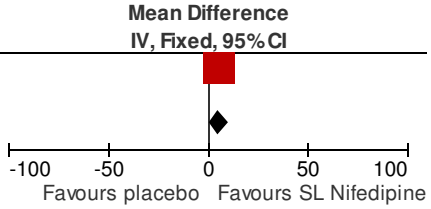
1 Sublingual nifedipine vs Placebo

1.1 Mean total work time for stepped increase in load (mins)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Atterhog 1975	5.2	2.24	100.0%	5.20 [0.81, 9.59]
Total (95% CI)			**100.0%**	**5.20 [0.81, 9.59]**

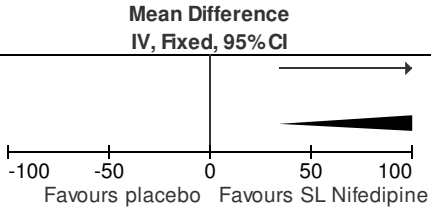
Heterogeneity: Not applicable
Test for overall effect: Z = 2.32 (P = 0.02)



1.2 Estimated workload at breakpoint for stepped increase in load (kpm/min)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Atterhog 1975	146	57	100.0%	146.00 [34.28, 257.72]
Total (95% CI)			**100.0%**	**146.00 [34.28, 257.72]**

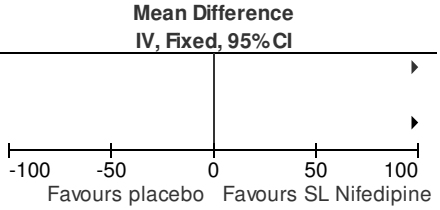
Heterogeneity: Not applicable
Test for overall effect: Z = 2.56 (P = 0.01)



1.3 Total work for stepped increase in load (kpm)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Atterhog 1975	3,685	1,431	100.0%	3685.00 [880.29, 6489.71]
Total (95% CI)			**100.0%**	**3685.00 [880.29, 6489.71]**

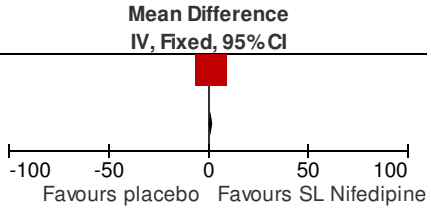
Heterogeneity: Not applicable
Test for overall effect: Z = 2.58 (P = 0.01)



1.4 Mean total work time for continuous increase in load (mins)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Atterhog 1975	1.1	0.56	100.0%	1.10 [0.00, 2.20]
Total (95% CI)			**100.0%**	**1.10 [0.00, 2.20]**

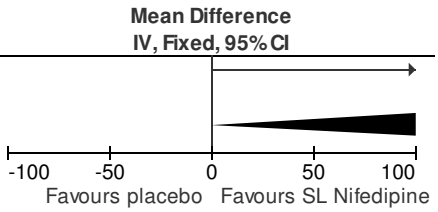
Heterogeneity: Not applicable
Test for overall effect: Z = 1.96 (P = 0.05)



1.5 Estimated workload at breakpoint for continuous increase in load (kpm/min)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Atterhog 1975	112	57.1	100.0%	112.00 [0.09, 223.91]
Total (95% CI)			**100.0%**	**112.00 [0.09, 223.91]**

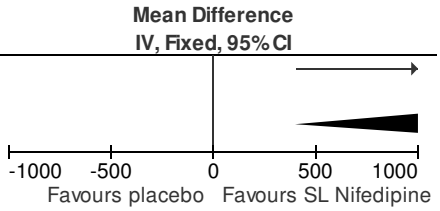
Heterogeneity: Not applicable
Test for overall effect: Z = 1.96 (P = 0.05)



1.6 Total work for continuous increase in load (kpm)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Atterhog 1975	1,146	379	100.0%	1146.00 [403.17, 1888.83]
Total (95% CI)			**100.0%**	**1146.00 [403.17, 1888.83]**

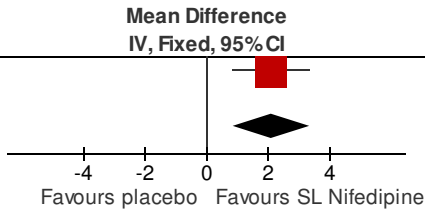
Heterogeneity: Not applicable
Test for overall effect: Z = 3.02 (P = 0.002)



1.7 Mean work capacity at angina threshold (minutes of exercise)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Marra 1983	2.1	0.64	100.0%	2.10 [0.85, 3.35]
Total (95% CI)			**100.0%**	**2.10 [0.85, 3.35]**

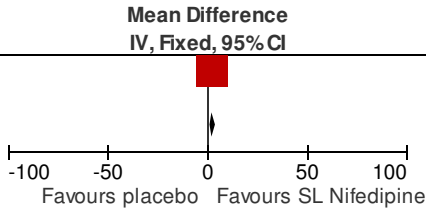
Heterogeneity: Not applicable
Test for overall effect: Z = 3.28 (P = 0.001)



1.8 Maximal work capacity at maximal exercise level (minutes of exercise)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Marra 1983	2.3	0.698	100.0%	2.30 [0.93, 3.67]
Total (95% CI)			**100.0%**	**2.30 [0.93, 3.67]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.30 (P = 0.0010)

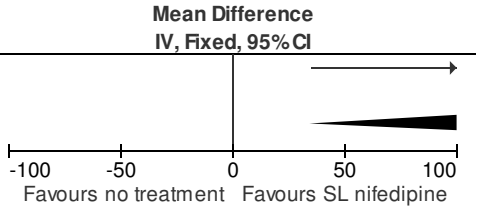


2 Sublingual nifedipine vs no treatment

2.1 Mean exercise time to 1mm ST segment depression (secs)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Pupita 1993	146	56.7	100.0%	146.00 [34.87, 257.13]
Total (95% CI)			**100.0%**	**146.00 [34.87, 257.13]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.57 (P = 0.01)

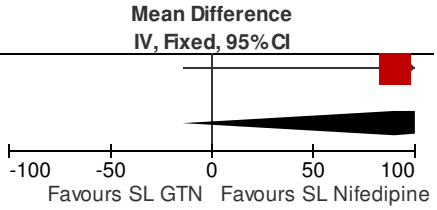


3 Sublingual GTN vs sublingual nifedipine

3.1 Mean exercise time to 1mm ST segment depression (secs)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Pupita 1993	90	53.1	100.0%	90.00 [-14.07, 194.07]
Total (95% CI)			**100.0%**	**90.00 [-14.07, 194.07]**

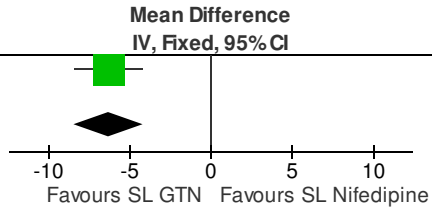
Heterogeneity: Not applicable
Test for overall effect: Z = 1.69 (P = 0.09)



3.2 Mean pain severity at 2 minutes post treatment

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Mooss 1989	1	1.7	7	7.3	2.1	6	100.0%	-6.30 [-8.40, -4.20]
Total (95% CI)			**7**			**6**	**100.0%**	**-6.30 [-8.40, -4.20]**

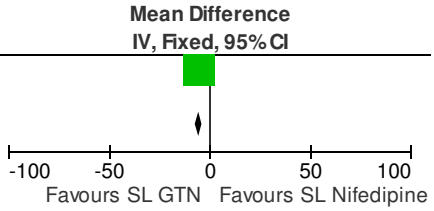
Heterogeneity: Not applicable
Test for overall effect: Z = 5.88 (P < 0.00001)



3.3 Mean pain severity at 4 minutes post treatment

Study or Subgroup	SL GTN Mean	SD	Total	SL nifedipine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Mooss 1989	0.4	0.8	7	6	1.7	6	100.0%	-5.60 [-7.08, -4.12]
Total (95% CI)			**7**			**6**	**100.0%**	**-5.60 [-7.08, -4.12]**

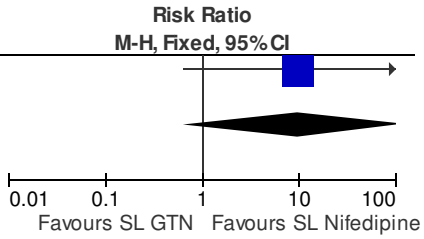
Heterogeneity: Not applicable
Test for overall effect: Z = 7.40 (P < 0.00001)



3.4 No participants with complete pain resolution at 2 minutes post treatment

Study or Subgroup	SL GTN Events	Total	SL Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Mooss 1989	5	7	0	6	100.0%	9.63 [0.64, 144.88]
Total (95% CI)		**7**		**6**	**100.0%**	**9.63 [0.64, 144.88]**
Total events	5		0			

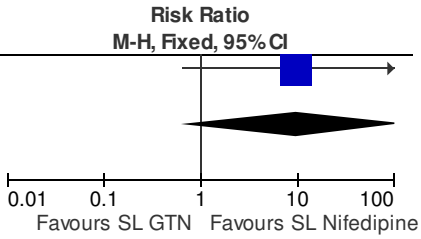
Heterogeneity: Not applicable
Test for overall effect: Z = 1.64 (P = 0.10)



3.5 No participants with complete pain resolution at 4 minutes post treatment

Study or Subgroup	SL GTN Events	Total	SL nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Mooss 1989	5	7	0	6	100.0%	9.63 [0.64, 144.88]
Total (95% CI)		**7**		**6**	**100.0%**	**9.63 [0.64, 144.88]**
Total events	5		0			

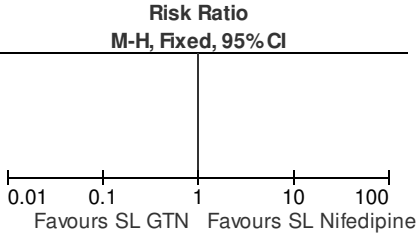
Heterogeneity: Not applicable
Test for overall effect: Z = 1.64 (P = 0.10)



3.6 No participants with complete pain resolution at 2 mins after cross over therapy

Study or Subgroup	SL GTN Events	Total	SL Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Mooss 1989	0	0	0	0		Not estimable
Total (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			

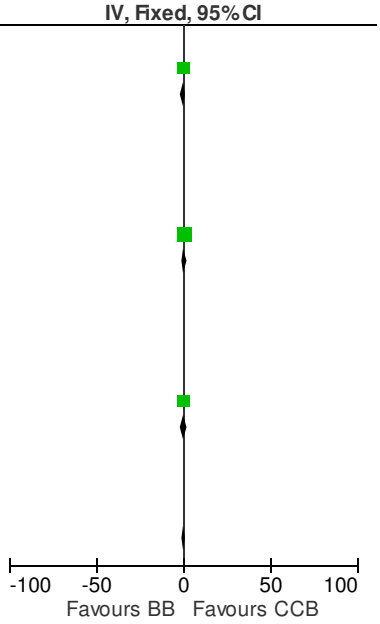
Heterogeneity: Not applicable
Test for overall effect: Not applicable



1 BB vs. CCB

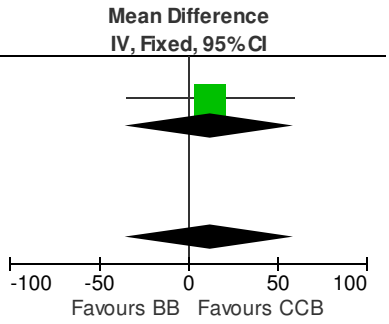
1.1 Exercise duration (min)

Study or Subgroup	BB Mean	BB SD	BB Total	CCB Mean	CCB SD	CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 Metoprolol vs. Diltiazem								
Van Dijk 1988	9.8	3.1	33	10	3.4	33	30.8%	-0.20 [-1.77, 1.37]
Subtotal (95% CI)			**33**			**33**	**30.8%**	**-0.20 [-1.77, 1.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.25 (P = 0.80)								
1.1.2 Propranolol vs. Diltiazem								
O'Hara 1987	6.8	3.5	34	6.5	2.3	34	38.3%	0.30 [-1.11, 1.71]
Subtotal (95% CI)			**34**			**34**	**38.3%**	**0.30 [-1.11, 1.71]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.42 (P = 0.68)								
1.1.3 Propranolol vs. Nifedipine								
Kawanishi 1992	7.2	2.65	21	7.2	2.2	16	31.0%	0.00 [-1.56, 1.56]
Subtotal (95% CI)			**21**			**16**	**31.0%**	**0.00 [-1.56, 1.56]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Total (95% CI)			**88**			**83**	**100.0%**	**0.05 [-0.82, 0.92]**
Heterogeneity: Chi² = 0.22, df = 2 (P = 0.89); I² = 0%								
Test for overall effect: Z = 0.12 (P = 0.90)								
Test for subgroup differences: Chi² = 0.22, df = 2 (P = 0.89), I² = 0%								



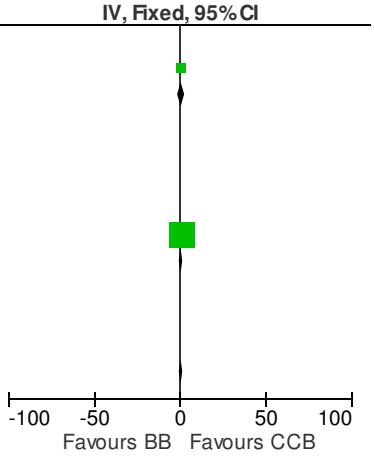
1.2 Time to 1mm ST depression (sec)

Study or Subgroup	BB Mean	BB SD	BB Total	CCB Mean	CCB SD	CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.2.1 Metoprolol vs. Nifedipine								
Savonitto 1996 (IMAGE)	49	128.6	65	37	141.3	62	100.0%	12.00 [-35.06, 59.06]
Subtotal (95% CI)			**65**			**62**	**100.0%**	**12.00 [-35.06, 59.06]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.50 (P = 0.62)								
Total (95% CI)			**65**			**62**	**100.0%**	**12.00 [-35.06, 59.06]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.50 (P = 0.62)								
Test for subgroup differences: Not applicable								



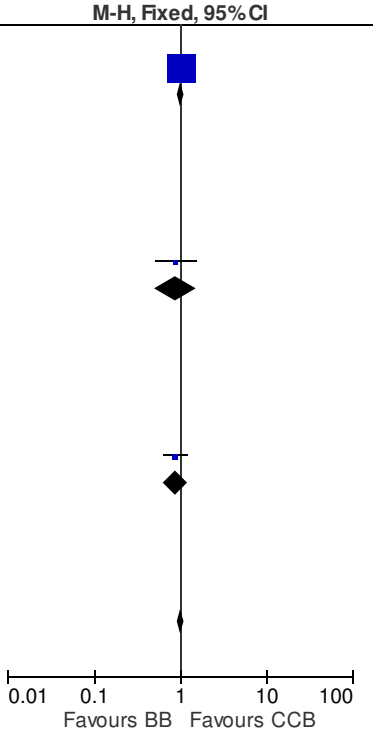
1.3 Time to onset of angina (min)

Study or Subgroup	BB Mean	BB SD	BB Total	CCB Mean	CCB SD	CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.3.1 Metoprolol vs. Diltiazem								
Van Dijk 1988	7.4	4.4	33	7	3.5	33	22.1%	0.40 [-1.52, 2.32]
Subtotal (95% CI)			**33**			**33**	**22.1%**	**0.40 [-1.52, 2.32]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.41 (P = 0.68)								
1.3.2 Propranolol vs. Nifedipine								
Kawanishi 1992	5.7	1.2	21	5	1.8	16	77.9%	0.70 [-0.32, 1.72]
Subtotal (95% CI)			**21**			**16**	**77.9%**	**0.70 [-0.32, 1.72]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.34 (P = 0.18)								
Total (95% CI)			**54**			**49**	**100.0%**	**0.63 [-0.27, 1.53]**
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.79); I² = 0%								
Test for overall effect: Z = 1.38 (P = 0.17)								
Test for subgroup differences: Chi² = 0.07, df = 1 (P = 0.79), I² = 0%								



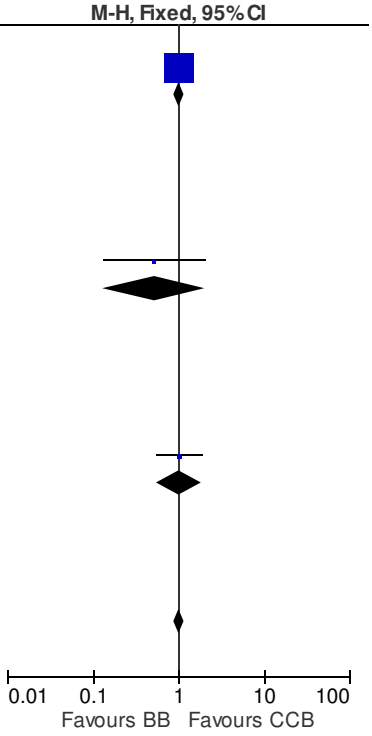
1.4 Total mortality

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 Atenolol vs. Verapamil						
Pepine 2003 (INVEST)	893	11309	873	11267	90.5%	1.02 [0.93, 1.11]
Subtotal (95% CI)		**11309**		**11267**	**90.5%**	**1.02 [0.93, 1.11]**
Total events	893		873			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.41 (P = 0.68)						
1.4.2 Metoprolol vs. Verapamil						
Rehnqvist 1996 (APSIS)	22	406	25	403	2.6%	0.87 [0.50, 1.52]
Subtotal (95% CI)		**406**		**403**	**2.6%**	**0.87 [0.50, 1.52]**
Total events	22		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.48 (P = 0.63)						
1.4.3 Metoprolol vs. Verapamil						
Hjemdahl 2006 (APSIS)	57	406	66	403	6.9%	0.86 [0.62, 1.19]
Subtotal (95% CI)		**406**		**403**	**6.9%**	**0.86 [0.62, 1.19]**
Total events	57		66			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.92 (P = 0.36)						
Total (95% CI)		**12121**		**12073**	**100.0%**	**1.00 [0.92, 1.09]**
Total events	972		964			
Heterogeneity: Chi² = 1.25, df = 2 (P = 0.54); I² = 0%						
Test for overall effect: Z = 0.10 (P = 0.92)						
Test for subgroup differences: Not applicable						



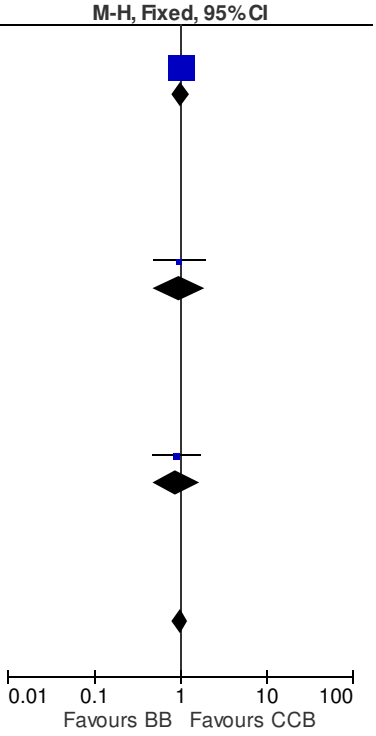
1.5 Cardiovascular death

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.5.1 Atenolol vs. Verapamil						
Pepine 2003 (INVEST)	431	11309	431	11267	94.5%	1.00 [0.87, 1.14]
Subtotal (95% CI)		**11309**		**11267**	**94.5%**	**1.00 [0.87, 1.14]**
Total events	431		431			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.06 (P = 0.96)						
1.5.2 Atenolol vs. Nifedipine						
Dargie1996 (TIBET)	3	226	6	232	1.3%	0.51 [0.13, 2.03]
Subtotal (95% CI)		**226**		**232**	**1.3%**	**0.51 [0.13, 2.03]**
Total events	3		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						
1.5.3 Metoprolol vs. Verapamil						
Rehnqvist 1996 (APSIS)	19	406	19	403	4.2%	0.99 [0.53, 1.85]
Subtotal (95% CI)		**406**		**403**	**4.2%**	**0.99 [0.53, 1.85]**
Total events	19		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.98)						
Total (95% CI)		**11941**		**11902**	**100.0%**	**0.99 [0.87, 1.12]**
Total events	453		456			
Heterogeneity: Chi² = 0.89, df = 2 (P = 0.64); I² = 0%						
Test for overall effect: Z = 0.16 (P = 0.88)						
Test for subgroup differences: Not applicable						



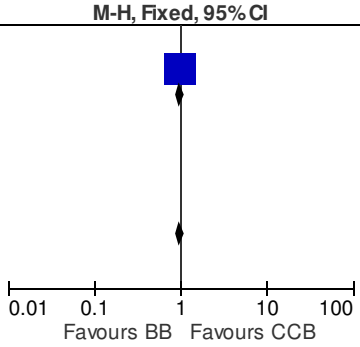
1.6 Non fatal MI

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 Atenolol vs. Verapamil						
Pepine 2003 (INVEST)	153	11309	151	11267	81.7%	1.01 [0.81, 1.26]
Subtotal (95% CI)		**11309**		**11267**	**81.7%**	**1.01 [0.81, 1.26]**
Total events	153		151			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.08 (P = 0.93)						
1.6.2 Atenolol vs. Nifedipine						
Dargie1996 (TIBET)	14	226	15	232	8.0%	0.96 [0.47, 1.94]
Subtotal (95% CI)		**226**		**232**	**8.0%**	**0.96 [0.47, 1.94]**
Total events	14		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.12 (P = 0.91)						
1.6.3 Metoprolol vs. Verapamil						
Hjemdahl 2006 (APSIS)	17	406	19	403	10.3%	0.89 [0.47, 1.68]
Subtotal (95% CI)		**406**		**403**	**10.3%**	**0.89 [0.47, 1.68]**
Total events	17		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.36 (P = 0.72)						
Total (95% CI)		**11941**		**11902**	**100.0%**	**0.99 [0.81, 1.22]**
Total events	184		185			
Heterogeneity: Chi² = 0.15, df = 2 (P = 0.93); I² = 0%						
Test for overall effect: Z = 0.07 (P = 0.94)						
Test for subgroup differences: Not applicable						



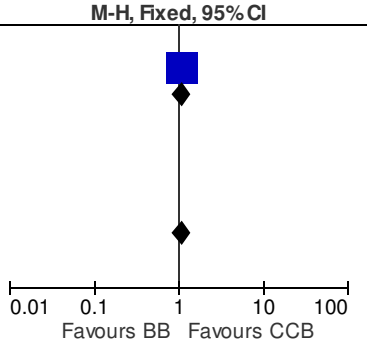
1.7 CV related hospitalisation

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.7.1 Atenolol vs. Verapamil						
Pepine 2003 (INVEST)	709	11309	726	11267	100.0%	0.97 [0.88, 1.08]
Subtotal (95% CI)		**11309**		**11267**	**100.0%**	**0.97 [0.88, 1.08]**
Total events	709		726			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.54 (P = 0.59)						
Total (95% CI)		**11309**		**11267**	**100.0%**	**0.97 [0.88, 1.08]**
Total events	709		726			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.54 (P = 0.59)						
Test for subgroup differences: Not applicable						



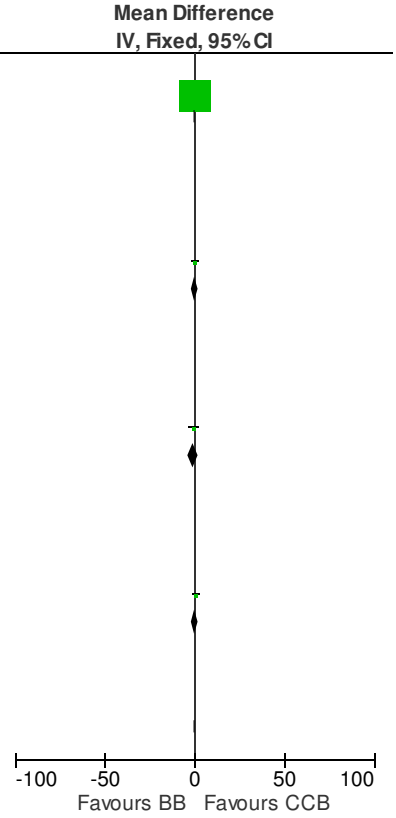
1.8 Non fatal CV events (combined)

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.8.1 Metoprolol vs. Verapamil						
Rehnqvist 1996 (APSIS)	106	406	98	403	100.0%	1.07 [0.85, 1.36]
Subtotal (95% CI)		**406**		**403**	**100.0%**	**1.07 [0.85, 1.36]**
Total events	106		98			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.56)						
Total (95% CI)		**406**		**403**	**100.0%**	**1.07 [0.85, 1.36]**
Total events	106		98			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.56)						
Test for subgroup differences: Not applicable						



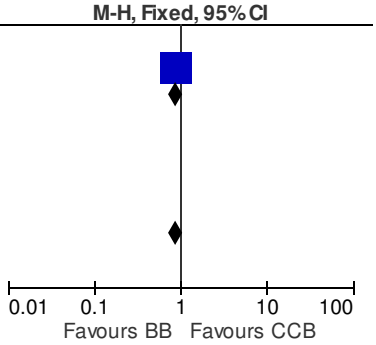
1.9 Angina episodes/week

Study or Subgroup	BB Mean	BB SD	BB Total	CCB Mean	CCB SD	CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.9.1 Atenolol vs. Verapamil								
Pepine 2003 (INVEST)	0.88	1.62	11309	0.77	1.31	11267	99.9%	0.11 [0.07, 0.15]
Subtotal (95% CI)			**11309**			**11267**	**99.9%**	**0.11 [0.07, 0.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.61 (P < 0.00001)								
1.9.2 Metoprolol vs. Diltiazem								
Van Dijk 1988	2.5	3	33	2.5	5.2	33	0.0%	0.00 [-2.05, 2.05]
Subtotal (95% CI)			**33**			**33**	**0.0%**	**0.00 [-2.05, 2.05]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
1.9.3 Propranolol vs. Nifedipine								
Kawanishi 1992	2	2.3	21	2.7	5.6	16	0.0%	-0.70 [-3.61, 2.21]
Subtotal (95% CI)			**21**			**16**	**0.0%**	**-0.70 [-3.61, 2.21]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.47 (P = 0.64)								
1.9.4 Metoprolol vs. Nifedipine								
Savonitto 1996 (IMAGE)	-2.01	4.72	61	-2.32	6.43	61	0.0%	0.31 [-1.69, 2.31]
Subtotal (95% CI)			**61**			**61**	**0.0%**	**0.31 [-1.69, 2.31]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.30 (P = 0.76)								
Total (95% CI)			**11424**			**11377**	**100.0%**	**0.11 [0.07, 0.15]**
Heterogeneity: Chi² = 0.35, df = 3 (P = 0.95); I² = 0%								
Test for overall effect: Z = 5.61 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.35, df = 3 (P = 0.95), I² = 0%								



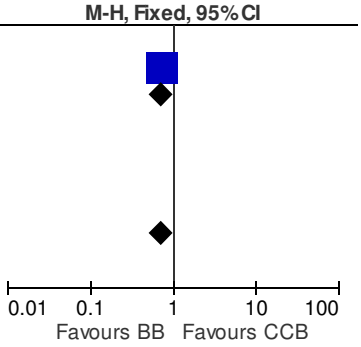
1.10 Prevalance of angina

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.10.1 Atenolol vs. Verapamil						
Pepine 2003 (INVEST)	228	11309	261	11267	100.0%	0.87 [0.73, 1.04]
Subtotal (95% CI)		**11309**		**11267**	**100.0%**	**0.87 [0.73, 1.04]**
Total events	228		261			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.55 (P = 0.12)						
Total (95% CI)		**11309**		**11267**	**100.0%**	**0.87 [0.73, 1.04]**
Total events	228		261			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.55 (P = 0.12)						
Test for subgroup differences: Not applicable						



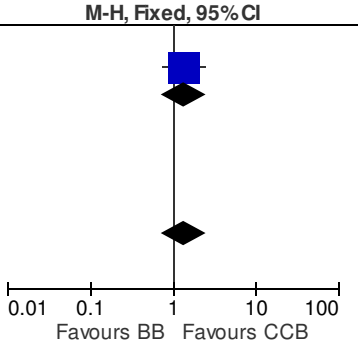
1.11 Severity of angina assessed by investigator (moderate/markedly improved)

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.11.1 Nadolol vs. Amlodipine						
Singh 1993	21	39	29	39	100.0%	0.72 [0.51, 1.02]
Subtotal (95% CI)		**39**		**39**	**100.0%**	**0.72 [0.51, 1.02]**
Total events	21		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.84 (P = 0.07)						
Total (95% CI)		**39**		**39**	**100.0%**	**0.72 [0.51, 1.02]**
Total events	21		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.84 (P = 0.07)						
Test for subgroup differences: Not applicable						



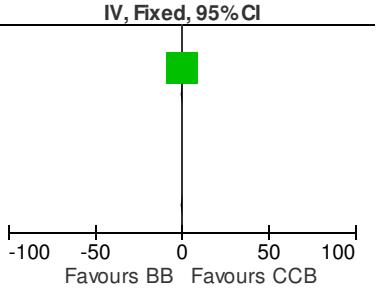
1.12 Severity of angina assessed by patients (moderate/severe)

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.12.1 Nadolol vs. Amlodipine						
Singh 1993	16	40	12	40	100.0%	1.33 [0.73, 2.45]
Subtotal (95% CI)		**40**		**40**	**100.0%**	**1.33 [0.73, 2.45]**
Total events	16		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.93 (P = 0.35)						
Total (95% CI)		**40**		**40**	**100.0%**	**1.33 [0.73, 2.45]**
Total events	16		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.93 (P = 0.35)						
Test for subgroup differences: Not applicable						



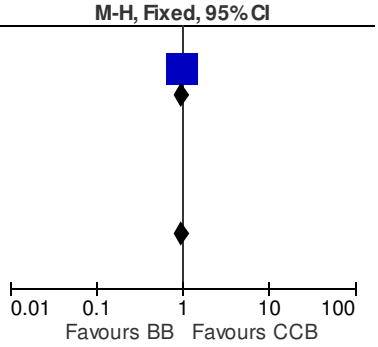
1.13 Nitroglycerin use

Study or Subgroup	BB Mean	BB SD	BB Total	CCB Mean	CCB SD	CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.13.1 Propranolol vs. Nifedipine								
Kawanishi 1992	0.7	1.2	21	0.7	1.6	16	100.0%	0.00 [-0.94, 0.94]
Subtotal (95% CI)			**21**			**16**	**100.0%**	**0.00 [-0.94, 0.94]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Total (95% CI)			**21**			**16**	**100.0%**	**0.00 [-0.94, 0.94]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Test for subgroup differences: Not applicable								



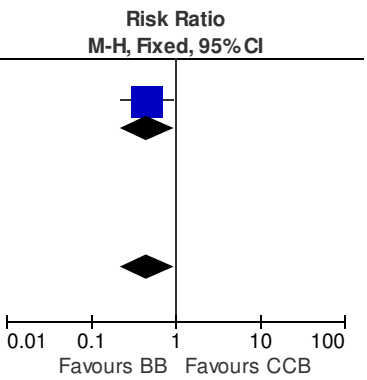
1.14 Adverse effects (dizziness)

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.14.1 Atenolol vs. verapamil						
Pepine 2003 (INVEST)	151	11309	154	11267	100.0%	0.98 [0.78, 1.22]
Subtotal (95% CI)		**11309**		**11267**	**100.0%**	**0.98 [0.78, 1.22]**
Total events	151		154			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.84)						
Total (95% CI)		**11309**		**11267**	**100.0%**	**0.98 [0.78, 1.22]**
Total events	151		154			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.84)						
Test for subgroup differences: Not applicable						



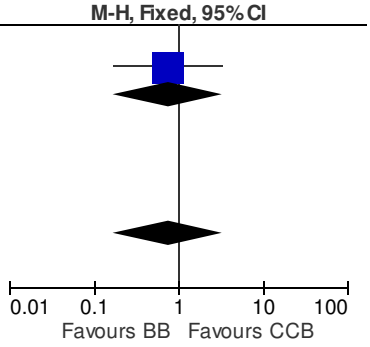
1.15 Adverse effects (GI events)

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.15.1 Metoprolol vs. Verapamil						
Rehnqvist 1996 (APSIS)	10	406	22	403	100.0%	0.45 [0.22, 0.94]
Subtotal (95% CI)		**406**		**403**	**100.0%**	**0.45 [0.22, 0.94]**
Total events	10		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.12 (P = 0.03)						
Total (95% CI)		**406**		**403**	**100.0%**	**0.45 [0.22, 0.94]**
Total events	10		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.12 (P = 0.03)						
Test for subgroup differences: Not applicable						



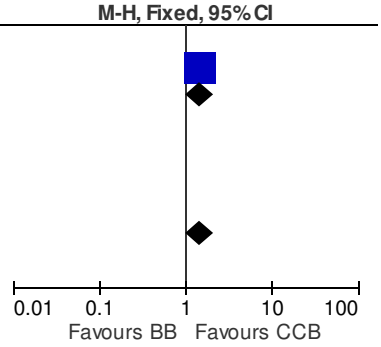
1.16 Adverse effects (head ache)

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.16.1 Metoprolol vs. Verapamil						
Rehnqvist 1996 (APSIS)	3	406	4	403	100.0%	0.74 [0.17, 3.31]
Subtotal (95% CI)		**406**		**403**	**100.0%**	**0.74 [0.17, 3.31]**
Total events	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.39 (P = 0.70)						
Total (95% CI)		**406**		**403**	**100.0%**	**0.74 [0.17, 3.31]**
Total events	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.39 (P = 0.70)						
Test for subgroup differences: Not applicable						



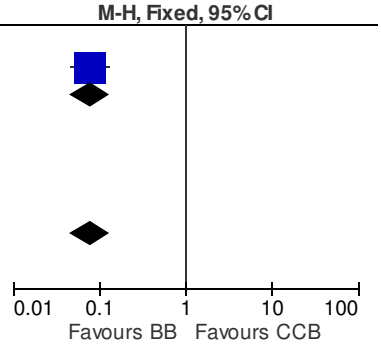
1.17 Adverse effects (light headedness)

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.17.1 Atenolol vs. Verapamil						
Pepine 2003 (INVEST)	70	11309	48	11267	100.0%	1.45 [1.01, 2.10]
Subtotal (95% CI)		**11309**		**11267**	**100.0%**	**1.45 [1.01, 2.10]**
Total events	70		48			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.00 (P = 0.05)						
Total (95% CI)		**11309**		**11267**	**100.0%**	**1.45 [1.01, 2.10]**
Total events	70		48			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.00 (P = 0.05)						
Test for subgroup differences: Not applicable						

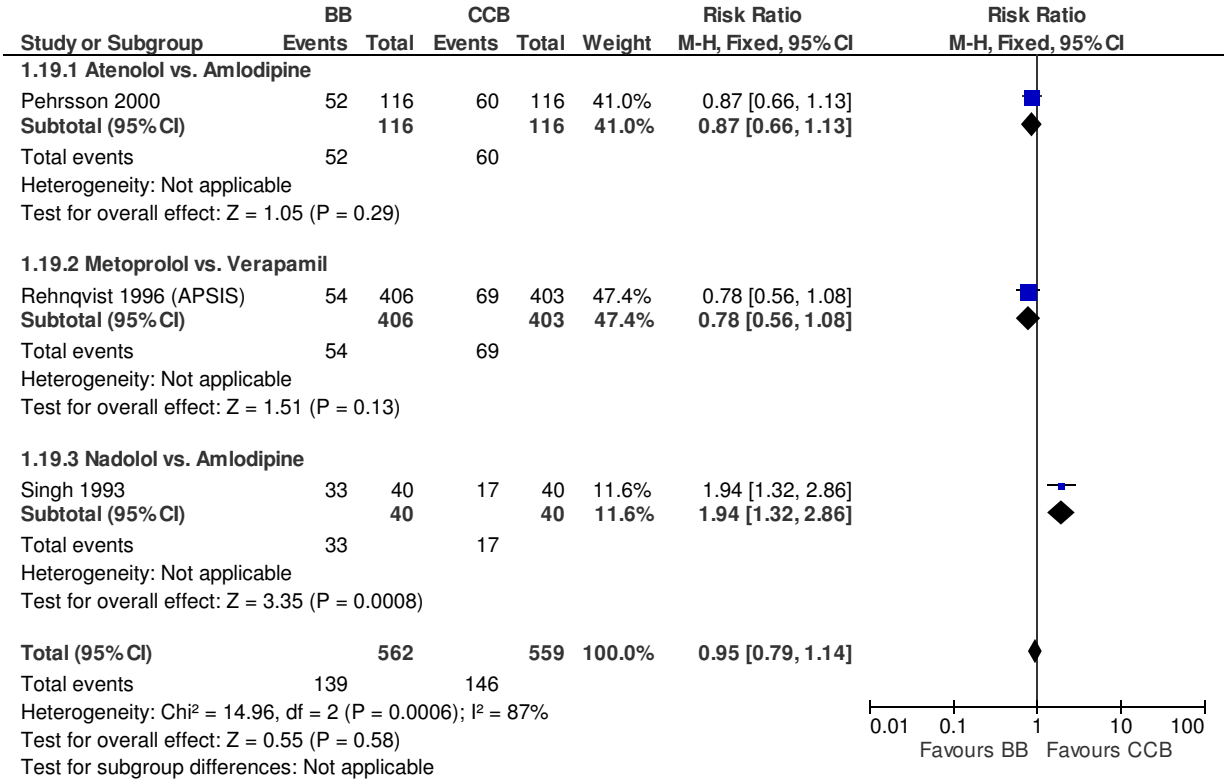


1.18 Adverse effects (constipation)

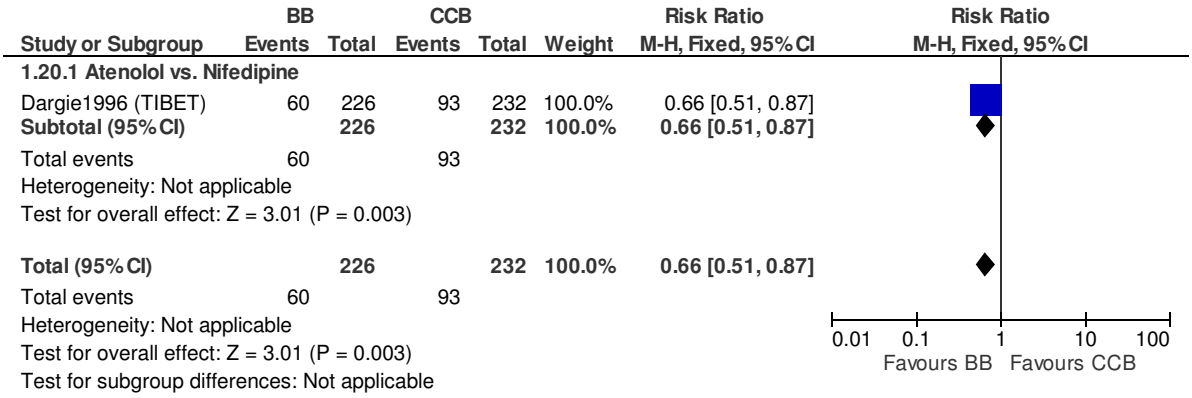
Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.18.1 Atenolol vs. Verapamil						
Pepine 2003 (INVEST)	15	11309	195	11267	100.0%	0.08 [0.05, 0.13]
Subtotal (95% CI)		**11309**		**11267**	**100.0%**	**0.08 [0.05, 0.13]**
Total events	15		195			
Heterogeneity: Not applicable						
Test for overall effect: Z = 9.60 (P < 0.00001)						
Total (95% CI)		**11309**		**11267**	**100.0%**	**0.08 [0.05, 0.13]**
Total events	15		195			
Heterogeneity: Not applicable						
Test for overall effect: Z = 9.60 (P < 0.00001)						
Test for subgroup differences: Not applicable						



1.19 Adverse effects (overall)

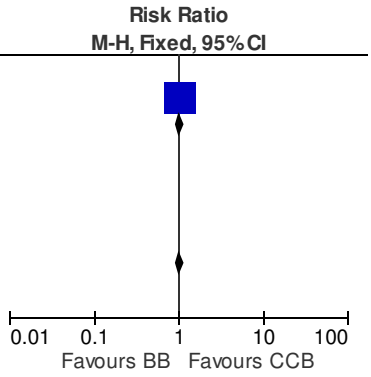


1.20 Withdrawals due to adverse effects



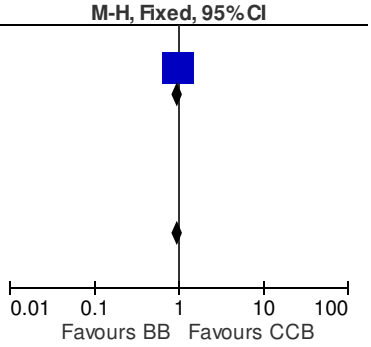
1.21 Combined outcomes (death, non fatal MI, non fatal stroke) (sub group females)

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.21.1 Atenolol vs. Verapamil						
Pepine 2003 (INVEST)	540	5920	524	5850	100.0%	1.02 [0.91, 1.14]
Subtotal (95% CI)		**5920**		**5850**	**100.0%**	**1.02 [0.91, 1.14]**
Total events	540		524			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.31 (P = 0.76)						
Total (95% CI)		**5920**		**5850**	**100.0%**	**1.02 [0.91, 1.14]**
Total events	540		524			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.31 (P = 0.76)						
Test for subgroup differences: Not applicable						



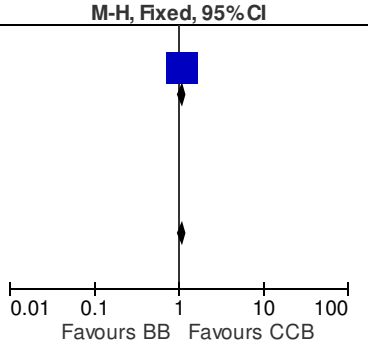
1.22 Combined outcome (death, non fatal MI, non fatal stroke) (sub group diabetes)

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.22.1 Atenolol vs. Verapamil						
Pepine 2003 (INVEST)	450	3231	463	3169	100.0%	0.95 [0.85, 1.07]
Subtotal (95% CI)		**3231**		**3169**	**100.0%**	**0.95 [0.85, 1.07]**
Total events	450		463			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.78 (P = 0.43)						
Total (95% CI)		**3231**		**3169**	**100.0%**	**0.95 [0.85, 1.07]**
Total events	450		463			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.78 (P = 0.43)						
Test for subgroup differences: Not applicable						



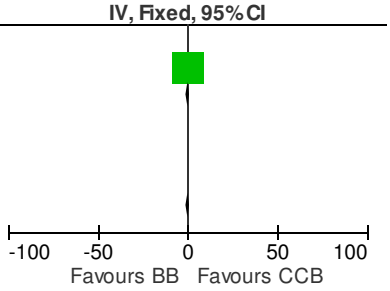
1.23 Combined (death, non fatal MI, Non fatal stroke)- Subgroup Age>70

Study or Subgroup	BB Events	BB Total	CCB Events	CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.23.1 Atenolol vs. Verapamil						
Pepine 2003 (INVEST)	664	3829	596	3694	100.0%	1.07 [0.97, 1.19]
Subtotal (95% CI)		**3829**		**3694**	**100.0%**	**1.07 [0.97, 1.19]**
Total events	664		596			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.40 (P = 0.16)						
Total (95% CI)		**3829**		**3694**	**100.0%**	**1.07 [0.97, 1.19]**
Total events	664		596			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.40 (P = 0.16)						
Test for subgroup differences: Not applicable						



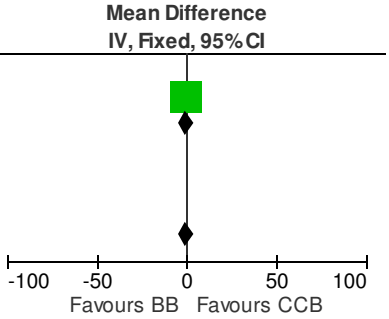
1.24 Quality of life (sleep disturbance)

Study or Subgroup	BB Mean	BB SD	BB Total	CCB Mean	CCB SD	CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.24.1 Metoprolol vs. Verapamil								
Rehnqvist 1996 (APSIS)	16.2	5.2	270	16.6	5.5	275	100.0%	-0.40 [-1.30, 0.50]
Subtotal (95% CI)			**270**			**275**	**100.0%**	**-0.40 [-1.30, 0.50]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.87 (P = 0.38)								
Total (95% CI)			**270**			**275**	**100.0%**	**-0.40 [-1.30, 0.50]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.87 (P = 0.38)								
Test for subgroup differences: Not applicable								



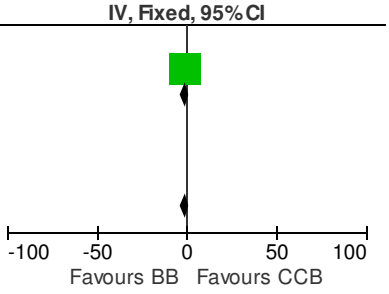
1.25 Quality of life (overall life satisfaction)

Study or Subgroup	BB Mean	BB SD	BB Total	CCB Mean	CCB SD	CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.25.1 Metoprolol vs. Verapamil								
Rehnqvist 1996 (APSIS)	75.2	25.6	268	75.9	26.3	275	100.0%	-0.70 [-5.07, 3.67]
Subtotal (95% CI)			**268**			**275**	**100.0%**	**-0.70 [-5.07, 3.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.31 (P = 0.75)								
Total (95% CI)			**268**			**275**	**100.0%**	**-0.70 [-5.07, 3.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.31 (P = 0.75)								
Test for subgroup differences: Not applicable								



1.26 Quality of life (psychosomatic symptoms)

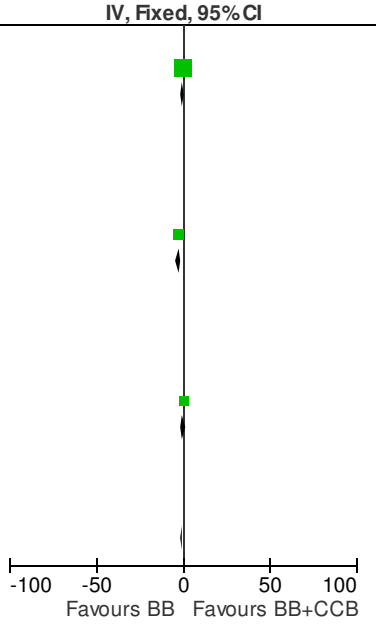
Study or Subgroup	BB Mean	BB SD	BB Total	CCB Mean	CCB SD	CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.26.1 Metoprolol vs. Verapamil								
Rehnqvist 1996 (APSIS)	60.5	15.6	275	61.8	15.6	282	100.0%	-1.30 [-3.89, 1.29]
Subtotal (95% CI)			**275**			**282**	**100.0%**	**-1.30 [-3.89, 1.29]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.98 (P = 0.33)								
Total (95% CI)			**275**			**282**	**100.0%**	**-1.30 [-3.89, 1.29]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.98 (P = 0.33)								
Test for subgroup differences: Not applicable								



1 BB vs. BB +CCB

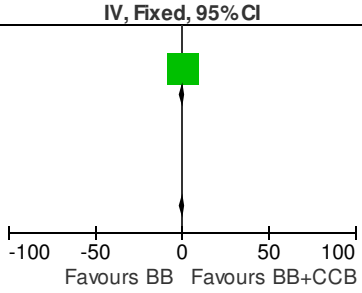
1.1 Exercise time (min)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 Propranolol vs. Propranolol +Nifedipine								
Tweddel 1981	4.8	1.68	18	5.06	1.68	18	50.5%	-0.26 [-1.36, 0.84]
Subtotal (95% CI)			**18**			**18**	**50.5%**	**-0.26 [-1.36, 0.84]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.46 (P = 0.64)								
1.1.2 Propranolol vs. Propranolol +Dilitazem								
O' hara 1987	6.8	3.5	34	9.6	1.3	7	26.3%	-2.80 [-4.32, -1.28]
Subtotal (95% CI)			**34**			**7**	**26.3%**	**-2.80 [-4.32, -1.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.61 (P = 0.0003)								
1.1.3 Propranolol vs. Propranolol +Nifedipine								
Kawanishi 1992	7.2	2.6	21	7.3	2.4	16	23.2%	-0.10 [-1.72, 1.52]
Subtotal (95% CI)			**21**			**16**	**23.2%**	**-0.10 [-1.72, 1.52]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.12 (P = 0.90)								
Total (95% CI)			**73**			**41**	**100.0%**	**-0.89 [-1.67, -0.11]**
Heterogeneity: Chi² = 8.24, df = 2 (P = 0.02); I² = 76%								
Test for overall effect: Z = 2.24 (P = 0.03)								
Test for subgroup differences: Chi² = 8.24, df = 2 (P = 0.02), I² = 75.7%								



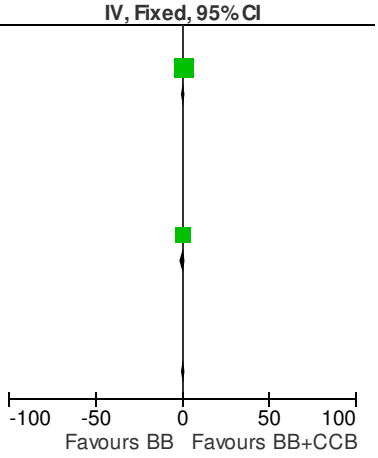
1.2 Time to onset of angina (min)

Study or Subgroup	BB Mean	SD	Total	BB+CCB Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.2.1 Propranolol vs. Propranolol +Nifedipine								
Kawanishi 1992	5.7	1.2	21	5.5	2.5	16	100.0%	0.20 [-1.13, 1.53]
Subtotal (95% CI)			**21**			**16**	**100.0%**	**0.20 [-1.13, 1.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.30 (P = 0.77)								
Total (95% CI)			**21**			**16**	**100.0%**	**0.20 [-1.13, 1.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.30 (P = 0.77)								
Test for subgroup differences: Not applicable								



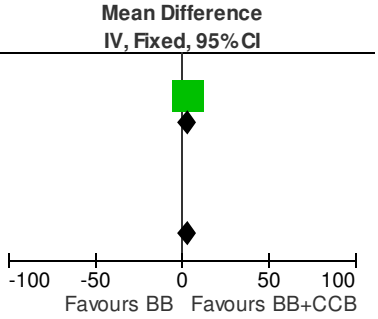
1.3 Angina attacks/week

Study or Subgroup	BB Mean	BB SD	BB Total	BB+CCB Mean	BB+CCB SD	BB+CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.3.1 Propranolol vs. Propranolol +Nifedipine								
Kawanishi 1992	2	2.3	21	1.3	1.7	16	58.2%	0.70 [-0.59, 1.99]
Subtotal (95% CI)			**21**			**16**	**58.2%**	**0.70 [-0.59, 1.99]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.06 (P = 0.29)								
1.3.2 Metoprolol vs. Metoprolol +Nifedipine								
Savonitto 1996 (IMAGE)	-2.01	4.72	61	-2.06	3.8	61	41.8%	0.05 [-1.47, 1.57]
Subtotal (95% CI)			**61**			**61**	**41.8%**	**0.05 [-1.47, 1.57]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.06 (P = 0.95)								
Total (95% CI)			**82**			**77**	**100.0%**	**0.43 [-0.56, 1.41]**
Heterogeneity: Chi² = 0.41, df = 1 (P = 0.52); I² = 0%								
Test for overall effect: Z = 0.85 (P = 0.39)								
Test for subgroup differences: Chi² = 0.41, df = 1 (P = 0.52), I² = 0%								



