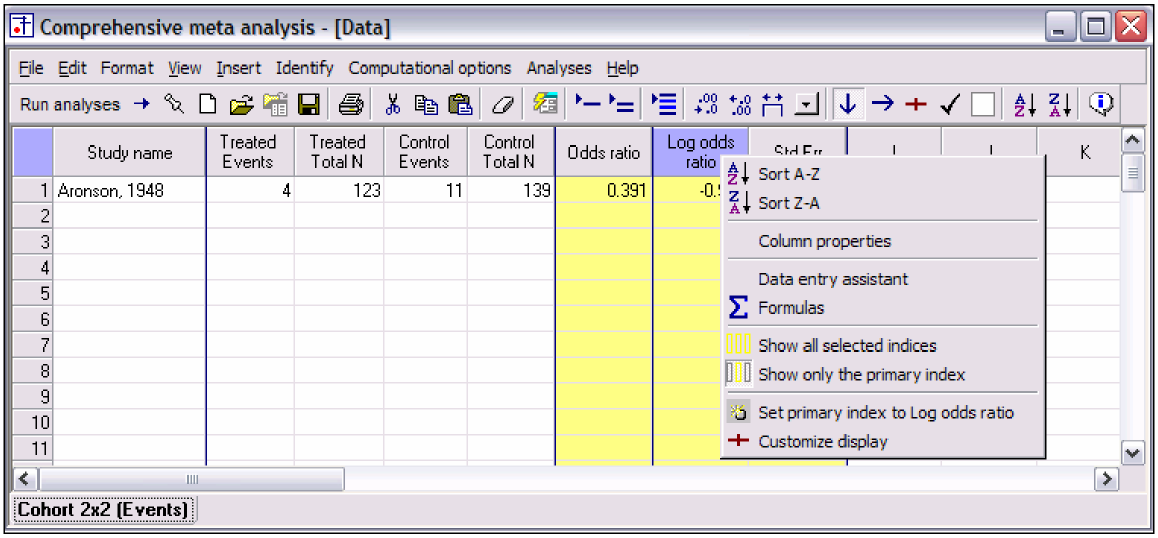
It is sometimes helpful to bookmark the current data entry state. This step allows you to discard subsequent changes and return to the bookmarked state.

First, click on the **Bookmark** icon, circled above. In this example, the icon was clicked before entry of the second study.

To restore the bookmarked state, click on **Edit… Restore data**. After a confirmation prompt, the data are restored, as displayed in the image below.

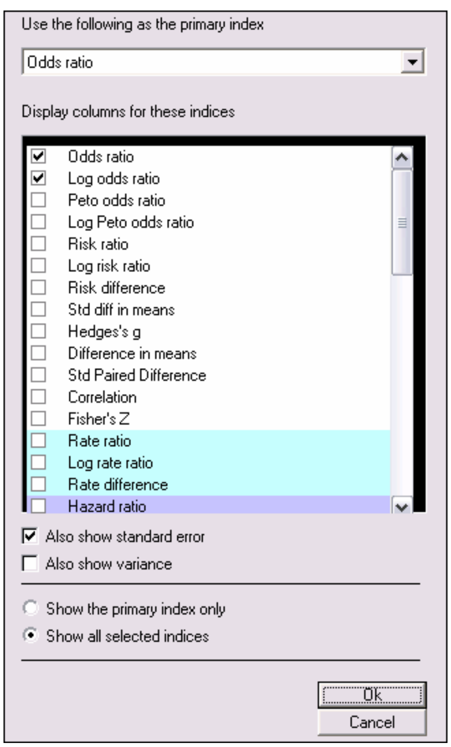


Customize effect size index display



By default the program will display one or two indices (in this case, odds ratio and log odds ratio), which are based on the format selected for data entry. However, the user can customize the screen to display other indices as well.

Right-click on the yellow columns to open the pop-up menu (below). Then click **Set primary index** or **Customize display** to launch the index dialog box shown below. (Note that indices in the same color group are compatible with each other. Entry formats associated with indices in one of the color groups can't be combined in an analysis with formats whose indices belong to another color group).



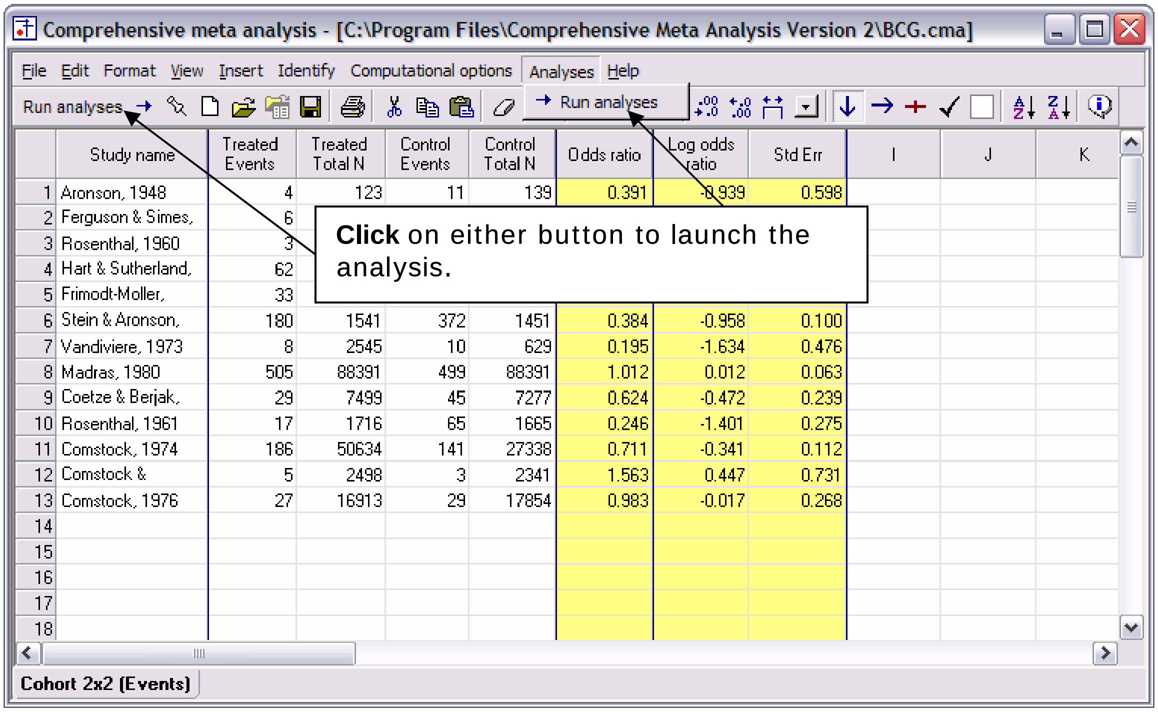
Open data set

Before proceeding to the analysis screen, the user would need to enter data for all studies.

As a time-saving device a copy of this data set has been included on the CD. To open this data set select **File… Open** and then drill down to the location of the data set.

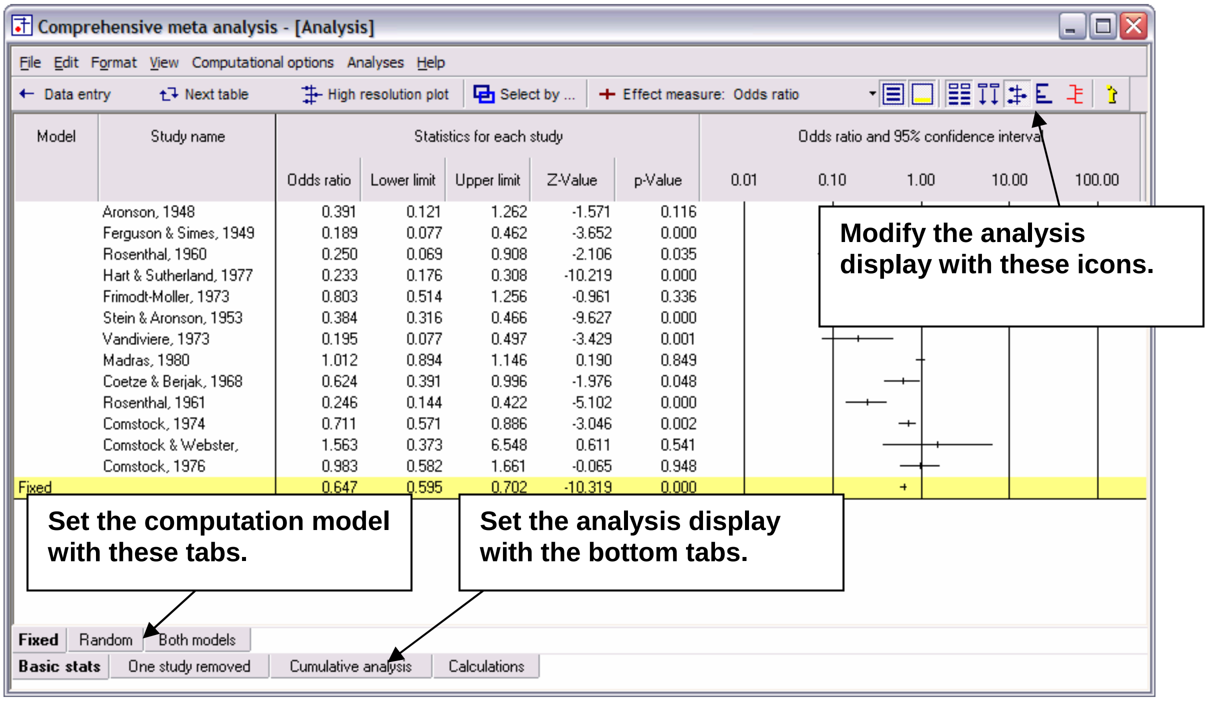
By default, the data set will be in the directory
C:\Program Files\Comprehensive Meta Analysis Version 2\Demo Files.
The data set name is BCG.

Launch analysis module



Note: The BCG meta analysis data set is the basis for this and other examples. It will be altered at certain points for the purposes of the presentation.

Analysis



The primary index from the Data Entry module (in this case odds ratio) is used for the initial Analysis display. The columns labeled **Statistics for each study** include the odds ratio and 95% confidence interval for each study. The last row in the spreadsheet shows the summary data. Under the fixed effect model the point estimate is 0.647 (0.595, 0.702).

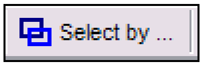
The same information is captured by the Forest plot at the center of the screen. This plot shows each study as a point estimate with its lower and upper limit, and provides a sense of the study-to-study dispersion.

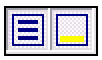
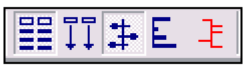
This screen may be customized in many ways, including the following (see toolbar):

- In the **Format** menu dropdown there are options to:
  - Display, hide and modify the appearance of the individual column blocks: **Basic stats, Forest plot, Counts, Weights** and **Residuals.**
  - Modify the appearance (font, decimal precision etc.) of the screen as a whole.
- From the **View… Columns** menu dropdown, the **Moderators** option will present a list of moderators. The user can select from the list and place the selected column where desired in the Analysis display.
- In the **Computational options** menu dropdown:
  - The **Group by…** entry allows the user to run the analysis grouped by a moderator (if moderators are included in the data set), and to compare the treatment effect across groups.

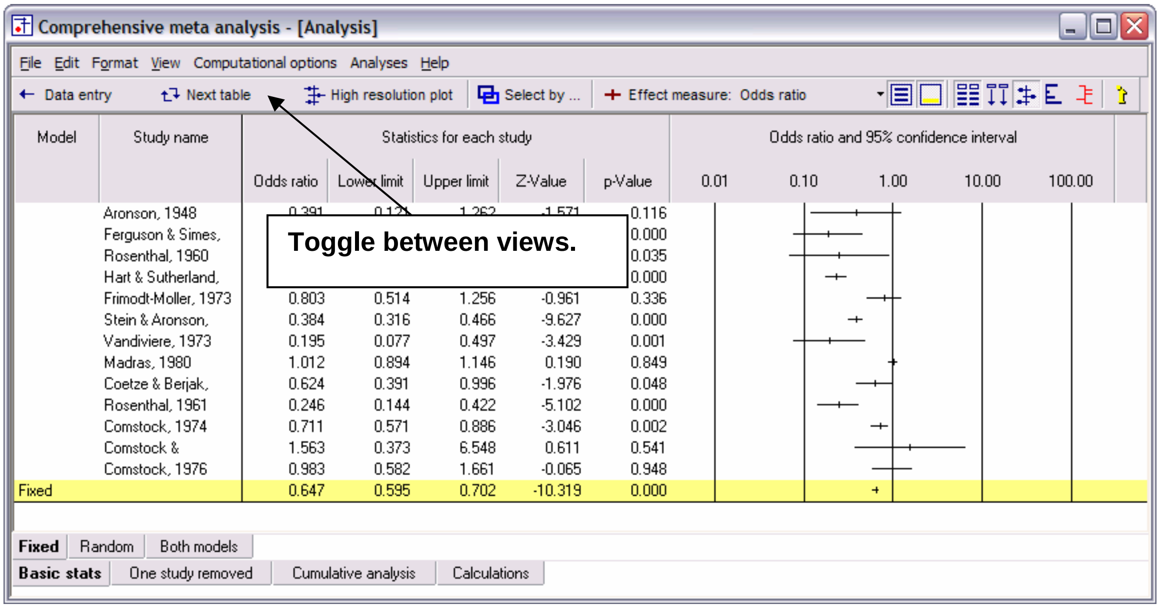
- o A drop-down box allows the user to set the **Confidence level** (95% in this example).

- Right-clicking on a column's heading area offers a list of context-sensitive entries, including:
  - o **Sort** options, both ascending and descending.
  - o A **Customization** option which allows the user to modify an individual column's display (alignment, decimal precision etc.).
  - o A **Scale** option (applicable to Forest plot) which allows the user to modify the display scale.

- 

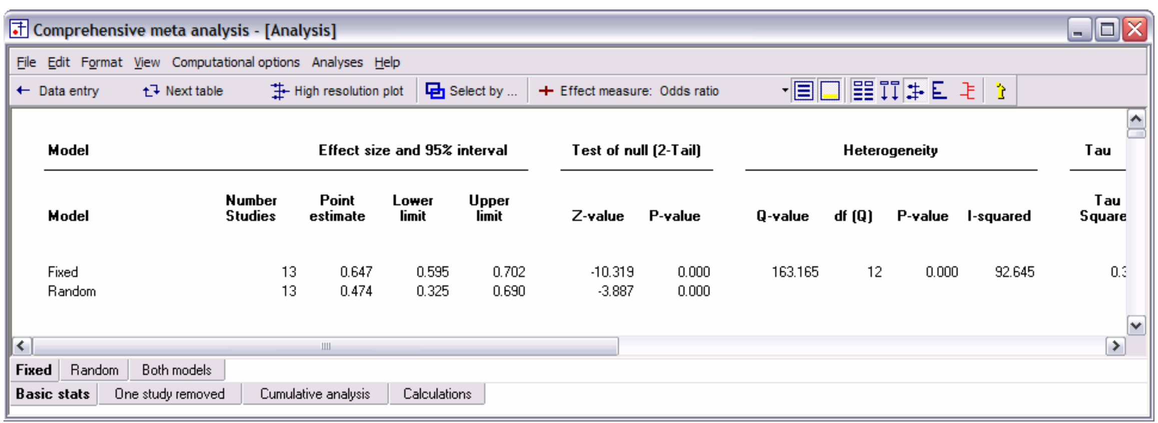
The **Select by…** toolbar icon allows the user to select which studies to include in the analysis, based on study name or moderator variables.
- The **Effect measure** toolbar option displays a selection of available effect measures. In this example the program would allow the user to toggle between odds ratio, risk ratio, risk difference, and other measures of effect size.
-  These toolbar icons allow the user to display and hide individual row results as well as overall results.
-  These toolbar icons allow the user to display and hide the following column blocks: **Basic stats, Individual study counts, Forest plot, Weights** and **Residuals.** This set of icons is determined by the selected data view; only icons relevant to that view will display.
- Tabs at the bottom of the screen allow the user to select the computational model (in this example, fixed or random effects, or both).
- Tabs at the bottom of the screen allow the user to select data views that include analyses with **One study removed** as well as **Cumulative analyses**.

View summary statistics



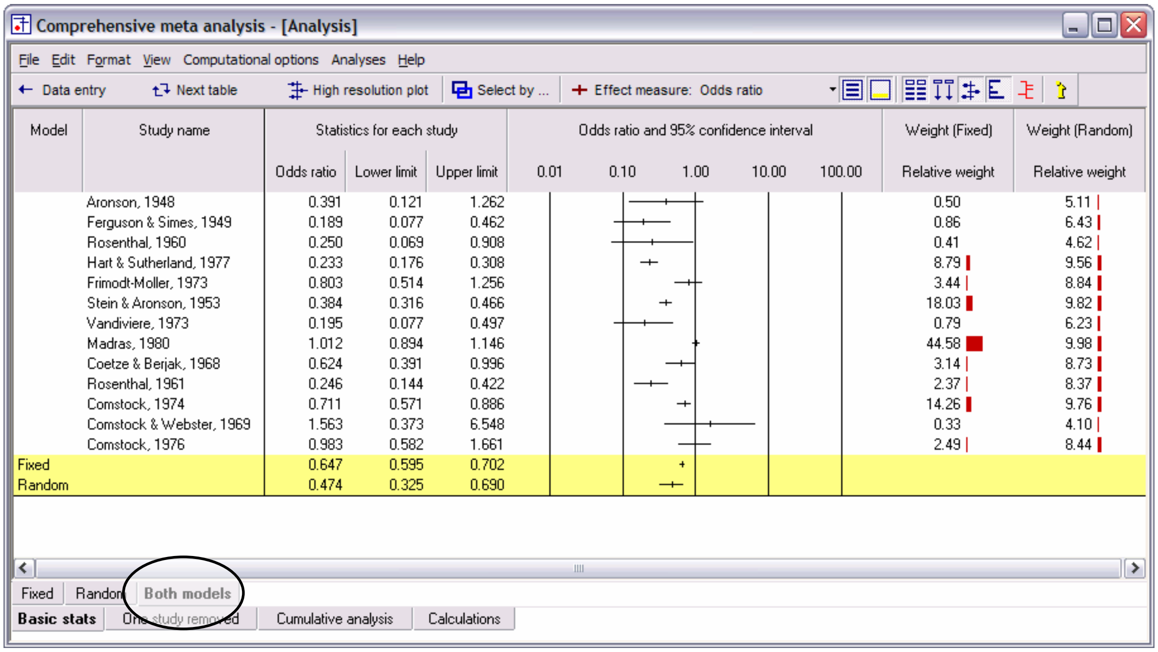
Model	Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
	Aronson, 1948					0.116
	Ferguson & Simes,					0.000
	Rosenthal, 1960					0.035
	Hart & Sutherland,					0.000
	Frimodt-Moller, 1973	0.803	0.514	1.256	-0.961	0.336
	Stein & Aronson,	0.384	0.316	0.466	-9.627	0.000
	Vandiviere, 1973	0.195	0.077	0.497	-3.429	0.001
	Madras, 1980	1.012	0.894	1.146	0.190	0.849
	Coetze & Berjak,	0.624	0.391	0.996	-1.976	0.048
	Rosenthal, 1961	0.246	0.144	0.422	-5.102	0.000
	Comstock, 1974	0.711	0.571	0.886	-3.046	0.002
	Comstock &	1.563	0.373	6.548	0.611	0.541
	Comstock, 1976	0.983	0.582	1.661	-0.065	0.948
Fixed		0.647	0.595	0.702	-10.319	0.000

The **Next table** button on the toolbar allows you to toggle between two windows, the analysis spreadsheet above and the table below (which provides more detail on the point estimate and heterogeneity).



Model	Effect size and 95% interval				Test of null (2-Tail)		Heterogeneity				Tau
Model	Number Studies	Point estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Square
Fixed	13	0.647	0.595	0.702	-10.319	0.000	163.165	12	0.000	92.645	0.3
Random	13	0.474	0.325	0.690	-3.887	0.000					

View study weights



Model	Study name	Statistics for each study			Odds ratio and 95% confidence interval	Weight (Fixed)	Weight (Random)
		Odds ratio	Lower limit	Upper limit	0.01 0.10 1.00 10.00 100.00	Relative weight	Relative weight
	Aronson, 1948	0.391	0.121	1.262		0.50	5.11
	Ferguson & Simes, 1949	0.189	0.077	0.462		0.86	6.43
	Rosenthal, 1960	0.250	0.069	0.908		0.41	4.62
	Hart & Sutherland, 1977	0.233	0.176	0.308		8.79	9.56
	Frimodt-Moller, 1973	0.803	0.514	1.256		3.44	8.84
	Stein & Aronson, 1953	0.384	0.316	0.466		18.03	9.82
	Vandiviere, 1973	0.195	0.077	0.497		0.79	6.23
	Madras, 1980	1.012	0.894	1.146		44.58	9.98
	Coetze & Berjak, 1968	0.624	0.391	0.996		3.14	8.73
	Rosenthal, 1961	0.246	0.144	0.422		2.37	8.37
	Comstock, 1974	0.711	0.571	0.886		14.26	9.76
	Comstock & Webster, 1969	1.563	0.373	6.548		0.33	4.10
	Comstock, 1976	0.983	0.582	1.661		2.49	8.44
Fixed		0.647	0.595	0.702			
Random		0.474	0.325	0.690			

- Click on the icon at the top of the screen to display **Study weights.** (The option is also accessible from the **View… Columns** menu dropdown.)
- Click on the **Both models** tab, circled at the bottom of the screen.

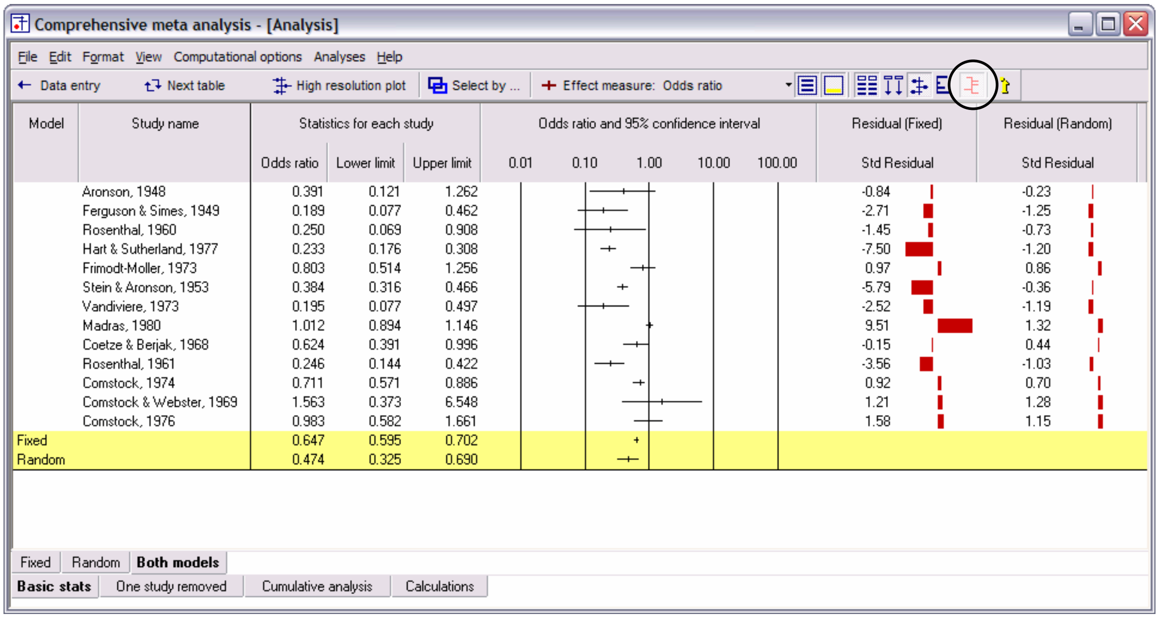
The spreadsheet now includes two rows at the bottom – labeled **Fixed** and **Random**

At the right, the program shows the weight assigned to each study under the fixed or random effects model. Compare, for example, the fixed effect and random effects weights for the "Madras, 1980" study.

In this display, the **Z-value** and **p-value** columns and the **Events / Total** block have been hidden. To hide a block, click on its toggle icon at the top of the screen, or right-click on the block itself and turn off the toggle icon from the resulting dropdown list.

The dropdown list also allows the user to display or hide individual columns within a block. To hide individual columns in the 'Basic stats' block, as is done above, right-click on the block and select the 'Customize display' option. In the customization dialog, uncheck the column(s) to be hidden.

View standardized residuals

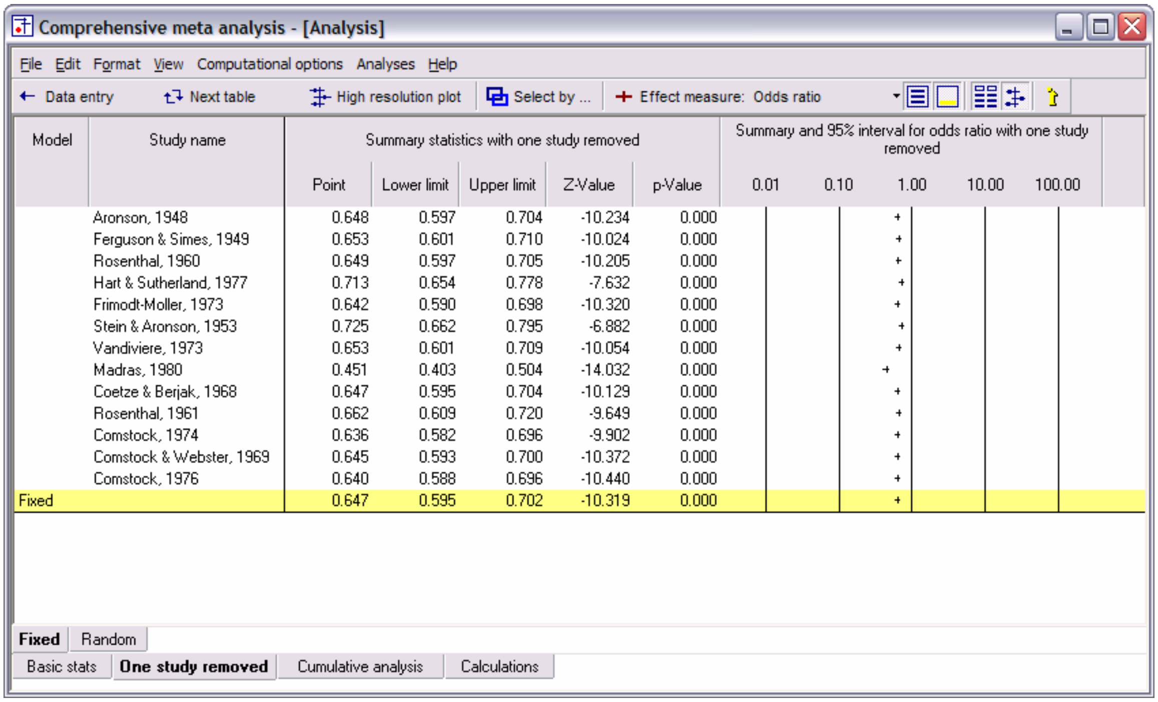


Model	Study name	Odds ratio	Lower limit	Upper limit	Residual (Fixed) Std Residual	Residual (Random) Std Residual
	Aronson, 1948	0.391	0.121	1.262	-0.84	-0.23
	Ferguson & Simes, 1949	0.189	0.077	0.462	-2.71	-1.25
	Rosenthal, 1960	0.250	0.069	0.908	-1.45	-0.73
	Hart & Sutherland, 1977	0.233	0.176	0.308	-7.50	-1.20
	Frimodt-Moller, 1973	0.803	0.514	1.256	0.97	0.86
	Stein & Aronson, 1953	0.384	0.316	0.466	-5.79	-0.36
	Vandiviere, 1973	0.195	0.077	0.497	-2.52	-1.19
	Madras, 1980	1.012	0.894	1.146	9.51	1.32
	Coetze & Berjak, 1968	0.624	0.391	0.996	-0.15	0.44
	Rosenthal, 1961	0.246	0.144	0.422	-3.56	-1.03
	Comstock, 1974	0.711	0.571	0.886	0.92	0.70
	Comstock & Webster, 1969	1.563	0.373	6.548	1.21	1.28
	Comstock, 1976	0.983	0.582	1.661	1.58	1.15
Fixed		0.647	0.595	0.702		
Random		0.474	0.325	0.690		

Here, the user has clicked on the **Residuals** icon, circled at the top.

Note, once again, how the display clarifies the contrast in results between the fixed and random models.

View ‘One study removed’ results

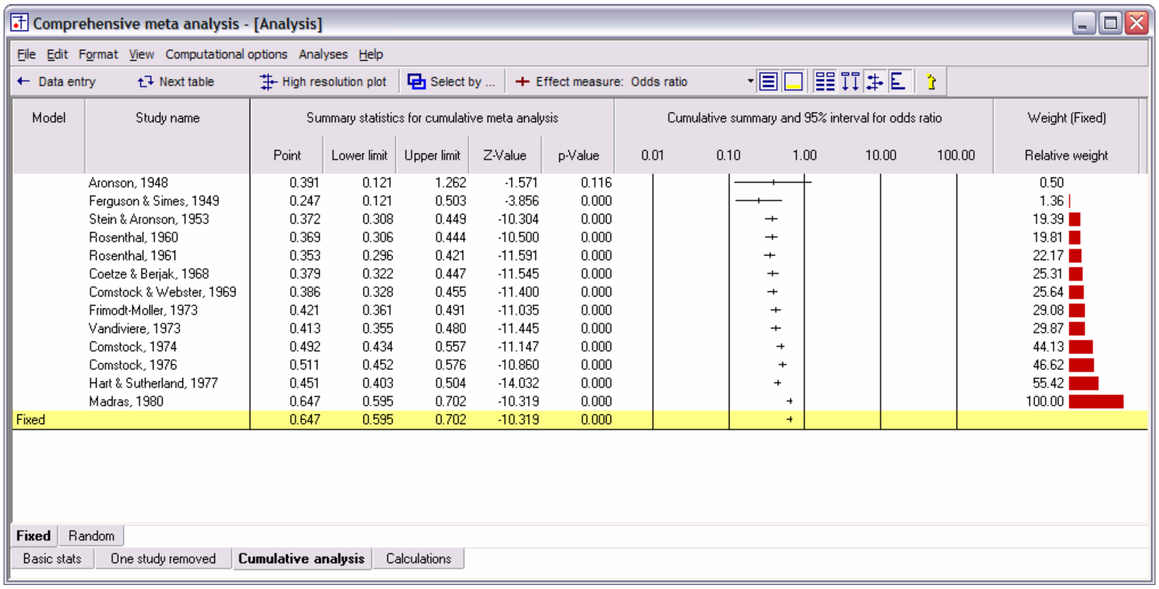


Model	Study name	Summary statistics with one study removed					Summary and 95% interval for odds ratio with one study removed
		Point	Lower limit	Upper limit	Z-Value	p-Value	0.01 0.10 1.00 10.00 100.00
	Aronson, 1948	0.648	0.597	0.704	-10.234	0.000	
	Ferguson & Simes, 1949	0.653	0.601	0.710	-10.024	0.000	
	Rosenthal, 1960	0.649	0.597	0.705	-10.205	0.000	
	Hart & Sutherland, 1977	0.713	0.654	0.778	-7.632	0.000	
	Frimodt-Moller, 1973	0.642	0.590	0.698	-10.320	0.000	
	Stein & Aronson, 1953	0.725	0.662	0.795	-6.882	0.000	
	Vandiviere, 1973	0.653	0.601	0.709	-10.054	0.000	
	Madras, 1980	0.451	0.403	0.504	-14.032	0.000	
	Coetze & Berjak, 1968	0.647	0.595	0.704	-10.129	0.000	
	Rosenthal, 1961	0.662	0.609	0.720	-9.649	0.000	
	Comstock, 1974	0.636	0.582	0.696	-9.902	0.000	
	Comstock & Webster, 1969	0.645	0.593	0.700	-10.372	0.000	
	Comstock, 1976	0.640	0.588	0.696	-10.440	0.000	
Fixed		0.647	0.595	0.702	-10.319	0.000	

In this view, each row displays not the results of a single study, but rather the summary values computed when that row’s study is removed from the meta analysis. For example, the values in the first row, “Aronson, 1948”, represent the summary computations for twelve studies, when “Aronson, 1948” is excluded.

Note that the **Both models** tab is not available in this display. The tab appears only when appropriate.

View cumulative analysis

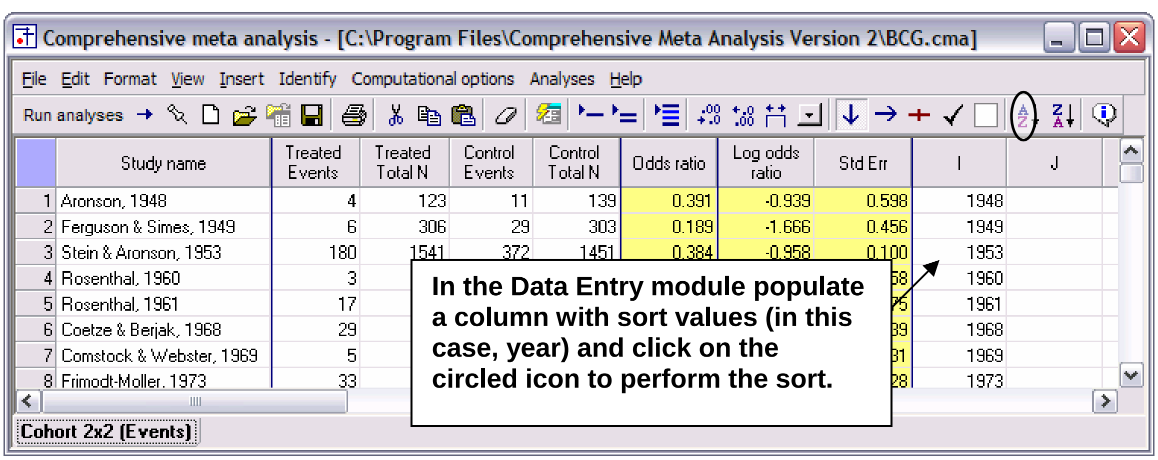


Model	Study name	Point	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
	Aronson, 1948	0.391	0.121	1.262	-1.571	0.116	0.50
	Ferguson & Simes, 1949	0.247	0.121	0.503	-3.856	0.000	1.36
	Stein & Aronson, 1953	0.372	0.308	0.449	-10.304	0.000	19.39
	Rosenthal, 1960	0.369	0.306	0.444	-10.500	0.000	19.81
	Rosenthal, 1961	0.353	0.296	0.421	-11.591	0.000	22.17
	Coetze & Berjak, 1968	0.379	0.322	0.447	-11.545	0.000	25.31
	Comstock & Webster, 1969	0.386	0.328	0.455	-11.400	0.000	25.64
	Frimodt-Moller, 1973	0.421	0.361	0.491	-11.035	0.000	29.08
	Vandiviere, 1973	0.413	0.355	0.480	-11.445	0.000	29.87
	Comstock, 1974	0.492	0.434	0.557	-11.147	0.000	44.13
	Comstock, 1976	0.511	0.452	0.576	-10.860	0.000	46.62
	Hart & Sutherland, 1977	0.451	0.403	0.504	-14.032	0.000	55.42
	Madras, 1980	0.647	0.595	0.702	-10.319	0.000	100.00
Fixed		0.647	0.595	0.702	-10.319	0.000	

The **Cumulative analysis** option displays results accumulated over successive studies. That is, the second row presents a summary analysis comprising the first two studies (in this case, “Aronson, 1948” and “Ferguson & Simes, 1949”), the third row presents a summary analysis comprising the first three studies, and so on through the final row. When the data are sorted by year, this would show the conclusions that could have been obtained at any point in time with each new study’s appearance.

The Forest plot and the study weight block also display cumulative values.

Note that the studies have been sorted (by year in this case) in order to make the display more meaningful. The image below shows one way such a sort could be done.



