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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 metaanalysis 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 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.

	/
Only needs to be inputted once for each s	tudy (in
Study The name of the study String Yes	
background colour is set to red the row is	not
included in the analysis.	
The type of the design (RTC, String No. Only needs to be inputted once for each s	tudy (in
Observational study etc) String No the first outcome/variable row)	
Will be truncated to 28 characters in grap	ns. If the
cell background colour is set to <mark>yellow</mark> the	row is
not included in the analysis. The font style	s used
( <b>bold</b> , <i>italics</i> , normal) are carried over to t	ne result
Variables Outcome variable names String Yes sheets. It is advised to set power outcome	names
in bold and secondary outcomes ones in i	alics.
Outcomes with names in italics are plotter	ł
separately in the outcomes scatter plot. N	o action
has be set for bold font style names	
Nub Intervention group size, Not used in any of the methods, column p	rovided
before treatment for information purposes and/or future use	!
Alla	
treatment	
Control group size, before Not used in any of the methods, column p	rovided
treatment for information purposes and/or future use	!
Control group size, after	
treatment	
Not used in any of the methods, column p	rovided
N(tot)b NIb + NCb Integer - for information purposes (certain old studi	es
provide the sum instead of the individual i	ems)
Not used in any of the methods, column p	rovided
N(tot)a Nla + NCa Integer - for information purposes (certain old studi	es
provide the sum instead of the individual i	ems)

Name	Label	Туре	Required	Information
lb	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
la	Number of events in intervention group, after treatment	Integer	Yes* (1a, 1b)	
Cb	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
Ca	Number of events in control group, after treatment	Integer	Yes* (1a, 1b)	
mean(lb)	Mean effect, intervention group, before treatment	Real	-	Not used in any of the methods, column provided for information purposes and/or future use
mean(la)	Mean effect, intervention group, after treatment	Real	Yes* (3, 4, 5, 6)	
mean(Cb)	Mean effect, control group, before treatment	Real	-	Not used in any of the methods, column provided for information purposes and/or future use
mean(Ca)	Mean effect, control group, after treatment	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)	
uCl95(MD)	Upper limit of 95% Confidence Interval for the means difference.	Real	Yes* (3)	
median(Ia)	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

Name	Label	Туре	Required	Information
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 intervention group, after treatment.	Real	Yes* (5)	
uCl95(Ca)	Upper limit of 95% Confidence Interval for the mean of the intervention group, after treatment.	Real	Yes* (5)	
OR	Odds ratio: $OR = \frac{la/(Nla - la)}{Ca/(NCa - Ca)}$	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

Name	Label	Туре	Required	Information				
				Evaluation of each study (only needs to be inputted				
quality	Quality of the study	Integer	No	once for each study). For future use and				
				information purposes only.				
cubaroup	Subgroup information for an	Ctring	No	Information on subgroup outcomes. They are used				
subgroup	outcome	String	NO	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.

Meta-analysis StatsDire	t <u>H</u> elp
D Eormat sheets	X   🛄 📣 100% 👻 🕜 💂
Execute meta +	Include all secondary outcomes
	Secondary only when no primary ones

#### 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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Sinoking status (nor-smoking)         0.1598         0.0600         0.252         0.172/         0.1409         0.1410         0.1412 </td <td>121</td> <td></td> <td></td> <td>Diet</td> <td>0.1307</td> <td>0.1741</td> <td>0.0328</td> <td>0.3153</td> <td>0.1412</td> <td>0.0812</td> <td>0.2124</td> <td>0.0532</td> <td>0.3716</td> <td>0.1592</td> <td></td> <td></td>	121			Diet	0.1307	0.1741	0.0328	0.3153	0.1412	0.0812	0.2124	0.0532	0.3716	0.1592		
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34       manage next LBP  <	133		)	regular exercise												
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41         Exercise (no of 20 min episode)         0         0         0         0         0.1766         0           42         Stop Smoking         0.5249         -0.2800         -0.8472         0.5672         0.5672         0         -	140	1		Diet (frequency of eating certain I											0.3827	0.
42         Stop Smoking         0.5249         -0.2800         -0.8472         0.2672         0.5672 <th< th=""> <th< th=""> <th< td=""><td>141</td><td></td><td></td><td>Exersise (no of 20 min episode )</td><td></td><td></td><td></td><td></td><td>8</td><td></td><td></td><td></td><td></td><td></td><td>0.1786</td><td>0.</td></th<></th<></th<>	141			Exersise (no of 20 min episode )					8						0.1786	0.
A3         angina episodes per week <th< th=""> <th< th="">          &lt;</th<></th<>	142			Stop Smoking	0.5249	-0.2800	-0.8472	0.2872	0.5672							
44         Emotion         2.7551         0.           45         Energy         45	143			angina episodes per week												
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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)

