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1. Installation

- Download and save setup.zip to a location in your hard disk drive
- Extract files to your desktop
- Install *setup.exe* by double-clicking on it and following the instructions
- After setup has been completed every time you open an Excel instance a meta-analysis menu will be available (Figure 1)

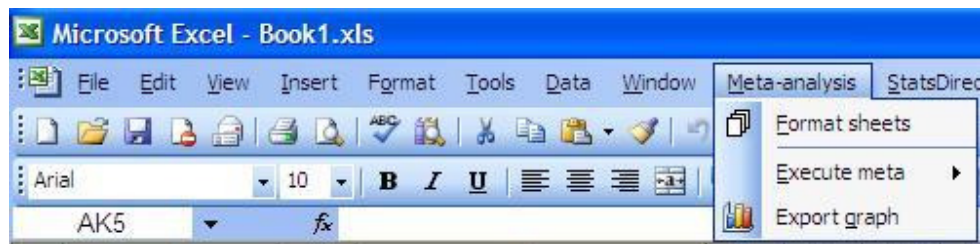


Figure 1

2. Format Sheets

Before inputting data the data and report sheets need to be formatted accordingly. Select the format sheet option and input the number of meta-analysis you want to include in a single excel workbook (Figure 2). For each meta-analysis 5 sheets are created (Figure 3) which will be explained below

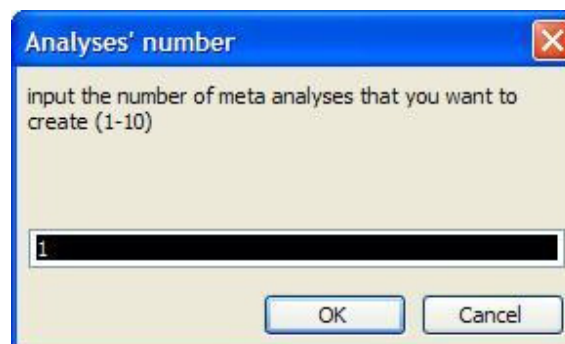


Figure 2

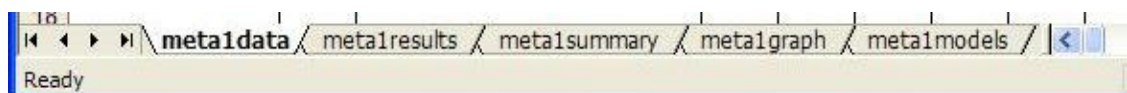


Figure 3

2.1. Data Sheet

The data sheet is the only sheet that is unlocked and on which data needs to be inputted. Each row corresponds to a study outcome for which information needs to be inputted in the appropriate information field so that the outcome effect and its standard error can be computed. Although there number of fields is large (Table I), completion of only a few may be sufficient. Nevertheless, you are advised to input all available information since the most robust effect calculation method will be automatically selected. More details on the used methods can be found in 3.2.

Name	Label	Type	Required	Information
<i>Study</i>	The name of the study	String	Yes	Only needs to be inputted once for each study (in the first outcome/variable row). If the cell background colour is set to red the row is not included in the analysis.
<i>Design</i>	The type of the design (RTC, Observational study etc)	String	No	Only needs to be inputted once for each study (in the first outcome/variable row)
<i>Variables</i>	Outcome variable names	String	Yes	Will be truncated to 28 characters in graphs. If the cell background colour is set to yellow the row is not included in the analysis. The font styles used (bold , <i>italics</i> , normal) are carried over to the result sheets. It is advised to set power outcome names in bold and secondary outcomes ones in italics. Outcomes with names in italics are plotted separately in the outcomes scatter plot. No action has be set for bold font style names
<i>Nlb</i>	Intervention group size, before treatment	Integer	-	Not used in any of the methods, column provided for information purposes and/or future use
<i>Nla</i>	Intervention group size, after treatment	Integer	Yes	
<i>NCb</i>	Control group size, before treatment	Integer	-	Not used in any of the methods, column provided for information purposes and/or future use
<i>Nca</i>	Control group size, after treatment	Integer	Yes	
<i>N(tot)b</i>	$Nlb + NCb$	Integer	-	Not used in any of the methods, column provided for information purposes (certain old studies provide the sum instead of the individual items)
<i>N(tot)a</i>	$Nla + Nca$	Integer	-	Not used in any of the methods, column provided for information purposes (certain old studies provide the sum instead of the individual items)

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Name	Label	Type	Required	Information
<i>Ib</i>	Number of events in intervention group, after treatment	Integer	-	Not used in any of the methods, column provided for information purposes and/or future use
<i>Ia</i>	Number of events in intervention group, after treatment	Integer	Yes* (1a, 1b)	
<i>Cb</i>	Number of events in control group, before treatment	Integer	-	Not used in any of the methods, column provided for information purposes and/or future use
<i>Ca</i>	Number of events in control group, after treatment	Integer	Yes* (1a, 1b)	
<i>mean(Ib)</i>	Mean effect, intervention group, before treatment	Real	-	Not used in any of the methods, column provided for information purposes and/or future use
<i>mean(Ia)</i>	Mean effect, intervention group, after treatment	Real	Yes* (3, 4, 5, 6)	
<i>mean(Cb)</i>	Mean effect, control group, before treatment	Real	-	Not used in any of the methods, column provided for information purposes and/or future use
<i>mean(Ca)</i>	Mean effect, control group, after treatment	Real	Yes* (3, 4, 5, 6)	
<i>SD(Ia)</i>	Standard deviation of the effect, intervention group, after treatment	Real	Yes* (4)	
<i>SD(Ca)</i>	Standard deviation of the effect, control group, after treatment	Real	Yes* (4)	
<i>MD</i>	Means difference $MD = mean(Ia) - mean(Ca)$	Real	Yes* (3, 4, 5, 6)	If <i>MD</i> has not been inputted it is calculated by the formula. If it has, the inputted value is used instead (to take into account adjusted <i>MD</i> values)
<i>LCI95(MD)</i>	Lower limit of 95% Confidence Interval for the means difference.	Real	Yes* (3)	
<i>UCI95(MD)</i>	Upper limit of 95% Confidence Interval for the means difference.	Real	Yes* (3)	
<i>median(Ia)</i>	Median of effect, intervention group, after treatment	Real	-	Not used in any of the methods, column provided for information purposes and/or future use
<i>median(Ca)</i>	Median of effect, control group, after treatment	Real	-	Not used in any of the methods, column provided for information purposes and/or future use

