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1. Introduction

This file provides information on MetaEasy, a Microsoft Excel add-in for performing meta-analyses. More details on the module can be found in the technical paper in which it was described (paper available in http://www.jstatsoft.org/v30/i07 but download the software from www.statanalysis.co.uk to get the latest version). Please note that the software's main aim is to help novice meta-analysts in combining outcomes from various studies, which were disseminated in different formats. To that end dichotomous outcomes are always transformed to Standardized Mean Differences so that they can be combined with continuous outcomes.

If you want to meta-analyse only dichotomous outcomes, avoid using MetaEasy since it will introduce another degree of bias via the transformation. Finally, if you already have computed effect sizes and their standard errors, MetaEasy is not going to be of any help since its primary function is the computation of these using various methods. If MetaEasy is not right for you try RevMan which is also free (and a very good piece of software). The functions included in MetaEasy have been implemented in Stata in two commands named metaeff and metaan (type "ssc describe metaan" or "ssc describe metaeff" in STATA, for a desccription)

2. Installation

- Download an 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 metaanalysis menu will be available (Figure 1)

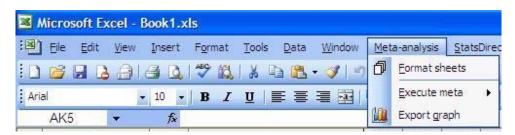


Figure 1

3. 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

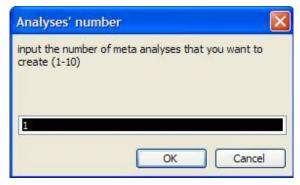


Figure 2



Figure 3

3.1. 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 4.2.

Name	Label	Туре	Required	Information
				Only needs to be inputted once for each study (in
04		0		the first outcome/variable row). If the cell
Study	The name of the study	String	Yes	background colour is set to red the row is not
				included in the analysis.
Decim	The type of the design (RTC,	Chrine er	Ne	Only needs to be inputted once for each study (in
Design	Observational study etc)	String	No	the first outcome/variable row)

Name	Label	Туре	Required	Information
				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
Variables	: Outcome variable names	: String	Yes	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
	: Intervention group size,			Not used in any of the methods, column provided
NIb	before treatment	Integer	-	for information purposes and/or future use
	: Intervention group size, after	:	:	
Nla	treatment	Integer	Yes	
	Control group size, before	:	:	Not used in any of the methods, column provided
NCb	treatment	Integer	-	for information purposes and/or future use
	Control group size, after	-	:	
NCa	treatment	Integer	Yes	
				Not used in any of the methods, column provided
N(tot)b	NIb + NCb	: Integer	-	for information purposes (certain old studies
()				provide the sum instead of the individual items)
				Not used in any of the methods, column provided
N(tot)a	Nla+NCa	Integer	-	for information purposes (certain old studies
()			•	provide the sum instead of the individual items)
	Number of events in			
lb	intervention group, after	Integer	-	Not used in any of the methods, column provided
	treatment	U		for information purposes and/or future use
	Number of events in			
la	intervention group, after	Integer	Yes* (1a,	
	treatment		: 1b)	
	Number of events in control		:	Not used in any of the methods, column provided
Cb	group, before treatment	Integer	-	for information purposes and/or future use
		:		
Ca	Number of events in control	Integer	Yes* (1a,	
UU	group, after treatment	integer	1b)	
moon(lb)	Mean effect, intervention	Back		Not used in any of the methods, column provided
mean(lb)	group, before treatment	Real	-	for information purposes and/or future use
maan(1-)	Mean effect, intervention	D. I	Yes* (3, 4,	
mean(la)	group, after treatment	Real	5, 6)	
	Mean effect, control group,			Not used in any of the methods, column provided
mean(Cb)	before treatment	Real	-	for information purposes and/or future use

