

Example name	Relenza Symptom relief
Effect size	Mean difference (Days to relief)
Analysis type	Basic
Version	Long
Reference	Cochrane Figure 5

Synopsis

We have a series of studies that evaluated the effect of Relenza on duration of flu symptoms. Each study compared Relenza vs. Placebo and reported the mean difference in time to relief. If the Drug yielded a shorter time to relief, the mean difference will be negative.

Since all studies used the same outcome (days to relief) we can use either Raw Mean Difference or Standardized mean difference as the outcome. We do both, to show where they are similar and where they differ.

We show

- How to enter data for means and standard deviation in two independent groups
- How to run a fixed-effect and a random-effects analysis
- How to get a visual sense of the dispersion
- How to see the weight assigned to each study
- How to understand the statistics for the summary effect and the dispersion
- The correspondence between the raw mean difference and the standardized mean difference
- How to create a high-resolution plot

To open a CMA file > [Download and Save file](#) | [Start CMA](#) | [Open file from within CMA](#)

[Download CMA file for computers that use a period to indicate decimals](#)

[Download CMA file for computers that use a comma to indicate decimals](#)

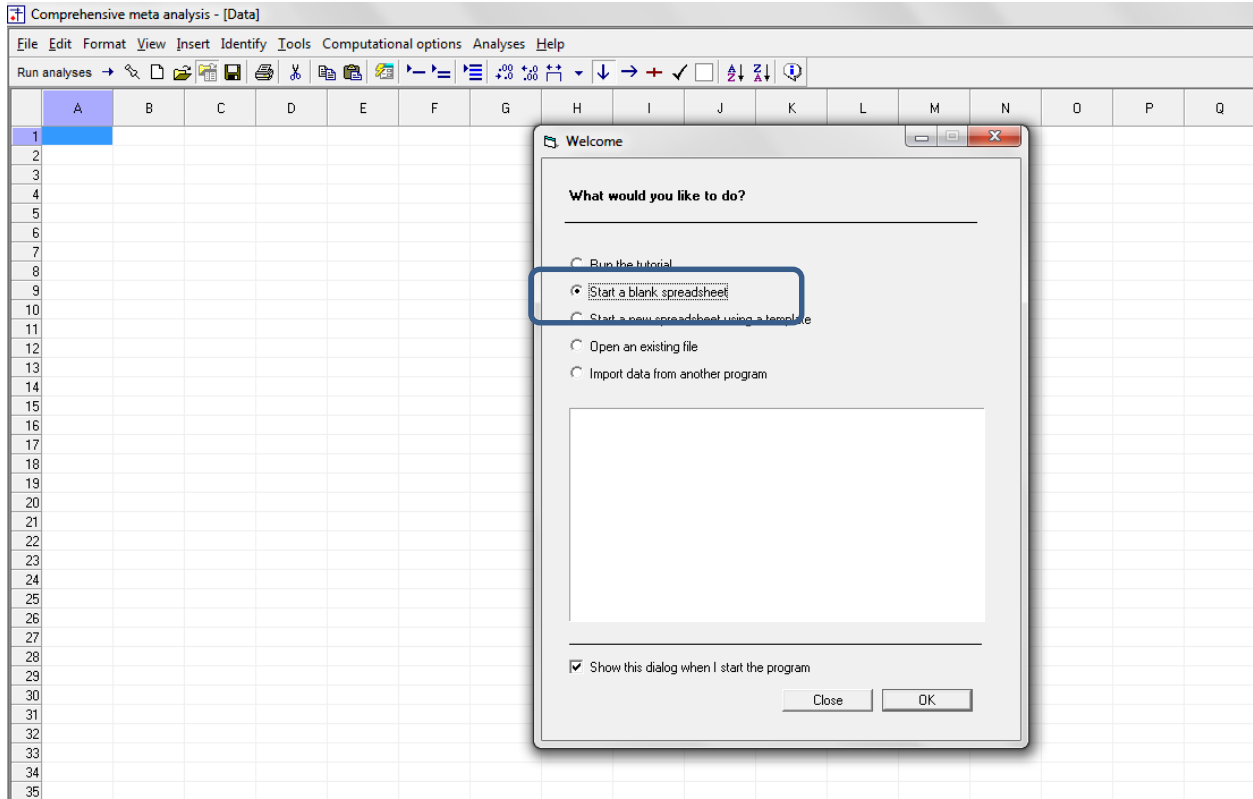
[Download this PDF](#)

[Download data in Excel](#)

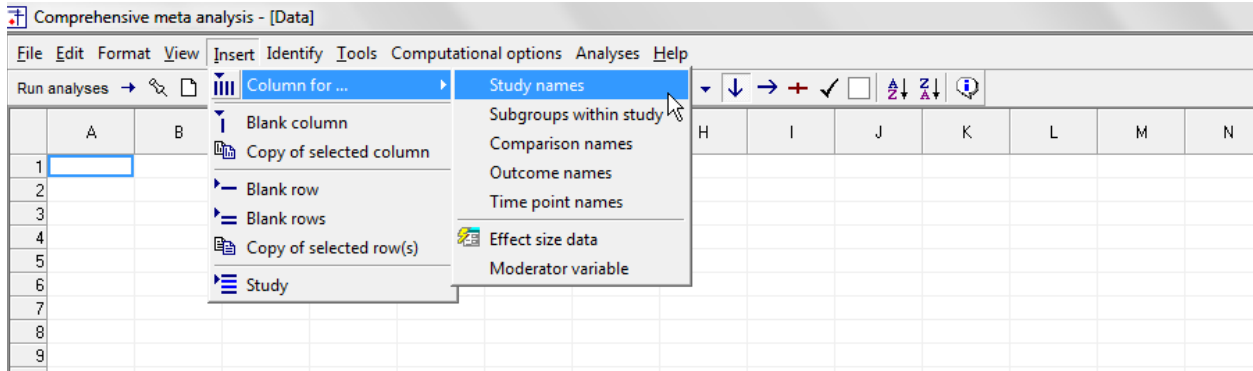
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Start the program

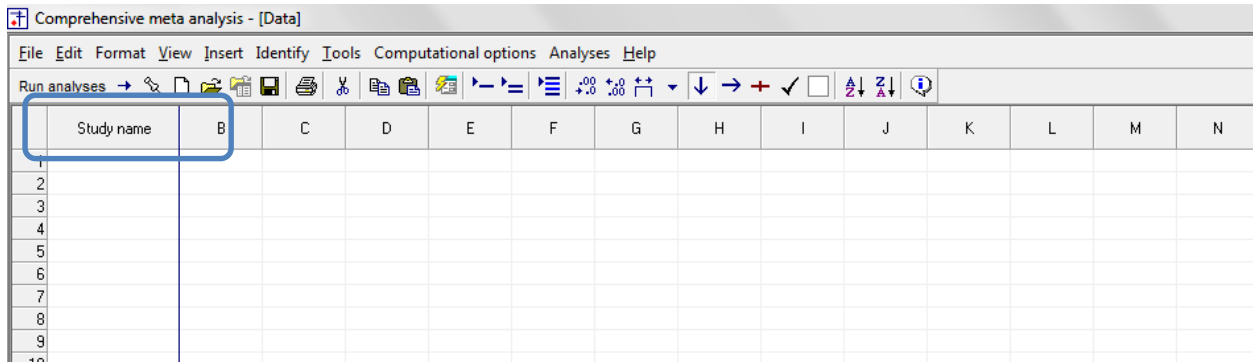
- Select the option [Start a blank spreadsheet]
- Click [OK]



