Example name Caffeine by subgroups

Effect sizeRisk ratioAnalysis typeSubgroups analysis, Meta-RegressionLevelIntermediate

Synopsis

This analysis includes 25 studies where patients were randomized to receive either analgesic alone or analgesic plus caffeine. Outcome was the proportion of patients who reported a "good" level of pain relief. The effect size was the risk ratio.

For the 25 studies there was clear evidence that patients treated with caffeine were about 10% more likely to report success as compared with the control group. However, there was substantial dispersion in the effect size. The true effect size probably ranges from a risk ratio of 1.02 to 1.22. We ran additional analyses to see if this variation could be explained by various factors.

We used subgroup analyses to compare the effect size in studies -

- That employed a low dose, moderate dose, or high dose of caffeine
- Where the basic analgesic was Ibuprofen vs. studies where it was Paracetamol
- Where the pain was from headache vs. studies where the pain was from surgery

We use this example to show

- How to enter data from 2x2 tables
- How to perform a basic analysis
- How to interpret statistics for heterogeneity
- How to estimate the dispersion in true effects
- How to compare the effect size in different subgroups using subgroup analysis
- How to compare the effect size in different subgroups using meta-regression

To open a CMA file > Download and Save file | Start CMA | Open file from within CMA

Download CMA file for computers that use a period to indicate decimals Download CMA file for computers that use a comma to indicate decimals

Download this PDF Download data in Excel Download trial of CMA

Start the program

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

T Comprehensive meta analysis - [Data]														
<u>File Edit</u> Format <u>View</u> Insert Identify <u>T</u> ools Computational options Analyses	s <u>H</u> elp													
Run analyses 🔸 🔨 🗅 🚅 🚟 🖬 🎒 🐰 🗈 🛍 🛍 🚈 🍋 🛬 🕫	協 봄 ▾ ↓ → + ✔ □ 刻 및 ③													
1	S. Welcome													
2														
3	With the world way Film to de 2													
5	what would you like to do?													
6														
7														
8	C. Bun the tutorial													
9	 Start a blank spreadsheet 													
10	C. Start a new spreadsheet using a tempting													
C Open an existing file														
C Open an existing file														
13	C Import data from another program													
14														
16														
17														
18														
19														
20														
21														
22														
23														
24														
26														
27														
28														
29	I Show this dialog when I start the program													
30	Close OK													
31														
32														
33														
34														
30														

Click Insert > Column for > Study names

🕂 Comprehensive meta a	analysis - [Data]							
<u>File Edit Format View</u>	Insert Identify Tools Compu	tational options Analyses <u>H</u> elp						
Run analyses → 🏷 🗋	Column for 🕨 🕨	Study names	$\downarrow \downarrow \rightarrow + \checkmark$	 / □ ੈ‡↓ 	ZI 🔍			
A B	Blank column	Subgroups within study	н і	J	к	L	м	N
1 2 3 4 5 6 7 8 9	Copy of selected column Blank row Blank rows Copy of selected row(s) Study	Outcome names Time point names Time point names Comparison Moderator variable						

The screen should look like this

🕂 Co	mprehensive met	a analysis - [[Data]											
<u>F</u> ile	<u>E</u> dit Format <u>V</u> ie	ew <u>I</u> nsert I	dentify <u>T</u> o	ols Compu	tational opt	ions Analys	ses <u>H</u> elp							
Run a	nalyses 🔸 🗞 [<u>) 🛋 </u> 🕯 I		X 🖻 🛍	∕≣ ►-•	= *≣ #3	8 號 🛗 🔻	$\downarrow \rightarrow \neg$	- ✓ 🗆	AL AL				
	Study name	в	С	D	E	F	G	н	I	J	к	L	м	N
2														
3														
4														
6														
8														
10														

Click Insert > Column for > Effect size data

Comprehensive meta	analysis - [Data]									
<u>File Edit Format Viev</u>	v Insert Identify <u>T</u> ools Compu	tational options Analyses <u>H</u> elp)							
Run analyses 🔸 🏷 🗋	Column for 🕨	Study names	$\downarrow \downarrow \rightarrow \downarrow$	⊢ ✓ 🖂	21 Z1 🤅					
Study name	Blank column	Subgroups within study Comparison names	н	I	J	к	L	м	N	
1 2 3	Blank row	Outcome names Time point names								
4	Copy of selected row(s)	Effect size data Moderator variable								
7 8	'≡ Study									

The program displays this wizard

Select [Comparison of two groups...]

Select [Show all 100 formats] Click [Next]



Drill down to

Click [Next]

Dichotomous (number of events) Unmatched groups, prospective ... Events and sample size in each group



© www.Meta-Analysis.com

Caffeine by subgroups

The program displays this wizard

Enter the following labels into the wizard

- First group > Caffeine
- Second group > Control
- Name for events > Relief
- Name for non-events > Pain

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

Ele Edit Format View Incer Indertify Tools Computational options Analyses Help Run analyses + Colspan="2">Colfeine Calfeine Control Study name Calfeine Control Relief Total N Relief Total N Relief Colspan="2">Control Control Control	Comprehensive meta analysis - [Data]													
Run analyses Run analyses <td>File Edit Format Liew Insert Identify Tools Computed</td> <td>tional options Ana</td> <td>ılyses <u>H</u>elp</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	File Edit Format Liew Insert Identify Tools Computed	tional options Ana	ılyses <u>H</u> elp											
Study name Caffeire Relief Control Total N Odds ratio Log adds ratio Std Err Variance J K L M N 1	Run analyses 🔸 🔨 🗅 😅 🚟 🖬 🚭 👗 🗈 🛍 😤	<u>≣ +</u> _ = + <u>≡</u>	÷00 tao tt →	• + 🗸 🗌	Ž↓ Z↓	Q								
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23	Study name Caffeine Caffeine Control Con Relief Total N Relief Tot	ntrol tal N Ddds ratio	Log odds ratio Std Err	Variance	J	к	L	м	N					
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23	1													
3 4 5 6 7 9 9 10 11 11 12 13 14 15 16 17 18 19 20 21 22 23	2													
3 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 23 24	3													
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 24	5													
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 24	6		(De Carrowent					a 53)					
8 9 Group names for cohort or prospective studies 10 Name for first group (e.g., Treated) Caffeine 12 Name for second group (e.g., Control) Control 13 Mame for events (e.g., Control) Control 14 Mame for events (e.g., Dead) Relief 17 Name for non-events (e.g., Alive) Pain 18 Cancel Apply Ok 20 Cancel Apply Ok 21 Cancel Apply Ok 22 Cancel Apply Ok 23 Cancel Apply Ok	7		G. Group names											
3 Cardin rames for Control in prospective studies 10 Name for first group (e.g., Treated) 12 Name for second group (e.g., Control) 13 Control 14 Binary outcome in cohort or prospective studies 16 Name for events (e.g., Dead) 17 Name for non-events (e.g., Alive) 19 Cancel Apply 20 Cancel Apply 21 Cancel Apply 22 Cancel Apply	8		Group pamee	for ophart or	prospectiv	va studias			_					
10 Name for first group (e.g., Treated) Caffeine 12 Name for second group (e.g., Control) Control 13 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 14 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 14 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 15 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 16 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 17 Image: Control of the second group (e.g., Alive) Image: Control of the second group (e.g., Alive) 18 Image: Control of the second group (e.g., Alive) Image: Control of the second group (e.g., Alive) 19 Image: Control of the second group (e.g., Alive) Image: Control of the second group (e.g., Alive) 20 Image: Control of the second group (e.g., Alive) Image: Control of the second group (e.g., Alive) 21 Image: Control of the second group (e.g., Alive) Image: Control of the second group (e.g., Alive) 22 Image: Control of the second group (e.g., Alive) Image: Control of the second group (e.g., Alive) 23 Image: Control of the second group (e.g., Alive) Image: Control of th	10				prospecus	E 3.			-					
12 Name for second group (e.g., Control) Control 13 Image: Control of the second group (e.g., Control) Control 14 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 14 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 14 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 16 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 16 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 16 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 17 Image: Control of the second group (e.g., Control) Image: Control of the second group (e.g., Control) 18 Image: Control of the second group (e.g., Alive) Image: Control of the second group (e.g., Alive) 19 Image: Control of the second group (e.g., Alive) Image: Control of the second group (e.g., Alive) 20 Image: Control of the second group (e.g., Alive) Image: Control of the second group (e.g., Alive) 21 Image: Control of the second group (e.g., Alive) Image: Control of the second group (e.g., Alive) 22 Image: Control of the second group (e.g., Alive) <td< td=""><td>11</td><td></td><td>Name for first gro</td><td>up (e.g., Treat</td><td>ed)</td><td></td><td>Caffeine</td><td></td><td></td></td<>	11		Name for first gro	up (e.g., Treat	ed)		Caffeine							
13 Image: Second seco	12		Name for second	l group (e.g., C	ontrol)		Control							
14 15 16 17 18 19 20 21 22 23 24	13													
15 Binary outcome in cohort or prospective studies 16 Name for events (e.g., Dead) 17 Name for non-events (e.g., Alive) 19 Cancel 20 Cancel 21 Cancel 22 Cancel 23 Cancel	14													
Ib Name for events (e.g., Dead) Relief 17 Name for non-events (e.g., Alive) Pain 19 20 Cancel Apply Ok 21 Cancel Apply Ok 23 24 Image: State	15		Binary outcom	e in cohort (or prospect	tive studies	•							
In 18 19 20 21 22 23 24	17		Name for events	(e.g., Dead)			Relief		-					
19 20 21 23 23 24	18		Name for non-ev	ents (e.g., Aliv	e)		Pain	_						
20 21 22 23 24	19							— JI						
21 Cancel Apply 0k 22	20													
22 23 24	21			0	Cancel	Apply	Ok							
23 24	22													
	23													
25	24													

We need to add a column for the moderator, Dose

Click Insert > Column for > Moderator variable

Comprehensive meta analysis - [Data]									
File Edit Format View Insert Identify Tools Comput	tational options Analyses <u>H</u> elp								
Run analyses → 🎕 🗋 🚻 Column for →	Study names	$\star \hspace{0.1cm} \downarrow \hspace{0.1cm} \rightarrow \hspace{0.1cm}$	+ 🗸 🗌		Q				
Study name	Subgroups within study Comparison names	Std Err	Variance	J	к	L	м	N	O
1 2 Blank row 3 Copy of decede column	Outcome names Time point names								
4 5 Copy of selected row(s)	Effect size data								
6 ▶ Study									
8									
10									
12									

- Name the moderator > Dose
- Set the data type to Categorical
- Click Ok

🛃 Comprehensive meta analysi	s - [Data]										
<u>File Edit Format View Inser</u>	t Identify <u>T</u> ools Cor	nputational optic	ons Analyses	<u>H</u> elp							
Run analyses 🔸 🗞 🗋 🚅 🕯	f 🖬 🎒 🐰 🖻	🛍 🖉 🛏 ۲=	= ▶≣ 2% ta	∺ - ↓ -	+ √ 🗌		Q				
Study name Caffein Relief	e Caffeine Control Total N Relief	Control Total N Od	lds ratio Log c rati	dds Std Err	Variance	Dose	к	L	м	N	0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27			Es Column Name Valu Variable na Column fur Data type Alignment	ormat es etion (Ca Let	se derator regorical t	Cance Ok					

- Insert a column for > Moderator > Categorical with the name Analgesic. This will be used to code the type of medication (e.g. ibuprofen)
- Insert a column for > Moderator > Categorical with the name Pain Type. This will be used to code the type of pain (e.g. post-surgical)

The screen should look like this

👬 Co	omprehensive met	a analysis -	[Data]												
<u>F</u> ile	<u>E</u> dit Format <u>V</u> ie	w Insert	Identify <u>T</u> o	ools Com	putational (options An	alyses <u>H</u> elp)							
$Run \text{ analyses } \rightarrow \ \& \ \square \cong \ \textcircled{m} \boxtimes \boxtimes \boxtimes \boxtimes \boxtimes \boxtimes \boxtimes \boxtimes \square \rightarrow + \downarrow \square \Rightarrow + \checkmark \square \textcircled{m} \textcircled{m} \swarrow \bigcirc \bigcirc$													ר		
	Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Dose	Analgesic	Pain Type	м	N	O
1															
2															
3															
4															
5															
6															

There are three options at this point

- Enter the data directly into CMA
- - or Open the CMA data file "Caffeine.cma"
- - or Copy the data from Excel"Caffeine.xls"

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

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

X≣	🔒 🕤 🖓 ÷ ÷						Caffeine.xlsx - I	Excel		
F	LE HOME INSER	T PAGE LAYO	UT FORMUL	AS DATA	REVIEW VIE	W ACRO	BAT			
Δ1		√ fr								
-4	Α	В	С	D	E	F	G	Н	I	J
1		Caffeine Relief	Caffeine N	Ctrl Relief	Ctrl N	Dose	Analgesic	Pain Type		
2	Forbes, 1990	17	66	17	68	a Low	Unknown	Post-op		
3	Laska 1983a	32	56	26	54	a Low	Paracetamol	Post-op		
4	Laska 1983b	51	80	47	81	a Low	Paracetamol	Post-op		
5	Laska 1983c	38	62	40	68	a Low	Paracetamol	Post-op		
6	McQuay 1996a	8	30	2	31	a Low	Ibuprofen	Post-op		
7	Ali, 2007	134	310	121	310	b Medium	Paracetamol	Dysmenorrhoea		
8	Diener, 2005	429	482	418	498	b Medium	Unknown	Headache		
9	Forbes, 1991a	24	44	17	48	b Medium	Ibuprofen	Post-op		
10	Forbes, 1991b	19	49	13	49	b Medium	Ibuprofen	Post-op		
11	Laska, 1983d	50	78	52	81	b Medium	Paracetamol	Post-op		
12	Laska, 1983e	39	62	42	68	b Medium	Paracetamol	Post-op		
13	Laska, 1983f	42	57	28	50	b Medium	Paracetamol	Post-op		
14	Laska, 1983g	42	45	37	46	b Medium	Paracetamol	Post-op		
15	McQuay 1996b	14	30	2	31	b Medium	Ibuprofen	Post-op		
16	Migliardi, 1994a	258	339	229	337	b Medium	Paracetamol	Headache		
17	Migliardi, 1994b	253	336	221	332	b Medium	Paracetamol	Headache		
18	Sunshine, 1996a	24	50	17	51	b Medium	Ibuprofen	Post-op		
19	Sunshine, 1996b	36	50	33	50	b Medium	Ibuprofen	Post-op		
20	Winter, 1983	19	40	20	41	b Medium	Paracetamol	Post-op		
21	Diamond, 2000	65	97	55	99	c High	Ibuprofen	Headache		
22	Laska, 1983h	42	56	38	60	c High	Paracetamol	Post-op		
23	Laska, 1983i	57	80	56	81	c High	Paracetamol	Post-op		
24	Laska, 1983j	45	64	43	66	c High	Paracetamol	Post-op		
25	Laska, 1983k	34	40	33	42	c High	Paracetamol	Post-op		
26	McQuay 1996c	12	29	2	31	c High	Ibuprofen	Post-op		
_										

- Switch to CMA
- Click in cell Study-name 1

Click here

👬 Co	mprehensive meta	a analysis -	[Data]										-		
<u>F</u> ile	Eile Edit Format View Insert Identify Tools Computational options Analyses Help														
Run a															
	Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Dose	Analgesic	Pain Type	м	N	0
1															
3															
4															
-															

- Press [CTRL-V] to paste the data
- The screen should look like this

n analyses 🔸 🗞	🗅 📂 🚟		X 🖻 🛍	y 🖅 🕨	-'= ' <u>=</u>	÷** 80. **	$\star \downarrow \rightarrow$	+ 🗸 🗌	≜ ↓ Z ↓	Q				
Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Dose	Analgesic	Pain Type	м	N	(
1	Caffeine	Caffeine N	Ctrl Relief	Ctrl N										
2 Forbes, 1990	17	66	17	68	1.041	0.040	0.397	0.158						
3 Laska 1983a	32	56	26	54	1.436	0.362	0.384	0.147						
4 Laska 1983b	51	80	47	81	1.272	0.241	0.324	0.105						
5 Laska 1983c	38	62	40	68	1.108	0.103	0.359	0.129						
5 McQuay 1996a	8	30	2	31	5.273	1.663	0.840	0.705						
7 Ali, 2007	134	310	121	310	1.189	0.173	0.163	0.027						
B Diener, 2005	429	482	418	498	1.549	0.438	0.190	0.036						
9 Forbes, 1991a	24	44	17	48	2.188	0.783	0.427	0.183						
J Forbes, 1991b	19	49	13	49	1.754	0.562	0.437	0.191						
1 Laska, 1983d	50	78	52	81	0.996	-0.004	0.331	0.109						
2 Laska, 1983e	39	62	42	68	1.050	0.048	0.362	0.131						
3 Laska, 1983f	42	57	28	50	2.200	0.788	0.414	0.172						
4 Laska, 1983g	42	45	37	46	3.405	1.225	0.704	0.495						
5 McQuay 1996b	14	30	2	31	12.688	2.541	0.818	0.668						
6 Migliardi, 1994a	258	339	229	337	1.502	0.407	0.173	0.030						
7 Migliardi, 1994b	253	336	221	332	1.531	0.426	0.172	0.030						
B Sunshine, 1996a	24	50	17	51	1.846	0.613	0.410	0.168						
9 Sunshine, 1996b	36	50	33	50	1.325	0.281	0.434	0.188						
0 Winter, 1983	19	40	20	41	0.950	-0.051	0.445	0.198						
1 Diamond, 2000	65	97	55	99	1.625	0.486	0.296	0.088						
2 Laska, 1983h	42	56	38	60	1.737	0.552	0.409	0.167						
3 Laska, 1983i	57	80	56	81	1.106	0.101	0.345	0.119						
4 Laska, 1983j	45	64	43	66	1.267	0.237	0.376	0.142						
5 Laska, 1983k	34	40	33	42	1.545	0.435	0.581	0.337						
6 McQuay 1996c	12	29	2	31	10.235	2.326	0.823	0.677						

- Switch to Excel
- Highlight the columns for Dose, Analgesic, and Pain Type as shown and click [CTRL-C]

