Example name Avandia

Effect sizePeto odds ratioAnalysis typeMultiple outcomes from same subjectsLevelAdvanced

Synopsis

Avandia a drug for treating diabetes, but these analyses focused on side-effects. The analysis uses data from 42 studies where patients were randomized to receive Avandia or Placebo. Each study reports data for two outcomes – (a) Myocardial infarction and (b) Death from Cardiovascular causes. The effect size is the Peto odds ratio.

We use this example to show

- How to enter data for multiple outcomes within a study
- How to perform the analysis for one outcome at a time

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]

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# Click Insert > Column for > Study names

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#### Click Insert > Column for > Effect size data

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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



Avandia

The program displays this wizard

Enter the following labels into the wizard

- First group > Avandia
- Second group > Control
- Events > Event
- Non-events > Non-event

(If all rows had the same outcome we would use "Dead" or "MI" as the label for Events. However, the event will vary (Dead or MI depending on the row) so we use the generic "Event" as the label here.

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

🕂 Co	omprehensive met	a analysis -	[Data]													
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All studies will include data for two or more outcomes. These outcomes are based on THE SAME subjects.

The possible outcomes are MI and Death. We will be using multiple rows for each study, and need a column that will identify the outcome for each row.

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1 2 3 4 5 6 7 8 9	Blank row Blank rows Copy of selected row(s) Study	Outcome names Time point names								

Click Insert > Column for > Outcome names

#### The screen should look like this

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Rather than enter the data directly into CMA we will copy the data from Excel

- Switch to Excel and open the file "Avandia"
- Highlight all rows and columns as shown, and press CTRL-C to copy to clipboard

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HOME

INSERT PAGE LAYOUT FORMULAS

DATA

REVIEW

VIEW

ACROBAT

Avandia.xlsx - Excel

A	L • ÷ ×	$\checkmark f_x$	Study					
	Α	В	С	D	E	F	G	Н
1	Study	Outcome	Avandia Events	Avandia N	CTRL Events	CTRL N		
2	49653/011	MI	2	357	0	176	1-Small	
3	49653/020	MI	2	391	1	207	1-Small	
4	49653/024	MI	1	774	1	185	1-Small	
5	49653/093	MI	0	213	1	109	1-Small	
6	49653/094	MI	1	232	0	116	1-Small	
7	100684	MI	0	43	1	47	1-Small	
8	49653/143	MI	1	121	0	124	1-Small	
9	49653/211	MI	5	110	2	114	1-Small	
10	49653/284	MI	1	382	0	384	1-Small	
11	712753/008	MI	1	284	0	135	1-Small	
12	AVM100264	MI	0	294	1	302	1-Small	
13	BRL 49653C/185	MI	2	563	0	142	1-Small	
14	BRL 49653/334	MI	2	278	1	279	1-Small	
15	BRL 49653/347	MI	2	418	0	212	1-Small	
16	49653/015	MI	2	395	1	198	1-Small	
17	49653/079	MI	1	203	1	106	1-Small	
18	49653/080	MI	1	104	2	99	1-Small	
19	49653/082	MI	2	212	0	107	1-Small	
20	49653/085	MI	3	138	1	139	1-Small	
21	49653/095	MI	0	196	0	96	1-Small	
22	49653/097	MI	0	122	1	120	1-Small	
23	49653/125	MI	0	175	1	173	1-Small	
24	49653/127	MI	1	56	0	58	1-Small	
25	49653/128	MI	1	39	0	38	1-Small	
26	49653/134	MI	0	561	2	276	1-Small	
27	49653/135	MI	2	116	3	111	1-Small	
28	49653/136	MI	1	148	0	143	1-Small	
29	49653/145	MI	1	231	0	242	1-Small	
30	49653/147	MI	1	89	0	88	1-Small	
31	49653/162	MI	1	168	0	172	1-Small	
32	49653/234	MI	0	116	0	61	1-Small	
33	49653/330	MI	1	1172	0	377	1-Small	
34	49653/331	MI	0	706	0	325	1-Small	
35	49653/137	MI	1	204	2	185	1-Small	
36	SB-712753/002	MI	1	288	0	280	1-Small	
37	SB-712753/003	MI	1	254	0	272	1-Small	
38	SB-712753/007	MI	1	314	0	154	1-Small	
39	SB-712753/009	MI	0	162	0	160	1-Small	
40	49653/132	MI	1	442	0	112	1-Small	
41	AVA100193	MI	1	394	0	124	1-Small	
42	DREAM	MI	15	2635	9	2634	3-DREAM	