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A	В	C	AZ	BA	BB	BC	BD	BE	BF	BG BH	BI	BJ	BK 🔨
1	ie -								Missing data from	method			
2 5 <sup>10</sup> 0 <sup>1</sup>	Desig	S Valuples	calculated b	tevelsed affect?	method	× ×*	10 00	<u>م</u>	5 1.95% OF 11.95SD		5 11 CI95(b)	<u></u>	195(Ca)
100 Campbell A, 1996	RUI	Physical	VES		3	la Ca	la Ca		195% OR # 94SD	(ia), SD(CL_CI95(ia) (ia), SD(CL_CI95(ia)	u_Cl95(la)	_CI95(Ca), u_C	195(Ca)
110	-	Social	YES		3	la Ca	la Ca	OR OR	195% OR # 950	(la), SD(CL_CI95(la) (la), SD(CL_CI95(la)	u_Cl95(la)	CI95(Ca), uC	:195(Ca)
111		Bole physical	YES		3	la Ca	la Ca	OR OR	1.95% OR 11.94SD	(la) SD(CLCI95(la)	u Cl95(la)	CI95(Ca) II C	:195(Ca)
112		Role emotional	YES		3	la. Ca	la, Ca	OR, OR	1 95%, OR u 95SD	(la), SD(CI CI95(la)	u Cl95(la), I	CI95(Ca). u C	195(Ca)
113		Mental	YES		3	la, Ca	la, Ca	OR, OR	1 95%, OR u 95SD	(la), SD(CI_CI95(la)	. u Cl95(la), l	CI95(Ca), u C	:195(Ca)
114	1	Energy	YES		3	la, Ca	la, Ca	OR, OR	1 95%, OR u 95SD	(la), SD(CI CI95(la)	u Cl95(la), l	CI95(Ca), u C	195(Ca)
115		Pain	YES		3	la, Ca	la, Ca	OR, OR	1 95%, OR u 95SD	(la), SD(CI CI95(la)	, u Cl95(la), l	CI95(Ca), u C	195(Ca)
116		Anxiety	YES	YES	3	la, Ca	la, Ca	OR, OR	1 95%, OR u 95SD	(la), SD(CI Cl95(la)	u Cl95(la), l	CI95(Ca), u C	195(Ca)
117	)	Depression	YES	YES	3	la, Ca	la, Ca	OR, OR	1 95%, OR u 95SD	(la), SD(CI_Cl95(la)	, u Cl95(la), l	CI95(Ca), u C	:195(Ca)
118		Chest Pain	YES	YES	1a			OR, OR	1_94 (MD, 1_CI95_SD	(la), SD(CMD, I_CIS	5(I MD		
119		Course of Chest Pain getting wo	YES	YES	1a			OR, OR	1_9(MD, 1_CI95_SD	(Ia), SD(CMD, I_CI9	5(I MD		
120	-	Exercise	YES		2				(MD, I_CI95_SD	(la), SD(CMD, I_CI9	5(I MD		
121		Diet	YES		2				(MD, I_CI95_SD	(la), SD(CMD, I_CI9	5(I MD		
122	2	Smoking status (non-smoking)	YES		2				(MD, I_CI95_SD	(Ia), SD(CMD, I_CI9	6(I MD		
123 Cherkin, 1996	RCT	worry (0-10)				la, Ca	la, Ca	OR, OR	_I_9! (I_CI95_MD, SD	(la), SD(CI_Cl95(la)	, u_p	р	
124		bothersomeness (0-10)				la, Ca	la, Ca	OR, OR	_I_9! (I_CI95_MD, SD	(la), SD(CI_Cl95(la)	, u_p	р	
125		pain control (?)				la, Ca	la, Ca	OR, OR	_I_9{(I_Cl95_MD, SD	(la), SD(CI_Cl95(la)	,u_p	р	
126		Function (0-23)				la, Ca	la, Ca	OR, OR	_I_94 (I_CI95_MD, SD	(la), SD(CI_Cl95(la)	, u_p	р	
127		cut days				Nla, NCa	, la Nia, NCa	i, la Nla, NCa	a, Ol (Nia, NCa, I_Nia	, NCa, SENIa, NCa,	I_INIa, NCa,	p Nla, NCa, p	