х] ⊟ 5 • ∂• ∓						Caffeine.xlsx - I	Excel			
	FILE HOME INSER	T PAGE LAYO	OUT FORMUL	AS DATA	REVIEW VIE	W ACRO	BAT				
F	1 * : ×	√ <i>f</i> _x [Dose								
	A	В	С	D	E	F	G	Н	I	J	К
1		Caffeine Relief	Caffeine N	Ctrl Relief	Ctrl N	Dose	Analgesic	Pain Type			
2	Forbes, 1990	17	66	17	68	a Low	Unknown	Post-op			
3	Laska 1983a	32	56	26	54	a Low	Paracetamol	Post-op			
4	Laska 1983b	51	80	47	81	a Low	Paracetamol	Post-op			
5	Laska 1983c	38	62	40	68	a Low	Paracetamol	Post-op			
6	McQuay 1996a	8	30	2	31	a Low	Ibuprofen	Post-op			
7	Ali, 2007	134	310	121	310	b Medium	Paracetamol	Dysmenorrhoea			
8	Diener, 2005	429	482	418	498	b Medium	Unknown	Headache			
9	Forbes, 1991a	24	44	17	48	b Medium	Ibuprofen	Post-op			
10	Forbes, 1991b	19	49	13	49	b Medium	Ibuprofen	Post-op			
11	Laska, 1983d	50	78	52	81	b Medium	Paracetamol	Post-op			
12	Laska, 1983e	39	62	42	68	b Medium	Paracetamol	Post-op			
13	Laska, 1983f	42	57	28	50	b Medium	Paracetamol	Post-op			
14	Laska, 1983g	42	45	37	46	b Medium	Paracetamol	Post-op			
15	McQuay 1996b	14	30	2	31	b Medium	Ibuprofen	Post-op			
16	Migliardi, 1994a	258	339	229	337	b Medium	Paracetamol	Headache			
17	Migliardi, 1994b	253	336	221	332	b Medium	Paracetamol	Headache			
18	Sunshine, 1996a	24	50	17	51	b Medium	Ibuprofen	Post-op			
19	Sunshine, 1996b	36	50	33	50	b Medium	Ibuprofen	Post-op			
20	Winter, 1983	19	40	20	41	b Medium	Paracetamol	Post-op			
21	Diamond, 2000	65	97	55	99	c High	Ibuprofen	Headache			
22	Laska, 1983h	42	56	38	60	c High	Paracetamol	Post-op			
23	Laska, 1983i	57	80	56	81	c High	Paracetamol	Post-op			
24	Laska, 1983j	45	64	43	66	c High	Paracetamol	Post-op			
25	Laska, 1983k	34	40	33	42	c High	Paracetamol	Post-op			
26	McQuay 1996c	12	29	2	31	c High	Ibuprofen	Post-op			
27									45		
28											
		i								i	1

- Switch to CMA
- Click the cell Dose 1
- Press CTRL-V to paste the data

Comprehensive meta analysis - [Data]
 Eile Edit Format View Insert Identify Tools Computational options Analyses Help

Run	analyses → 🏷 [ጋ 😅 🖷		X 🖻 🖬	s 🚈 🛌	-*= *=	.00 +.0 ++ +.0 .00 □	$\overline{} \rightarrow$	+ 🗸 🗌] ≜∔ ∡∔	Q					
	Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Dose	Analgesic	Pain Type	м	N	0	
1		Caffeine	Caffeine N	Ctrl Relief	Ctrl N					Dose	Analgesic	Pain Type				T
2	Forbes, 1990	17	66	17	68	1.041	0.040	0.397	0.158	a Low	Unknown	Post-op				
3	Laska 1983a	32	56	26	54	1.436	0.362	0.384	0.147	a Low	Paracetamo	Post-op				
4	Laska 1983b	51	80	47	81	1.272	0.241	0.324	0.105	a Low	Paracetamo	Post-op				
5	Laska 1983c	38	62	40	68	1.108	0.103	0.359	0.129	a Low	Paracetamo	Post-op				
6	McQuay 1996a	8	30	2	31	5.273	1.663	0.840	0.705	a Low	Ibuprofen	Post-op				
7	Ali, 2007	134	310	121	310	1.189	0.173	0.163	0.027	b Medium	Paracetamo	Dysmenorrh				
8	Diener, 2005	429	482	418	498	1.549	0.438	0.190	0.036	b Medium	Unknown	Headache				
9	Forbes, 1991a	24	44	17	48	2.188	0.783	0.427	0.183	b Medium	Ibuprofen	Post-op				
10	Forbes, 1991b	19	49	13	49	1.754	0.562	0.437	0.191	b Medium	Ibuprofen	Post-op				
11	Laska, 1983d	50	78	52	81	0.996	-0.004	0.331	0.109	b Medium	Paracetamo	Post-op				
12	Laska, 1983e	39	62	42	68	1.050	0.048	0.362	0.131	b Medium	Paracetamo	Post-op				
13	Laska, 1983f	42	57	28	50	2.200	0.788	0.414	0.172	b Medium	Paracetamo	Post-op				
14	Laska, 1983g	42	45	37	46	3.405	1.225	0.704	0.495	b Medium	Paracetamo	Post-op				
15	McQuay 1996b	14	30	2	31	12.688	2.541	0.818	0.668	b Medium	Ibuprofen	Post-op				
16	Migliardi, 1994a	258	339	229	337	1.502	0.407	0.173	0.030	b Medium	Paracetamo	Headache				
17	Migliardi, 1994b	253	336	221	332	1.531	0.426	0.172	0.030	b Medium	Paracetamo	Headache				
18	Sunshine, 1996a	24	50	17	51	1.846	0.613	0.410	0.168	b Medium	Ibuprofen	Post-op				
19	Sunshine, 1996b	36	50	33	50	1.325	0.281	0.434	0.188	b Medium	Ibuprofen	Post-op				
20	Winter, 1983	19	40	20	41	0.950	-0.051	0.445	0.198	b Medium	Paracetamo	Post-op				
21	Diamond, 2000	65	97	55	99	1.625	0.486	0.296	0.088	c High	Ibuprofen	Headache				
22	Laska, 1983h	42	56	38	60	1.737	0.552	0.409	0.167	c High	Paracetamo	Post-op				
23	Laska, 1983i	57	80	56	81	1.106	0.101	0.345	0.119	c High	Paracetamo	Post-op				
24	Laska, 1983j	45	64	43	66	1.267	0.237	0.376	0.142	c High	Paracetamo	Post-op				
25	Laska, 1983k	34	40	33	42	1.545	0.435	0.581	0.337	c High	Paracetamo	Post-op				
26	McQuay 1996c	12	29	2	31	10.235	2.326	0.823	0.677	c High	Ibuprofen	Post-op				
27																
28																

At this point we should check that the data has been copied correctly

•†	Comprehensive met	a analysis -	[Data]													
Ei	le <u>E</u> dit Format <u>V</u> ie	ew <u>I</u> nsert I	ldentify <u>T</u> o	ols Com	putational o	ptions Ana	lyses <u>H</u> elp									
R	un analyses 🔸 🗞 [ב 🔁 🗂		X 🖻 🛍	3 ⁄ 🔁	- * = *	++ + 00. *.0 + 00. *.+	$\bullet \hspace{0.1cm} \downarrow \hspace{0.1cm} \rightarrow \hspace{0.1cm}$	+ 🗸 🗌		Q					
	Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Dose	Analgesic	Pain Type	м	N	0	
	1	Caffeine	Caffeine N	Ctrl Relief	Ctrl N					Dose	Analgesic	Pain Type				
	2 Forbes, 1990	17	66	17	68	1.041	0.040	0.397	0.158	a Low	Unknown	Post-op				
	3 Laska 1983a	32	56	26	54	1.436	0.362	0.384	0.147	a Low	Paracetamo	Post-op				
	4 Laska 1983b	51	80	47	81	1.272	0.241	0.324	0.105	a Low	Paracetamo	Post-op				
	5 Laska 1983c	38	62	40	68	1.108	0.103	0.359	0.129	a Low	Paracetamo	Post-op				
	6 McQuay 1996a	8	30	2	31	5.273	1.663	0.840	0.705	a Low	Ibuprofen	Post-op				
	7 Ali, 2007	134	310	121	310	1.189	0.173	0.163	0.027	b Medium	Paracetamo	Dysmenorrh				

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

Click here

,† 0	omp	rehensive meta an	alysis - [D	ata]													
<u>F</u> ile	Edi	t Format <u>V</u> iew	<u>I</u> nsert Ide	entify <u>T</u> o	ols Com	putational o	options Ana	ilyses <u>H</u> elp									
Run	ŝ	Bookmark data		1 3 3	X 🖻 🛍	1 🔁 🕨	- *= *≣	*** 00. 00+	$\star \hspace{0.1cm} \downarrow \hspace{0.1cm} \rightarrow \hspace{0.1cm}$	+ 🗸 🗌		•					
	l no	Restore data Column properti	es	Caffeine Total N	Control Relief	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Dose	Analgesic	Pain Type	м	N	0	
1		Convertention	Chill C	affeine N	Ctrl Relief	Ctrl N					Dose	Analgesic	Pain Type				
2	43	Copy selection	Ctri+C	66	17	68	1.041	0.040	0.397	0.158	a Low	Unknown	Post-op				
3	L L	Copy with heade	r	56	26	54	1.436	0.362	0.384	0.147	a Low	Paracetamo	Post-op				
4	8	Copy entire grid		80	47	81	1.272	0.241	0.324	0.105	a Low	Paracetamo	Post-op				
5	-	D .	C1 1 1	62	40	68	1.108	0.103	0.359	0.129	a Low	Paracetamo	Post-op				
E	•	Paste	Ctrl+v	30	2	31	5.273	1.663	0.840	0.705	a Low	Ibuprofen	Post-op				
7	*	Cut	Ctrl+X	310	121	310	1.189	0.173	0.163	0.027	b Medium	Paracetamo	Dysmenorrh				
8	0	_ Delete	Del	482	418	498	1.549	0.438	0.190	0.036	b Medium	Unknown	Headache				
9	6	Delete	Dei	44	17	48	2.188	0.783	0.427	0.183	b Medium	Ibuprofen	Post-op				
10		Delete row		49	13	49	1.754	0.562	0.437	0.191	b Medium	Ibuprofen	Post-op				
11		Delete study	43	78	52	81	0.996	-0.004	0.331	0.109	b Medium	Paracetamo	Post-op				
12		Delete column		62	42	68	1.050	0.048	0.362	0.131	b Medium	Paracetamo	Post-op				
13				57	28	50	2.200	0.788	0.414	0.172	b Medium	Paracetamo	Post-op				
14		Edit group name	s	45	37	46	3.405	1.225	0.704	0.495	b Medium	Paracetamo	Post-op				
15	McG	luay 1996b	14	30	2	31	12.688	2.541	0.818	0.668	b Medium	Ibuprofen	Post-op				
16	Migl	ardi, 1994a	258	339	229	337	1.502	0.407	0.173	0.030	b Medium	Paracetamo	Headache				
17	Migl	ardi, 1994b	253	336	221	332	1.531	0.426	0.172	0.030	b Medium	Paracetamo	Headache				

The screen should look like this

÷	Comprehensive meta analysi	s - [Data]
•	comprehensive meta analysi	is [bata]

<u>E</u> dit Format <u>V</u> ie	w <u>I</u> nsert I	dentify <u>T</u> o	ols Comp	outational	options Ana	alyses <u>H</u> elp								
analyses → 🗞 [ן 🚔 🛥 נ	8 3	6 🖻 🛍	y 🖅 🕨	-*= *≣	+++ 00. *++ → 00. *++	$\star \downarrow \rightarrow$	+ 🗸 🗌] <u>A</u> ↓ <u>A</u> ↓	•				
Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Dose	Analgesic	Pain Type	М	N	0
Forbes, 1990	17	66	17	68	1.041	0.040	0.397	0.158	a Low	Unknown	Post-op			
Laska 1983a	32	56	26	54	1.436	0.362	0.384	0.147	a Low	Paracetamo	Post-op			
Laska 1983b	51	80	47	81	1.272	0.241	0.324	0.105	a Low	Paracetamo	Post-op			
Laska 1983c	38	62	40	68	1.108	0.103	0.359	0.129	a Low	Paracetamo	Post-op			
McQuay 1996a	8	30	2	31	5.273	1.663	0.840	0.705	a Low	Ibuprofen	Post-op			
Ali, 2007	134	310	121	310	1.189	0.173	0.163	0.027	b Medium	Paracetamo	Dysmenorrh			
Diener, 2005	429	482	418	498	1.549	0.438	0.190	0.036	b Medium	Unknown	Headache			
Forbes, 1991a	24	44	17	48	2.188	0.783	0.427	0.183	b Medium	Ibuprofen	Post-op			
Forbes, 1991b	19	49	13	49	1.754	0.562	0.437	0.191	b Medium	Ibuprofen	Post-op			
Laska, 1983d	50	78	52	81	0.996	-0.004	0.331	0.109	b Medium	Paracetamo	Post-op			
Laska, 1983e	39	62	42	68	1.050	0.048	0.362	0.131	b Medium	Paracetamo	Post-op			
Laska, 1983f	42	57	28	50	2.200	0.788	0.414	0.172	b Medium	Paracetamo	Post-op			
Laska, 1983g	42	45	37	46	3.405	1.225	0.704	0.495	b Medium	Paracetamo	Post-op			
McQuay 1996b	14	30	2	31	12.688	2.541	0.818	0.668	b Medium	Ibuprofen	Post-op			
Migliardi, 1994a	258	339	229	337	1.502	0.407	0.173	0.030	b Medium	Paracetamo	Headache			
Migliardi, 1994b	253	336	221	332	1.531	0.426	0.172	0.030	b Medium	Paracetamo	Headache			
Sunshine, 1996a	24	50	17	51	1.846	0.613	0.410	0.168	b Medium	Ibuprofen	Post-op			
Sunshine, 1996b	36	50	33	50	1.325	0.281	0.434	0.188	b Medium	Ibuprofen	Post-op			
Winter, 1983	19	40	20	41	0.950	-0.051	0.445	0.198	b Medium	Paracetamo	Post-op			
Diamond, 2000	65	97	55	99	1.625	0.486	0.296	0.088	c High	Ibuprofen	Headache			
Laska, 1983h	42	56	38	60	1.737	0.552	0.409	0.167	c High	Paracetamo	Post-op			
Laska, 1983i	57	80	56	81	1.106	0.101	0.345	0.119	c High	Paracetamo	Post-op			
Laska, 1983j	45	64	43	66	1.267	0.237	0.376	0.142	c High	Paracetamo	Post-op			
Laska, 1983k	34	40	33	42	1.545	0.435	0.581	0.337	c High	Paracetamo	Post-op			
McQuay 1996c	12	29	2	31	10.235	2.326	0.823	0.677	c High	Ibuprofen	Post-op			
	Edit Format Vie analyses → Study name Forbes, 1980 Laska 1983a Laska 1983a Laska 1983a Laska 1983a Laska 1983a Laska 1983a Joiner, 2005 Forbes, 1991b Laska, 1983d Laska, 1983d Laska, 1983d Laska, 1983f Laska, 1983g Sunshine, 1396a Sunshine, 13983 Laska, 1983i Laska, 1983i	Edit Format View Insert J analyses → Caffeire Relief Forbes, 1990 17 Laska 1983a 32 Laska 1983b 51 Laska 1983b 51 Laska 1983c 38 McQuay 1996a 8 Ali, 2007 134 Diener, 2005 429 Forbes, 1991b 19 Laska, 1983d 50 Laska, 1983d 42 Laska, 1983d 42 Laska, 1983f 42 Laska, 1983f 42 Sunshine, 1996b 36 Winter, 1983 19 Diamond, 2000 65 Laska, 1983h 42 Laska, 1983h 42 Laska, 1983h 45 Laska, 1983h 45 Laska, 1983k 34 <td>Edit Format View Insert Identify Ior analyses → > ></td> <td>Edit Format View Insert Identify Iools Comp analyses ◆ > ></td> <td>Edit Format View Insert Identify Tools Computational of tools analyses N D P</td> <td>Edit Format View Insert Identify Loois Computational options Analyses analyses \mathbb{N} \mathbb{P} <</td> <td>Edit Format View Insert Identify Loois Computational options Analyses Help analyses \below \below</td> <td>Edit Format View Insert Identify iools Computational options Analyses Help analyses</td> <td>Edit Format View Insert Identify Tools Computational options Analyses Help analyses → □ <td□< td=""><td>Edit Format Yiew Insert Identify Tools Computational options Analyses Heip analyses Image: Protein State I</td><td>Edit Format View Inset Identify Tools Computational options Analyses Heip analyses ↑ ↑ ↑ ↑ ↑ ↑ ↓<</td><td>Édit Format View Insert Identify Tools Computational options Analyses Height A Pain Type analyses • •</td><td>Édit Format View Inset Identify Iools Computational options Analyses Help analyses →</td><td>Édit Format View Insert Identify Iools Computational options Analyses Help analyses → 0 0</td></td□<></td>	Edit Format View Insert Identify Ior analyses → >	Edit Format View Insert Identify Iools Comp analyses ◆ >	Edit Format View Insert Identify Tools Computational of tools analyses N D P	Edit Format View Insert Identify Loois Computational options Analyses analyses \mathbb{N} \mathbb{P} <	Edit Format View Insert Identify Loois Computational options Analyses Help analyses \below	Edit Format View Insert Identify iools Computational options Analyses Help analyses	Edit Format View Insert Identify Tools Computational options Analyses Help analyses → □ <td□< td=""><td>Edit Format Yiew Insert Identify Tools Computational options Analyses Heip analyses Image: Protein State I</td><td>Edit Format View Inset Identify Tools Computational options Analyses Heip analyses ↑ ↑ ↑ ↑ ↑ ↑ ↓<</td><td>Édit Format View Insert Identify Tools Computational options Analyses Height A Pain Type analyses • •</td><td>Édit Format View Inset Identify Iools Computational options Analyses Help analyses →</td><td>Édit Format View Insert Identify Iools Computational options Analyses Help analyses → 0 0</td></td□<>	Edit Format Yiew Insert Identify Tools Computational options Analyses Heip analyses Image: Protein State I	Edit Format View Inset Identify Tools Computational options Analyses Heip analyses ↑ ↑ ↑ ↑ ↑ ↑ ↓<	Édit Format View Insert Identify Tools Computational options Analyses Height A Pain Type analyses • •	Édit Format View Inset Identify Iools Computational options Analyses Help analyses →	Édit Format View Insert Identify Iools Computational options Analyses Help analyses → 0 0