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Name	Label	Type	Required	Information
<i>lCI95(Ia)</i>	Lower limit of 95% Confidence Interval for the mean of the intervention group, after treatment.	Real	Yes* (5)	
<i>uCI95(Ia)</i>	Upper limit of 95% Confidence Interval for the mean of the intervention group, after treatment.	Real	Yes* (5)	
<i>lCI95(Ca)</i>	Lower limit of 95% Confidence Interval for the mean of the intervention group, after treatment.	Real	Yes* (5)	
<i>uCI95(Ca)</i>	Upper limit of 95% Confidence Interval for the mean of the intervention group, after treatment.	Real	Yes* (5)	
<i>OR</i>	Odds ratio: $OR = \frac{Ia/(NIa - Ia)}{Ca/(NCa - Ca)}$	Real	Yes* (2)	
<i>ORI95%</i>	Lower limit of 95% Confidence Interval for after treatment Odds Ratio	Real	Yes* (2)	
<i>ORu95%</i>	Upper limit of 95% Confidence Interval for after treatment Odds Ratio	Real	Yes* (2)	
<i>p – value</i>	P-value of a two way test that compares between groups	Real	Yes* (6, 7)	
<i>t – value</i>	T-value of a two way t-test that compares between groups	Real	Yes* (6, 7)	A p-value is calculated using this value, which always overrides an inputted p-value in the previous field
<i>df</i>	Degrees of freedom of a two way t-test that compares between groups	Integer	Yes* (6, 7)	Degrees of freedom are automatically computed (if not provided) as $NIa + NCa - 2$
<i>SEdiff</i>	Standard Error of Difference between the means of the two groups.	Real	Yes* (3)	
<i>direction</i>	Direction of the effect	Char	Yes	Leave empty if effect favours intervention. Input a single minus sign to reverse effect, if it favours control

Name	Label	Type	Required	Information
<i>quality</i>	Quality of the study	Integer	No	Evaluation of each study (only needs to be inputted once for each study). For future use and information purposes only.
<i>subgroup</i>	Subgroup information for an outcome	String	No	Information on subgroup outcomes. They are used to label outcomes in the results.

Table I

*Requisite for one effect size calculation method or more, but not all. The method(s) involved are shown in brackets

3. Execute meta

After the data sheet has been updated you can run a meta-analysis using one of two options.

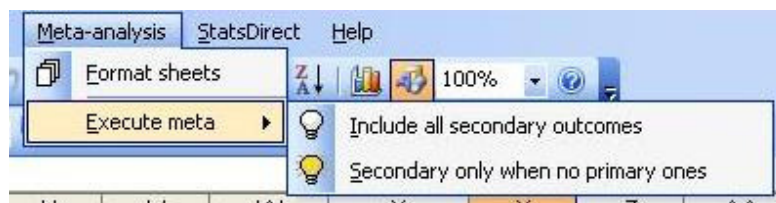


Figure 4

The first option will include all outcomes in the analysis, even secondary ones. The second will only include secondary outcomes for studies that totally lack primary ones. The option you select at this point can only affect the results in the last sheet (models). After the code is executed the four result sheets (results, summary, graph & models) are updated. It is likely that you will receive an error at this stage if the data sheet has not been completed with appropriate values (probability values above 1, negative group sizes or counts etc)

3.1. Results Sheet

As previously mentioned, eight different methods are used to compute the effect and SE of an outcome and their results are listed on this sheet. Once more, each row corresponds to a single outcome and the various results are provided just for comparison since the most robust method is automatically selected and used in the meta-analysis. Empty fields indicate that a particular method could not be used due to missing data (Figure 5). Additional information regarding the outcome is provided at the far right end of the worksheet (Figure 6). These additional fields are interpreted in Table II. The sheet is protected and cannot be changed but data can be copied from it.

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Microsoft Excel - Book1

File Edit View Insert Format Tools Data Window Meta-analysis StatsDirect Help

Type a question for help

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9

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1

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A B C K L M N O P Q R S T U V

1

Method 1b (based on OR) - Dichotomous Data - Q=ln(OR)

Method 2 (based on OR and its CI) - Dichotomous Data

2

Study Design Variables

seoff(Q) effect(SMD) effect I95 effect U95 Value for error bars SEeffect effect(SMD) effect I95 effect U95 Value for error bars seoff(QD) seoffr

108

Campbell A, 1998 RCT General

109

Physical

110

Social

111

Role physical

112

Role emotional

113

Mental

114

Energy

115

Pain

116

Anxiety

117

Depression

118

Chest Pain

0.1264 0.1002 -0.0364 0.2367 0.1365

119

Course of Chest Pain getting wo

0.2233 0.2512 0.0099 0.4925 0.2413

120

Exercise

0.1233 0.2608 0.1276 0.3940 0.1332

0.0856 0.2827 0.1150 0.4504 0.1677

121

Diet

0.1307 0.1741 0.0328 0.3153 0.1412

0.0812 0.2124 0.0532 0.3716 0.1592

122

Smoking status (non-smoking)

0.1598 -0.0800 -0.2527 0.0927 0.1727

0.1409 -0.1370 -0.4132 0.1392 0.2762

123

Cherkin, 1996 RCT worry (0-10)

124

bothersomeness (0-10)

125

pain control (?)