Name	Label	Туре	Required	Information
mean(Ca)	Mean effect, control group,	Real	Yes* (3, 4, 5, 6)	
SD(Ia)	Standard deviation of the effect, intervention group, after treatment	Real	Yes* (4)	· · · · · · · · · · · · · · · · · · ·
SD(Ca)	Standard deviation of the effect, control group, after treatment	Real	Yes* (4)	
MD	Means difference <i>MD = mean(Ia) – mean(Ca</i>)	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)
ICI95(MD)	Lower limit of 95% Confidence Interval for the means difference.	Real	Yes* (3)	L - - - - - - - - - - - - - - - - - - -
uCl95(MD)	Upper limit of 95% Confidence Interval for the means difference.	Real	Yes* (3)	
median(la)	Median of effect, intervention group, after treatment	Real	-	Not used in any of the methods, column provided for information purposes and/or future use
median(Ca)	Median of effect, control group, after treatment	Real	-	Not used in any of the methods, column provided for information purposes and/or future use
ICI95(Ia)	Lower limit of 95% Confidence Interval for the mean of the intervention group, after treatment.	Real	Yes* (5)	
uCl95(la)	Upper limit of 95% Confidence Interval for the mean of the intervention group, after treatment.	Real	Yes* (5)	
ICI95(Ca)	Lower limit of 95% Confidence Interval for the mean of the control group, after treatment.	Real	Yes* (5)	
uCl95(Ca)	Upper limit of 95% Confidence Interval for the mean of the control group, after treatment.	Real	Yes* (5)	

Name	Label	Туре	Required	Information
	Odds ratio:	-		-
OR	$OR = \frac{Ia/(NIa - Ia)}{Ca/(NCa - Ca)}$	Real	Yes* (2)	- - - - - - - - - -
ORI95%	Lower limit of 95% Confidence Interval for after treatment Odds Ratio	Real	Yes* (2)	- - - - - - - - - - - - - - - - - - -
ORu95%	Upper limit of 95% Confidence Interval for after treatment Odds Ratio	Real	Yes* (2)	
p–value	P-value of a two way test that compares between groups	Real	Yes* (6, 7)	
t – value	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
df	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 <i>NIa</i> + <i>NCa</i> -2
SEdiff	Standard Error of Difference between the means of the two groups.	Real	Yes* (3)	- - - - - - - - - - - - - - -
direction	Direction of the effect	Char	Yes	Leave empty if effect favours intervention. Input a single minus sign to reverse effect, if it favours control
quality	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.
subgroup	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

4. Execute meta

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

Meta-analysis	StatsDirect	Help				
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<u>Execute me</u>	ta 🔸 💡	Include	all second	dary out	comes	
0 	<u></u>	Seconda	ary only v	vhen no	primary or	nes
H N	507	V		V	7	A A

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)

4.1. 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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Campber	17, 1990	NOT .	Physical											1.1276	
			Social											1.3367	
-			Role physical											2.2245	
			Role emotional					1						2.2985	
			Mental											0.7934	
			Energy			1.								0.8929	
h		8	Pain											1.1862	
			Anxiety								-			0.1658	
			Depression											0.1454	
			Chest Pain	0.1264	0.1002	-0.0364	0.2367	0.1365						510.150A	
			Course of Chest Pain getting wo	0.2233	0.2512	0.0099	0.4925	0.2413							
1			Exercise	0.1233	0.2608	0.1276	0.3940	0.1332	0.0856	0.2827	0.1150	0.4504	0.1677		
			Diet	0.1307	0.1741	0.0328	0.3153	0.1412	0.0812	0.2124	0.0532	0.3716	0.1592		
8			Smoking status (non-smoking)	0.1598	-0.0800	-0.2527	0.0927	0.1727	0.1409	-0.1370	-0.4132	0.1392	0.2762		
Cherkin, "	1996	RCT	worry (0-10)												
			bothersomeness (0-10)												
			pain control (?)												
			Function (0-23)												
			cut days												
1		v	bed days					2							
			work-loss days												
			overall score (0-100)												
			information subscale (0-100)												
			general care subscale (0-100)												
			regular exercise												
			manage next LBP												
			perceived knowledge (0-100)												
Cupples,	1994	RCT	Serum cholesterol (mmol/L)			5								0.1046	
			Diastolic Blood Pressure (mm/H											1.1735	
			Systolic Blood Pressure (mm/Hg											2.2194	
		-	BMI											0.4082	
(-	Diet (frequency of eating certain I											0.3827	
			Exersise (no of 20 min episode ;	0.7040	-0.2800	0.0472	0.2872	0.5672						0.1786	
		-	Stop Smoking	0.5249	-0.2800	-0.8472	0.2872	0.56/2							
		-	angina episodes per week											2,7551	
		5	Emotion		7			2						4.3112	
			Energy Mobility			10								2.5255	
			Pain											2.5255	
			Sleep											3.5204	
* NA	meta1deta	metal	results / meta1summary / meta1g	ranh / meta:	modek /	10		1						3.5204	
- offi	motorcate					-		1	al munul						