By default, the program is displaying the odds ratio as the effect size

We want to switch to the risk ratio

Comprehensive meta	a analysis - [[Data]												
<u>File E</u> dit Format <u>V</u> ie	w <u>I</u> nsert I	dentify <u>T</u> oo	ols Comp	utational o	options Ana	alyses <u>H</u> elp								
Run analyses → 🍫 [ן 🚔 🛥 נ	🖬 🚳 🐰	- B	y 🖅 🕨	-*= *=	÷*8 ta8 t++	$\bullet \downarrow \rightarrow$	+ 🗸 🗌] ≜↓ ≩↓	Q				
Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	Dose	Analgesic	Pain Type	м	N	O
1 Forbes, 1990	17	66	17	68	1.041	0.040	0.397	0.158	a Low	Unknown	Post-op			
2 Laska 1983a	32	56	26	54	1.436	0.362	0.384	0.147	a Low	Paracetamo	Post-op			
3 Laska 1983b	51	80	47	81	1.272	0.241	0.324	0.105	a Low	Paracetamo	Post-op			
4 Laska 1983c	38	62	40	68	1.108	0.103	0.359	0.129	a Low	Paracetamo	Post-op			
5 McQuay 1996a	8	30	2	31	5.273	1.663	0.840	0.705	a Low	Ibuprofen	Post-op			
6 Ali, 2007	134	310	121	310	1.189	0.173	0.163	0.027	b Medium	Paracetamo	Dysmenorrh			
7 Diener, 2005	429	482	418	498	1.549	0.438	0.190	0.036	b Medium	Unknown	Headache			
8 Forbes, 1991a	24	44	17	48	2.188	0.783	0.427	0.183	b Medium	Ibuprofen	Post-op			
9 Forbes, 1991b	19	49	13	49	1.754	0.562	0.437	AL co	+ 1 7					
10 Laska, 1983d	50	78	52	81	0.996	-0.004	0.331	Z+ 30	IL A-2					
11 Laska, 1983e	39	62	42	68	1.050	0.048	0.362	⊼↓ So	rt Z-A					
12 Laska, 1983f	42	57	28	50	2.200	0.788	0.414	Co	lumn pror	erties				
13 Laska, 1983g	42	45	37	46	3.405	1.225	0.704					-		
14 McQuay 1996b	14	30	2	31	12.688	2.541	0.818	Da	ta entry as	sistant				
15 Migliardi, 1994a	258	339	229	337	1.502	0.407	0.173	Σ Fo	rmulas					
16 Migliardi, 1994b	253	336	221	332	1.531	0.426	0.172	000				-		
17 Sunshine, 1996a	24	50	17	51	1.846	0.613	0.410	UUU Sh	ow all sele	cted indices				
18 Sunshine, 1996b	36	50	33	50	1.325	0.281	0.434	🚺 Sh	ow only th	e primary ind	lex			
19 Winter, 1983	19	40	20	41	0.950	-0.051	0.445	M4 C-4						
20 Diamond, 2000	65	97	55	99	1.625	0.486	0.296	io se	t primary ii	ndex to Log o	dds ratio			
21 Laska, 1983h	42	56	38	60	1.737	0.552	0.409	+ Cu	istomize co	omputed effe	ct size display	/		
22 Laska, 1983i	57	80	56	81	1,106	0.101	0.345	0.119	c Hiah	Paracetamo	Post-op			
23 Laska, 1983i	45	64	43	66	1.267	0.237	0.376	0.142	c High	Paracetamo	Post-op			
24 Laska, 1983k	34	40	33	42	1.545	0.435	0.581	0.337	c High	Paracetamo	Post-op			
25 McQuay 1996c	12	29	2	31	10.235	2.326	0.823	0.677	c High	Ibuprofen	Post-op			
26														
27														
28														

- Right-click on any of the yellow columns
- Click Customize computed effect size display

; † C	omprehensive meta	analysis -	[C:\Users\Bic	ostat\Drop	box\Work	shops Three	-Day\Caffeir	e\Caffeine.cma]	
<u>F</u> ile	<u>E</u> dit Format <u>V</u> ie	w <u>I</u> nsert	Identify <u>T</u> oo	ols Comp	utational	options An	alyses <u>H</u> elp		
Run	analyses 🔸 🗞 [) 🚅 🖷	🖬 🎒 🐰	; 🖻 🛍	y 🖅 🕨	-*= * <u>=</u>	+** 00. ***	$\begin{array}{c c} \bullet & \bullet \\ \bullet & \\ \bullet & \bullet \\$	
	Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Odds ratio	Log odds ratio	Pa Effect size indices	0
1	Forbes, 1990	17	66	17	68	1.041	0.040		
2	Laska 1983a	32	56	26	54	1.436	0.362	Use the following as the primary index	
3	Laska 1983b	51	80	47	81	1.272	0.241		
4	Laska 1983c	38	62	40	68	1.108	0.103	Risk ratio	
5	McQuay 1996a	8	30	2	31	5.273	1.663		
6	Ali, 2007	134	310	121	310	1.189	0.173	Display columns for these indices	
7	Diener, 2005	429	482	418	498	1.549	0.438		
8	Forbes, 1991a	24	44	17	48	2.188	0.783	Odds ratio	
9	Forbes, 1991b	19	I 49	13	49	1.754	0.562	Log odds ratio	
10	Laska, 1983d	50	78	52	81	0.996	-0.004	Peto odds ratio	
11	Laska, 1983e	39	62	42	68	1.050	0.048	Log Peto odds ratio	
12	Laska, 1983f	42	! 57	28	50	2.200	0.788	Risk ratio	
13	Laska, 1983g	42	: 45	37	46	3.405	1.225		
14	McQuay 1996b	14	30	2	31	12.688	2.541		
15	Migliardi, 1994a	258	339	229	337	1.502	0.407		
16	Migliardi, 1994b	253	336	221	332	1.531	0.426	Difference in means	
17	Sunshine, 1996a	24	50	17	51	1.846	0.613		
18	Sunshine, 1996b	36	50	33	50	1.325	0.281		
19	Winter, 1983	19	40	20	41	0.950	-0.051	Fisher's Z	
20	Diamond, 2000	65	i 97	55	99	1.625	0.486	Rate ratio	
21	Laska, 1983h	42	: 56	38	60	1.737	0.552	Log rate ratio	
22	Laska, 1983i	57	' 80	56	81	1.106	0.101	Rate difference	
23	Laska, 1983j	45	i 64	43	66	1.267	0.237	Hazard ratio	
24	Laska, 1983k	34	40	33	42	1.545	0.435	Also show standard error	
25	McQuay 1996c	12	29	2	31	10.235	2.326	Also show variance	
26									
27								C Show the primary index only	
28								Chow all calented indices	
29								 Summaria selected indices 	
- 30									
31								Ok	
32								Cancel	
33									
34									

- Tick Risk ratio
- Tick Log risk ratio
- Select Risk ratio in the drop-down box in the wizard
- De-select Odds ratio
- De-select log odds ratio
- Click Ok

The program now display the risk ratio rather than the odds ratio

; † 0	Comprehensive meta	a analysis -	[Data]						A						
<u>F</u> ile	<u>E</u> dit Format <u>V</u> iev	w <u>I</u> nsert I	dentify <u>T</u> o	ols Comp	outational o	options Ana	ilyses <u>H</u> elp								
Run	nanalyses → 🏷 [נ 🚔 🐔	🖬 🎒 🖇	6 🖻 🛍	y 🚈 🕨	· *= *≣	*** 80.* 8°*	$\bullet \hspace{0.1cm} \downarrow \hspace{0.1cm} \rightarrow \hspace{0.1cm}$	+ 🗸 🗌		\bigcirc				
	Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Risk ratio	Log risk ratio	Std Err	Variance	Dose	Analgesic	Pain Type	м	N	0
1	Forbes, 1990	17	66	17	68	1.030	0.030	0.296	0.088	a Low	Unknown	Post-op			
2	2 Laska 1983a	32	56	26	54	1.187	0.171	0.183	0.033	a Low	Paracetamo	Post-op			
3	3 Laska 1983b	51	80	47	81	1.099	0.094	0.127	0.016	a Low	Paracetamo	Post-op			
4	Laska 1983c	38	62	40	68	1.042	0.041	0.143	0.020	a Low	Paracetamo	Post-op			
5	i McQuay 1996a	8	30	2	31	4.133	1.419	0.748	0.559	a Low	Ibuprofen	Post-op			
E	6 Ali, 2007	134	310	121	310	1.107	0.102	0.096	0.009	b Medium	Paracetamo	Dysmenorrh			
7	7 Diener, 2005	429	482	418	498	1.060	0.059	0.025	0.001	b Medium	Unknown	Headache			
8	Forbes, 1991a	24	44	17	48	1.540	0.432	0.239	0.057	b Medium	Ibuprofen	Post-op			
9	Forbes, 1991b	19	49	13	49	1.462	0.379	0.298	0.089	b Medium	Ibuprofen	Post-op			
10) Laska, 1983d	50	78	52	81	0.999	-0.001	0.119	0.014	b Medium	Paracetamo	Post-op			
11	Laska, 1983e	39	62	42	68	1.018	0.018	0.136	0.019	b Medium	Paracetamo	Post-op			
10	1 - J 10004	40	57	20	EO	1.010	0.074	0.140	0.000	L SALAD	Daraaatama	D			

© www.Meta-Analysis.com

Caffeine by subgroups

Click File > Save As and save the file

<u>+</u> C	omprehensive meta	a analysis -	[C:\Users\Bi	ostat\Drop	box\Work	shops Three	-Day\Caffein	e\Caffeine.c	maj	-		Contract States				
<u>F</u> ile	<u>E</u> dit Format <u>V</u> ie	w <u>I</u> nsert I	dentify <u>T</u> o	ols Comp	outational o	ptions Ana	ilyses <u>H</u> elp									
Run	analyses → 🏷 [ן 🚔 🛥 ב	883	K 🖻 🛍	y 🕫 🕨	· *=	••• 00. ••• → 00. •••	$\bullet \hspace{0.1cm} \downarrow \hspace{0.1cm} \rightarrow \hspace{0.1cm}$	+ 🗸 🗌		Q					
	Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Risk ratio	Log risk ratio	Std Err	Variance	Dose	Analgesic	Pain Type	м	N	0	
1	Forbes, 1990	17	66	17	68	1.030	0.030	0.296	0.088	a Low	Unknown	Post-op				
2	Laska 1983a	32	56	26	54	1.187	0.171	0.183	0.033	a Low	Paracetamo	Post-op				
3	Laska 1983b	51	80	47	81	1.099	0.094	0.127	0.016	a Low	Paracetamo	Post-op				
4	Laska 1983c	38	62	40	68	1.042	0.041	0.143	0.020	a Low	Paracetamo	Post-op				
5	McQuay 1996a	8	30	2	31	4.133	1.419	0.748	0.559	a Low	Ibuprofen	Post-op				
6	Ali, 2007	134	310	121	310	1.107	0.102	0.096	0.009	b Medium	Paracetamo	Dysmenorrh				
7	Diener, 2005	429	482	418	498	1.060	0.059	0.025	0.001	b Medium	Unknown	Headache				
8	Forbes, 1991a	24	44	17	48	1.540	0.432	0.239	0.057	b Medium	Ibuprofen	Post-op				
9	Forbes, 1991b	19	49	13	49	1.462	0.379	0.298	0.089	b Medium	Ibuprofen	Post-op				

T Comprehensive meta analysis (CAUsers) Piestath Dranbay/Workshops Three Day/Coffeine/Coffeine small

Note that the file name is now in the header.

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

. † c	omprehensive meta	a analysis -	[C:\Users\Bi	ostat\Drop	box\Work	shops Three	-Day\Caffein	e\Caffeine.c	ma]		-					
<u>F</u> ile	<u>E</u> dit Format <u>V</u> ie	w <u>I</u> nse r I	Identify <u>T</u> o	ole Comp	utational	ptions And	lycos <u>H</u> olp									
Run	analyses → 🏷 [נ 🚔 🐔		6 🖻 🛍	y 🕫 🕨	- *= *≣	+++ 00.† 00.+	$ \checkmark \checkmark \rightarrow$	+ 🗸 🗌		Q					
	Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Risk ratio	Log risk ratio	Std Err	Variance	Dose	Analgesic	Pain Type	м	N	0	
1	Forbes, 1990	17	66	17	68	1.030	0.030	0.296	0.088	a Low	Unknown	Post-op				_
2	Laska 1983a	32	56	26	54	1.187	0.171	0.183	0.033	a Low	Paracetamo	Post-op				
3	Laska 1983b	51	80	47	81	1.099	0.094	0.127	0.016	a Low	Paracetamo	Post-op				
4	Laska 1983c	38	62	40	68	1.042	0.041	0.143	0.020	a Low	Paracetamo	Post-op				
5	McQuay 1996a	8	30	2	31	4.133	1.419	0.748	0.559	a Low	Ibuprofen	Post-op				
6	Ali, 2007	134	310	121	310	1.107	0.102	0.096	0.009	b Medium	Paracetamo	Dysmenorrh				
7	Diener, 2005	429	482	418	498	1.060	0.059	0.025	0.001	b Medium	Unknown	Headache				
8	Forbes, 1991a	24	44	17	48	1.540	0.432	0.239	0.057	b Medium	Ibuprofen	Post-op				
9	Forbes, 1991b	19	49	13	49	1.462	0.379	0.298	0.089	b Medium	Ibuprofen	Post-op				

By convention we've put the treated group (caffeine plus analgesic) in the first two columns and the control (analgesic alone) in the second two columns. Also by convention, we've defined "Event" as the presence of the outcome (relief).

When we follow these conventions, and if the treated group does better than the control, then

- If the "event" is a bad outcome (such as relapse), the risk ratio will be less than 1.
- If the "event" is a good outcome (such as relief), the risk ratio will be greater than 1.

Therefore, in the present case, a risk ratio greater than 1 indicates that patients treated with caffeine were more likely to get relief.

It's always a good idea to check at least one study and make sure that we have the direction right. For this purpose we'll use the last study (McQauy), where the risk ratio is very high, and the distinction between groups should be clear.

🕇 C	omprehensive me	eta analysis -	C:\Users\Bi	ostat\Drop	box\Work	shops Three	-Day\Caffeir	ne\Caffeine.c	:ma]	-					
<u>F</u> ile	<u>E</u> dit Format <u>V</u>	iew <u>I</u> nsert	Identify <u>T</u> o	ols Comp	outational	options An	alyses <u>H</u> elp								
Run	analyses 🔸 📎	D 🚅 🖷		% 🖹 🖻 🛍	s 🕫 🕨	-*= *≣	.00 +.0 ++ +.0 00. □	▼ ↓ →	+ 🗸 🗌] <u></u> ≹↓ <mark>Z</mark> ↓	\mathbb{Q}				
	Study name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Risk ratio	Log risk ratio	Std Err	Variance	Dose	Analgesic	Pain Type	М	N	0
1	Forbes, 1990	17	7 66	17	68	1.030	0.030	0.296	0.088	a Low	Unknown	Post-op			
2	Laska 1983a	32	2 56	26	54	1.187	0.171	0.183	0.033	a Low	Paracetamo	Post-op			
3	Laska 1983b	51	1 80	47	81	1.099	0.094	0.127	0.016	a Low	Paracetamo	Post-op			
4	Laska 1983c	38	3 62	40	68	1.042	0.041	0.143	0.020	a Low	Paracetamo	Post-op			
5	McQuay 1996a	8	3 30	2	31	4.133	1.419	0.748	0.559	a Low	Ibuprofen	Post-op			
6	Ali, 2007	134	4 310	121	310	1.107	0.102	0.096	0.009	b Medium	Paracetamo	Dysmenorrh			
7	Diener, 2005	429	9 482	418	498	1.060	0.059	0.025	0.001	b Medium	Unknown	Headache			
8	Forbes, 1991a	24	4 44	17	48	1.540	0.432	0.239	0.057	b Medium	Ibuprofen	Post-op			
9	Forbes, 1991b	19	9 49	13	49	1.462	0.379	0.298	0.089	b Medium	Ibuprofen	Post-op			
10	Laska, 1983d	50) 78	52	81	0.999	-0.001	0.119	0.014	b Medium	Paracetamo	Post-op			
11	Laska, 1983e	39	9 62	42	68	1.018	0.018	0.136	0.019	b Medium	Paracetamo	Post-op			
12	Laska, 1983f	42	2 57	28	50	1.316	0.274	0.148	0.022	b Medium	Paracetamo	Post-op			
13	Laska, 1983g	42	2 45	37	46	1.160	0.149	0.083	0.007	b Medium	Paracetamo	Post-op			
14	McQuay 1996b	14	4 30	2	31	7.233	1.979	0.711	0.506	b Medium	Ibuprofen	Post-op			
15	Migliardi, 1994a	258	3 339	229	337	1.120	0.113	0.048	0.002	b Medium	Paracetamo	Headache			
16	Migliardi, 1994b	253	3 336	221	332	1.131	0.123	0.050	0.002	b Medium	Paracetamo	Headache			
17	Sunshine, 1996a	24	4 50	17	51	1.440	0.365	0.247	0.061	b Medium	Ibuprofen	Post-op			
18	Sunshine, 1996b	36	5 50	33	50	1.091	0.087	0.134	0.018	b Medium	Ibuprofen	Post-op			
19	Winter, 1983	19	9 40	20	41	0.974	-0.027	0.231	0.053	b Medium	Paracetamo	Post-op			
20	Diamond, 2000	65	5 97	55	99	1.206	0.187	0.115	0.013	c High	Ibuprofen	Headache			
21	Laska, 1983h	42	2 56	38	60	1.184	0.169	0.125	0.016	c High	Paracetamo	Post-op			
22	Laska, 1983i	57	7 80	56	81	1.031	0.030	0.103	0.011	c High	Paracetamo	Post-op			
23	Laska, 1983j	45	5 64	43	66	1.079	0.076	0.121	0.015	c High	Paracetamo	Post-op			
24	Laska, 1983k	34	4 40	33	42	1.082	0.079	0.104	0.011	c High	Paracetamo	Post-op			
25	McQuay 1996c	12	2 29	2	31	6.414	1.858	0.719	0.517	c High	Ibuprofen	Post-op			
26	-														
27															

For the caffeine group, more than half the patients (12/29) improved. For the control group, less than 10% (2/31) improved. Clearly, the treated group did better, and the risk ratio (6.414) is greater than one. This tells us that we are interpreting the direction of the effect size properly.