126

Function (0-23)

127

cut days

128

bed days

129

work-loss days

130

overall score (0-100)

131

information subscale (0-100)

132

general care subscale (0-100)

133

regular exercise

134

manage next LBP

135

perceived knowledge (0-100)

136

Cupples, 1994 RCT Serum cholesterol (mmol/L)

0.1046

137

Diastolic Blood Pressure (mmHg)

1.1735

138

Systolic Blood Pressure (mmHg)

2.2194

139

BMI

0.4082

140

Diet (frequency of eating certain

0.3827

141

Exercise (no of 20 min episode

0.1786

142

Stop Smoking

0.5249 -0.2800 -0.8472 0.2872 0.5672

143

angina episodes per week

144

Emotion

2.7551

145

Energy

4.3112

146

Mobility

2.5255

147

Pain

2.9337

148

Sleep

3.5204

meta1data \meta1results \meta1summary \meta1graph \meta1models \

Draw

AutoShapes

Ready

NUM

Figure 5

Field name	Information
Calculated & wanted?	YES if the effect could be calculated with any of the methods and the outcome hasn't been excluded from the analysis by highlighting the <i>study</i> or <i>variables</i> field in the data sheet (see Table I). Empty otherwise
Reversed effect?	YES if the effect has been reversed using field <i>direction</i> in the data sheet. Empty otherwise
Method selected	Displays the method that will be used in the meta-analysis. Empty if the effect could not be computed with any of the methods.
Missing data from method...	For each method lists the data that are missing to compute results. Empty if the method has been successfully used. Select a cell of interest and see its full contents in the formula bar (Figure 7)

Table II

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Study	Design	Variables	calculated & wanted?	reversed effect?	method selected	1a	1b	2	3	4	5	6	7
Campbell A, 1998	RCT	General	YES		3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), I_C195(Ca), u_C195(Ca)					
		Physical	YES		3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Social	YES		3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Role physical	YES		3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Role emotional	YES		3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Mental	YES		3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Energy	YES		3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Pain	YES		3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Anxiety	YES	YES	3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Depression	YES	YES	3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Chest Pain	YES	YES	1a			OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Course of Chest Pain getting wo	YES	YES	1a			OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Exercise	YES		2			(MD, I_C195 SD(la), SD(CMD, I_C195(I MD					
		Diet	YES		2			(MD, I_C195 SD(la), SD(CMD, I_C195(I MD					
		Smoking status (non-smoking)	YES		2			(MD, I_C195 SD(la), SD(CMD, I_C195(I MD					
Cherkin, 1996	RCT	worry (0-10)				la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		bothersomeness (0-10)				la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		pain control (?)				la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Function (0-23)				la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		cut days				Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la					
		bed days				Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la					
		work-loss days				Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la					
		overall score (0-100)				la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Information subscale (0-100)				la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		general care subscale (0-100)				la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		regular exercise				la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		manage next LBP				la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		perceived knowledge (0-100)				la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
Cupples, 1994	RCT	Serum cholesterol (mmol/L)	YES	YES	3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Diastolic Blood Pressure (mmHg)	YES	YES	3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Systolic Blood Pressure (mmHg)	YES	YES	3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		BMI	YES	YES	3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Diet (frequency of eating certain	YES		3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Exercise (no of 20 min episode	YES		3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Stop Smoking	YES		1a			OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		angina episodes per week				Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la					
		Emotion	YES	YES	3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Energy	YES	YES	3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Mobility	YES	YES	3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Pain	YES	YES	3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		Sleep	YES	YES	3	la, Ca	la, Ca	OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					

Figure 6

Study	Design	Variables	calculated & wanted?	reversed effect?	method selected	1a	1b	2	3	4	5	6	7
Batchelor	CBA	Smoking (% stopped)						OR, OR, I_95%, OR_u_95SD(la), SD(CI_C195(la), u_C195(Ca), I_C195(Ca), u_C195(Ca)					
		health care could be improved				Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la					
		establishment of family centre				Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la	Nla, NCa, la Nla, NCa, la					

Figure 7

3.2. Methods description

The methods used are labelled 1a, 1b, 2, 3, 4, 5, 6 & 7. The first three refer to dichotomous data, 3 to 6 to continuous and method 7 applies to both types. Table III provides information on the input needed by each method. All methods have been inferred from The Cochrane Collaboration Handbook for Systematic Reviews of Interventions v.4.2.6, §8.5 - <http://www.cochrane.org/resources/handbook/>.