	Study name	Treated Events	Treated Total N	Control Events	Control Total N	Odds ratio	Log odds ratio	Std Err	I	J
1	Aronson, 1948	4	123	11	139	0.391	-0.939	0.598	1948	
2	Ferguson & Simes, 1949	6	306	29	303	0.189	-1.666	0.456	1949	
3	Stein & Aronson, 1953	180	1541	372	1451	0.384	-0.958	0.100	1953	
4	Rosenthal, 1960	3						58	1960	
5	Rosenthal, 1961	17						75	1961	
6	Coetze & Berjak, 1968	29						39	1968	
7	Comstock & Webster, 1969	5						31	1969	
8	Frimodt-Moller, 1973	33						28	1973	

View calculations

Comprehensive meta analysis - [Analysis]

File Edit Format View Computational options Analyses Help

Data entry | Next table | High resolution plot | Select by ... | Effect measure: Odds ratio

Model	Study name	Calculations (Fixed)									
		Point	Study Variance	Tau^2 Within	Tau^2 Between	Total Variance	IV-Weight	W	T*W	T^2*W	W^2
	Aronson, 1948	-0.939	0.357	0.000	0.000	0.357	2.800	2.800	-2.628	2.467	7.841
	Ferguson & Simes, 1949	-1.666	0.208	0.000	0.000	0.208	4.805	4.805	-8.005	13.339	23.085
	Stein & Aronson, 1953	-0.958	0.010	0.000	0.000	0.010	100.956	100.956	-96.729	92.678	10192.196
	Rosenthal, 1960	-1.386	0.433	0.000	0.000	0.433	2.307	2.307	-3.199	4.434	5.323
	Rosenthal, 1961	-1.401	0.075	0.000	0.000	0.075	13.259	13.259	-18.578	26.032	175.795
	Coetze & Berjak, 1968	-0.472	0.057	0.000	0.000	0.057	17.551	17.551	-8.280	3.906	308.034
	Comstock & Webster, 1969	0.447	0.534	0.000	0.000	0.534	1.872	1.872	0.836	0.373	3.505
	Frimodt-Moller, 1973	-0.219	0.052	0.000	0.000	0.052	19.249	19.249	-4.218	0.924	370.509
	Vandiviere, 1973	-1.634	0.227	0.000	0.000	0.227	4.405	4.405	-7.197	11.758	19.405
	Comstock, 1974	-0.341	0.013	0.000	0.000	0.013	79.839	79.839	-27.213	9.276	6374.340
	Comstock, 1976	-0.017	0.072	0.000	0.000	0.072	13.960	13.960	-0.242	0.004	194.871
	Hart & Sutherland, 1977	-1.456	0.020	0.000	0.000	0.020	49.226	49.226	-71.695	104.420	2423.212
	Madras, 1980	0.012	0.004	0.000	0.000	0.004	249.566	249.566	3.000	0.036	62283.004
		-10.031	2.063	0.000	0.000	2.063	559.795	559.795	-244.148	269.648	82381.121

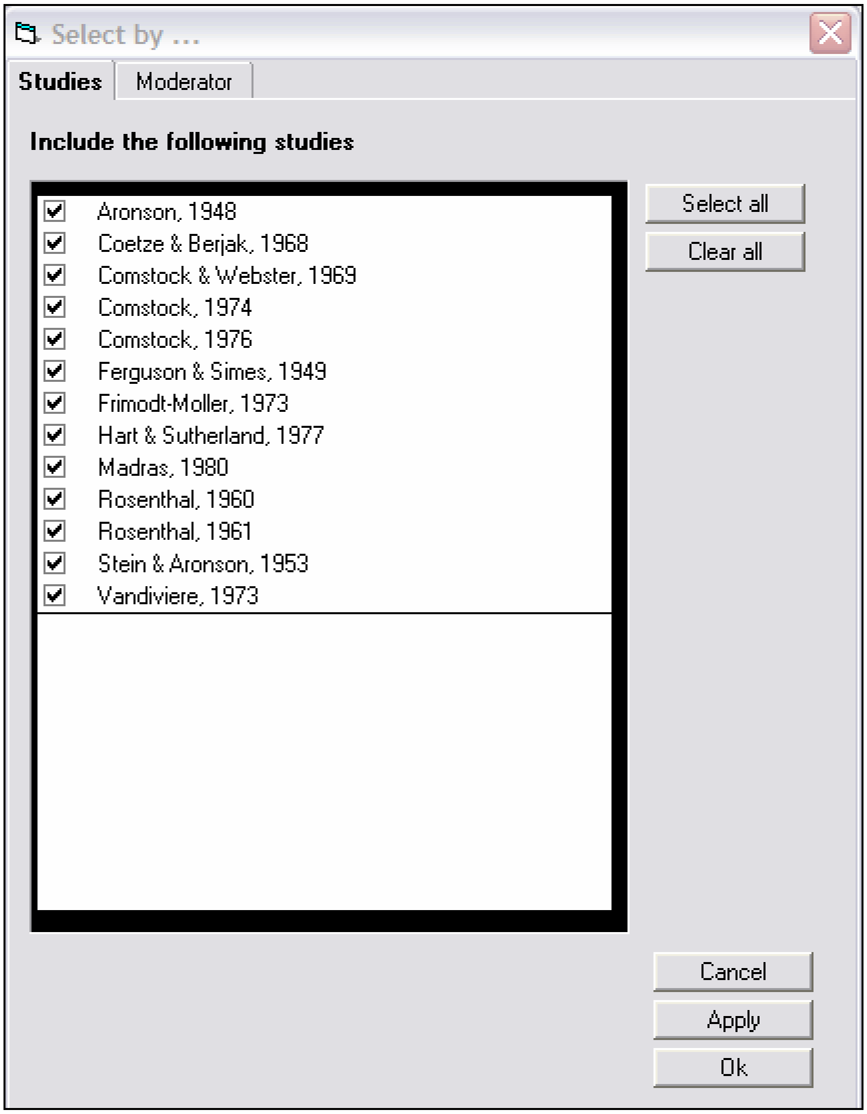
Fixed | Random

Basic stats | One study removed | Cumulative analysis | **Calculations**

This tab shows how data in each row are summed to yield totals, which are then used to compute the point estimates and standard errors.

This is intended both as a teaching tool and also to allow researchers to understand the precise formula being used. As development continues, the user will be allowed to open a box that shows the precise formula used for each computation, and how these values were inserted into that formula to yield the reported statistics.

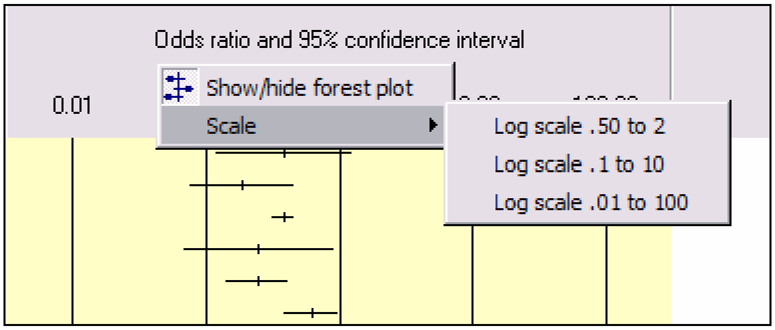
Select by…



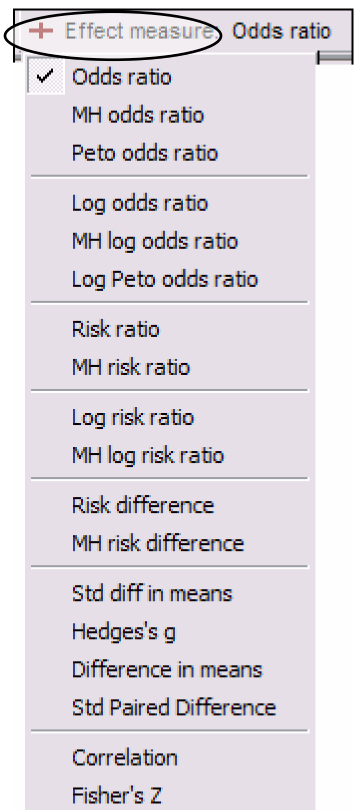
Click on the **Select by…** icon to launch this dialog. Here you can change the set of studies to include in the meta analysis. If the data set included subgroups or moderator variables, they would appear here as well.

Click on **Apply** or **OK** to apply the changes.

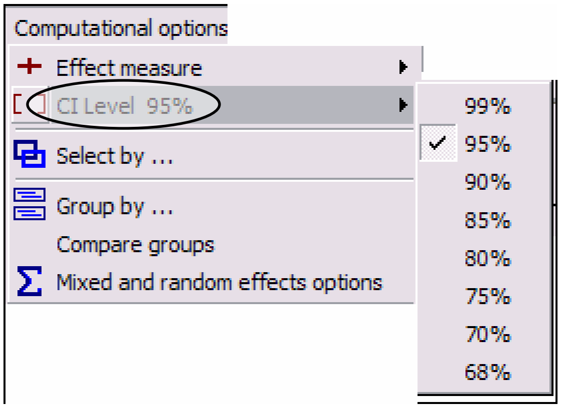
Some tools for customizing the analysis display



Right-click on the Forest plot block and click on the **Scale** option to select a different scale setting for the Forest plot. The options for log scales appear when odds ratios, risk ratios, rate ratios, or hazard ratios are used as the effect size index. Otherwise, options for raw scales appear.



Click on the **Effect measure** option and select a setting in this dropdown to use an alternate measure for the meta analysis computations.



Click on the **Computational Options... CI level** option and select a setting in this dropdown to change the confidence level used in the computations and the Forest plot.

Section 2. Multiple data entry formats

If the effect size for all studies is in the same format (e.g., number of events and total N for treated and control groups, or the odds ratio and confidence interval) the user would create one set of columns for effect size data as described in the previous section.

In the event that some studies report the effect size in one format while others report it using another format, the user will need to create two (or more) sets of data entry columns. The options are explained in this section.

This section uses the “Strepokinase” example, which is patterned after a published meta analysis but includes fictional data.

For all studies in this meta analysis, patients who arrive at a hospital following a myocardial infarction are randomized to one of two groups: (A) standard treatment alone, or (B) standard treatment plus streptokinase.

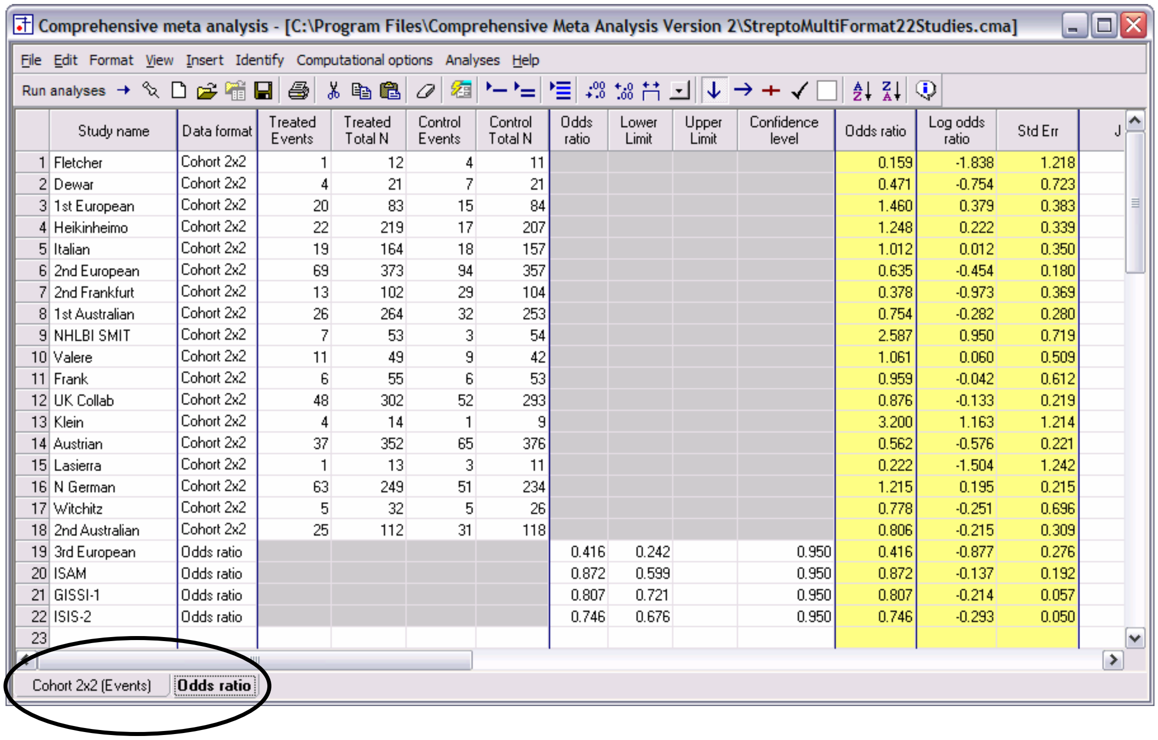
Some studies report the number of events (deaths) and the total number of patients in each group. This data will be used to compute an odds ratio, with odds ratios less than one indicating that patients in the treated group were less likely to die.

Other studies report the odds ratio and the 95% confidence interval.

By default, data sets are copied to
C:\Program Files\Comprehensive Meta Analysis Version 2\Demo Files.

The two datasets used in this section are
StreptoMultiformat18 studies, which includes the 18 studies in the first format, and
StreptoMultiformat22 studies, which includes all 22 studies.

Overview



	Study name	Data format	Treated Events	Treated Total N	Control Events	Control Total N	Odds ratio	Lower Limit	Upper Limit	Confidence level	Odds ratio	Log odds ratio	Std Err	J
1	Fletcher	Cohort 2x2	1	12	4	11					0.159	-1.838	1.218	
2	Dewar	Cohort 2x2	4	21	7	21					0.471	-0.754	0.723	
3	1st European	Cohort 2x2	20	83	15	84					1.460	0.379	0.383	
4	Heikinheimo	Cohort 2x2	22	219	17	207					1.248	0.222	0.339	
5	Italian	Cohort 2x2	19	164	18	157					1.012	0.012	0.350	
6	2nd European	Cohort 2x2	69	373	94	357					0.635	-0.454	0.180	
7	2nd Frankfurt	Cohort 2x2	13	102	29	104					0.378	-0.973	0.369	
8	1st Australian	Cohort 2x2	26	264	32	253					0.754	-0.282	0.280	
9	NHLBI SMIT	Cohort 2x2	7	53	3	54					2.587	0.950	0.719	
10	Valere	Cohort 2x2	11	49	9	42					1.061	0.060	0.509	
11	Frank	Cohort 2x2	6	55	6	53					0.959	-0.042	0.612	
12	UK Collab	Cohort 2x2	48	302	52	293					0.876	-0.133	0.219	
13	Klein	Cohort 2x2	4	14	1	9					3.200	1.163	1.214	
14	Austrian	Cohort 2x2	37	352	65	376					0.562	-0.576	0.221	
15	Lasierra	Cohort 2x2	1	13	3	11					0.222	-1.504	1.242	
16	N German	Cohort 2x2	63	249	51	234					1.215	0.195	0.215	
17	Witchitz	Cohort 2x2	5	32	5	26					0.778	-0.251	0.696	
18	2nd Australian	Cohort 2x2	25	112	31	118					0.806	-0.215	0.309	
19	3rd European	Odds ratio					0.416	0.242		0.950	0.416	-0.877	0.276	
20	ISAM	Odds ratio					0.872	0.599		0.950	0.872	-0.137	0.192	
21	GISSI-1	Odds ratio					0.807	0.721		0.950	0.807	-0.214	0.057	
22	ISIS-2	Odds ratio					0.746	0.676		0.950	0.746	-0.293	0.050	
23														

The mechanism for entering effect size data in several formats is shown here. The spreadsheet includes a block of columns labeled ‘Treated Events, Treated Total N’, etc. And, a second block of columns labeled ‘Odds ratio, Lower limit’, etc.

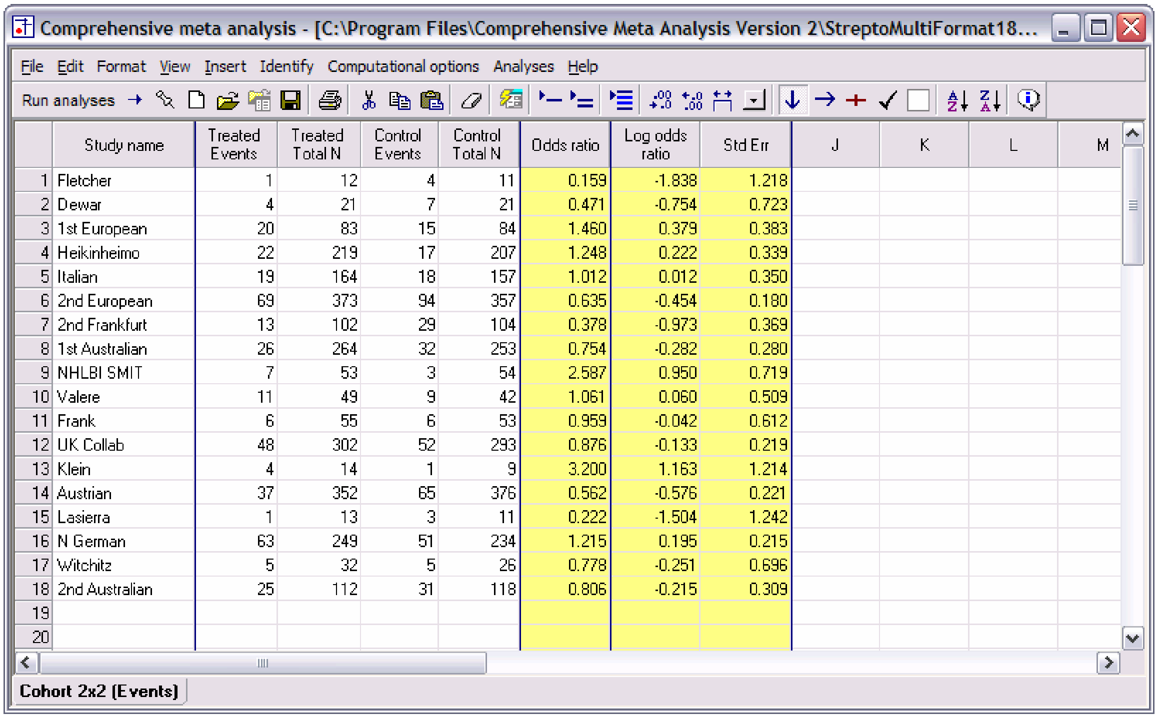
For the first 18 studies the data are entered into the first block, and the second block is grayed out. For the next 4 studies the data are entered into the second block and the first block is grayed out. However, for all 22 studies the computed effect is displayed in the same columns (at the right). Since it is these columns which are used in the analysis, all studies can be included in the analysis without regard to the original format (with the caveat that the data provided allows us to compute the required effect size index).

- To create multiple effect size blocks, simply **Insert… Columns for… Effect size data** as many times as needed. Each time, the program will allow the user to select an additional format from the hierarchy.

- By default, the program shows only one data entry block at a time. If only one block is displayed, use the tabs at the bottom of the screen to switch between blocks.

- To view all the blocks (as above), right-click on the data entry column and use the pop-up menu.

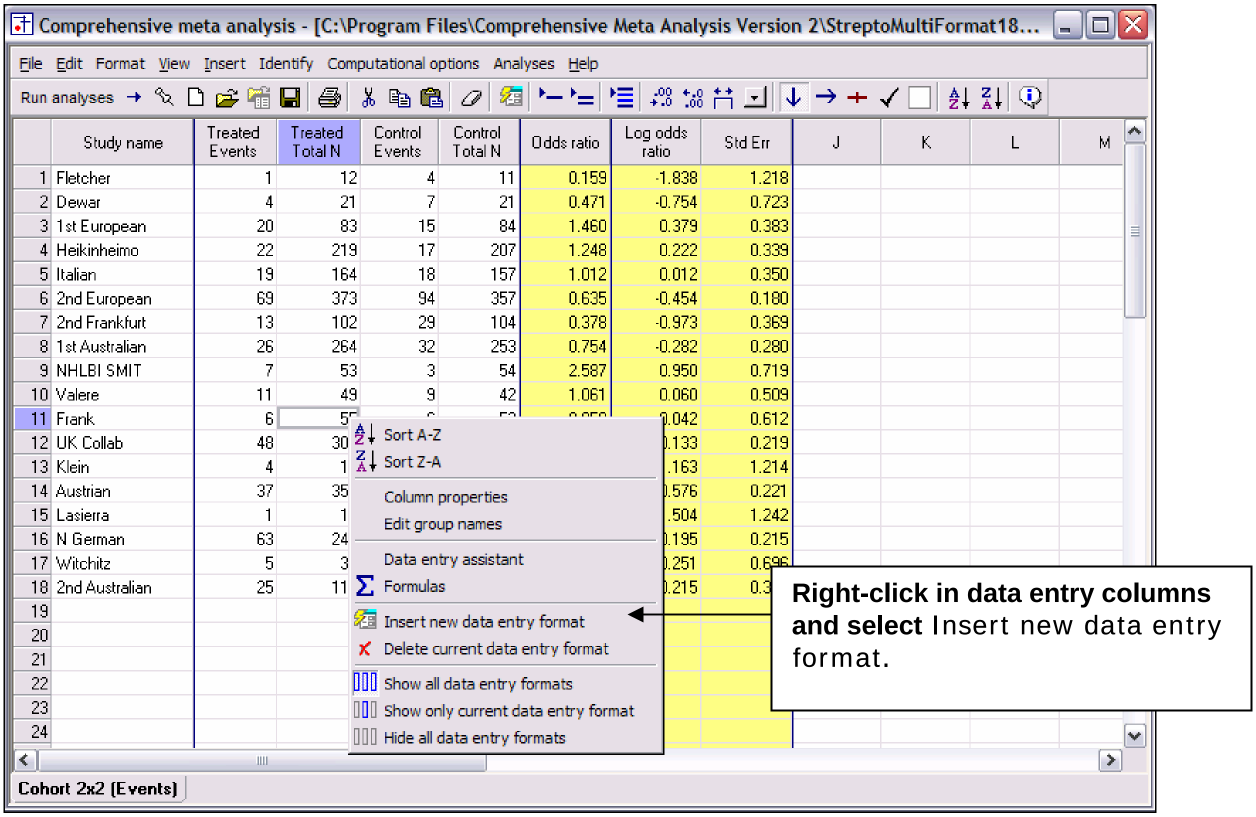
Step-by-step instructions for multiple formats



	Study name	Treated Events	Treated Total N	Control Events	Control Total N	Odds ratio	Log odds ratio	Std Err	J	K	L	M
1	Fletcher	1	12	4	11	0.159	-1.838	1.218				
2	Dewar	4	21	7	21	0.471	-0.754	0.723				
3	1st European	20	83	15	84	1.460	0.379	0.383				
4	Heikinheimo	22	219	17	207	1.248	0.222	0.339				
5	Italian	19	164	18	157	1.012	0.012	0.350				
6	2nd European	69	373	94	357	0.635	-0.454	0.180				
7	2nd Frankfurt	13	102	29	104	0.378	-0.973	0.369				
8	1st Australian	26	264	32	253	0.754	-0.282	0.280				
9	NHLBI SMIT	7	53	3	54	2.587	0.950	0.719				
10	Valere	11	49	9	42	1.061	0.060	0.509				
11	Frank	6	55	6	53	0.959	-0.042	0.612				
12	UK Collab	48	302	52	293	0.876	-0.133	0.219				
13	Klein	4	14	1	9	3.200	1.163	1.214				
14	Austrian	37	352	65	376	0.562	-0.576	0.221				
15	Lasierra	1	13	3	11	0.222	-1.504	1.242				
16	N German	63	249	51	234	1.215	0.195	0.215				
17	Witchitz	5	32	5	26	0.778	-0.251	0.696				
18	2nd Australian	25	112	31	118	0.806	-0.215	0.309				
19												
20												

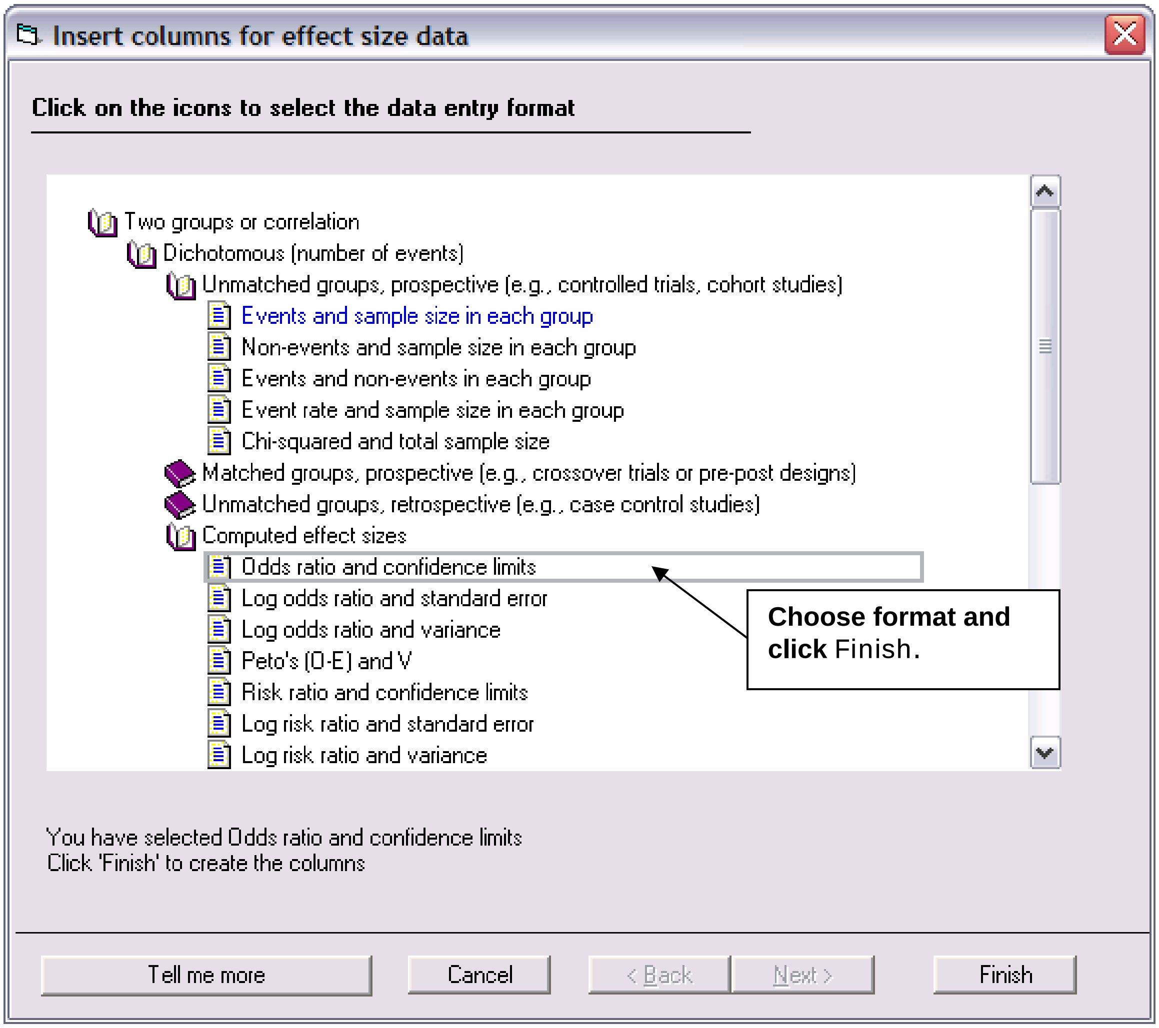
Create the first block (for events and total N in each group) as described in the previous section, and enter data for the first 18 studies as shown here.

Create the second effect size entry block



To create the second block, simply repeat the procedure (**Insert… Column for… Effect size data**). Or, right-click on the data entry columns to launch a pop-up menu and select **Insert new data entry format.**

Select second effect size entry format



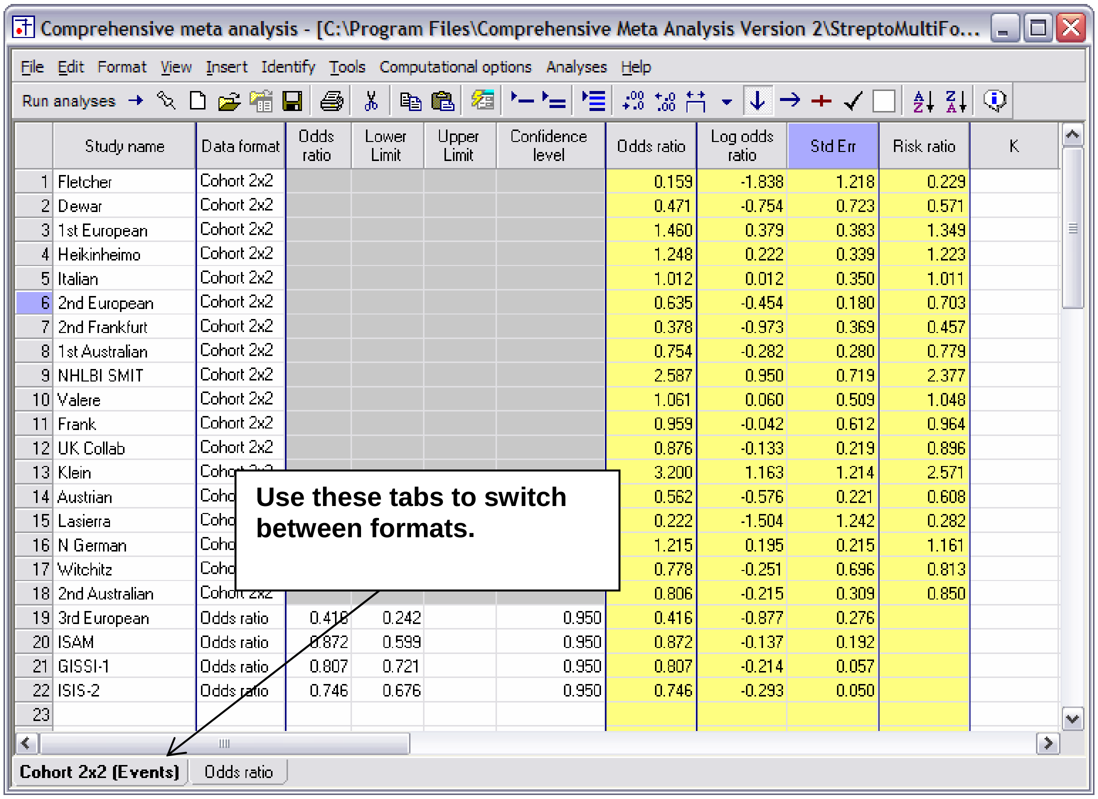
Note that the **Dichotomous (number of events)** book icon remains open from the selection of the first effect size entry format.

In this example we want to create a block of columns to enter the odds ratio and confidence interval. Drill down in the hierarchy to select the following:

- **Dichotomous (number of events)**
    - **Computed effect sizes**
        - **Odds ratio and confidence limits**

At this point, the **Finish** button will be activated. Click on it to create the columns for data entry.

Enter data for second effect size



	Study name	Data format	Odds ratio	Lower Limit	Upper Limit	Confidence level	Odds ratio	Log odds ratio	Std Err	Risk ratio	K
1	Fletcher	Cohort 2x2					0.159	-1.838	1.218	0.229	
2	Dewar	Cohort 2x2					0.471	-0.754	0.723	0.571	
3	1st European	Cohort 2x2					1.460	0.379	0.383	1.349	
4	Heikinheimo	Cohort 2x2					1.248	0.222	0.339	1.223	
5	Italian	Cohort 2x2					1.012	0.012	0.350	1.011	
6	2nd European	Cohort 2x2					0.635	-0.454	0.180	0.703	
7	2nd Frankfurt	Cohort 2x2					0.378	-0.973	0.369	0.457	
8	1st Australian	Cohort 2x2					0.754	-0.282	0.280	0.779	
9	NHLBI SMIT	Cohort 2x2					2.587	0.950	0.719	2.377	
10	Valere	Cohort 2x2					1.061	0.060	0.509	1.048	
11	Frank	Cohort 2x2					0.959	-0.042	0.612	0.964	
12	UK Collab	Cohort 2x2					0.876	-0.133	0.219	0.896	
13	Klein	Cohort 2x2					3.200	1.163	1.214	2.571	
14	Austrian	Coho					0.562	-0.576	0.221	0.608	
15	Lasierra	Coho					0.222	-1.504	1.242	0.282	
16	N German	Coho					1.215	0.195	0.215	1.161	
17	Witchitz	Coho					0.778	-0.251	0.696	0.813	
18	2nd Australian	Cohort 2x2					0.806	-0.215	0.309	0.850	
19	3rd European	Odds ratio	0.416	0.242		0.950	0.416	-0.877	0.276		
20	ISAM	Odds ratio	0.872	0.599		0.950	0.872	-0.137	0.192		
21	GISSI-1	Odds ratio	0.807	0.721		0.950	0.807	-0.214	0.057		
22	ISIS-2	Odds ratio	0.746	0.676		0.950	0.746	-0.293	0.050		
23											

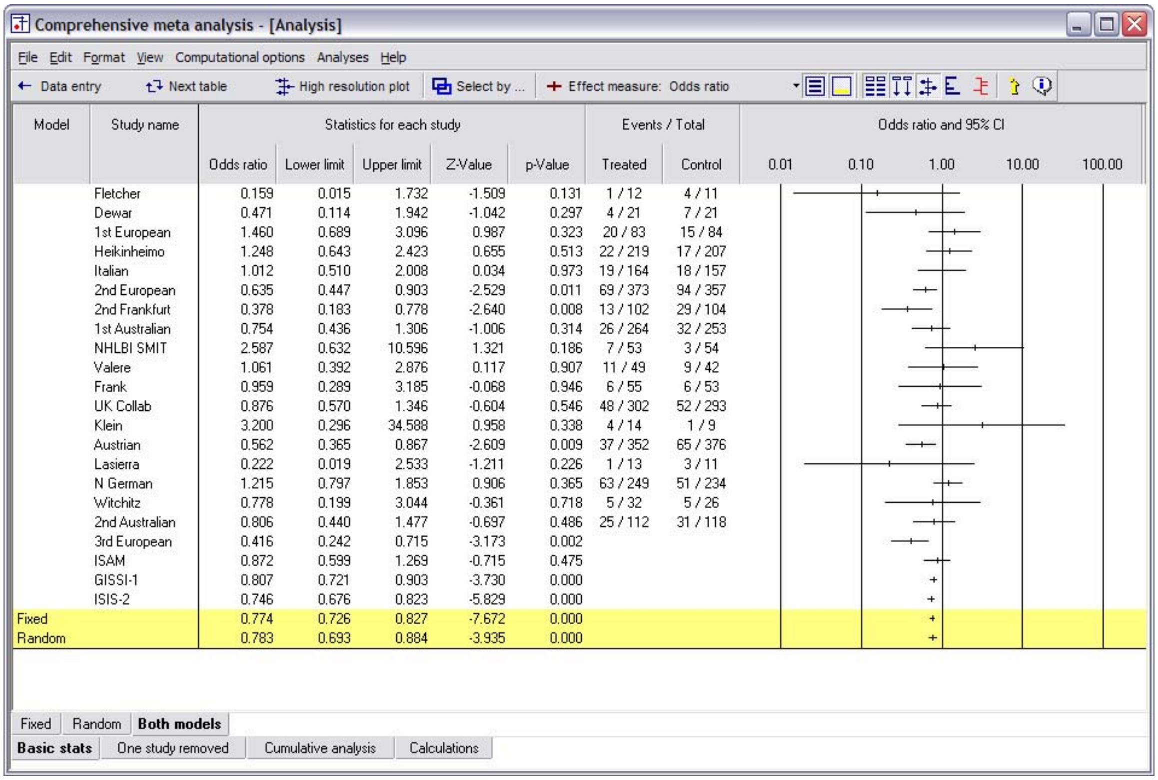
Data are now entered in the second effect size block for the final four studies.

Effect size index results are automatically calculated and display in the yellow columns. Note that it is not necessary to enter both 'Lower limit' and 'Upper limit' values in this format. (If both are entered, the program will check to ensure that the values are consistent. For example, if the 'Odds ratio' is 1.000 and the 'Lower limit' is 0.500, the 'Upper limit' must be 2.000. Currently, the program allows a small margin for rounding error. (This margin value can be modified through the **Computational options** on the top menu).

Since there is now more than one format, the program has added a column to identify the format for each row. The formats, **Cohort 2x2 (Events)** and **Odds ratio** are inserted by the program automatically when the user enters data.

- Right-click on the data entry columns and select **Show all data entry formats** to modify the display. If you elect to **Hide all data entry formats** they can be re-displayed by right-clicking on the tab at the bottom of the screen.
- Right-click on the yellow columns and add "Risk ratio" as an index. As shown above, this ratio will display for the first 18 studies (since it can be computed from the data provided) but not for the last four.