• To run the analysis, click [Run analysis]

							-										-
ſ	<u>F</u> ile	<u>E</u> dit Format <u>V</u> i	w <u>I</u> nsert I	dentify <u>T</u> o	ols Comp	utational o	ptions Ana	ilyses <u>H</u> elp									
	Run	analyses → 🎗	ן 🚔 🛥 נ	88	% 🖻 🛍	l 🖅 🛏	- `= ` ≣	••• 00. ••• → 00. •••	$\bullet \downarrow \rightarrow$	+ 🗸 🗌		•					
L		Studu name	Caffeine Relief	Caffeine Total N	Control Relief	Control Total N	Risk ratio	Log risk ratio	Std Err	Variance	Dose	Analgesic	Pain Type	м	N	0	Ι
	1	Forbes, 1990	17	66	17	68	1.030	0.030	0.296	0.088	a Low	Unknown	Post-op				Ι
	2	Laska 1983a	32	56	26	54	1.187	0.171	0.183	0.033	a Low	Paracetamo	Post-op				
	3	Laska 1983b	51	80	47	81	1.099	0.094	0.127	0.016	a Low	Paracetamo	Post-op				
	4	Laska 1983c	38	62	40	68	1.042	0.041	0.143	0.020	a Low	Paracetamo	Post-op				
	5	McQuay 1996a	8	30	2	31	4.133	1.419	0.748	0.559	a Low	Ibuprofen	Post-op				
	6	Ali, 2007	134	310	121	310	1.107	0.102	0.096	0.009	b Medium	Paracetamo	Dysmenorrh				
	7	Diener, 2005	429	482	418	498	1.060	0.059	0.025	0.001	b Medium	Unknown	Headache				
	8	Forbes, 1991a	24	44	17	48	1.540	0.432	0.239	0.057	b Medium	Ibuprofen	Post-op				
	9	Forbes, 1991b	19	49	13	49	1.462	0.379	0.298	0.089	b Medium	Ibuprofen	Post-op				
	10	Laska 1983d	50	78	52	81	0.999	-0.001	0.119	0.014	h Medium	Paracetamo	Post-on				

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

This is the basic analysis screen

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

Compre	ehensive meta analysis -	[Analysis]					1.000				-	
<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> iew Comput	tational optic	ons Analyse	s <u>H</u> elp								
← Data er	ntry t⊒ Next table	井 Higt	h resolution pl	ot 🛛 🔁 Sele	ect by 🛛 🕇	 Effect mea 	sure: Risk ratio			III II 🚁 E	t∣£	Q
Model	Study name		Statis	tics for each s	study			Risł	< ratio and 95	% CI		
		Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00	
	Forbes, 1990	1.030	0.576	1.841	0.101	0.920			+			
	Laska 1983a	1.187	0.830	1.697	0.938	0.348			+-			
	Laska 1983b	1.099	0.857	1.408	0.743	0.457			+			
	Laska 1983c	1.042	0.787	1.379	0.287	0.774			+			
1	McQuay 1996a	4.133	0.954	17.904	1.897	0.058						
1	Ali, 2007	1.107	0.917	1.338	1.060	0.289			+			
1	Diener, 2005	1.060	1.009	1.114	2.316	0.021						
1	Forbes, 1991a	1.540	0.965	2.458	1.810	0.070			<u> </u>			
1	Forbes, 1991b	1.462	0.815	2.620	1.274	0.203						
1	Laska, 19830 Laska, 1992a	1.010	0.791	1.250	-0.012	0.990			T			
	Laska, 13036 Laska, 19936	1.010	0.773	1.331	1.051	0.054			T.			
	Laska, 1303i Laska 1993a	1.310	0.304	1.703	1.001	0.004			Ľ			
1	McOueu 1996b	7 233	1 795	29.156	2 782	0.075			ľ			
	Midliardi 1994a	1 1 2 0	1.019	1 231	2.702	0.003			4			
	Migliardi, 1994b	1 1 31	1.076	1 247	2.000	0.013			Ļ.			
1	Sunshine 1996a	1 440	0.888	2,336	1 478	0.0139			<u> </u>			
1	Sunshine, 1996b	1.091	0.838	1.420	0.647	0.518			+			
1	Winter, 1983	0.974	0.619	1.531	-0.115	0.908			-			
1	Diamond, 2000	1.206	0.963	1.510	1.634	0.102			+-			
1	Laska, 1983h	1.184	0.927	1.513	1.354	0.176			+-			
1	Laska, 1983i	1.031	0.843	1.260	0.293	0.769			+			
1	Laska, 1983j	1.079	0.851	1.369	0.629	0.530			+			
	Laska, 1983k	1.082	0.882	1.328	0.753	0.451			+			
	N cQuay 1996c	6.414	1.568	26.237	2.586	0.010						
Fixed		1.097	1.061	1.134	5.446	0.000			1			
Finad D												
Fixed H	Both models			01.17								
Basic sta	Une study removed	Cumulativ	e analysis	Lalculations	:							

Virtually all studies have risk ratios over 1.0, which means that the caffeine group (analgesic plus caffeine) did better than the control (analgesic alone), but the effect is statistically significant in only a few of the studies.

The effects seem to be reasonably consistent. Aside from three exceptions, all of the studies have effect sizes that line up in a fairly narrow range.

The pooled effect is 1.097, which means that the addition of caffeine increases the chance of relief by about 10%. This is a modest increase but statistically significant (p < 0.001).

Click [Both models]

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

🕂 Compre	hensive meta analysis - [Analysis]										-	
<u>File</u> <u>E</u> dit	Format View Comput	ational optic	ons Analyse	es <u>H</u> elp									
← Data en	try try Next table	井 Higi	h resolution p	lot 🔁 Sele	ct by 🛛 🚽	Effect mea	sure: Risk ratio		-=-	îī ≇ E ₹	í	Q	
Model	Study name		Stati	stics for each s	tudy			Ris	sk ratio and 95% Cl				
		Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00 10	0.00		
Fixed Random	Forbes, 1990 Laska 1983a Laska 1983b Laska 1983c McQuay 1996a Ali, 2007 Diener, 2005 Forbes, 1991a Forbes, 1991b Laska, 1983d Laska, 1983e Laska, 1983e Laska, 1983e McQuay 1996b Migliardi, 1994b Sunshine, 1996b Sunshine, 1996b Sunshine, 1996b Sunshine, 1996b Winter, 1983 Diamond, 2000 Laska, 1983i Laska, 1983i Laska, 1983i Laska, 1983i	1.030 1.187 1.099 1.042 4.133 1.107 1.060 1.540 1.462 0.999 1.018 1.316 1.160 7.233 1.120 1.131 1.440 1.031 0.974 1.206 1.184 1.007 1.082 6.414 1.007 1.011	0.576 0.830 0.857 0.787 0.954 0.917 1.009 0.965 0.815 0.791 0.984 0.396 1.079 1.026 0.888 0.619 0.963 0.963 0.963 0.963 0.963 0.963 0.965 0.888 0.619 0.963 0.965 0.888 0.619 0.965 0.888 0.888 0.619 0.965 0.886 0.888 0.619 0.965 0.886 0.965	1.841 1.637 1.408 1.379 17.904 1.338 1.114 2.458 2.620 1.260 1.260 1.260 1.331 1.759 1.365 2.9.156 1.231 1.247 2.336 1.247 2.336 1.247 1.513 1.510 1.513 1.513 1.513 1.513 1.260 1.369 1.328 1.328 2.6237 1.134 1.161	0.101 0.338 0.743 0.287 1.897 1.060 2.316 1.810 1.274 -0.012 0.134 1.851 1.794 2.730 2.470 1.478 0.647 -0.115 1.634 1.634 1.634 0.293 0.629 0.753 2.566 5.446 4.721	0.920 0.348 0.457 0.774 0.058 0.021 0.070 0.203 0.990 0.834 0.064 0.073 0.005 0.019 0.013 0.019 0.013 0.019 0.013 0.019 0.013 0.019 0.012 0.176 0.300 0.451 0.010 0.000							
Fixed Ra	an lom Both models												
Basic stat	s Une study removed	Cumulativ	e analysis	Calculations									

Under the fixed-effect model the pooled effect size is 1.097, while under the random-effects model the pooled effect size is 1.111. While the two models yield very similar results, the random-effects model is a better fit for the way the studies were sampled, and therefore that is the model we will use in the analysis.

- The fixed-effect model would be appropriate if all the studies were virtual replicates of each other, which is not the case here. The dose varied, the analgesic varied, the patients varied.
- The random-effects model would be appropriate if the studies vary in ways that may impact the effect size (such as those mentioned immediately above). Therefore, we will use the random-effects model.

• Click Random on the tab at the bottom

The plot now displays the random-effects analysis alone.

← Data entry Model SI Forbe Laska Laska Laska McQu Ali, 20 Diene Forbe Forbe Laska Laska Laska Laska Laska Sunsł Sunsł Sunsł Winte Diamo Laska	t7 Next table itudy name a 1983a a 1983b a 1983c uay 1996a 007 er, 2005 a, 1991b a, 1983d a, 1983d a, 1983d	ния isk ratio Lov 1.030 1.187 1.099 1.042 4.133 1.107 1.060 1.540 1.540 1.540 0.939	gh resolution Statistic www.er limit 1 0.576 0.830 0.857 0.787 0.954 0.917 0.0965 0.815	n plot cs for each s Upper limit 1.841 1.697 1.408 1.379 17.904 1.338 1.114 2.458	Select by tudy Z-Value 0.101 0.938 0.743 0.287 1.897 1.060	+ Effect p-Value 0.920 0.348 0.457 0.774	0.01	Risk ratio R 0.10	sk ratio and 955	□ <u>==</u> ŢŢ ; CI 10.00	<u>∔ E_</u> 100.00	() (
Model Si Forbe Laska Laska Laska McQu Ali, 20 Diene Forbe Forbe Laska Laska Laska Laska Laska McQu Miglia Sunst Sunst Sunst	Ri s; 1990 a 1983a a 1983b a 1983c uay 1996a 007 er, 2005 s; 1991b a; 1983d a, 1983d a, 1983e	isk ratio Low 1.030 1.187 1.099 1.042 4.133 1.107 1.060 1.540 1.540 0.999	Statistic wer limit 0.576 0.830 0.857 0.787 0.954 0.917 1.009 0.965 0.815	cs for each s Upper limit 1.841 1.697 1.408 1.379 17.904 1.338 1.114 2.458	tudy Z-Value 0.101 0.938 0.743 0.287 1.897 1.050	p-Value 0.920 0.348 0.457 0.774	0.01	0.10	sk ratio and 95% 1.00	CI 10.00	100.00		
Forbe Laska Laska Laska Laska McQu Ali, 20 Diene Forbe Forbe Forbe Laska Laska Laska Laska McQu Miglia Sunst Sunst Sunst	Ri a 1983a a 1983b a 1983c uay 1996a 007 er, 2005 sc, 1991a sc, 1991b a, 1983d a, 1983d a, 1983d	isk ratio Low 1.030 1.187 1.099 1.042 4.133 1.107 1.060 1.540 1.462 0.999	wer limit 0.576 0.830 0.857 0.787 0.954 0.917 1.009 0.965 0.815	Upper limit 1.841 1.697 1.408 1.379 17.904 1.338 1.114 2.458	Z-Value 0.101 0.938 0.743 0.287 1.897 1.60	p-Value 0.920 0.348 0.457 0.774	0.01	0.10	1.00	10.00	100.00		
Forbe Laska Laska McQu Ali, 20 Diene Forbe Forbe Laska Laska Laska Laska McQu Miglia Sunst Sunst Sunst	es, 1990 a 1983a a 1983b a 1983c uay 1996a 007 er, 2005 es, 1991a as, 1991b a, 1983d a, 1983d	1.030 1.187 1.099 1.042 4.133 1.107 1.060 1.540 1.462 0.999	0.576 0.830 0.857 0.787 0.954 0.917 1.009 0.965 0.815	1.841 1.697 1.408 1.379 17.904 1.338 1.114 2.458	0.101 0.938 0.743 0.287 1.897 1.050	0.920 0.348 0.457 0.774			+-				
Laska Laska McQu Ali, 20 Diene Forbe Forbe Laska Laska Laska McQu Miglia Sunsh Sunsh Sunsh Uvinte Diamo Laska	a 1983a a 1983b a 1983c uay 1996a 007 er, 2005 ss, 1991a as, 1991b a, 1983d a, 1983d	1.187 1.099 1.042 4.133 1.107 1.060 1.540 1.462 0.999	0.830 0.857 0.787 0.954 0.917 1.009 0.965 0.815	1.697 1.408 1.379 17.904 1.338 1.114 2.458	0.938 0.743 0.287 1.897 1.050	0.348 0.457 0.774			+				
Laska Laska McQu Ai, 20 Diene Forbe Laska Laska Laska Laska Laska McQu Miglia Sunst Sunst Sunst Sunst	a 1983b a 1983c uay 1996a 007 er, 2005 es, 1991a es, 1991b a, 1983d a, 1983e	1.099 1.042 4.133 1.107 1.060 1.540 1.462 0.999	0.857 0.787 0.954 0.917 1.009 0.965 0.815	1.408 1.379 17.904 1.338 1.114 2.459	0.743 0.287 1.897 1.060	0.457 0.774							
Laska McQu Ali, 20 Forbe Forbe Laska Laska Laska Laska McQu Miglia Sunst Sunst Sunst Sunst	a 1983c uay 1996a 007 er, 2005 es, 1991a es, 1991b a, 1983d a, 1983e	1.042 4.133 1.107 1.060 1.540 1.462 0.999	0.787 0.954 0.917 1.009 0.965 0.815	1.379 17.904 1.338 1.114 2.459	0.287 1.897 1.060	0.774			+				
McQu Ali, 20 Diene Forbe Laska Laska Laska McQu Miglia Sunst Sunst Sunst Diamo Laska	uay 1996a 007 er, 2005 es, 1991a es, 1991b a, 1983d a, 1983e	4.133 1.107 1.060 1.540 1.462 0.999	0.954 0.917 1.009 0.965 0.815	17.904 1.338 1.114 2.458	1.897 1.060				+-				
Ali, 20 Diene Forbe Laska Laska Laska Laska McQu Miglia Sunst Sunst Sunst Sunst	007 er, 2005 es, 1991a es, 1991b a, 1983d a, 1983e	1.107 1.060 1.540 1.462 0.999	0.917 1.009 0.965 0.815	1.338 1.114 2. 4 59	1.060	0.058				+ +			
Diene Forbe Laska Laska Laska Laska McQu Miglia Sunsł Sunsł Winte Diamo Laska	er, 2005 es, 1991a es, 1991b a, 1983d a, 1983e	1.060 1.540 1.462 0.999	1.009 0.965 0.815	1.114 2.459	1.000	0.289			+-				
Forbe Forbe Laska Laska Laska McQu Miglia Sunst Sunst Sunst Diamo Laska	es, 1991a es, 1991b a, 1983d a, 1983e	1.540 1.462 0.999	0.965 0.815	2 459	2.316	0.021			+				
Forbe Laska Laska Laska Laska McQu Miglia Sunst Sunst Sunst Sunst Diamo Laska	es, 1991b a, 1983d a, 1983e	1.462 0.999	0.815	2.400	1.810	0.070			<u> </u>				
Laska Laska Laska McQu Miglia Sunst Sunst Winte Diamo Laska	a, 1983d a, 1983e	0.999		2.620	1.274	0.203			++				
Laska Laska KcQu Miglia Sunsh Sunsh Sunsh Diamo Laska	a, 1983e		0.791	1.260	-0.012	0.990			+				
Laska Laska McQu Miglia Sunsh Sunsh Winte Diamo Laska		1.018	0.779	1.331	0.134	0.894			+				
Laska McQu Miglia Sunsh Sunsh Winte Diamo Laska	a, 1983f	1.316	0.984	1.759	1.851	0.064			⊢ +-				
McQu Miglia Sunsł Sunsł Winte Diamc Laska	a, 1983g	1.160	0.986	1.365	1.794	0.073			+				
Miglia Miglia Sunsł Sunsł Winte Diamo Laska	uay 1996b	7.233	1.795	29.156	2.782	0.005							
Miglia Sunsł Sunsł Winte Diamo Laska	ardi, 1994a	1.120	1.019	1.231	2.350	0.019			+				
Sunsh Sunsh Winte Diamo Laska	ardi, 1994b	1.131	1.026	1.247	2.470	0.013			+				
Sunsh Winte Diamo Laska	hine, 1996a	1.440	0.888	2.336	1.478	0.139			++-				
Winte Diamo Laska	hine, 1996b	1.091	0.838	1.420	0.647	0.518			+-				
Diamo Laska	er, 1983	0.974	0.619	1.531	-0.115	0.908			+				
Laska	ond, 2000	1.206	0.963	1.510	1.634	0.102			+-				
	a, 1983h	1.184	0.927	1.513	1.354	0.176			+-				
Laska	a, 1983i	1.031	0.843	1.260	0.293	0.769			+				
Laska	a, 1983j	1.079	0.851	1.369	0.629	0.530			+-				
Laska	a, 1983k	1.082	0.882	1.328	0.753	0.451			+				
licQu	uay 1996c	6.414	1.568	26.237	2.586	0.010							
Random		1.111	1.064	1.161	4.721	0.000			4				
Fixed Bandom													
rixed nandom	Path madels												

A quick view of the plot suggests the following

- Most of the studies suggest an advantage for caffeine
- The observed effects are pretty consistent, with three exceptions.
- The summary effect is 1.111 with a CI of 1.064 to 1.161. Thus, the mean effect is small (only about a 10% increase in response as compared with the control).
- The summary effect has a Z-value 4.721 a *p*-value of < 0.001. Thus we can reject the null hypotheses that the true risk ratio is 1.0.

Click [Next table] Click here 🕂 Comprehensive meta analysis - [Analysis File Edit Format nputational options Analyses Help Data entry t⊋ Next table - High resolution plot 🛛 🔁 Select by .. + Effect measure: Risk ratio · 🗏 🗌 🏥 🎞 🏦 🖺 🕄 🔍 Effect size and 95% interval Tau-squared Model Test of null (2-Tail) Heterogeneity Number Studies Point Lowe limit Upper Tau Standard Error Model Squared estimate Z-value P-value at ron P-value l-squared Fixed 25 25 1.097 1.061 1.134 5.446 0.000 27.734 24 0.271 13.462 0.001 0.003 0.000 0.037 Random 1.111 1.064 1.161 4.721 0.000

Figure 1

The statistics at the left duplicate those we saw on the prior screen.