MI

Dead

Dead

Dead

Dead

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Dead

Dead

43 ADOPT

44 49653/011

45 49653/020

46 49653/024

48 49653/094

50 49653/143

49 100684

49653/093

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121

2895 2-ADOPT

176 1-Small

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109 1-Small

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51	49653/211	Dead	3	110	2	114	1-Small	
52	49653/284	Dead	0	382	0	384	1-Small	
53	712753/008	Dead	0	284	0	135	1-Small	
54	AVM100264	Dead	2	294	1	302	1-Small	
55	BRL 49653C/185	Dead	0	563	0	142	1-Small	
56	BRL 49653/334	Dead	0	278	1	279	1-Small	
57	BRL 49653/347	Dead	0	418	0	212	1-Small	
58	49653/015	Dead	2	395	0	198	1-Small	
59	49653/079	Dead	1	203	1	106	1-Small	
60	49653/080	Dead	0	104	0	99	1-Small	
61	49653/082	Dead	1	212	0	107	1-Small	
62	49653/085	Dead	1	138	0	139	1-Small	
63	49653/095	Dead	1	196	0	96	1-Small	
64	49653/097	Dead	0	122	0	120	1-Small	
65	49653/125	Dead	0	175	0	173	1-Small	
66	49653/127	Dead	0	56	0	58	1-Small	
67	49653/128	Dead	0	39	0	38	1-Small	
68	49653/134	Dead	1	561	0	276	1-Small	
69	49653/135	Dead	2	116	1	111	1-Small	
70	49653/136	Dead	2	148	0	143	1-Small	
71	49653/145	Dead	1	231	0	242	1-Small	
72	49653/147	Dead	0	89	0	88	1-Small	
73	49653/162	Dead	1	168	0	172	1-Small	
74	49653/234	Dead	0	116	0	61	1-Small	
75	49653/330	Dead	1	1172	0	377	1-Small	
76	49653/331	Dead	1	706	0	325	1-Small	
77	49653/137	Dead	0	204	1	185	1-Small	
78	SB-712753/002	Dead	1	288	0	280	1-Small	
79	SB-712753/003	Dead	0	254	0	272	1-Small	
80	SB-712753/007	Dead	0	314	0	154	1-Small	
81	SB-712753/009	Dead	0	162	0	160	1-Small	
82	49653/132	Dead	1	442	0	112	1-Small	
83	AVA100193	Dead	1	394	0	124	1-Small	
84	DREAM	Dead	12	2635	10	2634	3-DREAM	
85	ADOPT	Dead	2	1456	5	2895	2-ADOPT	

- Switch to CMA
- Click in cell Study-name 1
- Press [CTRL-V] to paste the data

Click here

• The screen should look like this

#### 📑 Comprehensive meta analysis - [Data]

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	Study name	Outcome	Avandia Event	Avandia Total N	Control Event	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	к	L	м	N	0
1	Study 🧹	Outcome	Avandia	Avandia N	CTRL	CTRL N									
2	49653/011	ML	2	357	0	176	2.482	0.909	1.552	2.408					
3	49653/020	MI	2	2 391	1	207	1.059	0.057	1.228	1.507					
4	49653/024	MI	1	774	1	185	0.238	-1.435	1.417	2.007					
5	49653/093	ML	0	213	1	109	0.169	-1.775	1.637	2.681					
6	49653/094	MI	1	232	0	116	1.510	0.412	1.637	2.680					
7	100684	ML	0	43	1	47	0.356	-1.032	1.647	2.711					
8	49653/143	ML	1	121	0	124	3.100	1.131	1.638	2.683					
9	49653/211	MI	5	5 110	2	114	2.667	0.981	0.848	0.718					
10	49653/284	ML	1	382	0	384	3.024	1.106	1.635	2.672					
11	712753/008	MI	1	284	0	135	1.434	0.360	1.636	2.678					
12	AVM100264	ML	0	294	1	302	0.341	-1.075	1.635	2.673					
13	BRL 49653C/185	ML	2	563	0	142	1.269	0.238	1.552	2.409					
14	BRL 49653/334	MI	2	278	1	279	2.014	0.700	1.228	1.507					
15	BRL 49653/347	ML	2	418	0	212	2.551	0.936	1.551	2.407					
16	49653/015	MI	2	395	1	198	1.003	0.003	1.228	1.508					
17	49653/079	ML	1	203	1	106	0.520	-0.654	1.419	2.014					
18	49653/080	MI	1	104	2	99	0.471	-0.753	1.233	1.520					
19	49653/082	MI	2	212	0	107	2.553	0.937	1.554	2.414					
20	49653/085	ML	3	138	1	139	3.067	1.121	1.161	1.348					
21	49653/095	ML	0	196	0	96									
22	49653/097	ML	0	122	1	120	0.325	-1.123	1.638	2.683					
23	49653/125	ML	0	175	1	173	0.328	-1.116	1.637	2.678					
24	49653/127	MI	1	56	0	58	3.162	1.151	1.644	2.702					
25	49653/128	ML	1	39	0	38	3.000	1.099	1.649	2.719					
26	49653/134	ML	0	561	2	276	0.098	-2.325	1.551	2.405					
27	49653/135	MI	2	2 116	3	111	0.632	-0.460	0.923	0.851					
28	49653/136	MI	1	148	0	143	2.919	1.071	1.637	2.680					
29	49653/145	ML	1	231	0	242	3.156	1.149	1.636	2.675					
30	49653/147	MI	1	89	0	88	3.000	1.099	1.640	2.689					
31	49653/162	ML	1	168	0	172	3.090	1.128	1.637	2.678					
32	49653/234	ML	0	116	0	61									
33	49653/330	М	1	1172	0	377	0.967	-0.034	1.634	2.670					

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

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3		Image: Copy selection         Ctrl+C         2         357         0         176         2.482         0.009         1.552         2.408           Image: Copy with header         2         391         1         207         1.059         0.057         1.228         1.507           Image: Copy entire grid         1         774         1         185         0.238         -1.435         1.417         2.007           Image: Copy entire grid         0         213         1         109         0.0169         -1.775         1.637         2.680           Image: Copy entire grid         1         232         0         116         1.510         0.412         1.637         2.680															
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9		Delete	Der		5	110	2	114	2.667	0.981	0.848	0.718					
10		Delete row			1	382	0	384	3.024	1.106	1.635	2.672					
11		Delete study			1	284	0	135	1.434	0.360	1.636	2.678					
12	2	Delete column			0	294	1	302	0.341	-1.075	1.635	2.673					
13	- 1				2	563	0	142	1.269	0.238	1.552	2.409					
14	Ļ	Edit group names			2	278	1	279	2.014	0.700	1.228	1.507					
15	BR	L 49653/347 MI			2	418	0	212	2.551	0.936	1.551	2.407					
16	19	53/015 MI			2	295	1	199	1 003	0.003	1 229	1 509					