128		bed days				Nla, NCa	, la Nla, NCa	i, la Nla, NCa	i, Ol (Nia, NCa, I_Nia	, NCa, SENIa, NCa,	I_INIa, NCa,	p NIa, NCa, p	<u></u>
129		work-loss days				Nia, NCa	, la Nia, NCa	i, la Nia, NCa	a, OI (NIa, NCa, I_ NIa	, NCa, SENIa, NCa,	I_INIa, NCa,	p Nia, NCa, p	3
130		overall score (0-100)				la, Ca	la, Ca	OR, OR	1_94(I_CI95_MD, SD	(Ia), SD(CI_CI95(Ia)	, u_p	р	
131	-	information subscale (0-100)				la, Ca	la, Ca	UR, UR	1_94(I_CI95_MD, SD	(Ia), SD(UI_CI95(Ia)	, u_p	р	
132		general care subscale (U-1UU)				la, Ca	la, Ca	UR, UR	1_94 (I_CI95_MD, SD	(Ia), SD(CI_CI95(Ia)	, u_p	р	
133	-	regular exercise				la, Ca	la, Ca	UR, UR	194 (I_CI95_MD, SD	(Ia), SD(CI_CI95(Ia)	, u_p	р	
134	-	manage next LBP		· · · · · · · · · · · · · · · · · · ·		la, Ca	la, Ca	OR, OR	1_91(I_CI95_MD, SD	(ia), SD(CI_CI95(ia) (ia), SD(CI_CI95(ia)	, u_p	р	
130 130 Outralian 4004	DOT	perceived knowledge (U-100)	VEC	VEC	-	la, Ca	la, Ca	OR, OR	1_94(I_CB95_MD, SD	(ia), SD(CI_CI95(ia) (ia), SD(CI_CI95(ia)	, u_p	p	
100 Cupples, 1994	RUI	Diactolic Blood Brocouro (mm/H	VEC	VES	3	la, Ca	la, Ca	OR, OR	195%, OR_U_93D	(ia), 3D(CI_CI95(ia) (ia), SD(CI_CI95(ia)	, u p	p	
138	1	Svetalic Blood Pressure (mm/He	VES	VES	3	la, Ca	la, Ca		195%, OR_U_9(3D	(ia), SD(CL_CI95(ia) (ia), SD(CL_CI95(ia)	, u p	P	
130		DMI	VES	VES	3	la Ca	la, Ca		195% OR 1953D	(ia), SD(CL_CISS(ia) (ia), SD(CL_CI95(ia)	, u p	P	
140		Diet (frequency of eating certain I	YES	120	3	la Ca	la Ca	OR OR	195% OR # 950	(la) SD(CL CI95(la)		n	-
140		Exercise (no of 20 min episode r	YES		3	la Ca	la Ca	OR OR	195% OR # 95D	(la), SD(CL_CI95(la) (la), SD(CL_CI95(la)	, одр п. Сl95(la), I	095(Ca) u C	(195(Ca)
142		Stop Smoking	YES		1a	14, 04	14, 54	OR OR	1.9/ (MD 1.095 SD	(la) SD(CMD L CIS	5/1 MD n	n	
143		angina episodes per week				NIa NCa	la NIa NCa	la NIa NCa	OL(NIa_NCa) CNIa	NCa SINIa NCa	L INIa NCa	n Nia NCa n	
144		Emotion	YES	YES	3	la, Ca	la, Ca	OR, OR	1 95%, OR u 95SD	(la), SD(CI CI95(la)	up	p	
145		Energy	YES	YES	3	la, Ca	la, Ca	OR, OR	1 95%, OR u 95SD	(la), SD(CI CI95(la)	up	p	
146		Mobility	YES	YES	3	la, Ca	la, Ca	OR, OR	1_95%, OR_u_95SD	(la), SD(CI_CI95(la)	, u_Cl95(la), l	_CI95(Ca), u C	:195(Ca)
147		Pain	YES	YES	3	la, Ca	la, Ca	OR, OR	1_95%, OR_u_95SD	(la), SD(CI_CI95(la)	, u_Cl95(la), l	_CI95(Ca), u C	195(Ca)
148		Sleep	YES	YES	3	la, Ca	la, Ca	OR, OR	1 95%, OR u 95SD	(la), SD(CI CI95(la)	, u p	p	~
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Figure 6