- Under the random-effects model the risk ratio is 1.111 with a 95% confidence interval of 1.064 to 1.161. The test of the null (that the true risk ratio is 1.0) yields a Z-value of 4.721 and a corresponding p-value of < 0.001.
- The statistics at the upper right relate to the dispersion of effect sizes across studies.
- The Q-value is 27.7234 with df=24 and p=0.271. Q reflects the distance of each study from the mean effect (weighted, squared, and summed over all studies). Q is always computed using FE weights (which is the reason it is displayed on the "Fixed" row, but applies to both FE and RE analyses.
- If all studies actually shared the same true effect size, the expected value of Q would be equal to
 df (which is 24). Here, Q is greater than that value, and so there is some evidence of variance in
 true effects. However, this excess variance falls within the range that could be attributed to
 random sampling error in effect sizes (not statistically significant).
- While the heterogeneity is not statistically significant, we will still use the random-effects model, since this matches the sampling frame for the studies.
- T^2 is the estimate of the between-study variance in true effects. This estimate is 0.001. *T* is the estimate of the between-study standard deviation in true effects. This estimate is 0.037. These value are both in log units.
- *I*² reflects the proportion of true variance to observed variance. This is 13.46, which tells us that only about 13% of the observed variance in effects is real. Put another way, if we were looking at a plot of the true effects rather than the observed effects, the variance in effects would be decreased by (1 minus .13) some 87%.
- Click [Next table] to return to this screen

Under the random-effects model the risk ratio is 1.111 with a 95% confidence interval of 1.064 to 1.161. This tells is that the <u>mean</u> true effect probably falls in the range of 1.064 to 1.161. However, since the true risk ratio varies from study to study, we might also want to know how widely the true risk ratios vary from the mean. This is the role of the prediction interval. We can use the spreadsheet [Prediction intervals] as follows.

Since we have select Risk ratio as the effect size, some of the statistics in this table are presented in risk ratio units. To compute the prediction interval we'll need to see statistics in log units.

🕂 Comprehensive	meta analysis - [Anal	ysis]								-				
<u>F</u> ile <u>E</u> dit F <u>o</u> rmat	t <u>V</u> iew Computation	al options Ana	alyses <u>H</u> elp											
← Data entry	t↓ Next table	🕂 High resoluti	on plot 🛛 🔁	Select by	Effect measu	re: Risk ratio	- = [] = 1	1 # E	ê 👔				
Model		Effect	size and 95%	interval	Test of nu	ıll (2-Tail)		Hetero	ogeneity			Tau-so	quared	
Model	Numbe Studie	er Point s estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	l-squared	Tau Squared	Standard Error	Variance	Tau
Fixed Random		25 1.09 25 1.11	7 1.061 1 1.064	1.134 1.161	5.446 4.721	0.000 0.000	27.734	24	0.271	13.462	0.001	0.003	0.000	0.037

- Open the spreadsheet [Prediction Intervals.xls]
- Select the tab for [Ratios]
- In CMA select Log risk ratio as the index
- Select Format > Increase decimals
- Copy the A|B|C|D values as shown from CMA to Excel

T Comprehensiv	e meta analysis - [Analysis	5]				C. Marca										
<u>F</u> ile <u>E</u> dit F <u>o</u> rma ← Data entry	t ³ Next table #	options Ana - High resolutio	lyses <u>H</u> elp on plot H elp	Select by	+ Effect m	easure: Log ni	sk ratio		11 # E ł	0 1	1					
Model		Eſ	fect size an	d 95% confi	dence interv	val	Test of n	ıll (2-Tail)		Heter	ogeneity			Tau-s	quared	
Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	l-squared	Tau Squared	Standard Error	Variance	Tau
Fixed Random		25 0.092; 25 0.1059 A	B	0.0003 0.0005	0.0590	0.1254 0.1492	5.4460 4.7214	0.0000	27.7335	24.0000	0.2714	13.4622	0.0014	0.0031	0.0000	0.0374
Figure 2																
XI 🔒 🗧	5 - ¢ - ∓								Predi	ction in	tervals.xls	sx - Excel				

FILE HOME INSERT PAGE LAYOUT FORMULAS DATA REVIEW VIEW ACROBAT

N12	2	\bullet : \times \checkmark f_x								
	А		В	С	D	Е	F	G	н	I
1		F	rediction intervals for OR, I	RR, HR						
2										
3		Enter values in shaded o	ells only							
4		Values must be entered	in log units							
5										
6		Number of studies		25			Α			
7		Degrees of freedom		23	p. 130					
8		Critical value for t (95%	interval)	2.068658	p. 131					
9		Mean effect (random ef	fect weights) in log units	0.105500	12.7		В			
10		Tau-squared in log units		0.001400	16.5		С			
11		Variance of M * in log u	nits	0.000500	12.8		D			
12										
13		Prediction interval in log	units							
14		Mean		0.105500						
15		Prediction interval (95%	lower limit	0.015329	17.7					
16		Prediction interval (95%)) upper limit	0.195671	17.8					
17										
18		Prediction interval in rat	io units							
19		Mean		1.111266						
20		Prediction interval (95%	lower limit	1.015447						
21		Prediction interval (95%	upper limit	1.216126						
22										
22										

The confidence interval is 1.064 to 1.161 (we read this from Figure 1 which shows the risk ratios rather than the log values). The prediction interval (from Excel) is 1.015 to 1.216.

The true risk ratio varies from study to study. The mean risk ratio probably falls in the range of 1.064 to 1.161. The true effect size for any single study will usually fall in the range of 1.015 to 1.216.

© www.Meta-Analysis.com

Caffeine by subgroups

In 95% of all possible meta-analyses, the true mean will fall in the range indicated by the Cl. In 95% of all meta-analyses, 95% of all studies will fall inside the range indicated by the Pl. This assumes that the true effect sizes are normally distributed.

To this point we've established that caffeine is effective, but the effect is rather small. However, we know that the dose of caffeine varied among studies. We're going to group by dose (low, moderate, or high) and see if the effect size was related to dose.

When we're dividing the studies into subgroups, the between-studies variance (T^2) must be computed within subgroups. However, we have two options. We can then pool the separate estimates, and use the pooled value for all subgroups. Or, we can use a separate estimate for each subgroup.

Our plan is to pool the estimates. To select that option

Click Computational options > Mixed and random effects options

🕂 Comprehe	ensive meta ar	nalysis - [Analysis]										
<u>File Edit Fo</u>	<u>o</u> rmat <u>V</u> iew	Computational options Analyses	<u>H</u> elp									
← Data entry	y t∓Ne	+ Effect measure	elect by	+ Effect	measure: Ris	k ratio	- = _		‡ E ₹	🗘		
Model	Study name	[] CI Level 95%				Risk	ratio and 95%	a				
	, i	🔁 Select by										
		🚍 Group by	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00			
F	Forbes, 199	Compare groups	0.101	0.920			+					
	Laska 1983 i Laska 1983 i j	D Mixed and random effects opti	0.938 0.743	0.348 0.457			+-					
L	Laska 1983	1.042 0.787 1	.37\$ 0.287	0.774			+					
N N	McQuay 1995	1.133 0.051 17	1.001 1.007	0.058				++-				

The program displays this wizard

- At the top select the first option, to "Assume a common among-study variance"
- At the bottom select the first option, to "Combine subgroups using a fixed-effect model"

Data en	trv tr Next ta	ble 👎	- High resolut	tion plot	- B Select by	+ Effect	t measure: Ris	ratio	- 🗐		° ≒ E }	0 1
		++										2 4
lodel	Study name		Stati	stics for each	n study			F	Risk ratio and 95	5% CI		
		Bisk ratio	Lower limit	Lloper limit	Z.Value	o.Value	0.01	0.10	1.00	10.00	100.00	
		That I duo	Lottor limit	opportant	2.4000	pvalue	0.01	0.10	1.00	10.00	100.00	
	Forbes, 1990	1.030	0.576	1.8	Et. Mixed and	d random ef	fects options				×	
	Laska 1983a	1.187	0.830	1.6	~	1.000			-		_	
	Laska 1983b	1.099	0.857	1.4	C							
	Laska 1983c	1.042	0.787	1.3	Combining	i studies wi	inin a subgro	чр				
	McQuay 1996a	4.133	0.954	17.9	(
	Ali, 2007	1.107	0.917	1.3	 Assume (neel with 	a common an	nong-study vari	ince com	ponent across s	ubgroups		
	Diener, 2005	1.060	1.009	1.1	(poor wi	nin-group esu	mates or tau-sy	Jareuj.				
	Forbes, 1991a	1.540	0.965	2.4								
	Forbes, 1991b	1.462	0.815	2.6	O Do not a	assume a com within-group.	mon among-stu	dy variani oguarad)	ce component a	icross subgro	ups (do	
	Laska, 1983d	0.999	0.791	1.2	I not poor	waanngooup	estimates or tac	squareuj	. This is the opt	onuseu by n		
	Laska, 1983e	1.018	0.779	1.3								
	Laska, 1983	1.316	0.984	1.7								
	Laska, 1983g	1.160	0.986	1.3	Combining	ı subgroups	to yield an o	verall e	fect			
	McQuay 1996b	7.233	1.795	29.1								
	Migliardi, 1994a	1.120	1.019	1.2	 Combine 	e subgroups u	sing fixed effec	model				
	Migliardi, 1994b Cumahina, 1996a	1.131	1.025	1.2	C. Combine		oing random off	ooto mode	4			
	Sunshine, 1996a Sunshine, 19965	1.440	0.888	2.3	Combine	s subgroups u	sing random en	sots mout	51			
	Sunstine, 1336D	0.974	0.638	1.4								
	Diamond 2000	1 206	0.013	1.0								
	Laska 1983h	1 194	0.363	15			Car	cel	Apply	Ok		
	Laska 1983i	1.031	0.327	12								
	Laska 1983i	1.031	0.851	13								
	Laska, 1983k	1.082	0.882	1.328	3 0.753	0.451			+			
	McQuay 1996c	6.414	1.568	26.237	2.586	0.010					-	
lom		1 111	1.064	1 161	4 721	0.000			4			

Now, we can tell the program to run the analysis by subgroups.

Click Computational options > Group by

🕂 Comprei	nensive meta ar	naly:	sis - [Analysis]				-						William Trees	
<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> iew	Co	mputational op	ptions Anal	yses <u>H</u> elp									
+ Data ent	ry t구 Ne	+	Effect measu	re	•	elect by	+ Effec	t measure:	Risk ratio	- 3		± E ₹	😲 🖞	
Model	Study name	[]	CI Level 95%		•	Нv			F	Risk ratio and 95	% CI			
	ſ	2	Select by											
			Group by		N	2-Value	p-Value	0.01	0.10	1.00	10.00	100.00		
	Forbes, 1990		Compare gro	unc	ЬČ	0.10	0.920			-				
	Laska 1983a Laska 1983b	Σ	Mixed and rai	ndom effect	s options	0.938	0.348 0.457			+				
	Laska 1983c		1.042	0.787	1.379	0.287	0.774			+-				
	McQuay 1996a		4.133	0.954	17.904	1.897	0.058							
	Ali, 2007		1.107	0.917	1.338	1.060	0.289			+				
	Diener, 2005		1.060	1.009	1.114	2.316	0.021			ŀ				
	Forbes, 1991a		1.540	0.965	2.458	1.810	0.070							
1	Forber 1991b		1 / 1 / 1 / 2	0.915	2 620	1 27/	0.203	I	I	<u> </u>	I	I		

- Select Dose
- Check the two boxes
- Click Ok

🕂 Compre	hensive meta analy	sis - [Analysi	s]			-			-					
<u>F</u> ile <u>E</u> dit	Format <u>V</u> iew Co	mputational	options Ai	nalyses <u>H</u> elp	p									
🔶 Data er	ntry t⊒ Next ta	able 🚦	- High resolu	ition plot	Select by	+ Effect	t measure: F	Risk ratio	- 🔳 [‡E ₹	🖸 🥵		
Model	Study name		Stat	istics for each	study			Ris	k ratio and 95	% CI				
		Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00			
	Forbes, 1990	1.030	0.576	1.841	0.101	0.920			+					
	Laska 1983a	1.187	C G	oup by		0.040			×					
	Laska 1983b	1.099		oup by	1.100									
	Laska 1983c	1.042												
I	McQuay 1996a	4.133	Bu	n a senarate	e analysis fo	or each leve	of							
	All, 2007 Disease 2005	1.107												
	Diener, 2005	1.060	Do	se		-								
	Forbes, 1991a	1.340												
	Foldes, 1997d	0.000		Also run analu	eie across lav	els of dose								
	Laska, 1903u	1 010		nico rain analy	010 0010000 1011	010 01 0000								
	Laska, 1993f	1 316		Compare effec	t at different l	evels of dose								
	Laska, 1983n	1 160												
	McQuau 1996b	7 233									.			
	Migliardi 1994a	1 120				Cancel	Reset	0	k 🛛					
1	Migliardi, 1994b	1,131												
1	Sunshine, 1996a	1.440												
1	Sunshine, 1996b	1.091	0.000	1.420	0.047	0.010	-							
1	Winter, 1983	0.974	0.619	1.531	-0.115	0.908								