#### The screen should look like this

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	Study name	Outcome	Avandia Event	Avandia Total N	Control Event	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	к	L	м	N	0
1	49653/011	MI	2	357	0	176	2.482	0.909	1.552	2.408					
2	49653/020	MI	2	391	1	207	1.059	0.057	1.228	1.507					
3	49653/024	MI	1	774	1	185	0.238	-1.435	1.417	2.007					
4	49653/093	MI	0	213	1	109	0.169	-1.775	1.637	2.681					
5	49653/094	MI	1	232	0	116	1.510	0.412	1.637	2.680					
6	100684	MI	0	43	1	47	0.356	-1.032	1.647	2.711					
7	49653/143	MI	1	121	0	124	3.100	1.131	1.638	2.683					
8	49653/211	MI	5	110	2	114	2.667	0.981	0.848	0.718					
9	49653/284	MI	1	382	0	384	3.024	1.106	1.635	2.672					
10	712753/008	MI	1	284	0	135	1.434	0.360	1.636	2.678					
11	AVM100264	MI	0	294	1	302	0.341	-1.075	1.635	2.673					
12	BRL 49653C/185	MI	2	563	0	142	1.269	0.238	1.552	2.409					
13	BRL 49653/334	MI	2	278	1	279	2.014	0.700	1.228	1.507					
1.4	DD1 400507047	MI	2	/10	0	212	2 551	0.000	1 551	2.407					

#### Click File > Save As and save the file

<b>;</b> †	Comprehensive met	ta analysis	- [C:\Use	rs\Biostat\D	ropbox\Wo	rkshops Th	nree-Day\A	vandia\Avar	idia.cma]							
Eil	e <u>E</u> dit Format <u>V</u> i	ew <u>I</u> nsert	Identify	<u>T</u> ools Co	mputationa	I options	Analyses	<u>H</u> elp								
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	Open	Ctrl+O	ome	Avandia Event	Avandia Total N	Control E vent	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	к	L	м	N	0
	g opening sereer n	in concernation of the second s		2	357	0	176	2.482	0.909	1.552	2.408					
_	Import			2	391	1	207	1.059	0.057	1.228	1.507					
	Save	Ctrl+S		1	774	1	185	0.238	-1.435	1.417	2.007					
	Save Ar			0	213	1	109	0.169	-1.775	1.637	2.681					
	Jave Z			1	232	0	116	1.510	0.412	1.637	2.680					
8	Print	Ctrl+P		0	43	1	47	0.356	-1.032	1.647	2.711					
l m	Print setup			1	121	0	124	3.100	1.131	1.638	2.683					
[ =				5	110	2	114	2.667	0.981	0.848	0.718					
	Exit			1	382	0	384	3.024	1.106	1.635	2.672					
1	0 712753/008	MI		1	284	0	135	1.434	0.360	1.636	2.678					
1	1 AVM100264	MI		0	294	1	302	0.341	-1.075	1.635	2.673					
1	2 BRL 49653C/185	MI		2	563	0	142	1.269	0.238	1.552	2.409					
1	3 BRL 49653/334	MI		2	278	1	279	2.014	0.700	1.228	1.507					
1	4 BBI 49653/347	MI		2	418	Π	212	2 551	0.936	1 551	2 407					

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

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Run	analyses 🔸 🗞	D 🚅 👬 🖬 🗧	3 × P	<b>B</b>		≣ ;% ta	: 🕂 🗕 🗍	, → + √	/ 🗌 🔳	≡ <mark>≵↓</mark>					
	Study name	Outcome	Avandia Event	Avandia Total N	Control Event	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	к	L	м	N	0
1	49653/011	MI	2	357	0	176	2.482	0.909	1.552	2.408					
2	49653/020	MI	2	391	1	207	1.059	0.057	1.228	1.507					
3	49653/024	MI	1	774	1	185	0.238	-1.435	1.417	2.007					
4	49653/093	MI	0	213	1	109	0.169	-1.775	1.637	2.681					
5	6 49653/094	MI	1	232	0	116	1.510	0.412	1.637	2.680					
E	100684	MI	0	43	1	47	0.356	-1.032	1.647	2.711					
7	49653/143	MI	1	121	0	124	3.100	1.131	1.638	2.683					
8	49653/211	MI	5	110	2	114	2.667	0.981	0.848	0.718					
9	49653/284	MI	1	382	0	384	3.024	1.106	1.635	2.672					
10	712753/008	MI	1	284	0	135	1.434	0.360	1.636	2.678					
11	AVM100264	MI	0	294	1	302	0.341	-1.075	1.635	2.673					
12	BRL 49653C/185	MI	2	563	0	142	1.269	0.238	1.552	2.409					

- Click on the Header for the Study column
- Click Sort A-Z
- Click the Merge Rows icon

<u>F</u> ile <u>E</u> dit Forma	at <u>V</u> iew <u>I</u> nsert Identify	<u>T</u> ools Co	mputationa	al options	Analyses	<u>H</u> elp								
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Stud	Sort A-Z	Avandia Event	Avandia Total N	Control E vent	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	к	L	м	N	0
1 49653/0 Z	Sert 7 A	2	357	0	176	2.482	0.909	1.552	2.408					
2 49653/0 *	SOIL Z-A	2	391	1	207	1.059	0.057	1.228	1.507					
3 49653/0	Column properties	1	774	1	185	0.238	-1.435	1.417	2.007					
4 49653/093	MI	0	213	1	109	0.169	-1.775	1.637	2.681					
5 49653/094	MI	1	232	0	116	1.510	0.412	1.637	2.680					
6 100684	MI	0	43	1	47	0.356	-1.032	1.647	2.711					
7 49653/143	MI	1	121	0	124	3.100	1.131	1.638	2.683					
8 49653/211	MI	5	110	2	114	2.667	0.981	0.848	0.718					
9 49653/284	MI	1	382	0	384	3.024	1.106	1.635	2.672					
10 712753/008	MI	1	284	0	135	1.434	0.360	1.636	2.678					
11 AVM100264	MI	0	294	1	302	0.341	-1.075	1.635	2.673					