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

Eile Edit View	Insert Forn	nat <u>T</u> ools <u>D</u> ata <u>W</u> indow <u>M</u> eta-	analysis <u>S</u> t	atsDirect <u>H</u> elp)			Type a question for help 🚽 🚽 🗗
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8 Campbell A, 1998	RCT	General	YES		3	la, Ca	la, Ca	OR, OR_L95%, OR_u9(SD(la), SD(CLCl95(la), u_Cl95(la), LCl95(Ca), u_Cl95(Ca)
9	-	Physical	YES	-	3	la, Ca	la, Ca	OR, OR_I_95%, OR_u_9(SD(la), SD(CI_Cl95(la), u_Cl95(la), I_Cl95(Ca), u_Cl95(Ca)
0	-	Social	YES		3	la, Ca	la, Ca	OR, OR L 95%, OR u 95 SD(la), SD(CLCI95(la), u CI95(la), L CI95(Ca), u CI95(Ca)
2	2	Role physical Role emotional	YES		3	la, Ca la, Ca	la, Ca la, Ca	OR, OR_I_95%, OR_u_9(SD(a), SD(CI_CI95(la), u_CI95(la), I_CI95(Ca), u_CI95(Ca) OR, OR_I_95%, OR_u_9(SD(la), SD(CI_CI95(la), u_CI95(la), I_CI95(Ca), u_CI95(Ca)
3		Mental	YES		3	la, Ca la, Ca	la, Ca	OR, OR_195%, OR_0.95 SD(la), SD(C1_Cl95(la), U_Cl95(la), I_Cl95(Ca), U_Cl95(Ca), OR_0.95 (Ca), U_Cl95(Ca), U_Cl95(
4	8	Energy	YES		3	la, Ca	la, Ca	OR, OR I 95%, OR u 95 SD(la), SD(CI Cl95(la), u Cl95(la), I Cl95(Ca), u Cl95(Ca)
5	8	Pain	YES	-	3	la, Ca	la, Ca	OR, OR I 95%, OR u 95 SD(la), SD(CI Cl95(la), u Cl95(la), I Cl95(Ca), u Cl95(Ca)
6		Anxiety	YES	YES	3	la, Ca	la, Ca	OR, OR I 95%, OR u 95 SD(la), SD(CI Cl95(la), u Cl95(la), I Cl95(Ca), u Cl95(Ca)
7	1	Depression	YES	YES	3	la, Ca	la, Ca	OR, OR I 95%, OR u 95 SD(la), SD(CI Cl95(la), u Cl95(la), I Cl95(Ca), u Cl95(Ca)
8		Chest Pain	YES	YES	1a			OR, OR I 9((MD, I CI95 SD(Ia), SD(CMD, I CI95(I MD
9		Course of Chest Pain getting wo	YES	YES	1a			OR, OR [94 (MD, I_CI95] SD(Ia), SD(CMD, I_CI95(I MD
0		Exercise	YES		2			(MD, I_CI95]SD(Ia), SD(CMD, I_CI95(I MD
1		Diet	YES		2			(MD, I_CI95_SD(Ia), SD(CMD, I_CI95(I MD
2	S.	Smoking status (non-smoking)	YES		2			(MD, I_CI95_SD(Ia), SD(CMD, I_CI95(I MD
3 Cherkin, 1996	RCT	worry (0-10)				la, Ca	la, Ca	OR, OR_I_9((I_CI95_MD, SD(Ia), SD(CI_CI95(Ia), u_p p
4		bothersomeness (0-10)				la, Ca	la, Ca	OR, OR_I_9!(I_CI95_MD, SD(Ia), SD(CI_CI95(Ia), u_p p
5	-	pain control (?)				la, Ca	la, Ca	OR, OR_I_9((I_CI95_MD, SD(Ia), SD(CI_CI95(Ia), u_p p
6 7	-	Function (0-23)				la, Ca	la, Ca	OR, OR_L9((_Cl95_MD, SD(la), SD(Cl_Cl95(la), u p p
8		cut days bed days						, la Nia, NCa, Ol (Nia, NCa, L_Nia, NCa, S[Nia, NCa, L_Nia, NCa, p_Nia, NCa, p_ , la Nia, NCa, Ol (Nia, NCa, INia, NCa, S[Nia, NCa, I] (Nia, NCa, p_Nia, NCa, p_