Method	Data type	Input needed	Effect Estimate Measure
1a	Dichotomous	N_{Ia} and N_{Ca} and Ia and Ca	Risk Difference
1b	Dichotomous	N_{Ia} and N_{Ca} and Ia and Ca	Odds Ratio
2	Dichotomous	N_{Ia} and N_{Ca} and OR and $CI_{95\%}(OR)$	Odds Ratio
3	Continuous	N_{Ia} and N_{Ca} and MD and $(CI_{95\%}(MD) \text{ or } SE_{diff}(m))$	Mean Difference
4	Continuous	N_{Ia} and N_{Ca} and MD and $SD(Ia)$ and $SD(Ca)$	Mean Difference
5	Continuous	N_{Ia} and N_{Ca} and MD and $CI_{95\%}(mean_{Ia})$ and $CI_{95\%}(mean_{Ca})$	Mean Difference
6	Continuous	N_{Ia} and N_{Ca} and MD and $(P \text{ or } (T \text{ and } DF))$	Mean Difference
7	Continuous	N_{Ia} and N_{Ca} and $(P \text{ or } (T \text{ and } DF))$	Any

Table III

Where:

- N_{Ia} is the size of the intervention group.
- N_{Ca} is the size of the control group.
- Ia is the number of events in the intervention group (always stands that $Ia < N_{Ia}$).
- Ca is the number of events in the control group (always stands that $Ca < N_{Ca}$).
- OR is the Odds Ratio ($OR = \frac{Ia/(N_{Ia} - Ia)}{Ca/(N_{Ca} - Ca)}$).
- $CI_{95\%}(OR)$ is the 95% Confidence Interval for the Odds Ratio
- MD is the means difference of the two groups, either provided or calculated with:
 $MD = mean(Ia) - mean(Ca)$.
- $CI_{95\%}(MD)$ is the 95% Confidence Interval for the means difference.

- $SE_{diff}(m)$ is the Standard Error of Difference between the means of the two groups.
- $SD(Ia)$ is the Standard Deviation for the intervention group.
- $SD(Ca)$ is the Standard Deviation for the control group.
- $CI95\%(mean_{Ia})$ is the 95% Confidence Interval for the mean of the intervention group.
- $CI95\%(mean_{Ca})$ is the 95% Confidence Interval for the mean of the control group.
- P is the p-value of the test.
- T is the t-value of the t-test.
- DF the degrees of freedom of the t-test.

As one would expect, there are studies for which we have enough data to employ more than one method. In cases as such all the possible 'paths' are used so that we can compare the results and identify possible errors. However, only one method is finally selected to provide us with data for the forest plot. The priority lists follow:

Data type	Priority list
Dichotomous	2, 1a, 1b, 7
Continuous	4, 5, 3, 6, 7

Table IV

For some outcomes enough data is provided for the application of more than one of the methods. In such cases, the effect size and SE are calculated using all possible 'options' which enables the user to compare the results and the accuracy of the information supplied by the study in question (Figure 5). Nevertheless, only one method is finally selected to provide us with effect sizes and SEs for the plots and the meta-analysis. The methods have been prioritised according to expected precision: that is, the expectation that the effect size and associated variance computed from the input data will be accurate. As a general rule, the fewer the number of mathematical transformations involved in getting from the "raw data" to the statistical parameters used as input for the method, the higher the expected precision.. As for 1a and 2a, they require exactly the same data but while the first one uses the Risk Difference to produce the results, the second one employs the Odds Ratio (OR). Since they both require exactly the same input, the former is arbitrarily prioritised over the latter, which – in effect – is never used in further analyses but is provided for comparison.

3.2.1. Method 1a (based on RD) – Dichotomous Data

We need:

- N_{Ia} , N_{Ca} , Ia , Ca

Step1

$$SE_{diff}(RD) = \sqrt{\frac{P_{Ia}(1-P_{Ia})}{N_{Ia}} + \frac{P_{Ca}(1-P_{Ca})}{N_{Ca}}} \text{ where } P_{Ia} = \frac{Ia}{N_{Ia}} \text{ \& } P_{Ca} = \frac{Ca}{N_{Ca}}$$

Step2

$$SE_{effect} = \sqrt{\frac{1}{N_{Ia}} + \frac{1}{N_{Ca}}}$$

Step3

$$SD = \frac{SE_{diff}}{SE_{effect}}$$

Step4

$$effect = \frac{RD}{SD}$$

Step5

$$CI_{95\%}(effect) = effect \pm 1.96 \cdot SE_{effect}$$

Step6

$$value_error_bars = SE_{effect} \cdot 1.96$$

3.2.2. Method 1b (based on OR) – Dichotomous Data

We need:

- N_{Ia} , N_{Ca} , Ia , Ca

Step1

$$\text{Let } Q = \ln(OR) \text{ where } OR = \frac{Ia/(N_{Ia} - Ia)}{Ca/(N_{Ca} - Ca)}^1$$

Step2

$$SE_{diff}(Q) = \sqrt{\frac{1}{Ia} + \frac{1}{N_{Ia} - Ia} + \frac{1}{Ca} + \frac{1}{N_{Ca} - Ca}}$$

Step3

¹ There are some cases where $N_{Ia} = Ia$ or $N_{Ca} = Ca$ and therefore the Odds Ratio cannot be computed.

$$upperCI95\%(Q) = Q + 1.96 \cdot SE_{diff}(Q)$$

$$lowerCI95\%(Q) = Q - 1.96 \cdot SE_{diff}(Q)$$

Step4

$$effect = \sqrt{3} / \pi \cdot Q$$

Step5

$$upperCI95\%(effect) = upperCI95\%(Q) \cdot \frac{\sqrt{3}}{\pi}$$

$$lowerCI95\%(effect) = lowerCI95\%(Q) \cdot \frac{\sqrt{3}}{\pi}$$

Step6

$$value_error_bars = \frac{\sqrt{3}}{\pi} SE_{diff}(Q) \cdot 1.96$$

3.2.3. Method 2 (based on OR and its CI) – Dichotomous Data

We need:

- $Nla, NCa, OR, CI95\%(OR)$

Step1

Calculate 'absolute' confidence intervals for Standardised Mean Difference (SMD)

$$upperCI95\%(SMD) = \sqrt{3} / \pi \ln(upperCI95\%(OR))$$

$$lowerCI95\%(SMD) = \sqrt{3} / \pi \ln(lowerCI95\%(OR))$$

Step2

$$SE_{effect} = \frac{upperCI95\%(SMD) - lowerCI95\%(SMD)}{3.92} \text{ when } Nla \geq 60 \text{ \& } NCa \geq 60$$

$$(\text{when sample size is small: } SE_{effect} = \frac{upperCI95\%(SMD) - lowerCI95\%(SMD)}{= 2 \cdot tinv(1 - 0.95, Nla + NCa - 2)})$$

where the denominator is an excel function returning the t-value for specific CI and dfs)

Step3

$$effect = \sqrt{3} / \pi \ln OR$$

effect is actually SMD

Step4

$$CI95\%(effect) = effect \pm 1.96 \cdot SE_{effect}$$

Step5

$$value_error_bars = SE_{effect} \cdot 1.96$$

3.2.4. Method 3 – Continuous data

We need:

- N_{Ia} , N_{Ca} , Mean Difference (MD) and Confidence Interval for the mean difference $CI95\%(MD)^2$

Step1

$$SE_{diff}(MD) = \frac{upperCI95\%(MD) - lowerCI95\%(MD)}{3.92} \text{ when } N_{Ia} \geq 60 \text{ \& } N_{Ca} \geq 60$$

$$(\text{when sample size is small: } SE_{diff}(MD) = \frac{upperCI95\%(MD) - lowerCI95\%(MD)}{= 2 \cdot tinv(1 - 0.95, N_{Ia} + N_{Ca} - 2)})$$

where the denominator is an excel function returning the t-value for specific CI and DFs)

Step2

$$SE_{effect} = \sqrt{\frac{1}{N_{Ia}} + \frac{1}{N_{Ca}}}$$

Step3

$$SD = \frac{SE_{diff}}{SE_{effect}}$$

Step4

$$effect = \frac{MD}{SD}$$

Step5

$$CI95\%(effect) = effect \pm 1.96 \cdot SE_{effect}$$

Step6

$$value_error_bars = SE_{effect} \cdot 1.96$$

3.2.5. Method 4 – Continuous data

We need:

- N_{Ia} , N_{Ca} , MD , $SD(Ia)$, $SD(Ca)$ ³

² Instead of the $CI95\%(MD)$ the $SE_{diff}(MD)$ may be provided instead

Step1

$$SD = \sqrt{\frac{SD(Ia)^2 \cdot Nla + SD(Ca)^2 \cdot NCa}{Nla + NCa}}$$

Step2

$$SE_{effect} = \sqrt{\frac{1}{Nla} + \frac{1}{NCa}}$$

Step3

$$effect = \frac{MD}{SD}$$

Step4

$$CI95\%(effect) = effect \pm 1.96 \cdot SE_{effect}$$

Step5

$$value_error_bars = SE_{effect} \cdot 1.96$$

3.2.6. Method 5 – Continuous data

We need:

- $Nla, NCa, MD, CI(Ia), CI(Ca)$

Step1

$$SD(Ia) = \sqrt{Nla} \cdot \frac{upperCI95\%(Ia) - lowerCI95\%(Ia)}{3.92} \quad \text{if } Nla \geq 60$$

$$\text{(if } Nla < 60 \text{ then } SD(Ia) = \sqrt{Nla} \cdot \frac{upperCI95\%(Ia) - lowerCI95\%(Ia)}{2 \cdot tinv(1 - 0.95, Nla - 1)})$$

Step2

$$SD(Ca) = \sqrt{NCa} \cdot \frac{upperCI95\%(Ca) - lowerCI95\%(Ca)}{3.92} \quad \text{if } NCa \geq 60$$

$$\text{(if } NCa < 60 \text{ then } SD(Ca) = \sqrt{NCa} \cdot \frac{upperCI95\%(Ca) - lowerCI95\%(Ca)}{2 \cdot tinv(1 - 0.95, NCa - 1)})$$

Step3

$$SD = \sqrt{\frac{SD(Ia)^2 \cdot Nla + SD(Ca)^2 \cdot NCa}{Nla + NCa}}$$

³ Instead of $SD(Ia)$ and $SD(Ca)$ we may have $SEM(Ia)$ & $SEM(Ca)$. Then we use: $SEM = \frac{SD}{\sqrt{N}}$ to convert SEM to SD .

Step4

$$SE_{effect} = \sqrt{\frac{1}{Nla} + \frac{1}{NCa}}$$

Step5

$$effect = \frac{MD}{SD}$$

Step6

$$CI95\%(effect) = effect \pm 1.96 \cdot SE_{effect}$$

Step7

$$value_error_bars = SE_{effect} \cdot 1.96$$

3.2.7. Method 6 – Continuous data

We need:

- Nla , NCa , MD and P value

Step1

$$SE_{diff}(MD) = \frac{MD}{= tinv(P, Nla + NCa - 2)}$$

Step2

$$SE_{effect} = \sqrt{\frac{1}{Nla} + \frac{1}{NCa}}$$

Step3

$$SD = \frac{SE_{diff}}{SE_{effect}}$$

Step4

$$effect = \frac{MD}{SD}$$

Step5

$$CI95\%(effect) = effect \pm 1.96 \cdot SE_{effect}$$

Step6

$$value_error_bars = SE_{effect} \cdot 1.96$$

3.2.8. Method 7 – Continuous data

We need:

- N_{Ia} , N_{Ca} and P value

Step1

$$z = \text{abs}(\text{normsin } v(P / 2))$$

Step2

$$SE_{\text{effect}} = \sqrt{\frac{1}{N_{Ia}} + \frac{1}{N_{Ca}}}$$

Step3

$$\text{effect} = z * SE_{\text{effect}}$$

Step4

$$CI95\%(\text{effect}) = \text{effect} \pm 1.96 \cdot SE_{\text{effect}}$$

Step5

$$\text{value_error_bars} = SE_{\text{effect}} \cdot 1.96$$

3.3. Summary Sheet

The outcomes for which an effect was computed are presented in this sheet (Figure 8). Details for the fields in the sheet are presented in Table V.