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

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Study name	Outcome	Avandia Event	Avandia Total N	Control Eivent	Control Total N	Odds ratio	Log odds ratio	Std Err	Variance	к	L	м	N	0
1 100694	MI	0	43	1	47	0.356	-1.032	1.647	2.711					
2	Dead	0	43	0	47									
3 49652/011	MI	2	357	0	176	2.482	0.909	1.552	2.408					
430337011	Dead	1	357	0	176	1.485	0.396	1.636	2.675					
5 49652/015	MI	2	395	1	198	1.003	0.003	1.228	1.508					
6	Dead	2	395	0	198	2.522	0.925	1.552	2.408					
7 49652/020	MI	2	391	1	207	1.059	0.057	1.228	1.507					
8 436337020	Dead	0	391	0	207									
9 496527024	MI	1	774	1	185	0.238	-1.435	1.417	2.007					
10 43653/024	Dead	0	774	0	185									
11 400504070	MI	1	203	1	106	0.520	-0.654	1.419	2.014					
12 43653/079	Dead	1	203	1	106	0.520	-0.654	1.419	2.014					
13 400504000	MI	1	104	2	99	0.471	-0.753	1.233	1.520					
43653/080	Dead	0	104	0	99									

• To run the analysis, click [Run analysis]

The issue we need to address when working with multiple outcomes is the fact that the outcomes are not independent of each other, and therefore do not contain independent information

If we compute an effect size for MI only, or for Death only, or for MI and Death separately, the effect size and its variance are valid. But, if we compute an effect size based on MI and Death, a variance that is based on the combined sample size (counting each subject twice) overstates the amount of information contained in the data, over-estimates the precision of the summary effect and under-estimates the variance.

We can see how this plays out in the analyses that follow.

By default the program picks one outcome for each study. Since each study had a row for Death and a row for MI, the program would normally pick the first (Death) for each.

However, some studies have zero outcomes in both groups for Death. When this happens, the program will pick MI. Therefore, the initial screen looks like this. Each study is included only once, but the analysis includes MI for some studies and Death for others.

🕂 Compre	hensive meta analy	/sis - [Analysi	s]					Sec. 1			-	
<u>F</u> ile <u>E</u> dit	F <u>o</u> rmat <u>V</u> iew Co	mputational	options Ana	alyses <u>H</u> elp	)							
+ Data en	try t⊒ Next ta	able 🚦	- High resoluti	on plot 🛛 📮	Select by	+ Effect	measure: O	dds ratio	- 🔳		‡E ₹	Q 1
Model	Study name	Outcome		Statis	stics for each s	tudy			Od	ds ratio and 95	% CI	
			Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00
	100684.000	MI	0.356	0.014	8.982	-0.627	0.531			+		
	49653/011	Dead	1.485	0.060	36.645	0.242	0.809					-
	49653/015	Dead	2.522	0.121	52.789	0.596	0.551					-
	49653/020	мі	1.059	0.095	11.750	0.047	0.963					
	49653/024	MI	0.238	0.015	3.823	-1.013	0.311				-	
	49653/079	Dead	0.520	0.032	8.394	-0.461	0.645					
	49653/080	MI	0.471	0.042	5.276	-0.611	0.541				-	
	49653/082	Dead	1.525	0.062	37.747	0.258	0.797					-
	49653/085	Dead	3.044	0.123	75.363	0.680	0.497				· · · · ·	— I
	49653/093	MI	0.169	0.007	4.193	-1.084	0.278				-	
	49653/094	Dead	1.510	0.061	37.347	0.252	0.801					-
	49653/095	Dead	1.481	0.060	36.689	0.240	0.811					-
	49653/097	MI	0.325	0.013	8.062	-0.686	0.493			·		
	49653/125	MI	0.328	0.013	8.098	-0.682	0.495			+ +		
	49653/127	MI	3.162	0.126	79.271	0.700	0.484		—		•	<u> </u>
	49653/128	MI	3.000	0.118	75.963	0.666	0.505		<u> </u>			<u> </u>
	49653/132	Dead	0.764	0.031	18.891	-0.164	0.870					
	49653/134	Dead	1.480	0.060	36.446	0.240	0.810					-
	49653/135	Dead	1.930	0.173	21.588	0.534	0.594		-			
	49653/136	Dead	4.898	0.233	102.907	1.023	0.306		-			
	49653/137	Dead	0.301	0.012	7.428	-0.734	0.463			·		
	49653/143	MI	3.100	0.125	76.835	0.691	0.490					<u> </u>
	49653/145	Dead	3.156	0.128	77.870	0.703	0.482					<u> </u>
	49653/147	MI	3.000	0.121	74.646	0.670	0.503					<u> </u>
	49653/162	Dead	3.090	0.125	76.377	0.689	0.491					— I
	49653/211	Dead	1.570	0.257	9.582	0.489	0.625		·			
	49653/284	MI	3.024	0.123	74.454	0.677	0.498					— I
	49653/330	Dead	0.967	0.039	23.780	-0.021	0.983					
	49653/331	Dead	1.384	0.056	34.068	0.199	0.842					-
	712753/008	MI	1.434	0.058	35.429	0.220	0.826					-
	ADOPT	Dead	0.795	0.154	4.103	-0.274	0.784		—		-	
	AVA100193	Dead	0.949	0.038	23.448	-0.032	0.975				<u> </u>	

We can run an analysis for MI only (that is, selecting MI for studies that report an effect size for MI, and omitting studies that do not)

- Right-click on the Outcome column and click [Select by outcome]
- De-Select Death