9		work-loss days						, la Nia, NCa, Ol (Nia, NCa, I_Nia, NCa, St Nia, NCa, I_Nia, NCa, p_Nia, NCa, p_ , la Nia, NCa, Ol (Nia, NCa, I_Nia, NCa, St Nia, NCa, I_Nia, NCa, p_Nia, NCa, p_
0	8	overall score (0-100)				la, Ca	la, Ca	OR, OR I 9: (I Cl95 MD, SD(la), SD(CI Cl95(la), u p p
1	10	information subscale (0-100)		-		la, Ca	la, Ca	OR, OR I 9! (I CI95 MD, SD(Ia), SD(CI CI95(Ia), u p p
2		general care subscale (0-100)				la, Ca	la, Ca	OR, OR_L9!(I_CI95_MD, SD(la), SD(CI_CI95(la), u p p
3	1	regular exercise				la, Ca	la, Ca	OR, OR I 9((I CI95 MD, SD(Ia), SD(CI CI95(Ia), u p p
4		manage next LBP				la, Ca	la, Ca	OR, OR I 9((I CI95 MD, SD(Ia), SD(CI CI95(Ia), u p p
5		perceived knowledge (0-100)				la, Ca	la, Ca	OR, OR [9/(I_CI95_MD, SD(Ia), SD(CI_CI95(Ia), u p p
6 Cupples, 1994	RCT	Serum cholesterol (mmol/L)	YES	YES	3	la, Ca	la, Ca	OR, OR_I_95%, OR_u_95SD(la), SD(CI_Cl95(la), u]p p
7		Diastolic Blood Pressure (mm/H	YES	YES	3	la, Ca	la, Ca	OR, OR_I_95%, OR_u_95SD(la), SD(CI_Cl95(la), u_p p
8	S.	Systolic Blood Pressure (mm/Hg	YES	YES	3	la, Ca	la, Ca	OR, OR_I_95%, OR_u_95SD(la), SD(CI_Cl95(la), u]p p
9		BMI	YES	YES	3	la, Ca	la, Ca	OR, OR_I_95%, OR_u_9(SD(Ia), SD(CI_CI95(Ia), u_p p
	-	Diet (frequency of eating certain	YES		3	la, Ca	la, Ca	OR, OR_I_95%, OR_u_9(SD(la), SD(CI_Cl95(la), u_p p
2		Exersise (no of 20 min episode :	YES		3	la, Ca	la, Ca	OR, OR I 95%, OR u 95 SD(la), SD(CI_CI95(la), u_CI95(la), I_CI95(Ca), u_CI95(Ca)
3	-	Stop Smoking	YES	-	1a	NIL NO.	I. NIL NO.	OR, OR_L9(MD, I_CI95_SD(Ia), SD(CMD, I_CI95(I MD, p p
4		angina episodes per week	YES	YES	3			Ia Nia, NCa, Ol (Nia, NCa) CNia, NCa, SI Nia, NCa, I_INia, NCa, p_Nia, NCa, p_
5		Emotion Energy	YES	YES	3	la, Ca la, Ca	la, Ca la, Ca	OR, OR_I_95%, OR_u_95D(la), SD(CI_CI95(la), u_p p OR, OR_I 95%, OR_u_95D(la), SD(CI_CI95(la), u_p p
6	2	Mobility	YES	YES	3	la, Ca la, Ca	la, Ca	OR, OR 1 95%, OR u 95 D(la), SD(CI Cl95(la), u Cl95(la), I Cl95(Ca), u Cl95(Ca)
7		Pain	YES	YES	3	la, Ca la, Ca	la, Ca	OR, OR I 95%, OR u 95 D(la), SD(CI Cl95(la), u Cl95(la), I Cl95(Ca), u Cl95(Ca)
B		Sleep	YES	YES	3	la, Ca	la, Ca	OR, OR I 95%, OR u 95 SD(la), SD(CI Cl95(la), u p p
	· · · · · · · · · · · · · · · · · · ·	sults / meta1summary / meta1c			· -			

Figure 6

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Figure 7

4.2. 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 - <u>http://www.cochrane.org/resources/handbook/</u>.