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1	BE91 🚽 🗸	f⊱ Nla, N	Ca, OR, OR_I_	95%, OR_u_9	95%			
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2	51004	Desil	`	Variables	2	ზ	۵	6
90			Smoking (% sto	ipped)	OR, OR	<u>I 9(</u> (MD, I_Cl9	5_SD(la), SD(	CMD, I_CI
91	Batchelor	CBA	health care cou	ld be improved	t Nla, NCa	<u>, O]</u> (NIa, NCa,	MNIa, NCa, S	GENIa, NCa
92			establishemen	t of family cent	re i Nla, NCa	, OĪ (NIa, NCa,	MNIa, NCa, S	SENIa, NCa

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	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	<i>NIa</i> and <i>NCa</i> and <i>MD</i> and <i>SD(Ia)</i> and <i>SD(Ca)</i>	Mean Difference
5	Continuous	NIa and NCa and MD and CI95%(mean <sub>Ia</sub> ) and CI95%(mean <sub>Ca</sub> )	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<sub>la</sub>) is the 95% Confidence Interval for the mean of the intervention group.
- *Cl95%(mean<sub>ca</sub>)* 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
Tal	he IV

#### 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 metaanalysis. 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:

• Nla, NCa, la, Ca

Step1

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

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 =  $SE_{effect} \cdot 1.96$ 

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

#### We need:

• NIa, NCa, Ia, Ca

### Step1

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

Step2

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

<sup>&</sup>lt;sup>1</sup> There are some cases where NIa = Ia or NCa = Ca and therefore the Odds Ratio cannot be computed.

$$upperCl_{95\%}(Q) = Q + 1.96 \cdot SE_{diff}(Q)$$

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

Step4

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

Step5

$$upperCl95\%(effect) = upperCl95\%(Q) \cdot \frac{\sqrt{3}}{\pi}$$
$$lowerCl95\%(effect) = lowerCl95\%(Q) \cdot \frac{\sqrt{3}}{\pi}$$

#### 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:

• NIa, NCa, OR, Cl95%(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

$$SE_{effect} = \frac{upperCl95\%(SMD) - lowerCl95\%(SMD)}{3.92}$$
 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* =  $SE_{effect} \cdot 1.96$ 

## 3.2.4. Method 3 – Continuous data

#### We need:

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

#### Step1

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

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

where the denominator is an excel function returning the t-value for specific CI and DFs) **Step2** 

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

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* =  $SE_{effect} \cdot 1.96$ 

### 3.2.5. Method 4 – Continuous data

#### We need:

• NIa, NCa, MD, SD(Ia), SD(Ca)<sup>3</sup>

 $<sup>^{\</sup>rm 2}$  Instead of the CI95%(MD) the SE\_{diff}(MD) may be provided instead

Step1

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

Step2

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

Step3

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

#### Step4

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

#### Step5

 $value\_error\_bars = SE_{effect} \cdot 1.96$ 

## 3.2.6. 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

$$SD(Ca) = \sqrt{NCa} \cdot \frac{upperCl95\%(Ca) - lowerCl95\%(Ca)}{3.92}$$
 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

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

<sup>3</sup> 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

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

Step7

*value\_error\_bars* =  $SE_{effect} \cdot 1.96$ 

### 3.2.7. Method 6 – Continuous data

### We need:

• NIa, NCa, MD and P value

#### Step1

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

Step2

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

Step3

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

Step4

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

Step5

 $Cl95\%(effect) = effect \pm 1.96 \cdot SE_{effect}$ 

#### Step6

 $value\_error\_bars = SE_{effect} \cdot 1.96$ 

## 3.2.8. Method 7 - Continuous data

#### We need:

• *NIa*, *NCa* and *P* value

#### Step1

z = abs(normsinv(P/2))