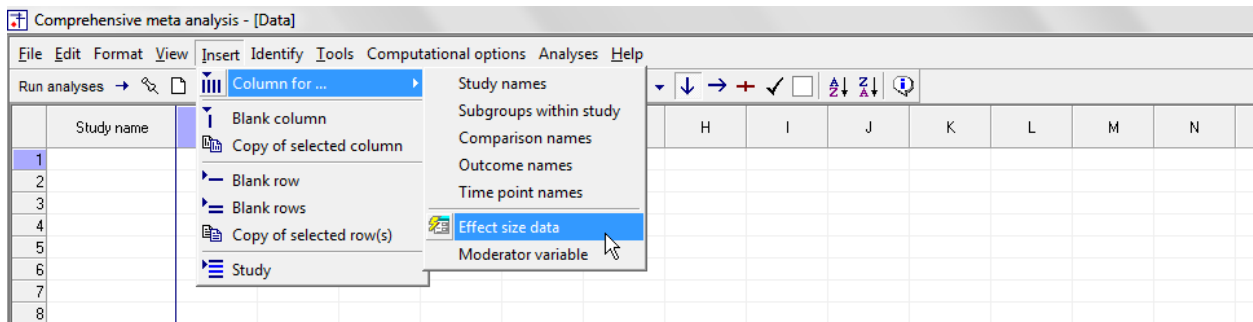
Click Insert > Column for > Study names



The screen should look like this

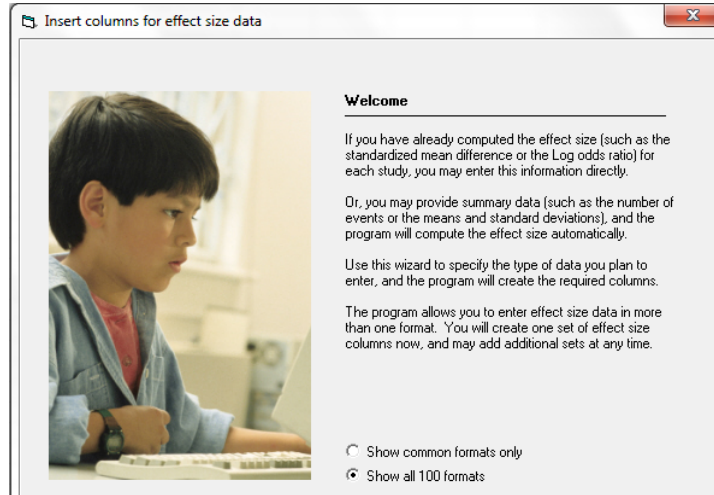


Click Insert > Column for > Effect size data

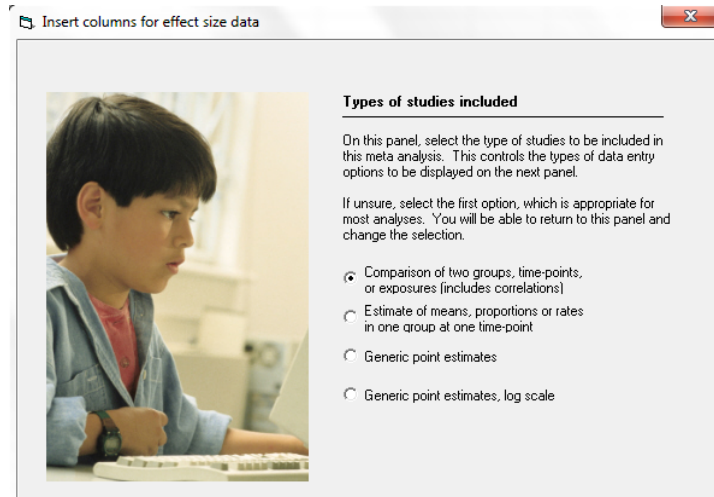


The program displays this wizard

Select [Show all 100 formats]
Click [Next]

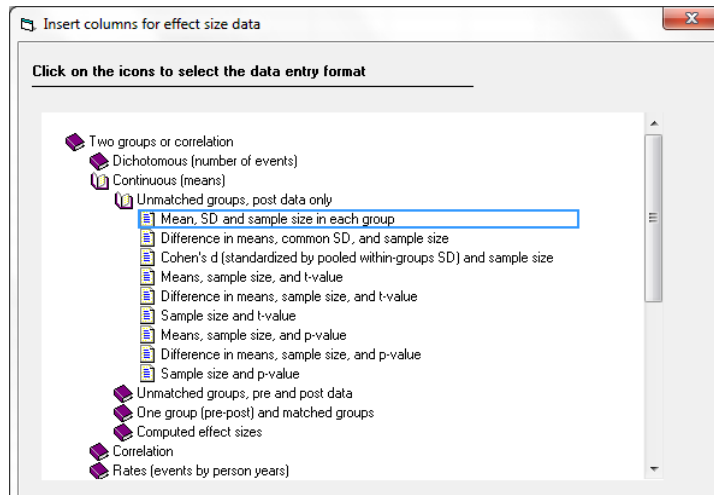


Select [Comparison of two groups...]
Click [Next]



Drill down to

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

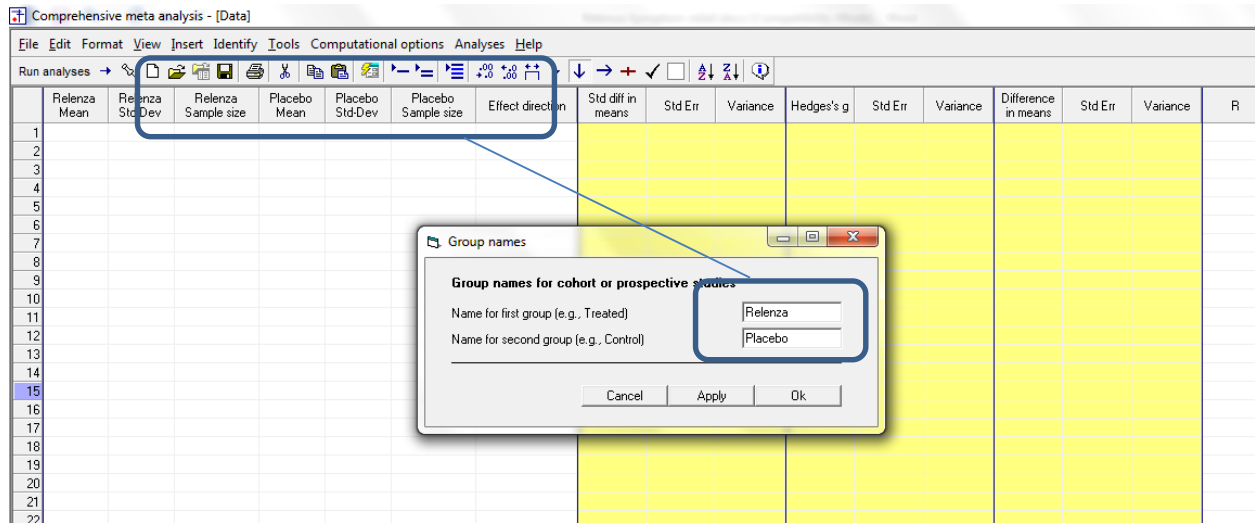


The program displays this wizard

Enter the following labels into the wizard

- First group > Relenza
- Second group > Placebo

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



There are three options at this point

- Enter the data directly into CMA
- – or – Open the CMA data file “Relenza Symptom Relief.cma”
- – or – Copy the data from Excel “Relenza Symptom Relief.xls”

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

- Switch to Excel and open the file
- Highlight the rows and columns as shown (Columns A to G), and press CTRL-C to copy to clipboard
-

	A	B	C	D	E	F	G	H	I
1	Study	Tx Mean	Tx SD	Tx N	Pbo Mean	Pbo SD	Pbo N		
2	JNAI-01	3.13	1.33	29	3.9	0.96	31		
3	JNAI-04	3.84	2.06	32	5.68	2.75	16		
4	JNAI-07	4.41	1.95	211	4.67	1.98	107		
5	NAI30008	9.61	8.11	262	10.72	8.46	263		
6	NAI30010	7.11	6.52	163	7.93	6.58	158		
7	NAI30012	10.45	8.89	191	10.93	8.47	169		
8	NAI30015	4.29	5.23	293	4.86	5.64	295		
9	NAIAB2008	5.87	2.46	834	6.34	2.25	422		
10	NAIA2005	5.29	2.31	139	5.7	2.49	81		
11	NAIA3002	8.34	7.4	412	8.9	7.77	365		
12	NAIB20005	5.06	2.33	64	5.9	2.73	63		
13	NAIB3001	6.48	3.74	227	7.35	3.83	228		
14	NAIB3002	7.97	7.32	174	10.58	8.53	182		
15									
16									

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

Click here

Comprehensive meta analysis - [Data]

File Edit Format View Insert Identify Tools Computational options Analyses Help

Run analyses → [Icons]

Study name	Relenza Mean	Relenza Std-Dev	Relenza Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges's g
1 Study	Tx Mean	Tx SD	Tx N	Pbo Mean	Pbo SD	Pbo N					
2 JNAI-01	3.130	1.330	29	3.900	0.960	31					
3 JNAI-04	3.840	2.060	32	5.680	2.750	16					
4 JNAI-07	4.410	1.950	211	4.670	1.980	107					
5 NAI30008	9.610	8.110	262	10.720	8.460	263					
6 NAI30010	7.110	6.520	163	7.930	6.580	158					
7 NAI30012	10.450	8.890	191	10.930	8.470	169					
8 NAI30015	4.290	5.230	293	4.860	5.640	295					
9 NAIAB2008	5.870	2.460	834	6.340	2.250	422					
10 NAIA2005	5.290	2.310	139	5.700	2.490	81					
11 NAIA3002	8.340	7.400	412	8.900	7.770	365					
12 NAIB20005	5.060	2.330	64	5.900	2.730	63					
13 NAIB3001	6.480	3.740	227	7.350	3.830	228					
14 NAIB3002	7.970	7.320	174	10.580	8.530	182					
15											
16											
17											

After checking that the data has been copied correctly, we can delete Row 1

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

Click here

Comprehensive meta analysis - [Data]

File Edit Format View Insert Identify Tools Computational options Analyses Help

Run: [Icons]