Method	Data type	Input needed	Effect Estimate Measure
1a	Dichotomous	NIa and NCa and Ia and Ca	Risk Difference
1b	Dichotomous	NIa and NCa and Ia and Ca	Odds Ratio
2	Dichotomous	NIa and NCa and OR and CI95%(OR)	Odds Ratio
3	Continuous	NIa and NCa and MD and (CI95%(MD) or SEdiff(m))	Mean Difference
4	Continuous	NIa and NCa and MD and SD(Ia) and SD(Ca)	Mean Difference
5	Continuous	NIa and NCa and MD and CI95%(mean _{la}) and CI95%(mean _{Ca})	Mean Difference
6	Continuous	<i>NIa</i> and <i>NCa</i> and <i>MD</i> and (<i>P</i> or (<i>T</i> and <i>DF</i>))	Mean Difference
7	Continuous	NIa and NCa and (P or (T and DF))	Any

Table III

Where:

- *NIa* is the size of the intervention group.
- *NCa* is the size of the control group.
- *Ia* is the number of events in the intervention group (always stands that *Ia*<*NIa*).
- Ca is the number of events in the control group (always stands that Ca<NCa).

• OR is the Odds Ratio
$$(OR = \frac{Ia/(NIa - Ia)}{Ca/(NCa - Ca)}).$$

- CI95%(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).
- *CI95%(MD)* is the 95% Confidence Interval for the means difference.

- *SEdiff(m)* is the Standard Error of Difference between the means of the two groups.
- *SD(la)* is the Standard Deviation for the intervention group.
- *SD(Ca)* is the Standard Deviation for the control group.
- Cl95%(mean_{la}) is the 95% Confidence Interval for the mean of the intervention group.
- *Cl95%(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.

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

We need:

• Nla, NCa, la, Ca

Step1

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

Step2

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

Step3

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

Step4

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

Step5

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

Step6

value _ error _ bars = $SE_{effect} \cdot 1.96$

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

We need:

• Nla, NCa, la, Ca

Step1

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

Step2

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

Step3

¹ There are some cases where NIa = Ia or NCa = Ca and therefore the Odds Ratio cannot be computed.

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

 $lowerCl95\%(Q) = Q - 1.96 \cdot SE_{diff}(Q)$

Step4

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

Step5

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

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

Step6

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

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

_

We need:

• NIa, NCa, OR, CI95%(OR)

Step1

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

$$upperCI95\%(SMD) = \frac{\sqrt{3}}{\pi} \ln(upperCI95\%(OR))$$
$$lowerCI95\%(SMD) = \frac{\sqrt{3}}{\pi} \ln(lowerCI95\%(OR))$$

Step2

$$SE_{effect} = \frac{upperCl95\%(SMD) - lowerCl95\%(SMD)}{3.92} \text{ when } Nla \ge 60 \& NCa \ge 60$$

(when sample size is small: $SE_{effect} = \frac{upperCl95\%(SMD) - lowerCl95\%(SMD)}{= 2 \cdot tinv(1 - 0.95, Nla + NCa - 2)}$

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

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

Step5

value_error_bars = $SE_{effect} \cdot 1.96$

4.2.4. Method 3 – Continuous data

We need:

 NIa, NCa, Mean Difference (MD) and Confidence Interval for the mean difference CI95%(MD)²

Step1

$$SE_{diff}(MD) = \frac{upperCI95\%(MD) - lowerCI95\%(MD)}{3.92} \text{ when } NIa \ge 60 \& NCa \ge 60$$

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

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

Step2

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

Step3

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

Step4

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

Step5

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

Step6

value_error_bars = $SE_{effect} \cdot 1.96$

4.2.5. Method 4 – Continuous data

We need:

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

Step1

$$SD = \sqrt{\frac{SD(Ia)^2 \cdot (NIa - 1) + SD(Ca)^2 \cdot (NCa - 1)}{NIa + NCa - 2}}$$