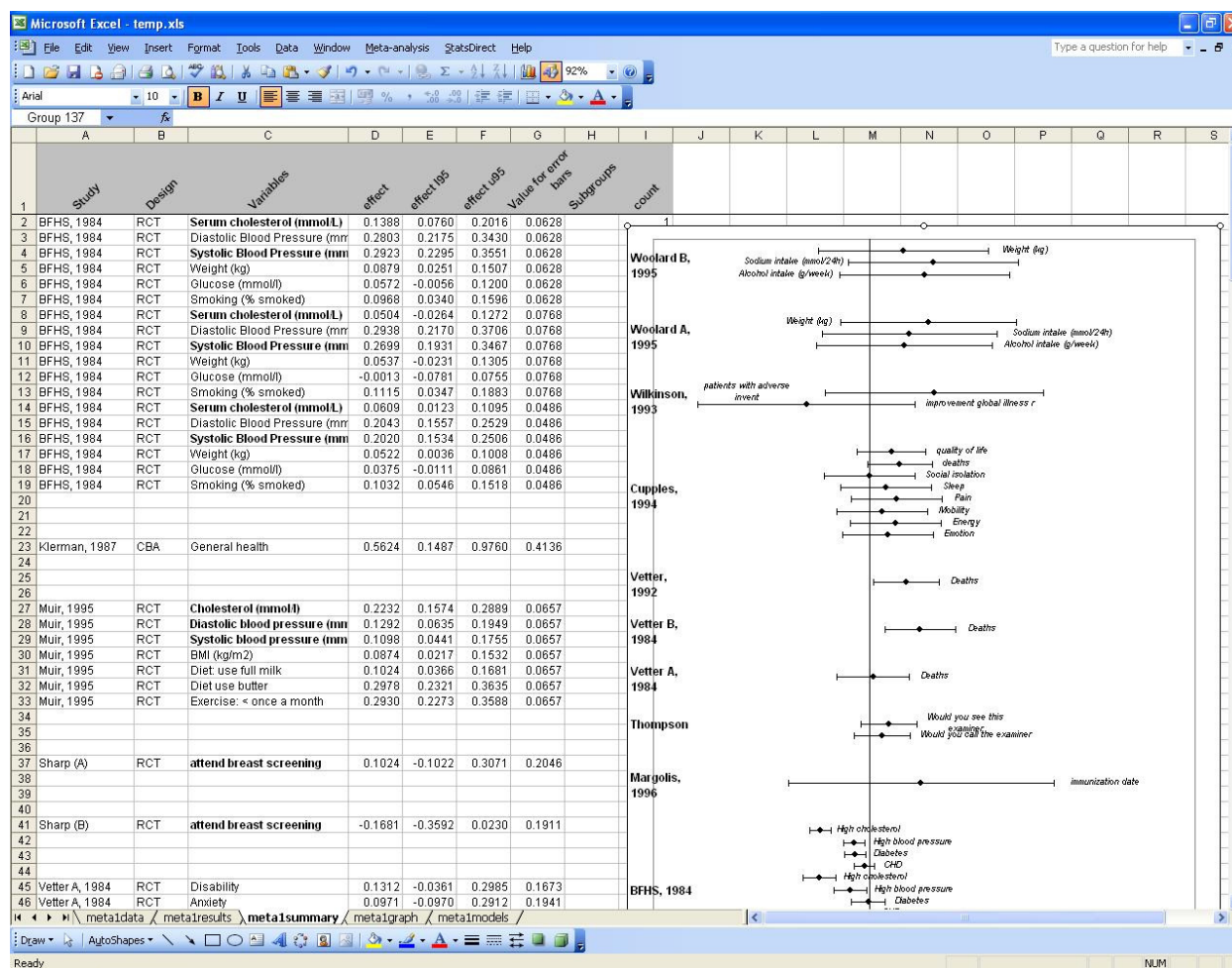


Figure 8

Primary outcomes are listed first followed by the secondary ones, grouped by study. The same style applies to the forest plot. The sheet is protected and cell values cannot be changed but data can be copied from it. The forest plot can also be selected and copied.

Field name	Information
effect	The outcome's effect, as computed by the "best" possible method
effectl95	Lower lever of the 95% CI for the effect, as computed by the "best" possible method

Field name	Information
effectu95	Upper lever of the 95% CI for the effect, as computed by the “best” possible method
value for error bars	1.96*SE as stated in the methods. Used to display the effect’s variability in the forest plot
subgroups	Displays subgroup information if any was inputted in the first data sheet
count	Counter that is used in the forest plot

Table V

3.4. Models Sheet

The last sheet calculates a single effect size and its variance for each study using the available outcomes (Figure 9).