1	Relenza Std-Dev	Relenza Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges's g
2	1.330	29	3.900	0.960	31					
3	2.060	32	5.680	2.750	16					
4	1.950	211	4.670	1.980	107					
5	8.110	262	10.720	8.460	263					
6	6.520	163	7.930	6.580	158					
7	8.890	191	10.930	8.470	169					
8	5.230	293	4.860	5.640	295					
9	2.460	834	6.340	2.250	422					
10	2.310	139	5.700	2.490	81					
11	7.400	412	8.900	7.770	365					
12	2.330	64	5.900	2.730	63					
13	3.740	227	7.350	3.830	228					
14	7.320	174	10.580	8.530	182					
15										
16										
17										

We need to enter a value for “Effect Direction”

Enter “Auto” for each study

Click here

Comprehensive meta analysis - [Data]

Study name	Relenza Mean	Relenza Std-Dev	Relenza Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance
1 JNAI-01	3.130	1.330	29	3.900	0.960	31	Auto	-0.668	0.265	0.070	-0.659	0.262	0.069	-0.770	0.301	0.091
2 JNAI-04	3.840	2.060	32	5.680	2.750	16	Auto	-0.797	0.317	0.100	-0.784	0.312	0.097	-1.840	0.778	0.605
3 JNAI-07	4.410	1.950	211	4.670	1.980	107	Auto	-0.133	0.119	0.014	-0.132	0.119	0.014	-0.260	0.234	0.055
4 NAI30008	9.610	8.110	262	10.720	8.460	263	Auto	-0.134	0.087	0.008	-0.134	0.087	0.008	-1.110	0.723	0.523
5 NAI30010	7.110	6.520	163	7.930	6.580	158	Auto	-0.125	0.112	0.012	-0.125	0.111	0.012	-0.820	0.731	0.535
6 NAI30012	10.450	8.890	191	10.930	8.470	169	Auto	-0.065	0.106	0.011	-0.065	0.105	0.011	-0.480	0.916	0.838
7 NAI30015	4.290	5.230	293	4.860	5.640	295	Auto	-0.105	0.083	0.007	-0.105	0.082	0.007	-0.570	0.449	0.201
8 NAIAB2008	5.870	2.460	834	6.340	2.250	422	Auto	-0.197	0.060	0.004	-0.196	0.060	0.004	-0.470	0.139	0.019
9 NAI2005	5.290	2.310	139	5.700	2.490	81	Auto	-0.172	0.140	0.020	-0.172	0.140	0.019	-0.410	0.339	0.115
10 NAI3002	8.340	7.400	412	8.900	7.770	365	Auto	-0.074	0.072	0.005	-0.074	0.072	0.005	-0.560	0.546	0.298
11 NAI20005	5.060	2.330	64	5.900	2.730	63	Auto	-0.331	0.179	0.032	-0.329	0.178	0.032	-0.840	0.451	0.203
12 NAI20001	6.480	3.740	227	7.350	3.830	228	Auto	-0.230	0.094	0.009	-0.229	0.094	0.009	-0.870	0.355	0.126
13 NAI20002	7.970	7.320	174	10.580	8.530	182	Auto	-0.328	0.107	0.011	-0.327	0.107	0.011	-2.610	0.841	0.708

The program displays three effect sizes – d , g , and raw mean difference

- We want to hide the index d
- We want to set the raw mean difference as the primary index

Comprehensive meta analysis - [Data]

Study name	Relenza Mean	Relenza Std-Dev	Relenza Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Std diff in means	Std Err	Variance	Hedges's g	Std Err	Variance
1 JNAI-01	3.130	1.330	29	3.900	0.960	31	Auto	-0.668	0.265	0.070	-0.659	0.262	0.069
2 JNAI-04	3.840	2.060	32	5.680	2.750	16	Auto	-0.797	0.317	0.100	-0.784	0.312	0.097
3 JNAI-07	4.410	1.950	211	4.670	1.980	107	Auto	-0.133	0.119	0.014	-0.132	0.119	0.014
4 NAI30008	9.610	8.110	262	10.720	8.460	263	Auto	-0.134	0.087	0.008	-0.134	0.087	0.008
5 NAI30010	7.110	6.520	163	7.930	6.580	158	Auto	-0.125	0.112	0.012	-0.125	0.111	0.012
6 NAI30012	10.450	8.890	191	10.930	8.470	169	Auto	-0.065	0.106	0.011	-0.065	0.105	0.011
7 NAI30015	4.290	5.230	293	4.860	5.640	295	Auto	-0.105	0.083	0.007	-0.105	0.082	0.007
8 NAIAB2008	5.870	2.460	834	6.340	2.250	422	Auto	-0.197	0.060	0.004	-0.196	0.060	0.004
9 NAI2005	5.290	2.310	139	5.700	2.490	81	Auto	-0.172	0.140	0.020	-0.172	0.140	0.019
10 NAI3002	8.340	7.400	412	8.900	7.770	365	Auto	-0.074	0.072	0.005	-0.074	0.072	0.005
11 NAI20005	5.060	2.330	64	5.900	2.730	63	Auto	-0.331	0.179	0.032	-0.329	0.178	0.032
12 NAI20001	6.480	3.740	227	7.350	3.830	228	Auto	-0.230	0.094	0.009	-0.229	0.094	0.009
13 NAI20002	7.970	7.320	174	10.580	8.530	182	Auto	-0.328	0.107	0.011	-0.327	0.107	0.011

- Right-click in any yellow column
- Click “Customize computed effect size display”

In the wizard,

- Select “Difference in means” in the drop-down box
- Un-check “Std diff in means”
- Click [OK]

Effect size indices

Use the following as the primary index

Difference in means

Display columns for these indices

- Odds ratio
- Log odds ratio
- Peto odds ratio
- Log Peto odds ratio
- Risk ratio
- Log risk ratio
- Risk difference
- Std diff in means
- Hedges's g
- Difference in means
- Std Paired Difference
- Correlation
- Fisher's Z
- Rate ratio
- Log rate ratio
- Rate difference
- Hazard ratio

Also show standard error

Also show variance

Show the primary index only

Show all selected indices

Ok
Cancel

Study name	Relenza Mean	Relenza Std-Dev	Relenza Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size
1 JNAI-01	3.130	1.330	29	3.900	0.960	
2 JNAI-04	3.840	2.060	32	5.680	2.750	
3 JNAI-07	4.410	1.950	211	4.670	1.980	
4 NAI30008	9.610	8.110	262	10.720	8.460	
5 NAI30010	7.110	6.520	163	7.930	6.580	
6 NAI30012	10.450	8.890	191	10.930	8.470	
7 NAI30015	4.290	5.230	293	4.860	5.640	
8 NAIAB2008	5.870	2.460	834	6.340	2.250	
9 NAI A2005	5.290	2.310	139	5.700	2.490	
10 NAI A3002	8.340	7.400	412	8.900	7.770	
11 NAI B20005	5.060	2.330	64	5.900	2.730	
12 NAI B3001	6.480	3.740	227	7.350	3.830	
13 NAI B3002	7.970	7.320	174	10.580	8.530	

The screen should look like this

Study name	Relenza Mean	Relenza Std-Dev	Relenza Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance	I-squared
1 JNAI-01	3.130	1.330	29	3.900	0.960	31	Auto	-0.659	0.262	0.069	-0.770	0.301	0.091	0
2 JNAI-04	3.840	2.060	32	5.680	2.750	16	Auto	-0.784	0.312	0.097	-1.940	0.778	0.605	
3 JNAI-07	4.410	1.950	211	4.670	1.980	107	Auto	-0.132	0.119	0.014	-0.260	0.234	0.055	
4 NAI30008	9.610	8.110	262	10.720	8.460	263	Auto	-0.134	0.087	0.008	-1.110	0.723	0.523	
5 NAI30010	7.110	6.520	163	7.930	6.580	158	Auto	-0.125	0.111	0.012	-0.820	0.731	0.535	
6 NAI30012	10.450	8.890	191	10.930	8.470	169	Auto	-0.055	0.105	0.011	-0.480	0.916	0.838	
7 NAI30015	4.290	5.230	293	4.860	5.640	295	Auto	-0.105	0.082	0.007	-0.570	0.449	0.201	
8 NAIAB2008	5.870	2.460	834	6.340	2.250	422	Auto	-0.196	0.060	0.004	-0.470	0.139	0.019	
9 NAI A2005	5.290	2.310	139	5.700	2.490	81	Auto	-0.172	0.140	0.019	-0.410	0.339	0.115	
10 NAI A3002	8.340	7.400	412	8.900	7.770	365	Auto	-0.074	0.072	0.005	-0.560	0.546	0.298	
11 NAI B20005	5.060	2.330	64	5.900	2.730	63	Auto	-0.329	0.178	0.032	-0.840	0.451	0.203	
12 NAI B3001	6.480	3.740	227	7.350	3.830	228	Auto	-0.229	0.094	0.009	-0.870	0.355	0.126	
13 NAI B3002	7.970	7.320	174	10.580	8.530	182	Auto	-0.327	0.107	0.011	-2.610	0.841	0.708	

There are two options for computing the variance of the mean difference. We can pool the estimates from the two groups, or keep them separate. The authors of this analysis chose to keep them separate, and so we will use that option as well.