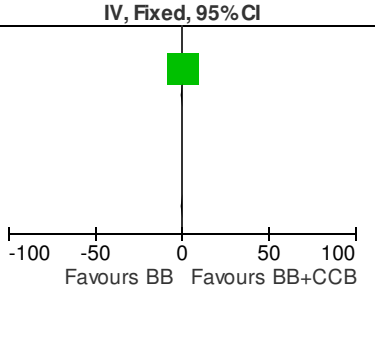
1.4 Angina attacks/day

Study or Subgroup	BB Mean	BB SD	BB Total	BB+CCB Mean	BB+CCB SD	BB+CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.4.1 Propranolol vs. Propranolol +Nifedipine								
Tweddel 1981	7	8.4	18	4	8.4	18	100.0%	3.00 [-2.49, 8.49]
Subtotal (95% CI)			**18**			**18**	**100.0%**	**3.00 [-2.49, 8.49]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.07 (P = 0.28)								
Total (95% CI)			**18**			**18**	**100.0%**	**3.00 [-2.49, 8.49]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.07 (P = 0.28)								
Test for subgroup differences: Not applicable								



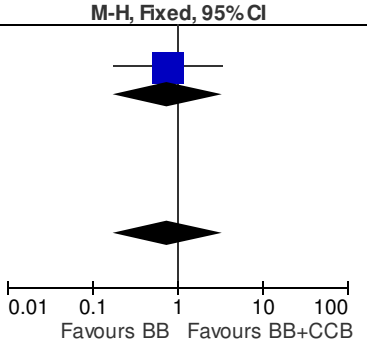
1.5 Nitroglycerin tablets/week

Study or Subgroup	BB Mean	BB SD	BB Total	BB+CCB Mean	BB+CCB SD	BB+CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.5.1 Propranolol vs. Propranolol +Nifedipine								
Kawanishi 1992	0.7	1.2	21	0.3	0.4	16	100.0%	0.40 [-0.15, 0.95]
Subtotal (95% CI)			**21**			**16**	**100.0%**	**0.40 [-0.15, 0.95]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.43 (P = 0.15)								
Total (95% CI)			**21**			**16**	**100.0%**	**0.40 [-0.15, 0.95]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.43 (P = 0.15)								
Test for subgroup differences: Not applicable								



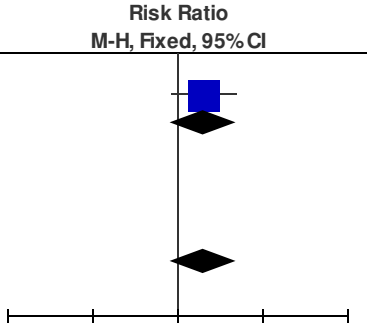
1.6 Cardiac death

Study or Subgroup	BB Events	BB Total	BB+CCB Events	BB+CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 Atenolol vs. Atenolol+Nifedipine						
Dargie 1996 (TIBET)	3	226	4	224	100.0%	0.74 [0.17, 3.28]
Subtotal (95% CI)		**226**		**224**	**100.0%**	**0.74 [0.17, 3.28]**
Total events	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.39 (P = 0.70)						
Total (95% CI)		**226**		**224**	**100.0%**	**0.74 [0.17, 3.28]**
Total events	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.39 (P = 0.70)						
Test for subgroup differences: Not applicable						



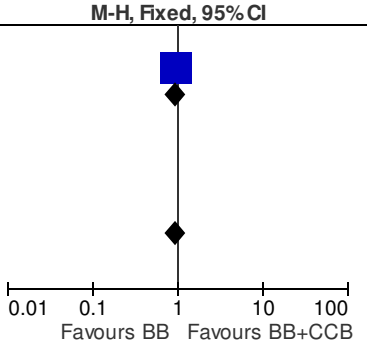
1.7 Non fatal MI

Study or Subgroup	BB Events	BB Total	BB+CCB Events	BB+CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.7.1 Atenolol +Atenolol +Nifedipine						
Dargie 1996 (TIBET)	14	226	7	224	100.0%	1.98 [0.82, 4.82]
Subtotal (95% CI)		**226**		**224**	**100.0%**	**1.98 [0.82, 4.82]**
Total events	14		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.51 (P = 0.13)						
Total (95% CI)		**226**		**224**	**100.0%**	**1.98 [0.82, 4.82]**
Total events	14		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.51 (P = 0.13)						
Test for subgroup differences: Not applicable						



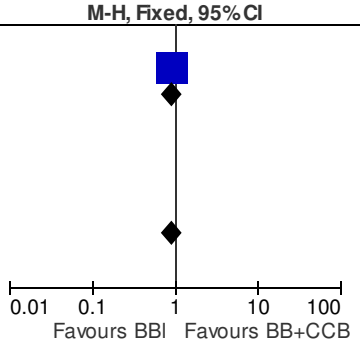
1.8 Withdarwals due to side effects

Study or Subgroup	BB Events	BB Total	BB+CCB Events	BB+CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.8.1 Atenolol vs. Atenolol +Nifedipine						
Dargie 1996 (TIBET)	60	226	64	224	100.0%	0.93 [0.69, 1.25]
Subtotal (95% CI)		**226**		**224**	**100.0%**	**0.93 [0.69, 1.25]**
Total events	60		64			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.48 (P = 0.63)						
Total (95% CI)		**226**		**224**	**100.0%**	**0.93 [0.69, 1.25]**
Total events	60		64			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.48 (P = 0.63)						
Test for subgroup differences: Not applicable						



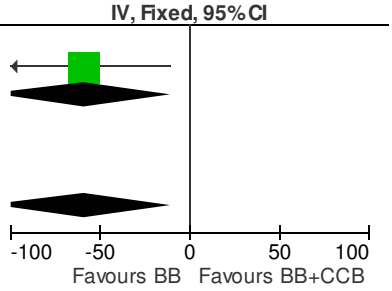
1.9 Adverse effects (overall)

Study or Subgroup	BB Events	BB Total	BB+CCB Events	BB+CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.9.1 Atenolol vs. Atenolol+Amlodipine						
Pehrsson 2000	52	116	59	119	100.0%	0.90 [0.69, 1.19]
Subtotal (95% CI)		**116**		**119**	**100.0%**	**0.90 [0.69, 1.19]**
Total events	52		59			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.73 (P = 0.47)						
Total (95% CI)		**116**		**119**	**100.0%**	**0.90 [0.69, 1.19]**
Total events	52		59			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.73 (P = 0.47)						
Test for subgroup differences: Not applicable						



1.10 Time to 1mm ST depression (sec)

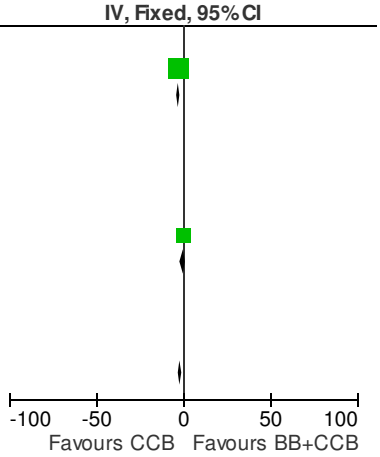
Study or Subgroup	BB Mean	BB SD	BB Total	BB+CCB Mean	BB+CCB SD	BB+CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
1.10.1 Metoprolol vs. Metoprolol +Nifedipine								
Savonitto 1996 (IMAGE)	49	128.6	65	108	149.1	63	100.0%	-59.00 [-107.30, -10.70]
Subtotal (95% CI)			**65**			**63**	**100.0%**	**-59.00 [-107.30, -10.70]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.39 (P = 0.02)								
Total (95% CI)			**65**			**63**	**100.0%**	**-59.00 [-107.30, -10.70]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.39 (P = 0.02)								
Test for subgroup differences: Not applicable								



2 CCB vs. BB +CCB

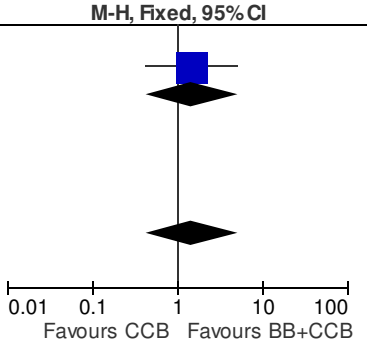
2.1 Exercise time (min)

Study or Subgroup	CCB Mean	CCB SD	CCB Total	BB+CCB Mean	BB+CCB SD	BB+CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
2.1.1 Diltiazem vs. Propranolol+Diltiazem								
O' hara 1987	6.5	2.3	34	9.6	1.3	7	60.4%	-3.10 [-4.33, -1.87]
Subtotal (95% CI)			**34**			**7**	**60.4%**	**-3.10 [-4.33, -1.87]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.92 (P < 0.00001)								
2.1.2 Nifedipine vs. Propranolol +Nifedipine								
Kawanishi 1992	7.2	2.2	16	7.3	2.4	19	39.6%	-0.10 [-1.63, 1.43]
Subtotal (95% CI)			**16**			**19**	**39.6%**	**-0.10 [-1.63, 1.43]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.13 (P = 0.90)								
Total (95% CI)			**50**			**26**	**100.0%**	**-1.91 [-2.87, -0.95]**
Heterogeneity: Chi² = 8.98, df = 1 (P = 0.003); I² = 89%								
Test for overall effect: Z = 3.90 (P < 0.0001)								
Test for subgroup differences: Chi² = 8.98, df = 1 (P = 0.003), I² = 88.9%								



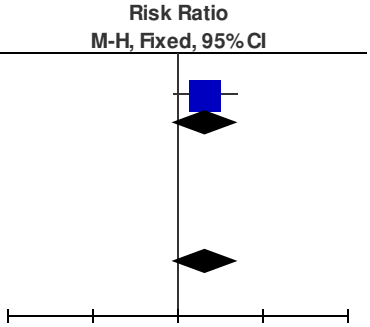
2.2 Cardiac death

Study or Subgroup	CCB Events	CCB Total	BB+CCB Events	BB+CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 Nifedipine vs. Atenolol +Nifedipine						
Dargie 1996 (TIBET)	6	232	4	224	100.0%	1.45 [0.41, 5.06]
Subtotal (95% CI)		**232**		**224**	**100.0%**	**1.45 [0.41, 5.06]**
Total events	6		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.58 (P = 0.56)						
Total (95% CI)		**232**		**224**	**100.0%**	**1.45 [0.41, 5.06]**
Total events	6		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.58 (P = 0.56)						
Test for subgroup differences: Not applicable						



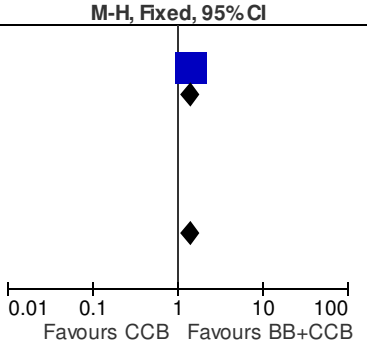
2.3 Non fatal MI

Study or Subgroup	CCB Events	CCB Total	BB+CCB Events	BB+CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.3.1 Nifedipine vs. Atenolol +Nifedipine						
Dargie 1996 (TIBET)	15	232	7	224	100.0%	2.07 [0.86, 4.98]
Subtotal (95% CI)		**232**		**224**	**100.0%**	**2.07 [0.86, 4.98]**
Total events	15		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.62 (P = 0.10)						
Total (95% CI)		**232**		**224**	**100.0%**	**2.07 [0.86, 4.98]**
Total events	15		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.62 (P = 0.10)						
Test for subgroup differences: Not applicable						



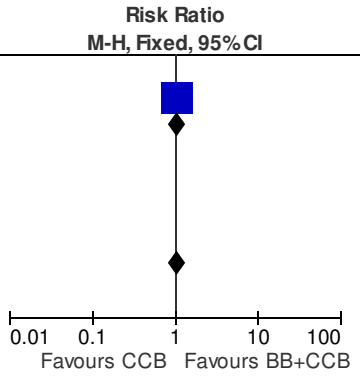
2.4 Withdrawals due to side effects

Study or Subgroup	CCB Events	CCB Total	BB+CCB Events	BB+CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.4.1 Nifedipine vs. Atenolol +Nifedipine						
Dargie 1996 (TIBET)	93	232	64	224	100.0%	1.40 [1.08, 1.82]
Subtotal (95% CI)		**232**		**224**	**100.0%**	**1.40 [1.08, 1.82]**
Total events	93		64			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.55 (P = 0.01)						
Total (95% CI)		**232**		**224**	**100.0%**	**1.40 [1.08, 1.82]**
Total events	93		64			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.55 (P = 0.01)						
Test for subgroup differences: Not applicable						



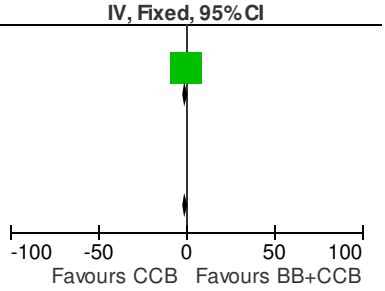
2.5 Adverse effects (overall)

Study or Subgroup	CCB Events	CCB Total	BB+CCB Events	BB+CCB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.5.1 Amlodipine vs. Atenolol +Amlodipine						
Pehrsson 2000	60	116	59	119	100.0%	1.04 [0.81, 1.34]
Subtotal (95% CI)		**116**		**119**	**100.0%**	**1.04 [0.81, 1.34]**
Total events	60		59			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.33 (P = 0.74)						
Total (95% CI)		**116**		**119**	**100.0%**	**1.04 [0.81, 1.34]**
Total events	60		59			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.33 (P = 0.74)						
Test for subgroup differences: Not applicable						



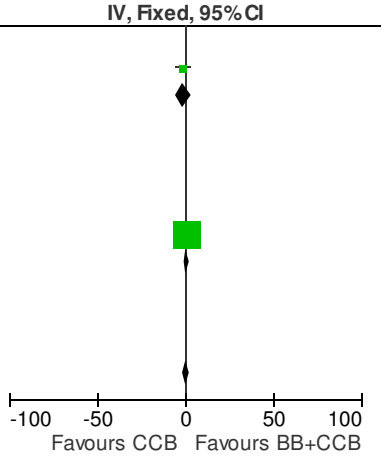
2.6 Time to onset of angina (min)

Study or Subgroup	CCB Mean	CCB SD	CCB Total	BB+CCB Mean	BB+CCB SD	BB+CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
2.6.1 Nifedipine vs. Propranolol +Nifedipine								
Kawanishi 1992	5	1.8	16	5.5	2.5	19	100.0%	-0.50 [-1.93, 0.93]
Subtotal (95% CI)			**16**			**19**	**100.0%**	**-0.50 [-1.93, 0.93]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.69 (P = 0.49)								
Total (95% CI)			**16**			**19**	**100.0%**	**-0.50 [-1.93, 0.93]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.69 (P = 0.49)								
Test for subgroup differences: Not applicable								



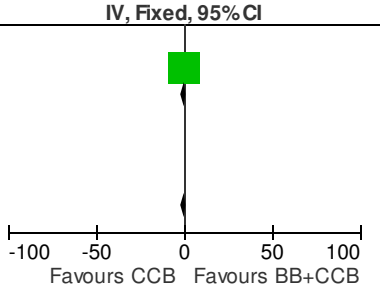
2.7 Angina episodes/week

Study or Subgroup	CCB Mean	CCB SD	CCB Total	BB+CCB Mean	BB+CCB SD	BB+CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
2.7.1 Nifedipine vs. Propranolol+Nifedipine								
Kawanishi 1992	2.7	5.6	16	4.3	7.9	19	14.7%	-1.60 [-6.09, 2.89]
Subtotal (95% CI)			**16**			**19**	**14.7%**	**-1.60 [-6.09, 2.89]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.70 (P = 0.48)								
2.7.2 Nifedipine vs. Metoprolol +Nifedipine								
Savonitto 1996 (IMAGE)	-2.32	6.43	61	-2.71	3.58	57	85.3%	0.39 [-1.47, 2.25]
Subtotal (95% CI)			**61**			**57**	**85.3%**	**0.39 [-1.47, 2.25]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.41 (P = 0.68)								
Total (95% CI)			**77**			**76**	**100.0%**	**0.10 [-1.62, 1.82]**
Heterogeneity: Chi² = 0.64, df = 1 (P = 0.42); I² = 0%								
Test for overall effect: Z = 0.11 (P = 0.91)								
Test for subgroup differences: Chi² = 0.64, df = 1 (P = 0.42), I² = 0%								



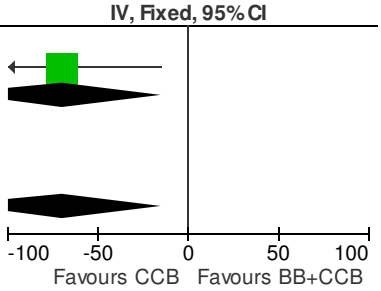
2.8 Nitroglycerin tablets/week

Study or Subgroup	CCB Mean	CCB SD	CCB Total	BB+CCB Mean	BB+CCB SD	BB+CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
2.8.1 Nifedipine vs. Propranolol+Nifedipine								
Kawanishi 1992	0.7	1.6	16	1.1	2.2	19	100.0%	-0.40 [-1.66, 0.86]
Subtotal (95% CI)			**16**			**19**	**100.0%**	**-0.40 [-1.66, 0.86]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.62 (P = 0.53)								
Total (95% CI)			**16**			**19**	**100.0%**	**-0.40 [-1.66, 0.86]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.62 (P = 0.53)								
Test for subgroup differences: Not applicable								



2.9 Time to 1 mm ST segment depression

Study or Subgroup	CCB Mean	CCB SD	CCB Total	BB+CCB Mean	BB+CCB SD	BB+CCB Total	Weight	Mean Difference IV, Fixed, 95% CI
2.9.1 Nifedipine vs. Metoprolol+Nifedipine								
Savonitto 1996 (IMAGE)	37	141.28	62	107	166.4	59	100.0%	-70.00 [-125.13, -14.87]
Subtotal (95% CI)			**62**			**59**	**100.0%**	**-70.00 [-125.13, -14.87]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.49 (P = 0.01)								
Total (95% CI)			**62**			**59**	**100.0%**	**-70.00 [-125.13, -14.87]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.49 (P = 0.01)								
Test for subgroup differences: Not applicable								

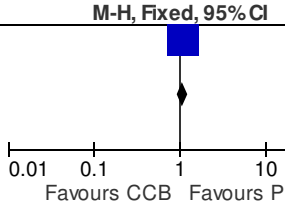


1 CCB +basic regimen vs. Placebo +basic regimen

1.1 All cause mortality

Study or Subgroup	CCB +basic regimen Events	Total	Placebo +basic regimen Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poole-Wilson 2004(ACTION)	310	3825	291	3840	100.0%	1.07 [0.92, 1.25]
Total (95% CI)		**3825**		**3840**	**100.0%**	**1.07 [0.92, 1.25]**
Total events	310		291			

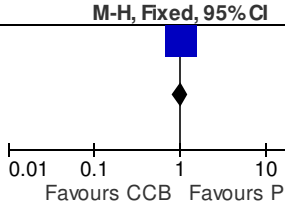
Heterogeneity: Not applicable
Test for overall effect: Z = 0.86 (P = 0.39)



1.2 Cardiovascular or unknown death

Study or Subgroup	CCB +basic regimen Events	Total	Placebo +basic regimen Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poole-Wilson 2004(ACTION)	178	3825	177	3840	100.0%	1.01 [0.82, 1.24]
Total (95% CI)		**3825**		**3840**	**100.0%**	**1.01 [0.82, 1.24]**
Total events	178		177			

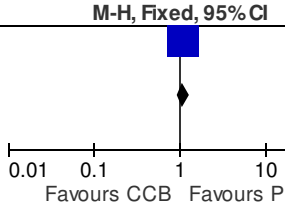
Heterogeneity: Not applicable
Test for overall effect: Z = 0.09 (P = 0.93)



1.3 MI

Study or Subgroup	CCB +basic regimen Events	Total	Placebo +basic regimen Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poole-Wilson 2004(ACTION)	320	3825	296	3840	100.0%	1.09 [0.93, 1.26]
Total (95% CI)		**3825**		**3840**	**100.0%**	**1.09 [0.93, 1.26]**
Total events	320		296			

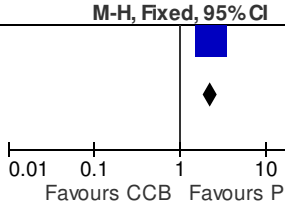
Heterogeneity: Not applicable
Test for overall effect: Z = 1.06 (P = 0.29)



1.4 Withdrawal due to adverse effects

Study or Subgroup	CCB +basic regimen Events	Total	Placebo +basic regimen Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poole-Wilson 2004(ACTION)	389	3825	172	3840	100.0%	2.27 [1.91, 2.70]
Total (95% CI)		**3825**		**3840**	**100.0%**	**2.27 [1.91, 2.70]**
Total events	389		172			

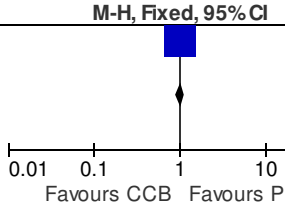
Heterogeneity: Not applicable
Test for overall effect: Z = 9.25 (P < 0.00001)



1.5 combined outcome (death, acute MI, refractory angina, new overt HF, debilitating stroke, peripheral revas) (age >65yrs)

Study or Subgroup	CCB +basic regimen Events	Total	Placebo +basic regimen Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poole-Wilson 2004(ACTION)	467	1772	466	1776	100.0%	1.00 [0.90, 1.12]
Total (95% CI)		**1772**		**1776**	**100.0%**	**1.00 [0.90, 1.12]**
Total events	467		466			

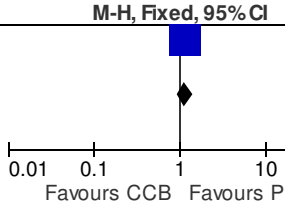
Heterogeneity: Not applicable
Test for overall effect: Z = 0.08 (P = 0.94)



1.6 combined outcome (death, acute MI, refractory angina, new overt HF, debilitating stroke, peripheral revas) (females)

Study or Subgroup	CCB +basic regimen Events	Total	Placebo +basic regimen Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poole-Wilson 2004(ACTION)	166	784	147	797	100.0%	1.15 [0.94, 1.40]
Total (95% CI)		**784**		**797**	**100.0%**	**1.15 [0.94, 1.40]**
Total events	166		147			

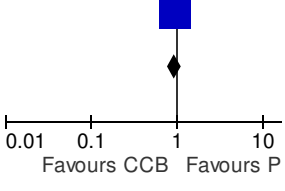
Heterogeneity: Not applicable
Test for overall effect: Z = 1.36 (P = 0.17)



1.7 combined outcome (death, acute MI, refractory angina, new overt HF, debilitating stroke, peripheral revas) (diabetes)

Study or Subgroup	CCB +basic regimen Events	Total	Placebo +basic regimen Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poole-Wilson 2004(ACTION)	164	565	170	545	100.0%	0.93 [0.78, 1.11]
Total (95% CI)		**565**		**545**	**100.0%**	**0.93 [0.78, 1.11]**
Total events	164		170			

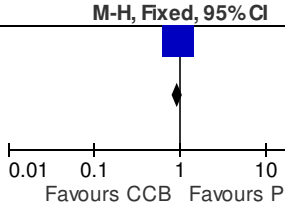
Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)



1.8 Combined outcome (death from any cause, acute MI, refractory angina, new overt HF, debilitating stroke , peripheral revas)(age <65 years)

Study or Subgroup	CCB +basic regimen Events	Total	Placebo +basic regimen Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poole-Wilson 2004(ACTION)	337	2053	362	2064	100.0%	0.94 [0.82, 1.07]
Total (95% CI)		**2053**		**2064**	**100.0%**	**0.94 [0.82, 1.07]**
Total events	337		362			

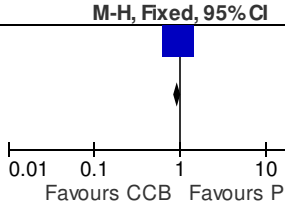
Heterogeneity: Not applicable
Test for overall effect: Z = 0.96 (P = 0.34)



1.9 combined outcome (death from any cause, acute MI, refractory angina, new overt HF, debilitating stroke ,peripheral revas)(males)

Study or Subgroup	CCB +basic regimen Events	Total	Placebo +basic regimen Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poole-Wilson 2004(ACTION)	638	3041	681	3043	100.0%	0.94 [0.85, 1.03]
Total (95% CI)		**3041**		**3043**	**100.0%**	**0.94 [0.85, 1.03]**
Total events	638		681			

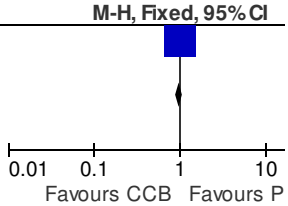
Heterogeneity: Not applicable
Test for overall effect: Z = 1.32 (P = 0.19)



1.10 combined outcome (death from any cause, acute MI, refractory angina, new overt HF, debilitating stroke ,peripheral revas)(no diabetes)

Study or Subgroup	CCB +basic regimen Events	Total	Placebo +basic regimen Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Poole-Wilson 2004(ACTION)	640	3260	658	3295	100.0%	0.98 [0.89, 1.08]
Total (95% CI)		**3260**		**3295**	**100.0%**	**0.98 [0.89, 1.08]**
Total events	640		658			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.34 (P = 0.73)

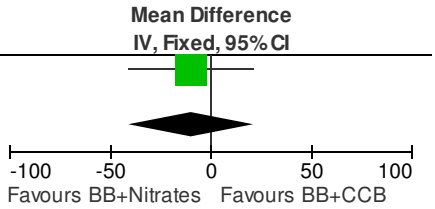


1 BB+Nitrates vs. BB+CCB

1.1 Exercise time (Sec)

Study or Subgroup	BB +Nitrates Mean	SD	Total	BB +CCB Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
De Vries 1994	12	77.2	46	22	75.2	46	100.0%	-10.00 [-41.14, 21.14]
Total (95% CI)			**46**			**46**	**100.0%**	**-10.00 [-41.14, 21.14]**

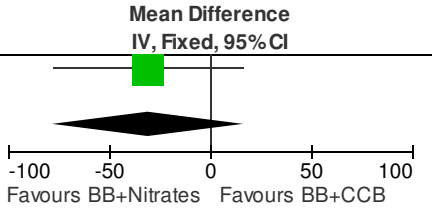
Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)



1.2 Time to onset of angina (Sec)

Study or Subgroup	BB +Nitrates Mean	SD	Total	BB +CCB Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
De Vries 1994	21	115.9	46	52	114.5	46	100.0%	-31.00 [-78.08, 16.08]
Total (95% CI)			**46**			**46**	**100.0%**	**-31.00 [-78.08, 16.08]**

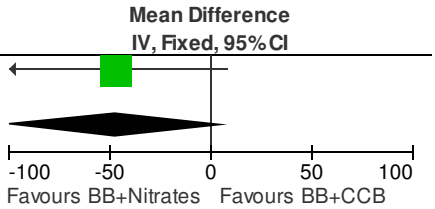
Heterogeneity: Not applicable
Test for overall effect: Z = 1.29 (P = 0.20)



1.3 Time to ST segment depression (sec)

Study or Subgroup	BB +Nitrates Mean	SD	Total	BB +CCB Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
De Vries 1994	3	136.2	46	50	134.9	46	100.0%	-47.00 [-102.40, 8.40]
Total (95% CI)			**46**			**46**	**100.0%**	**-47.00 [-102.40, 8.40]**

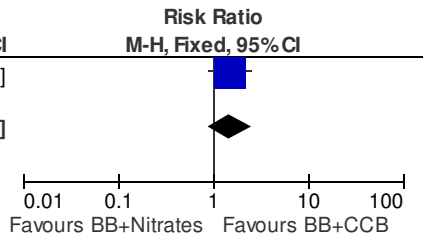
Heterogeneity: Not applicable
Test for overall effect: Z = 1.66 (P = 0.10)



1.4 Adverse effects (overall)

Study or Subgroup	BB +Nitrates Events	Total	BB +CCB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
De Vries 1994	22	46	14	43	100.0%	1.47 [0.87, 2.48]
Total (95% CI)		**46**		**43**	**100.0%**	**1.47 [0.87, 2.48]**
Total events	22		14			

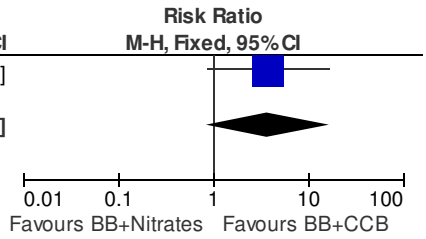
Heterogeneity: Not applicable
Test for overall effect: Z = 1.43 (P = 0.15)



1.5 Stopping due to adverse events

Study or Subgroup	BB +Nitrates Events	Total	BB +CCB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
De Vries 1994	8	46	2	43	100.0%	3.74 [0.84, 16.64]
Total (95% CI)		**46**		**43**	**100.0%**	**3.74 [0.84, 16.64]**
Total events	8		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.73 (P = 0.08)

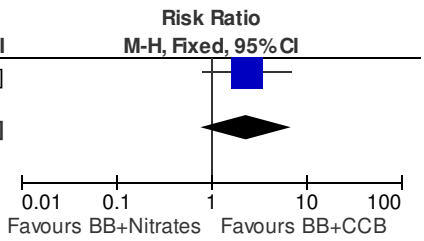


1.6 Headache

Study or Subgroup	BB +Nitrates Events	Total	BB +CCB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
De Vries 1994	10	46	4	43	100.0%	2.34 [0.79, 6.90]
Total (95% CI)		**46**		**43**	**100.0%**	**2.34 [0.79, 6.90]**
Total events	10		4			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.54 (P = 0.12)

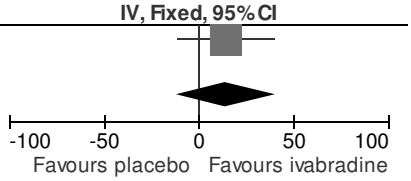


1 Ivabradine vs placebo

1.1 Time to angina onset (sec) (trough change from baseline) - 14 days

Study or Subgroup	Ivabradine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Borer 2003	38.8	81.7	59	24.7	64.2	68	100.0%	14.10 [-11.73, 39.93]
Total (95% CI)			**59**			**68**	**100.0%**	**14.10 [-11.73, 39.93]**

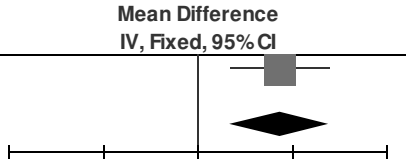
Heterogeneity: Not applicable
Test for overall effect: Z = 1.07 (P = 0.28)



1.2 Time to angina onset (sec) (peak change from baseline - 14 days

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Borer 2003	72.1	83.1	59	28.9	66.5	68	100.0%	43.20 [16.75, 69.65]
Total (95% CI)			**59**			**68**	**100.0%**	**43.20 [16.75, 69.65]**

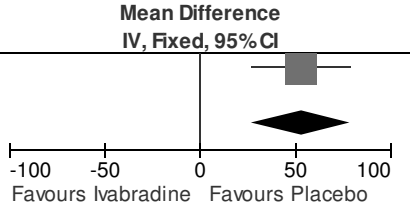
Heterogeneity: Not applicable
Test for overall effect: Z = 3.20 (P = 0.001)



1.3 Time to 1 mm S depression (sec) (at peak of drug activity) - 14 days

Study or Subgroup	Ivabradine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Borer 2003	62.8	79.7	59	9.9	68.5	68	100.0%	52.90 [26.85, 78.95]
Total (95% CI)			**59**			**68**	**100.0%**	**52.90 [26.85, 78.95]**

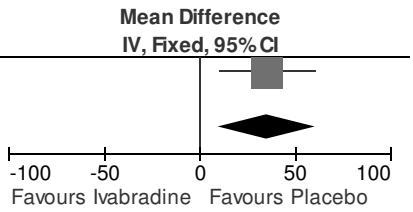
Heterogeneity: Not applicable
Test for overall effect: Z = 3.98 (P < 0.0001)



1.4 Time to 1 mm ST depression (sec) (at trough) - 14 days

Study or Subgroup	Ivabradine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Borer 2003	44.1	80.1	59	9	63.6	68	100.0%	35.10 [9.68, 60.52]
Total (95% CI)			**59**			**68**	**100.0%**	**35.10 [9.68, 60.52]**

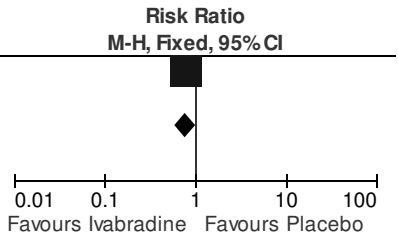
Heterogeneity: Not applicable
Test for overall effect: Z = 2.71 (P = 0.007)



1.5 With limiting angina - CV death or hospitalisation for MI or HF - median 18 months

Study or Subgroup	Ivabradine Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fox 2009 (BEAUTIFUL)	88	734	120	773	100.0%	0.77 [0.60, 1.00]
Total (95% CI)		**734**		**773**	**100.0%**	**0.77 [0.60, 1.00]**
Total events	88		120			

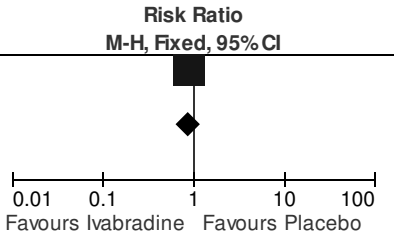
Heterogeneity: Not applicable
Test for overall effect: Z = 1.98 (P = 0.05)



1.6 With limiting angina - all cause mortality - median 18 months

Study or Subgroup	Ivabradine Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fox 2009 (BEAUTIFUL)	64	734	77	773	100.0%	0.88 [0.64, 1.20]
Total (95% CI)		**734**		**773**	**100.0%**	**0.88 [0.64, 1.20]**
Total events	64		77			

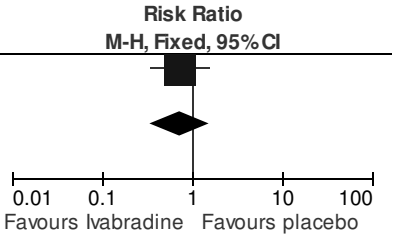
Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)



1.7 With limiting angina - Cardiac death - median 18 months

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fox 2009 (BEAUTIFUL)	11	734	16	773	100.0%	0.72 [0.34, 1.55]
Total (95% CI)		**734**		**773**	**100.0%**	**0.72 [0.34, 1.55]**
Total events	11		16			

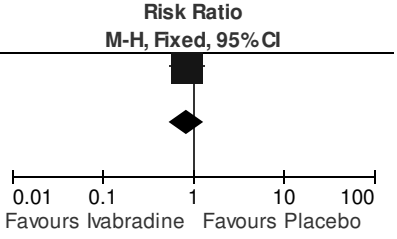
Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)



1.8 With limiting angina - hospitalisation for HF - median 18 months

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fox 2009 (BEAUTIFUL)	33	734	41	773	100.0%	0.85 [0.54, 1.33]
Total (95% CI)		**734**		**773**	**100.0%**	**0.85 [0.54, 1.33]**
Total events	33		41			

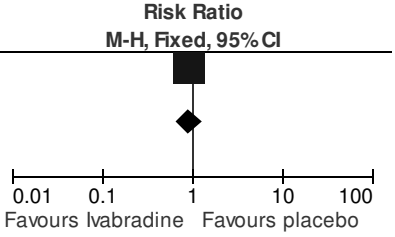
Heterogeneity: Not applicable
Test for overall effect: Z = 0.72 (P = 0.47)



1.9 With limiting angina - Hospitalisation for MI or unstable angina - median 18 months

Study or Subgroup	Ivabradine Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fox 2009 (BEAUTIFUL)	56	734	65	773	100.0%	0.91 [0.64, 1.28]
Total (95% CI)		**734**		**773**	**100.0%**	**0.91 [0.64, 1.28]**
Total events	56		65			

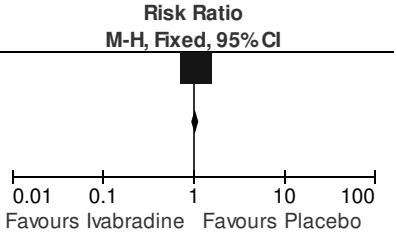
Heterogeneity: Not applicable
Test for overall effect: Z = 0.56 (P = 0.58)



1.10 Without limiting angina - CV death or hospitalisation for MI or HF - median 18 months

Study or Subgroup	Ivabradine Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fox 2009 (BEAUTIFUL)	756	4745	712	4665	100.0%	1.04 [0.95, 1.15]
Total (95% CI)		**4745**		**4665**	**100.0%**	**1.04 [0.95, 1.15]**
Total events	756		712			

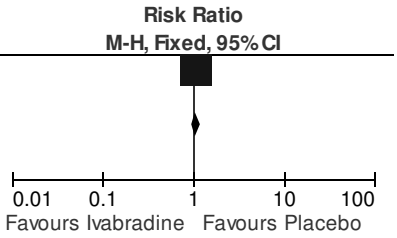
Heterogeneity: Not applicable
Test for overall effect: Z = 0.90 (P = 0.37)



1.11 Without limiting angina - all cause mortality - median 18 months

Study or Subgroup	Ivabradine Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fox 2009 (BEAUTIFUL)	508	4745	470	4665	100.0%	1.06 [0.94, 1.20]
Total (95% CI)		**4745**		**4665**	**100.0%**	**1.06 [0.94, 1.20]**
Total events	508		470			

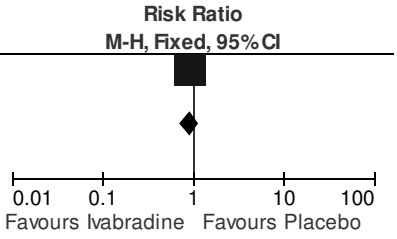
Heterogeneity: Not applicable
Test for overall effect: Z = 1.00 (P = 0.32)



1.12 Without limiting angina - Cardiac death - median 18 months

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fox 2009 (BEAUTIFUL)	125	4745	135	4665	100.0%	0.91 [0.72, 1.16]
Total (95% CI)		**4745**		**4665**	**100.0%**	**0.91 [0.72, 1.16]**
Total events	125		135			

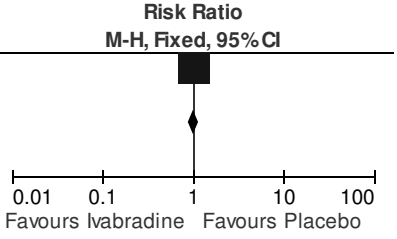
Heterogeneity: Not applicable
Test for overall effect: Z = 0.77 (P = 0.44)



1.13 Without limiting angina - hospitalisation for HF - median 18 months

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fox 2009 (BEAUTIFUL)	393	4745	386	4665	100.0%	1.00 [0.87, 1.15]
Total (95% CI)		**4745**		**4665**	**100.0%**	**1.00 [0.87, 1.15]**
Total events	393		386			

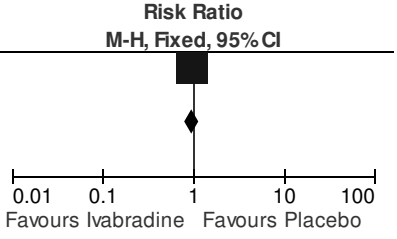
Heterogeneity: Not applicable
Test for overall effect: Z = 0.01 (P = 0.99)



1.14 Without limiting angina - Hospitalisation for MI or unstable angina - median 18 months

Study or Subgroup	Ivabradine Events	Total	Palcebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fox 2009 (BEAUTIFUL)	247	4745	252	4665	100.0%	0.96 [0.81, 1.14]
Total (95% CI)		**4745**		**4665**	**100.0%**	**0.96 [0.81, 1.14]**
Total events	247		252			

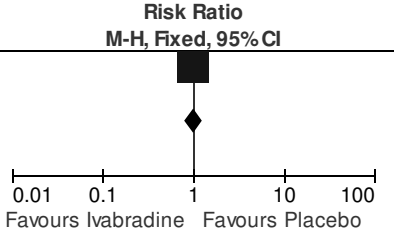
Heterogeneity: Not applicable
Test for overall effect: Z = 0.43 (P = 0.67)



1.15 All serious adverse events

Study or Subgroup	Ivabradine Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fox 2009 (BEAUTIFUL)	135	734	144	773	100.0%	0.99 [0.80, 1.22]
Total (95% CI)		**734**		**773**	**100.0%**	**0.99 [0.80, 1.22]**
Total events	135		144			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.12 (P = 0.91)

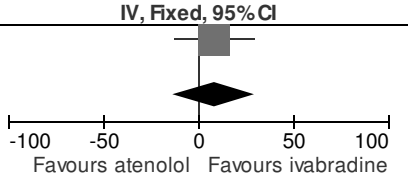


2 Ivabradine vs atenolol

2.1 Total exercise duration (sec)(trough change from baseline) - 16 weeks

Study or Subgroup	Ivabradine Mean	SD	Total	Atenolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tardif 2005	86.8	129	300	78.8	133.4	286	100.0%	8.00 [-13.26, 29.26]
Total (95% CI)			**300**			**286**	**100.0%**	**8.00 [-13.26, 29.26]**

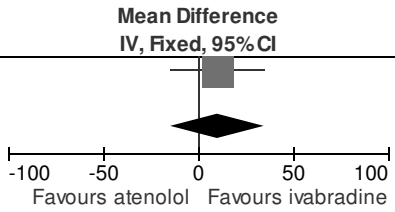
Heterogeneity: Not applicable
Test for overall effect: Z = 0.74 (P = 0.46)



2.2 Time to angina onset (sec) (trough change from baseline) - 16 weeks

Study or Subgroup	Ivabradine Mean	SD	Total	Atenolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tardif 2005	145.2	153.4	300	135.2	154.7	286	100.0%	10.00 [-14.96, 34.96]
Total (95% CI)			**300**			**286**	**100.0%**	**10.00 [-14.96, 34.96]**

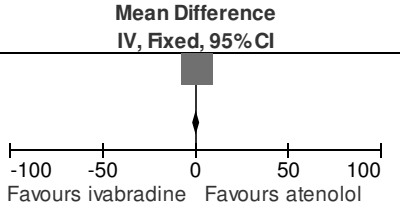
Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)



2.3 Weekly number of angina attacks - 16 weeks

Study or Subgroup	Ivabradine Mean	SD	Total	Atenolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tardif 2005	-2.2	4.4	307	-2.7	12.3	294	100.0%	0.50 [-0.99, 1.99]
Total (95% CI)			**307**			**294**	**100.0%**	**0.50 [-0.99, 1.99]**

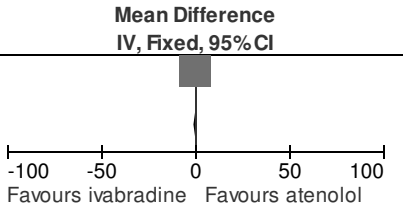
Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)



2.4 Short-acting nitrate consumption units/week - 16 weeks

Study or Subgroup	Ivabradine Mean	SD	Total	Atenolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tardif 2005	-1.6	4.1	307	-1.2	3.4	294	100.0%	-0.40 [-1.00, 0.20]
Total (95% CI)			**307**			**294**	**100.0%**	**-0.40 [-1.00, 0.20]**

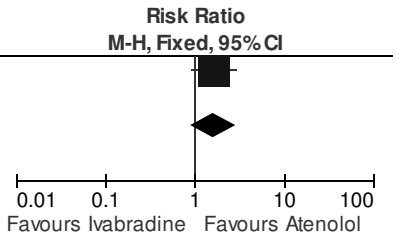
Heterogeneity: Not applicable
Test for overall effect: Z = 1.30 (P = 0.19)



2.5 Withdrawal due to AEs-16 weeks

Study or Subgroup	Ivabradine Events	Total	Atenolol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tardif 2005	28	315	17	307	100.0%	1.61 [0.90, 2.87]
Total (95% CI)		**315**		**307**	**100.0%**	**1.61 [0.90, 2.87]**
Total events	28		17			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.59 (P = 0.11)

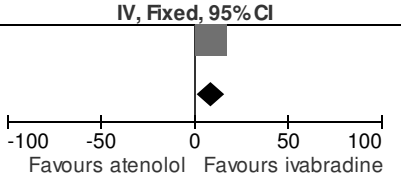


3 Ivabradine +atenolol vs atenolol+ placebo

3.1 Total exercise duration (sec) (change from baseline) - 2 months

Study or Subgroup	Ivabradine + atenolol Mean	SD	Total	atenolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tardif 2009	15.5	60	441	6.8	56.5	434	100.0%	8.70 [0.98, 16.42]
Total (95% CI)			**441**			**434**	**100.0%**	**8.70 [0.98, 16.42]**

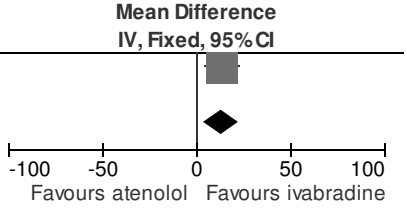
Heterogeneity: Not applicable
Test for overall effect: Z = 2.21 (P = 0.03)



3.2 Time to angina onset (sec) (change from baseline) - 2 mths

Study or Subgroup	Ivabradine + atenolol Mean	SD	Total	atenolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tardif 2009	30.2	72.2	441	17.2	72.3	434	100.0%	13.00 [3.43, 22.57]
Total (95% CI)			**441**			**434**	**100.0%**	**13.00 [3.43, 22.57]**

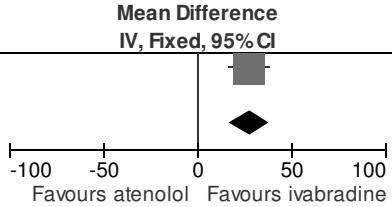
Heterogeneity: Not applicable
Test for overall effect: Z = 2.66 (P = 0.008)



3.3 Time to 1 mm S depression (sec) (change from baseline)- 2months

Study or Subgroup	Ivabradine + atenolol Mean	SD	Total	atenolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tardif 2009	35	84.1	441	7.8	82.6	434	100.0%	27.20 [16.15, 38.25]
Total (95% CI)			**441**			**434**	**100.0%**	**27.20 [16.15, 38.25]**

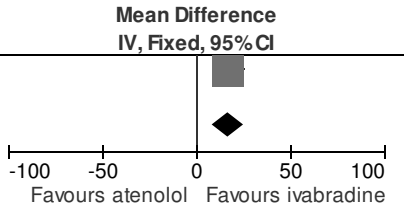
Heterogeneity: Not applicable
Test for overall effect: Z = 4.83 (P < 0.00001)



3.4 Total exercise duration (sec) (change from baseline-4 months

Study or Subgroup	Ivabradine + atenolol Mean	SD	Total	atenolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tardif 2009	24.3	65.3	441	7.7	63.8	434	100.0%	16.60 [8.05, 25.15]
Total (95% CI)			**441**			**434**	**100.0%**	**16.60 [8.05, 25.15]**

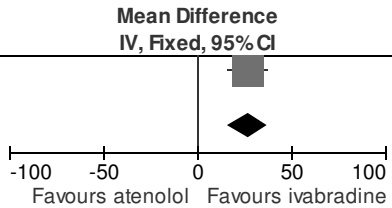
Heterogeneity: Not applicable
Test for overall effect: Z = 3.80 (P = 0.0001)



3.5 Time to onset of angina(sec) (change from baseline) - 4 months

Study or Subgroup	Ivabradine + atenolol Mean	SD	Total	atenolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tardif 2009	49.1	83.3	441	22.7	79.1	434	100.0%	26.40 [15.64, 37.16]
Total (95% CI)			**441**			**434**	**100.0%**	**26.40 [15.64, 37.16]**

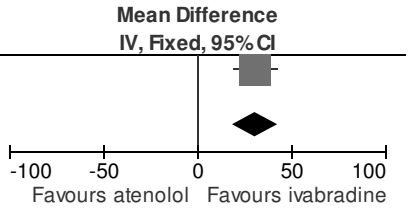
Heterogeneity: Not applicable
Test for overall effect: Z = 4.81 (P < 0.00001)



3.6 Time to 1 mm ST depression (sec) (change from baseline-4 months

Study or Subgroup	Ivabradine + atenolol Mean	SD	Total	atenolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tardif 2009	45.7	93	441	15.4	86.6	434	100.0%	30.30 [18.40, 42.20]
Total (95% CI)			**441**			**434**	**100.0%**	**30.30 [18.40, 42.20]**

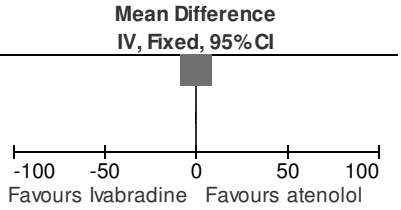
Heterogeneity: Not applicable
Test for overall effect: Z = 4.99 (P < 0.00001)



3.7 angina attacks/week

Study or Subgroup	Ivabradine + atenolol Mean	SD	Total	atenolol+placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tardif 2009	0.9	2.4	441	0.9	2.1	434	100.0%	0.00 [-0.30, 0.30]
Total (95% CI)			**441**			**434**	**100.0%**	**0.00 [-0.30, 0.30]**

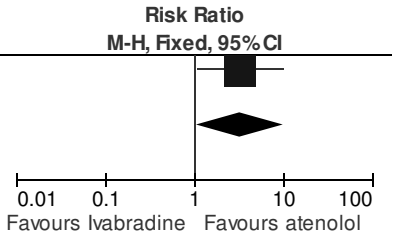
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



3.8 Adverse events (4 months)

Study or Subgroup	Ivabradine + atenolol Events	Total	atenolol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tardif 2009	13	441	4	434	100.0%	3.20 [1.05, 9.73]
Total (95% CI)		**441**		**434**	**100.0%**	**3.20 [1.05, 9.73]**
Total events	13		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.05 (P = 0.04)

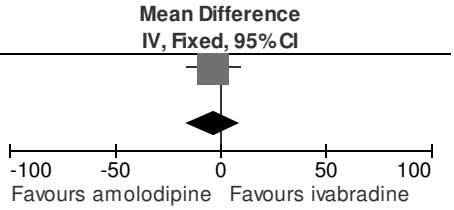


4 Ivabradine vs amolodipine

4.1 Total exercise duration (sec) - 3 months

Study or Subgroup	Ivabradine Mean	SD	Total	amolodipine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ruzyllo 2007	27.6	91.7	381	31.2	92	398	100.0%	-3.60 [-16.50, 9.30]
Total (95% CI)			**381**			**398**	**100.0%**	**-3.60 [-16.50, 9.30]**