View analysis



Model	Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	Treated	Control
		Statistics for each study					Events / Total	
	Fletcher	0.159	0.015	1.732	-1.509	0.131	1 / 12	4 / 11
	Dewar	0.471	0.114	1.942	-1.042	0.297	4 / 21	7 / 21
	1st European	1.460	0.689	3.096	0.987	0.323	20 / 83	15 / 84
	Heikinheimo	1.248	0.643	2.423	0.655	0.513	22 / 219	17 / 207
	Italian	1.012	0.510	2.008	0.034	0.973	19 / 164	18 / 157
	2nd European	0.635	0.447	0.903	-2.529	0.011	69 / 373	94 / 357
	2nd Frankfurt	0.378	0.183	0.778	-2.640	0.008	13 / 102	29 / 104
	1st Australian	0.754	0.436	1.306	-1.006	0.314	26 / 264	32 / 253
	NHLBI SMIT	2.587	0.632	10.596	1.321	0.186	7 / 53	3 / 54
	Valere	1.061	0.392	2.876	0.117	0.907	11 / 49	9 / 42
	Frank	0.959	0.289	3.185	-0.068	0.946	6 / 55	6 / 53
	UK Collab	0.876	0.570	1.346	-0.604	0.546	48 / 302	52 / 293
	Klein	3.200	0.296	34.588	0.958	0.338	4 / 14	1 / 9
	Austrian	0.562	0.365	0.867	-2.609	0.009	37 / 352	65 / 376
	Lasierra	0.222	0.019	2.533	-1.211	0.226	1 / 13	3 / 11
	N German	1.215	0.797	1.853	0.906	0.365	63 / 249	51 / 234
	Witchitz	0.778	0.199	3.044	-0.361	0.718	5 / 32	5 / 26
	2nd Australian	0.806	0.440	1.477	-0.697	0.486	25 / 112	31 / 118
	3rd European	0.416	0.242	0.715	-3.173	0.002		
	ISAM	0.872	0.599	1.269	-0.715	0.475		
	GISSI-1	0.807	0.721	0.903	-3.730	0.000		
	ISIS-2	0.746	0.676	0.823	-5.829	0.000		
Fixed		0.774	0.726	0.827	-7.672	0.000		
Random		0.783	0.693	0.884	-3.935	0.000		

For an analysis using odds ratios (as shown here), data from all studies would be available. Note that **Events / Total** counts display where relevant.

For an analysis using risk ratios, only data from the first 18 studies would be available, since the data from the last 4 studies cannot be used to compute a risk ratio.

Section 3. Working with moderator variables

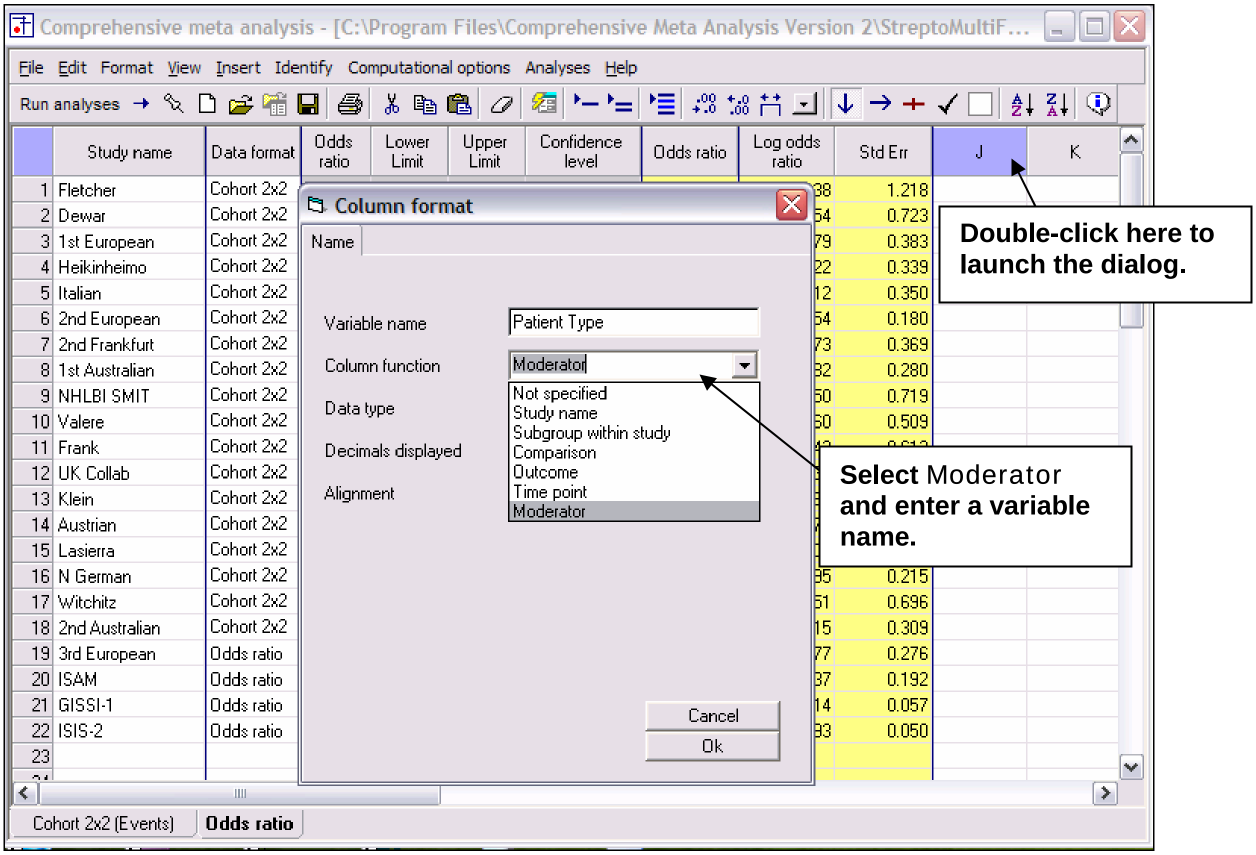
The program allows you to create two types of moderator variables which can then be used in the analysis. This chapter will describe the use of categorical moderators. (Chapter 9, on ‘Meta regression’, describes the use of numeric moderators.)

Once a categorical moderator variable is defined the user will be able to group by that variable. The program will also offer options for fixed effect, multiple mixed effect models, and a fully random effects model.

These options, still in development, are explained in this section.

By default, data sets are copied to
C:\Program Files\Comprehensive Meta Analysis Version 2\Demo Files.
The dataset used in this section is StreptoModerator.

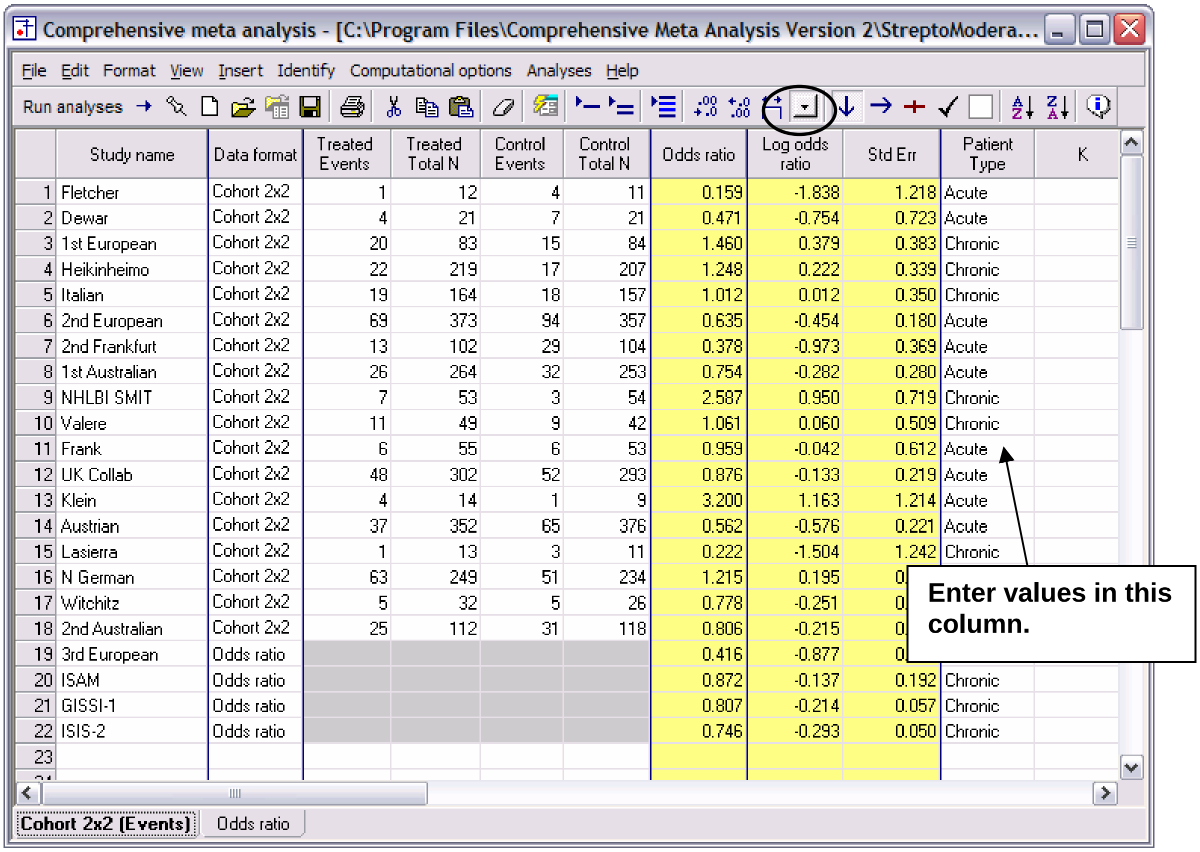
Create the moderator column



The program allows you to compare the effect size in two groups of outcomes. For example, you may want to compare the effect size in studies using acute patients with the effect size in studies using chronic patients. In order to group the studies for such a comparison you must first set up a moderator variable column.

- Double-click on an unassigned column header to launch the column format dialog. The dialog allows you to select a column function, in this case **Moderator**, and to enter a variable name, in this case, 'Patient Type'.
- Specify that the variable data type is **Categorical**.
- Click on **OK** to create the moderator column and to begin data entry.

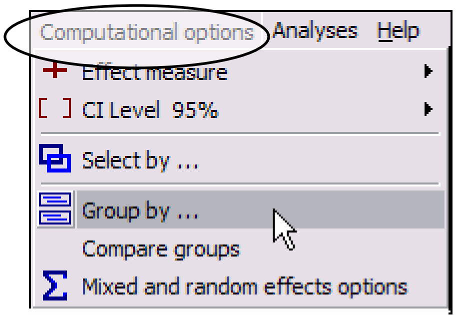
Enter moderator values



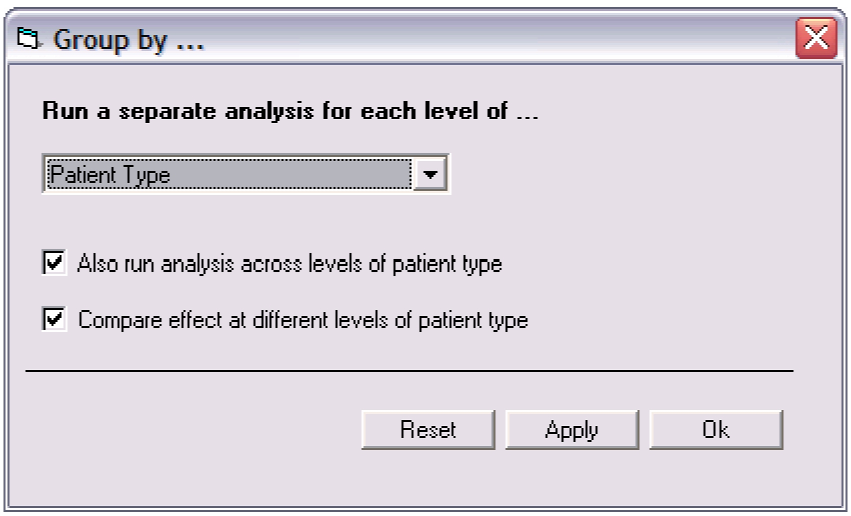
	Study name	Data format	Treated Events	Treated Total N	Control Events	Control Total N	Odds ratio	Log odds ratio	Std Err	Patient Type	K
1	Fletcher	Cohort 2x2	1	12	4	11	0.159	-1.838	1.218	Acute	
2	Dewar	Cohort 2x2	4	21	7	21	0.471	-0.754	0.723	Acute	
3	1st European	Cohort 2x2	20	83	15	84	1.460	0.379	0.383	Chronic	
4	Heikinheimo	Cohort 2x2	22	219	17	207	1.248	0.222	0.339	Chronic	
5	Italian	Cohort 2x2	19	164	18	157	1.012	0.012	0.350	Chronic	
6	2nd European	Cohort 2x2	69	373	94	357	0.635	-0.454	0.180	Acute	
7	2nd Frankfurt	Cohort 2x2	13	102	29	104	0.378	-0.973	0.369	Acute	
8	1st Australian	Cohort 2x2	26	264	32	253	0.754	-0.282	0.280	Acute	
9	NHLBI SMIT	Cohort 2x2	7	53	3	54	2.587	0.950	0.719	Chronic	
10	Valere	Cohort 2x2	11	49	9	42	1.061	0.060	0.509	Chronic	
11	Frank	Cohort 2x2	6	55	6	53	0.959	-0.042	0.612	Acute	
12	UK Collab	Cohort 2x2	48	302	52	293	0.876	-0.133	0.219	Acute	
13	Klein	Cohort 2x2	4	14	1	9	3.200	1.163	1.214	Acute	
14	Austrian	Cohort 2x2	37	352	65	376	0.562	-0.576	0.221	Acute	
15	Lasierra	Cohort 2x2	1	13	3	11	0.222	-1.504	1.242	Chronic	
16	N German	Cohort 2x2	63	249	51	234	1.215	0.195	[illegible]	[illegible]	
17	Witchitz	Cohort 2x2	5	32	5	26	0.778	-0.251	[illegible]	[illegible]	
18	2nd Australian	Cohort 2x2	25	112	31	118	0.806	-0.215	[illegible]	[illegible]	
19	3rd European	Odds ratio					0.416	-0.877	[illegible]	[illegible]	
20	ISAM	Odds ratio					0.872	-0.137	0.192	Chronic	
21	GISSI-1	Odds ratio					0.807	-0.214	0.057	Chronic	
22	ISIS-2	Odds ratio					0.746	-0.293	0.050	Chronic	
23											

The moderator values, either “Acute” or “Chronic”, are now entered for each study in the ‘Patient Type’ column. The toggle button circled above allows you to switch to dropdown data entry, so that you can enter “Acute” or “Chronic” by typing only the first letter of either word.

Select a grouping variable



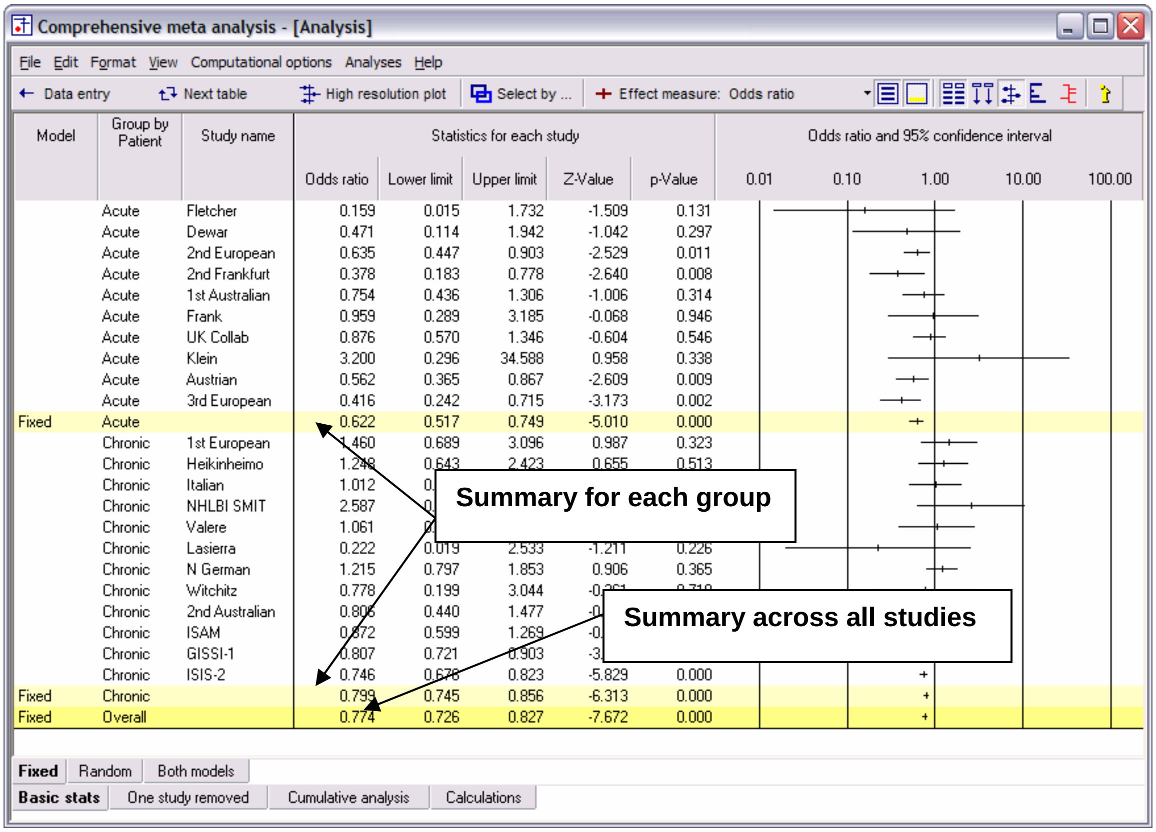
Click on the **Computational options… Group by** selection to launch the **Group by** dialog.



Select 'Patient Type' as the moderator.

In this example we will run an analysis within each patient level and an 'overall analysis' across all levels. Because the second box is checked, within-groups and between-groups heterogeneity values will be provided in the appropriate view (described below).

Run Group by… analysis

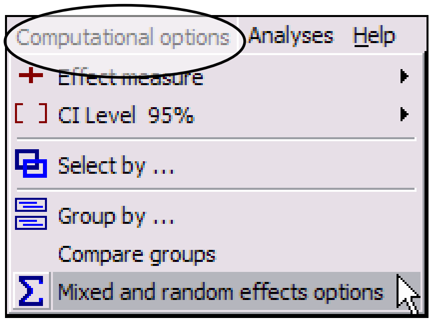


Model	Group by Patient	Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
	Acute	Fletcher	0.159	0.015	1.732	-1.509	0.131
	Acute	Dewar	0.471	0.114	1.942	-1.042	0.297
	Acute	2nd European	0.635	0.447	0.903	-2.529	0.011
	Acute	2nd Frankfurt	0.378	0.183	0.778	-2.640	0.008
	Acute	1st Australian	0.754	0.436	1.306	-1.006	0.314
	Acute	Frank	0.959	0.289	3.185	-0.068	0.946
	Acute	UK Collab	0.876	0.570	1.346	-0.604	0.546
	Acute	Klein	3.200	0.296	34.588	0.958	0.338
	Acute	Austrian	0.562	0.365	0.867	-2.609	0.009
	Acute	3rd European	0.416	0.242	0.715	-3.173	0.002
Fixed	Acute		0.622	0.517	0.749	-5.010	0.000
	Chronic	1st European	1.460	0.689	3.096	0.987	0.323
	Chronic	Heikinheimo	1.248	0.643	2.423	0.655	0.513
	Chronic	Italian	1.012	[illegible]	[illegible]	[illegible]	[illegible]
	Chronic	NHLBI SMIT	2.587	[illegible]	[illegible]	[illegible]	[illegible]
	Chronic	Valere	1.061	[illegible]	[illegible]	[illegible]	[illegible]
	Chronic	Lasierra	0.222	0.019	2.533	-1.211	0.226
	Chronic	N German	1.215	0.797	1.853	0.906	0.365
	Chronic	Witchitz	0.778	0.199	3.044	[illegible]	[illegible]
	Chronic	2nd Australian	0.806	0.440	1.477	[illegible]	[illegible]
	Chronic	ISAM	0.872	0.599	1.269	[illegible]	[illegible]
	Chronic	GISSI-1	0.807	0.721	0.903	[illegible]	[illegible]
	Chronic	ISIS-2	0.746	0.676	0.823	-5.829	0.000
Fixed	Chronic		0.799	0.745	0.856	-6.313	0.000
Fixed	Overall		0.774	0.726	0.827	-7.672	0.000

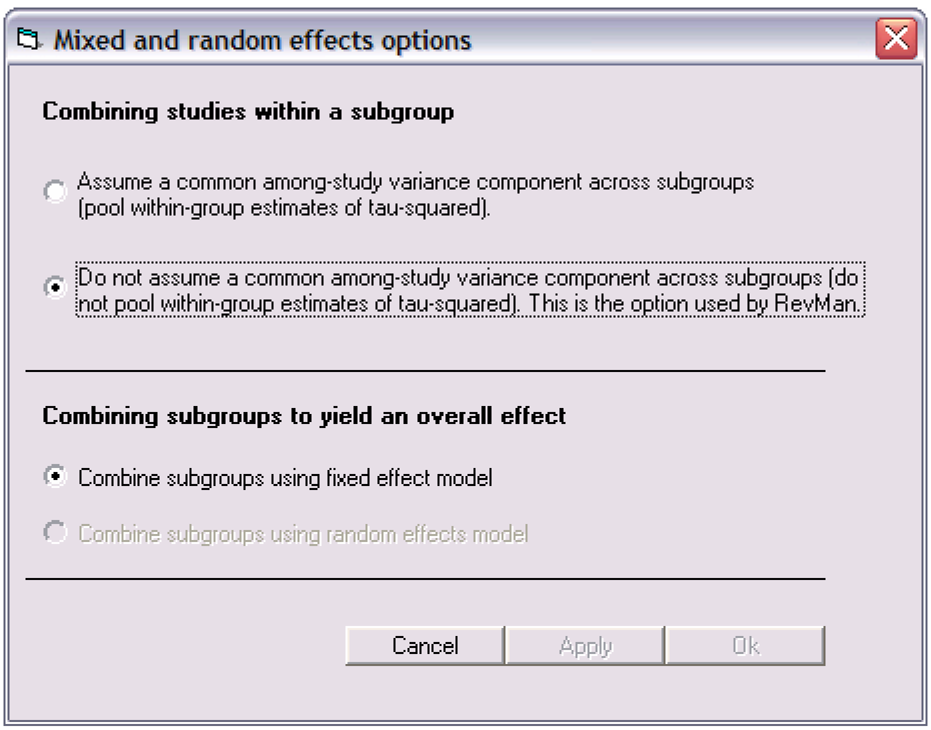
The pale yellow rows provide summaries at each level, "Acute" and "Chronic". The bold yellow 'Overall' row provides a summary for both levels.

Select a computational model

Select **View… Analysis** to switch to the 'Analysis' screen.

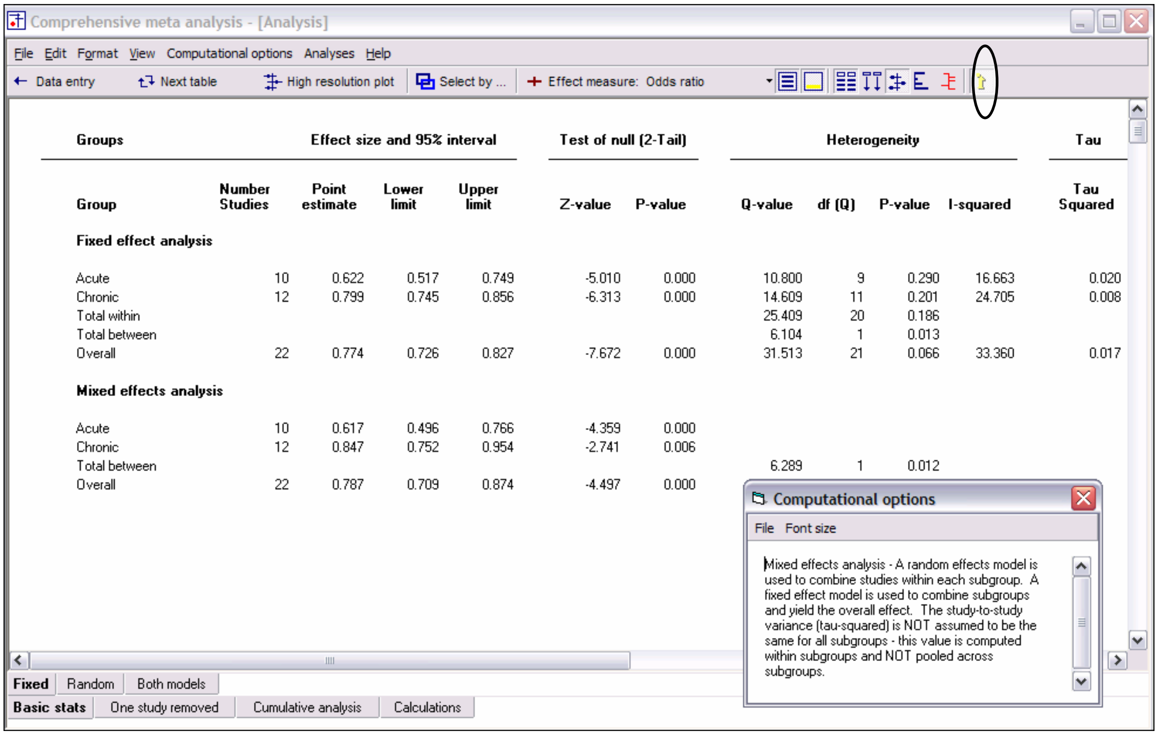


Click on the **Computational options… Mixed and random effects options** selection to launch the dialog.



The options selected here will determine the model to be used for calculating group summary and overall summary values.

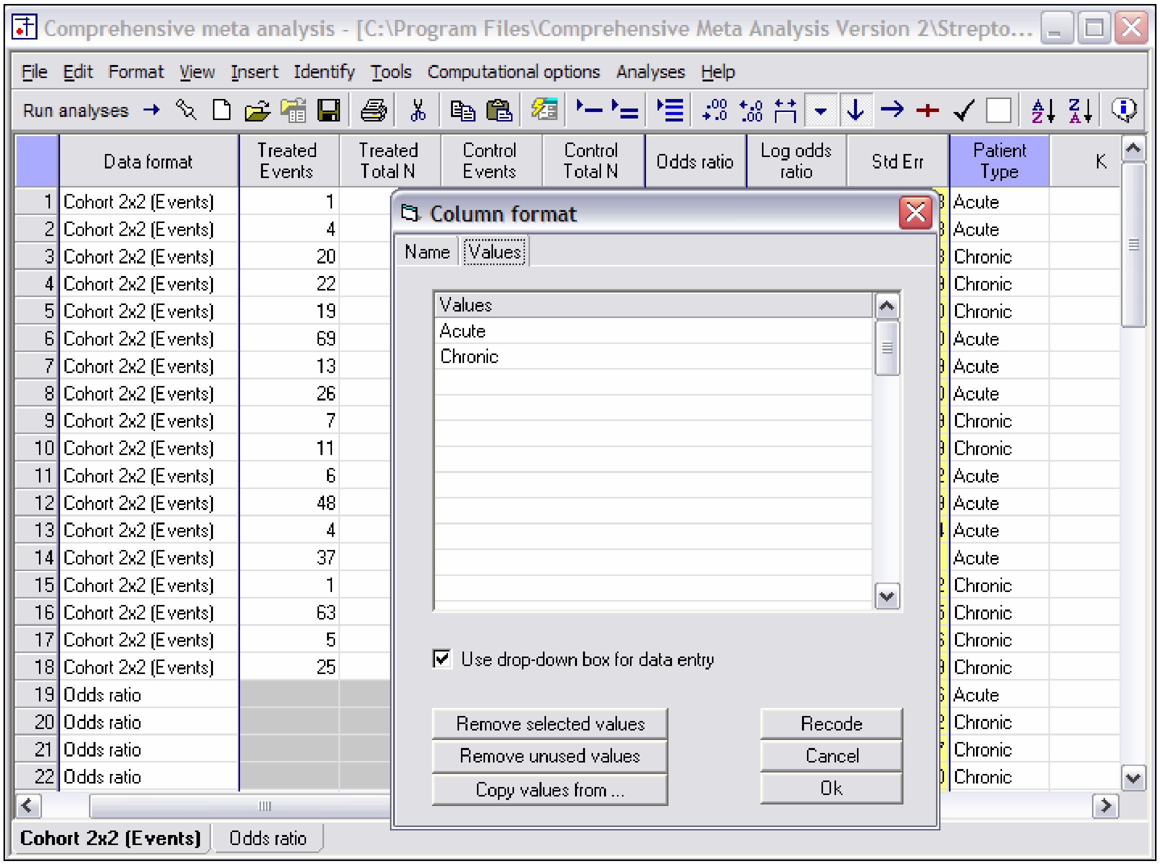
View additional statistics by group



Groups	Effect size and 95% interval				Test of null (2-Tail)		Heterogeneity				Tau
Group	Number Studies	Point estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared
Fixed effect analysis											
Acute	10	0.622	0.517	0.749	-5.010	0.000	10.800	9	0.290	16.663	0.020
Chronic	12	0.799	0.745	0.856	-6.313	0.000	14.609	11	0.201	24.705	0.008
Total within							25.409	20	0.186		
Total between							6.104	1	0.013		
Overall	22	0.774	0.726	0.827	-7.672	0.000	31.513	21	0.066	33.360	0.017
Mixed effects analysis											
Acute	10	0.617	0.496	0.766	-4.359	0.000					
Chronic	12	0.847	0.752	0.954	-2.741	0.006					
Total between							6.289	1	0.012		
Overall	22	0.787	0.709	0.874	-4.497	0.000					

Click on the **Next table** toggle option to display this window, showing additional statistics at each level and overall. The within-groups and between-groups heterogeneity values are also broken out. In the report pop-up is a brief explanation of the assumptions which underlie the selected models. The circled icon allows the user to display and hide the report pop-up.

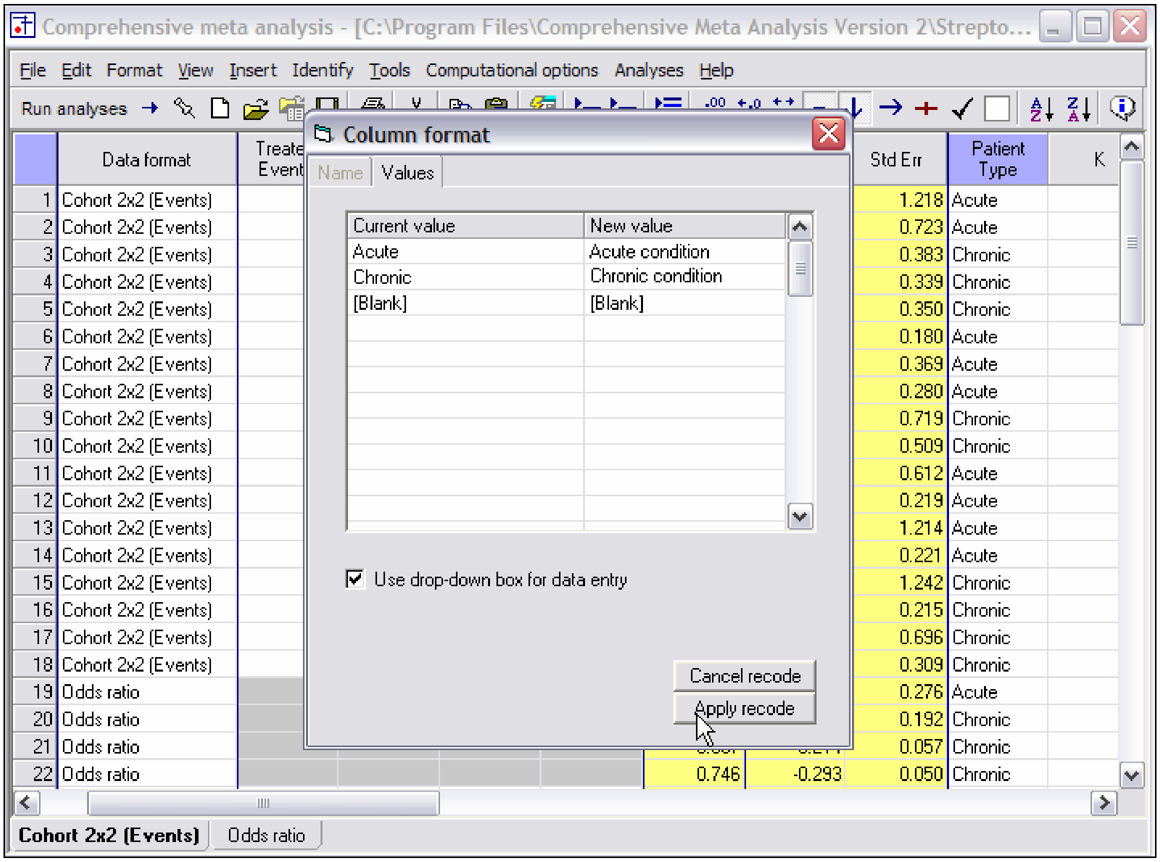
Recode column values



The program offers a set of options for making general changes to the contents of a column. To make such changes to the 'Patient Type' column, you would double-click on the column header and select the **Values** tab in the dialog, as shown above.

You could then do the following:

- **Remove selected values** or **Remove unused values.** The removed values will no longer appear in the 'Patient Type' data entry dropdown.
- **Copy values from.** Copy values from another column so that they are available for selection in the 'Patient Type' data entry dropdown.
- **Recode.** Modify all instances of a value in the column. As an example, the following image shows how to change "Chronic" and "Acute" to "Chronic condition" and "Acute condition" throughout the 'Patient Type' column.



Click on **Apply recode** to replace the current column values with new values.

Section 4. Subgroups within studies

In the main example summary data were recorded for the full sample in each study.

The program also allows the user to record data for subgroups within the study. For example, if there were reason to believe that the treatment effect varied as a function of gender, some (or all) studies might report the treatment effect separately for males and females.

In this case we would enter the data for each study on two rows – one for males and one for females.

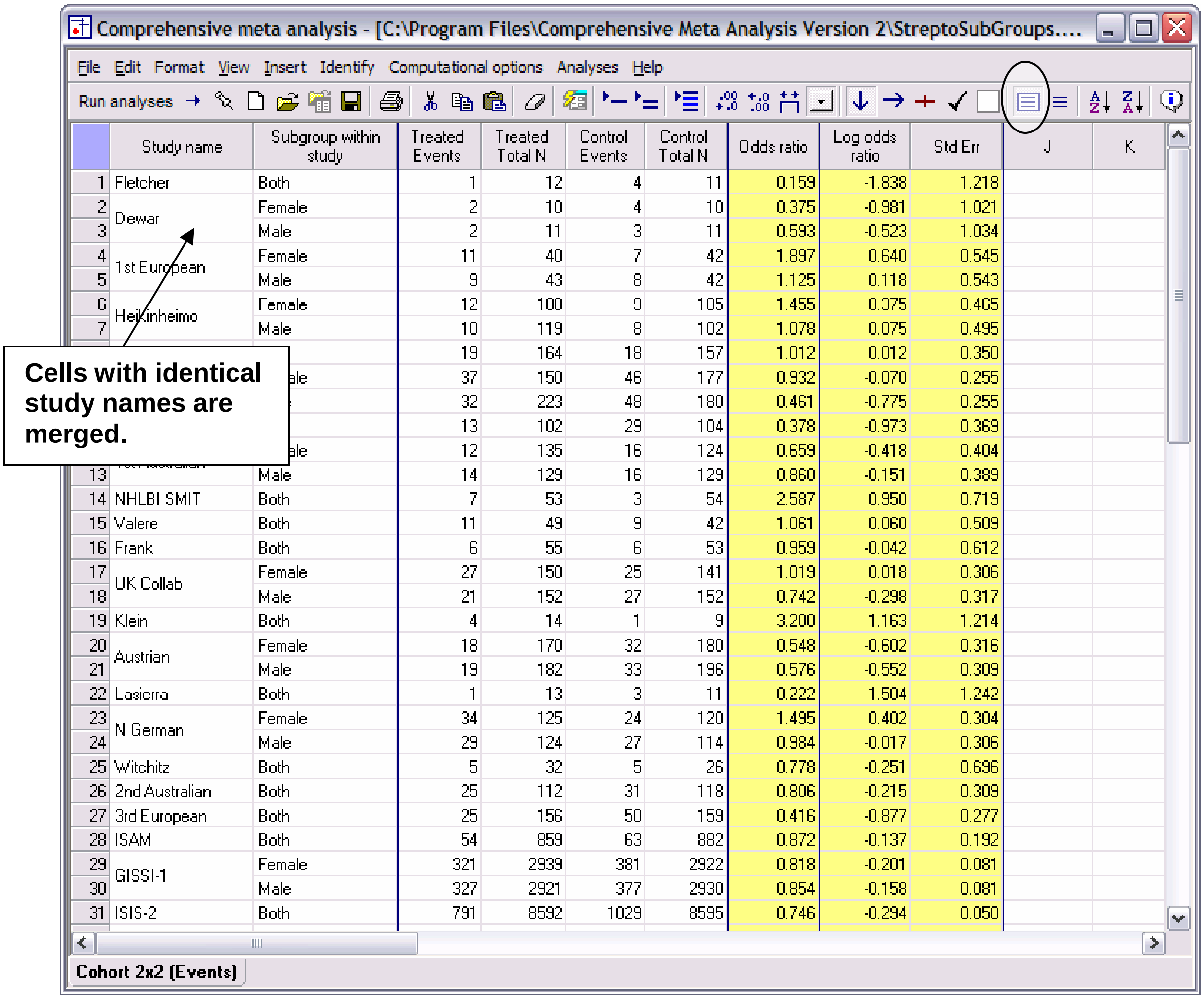
In the analyses we would want to do some (or all) of the following:

- Using subgroup as the unit of analysis, run an analysis grouped by gender. This would report the treatment effect for each gender, and assess the impact of gender on the treatment effect. We could also run an overall analysis.
- Using subgroup as the unit of analysis, run the analysis for either gender alone.
- If it emerged that the treatment effect was comparable for males and females, the researcher might elect to use study as the unit of analysis. This would require having the program collapse the rows for male and female within each study, and impute the values for the full group.