Step2

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

Step3

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

Step4

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

Step5

value_error_bars = $SE_{effect} \cdot 1.96$

4.2.6. Method 5 - Continuous data

We need:

• NIa, NCa, MD, CI(Ia), CI(Ca)

Step1

$$SD(Ia) = \sqrt{NIa} \cdot \frac{upperCl95\%(Ia) - lowerCl95\%(Ia)}{3.92}$$
 if $NIa \ge 60$
(if $NIa < 60$ then $SD(Ia) = \sqrt{NIa} \cdot \frac{upperCl95\%(Ia) - lowerCl95\%(Ia)}{= 2 \cdot tinv(1 - 0.95, NIa - 1)}$

Step2

$$SD(Ca) = \sqrt{NCa} \cdot \frac{upperCl95\%(Ca) - lowerCl95\%(Ca)}{3.92} \quad \text{if } NCa \ge 60$$

(if $NCa < 60$ then $SD(Ca) = \sqrt{NCa} \cdot \frac{upperCl95\%(Ca) - lowerCl95\%(Ca)}{= 2 \cdot tinv(1 - 0.95, NCa - 1)}$

Step3

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*.

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

Step4

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

Step5

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

Step6

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

Step7

value _ error _ bars = $SE_{effect} \cdot 1.96$

4.2.7. Method 6 - Continuous data

We need:

• NIa, NCa, MD and P value

Step1

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

Step2

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

Step3

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

Step4

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

Step5

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

Step6

value_error_bars = $SE_{effect} \cdot 1.96$

4.2.8. Method 7 – Continuous data

We need:

• Nla, NCa and P value

Step1

z = abs(normsinv(P/2))

Step2

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

Step3

effect = $z * SE_{effect}$

Step4

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

Step5

 $value_error_bars = SE_{effect} \cdot 1.96$

4.3. 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.

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BFHS, 1984	RCT	Serum cholesterol (mmol/L)	0.1388	0.0760	0.2016	0.0628	9 1			10	-0		()			
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BFHS, 1984	RCT	Systolic Blood Pressure (mm Weight (kg)	0.2923	0.0251	0.3551	0.0628	Woolard B,		alve (mmol/24h) ⊨	1.0	+	1 200	1			
BFHS, 1984	RCT	Glucose (mmol/l)	0.0879	-0.0056	0.1307	0.0628	1995	Alcohol inta	ke (g/week) 🛏	-	•					
BFHS, 1984	RCT	Smoking (% smoked)	0.0968	0.0340	0.1596	0.0628				1						
BFHS, 1984	RCT	Serum cholesterol (mmol/L)	0.0504	-0.0264	0.1330	0.0768				1						
BFHS, 1984	RCT	Diastolic Blood Pressure (mm	0.2938	0.2170	0.3706	0.0768	Woolard A,		Weight (kg)				odium intake	(mmol/24h)		
BFHS, 1984	RCT	Systolic Blood Pressure (mm		0.1931	0.3467	0.0768	1995		1	- •		Alc	ohol intake (g.	/week)		
BFHS, 1984	RCT	Weight (kg)	0.0537	-0.0231	0.1305	0.0768										
BFHS, 1984	RCT	Glucose (mmol/l)	-0.0013	-0.0781	0.0755	0.0768				1						
BFHS, 1984	RCT	Smoking (% smoked)	0.1115	0.0347	0.1883	0.0768	Wilkinson,	patients with advers invent	* —	-	•					
BFHS, 1984	RCT	Serum cholesterol (mmol/L)	0.0609	0.0123	0.1095	0.0486	1993	arrent	•	-	→ improven	ent global illne	55 r			
BFHS, 1984	RCT	Diastolic Blood Pressure (mm	0.2043	0.1557	0.2529	0.0486	9000			1						
BFHS, 1984	RCT	Systolic Blood Pressure (mm	0.2020	0.1534	0.2506	0.0486					100 K217+1+4	- Taken of				
BFHS, 1984	RCT	Weight (kg)	0.0522	0.0036	0.1008	0.0486			1	•	quality					
BFHS, 1984	RCT	Glucose (mmol/l)	0.0375	-0.0111	0.0861	0.0486			-	+	deati					
BFHS, 1984	RCT	Smoking (% smoked)	0.1032	0.0546	0.1518	0.0486	Cupples,		- E-	+	Slee	0				
							1994		_ ⊢		Pi Mobili					
									-		- En	ergy				
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Klerman, 198	7 CBA	General health	0.5624	0.1487	0.9760	0.4136										
							Vetter,									
		-					1992					aths				
Muir, 1995	RCT	Cholesterol (mmol/l)	0.2232	0.1574	0.2889	0.0657	1002			1						
Muir, 1995 Muir, 1995	RCT	Diastolic blood pressure (mn	0.1292	0.0635	0.1949	0.0657	Vetter B.					D - 11 -				
Muir, 1995	RCT	Systolic blood pressure (mm	0.1098	0.0441	0.1345	0.0657	1984			<u> </u>	•	Deaths				
Muir, 1995 Muir, 1995	RCT	BMI (kg/m2)	0.0874	0.0217	0.1532	0.0657				1						
Muir, 1995	RCT	Diet: use full milk	0.1024	0.0366	0.1681	0.0657	Vetter A,		14		- Deaths					
Muir, 1995	RCT	Diet use butter	0.2978	0.2321	0.3635	0.0657	1984			100	- Ceatris					
Muir, 1995	RCT	Exercise: < once a month	0.2930	0.2273	0.3588	0.0657				1						
							Thomas				Would yo	u see this				
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Sharp (A)	RCT	attend breast screening	0.1024	-0.1022	0.3071	0.2046				1						
							Margolis,		·	-	•			immunization dat	e	
							1996			1						
										1						
Sharp (B)	RCT	attend breast screening	-0.1681	-0.3592	0.0230	0.1911			High							
									H		od pressure					
									H.	→ Liabetes						
V-H 0 400-	DOT	Dischille	0.4.04.0	0.0001	0.0005	0.4070			Hal	t cholesterol						
Vetter A, 1984	RCT	Disability	0.1312		0.2985	0.1673	BFHS, 1984		⊢+	High blo	od pressure ibetes					
Vetter A, 1984		Anxiety		-0.0970	0.2912	0.1941			H	- <u>Cia</u>	ine:62					_
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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	1.96*SE as stated in the methods. Used to display the effect's variability in the
bars	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