	A	B	C	D	E	F	G	H	I	J
	Study	Effect	lower 95%CI	upper 95%CI	error bars	count				
9	Sharp (B)	-0.1681	-0.3592	0.0230	0.1911	8				
10	Thompson	0.0721	-0.0567	0.2008	0.1288	9				
11	Vetter A, 1984	0.1018	-0.0789	0.2825	0.1807	10				
12	Vetter B, 1984	0.1290	-0.0439	0.3018	0.1729	11				
13	Vetter, 1992	0.0837	-0.0845	0.2518	0.1682	12				
14	Bakx A, 1985	0.6663	0.3851	0.9474	0.2812	13				
15	Batchelor	0.1549	-0.0134	0.3232	0.1683	14				
16	Campbell A, 1998	0.1285	0.0057	0.2514	0.1228	15				
17	Cupples, 1994	0.0815	-0.0962	0.2592	0.1777	16				
18	Eckerlund	0.3842	0.1593	0.6092	0.2249	17				
19	Fall, 1997	0.3187	0.1453	0.4920	0.1734	18				
20	Mann, 1998 A	-0.0767	-0.4099	0.2565	0.3332	19				
21	Mann, 1998 B	-0.0935	-0.3032	0.1162	0.2097	20				
22	Moher, 2001	0.0489	-0.0867	0.1844	0.1355	21				
23	Mynors, 1997	0.6336	0.0658	1.2013	0.5678	22				
24	Pine, 1997	-0.1497	-0.5361	0.2367	0.3864	23				
25	Wilkinson, 1993	0.2966	-0.2054	0.7985	0.5020	24				
26	Woolard A, 1995	0.3509	-0.0535	0.7553	0.4044	25				
27	Woolard B, 1995	0.3095	-0.0828	0.7018	0.3923	26				
28										
29		mean eff	var eff	l95%CI	u95%CI					
30	FE model	0.1124	0.0003	0.0811	0.1436					
31	DL model	0.1578	0.0012	0.0891	0.2266					
32	Q model	0.1578	0.0012	0.0891	0.2266					
33	ML model	0.1732	0.0020	0.0851	0.2612					
34	PL model	0.1732	0.0020	0.0842	0.2762					
35	T-test	0.2054	0.0036	0.0812	0.3296					
36	PE method	0.1578	NA	0.0710	0.2326					

Figure 9

Each study's effect size is the median of the effect sizes of the respective outcomes, while the variance of the effect is the median of their variances. The computed values are used in various meta-analysis models in order to determine an overall effect for the intervention. For all methods (*Fixed*, *DerSimonian-Laird*, *Q*, *Maximum-Likelihood*, *Profile-Likelihood*, *Permutations* and *T-test*) an overall effect is computed along with a variance and confidence interval. References for all the used methods are provided in Table VI.

Name	Reference / Information
Fixed Effects (FE)	Brockwell SE, Gordon IR. A comparison of statistical methods for meta-analysis. <i>Stat.Med.</i> 2001; 20(6):825-840.
DerSimonian-Laird (DL)	DerSimonian R, Laird N. Meta-analysis in clinical trials. <i>Control Clin.Trials</i> 1986; 7(3):177-188
Q method (Q)	Brockwell SE, Gordon IR. A comparison of statistical methods for meta-analysis. <i>Stat.Med.</i> 2001; 20(6):825-840.
Maximum-Likelihood (ML)	Brockwell SE, Gordon IR. A comparison of statistical methods for meta-analysis. <i>Stat.Med.</i> 2001; 20(6):825-840.
Profile-Likelihood (PL)	Brockwell SE, Gordon IR. A comparison of statistical methods for meta-analysis. <i>Stat.Med.</i> 2001; 20(6):825-840.
T-test (T)	One sample t-test that compares the (median) study effects to zero. Variances of the effects are ignored.
Permutations method (PE)	Follmann DA, Proschan MA. Valid inference in random effects meta-analysis. <i>Biometrics</i> 1999; 55(3):732-737.

Table VI

A forest plot is also created that includes the individual study effects and the overall effects (Figure 10).

Finally measures of heterogeneity are displayed to help the user decide on the appropriate model for his/her analysis (Figure 11). The measures are: Cochran's Q (for p-value below α homogeneity is rejected), estimates of the between-study variance τ^2 with three methods. In addition I^2 and H_m^2 are reported (their calculation is based on the DL method)