Avandia

## Select Peto Odds ratio as the Index

diff. Farmat. View Computational options: Analyses. Help         + Effect measure: Peto odds ratio         + Effect m	Comprehe	ensive meta analy	sis - [Analysi	s]					_	_		-		
is entry         t-3 Next table         High resolution pol         Select by Table         + Effect measure: Peto odds ratio         + Effect	ile <u>E</u> dit F	<u>o</u> rmat <u>V</u> iew Co	mputational	options An	alyses <u>H</u> elp									
Idel         Study name         Outcome         Estatistics for each stog         Pero odds ratio and 95% Cl         Weight (Random)           49553/073         MI         0.497         0.027         9.257         0.468         0.640         1.00         10.00         100.00         Relative weight           49553/082         MI         0.497         0.027         9.257         0.468         0.640         1.01         1.00         10.00         12.41           49553/082         MI         4.278         0.386         19.666         1.013         0.311         1.231         1.231           49553/083         MI         0.026         0.001         3.280         1.398         0.162         0.661         0.651           49553/054         MI         0.134         0.003         6.743         -1.006         0.315	- Data entry	y t⊒ Next ta	ible 🚦	<ul> <li>High resolut</li> </ul>	on plot	Select by	+ Effect	measure: Pe	to odds ratio	• 🔳		₽E₹	🖓 🗘	
R         Procession         Lower limit         Upper limit         Z-Value         p-Value         0.01         0.00         10.00         100.00         Relative weight           49653/075         MI         0.497         0.027         9.577         0.468         0.640         1.533         1.24         2.061         0.611         0.621         0.621         0.651	Model	Study name	Outcome		Stati	stics for each s	stuay			Peto d	odds ratio and 9	5% CI		Weight (Random)
49653/079         MI         0.497         0.027         9.257         0.468         0.640           49653/060         MI         0.495         0.007         4.719         0.623         0.533				Peto odds ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00	Relative weight
49653/080         MI         0.465         0.050         4.719         0.623         0.533		49653/079	MI	0.497	0.027	9.257	-0.468	0.640						1.24
4963/082         MI         4.524         0.233         85.581         1.006         0.314		49653/080	MI	0.485	0.050	4.719	-0.623	0.533				-		2.05
4963/026       MI       2.788       0.386       19.866       1.013       0.011       2.74         49653/084       MI       0.052       0.001       3.280       -1.398       0.162       0.601         49653/094       MI       0.133       0.003       6.709       -1.008       0.315       0.61       0.651         49653/097       MI       0.133       0.003       6.709       -1.008       0.315       0.61       0.681         49653/125       MI       7.020       0.143       380.078       0.387       0.324       0.681         49653/127       MI       7.658       0.152       386.158       1.018       0.309       0.445       0.681         49653/132       MI       7.022       0.143       380.078       0.897       0.224       0.445       0.681         49653/136       MI       7.144       0.142       360.223       0.983       0.328       0.445       0.681         49653/136       MI       7.749       0.154       390.961       1.024       0.362       0.445       0.681         49653/145       MI       7.757       0.150       381.445       1.012       0.312       0.447       0.681     <		49653/082	MI	4.524	0.239	85.581	1.006	0.314						1.23
49653/033       MI       0.052       0.001       3.280       -1.398       0.162        0.62         49653/037       MI       0.133       0.003       6.709       -1.008       0.313       0.61       0.661         49653/037       MI       0.134       0.003       6.703       -1.008       0.313       0.631         49653/125       MI       0.134       0.003       6.743       -1.006       0.315        0.681         49653/128       MI       7.202       0.143       363.078       0.987       0.244       0.631         49653/132       MI       3.002       0.027       461.091       0.503       0.616        0.451         49653/135       MI       0.636       0.108       3.732       0.501       0.616        3.40         49653/137       MI       0.433       0.404       4.499       0.566        2.061         49653/143       MI       7.759       0.150       381.465       1.012       0.211        0.681         49653/147       MI       7.657       0.150       381.461       1.012       0.211        0.691 <td></td> <td>49653/085</td> <td>MI</td> <td>2.768</td> <td>0.386</td> <td>19.866</td> <td>1.013</td> <td>0.311</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>2.74</td>		49653/085	MI	2.768	0.386	19.866	1.013	0.311						2.74
4963/094       MI       4.462       0.070       286.492       0.707       0.400		49653/093	MI	0.052	0.001	3.280	-1.398	0.162						0.62
49653/097       MI       0.133       0.003       6.709       -1.008       0.313       0.69         49653/127       MI       7.658       0.152       386.158       1.018       0.309         49653/127       MI       7.658       0.152       386.158       1.018       0.309         49653/128       MI       7.202       0.143       953.078       0.997       0.224         49653/132       MI       0.048       0.003       0.917       -2.017       0.044         49653/135       MI       0.636       0.108       3.732       -0.501       0.615         49653/137       MI       0.643       0.044       4.489       -0.644       0.656         49653/137       MI       0.432       0.0223       0.983       0.326		49653/094	MI	4.482	0.070	286.492	0.707	0.480						0.61
49653/125       MI       0.134       0.003       6.743       -1.006       0.315		49653/097	М	0.133	0.003	6,709	-1.008	0.313				_		0.69
49653/127       MI       7.658       0.152       386.158       1.018       0.309         49653/128       MI       7.202       0.143       363.078       0.987       0.324         49653/132       MI       3.502       0.027       46.1091       0.503       0.615         49653/134       MI       0.648       0.003       0.917       -2.017       0.044         49653/135       MI       0.638       0.1142       380.0223       0.983       0.326         49653/135       MI       7.144       0.142       380.0223       0.983       0.326         49653/143       MI       7.575       0.150       361.845       1.012       0.311         49653/143       MI       7.575       0.150       381.845       1.012       0.312         49653/145       MI       7.567       0.150       381.845       1.003       0.312         49653/142       MI       7.567       0.150       381.451       1.012       0.312         49653/2145       MI       7.567       0.150       381.451       1.033       0.316         49653/2145       MI       7.567       0.150       381.451       1.033       0.316       4.		49653/125	М	0.134	0.003	6,743	-1.006	0.315				_		0.69
49653/128       MI       7.202       0.143       363.078       0.987       0.324       0.69         49653/132       MI       3.502       0.027       461.091       0.503       0.615       0.45         49653/135       MI       0.636       0.108       3.732       0.501       0.616       1.22         49653/135       MI       7.144       0.142       360.023       0.983       0.326       0.616         49653/137       MI       0.648       0.003       0.917       2.011       0.616       0.59         49653/137       MI       0.463       0.048       4.483       0.664       0.506		49653/127	м	7,658	0.152	386 158	1.018	0.309						0.69