The program offers all of these options, which are outlined in this section.

By default, data sets are copied to
C:\Program Files\Comprehensive Meta Analysis Version 2\Demo Files.
The dataset used in this section is StreptoSubGroups.

Create column for subgroups within study

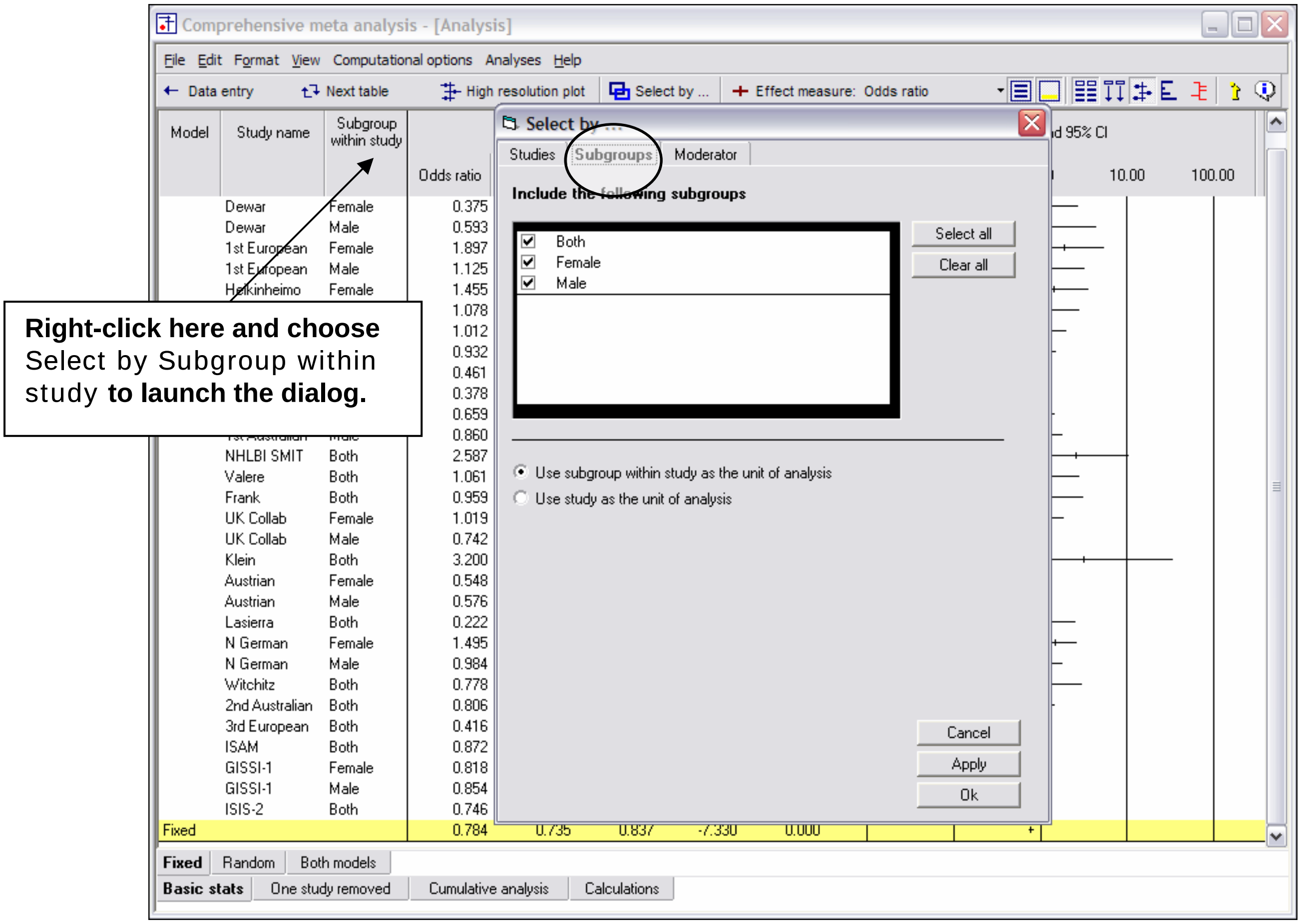


	Study name	Subgroup within study	Treated Events	Treated Total N	Control Events	Control Total N	Odds ratio	Log odds ratio	Std Err	J	K
1	Fletcher	Both	1	12	4	11	0.159	-1.838	1.218		
2	Dewar	Female	2	10	4	10	0.375	-0.981	1.021		
3		Male	2	11	3	11	0.593	-0.523	1.034		
4	1st European	Female	11	40	7	42	1.897	0.640	0.545		
5		Male	9	43	8	42	1.125	0.118	0.543		
6	Heikinheimo	Female	12	100	9	105	1.455	0.375	0.465		
7		Male	10	119	8	102	1.078	0.075	0.495		
[illegible]	[illegible]	[illegible]	19	164	18	157	1.012	0.012	0.350		
[illegible]	[illegible]	[illegible]	37	150	46	177	0.932	-0.070	0.255		
[illegible]	[illegible]	[illegible]	32	223	48	180	0.461	-0.775	0.255		
[illegible]	[illegible]	[illegible]	13	102	29	104	0.378	-0.973	0.369		
[illegible]	[illegible]	[illegible]	12	135	16	124	0.659	-0.418	0.404		
13	[illegible]	Male	14	129	16	129	0.860	-0.151	0.389		
14	NHLBI SMIT	Both	7	53	3	54	2.587	0.950	0.719		
15	Valere	Both	11	49	9	42	1.061	0.060	0.509		
16	Frank	Both	6	55	6	53	0.959	-0.042	0.612		
17	UK Collab	Female	27	150	25	141	1.019	0.018	0.306		
18		Male	21	152	27	152	0.742	-0.298	0.317		
19	Klein	Both	4	14	1	9	3.200	1.163	1.214		
20	Austrian	Female	18	170	32	180	0.548	-0.602	0.316		
21		Male	19	182	33	196	0.576	-0.552	0.309		
22	Lasierra	Both	1	13	3	11	0.222	-1.504	1.242		
23	N German	Female	34	125	24	120	1.495	0.402	0.304		
24		Male	29	124	27	114	0.984	-0.017	0.306		
25	Witchitz	Both	5	32	5	26	0.778	-0.251	0.696		
26	2nd Australian	Both	25	112	31	118	0.806	-0.215	0.309		
27	3rd European	Both	25	156	50	159	0.416	-0.877	0.277		
28	ISAM	Both	54	859	63	882	0.872	-0.137	0.192		
29	GISSI-1	Female	321	2939	381	2922	0.818	-0.201	0.081		
30		Male	327	2921	377	2930	0.854	-0.158	0.081		
31	ISIS-2	Both	791	8592	1029	8595	0.746	-0.294	0.050		

Select **Insert… Column for… Study names**
Select **Insert… Column for… Subgroups within studies**

In this example the study name "Dewar" extends across two rows to accommodate the two subgroups. This is controlled by toggling the **Merge** icon, circled on the toolbar.

View analysis

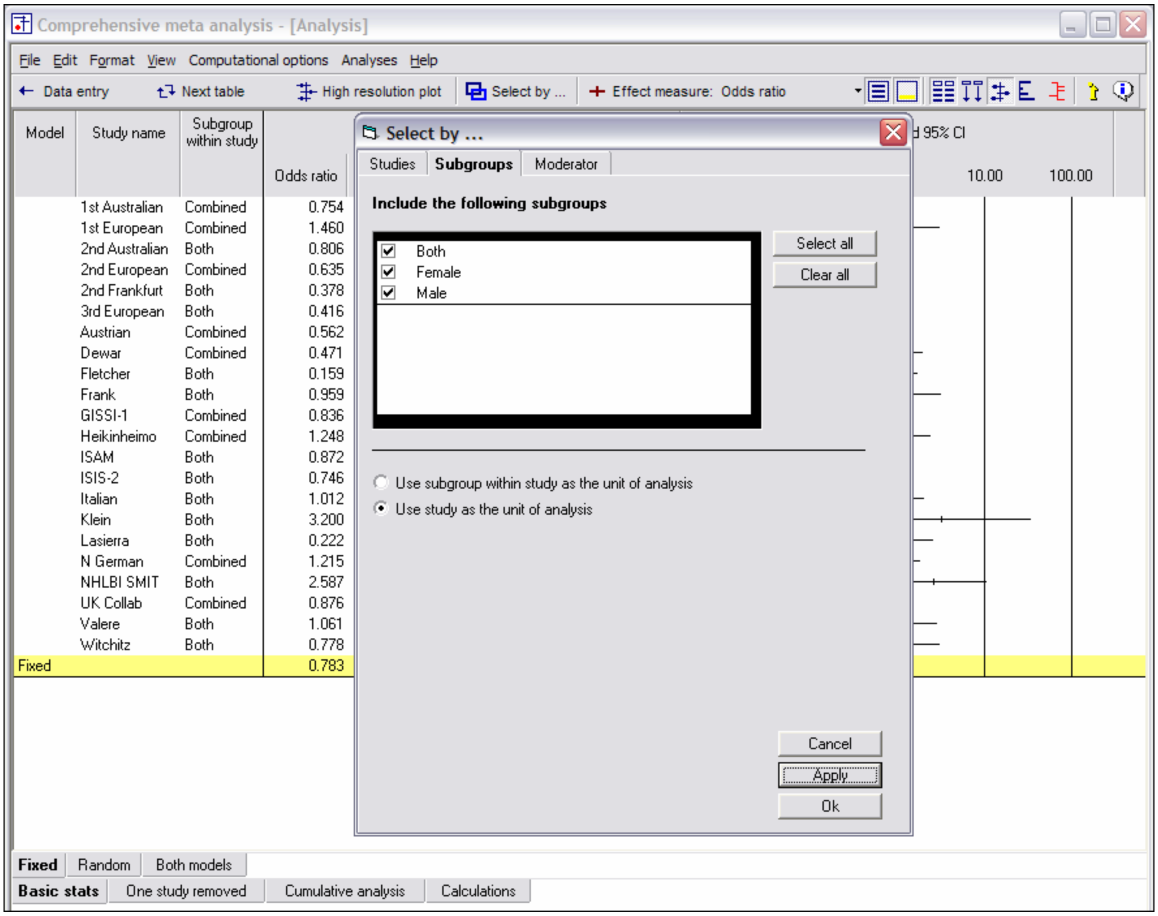


At the top of the dialog box, use check-marks to select which subgroups should be included in the analysis.

At the bottom of the dialog box, specify whether to use subgroup within study or study as the unit of analysis.

If subgroup is the unit of analysis, you may use the **Group by** button and run an analysis using gender as the moderator variable.

Use study as the unit of analysis



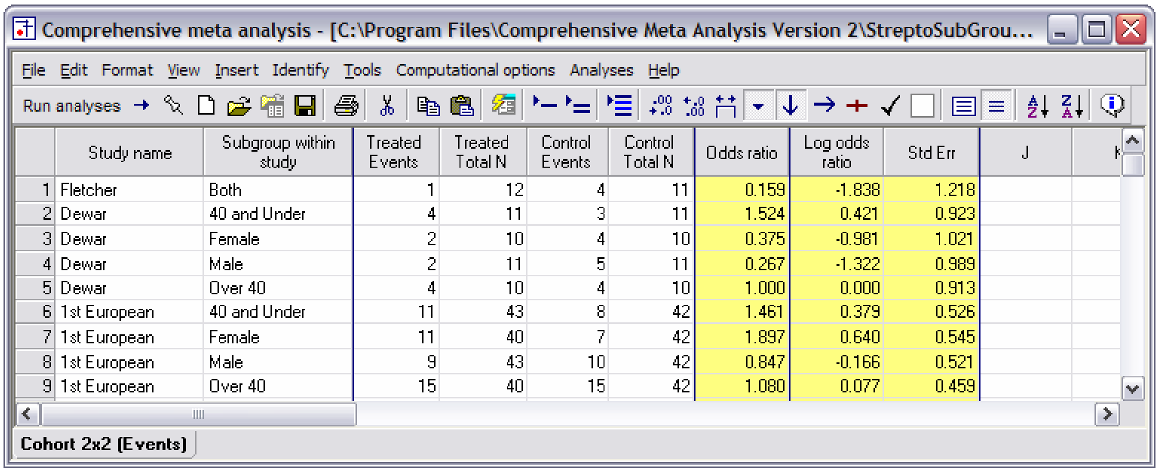
This analysis is run according to the selection: **Use study as the unit of analysis**.

Those studies with multiple subgroups display the term 'Combined' in the **Subgroups within study** column. Those studies that had initially been entered on one line as "Both" are displayed here as they had been entered, since there is no imputation required.

Multiple sets of subgroups

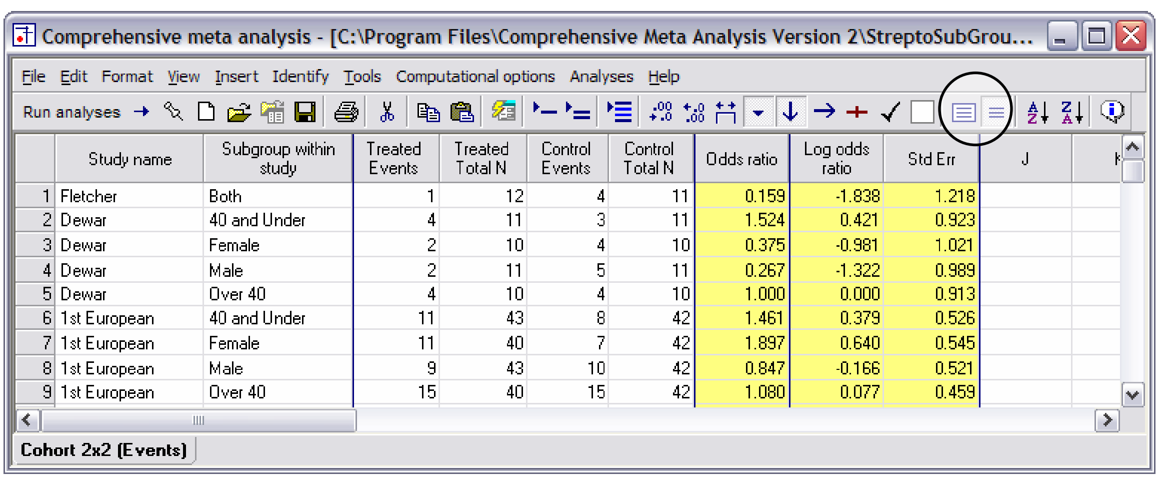
The program can accommodate studies which report treatment effect for more than one set of subgroups.

For instance, certain studies may report results by age level as well as by gender. Such subgroup sets are not independent; they share subjects. It is therefore necessary to limit the analysis to one set at a time.



	Study name	Subgroup within study	Treated Events	Treated Total N	Control Events	Control Total N	Odds ratio	Log odds ratio	Std Err	J
1	Fletcher	Both	1	12	4	11	0.159	-1.838	1.218	
2	Dewar	40 and Under	4	11	3	11	1.524	0.421	0.923	
3	Dewar	Female	2	10	4	10	0.375	-0.981	1.021	
4	Dewar	Male	2	11	5	11	0.267	-1.322	0.989	
5	Dewar	Over 40	4	10	4	10	1.000	0.000	0.913	
6	1st European	40 and Under	11	43	8	42	1.461	0.379	0.526	
7	1st European	Female	11	40	7	42	1.897	0.640	0.545	
8	1st European	Male	9	43	10	42	0.847	-0.166	0.521	
9	1st European	Over 40	15	40	15	42	1.080	0.077	0.459	

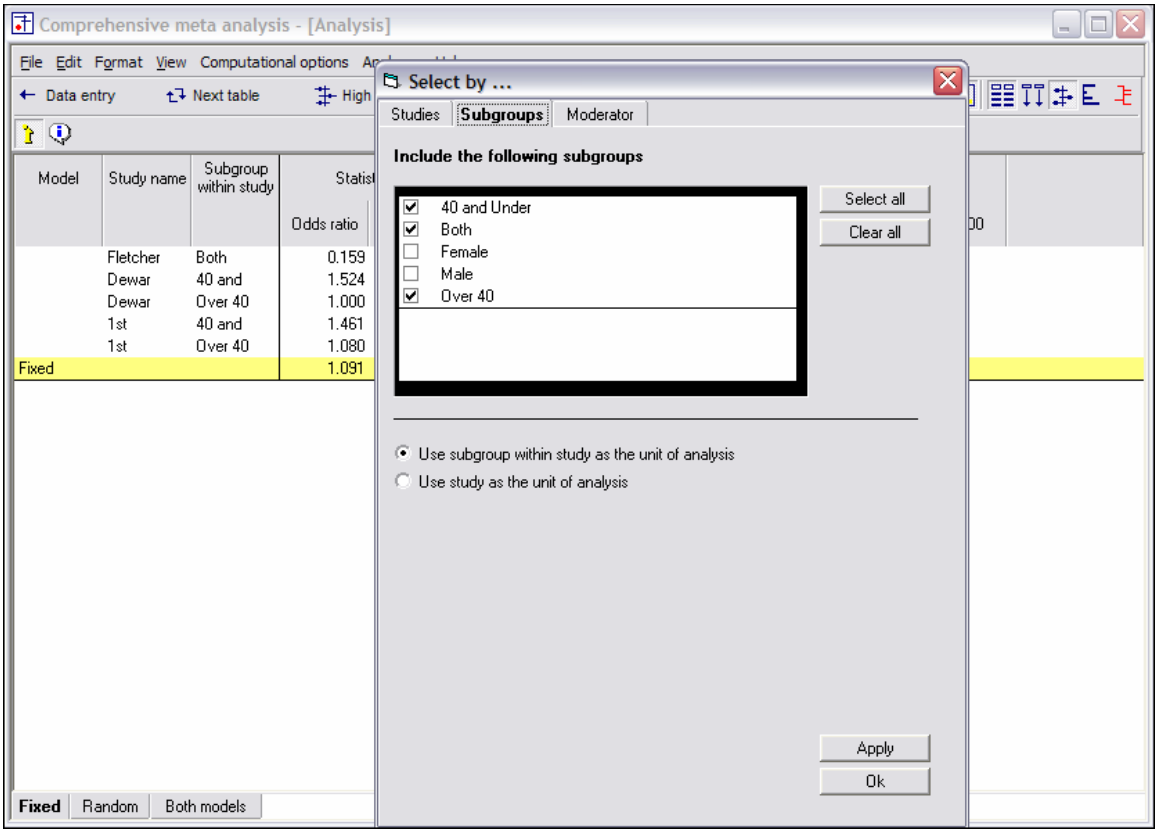
As an example, to accommodate both age and gender subgroup sets, first enter the data as shown above.



	Study name	Subgroup within study	Treated Events	Treated Total N	Control Events	Control Total N	Odds ratio	Log odds ratio	Std Err	J
1	Fletcher	Both	1	12	4	11	0.159	-1.838	1.218	
2	Dewar	40 and Under	4	11	3	11	1.524	0.421	0.923	
3	Dewar	Female	2	10	4	10	0.375	-0.981	1.021	
4	Dewar	Male	2	11	5	11	0.267	-1.322	0.989	
5	Dewar	Over 40	4	10	4	10	1.000	0.000	0.913	
6	1st European	40 and Under	11	43	8	42	1.461	0.379	0.526	
7	1st European	Female	11	40	7	42	1.897	0.640	0.545	
8	1st European	Male	9	43	10	42	0.847	-0.166	0.521	
9	1st European	Over 40	15	40	15	42	1.080	0.077	0.459	

To merge contiguous study names, click on the circled icon.

Filter subgroup sets for analysis



In the **Select by…** dialog, uncheck those subgroups which don't belong to the set you wish to include in the current analysis. In this example, the gender subgroups, 'Male' and 'Female', are excluded from the analysis.

This approach should also be used to manage multiple sets of comparisons, outcomes or time points.

Section 5. Multiple outcomes within studies

In the initial example, we assumed that we needed to record one treatment effect for each study. However, there are situations where the user will want to record more than one treatment effect per study. These are outlined here.

- More than one comparison per study. Assume that some (or all) studies report the treatment effect for Control vs Treatment-A and also Control vs Treatment-B. We would want to record each treatment effect, and then use this information in the analysis.

- More than one outcome per study. Assume that some (or all) studies report the treatment effect for more than one dependent variable – for example, the impact of the treatment in preventing myocardial infarction and also its impact in preventing death. We may want to run one analysis for the first outcome and a separate analysis for the second.

- More than one time point. Assume that studies record the treatment effect at six months and also at one year. We would want to record both, and then run the analysis on one or the other.

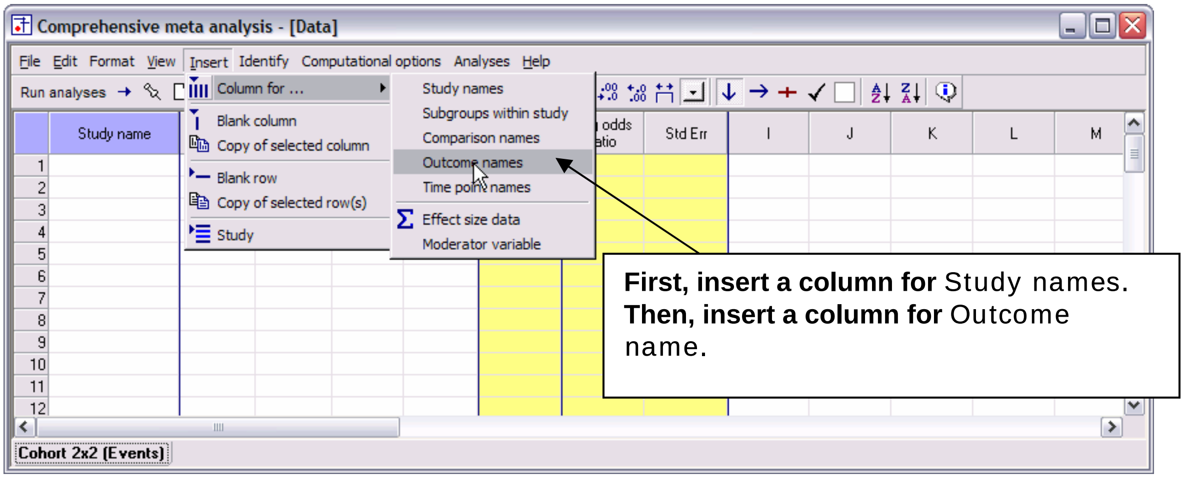
This synopsis is meant only to introduce the topic of multiple, non-independent data points. The ability of the program to work with these will be much more extensive than alluded to here.

In this example we limit ourselves to the simplest case, where the user selects one item of information from each study. This example focuses on outcomes, but the same options are available for comparisons or time points.

A separate section in this document addresses the use of multiple subgroups within studies.

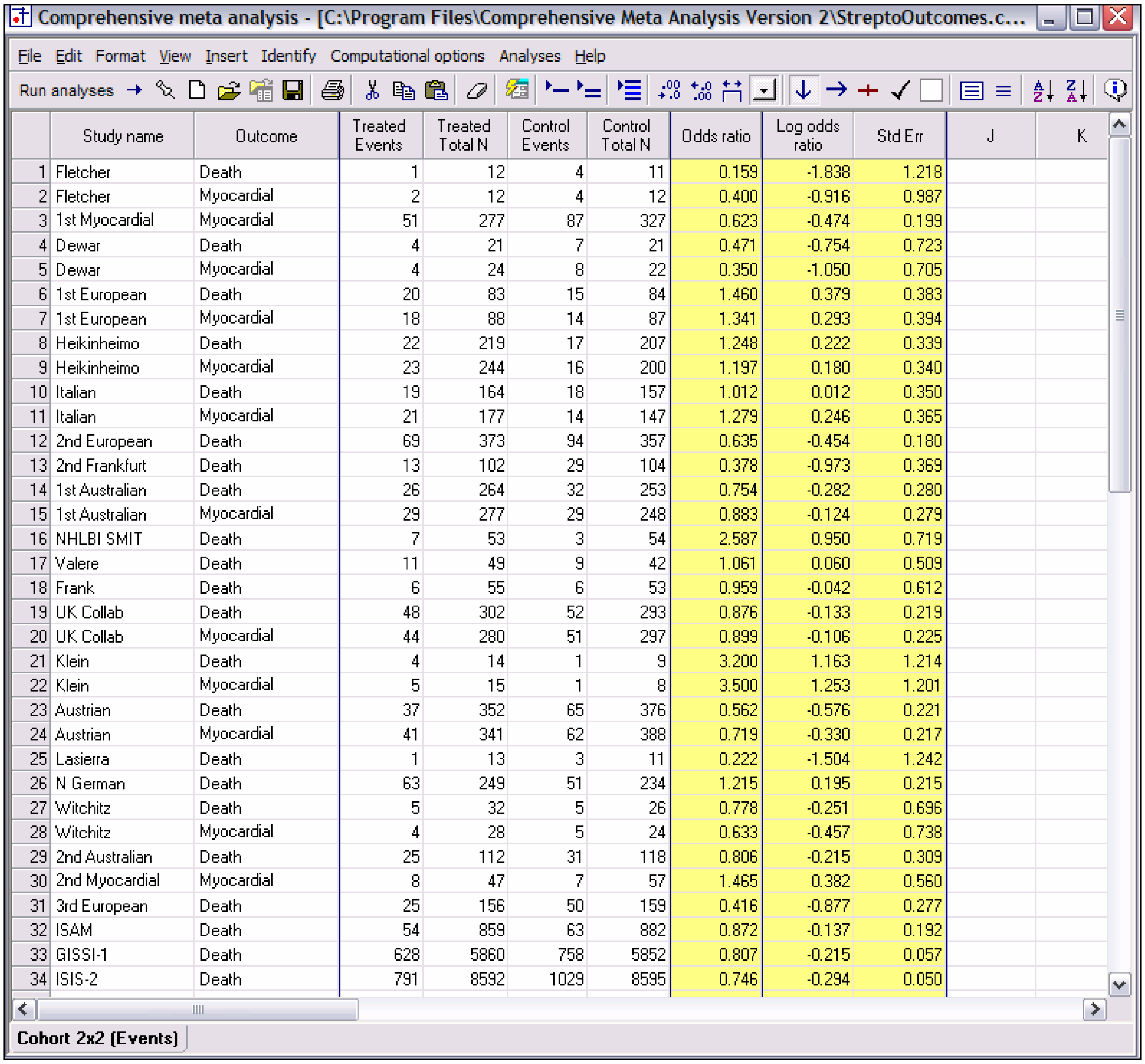
By default, data sets are copied to
C:\Program Files\Comprehensive Meta Analysis Version 2\Demo Files.
The dataset used in this section is StreptoOutcomes.

Create the outcome column



Select **Insert… Column for… Study names.**
Select **Insert… Column for… Outcome name.**

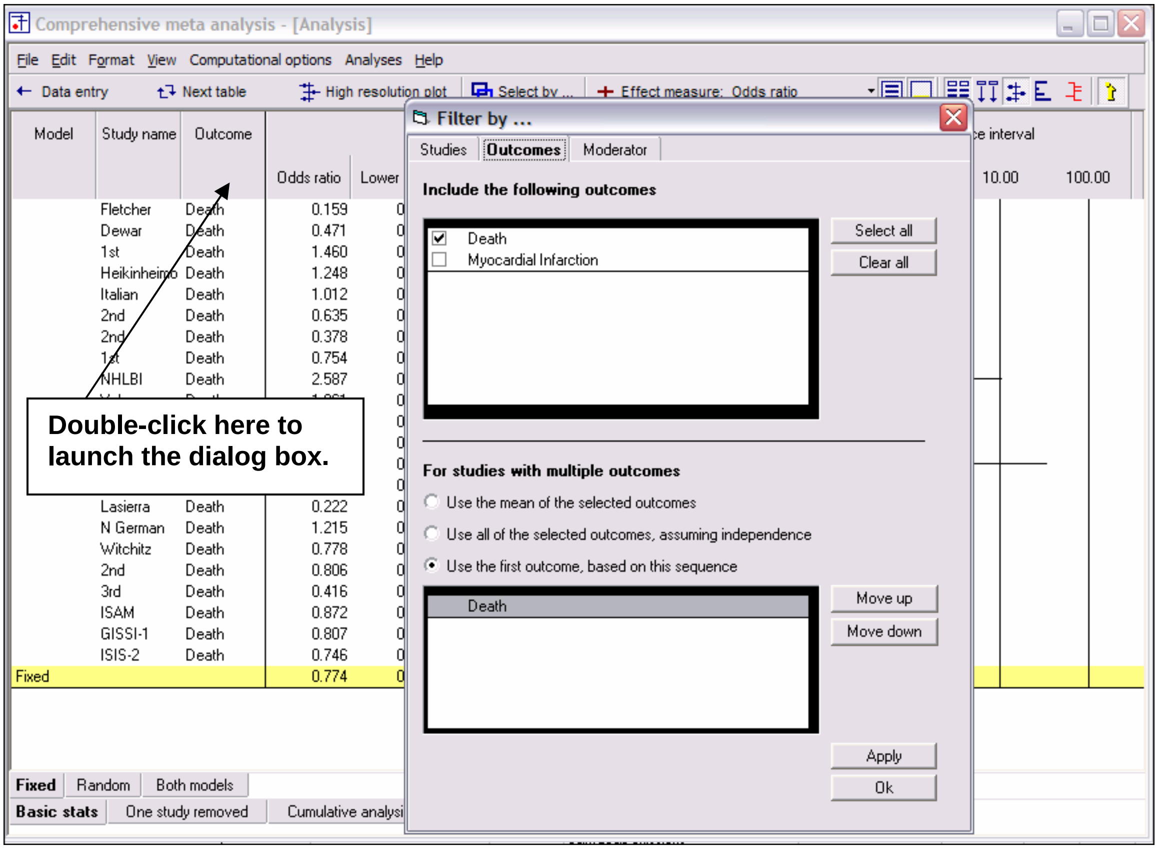
Enter outcome values



	Study name	Outcome	Treated Events	Treated Total N	Control Events	Control Total N	Odds ratio	Log odds ratio	Std Err	J	K
1	Fletcher	Death	1	12	4	11	0.159	-1.838	1.218		
2	Fletcher	Myocardial	2	12	4	12	0.400	-0.916	0.987		
3	1st Myocardial	Myocardial	51	277	87	327	0.623	-0.474	0.199		
4	Dewar	Death	4	21	7	21	0.471	-0.754	0.723		
5	Dewar	Myocardial	4	24	8	22	0.350	-1.050	0.705		
6	1st European	Death	20	83	15	84	1.460	0.379	0.383		
7	1st European	Myocardial	18	88	14	87	1.341	0.293	0.394		
8	Heikinheimo	Death	22	219	17	207	1.248	0.222	0.339		
9	Heikinheimo	Myocardial	23	244	16	200	1.197	0.180	0.340		
10	Italian	Death	19	164	18	157	1.012	0.012	0.350		
11	Italian	Myocardial	21	177	14	147	1.279	0.246	0.365		
12	2nd European	Death	69	373	94	357	0.635	-0.454	0.180		
13	2nd Frankfurt	Death	13	102	29	104	0.378	-0.973	0.369		
14	1st Australian	Death	26	264	32	253	0.754	-0.282	0.280		
15	1st Australian	Myocardial	29	277	29	248	0.883	-0.124	0.279		
16	NHLBI SMIT	Death	7	53	3	54	2.587	0.950	0.719		
17	Valere	Death	11	49	9	42	1.061	0.060	0.509		
18	Frank	Death	6	55	6	53	0.959	-0.042	0.612		
19	UK Collab	Death	48	302	52	293	0.876	-0.133	0.219		
20	UK Collab	Myocardial	44	280	51	297	0.899	-0.106	0.225		
21	Klein	Death	4	14	1	9	3.200	1.163	1.214		
22	Klein	Myocardial	5	15	1	8	3.500	1.253	1.201		
23	Austrian	Death	37	352	65	376	0.562	-0.576	0.221		
24	Austrian	Myocardial	41	341	62	388	0.719	-0.330	0.217		
25	Lasierra	Death	1	13	3	11	0.222	-1.504	1.242		
26	N German	Death	63	249	51	234	1.215	0.195	0.215		
27	Witchitz	Death	5	32	5	26	0.778	-0.251	0.696		
28	Witchitz	Myocardial	4	28	5	24	0.633	-0.457	0.738		
29	2nd Australian	Death	25	112	31	118	0.806	-0.215	0.309		
30	2nd Myocardial	Myocardial	8	47	7	57	1.465	0.382	0.560		
31	3rd European	Death	25	156	50	159	0.416	-0.877	0.277		
32	ISAM	Death	54	859	63	882	0.872	-0.137	0.192		
33	GISSI-1	Death	628	5860	758	5852	0.807	-0.215	0.057		
34	ISIS-2	Death	791	8592	1029	8595	0.746	-0.294	0.050		

In this example some studies contain both outcomes, some only one.

View analysis for one outcome



Note that only one outcome displays in the **Outcome** column. That is the only outcome selected in the dialog.

With the settings provided in the **Group by** dialog, you can also produce analyses which group results by outcome across multiple outcomes.

Section 6. Importing data from other programs

The data entry screen is a spreadsheet, and the user may cut and paste data from most programs, such as Excel, STATA, or SPSS, which are able to display the data in spreadsheet form.

To import data

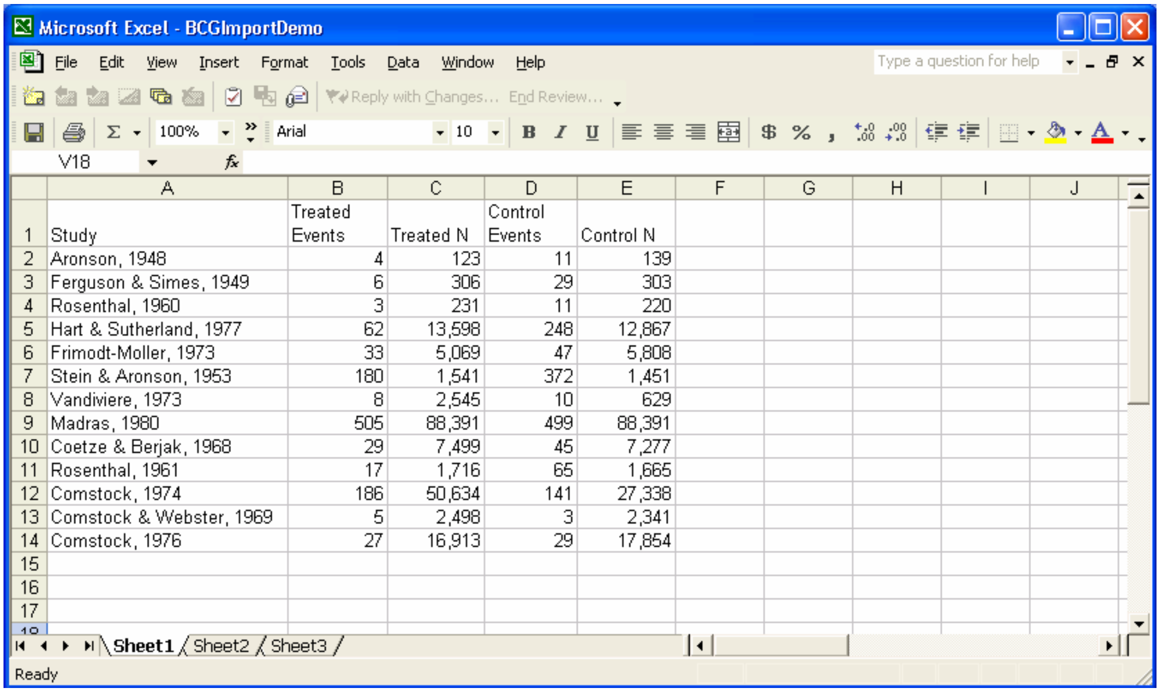
- Switch to the other program and display the data in the Grid View.
- Copy the data to the Windows clipboard (CTRL-C)
- Switch to this program and paste the data into the spreadsheet (CTRL-V)

One step remains – the user must identify the column with the study names, and the columns with the effect size data. Instructions follow.

By default, data sets are copied to
C:\Program Files\Comprehensive Meta Analysis Version 2\Demo Files.

The Excel spreadsheet is BCG.xls.
The CMA data file is BCG.cma.