#### Step2

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

#### Step3

effect =  $z * SE_{effect}$ 

## Step4

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

### Step5

*value\_error\_bars* =  $SE_{effect} \cdot 1.96$ 

## 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.

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BFHS, 1984	RCT	Serum cholesterol (mmol/L)	0.1388	0.0760	0.2016	0.0628	Q 1 0	
BFHS, 1984	RCT	Diastolic Blood Pressure (mm	0.2803	0.2175	0.3430	0.0628		
BFHS, 1984	RCT	Systolic Blood Pressure (mm	0.2923	0.2295	0.3551	0.0628	Woolard B, Socium intalie (mnol/24h)	
BFHS, 1984	RCT	VVeight (kg)	0.0879	0.0251	0.1507	0.0628	1995 Alcohol intake (g/week)	
BFHS, 1984	RCI	Glucose (mmol/l)	0.0572	-0.0056	0.1200	0.0628		
BFHS, 1984	RCI	Smoking (% smoked)	0.0968	0.0340	0.1596	0.0628		
BFHS, 1984	RCI	Serum cholesterol (mmol/L)	0.0504	-0.0264	0.1272	0.0768	Weight (kg)	
BEHS, 1984	RCI	Diastolic Blood Pressure (mm	0.2938	0.2170	0.3706	0.0768	Sodium intake (mmol/24h)	
or HS, 1984	RCI	Systolic Blood Pressure (mm	0.2099	0.1931	0.346/	0.0760	- Anonor intake (g/week)	
BFH5, 1984	RUT ROT	Weight (kg)	0.0037	-0.0231	0.1305	0.0768		
DELLO 1004	RCT	Glucose (mmon)	-0.0013	-0.0781	0.0755	0.0760	patients with adverse	
DELLO 1004		Smoking (% smokeu)	0.1113	0.0347	0.1003	0.0700	Wilkinson, invent improvement global illness r	
3FH5, 1984	RCT	Diestelie Diesd Dressure (mm	0.0009	0.0123	0.1095	0.0486	1993	
DELIO, 1904	RCT	Custolic Blood Pressure (min	0.2043	0.1557	0.2529	0.0400		
DELIO, 4004	RCT	Systolic Blood Pressure (mm	0.2020	0.1534	0.2506	0.0486	public of He	
3FH3, 1964	RCT	Clusses (mms//l)	0.0022	0.0036	0.1008	0.0486	• deaths	
3FH5, 1984	RCT	Glucose (mmol/l)	0.03/5	-0.0111	0.0801	0.0486	Social isolation	
BFH5, 1984	RUI	Smoking (% smoked)	0.1032	0.0546	0.1518	0.0486	Cupples, Steep	
							1994 Asobility	
							Energy Energy	
Klormon 10	07 004	Conorol hoolth	0.5604	0.1.407	0.0760	0.41.06		
Kiennan, rs	SOT CBA	General fieatur	0.0024	0.1407	0.9700	0.4130		
	-						Vettor	
							1992	
Muir 1995	RCT	Cholesterol (mmolil)	0 2222	0.1574	0.2999	0.0657	1002	
Muir 1005	RCT	Diastolic blood pressure (mn	0.1202	0.0635	0.2003	0.0657	Vetter B	
Muir 1995	RCT	Systelic blood pressure (mm	0.1292	0.0033	0.1755	0.0657	1984	
Muir 1005	RCT	BMI (ka(m2)	0.0974	0.0441	0.1733	0.0657	1504	
Muir 1005	RCT	Diet use full milk	0.0074	0.0211	0.1691	0.0657	Vettor A	
Muir 1995	RCT	Diet use hutter	0.7978	0.0000	0.3635	0.0657	1984	
Muir 1995	RCT	Exercise: < once a month	0.2930	0.2273	0.3588	0.0657	1304	
		Excluse: once a month	0.2000	0.2210	0.0000	0.0001	Would you see this	
							Thompson	
							The second	
Sharp (A)	RCT	attend breast screening	0.1024	-0.1022	0.3071	0.2046		
		in the second					Margolis,	
							1996	
Sharp (B)	RCT	attend breast screening	-0.1681	-0.3592	0.0230	0.1911	L A J Herb shale them	
/							High blood pressure	
							Diabetes	
Vetter A, 198	84 RCT	Disability	0.1312	-0.0361	0.2985	0.1673	BEHS 1984	
Vetter A, 198	84 RCT	Anxiety	0.0971	-0.0970	0.2912	0.1941	Dabetes	
> N me	eta1data / n	neta1results ) meta1summary /	meta1ora	aph / met	a1models	/		1
N			11.8	4		+ a a =		
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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
offoctIQ5	Lower lever of the 95% CI for the effect, as computed by the "best" possible
enecties	method

Field name	Information
offootu05	Upper lever of the 95% CI for the effect, as computed by the "best" possible
enectuso	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