Click Computational options < Variance for mean difference

Comprehensive meta analysis - [Data]

File Edit Format View Insert Identify Tools Computational options Analyses Help

Run analyses → [Icons]

Correlation for imputing paired SD
Variance for mean difference
 Symmetry for confidence intervals
 Variance for Hedges's g

Study name	Relenza Mean	Relenza Std-Dev	Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance	I ²
1 JNAI-01	3.130	1.330	29	3.900	0.960	31	Auto	-0.659	0.262	0.069	-0.770	0.301	0.091	
2 JNAI-04	3.840	2.060	32	5.680	2.750	16	Auto	-0.784	0.312	0.097	-1.840	0.778	0.605	
3 JNAI-07	4.410	1.950	211	4.670	1.980	107	Auto	-0.132	0.119	0.014	-0.260	0.234	0.055	
4 NAI30008	9.610	8.110	262	10.720	8.460	263	Auto	-0.134	0.087	0.008	-1.110	0.723	0.523	
5 NAI30010	7.110	6.520	163	7.930	6.580	158	Auto	-0.125	0.111	0.012	-0.820	0.731	0.535	
6 NAI30012	10.450	8.890	191	10.930	8.470	169	Auto	-0.055	0.105	0.011	-0.480	0.916	0.838	
7 NAI30015	4.290	5.230	293	4.860	5.640	295	Auto	-0.105	0.082	0.007	-0.570	0.449	0.201	
8 NAIAB2008	5.870	2.460	834	6.340	2.250	422	Auto	-0.196	0.060	0.004	-0.470	0.139	0.019	
9 NAI2005	5.290	2.310	139	5.700	2.490	81	Auto	-0.172	0.140	0.019	-0.410	0.339	0.115	
10 NAI3002	8.340	7.400	412	8.900	7.770	365	Auto	-0.074	0.072	0.005	-0.560	0.546	0.298	
11 NAI20005	5.060	2.330	64	5.900	2.730	63	Auto	-0.329	0.178	0.032	-0.840	0.451	0.203	
12 NAI20001	6.480	3.740	227	7.350	3.830	228	Auto	-0.229	0.094	0.009	-0.870	0.395	0.126	
13 NAI20002	7.970	7.320	174	10.580	8.530	182	Auto	-0.327	0.107	0.011	-2.610	0.841	0.708	

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

Comprehensive meta analysis - [Data]

File Edit Format View Insert Identify Tools Computational options Analyses Help

Run analyses → [Icons]

Options for computing treatment effects

Variance for raw mean difference in independent groups

When a study includes data for two independent groups, the user may elect to enter the SD for each of the groups separately. In this case the program can pool the variance in the two groups (option 1) or not pool them (option 2).

This option affects the variance (and weights) used in an analysis of raw mean differences. It has no impact on analyses of standardized mean differences.

Assume a common variance

Do not assume a common variance (Revman, STATA)

Cancel Apply Ok

Study name	Relenza Mean	Relenza Std-Dev	Relenza Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance	I ²
1 JNAI-01	3.130	1.330	29	3.900	0.960	31	Auto	-0.659	0.262	0.069	-0.770	0.301	0.091	
2 JNAI-04	3.840	2.060	32	5.680	2.750	16	Auto	-0.784	0.312	0.097	-1.840	0.778	0.605	
3 JNAI-07	4.410	1.950	211	4.670	1.980	107	Auto	-0.132	0.119	0.014	-0.260	0.234	0.055	
4 NAI30008	9.610	8.110	262	10.720	8.460	263	Auto	-0.134	0.087	0.008	-1.110	0.723	0.523	
5 NAI30010	7.110	6.520	163	7.930	6.580	158	Auto	-0.125	0.111	0.012	-0.820	0.731	0.535	
6 NAI30012	10.450	8.890	191	10.930	8.470	169	Auto	-0.055	0.105	0.011	-0.480	0.916	0.838	
7 NAI30015	4.290	5.230	293	4.860	5.640	295	Auto	-0.105	0.082	0.007	-0.570	0.449	0.201	
8 NAIAB2008	5.870	2.460	834	6.340	2.250	422	Auto	-0.196	0.060	0.004	-0.470	0.139	0.019	
9 NAI2005	5.290	2.310	139	5.700	2.490	81	Auto	-0.172	0.140	0.019	-0.410	0.339	0.115	
10 NAI3002	8.340	7.400	412	8.900	7.770	365	Auto	-0.074	0.072	0.005	-0.560	0.546	0.298	
11 NAI20005	5.060	2.330	64	5.900	2.730	63	Auto	-0.329	0.178	0.032	-0.840	0.451	0.203	
12 NAI20001	6.480	3.740	227	7.350	3.830	228	Auto	-0.229	0.094	0.009	-0.870	0.395	0.126	
13 NAI20002	7.970	7.320	174	10.580	8.530	182	Auto	-0.327	0.107	0.011	-2.610	0.841	0.708	

Click File > Save As and save the file

	Relenza Std-Dev	Relenza Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance		
0	1.330	29	3.900	0.960	31	Auto	-0.659	0.262	0.069	-0.770	0.301	0.091		
0	2.060	32	5.680	2.750	16	Auto	-0.784	0.312	0.097	-1.840	0.778	0.605		
0	1.950	211	4.670	1.980	107	Auto	-0.132	0.119	0.014	-0.260	0.234	0.055		
0	8.110	262	10.720	8.460	263	Auto	-0.134	0.087	0.008	-1.110	0.723	0.523		
0	6.520	163	7.930	6.580	158	Auto	-0.125	0.111	0.012	-0.820	0.731	0.535		
0	8.890	191	10.930	8.470	169	Auto	-0.055	0.105	0.011	-0.480	0.916	0.838		
0	5.230	293	4.860	5.640	295	Auto	-0.105	0.082	0.007	-0.570	0.449	0.201		
0	2.460	834	6.340	2.250	422	Auto	-0.196	0.060	0.004	-0.470	0.139	0.019		
0	2.310	139	5.700	2.490	81	Auto	-0.172	0.140	0.019	-0.410	0.339	0.115		
10	NAIA3002	7.400	412	8.900	7.770	365	Auto	-0.074	0.072	0.005	-0.560	0.546	0.298	
11	NAIB20005	5.060	64	5.900	2.730	63	Auto	-0.329	0.178	0.032	-0.840	0.451	0.203	
12	NAIB3001	6.480	3.740	227	7.350	3.830	228	Auto	-0.229	0.094	0.009	-0.870	0.355	0.126
13	NAIB3002	7.970	7.320	174	10.580	8.530	182	Auto	-0.327	0.107	0.011	-2.610	0.841	0.708

Note that the file name is now in the header.

- [Save] will over-write the prior version of this file without warning
- [Save As...] will allow you to save the file with a new name

Study name	Relenza Mean	Relenza Std-Dev	Relenza Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance	0
1	JNAI-01	3.130	1.330	29	3.900	0.960	31	Auto	-0.659	0.262	0.069	-0.770	0.301	0.091
2	JNAI-04	3.840	2.060	32	5.680	2.750	16	Auto	-0.784	0.312	0.097	-1.840	0.778	0.605
3	JNAI-07	4.410	1.950	211	4.670	1.980	107	Auto	-0.132	0.119	0.014	-0.260	0.234	0.055
4	NAI30008	9.610	8.110	262	10.720	8.460	263	Auto	-0.134	0.087	0.008	-1.110	0.723	0.523
5	NAI30010	7.110	6.520	163	7.930	6.580	158	Auto	-0.125	0.111	0.012	-0.820	0.731	0.535
6	NAI30012	10.450	8.890	191	10.930	8.470	169	Auto	-0.055	0.105	0.011	-0.480	0.916	0.838
7	NAI30015	4.290	5.230	293	4.860	5.640	295	Auto	-0.105	0.082	0.007	-0.570	0.449	0.201
8	NAIAB2008	5.870	2.460	834	6.340	2.250	422	Auto	-0.196	0.060	0.004	-0.470	0.139	0.019
9	NAIA2005	5.290	2.310	139	5.700	2.490	81	Auto	-0.172	0.140	0.019	-0.410	0.339	0.115
10	NAIA3002	8.340	7.400	412	8.900	7.770	365	Auto	-0.074	0.072	0.005	-0.560	0.546	0.298
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12	NAIB3001	6.480	3.740	227	7.350	3.830	228	Auto	-0.229	0.094	0.009	-0.870	0.355	0.126
13	NAIB3002	7.970	7.320	174	10.580	8.530	182	Auto	-0.327	0.107	0.011	-2.610	0.841	0.708

By convention we've put the Treated group (Relenza) in the first columns and the control group in the next columns.

The program will compute the mean difference as Treated minus Control. Thus, a negative difference means that the treated group responded in less time.