Import data from Excel



	A	B	C	D	E
1	Study	Treated Events	Treated N	Control Events	Control N
2	Aronson, 1948	4	123	11	139
3	Ferguson & Simes, 1949	6	306	29	303
4	Rosenthal, 1960	3	231	11	220
5	Hart & Sutherland, 1977	62	13,598	248	12,867
6	Frimodt-Moller, 1973	33	5,069	47	5,808
7	Stein & Aronson, 1953	180	1,541	372	1,451
8	Vandiviere, 1973	8	2,545	10	629
9	Madras, 1980	505	88,391	499	88,391
10	Coetze & Berjak, 1968	29	7,499	45	7,277
11	Rosenthal, 1961	17	1,716	65	1,665
12	Comstock, 1974	186	50,634	141	27,338
13	Comstock & Webster, 1969	5	2,498	3	2,341
14	Comstock, 1976	27	16,913	29	17,854
15					
16					
17					

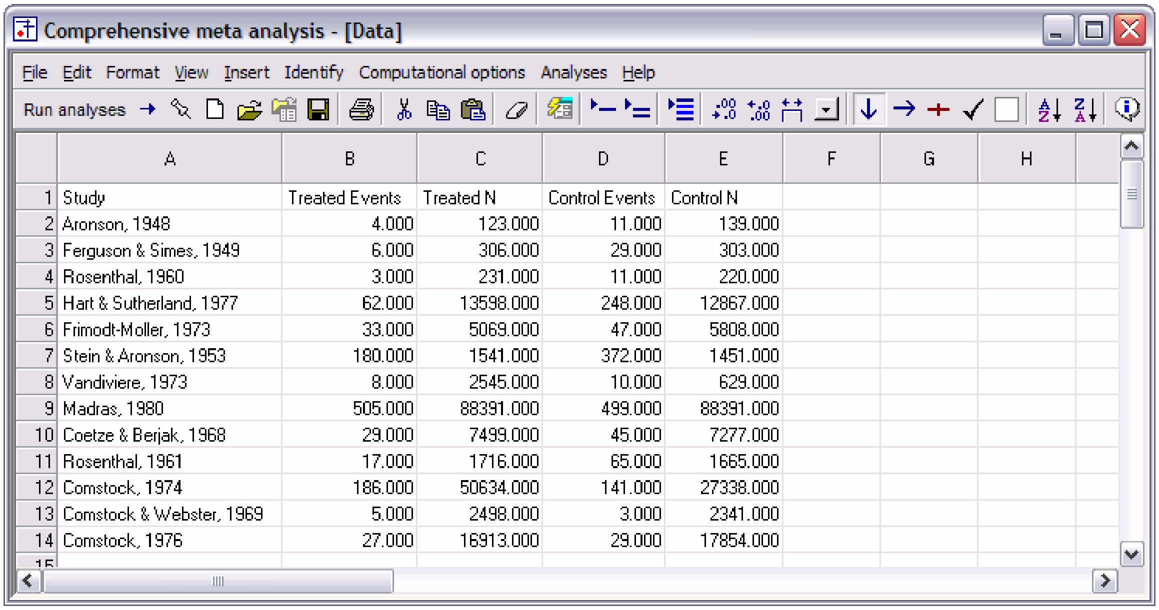
The program allows you to import data already stored on an Excel spreadsheet. It provides simple procedures to assign the imported data to population and effect size entry columns in the Data Entry module.

The Excel spreadsheet above contains the BCG data used in an earlier sequence.

Copy the Excel data into a buffer (using 'Ctrl-C', for instance).

(The same approach will work with SPSS, STATA, and most programs that can display the data in a grid).

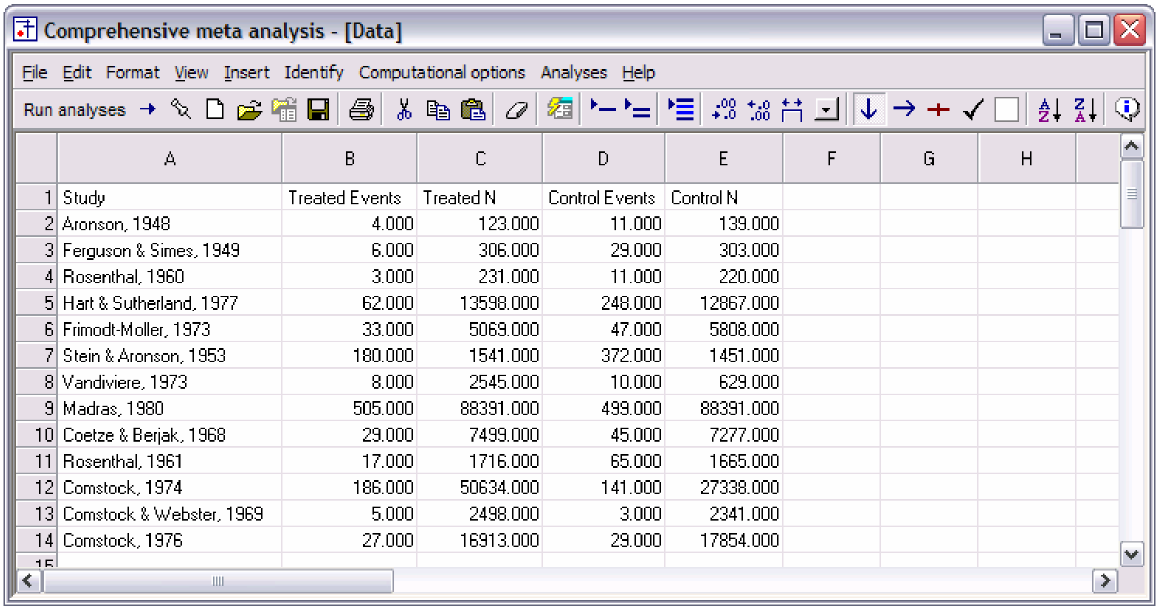
Paste data into the data entry module



	A	B	C	D	E	F	G	H
1	Study	Treated Events	Treated N	Control Events	Control N			
2	Aronson, 1948	4.000	123.000	11.000	139.000			
3	Ferguson & Simes, 1949	6.000	306.000	29.000	303.000			
4	Rosenthal, 1960	3.000	231.000	11.000	220.000			
5	Hart & Sutherland, 1977	62.000	13598.000	248.000	12867.000			
6	Frimodt-Moller, 1973	33.000	5069.000	47.000	5808.000			
7	Stein & Aronson, 1953	180.000	1541.000	372.000	1451.000			
8	Vandiviere, 1973	8.000	2545.000	10.000	629.000			
9	Madras, 1980	505.000	88391.000	499.000	88391.000			
10	Coetze & Berjak, 1968	29.000	7499.000	45.000	7277.000			
11	Rosenthal, 1961	17.000	1716.000	65.000	1665.000			
12	Comstock, 1974	186.000	50634.000	141.000	27338.000			
13	Comstock & Webster, 1969	5.000	2498.000	3.000	2341.000			
14	Comstock, 1976	27.000	16913.000	29.000	17854.000			
15								

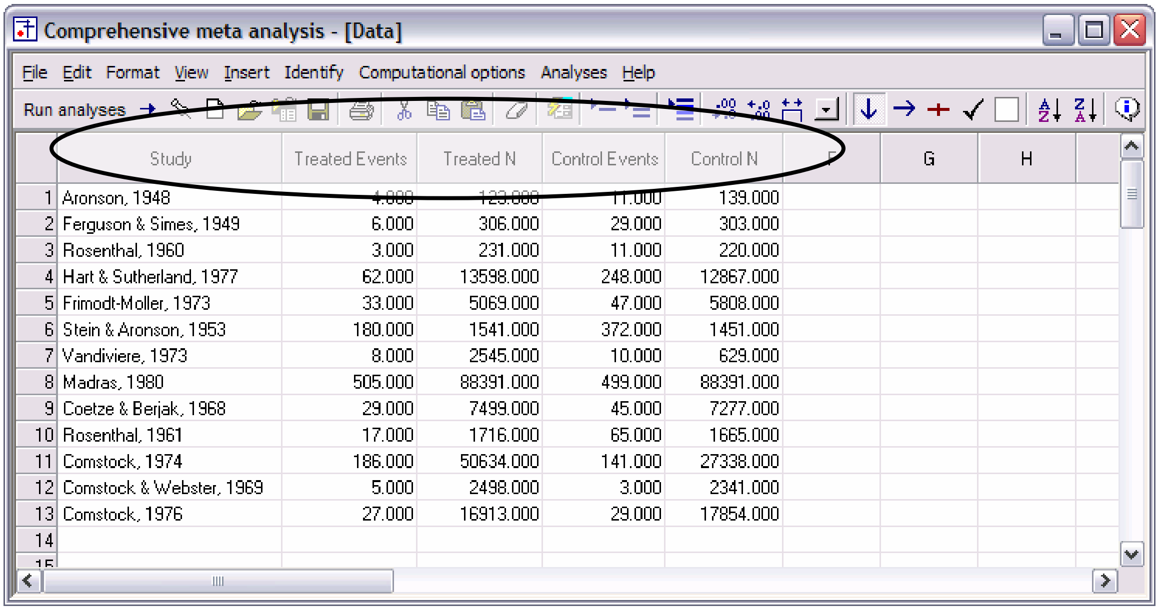
Switch to Comprehensive Meta Analysis and use ‘Ctrl-V’ to paste the data into the spreadsheet.

Assign column header titles



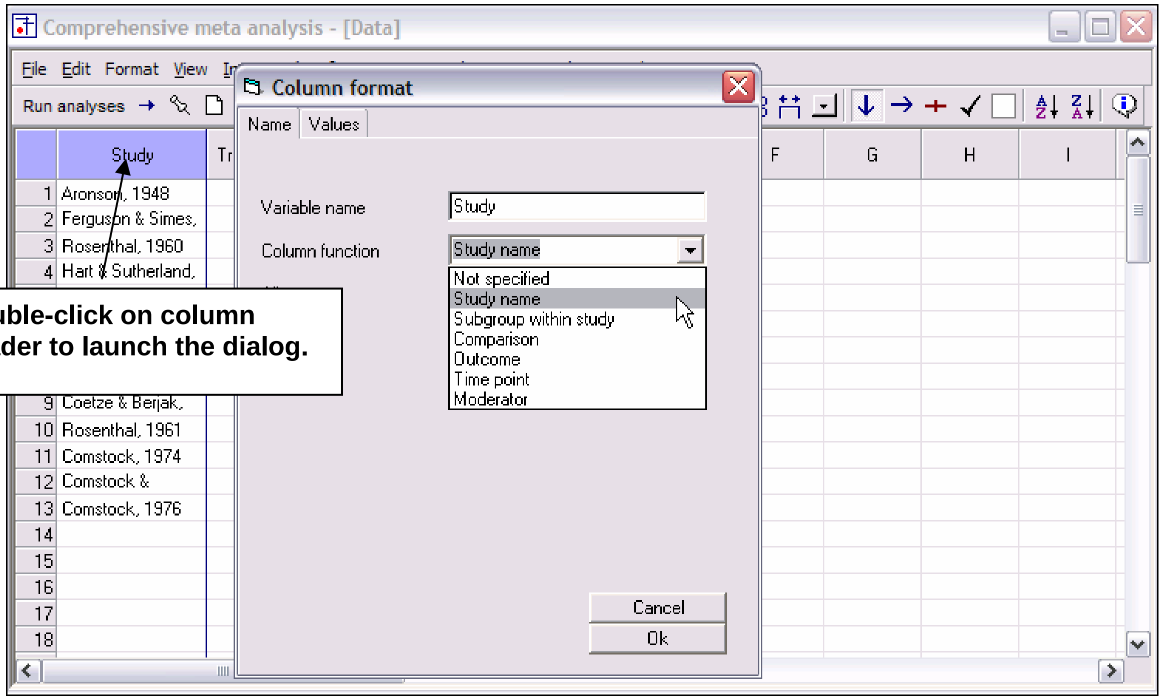
	A	B	C	D	E	F	G	H
1	Study	Treated Events	Treated N	Control Events	Control N			
2	Aronson, 1948	4.000	123.000	11.000	139.000			
3	Ferguson & Simes, 1949	6.000	306.000	29.000	303.000			
4	Rosenthal, 1960	3.000	231.000	11.000	220.000			
5	Hart & Sutherland, 1977	62.000	13598.000	248.000	12867.000			
6	Frimodt-Moller, 1973	33.000	5069.000	47.000	5808.000			
7	Stein & Aronson, 1953	180.000	1541.000	372.000	1451.000			
8	Vandiviere, 1973	8.000	2545.000	10.000	629.000			
9	Madras, 1980	505.000	88391.000	499.000	88391.000			
10	Coetze & Berjak, 1968	29.000	7499.000	45.000	7277.000			
11	Rosenthal, 1961	17.000	1716.000	65.000	1665.000			
12	Comstock, 1974	186.000	50634.000	141.000	27338.000			
13	Comstock & Webster, 1969	5.000	2498.000	3.000	2341.000			
14	Comstock, 1976	27.000	16913.000	29.000	17854.000			

In this example the top row of the data file contains titles ("Study", etc). Click on **Format** and select **Use first row as labels.**



	Study	Treated Events	Treated N	Control Events	Control N	F	G	H
1	Aronson, 1948	4.000	123.000	11.000	139.000			
2	Ferguson & Simes, 1949	6.000	306.000	29.000	303.000			
3	Rosenthal, 1960	3.000	231.000	11.000	220.000			
4	Hart & Sutherland, 1977	62.000	13598.000	248.000	12867.000			
5	Frimodt-Moller, 1973	33.000	5069.000	47.000	5808.000			
6	Stein & Aronson, 1953	180.000	1541.000	372.000	1451.000			
7	Vandiviere, 1973	8.000	2545.000	10.000	629.000			
8	Madras, 1980	505.000	88391.000	499.000	88391.000			
9	Coetze & Berjak, 1968	29.000	7499.000	45.000	7277.000			
10	Rosenthal, 1961	17.000	1716.000	65.000	1665.000			
11	Comstock, 1974	186.000	50634.000	141.000	27338.000			
12	Comstock & Webster, 1969	5.000	2498.000	3.000	2341.000			
13	Comstock, 1976	27.000	16913.000	29.000	17854.000			
14								

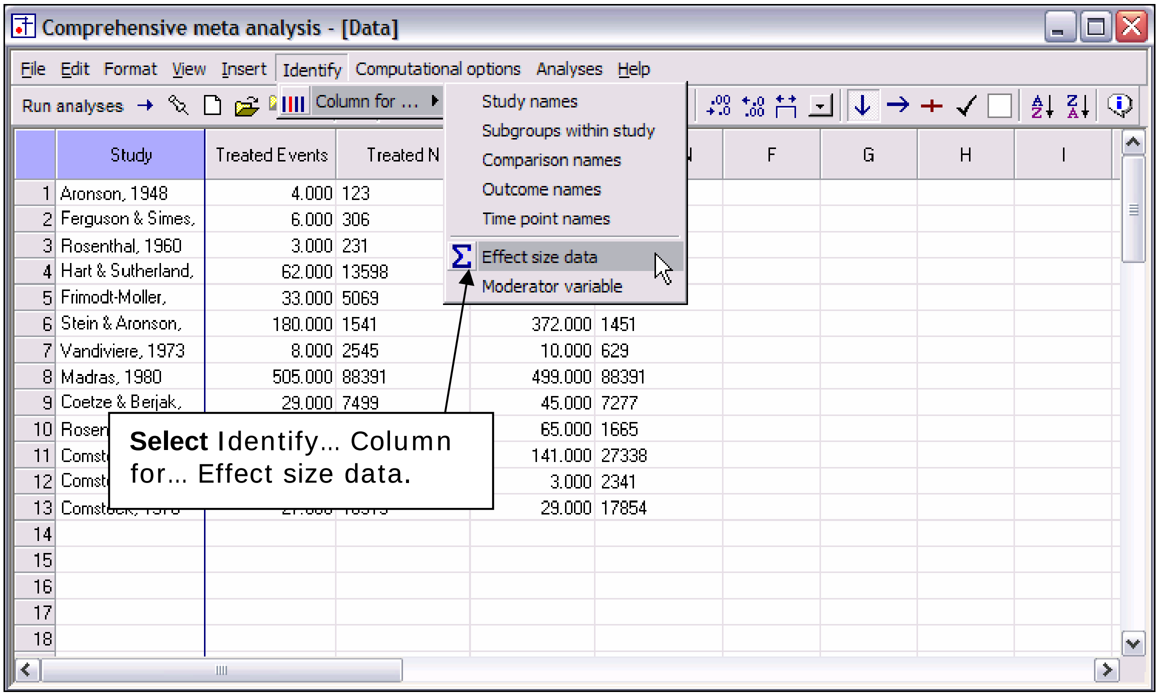
Assign a 'Study name' column



Double-click on the header for the "Study" column and identify the function of the column as 'Study name'.

Note: This is required even though the column is named "Study".

Identify the effect size columns

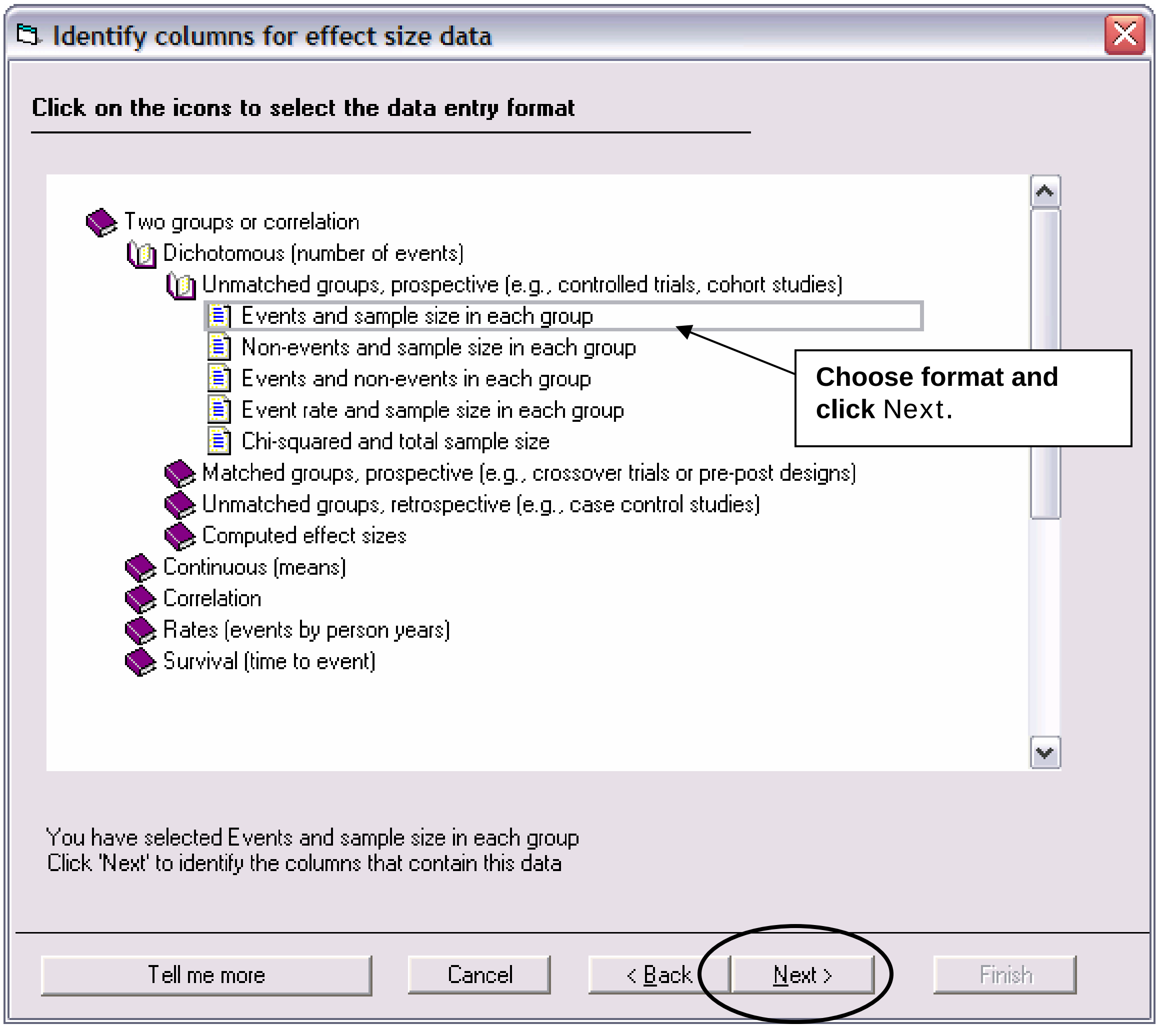


Select **Identify… Column for… Effect size data**

Be sure to use **Identify** to identify the existing columns, rather than **Insert**, which would create new columns.

The program will launch the effect size entry wizard. The function is identical to that for creating a new spreadsheet, until the last panel of the wizard. There, instead of <u>creating</u> the columns, the program will ask you to <u>identify</u> their location.

Select effect size entry format

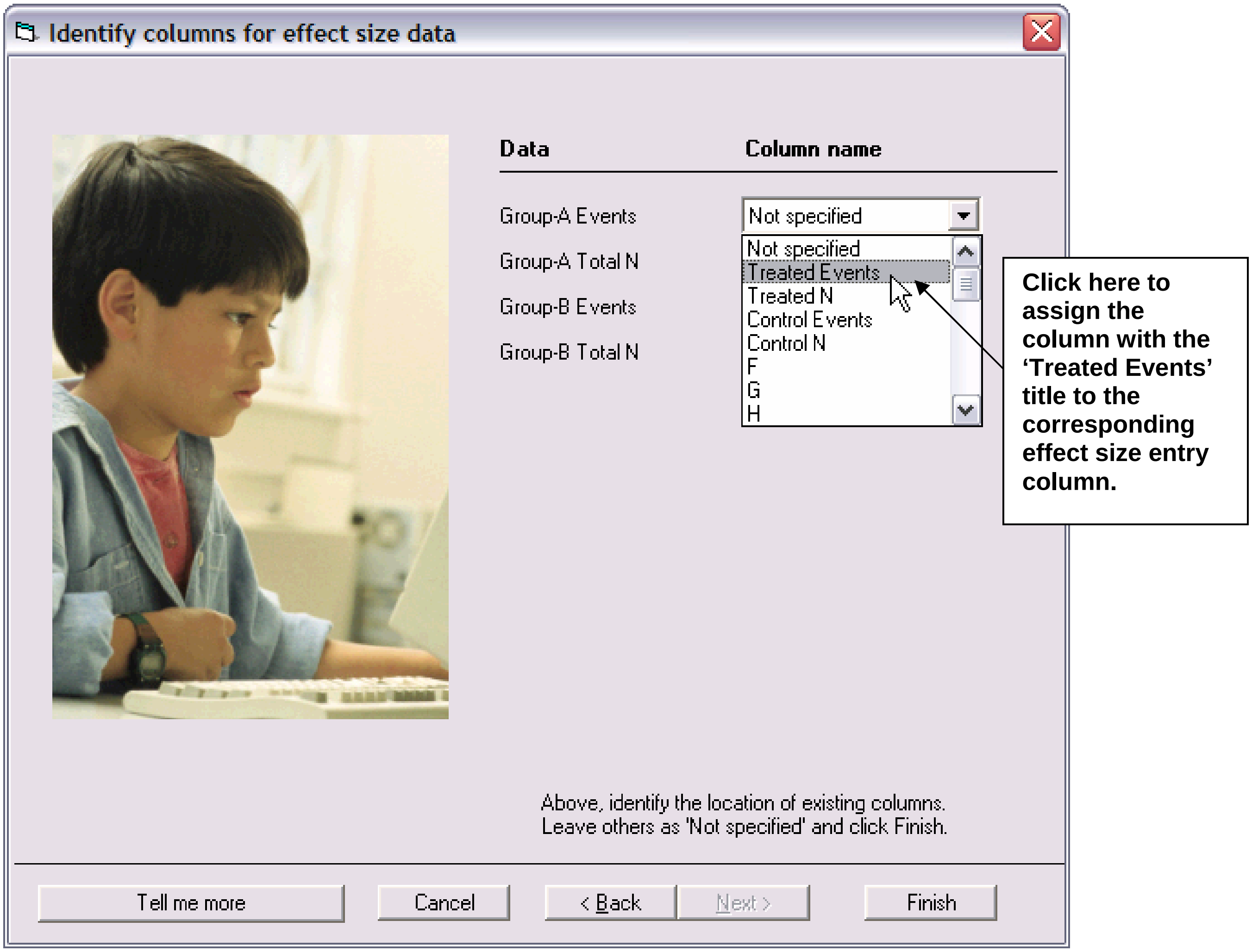


The third screen shows the list of formats arranged hierarchically. In the running example, drill down in the hierarchy to select the following:

- **Dichotomous (number of events)**
    - **Unmatched groups, prospective (e.g., controlled trials, cohort studies)**
        - **Events and sample size in each group**

At this point, the **Next** button will be activated. Click on it to proceed to the final screen.

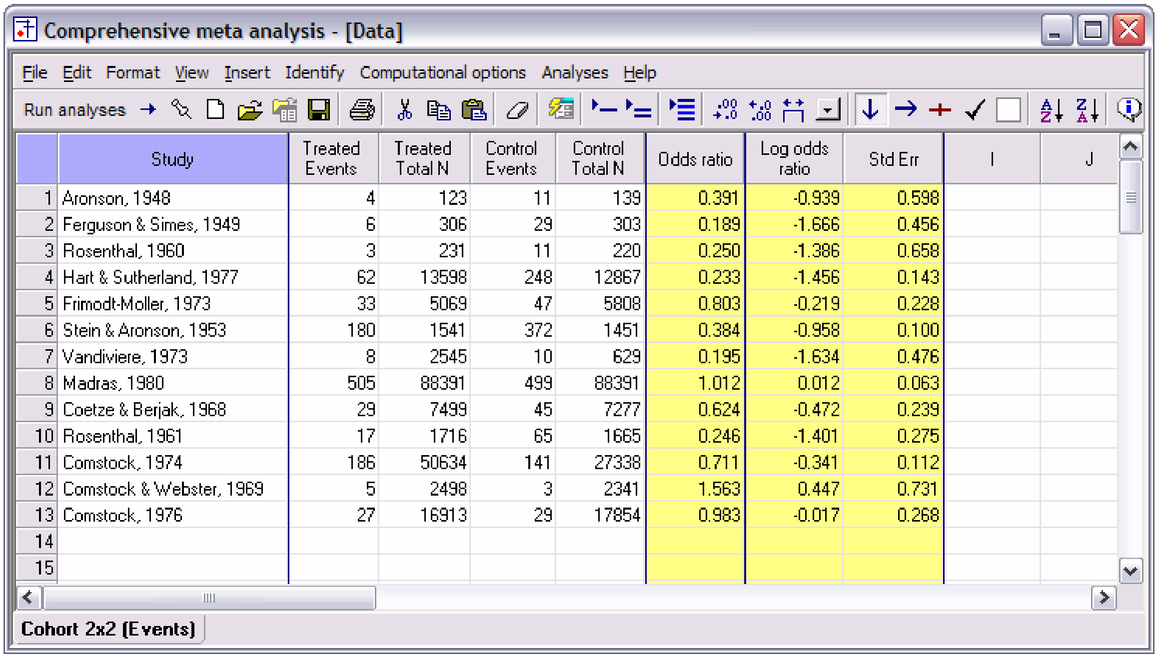
Assign effect size entry columns



Select a column title from the dropdown in order to assign that column's data to the corresponding effect size entry column.

Then, click **Finish**.

All imported columns assigned



	Study	Treated Events	Treated Total N	Control Events	Control Total N	Odds ratio	Log odds ratio	Std Err	I	J
1	Aronson, 1948	4	123	11	139	0.391	-0.939	0.598		
2	Ferguson & Simes, 1949	6	306	29	303	0.189	-1.666	0.456		
3	Rosenthal, 1960	3	231	11	220	0.250	-1.386	0.658		
4	Hart & Sutherland, 1977	62	13598	248	12867	0.233	-1.456	0.143		
5	Frimodt-Moller, 1973	33	5069	47	5808	0.803	-0.219	0.228		
6	Stein & Aronson, 1953	180	1541	372	1451	0.384	-0.958	0.100		
7	Vandiviere, 1973	8	2545	10	629	0.195	-1.634	0.476		
8	Madras, 1980	505	88391	499	88391	1.012	0.012	0.063		
9	Coetze & Berjak, 1968	29	7499	45	7277	0.624	-0.472	0.239		
10	Rosenthal, 1961	17	1716	65	1665	0.246	-1.401	0.275		
11	Comstock, 1974	186	50634	141	27338	0.711	-0.341	0.112		
12	Comstock & Webster, 1969	5	2498	3	2341	1.563	0.447	0.731		
13	Comstock, 1976	27	16913	29	17854	0.983	-0.017	0.268		
14										
15										

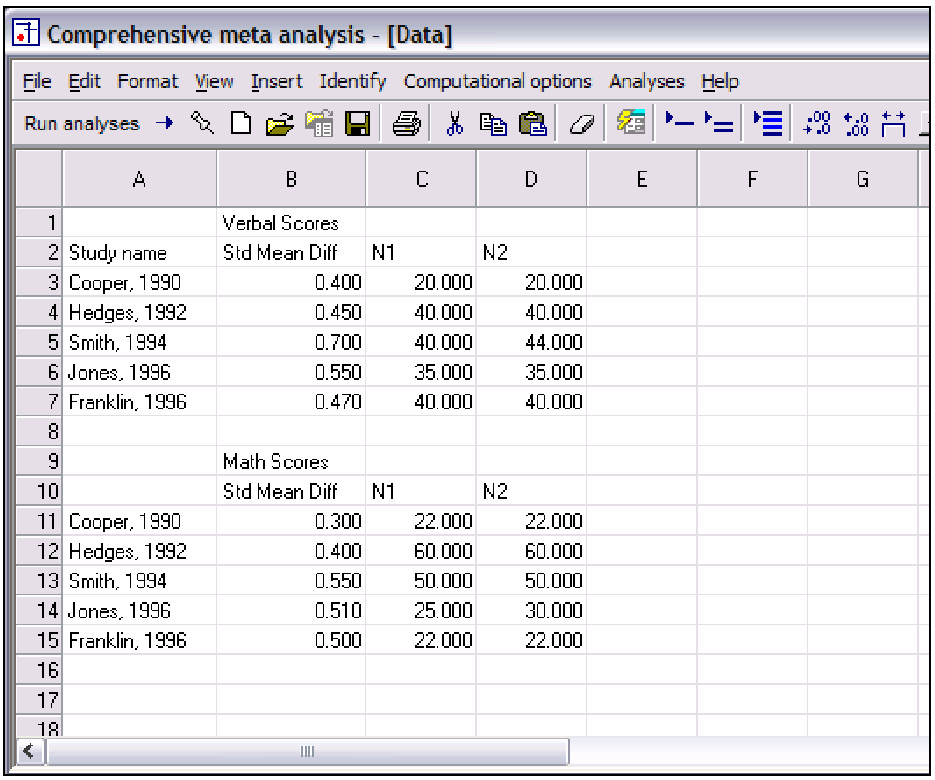
The study names and effect size entry columns are now appropriately assigned. The effect size results are automatically calculated and display in the yellow columns.

At this point, the program behaves exactly as if the spreadsheet had been created from scratch.

Importing data with multiple outcomes per row

	A	B	C	D	E	F	G	H
1		Verbal Scores			Math Scores			
2	Study name	Std Mean Diff	N1	N2	Std Mean Diff	N1	N2	
3	Cooper, 1990	0.4	20	20	0.3	22	22	
4	Hedges, 1992	0.45	40	40	0.4	60	60	
5	Smith, 1994	0.7	40	44	0.55	50	50	
6	Jones, 1996	0.55	35	35	0.51	25	30	
7	Franklin, 1996	0.47	40	40	0.5	22	22	
8								

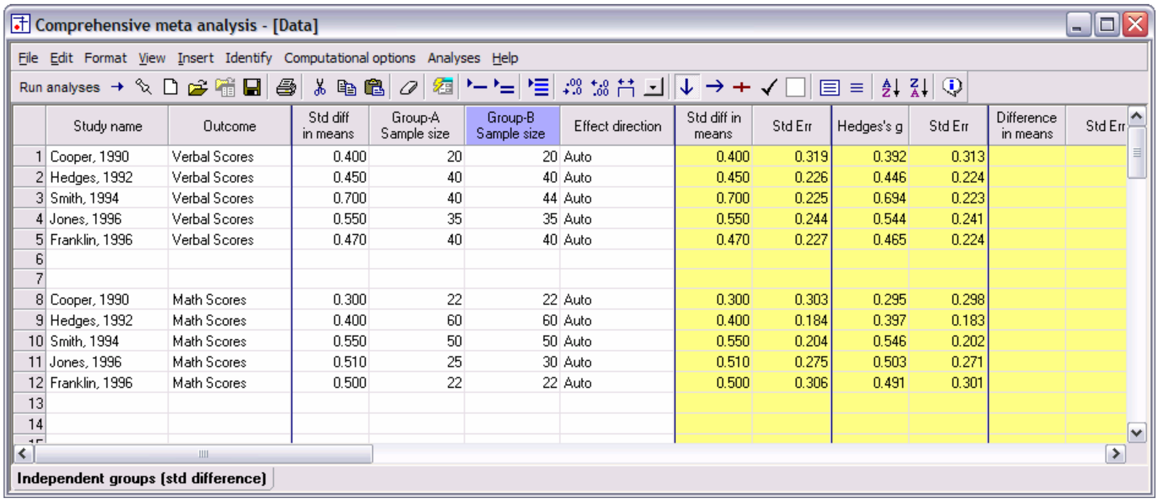
Data are often stored as above, one row per study, with multiple outcomes per row. The following steps explain how to export this data and format it so that it fits the structure of the Data Entry module.



	A	B	C	D	E	F	G
1		Verbal Scores					
2	Study name	Std Mean Diff	N1	N2			
3	Cooper, 1990	0.400	20.000	20.000			
4	Hedges, 1992	0.450	40.000	40.000			
5	Smith, 1994	0.700	40.000	44.000			
6	Jones, 1996	0.550	35.000	35.000			
7	Franklin, 1996	0.470	40.000	40.000			
8							
9		Math Scores					
10		Std Mean Diff	N1	N2			
11	Cooper, 1990	0.300	22.000	22.000			
12	Hedges, 1992	0.400	60.000	60.000			
13	Smith, 1994	0.550	50.000	50.000			
14	Jones, 1996	0.510	25.000	30.000			
15	Franklin, 1996	0.500	22.000	22.000			
16							
17							
18							

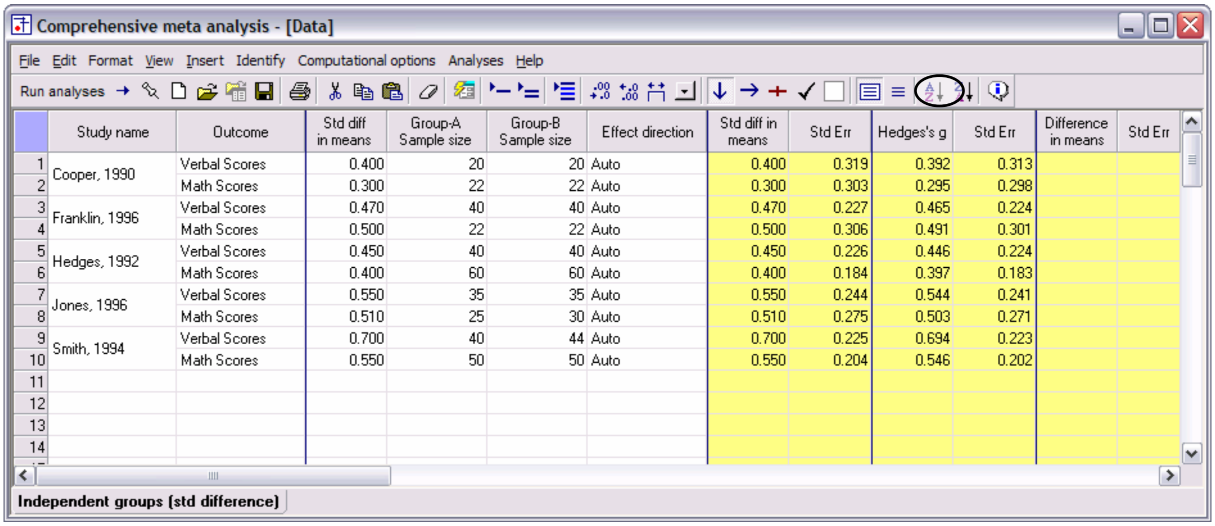
First, paste the Excel data directly onto the Data Entry spreadsheet.

Then cut and paste the data into vertical blocks, one for each outcome.