## 3.4. Models Sheet

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

<b>X</b> 1	Aicrosoft Excel - B	ook2								
:2)	<u>File Edit V</u> iew	Insert Fo	rmat <u>T</u> ools	<u>D</u> ata <u>V</u>	<u>V</u> indow <u>M</u> et	a-analysis	<u>H</u> elp			
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	-		950	95	pars					
4	CTU D	Hec	. ONC	. open	NOT	ount				
a	Sharp (B)	-0 1681	0 3592	0.0230	0 1011	8		Woola	rd A 1995	
10	Thompson	0.0721	-0.0567	0.0230	0.1288	9		Wooldiu A, 1555		
11	Vetter A 1984	0 1018	-0.0789	0.2825	0.1200	10				
12	Vetter B 1984	0 1290	-0.0439	0.3018	0 1729	11		Wilkinson, 1993		
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		Pine, 1997		
16	Campbell A, 1998	0.1285	0.0057	0.2514	0.1228	15		Mynors, 1997		
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		Moher, 2001		
21	Mann, 1998 B	-0.0935	-0.3032	0.1162	0.2097	20	N			
22	Moher, 2001	0.0489	-0.0867	0.1844	0.1355	21	13			
23	Mynors, 1997	0.6336	0.0658	1.2013	0.5678	22		Mann	1008 B	
24	Pine, 1997	-0.1497	-0.5361	0.2367	0.3864	23		Mann, 1998 B		
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		incarin,	1000 11	
28										
29		mean eff	var eff	195%CI	u95%Cl			Fall, 1	1997	
30	FE model	0.1124	0.0003	0.0811	0.1436					
31	DL model	0.1578	0.0012	0.0891	0.2266			2010-000		
32	Q model	0.15/8	0.0012	0.0891	0.2266			Ecker	lund	
33	IVIL model	0.1/32	0.0020	0.0851	0.2612					
34	PL model	0.1/32	0.0020	0.0842	0.2762					
35	I-test	0.2054	0.0036	0.0812	0.3296			Cupp	les, 1994	
30	PE method	0.15/8	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*, *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.

Name	Reference / Information
Fixed Effects	Brockwell SE, Gordon IR. A comparison of statistical methods
(FE)	for meta-analysis. <i>Stat.Med.</i> 2001; 20(6):825-840.
DerSimonial-	DerSimonian R, Laird N. Meta-analysis in clinical trials. Control
Laird (DL)	<i>Clin.Trials</i> 1986; 7(3):177-188
O mothod $(O)$	Brockwell SE, Gordon IR. A comparison of statistical methods
	for meta-analysis. <i>Stat.Med.</i> 2001; 20(6):825-840.
Maximum-	Brockwell SE, Gordon IR. A comparison of statistical methods
Likelihood (ML)	for meta-analysis. <i>Stat.Med.</i> 2001; 20(6):825-840.
Profile-	Brockwell SE, Gordon IR. A comparison of statistical methods
Likelihood (PL)	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	Follmann DA, Proschan MA. Valid inference in random effects
method (PE)	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: Cochrane's Q (for p-value below  $\alpha$  homogeneity is rejected), estimates of the between-study variance  $\tau^2$  with three methods. In addition  $I^2$  and  $H^2_{M}$  are reported (their calculation is based on the DL method)



Figure 10

Heterogeneity mea	erogeneity measures		
	value	df	p-value
Cochrane Q	119.05	16	0.0000
τ <sup>2</sup> estimate (DL)	0.0573		
τ <sup>2</sup> estimate (ML)	0.0591		
τ <sup>2</sup> estimate (PL)	0.0813		
<sup>2</sup>	%86.56		
H <sup>2</sup> <sub>M</sub>	6.4409		
-	Figure 1	1	

## 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 (<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>).

# 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

	Currently installed programs: Show	v up <u>d</u> ates	Sort by: Name		~
Change or Remove	MathType 5	2200203	Size	9.24MB	^
Programs	🔯 McAfee VirusScan Enterprise		Size	38.82MB	
<b>A</b>	MEL.		Size	32.49MB	
Add New	# Meta-analysis Excel Add-In ver 1.0		Size	<u>1.15MB</u>	Í.
Programs			Used	<u>rarely</u>	J
-			Last Used On	14/10/2007	
	To remove this program from your computer, dick Ren	nove.		Remove	
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mponents	🕼 Microsoft .NET Framework 1.1 Hotfix (KB928366)				
	A Microsoft NET Framework 2.0		Sizo	00 25MD	1

Figure 13