(The column labeled Direction allows you to control this process. "Auto" means that the program will assign a "+" if the first group was higher and a "-" if the second group was higher. In this example, studies will have a negative sign if the treated group had a lower value (which means they responded more quickly).

It's always a good idea to check at least one study and make sure that we have the direction right. For this purpose we'll use the first study. The mean time to response was 3.130 days for Relenza and 3.900 days for Control. The Difference in means is negative (-0.770 days) which means that the treated group responded more quickly.

Comprehensive meta analysis - [C:\Users\Biostat\Dropbox\Workshops Three-Day\Tamiflu\Relenzaf.cma]

File Edit Format View Insert Identify Tools Computational options Analyses Help

Run analyses → [Icons]

	Study name	Relenza Mean	Relenza Std-Dev	Relenza Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance	0
1	JNAI-01	3.130	1.330	29	3.900	0.960	31	Auto	-0.659	0.262	0.069	-0.770	0.301	0.091	
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13	NAIB3002	7.970	7.320	174	10.580	8.530	182	Auto	-0.327	0.107	0.011	-2.610	0.841	0.708	
14															
15															

- To run the analysis, click [Run analysis]

Comprehensive meta analysis - [C:\Users\Biostat\Dropbox\Workshops Three-Day\Tamiflu\Relenzaf.cma]

File Edit Format View Insert Identify Tools Computational options Analyses Help

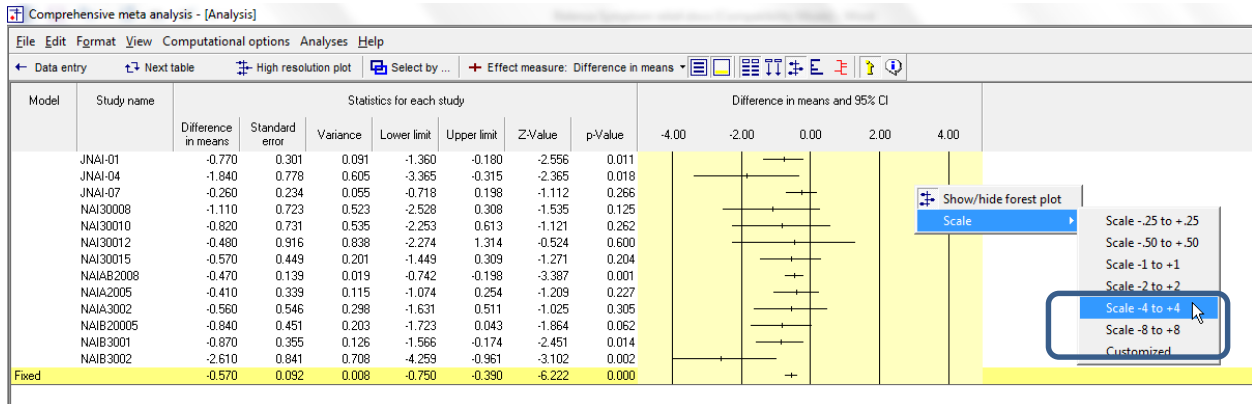
Run analyses → [Icons]

	Study name	Relenza Mean	Relenza Std-Dev	Relenza Sample size	Placebo Mean	Placebo Std-Dev	Placebo Sample size	Effect direction	Hedges's g	Std Err	Variance	Difference in means	Std Err	Variance	0
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3	JNAI-07	4.410	1.950	211	4.670	1.980	107	Auto	-0.132	0.119	0.014	-0.260	0.234	0.055	
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7	NAI30015	4.290	5.230	293	4.860	5.640	295	Auto	-0.105	0.082	0.007	-0.570	0.449	0.201	
8	NAIAB2008	5.870	2.460	834	6.340	2.250	422	Auto	-0.196	0.060	0.004	-0.470	0.139	0.019	
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10	NAIA3002	8.340	7.400	412	8.900	7.770	365	Auto	-0.074	0.072	0.005	-0.560	0.546	0.298	
11	NAIB20005	5.060	2.330	64	5.900	2.730	63	Auto	-0.329	0.178	0.032	-0.840	0.451	0.203	
12	NAIB3001	6.480	3.740	227	7.350	3.830	228	Auto	-0.229	0.094	0.009	-0.870	0.355	0.126	
13	NAIB3002	7.970	7.320	174	10.580	8.530	182	Auto	-0.327	0.107	0.011	-2.610	0.841	0.708	
14															
15															

This is the basic analysis screen

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

- Right-click on the forest plot > Customized > Set the scale to [-4 to +4]



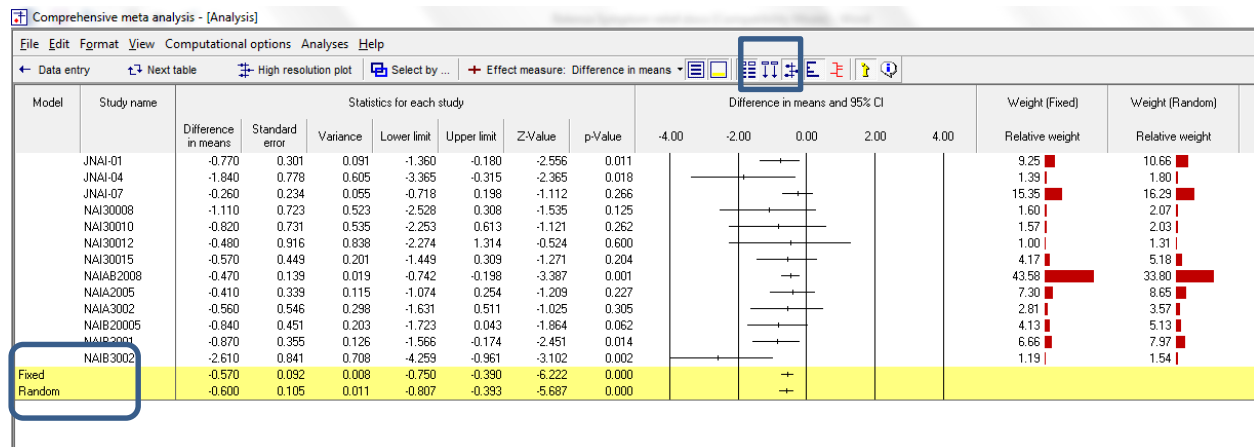
All studies have mean differences less than 0.0, which means that the Relenza group had symptom relief sooner than the control group.

There seems to be some variation in the observed effect sizes. However, the effect sizes (in particular for the two extreme studies) are wide. The confidence interval for most studies overlaps the mean effect size.

The pooled effect is -0.570 , which means that the mean Relenza group reported symptom relief about 0.57 days (14 hours) sooner than the placebo group.

- Click [Both models]
- Click the tool to display weights

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



Under the fixed-effect model the pooled mean difference is -0.560 . Under the random-effects model the pooled mean difference is -0.600 .

This tells us that the between-study variance in the observed effects is outside the range we would expect based on sampling error. Our estimate of the between-study variance in true effects is not zero. Therefore, the fixed-effect weights and random-effects weights are not identical.

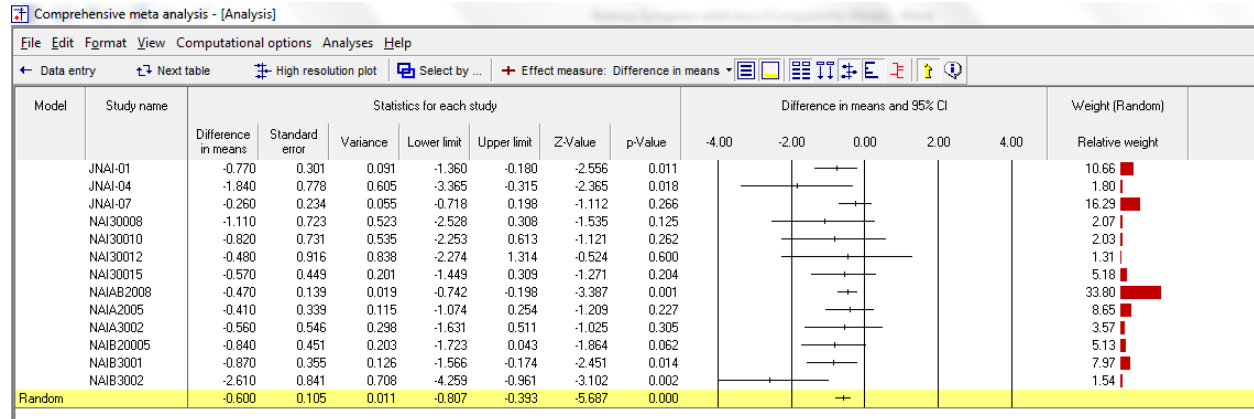
We need to select a statistical model for the analysis

- The fixed-effect model would be appropriate if all the studies were virtual replicates of each other. This is not the case, which is not the case here since the study populations varied in numerous (if unknown) ways.
- The random-effects model would be appropriate if the studies vary in ways that may impact the effect size. Therefore, we will use the random-effects model.