	Study name	Outcome	Std diff in means	Group-A Sample size	Group-B Sample size	Effect direction	Std diff in means	Std Err	Hedges's g	Std Err	Difference in means	Std Err
1	Cooper, 1990	Verbal Scores	0.400	20	20	Auto	0.400	0.319	0.392	0.313		
2	Hedges, 1992	Verbal Scores	0.450	40	40	Auto	0.450	0.226	0.446	0.224		
3	Smith, 1994	Verbal Scores	0.700	40	44	Auto	0.700	0.225	0.694	0.223		
4	Jones, 1996	Verbal Scores	0.550	35	35	Auto	0.550	0.244	0.544	0.241		
5	Franklin, 1996	Verbal Scores	0.470	40	40	Auto	0.470	0.227	0.465	0.224		
6												
7												
8	Cooper, 1990	Math Scores	0.300	22	22	Auto	0.300	0.303	0.295	0.298		
9	Hedges, 1992	Math Scores	0.400	60	60	Auto	0.400	0.184	0.397	0.183		
10	Smith, 1994	Math Scores	0.550	50	50	Auto	0.550	0.204	0.546	0.202		
11	Jones, 1996	Math Scores	0.510	25	30	Auto	0.510	0.275	0.503	0.271		
12	Franklin, 1996	Math Scores	0.500	22	22	Auto	0.500	0.306	0.491	0.301		
13												
14												

- Click on **Identify… Column for… Study names** to assign that column.
- Click on **Insert… Column for… Outcome names** to create that column. Populate the column with the appropriate outcome value, “Verbal Score” or “Math Score”.
- Identify the effect size format columns via **Identify… Columns… For effect size data.** Within the effect size identification wizard, select the appropriate format, in this case: **Continuous (means)… Unmatched groups…Cohen's d (standardized by pooled within-groups SD) and sample size**



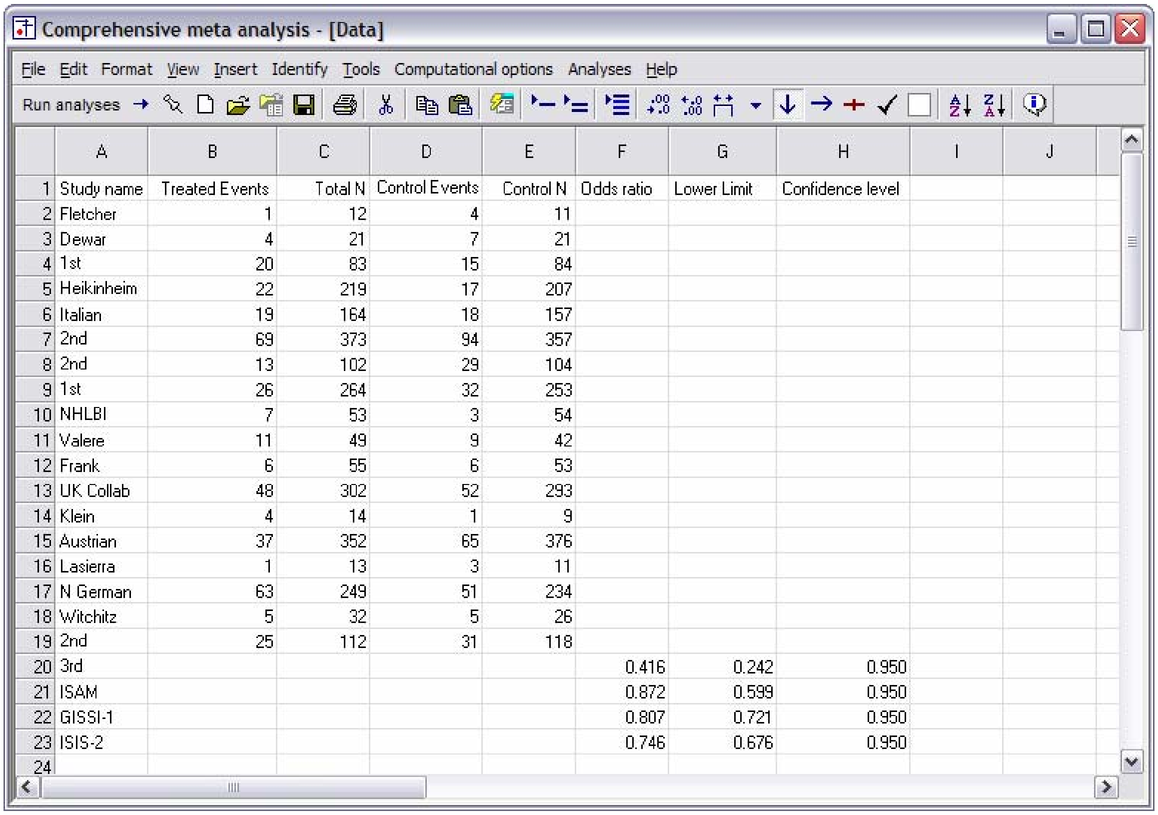
	Study name	Outcome	Std diff in means	Group-A Sample size	Group-B Sample size	Effect direction	Std diff in means	Std Err	Hedges's g	Std Err	Difference in means	Std Err
1	Cooper, 1990	Verbal Scores	0.400	20	20	Auto	0.400	0.319	0.392	0.313		
2		Math Scores	0.300	22	22	Auto	0.300	0.303	0.295	0.298		
3	Franklin, 1996	Verbal Scores	0.470	40	40	Auto	0.470	0.227	0.465	0.224		
4		Math Scores	0.500	22	22	Auto	0.500	0.306	0.491	0.301		
5	Hedges, 1992	Verbal Scores	0.450	40	40	Auto	0.450	0.226	0.446	0.224		
6		Math Scores	0.400	60	60	Auto	0.400	0.184	0.397	0.183		
7	Jones, 1996	Verbal Scores	0.550	35	35	Auto	0.550	0.244	0.544	0.241		
8		Math Scores	0.510	25	30	Auto	0.510	0.275	0.503	0.271		
9	Smith, 1994	Verbal Scores	0.700	40	44	Auto	0.700	0.225	0.694	0.223		
10		Math Scores	0.550	50	50	Auto	0.550	0.204	0.546	0.202		
11												
12												
13												
14												

Click on the study names column and then on the ascending sort icon, circled above. The data are now sorted by study name so that multiple outcomes for a given study display on contiguous rows.

The **Merge** icon has been clicked so that contiguous study names are merged.

(Note that ascending and descending sorts can be performed on any column. To order studies by date, you could enter study dates into an unassigned column or a moderator column and then sort on that column.)

Import data with multiple effect size entry formats



	A	B	C	D	E	F	G	H	I	J
1	Study name	Treated Events	Total N	Control Events	Control N	Odds ratio	Lower Limit	Confidence level		
2	Fletcher	1	12	4	11					
3	Dewar	4	21	7	21					
4	1st	20	83	15	84					
5	Heikinheim	22	219	17	207					
6	Italian	19	164	18	157					
7	2nd	69	373	94	357					
8	2nd	13	102	29	104					
9	1st	26	264	32	253					
10	NHLBI	7	53	3	54					
11	Valere	11	49	9	42					
12	Frank	6	55	6	53					
13	UK Collab	48	302	52	293					
14	Klein	4	14	1	9					
15	Austrian	37	352	65	376					
16	Lasierra	1	13	3	11					
17	N German	63	249	51	234					
18	Witchitz	5	32	5	26					
19	2nd	25	112	31	118					
20	3rd					0.416	0.242	0.950		
21	ISAM					0.872	0.599	0.950		
22	GISSI-1					0.807	0.721	0.950		
23	ISIS-2					0.746	0.676	0.950		
24										

When the study results to be imported require multiple entry formats, paste the data into the Data Entry module as above, with the second format's columns to the right of the first format's columns.

To assign the imported data shown above, follow these steps:

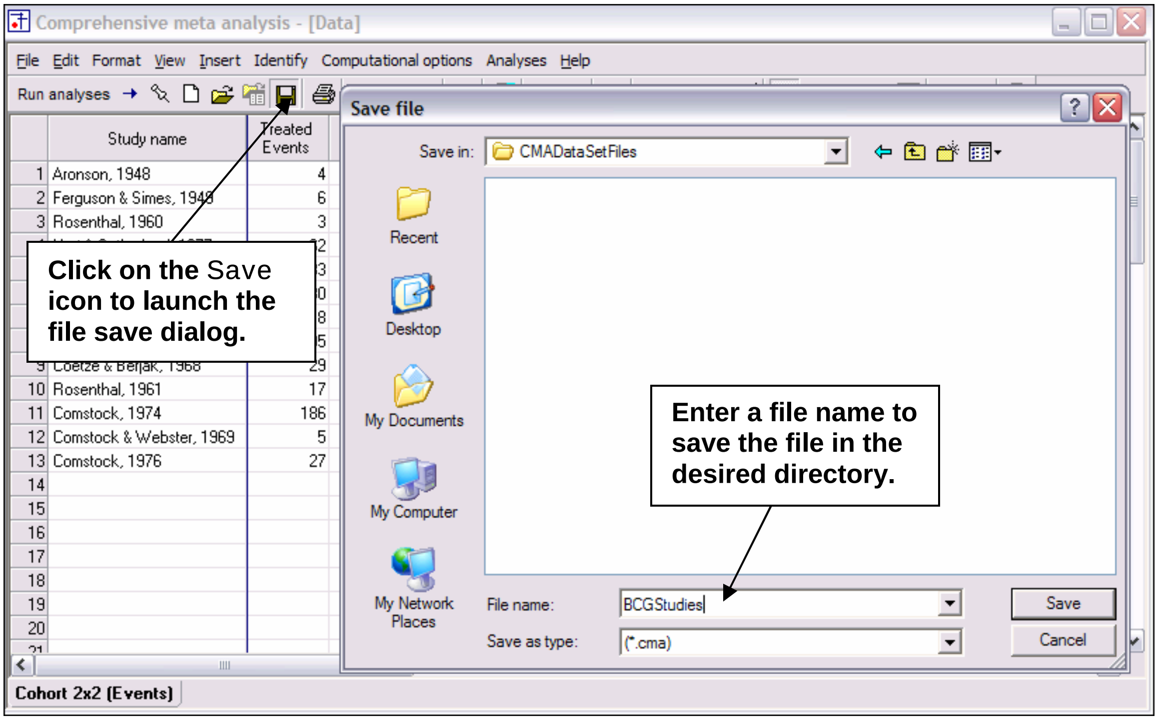
- Click on **Format** and select **Use first row as labels (**keep in mind that the column names must be unique).
- Double-click on the header for the "Study" column and identify the function of the column as 'Study name'.
- For rows 2 – 19, select **Identify… Column for… Effect size data** and assign the data columns to the **Events and sample size in each group** entry format**.**
- For rows 20 – 23, select **Identify… Column for… Effect size data** and assign the data columns to the **Odds ratio and confidence limits** entry format**.** (Note that **Upper limits** values are missing from the pasted data. The **Identify…** function will automatically create an empty **Upper limits** column.)

The data will display, fully formatted as it does in chapter 2 (which discusses multiple data entry formats).

Section 7. Saving and loading files

This section shows how to save and reload your data sets.

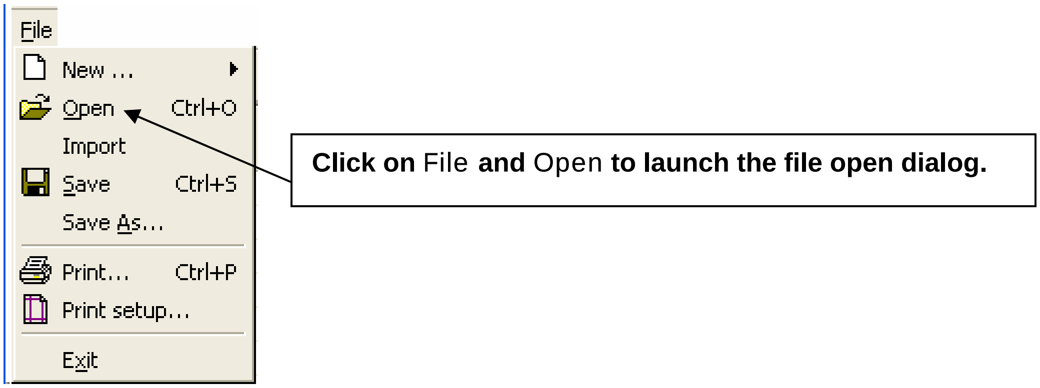
Save the data set

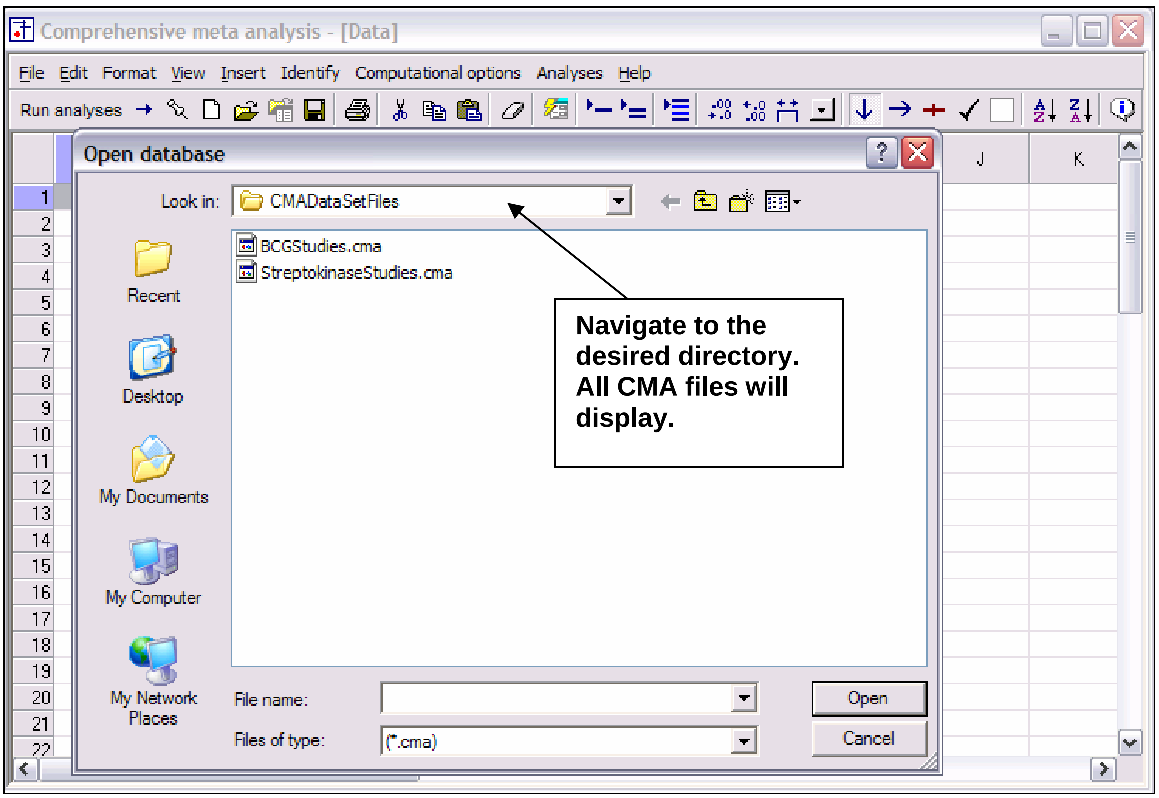


In order to save your data for future use, click on the file save icon to launch the save dialog. Here you can enter a file name for the data set.

The file type is '.cma'.

Open and load the saved data set





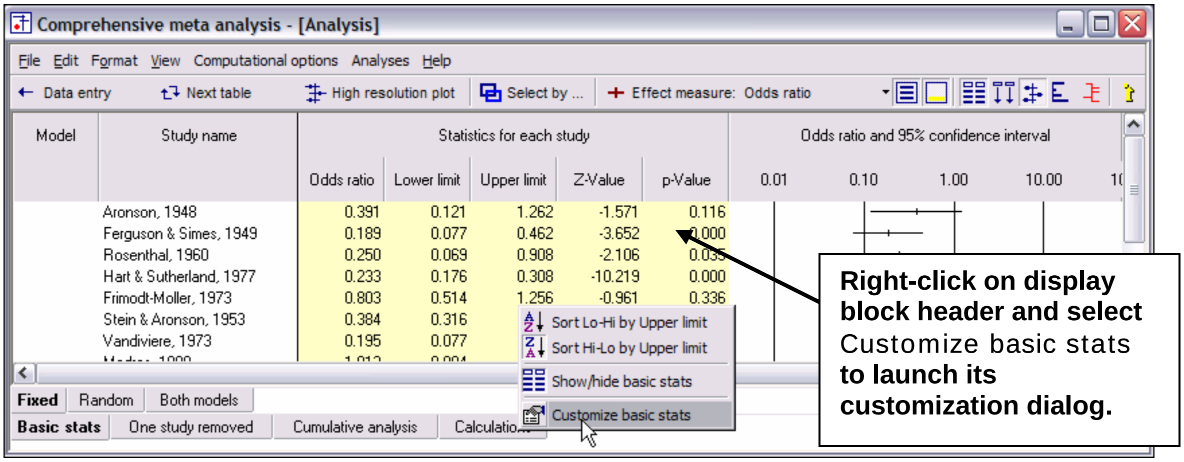
Use this file open dialog to locate, select and download previously saved data sets.

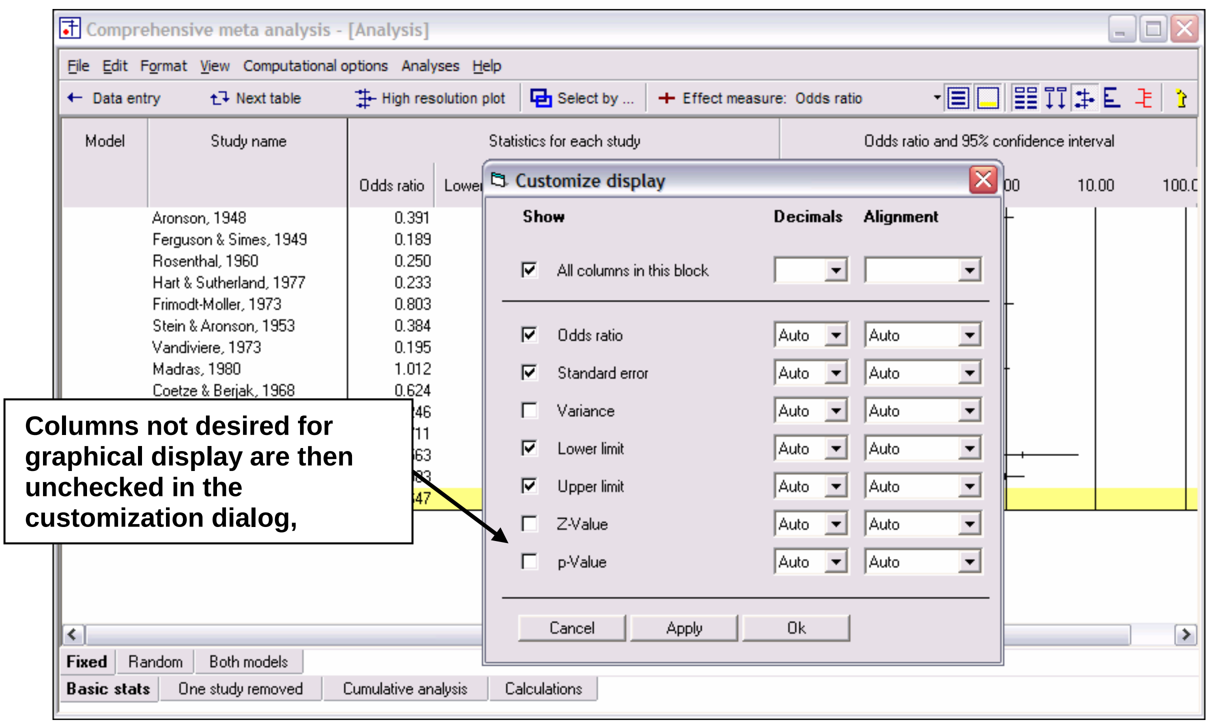
Section 8. Publication-quality graphics

The program enables you to create and easily format publication-quality graphics. The Graphics module will allow you to print the graphics, export them to common presentation formats, such as Word or PowerPoint, or save them in formats such as “PDF” or “WMF”.

Please note that, in this release, only the exports to Word and PowerPoint and the save as “WMF file” are operational.

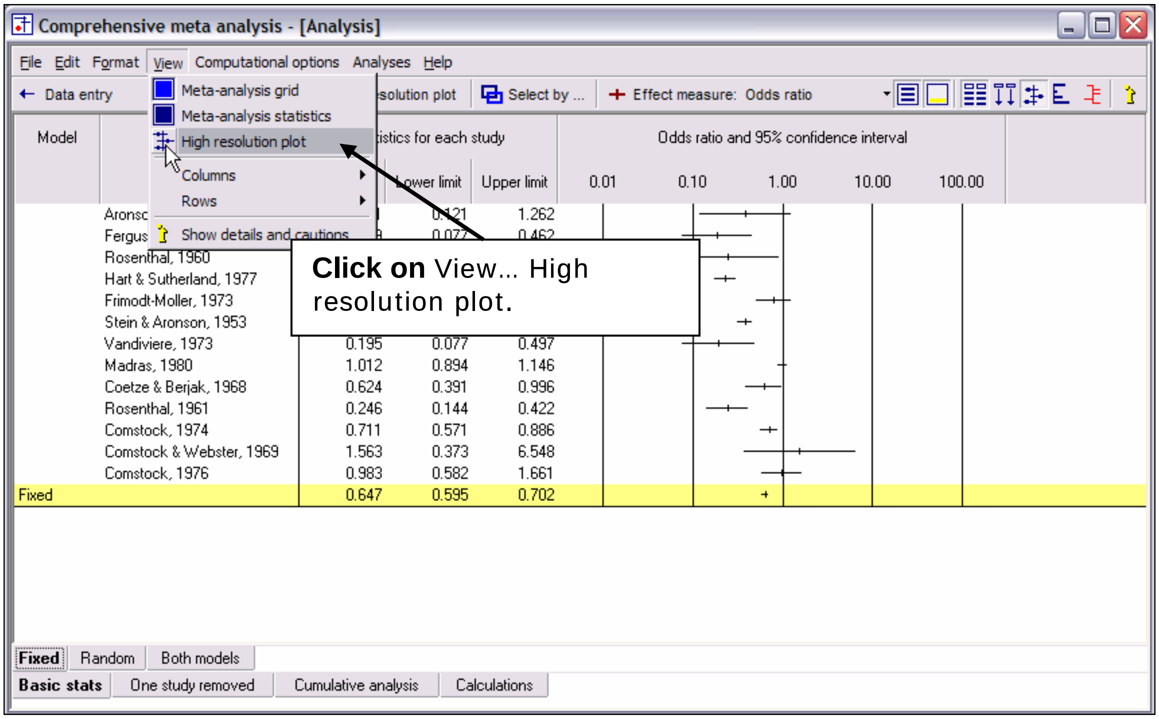
Modify analysis display



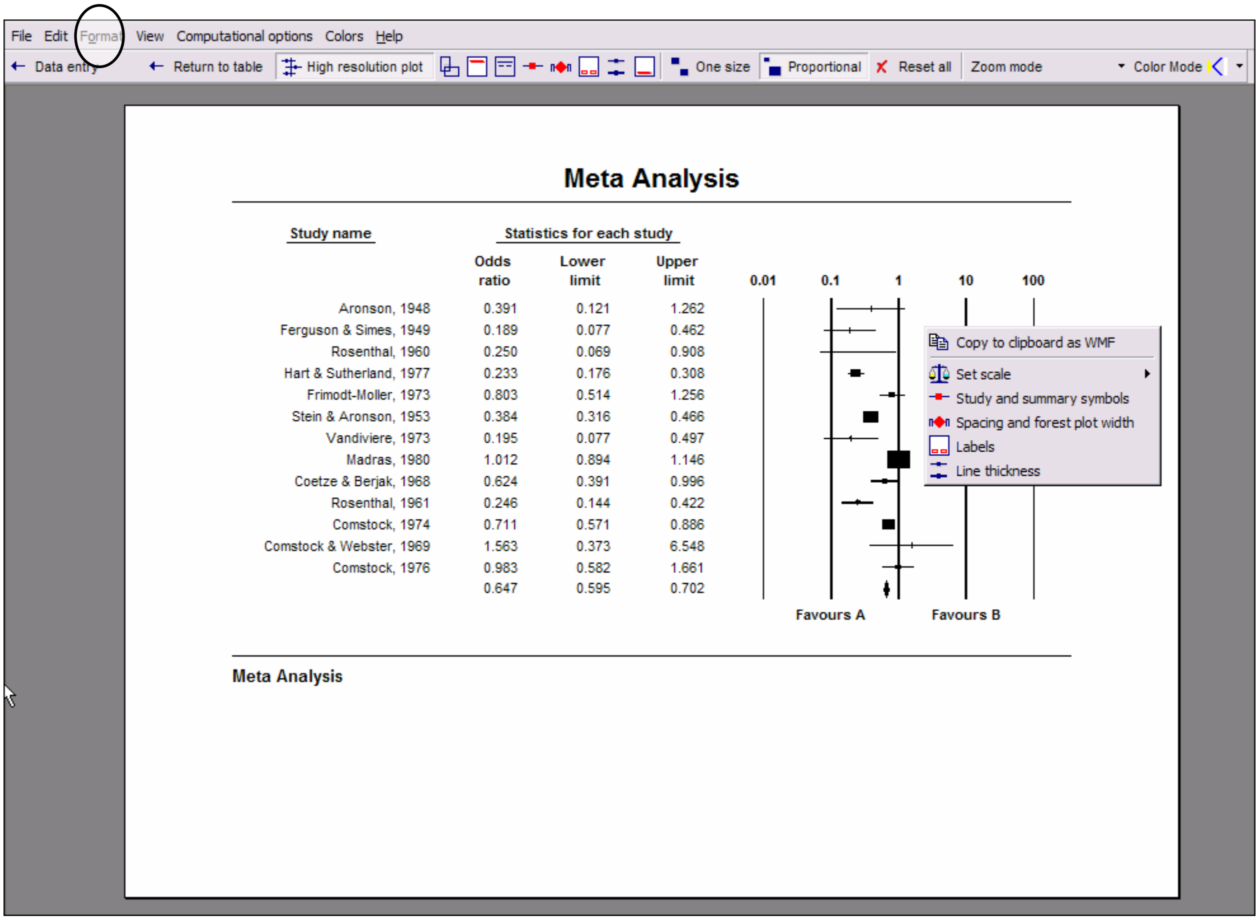


Modify the analysis display for graphics presentation.

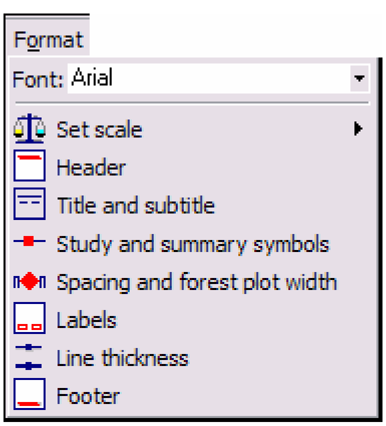
Launch graphics module



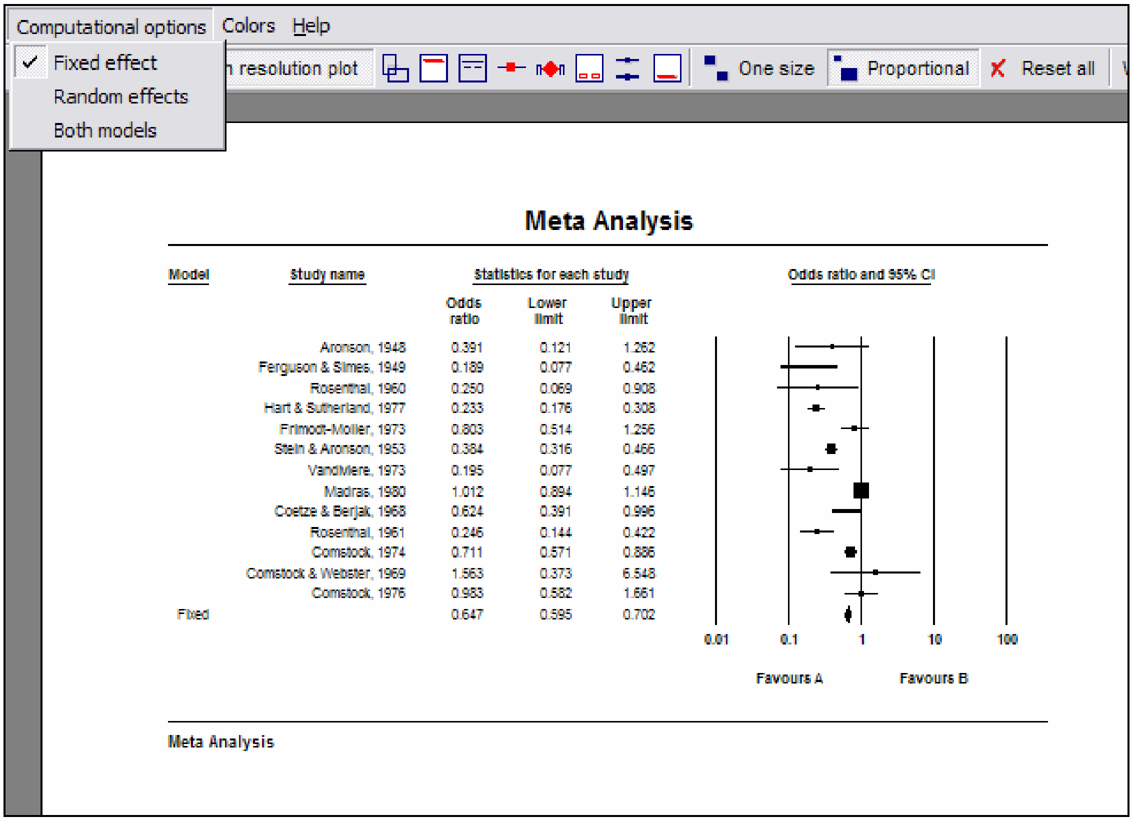
Format graphics display



The graphic first displays in a default mode. Right-clicking on any segment of the display will drop down a list of context-sensitive formatting options. Clicking on the **Format** icon circled on the toolbar will drop down the list below, displaying a more comprehensive set of adjustment options.

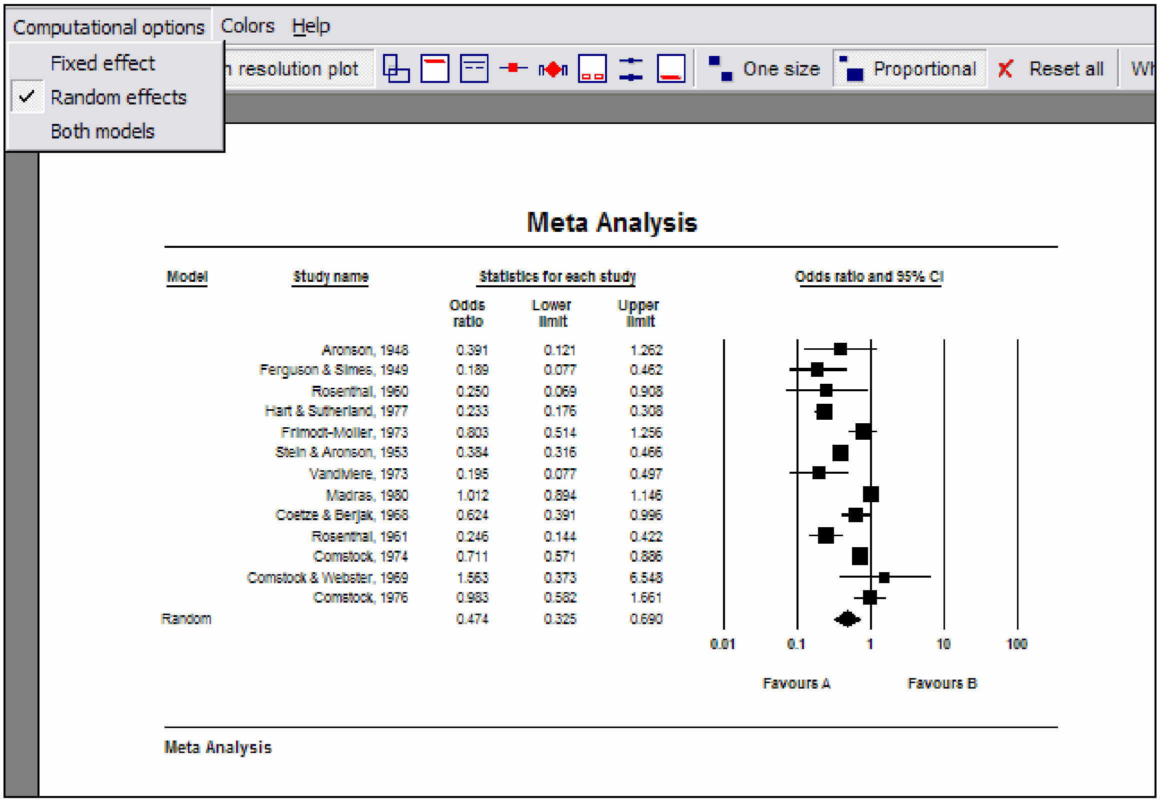


Change computational model



Click on the **Computational options** button to vary the model used for determining summary results (**Fixed effect, Random effects** or **Both models**).

In the Forest plot the studies are represented by symbols whose area is proportional to the study's weight in the analysis.

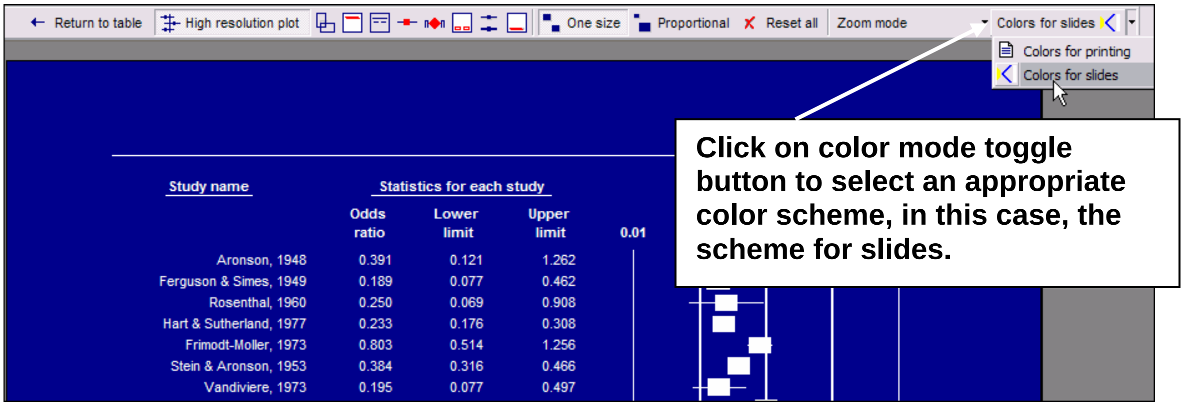


The weights assigned under the random effects model above are more balanced than those under the fixed effects model shown on the previous page. Under random effects, the smaller studies get more weight and the larger studies get less weight.

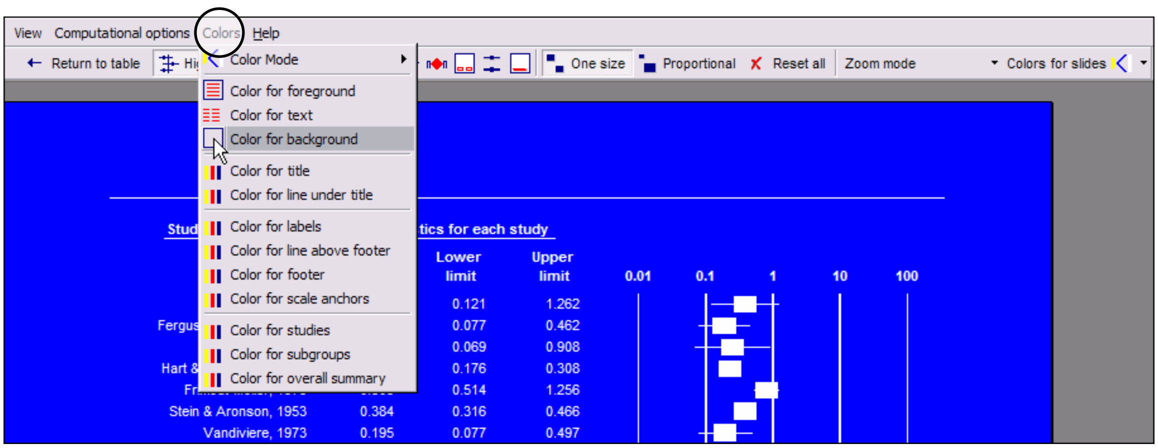
When the **Both models** option is selected, the weight symbols for each study will be identical in size.