The screen should look like this

	ta analysis - [Analy	sis]					A					
F <u>o</u> rmat <u>V</u> ie	ew Computationa	I options A	nalyses <u>H</u> e	р								
ny t∓	Next table	- High resolu	tion plot	Select by	. 🕂 Effec	t measure: F	lisk ratio	- 🔳	🗆 📰 II	∄ E ₹	🗘	
Group by	Study name		Stati	stics for each s	tudy			Ris	k ratio and 95%	i Cl		
2000		Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00	
alow	Forbes 1990	1.030	0.576	1.9/1	0.101	0.920	1		_	1		
alow	Looko 1002o	1.000	0.070	1.041	0.101	0.320			1			
alow	Laska 1983b	1.107	0.000	1.007	0.330	0.340			L.			
alow	Laska 19030	1.033	0.037	1.400	0.743	0.437			T.			
aLow	MaQuan 1990a	4 1 2 2	0.707	17.904	1.007	0.774						
aLow	MCQuay 1556a	4.133	0.334	1 011	1.037	0.000						
a Low	AE 2007	1.107	0.941	1.311	1.235	0.215			T.			
DMedium	All, 2007	1.107	0.917	1.338	1.060	0.289			t			
b Medium	Diener, 2005	1.060	1.009	1.114	2.316	0.021			t			
b Medium	Forbes, 1991a	1.540	0.965	2.458	1.810	0.070			-+-			
b Medium	Forbes, 1991b	1.462	0.815	2.620	1.274	0.203			+			
b Medium	Laska, 1983d	0.999	0.791	1.260	-0.012	0.990			+			
b Medium	Laska, 1983e	1.018	0.779	1.331	0.134	0.894			+			
b Medium	Laska, 1983f	1.316	0.984	1.759	1.851	0.064			+-			
b Medium	Laska, 1983g	1.160	0.986	1.365	1.794	0.073			+			
b Medium	McQuay 1996b	7.233	1.795	29.156	2.782	0.005						
b Medium	Migliardi, 1994a	1.120	1.019	1.231	2.350	0.019			+			
b Medium	Migliardi, 1994b	1.131	1.026	1.247	2.470	0.013			+			
b Medium	Sunshine, 1996a	1.440	0.888	2.336	1.478	0.139			++-			
b Medium	Sunshine, 1996b	1.091	0.838	1.420	0.647	0.518			+			
b Medium	Winter, 1983	0.974	0.619	1.531	-0.115	0.908			-			
b Medium		1.114	1.053	1.179	3,776	0.000			4			
e High	Diamond 2000	1 206	0.963	1 510	1.634	0.102			++			
c High	Laska 1983b	1 184	0.000	1 513	1 354	0.176			<u> </u>			
e High	Laska, 1983i	1.031	0.021	1.010	0.293	0.769			L.			
e High	Lacka 1983i	1.001	0.040	1 369	0.629	0.530			4			
o High	Laska, 1993k	1.073	0.001	1 229	0.752	0.350			Ĺ			
- High	Moffung 1996a	6 414	1 569	26,227	2 596	0.431			í			
	MCQuay 15560	0.414	1.000	1 247	2.300	0.010						
c High			1.005	1.247	2.073	0.030			L. L.			
	a Low a Low a Low a Low a Low a Low a Low b Medium b Medium	Group by Dose Study name Group by Dose Study name a Low Laska 1983a a Low Laska 1983c a Low Laska 1983c a Low Laska 1983c a Low Laska 1983c b Medium Forbes, 1991a b Medium Dener, 2005 b Medium Laska, 1983d b Medium Laska, 1983d b Medium Laska, 1983g b Medium Laska, 1983g b Medium Migliardi, 1934b b Medium Sunshine, 1996b <	Group by Dose Study name Group by Dose Study name Brisk ratio Risk ratio a Low Forbes, 1990 a Low Laska 1983a a Low Laska 1983a a Low Laska 1983b a Low Laska 1983c a Low McQuay 1996a McGuay 1996a 1.130 b Medium Forbes, 1991a b Medium Laska, 1983e b Medium Laska, 1983g b Medium Laska, 1983g b Medium Migliardi, 1994b b Medium Sunshine, 1996a b Medium Sunshine, 1996a b Medium Sunshine, 1996b b Medium Sunshine, 1996b b Medium Sunshine, 1996b b Medium Sunshine, 1996b b Medium	Group by Dose Study name Risk ratio Lower limit a Low Forbes, 1990 1.030 0.576 a Low Laska 1983a 1.030 0.576 a Low Laska 1983a 1.087 0.830 a Low Laska 1983a 1.099 0.857 a Low Laska 1983c 1.042 0.787 a Low Laska 1983c 1.042 0.787 a Low Laska 1983c 1.042 0.787 a Low McQuay 1996a 4.133 0.994 a Low McQuay 1996a 1.100 0.941 b Medium Diener, 2005 1.060 1.009 b Medium Forbes, 1991a 1.462 0.815 b Medium Laska, 1983g 1.018 0.773 b Medium Laska, 1983g 1.160 0.986 b Medium Laska, 1983g 1.160 0.868 b Medium Migliardi, 1994a 1.120 1.019 b Medium Surshine, 1996a 1.440 0.838 <td>Group by Dose Study name Risk ratio Lower limit Upper limit a Low Forbes, 1990 1.030 0.576 1.841 a Low Laska 1983a 1.187 0.830 1.697 a Low Laska 1983b 1.099 0.857 1.408 a Low Laska 1983b 1.042 0.787 1.379 a Low Laska 1983b 1.042 0.787 1.379 a Low Laska 1983b 1.042 0.787 1.379 a Low McQuay 1996a 4.133 0.954 1.338 b Medium Diener, 2005 1.060 1.009 1.114 b Medium Forbes, 1991a 1.540 0.965 2.458 b Medium Laska, 1983d 0.999 0.791 1.260 b Medium Laska, 1983d 1.018 0.779 1.331 b Medium Laska, 1983g 1.160 0.986 1.285 b Medium Laska, 1983g 1.161 0.986 1.285 b Medium<td>group by Dose Study name Statistics for each study Broup by Dose Study name Risk ratio Lower limit Upper limit Z-Value a Low Laska 1983a 1.030 0.576 1.841 0.101 a Low Laska 1983b 1.039 0.576 1.841 0.101 a Low Laska 1983b 1.039 0.577 1.408 0.743 a Low Laska 1983b 1.042 0.787 1.379 0.287 a Low Laska 1983b 1.042 0.787 1.379 0.287 a Low Laska 1983b 1.042 0.787 1.379 0.287 a Low Laska 1983c 1.042 0.787 1.379 0.287 b Medium Disener, 2005 1.060 1.009 1.114 2.316 b Medium Easka, 1983e 1.018 0.779 1.331 1.0134 b Medium Laska, 1983g 1.150 0.986 1.355 1.794 b Medium Laska, 1983g 1.160</td><td>Group by Dose Study name Fisk ratio Lower limit Upper limit Z-Value p-Value a Low Forbes, 1990 1.030 0.576 1.641 0.101 0.320 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 a Low Laska 1983a 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983b 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983c 1.042 0.787 1.379 0.287 0.774 a Low McQuay 1996a 4.133 0.954 1.7304 1.897 0.058 a Low McQuay 1996a 1.107 0.917 1.338 1.060 0.289 b Medium Derner, 2005 1.060 1.009 1.114 2.316 0.021 0.393 b Medium Forbes, 1991a 1.642 0.815 2.620 1.274 0.203 b Medium Laska, 1983g 1.018 0.779 <</td><td>group by Dose Study name Statistics for each study P-Value 0.01 a Low Forbes, 1990 1.030 0.576 1.841 0.101 0.320 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 a Low Laska 1983b 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983b 1.099 0.857 1.348 0.743 0.457 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low McGuay 1996a 4.133 0.954 1.7304 1.897 0.058 a Low McGuay 1996a 1.110 0.941 1.311 1.226 0.216 b Medium Statista 1983 1.060 0.965 2.458 1.810 0.070 <tr< td=""><td>group by Dose Study name Statistics for each study percent finit Upper limit ZValue p-Value 0.01 0.10 a Low Laska 1983a 1.030 0.576 1.841 0.101 0.920 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 a Low Laska 1983b 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983b 1.042 0.777 1.408 0.743 0.457 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low McQuay 1996a 4.133 0.954 17.904 1.897 0.058 a Low McGuay 1996a 4.133 0.954 1.7304 1.897 0.058 a Low McGuay 1996a 4.133 0.954 1.7304 1.897 0.058 b Medium Diener, 2005 1.060 1.009 1.114 2.316 0.021 0.999 b Medium Laska, 1983g<td>group Dose Study name Statistics for each study public field public field public field public field public field public field field</td><td>group Dose Study name Statistics for each study performation peri</td><td>Group Dose Study name Statistics for each study P-Value 0.01 0.10 1.00 10.00 100.00 a Low Laska 1983a 1.030 0.576 1.841 0.101 0.920 0.01 0.10 1.000 100.00 100.00 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 0.444 4<!--</td--></td></td></tr<></td></td>	Group by Dose Study name Risk ratio Lower limit Upper limit a Low Forbes, 1990 1.030 0.576 1.841 a Low Laska 1983a 1.187 0.830 1.697 a Low Laska 1983b 1.099 0.857 1.408 a Low Laska 1983b 1.042 0.787 1.379 a Low Laska 1983b 1.042 0.787 1.379 a Low Laska 1983b 1.042 0.787 1.379 a Low McQuay 1996a 4.133 0.954 1.338 b Medium Diener, 2005 1.060 1.009 1.114 b Medium Forbes, 1991a 1.540 0.965 2.458 b Medium Laska, 1983d 0.999 0.791 1.260 b Medium Laska, 1983d 1.018 0.779 1.331 b Medium Laska, 1983g 1.160 0.986 1.285 b Medium Laska, 1983g 1.161 0.986 1.285 b Medium <td>group by Dose Study name Statistics for each study Broup by Dose Study name Risk ratio Lower limit Upper limit Z-Value a Low Laska 1983a 1.030 0.576 1.841 0.101 a Low Laska 1983b 1.039 0.576 1.841 0.101 a Low Laska 1983b 1.039 0.577 1.408 0.743 a Low Laska 1983b 1.042 0.787 1.379 0.287 a Low Laska 1983b 1.042 0.787 1.379 0.287 a Low Laska 1983b 1.042 0.787 1.379 0.287 a Low Laska 1983c 1.042 0.787 1.379 0.287 b Medium Disener, 2005 1.060 1.009 1.114 2.316 b Medium Easka, 1983e 1.018 0.779 1.331 1.0134 b Medium Laska, 1983g 1.150 0.986 1.355 1.794 b Medium Laska, 1983g 1.160</td> <td>Group by Dose Study name Fisk ratio Lower limit Upper limit Z-Value p-Value a Low Forbes, 1990 1.030 0.576 1.641 0.101 0.320 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 a Low Laska 1983a 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983b 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983c 1.042 0.787 1.379 0.287 0.774 a Low McQuay 1996a 4.133 0.954 1.7304 1.897 0.058 a Low McQuay 1996a 1.107 0.917 1.338 1.060 0.289 b Medium Derner, 2005 1.060 1.009 1.114 2.316 0.021 0.393 b Medium Forbes, 1991a 1.642 0.815 2.620 1.274 0.203 b Medium Laska, 1983g 1.018 0.779 <</td> <td>group by Dose Study name Statistics for each study P-Value 0.01 a Low Forbes, 1990 1.030 0.576 1.841 0.101 0.320 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 a Low Laska 1983b 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983b 1.099 0.857 1.348 0.743 0.457 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low McGuay 1996a 4.133 0.954 1.7304 1.897 0.058 a Low McGuay 1996a 1.110 0.941 1.311 1.226 0.216 b Medium Statista 1983 1.060 0.965 2.458 1.810 0.070 <tr< td=""><td>group by Dose Study name Statistics for each study percent finit Upper limit ZValue p-Value 0.01 0.10 a Low Laska 1983a 1.030 0.576 1.841 0.101 0.920 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 a Low Laska 1983b 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983b 1.042 0.777 1.408 0.743 0.457 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low McQuay 1996a 4.133 0.954 17.904 1.897 0.058 a Low McGuay 1996a 4.133 0.954 1.7304 1.897 0.058 a Low McGuay 1996a 4.133 0.954 1.7304 1.897 0.058 b Medium Diener, 2005 1.060 1.009 1.114 2.316 0.021 0.999 b Medium Laska, 1983g<td>group Dose Study name Statistics for each study public field public field public field public field public field public field field</td><td>group Dose Study name Statistics for each study performation peri</td><td>Group Dose Study name Statistics for each study P-Value 0.01 0.10 1.00 10.00 100.00 a Low Laska 1983a 1.030 0.576 1.841 0.101 0.920 0.01 0.10 1.000 100.00 100.00 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 0.444 4<!--</td--></td></td></tr<></td>	group by Dose Study name Statistics for each study Broup by Dose Study name Risk ratio Lower limit Upper limit Z-Value a Low Laska 1983a 1.030 0.576 1.841 0.101 a Low Laska 1983b 1.039 0.576 1.841 0.101 a Low Laska 1983b 1.039 0.577 1.408 0.743 a Low Laska 1983b 1.042 0.787 1.379 0.287 a Low Laska 1983b 1.042 0.787 1.379 0.287 a Low Laska 1983b 1.042 0.787 1.379 0.287 a Low Laska 1983c 1.042 0.787 1.379 0.287 b Medium Disener, 2005 1.060 1.009 1.114 2.316 b Medium Easka, 1983e 1.018 0.779 1.331 1.0134 b Medium Laska, 1983g 1.150 0.986 1.355 1.794 b Medium Laska, 1983g 1.160	Group by Dose Study name Fisk ratio Lower limit Upper limit Z-Value p-Value a Low Forbes, 1990 1.030 0.576 1.641 0.101 0.320 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 a Low Laska 1983a 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983b 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983c 1.042 0.787 1.379 0.287 0.774 a Low McQuay 1996a 4.133 0.954 1.7304 1.897 0.058 a Low McQuay 1996a 1.107 0.917 1.338 1.060 0.289 b Medium Derner, 2005 1.060 1.009 1.114 2.316 0.021 0.393 b Medium Forbes, 1991a 1.642 0.815 2.620 1.274 0.203 b Medium Laska, 1983g 1.018 0.779 <	group by Dose Study name Statistics for each study P-Value 0.01 a Low Forbes, 1990 1.030 0.576 1.841 0.101 0.320 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 a Low Laska 1983b 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983b 1.099 0.857 1.348 0.743 0.457 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low McGuay 1996a 4.133 0.954 1.7304 1.897 0.058 a Low McGuay 1996a 1.110 0.941 1.311 1.226 0.216 b Medium Statista 1983 1.060 0.965 2.458 1.810 0.070 <tr< td=""><td>group by Dose Study name Statistics for each study percent finit Upper limit ZValue p-Value 0.01 0.10 a Low Laska 1983a 1.030 0.576 1.841 0.101 0.920 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 a Low Laska 1983b 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983b 1.042 0.777 1.408 0.743 0.457 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low McQuay 1996a 4.133 0.954 17.904 1.897 0.058 a Low McGuay 1996a 4.133 0.954 1.7304 1.897 0.058 a Low McGuay 1996a 4.133 0.954 1.7304 1.897 0.058 b Medium Diener, 2005 1.060 1.009 1.114 2.316 0.021 0.999 b Medium Laska, 1983g<td>group Dose Study name Statistics for each study public field public field public field public field public field public field field</td><td>group Dose Study name Statistics for each study performation peri</td><td>Group Dose Study name Statistics for each study P-Value 0.01 0.10 1.00 10.00 100.00 a Low Laska 1983a 1.030 0.576 1.841 0.101 0.920 0.01 0.10 1.000 100.00 100.00 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 0.444 4<!--</td--></td></td></tr<>	group by Dose Study name Statistics for each study percent finit Upper limit ZValue p-Value 0.01 0.10 a Low Laska 1983a 1.030 0.576 1.841 0.101 0.920 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 a Low Laska 1983b 1.099 0.857 1.408 0.743 0.457 a Low Laska 1983b 1.042 0.777 1.408 0.743 0.457 a Low Laska 1983b 1.042 0.787 1.379 0.287 0.774 a Low McQuay 1996a 4.133 0.954 17.904 1.897 0.058 a Low McGuay 1996a 4.133 0.954 1.7304 1.897 0.058 a Low McGuay 1996a 4.133 0.954 1.7304 1.897 0.058 b Medium Diener, 2005 1.060 1.009 1.114 2.316 0.021 0.999 b Medium Laska, 1983g <td>group Dose Study name Statistics for each study public field public field public field public field public field public field field</td> <td>group Dose Study name Statistics for each study performation peri</td> <td>Group Dose Study name Statistics for each study P-Value 0.01 0.10 1.00 10.00 100.00 a Low Laska 1983a 1.030 0.576 1.841 0.101 0.920 0.01 0.10 1.000 100.00 100.00 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 0.444 4<!--</td--></td>	group Dose Study name Statistics for each study public field public field public field public field public field public field field	group Dose Study name Statistics for each study performation peri	Group Dose Study name Statistics for each study P-Value 0.01 0.10 1.00 10.00 100.00 a Low Laska 1983a 1.030 0.576 1.841 0.101 0.920 0.01 0.10 1.000 100.00 100.00 a Low Laska 1983a 1.187 0.830 1.697 0.938 0.348 0.444 4 </td

For the low, medium, and high-dose studies the mean risk ratio is 1.110, 1.114, and 1.120, respectively. Therefore, there's no evidence that the impact varies by dose.

Click the "Show individual studies" button. This will hide all of the individual studies and display the summary effects only as shown here.

🕂 Compre	hensive meta	analysis - [Analy	/sis]											
<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> ie	w Computation	al options A	nalyses <u>H</u> e	lp									
+ Data en	try t∓	Next table	🕂 High resolu	ution plot	Belect by .	🕂 🕂 Effe	ct measure: F	Risk rati	• · ·		III II	‡E ₹	🗘	
Model	Group by Dose	Study name		Stati	stics for each :	study				Show i	individal	studies		
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.0	1 0.1	0	1.00	10.00	100.00	
Random	a Low		1.110	0.941	1.311	1.236	0.216				+			
Random	b Medium		1.114	1.053	1.179	3.776	0.000				4			
Random	c High		1.120	1.006	1.247	2.073	0.038				+			
Random	Overall		1.115	1.063	1.169	4.480	0.000				+			

Right-click on the forest plot and change the scale to 0.50 to 2

計 Compre	hensive meta	a analysis - [Analy	sis]						a tea tea " any second teat they a				
<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> ie	w Computationa	al options A	nalyses <u>H</u> el	p								
🔶 Data en	itry t∓	Next table	🕂 High resolu	ution plot	Belect by .	🕂 Effe	ct measure:	Risk ratio	· 🗏 🛄 🏥 🗊 🏦 🗞 🧎 🏅	Q			
Model	Group by Dose	Study name		Stati	stics for each	study			Risk ratio and 95% Cl				
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.50	1.00 2	2.00			
Random	a Low		1.110	0.941	1.311	1.236	0.216		+				
Random	b Medium		1.114	1.053	1.179	3.776	0.000						
Random	c High		1.120	1.006	1.247	2.073	0.038	.					
Random	Overall		1.115	1.063	1.169	4.480	0.000					1	
										Ŧ	Show/hide forest plot	L_	
												~	Log scale .50 to 2
										_			Log scale .1 to 10
													Log scale .01 to 100
1													

With the pooled effects clarified in this way, we can see clearly that the summary effect size is virtually identical in all three dose groups.

Note that the effect is statistically significant for the medium and high doses, but not for the low dose. However, it would be a serious mistake to conclude that the effect varies by dose. Clearly, the effect is essentially identical for all three doses. What distinguishes the low dose group from the others is not that the effect is smaller, but only that the estimate of the effect size is less precise. (And in this example that's solely because there are only four studies in the low-dose group).

It is fair to say that we have evidence of the effect in two groups only. It is not correct to say that the effect in the low dose group is smaller unless the test that compares the effects shows a statistically significant effect of dose (which it will not in this case).

Toggle the "All studies button" to display the studies again.

Given what we've seen, it's clear that there the test to compare doses will not be statistically significant, but we'll proceed to show the test.

Click Next table

a entry 🔁 Next tab	le 井 H	High resolution	plot 🔁 S	elect by	+ Effect measure	re: Risk ratio	•=] ∄ E.	E 3 Q				
Groups		Effect siz	e and 95%:	interval	Test of nu	ıll (2-Tail)		Hetero	geneity			Tau-so	quared	
Group	Number Studies	Point estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	l-squared	Tau Squared	Standard Error	Variance	Tau
Fixed effect analysis	5													
a Low	5	1.108	0.947	1.298	1.279	0.201	3.489	4	0.480	0.000	0.000	0.026	0.001	0.0
b Medium	14	1.093	1.054	1.133	4.831	0.000	16.692	13	0.214	22.119	0.002	0.004	0.000	0.0
c High	6	1.117	1.012	1.233	2.206	0.027	7.370	5	0.195	32.153	0.007	0.015	0.000	0.0
Total within							27.551	22	0.191					
Total between							0.183	2	0.913					
Overall	25	1.097	1.061	1.134	5.446	0.000	27.734	24	0.271	13.462	0.001	0.003	0.000	0.0
Mixed effects analy	sis													
a Low	5	1.110	0.941	1.311	1.236	0.216								
b Medium	14	1.114	1.053	1.179	3.776	0.000								
c High	6	1.120	1.006	1.247	2.073	0.038								
Total between							0.010	2	0.995					
Overall	25	1.115	1.063	1.169	4.480	0.000								

This screen displays two sets of statistics

The table labeled "Fixed-effect analysis" uses fixed-effect weights within subgroups. The table labeled "Mixed-effects analysis" uses random-effects weights within subgroups. This is the table we will use.

As we saw on the prior screen, the risk ratio within the three subgroups is 1.110, 1.114, and 1.117. The effect is not statistically significant in the low-dose group (p=0.216) but is statistically significant in the other two (p< 0.001, p=0.038). However, this does not suggest that the effect is smaller in the first group (clearly, the effect size in the sample is virtually identical in all three groups).

To test the hypothesis that the effect size varies by dose we look to the line labeled "Total between". The Q-value is 0.010 with 2 df, and the corresponding p-value is 0.995.

Click Next table to return to this screen.