4.4. Models Sheet

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

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1	Stu	4hr	10r	Nor	ST.	cov					
9	Sharp (B)	-0.1661	-0.3592	0.0230	0.1911	8		Woola	ard A, 1995	5	
	Thompson	0.0721		0.2008							
11	and the second	0.1018				a la contra de la		20000000000			
12	Vetter B, 1984	0.1290				and the second se		Wilkir	nson, 1993		
13	Vetter, 1992	0.0837		0.2518					Pine, 1997		
14	Bakx A, 1985	0.6663	0.3851	0.9474		1		212111			
	Batchelor	0.1549	-0.0134	0.3232				Pine,			
16	Campbell A, 1998	0.1285		0.2514		3.5.5.6					
17	Cupples, 1994	0.0815			0.1777			1922	Mynors, 1997		
18	Eckerlund	0.3842	0.1593	0.6092	0.2249	17		Myno			
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			2004		
21	Mann, 1998 B	-0.0935	-0.3032	0.1162	0.2097		N	Mon	Moher, 2001		
22	Moher, 2001	0.0489	-0.0867	0.1844	0.1355	21	- La				
23	Mynors, 1997	0.6336	0.0658	1.2013	0.5678	22		Manu	n, 1998 B		
24	Pine, 1997	-0.1497	-0.5361	0.2367	0.3864	23		Mann	I, 1990 D		
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		Mann	, 1998 A		
27	Woolard B, 1995	0.3095	-0.0828	0.7018	0.3923	26		walli	, 1330 A		
28											
29		mean eff	var eff	195%CI	u95%Cl			Fall	1997		
30	FE model	0.1124	0.0003	0.0811	0.1436			ran,	Fall, 1997		
	DL model	0.1578	0.0012	0.0891	0.2266						
32	Q model	0.1578	0.0012	0.0891	0.2266	i		Ecke	rlund		
33	ML model	0.1732	0.0020	0.0851	0.2612	1		Lono	Levenung		
34	PL model	0.1732	0.0020	0.0842	0.2762						
35	T-test	0.2054	0.0036	0.0812	0.3296	1		Cupr	oles, 1994		
	PE method	0.1578	NA	0.0710	0.2326	1			cuppies, 1554		
33 34 35	ML model PL model T-test PE method	0.1732 0.1732 0.2054	0.0020 0.0020 0.0036	0.0851 0.0842 0.0812	0.2612 0.2762 0.3296						

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*, *DerSimonial-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. Note that the Permutations method, in order to save on computational time, uses a randomisation method when the number of studies is above 10. Therefore results may be slightly different for its CIs from one execution to the next.