49653/132       MI       3.502       0.027       461.091       0.503       0.615		49653/128	MI	7.202	0.143	363.078	0.987	0.324						0.69
49653/134       MI       0.048       0.003       0.917       2.017       0.044       1.22         49653/135       MI       0.636       0.108       3.732       0.501       0.616       3.40         49653/136       MI       7.144       0.142       360.223       0.983       0.326       0.654       0.654         49653/137       MI       0.463       0.048       4.499       0.664       0.506       2.06         49653/137       MI       7.757       0.150       381.845       1.012       0.311       0.69         49653/145       MI       7.7567       0.150       381.845       1.012       0.312       0.69         49653/147       MI       7.366       0.145       380.8247       0.394       0.320       0.69         49653/162       MI       7.567       0.150       381.461       1.012       0.312       0.69         49653/300       MI       3.750       0.039       361.055       0.567       0.571       0.51       0.51         49653/330       MI       3.724       0.038       36.299       0.89       0.491       4.71       0.50         49653/330       MI       3.726       0.038	,	49653/132	MI	3.502	0.027	461 091	0.503	0.615						0.45
49653/135       MI       0.636       0.108       3.732       0.501       0.616       3.40         49653/135       MI       7.144       0.142       360.223       0.983       0.266       0.506       0.59         49653/137       MI       0.463       0.048       4.489       0.664       0.506       0.59       0.69         49653/143       MI       7.757       0.150       381.845       1.012       0.311       0.69       0.69         49653/147       MI       7.730       0.154       390.961       1.024       0.300       0.69       0.69         49653/147       MI       7.567       0.150       381.445       1.012       0.311       0.69       0.69         49653/244       MI       7.428       0.147       374.345       1.003       0.316       4.71       0.69         49653/284       MI       7.428       0.147       374.345       1.003       0.316       4.71       0.69         49653/284       MI       7.428       0.147       374.345       1.003       0.316       4.71       0.69         AVA100193       MI       3.724       0.69       0.87       0.57       0.57       0.51	,	49653/134	MI	0.048	0.003	0.917	-2 017	0.044						1.22
Hoson 103         Mile         C.144         Store         C.033         C.223         C.933         C.226         C.033         C.226         C.034         C.039         C.039 <thc.039< th="">         C.039         C.039         &lt;</thc.039<>		49653/135	MI	0.636	0.108	3 732	-0.501	0.616						3.40
49653/137       Mi       0.463       0.048       4.489       0.664       0.506       2.067         49653/143       Mi       7.759       0.150       381.845       1.012       0.311       0.691       0.691         49653/145       Mi       7.749       0.145       380.847       0.994       0.320       0.691       0.691         49653/145       Mi       7.366       0.145       386.247       0.994       0.320       0.691       0.691         49653/162       Mi       7.567       0.150       381.461       1.012       0.312       0.691       0.691         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       0.691       0.691         49653/330       Mi       3.3750       0.039       361.055       0.567       0.571       0.511       0.511         712753/008       Mi       4.373       0.666       289.668       0.699       0.272       0.691       0.501         AVA100133       Mi       3.724       0.038       367.954       0.561       0.575       0.561       0.591       0.591         AVA100284       Mi       0.139       0.003       7.006       0.387		49653/136	м	7 144	0.142	360.223	0.983	0.326						0.69
49653/143       Mi       7.575       0.500       4.002       0.300       1.024       0.300       0.300       0.69       0.69         49653/145       Mi       7.749       0.154       390.961       1.024       0.300       0.401       0.69       0.69         49653/147       Mi       7.360       0.145       368.247       0.994       0.320       0.69       0.69         49653/162       Mi       7.567       0.150       381.461       1.012       0.312       0.69       0.69         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       0.69       0.69         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       0.69       0.69         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       0.69       0.69         712753/008       Mi       4.373       0.066       289.868       0.699       0.491       0.69       0.60         AVA100193       Mi       3.274       0.038       36.755       0.577       0.50       0.50       0.50         AVA100284       Mi       0.139       0.003	,	19653/137	м	0.463	0.048	4 489	-0.664	0.506				_		2.06
49653/145       Mi       7.749       0.154       30.961       1.024       0.306         49653/145       Mi       7.306       0.145       368.247       0.994       0.320         49653/147       Mi       7.567       0.150       381.461       1.012       0.312       0.69         49653/162       Mi       7.567       0.150       381.461       1.012       0.312       0.69         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       0.69         49653/300       Mi       3.750       0.039       361.055       0.567       0.571       0.51         712753/008       Mi       4.373       0.066       289.868       0.689       0.491       0.51         AVA100133       Mi       3.724       0.038       367.954       0.561       0.575	,	49653/143	м	7 575	0.150	381.845	1.012	0.311						0.69
H3037147       Mil       7.306       0.145       368.247       0.394       0.302       0.531         49653/147       Mil       7.567       0.150       381.461       1.012       0.312       0.691         49653/211       Mil       2.567       0.150       381.461       1.012       0.312       0.691         49653/211       Mil       2.428       0.557       11.246       1.198       0.231       4.71         49653/284       Mil       7.428       0.147       374.345       1.003       0.316       0.691         49653/300       Mil       3.750       0.039       361.055       0.567       0.571       0.511       0.511         712753/008       Mil       4.373       0.660       229.968       0.699       0.272       41.25       0.501         AVA100193       Mil       3.724       0.039       367.954       0.561       0.575       41.25       0.501         AVM100264       Mil       0.139       0.003       7.006       0.987       0.324       0.591       0.591         BRL 49653/347       Mil       1.552       0.240       85.195       1.008       0.313       4.71       0.691         BR	,	49653/145	м	7 749	0.154	390.961	1.072	0.306						0.69
Holdson Hi       7.567       0.150       381.461       1.02       0.312       0.69         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       4.71       0.69         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       4.71       0.69         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       4.71       0.69         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       4.71       0.69         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       4.71       0.69         49653/284       Mi       3.750       0.039       36.1055       0.567       0.571       4.71       0.69         ADOPT       Mi       1.329       0.800       2.209       1.099       0.272       41.25       0.50         AVA100193       Mi       3.724       0.587       0.587       0.224       85.195       0.69       0.59         BRL 49653/247       Mi       4.525       0.240       85.195       0.060       0.313       4.47       0.89<	,	49653/143	м	7 306	0.145	368 247	0.994	0.320						0.69