Note that this selection of a model is based on the sampling frame, and not on the results. We presented the fixed-effect model here for educational reasons, but could have proceeded directly to the random-effects model.

- Click Random on the tab at the bottom

The plot now displays the random-effects analysis alone.



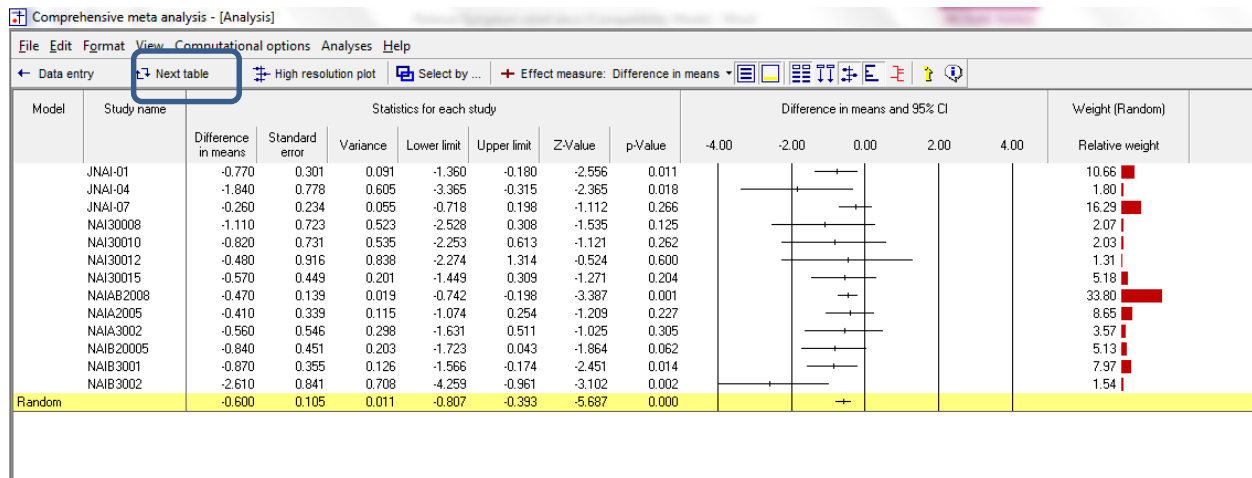
A quick view of the plot suggests the following

- The Relenza group responded more quickly than the placebo group in all studies
- The difference was statistically significant in five studies
- Excluding the second and the last studies, the observed effects ranged from 1.1 to 0.26 days. The two outliers had effects of 1.84 and 2.6 days, but with wide confidence intervals
- The summary effect is -0.600 days with a CI of -0.807 to -0.393 .
- The summary effect has a Z-value -5.687 a p -value of < 0.001 . Thus we can reject the null hypotheses that the true mean difference is 0.0.

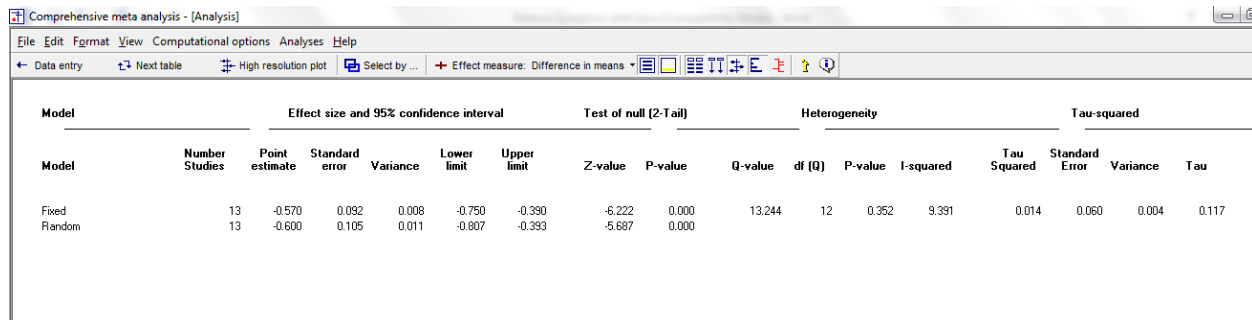
Our studies were sampled from a universe of studies defined by the patient types, dosage, and other factors as outlined in the inclusion/exclusion criteria for the meta-analysis. The confidence interval tells us that the mean effect size in this universe of studies probably falls in range of -0.807 to -0.393 . It tells us nothing about how widely the true effect size varies from study to study. This is an important clinical issue since we need to distinguish between various possibilities, such as

- Relenza consistently decreases the response time by 0.600 days (with a mean of 0.600)
- Relenza decreases the response time by 0 days in some studies, by 0.600 days in others, and by 1 or 2 days in others (with a mean of 0.600)

To address this we need not only the mean difference but also the standard deviation of the differences. For this we turn to the next screen.



The program displays this screen



The section labeled “Effect size and 95% confidence interval and the section labeled “Test of null” address the mean effect size and the null hypothesis that the mean difference is zero. These are the same statistics we saw on the previous screen. For the random-effects model the mean difference is -0.600 with a CI of -0.807 to -0.393 , the Z-value for a test of the null is -5.687 and the p-value for a test of the null is < 0.001 .

The section labeled Heterogeneity shows a test of the null hypothesis that the true effect size is identical in all thirteen studies and that 100% of the variation in the observed effects is due to sampling error. Put another way, if every one of the studies had an infinite sample size (so that we knew the true effect size in that study exactly) the observed effects would all be identical to each other.

To test this hypothesis we compute Q, which is basically a weighted sum of squares (we compute the difference of every effect size from the mean effect size, square that difference, assign larger weights to more precise studies, and then sum these weighted values). If the null hypothesis is true (that all the variation in effects is due to sampling error), the expected value of Q is equal to the number of studies minus 1 (here, 13 minus 1 equals 12).

The observed Q value is 13.244. This is more than we would expect if the null is true (12.0), but still within the range that could be due to sampling error. Therefore, we do not reject the null (it’s possible

that all studies share a common effect size). However, our best estimate is that there is some variance in effect sizes. This is expressed in several statistics.

I^2 is 9.391. This tells us that about 9% of the variance that we see in the forest plot reflects difference in the true effect sizes, while the other 91% reflects sampling error. Put another way, if we were able to plot the true effects rather than the observed effects, the data points would align one directly above the other.

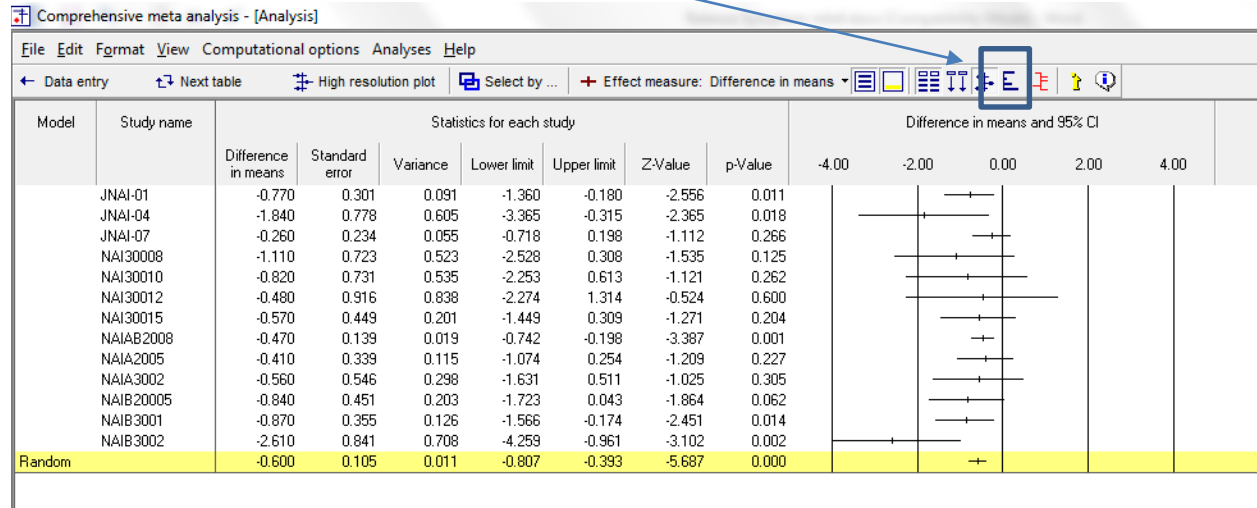
Importantly, I^2 is a proportion – it tells us what proportion of the observed variance is real (if our estimates are correct) but does not tell us how much variance there is.

- T^2 (shown as 0.014) is the estimate of variance in true effect sizes.
- T (shown 0.117) is the estimate of the standard deviation in true effect sizes.