Name	Reference / Information						
Fixed Effects (EE)	Brockwell SE, Gordon IR. A comparison of statistical methods for						
Fixed Effects (FE)	meta-analysis. Stat.Med. 2001; 20(6):825-840.						
DerSimonial-Laird	DerSimonian R, Laird N. Meta-analysis in clinical trials. Control						
(DL)	<i>Clin.Trials</i> 1986; 7(3):177-188						
	Brockwell SE, Gordon IR. A comparison of statistical methods for						
Q method (Q)	meta-analysis. Stat.Med. 2001; 20(6):825-840.						
Maximum-	Brockwell SE, Gordon IR. A comparison of statistical methods for						
Likelihood (ML)	meta-analysis. Stat.Med. 2001; 20(6):825-840.						
Profile-Likelihood	Brockwell SE, Gordon IR. A comparison of statistical methods for						
(PL)	meta-analysis. Stat.Med. 2001; 20(6):825-840.						
T toot (T)	One sample t-test that compares the (median) study effects to zero.						
T-test (T)	Variances of the effects are ignored.						
Permutations	Follmann DA, Proschan MA. Valid inference in random effects meta-						
method (PE)	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). The study weights in the graph relate to the fixed effects model, even though diamonds for all methods have been included. It should be noted however that the appropriate weights have been used in the calculations for the other models, despite the apparent discrepancy in the graph (weights are much more uniform for the RE models). This plot was created purely for information purposes and 'prettier'/publishable forest plots can be obtained in other application (i.e. RevMan, STATA).

Finally measures of heterogeneity are displayed to help the user decide on the appropriate model for his/her analysis (Figure 11). The measures are: Cochrane'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 $H^2_{\scriptscriptstyle M}$ (i.e. $H^2 - 1$ and in the $(0, +\infty)$ range) are reported (their calculation is based on the DL method)

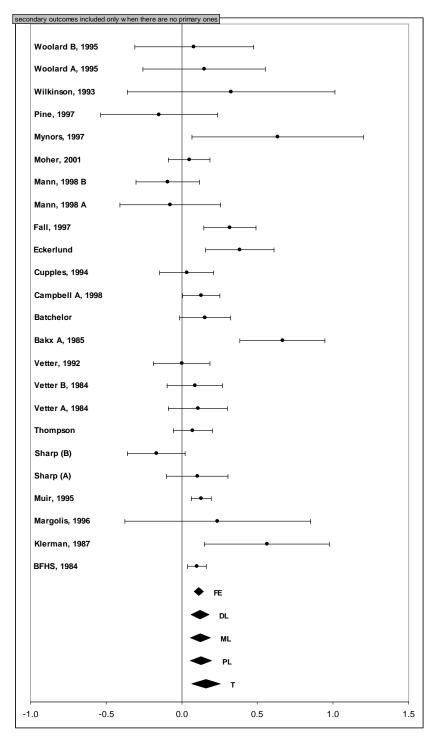


Figure 10

Heterogeneity mea								
	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							
²	%86.56							
H ² _M	6.4409							
Figure 11								



5. 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 (<u>http://www.mvps.org/dmcritchie/excel/xl2gif.htm</u>), David McRitchie, Stephen Bullen and Jon Peltier (<u>http://www.ac6la.com/makegif.html</u>). Currently only the GIF format is offered as an export option but we will consider adding more coding options if suggested by user feedback.

6. Uninstall

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

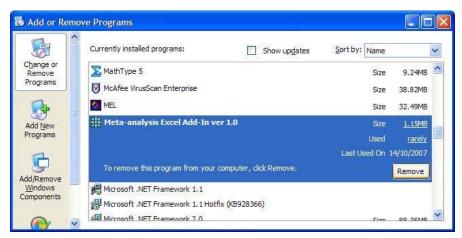


Figure 12