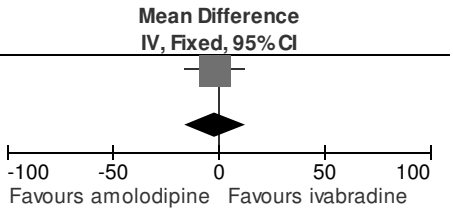
Heterogeneity: Not applicable
Test for overall effect: Z = 0.55 (P = 0.58)



4.2 Time angina onset (sec) - 3 months

Study or Subgroup	Ivabradine Mean	SD	Total	amolodipine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ruzyllo 2007	64.7	104.9	381	66.6	99.1	398	100.0%	-1.90 [-16.24, 12.44]
Total (95% CI)			**381**			**398**	**100.0%**	**-1.90 [-16.24, 12.44]**

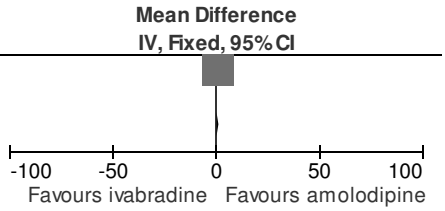
Heterogeneity: Not applicable
Test for overall effect: Z = 0.26 (P = 0.80)



4.3 Short-acting nitrate use (units/week) - 3 months

Study or Subgroup	Ivabradine Mean	SD	Total	amolodipine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ruzyllo 2007	-1.9	4.5	389	-2.7	6.3	398	100.0%	0.80 [0.04, 1.56]
Total (95% CI)			**389**			**398**	**100.0%**	**0.80 [0.04, 1.56]**

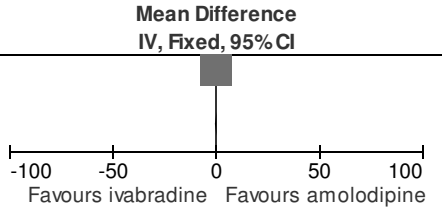
Heterogeneity: Not applicable
Test for overall effect: Z = 2.05 (P = 0.04)



4.4 Frequency of angina attacks/week - 3 months

Study or Subgroup	Ivabradine Mean	SD	Total	amolodipine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ruzyllo 2007	-3	5	389	-3	6	398	100.0%	0.00 [-0.77, 0.77]
Total (95% CI)			**389**			**398**	**100.0%**	**0.00 [-0.77, 0.77]**

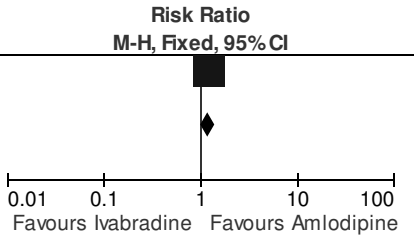
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



4.5 Adverse events - 3 months

Study or Subgroup	Ivabradine Events	Total	amolodipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ruzyllo 2007	181	400	152	404	100.0%	1.20 [1.02, 1.42]
Total (95% CI)		**400**		**404**	**100.0%**	**1.20 [1.02, 1.42]**
Total events	181		152			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.19 (P = 0.03)

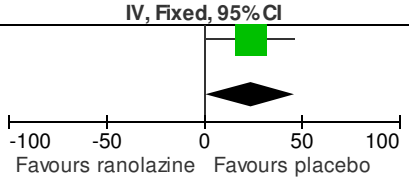


1 Ranolazine (750 mg bid) + antianginal vs Placebo + antianginal (Follow-up 12 weeks)

1.1 Exercise duration (trough - change from baseline), s - 12 wks

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Chaitman (CARISA) 2004	115.4	131.92	272	91.7	133.3	258	100.0%	23.70 [1.11, 46.29]
Total (95% CI)			**272**			**258**	**100.0%**	**23.70 [1.11, 46.29]**

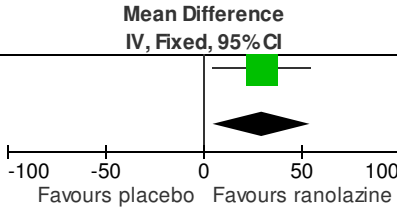
Heterogeneity: Not applicable
Test for overall effect: Z = 2.06 (P = 0.04)



1.2 Time to onset of angina (trough - change from baseline) s - 12 wks

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Chaitman (CARISA) 2004	144	146.76	272	114.3	147.75	258	100.0%	29.70 [4.62, 54.78]
Total (95% CI)			**272**			**258**	**100.0%**	**29.70 [4.62, 54.78]**

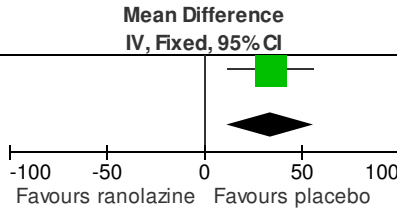
Heterogeneity: Not applicable
Test for overall effect: Z = 2.32 (P = 0.02)



1.3 Exercise duration (peak - change from baseline) s - 12 wks

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Chaitman (CARISA) 2004	99.4	128.15	270	65.4	129.6	256	100.0%	34.00 [11.96, 56.04]
Total (95% CI)			**270**			**256**	**100.0%**	**34.00 [11.96, 56.04]**

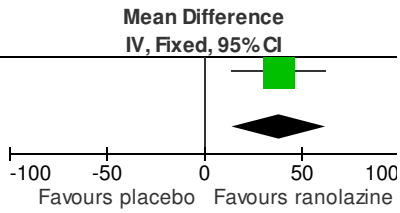
Heterogeneity: Not applicable
Test for overall effect: Z = 3.02 (P = 0.002)



1.4 Time to onset of angina (peak - change from baseline) s - 12 wks

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Chaitman (CARISA) 2004	126.9	149.51	272	88.9	132.8	256	100.0%	38.00 [13.91, 62.09]
Total (95% CI)			**272**			**256**	**100.0%**	**38.00 [13.91, 62.09]**

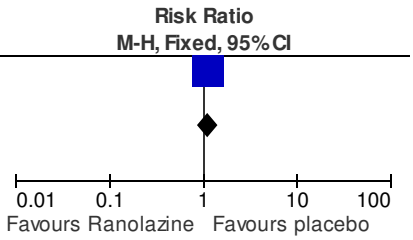
Heterogeneity: Not applicable
Test for overall effect: Z = 3.09 (P = 0.002)



1.5 Adverse events

Study or Subgroup	Ranolazine Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chaitman (CARISA) 2004	82	279	71	269	100.0%	1.11 [0.85, 1.46]
Total (95% CI)		**279**		**269**	**100.0%**	**1.11 [0.85, 1.46]**
Total events	82		71			

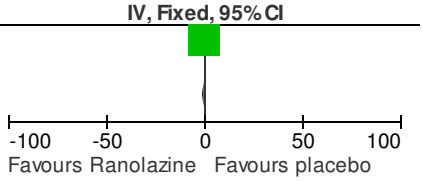
Heterogeneity: Not applicable
Test for overall effect: Z = 0.78 (P = 0.44)



1.6 Angina attacks per week

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Chaitman (CARISA) 2004	2.5	3.3	272	3.3	4.9	258	100.0%	-0.80 [-1.52, -0.08]
Total (95% CI)			**272**			**258**	**100.0%**	**-0.80 [-1.52, -0.08]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.19 (P = 0.03)

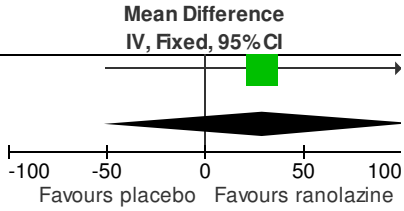


2 Ranolazine (750 mg bid) + antianginal treatment vs Placebo+antianginal treatment - diabetic patients (Follow-up 12 weeks)

2.1 Exercise duration (trough change from baseline) s - 12 wks

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Timmis (CARISA) 2006	114.1	213.13	68	85.4	236.5	57	100.0%	28.70 [-50.90, 108.30]
Total (95% CI)			**68**			**57**	**100.0%**	**28.70 [-50.90, 108.30]**

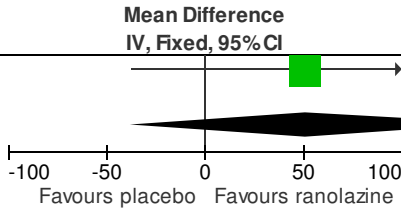
Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)



2.2 Time to onset of angina (trough change from baseline) s - 12 wks

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Timmis (CARISA) 2006	145.7	236.5	68	94.9	262.63	57	100.0%	50.80 [-37.56, 139.16]
Total (95% CI)			**68**			**57**	**100.0%**	**50.80 [-37.56, 139.16]**

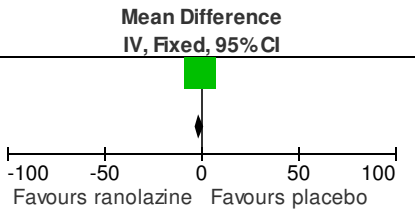
Heterogeneity: Not applicable
Test for overall effect: Z = 1.13 (P = 0.26)



2.3 Angina episodes per week - 12 wks

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Timmis (CARISA) 2006	2.08	5.09	68	2.99	7.7	57	100.0%	-0.91 [-3.25, 1.43]
Total (95% CI)			**68**			**57**	**100.0%**	**-0.91 [-3.25, 1.43]**

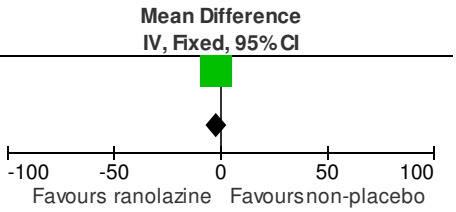
Heterogeneity: Not applicable
Test for overall effect: Z = 0.76 (P = 0.45)



2.4 Nitroglycerin consumption per week - 12 wks

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Timmis (CARISA) 2006	2.03	7.43	68	4.35	17.46	57	100.0%	-2.32 [-7.18, 2.54]
Total (95% CI)			**68**			**57**	**100.0%**	**-2.32 [-7.18, 2.54]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.93 (P = 0.35)

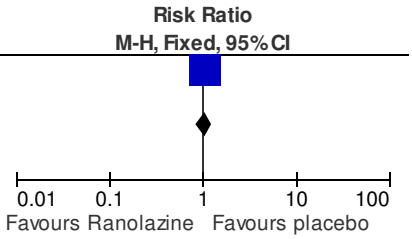


3 Ranolazine (1000 mg bid) + antianginal treatment vs Placebo +antianginal treatment- age (Follow-up 6 weeks)

3.1 Adverse events<70 years

Study or Subgroup	Ranolazine Events	Ranolazine Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rich (CARISA) 2007	194	604	131	420	100.0%	1.03 [0.86, 1.24]
Total (95% CI)		**604**		**420**	**100.0%**	**1.03 [0.86, 1.24]**
Total events	194		131			

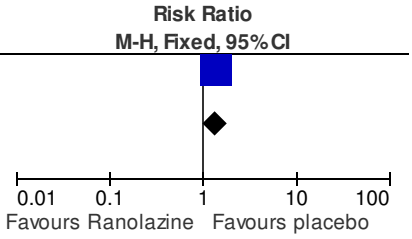
Heterogeneity: Not applicable
Test for overall effect: Z = 0.31 (P = 0.75)



3.2 Adverse events >70 years

Study or Subgroup	Ranolazine Events	Ranolazine Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rich (CARISA) 2007	102	231	43	132	100.0%	1.36 [1.02, 1.80]
Total (95% CI)		**231**		**132**	**100.0%**	**1.36 [1.02, 1.80]**
Total events	102		43			

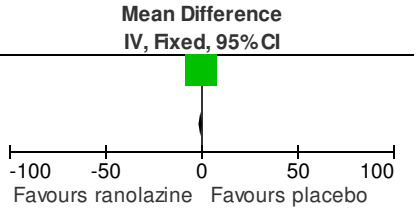
Heterogeneity: Not applicable
Test for overall effect: Z = 2.09 (P = 0.04)



3.5 Weekly angina attacks < 70 yrs

Study or Subgroup	Ranolazine Mean	Ranolazine SD	Ranolazine Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Fixed, 95% CI
Rich (CARISA) 2007	3.11	4.62	403	3.61	4.04	409	100.0%	-0.50 [-1.10, 0.10]
Total (95% CI)			**403**			**409**	**100.0%**	**-0.50 [-1.10, 0.10]**

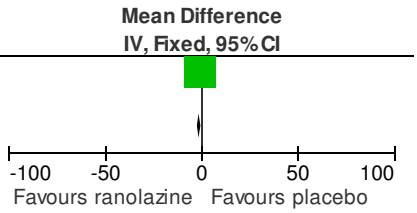
Heterogeneity: Not applicable
Test for overall effect: Z = 1.64 (P = 0.10)



3.6 Weekly angina attacks > 71 yrs

Study or Subgroup	Ranolazine Mean	Ranolazine SD	Ranolazine Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Fixed, 95% CI
Rich (CARISA) 2007	2.08	2.67	135	3.21	4.67	130	100.0%	-1.13 [-2.05, -0.21]
Total (95% CI)			**135**			**130**	**100.0%**	**-1.13 [-2.05, -0.21]**

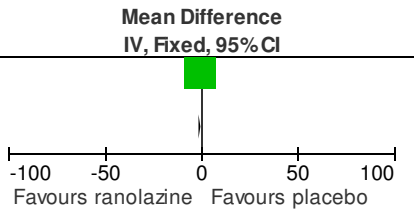
Heterogeneity: Not applicable
Test for overall effect: Z = 2.41 (P = 0.02)



3.7 Nitroglycerin consumption < 70 yrs

Study or Subgroup	Ranolazine Mean	Ranolazine SD	Ranolazine Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Fixed, 95% CI
Rich (CARISA) 2007	2.18	4.42	403	3.15	5.26	409	100.0%	-0.97 [-1.64, -0.30]
Total (95% CI)			**403**			**409**	**100.0%**	**-0.97 [-1.64, -0.30]**

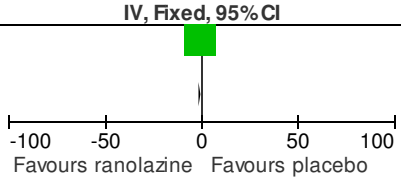
Heterogeneity: Not applicable
Test for overall effect: Z = 2.85 (P = 0.004)



3.8 Nitroglycerin consumption > 71 yrs

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Rich (CARISA) 2007	1.51	2.44	135	2.45	3.99	130	100.0%	-0.94 [-1.74, -0.14]
Total (95% CI)			**135**			**130**	**100.0%**	**-0.94 [-1.74, -0.14]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.30 (P = 0.02)

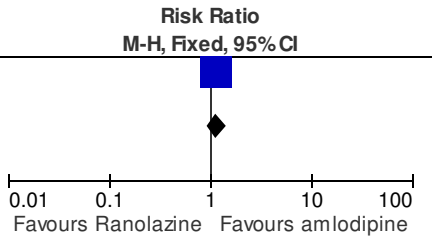


6 Ranolazine (1000 mg bid) plus amolodipine (10 mg) vs amolodipine (10mg) (Follow-up 6 weeks)

6.1 Adverse events

Study or Subgroup	Ranolazine Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Stone (ERICA) 2006	112	281	100	284	100.0%	1.13 [0.91, 1.40]
Total (95% CI)		**281**		**284**	**100.0%**	**1.13 [0.91, 1.40]**
Total events	112		100			

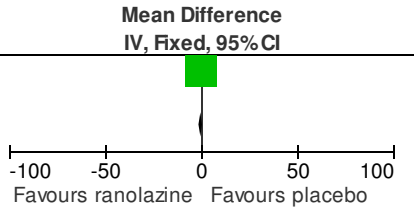
Heterogeneity: Not applicable
Test for overall effect: Z = 1.14 (P = 0.25)



6.5 Weekly angina frequency - 6 wks

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Stone (ERICA) 2006	2.88	3.16	277	3.31	3.69	281	100.0%	-0.43 [-1.00, 0.14]
Total (95% CI)			**277**			**281**	**100.0%**	**-0.43 [-1.00, 0.14]**

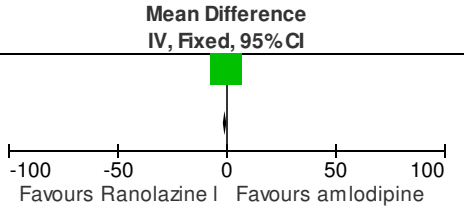
Heterogeneity: Not applicable
Test for overall effect: Z = 1.48 (P = 0.14)



6.6 Weekly nitroglycerin consumption - 6 wks

Study or Subgroup	Ranolazine Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Stone (ERICA) 2006	2.03	3.33	277	2.68	3.69	281	100.0%	-0.65 [-1.23, -0.07]
Total (95% CI)			**277**			**281**	**100.0%**	**-0.65 [-1.23, -0.07]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.19 (P = 0.03)

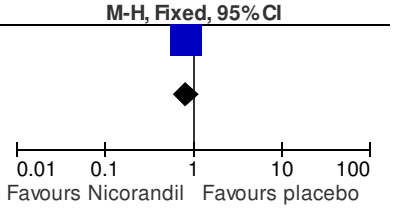


1 Nicorandil vs. Placebo (Follow-up 1.6 years)

1.1 CHD death

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2002)	60	2565	73	2561	100.0%	0.82 [0.59, 1.15]
Total (95% CI)		**2565**		**2561**	**100.0%**	**0.82 [0.59, 1.15]**
Total events	60		73			

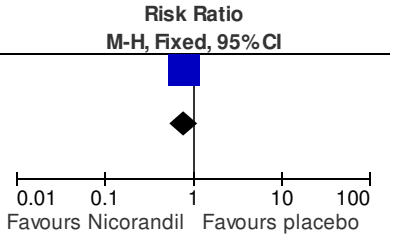
Heterogeneity: Not applicable
Test for overall effect: Z = 1.15 (P = 0.25)



1.2 Non fatal MI

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2002)	56	2565	72	2561	100.0%	0.78 [0.55, 1.10]
Total (95% CI)		**2565**		**2561**	**100.0%**	**0.78 [0.55, 1.10]**
Total events	56		72			

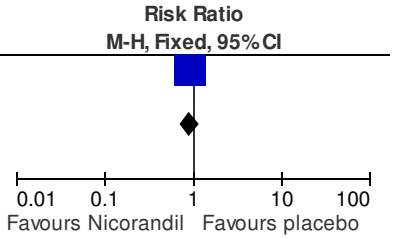
Heterogeneity: Not applicable
Test for overall effect: Z = 1.44 (P = 0.15)



1.3 Unstable Angina

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2002)	115	2565	127	2561	100.0%	0.90 [0.71, 1.16]
Total (95% CI)		**2565**		**2561**	**100.0%**	**0.90 [0.71, 1.16]**
Total events	115		127			

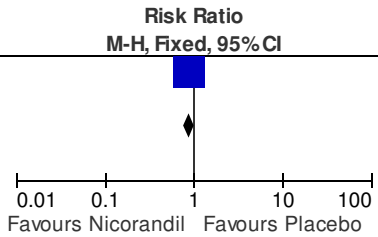
Heterogeneity: Not applicable
Test for overall effect: Z = 0.80 (P = 0.42)



1.4 All cardiovascular events

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2002)	378	2565	436	2561	100.0%	0.87 [0.76, 0.98]
Total (95% CI)		**2565**		**2561**	**100.0%**	**0.87 [0.76, 0.98]**
Total events	378		436			

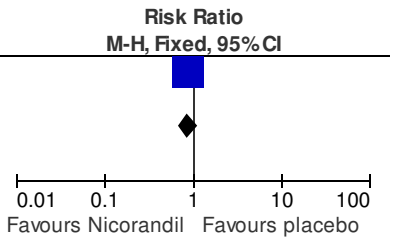
Heterogeneity: Not applicable
Test for overall effect: Z = 2.24 (P = 0.03)



1.5 All cause mortality

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2002)	111	2565	129	2561	100.0%	0.86 [0.67, 1.10]
Total (95% CI)		**2565**		**2561**	**100.0%**	**0.86 [0.67, 1.10]**
Total events	111		129			

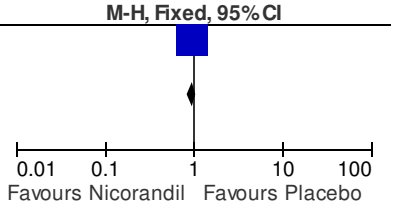
Heterogeneity: Not applicable
Test for overall effect: Z = 1.20 (P = 0.23)



1.6 Worsening of angina status

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2002)	569	2565	602	2561	100.0%	0.94 [0.85, 1.04]
Total (95% CI)		**2565**		**2561**	**100.0%**	**0.94 [0.85, 1.04]**
Total events	569		602			

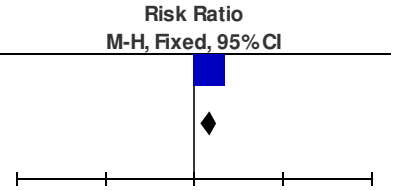
Heterogeneity: Not applicable
Test for overall effect: Z = 1.13 (P = 0.26)



1.7 GI disturbances

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2002)	194	2565	132	2561	100.0%	1.47 [1.18, 1.82]
Total (95% CI)		**2565**		**2561**	**100.0%**	**1.47 [1.18, 1.82]**
Total events	194		132			

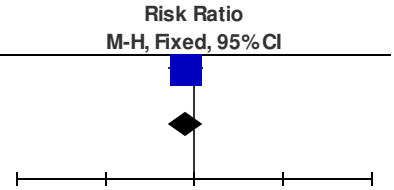
Heterogeneity: Not applicable
Test for overall effect: Z = 3.51 (P = 0.0005)



1.8 Combined outcome (diabetes subgroup)

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2004)	27	197	40	232	100.0%	0.79 [0.51, 1.25]
Total (95% CI)		**197**		**232**	**100.0%**	**0.79 [0.51, 1.25]**
Total events	27		40			

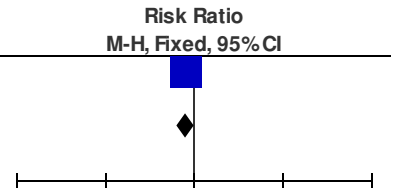
Heterogeneity: Not applicable
Test for overall effect: Z = 1.00 (P = 0.32)



1.9 Combined outcomes (age subgroup >70 yrs)

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2004)	131	927	167	948	100.0%	0.80 [0.65, 0.99]
Total (95% CI)		**927**		**948**	**100.0%**	**0.80 [0.65, 0.99]**
Total events	131		167			

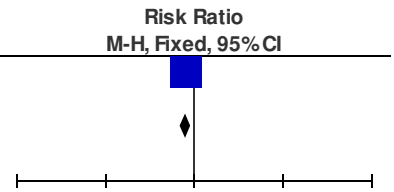
Heterogeneity: Not applicable
Test for overall effect: Z = 2.06 (P = 0.04)



1.10 combined outcomes (male subgroup)

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2004)	251	1962	311	1948	100.0%	0.80 [0.69, 0.93]
Total (95% CI)		**1962**		**1948**	**100.0%**	**0.80 [0.69, 0.93]**
Total events	251		311			

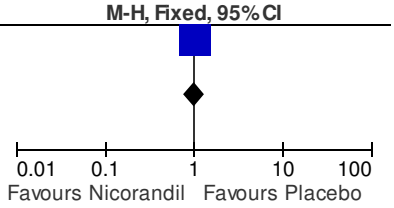
Heterogeneity: Not applicable
Test for overall effect: Z = 2.82 (P = 0.005)



1.11 Combined outcomes (female subgroup)

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2004)	86	603	87	613	100.0%	1.00 [0.76, 1.32]
Total (95% CI)		**603**		**613**	**100.0%**	**1.00 [0.76, 1.32]**
Total events	86		87			

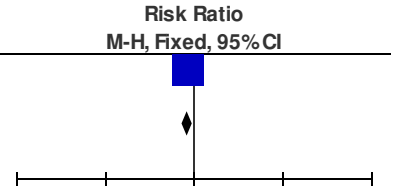
Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.97)



1.12 Composite (CHD death,non fatal MI or hospital adm. for chest pain)

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2002)	337	2565	398	2561	100.0%	0.85 [0.74, 0.97]
Total (95% CI)		**2565**		**2561**	**100.0%**	**0.85 [0.74, 0.97]**
Total events	337		398			

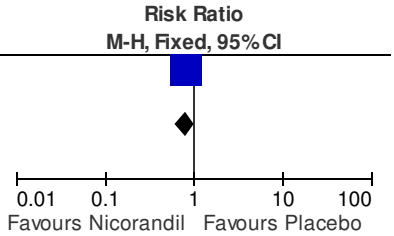
Heterogeneity: Not applicable
Test for overall effect: Z = 2.45 (P = 0.01)



1.13 composite (CHD death or non fatal MI)

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2002)	107	2565	134	2561	100.0%	0.80 [0.62, 1.02]
Total (95% CI)		**2565**		**2561**	**100.0%**	**0.80 [0.62, 1.02]**
Total events	107		134			

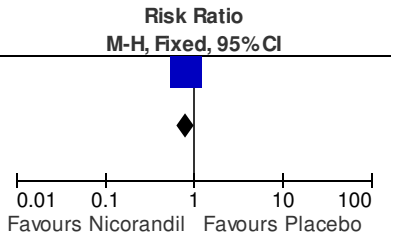
Heterogeneity: Not applicable
Test for overall effect: Z = 1.79 (P = 0.07)



1.14 Compiste (CHD death, non fatal MI, or unstable angina)

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2002)	156	2565	195	2561	100.0%	0.80 [0.65, 0.98]
Total (95% CI)		**2565**		**2561**	**100.0%**	**0.80 [0.65, 0.98]**
Total events	156		195			

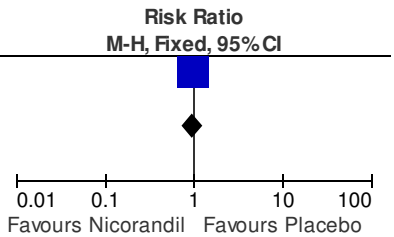
Heterogeneity: Not applicable
Test for overall effect: Z = 2.17 (P = 0.03)



1.15 Combined outcome (age subgroup 65-70 yrs)

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2004)	82	599	81	567	100.0%	0.96 [0.72, 1.27]
Total (95% CI)		**599**		**567**	**100.0%**	**0.96 [0.72, 1.27]**
Total events	82		81			

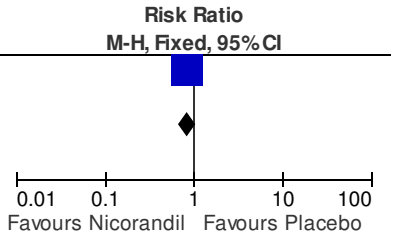
Heterogeneity: Not applicable
Test for overall effect: Z = 0.29 (P = 0.77)



1.16 Combined outcomes (age subgroup <65 yrs)

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2004)	124	1039	150	1046	100.0%	0.83 [0.67, 1.04]
Total (95% CI)		**1039**		**1046**	**100.0%**	**0.83 [0.67, 1.04]**
Total events	124		150			

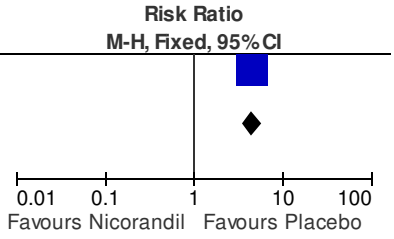
Heterogeneity: Not applicable
Test for overall effect: Z = 1.62 (P = 0.10)



1.17 Headache

Study or Subgroup	Nicorandil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
IONA (2002)	364	2565	81	2561	100.0%	4.49 [3.55, 5.67]
Total (95% CI)		**2565**		**2561**	**100.0%**	**4.49 [3.55, 5.67]**
Total events	364		81			

Heterogeneity: Not applicable
Test for overall effect: Z = 12.55 (P < 0.00001)

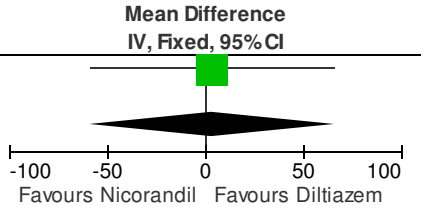


2 Nicorandil vs. Diltiazem (Follow-up 90 days)

2.1 Excercise capacity (work to angina onset)

Study or Subgroup	Nicorandil Mean	SD	Total	Diltiazem Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Guermonprez 1993	48.1	174.7	50	44.7	149.7	56	100.0%	3.40 [-58.91, 65.71]
Total (95% CI)			**50**			**56**	**100.0%**	**3.40 [-58.91, 65.71]**

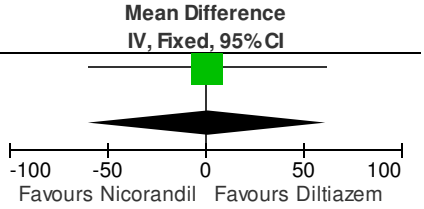
Heterogeneity: Not applicable
Test for overall effect: Z = 0.11 (P = 0.91)



2.2 Excercise capacity (work to ischemic threshold)

Study or Subgroup	Nicorandil Mean	SD	Total	Diltiazem Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Guermonprez 1993	38.7	171.1	50	37.8	145.2	56	100.0%	0.90 [-59.89, 61.69]
Total (95% CI)			**50**			**56**	**100.0%**	**0.90 [-59.89, 61.69]**

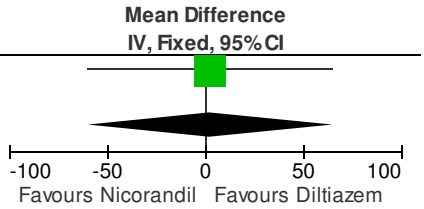
Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.98)



2.3 Excercise capacity (work to peak excercise)

Study or Subgroup	Nicorandil Mean	SD	Total	Diltiazem Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Guermonprez 1993	49.2	172.3	50	46.8	154.2	56	100.0%	2.40 [-60.15, 64.95]
Total (95% CI)			**50**			**56**	**100.0%**	**2.40 [-60.15, 64.95]**

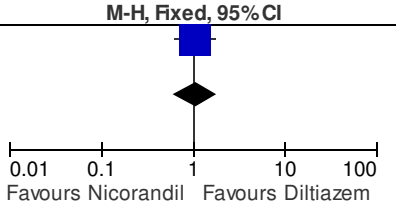
Heterogeneity: Not applicable
Test for overall effect: Z = 0.08 (P = 0.94)



2.4 Adverse events (combined)

Study or Subgroup	Nicorandil Events	Nicorandil Total	Diltiazem Events	Diltiazem Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Guermonprez 1993	19	60	19	63	100.0%	1.05 [0.62, 1.78]
Total (95% CI)		**60**		**63**	**100.0%**	**1.05 [0.62, 1.78]**
Total events	19		19			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.18 (P = 0.86)

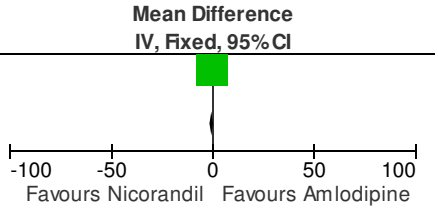


3 Nicorandil vs. Amlodipine (Follow-up 8 weeks)

3.1 ETT (Time to ST-segment depression)

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Chatterjee 1999	5.1	2.3	56	5.7	2.4	62	100.0%	-0.60 [-1.45, 0.25]
Total (95% CI)			**56**			**62**	**100.0%**	**-0.60 [-1.45, 0.25]**

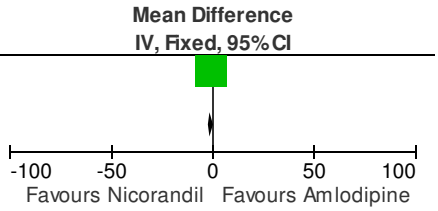
Heterogeneity: Not applicable
Test for overall effect: Z = 1.39 (P = 0.17)



3.2 ETT (Time to onset of anginal pain)

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Chatterjee 1999	6.1	3	56	7	3.1	62	100.0%	-0.90 [-2.00, 0.20]
Total (95% CI)			**56**			**62**	**100.0%**	**-0.90 [-2.00, 0.20]**

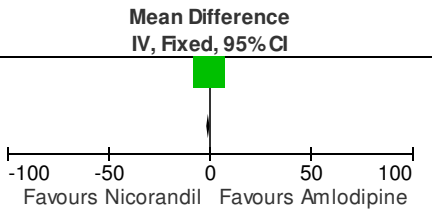
Heterogeneity: Not applicable
Test for overall effect: Z = 1.60 (P = 0.11)



3.3 ETT (Total excercise duration)

Study or Subgroup	Nicorandil Mean	Nicorandil SD	Nicorandil Total	Amlodipine Mean	Amlodipine SD	Amlodipine Total	Weight	Mean Difference IV, Fixed, 95% CI
Chatterjee 1999	7.2	3	56	7.9	2.4	62	100.0%	-0.70 [-1.69, 0.29]
Total (95% CI)			**56**			**62**	**100.0%**	**-0.70 [-1.69, 0.29]**

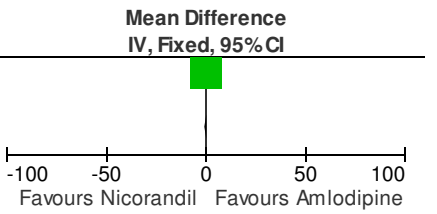
Heterogeneity: Not applicable
Test for overall effect: Z = 1.39 (P = 0.16)



3.4 ETT (Segment depression at maximal identical workload)

Study or Subgroup	Nicorandil Mean	Nicorandil SD	Nicorandil Total	Amlodipine Mean	Amlodipine SD	Amlodipine Total	Weight	Mean Difference IV, Fixed, 95% CI
Chatterjee 1999	0.13	0.1	56	0.12	0.1	62	100.0%	0.01 [-0.03, 0.05]
Total (95% CI)			**56**			**62**	**100.0%**	**0.01 [-0.03, 0.05]**

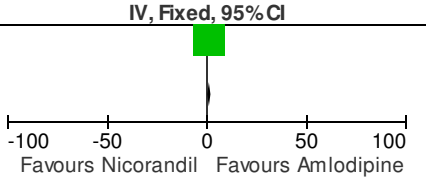
Heterogeneity: Not applicable
Test for overall effect: Z = 0.54 (P = 0.59)



3.5 Sum of weekly anginal attacks

Study or Subgroup	Nicorandil Mean	SD	Total	Amlodipine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Chatterjee 1999	2.1	2	56	0.9	1.6	62	100.0%	1.20 [0.54, 1.86]
Total (95% CI)			**56**			**62**	**100.0%**	**1.20 [0.54, 1.86]**

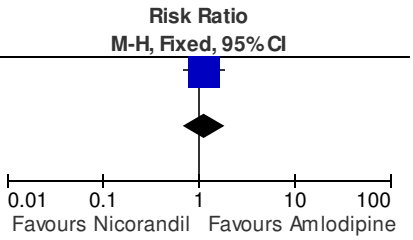
Heterogeneity: Not applicable
Test for overall effect: Z = 3.57 (P = 0.0004)



3.6 Adverse events (combined)

Study or Subgroup	Nicorandil Events	Total	Amlodipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chatterjee 1999	20	57	20	64	100.0%	1.12 [0.68, 1.86]
Total (95% CI)		**57**		**64**	**100.0%**	**1.12 [0.68, 1.86]**
Total events	20		20			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.45 (P = 0.65)

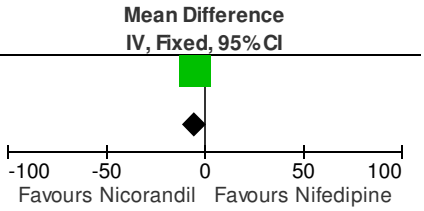


4 Nicorandil vs. Nifedipine (Follow-up immediately after 8 weeks of treatment)

4.1 Weekly anginal attack rate

Study or Subgroup	Nicorandil Mean	SD	Total	Nifedipine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ulvenstam1992	2.1	2.1	27	7.4	15	23	100.0%	-5.30 [-11.48, 0.88]
Total (95% CI)			**27**			**23**	**100.0%**	**-5.30 [-11.48, 0.88]**

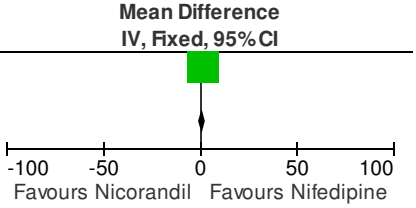
Heterogeneity: Not applicable
Test for overall effect: Z = 1.68 (P = 0.09)



4.2 Exercise duration (min)

Study or Subgroup	Nicorandil Mean	SD	Total	Nifedipine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ulvenstam1992	11.4	3.2	25	10.4	2.4	23	100.0%	1.00 [-0.59, 2.59]
Total (95% CI)			**25**			**23**	**100.0%**	**1.00 [-0.59, 2.59]**

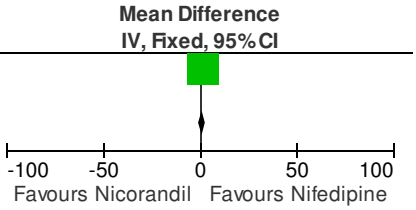
Heterogeneity: Not applicable
Test for overall effect: Z = 1.23 (P = 0.22)



4.3 Time to onset of angina pectoris (min)

Study or Subgroup	Nicorandil Mean	SD	Total	Nifedipine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ulvenstam1992	8.7	3.6	23	7.6	2.7	22	100.0%	1.10 [-0.75, 2.95]
Total (95% CI)			**23**			**22**	**100.0%**	**1.10 [-0.75, 2.95]**

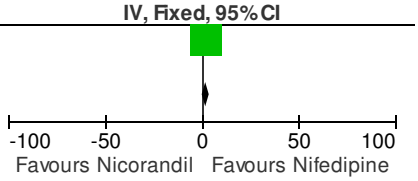
Heterogeneity: Not applicable
Test for overall effect: Z = 1.16 (P = 0.24)



4.4 Time to 1mm ST-depression (min)

Study or Subgroup	Nicorandil Mean	SD	Total	Nifedipine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ulvenstam1992	8	3.2	23	6.4	2.2	20	100.0%	1.60 [-0.02, 3.22]
Total (95% CI)			**23**			**20**	**100.0%**	**1.60 [-0.02, 3.22]**

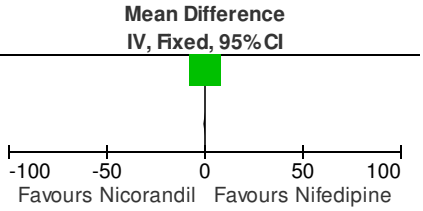
Heterogeneity: Not applicable
Test for overall effect: Z = 1.93 (P = 0.05)



4.5 ST depression on maximal identical workload (mm)

Study or Subgroup	Nicorandil Mean	SD	Total	Nifedipine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ulvenstam1992	1.9	0.89	24	1.7	0.75	20	100.0%	0.20 [-0.28, 0.68]
Total (95% CI)			**24**			**20**	**100.0%**	**0.20 [-0.28, 0.68]**

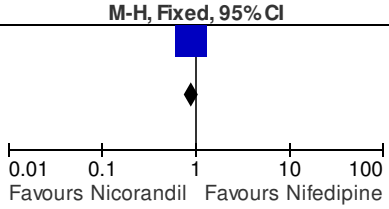
Heterogeneity: Not applicable
Test for overall effect: Z = 0.81 (P = 0.42)



4.6 Adverse events (combined)

Study or Subgroup	Nicorandil Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ulvenstam1992	25	29	28	29	100.0%	0.89 [0.76, 1.05]
Total (95% CI)		**29**		**29**	**100.0%**	**0.89 [0.76, 1.05]**
Total events	25		28			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.38 (P = 0.17)

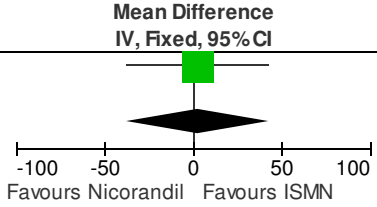


5 Nicorandil vs. ISMN (Follow-up 2 weeks)

5.1 ETT (Time to ST-depression)

Study or Subgroup	Nicorandil Mean	SD	Total	ISMN Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Zhu 2007	392.8	169.1	114	390.4	141.9	116	100.0%	2.40 [-37.98, 42.78]
Total (95% CI)			**114**			**116**	**100.0%**	**2.40 [-37.98, 42.78]**

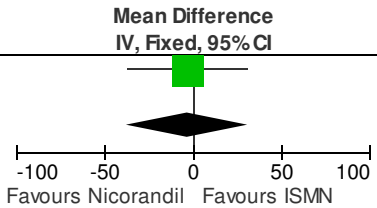
Heterogeneity: Not applicable
Test for overall effect: Z = 0.12 (P = 0.91)



5.2 ETT (Total excercise time)

Study or Subgroup	Nicorandil Mean	SD	Total	ISMN Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Zhu 2007	439.7	135.2	115	442.9	129.4	117	100.0%	-3.20 [-37.26, 30.86]
Total (95% CI)			**115**			**117**	**100.0%**	**-3.20 [-37.26, 30.86]**

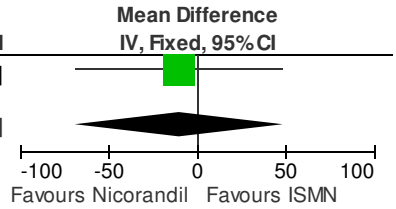
Heterogeneity: Not applicable
Test for overall effect: Z = 0.18 (P = 0.85)



5.3 ETT (Time to onset of chest pain)

Study or Subgroup	Nicorandil Mean	SD	Total	ISMN Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Zhu 2007	408.2	137.1	37	418.6	119.2	37	100.0%	-10.40 [-68.94, 48.14]
Total (95% CI)			**37**			**37**	**100.0%**	**-10.40 [-68.94, 48.14]**

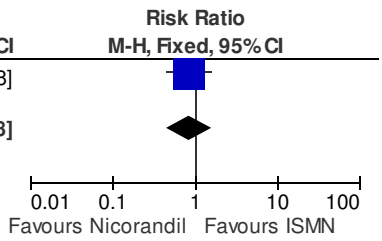
Heterogeneity: Not applicable
Test for overall effect: Z = 0.35 (P = 0.73)



5.4 Adverse event (Headache)

Study or Subgroup	Nicorandil Events	Total	ISMN Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zhu 2007	15	123	18	123	100.0%	0.83 [0.44, 1.58]
Total (95% CI)		**123**		**123**	**100.0%**	**0.83 [0.44, 1.58]**
Total events	15		18			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.56 (P = 0.58)

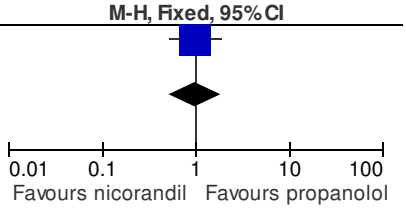


1 Nicorandil vs propanalol (Follow-up 6 weeks)

1.1 Angina free in daily life

Study or Subgroup	Nicorandil Events	Total	Propanolol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Meeter 1992	11	32	13	37	100.0%	0.98 [0.51, 1.87]
Total (95% CI)		**32**		**37**	**100.0%**	**0.98 [0.51, 1.87]**
Total events	11		13			

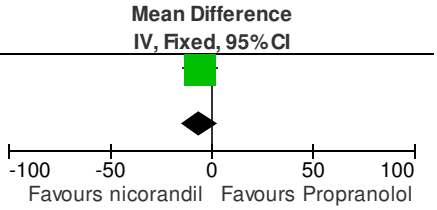
Heterogeneity: Not applicable
Test for overall effect: Z = 0.07 (P = 0.95)



1.2 12 hrs after medication - change in maximal work load (W) (baseline vs 3 weeks)

Study or Subgroup	Nicorandil Mean	SD	Total	Propanolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Meeter 1992	-1	19	32	5	18	37	100.0%	-6.00 [-14.77, 2.77]
Total (95% CI)			**32**			**37**	**100.0%**	**-6.00 [-14.77, 2.77]**

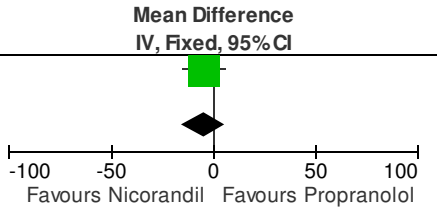
Heterogeneity: Not applicable
Test for overall effect: Z = 1.34 (P = 0.18)



1.3 12 hrs after medication - change in maximal work load (W) - baseline vs 6 wks

Study or Subgroup	Nicorandil Mean	SD	Total	Propanolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Meeter 1992	1	24	32	6	21	37	100.0%	-5.00 [-15.72, 5.72]
Total (95% CI)			**32**			**37**	**100.0%**	**-5.00 [-15.72, 5.72]**

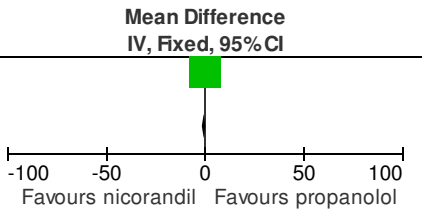
Heterogeneity: Not applicable
Test for overall effect: Z = 0.91 (P = 0.36)



1.4 12 hrs after medication - change in time to angina decimal min (baseline vs 3wks)

Study or Subgroup	Nicorandil Mean	SD	Total	Propanolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Meeter 1992	0.4	2	32	0.5	2	37	100.0%	-0.10 [-1.05, 0.85]
Total (95% CI)			**32**			**37**	**100.0%**	**-0.10 [-1.05, 0.85]**

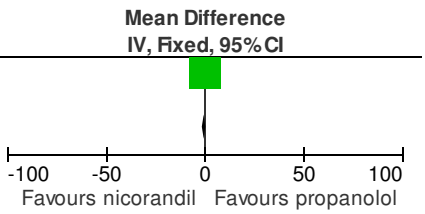
Heterogeneity: Not applicable
Test for overall effect: Z = 0.21 (P = 0.84)



1.5 12 hrs after medication - change in time to angina (baseline vs 6 wks)

Study or Subgroup	Nicorandil Mean	SD	Total	Propanolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Meeter 1992	0.4	2	32	0.8	2	37	100.0%	-0.40 [-1.35, 0.55]
Total (95% CI)			**32**			**37**	**100.0%**	**-0.40 [-1.35, 0.55]**

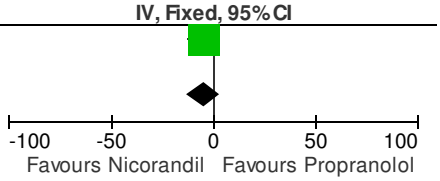
Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)



1.6 2 hrs after medication - change in maximal work load (W) (baseline vs 3ks)

Study or Subgroup	Nicorandil Mean	SD	Total	Propanolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Meeter 1992	3	14	32	8	20	37	100.0%	-5.00 [-13.07, 3.07]
Total (95% CI)			**32**			**37**	**100.0%**	**-5.00 [-13.07, 3.07]**

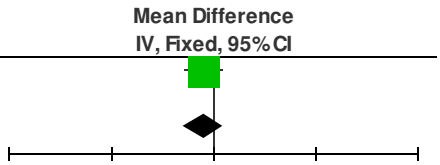
Heterogeneity: Not applicable
Test for overall effect: Z = 1.21 (P = 0.22)



1.7 2 hrs after medication - change in maximal work load (W) (baseline vs 6 wks)

Study or Subgroup	Nicorandil Mean	SD	Total	Propanolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Meeter 1992	4	17	32	9	23	37	100.0%	-5.00 [-14.47, 4.47]
Total (95% CI)			**32**			**37**	**100.0%**	**-5.00 [-14.47, 4.47]**

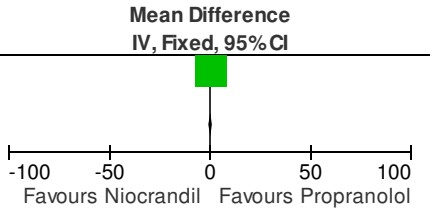
Heterogeneity: Not applicable
Test for overall effect: Z = 1.04 (P = 0.30)



1.8 2 hrs after medication time to angina

Study or Subgroup	Nicorandil Mean	SD	Total	Propanolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Meeter 1992	1	1	32	0.8	2	37	100.0%	0.20 [-0.53, 0.93]
Total (95% CI)			**32**			**37**	**100.0%**	**0.20 [-0.53, 0.93]**

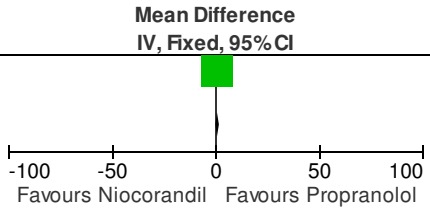
Heterogeneity: Not applicable
Test for overall effect: Z = 0.54 (P = 0.59)



1.9 2 hrs after medication time to angina

Study or Subgroup	Nicorandil Mean	SD	Total	Propanolol Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Meeter 1992	1.5	2	32	0.9	2	37	100.0%	0.60 [-0.35, 1.55]
Total (95% CI)			**32**			**37**	**100.0%**	**0.60 [-0.35, 1.55]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.24 (P = 0.21)

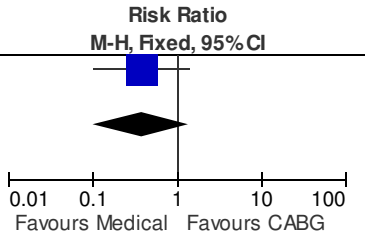


1 Multi vessel disease- Short term follow-up (1 year)

1.1 Death

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2004 (MASS-II)	3	203	8	203	100.0%	0.38 [0.10, 1.39]
Total (95% CI)		**203**		**203**	**100.0%**	**0.38 [0.10, 1.39]**
Total events	3		8			

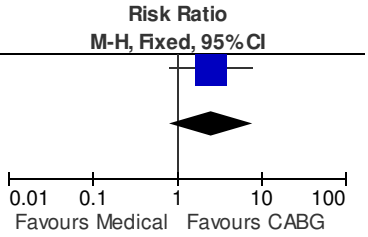
Heterogeneity: Not applicable
Test for overall effect: Z = 1.46 (P = 0.14)



1.2 Q wave MI

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2004 (MASS-II)	10	203	4	203	100.0%	2.50 [0.80, 7.84]
Total (95% CI)		**203**		**203**	**100.0%**	**2.50 [0.80, 7.84]**
Total events	10		4			

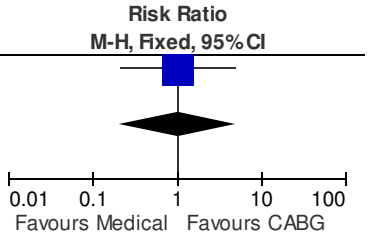
Heterogeneity: Not applicable
Test for overall effect: Z = 1.57 (P = 0.12)



1.3 Stroke

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2004 (MASS-II)	3	203	3	203	100.0%	1.00 [0.20, 4.90]
Total (95% CI)		**203**		**203**	**100.0%**	**1.00 [0.20, 4.90]**
Total events	3		3			

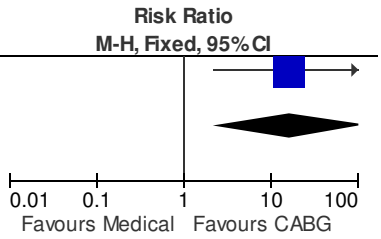
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