49653/102       Mi       7.057       0.160       0.0147       1.012       0.012       0.012       0.011         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       0.571       0.591       0.591         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       0.511       0.591       0.591         49653/284       Mi       7.428       0.147       374.345       1.003       0.316       0.511       0.591       0.591         49653/284       Mi       4.373       0.066       289.868       0.689       0.491       0.511       0.51       0.511		49653/162	м	7.567	0.150	391 /61	1 012	0.312						0.69
43653/211       Mi       2.054       0.037       11.246       1.136       0.231		40050/102	M	2.504	0.150	11 246	1 1 1 9 0	0.012						4 71
49653/204       Mi       7.228       0.147       375.04.04.0       1.003       0.510       0.031         49653/230       Mi       3.750       0.039       361.055       0.567       0.571       0.691         ADOPT       Mi       1.329       0.800       2.209       1.099       0.272       ++++++++++++++++++++++++++++++++++++		40050/211	M	7 420	0.147	274 245	1.100	0.231						0.00
4333/300       Mi       5/33       6/33       6/34       5/34       6/34         712753/008       Mi       4/373       0.066       289       6/491       41.25         AVA100193       Mi       3/24       0.038       367.354       0.561       0.575       441.25         AVM100264       Mi       0.139       0.003       7.006       0.987       0.324       0.561         BRL 49653/334       Mi       1.359       0.203       18.915       0.562       0.561		49653/204	M	2 750	0.147	201.055	0.567	0.510						0.03
ADDPT       Mil       1.329       0.000       2293.000       0.089       0.272       4       0.000         AVA100133       Mil       3.724       0.038       367.954       0.561       0.575       4       0.501         AVM100264       Mil       0.139       0.003       7.006       0.987       0.575       4       0.591         BRL 49653/334       Mil       1.559       0.203       18.915       0.582       0.561       0.575       0.591         BRL 49653/344       Mil       1.552       0.240       85.195       1.008       0.313       4       1.231         BRL 49653/347       Mil       3.504       0.110       111.261       0.711       0.477       0.891       1.231         BRL 49653/344       Mil       1.652       0.741       3.683       1.226       0.220       4       0.691         BR-12753/002       Mil       7.187       0.143       36.2324       0.986       0.331       4       0.691         SB-712753/002       Mil       7.139       0.051       1.035       0.301       4       0.691         SB-712753/007       Mil       4.439       0.069       287.643       0.700       0.484		+3033/330	M	4.272	0.035	200.000	0.007	0.371						0.01
AVA100193       Mil       3.724       0.038       3.67.954       0.651       0.672		ADODT	M	4.373	0.000	203.000	1.000	0.431				·		41.05
AVATIO1254     Mi     0.139     0.003     367.304     0.037     -     -     0.001       BRL 49653/334     Mi     1.959     0.003     18.915     0.582     0.561     -     -     2.07       BRL 49653/334     Mi     1.959     0.203     18.915     0.582     0.561     -     -     2.07       BRL 49653/347     Mi     4.525     0.240     85.195     1.008     0.313     -     -     2.07       BRL 49653/247     Mi     3.504     0.110     111.281     0.711     0.477     -     -     0.89       BRL 49653/2478     Mi     1.652     0.741     3.683     1.226     0.220     -     -     16.53       SB-712753/002     Mi     7.187     0.143     362.324     0.986     0.324     -     -     0.69       SB-712753/007     Mi     7.187     0.143     362.324     0.986     0.301     -     -     0.69       SB-712753/007     Mi     7.392     0.157     400.651     1.035     0.301     -     -     0.69       SB-712753/007     Mi     4.439     0.069     287.643     0.700     0.484     -     -     0.61	,	ADUET AV/A100102	M	2.724	0.000	2.203	0.661	0.272						41.23
NYM 106204         Imil         0.139         0.039         0.039         0.039         0.034           BRL 49653/334         MI         1.959         0.203         18.915         0.582         0.661           BRL 49653/347         MI         4.525         0.240         85.195         1.008         0.313           BRL 49653/347         MI         3.504         0.110         111.281         0.711         0.477           DREAM         MI         1.652         0.741         3.683         1.226         0.220         16.53           SB-712753/002         MI         7.187         0.143         362.324         0.966         0.324         0.69           SB-712753/003         MI         7.392         0.157         400.651         1.035         0.301         4         0.69           SB-712753/007         MI         4.439         0.069         287.643         0.700         0.484         4         0.61		47A100133	ent Mi	0.120	0.030	307.334	0.061	0.070						0.00
b n L 43633/337     mi     1.535     0.240     85.195     1.008     0.311     1.011     1.011     1.011     1.011     1.011     1.011     0.011     1.011     0.011<	, ,		ivit Kal	1.050	0.003	10.015	-0.387	0.524						0.63
b = 1.4 3903/34/r     Mi     4.325     0.240     80.150     1.008     0.313	t r	DEL 43033/334	MI MI	1.959	0.203	18.915 0E 105	0.582	0.051			'			2.07
bit         43034/11         0.110         0.11.281         0.711         0.477         0.89           DREAM         MI         1.652         0.741         3.683         1.226         0.220         16.53         16.53           SB-712753/002         MI         7.187         0.0157         400.651         1.035         0.301         0.69         0.69         0.69         0.69         0.69         0.69         0.69         0.69         0.69         0.69         0.61	t,	DIL 43603/34/	MI MI	4.025	0.240	85.195	1.008	0.313						1.23
DHEAM         MI         1.652         0.741         3.683         1.226         0.220         ++++         16.53           SB-712753/002         MI         7.187         0.143         362.324         0.986         0.324         -+++++         0.69             SB-712753/003         MI         7.932         0.157         400.651         1.035         0.301         -+++++++         0.69             SB-712753/007         MI         4.439         0.069         287.643         0.700         0.484         -+++++++++++         0.61             n         1.428         1.031         1.379         2.143         0.032         ++++++++++++++++++++++++++++++++++++	t	5HL 49603L/185	MI	3.504	0.110	111.281	0.711	0.477						0.89
S8-712753/002         MI         7.187         U.143         362.324         U.386         U.324           S8-712753/003         MI         7.932         0.157         400.651         1.035         0.301	l	UREAM	MI	1.652	0.741	3.683	1.226	0.220			+			16.53
SB-712753/007         MI         7.352         0.157         400.651         1.035         0.301		58-712753/002	MI	7.187	0.143	362.324	0.986	0.324						0.69
SB-/12/53/00/ MI 4.439 0.069 287.643 0.700 0.484 0.61 0.61	ę	58-712753/003	MI	7.932	0.157	400.651	1.035	0.301						0.69
m l 1.428 1.031 1.979 2.143 0.032 l l ⊢⊷ l l	ç	5B-712753/007	MI	4.439	0.069	287.643	0.700	0.484		_				0.61
	ndom			1.428	1.031	1.979	2.143	0.032						