Re-set the scale to 0.01 to 100

<u>File</u> <u>E</u> dit	Format V	iew Computational op	tions Analys	ies <u>H</u> elp								
← Data ei	ntry 🖞	Next table	ligh resolution	plot 🛛 🔁 Se	elect by	+ Effect mea	asure: Risk n	atio	- 🔳 🗖	₩II \$•	E -E 1	Q 1
Model	Group by Dose	Study name		Statis	stics for each :	study			Ris	k ratio and 95%	s Cl	
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00
	a Low	Forbes, 1990	1.030	0.576	1.841	0.101	0.920			- -		
	a Low	Laska 1983a	1.187	0.830	1.697	0.938	0.348			+		
	a Low	Laska 1983b	1.099	0.857	1.408	0.743	0.457			+		
	a Low	Laska 1983c	1.042	0.787	1.379	0.287	0.774			+		
	a Low	McQuay 1996a	4.133	0.954	17.904	1.897	0.058					
Random	a Low		1.110	0.941	1.311	1.236	0.216			+		
	b Medium	Ali, 2007	1.107	0.917	1.338	1.060	0.289			+-		
	b Medium	Diener, 2005	1.060	1.009	1.114	2.316	0.021			+		
	b Medium	Forbes, 1991a	1.540	0.965	2.458	1.810	0.070			<u> </u>		
	b Medium	Forbes, 1991b	1.462	0.815	2.620	1.274	0.203			++		
	b Medium	Laska, 1983d	0.999	0.791	1.260	-0.012	0.990			+		
	b Medium	Laska, 1983e	1.018	0.779	1.331	0.134	0.894			+		
	b Medium	Laska, 1983f	1.316	0.984	1.759	1.851	0.064			<u> </u> +-		
	b Medium	Laska, 1983g	1.160	0.986	1.365	1.794	0.073			+		
	b Medium	McQuay 1996b	7.233	1.795	29.156	2.782	0.005					-
	b Medium	Migliardi, 1994a	1.120	1.019	1.231	2.350	0.019			÷		
	b Medium	Migliardi, 1994b	1.131	1.026	1.247	2.470	0.013			+		
	b Medium	Sunshine, 1996a	1.440	0.888	2.336	1.478	0.139			++-		
	b Medium	Sunshine, 1996b	1.091	0.838	1.420	0.647	0.518			+		
	b Medium	Winter, 1983	0.974	0.619	1.531	-0.115	0.908			+		
Random	b Medium		1.114	1.053	1.179	3.776	0.000			4		
	c High	Diamond, 2000	1.206	0.963	1.510	1.634	0.102			++		
	c High	Laska, 1983h	1.184	0.927	1.513	1.354	0.176			+-		
	c High	Laska, 1983i	1.031	0.843	1.260	0.293	0.769			+		
	c High	Laska, 1983j	1.079	0.851	1.369	0.629	0.530			+-		
	c High	Laska, 1983k	1.082	0.882	1.328	0.753	0.451			+		
	c High	McQuay 1996c	6.414	1.568	26.237	2.586	0.010			1 —		.
Random	c High		1.120	1.006	1.247	2.073	0.038			+		
Random	Overall		1.115	1.063	1.169	4.480	0.000			+		

Fixed Random Both models

Basic stats Calculations

Above, we ran an analysis to see if the effect size varied by dose. Now, we'll run an analysis to see if the effect size varies by the type of analgesic.

Click Computational options > Group by > Analgesic

👬 Compre	hensive meta	analysis - [Analysis]									-			
<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> iew	Computational option	ns Analyses	<u>H</u> elp										
🔶 Data er	itry 1구 N	ext table 🚦 High	resolution plot	t 🔁 Selec	:t by 🕇 🛨	Effect measu	re: Risk ratio		-=	11 11 14 E	£ 👔 🤇)		
Model	Group by Analgesic	Study name		Stati	stics for each :	study			F	isk ratio and 95% (51			
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00		
	Ibuprofen	McQuay 1996a	4,133	0.954	17.904	1.897	0.058			+				
1	Ibuprofen	Forbes, 1991a	1.540	0.965	2.458	1.810	0.070			<u> </u>				
	Ibuprofen	Forbes, 1991b	1.462	0.815	2.620	1.274	0.203			++				
	Ibuprofen	McQuay 1996b	7.233	1.795	29.156	2.782	0.005							
	Ibuprofen	Sunshine, 1996a	1.440	0.888	2.336	1.478	0.139			++-				
	Ibuprofen	Sunshine, 1996b	1.091	0.838	1.420	0.647	0.518			+				
	Ibuprofen	Diamond, 2000	1.206	0.963	1.510	1.634	0.102			+-				
	Ibuprofen	McQuay 1996c	6.414	1.568	26.237	2.586	0.010							
Random	Ibuprofen		1.294	1.119	1.496	3.478	0.001			+				
	Paracetamol	Laska 1983a	1.187	0.830	1.697	0.938	0.348			+-				
	Paracetamol	Laska 1983b	1.099	0.857	1.408	0.743	0.457			+				
	Paracetamol	Laska 1983c	1.042	0.787	1.379	0.287	0.774			+				
	Paracetamol	Ali, 2007	1.107	0.917	1.338	1.060	0.289			+				
	Paracetamol	Laska, 1983d	0.999	0.791	1.260	-0.012	0.990			+				
	Paracetamol	Laska, 1983e	1.018	0.779	1.331	0.134	0.894			+				
	Paracetamol	Laska, 1983f	1.316	0.984	1.759	1.851	0.064			+-				
	Paracetamol	Laska, 1983g	1.160	0.986	1.365	1.794	0.073			+				
	Paracetamol	Migliardi, 1994a	1.120	1.019	1.231	2.350	0.019			+				
	Paracetamol	Migliardi, 1994b	1.131	1.026	1.247	2.470	0.013			+				
	Paracetamol	Winter, 1983	0.974	0.619	1.531	-0.115	0.908			-				
	Paracetamol	Laska, 1983h	1.184	0.927	1.513	1.354	0.176			#				
	Paracetamol	Laska, 1983i	1.031	0.843	1.260	0.293	0.769			T				
	Paracetamol	Laska, 1983 Laska, 1983	1.079	0.851	1.363	0.623	0.530			Ť				
Pandom	Paracetamol	LdSKd, TJOJK	1.002	1.002	1.520	4 201	0.401			T				
nanuoin	Unknown	Forbes 1990	1.020	0.576	1.105	9.001	0.000							
	Unknown	Diener 2005	1.050	1.009	1 114	2 316	0.020							
Bandom	Unknown	Dicitici, 2003	1.000	1.005	1 114	2.317	0.021							
Bandom	Overall		1.097	1.061	1 134	5 446	0.000							
Fixed Ra Basic stal	andom Both ts Calculation	models												
			11								-		 	

We see that there are a number of studies that used Ibuprofen or Paracetamol, but only a few that are classified as "Unknown". Let's limit the analysis to those the first two groups.

Click Computational options > Select by > Analgesic

- Select Ibupfrofen and Paracetamol
- De-select "Unknown"
- Click Ok

🕂 Compre	hensive meta ar	nalysis - [Analysis]					California		teres if an opposite		1000		
<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> iew	Computational option	ns Analyses <u>H</u> elp										
+ Data en	try t⊒ Ne	+ Effect measure		elec	t by 🕇 🕂	Effect measu	ure: Risk ratio		-=-	≣ II ‡ E	. E 🚹	.	
Model	Group by	[] CI Level 95%		► Statis	stics for each :	studv			Bis	k ratio and 95	% CI		
	Analgesic	🔁 Select by											
		🖶 Group by	M	mit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00	
	Ibuprofen	 Compare groups 		954	17.904	1.897	0.058			<u> </u>			
	Ibuprofen	Mixed and randor	n effects options	815	2.458	1.810	0.070						
	Ibuprofen	McQuay 1996b	7.233	1.795	29.156	2.782	0.005			-		-	
	Ibuprofen	Sunshine, 1996a	1.440	0.888	2.336	1.478	0.139			+			
	Ibuprofen	Sunshine, 1996b	1.091	0.838	1.420	0.647	0.518			+			
	Ibuprofen	Diamond, 2000	1.206	0.963	1.510	1.634	0.102			++			
	Ibuprofen	McQuay 1996c	6.414	1.568	26.237	2.586	0.010						
Random	Ibuprofen		1.294	1.119	1.496	3.478	0.001			+			

Comprehensive meta analysis - [Analysis]

<u>File</u> Edit	Format View	Computational optio	is Analyses <u>H</u> elp	
🔶 Data en	try 1구 N	ext table 🕀 High	resolution plot 🛛 🖶 Select by 🔸 Effect measure: Risk ratio 🔹 🗐 🛄 🖽 💭 😩 🗜 🌓 🏠 😳	
Model	Group by Analgesic	Study name	Statistics for each study Risk ratio and 95% Cl	
	Ibuprofen Ibuprofen Ibuprofen Ibuprofen Ibuprofen Ibuprofen Ibuprofen Ibuprofen	McQuay 1996a Forbes, 1991a Forbes, 1991b McQuay 1996b Sunshine, 1996a Sunshine, 1996b Diamond, 2000 McQuay 1996c	Studies Analgesic Select based on Analgesic Analgesic Analgesic U bucrofen Select all	
Random	Ibuprofen Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol	Laska 1983a Laska 1983b Laska 1983c Ali, 2007 Laska, 1983d Laska, 1983e	Paracetamol Clear all Clear all Reset filter Add filter	

The screen should look like this

👬 Compre	ehensive meta a	analysis - [Analysis]					1.000									
<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> iew	Computational option	s Analyses	<u>H</u> elp												
+ Data er	ntry t구 N	ext table 🕀 High	resolution plot	🔁 Selec	t by 🕇 🕂	Effect measu	re: Risk ratio		• 🔳 🗖] == 11	: 🚁 E	£ 👔	Q			
Model	Group by Analgesic	Study name		Stati	stics for each s	tudy				Risk ratio	o and 95% (21				
			Risk ratio	Lower limit	Upper limit	Z-Value	p∙Value	0.01	0.1	0	1.00	10.00	100.00			
	Ibuprofen Ibuprofen Ibuprofen Ibuprofen Ibuprofen Ibuprofen	McQuay 1996a Forbes, 1991a Forbes, 1991b McQuay 1996b Sunshine, 1996a Sunshine, 1996b Diamond, 2000	4.133 1.540 1.462 7.233 1.440 1.091 1.206	0.954 0.965 0.815 1.795 0.888 0.838 0.963 1.500	17.904 2.458 2.620 29.156 2.336 1.420 1.510	1.897 1.810 1.274 2.782 1.478 0.647 1.634	0.058 0.070 0.203 0.005 0.139 0.518 0.102									
Random	Ibuprofen	MCQUAY 1996C	1.294	1.568	26.237	2.586	0.010				+					
Dender	Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol Paracetamol	Laska 1983a Laska 1983b Laska 1983b Laska 1983b Laska, 1983d Laska, 1983d Laska, 1983a Miglardi, 1994a Miglardi, 1994a Miglardi, 1994b Vinter, 1983 Laska, 1983h Laska, 1983j Laska, 1983j Laska, 1983j	1.187 1.099 1.042 1.107 0.999 1.018 1.316 1.160 1.120 1.131 0.974 1.184 1.031 1.079 1.082 1.079	0.830 0.857 0.787 0.917 0.791 0.791 0.986 1.019 1.026 0.619 0.927 0.843 0.851 0.882	1.697 1.408 1.379 1.338 1.260 1.331 1.759 1.365 1.231 1.247 1.531 1.513 1.513 1.260 1.369 1.328	0.938 0.743 0.287 1.060 -0.012 0.134 1.851 1.794 2.350 2.470 -0.115 1.354 0.293 0.629 0.753 0.629	0.348 0.457 0.774 0.289 0.990 0.894 0.064 0.073 0.019 0.013 0.908 0.176 0.769 0.530 0.451			-	++ + + + + + + + + + + + + + + + + + +					
Random	Paracetamol Overall		1.111	1.060	1.165	4.391	0.000				+					
Fixed Ra	andom Both r	nodels														

Hide the individual studies and change the scale

🕂 Comprel	hensive meta	a analysis - [Analysis]					California es	And the Competence Margaret	1. A.	
<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> ie	w Comput	ational optic	ons Analyse	s <u>H</u> elp						
+ Data ent	try t∓	Next table	井 Higt	n resolution pl	ot 🛛 🔁 Sele	ect by 🚽	Effect mea	sure: Risk ratio	- 🗏 🛄 📰 🏗 🏝 E	£	Q
Model	Group by Analgesic	Study name		Stati	stics for each	study			Risk ratio and 95% Cl		
			Risk ratio	Lower limit	Upper limit	Z-Value	p·Value	0.50	1.00	2.00	
Random	Ibuprofen		1.294	1.119	1.496	3.478	0.001		· · · · · · · · · · · · · · · · · · ·		
Random	Paracetamo		1.111	1.060	1.165	4.391	0.000				
Random	Overall		1.127	1.078	1.179	5.250	0.000		-+-		
I											
1											

For studies that used ibuprofen, caffeine increased the response rate by 29%. For studies that used Paracetemol, caffeine increased the response rate by 11%. Thus, the difference in this sample is substantial.

However, there's a lot of overlap in the confidence intervals and it's not clear whether or not this difference is statistically significant. To compare the two effects, click Next table.

a entry t7 Next	table 🏦 H	ligh resolution	plot 🔁 S	elect by 🚽	 Effect measure 	re: Risk ratio	• 🔳		1 # E	Į <u>1</u> Į				
Groups		Effect siz	e and 95%	interval	Test of nu	ll (2-Tail)		Hetero	geneity			Tau-so	juared	
Group	Number Studies	Point estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed effect anal	ysis													
Ibuprofen	8	1.294	1.119	1.496	3.478	0.001	16.101	7	0.024	56.524	0.070	0.079	0.006	0.265
Paracetamol	15	1.111	1.060	1.165	4.391	0.000	4.537	14	0.991	0.000	0.000	0.004	0.000	0.000
Total within							20.638	21	0.481					
Total between							3.819	1	0.051					
Overall	23	1.127	1.078	1.179	5.250	0.000	24.457	22	0.324	10.046	0.001	0.004	0.000	0.038
Mixed effects an	alysis													
Ibuprofen	8	1.294	1.119	1.496	3.478	0.001								
Paracetamol	15	1.111	1.060	1.165	4.391	0.000								
Total between							3.819	1	0.051					
Overall	23	1 1 2 7	1.078	1 1 7 9	5 250	0.000								

As before, we're working with the section labeled "Mixed effects analysis" and the relevant line is the one labelled "Total between". The Q-value is 3.819 with 1 df, and the corresponding p-value is 0.051.

People have different ways of reacting to a p-value this close to 0.05. I would conclude that caffeine does have more of an impact for patients being treated with ibuprofen than for patients being treated with paracetamol.

Perhaps more to the point, this suggests that the overall effect size reported earlier (that caffeine increases the response rate by 11%) is really not that relevant to clinical practice. Rather, the utility of caffeine depends on the analgesic. For patients being treated with paracetamol, caffeine had a small impact. For patients being treated with ibuprofen, caffeine had a larger impact.

As always, the difference between groups is observational, not causal. It's possible that caffeine works better with ibuprofen. But it's also possible that the studies which used ibuprofen differed in some ways from the studies that used paracetamol and that it's this factor that was responsible (at least in part) for the difference in effect sizes.

It's worth noting that the higher response rate for the ibuprofen studies seems to be driven (at least in part) by three studies. If there was something unique about these studies that led to the higher response rate, then the difference between subgroups might be due to this factor, and not to the analgesic.

This is always a concern when we compare subgroups. While the allocation to caffeine vs control is based on random assignment, the "allocation" to one subgroup vs. another is observational. While we are referring to the subgroups as "Ibuprofen" vs. "Paracetamol", it's possible that they should be called "Ibuprofen young sample" vs. "Paracetamol older sample", and that caffeine works better with younger patients. (The age part of this example is purely hypothetical).

The studies were also coded for the nature of the pain, and we want to see if the effect size varies by this factor.

First, we need to remove the current filter.

Click Computation options > Select by and tick all the options

Compre	hensive met	a analysis - [/	Analysis]						1.000			and the second second			
<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> ie	w Comput	ational optio	ons Analyse	es <u>H</u> elp										
+ Data en	try t7	Next table	井 High	n resolution pl	lot 🔁 Selec	t by	+	 Effect meas 	ure: Risk ratio			111 # E 1	0		
Model	Group by Analgesic	Study name		Stati	stics for each st	udy				Risl	k ratio and 95%	: Cl			
			Risk ratio	Lower limit	Upper limit), Selec	t by	-		-	×			
	Ibuprofen	McQuay	4.133	0.954	17.904	H	studies	Analgesic	1						
	Ibuprofen	Forbes,	1.540	0.965	2.458		Select	based on th	nis moderator						
I	Ibuprofen	Forbes,	1.462	0.815	2.620										
I	Ibuprofen	McQuay	7.233	1.795	29.156					_					
I	Ibuprofen	Sunshine,	1.440	0.888	2.336		Anaige:	sic		•					
I	Ibuprofen	Sunshine,	1.091	0.838	1.420										
I	Ibuproten	Diamond,	1.206	0.963	1.510		v	buprofen				Select all			
Dandan	Ibuproten	McQuay	5.414	1.568	26.237		F F	Paracetamol				Clear all			
Handom	Duproren	Laska	1.294	1.119	1.495			Jnknown							
I	Paracetamo	Laska	1.107	0.030	1.657										
I	Paracetamo	Laska	1.033	0.001	1.379										
I	Paracetamo	Ali. 2007	1.107	0.917	1.338							Reset filter			
1	Paracetamo	Laska,	0.999	0.791	1.260							Add filter			
1	Paracetamo	Laska,	1.018	0.779	1.331										

Group by Pain type

Select Computational options > Group by > Pain type

← Data e	ntry t7 Next	table 🚦 High re	solution plot	🔁 Select b	y 🕂 Ef	fect measure	Risk ratio	-		11 🏦 E	🔱 🕻 🗐	
Model	Group by Pain Type	Study name		Statis	tics for each :	study			Ris	sk ratio and 95	% CI	
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.0
	Dysmenorrhoea	Ali, 2007	1.107	0.917	1.338	1.060	0.289			+		
Random	Dysmenorrhoea		1.107	0.897	1.367	0.950	0.342			+-		
	Headache	Diener, 2005	1.060	1.009	1.114	2.316	0.021			+		
	Headache	Migliardi, 1994a	1.120	1.019	1.231	2.350	0.019			ŀ		
	Headache	Migliardi, 1994b	1.131	1.026	1.247	2.470	0.013			+		
	Headache	Diamond, 2000	1.206	0.963	1.510	1.634	0.102			++		
landom	Headache		1.104	1.032	1.182	2.865	0.004			+		
	Post-op	Forbes, 1990	1.030	0.576	1.841	0.101	0.920					
	Post-op	Laska 1983a	1.187	0.830	1.697	0.938	0.348			+		
	Post-op	Laska 1983b	1.099	0.857	1.408	0.743	0.457			+-		
	Post-op	Laska 1983c	1.042	0.787	1.379	0.287	0.774			+		
	Post-op	McQuay 1996a	4.133	0.954	17.904	1.897	0.058					
	Post-op	Forbes, 1991a	1.540	0.965	2.458	1.810	0.070			<u>⊢</u> ,		
	Post-op	Forbes, 1991b	1.462	0.815	2.620	1.274	0.203			+		
	Post-op	Laska, 1983d	0.999	0.791	1.260	-0.012	0.990			+		
	Post-op	Laska, 1983e	1.018	0.779	1.331	0.134	0.894			+		
	Post-op	Laska, 1983f	1.316	0.984	1.759	1.851	0.064			⊢ +−		
	Post-op	Laska, 1983g	1.160	0.986	1.365	1.794	0.073			+		
	Post-op	McQuay 1996b	7.233	1.795	29.156	2.782	0.005					
	Post-op	Sunshine, 1996a	1.440	0.888	2.336	1.478	0.139			++-		
	Post-op	Sunshine, 1996b	1.091	0.838	1.420	0.647	0.518			+		
	Post-op	Winter, 1983	0.974	0.619	1.531	-0.115	0.908			+		
	Post-op	Laska, 1983h	1.184	0.927	1.513	1.354	0.176			+		
	Post-op	Laska, 1983i	1.031	0.843	1.260	0.293	0.769			+		
	Post-op	Laska, 1983j	1.079	0.851	1.369	0.629	0.530			+		
	Post-op	Laska, 1983k	1.082	0.882	1.328	0.753	0.451			+		
	Post-op	McQuay 1996c	6.414	1.568	26.237	2.586	0.010			- I -		
Random	Post-op		1.127	1.051	1.209	3.351	0.001			+		
Random	Overall		1.115	1.063	1.169	4.491	0.000			4		