Please note that the summary results for a particular model will only display if that model has first been selected in the Analysis module. In this case, the **Both models** tab was selected in the Analysis module before entering the Graphics module, enabling the display here of both fixed and random models.

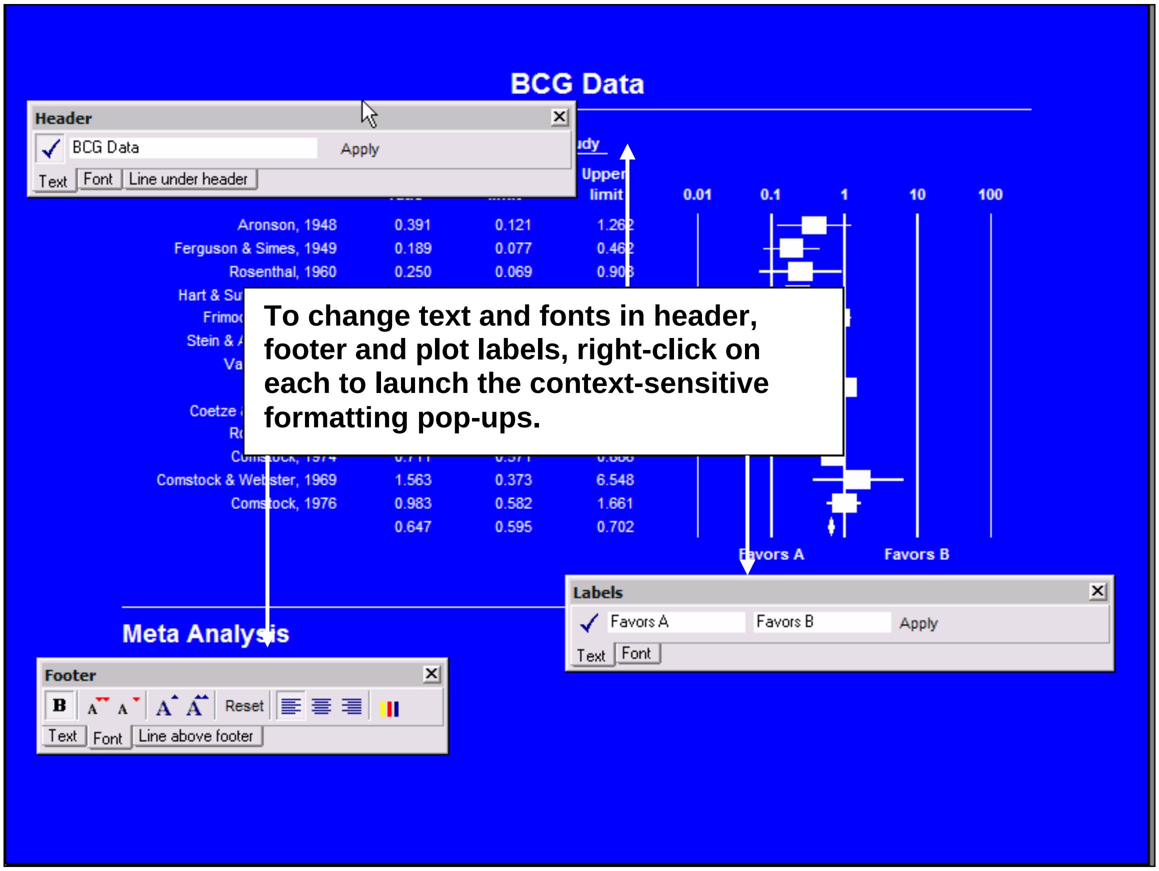
Select color scheme for presentation format



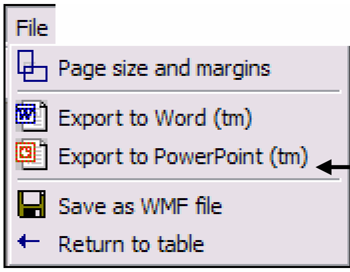
The color scheme can be further modified by clicking on the **Colors for slides** option. Clicking on the **Colors** button, circled below, will drop down a list which offers more extensive color editing options. In the image below, the background color has been changed via the **Color for background** list option.



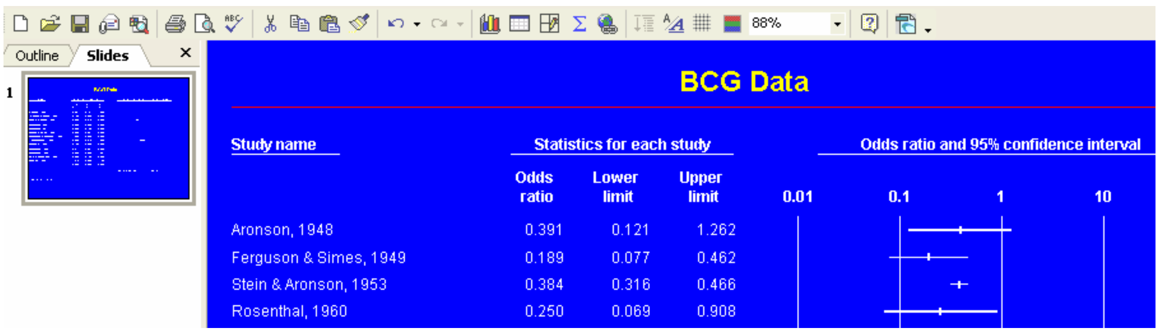
Format text


BCG Data
Header
BCG Data
Apply
Text
Font
Line under header
Upper limit
0.01
0.1
1
10
100
Aronson, 1948
0.391
0.121
Ferguson & Simes, 1949
0.189
0.077
Rosenthal, 1960
0.250
0.069
To change text and fonts in header, footer and plot labels, right-click on each to launch the context-sensitive formatting pop-ups.
Comstock & Webster, 1969
1.563
0.373
6.548
Comstock, 1976
0.983
0.582
1.661
0.647
0.595
0.702
Favors B
Labels
Favors A
Favors B
Apply
Text
Font
Meta Analysis
Footer
B
Reset
Text
Font
Line above footer

Export to file



Click on File **to select an option for printing, copying, exporting or saving the graphic display.**



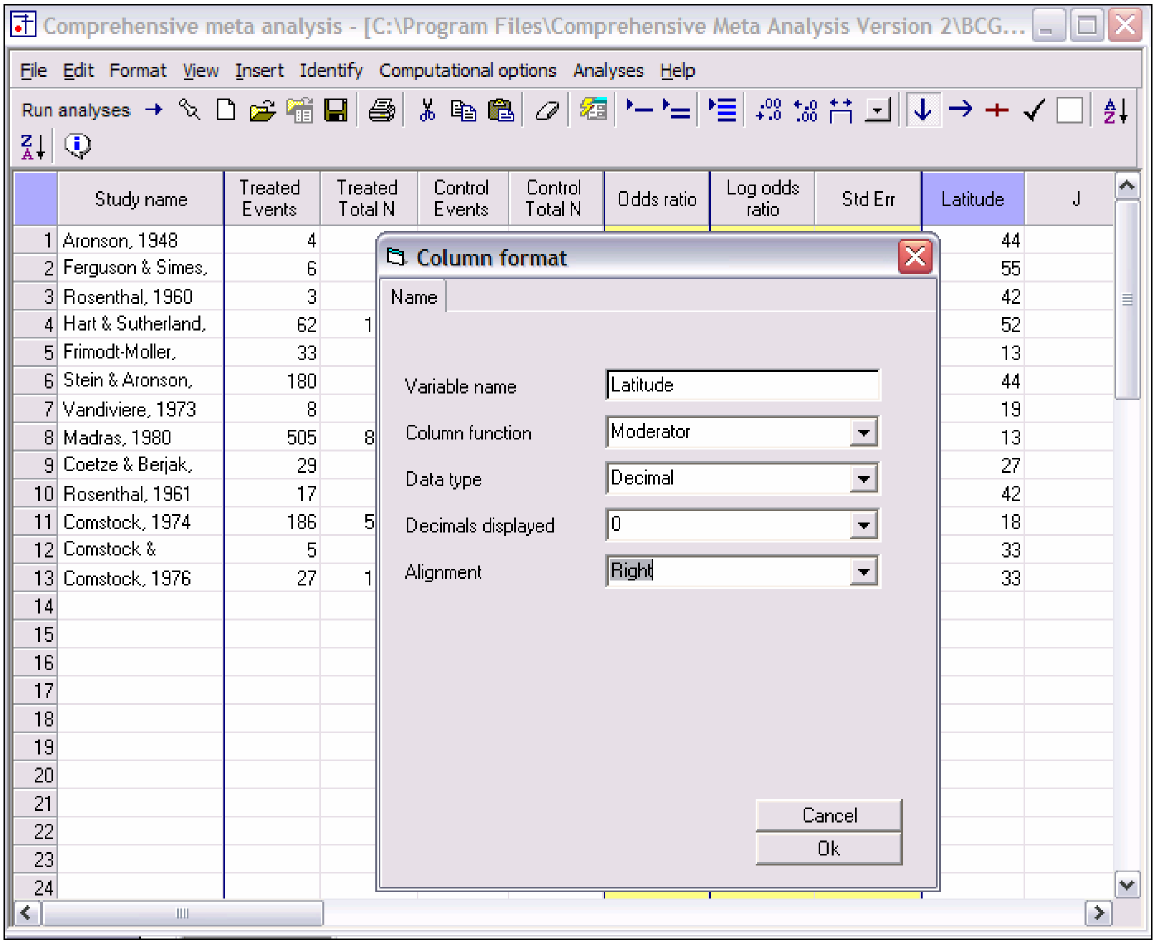
In this case, the graphics image has been exported to PowerPoint which opens automatically and displays the converted graphic.

Section 9. Meta regression

This module allows you to run a regression analysis to estimate the impact of continuous study moderators on overall heterogeneity.

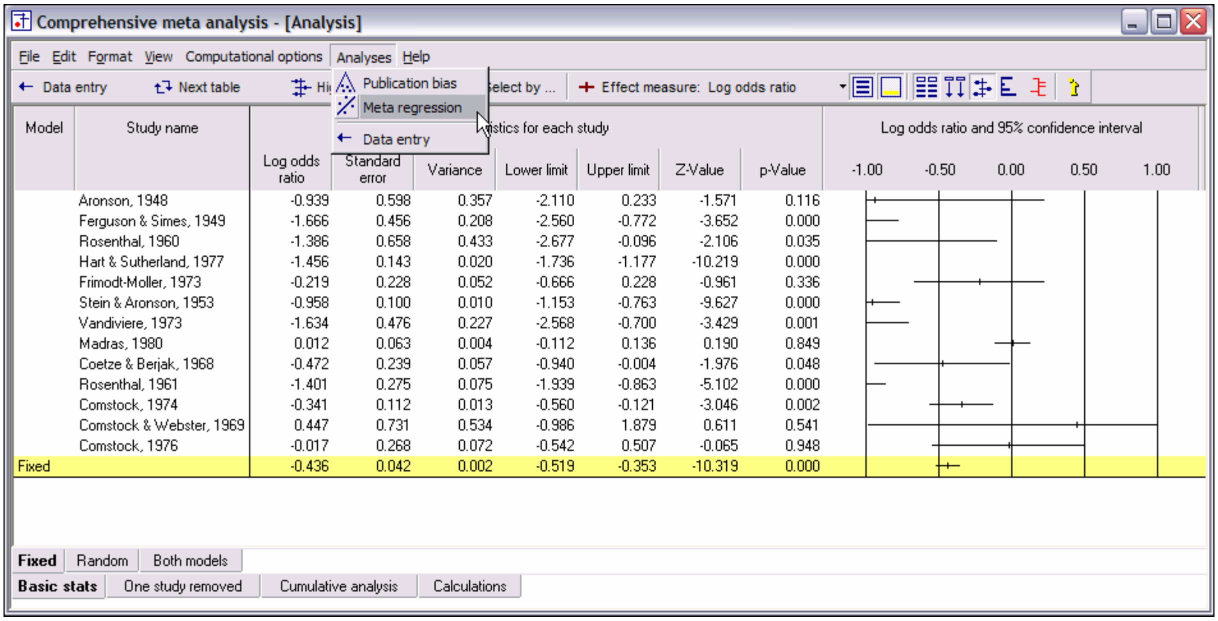
By default, data sets are copied to
C:\Program Files\Comprehensive Meta Analysis Version 2\Demo Files.
The dataset used in this section is BCGLatitude.

Define a moderator



In order to perform a meta-regression you must first create a continuous moderator and define it as decimal or numeric. In this example, using the BCGLatitude data set, the impact of a study location's latitude will be examined.

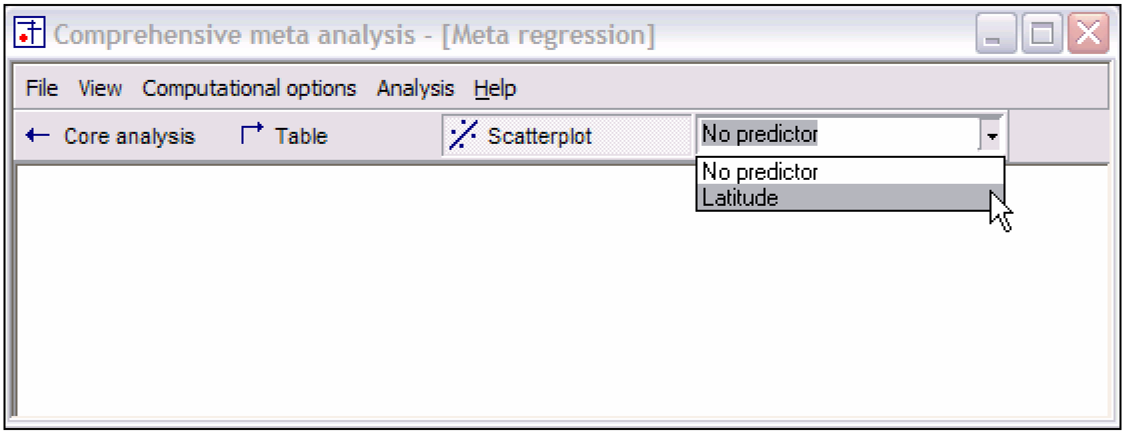
Launch the Meta regression module



Model	Study name	Log odds ratio	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Aronson, 1948	-0.939	0.598	0.357	-2.110	0.233	-1.571	0.116
	Ferguson & Simes, 1949	-1.666	0.456	0.208	-2.560	-0.772	-3.652	0.000
	Rosenthal, 1960	-1.386	0.658	0.433	-2.677	-0.096	-2.106	0.035
	Hart & Sutherland, 1977	-1.456	0.143	0.020	-1.736	-1.177	-10.219	0.000
	Frimodt-Moller, 1973	-0.219	0.228	0.052	-0.666	0.228	-0.961	0.336
	Stein & Aronson, 1953	-0.958	0.100	0.010	-1.153	-0.763	-9.627	0.000
	Vandiviere, 1973	-1.634	0.476	0.227	-2.568	-0.700	-3.429	0.001
	Madras, 1980	0.012	0.063	0.004	-0.112	0.136	0.190	0.849
	Coetze & Berjak, 1968	-0.472	0.239	0.057	-0.940	-0.004	-1.976	0.048
	Rosenthal, 1961	-1.401	0.275	0.075	-1.939	-0.863	-5.102	0.000
	Comstock, 1974	-0.341	0.112	0.013	-0.560	-0.121	-3.046	0.002
	Comstock & Webster, 1969	0.447	0.731	0.534	-0.986	1.879	0.611	0.541
	Comstock, 1976	-0.017	0.268	0.072	-0.542	0.507	-0.065	0.948
Fixed		-0.436	0.042	0.002	-0.519	-0.353	-10.319	0.000

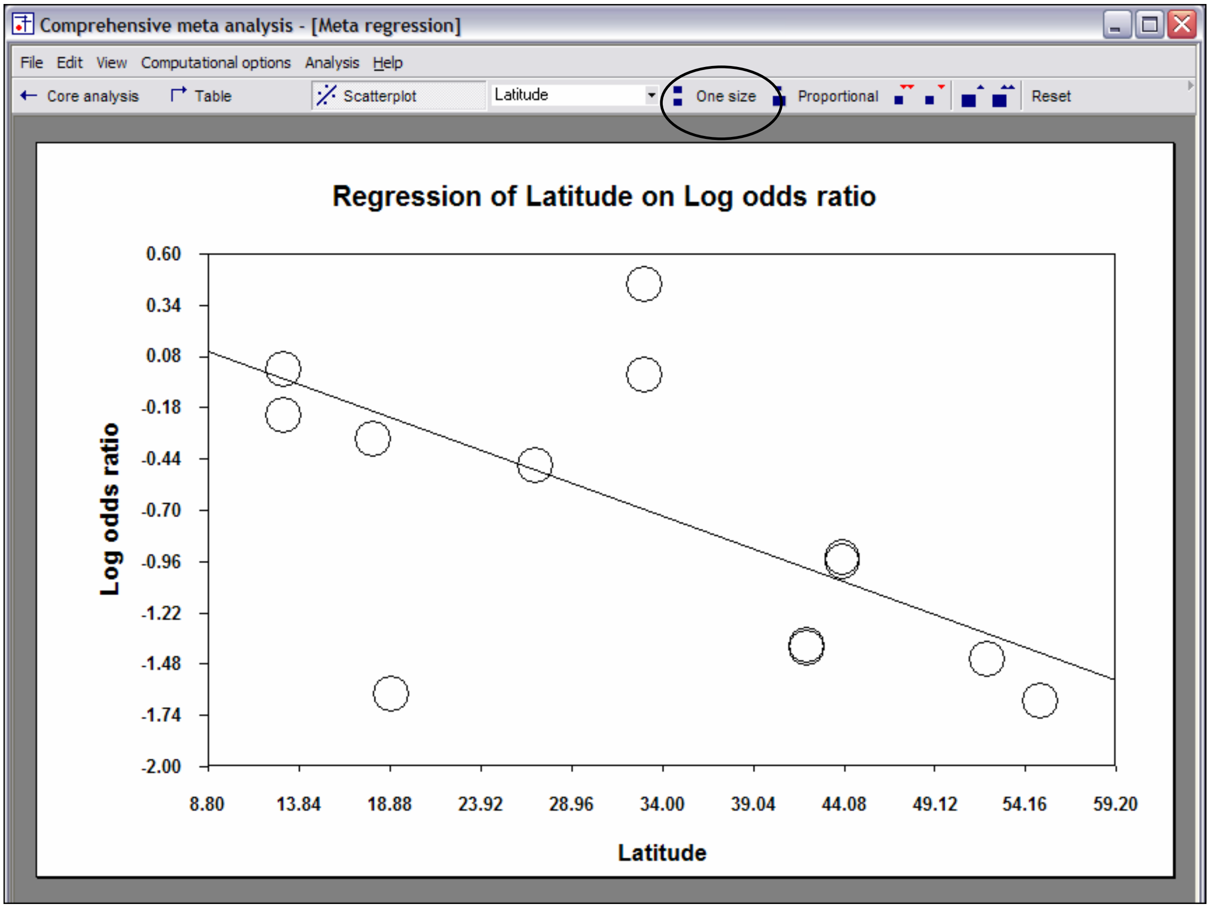
Select **Meta regression** from the **Windows** option dropdown. The effect size index used in the Analysis module (log odds ratio here) will also be used in the regression analysis.

Select the moderator



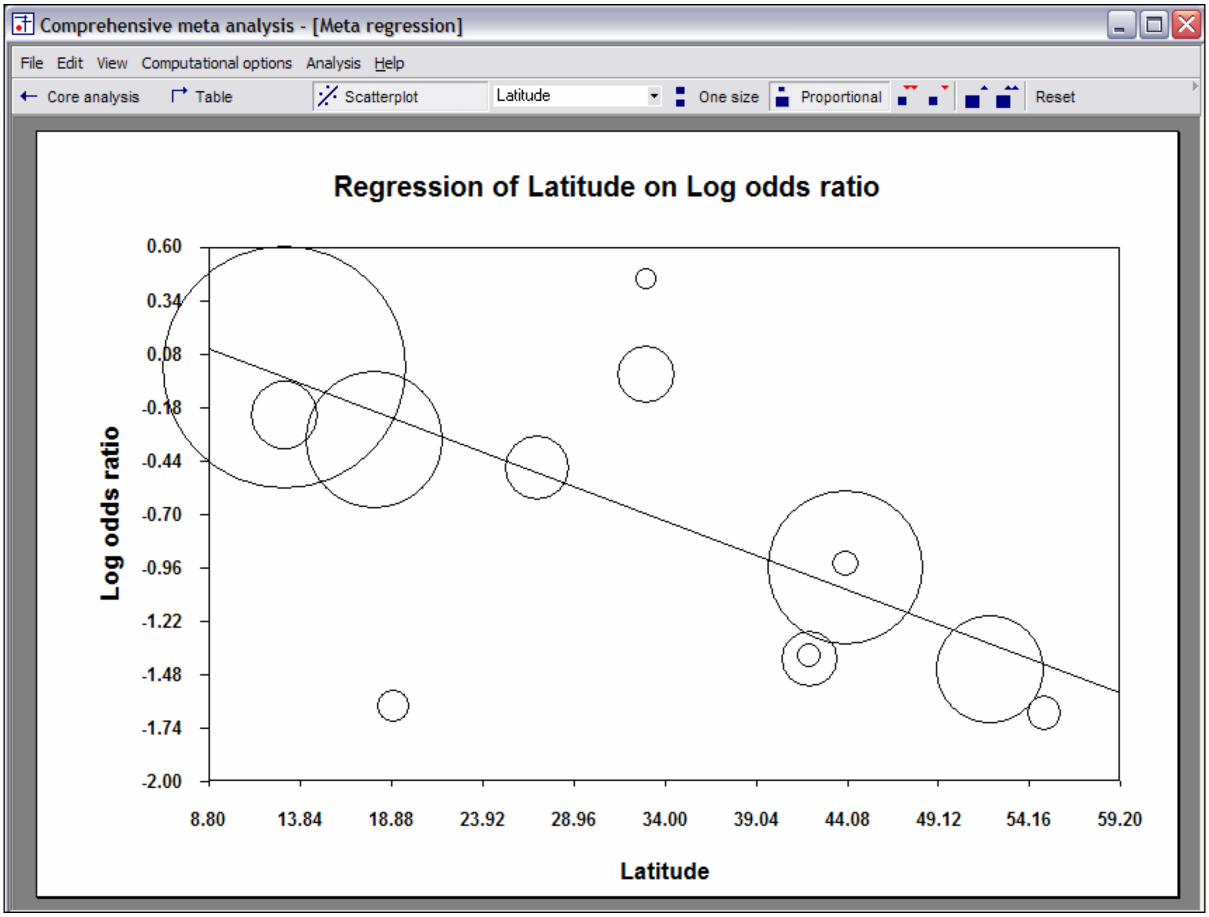
Select the moderator to be used as the covariate in the regression analysis. The dropdown list will contain all available numeric moderators.

View the regression scatter plot



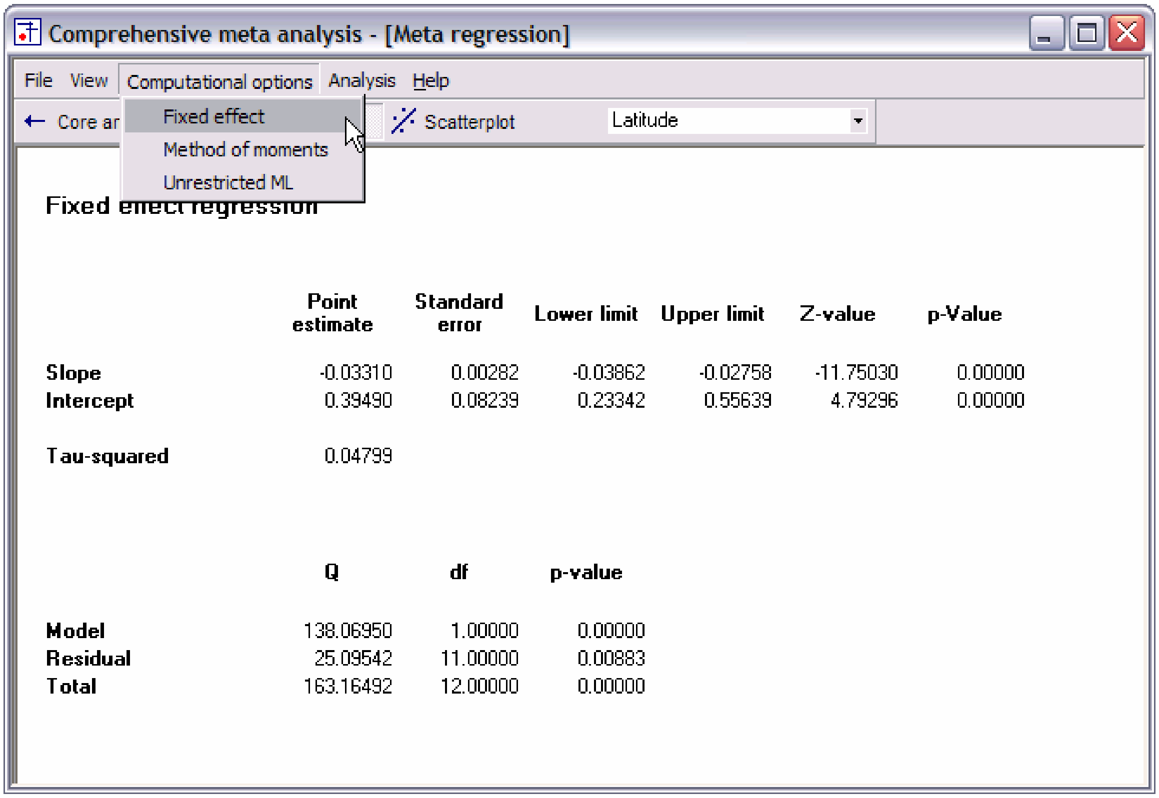
After selection of the moderator, the program displays the regression line and scatter plot of studies. In the default presentation, all studies are represented by circles of identical size, regardless of their individual weighting in the analysis. (Note the circled **One size** option.)

Adjust scatter plot display



Click on the **Proportional** option to view the same graph, but this time with each study represented by a circle proportional to its weight in the analysis. This view identifies which studies have the greatest impact on the slope of the regression line.

Select the regression model

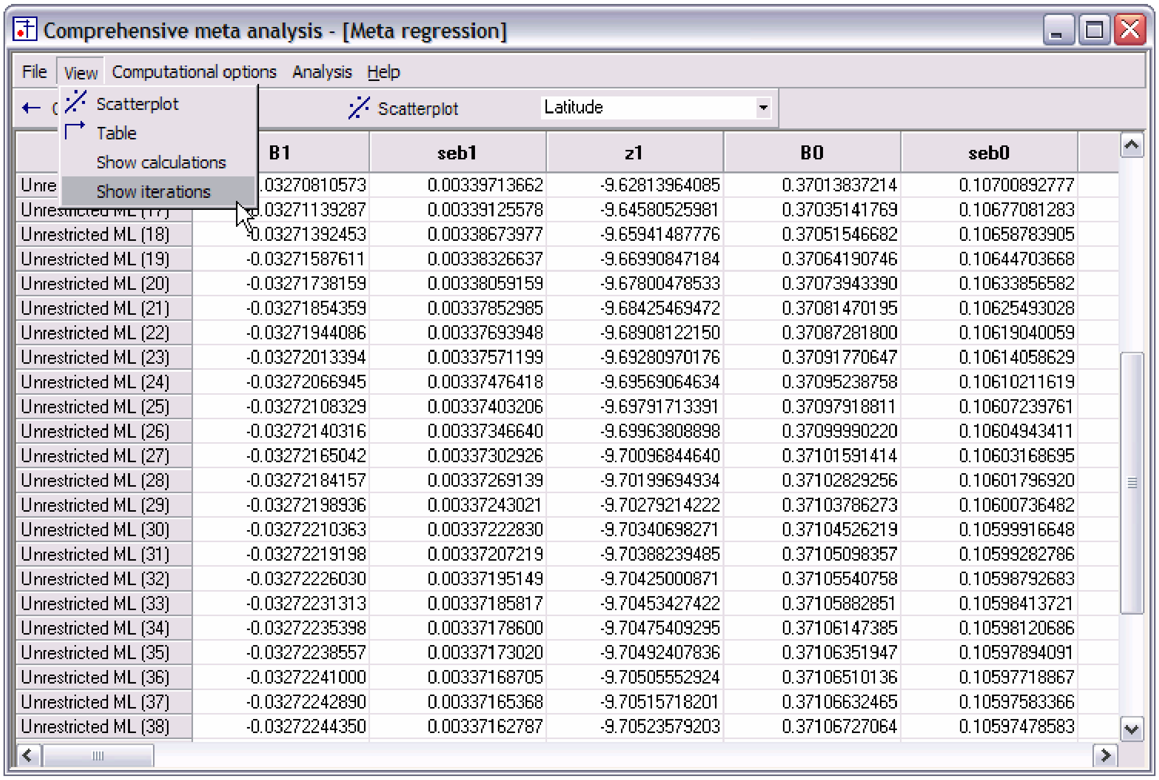


	Point estimate	Standard error	Lower limit	Upper limit	Z-value	p-Value
Slope	-0.03310	0.00282	-0.03862	-0.02758	-11.75030	0.00000
Intercept	0.39490	0.08239	0.23342	0.55639	4.79296	0.00000
Tau-squared	0.04799					

	Q	df	p-value
Model	138.06950	1.00000	0.00000
Residual	25.09542	11.00000	0.00883
Total	163.16492	12.00000	0.00000

Click on the **Computational options** button and select from among the three available models, **Fixed effect, Method of moments, Unrestricted ML** (maximum likelihood). Each of the displays in this module reflects the model chosen. Basic meta regression results are given in the display above, which is invoked by clicking on the **Table** toggle button.

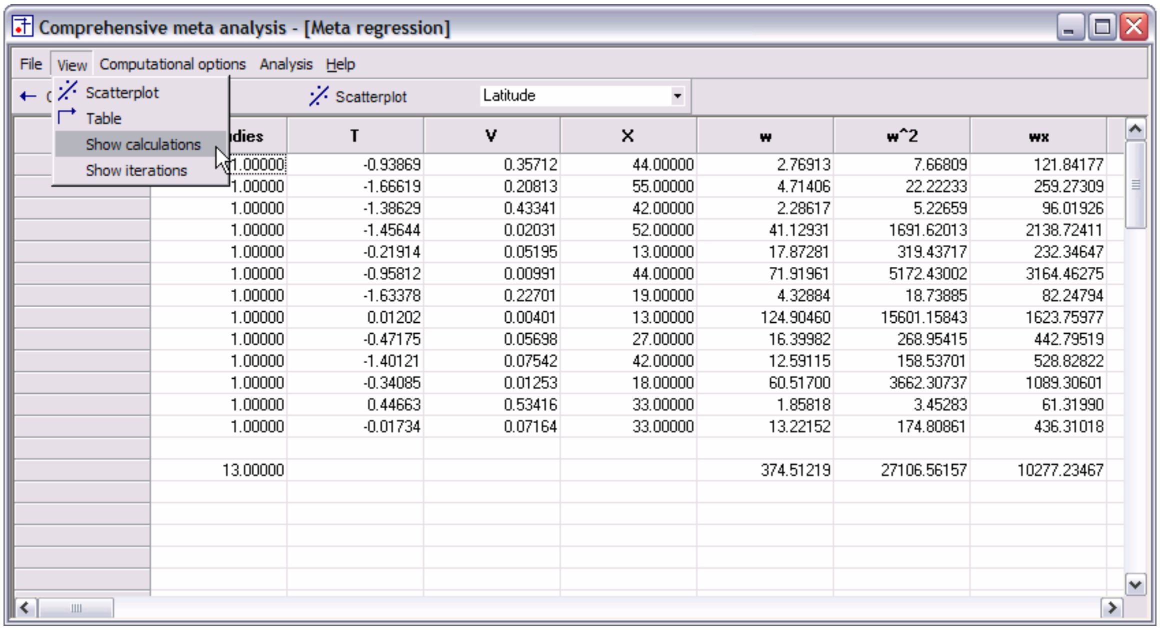
View iterations



	B1	seb1	z1	B0	seb0
Unre	.03270810573	0.00339713662	-9.62813964085	0.37013837214	0.10700892777
Unrestricted ML (17)	.03271139287	0.00339125578	-9.64580525981	0.37035141769	0.10677081283
Unrestricted ML (18)	0.03271392453	0.00338673977	-9.65941487776	0.37051546682	0.10658783905
Unrestricted ML (19)	-0.03271587611	0.00338326637	-9.66990847184	0.37064190746	0.10644703668
Unrestricted ML (20)	-0.03271738159	0.00338059159	-9.67800478533	0.37073943390	0.10633856582
Unrestricted ML (21)	-0.03271854359	0.00337852985	-9.68425469472	0.37081470195	0.10625493028
Unrestricted ML (22)	-0.03271944086	0.00337693948	-9.68908122150	0.37087281800	0.10619040059
Unrestricted ML (23)	-0.03272013394	0.00337571199	-9.69280970176	0.37091770647	0.10614058629
Unrestricted ML (24)	-0.03272066945	0.00337476418	-9.69569064634	0.37095238758	0.10610211619
Unrestricted ML (25)	-0.03272108329	0.00337403206	-9.69791713391	0.37097918811	0.10607239761
Unrestricted ML (26)	-0.03272140316	0.00337346640	-9.69963808898	0.37099990220	0.10604943411
Unrestricted ML (27)	-0.03272165042	0.00337302926	-9.70096844640	0.37101591414	0.10603168695
Unrestricted ML (28)	-0.03272184157	0.00337269139	-9.70199694934	0.37102829256	0.10601796920
Unrestricted ML (29)	-0.03272198936	0.00337243021	-9.70279214222	0.37103786273	0.10600736482
Unrestricted ML (30)	-0.03272210363	0.00337222830	-9.70340698271	0.37104526219	0.10599916648
Unrestricted ML (31)	-0.03272219198	0.00337207219	-9.70388239485	0.37105098357	0.10599282786
Unrestricted ML (32)	-0.03272226030	0.00337195149	-9.70425000871	0.37105540758	0.10598792683
Unrestricted ML (33)	-0.03272231313	0.00337185817	-9.70453427422	0.37105882851	0.10598413721
Unrestricted ML (34)	-0.03272235398	0.00337178600	-9.70475409295	0.37106147385	0.10598120686
Unrestricted ML (35)	-0.03272238557	0.00337173020	-9.70492407836	0.37106351947	0.10597894091
Unrestricted ML (36)	-0.03272241000	0.00337168705	-9.70505552924	0.37106510136	0.10597718867
Unrestricted ML (37)	-0.03272242890	0.00337165368	-9.70515718201	0.37106632465	0.10597583366
Unrestricted ML (38)	-0.03272244350	0.00337162787	-9.70523579203	0.37106727064	0.10597478583

Click on **View… Show Iterations** to display the iterations needed by the unrestricted maximum likelihood algorithm to bring successive 'Tau-squared' variance values into virtual convergence, at which point the final meta-regression values have been attained. As the above display makes clear, the model required 38 iterations in this case to arrive at final results.