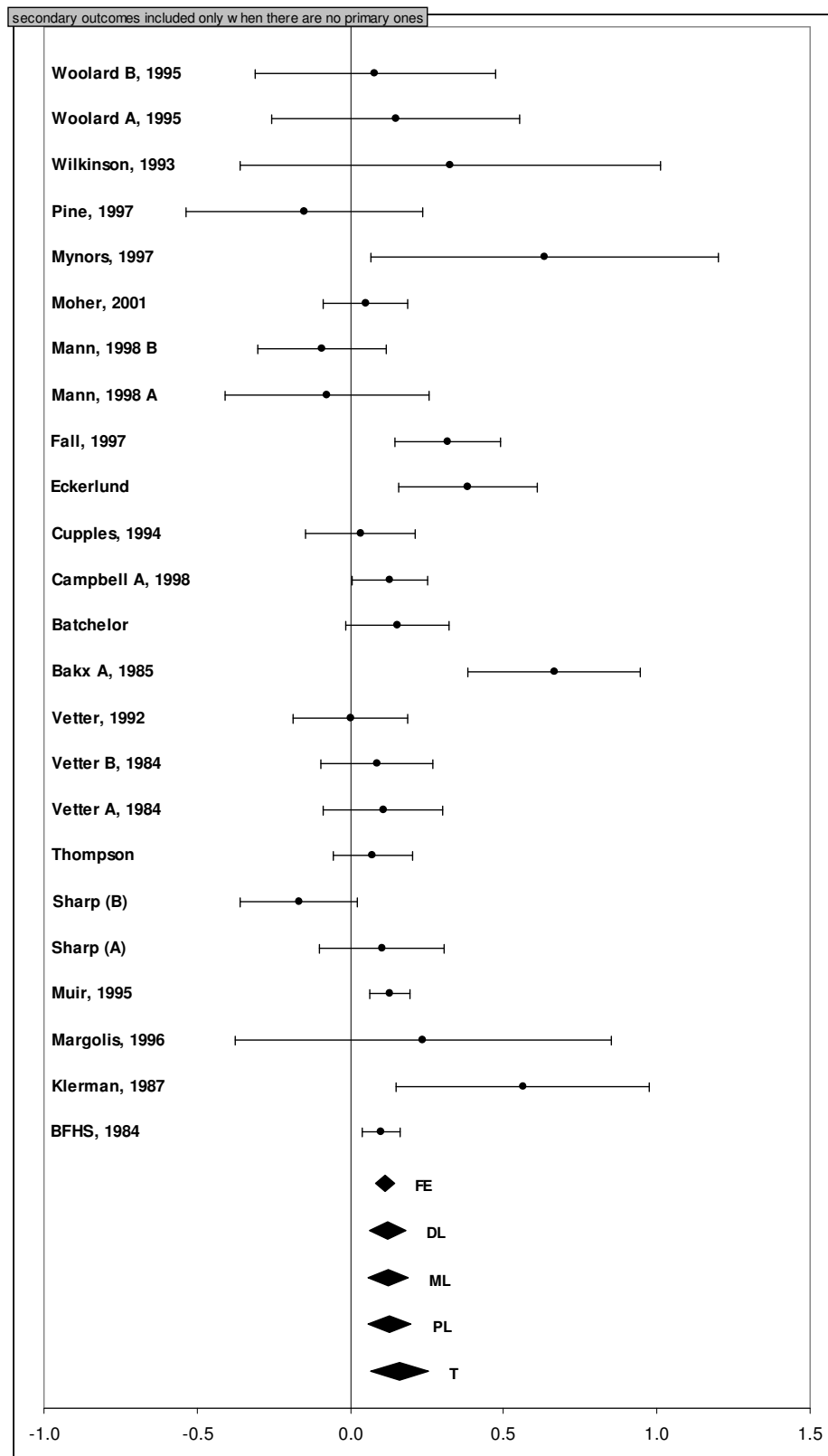


Figure 10

Heterogeneity measures			
	value	df	p-value
Cochrane Q	119.05	16	0.0000
τ^2 estimate (DL)	0.0573		
τ^2 estimate (ML)	0.0591		
τ^2 estimate (PL)	0.0813		
I^2	%86.56		
H^2_M	6.4409		

Figure 11

4. Exporting graphs

Using the *Export graph* command a user can export a selected picture (the forest plots) or range of cells (the evidence summary chart) as a Graphics Interchange Format (GIF) image. For pictures and graphs, the magnification factor can be edited to provide a better quality GIF image. The code for this command was collected from various websites and authors: Harold Staff (<http://www.mvps.org/dmccritchie/excel/xl2gif.htm>), David McRitchie, Stephen Bullen and Jon Peltier (<http://www.ac6la.com/makegif.html>).

5. Uninstall

Go to Control Panel and open add/remove programs (Figure 12). Scroll down, select the Meta-analysis add-in, click on remove and follow the instructions (Figure 13)

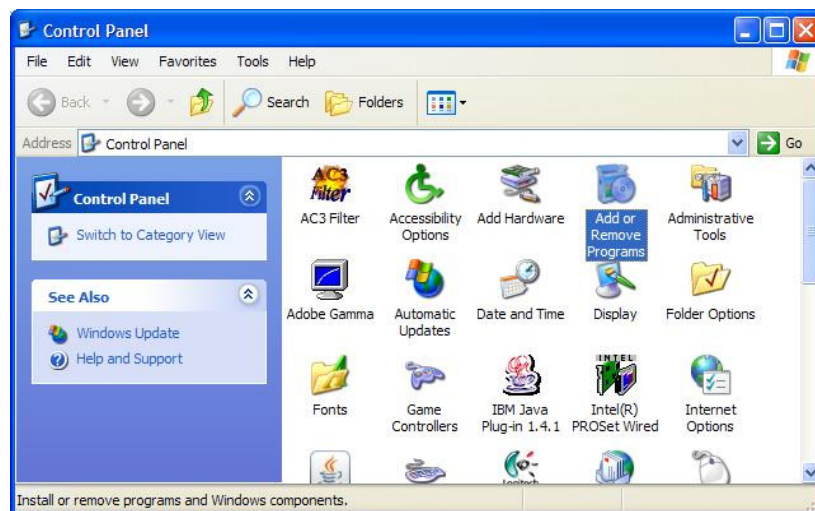


Figure 12

NPCRDC - Meta-analysis excel add-in v1.0

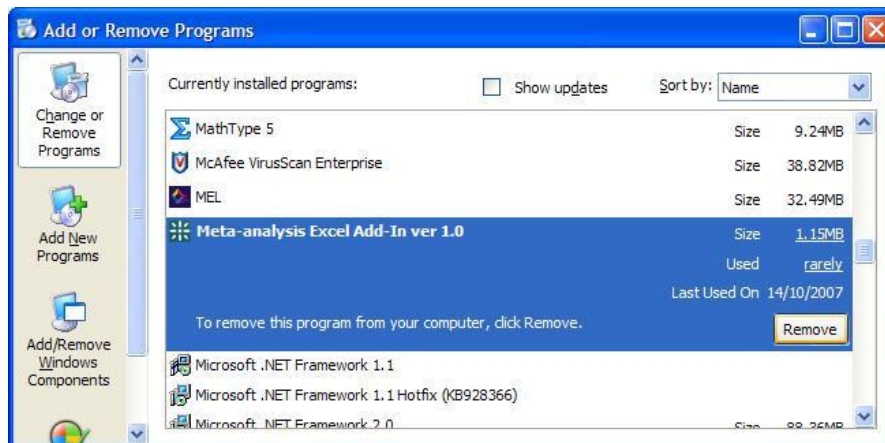


Figure 13