It seems that we have only one study where the pain type is Dysmenorrheea, and so let's remove that from this analysis

Click Computational options > Select by > Pain type

Select Headache and Post-op



Group by Pain type

Compre	enensive meta analy	/sis - [Analysis]								-			 _
<u>F</u> ile <u>E</u> dit	Format <u>V</u> iew Co	omputational options	Analyses H	lelp									
← Data er	ntry t⊋ Next t	able 井 High res	solution plot	🔁 Select b	y 🕇 🕂 Ef	fect measure	Risk ratio	•		11 # E	Q 1 3		
Model	Group by Pain Type	Study name		Stati	tics for each a	study			F	Risk ratio and 95%	i Cl		
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00	
	Headache	Diener, 2005	1.060	1.009	1.114	2.316	0.021			ŀ			
	Headache	Migliardi, 1994a	1.120	1.019	1.231	2.350	0.019			+			
	Headache	Migliardi, 1994b	1.131	1.026	1.247	2.470	0.013			+			
	Headache	Diamond, 2000	1.206	0.963	1.510	1.634	0.102			+-			
Random	Headache		1.104	1.032	1.182	2.865	0.004			+			
	Post-op	Forbes, 1990	1.030	0.576	1.841	0.101	0.920						
	Post-op	Laska 1983a	1.187	0.830	1.697	0.938	0.348			+			
	Post-op	Laska 1983b	1.099	0.857	1.408	0.743	0.457			+			
	Post-op	Laska 1983c	1.042	0.787	1.379	0.287	0.774			-			
	Post-op	McQuay 1996a	4.133	0.954	17.904	1.897	0.058						
	Post-op	Forbes, 1991a	1.540	0.965	2.458	1.810	0.070			<u> </u>			
	Post-op	Forbes, 1991b	1.462	0.815	2.620	1.274	0.203			++			
	Post-op	Laska, 1983d	0.999	0.791	1.260	-0.012	0.990			+			
	Post-op	Laska, 1983e	1.018	0.779	1.331	0.134	0.894			+			
	Post-op	Laska, 1983f	1.316	0.984	1.759	1.851	0.064			+-			
	Post-op	Laska, 1983g	1.160	0.986	1.365	1.794	0.073			+			
	Post-op	McQuay 1996b	7.233	1.795	29.156	2.782	0.005			— —			
	Post-op	Sunshine, 1996a	1.440	0.888	2.336	1.478	0.139			++-			
	Post-op	Sunshine, 1996b	1.091	0.838	1.420	0.647	0.518			+			
	Post-op	Winter, 1983	0.974	0.619	1.531	-0.115	0.908			+			
	Post-op	Laska, 1983h	1.184	0.927	1.513	1.354	0.176			+-			
	Post-op	Laska, 1983i	1.031	0.843	1.260	0.293	0.769			+			
	Post-op	Laska, 1983j	1.079	0.851	1.369	0.629	0.530			+			
	Post-op	Laska, 1983k	1.082	0.882	1.328	0.753	0.451			+			
	Post-op	McQuay 1996c	6.414	1.568	26.237	2.586	0.010						
Random	Post-op		1.127	1.051	1.209	3.351	0.001			+			
Random	Overall		1.115	1.062	1.171	4.389	0.000			+			

Hide the individual studies and expand the scale

🕂 Comprel] Comprehensive meta analysis - [Analysis]												
<u>F</u> ile <u>E</u> dit	Eile Edit Format View Computational options Analyses Help												
+ Data ent	- Data entry 🛟 Next table 🐉 High resolution plot 🛛 🖶 Select by 🔶 Effect measure: Risk ratio 🛛 🕫 🔲 🗒 🛱 🖓 😨												
Model	Group by Pain Type	Study name		Statistics for each study					Risk ratio and 95% CI				
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.50	1.00	2.00			
Random	Headache		1.104	1.032	1.182	2.865	0.004						
Random	Post-op		1.127	1.051	1.209	3.351	0.001		_ + _				
Random	Overall		1.115	1.062	1.171	4.389	0.000						
1													

The effect size seems to be almost identical for the two types of pain

Click Next table

		ngii reconstanti		elect by	+ Effect measu	re: Risk ratio	• 🗐 [비포트	-E 3 🔍				
Groups		Effect siz	e and 95%:	interval	Test of nu	ıll (2-Tail)	Heterogeneity			T au-squared				
Group	Number Studies	Point estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	l-squared	Tau Squared	Standard Error	Variance	Tau
Fixed effect analy	vsis													
Headache	4	1.086	1.044	1.130	4.106	0.000	2.802	3	0.423	0.000	0.000	0.002	0.000	0.000
Post-op	20	1.124	1.053	1.199	3.531	0.000	24.137	19	0.191	21.282	0.006	0.009	0.000	0.078
Total within							26.939	22	0.214					
Total between							0.784	1	0.376					
Overall	24	1.096	1.060	1.134	5.343	0.000	27.723	23	0.226	17.036	0.002	0.003	0.000	0.043
Mixed effects and	lysis													
Headache	4	1.104	1.032	1.182	2.865	0.004								
Post-op	20	1.127	1.051	1.209	3.351	0.001								
Total between							0.173	1	0.677					
Overall	24	1.115	1.062	1.171	4.389	0.000								

The risk ratio is 1.104 for Headache, and 1.127 for Post-op. The line total-between shows the Q-value that compares these two effects sizes. The Q-value is 0.173 with 1 df and p=0.677.

There's no evidence that the impact of caffeine differs by pain type.

Above, we found evidence that caffeine had a stronger effect for patients on ibuprofen than for patients on parecetamol.

It would be helpful to know if this relationship could be explained by a confound with type of pain, or with dose. For example, if the patients taking ibuprofen were more likely to have had a higher dose of caffeine, this could explain the larger effect for these patients. In the present case this seems unlikely, since we found essentially no effect for dose. However, for completeness we will proceed with a meta-regression.

As before, we will limit the analysis to studies that used ibuprofen or paracetamol. We will do this for all the regressions, to ensure that all are based on the same set of studies.

To select only the desired studies

On the main analysis screen (before proceeding to the regression)

- Click Computational options > Select by
- Select Analgesic
- Select Ibuprofen and Paracetamol
- De-select Unknown
- Click Ok

T Comprehensive meta analysis - [Analysis] <u>File Edit Format View</u> Computational options Analyses <u>H</u>elp t[⊋] Ne + Effect measure · 🗏 🛄 🏥 📜 🗦 🛯 🖓 + Data entry ۲ elect by ... + Effect measure: Risk ratio [] CI Level 95% ۲ Risk ratio and 95% Cl Model Study name 🔁 Select by h 10.00 p-Value 0.01 0.10 1.00 100.00 F 📑 Group by ... Laska 0.348 <u>k</u>8 Compare groups **\$**3 0.457 Laska **D** Mixed and random effects options 87 Laska 0.774 McQuay 4.133 0.954 17.904 1.897 0.058 Ali, 2007 1.107 0.917 1.338 1.060 0.289 Forboo 1 540 0.005 2 4E0 1 010 0 070

🕂 Comprehensive meta analysis - [Analysis]

<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> ie	w Computa	ational optio	ns Analyse	s <u>H</u> elp			
+ Data ent	try t∓	Next table	井 High	resolution pl	ot 🛛 🔁 Sele	ct by	+ Effect measure: Risk ratio	
Model	Study name		Stati	stics for each :	study		Risk ratio and 95% Cl	
		Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01 0.10 1.00 10.00 100.00	
Fixed	Laska Laska Laska McQuay Ali, 2007 Forbes, Forbes, Forbes, Laska, Laska, Laska, Laska, Laska, McQuay Migliardi, Sunshine, Winter, Diamond, Laska, Laska, Laska, Laska, Laska, McQuay	1.187 1.099 1.042 4.133 1.107 1.540 1.462 0.999 1.018 1.160 7.233 1.120 1.160 7.233 1.120 1.160 7.233 1.120 1.131 1.440 1.091 1.044 1.091 1.044 1.031 1.079 1.062 6.414 1.127	0.830 0.857 0.954 0.917 0.955 0.815 0.779 0.984 0.986 0.984 0.986 0.838 0.619 0.963 0.927 0.843 0.927 0.843 0.927 0.843 0.927	1.697 1.408 1.379 17.904 1.338 2.458 2.620 1.331 1.759 1.365 2.9.156 1.231 1.247 2.336 1.420 1.531 1.510 1.513 1.250 1.369 1.328 26.237 1.179	0.938 0.743 0.287 1.997 1.060 1.810 1.274 -0.012 0.134 1.734 2.782 2.350 2.470 1.478 0.647 -0.115 1.744 1.354 0.629 0.753 2.586 5.250	0.348 0.457 0.774 0.058 0.269 0.070 0.203 0.894 0.073 0.064 0.073 0.013 0.133 0.518 0.518 0.518 0.102 0.176 0.769 0.530 0.451 0.010	Image: Select by Studies Analgesic Analgesic Image: Select based on this moderator Image: Select based on this moderator Image: Select all Imag	

Click Analyses > Meta-regression 2

•	+ Compret	nensive meta	a analysis - [/	Analysis]						-	- 1			
	<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> ie	w Computa	ational optio	ns Analyse	s <u>H</u> elp								
	+ Data ent	ry t∓	Next table	井 High	res 🛕 Pub	lication bias	-	 Effect mea 	sure: Risk ratio			8 II 🏞 E	0 <mark>1</mark> 5	
	Model	Study name		Statis	tics Het	ta regression a entry	2 - k		Risk	ratio and 95	% CI			
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00		
		Laska	1.187	0.830	1.697	0.938	0.348			+				
		Laska	1.099	0.857	1.408	0.743	0.457			+				
		Laska	1.042	0.787	1.379	0.287	0.774			+				
		McQuay	4.133	0.954	17.904	1.897	0.058							
		Ali, 2007	1.107	0.917	1.338	1.060	0.289			┢				

First, we run the regression using only Analgesic as the covariate. The Q-value for the analgesic is 3.8193 with p= 0.0507, precisely the same values we saw in the subgroups analysis.

File Computational options D	ecimals Analyses	Help 😲					← Modify models	Main results	III Scatterplot		
Main results for Mo	odel 1, Rand	om effec	ts (MM),	Z-Distrib	ution,	Log risk rati	io	← Modify models			
Covariate	Coefficient	Standard Error	95% Lower	95% Upper	Z-value	2-sided P-value					
Intercept	0.2576237	0.0740685	0.1124521	0.4027953	3.4782	0.0005					
Analgesic: Paracetamol	-0.1521702	0.0778647	-0.3047822	0.0004417	-1.9543	0.0507					
Statistics for Model 1											
Test of the model: Simultar	neous test that al	l coefficient	s (excluding	intercept) a	re zero						
Q = 3.8193, df = 1, p = 0.0507	7										
Goodness of fit: Test that u	inexplained varia	ince is zero									
Tau ² = 0.000000000, Tau = 0.	000000000, l ² = 0.	00%, Q = 20.	6377, df = 21,	p = 0.4813							
Comparison of Model 1 wit	th the null model										
Total between-study variar	nce (intercept on	ly)									
Tau ² = 0.001453406, Tau = 0.	038123563, I ² = 10).05%, Q = 24	.4570, df = 22	2, p = 0.3237							
Proportion of total betwee	n-study variance	explained b	y Model 1								
R ² analog = 1.00											
Number of studies in the a	nalysis 23										
Fixed Random											
Hodel 1											

Now, we add Dose and Pain Type as covariates in addition to the analgesic. With these covariates in the model, the line for "Analgesic" tests the impact of this covariate controlling for the other covariates. The p-value is now 0.0451. As expected, since the other covariates had no relation to effect size, including them in the model made no real difference. The p-value for analgesic is essentially unchanged.

This tells us that the relationship between analgesic type and effect size is not due to a confound with these other two covariates. Unfortunately, it's still possible that it's due to a confound with some other (unknown) covariates (possibly some unique aspect of the three outlier studies in the ibuprofen group).

+ Comprehensive	meta analysis - [Meta-regression]				August 1						
<u>F</u> ile Computatio	nal options Decimals Analyses <u>H</u>	elp 😲					+ Modify	models	Main results	III Scatterplot	More results
	Main results for Mo	odel 1, Rand	om effe	cts (MM),	Z-Distrib	ution, I	og risk r	atio			
Set	Covariate	Coefficient	Standard Error	95% Lower	95% Upper	Z-value	2-sided P-value				
	Intercept	0.2742802	0.1783568	-0.0752926	0.6238530	1.5378	0.1241				
	Analgesic: Paracetamol	-0.1729541	0.0863088	-0.3421163	-0.0037919	-2.0039	0.0451				
Dasa	Dose: b Medium	0.0007231	0.1028412	-0.2008418	0.2022881	0.0070	0.9944	0-0.10	005 df-2 -0 00FF		
Dose	Dose: c High	-0.0295401	0.1073673	-0.2399763	0.1808960	-0.2751	0.7832	Q=0.15	986, at=2, p=0.9055		
Dain Turne	Pain Type: Headache	0.0057332	0.1212243	-0.2318620	0.2433284	0.0473	0.9623	0-0.00	17 df-2 -0 0076		
Pain Type	Pain Type: Post-op	0.0080776	0.1215739	-0.2302030	0.2463582	0.0664	0.9470	Q=0.00	147, di=2, p=0.9976		
	Statistics for Model 1 Test of the model: Simultar Q = 4.1384, df = 5, p = 0.5297 Goodness of fit: Test that u Tau ² = 0.002911441, Tau = 0.	neous test that a 7 Inexplained varia 053957769, I ² = 10	II coefficient ance is zero 5.30%, Q = 20	ts (excluding 0.3108, df = 17	intercept) ar 7, p = 0.2586	e zero					
	Comparison of Model 1 wit	h the null mode	I								
	Total between-study variar	nce (intercept on	ly)								
	Tau ² = 0.001453406, Tau = 0.	038123563, I ² = 10	0.05%, Q = 24	1.4570, df = 22	, p = 0.3237						
	Proportion of total betwee	n-study variance	explained b	oy Model 1							
	R ² analog = 0.00 (computed	value is -1.00)									
	Number of studies in the a	nalysis 23									
Fixed Random											
Model 1											



Summary

This analysis includes 25 studies where patients were randomized to receive either analgesic alone or analgesic plus caffeine. Outcome was the proportion of patients who reported a "good" level of pain relief. The effect size was the risk ratio.

Does caffeine affect the likelihood of a good response?

The mean risk ratio is 1.111, which means that caffeine increased the likelihood of a good response by about 11%.

These studies were sampled from a universe of possible studies defined by certain inclusion/exclusion rules as outlined in the full paper. The confidence interval for the risk ratio is 1.064 to 1.161, which tells us that the <u>mean</u> risk ratio in the universe of studies could fall anywhere in this range. This range does not include a risk ratio of 1.0, which tells us that the mean risk ratio is probably not 1.0.

Similarly, the *Z*-value for testing the null hypothesis (that the mean risk ratio is 1.0) is 4.721, with a corresponding *p*-value is < 0.001. We can reject the null hypothesis that caffeine has no effect on response, and conclude that the risk of death is lower in the high-dose group.

Does the effect size vary across studies?

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

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

The *Q*-value is 27.73 with 24 degrees of freedom and a p-value of 0.271. Since the observed variance falls within the range that can be attributed to sampling error, we cannot reject the null that the true effect size is the same in all studies. At the same time, since the observed variance does exceed the expected value, we can report statistics for the estimate of dispersion in true effects.

The l^2 statistic tells us what proportion of the observed variance reflects differences in true effect sizes rather than sampling error. Here, l^2 is 13.642%.

 T^2 is the variance of true effect sizes (in log units). Here, T^2 is 0.001. T is the standard deviation of true effects (in log units). Here, T is 0.037.

Does the effect size vary by subgroup?

While the <u>mean</u> effect size across all studies is modest (a risk ratio of 1.111), it's possible that the mean risk ratio varies by subgroup.

© www.Meta-Analysis.com

Caffeine by subgroups

We used subgroup analyses to compare the effect size in studies that employed a low dose, moderate dose, or high dose of caffeine. The mean risk ratio in these three groups was 1.11, 1.11, and 1.12, respectively. The *Q*-value for the difference is 0.010 with 2 *df* and p = 0.995. Thus, there was no evidence that the risk ratio varied as a function of caffeine dose.

We used subgroup analyses to compare the effect size in studies where patients were being treated for headache vs. studies were being treated for post-surgical pain. The mean risk ratio in these two groups was 1.10, 1.13, respectively. The *Q*-value for the difference is 0.173 with 1 *df* and p = 0.877. Thus, there was no evidence that the risk ratio varied as a function of the pain type.

We used subgroup analyses to compare the effect size in studies where the analgesic was Ibuprofen vs. studies where the analgesic was Paracetamol. The mean risk ratio in these two groups was 1.29, 1.11, respectively. The *Q*-value for the difference is 3.819 with 1 *df* and p = 0.051. Thus, there is evidence that the caffeine had more of an impact in the Ibuprofen studies than it did in the Paracetamol studies.

We used regression to see if this relationship could be explained by a confound with other moderators. The relationship between effect size and drug type remained even after we controlled for caffeine dose and for pain-type. Nevertheless, we cannot rule out the possibility that the selection of drug was related to other factors, and that these factors were responsible for the fact that caffeine was more effective in one subgroup than the other.