1.4 Non protocol revascularisation

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2004 (MASS-II)	16	203	1	203	100.0%	16.00 [2.14, 119.52]
Total (95% CI)		**203**		**203**	**100.0%**	**16.00 [2.14, 119.52]**
Total events	16		1			

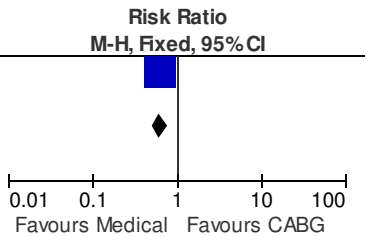
Heterogeneity: Not applicable
Test for overall effect: Z = 2.70 (P = 0.007)



1.5 Free of angina

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2004 (MASS-II)	74	203	120	203	100.0%	0.62 [0.50, 0.76]
Total (95% CI)		**203**		**203**	**100.0%**	**0.62 [0.50, 0.76]**
Total events	74		120			

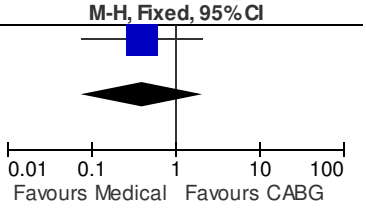
Heterogeneity: Not applicable
Test for overall effect: Z = 4.41 (P < 0.0001)



1.6 Death- subgroup diabetes

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Soares 2006 (MASS -II)	2	75	4	59	100.0%	0.39 [0.07, 2.07]
Total (95% CI)		**75**		**59**	**100.0%**	**0.39 [0.07, 2.07]**
Total events	2		4			

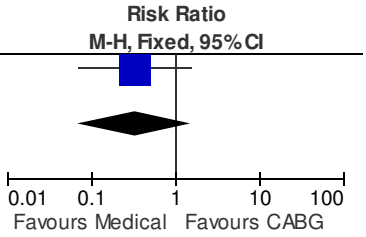
Heterogeneity: Not applicable
Test for overall effect: Z = 1.10 (P = 0.27)



1.7 Death- subgroup no diabetes

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Soares 2006 (MASS -II)	2	128	7	144	100.0%	0.32 [0.07, 1.52]
Total (95% CI)		**128**		**144**	**100.0%**	**0.32 [0.07, 1.52]**
Total events	2		7			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.43 (P = 0.15)

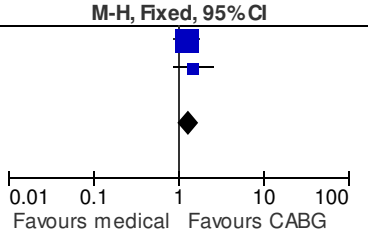


2 Multivessel disease- Medium term follow-up (2 to 4 years)

2.1 Death

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Read 1977 (VA study)	60	354	46	332	69.9%	1.22 [0.86, 1.74]
Varnauskas 1979 (ECSS)	29	373	21	394	30.1%	1.46 [0.85, 2.51]
Total (95% CI)		**727**		**726**	**100.0%**	**1.29 [0.96, 1.74]**
Total events	89		67			

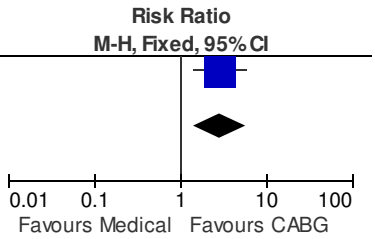
Heterogeneity: $Chi^2 = 0.28$, df = 1 (P = 0.59); $I^2 = 0\%$
Test for overall effect: Z = 1.70 (P = 0.09)



2.2 cardiac death`

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Varnauskas 1979 (ECSS)	27	373	10	394	100.0%	2.85 [1.40, 5.81]
Total (95% CI)		**373**		**394**	**100.0%**	**2.85 [1.40, 5.81]**
Total events	27		10			

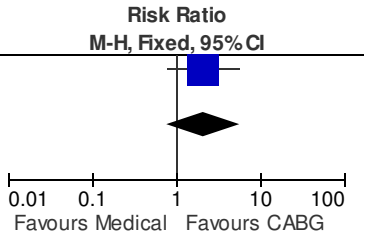
Heterogeneity: Not applicable
Test for overall effect: Z = 2.89 (P = 0.004)



2.3 MI

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Guinn 1976 (VA study)	11	60	5	56	100.0%	2.05 [0.76, 5.54]
Total (95% CI)		**60**		**56**	**100.0%**	**2.05 [0.76, 5.54]**
Total events	11		5			

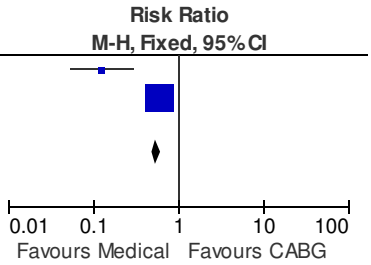
Heterogeneity: Not applicable
Test for overall effect: Z = 1.42 (P = 0.16)



2.4 Free of angina

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Guinn 1976 (VA study)	5	60	38	56	11.4%	0.12 [0.05, 0.29]
Varnauskas 1979 (ECSS)	175	373	315	394	88.6%	0.59 [0.52, 0.66]
Total (95% CI)		**433**		**450**	**100.0%**	**0.53 [0.47, 0.60]**
Total events	180		353			

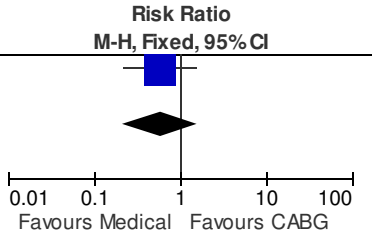
Heterogeneity: Chi² = 13.68, df = 1 (P = 0.0002); I² = 93%
Test for overall effect: Z = 10.26 (P < 0.00001)



2.5 Death- sub group 2 vessel disease

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Varnauskas 1979 (ECSS)	6	154	10	147	100.0%	0.57 [0.21, 1.54]
Total (95% CI)		**154**		**147**	**100.0%**	**0.57 [0.21, 1.54]**
Total events	6		10			

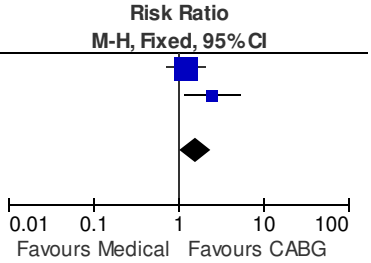
Heterogeneity: Not applicable
Test for overall effect: Z = 1.11 (P = 0.27)



2.6 Death - sub group 3 vessel disease

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Detre 1977 (VA study)	27	158	19	135	71.1%	1.21 [0.71, 2.08]
Varnauskas 1979 (ECSS)	19	188	9	219	28.9%	2.46 [1.14, 5.30]
Total (95% CI)		**346**		**354**	**100.0%**	**1.57 [1.02, 2.44]**
Total events	46		28			

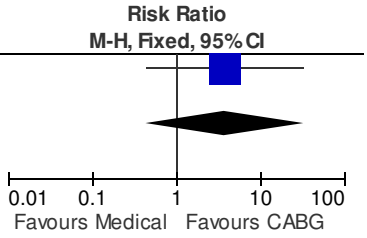
Heterogeneity: Chi² = 2.18, df = 1 (P = 0.14); I² = 54%
Test for overall effect: Z = 2.03 (P = 0.04)



2.7 Non protocol revascularisation

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Guinn 1976 (VA study)	4	60	1	56	100.0%	3.73 [0.43, 32.40]
Total (95% CI)		**60**		**56**	**100.0%**	**3.73 [0.43, 32.40]**
Total events	4		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.19 (P = 0.23)

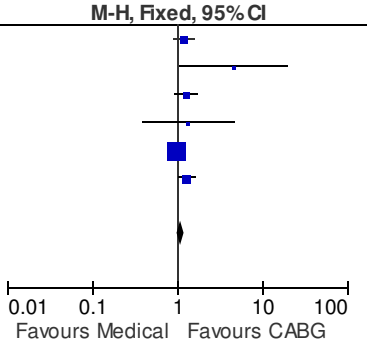


3 Multivessel disease -Long term follow-up (>4 years)

3.1 Death

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Alderman 1990 (CASS)	81	390	70	390	14.3%	1.16 [0.87, 1.54]
Frick 1985	10	50	2	45	0.4%	4.50 [1.04, 19.45]
Hueb 2010 (MASS-II)	63	203	51	203	10.4%	1.24 [0.90, 1.69]
Kloster 1979	5	49	4	51	0.8%	1.30 [0.37, 4.56]
Peduzzi 1998 (VA study)	265	354	265	332	55.8%	0.94 [0.86, 1.02]
Varnauaskas 1988 (ECSS)	109	373	92	394	18.3%	1.25 [0.99, 1.59]
Total (95% CI)		**1419**		**1415**	**100.0%**	**1.08 [0.99, 1.17]**
Total events	533		484			

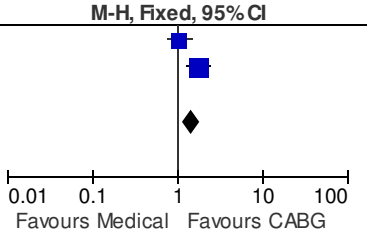
Heterogeneity: Chi² = 17.29, df = 5 (P = 0.004); I² = 71%
Test for overall effect: Z = 1.67 (P = 0.09)



3.2 cardiac death

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bhayana 1978 (VA study)	36	75	33	71	43.1%	1.03 [0.73, 1.46]
Varnauaskas 1988 (ECSS)	76	373	46	394	56.9%	1.75 [1.25, 2.45]
Total (95% CI)		**448**		**465**	**100.0%**	**1.44 [1.12, 1.84]**
Total events	112		79			

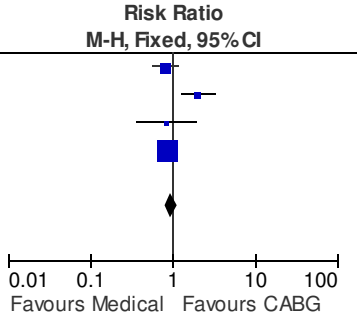
Heterogeneity: Chi² = 4.84, df = 1 (P = 0.03); I² = 79%
Test for overall effect: Z = 2.89 (P = 0.004)



3.3 MI

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fisher 1984 (CASS)	43	390	53	390	23.5%	0.81 [0.56, 1.18]
Hueb 2010 (MASS-II)	42	203	21	203	9.3%	2.00 [1.23, 3.25]
Kloster 1979	8	49	10	51	4.4%	0.83 [0.36, 1.93]
Peduzzi 1998 (VA study)	123	354	137	332	62.8%	0.84 [0.69, 1.02]
Total (95% CI)		**996**		**976**	**100.0%**	**0.94 [0.80, 1.10]**
Total events	216		221			

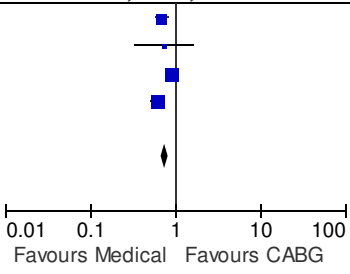
Heterogeneity: Chi² = 11.21, df = 3 (P = 0.01); I² = 73%
Test for overall effect: Z = 0.73 (P = 0.46)



3.4 Free of angina

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2010 (MASS-II)	88	203	130	203	25.9%	0.68 [0.56, 0.82]
Peduzzi 1992 (VA study)	10	354	13	332	2.7%	0.72 [0.32, 1.62]
Rogers 1990 (CASS)	163	390	183	390	36.4%	0.89 [0.76, 1.04]
Varnauskas 1982 (ECSS)	104	373	181	394	35.0%	0.61 [0.50, 0.74]
Total (95% CI)		**1320**		**1319**	**100.0%**	**0.73 [0.66, 0.81]**
Total events	365		507			

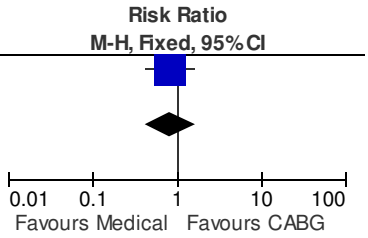
Heterogeneity: Chi² = 10.16, df = 3 (P = 0.02); I² = 70%
Test for overall effect: Z = 5.97 (P < 0.00001)



3.5 stroke

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2010 (MASS-II)	14	203	17	203	100.0%	0.82 [0.42, 1.63]
Total (95% CI)		**203**		**203**	**100.0%**	**0.82 [0.42, 1.63]**
Total events	14		17			

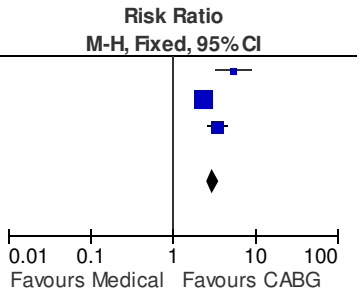
Heterogeneity: Not applicable
Test for overall effect: Z = 0.56 (P = 0.58)



3.6 Non protocol revascularisation

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2010 (MASS-II)	80	203	15	203	10.4%	5.33 [3.18, 8.94]
Peduzzi 1998 (VA study)	194	354	78	332	55.7%	2.33 [1.88, 2.89]
Rogers 1990 (CASS)	168	390	49	390	33.9%	3.43 [2.58, 4.56]
Total (95% CI)		**947**		**925**	**100.0%**	**3.02 [2.56, 3.55]**
Total events	442		142			

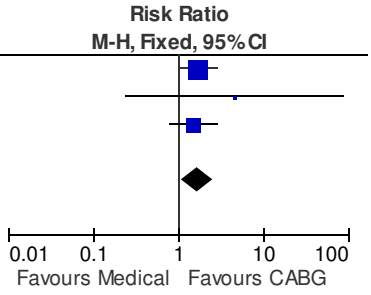
Heterogeneity: Chi² = 10.90, df = 2 (P = 0.004); I² = 82%
Test for overall effect: Z = 13.18 (P < 0.00001)



3.7 Death- sub group 2 vessel disease

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Alderman 1990 (CASS)	31	148	20	160	58.2%	1.68 [1.00, 2.81]
Kloster 1979	2	19	0	17	1.6%	4.50 [0.23, 87.61]
Varnauskas 1982 (ECSS)	20	154	13	147	40.2%	1.47 [0.76, 2.84]
Total (95% CI)		**321**		**324**	**100.0%**	**1.64 [1.10, 2.45]**
Total events	53		33			

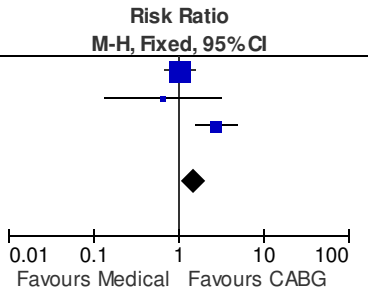
Heterogeneity: Chi² = 0.56, df = 2 (P = 0.76); I² = 0%
Test for overall effect: Z = 2.40 (P = 0.02)



3.8 Death- sub group 3 vessel disease

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Alderman 1990 (CASS)	34	135	30	123	64.4%	1.03 [0.67, 1.58]
Kloster 1979	2	20	4	26	7.1%	0.65 [0.13, 3.20]
Varnauskas 1982 (ECSS)	35	188	15	219	28.4%	2.72 [1.53, 4.82]
Total (95% CI)		**343**		**368**	**100.0%**	**1.48 [1.07, 2.06]**
Total events	71		49			

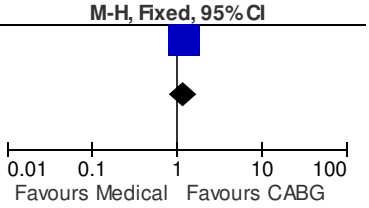
Heterogeneity: Chi² = 8.11, df = 2 (P = 0.02); I² = 75%
Test for overall effect: Z = 2.37 (P = 0.02)



3.9 Mortality- age >53 yrs

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Alderman 1990 (CASS)	46	163	39	163	100.0%	1.18 [0.82, 1.70]
Total (95% CI)		**163**		**163**	**100.0%**	**1.18 [0.82, 1.70]**
Total events	46		39			

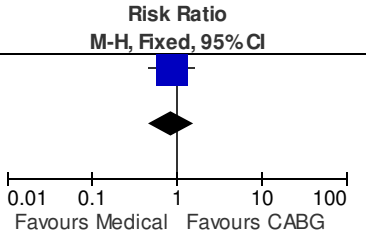
Heterogeneity: Not applicable
Test for overall effect: Z = 0.88 (P = 0.38)



3.10 Mortality- age <47 years

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Alderman 1990 (CASS)	16	101	17	92	100.0%	0.86 [0.46, 1.60]
Total (95% CI)		**101**		**92**	**100.0%**	**0.86 [0.46, 1.60]**
Total events	16		17			

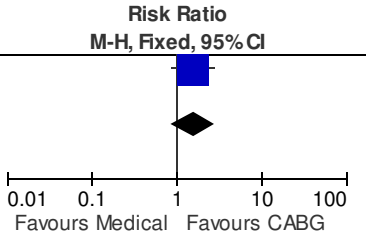
Heterogeneity: Not applicable
Test for overall effect: Z = 0.49 (P = 0.63)



3.11 Mortality- age 47-53 years

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Alderman 1990 (CASS)	23	126	16	135	100.0%	1.54 [0.85, 2.78]
Total (95% CI)		**126**		**135**	**100.0%**	**1.54 [0.85, 2.78]**
Total events	23		16			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.43 (P = 0.15)

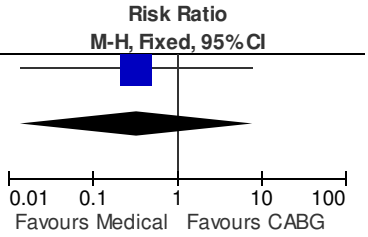


4 Single vessel disease- medium term follow-up (2-4 years)

4.1 Death

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1995 (MASS- I)	0	72	1	70	100.0%	0.32 [0.01, 7.83]
Total (95% CI)		**72**		**70**	**100.0%**	**0.32 [0.01, 7.83]**
Total events	0		1			

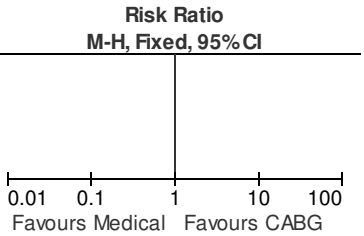
Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)



4.2 Stroke

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1995 (MASS- I)	0	72	0	70		Not estimable
Total (95% CI)		**72**		**70**		**Not estimable**
Total events	0		0			

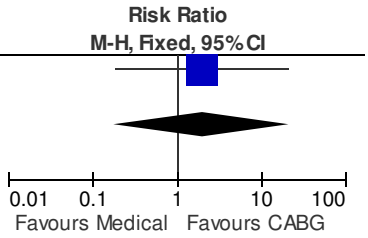
Heterogeneity: Not applicable
Test for overall effect: Not applicable



4.3 MI

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1995 (MASS- I)	2	72	1	70	100.0%	1.94 [0.18, 20.96]
Total (95% CI)		**72**		**70**	**100.0%**	**1.94 [0.18, 20.96]**
Total events	2		1			

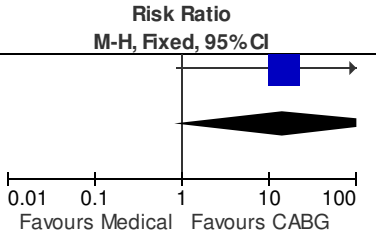
Heterogeneity: Not applicable
Test for overall effect: Z = 0.55 (P = 0.58)



4.4 Non protocol revascularisation

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1995 (MASS- I)	7	72	0	70	100.0%	14.59 [0.85, 250.71]
Total (95% CI)		**72**		**70**	**100.0%**	**14.59 [0.85, 250.71]**
Total events	7		0			

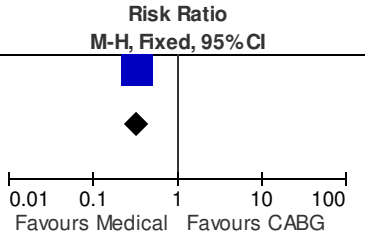
Heterogeneity: Not applicable
Test for overall effect: Z = 1.85 (P = 0.06)



4.5 Free of angina

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1995 (MASS- I)	23	72	68	70	100.0%	0.33 [0.23, 0.46]
Total (95% CI)		**72**		**70**	**100.0%**	**0.33 [0.23, 0.46]**
Total events	23		68			

Heterogeneity: Not applicable
Test for overall effect: Z = 6.42 (P < 0.00001)

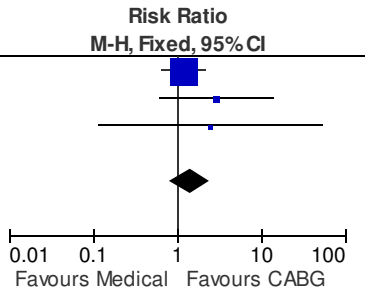


5 Single vessel disease -Long term follow-up (>4 years)

5.1 Death

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Alderman 1990 (CASS)	19	107	16	107	86.1%	1.19 [0.65, 2.18]
Hueb 1999 (MASS-I)	6	72	2	70	10.9%	2.92 [0.61, 13.97]
Kloster 1979	1	10	0	8	3.0%	2.45 [0.11, 53.25]
Total (95% CI)		**189**		**185**	**100.0%**	**1.41 [0.81, 2.46]**
Total events	26		18			

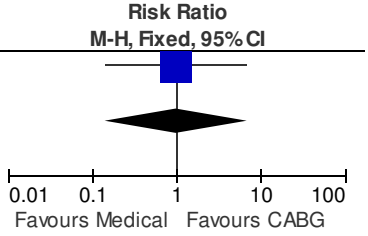
Heterogeneity: $Chi^2 = 1.26$, df = 2 (P = 0.53); $I^2 = 0\%$
Test for overall effect: Z = 1.23 (P = 0.22)



5.2 Cardiac death

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1999 (MASS-I)	2	72	2	70	100.0%	0.97 [0.14, 6.71]
Total (95% CI)		**72**		**70**	**100.0%**	**0.97 [0.14, 6.71]**
Total events	2		2			

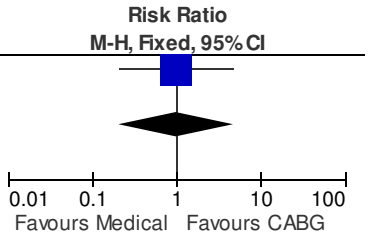
Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.98)



5.3 MI

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1999 (MASS-I)	3	72	3	70	100.0%	0.97 [0.20, 4.66]
Total (95% CI)		**72**		**70**	**100.0%**	**0.97 [0.20, 4.66]**
Total events	3		3			

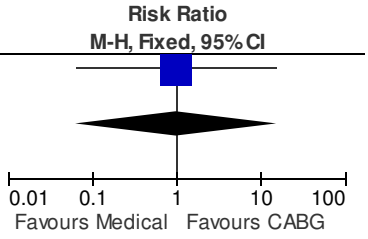
Heterogeneity: Not applicable
Test for overall effect: Z = 0.04 (P = 0.97)



5.4 Stroke

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1999 (MASS-I)	1	72	1	70	100.0%	0.97 [0.06, 15.24]
Total (95% CI)		**72**		**70**	**100.0%**	**0.97 [0.06, 15.24]**
Total events	1		1			

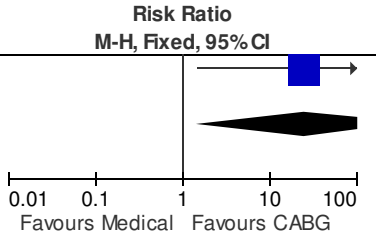
Heterogeneity: Not applicable
Test for overall effect: Z = 0.02 (P = 0.98)



5.5 Non protocol revascularisation

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1999 (MASS-I)	12	72	0	70	100.0%	24.32 [1.47, 402.97]
Total (95% CI)		**72**		**70**	**100.0%**	**24.32 [1.47, 402.97]**
Total events	12		0			

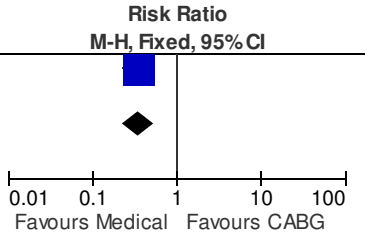
Heterogeneity: Not applicable
Test for overall effect: Z = 2.23 (P = 0.03)



5.6 Free of angina

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1999 (MASS-I)	17	72	48	70	100.0%	0.34 [0.22, 0.54]
Total (95% CI)		**72**		**70**	**100.0%**	**0.34 [0.22, 0.54]**
Total events	17		48			

Heterogeneity: Not applicable
Test for overall effect: Z = 4.70 (P < 0.00001)

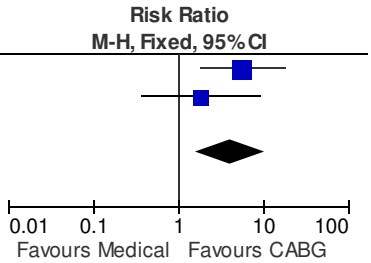


6 Left main stem disease- Medium term follow-up (2 to 4 years)

6.1 Death

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Detre 1977 (VA study)	16	44	3	46	58.3%	5.58 [1.74, 17.82]
Varnauskas 1979 (ECSS)	4	31	2	28	41.7%	1.81 [0.36, 9.12]
Total (95% CI)		**75**		**74**	**100.0%**	**4.00 [1.60, 10.03]**
Total events	20		5			

Heterogeneity: $Chi^2 = 1.24$, df = 1 (P = 0.27); $I^2 = 19\%$
Test for overall effect: Z = 2.96 (P = 0.003)

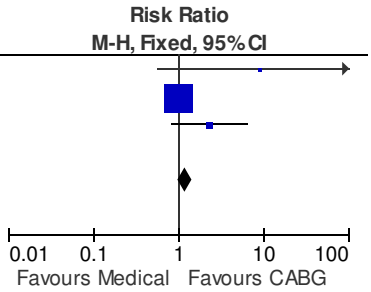


7 Left main stem disease- Long term follow-up (>4 years)

7.1 Death

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Alderman 1990 (CASS)	3	6	0	8	1.0%	9.00 [0.55, 147.08]
Peduzzi 1998 (VA study)	38	43	43	48	89.8%	0.99 [0.85, 1.14]
Varnauskas 1982 (ECSS)	10	31	4	28	9.3%	2.26 [0.80, 6.39]
Total (95% CI)		**80**		**84**	**100.0%**	**1.18 [0.97, 1.43]**
Total events	51		47			

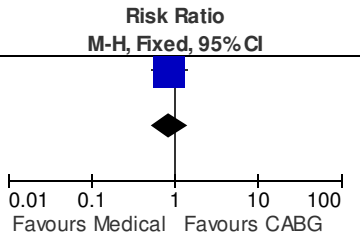
Heterogeneity: Chi² = 9.48, df = 2 (P = 0.009); I² = 79%
Test for overall effect: Z = 1.69 (P = 0.09)



7.2 MI

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Peduzzi 1998 (VA study)	16	43	21	48	100.0%	0.85 [0.51, 1.41]
Total (95% CI)		**43**		**48**	**100.0%**	**0.85 [0.51, 1.41]**
Total events	16		21			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)

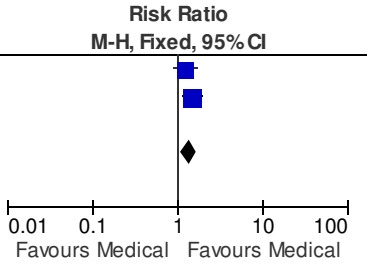


8 Left anterior descending artery - Long term follow-up (>4 years)

8.1 Death

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Alderman 1990 (CASS)	60	275	50	277	45.3%	1.21 [0.86, 1.69]
Varnauaskas 1988 (ECSS)	84	240	63	262	54.7%	1.46 [1.10, 1.92]
Total (95% CI)		**515**		**539**	**100.0%**	**1.34 [1.09, 1.66]**
Total events	144		113			

Heterogeneity: Chi² = 0.70, df = 1 (P = 0.40); I² = 0%
Test for overall effect: Z = 2.72 (P = 0.007)

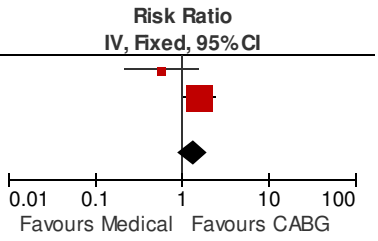


9 Sub group interaction

9.1 Sub group 2 vessel and 3 vessel (Death) - Multivessel medium term follow-up

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis- 2 vessel	-0.5621189	0.508273	16.1%	0.57 [0.21, 1.54]
meta analysis- 3 vessel	0.45107562	0.222499	83.9%	1.57 [1.02, 2.43]
Total (95% CI)			**100.0%**	**1.33 [0.89, 1.99]**

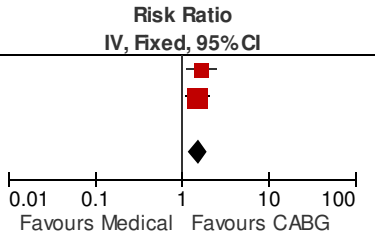
Heterogeneity: Chi² = 3.33, df = 1 (P = 0.07); I² = 70%
Test for overall effect: Z = 1.41 (P = 0.16)



9.2 Sub group 2 vessel and 3 vessel (Death) - Multivessel-long term follow-up

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis- 2 vessel	0.49469624	0.20428	40.1%	1.64 [1.10, 2.45]
meta analysis- 3 vessel	0.39204209	0.167104	59.9%	1.48 [1.07, 2.05]
Total (95% CI)			**100.0%**	**1.54 [1.20, 1.99]**

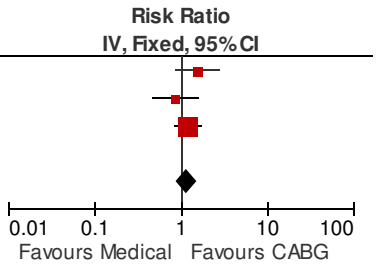
Heterogeneity: Chi² = 0.15, df = 1 (P = 0.70); I² = 0%
Test for overall effect: Z = 3.35 (P = 0.0008)



9.3 Sub group age <47, 47-53, >53 years (Death) - Multivessel -long term follow-up

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis- 47-53	0.43178242	0.302288	22.0%	1.54 [0.85, 2.79]
meta analysis- age <47	-0.1508229	0.317993	19.9%	0.86 [0.46, 1.60]
meta analysis->53	0.16551444	0.18599	58.1%	1.18 [0.82, 1.70]
Total (95% CI)			**100.0%**	**1.17 [0.89, 1.55]**

Heterogeneity: Chi² = 1.76, df = 2 (P = 0.41); I² = 0%
Test for overall effect: Z = 1.14 (P = 0.26)

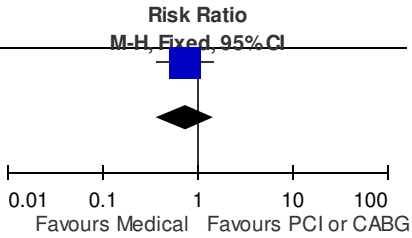


1 Multivessel disease- short term follow-up (1 year)

1.1 Death

Study or Subgroup	Medical Events	Total	PCI or CABG Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pfisterer 2003 (TIME)	12	148	17	153	100.0%	0.73 [0.36, 1.47]
Total (95% CI)		**148**		**153**	**100.0%**	**0.73 [0.36, 1.47]**
Total events	12		17			

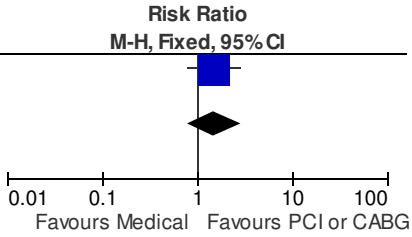
Heterogeneity: Not applicable
Test for overall effect: Z = 0.88 (P = 0.38)



1.2 MI

Study or Subgroup	Medical Events	Total	PCI or CABG Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pfisterer 2003 (TIME)	20	148	14	153	100.0%	1.48 [0.78, 2.81]
Total (95% CI)		**148**		**153**	**100.0%**	**1.48 [0.78, 2.81]**
Total events	20		14			

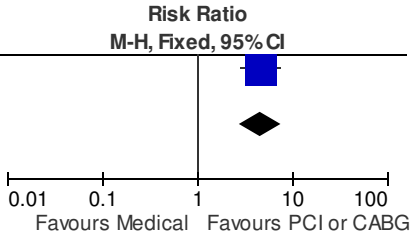
Heterogeneity: Not applicable
Test for overall effect: Z = 1.19 (P = 0.24)



1.3 Non protocol revascularisation

Study or Subgroup	Medical Events	Total	PCI or CABG Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pfisterer 2003 (TIME)	71	148	16	153	100.0%	4.59 [2.80, 7.51]
Total (95% CI)		**148**		**153**	**100.0%**	**4.59 [2.80, 7.51]**
Total events	71		16			

Heterogeneity: Not applicable
Test for overall effect: Z = 6.06 (P < 0.00001)

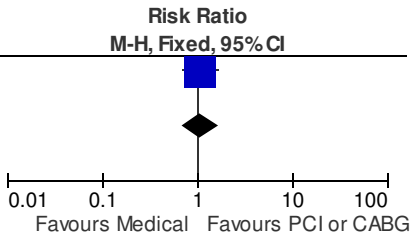


2 Multi vessel disease- medium term follow-up (2 to 4 years)

2.1 Death

Study or Subgroup	Medical Events	Total	PCI or CABG Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pfisterer 2004 (TIME)	31	139	29	137	100.0%	1.05 [0.67, 1.65]
Total (95% CI)		**139**		**137**	**100.0%**	**1.05 [0.67, 1.65]**
Total events	31		29			

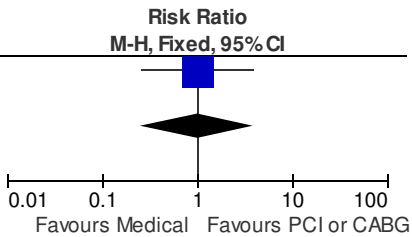
Heterogeneity: Not applicable
Test for overall effect: Z = 0.23 (P = 0.82)



2.2 Non protocol revascularisation

Study or Subgroup	Medical Events	Total	PCI or CABG Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pfisterer 2004 (TIME)	4	139	4	137	100.0%	0.99 [0.25, 3.86]
Total (95% CI)		**139**		**137**	**100.0%**	**0.99 [0.25, 3.86]**
Total events	4		4			

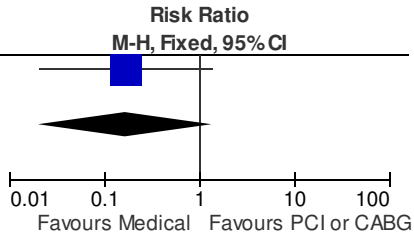
Heterogeneity: Not applicable
Test for overall effect: Z = 0.02 (P = 0.98)



2.3 Non fatal MI

Study or Subgroup	Medical Events	Medical Total	PCI or CABG Events	PCI or CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pfisterer 2004 (TIME)	1	139	6	137	100.0%	0.16 [0.02, 1.35]
Total (95% CI)		**139**		**137**	**100.0%**	**0.16 [0.02, 1.35]**
Total events	1		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.68 (P = 0.09)

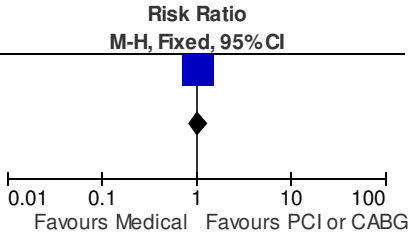


3 Multi vessel disease- Long term follow-up (5 years)

3.1 Death (all patients with type 2 diabetes)

Study or Subgroup	Medical Events	Medical Total	PCI or CABG Events	PCI or CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Frye et al 2009 (BARI-2D)	121	991	112	953	100.0%	1.04 [0.82, 1.32]
Total (95% CI)		**991**		**953**	**100.0%**	**1.04 [0.82, 1.32]**
Total events	121		112			

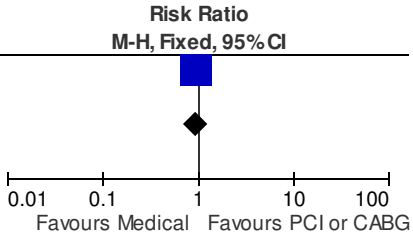
Heterogeneity: Not applicable
Test for overall effect: Z = 0.31 (P = 0.76)



3.2 Death (in PCI stratum in BARI-2D)

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Frye et al 2009 (BARI-2D)	82	807	86	798	100.0%	0.94 [0.71, 1.26]
Total (95% CI)		**807**		**798**	**100.0%**	**0.94 [0.71, 1.26]**
Total events	82		86			

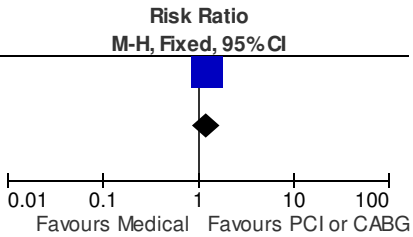
Heterogeneity: Not applicable
Test for overall effect: Z = 0.40 (P = 0.69)



3.3 Death (in CABG stratum in BARI-2D)

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Frye et al 2009 (BARI-2D)	63	385	51	378	100.0%	1.21 [0.86, 1.71]
Total (95% CI)		**385**		**378**	**100.0%**	**1.21 [0.86, 1.71]**
Total events	63		51			

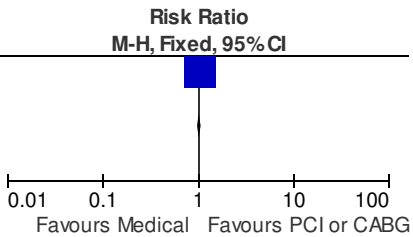
Heterogeneity: Not applicable
Test for overall effect: Z = 1.11 (P = 0.27)



3.4 Freedom from CV events (death, MI or stroke) - PCI stratum (BARI-2D)

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Frye et al 2009 (BARI-2D)	637	807	614	798	100.0%	1.03 [0.97, 1.08]
Total (95% CI)		**807**		**798**	**100.0%**	**1.03 [0.97, 1.08]**
Total events	637		614			

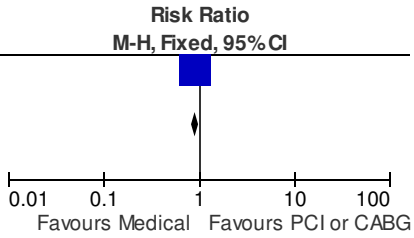
Heterogeneity: Not applicable
Test for overall effect: Z = 0.96 (P = 0.34)



3.5 Freedom from CV events (death, MI or stroke)- CABG stratum(BARI-2D)

Study or Subgroup	Medical Events	Medical Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Frye et al 2009 (BARI-2D)	268	385	293	378	100.0%	0.90 [0.82, 0.98]
Total (95% CI)		**385**		**378**	**100.0%**	**0.90 [0.82, 0.98]**
Total events	268		293			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.47 (P = 0.01)

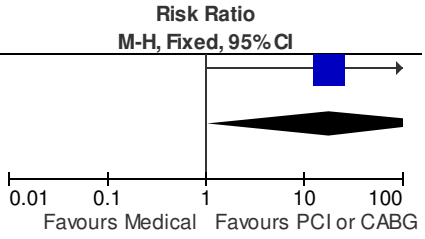


4 Angiography prior randomisation - Multivessel disease short term

4.1 Death

Study or Subgroup	Medical Events	Medical Total	PCI or CABG Events	PCI or CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rogers 1995 (ACIP)	8	183	0	192	100.0%	17.83 [1.04, 306.73]
Total (95% CI)		**183**		**192**	**100.0%**	**17.83 [1.04, 306.73]**
Total events	8		0			

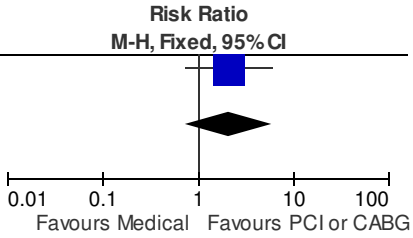
Heterogeneity: Not applicable
Test for overall effect: Z = 1.98 (P = 0.05)



4.2 MI

Study or Subgroup	Medical Events	Medical Total	PCI or CABG Events	PCI or CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rogers 1995 (ACIP)	10	183	5	192	100.0%	2.10 [0.73, 6.02]
Total (95% CI)		**183**		**192**	**100.0%**	**2.10 [0.73, 6.02]**
Total events	10		5			

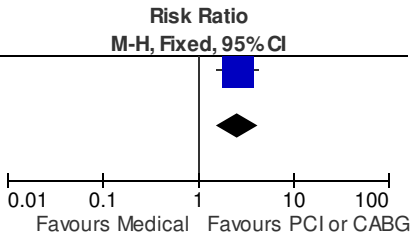
Heterogeneity: Not applicable
Test for overall effect: Z = 1.38 (P = 0.17)



4.3 Non protocol revascularisation

Study or Subgroup	Medical Events	Medical Total	PCI or CABG Events	PCI or CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rogers 1995 (ACIP)	44	183	18	192	100.0%	2.56 [1.54, 4.27]
Total (95% CI)		**183**		**192**	**100.0%**	**2.56 [1.54, 4.27]**
Total events	44		18			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.62 (P = 0.0003)

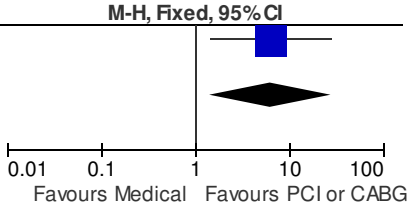


5 Angiography prior randomisation- Multivessel disease medium term follow-up

5.1 Death

Study or Subgroup	Medical Events	Medical Total	PCI or CABG Events	PCI or CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Davies 1997 (ACIP)	12	183	2	192	100.0%	6.30 [1.43, 27.74]
Total (95% CI)		**183**		**192**	**100.0%**	**6.30 [1.43, 27.74]**
Total events	12		2			

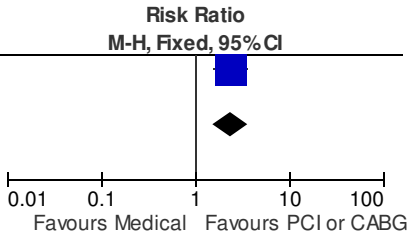
Heterogeneity: Not applicable
Test for overall effect: Z = 2.43 (P = 0.02)



5.2 Non protocol revascularisation

Study or Subgroup	Medical Events	Medical Total	PCI or CABG Events	PCI or CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Davies 1997 (ACIP)	56	183	25	192	100.0%	2.35 [1.54, 3.60]
Total (95% CI)		**183**		**192**	**100.0%**	**2.35 [1.54, 3.60]**
Total events	56		25			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.93 (P < 0.0001)

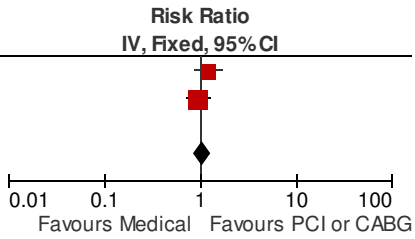


6 Interaction between study group assignment (BARI-2D trial)

6.1 Death in PCI stratum and CABG startum

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
CABG stratum-BARI 2D	0.19062036	0.175336	41.1%	1.21 [0.86, 1.71]
PCI stratum- BARI 2D	-0.0618754	0.146327	58.9%	0.94 [0.71, 1.25]
Total (95% CI)			**100.0%**	**1.04 [0.84, 1.30]**

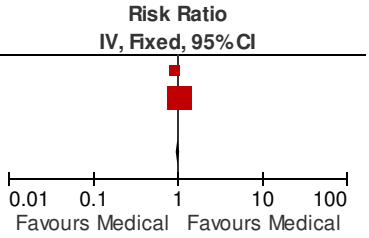
Heterogeneity: Chi² = 1.22, df = 1 (P = 0.27); I² = 18%
Test for overall effect: Z = 0.37 (P = 0.71)



6.2 Freedom from CV events- PCI stratum and CABG stratum

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
CABG stratum-BARI 2D	-0.1053605	0.045471	26.6%	0.90 [0.82, 0.98]
PCI stratum- BARI 2D	0.0295588	0.027403	73.4%	1.03 [0.98, 1.09]
Total (95% CI)			**100.0%**	**0.99 [0.95, 1.04]**

Heterogeneity: Chi² = 6.46, df = 1 (P = 0.01); I² = 85%
Test for overall effect: Z = 0.27 (P = 0.79)

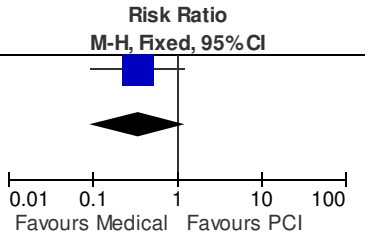


1 Multivessel disease - short term follow-up (1 year)

1.1 Death

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2004 (MASS-II)	3	203	9	205	100.0%	0.34 [0.09, 1.23]
Total (95% CI)		**203**		**205**	**100.0%**	**0.34 [0.09, 1.23]**
Total events	3		9			

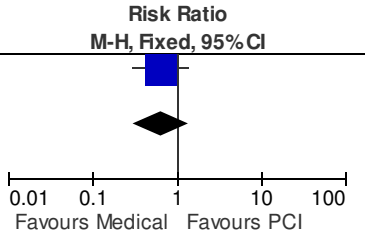
Heterogeneity: Not applicable
Test for overall effect: Z = 1.65 (P = 0.10)



1.2 Q wave MI

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2004 (MASS-II)	10	203	16	205	100.0%	0.63 [0.29, 1.36]
Total (95% CI)		**203**		**205**	**100.0%**	**0.63 [0.29, 1.36]**
Total events	10		16			

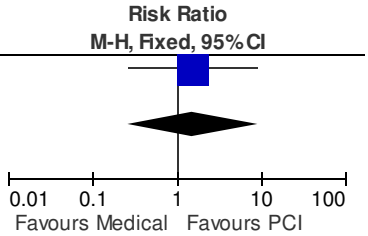
Heterogeneity: Not applicable
Test for overall effect: Z = 1.18 (P = 0.24)



1.3 Stroke

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2004 (MASS-II)	3	203	2	205	100.0%	1.51 [0.26, 8.97]
Total (95% CI)		**203**		**205**	**100.0%**	**1.51 [0.26, 8.97]**
Total events	3		2			

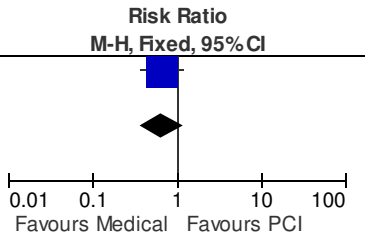
Heterogeneity: Not applicable
Test for overall effect: Z = 0.46 (P = 0.65)



1.4 Non protocol revascularisation

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2004 (MASS-II)	16	203	25	205	100.0%	0.65 [0.36, 1.17]
Total (95% CI)		**203**		**205**	**100.0%**	**0.65 [0.36, 1.17]**
Total events	16		25			

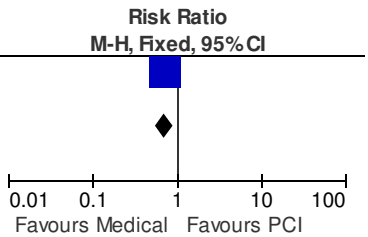
Heterogeneity: Not applicable
Test for overall effect: Z = 1.43 (P = 0.15)



1.5 Free of angina

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2004 (MASS-II)	74	203	107	205	100.0%	0.70 [0.56, 0.87]
Total (95% CI)		**203**		**205**	**100.0%**	**0.70 [0.56, 0.87]**
Total events	74		107			

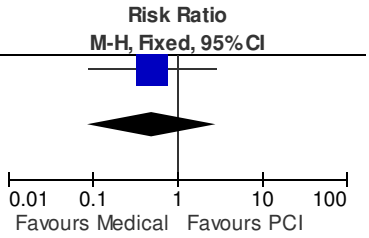
Heterogeneity: Not applicable
Test for overall effect: Z = 3.14 (P = 0.002)



1.6 Death- Sub group diabetes

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Soares 2006 (MASS-II)	2	75	3	56	100.0%	0.50 [0.09, 2.88]
Total (95% CI)		**75**		**56**	**100.0%**	**0.50 [0.09, 2.88]**
Total events	2		3			

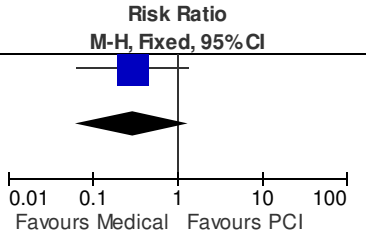
Heterogeneity: Not applicable
Test for overall effect: Z = 0.78 (P = 0.44)



1.7 Death- Subgroup no diabetes

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Soares 2006 (MASS-II)	2	128	8	149	100.0%	0.29 [0.06, 1.35]
Total (95% CI)		**128**		**149**	**100.0%**	**0.29 [0.06, 1.35]**
Total events	2		8			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.58 (P = 0.11)

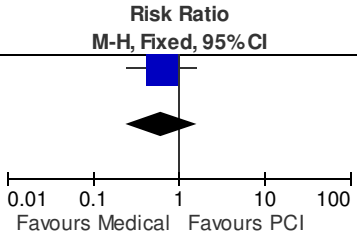


2 Multi vessel disease- medium term follow-up (2 to 4 years)

2.1 Death

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chamberlain 1997 (RITA-2)	7	514	11	504	100.0%	0.62 [0.24, 1.60]
Total (95% CI)		**514**		**504**	**100.0%**	**0.62 [0.24, 1.60]**
Total events	7		11			

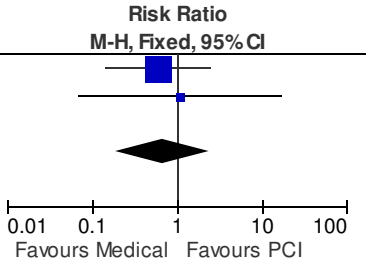
Heterogeneity: Not applicable
Test for overall effect: Z = 0.98 (P = 0.33)



2.2 cardiac death

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chamberlain 1997 (RITA-2)	3	514	5	504	84.0%	0.59 [0.14, 2.45]
Pitt 1999 (AVERT)	1	164	1	177	16.0%	1.08 [0.07, 17.11]
Total (95% CI)		**678**		**681**	**100.0%**	**0.67 [0.19, 2.35]**
Total events	4		6			

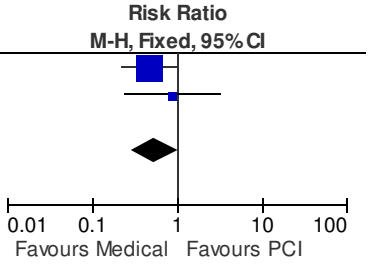
Heterogeneity: Chi² = 0.15, df = 1 (P = 0.70); I² = 0%
Test for overall effect: Z = 0.63 (P = 0.53)



