# **Systematic Review & Meta-analysis**

These are often considered the highest form of evidence and there is no doubt that they can be very helpful bringing together a variety of similar studies addressing the same question. That said, systematic reviews and meta-analyses can also have multiple biases, some profoundly altering interpretation and results. These can in turn lead to more, rather than less confusion. To enhance your understanding of systematic reviews and meta-analyses, it is important we lay a little groundwork first.

#### **DEFINITIONS**

#### **Systematic Review**

A careful, thorough, and rigorous review of evidence related to a focused clinical question. This includes a methodical search and identification of research, extraction of data and assessment of quality, and summation of the study results.

#### **Meta-analysis**

This is the mathematical action of adding the results of studies together. The graphs are called meta-graphs, Forest Plot, or Blobograms. Meta-analysis is not required for every systematic review but preferred if studies are suitable for combining.

## Sample Meta-graph

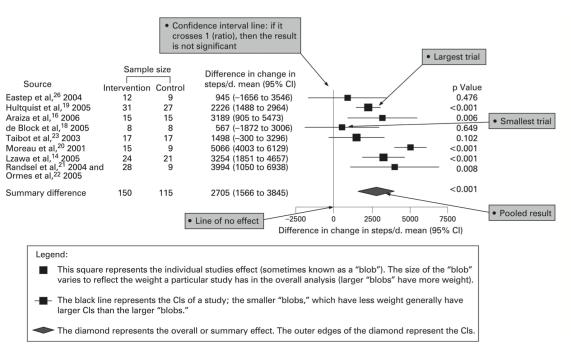
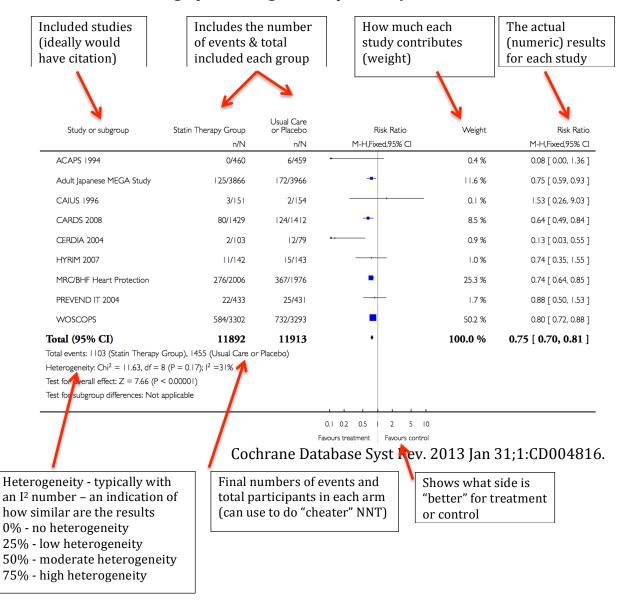


Figure. Basic components of a forest plot (based on Bravata DM, Smith-Spangler C, Sundaram V, et al. JAMA. 2007;298:2296-304.)

Ann Intern Med. 2009 Feb 17;150(4):JC2-2, JC2-3.

Here is an example of a good meta-graph (not the research per-se but what was included in the meta-graph allowing for interpretation).



# **Examples of Meta-analyses**

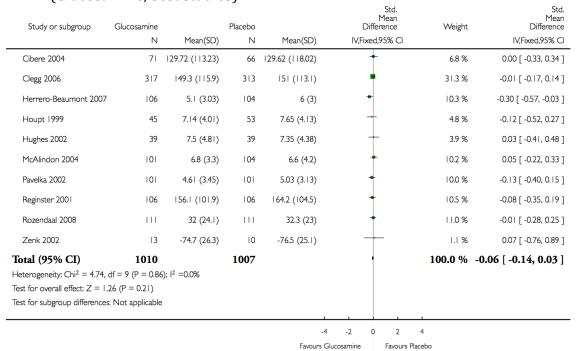
Have a look and see if you can figure out if the results were statistically significant and if the individual trial results were quite different (heterogeneous)?