View data and residuals



dies	T	V	X	w	w^2	wx
1.00000	-0.93869	0.35712	44.00000	2.76913	7.66809	121.84177
1.00000	-1.66619	0.20813	55.00000	4.71406	22.22233	259.27309
1.00000	-1.38629	0.43341	42.00000	2.28617	5.22659	96.01926
1.00000	-1.45644	0.02031	52.00000	41.12931	1691.62013	2138.72411
1.00000	-0.21914	0.05195	13.00000	17.87281	319.43717	232.34647
1.00000	-0.95812	0.00991	44.00000	71.91961	5172.43002	3164.46275
1.00000	-1.63378	0.22701	19.00000	4.32884	18.73885	82.24794
1.00000	0.01202	0.00401	13.00000	124.90460	15601.15843	1623.75977
1.00000	-0.47175	0.05698	27.00000	16.39982	268.95415	442.79519
1.00000	-1.40121	0.07542	42.00000	12.59115	158.53701	528.82822
1.00000	-0.34085	0.01253	18.00000	60.51700	3662.30737	1089.30601
1.00000	0.44663	0.53416	33.00000	1.85818	3.45283	61.31990
1.00000	-0.01734	0.07164	33.00000	13.22152	174.80861	436.31018
13.00000				374.51219	27106.56157	10277.23467

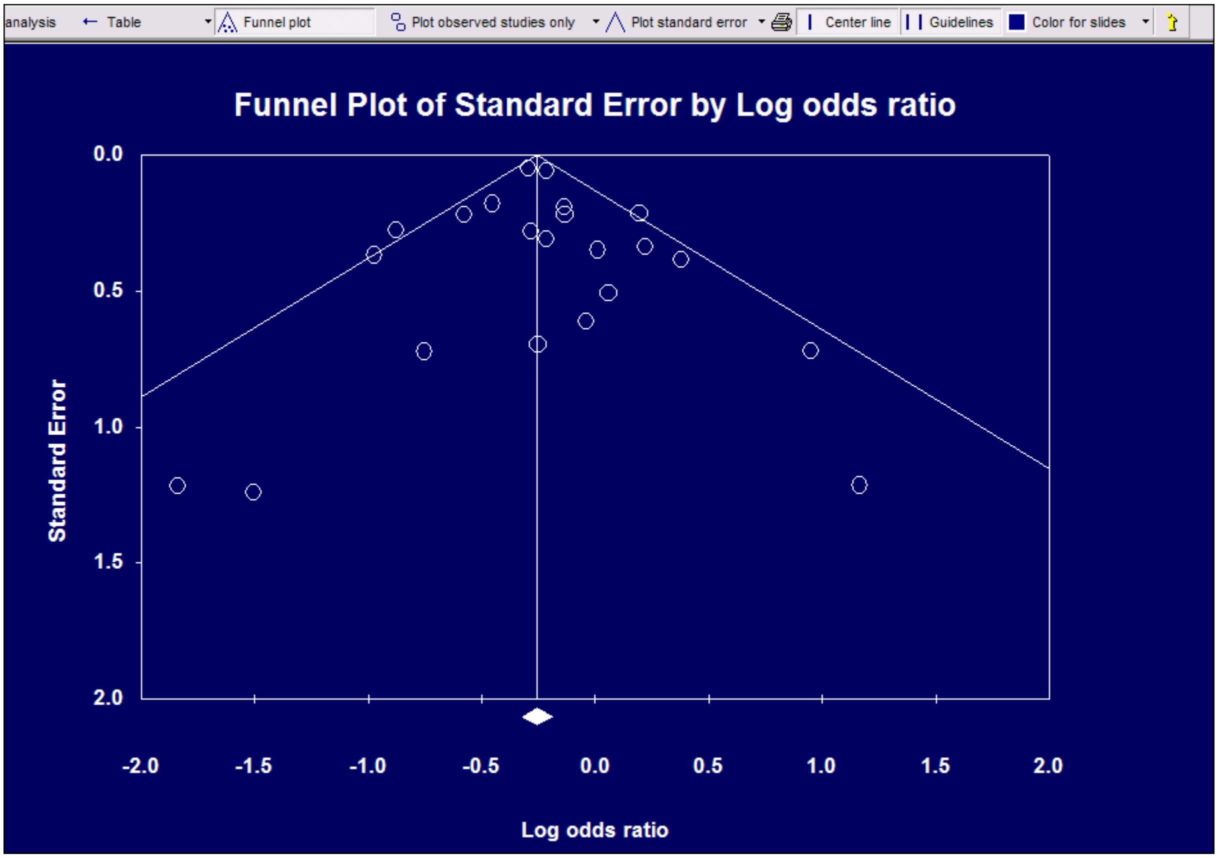
Click on **View… Show Calculations** to display the calculations involved in producing the regression analysis results.

Section 10. Publication Bias

This module offers multiple methods for detecting the presence of publication bias and assessing its impact on the analysis.

By default, data sets are copied to
C:\Program Files\Comprehensive Meta Analysis Version 2\Demo Files.
The dataset used in this section is StreptoModerator.

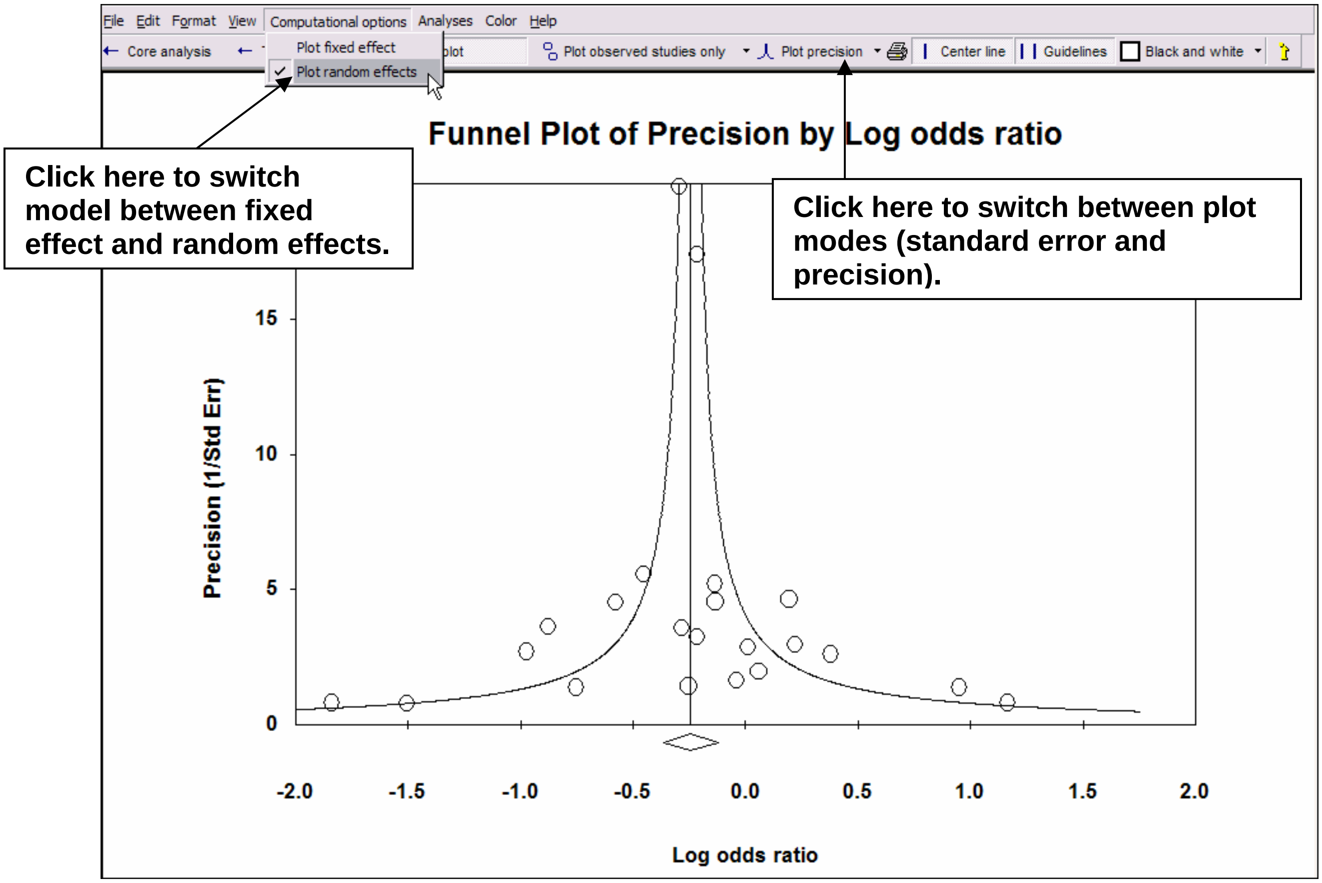
Funnel plot



To launch the Publication Bias module from the Analysis module, click on **Analyses… Publication bias.**

The default display, a funnel plot, has two modes, one which plots a study's effect size against its standard error (above) and another which plots effect size against precision, the inverse of standard error (next page).

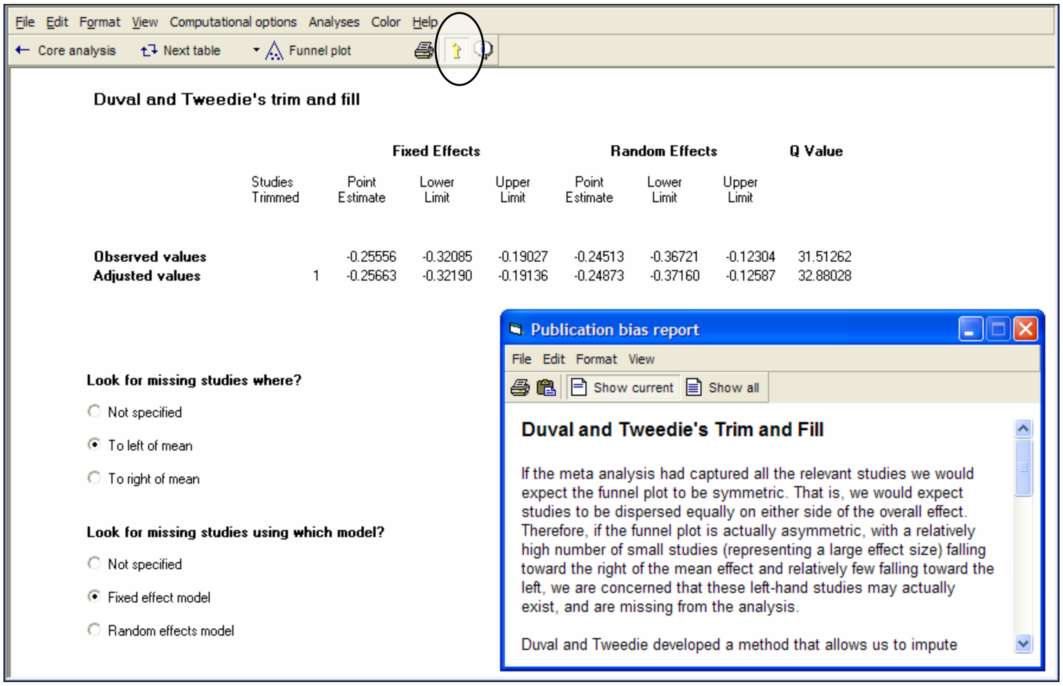
Toolbar icons allow the user to alter the color scheme and other plot attributes.



The plot by precision is the traditional form. Note that large studies appear toward the top of the graph, and tend to cluster near the mean effect size. Smaller studies appear toward the bottom of the graph, and (since there is more random variation in the small studies) are dispersed across a range of values. This pattern tends to resemble a funnel, which is the basis for the plot's name.

In the absence of publication bias the studies will be distributed symmetrically about the combined effect size. By contrast, in the presence of bias, the bottom of the plot would tend to show a higher concentration of studies on one side of the mean than the other. This would reflect the fact that smaller studies (which appear toward the bottom) are more likely to be published if they have larger than average effects, which makes them more likely to meet the criterion for statistical significance.

Duval and Tweedie’s trim and fill



The **View** option drops down a selection of methods for assessing publication bias, including the Trim and Fill procedure, shown here.

Trim and Fill builds on the key idea behind the funnel plot; that in the absence of bias the plot would be symmetric about the summary effect. If there are more small studies on the right than on the left, the concern is that studies may be missing from the left. The Trim and Fill procedure imputes these missing studies, adds them to the analysis, and then re-computes the summary effect size.

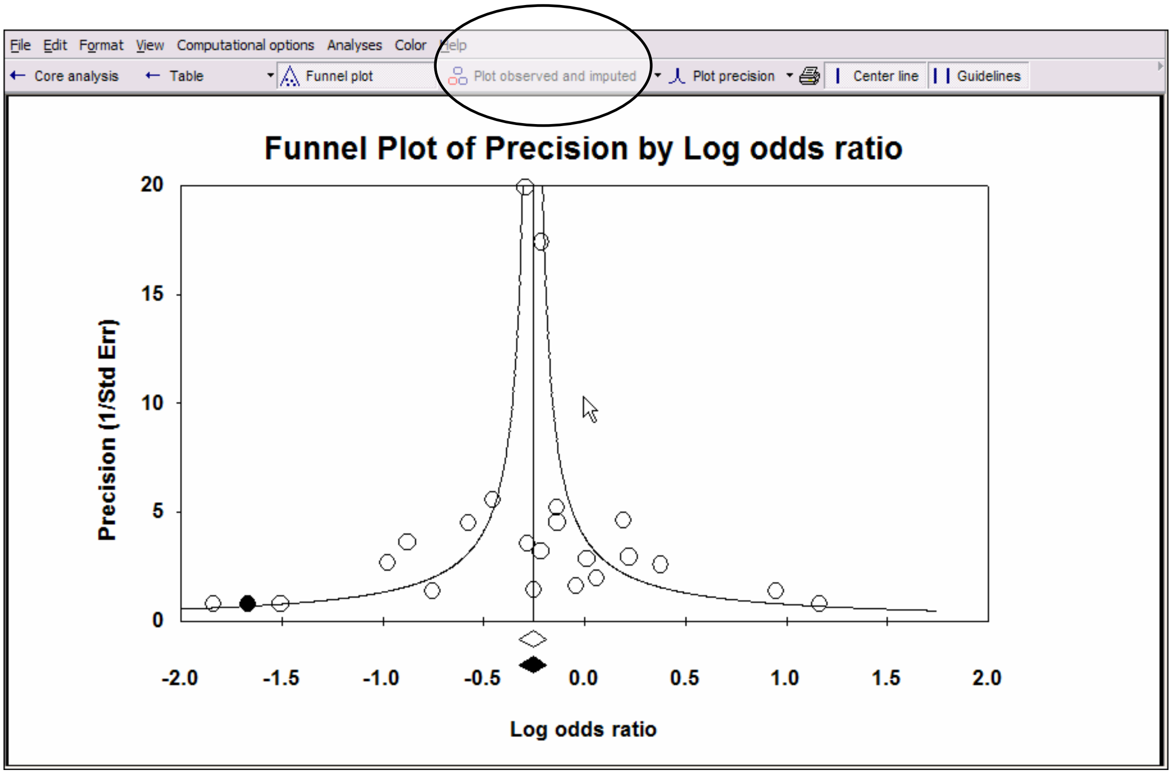
By default, the tool will look for missing studies to the left of the summary effect. The user can reverse the search direction by selecting the appropriate setting.

The report icon (circled above) launches a description of the statistical test and an explanation of the actual results it yields.

In our example there is one imputed missing study. In addition, the report tells us that:

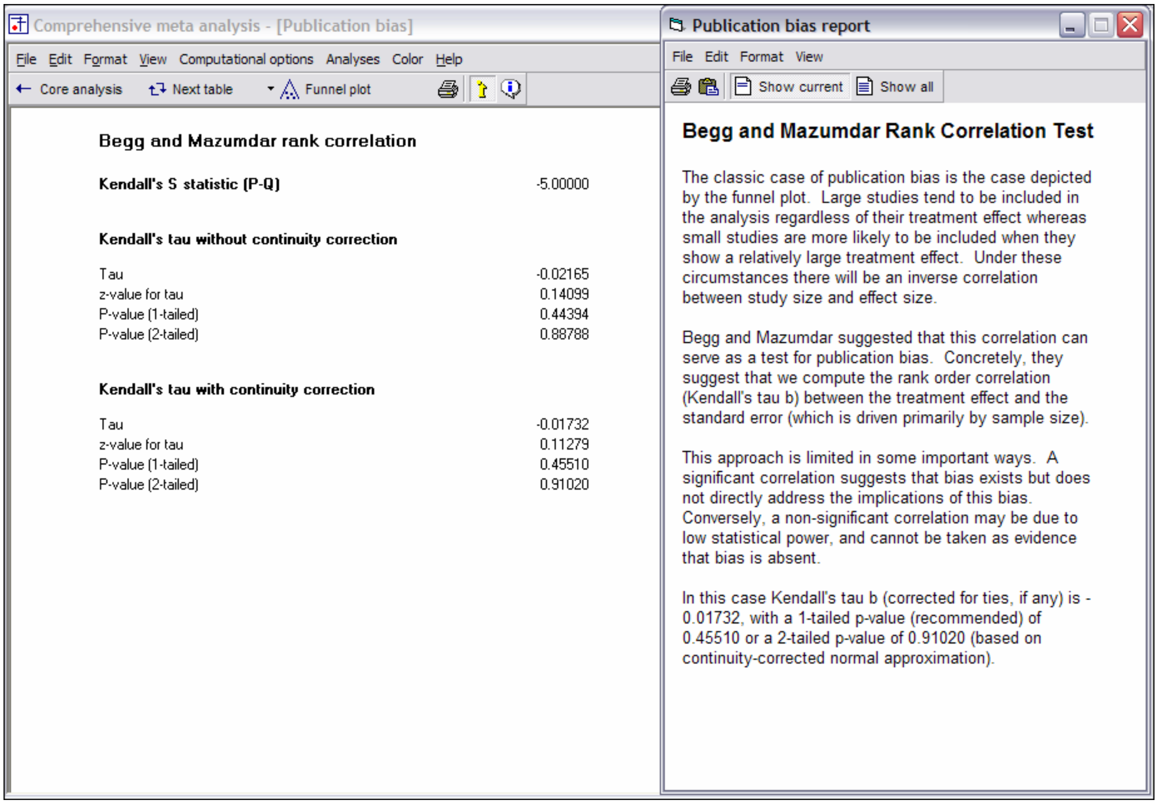
“Under the fixed effect model the point estimate and 95% confidence interval for the combined studies is -0.25556 (-0.32085, -0.19027). Using Trim and Fill the imputed point estimate is -0.25663 (-0.32190, -0.19136).

Under the random effects model the point estimate and 95% confidence interval for the combined studies is -0.24513 (-0.36721, -0.12304). Using Trim and Fill the imputed point estimate is -0.24873 (-0.37160, -0.12587).”



To view Trim and Fill's imputed studies on the funnel plot, click on the toggle icon circled above. In our example the data point for one imputed study is highlighted in black (near bottom left of plot).

Begg and Mazumdar rank correlation



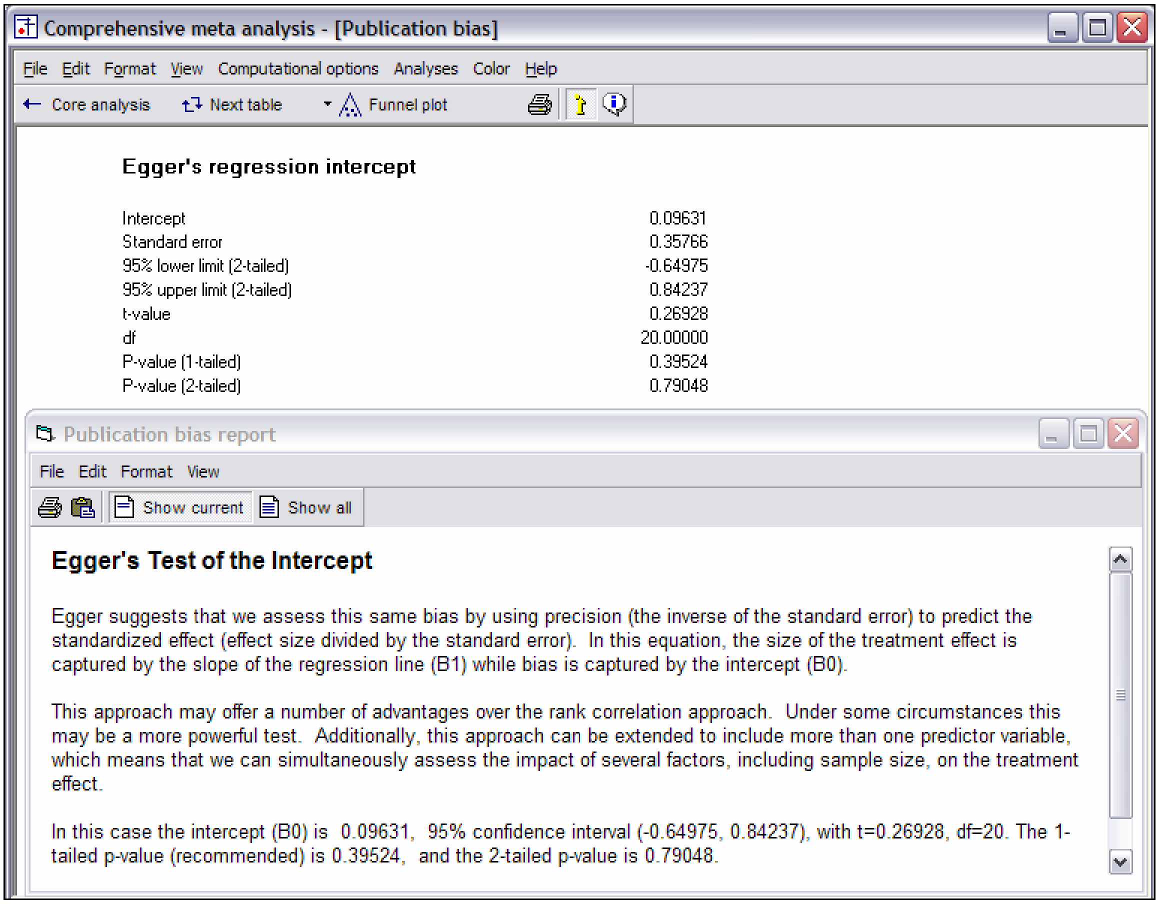
Begg and Mazumdar's rank correlation test reports the rank correlation (Kendall's tau) between the standardized effect size and the variances (or standard errors) of these effects. Tau would be interpreted much the same way as any correlation, with a value of zero indicating no relationship between effect size and precision, and deviations from zero indicating the presence of a relationship.

If asymmetry is caused by publication bias we would expect to see high standard errors (small studies) associated with larger effect sizes. If larger effects are represented by low values, tau would be positive, while if larger effects are represented by high values, tau would be negative. Since asymmetry could appear in the reverse direction, the significance test is two-sided.

In our example Kendall's tau b (corrected for ties, if any) is -0.01732, with a 1-tailed p-value (recommended) of 0.45510 or a 2-tailed p-value of 0.91020.

Note that the **Next table** button allows you to toggle among all the available publication bias tests.

Egger's regression intercept



Egger's linear regression method, like the rank correlation test, quantifies the bias captured by the funnel plot. While Begg and Mazumdar's test uses ranks, Egger's method uses the actual values of the effect sizes and their precision.

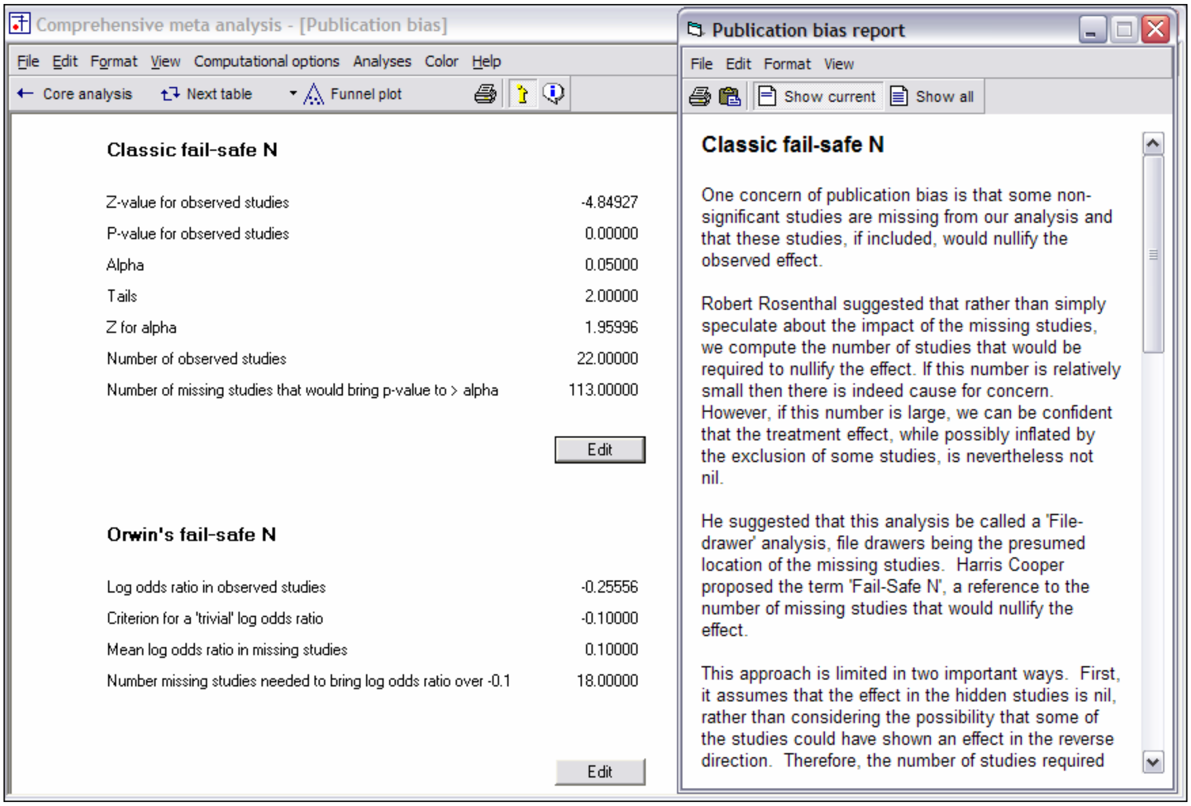
In the Egger test, the standardized effect (effect size divided by standard error) is regressed on precision (inverse of standard error). Small studies generally have a precision close to zero, due to their high standard error. In the absence of bias we would expect to see such studies associated with small standardized effects. We would expect to see large studies associated with large standardized effects. This would create a regression line whose intercept approached the origin.

If the intercept deviates from this expectation, publication bias may be the cause. This would occur, for instance, when small studies are disproportionately associated with larger effect sizes.

As was true for the rank correlation test, the significance test should be two-tailed.

In our example the intercept (B0) is 0.09631, 95% confidence interval (-0.64975, 0.84237), with t=0.26928, df=20. The one-tailed p-value is 0.39524, and the two-tailed p-value is 0.79048.

Fail-safe N



Rosenthal's Fail-safe N test computes the number of missing studies (with mean effect of zero) that would need to be added to the analysis to yield a statistically non-significant overall effect.

The user can edit the **Alpha** and **Tails** parameters

In our example Rosenthal's fail-safe N is 113. This means that we would need to locate and include 113 'null' studies in order for the combined 2-tailed p-value to exceed 0.050. Put another way, there would be need to be 5.1 missing studies for every observed study for the effect to be nullified.

The Orwin variant of this test addresses two problems with Rosenthal's method; that it focuses on statistical rather than clinical significance, and that it assumes a nil overall effect in the missing studies.

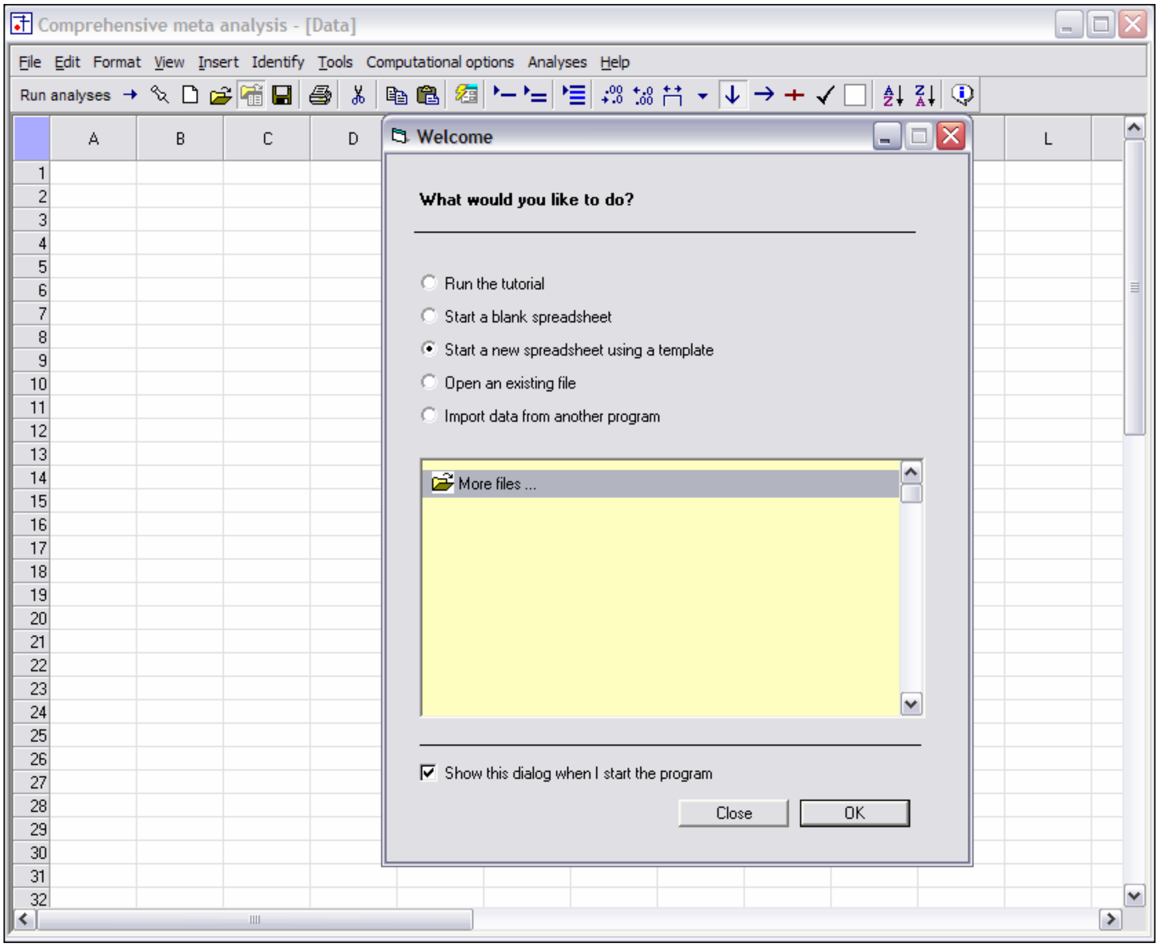
Orwin's test allows you to select both the smallest effect value deemed to be clinically important and a value other than nil for the mean effect in the missing studies. To vary these values, edit the relevant parameters, which in our example are **Criterion for a 'trivial' log odds ratio** and **Mean log odds ratio in missing studies**.

In our example Orwin's fail-safe N is 18. This means that we would need to locate 18 studies with mean log odds ratio of 0.1 to bring the combined log odds ratio over -0.1 (see the Orwin parameter settings in the image).

Section 11. Data Entry Templates

This module describes the basic templates provided to facilitate data entry.

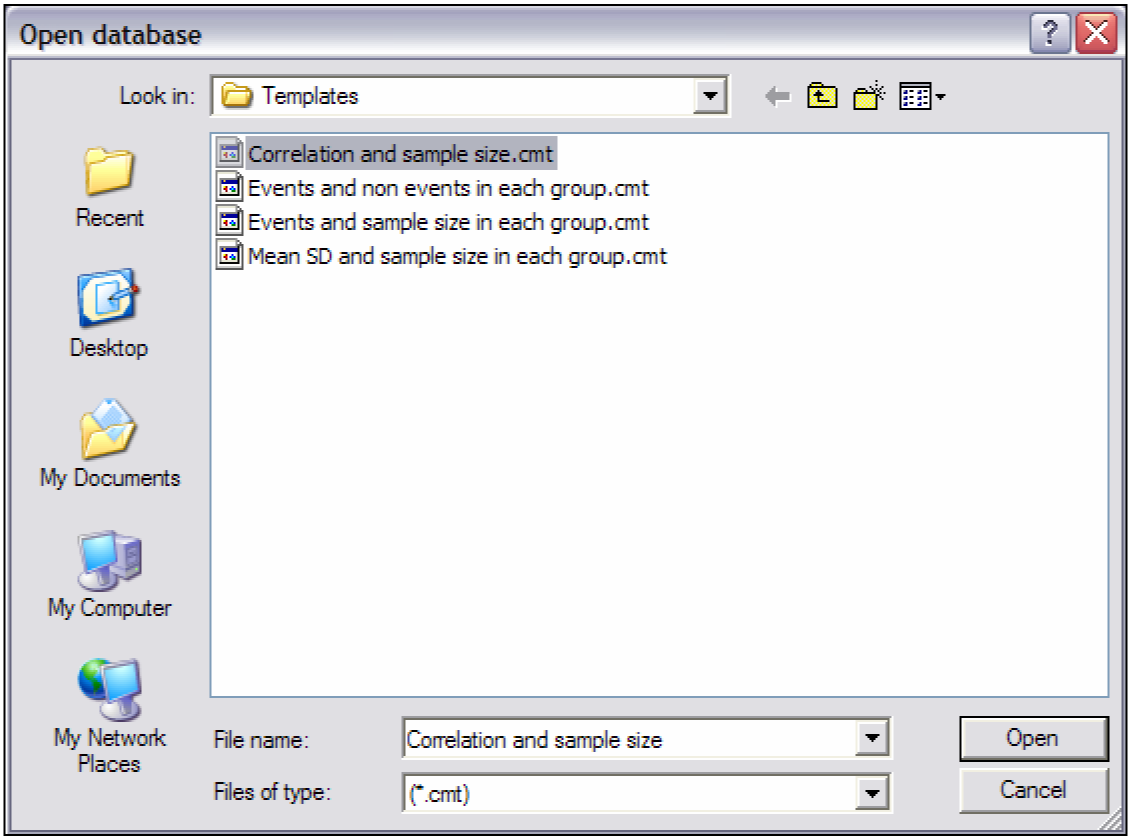
View templates



To expedite data entry, the program provides templates which contain pre-established columns for study names and commonly used entry formats.

To view the templates, click on the option selected above in the **Welcome** dialog.

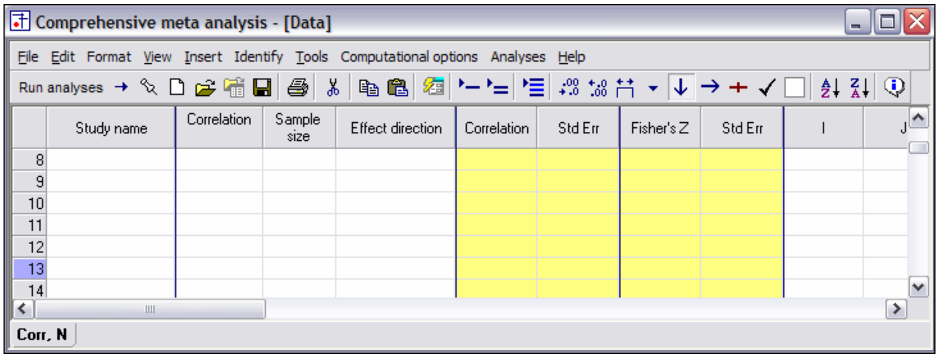
Select a template



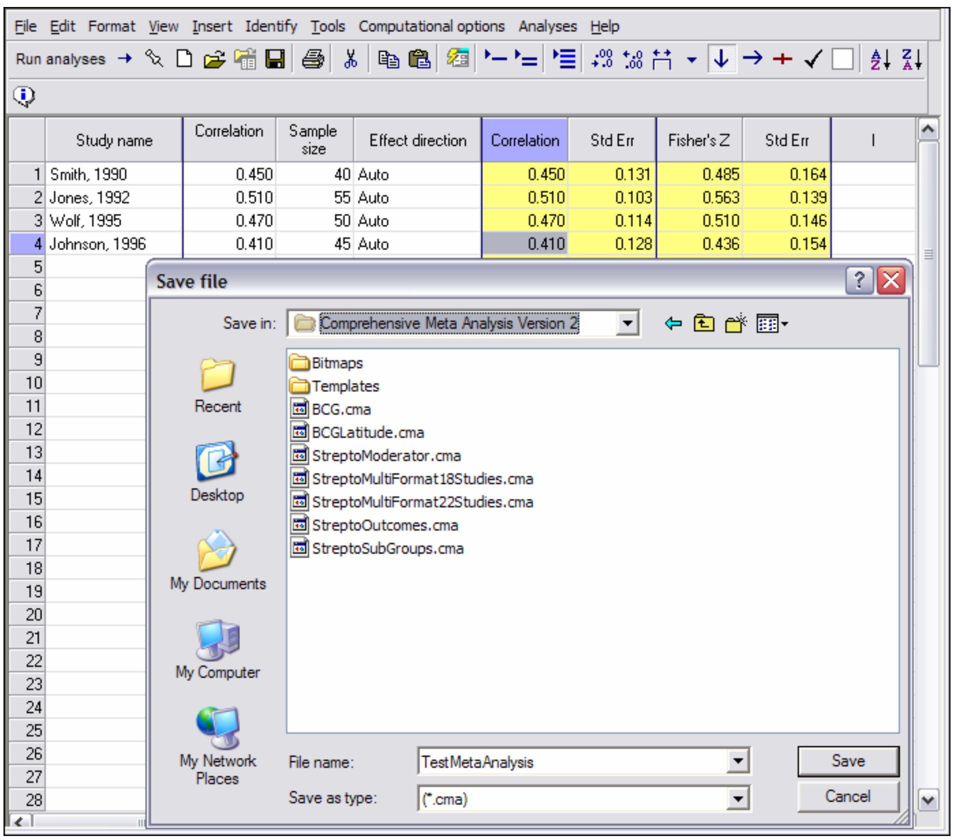
Select the template which fits your data format. Note the file extension of 'cmt', indicating template.

Additional templates will be included in future releases.

Enter data



The data entry module displays the pre-established columns associated with the selected template.



Enter data, modify as desired, and save as a normal data set (with extension 'cma'.) The newly created data set can be re-opened and modified.

The template remains intact and can be re-selected to begin entry of a new data set.