2.3 Non fatal MI

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chamberlain 1997 (RITA-2)	10	514	21	504	81.5%	0.47 [0.22, 0.98]
Pitt 1999 (AVERT)	4	164	5	177	18.5%	0.86 [0.24, 3.16]
Total (95% CI)		**678**		**681**	**100.0%**	**0.54 [0.28, 1.02]**
Total events	14		26			

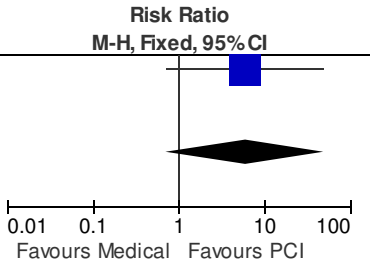
Heterogeneity: Chi² = 0.65, df = 1 (P = 0.42); I² = 0%
Test for overall effect: Z = 1.89 (P = 0.06)



2.4 Stroke

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chamberlain 1997 (RITA-2)	6	514	1	504	100.0%	5.88 [0.71, 48.69]
Pitt 1999 (AVERT)	0	164	0	164		Not estimable
Total (95% CI)		**678**		**668**	**100.0%**	**5.88 [0.71, 48.69]**
Total events	6		1			

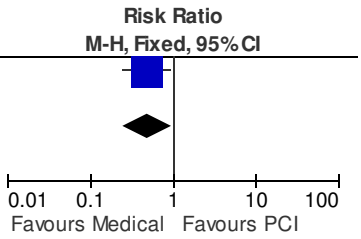
Heterogeneity: Not applicable
Test for overall effect: Z = 1.64 (P = 0.10)



2.5 Hospitalisation (for worsening of angina) no. of patients

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pitt 1999 (AVERT)	11	164	25	177	100.0%	0.47 [0.24, 0.93]
Total (95% CI)		**164**		**177**	**100.0%**	**0.47 [0.24, 0.93]**
Total events	11		25			

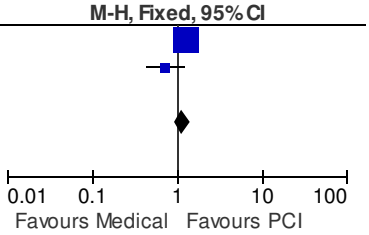
Heterogeneity: Not applicable
Test for overall effect: Z = 2.16 (P = 0.03)



2.6 Non protocol Revascularisation

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chamberlain 1997 (RITA-2)	131	514	102	504	78.1%	1.26 [1.00, 1.58]
Pitt 1999 (AVERT)	20	164	30	177	21.9%	0.72 [0.43, 1.22]
Total (95% CI)		**678**		**681**	**100.0%**	**1.14 [0.93, 1.40]**
Total events	151		132			

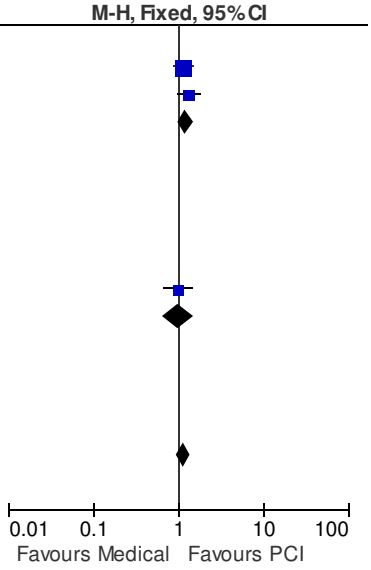
Heterogeneity: $Chi^2 = 3.69$, df = 1 (P = 0.05); $I^2 = 73\%$
Test for overall effect: Z = 1.24 (P = 0.21)



3 Multivessel disease-long term follow-up (> 4 years follow-up)

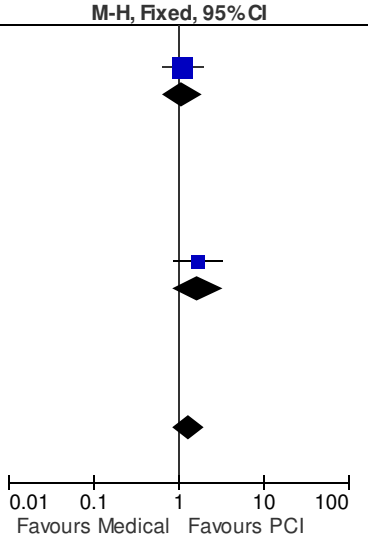
3.1 Death

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 angioplasty and stents						
Boden 2007 (COURAGE)	95	1138	85	1149	47.9%	1.13 [0.85, 1.49]
Hueb 2010 (MASS-II)	63	203	49	205	27.6%	1.30 [0.94, 1.79]
Subtotal (95% CI)		**1341**		**1354**	**75.4%**	**1.19 [0.96, 1.47]**
Total events	158		134			
Heterogeneity: Chi² = 0.42, df = 1 (P = 0.52); I² = 0%						
Test for overall effect: Z = 1.61 (P = 0.11)						
3.1.2 angioplasty						
Henderson 2003 (RITA-2)	43	514	43	504	24.6%	0.98 [0.65, 1.47]
Subtotal (95% CI)		**514**		**504**	**24.6%**	**0.98 [0.65, 1.47]**
Total events	43		43			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.10 (P = 0.92)						
Total (95% CI)		**1855**		**1858**	**100.0%**	**1.14 [0.94, 1.37]**
Total events	201		177			
Heterogeneity: Chi² = 1.18, df = 2 (P = 0.55); I² = 0%						
Test for overall effect: Z = 1.36 (P = 0.17)						
Test for subgroup differences: Not applicable						



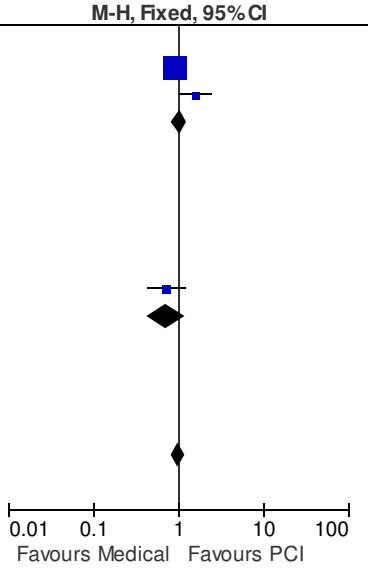
3.2 cardiac death

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.2.1 angioplasty and stents						
Boden 2007 (COURAGE)	25	1138	23	1149	63.6%	1.10 [0.63, 1.92]
Subtotal (95% CI)		**1138**		**1149**	**63.6%**	**1.10 [0.63, 1.92]**
Total events	25		23			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.33 (P = 0.74)						
3.2.2 angioplasty						
Henderson 2003 (RITA-2)	22	514	13	504	36.4%	1.66 [0.85, 3.26]
Subtotal (95% CI)		**514**		**504**	**36.4%**	**1.66 [0.85, 3.26]**
Total events	22		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.47 (P = 0.14)						
Total (95% CI)		**1652**		**1653**	**100.0%**	**1.30 [0.85, 2.00]**
Total events	47		36			
Heterogeneity: Chi² = 0.85, df = 1 (P = 0.36); I² = 0%						
Test for overall effect: Z = 1.21 (P = 0.23)						
Test for subgroup differences: Not applicable						



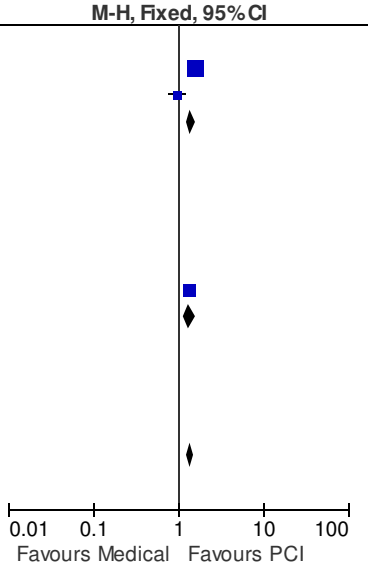
3.3 Non fatal MI

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.3.1 angioplasty and Stents						
Boden 2007 (COURAGE)	128	1138	143	1149	70.6%	0.90 [0.72, 1.13]
Hueb 2010 (MASS-II)	42	203	27	205	13.3%	1.57 [1.01, 2.45]
Subtotal (95% CI)		**1341**		**1354**	**84.0%**	**1.01 [0.83, 1.23]**
Total events	170		170			
Heterogeneity: Chi² = 4.77, df = 1 (P = 0.03); I² = 79%						
Test for overall effect: Z = 0.10 (P = 0.92)						
3.3.2 angioplasty						
Henderson 2003 (RITA-2)	23	514	32	504	16.0%	0.70 [0.42, 1.19]
Subtotal (95% CI)		**514**		**504**	**16.0%**	**0.70 [0.42, 1.19]**
Total events	23		32			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.31 (P = 0.19)						
Total (95% CI)		**1855**		**1858**	**100.0%**	**0.96 [0.80, 1.16]**
Total events	193		202			
Heterogeneity: Chi² = 6.38, df = 2 (P = 0.04); I² = 69%						
Test for overall effect: Z = 0.42 (P = 0.67)						
Test for subgroup differences: Not applicable						



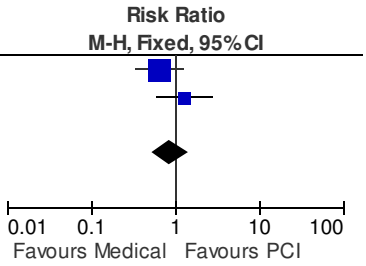
3.4 Non protocol Revascularisation

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.4.1 angioplasty and stents						
Boden 2007 (COURAGE)	348	1138	228	1149	49.0%	1.54 [1.33, 1.78]
Hueb 2010 (MASS-II)	80	203	85	205	18.3%	0.95 [0.75, 1.20]
Subtotal (95% CI)		**1341**		**1354**	**67.3%**	**1.38 [1.22, 1.56]**
Total events	428		313			
Heterogeneity: Chi² = 11.83, df = 1 (P = 0.0006); I² = 92%						
Test for overall effect: Z = 5.10 (P < 0.00001)						
3.4.2 angioplasty						
Henderson 2003 (RITA-2)	202	514	150	504	32.7%	1.32 [1.11, 1.57]
Subtotal (95% CI)		**514**		**504**	**32.7%**	**1.32 [1.11, 1.57]**
Total events	202		150			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.17 (P = 0.002)						
Total (95% CI)		**1855**		**1858**	**100.0%**	**1.36 [1.23, 1.51]**
Total events	630		463			
Heterogeneity: Chi² = 11.84, df = 2 (P = 0.003); I² = 83%						
Test for overall effect: Z = 6.00 (P < 0.00001)						
Test for subgroup differences: Not applicable						



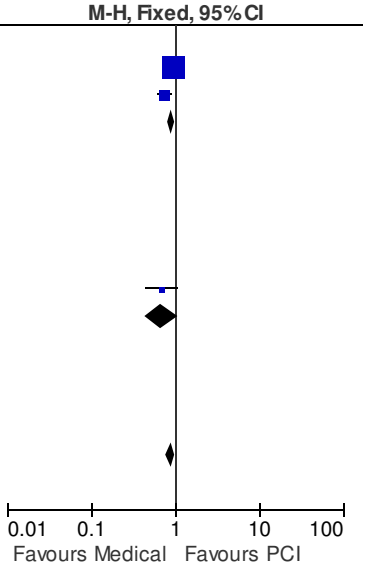
3.5 stroke

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Boden 2007 (COURAGE)	14	1138	22	1149	66.7%	0.64 [0.33, 1.25]
Hueb 2010 (MASS-II)	14	203	11	205	33.3%	1.29 [0.60, 2.76]
Total (95% CI)		**1341**		**1354**	**100.0%**	**0.86 [0.52, 1.41]**
Total events	28		33			
Heterogeneity: Chi² = 1.80, df = 1 (P = 0.18); I² = 44%						
Test for overall effect: Z = 0.61 (P = 0.54)						



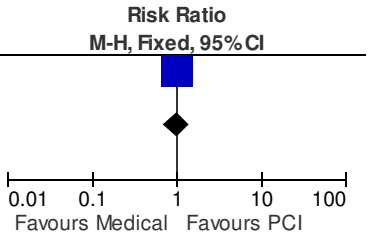
3.6 Free of angina

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.6.1 angioplasty and stents						
Boden 2007 (COURAGE)	296	1138	316	1149	68.3%	0.95 [0.83, 1.08]
Hueb 2010 (MASS-II)	88	203	120	205	25.9%	0.74 [0.61, 0.90]
Subtotal (95% CI)		**1341**		**1354**	**94.2%**	**0.89 [0.79, 1.00]**
Total events	384		436			
Heterogeneity: Chi² = 4.18, df = 1 (P = 0.04); I² = 76%						
Test for overall effect: Z = 2.04 (P = 0.04)						
3.6.2 angioplasty						
Folland 1997 (ACME)	18	50	27	51	5.8%	0.68 [0.43, 1.07]
Subtotal (95% CI)		**50**		**51**	**5.8%**	**0.68 [0.43, 1.07]**
Total events	18		27			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.68 (P = 0.09)						
Total (95% CI)		**1391**		**1405**	**100.0%**	**0.88 [0.79, 0.98]**
Total events	402		463			
Heterogeneity: Chi² = 5.30, df = 2 (P = 0.07); I² = 62%						
Test for overall effect: Z = 2.35 (P = 0.02)						
Test for subgroup differences: Not applicable						



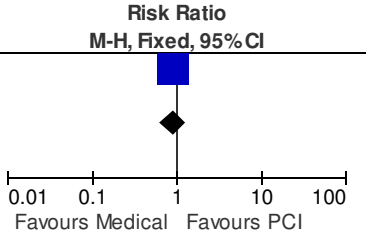
3.7 Death- sub group age >65 yrs

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Teo 2009 (COURAGE)	54	444	57	460	100.0%	0.98 [0.69, 1.39]
Total (95% CI)		**444**		**460**	**100.0%**	**0.98 [0.69, 1.39]**
Total events	54		57			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.10 (P = 0.92)						



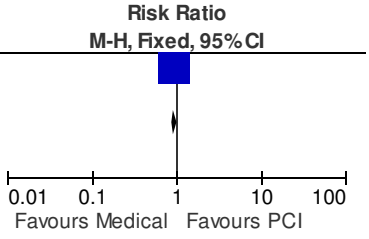
3.8 MI- sub group age >65 yrs

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Teo 2009 (COURAGE)	52	444	60	460	100.0%	0.90 [0.63, 1.27]
Total (95% CI)		**444**		**460**	**100.0%**	**0.90 [0.63, 1.27]**
Total events	52		60			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.61 (P = 0.54)						



3.9 Free of angina- sub group age >65 yrs

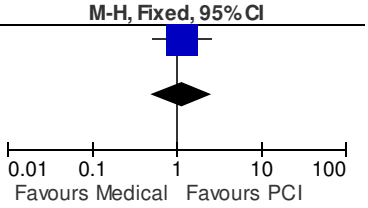
Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Teo 2009 (COURAGE)	324	444	368	460	100.0%	0.91 [0.85, 0.98]
Total (95% CI)		**444**		**460**	**100.0%**	**0.91 [0.85, 0.98]**
Total events	324		368			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.48 (P = 0.01)						



3.10 Death- sub group 2 vessel disease

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Folland 1997 (ACME)	10	50	9	51	100.0%	1.13 [0.50, 2.55]
Total (95% CI)		**50**		**51**	**100.0%**	**1.13 [0.50, 2.55]**
Total events	10		9			

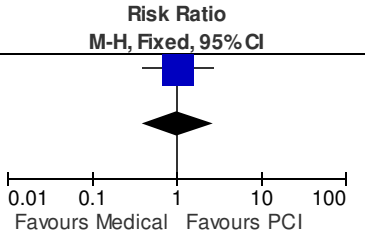
Heterogeneity: Not applicable
Test for overall effect: Z = 0.30 (P = 0.76)



3.11 Non fatal MI- sub group 2 vesel disease

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Folland 1997 (ACME)	7	50	7	51	100.0%	1.02 [0.39, 2.70]
Total (95% CI)		**50**		**51**	**100.0%**	**1.02 [0.39, 2.70]**
Total events	7		7			

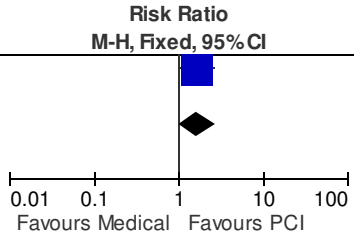
Heterogeneity: Not applicable
Test for overall effect: Z = 0.04 (P = 0.97)



3.12 Death- sub group age <65 yrs

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Teo 2009 (COURAGE)	41	693	25	688	100.0%	1.63 [1.00, 2.65]
Total (95% CI)		**693**		**688**	**100.0%**	**1.63 [1.00, 2.65]**
Total events	41		25			

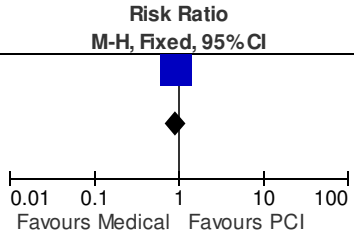
Heterogeneity: Not applicable
Test for overall effect: Z = 1.97 (P = 0.05)



3.13 MI - sub group age <65 yrs

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Teo 2009 (COURAGE)	76	693	83	688	100.0%	0.91 [0.68, 1.22]
Total (95% CI)		**693**		**688**	**100.0%**	**0.91 [0.68, 1.22]**
Total events	76		83			

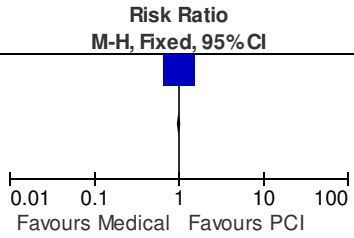
Heterogeneity: Not applicable
Test for overall effect: Z = 0.64 (P = 0.52)



3.14 Free of angina- sub group age<65 years

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Teo 2009 (COURAGE)	485	693	481	688	100.0%	1.00 [0.93, 1.07]
Total (95% CI)		**693**		**688**	**100.0%**	**1.00 [0.93, 1.07]**
Total events	485		481			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.98)

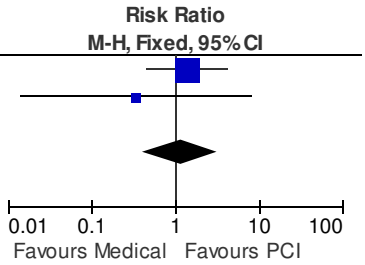


4 Single vessel disease - medium term follow-up (2 -4 years)

4.1 Death

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hartigan 1998 (ACME)	7	107	5	105	77.1%	1.37 [0.45, 4.19]
Hueb 1995 (MASS-I)	0	72	1	72	22.9%	0.33 [0.01, 8.05]
Total (95% CI)		**179**		**177**	**100.0%**	**1.14 [0.41, 3.17]**
Total events	7		6			

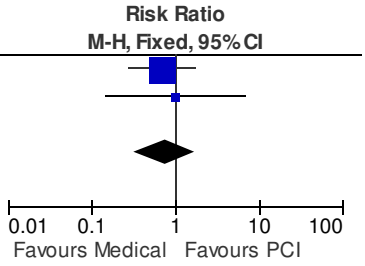
Heterogeneity: Chi² = 0.68, df = 1 (P = 0.41); I² = 0%
Test for overall effect: Z = 0.24 (P = 0.81)



4.2 MI

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hartigan 1998 (ACME)	7	107	10	105	83.5%	0.69 [0.27, 1.74]
Hueb 1995 (MASS-I)	2	72	2	72	16.5%	1.00 [0.14, 6.91]
Total (95% CI)		**179**		**177**	**100.0%**	**0.74 [0.32, 1.70]**
Total events	9		12			

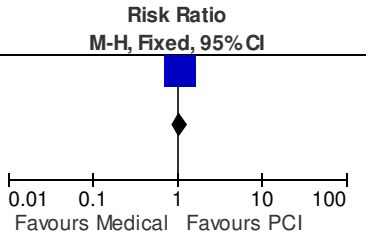
Heterogeneity: Chi² = 0.12, df = 1 (P = 0.73); I² = 0%
Test for overall effect: Z = 0.71 (P = 0.48)



4.3 Hospitalisation (no. of patients)

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hartigan 1998 (ACME)	69	107	64	105	100.0%	1.06 [0.86, 1.30]
Total (95% CI)		**107**		**105**	**100.0%**	**1.06 [0.86, 1.30]**
Total events	69		64			

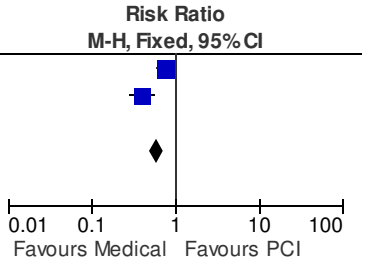
Heterogeneity: Not applicable
Test for overall effect: Z = 0.53 (P = 0.60)



4.4 Free of angina

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hartigan 1998 (ACME)	50	107	65	105	53.1%	0.75 [0.59, 0.97]
Hueb 1995 (MASS-I)	23	72	58	72	46.9%	0.40 [0.28, 0.57]
Total (95% CI)		**179**		**177**	**100.0%**	**0.59 [0.48, 0.72]**
Total events	73		123			

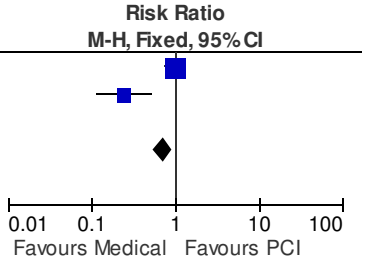
Heterogeneity: Chi² = 8.50, df = 1 (P = 0.004); I² = 88%
Test for overall effect: Z = 5.11 (P < 0.00001)



4.5 Non protocol revascularisation

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hartigan 1998 (ACME)	47	107	47	105	62.1%	0.98 [0.73, 1.33]
Hueb 1995 (MASS-I)	7	72	29	72	37.9%	0.24 [0.11, 0.52]
Total (95% CI)		**179**		**177**	**100.0%**	**0.70 [0.53, 0.93]**
Total events	54		76			

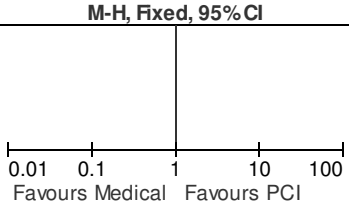
Heterogeneity: Chi² = 12.39, df = 1 (P = 0.0004); I² = 92%
Test for overall effect: Z = 2.50 (P = 0.01)



4.6 Stroke

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1995 (MASS-I)	0	72	0	72		Not estimable
Total (95% CI)		**72**		**72**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

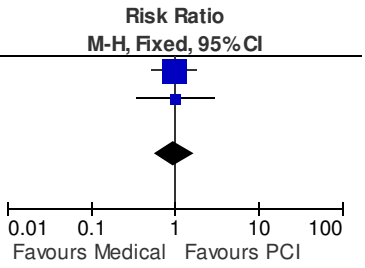


5 Single vessel disease - long term follow-up (>4 years)

5.1 Death

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Folland 1997 (ACME)	16	112	17	115	73.7%	0.97 [0.51, 1.82]
Hueb 1999 (MASS-I)	6	72	6	72	26.3%	1.00 [0.34, 2.95]
Total (95% CI)		**184**		**187**	**100.0%**	**0.98 [0.57, 1.68]**
Total events	22		23			

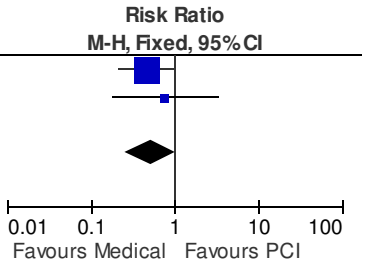
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.96); I² = 0%
Test for overall effect: Z = 0.09 (P = 0.93)



5.2 Non fatal MI

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Folland 1997 (ACME)	8	112	18	115	81.6%	0.46 [0.21, 1.01]
Hueb 1999 (MASS-I)	3	72	4	72	18.4%	0.75 [0.17, 3.23]
Total (95% CI)		**184**		**187**	**100.0%**	**0.51 [0.26, 1.02]**
Total events	11		22			

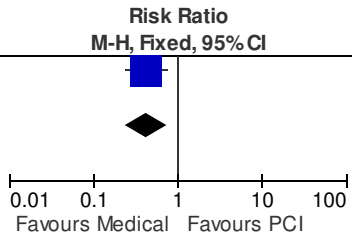
Heterogeneity: Chi² = 0.34, df = 1 (P = 0.56); I² = 0%
Test for overall effect: Z = 1.91 (P = 0.06)



5.3 Non protocol Revascularisation

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1999 (MASS-I)	12	72	29	72	100.0%	0.41 [0.23, 0.75]
Total (95% CI)		**72**		**72**	**100.0%**	**0.41 [0.23, 0.75]**
Total events	12		29			

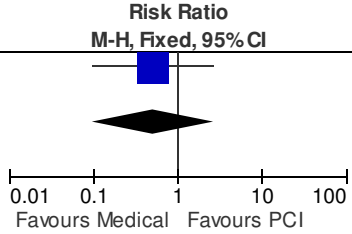
Heterogeneity: Not applicable
Test for overall effect: Z = 2.94 (P = 0.003)



5.4 cardiac death

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1999 (MASS-I)	2	72	4	72	100.0%	0.50 [0.09, 2.64]
Total (95% CI)		**72**		**72**	**100.0%**	**0.50 [0.09, 2.64]**
Total events	2		4			

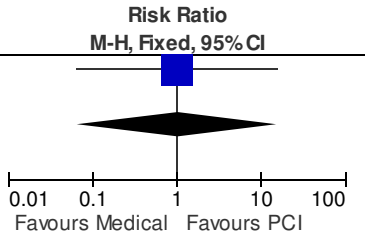
Heterogeneity: Not applicable
Test for overall effect: Z = 0.82 (P = 0.41)



5.5 stroke

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1999 (MASS-I)	1	72	1	72	100.0%	1.00 [0.06, 15.68]
Total (95% CI)		**72**		**72**	**100.0%**	**1.00 [0.06, 15.68]**
Total events	1		1			

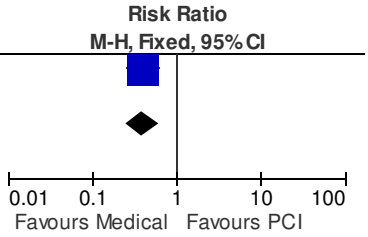
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



5.6 Free of angina

Study or Subgroup	Medical Events	Medical Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1999 (MASS-I)	17	72	44	72	100.0%	0.39 [0.25, 0.61]
Total (95% CI)		**72**		**72**	**100.0%**	**0.39 [0.25, 0.61]**
Total events	17		44			

Heterogeneity: Not applicable
Test for overall effect: Z = 4.10 (P < 0.0001)

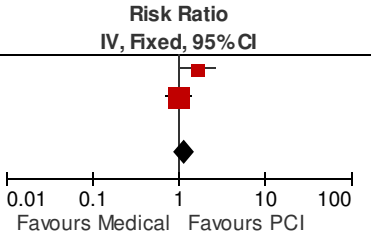


6 Sub group interaction

6.1 Age >and >65 yrs (Death) - Multivessel -LOng term follow-up

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis- age<65	0.48858001	0.248612	34.1%	1.63 [1.00, 2.65]
meta analysis-age>65	-0.0202027	0.178665	65.9%	0.98 [0.69, 1.39]
Total (95% CI)			**100.0%**	**1.17 [0.88, 1.55]**

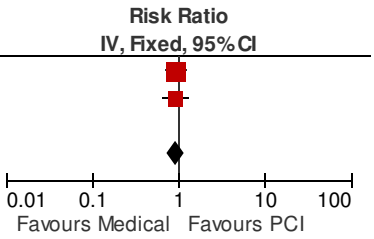
Heterogeneity: Chi² = 2.76, df = 1 (P = 0.10); I² = 64%
Test for overall effect: Z = 1.06 (P = 0.29)



6.2 Age < and >65 yrs (MI)-Multivessel -Long term follow-up

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis- age<65	-0.0943107	0.149111	59.0%	0.91 [0.68, 1.22]
meta analysis-age>65	-0.1053605	0.17884	41.0%	0.90 [0.63, 1.28]
Total (95% CI)			**100.0%**	**0.91 [0.72, 1.13]**

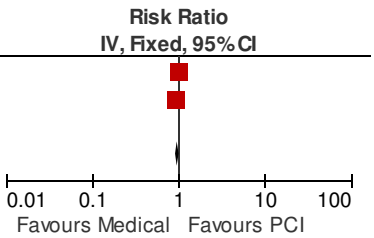
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.96); I² = 0%
Test for overall effect: Z = 0.86 (P = 0.39)



6.3 Age <65 and >65 yrs (Free of angina)- Multivessel- Long term follow-up)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis- age<65	0	0.035773	50.7%	1.00 [0.93, 1.07]
meta analysis-age>65	-0.0943107	0.036305	49.3%	0.91 [0.85, 0.98]
Total (95% CI)			**100.0%**	**0.95 [0.91, 1.00]**

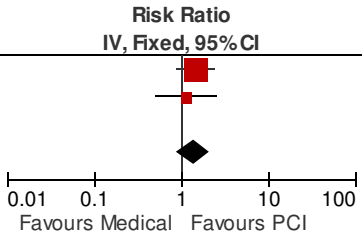
Heterogeneity: Chi² = 3.42, df = 1 (P = 0.06); I² = 71%
Test for overall effect: Z = 1.82 (P = 0.07)



6.4 Single vessel and 2 vessel (Death)- Long term follow-up

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis- single ves	0.37156356	0.255944	72.5%	1.45 [0.88, 2.39]
meta analysis-2 vessel	0.12221763	0.415623	27.5%	1.13 [0.50, 2.55]
Total (95% CI)			**100.0%**	**1.35 [0.88, 2.08]**

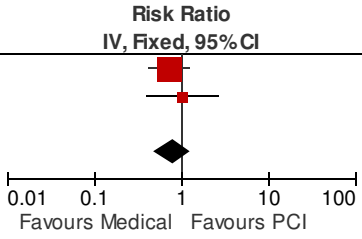
Heterogeneity: Chi² = 0.26, df = 1 (P = 0.61); I² = 0%
Test for overall effect: Z = 1.39 (P = 0.16)



6.5 Single vessel and 2 vessel (MI)- Long term follow-up

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis- single ves	-0.3285041	0.278226	75.9%	0.72 [0.42, 1.24]
meta analysis-2 vessel	0.01980263	0.493587	24.1%	1.02 [0.39, 2.68]
Total (95% CI)			**100.0%**	**0.78 [0.49, 1.26]**

Heterogeneity: Chi² = 0.38, df = 1 (P = 0.54); I² = 0%
Test for overall effect: Z = 1.01 (P = 0.31)

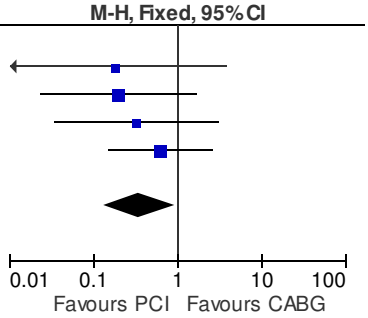


1 Multi vessel disease - Immediate follow-up

1.1 Stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Eefting 2003	0	138	0	142		Not estimable
Hamm 1994 (GABI)	0	176	2	161	16.7%	0.18 [0.01, 3.78]
Hampton 1993 (RITA)	1	509	5	498	32.3%	0.20 [0.02, 1.67]
King 1994 (EAST)	1	198	3	194	19.4%	0.33 [0.03, 3.11]
Zhang 2006 (SOS)	3	488	5	500	31.6%	0.61 [0.15, 2.56]
Total (95% CI)		**1509**		**1495**	**100.0%**	**0.35 [0.13, 0.92]**
Total events	5		15			

Heterogeneity: Chi² = 1.06, df = 3 (P = 0.79); I² = 0%
Test for overall effect: Z = 2.12 (P = 0.03)

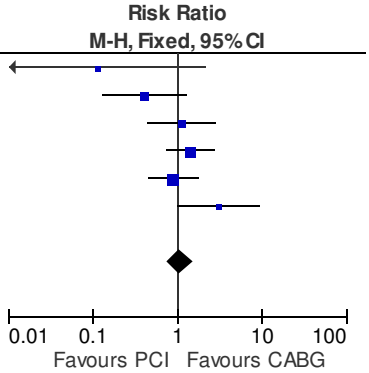


2 Multivessel disease -Short term follow-up (1 yr)

2.1 Death (all causes)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Eefting 2003	0	138	4	142	7.8%	0.11 [0.01, 2.10]
Hamm 1994 (GABI)	4	155	9	139	16.6%	0.40 [0.13, 1.27]
Hueb 2004 (MASS- II)	9	205	8	203	14.1%	1.11 [0.44, 2.83]
Rickards 1995 (CABRI)	21	541	14	513	25.1%	1.42 [0.73, 2.77]
Serruys 2001 (ARTS)	15	600	17	605	29.6%	0.89 [0.45, 1.77]
Sigwart 2002 (SOS)	12	488	4	500	6.9%	3.07 [1.00, 9.46]
Total (95% CI)		**2127**		**2102**	**100.0%**	**1.06 [0.75, 1.52]**
Total events	61		56			

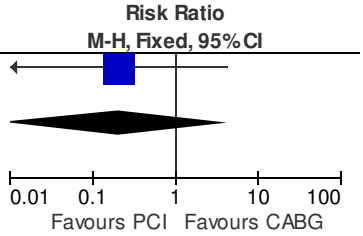
Heterogeneity: Chi² = 9.45, df = 5 (P = 0.09); I² = 47%
Test for overall effect: Z = 0.34 (P = 0.73)



2.2 Cardiac mortality

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Eefting 2003	0	138	2	142	100.0%	0.21 [0.01, 4.25]
Total (95% CI)		**138**		**142**	**100.0%**	**0.21 [0.01, 4.25]**
Total events	0		2			

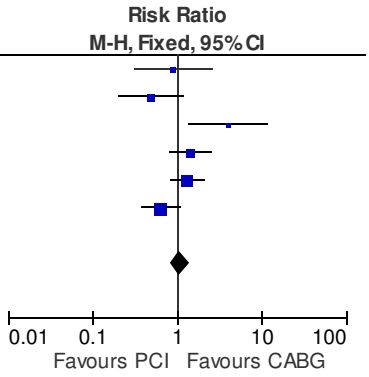
Heterogeneity: Not applicable
Test for overall effect: Z = 1.02 (P = 0.31)



2.3 Non fatal MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Eefting 2003	6	138	7	142	6.5%	0.88 [0.30, 2.56]
Hamm 1994 (GABI)	7	155	13	139	13.0%	0.48 [0.20, 1.18]
Hueb 2004 (MASS- II)	16	205	4	203	3.8%	3.96 [1.35, 11.64]
Rickards 1995 (CABRI)	27	541	18	513	17.5%	1.42 [0.79, 2.55]
Serruys 2001 (ARTS)	37	600	29	605	27.4%	1.29 [0.80, 2.06]
Sigwart 2002 (SOS)	21	488	34	500	31.8%	0.63 [0.37, 1.07]
Total (95% CI)		**2127**		**2102**	**100.0%**	**1.07 [0.83, 1.39]**
Total events	114		105			

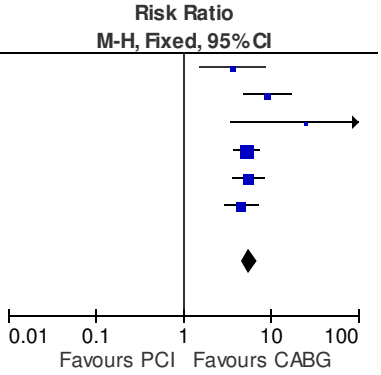
Heterogeneity: Chi² = 14.14, df = 5 (P = 0.01); I² = 65%
Test for overall effect: Z = 0.54 (P = 0.59)



2.4 Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Eefting 2003	21	138	6	142	6.3%	3.60 [1.50, 8.65]
Hamm 1994 (GABI)	91	155	9	139	10.1%	9.07 [4.76, 17.29]
Hueb 2004 (MASS- II)	25	205	1	203	1.1%	24.76 [3.39, 180.98]
Rickards 1995 (CABRI)	182	541	33	513	36.1%	5.23 [3.68, 7.43]
Serruys 2001 (ARTS)	126	600	23	605	24.4%	5.52 [3.59, 8.49]
Sigwart 2002 (SOS)	93	488	21	500	22.1%	4.54 [2.87, 7.16]
Total (95% CI)		**2127**		**2102**	**100.0%**	**5.64 [4.57, 6.97]**
Total events	538		93			

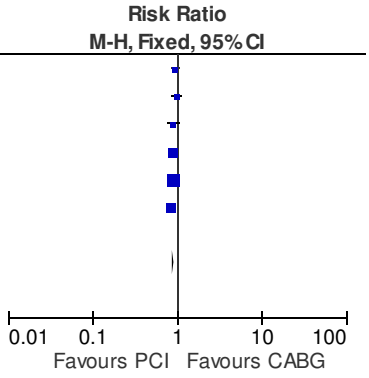
Heterogeneity: Chi² = 6.27, df = 5 (P = 0.28); I² = 20%
Test for overall effect: Z = 16.07 (P < 0.00001)



2.5 Free of angina

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Eefting 2003	108	138	120	142	7.3%	0.93 [0.83, 1.04]
Hamm 1994 (GABI)	110	155	102	139	6.6%	0.97 [0.84, 1.11]
Hueb 2004 (MASS- II)	107	205	120	203	7.4%	0.88 [0.74, 1.05]
Rickards 1995 (CABRI)	328	541	350	513	22.1%	0.89 [0.81, 0.97]
Serruys 2001 (ARTS)	473	600	541	605	33.2%	0.88 [0.84, 0.93]
Sigwart 2002 (SOS)	309	471	387	493	23.3%	0.84 [0.77, 0.91]
Total (95% CI)		**2110**		**2095**	**100.0%**	**0.88 [0.85, 0.91]**
Total events	1435		1620			

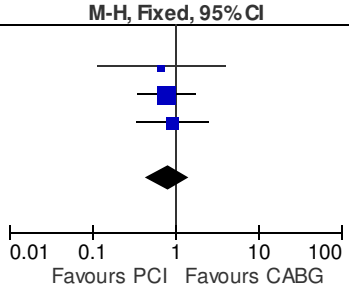
Heterogeneity: Chi² = 4.11, df = 5 (P = 0.53); I² = 0%
Test for overall effect: Z = 6.76 (P < 0.00001)



2.6 Stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Eefting 2003	0	138	0	142		Not estimable
Hueb 2004 (MASS- II)	2	205	3	203	12.6%	0.66 [0.11, 3.91]
Serruys 2001 (ARTS)	10	600	13	605	54.3%	0.78 [0.34, 1.76]
Sigwart 2002 (SOS)	7	488	8	500	33.1%	0.90 [0.33, 2.45]
Total (95% CI)		**1431**		**1450**	**100.0%**	**0.80 [0.44, 1.45]**
Total events	19		24			

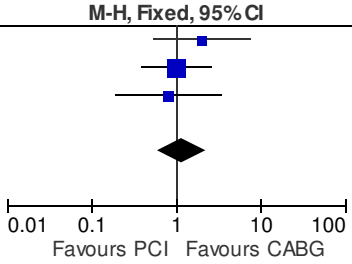
Heterogeneity: Chi² = 0.10, df = 2 (P = 0.95); I² = 0%
Test for overall effect: Z = 0.73 (P = 0.47)



2.7 Subgroup-diabetes- Death (all causes)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Abizaid 2001 (ARTS)	7	112	3	96	21.2%	2.00 [0.53, 7.52]
Kapur 2009 (CARDia trial)	8	254	8	248	53.2%	0.98 [0.37, 2.56]
Soares 2006 (MASS-II)	3	56	4	59	25.6%	0.79 [0.19, 3.37]
Total (95% CI)		**422**		**403**	**100.0%**	**1.15 [0.58, 2.25]**
Total events	18		15			

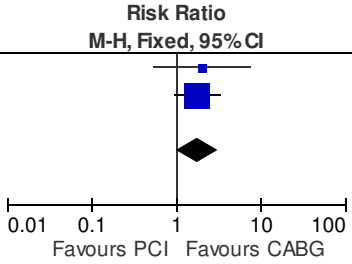
Heterogeneity: Chi² = 1.04, df = 2 (P = 0.60); I² = 0%
Test for overall effect: Z = 0.39 (P = 0.69)



2.8 Subgroup diabetes-MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Abizaid 2001 (ARTS)	7	112	3	96	18.6%	2.00 [0.53, 7.52]
Kapur 2009 (CARDia trial)	25	254	14	248	81.4%	1.74 [0.93, 3.28]
Total (95% CI)		**366**		**344**	**100.0%**	**1.79 [1.01, 3.17]**
Total events	32		17			

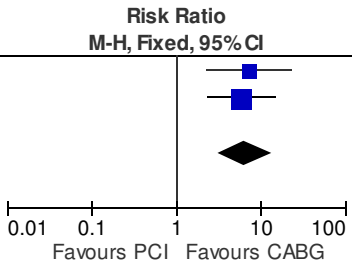
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.85); I² = 0%
Test for overall effect: Z = 2.01 (P = 0.04)



2.9 Subgroup diabetes- Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Abizaid 2001 (ARTS)	25	112	3	96	39.0%	7.14 [2.23, 22.93]
Kapur 2009 (CARDia trial)	30	254	5	248	61.0%	5.86 [2.31, 14.85]
Total (95% CI)		**366**		**344**	**100.0%**	**6.36 [3.07, 13.16]**
Total events	55		8			

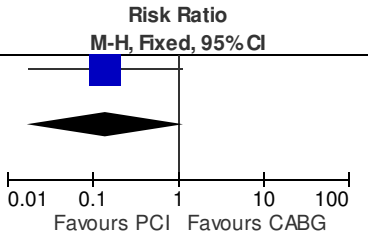
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.79); I² = 0%
Test for overall effect: Z = 4.98 (P < 0.00001)



2.10 Sub group diabetes- Non fatal stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kapur 2009 (CARDia trial)	1	254	7	248	100.0%	0.14 [0.02, 1.13]
Total (95% CI)		**254**		**248**	**100.0%**	**0.14 [0.02, 1.13]**
Total events	1		7			

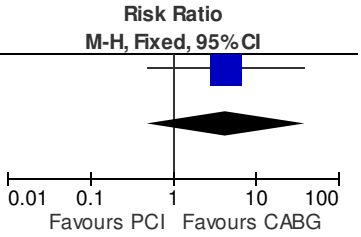
Heterogeneity: Not applicable
Test for overall effect: Z = 1.85 (P = 0.06)



2.11 Subgroup age>65 yrs- Death (all causes)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zhang 2006 (SOS)	4	190	1	205	100.0%	4.32 [0.49, 38.27]
Total (95% CI)		**190**		**205**	**100.0%**	**4.32 [0.49, 38.27]**
Total events	4		1			

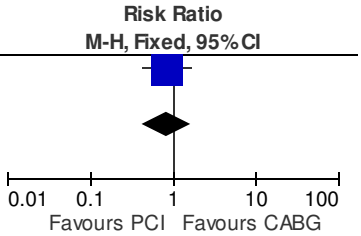
Heterogeneity: Not applicable
Test for overall effect: Z = 1.31 (P = 0.19)



2.12 subgroup age>65 yrs-MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zhang 2006 (SOS)	13	190	17	205	100.0%	0.83 [0.41, 1.65]
Total (95% CI)		**190**		**205**	**100.0%**	**0.83 [0.41, 1.65]**
Total events	13		17			

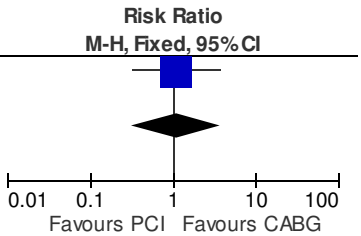
Heterogeneity: Not applicable
Test for overall effect: Z = 0.54 (P = 0.59)



2.13 Subgroup age>65 yrs- stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zhang 2006 (SOS)	5	190	5	205	100.0%	1.08 [0.32, 3.67]
Total (95% CI)		**190**		**205**	**100.0%**	**1.08 [0.32, 3.67]**
Total events	5		5			

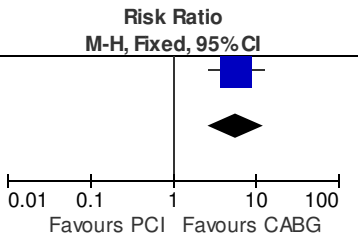
Heterogeneity: Not applicable
Test for overall effect: Z = 0.12 (P = 0.90)



2.14 subgroup age>65 yrs- repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zhang 2006 (SOS)	37	190	7	205	100.0%	5.70 [2.61, 12.48]
Total (95% CI)		**190**		**205**	**100.0%**	**5.70 [2.61, 12.48]**
Total events	37		7			

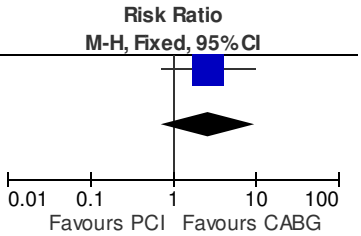
Heterogeneity: Not applicable
Test for overall effect: Z = 4.36 (P < 0.0001)



2.15 Sub group age <65 yrs- Death

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zhang 2006 (SOS)	8	298	3	295	100.0%	2.64 [0.71, 9.85]
Total (95% CI)		**298**		**295**	**100.0%**	**2.64 [0.71, 9.85]**
Total events	8		3			

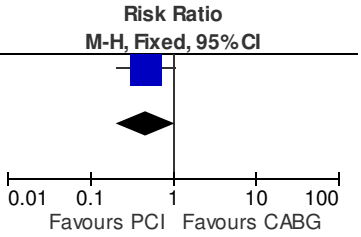
Heterogeneity: Not applicable
Test for overall effect: Z = 1.44 (P = 0.15)



2.16 Sub group age <65 yrs-MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zhang 2006 (SOS)	8	298	17	295	100.0%	0.47 [0.20, 1.06]
Total (95% CI)		**298**		**295**	**100.0%**	**0.47 [0.20, 1.06]**
Total events	8		17			

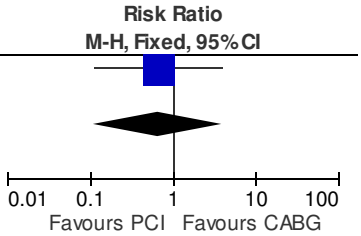
Heterogeneity: Not applicable
Test for overall effect: Z = 1.82 (P = 0.07)



2.17 Sub group age<65 yrs- Stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zhang 2006 (SOS)	2	298	3	295	100.0%	0.66 [0.11, 3.92]
Total (95% CI)		**298**		**295**	**100.0%**	**0.66 [0.11, 3.92]**
Total events	2		3			

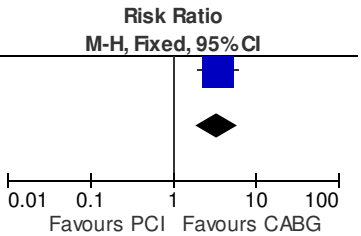
Heterogeneity: Not applicable
Test for overall effect: Z = 0.46 (P = 0.65)



2.18 Sub group age<65 yrs- Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Zhang 2006 (SOS)	48	298	14	295	100.0%	3.39 [1.91, 6.02]
Total (95% CI)		**298**		**295**	**100.0%**	**3.39 [1.91, 6.02]**
Total events	48		14			

Heterogeneity: Not applicable
Test for overall effect: Z = 4.18 (P < 0.0001)

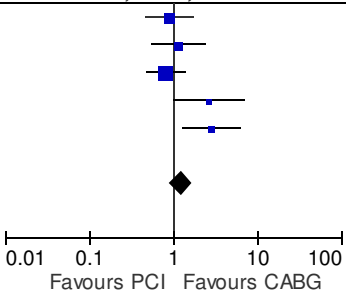


3 Multi vessel disease - Medium term follow-up (>1-4 yrs)

3.1 Death (all causes)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hampton 1993 (RITA)	16	510	18	501	25.4%	0.87 [0.45, 1.69]
King 1994 (EAST)	14	198	12	194	17.0%	1.14 [0.54, 2.41]
Legrand 2004 (ARTS)	22	600	28	605	39.0%	0.79 [0.46, 1.37]
Martuscelli 2008 (CABRI)	15	120	5	103	7.5%	2.58 [0.97, 6.84]
Sigwart 2002 (SOS)	22	488	8	500	11.1%	2.82 [1.27, 6.27]
Total (95% CI)		**1916**		**1903**	**100.0%**	**1.23 [0.91, 1.67]**
Total events	89		71			

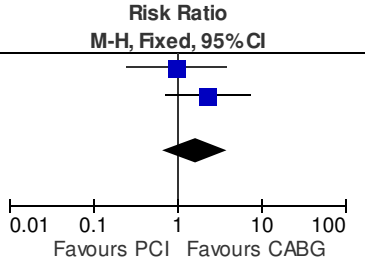
Heterogeneity: Chi² = 9.88, df = 4 (P = 0.04); I² = 60%
Test for overall effect: Z = 1.33 (P = 0.18)



3.2 Cardiac mortality

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hampton 1993 (RITA)	4	510	4	501	50.5%	0.98 [0.25, 3.91]
Sigwart 2002 (SOS)	9	488	4	500	49.5%	2.31 [0.71, 7.44]
Total (95% CI)		**998**		**1001**	**100.0%**	**1.64 [0.68, 3.92]**
Total events	13		8			

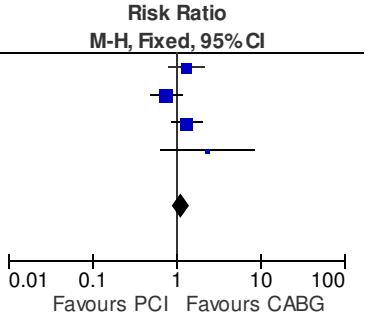
Heterogeneity: Chi² = 0.85, df = 1 (P = 0.36); I² = 0%
Test for overall effect: Z = 1.10 (P = 0.27)



3.3 Non fatal MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hampton 1993 (RITA)	34	510	26	501	25.8%	1.28 [0.78, 2.11]
King 1994 (EAST)	29	198	38	194	37.7%	0.75 [0.48, 1.16]
Legrand 2004 (ARTS)	44	600	34	605	33.3%	1.30 [0.85, 2.01]
Martuscelli 2008 (CABRI)	8	120	3	103	3.2%	2.29 [0.62, 8.40]
Total (95% CI)		**1428**		**1403**	**100.0%**	**1.12 [0.87, 1.45]**
Total events	115		101			

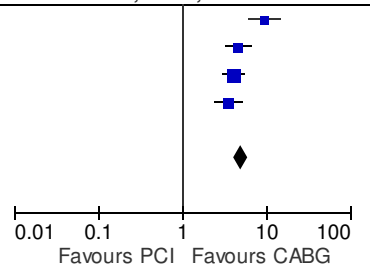
Heterogeneity: Chi² = 5.16, df = 3 (P = 0.16); I² = 42%
Test for overall effect: Z = 0.88 (P = 0.38)