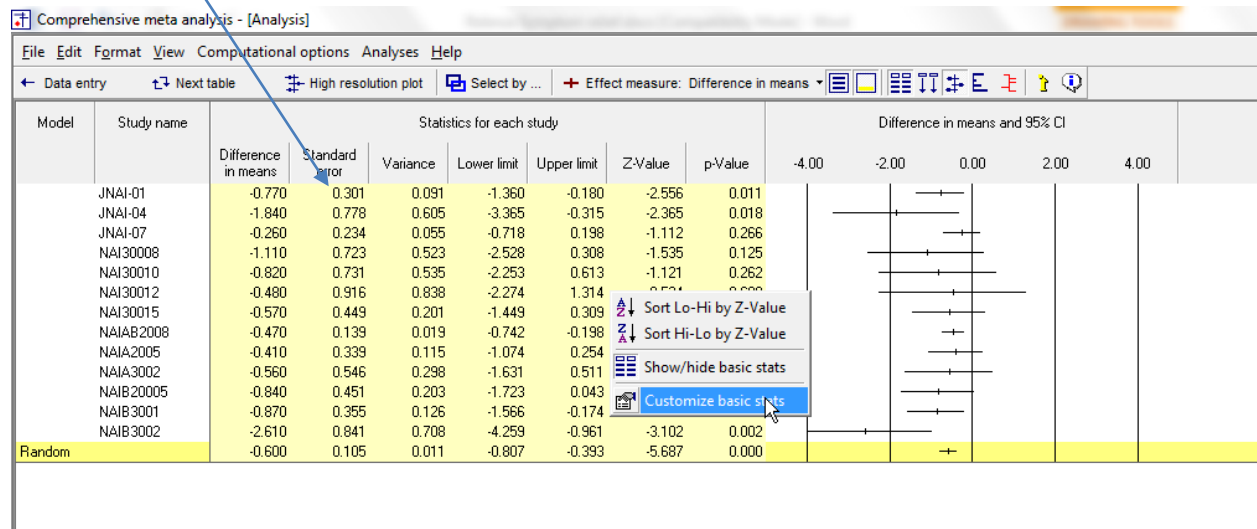
Click Next table

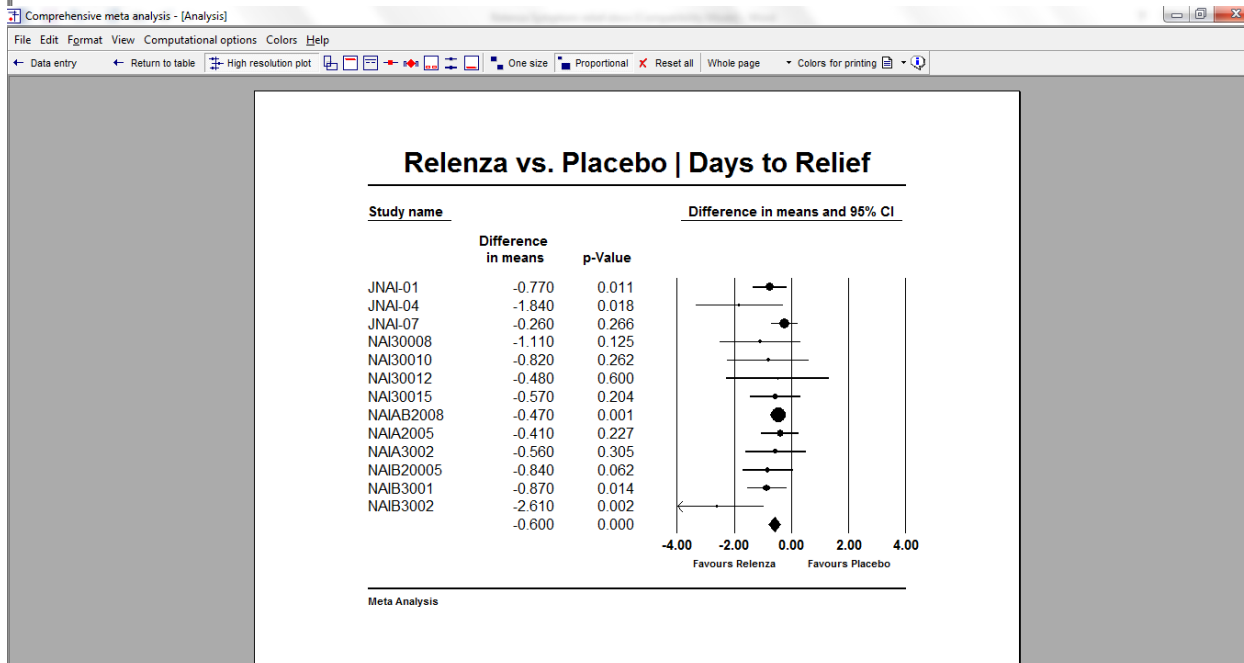
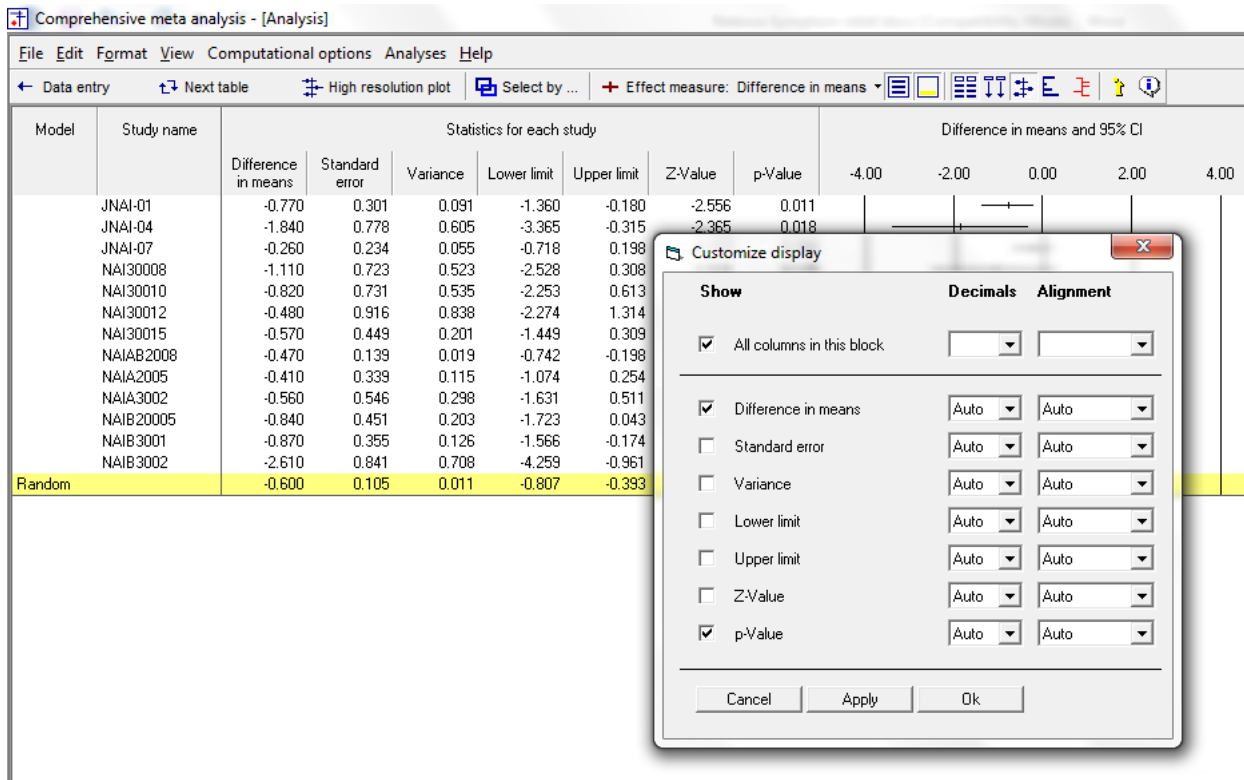
We want to create a high-resolution plot