Basic stats One study removed Cumulative analysis Calculations

# • Right-click on Outcome

## • Select Dead only

	o. 1										59.01		
odel	Study name	Uutcome		Statis	tics for each s	tudy			Peto o	dds ratio and :	15% LI		weight (Handom)
			Peto odds ratio	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00	Relative weight
	49653/011	Dead	4.450	0.069	287.317	0.702	0.483		-	-			1.53
	49653/015	Dead	4.499	0.238	85.200	1.002	0.316		-		•		3.06
	49653/079	Dead	0.497	0.027	9.257	-0.468	0.640						3.10
	49653/082	Dead	4.503	0.071	285.993	0.710	0.477		-		· ·		1.54
	49653/085	Dead	7.443	0.148	375.103	1.004	0.316						1.72
	49653/094	Dead	4.482	0.070	286.492	0.707	0.480		-		·		1.53
	49653/095	Dead	4.436	0.068	287.728	0.700	0.484						1.52
	49653/132	Dead	3.502	0.027	461.091	0.503	0.615	-					1.11
	49653/134	Dead	4.446	0.069	287.445	0.701	0.483						1.52
	49653/135	Dead	1.875	0.193	18.216	0.542	0.588		_		<u> </u>		5.13
	49653/136	Dead	7.192	0.448	115.588	1.393	0.164						3.44
	49653/137	Dead	0.122	0.002	6.184	-1.050	0.294				_		1.72
	49653/145	Dead	7.749	0.154	390.961	1.024	0.306						1.72
	49653/162	Dead	7.567	0.150	381.461	1.012	0.312						1.72
	49653/211	Dead	1.559	0.266	9.144	0.492	0.623		-				8.47
	49653/330	Dead	3,750	0.039	361.055	0.567	0.571						1.27
	49653/331	Dead	4.307	0.063	292.623	0.678	0.497		_				1.49
	ADOPT	Dead	0.803	0.167	3.861	-0.274	0.784				-		10.74
	AVA100193	Dead	3,724	0.038	367,954	0.561	0.575						1.26
	AVM100264	Dead	2.006	0.208	19.359	0.602	0.547		_				5.16
	BBL 49653/334	Dead	0.136	0.003	6.845	-0.998	0.318				_		1.72
	DBEAM	Dead	1 200	0.519	2 772	0.426	0.670						37.80
	SB-712753/002	Dead	7,187	0.143	362,324	0.986	0.324						1.72
om			1 640	0.980	2 744	1.883	0.060						

### Summary

This analysis uses data from 42 studies where patients were randomized to receive Avandia or Placebo. Avandia is used to treat diabetes, but these analyses focused on side-effects. Each study reports data for two outcomes – (a) Myocardial infarction and (b) Death from Cardiovascular causes. The effect size is the Peto odds ratio.

#### Is Avandia related to the risk of MI?

The Peto odds ratio is 1.428 with a Cl of 1.031 to 1.979. The Z-value for a test of the null is 2.143 with a corresponding p-value of 0.032.

### Is Avandia related to the risk of Death?

The Peto odds ratio is 1.640 with a CI of 0.980 to 2.744. The Z-value for a test of the null is 1.883 with a corresponding p-value of 0.060.