3.4 Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hampton 1993 (RITA)	189	510	20	501	16.7%	9.28 [5.95, 14.47]
King 1994 (EAST)	125	198	27	194	22.6%	4.54 [3.15, 6.54]
Legrand 2004 (ARTS)	175	600	44	605	36.2%	4.01 [2.94, 5.47]
Sigwart 2002 (SOS)	101	488	30	500	24.5%	3.45 [2.34, 5.08]
Total (95% CI)		**1796**		**1800**	**100.0%**	**4.87 [4.06, 5.85]**
Total events	590		121			

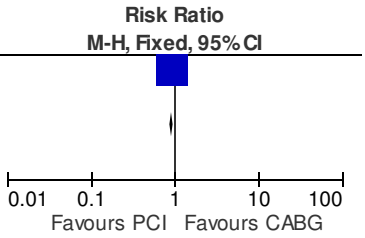
Heterogeneity: Chi² = 12.79, df = 3 (P = 0.005); I² = 77%
Test for overall effect: Z = 16.92 (P < 0.00001)



3.5 Free of angina

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Unger 2003 (ARTS)	478	600	527	605	100.0%	0.91 [0.87, 0.96]
Total (95% CI)		**600**		**605**	**100.0%**	**0.91 [0.87, 0.96]**
Total events	478		527			

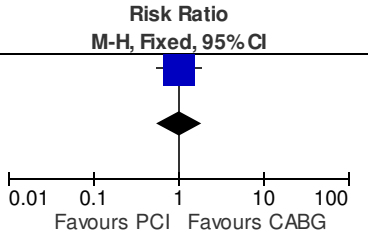
Heterogeneity: Not applicable
Test for overall effect: Z = 3.45 (P = 0.0006)



3.6 Stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Legrand 2004 (ARTS)	20	600	20	605	100.0%	1.01 [0.55, 1.85]
Total (95% CI)		**600**		**605**	**100.0%**	**1.01 [0.55, 1.85]**
Total events	20		20			

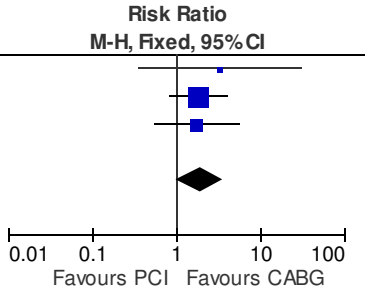
Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.98)



3.7 Sub group diabetes- Mortality

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Booth 2008 (SOS)	3	68	1	74	7.3%	3.26 [0.35, 30.64]
Kurbaan 2001 (CABRI)	14	62	8	63	60.1%	1.78 [0.80, 3.94]
Legrand 2004 (ARTS)	8	112	4	96	32.6%	1.71 [0.53, 5.52]
Total (95% CI)		**242**		**233**	**100.0%**	**1.87 [0.99, 3.50]**
Total events	25		13			

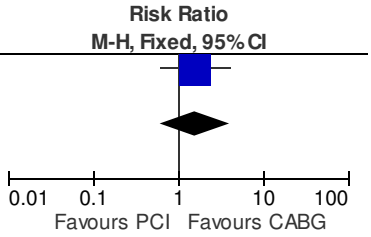
Heterogeneity: Chi² = 0.27, df = 2 (P = 0.87); I² = 0%
Test for overall effect: Z = 1.94 (P = 0.05)



3.8 Sub group diabetes- MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Legrand 2004 (ARTS)	11	112	6	96	100.0%	1.57 [0.60, 4.09]
Total (95% CI)		**112**		**96**	**100.0%**	**1.57 [0.60, 4.09]**
Total events	11		6			

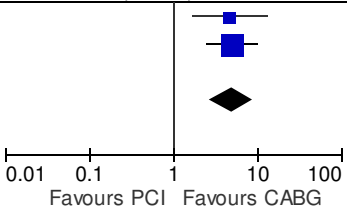
Heterogeneity: Not applicable
Test for overall effect: Z = 0.93 (P = 0.35)



3.9 Sub group diabetes- Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Booth 2008 (SOS)	17	68	4	74	30.8%	4.63 [1.64, 13.06]
Legrand 2004 (ARTS)	46	112	8	96	69.2%	4.93 [2.45, 9.92]
Total (95% CI)		**180**		**170**	**100.0%**	**4.84 [2.71, 8.64]**
Total events	63		12			

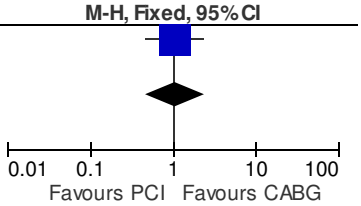
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.92); I² = 0%
Test for overall effect: Z = 5.32 (P < 0.00001)



3.10 Sub group- Left Anterior descending coronary artery proximally- Death

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Aoki 2004 (ARTS)	11	246	11	253	100.0%	1.03 [0.45, 2.33]
Total (95% CI)		**246**		**253**	**100.0%**	**1.03 [0.45, 2.33]**
Total events	11		11			

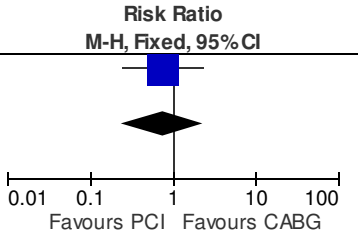
Heterogeneity: Not applicable
Test for overall effect: Z = 0.07 (P = 0.95)



3.11 Sub group LAD artery- Stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Aoki 2004 (ARTS)	5	246	7	253	100.0%	0.73 [0.24, 2.28]
Total (95% CI)		**246**		**253**	**100.0%**	**0.73 [0.24, 2.28]**
Total events	5		7			

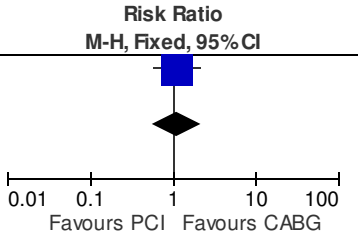
Heterogeneity: Not applicable
Test for overall effect: Z = 0.53 (P = 0.59)



3.12 Sub group LAD artery- MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Aoki 2004 (ARTS)	17	246	16	253	100.0%	1.09 [0.56, 2.11]
Total (95% CI)		**246**		**253**	**100.0%**	**1.09 [0.56, 2.11]**
Total events	17		16			

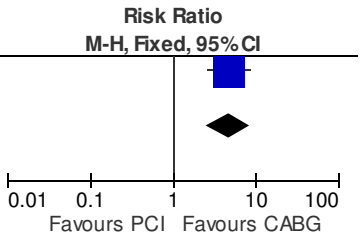
Heterogeneity: Not applicable
Test for overall effect: Z = 0.26 (P = 0.79)



3.13 Sub group LAD artery- Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Aoki 2004 (ARTS)	54	246	12	253	100.0%	4.63 [2.54, 8.44]
Total (95% CI)		**246**		**253**	**100.0%**	**4.63 [2.54, 8.44]**
Total events	54		12			

Heterogeneity: Not applicable
Test for overall effect: Z = 5.00 (P < 0.00001)

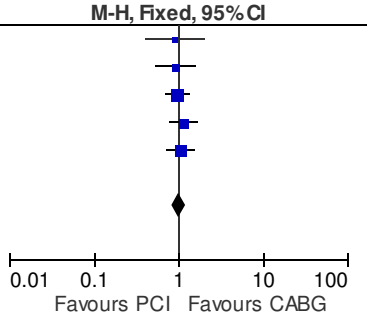


4 Multi vessel disease - Long term follow-up (> 5 yrs)

4.1 Death (all causes)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Buszman 2009 (SOS)	9	50	10	50	6.0%	0.90 [0.40, 2.02]
Henderson 1998 (RITA)	22	277	24	279	14.4%	0.92 [0.53, 1.61]
Hueb 2010 (MASS-II)	49	205	51	203	30.8%	0.95 [0.68, 1.34]
Kaehler (GABI 2005)	41	164	35	160	21.3%	1.14 [0.77, 1.70]
Serruys2005 (ARTS)	48	600	46	605	27.5%	1.05 [0.71, 1.55]
Total (95% CI)		**1296**		**1297**	**100.0%**	**1.01 [0.83, 1.23]**
Total events	169		166			

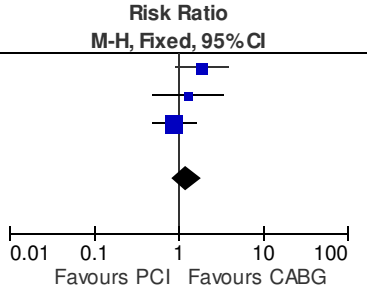
Heterogeneity: Chi² = 0.71, df = 4 (P = 0.95); I² = 0%
Test for overall effect: Z = 0.13 (P = 0.90)



4.2 Cardiac mortality

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Booth 2008 (SOS)	20	488	11	500	28.5%	1.86 [0.90, 3.85]
Henderson 1998 (RITA)	9	277	7	279	18.3%	1.29 [0.49, 3.43]
Kaehler (GABI 2005)	18	164	20	160	53.2%	0.88 [0.48, 1.60]
Total (95% CI)		**929**		**939**	**100.0%**	**1.24 [0.82, 1.87]**
Total events	47		38			

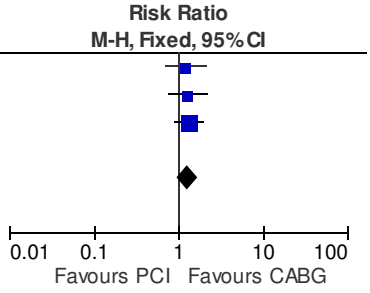
Heterogeneity: Chi² = 2.49, df = 2 (P = 0.29); I² = 20%
Test for overall effect: Z = 1.01 (P = 0.31)



4.3 Non fatal MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Henderson 1998 (RITA)	24	277	20	279	25.0%	1.21 [0.68, 2.14]
Hueb 2010 (MASS-II)	27	205	21	203	26.4%	1.27 [0.74, 2.18]
Serruys2005 (ARTS)	51	600	39	605	48.6%	1.32 [0.88, 1.97]
Total (95% CI)		**1082**		**1087**	**100.0%**	**1.28 [0.97, 1.69]**
Total events	102		80			

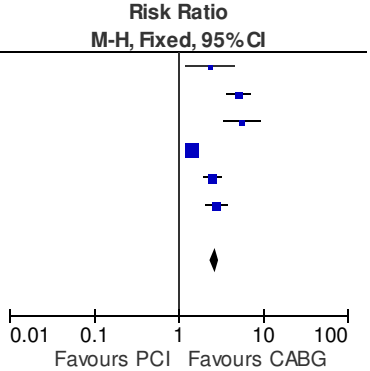
Heterogeneity: Chi² = 0.06, df = 2 (P = 0.97); I² = 0%
Test for overall effect: Z = 1.72 (P = 0.08)



4.4 Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Buszman 2009 (SOS)	21	50	9	50	3.6%	2.33 [1.19, 4.58]
Henderson 1998 (RITA)	161	277	32	279	12.6%	5.07 [3.60, 7.13]
Hueb 2010 (MASS-II)	85	205	15	203	6.0%	5.61 [3.36, 9.38]
Kaehler (GABI 2005)	136	164	94	160	37.7%	1.41 [1.22, 1.64]
King 2000 (EAST)	129	198	51	194	20.4%	2.48 [1.92, 3.20]
Serruys2005 (ARTS)	139	600	50	605	19.7%	2.80 [2.07, 3.79]
Total (95% CI)		**1494**		**1491**	**100.0%**	**2.65 [2.35, 2.98]**
Total events	671		251			

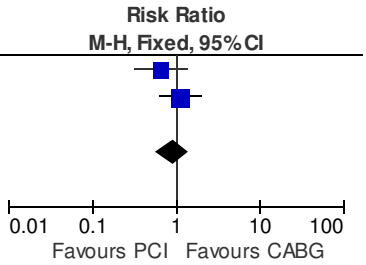
Heterogeneity: Chi² = 92.87, df = 5 (P < 0.00001); I² = 95%
Test for overall effect: Z = 16.12 (P < 0.00001)



4.5 Stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2010 (MASS-II)	11	205	17	203	45.0%	0.64 [0.31, 1.33]
Serruys2005 (ARTS)	23	600	21	605	55.0%	1.10 [0.62, 1.97]
Total (95% CI)		**805**		**808**	**100.0%**	**0.90 [0.57, 1.41]**
Total events	34		38			

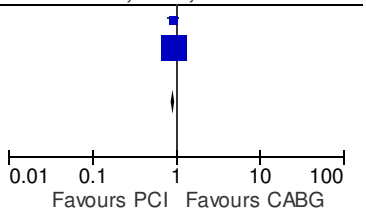
Heterogeneity: Chi² = 1.30, df = 1 (P = 0.25); I² = 23%
Test for overall effect: Z = 0.48 (P = 0.63)



4.6 Free of angina

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 2010 (MASS-II)	120	205	130	203	20.4%	0.91 [0.78, 1.07]
Serruys2005 (ARTS)	467	600	511	605	79.6%	0.92 [0.87, 0.97]
Total (95% CI)		**805**		**808**	**100.0%**	**0.92 [0.87, 0.97]**
Total events	587		641			

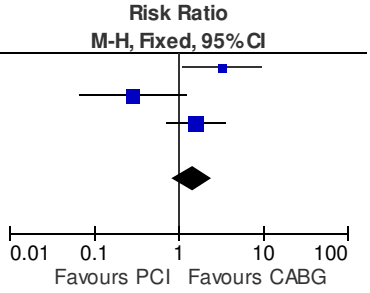
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.92); I² = 0%
Test for overall effect: Z = 3.04 (P = 0.002)



4.7 Sub group diabetes - Death (all causes)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Booth 2008 (SOS)	12	68	4	74	19.2%	3.26 [1.11, 9.64]
Henderson 1998 (RITA)	2	29	8	33	37.6%	0.28 [0.07, 1.23]
Serruys2005 (ARTS)	15	112	8	96	43.2%	1.61 [0.71, 3.63]
Total (95% CI)		**209**		**203**	**100.0%**	**1.43 [0.83, 2.47]**
Total events	29		20			

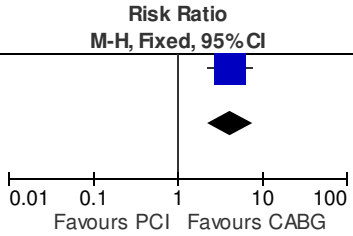
Heterogeneity: Chi² = 6.97, df = 2 (P = 0.03); I² = 71%
Test for overall effect: Z = 1.28 (P = 0.20)



4.8 Sub group diabetes- Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Serruys2005 (ARTS)	48	112	10	96	100.0%	4.11 [2.20, 7.68]
Total (95% CI)		**112**		**96**	**100.0%**	**4.11 [2.20, 7.68]**
Total events	48		10			

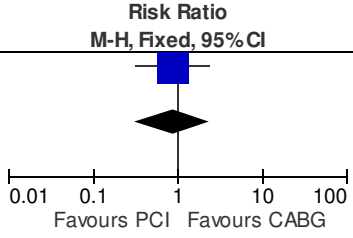
Heterogeneity: Not applicable
Test for overall effect: Z = 4.44 (P < 0.00001)



4.9 Sub group diabetes- stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Serruys2005 (ARTS)	7	112	7	96	100.0%	0.86 [0.31, 2.36]
Total (95% CI)		**112**		**96**	**100.0%**	**0.86 [0.31, 2.36]**
Total events	7		7			

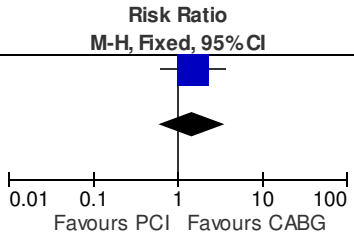
Heterogeneity: Not applicable
Test for overall effect: Z = 0.30 (P = 0.77)



4.10 Sub group diabetes- MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Serruys2005 (ARTS)	12	112	7	96	100.0%	1.47 [0.60, 3.58]
Total (95% CI)		**112**		**96**	**100.0%**	**1.47 [0.60, 3.58]**
Total events	12		7			

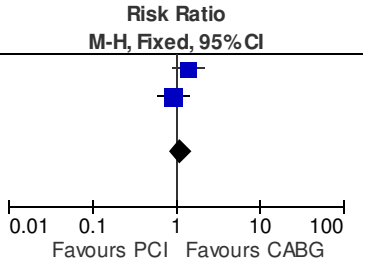
Heterogeneity: Not applicable
Test for overall effect: Z = 0.85 (P = 0.40)



4.11 Sub group-no diabetes -Death (all causes)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Booth 2008 (SOS)	41	420	30	426	44.5%	1.39 [0.88, 2.18]
Serruys2005 (ARTS)	33	488	38	509	55.5%	0.91 [0.58, 1.42]
Total (95% CI)		**908**		**935**	**100.0%**	**1.12 [0.82, 1.54]**
Total events	74		68			

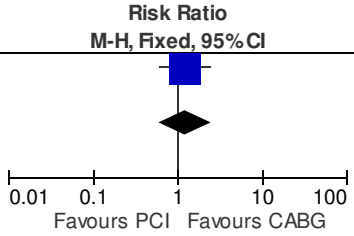
Heterogeneity: Chi² = 1.71, df = 1 (P = 0.19); I² = 42%
Test for overall effect: Z = 0.70 (P = 0.49)



4.12 Sub group no diabetes- stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Serruys2005 (ARTS)	16	488	14	509	100.0%	1.19 [0.59, 2.42]
Total (95% CI)		**488**		**509**	**100.0%**	**1.19 [0.59, 2.42]**
Total events	16		14			

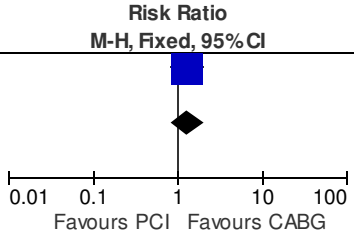
Heterogeneity: Not applicable
Test for overall effect: Z = 0.49 (P = 0.63)



4.13 Sub group no diabetes- MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Serruys2005 (ARTS)	38	488	31	509	100.0%	1.28 [0.81, 2.02]
Total (95% CI)		**488**		**509**	**100.0%**	**1.28 [0.81, 2.02]**
Total events	38		31			

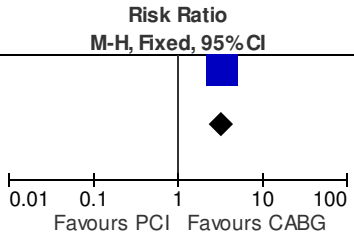
Heterogeneity: Not applicable
Test for overall effect: Z = 1.05 (P = 0.29)



4.14 Sub group no diabetes- Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Serruys2005 (ARTS)	134	488	43	509	100.0%	3.25 [2.36, 4.48]
Total (95% CI)		**488**		**509**	**100.0%**	**3.25 [2.36, 4.48]**
Total events	134		43			

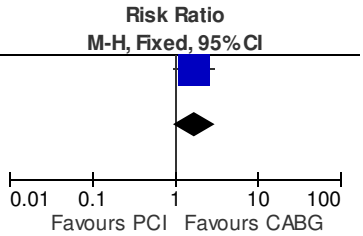
Heterogeneity: Not applicable
Test for overall effect: Z = 7.21 (P < 0.00001)



4.15 Sub group 2 vessel- Death

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Booth 2008 (SOS)	31	305	16	264	100.0%	1.68 [0.94, 3.00]
Total (95% CI)		**305**		**264**	**100.0%**	**1.68 [0.94, 3.00]**
Total events	31		16			

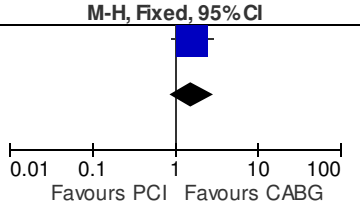
Heterogeneity: Not applicable
Test for overall effect: Z = 1.75 (P = 0.08)



4.16 Sub group 3 vessel -Death

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Booth 2008 (SOS)	22	183	18	236	100.0%	1.58 [0.87, 2.85]
Total (95% CI)		**183**		**236**	**100.0%**	**1.58 [0.87, 2.85]**
Total events	22		18			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.51 (P = 0.13)

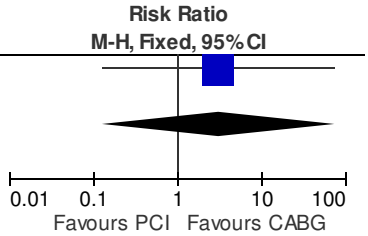


5 Single vessel disease - Short term follow-up (1 yr)

5.1 Death (all causes)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cisowski et al 2002	1	50	0	50	100.0%	3.00 [0.13, 71.92]
Total (95% CI)		**50**		**50**	**100.0%**	**3.00 [0.13, 71.92]**
Total events	1		0			

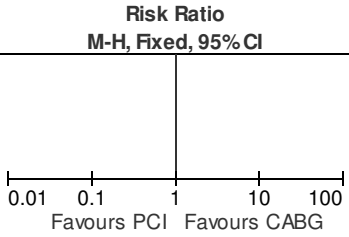
Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)



5.2 MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cisowski et al 2002	0	50	0	50		Not estimable
Total (95% CI)		**50**		**50**		**Not estimable**
Total events	0		0			

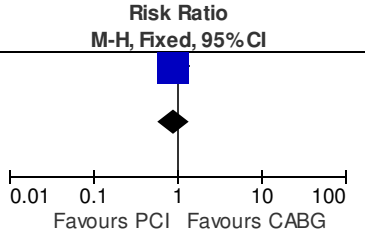
Heterogeneity: Not applicable
Test for overall effect: Not applicable



5.3 Free of angina

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cisowski et al 2002	21	50	24	50	100.0%	0.88 [0.57, 1.35]
Total (95% CI)		**50**		**50**	**100.0%**	**0.88 [0.57, 1.35]**
Total events	21		24			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.60 (P = 0.55)

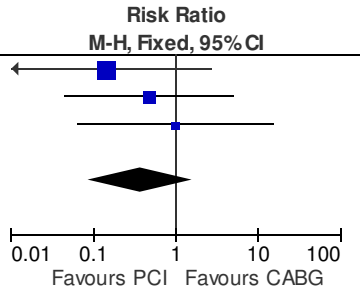


6 Single vessel disease - Medium term follow-up (>1-4 yrs)

6.1 Death (all causes)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Drenth et al 2004	0	51	3	51	53.3%	0.14 [0.01, 2.70]
Goy et al 2000 (SIMA)	1	62	2	59	31.2%	0.48 [0.04, 5.11]
Hueb 1995 (MASS-I)	1	72	1	70	15.4%	0.97 [0.06, 15.24]
Total (95% CI)		**185**		**180**	**100.0%**	**0.37 [0.09, 1.60]**
Total events	2		6			

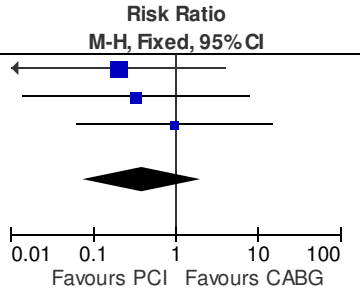
Heterogeneity: Chi² = 0.91, df = 2 (P = 0.63); I² = 0%
Test for overall effect: Z = 1.33 (P = 0.18)



6.2 Cardiac death

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Drenth et al 2004	0	51	2	51	49.5%	0.20 [0.01, 4.07]
Goy et al 1994	0	68	1	66	30.2%	0.32 [0.01, 7.81]
Goy et al 2000 (SIMA)	1	62	1	59	20.3%	0.95 [0.06, 14.87]
Total (95% CI)		**181**		**176**	**100.0%**	**0.39 [0.08, 2.00]**
Total events	1		4			

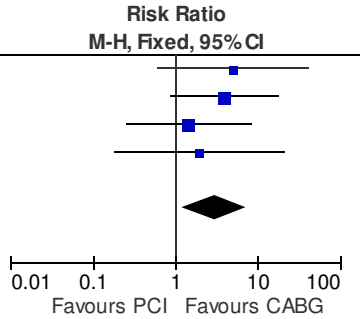
Heterogeneity: Chi² = 0.61, df = 2 (P = 0.74); I² = 0%
Test for overall effect: Z = 1.13 (P = 0.26)



6.3 MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Drenth et al 2004	5	51	1	51	16.4%	5.00 [0.61, 41.31]
Goy et al 1994	8	68	2	66	33.3%	3.88 [0.86, 17.61]
Goy et al 2000 (SIMA)	3	62	2	59	33.6%	1.43 [0.25, 8.24]
Hueb 1995 (MASS-I)	2	72	1	70	16.6%	1.94 [0.18, 20.96]
Total (95% CI)		**253**		**246**	**100.0%**	**2.92 [1.18, 7.21]**
Total events	18		6			

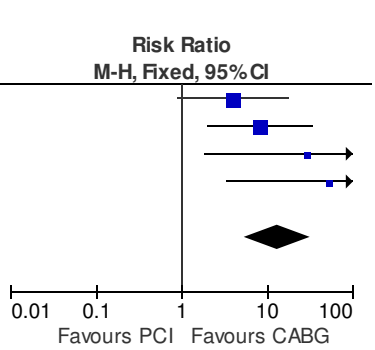
Heterogeneity: Chi² = 1.14, df = 3 (P = 0.77); I² = 0%
Test for overall effect: Z = 2.32 (P = 0.02)



6.4 Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Drenth et al 2004	8	51	2	51	39.6%	4.00 [0.89, 17.93]
Goy et al 1994	17	68	2	66	40.2%	8.25 [1.98, 34.32]
Goy et al 2000 (SIMA)	15	62	0	59	10.1%	29.52 [1.81, 482.55]
Hueb 1995 (MASS-I)	27	72	0	70	10.0%	53.49 [3.33, 860.32]
Total (95% CI)		**253**		**246**	**100.0%**	**13.27 [5.41, 32.51]**
Total events	67		4			

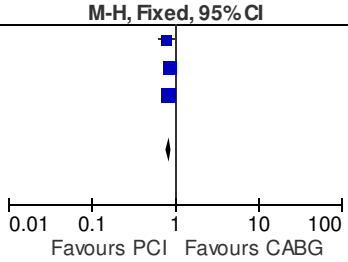
Heterogeneity: Chi² = 4.16, df = 3 (P = 0.24); I² = 28%
Test for overall effect: Z = 5.65 (P < 0.00001)



6.5 Free of angina

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Drenth et al 2004	34	51	41	48	24.7%	0.78 [0.62, 0.98]
Goy et al 1994	52	68	59	66	35.0%	0.86 [0.73, 1.00]
Hueb 1995 (MASS-I)	58	72	68	70	40.3%	0.83 [0.74, 0.94]
Total (95% CI)		**191**		**184**	**100.0%**	**0.83 [0.75, 0.91]**
Total events	144		168			

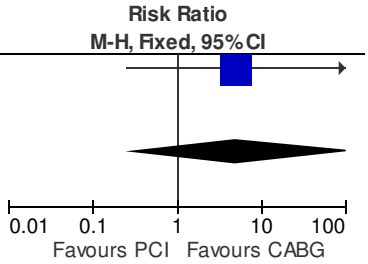
Heterogeneity: Chi² = 0.44, df = 2 (P = 0.80); I² = 0%
Test for overall effect: Z = 4.08 (P < 0.0001)



6.6 Stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Drenth et al 2004	2	51	0	51	100.0%	5.00 [0.25, 101.63]
Goy et al 2000 (SIMA)	0	62	0	59		Not estimable
Total (95% CI)		**113**		**110**	**100.0%**	**5.00 [0.25, 101.63]**
Total events	2		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.05 (P = 0.29)

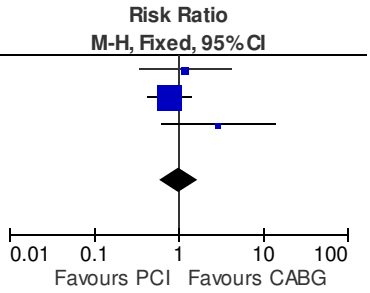


7 Single vessel disease - Long term follow-up (>5 yrs)

7.1 Death (all causes)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Goy 2008 (SIMA)	5	62	4	59	14.8%	1.19 [0.34, 4.22]
Henderson 1998 (RITA)	17	233	21	222	77.8%	0.77 [0.42, 1.42]
Hueb 1999 (MASS-I)	6	72	2	70	7.3%	2.92 [0.61, 13.97]
Total (95% CI)		**367**		**351**	**100.0%**	**0.99 [0.60, 1.65]**
Total events	28		27			

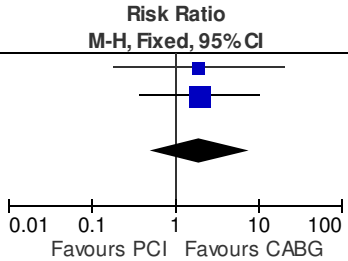
Heterogeneity: Chi² = 2.55, df = 2 (P = 0.28); I² = 22%
Test for overall effect: Z = 0.04 (P = 0.97)



7.2 Cardiac death

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Goy 2008 (SIMA)	2	62	1	59	33.6%	1.90 [0.18, 20.44]
Hueb 1999 (MASS-I)	4	72	2	70	66.4%	1.94 [0.37, 10.28]
Total (95% CI)		**134**		**129**	**100.0%**	**1.93 [0.49, 7.55]**
Total events	6		3			

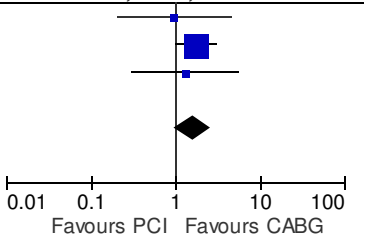
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.99); I² = 0%
Test for overall effect: Z = 0.95 (P = 0.34)



7.3 MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Goy 2008 (SIMA)	3	62	3	59	13.1%	0.95 [0.20, 4.53]
Henderson 1998 (RITA)	31	233	17	222	74.0%	1.74 [0.99, 3.05]
Hueb 1999 (MASS-I)	4	72	3	70	12.9%	1.30 [0.30, 5.58]
Total (95% CI)		**367**		**351**	**100.0%**	**1.58 [0.96, 2.59]**
Total events	38		23			

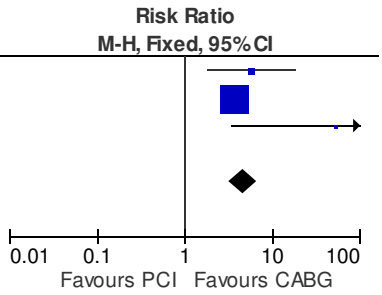
Heterogeneity: Chi² = 0.59, df = 2 (P = 0.75); I² = 0%
Test for overall effect: Z = 1.81 (P = 0.07)



7.4 Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Goy 2008 (SIMA)	18	62	3	59	9.2%	5.71 [1.77, 18.38]
Henderson 1998 (RITA)	111	233	29	222	89.2%	3.65 [2.53, 5.25]
Hueb 1999 (MASS-I)	27	72	0	70	1.5%	53.49 [3.33, 860.32]
Total (95% CI)		**367**		**351**	**100.0%**	**4.60 [3.25, 6.50]**
Total events	156		32			

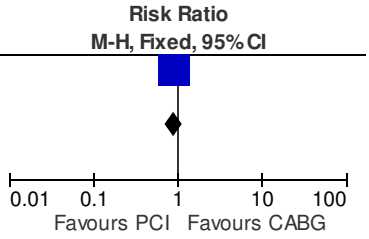
Heterogeneity: Chi² = 4.67, df = 2 (P = 0.10); I² = 57%
Test for overall effect: Z = 8.65 (P < 0.00001)



7.5 Free of angina

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hueb 1999 (MASS-I)	44	72	48	70	100.0%	0.89 [0.70, 1.14]
Total (95% CI)		**72**		**70**	**100.0%**	**0.89 [0.70, 1.14]**
Total events	44		48			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.93 (P = 0.35)

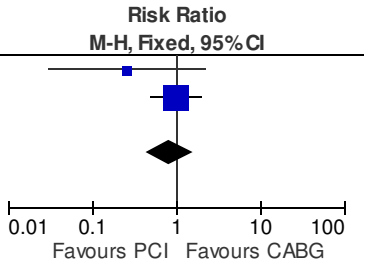


8 Left main coronary disease - Short term follow-up (1 yr)

8.1 Death

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Buszman 2008 (LE MANS)	1	52	4	53	20.7%	0.25 [0.03, 2.20]
Morice 2010 (SYNTAX)	15	357	15	348	79.3%	0.97 [0.48, 1.96]
Total (95% CI)		**409**		**401**	**100.0%**	**0.83 [0.43, 1.59]**
Total events	16		19			

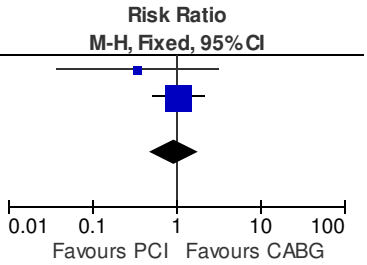
Heterogeneity: Chi² = 1.36, df = 1 (P = 0.24); I² = 26%
Test for overall effect: Z = 0.57 (P = 0.57)



8.2 non fatal MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Buszman 2008 (LE MANS)	1	52	3	53	17.3%	0.34 [0.04, 3.16]
Morice 2010 (SYNTAX)	15	357	14	348	82.7%	1.04 [0.51, 2.13]
Total (95% CI)		**409**		**401**	**100.0%**	**0.92 [0.47, 1.80]**
Total events	16		17			

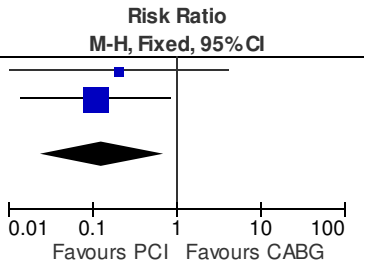
Heterogeneity: Chi² = 0.89, df = 1 (P = 0.35); I² = 0%
Test for overall effect: Z = 0.24 (P = 0.81)



8.3 Stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Buszman 2008 (LE MANS)	0	52	2	53	21.4%	0.20 [0.01, 4.14]
Morice 2010 (SYNTAX)	1	357	9	348	78.6%	0.11 [0.01, 0.85]
Total (95% CI)		**409**		**401**	**100.0%**	**0.13 [0.02, 0.70]**
Total events	1		11			

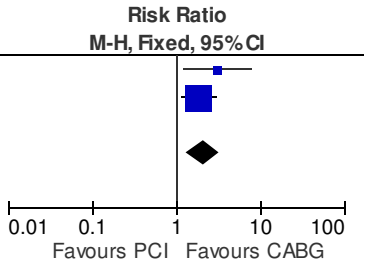
Heterogeneity: Chi² = 0.12, df = 1 (P = 0.73); I² = 0%
Test for overall effect: Z = 2.37 (P = 0.02)



8.4 Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Buszman 2008 (LE MANS)	15	52	5	53	17.5%	3.06 [1.20, 7.80]
Morice 2010 (SYNTAX)	43	357	23	348	82.5%	1.82 [1.12, 2.96]
Total (95% CI)		**409**		**401**	**100.0%**	**2.04 [1.33, 3.13]**
Total events	58		28			

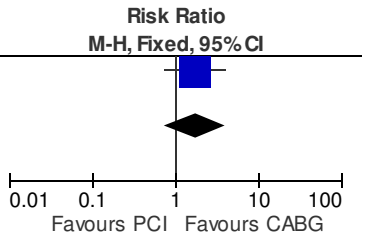
Heterogeneity: Chi² = 0.92, df = 1 (P = 0.34); I² = 0%
Test for overall effect: Z = 3.26 (P = 0.001)



8.5 Cardiac death

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Morice 2010 (SYNTAX)	14	357	8	348	100.0%	1.71 [0.72, 4.02]
Total (95% CI)		**357**		**348**	**100.0%**	**1.71 [0.72, 4.02]**
Total events	14		8			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.22 (P = 0.22)

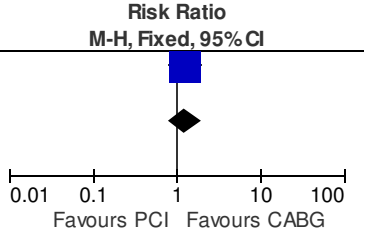


9 Left main coronary artery or 3 vessel disease -Short term follow-up (1yr)

9.1 Death (all causes)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Serruys 2009 (SYNTAX)	39	891	30	849	100.0%	1.24 [0.78, 1.98]
Total (95% CI)		**891**		**849**	**100.0%**	**1.24 [0.78, 1.98]**
Total events	39		30			

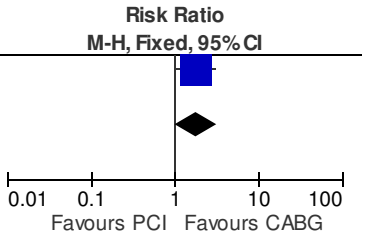
Heterogeneity: Not applicable
Test for overall effect: Z = 0.90 (P = 0.37)



9.2 cardiac mortality

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Serruys 2009 (SYNTAX)	33	891	18	849	100.0%	1.75 [0.99, 3.08]
Total (95% CI)		**891**		**849**	**100.0%**	**1.75 [0.99, 3.08]**
Total events	33		18			

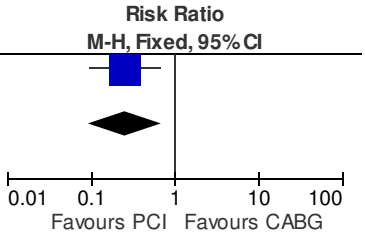
Heterogeneity: Not applicable
Test for overall effect: Z = 1.93 (P = 0.05)



9.3 Stroke

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Serruys 2009 (SYNTAX)	5	891	19	849	100.0%	0.25 [0.09, 0.67]
Total (95% CI)		**891**		**849**	**100.0%**	**0.25 [0.09, 0.67]**
Total events	5		19			

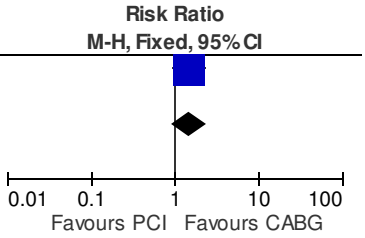
Heterogeneity: Not applicable
Test for overall effect: Z = 2.76 (P = 0.006)



9.4 MI

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Serruys 2009 (SYNTAX)	43	891	28	849	100.0%	1.46 [0.92, 2.33]
Total (95% CI)		**891**		**849**	**100.0%**	**1.46 [0.92, 2.33]**
Total events	43		28			

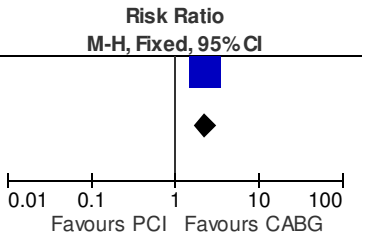
Heterogeneity: Not applicable
Test for overall effect: Z = 1.60 (P = 0.11)



9.5 Repeat revascularisation

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Serruys 2009 (SYNTAX)	120	891	50	849	100.0%	2.29 [1.67, 3.14]
Total (95% CI)		**891**		**849**	**100.0%**	**2.29 [1.67, 3.14]**
Total events	120		50			

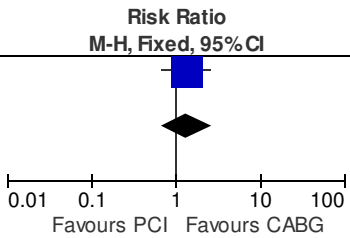
Heterogeneity: Not applicable
Test for overall effect: Z = 5.13 (P < 0.00001)



9.6 Sub group diabetes (Death)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Banning 2010 (SYNTAX)	19	227	13	204	100.0%	1.31 [0.67, 2.59]
Total (95% CI)		**227**		**204**	**100.0%**	**1.31 [0.67, 2.59]**
Total events	19		13			

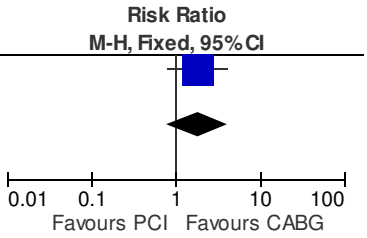
Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)



9.7 Sub group diabetes (cardiac death)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Banning 2010 (SYNTAX)	16	227	8	204	100.0%	1.80 [0.79, 4.11]
Total (95% CI)		**227**		**204**	**100.0%**	**1.80 [0.79, 4.11]**
Total events	16		8			

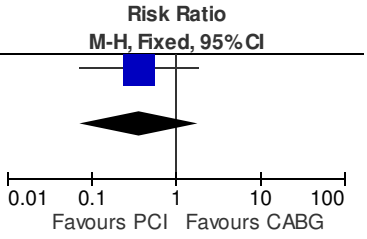
Heterogeneity: Not applicable
Test for overall effect: Z = 1.39 (P = 0.16)



9.8 Sub group diabetes (stroke)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Banning 2010 (SYNTAX)	2	227	5	204	100.0%	0.36 [0.07, 1.83]
Total (95% CI)		**227**		**204**	**100.0%**	**0.36 [0.07, 1.83]**
Total events	2		5			

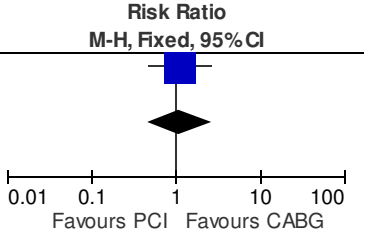
Heterogeneity: Not applicable
Test for overall effect: Z = 1.23 (P = 0.22)



9.9 Sub group diabetes (MI)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Banning 2010 (SYNTAX)	11	227	9	204	100.0%	1.10 [0.46, 2.60]
Total (95% CI)		**227**		**204**	**100.0%**	**1.10 [0.46, 2.60]**
Total events	11		9			

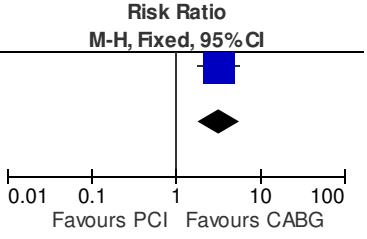
Heterogeneity: Not applicable
Test for overall effect: Z = 0.21 (P = 0.83)



9.10 Sub group diabetes (Repeat revascularisation)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Banning 2010 (SYNTAX)	46	227	13	204	100.0%	3.18 [1.77, 5.71]
Total (95% CI)		**227**		**204**	**100.0%**	**3.18 [1.77, 5.71]**
Total events	46		13			

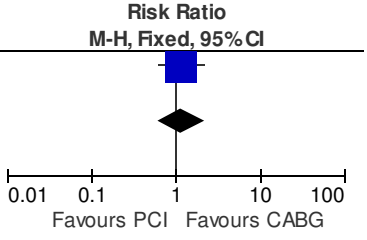
Heterogeneity: Not applicable
Test for overall effect: Z = 3.87 (P = 0.0001)



9.11 Sub group no diabetes (Death)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Banning 2010 (SYNTAX)	20	664	17	645	100.0%	1.14 [0.60, 2.16]
Total (95% CI)		**664**		**645**	**100.0%**	**1.14 [0.60, 2.16]**
Total events	20		17			

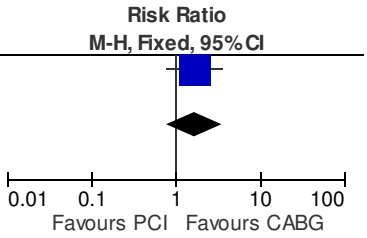
Heterogeneity: Not applicable
Test for overall effect: Z = 0.41 (P = 0.68)



9.12 Sub group no diabetes (no cardiac death)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Banning 2010 (SYNTAX)	17	664	10	645	100.0%	1.65 [0.76, 3.58]
Total (95% CI)		**664**		**645**	**100.0%**	**1.65 [0.76, 3.58]**
Total events	17		10			

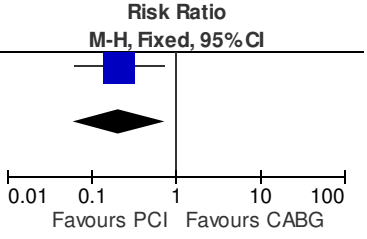
Heterogeneity: Not applicable
Test for overall effect: Z = 1.27 (P = 0.20)



9.13 Sub group no diabetes (stroke)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Banning 2010 (SYNTAX)	3	664	14	645	100.0%	0.21 [0.06, 0.72]
Total (95% CI)		**664**		**645**	**100.0%**	**0.21 [0.06, 0.72]**
Total events	3		14			

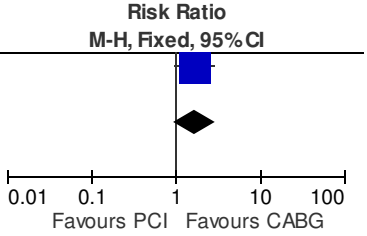
Heterogeneity: Not applicable
Test for overall effect: Z = 2.48 (P = 0.01)



9.14 Sub group no diabetes (MI)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Banning 2010 (SYNTAX)	32	664	19	645	100.0%	1.64 [0.94, 2.86]
Total (95% CI)		**664**		**645**	**100.0%**	**1.64 [0.94, 2.86]**
Total events	32		19			

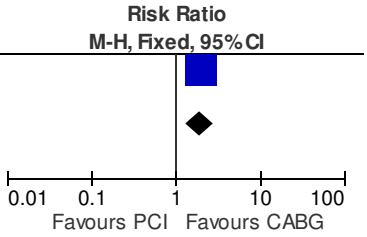
Heterogeneity: Not applicable
Test for overall effect: Z = 1.73 (P = 0.08)



9.15 Sub group no diabetes (Repeat revasc)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Banning 2010 (SYNTAX)	74	664	37	645	100.0%	1.94 [1.33, 2.84]
Total (95% CI)		**664**		**645**	**100.0%**	**1.94 [1.33, 2.84]**
Total events	74		37			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.43 (P = 0.0006)

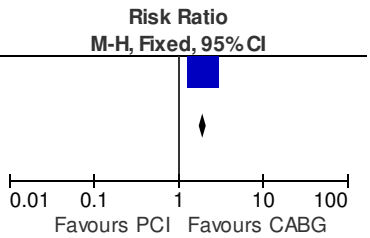


10 IPD meta analyses

10.1 Prevalance of angina

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hlatky et al 2009 (IPD)	856	3240	439	3228	100.0%	1.94 [1.75, 2.16]
Total (95% CI)		**3240**		**3228**	**100.0%**	**1.94 [1.75, 2.16]**
Total events	856		439			

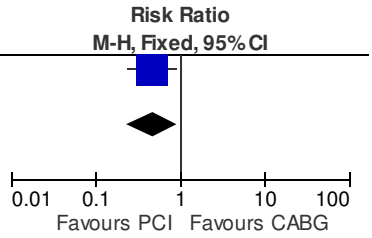
Heterogeneity: Not applicable
Test for overall effect: Z = 12.49 (P < 0.00001)



10.2 Stroke (90 days)

Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hlatky et al 2009 (IPD)	12	2269	26	2268	100.0%	0.46 [0.23, 0.91]
Total (95% CI)		**2269**		**2268**	**100.0%**	**0.46 [0.23, 0.91]**
Total events	12		26			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.22 (P = 0.03)

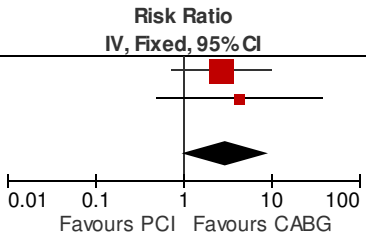


11 Sub group interaction

11.1 Age >65 yrs and age <65 yrs (Death) (Multi vessel short term)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis age <65 yrs	0.97077892	0.670909	73.3%	2.64 [0.71, 9.83]
meta analysis age >65 yrs	1.4632554	1.111739	26.7%	4.32 [0.49, 38.18]
Total (95% CI)			**100.0%**	**3.01 [0.98, 9.28]**

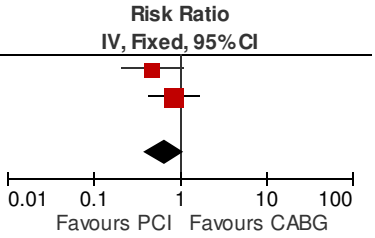
Heterogeneity: Chi² = 0.14, df = 1 (P = 0.70); I² = 0%
Test for overall effect: Z = 1.92 (P = 0.05)



11.2 Age >65 yrs and age <65 yrs (MI) (Multi vessel short term)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis age <65 yrs	-0.7550226	0.425435	41.1%	0.47 [0.20, 1.08]
meta analysis age >65 yrs	-0.1863296	0.355197	58.9%	0.83 [0.41, 1.67]
Total (95% CI)			**100.0%**	**0.66 [0.39, 1.12]**

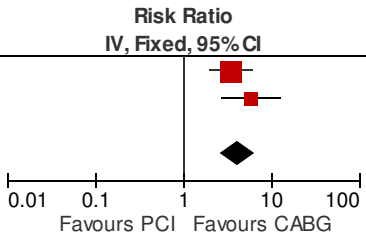
Heterogeneity: Chi² = 1.05, df = 1 (P = 0.30); I² = 5%
Test for overall effect: Z = 1.54 (P = 0.12)



11.3 Age >65 yrs and age <65 yrs (Repeat revasc) (Multi vessel short term)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis age <65 yrs	1.22082992	0.292853	65.0%	3.39 [1.91, 6.02]
meta analysis age >65 yrs	1.74046617	0.399178	35.0%	5.70 [2.61, 12.46]
Total (95% CI)			**100.0%**	**4.07 [2.56, 6.46]**

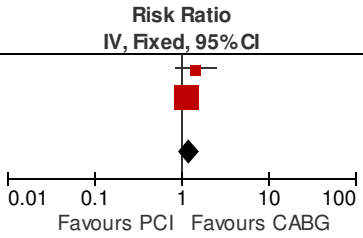
Heterogeneity: Chi² = 1.10, df = 1 (P = 0.29); I² = 9%
Test for overall effect: Z = 5.94 (P < 0.00001)



11.4 Diabetes and no diabetes (Death) (Multi vessel Long term)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis - diabetes	0.35767444	0.278201	25.0%	1.43 [0.83, 2.47]
meta analysis-no diabetes	0.11332869	0.160774	75.0%	1.12 [0.82, 1.53]
Total (95% CI)			**100.0%**	**1.19 [0.91, 1.56]**

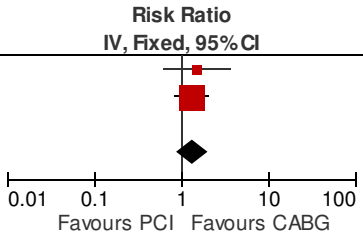
Heterogeneity: Chi² = 0.58, df = 1 (P = 0.45); I² = 0%
Test for overall effect: Z = 1.25 (P = 0.21)



11.5 Diabetes and no diabetes (MI) (Multi vessel long term)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis - diabetes	0.3852624	0.45566	20.7%	1.47 [0.60, 3.59]
meta analysis-no diabetes	0.24686008	0.233117	79.3%	1.28 [0.81, 2.02]
Total (95% CI)			**100.0%**	**1.32 [0.88, 1.98]**