Click here to hide the column of weights



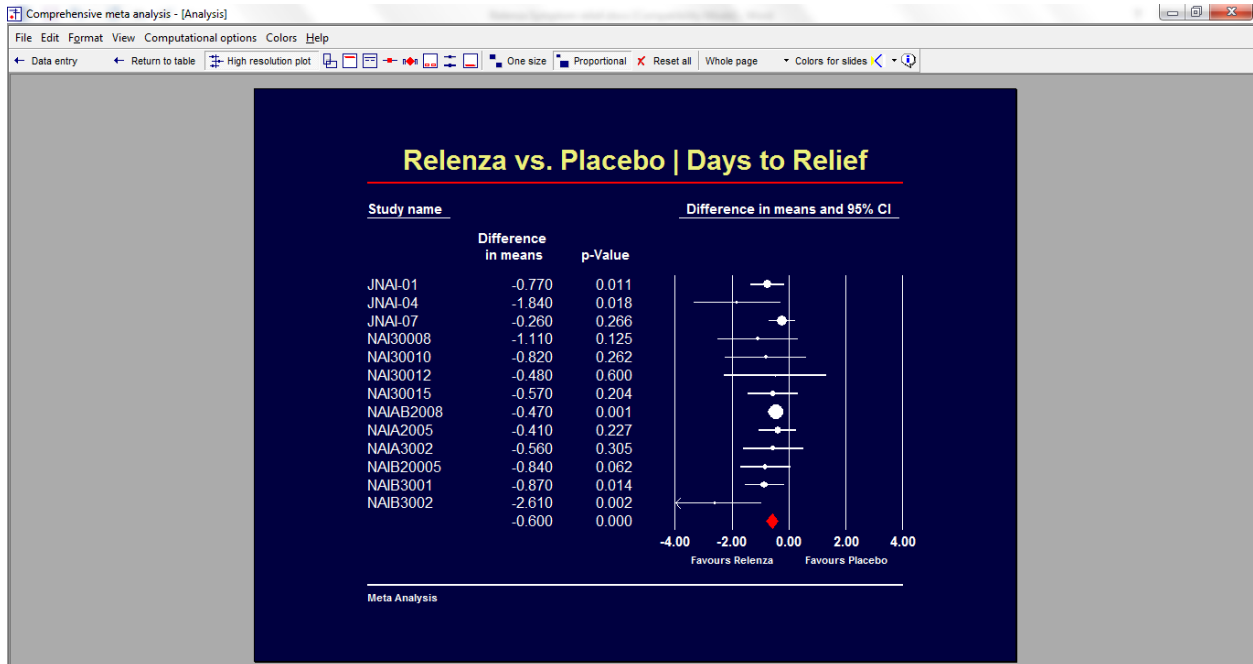
Right-click here and hide some of the statistics columns





Select "Random" rather than "Both" on the bottom tab

- Click Hi-Resolution plot
- Adjust the columns widths



In this analyses the effect size was the mean difference, which was reported in days. This is one of the cases where a raw mean difference is an appropriate effect size, because three conditions are met

- The outcome is in a metric that is meaningful and widely understood (days)
- All studies employed the same outcome
- The standard deviation is roughly comparable across studies

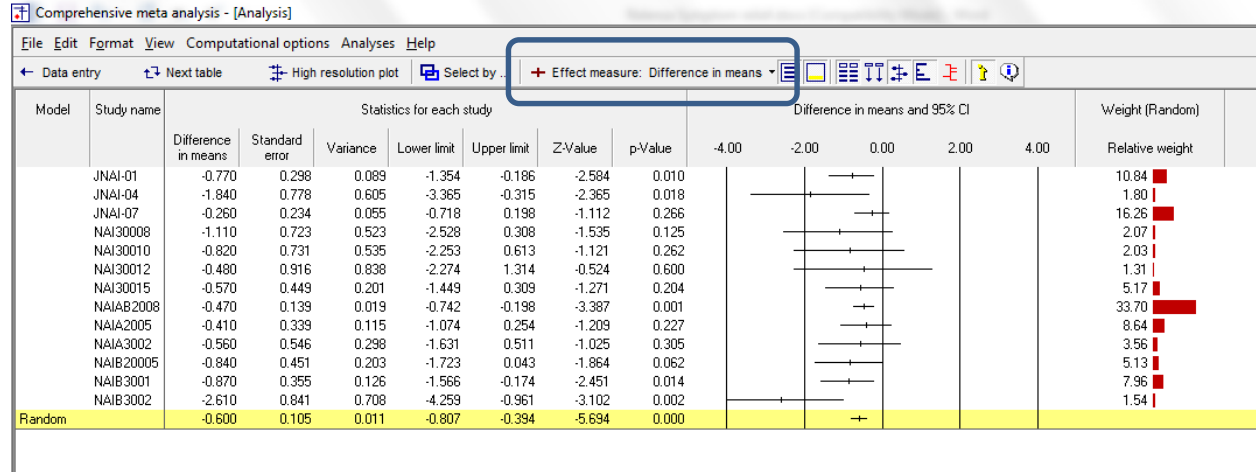
Alternatively, we could have used the standardized mean difference. This takes the mean difference and puts it on a standardized scale

- A difference of 0.25 indicates that the mean on Group-A is 0.25 standard deviations above the mean of Group-B.
- A difference of 0.50 indicates that the mean on Group-A is 0.50 standard deviations above the mean of Group-B.
- A difference of 0.75 indicates that the mean on Group-A is 0.75 standard deviations above the mean of Group-B.

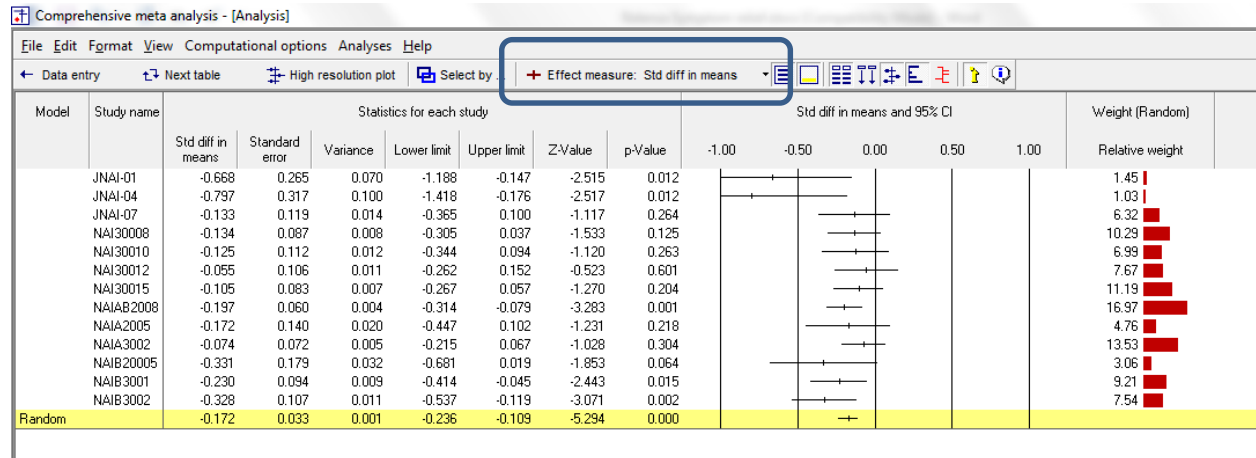
Let's see what the analysis would look like if we had used the standardized mean difference (g) rather than the mean difference.

We'll focus on the random-effects analysis

The analysis of raw mean differences looked like this



We can use the drop-down box and switch Hedge's g. Now the analysis looks like this



In the first analysis we reported a mean difference of 0.600 days. In the second we report a mean difference of 0.172 standard deviations. The first is more informative in that we get a sense of the actual time difference. The second gives us the sense that this is a fairly small effect inasmuch as the standard deviation of recovery times is about 6 times as large as the difference between groups.

Note that the weight assigned to each study differs somewhat in the two analysis. This reflects the fact that the standard deviation varied substantially from study to study, and affects the weight for the mean difference but not for the standardized mean difference.

The Z-value for testing the null is -5.694 ($p < 0.001$) in the first analysis and -5.294 ($p < 0.001$) in the second.

Summary

The analysis is based on seven studies that evaluated the effect of Relenza on duration of flu symptoms. Each study compared Relenza vs. Placebo and reported the time to relief in symptoms. The effect size is the raw mean difference.

Does Relenza decrease the time to symptom relief?

The difference in means is -0.600 days. On average, patients treated with Relenza reported symptom relief 0.600 days (14.4 hours) sooner than patients treated with placebo.

These studies were sampled from a universe of possible studies defined by certain inclusion/exclusion rules as outlined in the full paper. The confidence interval for the difference in means is -0.807 to -0.394 , which tell us that the mean raw difference in the universe of studies could fall anywhere in this range. This range does not include a difference of zero, which tells us that the true mean difference is probably not zero.

Similarly, the Z-value for testing the null hypothesis (that the mean difference is 0.0) is -5.694 , with a corresponding p -value is < 0.001 . We can reject the null that the drug has no impact on time to symptom relief.

Does the effect size vary across studies?

The *observed* effect size varies somewhat from study to study, but a certain amount of variation is expected due to sampling error. We need to determine if the observed variation falls within the range that can be attributed to sampling error (in which case there is no evidence of variation in true effects), or if it exceeds that range.

The Q -statistic provides a test of the null hypothesis that all studies in the analysis share a common effect size. If all studies shared the same effect size, the expected value of Q would be equal to the degrees of freedom (the number of studies minus 1).

The Q -value is 13.253 with 12 degrees of freedom and $p=0.351$. We cannot reject the null hypothesis that the true effect size is identical in all the studies. While the observed variation falls within the range that *could be* due to sampling error, our estimate of the variance in true effects is not zero, as reflected in the following statistics.

The I^2 statistic tells us what proportion of the observed variance reflects differences in true effect sizes rather than sampling error. Here, I^2 is 9.456.

T^2 is the variance of true effect sizes. Here, T^2 is 0.014. T is the standard deviation of true effects. Here, T is 0.117