# 1) Statistical significance Yes; Heterogeneity No (ADAS-cog changes with donepezil in dementia)

N         Mean(SD)         N           I donepezil (5mg/d) vs placebo at 12 weeks         Study 134         49         -2.99 (5.67)         52           Study 161         124         -3.04 (6.01)         110           Study 201         35         -2.13 (4.91)         36           Study 301/303         141         -2.23 (5.46)         139           Study 302         141         -1.28 (5.34)         137	Mean(SD) -1.89 (5.55) -0.74 (5.87) 1.04 (4.68)	IV,Fixed,95% CI	6.1 %	IV.Fixed,95% CI -1.10 [ -3.29, 1.09 ] -2.30 [ -3.82, -0.78 ]
Study 134     49     -2.99 (5.67)     52       Study 161     124     -3.04 (6.01)     110       Study 201     35     -2.13 (4.91)     36       Study 301/303     141     -2.23 (5.46)     139       Study 302     141     -1.28 (5.34)     137	-0.74 (5.87)	- <b>-</b>	12.5 %	
Study 161       124       -3.04 (6.01)       110         Study 201       35       -2.13 (4.91)       36         Study 301/303       141       -2.23 (5.46)       139         Study 302       141       -1.28 (5.34)       137	-0.74 (5.87)	- <b>-</b>	12.5 %	
Study 201       35       -2.13 (4.91)       36         Study 301/303       141       -2.23 (5.46)       139         Study 302       141       -1.28 (5.34)       137	, ,	<b>-</b>		-2.30 [ -3.82, -0.78 ]
Study 301/303 141 -2.23 (5.46) 139 Study 302 141 -1.28 (5.34) 137	1.04 (4.68)		F 0 0/	
Study 302 141 -1.28 (5.34) 137			5.8 %	-3.17 [ -5.40, -0.94 ]
, , ,	0.4 (5.42)	-	17.9 %	-2.63 [ -3.90, -1.36 ]
0.1.004	0.84 (5.38)	-	18.3 %	-2.12 [ -3.38, -0.86 ]
Study 304 235 -1.55 (4.75) 242	0.36 (4.82)	-	39.4 %	-1.91 [ -2.77, -1.05 ]
Subtotal (95% CI) 725 716		•	100.0 %	-2.15 [ -2.69, -1.61 ]

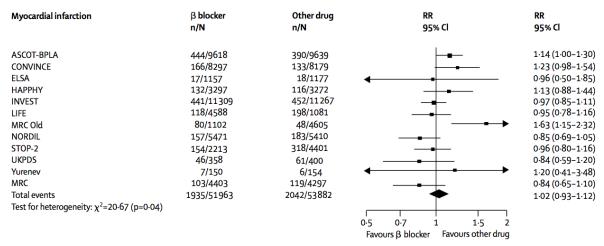
Cochrane Database Syst Rev. 2006 Jan 25;(1):CD001190.

## Statistical significance No; Heterogeneity No (Glucosamine, best studies)



Cochrane Database Syst Rev. 2005 Apr 18;(2):CD002946.

# 3) Statistical significance No; Heterogeneity Yes



Lancet. 2005 Oct 29-Nov 4;366(9496):1545-53.

## 4) Statistical significance Yes; Heterogeneity Yes

Stroke	β blocker n/N	Other drug n/N	RR 95% Cl	RR 95% Cl
	11/19	11/18	95% CI	95% CI
ASCOT-BPLA	422/9618	327/9639	_ <b></b>	1.29 (1.12-1.49)
CONVINCE	118/8297	133/8179		0.87 (0.68-1.12)
ELSA	14/1157	9/1177		1.58 (0.69-3.64)
HAPPHY	32/3297	41/3272	<b>←</b>	0.77 (0.49-1.23)
INVEST	201/11309	176/11267	<del></del>	1.14 (0.93-1.39)
LIFE	309/4588	232/4605		1.34 (1.13-1.58)
MRC Old	56/1102	45/1081		1.22 (0.83-1.79)
NORDIL	196/5471	159/5410	<del></del>	1.22 (0.99-1.50)
STOP-2	237/2213	422/4401	<b>⊢</b> ■	1.12 (0.96-1.30)
UKPDS	17/358	21/400	<b>←</b>	0.90 (0.48-1.69)
Yurenev	6/150	11/154	<b>+-</b>	0.56 (0.21-1.48)
MRC	42/4403	18/4297	<u> </u>	2.28 (1.31-3.95)
Total events	1650/51963	1594/53882	•	1.16 (1.04-1.30)
Test for heterogeneity: χ <sup>2</sup> =22·39 (	p=0-02)			•
2 ,			0.5 0.7 1 1.5	2
			Favours β blocker Favours other dru	ug.

Lancet. 2005 Oct 29-Nov 4;366(9496):1545-53.