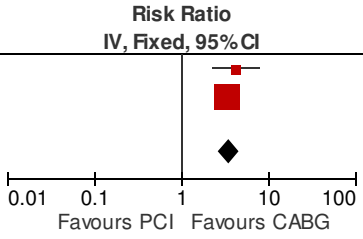
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.79); I² = 0%
Test for overall effect: Z = 1.33 (P = 0.18)



11.6 Diabetes and no diabetes (Repeat revasc) (Multi vessel long term)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis - diabetes	1.41342303	0.318919	20.8%	4.11 [2.20, 7.68]
meta analysis-no diabetes	1.178655	0.163511	79.2%	3.25 [2.36, 4.48]
Total (95% CI)			**100.0%**	**3.41 [2.57, 4.54]**

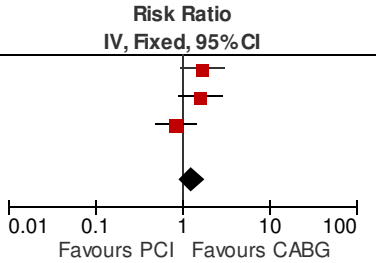
Heterogeneity: Chi² = 0.43, df = 1 (P = 0.51); I² = 0%
Test for overall effect: Z = 8.44 (P < 0.00001)



11.7 Single, 2 vessel and 3 vessel (Death) (long term)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis - 2 vessel	0.51879379	0.296043	32.7%	1.68 [0.94, 3.00]
meta analysis -3 vessel	0.45742485	0.302699	31.3%	1.58 [0.87, 2.86]
meta analysis -single ves	-0.1743534	0.282024	36.0%	0.84 [0.48, 1.46]
Total (95% CI)			**100.0%**	**1.28 [0.92, 1.79]**

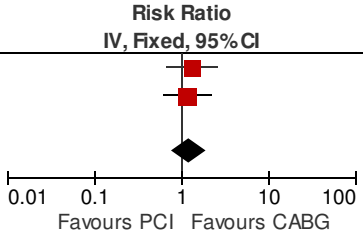
Heterogeneity: Chi² = 3.56, df = 2 (P = 0.17); I² = 44%
Test for overall effect: Z = 1.48 (P = 0.14)



11.8 Diabetes and no diabetes (Death) (LMD or 3 vessel-short term)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis - diabetes	0.27002714	0.344933	47.3%	1.31 [0.67, 2.58]
meta analysis-no diabetes	0.13102826	0.326769	52.7%	1.14 [0.60, 2.16]
Total (95% CI)			**100.0%**	**1.22 [0.76, 1.94]**

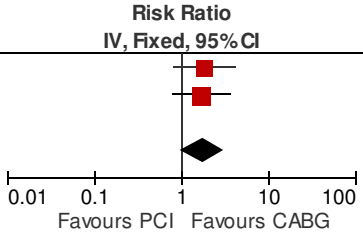
Heterogeneity: Chi² = 0.09, df = 1 (P = 0.77); I² = 0%
Test for overall effect: Z = 0.83 (P = 0.41)



11.9 Diabetes and no diabetes (cardiac Death) (LMD or 3 ves sel -s

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis - diabetes	0.58778666	0.4207	46.9%	1.80 [0.79, 4.11]
meta analysis-no diabetes	0.50077529	0.395357	53.1%	1.65 [0.76, 3.58]
Total (95% CI)			**100.0%**	**1.72 [0.98, 3.02]**

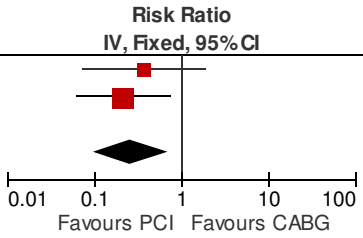
Heterogeneity: Chi² = 0.02, df = 1 (P = 0.88); I² = 0%
Test for overall effect: Z = 1.88 (P = 0.06)



11.10 Diabetes and no diabetes (stroke) (LMD or 3 vessel short term)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis - diabetes	-1.0216512	0.832545	36.7%	0.36 [0.07, 1.84]
meta analysis-no diabetes	-1.5606477	0.633905	63.3%	0.21 [0.06, 0.73]
Total (95% CI)			**100.0%**	**0.26 [0.10, 0.69]**

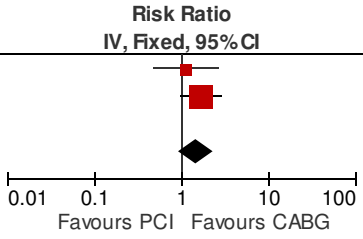
Heterogeneity: Chi² = 0.27, df = 1 (P = 0.61); I² = 0%
Test for overall effect: Z = 2.70 (P = 0.007)



11.11 Diabetes and no diabetes (MI) (LMD or 3 vessel short term)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis - diabetes	0.09531018	0.441847	29.2%	1.10 [0.46, 2.62]
meta analysis-no diabetes	0.49469624	0.283851	70.8%	1.64 [0.94, 2.86]
Total (95% CI)			**100.0%**	**1.46 [0.91, 2.33]**

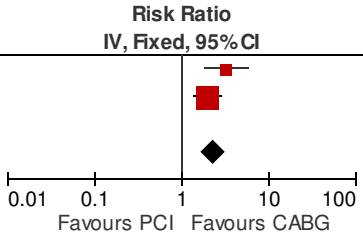
Heterogeneity: Chi² = 0.58, df = 1 (P = 0.45); I² = 0%
Test for overall effect: Z = 1.58 (P = 0.11)



11.12 Diabetes and no diabetes (repeat revasc) (LMD or 3 vessel short term)

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
meta analysis - diabetes	1.1568812	0.298786	29.6%	3.18 [1.77, 5.71]
meta analysis-no diabetes	0.66268797	0.193527	70.4%	1.94 [1.33, 2.83]
Total (95% CI)			**100.0%**	**2.25 [1.63, 3.09]**

Heterogeneity: Chi² = 1.93, df = 1 (P = 0.17); I² = 48%
Test for overall effect: Z = 4.98 (P < 0.00001)

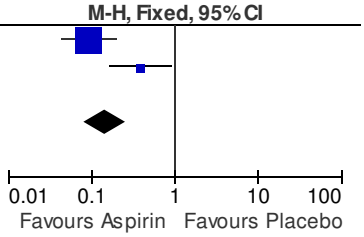


1 Aspirin vs. Placebo

1.1 Non fatal MI (follow-up 50-60 months)

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Moller 1992 (SAPAT trial)	7	1009	78	1026	81.9%	0.09 [0.04, 0.20]
Ridker 1991	7	178	16	155	18.1%	0.38 [0.16, 0.90]
Total (95% CI)		**1187**		**1181**	**100.0%**	**0.14 [0.08, 0.25]**
Total events	14		94			

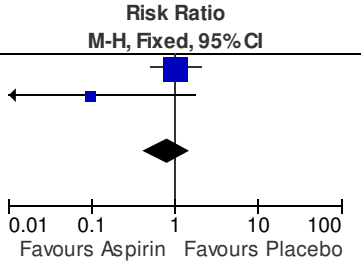
Heterogeneity: Chi² = 6.26, df = 1 (P = 0.01); I² = 84%
Test for overall effect: Z = 6.76 (P < 0.00001)



1.2 Fatal MI (follow-up 50-60 months)

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Moller 1992 (SAPAT trial)	15	1009	15	1026	75.6%	1.02 [0.50, 2.07]
Ridker 1991	0	178	4	155	24.4%	0.10 [0.01, 1.78]
Total (95% CI)		**1187**		**1181**	**100.0%**	**0.79 [0.41, 1.53]**
Total events	15		19			

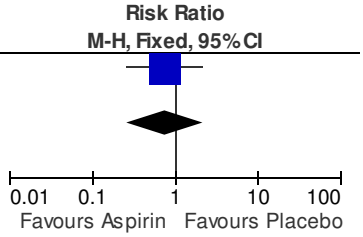
Heterogeneity: Chi² = 2.47, df = 1 (P = 0.12); I² = 60%
Test for overall effect: Z = 0.70 (P = 0.49)



1.3 Cardiovascular death (follow-up 60.2 months)

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ridker 1991	6	178	7	155	100.0%	0.75 [0.26, 2.17]
Total (95% CI)		**178**		**155**	**100.0%**	**0.75 [0.26, 2.17]**
Total events	6		7			

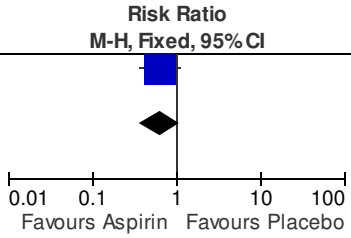
Heterogeneity: Not applicable
Test for overall effect: Z = 0.54 (P = 0.59)



1.4 Sudden death (follow-up median 50 months)

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Moller 1992 (SAPAT trial)	19	1009	31	1026	100.0%	0.62 [0.35, 1.10]
Total (95% CI)		**1009**		**1026**	**100.0%**	**0.62 [0.35, 1.10]**
Total events	19		31			

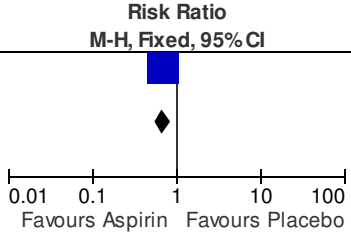
Heterogeneity: Not applicable
Test for overall effect: Z = 1.64 (P = 0.10)



1.5 Vascular events (follow-up median 50 months)

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Moller 1992 (SAPAT trial)	108	1009	161	1026	100.0%	0.68 [0.54, 0.86]
Total (95% CI)		**1009**		**1026**	**100.0%**	**0.68 [0.54, 0.86]**
Total events	108		161			

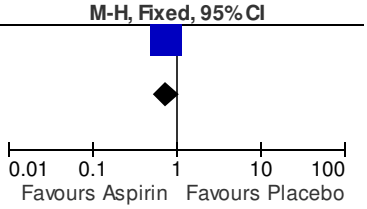
Heterogeneity: Not applicable
Test for overall effect: Z = 3.29 (P = 0.0010)



1.6 Vascular deaths (follow-up median 50 months)

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Moller 1992 (SAPAT trial)	51	1009	70	1026	100.0%	0.74 [0.52, 1.05]
Total (95% CI)		**1009**		**1026**	**100.0%**	**0.74 [0.52, 1.05]**
Total events	51		70			

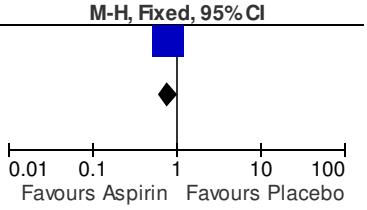
Heterogeneity: Not applicable
Test for overall effect: Z = 1.68 (P = 0.09)



1.7 All cause mortality (follow-up median 50 months)

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Moller 1992 (SAPAT trial)	82	1009	106	1026	100.0%	0.79 [0.60, 1.04]
Total (95% CI)		**1009**		**1026**	**100.0%**	**0.79 [0.60, 1.04]**
Total events	82		106			

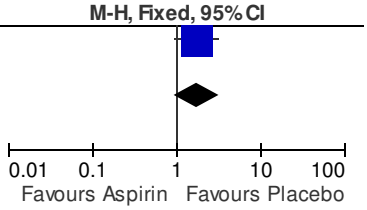
Heterogeneity: Not applicable
Test for overall effect: Z = 1.71 (P = 0.09)



1.8 Haemorrhagic adverse events (follow-up median 50 months)

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Moller 1992 (SAPAT trial)	27	1009	16	1026	100.0%	1.72 [0.93, 3.17]
Total (95% CI)		**1009**		**1026**	**100.0%**	**1.72 [0.93, 3.17]**
Total events	27		16			

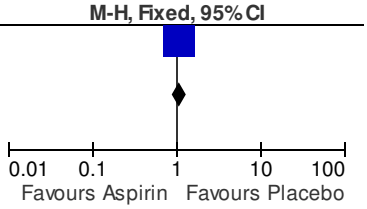
Heterogeneity: Not applicable
Test for overall effect: Z = 1.73 (P = 0.08)



1.9 Non haemorrhagic adverse events (follow-up median 50 months)

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Moller 1992 (SAPAT trial)	174	1009	168	1026	100.0%	1.05 [0.87, 1.28]
Total (95% CI)		**1009**		**1026**	**100.0%**	**1.05 [0.87, 1.28]**
Total events	174		168			

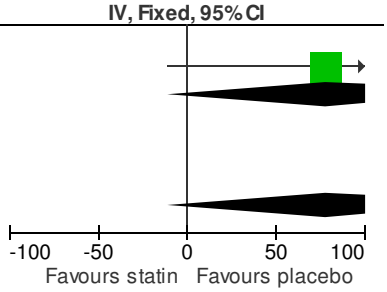
Heterogeneity: Not applicable
Test for overall effect: Z = 0.53 (P = 0.60)



1 Statins vs. Placebo

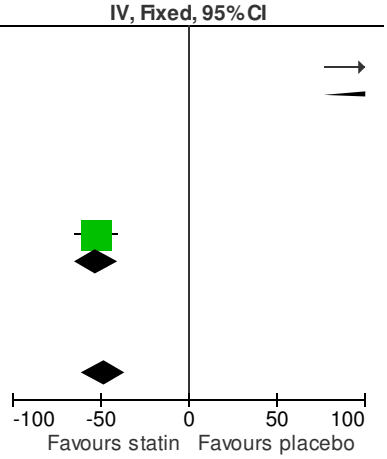
1.1 Total exercise time (Sec)

Study or Subgroup	Statin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 Pravastatin vs. placebo								
Kayikcioglu 2005	585	165	19	507	110	19	100.0%	78.00 [-11.17, 167.17]
Subtotal (95% CI)			**19**			**19**	**100.0%**	**78.00 [-11.17, 167.17]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.71 (P = 0.09)								
Total (95% CI)			**19**			**19**	**100.0%**	**78.00 [-11.17, 167.17]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.71 (P = 0.09)								
Test for subgroup differences: Not applicable								



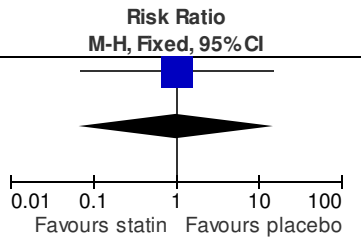
1.2 Time to 1mm ST depression (Sec)

Study or Subgroup	Statin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.2.1 Pravastatin vs. Placebo								
Kayikcioglu 2005	419	162	19	256	102	19	2.1%	163.00 [76.92, 249.08]
Subtotal (95% CI)			**19**			**19**	**2.1%**	**163.00 [76.92, 249.08]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.71 (P = 0.0002)								
1.2.2 Simvastatin vs. Placebo								
Fabian 2004	267	23.4	20	319.8	16.2	20	97.9%	-52.80 [-65.27, -40.33]
Subtotal (95% CI)			**20**			**20**	**97.9%**	**-52.80 [-65.27, -40.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 8.30 (P < 0.00001)								
Total (95% CI)			**39**			**39**	**100.0%**	**-48.36 [-60.71, -36.02]**
Heterogeneity: Chi² = 23.65, df = 1 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 7.68 (P < 0.00001)								
Test for subgroup differences: Chi² = 23.65, df = 1 (P < 0.00001), I² = 95.8%								



1.3 Hospitalisation for worsening of angina

Study or Subgroup	Statin Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kayikcioglu 2005	1	19	1	19	100.0%	1.00 [0.07, 14.85]
Total (95% CI)		**19**		**19**	**100.0%**	**1.00 [0.07, 14.85]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						

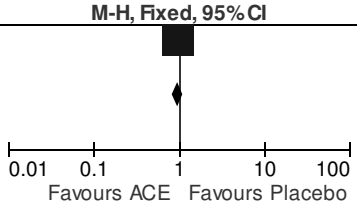


1 ACE +background medication vs. Placebo +background medication

1.1 Combined (death from cv causes or non fatal MI)

Study or Subgroup	ACE Events	ACE Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Braunwald 2004(PEACE)	344	4158	352	4132	100.0%	0.97 [0.84, 1.12]
Total (95% CI)		**4158**		**4132**	**100.0%**	**0.97 [0.84, 1.12]**
Total events	344		352			

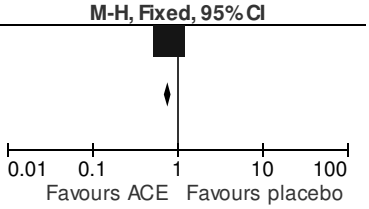
Heterogeneity: Not applicable
Test for overall effect: Z = 0.40 (P = 0.69)



1.2 Combined (MI, stroke, or death from CV causes)

Study or Subgroup	ACE Events	ACE Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yusuf 2000 (HOPE trial)	651	4645	826	4652	100.0%	0.79 [0.72, 0.87]
Total (95% CI)		**4645**		**4652**	**100.0%**	**0.79 [0.72, 0.87]**
Total events	651		826			

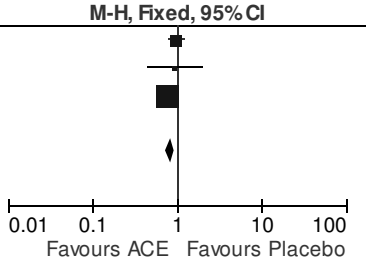
Heterogeneity: Not applicable
Test for overall effect: Z = 4.92 (P < 0.00001)



1.3 Death from cardio vascular causes

Study or Subgroup	ACE Events	ACE Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Braunwald 2004(PEACE)	146	4158	152	4132	28.1%	0.95 [0.76, 1.19]
Pitt 2001 (QUIET)	13	878	14	872	2.6%	0.92 [0.44, 1.95]
Yusuf 2000 (HOPE trial)	282	4645	377	4652	69.3%	0.75 [0.65, 0.87]
Total (95% CI)		**9681**		**9656**	**100.0%**	**0.81 [0.72, 0.92]**
Total events	441		543			

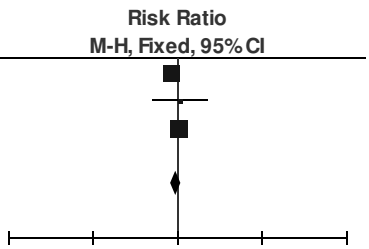
Heterogeneity: $Chi^2 = 3.26$, df = 2 (P = 0.20); $I^2 = 39\%$
Test for overall effect: Z = 3.36 (P = 0.0008)



1.4 Death from non cardiovascular or unknown causes

Study or Subgroup	ACE Events	ACE Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Braunwald 2004(PEACE)	153	4158	182	4132	47.1%	0.84 [0.68, 1.03]
Pitt 2001 (QUIET)	14	878	13	872	3.4%	1.07 [0.51, 2.26]
Yusuf 2000 (HOPE trial)	200	4645	192	4652	49.5%	1.04 [0.86, 1.27]
Total (95% CI)		**9681**		**9656**	**100.0%**	**0.95 [0.82, 1.09]**
Total events	367		387			

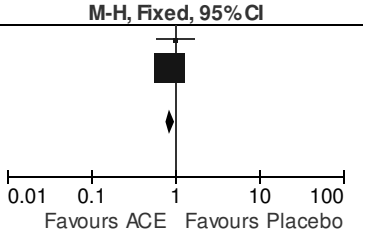
Heterogeneity: $Chi^2 = 2.42$, df = 2 (P = 0.30); $I^2 = 17\%$
Test for overall effect: Z = 0.77 (P = 0.44)



1.5 All causes death

Study or Subgroup	ACE Events	ACE Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pitt 2001 (QUIET)	27	878	27	872	4.5%	0.99 [0.59, 1.68]
Yusuf 2000 (HOPE trial)	482	4645	569	4652	95.5%	0.85 [0.76, 0.95]
Total (95% CI)		**5523**		**5524**	**100.0%**	**0.85 [0.76, 0.96]**
Total events	509		596			

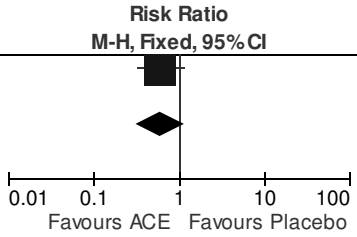
Heterogeneity: Chi² = 0.33, df = 1 (P = 0.57); I² = 0%
Test for overall effect: Z = 2.75 (P = 0.006)



1.6 Death from CHF

Study or Subgroup	ACE Events	ACE Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Braunwald 2004(PEACE)	15	4158	25	4132	100.0%	0.60 [0.31, 1.13]
Total (95% CI)		**4158**		**4132**	**100.0%**	**0.60 [0.31, 1.13]**
Total events	15		25			

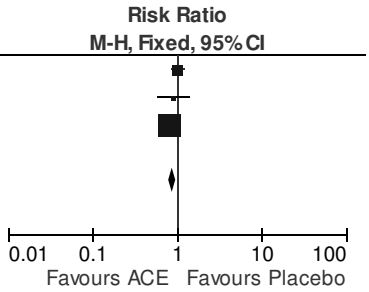
Heterogeneity: Not applicable
Test for overall effect: Z = 1.59 (P = 0.11)



1.7 Non fatal MI (MI in HOPE trial)

Study or Subgroup	ACE Events	ACE Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Braunwald 2004(PEACE)	222	4158	220	4132	26.6%	1.00 [0.84, 1.20]
Pitt 2001 (QUIET)	36	878	40	872	4.8%	0.89 [0.58, 1.39]
Yusuf 2000 (HOPE trial)	459	4645	570	4652	68.6%	0.81 [0.72, 0.91]
Total (95% CI)		**9681**		**9656**	**100.0%**	**0.86 [0.78, 0.95]**
Total events	717		830			

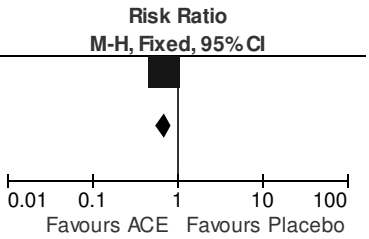
Heterogeneity: Chi² = 3.96, df = 2 (P = 0.14); I² = 50%
Test for overall effect: Z = 3.03 (P = 0.002)



1.8 Stroke

Study or Subgroup	ACE Events	ACE Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yusuf 2000 (HOPE trial)	156	4645	226	4652	100.0%	0.69 [0.57, 0.84]
Total (95% CI)		**4645**		**4652**	**100.0%**	**0.69 [0.57, 0.84]**
Total events	156		226			

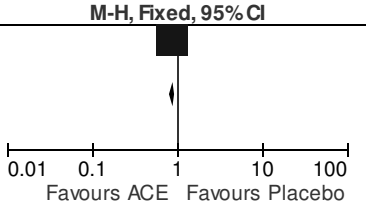
Heterogeneity: Not applicable
Test for overall effect: Z = 3.62 (P = 0.0003)



1.9 Revascularisation

Study or Subgroup	ACE Events	ACE Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yusuf 2000 (HOPE trial)	742	4645	852	4652	100.0%	0.87 [0.80, 0.95]
Total (95% CI)		**4645**		**4652**	**100.0%**	**0.87 [0.80, 0.95]**
Total events	742		852			

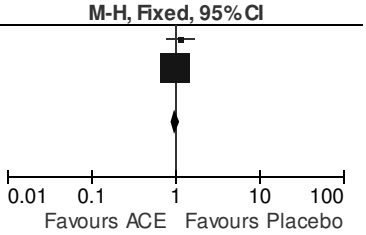
Heterogeneity: Not applicable
Test for overall effect: Z = 2.99 (P = 0.003)



1.10 Hospitalised with unstable angina

Study or Subgroup	ACE Events	ACE Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pitt 2001 (QUIET)	52	878	45	872	7.4%	1.15 [0.78, 1.69]
Yusuf 2000 (HOPE trial)	554	4645	565	4652	92.6%	0.98 [0.88, 1.10]
Total (95% CI)		**5523**		**5524**	**100.0%**	**0.99 [0.89, 1.11]**
Total events	606		610			

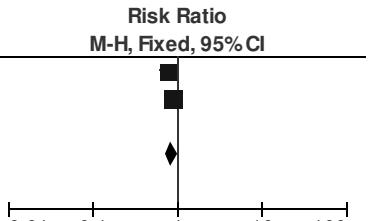
Heterogeneity: Chi² = 0.57, df = 1 (P = 0.45); I² = 0%
Test for overall effect: Z = 0.11 (P = 0.92)



1.11 Hospitalisation due to CHF

Study or Subgroup	ACE Events	ACE Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Braunwald 2004(PEACE)	105	4158	134	4132	45.7%	0.78 [0.61, 1.00]
Yusuf 2000 (HOPE trial)	141	4645	160	4652	54.3%	0.88 [0.71, 1.10]
Total (95% CI)		**8803**		**8784**	**100.0%**	**0.84 [0.71, 0.99]**
Total events	246		294			

Heterogeneity: Chi² = 0.53, df = 1 (P = 0.47); I² = 0%
Test for overall effect: Z = 2.12 (P = 0.03)

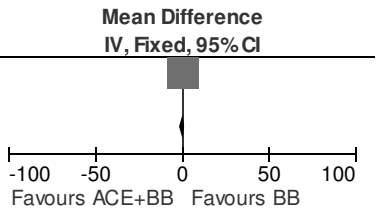


2 ACE+BB vs. BB

2.1 Exercise time (min)

Study or Subgroup	ACE Mean	ACE SD	ACE Total	BB Mean	BB SD	BB Total	Weight	Mean Difference IV, Fixed, 95% CI
Klein 1990	9.6	2.35	23	9.4	2.35	23	100.0%	0.20 [-1.16, 1.56]
Total (95% CI)			**23**			**23**	**100.0%**	**0.20 [-1.16, 1.56]**

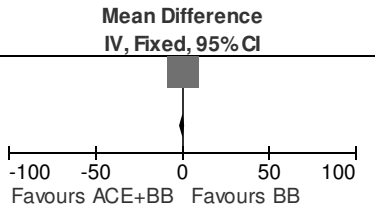
Heterogeneity: Not applicable
Test for overall effect: Z = 0.29 (P = 0.77)



2.2 Time to 1mm ST segment depression (min)

Study or Subgroup	ACE Mean	ACE SD	ACE Total	BB Mean	BB SD	BB Total	Weight	Mean Difference IV, Fixed, 95% CI
Klein 1990	8.1	2.82	23	7.9	2.35	23	100.0%	0.20 [-1.30, 1.70]
Total (95% CI)			**23**			**23**	**100.0%**	**0.20 [-1.30, 1.70]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.26 (P = 0.79)

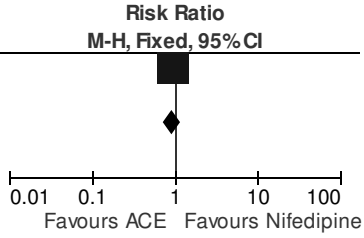


3 ACE +background medication vs. Nifedipine + background medication

3.1 Combined Cardiac events

Study or Subgroup	ACE Events	ACE Total	Nifedipine Events	Nifedipine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	106	822	116	828	100.0%	0.92 [0.72, 1.18]
Total (95% CI)		**822**		**828**	**100.0%**	**0.92 [0.72, 1.18]**
Total events	106		116			

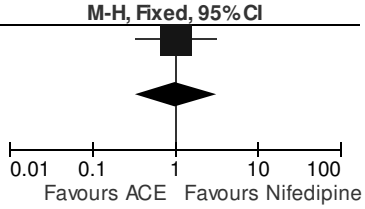
Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)



3.2 sudden death or cardiac death

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	6	822	6	828	100.0%	1.01 [0.33, 3.11]
Total (95% CI)		**822**		**828**	**100.0%**	**1.01 [0.33, 3.11]**
Total events	6		6			

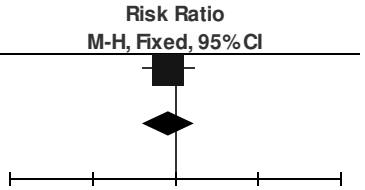
Heterogeneity: Not applicable
Test for overall effect: Z = 0.01 (P = 0.99)



3.3 MI

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	13	822	16	828	100.0%	0.82 [0.40, 1.69]
Total (95% CI)		**822**		**828**	**100.0%**	**0.82 [0.40, 1.69]**
Total events	13		16			

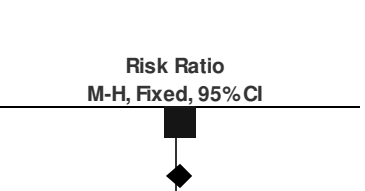
Heterogeneity: Not applicable
Test for overall effect: Z = 0.54 (P = 0.59)



3.4 Hospitalisation for angina pectoris

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	56	822	50	828	100.0%	1.13 [0.78, 1.63]
Total (95% CI)		**822**		**828**	**100.0%**	**1.13 [0.78, 1.63]**
Total events	56		50			

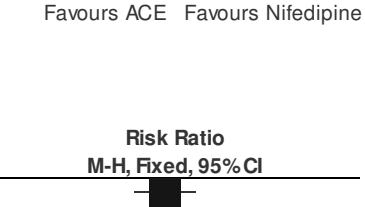
Heterogeneity: Not applicable
Test for overall effect: Z = 0.64 (P = 0.52)



3.5 Hospitalisation for HF

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	9	822	12	828	100.0%	0.76 [0.32, 1.78]
Total (95% CI)		**822**		**828**	**100.0%**	**0.76 [0.32, 1.78]**
Total events	9		12			

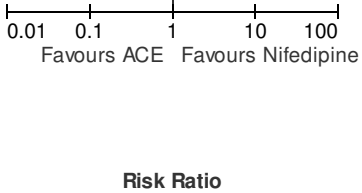
Heterogeneity: Not applicable
Test for overall effect: Z = 0.64 (P = 0.52)



3.6 Non cardiac death

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	9	822	6	828	100.0%	1.51 [0.54, 4.23]
Total (95% CI)		**822**		**828**	**100.0%**	**1.51 [0.54, 4.23]**
Total events	9		6			

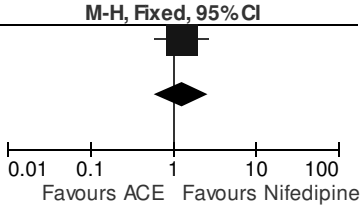
Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)



3.7 Total mortality

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	15	822	12	828	100.0%	1.26 [0.59, 2.67]
Total (95% CI)		**822**		**828**	**100.0%**	**1.26 [0.59, 2.67]**
Total events	15		12			

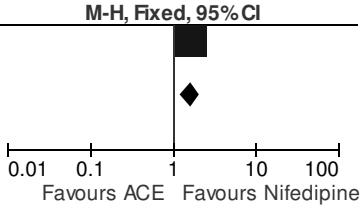
Heterogeneity: Not applicable
Test for overall effect: Z = 0.60 (P = 0.55)



3.8 Adverse events

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	121	822	76	828	100.0%	1.60 [1.22, 2.10]
Total (95% CI)		**822**		**828**	**100.0%**	**1.60 [1.22, 2.10]**
Total events	121		76			

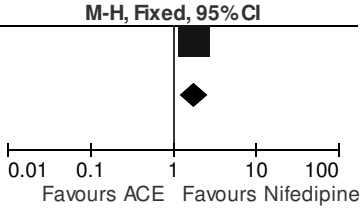
Heterogeneity: Not applicable
Test for overall effect: Z = 3.43 (P = 0.0006)



3.9 Withdrawal due to adverse effects

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	72	822	41	828	100.0%	1.77 [1.22, 2.56]
Total (95% CI)		**822**		**828**	**100.0%**	**1.77 [1.22, 2.56]**
Total events	72		41			

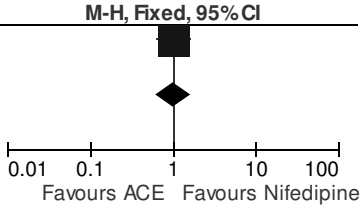
Heterogeneity: Not applicable
Test for overall effect: Z = 3.01 (P = 0.003)



3.10 Diabetes sub group (combined cardiac events)

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	26	173	30	199	100.0%	1.00 [0.61, 1.62]
Total (95% CI)		**173**		**199**	**100.0%**	**1.00 [0.61, 1.62]**
Total events	26		30			

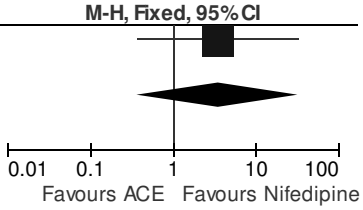
Heterogeneity: Not applicable
Test for overall effect: Z = 0.01 (P = 0.99)



3.11 Diabetes sub group (cardiac death or sudden death)

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	3	173	1	199	100.0%	3.45 [0.36, 32.87]
Total (95% CI)		**173**		**199**	**100.0%**	**3.45 [0.36, 32.87]**
Total events	3		1			

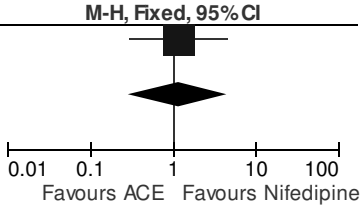
Heterogeneity: Not applicable
Test for overall effect: Z = 1.08 (P = 0.28)



3.12 Diabetes sub group (MI)

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	4	173	4	199	100.0%	1.15 [0.29, 4.53]
Total (95% CI)		**173**		**199**	**100.0%**	**1.15 [0.29, 4.53]**
Total events	4		4			

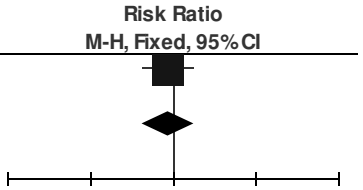
Heterogeneity: Not applicable
Test for overall effect: Z = 0.20 (P = 0.84)



3.13 Diabetes sub group (hospitalisation for angina pectoris)

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	12	173	16	199	100.0%	0.86 [0.42, 1.77]
Total (95% CI)		**173**		**199**	**100.0%**	**0.86 [0.42, 1.77]**
Total events	12		16			

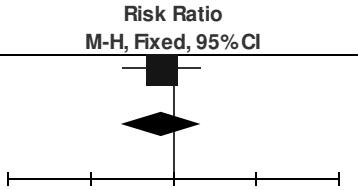
Heterogeneity: Not applicable
Test for overall effect: Z = 0.40 (P = 0.69)



3.14 Diabetes sub group (Hospitalisation for HF)

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	5	173	8	199	100.0%	0.72 [0.24, 2.16]
Total (95% CI)		**173**		**199**	**100.0%**	**0.72 [0.24, 2.16]**
Total events	5		8			

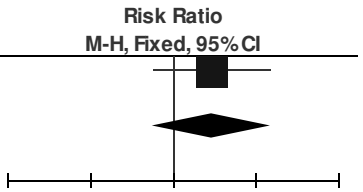
Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)



3.15 Diabetes sub group (Total mortality)

Study or Subgroup	ACE Events	Total	Nifedipine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Yui 2004 (JMIC-B)	5	173	2	199	100.0%	2.88 [0.57, 14.64]
Total (95% CI)		**173**		**199**	**100.0%**	**2.88 [0.57, 14.64]**
Total events	5		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.27 (P = 0.20)

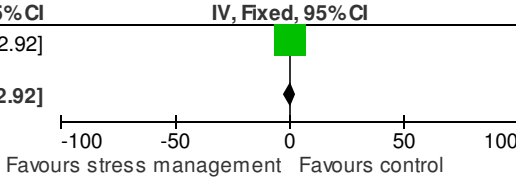


1 Stress management vs. routine care control

1.1 Frequency of angina (average no. of. daily attacks) (8 weeks)

Study or Subgroup	stress management Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bundy 1998	7.4	4.7	42	7.4	5.2	16	100.0%	0.00 [-2.92, 2.92]
Total (95% CI)			**42**			**16**	**100.0%**	**0.00 [-2.92, 2.92]**

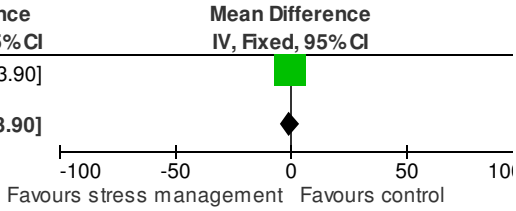
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



1.2 Average duration of angina per attack (mins) (8 weeks)

Study or Subgroup	stress management Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bundy 1998	11	7.4	42	11.4	7.5	16	100.0%	-0.40 [-4.70, 3.90]
Total (95% CI)			**42**			**16**	**100.0%**	**-0.40 [-4.70, 3.90]**

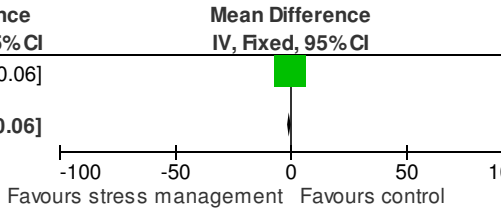
Heterogeneity: Not applicable
Test for overall effect: Z = 0.18 (P = 0.86)



1.3 Frequency of chest pain at rest (days per fortnight) (6 months)

Study or Subgroup	stress management Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Gallacher 1997	1.83	2.92	158	2.42	3.19	179	100.0%	-0.59 [-1.24, 0.06]
Total (95% CI)			**158**			**179**	**100.0%**	**-0.59 [-1.24, 0.06]**

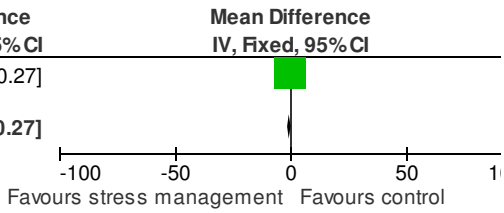
Heterogeneity: Not applicable
Test for overall effect: Z = 1.77 (P = 0.08)



1.4 Frequency of chest pain on exertion (days per fortnight) (6 months)

Study or Subgroup	stress management Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Gallacher 1997	3.42	3.71	158	3.96	3.86	179	100.0%	-0.54 [-1.35, 0.27]
Total (95% CI)			**158**			**179**	**100.0%**	**-0.54 [-1.35, 0.27]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.31 (P = 0.19)

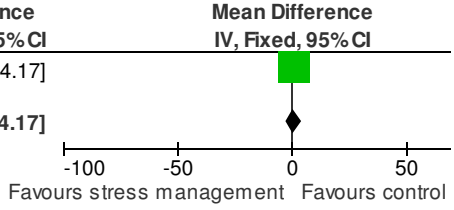


2 Stress management + exercise vs. routine care control (8 weeks)

2.1 Frequency of angina (average no. of daily attacks

Study or Subgroup	stress management+exerc Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bundy 1998	8	5.7	20	7.4	5.2	16	100.0%	0.60 [-2.97, 4.17]
Total (95% CI)			**20**			**16**	**100.0%**	**0.60 [-2.97, 4.17]**

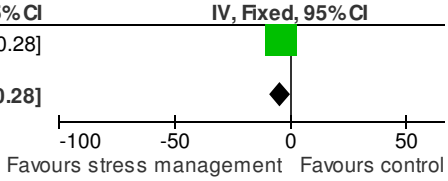
Heterogeneity: Not applicable
Test for overall effect: Z = 0.33 (P = 0.74)



2.2 Duration of angina (min)

Study or Subgroup	stress management+exerc Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bundy 1998	7	6.6	20	11.4	7.5	16	100.0%	-4.40 [-9.08, 0.28]
Total (95% CI)			**20**			**16**	**100.0%**	**-4.40 [-9.08, 0.28]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.84 (P = 0.07)

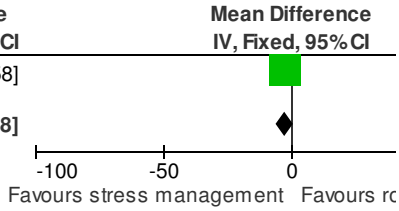


3 Stress management + exercise vs. routine care (8 weeks) (change scores)

3.1 Frequency of angina

Study or Subgroup	Stress management +exerci Mean	SD	Total	routine care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bundy 1994	4.3	3	14	7	5.7	15	100.0%	-2.70 [-5.98, 0.58]
Total (95% CI)			**14**			**15**	**100.0%**	**-2.70 [-5.98, 0.58]**

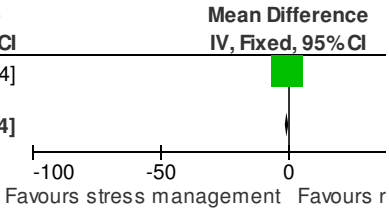
Heterogeneity: Not applicable
Test for overall effect: Z = 1.61 (P = 0.11)



3.2 Duration of angina

Study or Subgroup	Stress management +exerci Mean	SD	Total	routine care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bundy 1994	1.2	0.5	14	1.9	0.5	15	100.0%	-0.70 [-1.06, -0.34]
Total (95% CI)			**14**			**15**	**100.0%**	**-0.70 [-1.06, -0.34]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.77 (P = 0.0002)

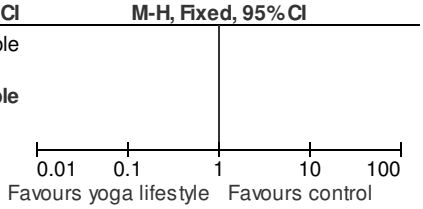


4 Yoga life style intervention programme vs. Control (1 year)

4.1 Mortality

Study or Subgroup	Yoga life style Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Manchanda 2000	0	21	0	21		Not estimable
Total (95% CI)		**21**		**21**		**Not estimable**
Total events	0		0			

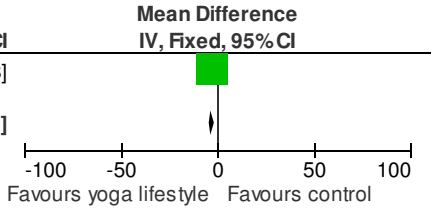
Heterogeneity: Not applicable
Test for overall effect: Not applicable



4.2 Angina episodes per week

Study or Subgroup	Yoga life style Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Manchanda 2000	2.1	2.7	21	5.4	2.3	21	100.0%	-3.30 [-4.82, -1.78]
Total (95% CI)			**21**			**21**	**100.0%**	**-3.30 [-4.82, -1.78]**

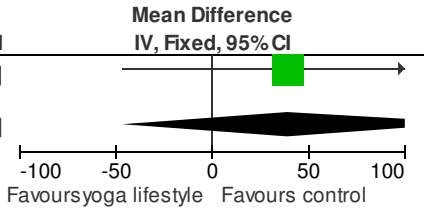
Heterogeneity: Not applicable
Test for overall effect: Z = 4.26 (P < 0.0001)



4.3 Exercise duration (sec)

Study or Subgroup	Yoga life style Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Manchanda 2000	413	132	21	374	151	21	100.0%	39.00 [-46.78, 124.78]
Total (95% CI)			**21**			**21**	**100.0%**	**39.00 [-46.78, 124.78]**

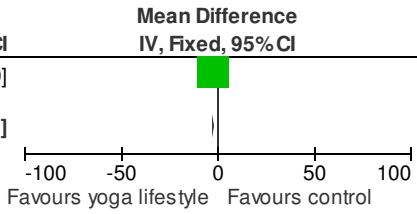
Heterogeneity: Not applicable
Test for overall effect: Z = 0.89 (P = 0.37)



4.4 ST segment depression (mm)

Study or Subgroup	Yoga life style Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Manchanda 2000	0.18	0.8	21	2.7	0.6	21	100.0%	-2.52 [-2.95, -2.09]
Total (95% CI)			**21**			**21**	**100.0%**	**-2.52 [-2.95, -2.09]**

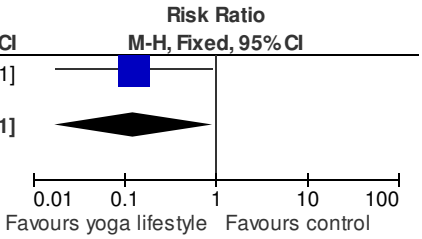
Heterogeneity: Not applicable
Test for overall effect: Z = 11.55 (P < 0.00001)



4.5 Revascularisation

Study or Subgroup	Yoga life style Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Manchanda 2000	1	21	8	21	100.0%	0.13 [0.02, 0.91]
Total (95% CI)		**21**		**21**	**100.0%**	**0.13 [0.02, 0.91]**
Total events	1		8			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.05 (P = 0.04)

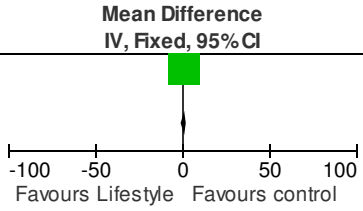


5 Intensive lifestyle programme vs. control (5 years)

5.1 Angina frequency (times per week)

Study or Subgroup	lifestyle programme Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ornish 1998	1.6	2.7	18	0.9	1.9	14	100.0%	0.70 [-0.90, 2.30]
Total (95% CI)			**18**			**14**	**100.0%**	**0.70 [-0.90, 2.30]**

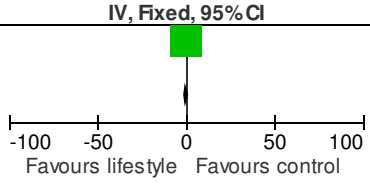
Heterogeneity: Not applicable
Test for overall effect: Z = 0.86 (P = 0.39)



5.2 chest pain duration (min)

Study or Subgroup	lifestyle programme Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ornish 1998	0.9	1.3	18	1	2.7	14	100.0%	-0.10 [-1.64, 1.44]
Total (95% CI)			**18**			**14**	**100.0%**	**-0.10 [-1.64, 1.44]**

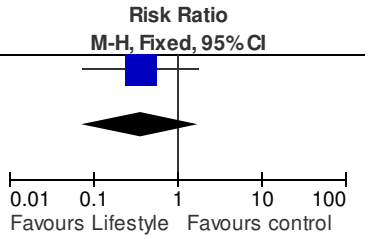
Heterogeneity: Not applicable
Test for overall effect: Z = 0.13 (P = 0.90)



5.3 MI

Study or Subgroup	lifestyle programme Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ornish 1998	2	28	4	20	100.0%	0.36 [0.07, 1.76]
Total (95% CI)		**28**		**20**	**100.0%**	**0.36 [0.07, 1.76]**
Total events	2		4			

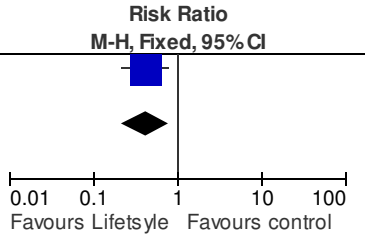
Heterogeneity: Not applicable
Test for overall effect: Z = 1.26 (P = 0.21)



5.4 PTCA

Study or Subgroup	lifestyle programme Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ornish 1998	8	28	14	20	100.0%	0.41 [0.21, 0.78]
Total (95% CI)		**28**		**20**	**100.0%**	**0.41 [0.21, 0.78]**
Total events	8		14			

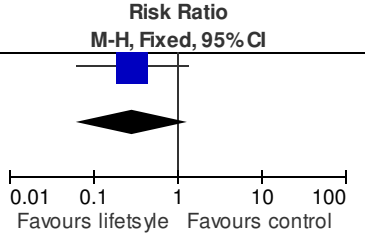
Heterogeneity: Not applicable
Test for overall effect: Z = 2.69 (P = 0.007)



5.5 CABG

Study or Subgroup	lifestyle programme Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ornish 1998	2	28	5	20	100.0%	0.29 [0.06, 1.33]
Total (95% CI)		**28**		**20**	**100.0%**	**0.29 [0.06, 1.33]**
Total events	2		5			

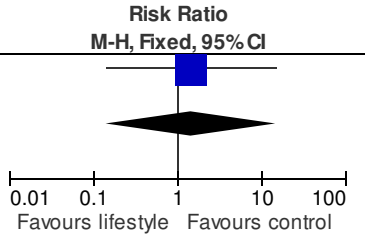
Heterogeneity: Not applicable
Test for overall effect: Z = 1.60 (P = 0.11)



5.6 Death

Study or Subgroup	lifestyle programme Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ornish 1998	2	28	1	20	100.0%	1.43 [0.14, 14.70]
Total (95% CI)		**28**		**20**	**100.0%**	**1.43 [0.14, 14.70]**
Total events	2		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.30 (P = 0.76)

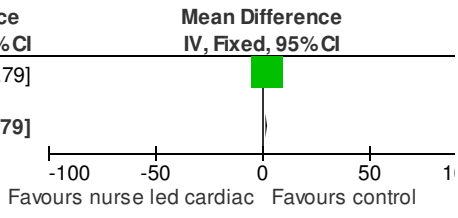


6 Nurse led cardiac rehab vs. routine care (6 months)

6.1 Walking performance (Jenkins activity checklist for walking)

Study or Subgroup	nurse led cardiac rehab Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Jiang 2007	10.63	2.13	83	8.62	2.98	84	100.0%	2.01 [1.23, 2.79]
Total (95% CI)			**83**			**84**	**100.0%**	**2.01 [1.23, 2.79]**

Heterogeneity: Not applicable
Test for overall effect: Z = 5.02 (P < 0.00001)

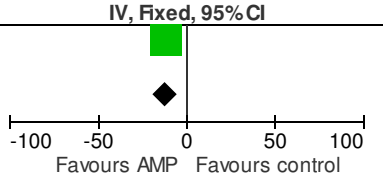


7 Angina management programme (AMP) vs. control (at the end of 8 week treatment period)

7.1 Mean no. of Episodes of angina per week

Study or Subgroup	AMP Mean	AMP SD	AMP Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 1995 (AMP)	4.5	5.7	34	16.6	17.8	31	100.0%	-12.10 [-18.65, -5.55]
Total (95% CI)			**34**			**31**	**100.0%**	**-12.10 [-18.65, -5.55]**

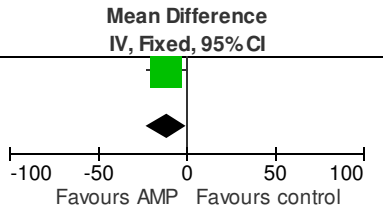
Heterogeneity: Not applicable
Test for overall effect: Z = 3.62 (P = 0.0003)



7.2 Severity of angina (self rated out of 100 with scores being worse)

Study or Subgroup	AMP Mean	AMP SD	AMP Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 1995 (AMP)	21.2	21.8	34	32.9	24.6	31	100.0%	-11.70 [-23.04, -0.36]
Total (95% CI)			**34**			**31**	**100.0%**	**-11.70 [-23.04, -0.36]**

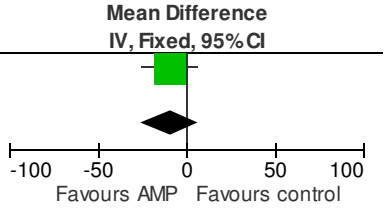
Heterogeneity: Not applicable
Test for overall effect: Z = 2.02 (P = 0.04)



7.3 Duration of angina (mins)

Study or Subgroup	AMP Mean	AMP SD	AMP Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 1995 (AMP)	16.3	23.8	34	26	39.7	31	100.0%	-9.70 [-25.80, 6.40]
Total (95% CI)			**34**			**31**	**100.0%**	**-9.70 [-25.80, 6.40]**

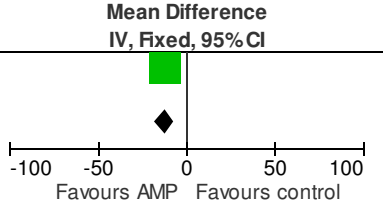
Heterogeneity: Not applicable
Test for overall effect: Z = 1.18 (P = 0.24)



7.4 Disability (Sickness Impact Profile) (100 being completely medically dependent and 0 indicating no measurable impairment)

Study or Subgroup	AMP Mean	AMP SD	AMP Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 1995 (AMP)	6.8	6.3	34	19.5	12.9	31	100.0%	-12.70 [-17.71, -7.69]
Total (95% CI)			**34**			**31**	**100.0%**	**-12.70 [-17.71, -7.69]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.97 (P < 0.00001)

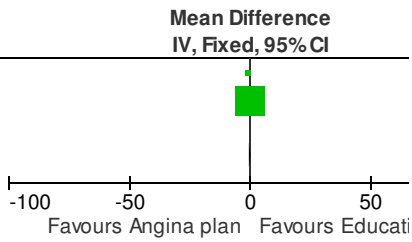


8 Angina Plan vs. Education session (6 months) (all of the outcomes below report change scores)

8.1 Anxiety (HAD scale) (scores between 8 and 10 indicate bordeline presence of anxiety)

Study or Subgroup	Angina Plan Mean	Angina Plan SD	Angina Plan Total	Education session Mean	Education session SD	Education session Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 2002 (Angina plan)	-1.03	2.61	68	0	3.07	74	5.9%	-1.03 [-1.96, -0.10]
Zetta 2009 (Angina Plan)	-0.35	0.92	109	-0.24	0.84	109	94.1%	-0.11 [-0.34, 0.12]
Total (95% CI)			**177**			**183**	**100.0%**	**-0.16 [-0.39, 0.06]**

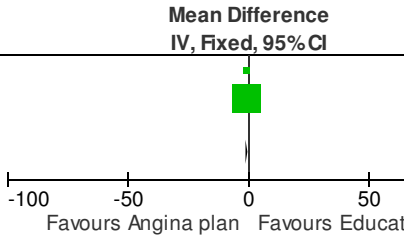
Heterogeneity: Chi² = 3.50, df = 1 (P = 0.06); I² = 71%
Test for overall effect: Z = 1.42 (P = 0.16)



8.2 Depression (HAD scale) (scores between 8 and 10 indicate borderline presence of depression)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 2002 (Angina plan)	-0.48	1.89	68	0.41	2.1	74	9.9%	-0.89 [-1.55, -0.23]
Zetta 2009 (Angina Plan)	-0.07	0.87	109	0.79	0.77	109	90.1%	-0.86 [-1.08, -0.64]
Total (95% CI)			**177**			**183**	**100.0%**	**-0.86 [-1.07, -0.66]**

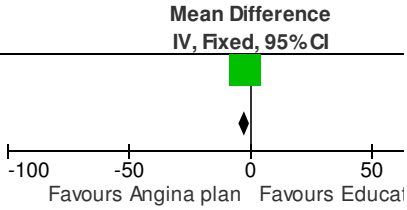
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.93); I² = 0%
Test for overall effect: Z = 8.17 (P < 0.00001)



8.3 Angina attacks per week

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 2002 (Angina plan)	-2.98	5.54	68	-0.41	5.97	74	100.0%	-2.57 [-4.46, -0.68]
Total (95% CI)			**68**			**74**	**100.0%**	**-2.57 [-4.46, -0.68]**

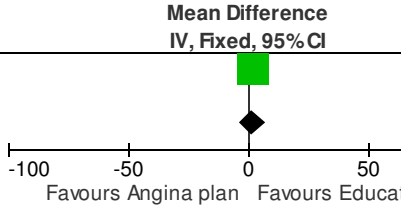
Heterogeneity: Not applicable
Test for overall effect: Z = 2.66 (P = 0.008)



8.4 Mean pain score

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 2002 (Angina plan)	-1.69	14.78	68	-3.48	17.35	74	100.0%	1.79 [-3.50, 7.08]
Total (95% CI)			**68**			**74**	**100.0%**	**1.79 [-3.50, 7.08]**

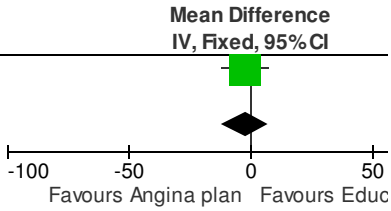
Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)



8.5 Mean duration of pain

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 2002 (Angina plan)	-9.21	34.87	68	-6.78	22.98	74	100.0%	-2.43 [-12.23, 7.37]
Total (95% CI)			**68**			**74**	**100.0%**	**-2.43 [-12.23, 7.37]**

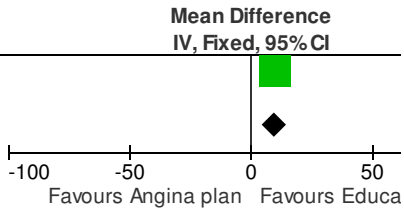
Heterogeneity: Not applicable
Test for overall effect: Z = 0.49 (P = 0.63)



8.6 Physical limitation (Seattle Angina questionnaire) (0 to 100 scale with higher scores indicating better functioning)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 2002 (Angina plan)	8.42	16.07	68	-1.43	14.24	74	100.0%	9.85 [4.84, 14.86]
Total (95% CI)			**68**			**74**	**100.0%**	**9.85 [4.84, 14.86]**

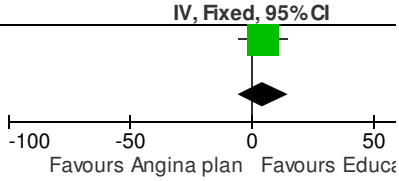
Heterogeneity: Not applicable
Test for overall effect: Z = 3.85 (P = 0.0001)



8.7 Angina stability (Seattle Angina questionnaire)(0 to 100 scale with higher scores indicating better functioning)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 2002 (Angina plan)	8.73	31.48	68	4.17	29.93	74	100.0%	4.56 [-5.56, 14.68]
Total (95% CI)			**68**			**74**	**100.0%**	**4.56 [-5.56, 14.68]**

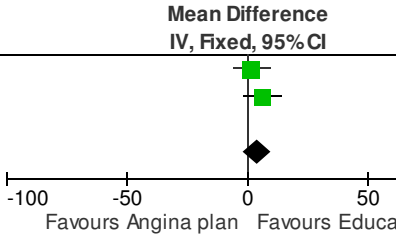
Heterogeneity: Not applicable
Test for overall effect: Z = 0.88 (P = 0.38)



8.8 Angina frequency (Seattle Angina questionnaire)(0 to 100 scale with higher scores indicating better functioning)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 2002 (Angina plan)	5.71	23.54	68	4.24	24.06	74	51.2%	1.47 [-6.36, 9.30]
Zetta 2009 (Angina Plan)	24.54	31.29	109	18.33	29.11	109	48.8%	6.21 [-1.81, 14.23]
Total (95% CI)			**177**			**183**	**100.0%**	**3.78 [-1.82, 9.39]**

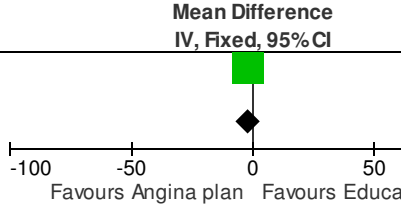
Heterogeneity: Chi² = 0.69, df = 1 (P = 0.41); I² = 0%
Test for overall effect: Z = 1.32 (P = 0.19)



8.9 Treatment satisfaction (Seattle Angina questionnaire)(0 to 100 scale with higher scores indicating better functioning)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 2002 (Angina plan)	0.81	16.82	68	2.75	13.52	74	100.0%	-1.94 [-6.99, 3.11]
Total (95% CI)			**68**			**74**	**100.0%**	**-1.94 [-6.99, 3.11]**

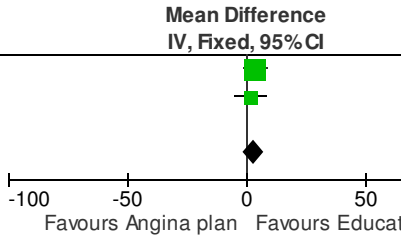
Heterogeneity: Not applicable
Test for overall effect: Z = 0.75 (P = 0.45)



8.10 Disease perception (Seattle Angina questionnaire)(0 to 100 scale with higher scores indicating better functioning)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lewin 2002 (Angina plan)	7.8	14.35	68	4.29	16.94	74	63.4%	3.51 [-1.64, 8.66]
Zetta 2009 (Angina Plan)	21.16	28.2	109	19.43	22.51	109	36.6%	1.73 [-5.04, 8.50]
Total (95% CI)			**177**			**183**	**100.0%**	**2.86 [-1.24, 6.96]**

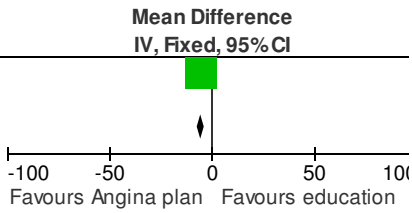
Heterogeneity: Chi² = 0.17, df = 1 (P = 0.68); I² = 0%
Test for overall effect: Z = 1.37 (P = 0.17)



8.11 Misconceptions/knowledge

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Zetta 2009 (Angina Plan)	-7.51	7.76	109	-2.01	6.39	109	100.0%	-5.50 [-7.39, -3.61]
Total (95% CI)			**109**			**109**	**100.0%**	**-5.50 [-7.39, -3.61]**

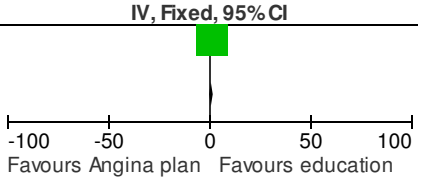
Heterogeneity: Not applicable
Test for overall effect: Z = 5.71 (P < 0.00001)



8.12 CLASP angina

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Zetta 2009 (Angina Plan)	-1.64	2.87	109	-2.44	3.23	109	100.0%	0.80 [-0.01, 1.61]
Total (95% CI)			**109**			**109**	**100.0%**	**0.80 [-0.01, 1.61]**

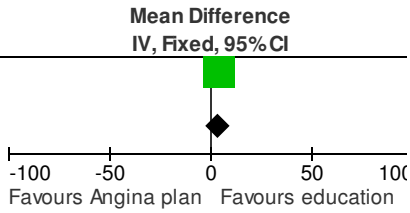
Heterogeneity: Not applicable
Test for overall effect: Z = 1.93 (P = 0.05)



8.13 Physical function (SF-36) (scores between 0 to 100 with higher scores representing better health status)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Zetta 2009 (Angina Plan)	3.69	21.77	109	0.02	23.22	109	100.0%	3.67 [-2.31, 9.65]
Total (95% CI)			**109**			**109**	**100.0%**	**3.67 [-2.31, 9.65]**

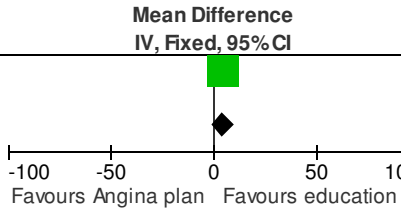
Heterogeneity: Not applicable
Test for overall effect: Z = 1.20 (P = 0.23)



8.14 Energy and and vitality (SF-36)(scores between 0 to 100 with higher scores representing better health status)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Zetta 2009 (Angina Plan)	5.82	20.35	109	1.3	21.34	109	100.0%	4.52 [-1.02, 10.06]
Total (95% CI)			**109**			**109**	**100.0%**	**4.52 [-1.02, 10.06]**

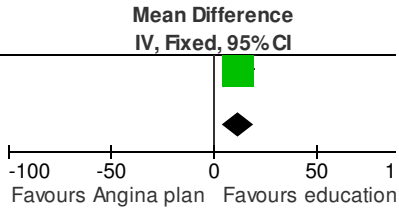
Heterogeneity: Not applicable
Test for overall effect: Z = 1.60 (P = 0.11)



8.15 Pain (SF-36)(scores between 0 to 100 with higher scores representing better health status)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Zetta 2009 (Angina Plan)	11.89	27.75	109	0.02	31.15	109	100.0%	11.87 [4.04, 19.70]
Total (95% CI)			**109**			**109**	**100.0%**	**11.87 [4.04, 19.70]**

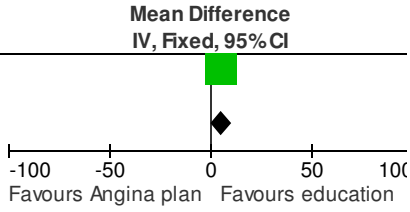
Heterogeneity: Not applicable
Test for overall effect: Z = 2.97 (P = 0.003)



8.16 GH perception (SF-36)(scores between 0 to 100 with higher scores representing better health status)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Zetta 2009 (Angina Plan)	6.37	16.74	109	1.34	20.1	109	100.0%	5.03 [0.12, 9.94]
Total (95% CI)			**109**			**109**	**100.0%**	**5.03 [0.12, 9.94]**

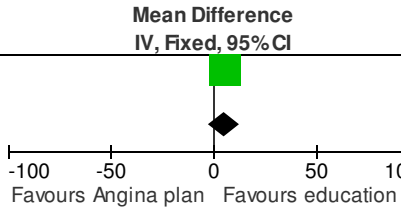
Heterogeneity: Not applicable
Test for overall effect: Z = 2.01 (P = 0.04)



8.17 Change in health (SF-36)(scores between 0 to 100 with higher scores representing better health status)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Zetta 2009 (Angina Plan)	15.24	27.19	109	9.99	31.2	109	100.0%	5.25 [-2.52, 13.02]
Total (95% CI)			**109**			**109**	**100.0%**	**5.25 [-2.52, 13.02]**

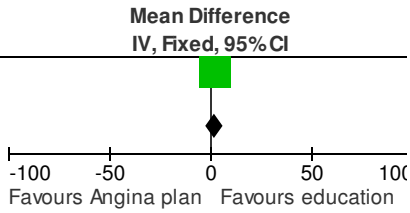
Heterogeneity: Not applicable
Test for overall effect: Z = 1.32 (P = 0.19)



8.18 SEI QOL- DW QOL score (overall score ranging from 0-100 with higher scores reflecting better quality of life)

Study or Subgroup	Angina Plan Mean	SD	Total	Education session Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Zetta 2009 (Angina Plan)	6.53	15.02	109	4.83	16.57	109	100.0%	1.70 [-2.50, 5.90]
Total (95% CI)			**109**			**109**	**100.0%**	**1.70 [-2.50, 5.90]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)

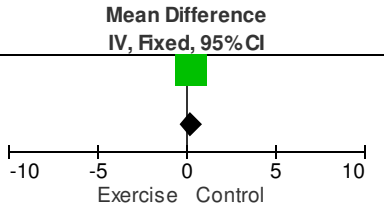


1 Exercise (1 year intensive) vs Control

1.1 Max ST depression (mm)

Study or Subgroup	Exercise Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Todd & Ballantyne 1990	1.6	1.2	20	1.4	0.8	20	100.0%	0.20 [-0.43, 0.83]
Total (95% CI)			**20**			**20**	**100.0%**	**0.20 [-0.43, 0.83]**

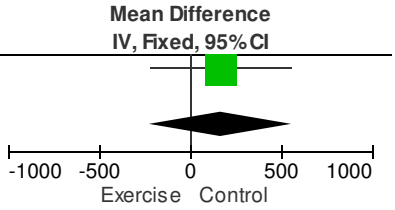
Heterogeneity: Not applicable
Test for overall effect: Z = 0.62 (P = 0.54)



1.2 Time to 1mm ST depression (sec)

Study or Subgroup	Exercise Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Todd & Ballantyne 1990	881	668	20	715	580	20	100.0%	166.00 [-221.71, 553.71]
Total (95% CI)			**20**			**20**	**100.0%**	**166.00 [-221.71, 553.71]**

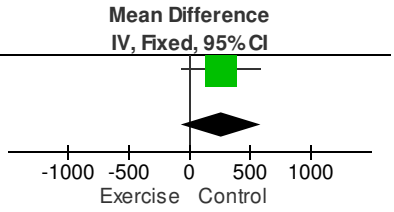
Heterogeneity: Not applicable
Test for overall effect: Z = 0.84 (P = 0.40)



1.3 Treadmill time (s)

Study or Subgroup	Exercise Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Todd & Ballantyne 1990	1,272	514	20	1,010	546	20	100.0%	262.00 [-66.64, 590.64]
Total (95% CI)			**20**			**20**	**100.0%**	**262.00 [-66.64, 590.64]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.56 (P = 0.12)

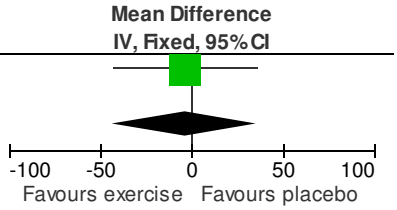


2 Exercise (and placebo) vs. Placebo

2.1 Maximal working capacity kpm/min

Study or Subgroup	Exercise (and placebo) Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Malmborg et al. 1974	15	21	8	19	53	8	100.0%	-4.00 [-43.50, 35.50]
Total (95% CI)			**8**			**8**	**100.0%**	**-4.00 [-43.50, 35.50]**

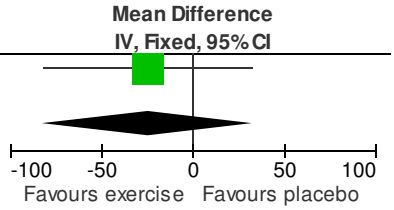
Heterogeneity: Not applicable
Test for overall effect: Z = 0.20 (P = 0.84)



2.2 Anginal attacks / week

Study or Subgroup	Exercise (and placebo) Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Malmborg et al. 1974	24	50	8	49	66	8	100.0%	-25.00 [-82.38, 32.38]
Total (95% CI)			**8**			**8**	**100.0%**	**-25.00 [-82.38, 32.38]**

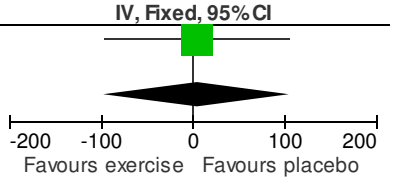
Heterogeneity: Not applicable
Test for overall effect: Z = 0.85 (P = 0.39)



2.3 Nitroglycerin tabl / week

Study or Subgroup	Exercise (and placebo) Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Malmborg et al. 1974	4	54	8	0	135	8	100.0%	4.00 [-96.75, 104.75]
Total (95% CI)			**8**			**8**	**100.0%**	**4.00 [-96.75, 104.75]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.08 (P = 0.94)

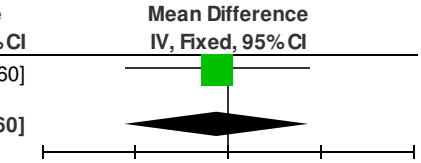


3 Exercise and beta blockers vs. Beta blocker

3.1 Maximal working capacity kpm/min

Study or Subgroup	Exercise + beta blocker Mean	SD	Total	Beta blocker Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Malmborg et al. 1974	42	49	6	48	41	7	100.0%	-6.00 [-55.60, 43.60]
Total (95% CI)			**6**			**7**	**100.0%**	**-6.00 [-55.60, 43.60]**

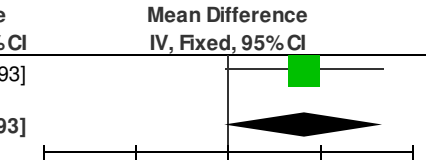
Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)



3.2 Anginal attacks / week

Study or Subgroup	Exercise + beta blocker Mean	SD	Total	Beta blocker Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Malmborg et al. 1974	-44	50	6	-85	21	7	100.0%	41.00 [-1.93, 83.93]
Total (95% CI)			**6**			**7**	**100.0%**	**41.00 [-1.93, 83.93]**

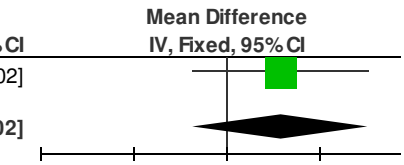
Heterogeneity: Not applicable
Test for overall effect: Z = 1.87 (P = 0.06)



3.3 Nitroglycerin tabl / week

Study or Subgroup	Exercise + beta blocker Mean	SD	Total	Beta blocker Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Malmborg et al. 1974	-15	115	6	-73	32	7	100.0%	58.00 [-37.02, 153.02]
Total (95% CI)			**6**			**7**	**100.0%**	**58.00 [-37.02, 153.02]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.20 (P = 0.23)

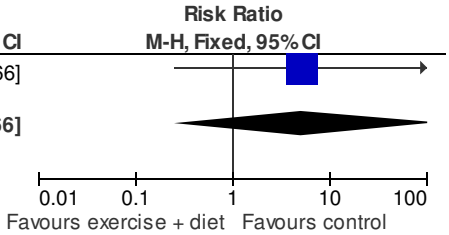


4 Exercise + low fat diet vs. Control

4.1 Cardiac mortality

Study or Subgroup	Exercise + low fat diet Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Schuler et al. 1992	2	56	0	57	100.0%	5.09 [0.25, 103.66]
Total (95% CI)		**56**		**57**	**100.0%**	**5.09 [0.25, 103.66]**
Total events	2		0			

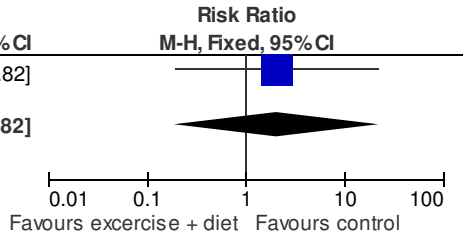
Heterogeneity: Not applicable
Test for overall effect: Z = 1.06 (P = 0.29)



4.2 Mortality (all)

Study or Subgroup	Exercise + low fat diet Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Schuler et al. 1992	2	56	1	57	100.0%	2.04 [0.19, 21.82]
Total (95% CI)		**56**		**57**	**100.0%**	**2.04 [0.19, 21.82]**
Total events	2		1			

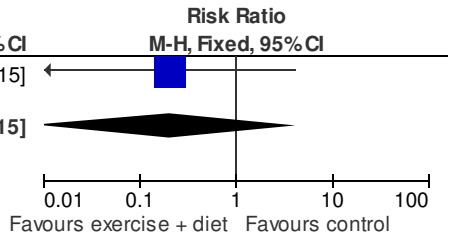
Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)



4.3 Non-fatal MI

Study or Subgroup	Exercise + low fat diet Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Schuler et al. 1992	0	56	2	57	100.0%	0.20 [0.01, 4.15]
Total (95% CI)		**56**		**57**	**100.0%**	**0.20 [0.01, 4.15]**
Total events	0		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.04 (P = 0.30)

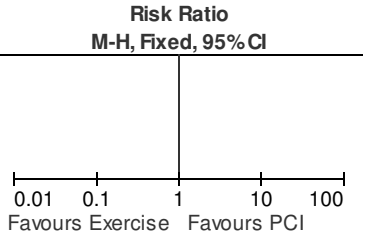


5 Exercise vs. PCI

5.1 Death of cardiac causes

Study or Subgroup	Exercise Events	Total	PCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hambrecht 2004	0	51	0	50		Not estimable
Total (95% CI)		**51**		**50**		**Not estimable**
Total events	0		0			

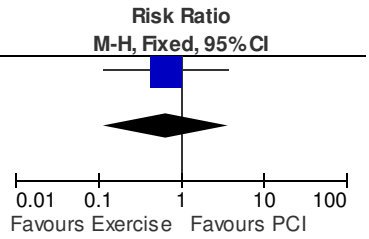
Heterogeneity: Not applicable
Test for overall effect: Not applicable



5.2 Cerebrovascular accident

Study or Subgroup	Exercise Events	Total	PCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hambrecht 2004	2	51	3	50	100.0%	0.65 [0.11, 3.75]
Total (95% CI)		**51**		**50**	**100.0%**	**0.65 [0.11, 3.75]**
Total events	2		3			

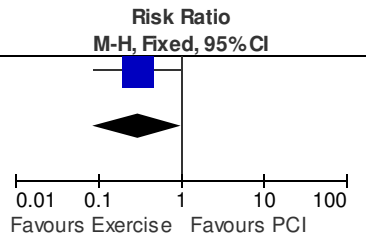
Heterogeneity: Not applicable
Test for overall effect: Z = 0.48 (P = 0.63)



5.3 Revascularisation

Study or Subgroup	Exercise Events	Total	PCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hambrecht 2004	3	51	10	50	100.0%	0.29 [0.09, 1.01]
Total (95% CI)		**51**		**50**	**100.0%**	**0.29 [0.09, 1.01]**
Total events	3		10			

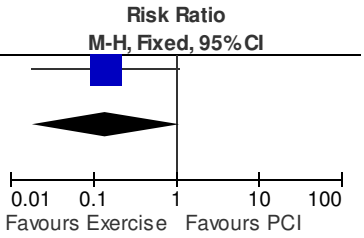
Heterogeneity: Not applicable
Test for overall effect: Z = 1.95 (P = 0.05)



5.4 Hospitalisation and coronary angiography owing to worsening angina

Study or Subgroup	Exercise Events	Total	PCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hambrecht 2004	1	51	7	50	100.0%	0.14 [0.02, 1.10]
Total (95% CI)		**51**		**50**	**100.0%**	**0.14 [0.02, 1.10]**
Total events	1		7			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.87 (P = 0.06)

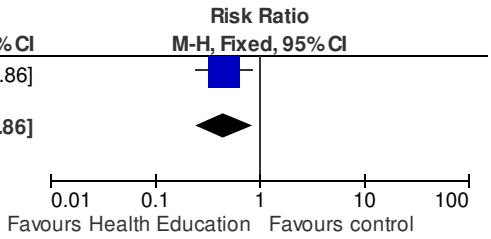


6 Health Education vs Control

6.1 Mortality

Study or Subgroup	Health Education Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cupples & McKnight, 1994	13	342	29	346	100.0%	0.45 [0.24, 0.86]
Total (95% CI)		**342**		**346**	**100.0%**	**0.45 [0.24, 0.86]**
Total events	13		29			

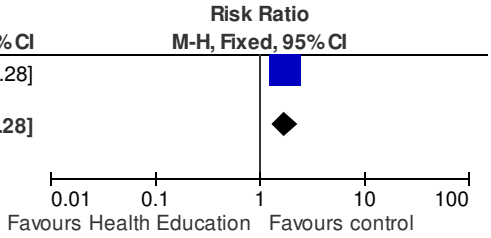
Heterogeneity: Not applicable
Test for overall effect: Z = 2.43 (P = 0.01)



6.2 Increase in frequency of exercise

Study or Subgroup	Health Education Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cupples & McKnight, 1994	108	342	63	346	100.0%	1.73 [1.32, 2.28]
Total (95% CI)		**342**		**346**	**100.0%**	**1.73 [1.32, 2.28]**
Total events	108		63			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.96 (P < 0.0001)

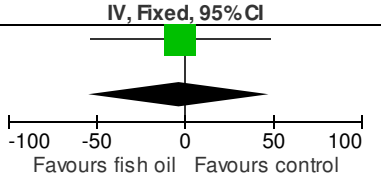


1 Fish oil capsules vs. Placebo (Follow-up at end of treatment period)

1.1 Anginal episodes per week

Study or Subgroup	Fish oil Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Salachas 1994	8.36	103.6	20	11.36	51.7	19	100.0%	-3.00 [-54.01, 48.01]
Total (95% CI)			**20**			**19**	**100.0%**	**-3.00 [-54.01, 48.01]**

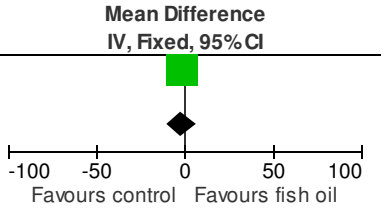
Heterogeneity: Not applicable
Test for overall effect: Z = 0.12 (P = 0.91)



1.2 GTN consumption per week

Study or Subgroup	Fish oil Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Salachas 1994	10.43	15.07	20	12.42	12.61	19	100.0%	-1.99 [-10.69, 6.71]
Total (95% CI)			**20**			**19**	**100.0%**	**-1.99 [-10.69, 6.71]**

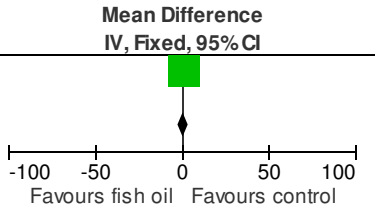
Heterogeneity: Not applicable
Test for overall effect: Z = 0.45 (P = 0.65)



1.3 Exercise test duration (min)

Study or Subgroup	Fish oil Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Salachas 1994	10.09	5.16	20	9.1	4.38	19	100.0%	0.99 [-2.01, 3.99]
Total (95% CI)			**20**			**19**	**100.0%**	**0.99 [-2.01, 3.99]**

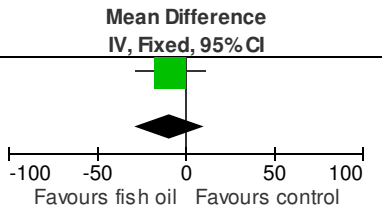
Heterogeneity: Not applicable
Test for overall effect: Z = 0.65 (P = 0.52)



1.4 Number of anginal attacks per 30 days

Study or Subgroup	Fish oil Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Aucamp 1993	12.9	13.7	12	22.1	31.1	11	100.0%	-9.20 [-29.15, 10.75]
Total (95% CI)			**12**			**11**	**100.0%**	**-9.20 [-29.15, 10.75]**

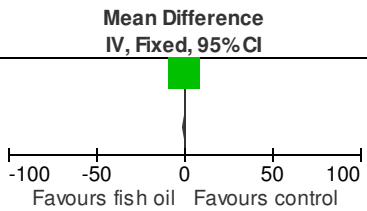
Heterogeneity: Not applicable
Test for overall effect: Z = 0.90 (P = 0.37)



1.5 Duration of angina attacks per minute

Study or Subgroup	Fish oil Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Aucamp 1993	1.8	0.5	12	2.2	0.8	11	100.0%	-0.40 [-0.95, 0.15]
Total (95% CI)			**12**			**11**	**100.0%**	**-0.40 [-0.95, 0.15]**

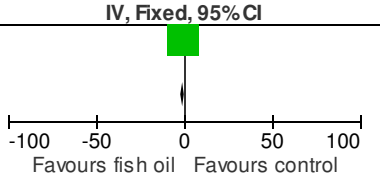
Heterogeneity: Not applicable
Test for overall effect: Z = 1.42 (P = 0.15)



1.6 Intensity of pain per attack per patient (on a 10 cm visual analogue scale)

Study or Subgroup	Fish oil Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Aucamp 1993	2.5	1.2	12	3.5	1.5	11	100.0%	-1.00 [-2.12, 0.12]
Total (95% CI)			**12**			**11**	**100.0%**	**-1.00 [-2.12, 0.12]**

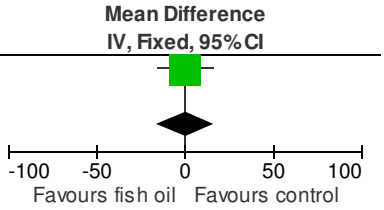
Heterogeneity: Not applicable
Test for overall effect: Z = 1.76 (P = 0.08)



1.7 No. of sublingual isosorbide dinitrate tablets taken per 30 days

Study or Subgroup	Fish oil Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Aucamp 1993	17	22.5	12	17	16.8	11	100.0%	0.00 [-16.14, 16.14]
Total (95% CI)			**12**			**11**	**100.0%**	**0.00 [-16.14, 16.14]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

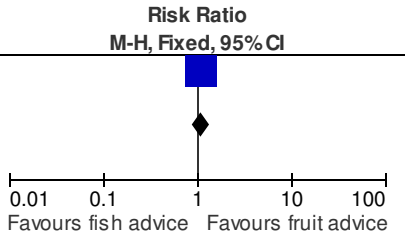


2 Fish advice (dietary fish advice + fish oil capsule) vs. Fruit advice (Mortality ascertained after 3 to 9 yrs)

2.1 All death

Study or Subgroup	Fish oil advice Events	Total	Fruit advice Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Burr 2003	141	764	133	779	100.0%	1.08 [0.87, 1.34]
Total (95% CI)		**764**		**779**	**100.0%**	**1.08 [0.87, 1.34]**
Total events	141		133			

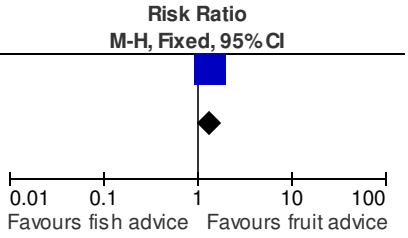
Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)



2.2 Cardiac death

Study or Subgroup	Fish oil advice Events	Total	Fruit advice Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Burr 2003	94	764	72	779	100.0%	1.33 [1.00, 1.78]
Total (95% CI)		**764**		**779**	**100.0%**	**1.33 [1.00, 1.78]**
Total events	94		72			

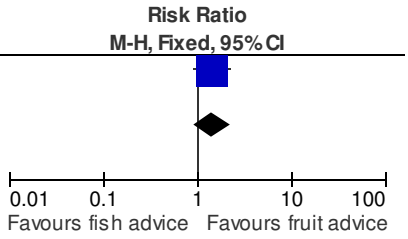
Heterogeneity: Not applicable
Test for overall effect: Z = 1.93 (P = 0.05)



2.3 Sudden death

Study or Subgroup	Fish oil advice Events	Total	Fruit advice Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Burr 2003	42	764	30	779	100.0%	1.43 [0.90, 2.26]
Total (95% CI)		**764**		**779**	**100.0%**	**1.43 [0.90, 2.26]**
Total events	42		30			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.52 (P = 0.13)

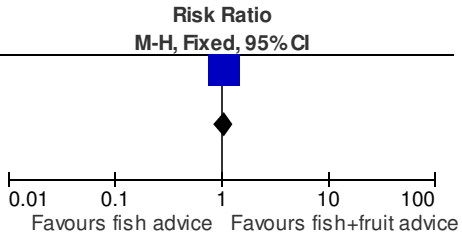


3 Fish advice (dietary fish advice+ fish oil capsule) vs. Fish +Fruit advice (Mortality ascertained after 3 to 9 yrs)

3.1 All death

Study or Subgroup	Fish advice Events	Total	.Fish+fruit Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Burr 2003	141	764	142	807	100.0%	1.05 [0.85, 1.30]
Total (95% CI)		**764**		**807**	**100.0%**	**1.05 [0.85, 1.30]**
Total events	141		142			

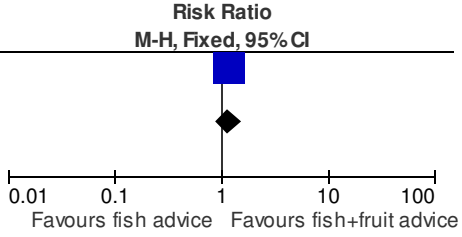
Heterogeneity: Not applicable
Test for overall effect: Z = 0.44 (P = 0.66)



3.2 Cardiac death

Study or Subgroup	Fish advice Events	Total	.Fish+fruit Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Burr 2003	94	764	86	807	100.0%	1.15 [0.88, 1.52]
Total (95% CI)		**764**		**807**	**100.0%**	**1.15 [0.88, 1.52]**
Total events	94		86			

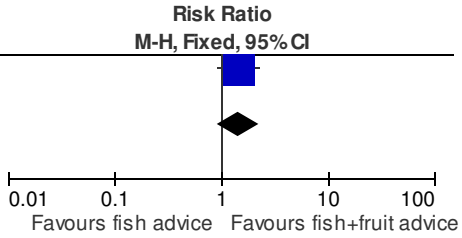
Heterogeneity: Not applicable
Test for overall effect: Z = 1.02 (P = 0.31)



3.3 Sudden death

Study or Subgroup	Fish advice Events	Total	.Fish+fruit Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Burr 2003	42	764	31	807	100.0%	1.43 [0.91, 2.25]
Total (95% CI)		**764**		**807**	**100.0%**	**1.43 [0.91, 2.25]**
Total events	42		31			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.55 (P = 0.12)

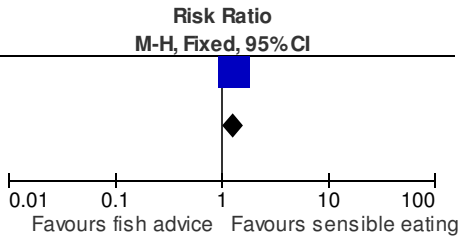


4 Fish advice (dietary fish advice + fish oil capsule) vs. Sensible eating (non -specific advice) (Mortality ascertained after 3 to 9 yrs)

4.1 All deaths

Study or Subgroup	Fish oil advice Events	Total	Sensible eating Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Burr 2003	141	764	109	764	100.0%	1.29 [1.03, 1.63]
Total (95% CI)		**764**		**764**	**100.0%**	**1.29 [1.03, 1.63]**
Total events	141		109			

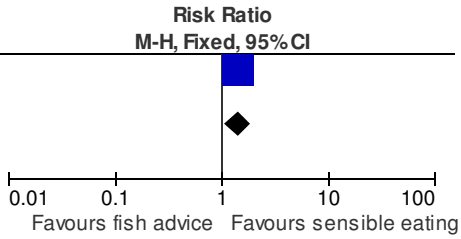
Heterogeneity: Not applicable
Test for overall effect: Z = 2.20 (P = 0.03)



4.2 Cardiac death

Study or Subgroup	Fish oil advice Events	Total	Sensible eating Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Burr 2003	94	764	67	764	100.0%	1.40 [1.04, 1.89]
Total (95% CI)		**764**		**764**	**100.0%**	**1.40 [1.04, 1.89]**
Total events	94		67			

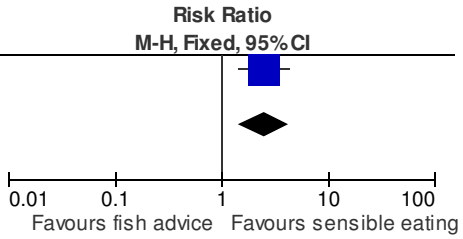
Heterogeneity: Not applicable
Test for overall effect: Z = 2.24 (P = 0.03)



4.3 Sudden death

Study or Subgroup	Fish oil advice Events	Total	Sensible eating Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Burr 2003	42	764	17	764	100.0%	2.47 [1.42, 4.30]
Total (95% CI)		**764**		**764**	**100.0%**	**2.47 [1.42, 4.30]**
Total events	42		17			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.20 (P = 0.001)

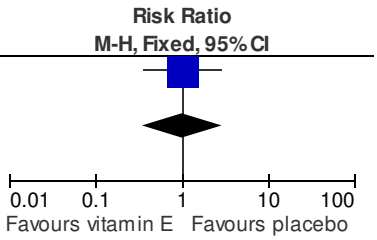


6 Vitamin E vs. Placebo ((Follow-up at the end of treatment period))

6.1 Improved anginal symptoms

Study or Subgroup	Vitamin E Events	Total	control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Anderson 1974	5	18	5	18	100.0%	1.00 [0.35, 2.87]
Total (95% CI)		**18**		**18**	**100.0%**	**1.00 [0.35, 2.87]**
Total events	5		5			

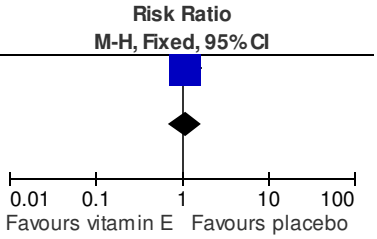
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



6.2 No change in anginal symptoms

Study or Subgroup	Vitamin E Events	Total	control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Anderson 1974	13	18	12	18	100.0%	1.08 [0.70, 1.67]
Total (95% CI)		**18**		**18**	**100.0%**	**1.08 [0.70, 1.67]**
Total events	13		12			

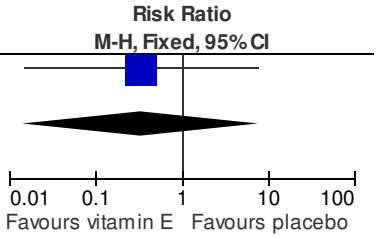
Heterogeneity: Not applicable
Test for overall effect: Z = 0.36 (P = 0.72)



6.3 Slightly worse anginal symptoms

Study or Subgroup	Vitamin E Events	Total	control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Anderson 1974	0	18	1	18	100.0%	0.33 [0.01, 7.68]
Total (95% CI)		**18**		**18**	**100.0%**	**0.33 [0.01, 7.68]**
Total events	0		1			

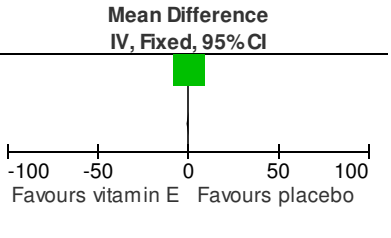
Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)



6.4 Duration treadmill (min)

Study or Subgroup	Vitamin E Mean	SD	Total	control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Gillian 1977	5.48	1.69	48	5.3	1.6	40	100.0%	0.18 [-0.51, 0.87]
Total (95% CI)			**48**			**40**	**100.0%**	**0.18 [-0.51, 0.87]**

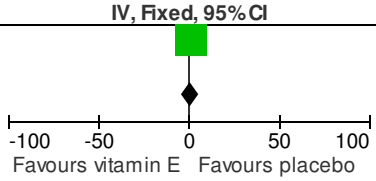
Heterogeneity: Not applicable
Test for overall effect: Z = 0.51 (P = 0.61)



6.5 Angina attacks per week

Study or Subgroup	Vitamin E Mean	SD	Total	control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Gillian 1977	7.3	12.6	48	6.7	10.5	48	100.0%	0.60 [-4.04, 5.24]
Total (95% CI)			**48**			**48**	**100.0%**	**0.60 [-4.04, 5.24]**

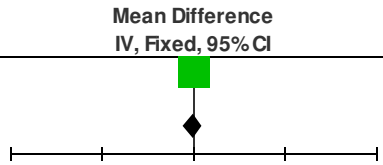
Heterogeneity: Not applicable
Test for overall effect: Z = 0.25 (P = 0.80)



6.6 Nitroglycerin consumption per week

Study or Subgroup	Vitamin E Mean	SD	Total	control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Gillian 1977	7.6	12.1	48	7.7	14.2	48	100.0%	-0.10 [-5.38, 5.18]
Total (95% CI)			**48**			**48**	**100.0%**	**-0.10 [-5.38, 5.18]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.04 (P = 0.97)

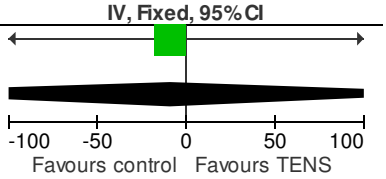


1 TENS vs.control (no TENS) (Follow-up 2 weeks after treatment)

1.1 Exercise tolerance (W.min)

Study or Subgroup	TENS Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Mannheimer 1985	523	231	11	532	139	10	100.0%	-9.00 [-170.42, 152.42]
Total (95% CI)			**11**			**10**	**100.0%**	**-9.00 [-170.42, 152.42]**

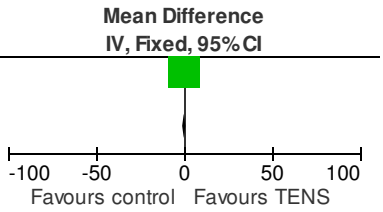
Heterogeneity: Not applicable
Test for overall effect: Z = 0.11 (P = 0.91)



1.2 ST segment depression (mm) during exercise

Study or Subgroup	TENS Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Mannheimer 1985	2.8	1.3	11	3	1.4	10	100.0%	-0.20 [-1.36, 0.96]
Total (95% CI)			**11**			**10**	**100.0%**	**-0.20 [-1.36, 0.96]**

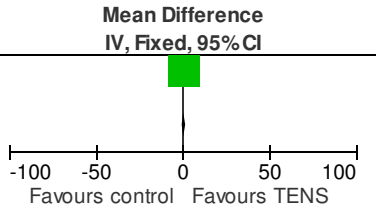
Heterogeneity: Not applicable
Test for overall effect: Z = 0.34 (P = 0.74)



1.3 ST segment depression (mm) after exercise

Study or Subgroup	TENS Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Mannheimer 1985	3	1.2	11	2.8	1.5	10	100.0%	0.20 [-0.97, 1.37]
Total (95% CI)			**11**			**10**	**100.0%**	**0.20 [-0.97, 1.37]**

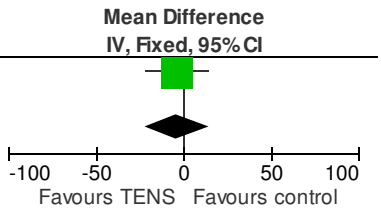
Heterogeneity: Not applicable
Test for overall effect: Z = 0.34 (P = 0.74)



1.4 Frequency of angina attacks per week

Study or Subgroup	TENS Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Mannheimer 1985	19	23	11	23	19	10	100.0%	-4.00 [-21.98, 13.98]
Total (95% CI)			**11**			**10**	**100.0%**	**-4.00 [-21.98, 13.98]**

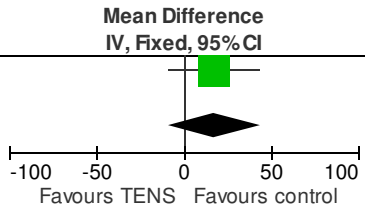
Heterogeneity: Not applicable
Test for overall effect: Z = 0.44 (P = 0.66)



1.5 Nitroglycerin consumption per week

Study or Subgroup	Favours TENS Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Mannheimer 1985	31	43	11	14	11	10	100.0%	17.00 [-9.31, 43.31]
Total (95% CI)			**11**			**10**	**100.0%**	**17.00 [-9.31, 43.31]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.27 (P = 0.21)

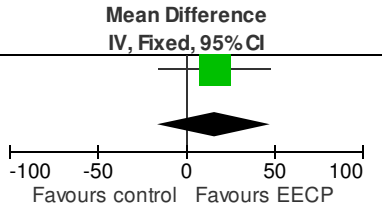


2 EECP vs. inactive CP (Follow-up 3 days after treatment for angina pain counts, one week after treatment for exercise duration)

2.1 Exercise duration (sec) (change scores) (follow-up after 1 week)

Study or Subgroup	EECP Mean	EECP SD	EECP Total	Inactive CP Mean	Inactive CP SD	Inactive CP Total	Weight	Mean Difference IV, Fixed, 95% CI
Arora 2010	42	82.9	57	26	91.3	58	100.0%	16.00 [-15.86, 47.86]
Total (95% CI)			**57**			**58**	**100.0%**	**16.00 [-15.86, 47.86]**

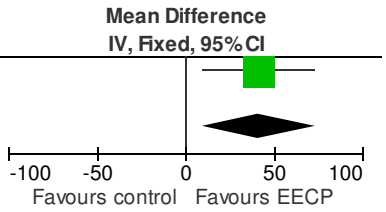
Heterogeneity: Not applicable
Test for overall effect: Z = 0.98 (P = 0.33)



2.2 Time to >1mm ST segment depression (Sec) (change scores) (follow-up after 1 week)

Study or Subgroup	EECP Mean	EECP SD	EECP Total	Inactive CP Mean	Inactive CP SD	Inactive CP Total	Weight	Mean Difference IV, Fixed, 95% CI
Arora 2010	37	82.2	56	-4	89.7	56	100.0%	41.00 [9.13, 72.87]
Total (95% CI)			**56**			**56**	**100.0%**	**41.00 [9.13, 72.87]**

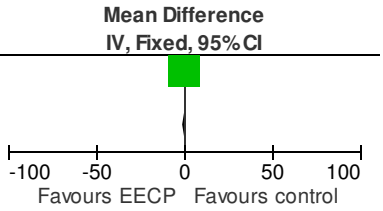
Heterogeneity: Not applicable
Test for overall effect: Z = 2.52 (P = 0.01)



2.3 Angina episodes/day (change scores) (follow-up after 3 days)

Study or Subgroup	EECP Mean	EECP SD	EECP Total	Inactive CP Mean	Inactive CP SD	Inactive CP Total	Weight	Mean Difference IV, Fixed, 95% CI
Arora 2010	-0.11	1.76	71	0.13	1.78	66	100.0%	-0.24 [-0.83, 0.35]
Total (95% CI)			**71**			**66**	**100.0%**	**-0.24 [-0.83, 0.35]**

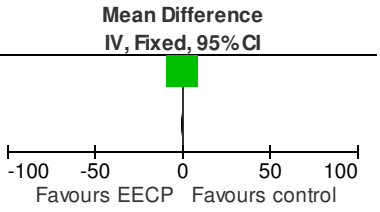
Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)



2.4 NTG use/day (change scores) (follow-up after 3 days)

Study or Subgroup	EECP Mean	EECP SD	EECP Total	Inactive CP Mean	Inactive CP SD	Inactive CP Total	Weight	Mean Difference IV, Fixed, 95% CI
Arora 2010	-0.32	1	71	-0.1	0.97	66	100.0%	-0.22 [-0.55, 0.11]
Total (95% CI)			**71**			**66**	**100.0%**	**-0.22 [-0.55, 0.11]**

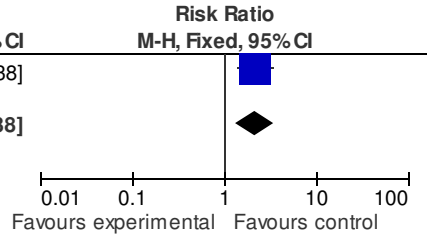
Heterogeneity: Not applicable
Test for overall effect: Z = 1.31 (P = 0.19)



2.5 Adverse events (no. of patients) (up to the end of treatment)

Study or Subgroup	EECP Events	EECP Total	Inactive CP Events	Inactive CP Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Arora 2010	39	71	17	66	100.0%	2.13 [1.35, 3.38]
Total (95% CI)		**71**		**66**	**100.0%**	**2.13 [1.35, 3.38]**
Total events	39		17			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.22 (P = 0.001)

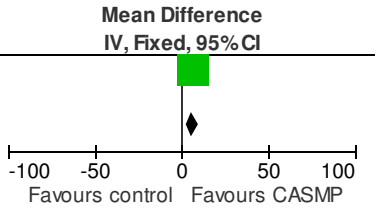


3 Chronic angina self management Program (CASMP) vs. control (Follow-up 3 months from start of treatment)

3.1 Physical functioning (SF-36) (range 0-100 -higher score better functioning) (change scores)

Study or Subgroup	CASMP Mean	CASMP SD	CASMP Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
McGillion 2008	5.3	9.4	57	-0.68	9.3	60	100.0%	5.98 [2.59, 9.37]
Total (95% CI)			**57**			**60**	**100.0%**	**5.98 [2.59, 9.37]**

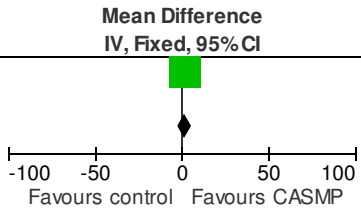
Heterogeneity: Not applicable
Test for overall effect: Z = 3.46 (P = 0.0005)



3.2 Role physical functioning (SF-36) (change scores) (range 0-100)

Study or Subgroup	CASMP Mean	CASMP SD	CASMP Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
McGillion 2008	4.8	12.7	57	3.2	9.6	60	100.0%	1.60 [-2.50, 5.70]
Total (95% CI)			**57**			**60**	**100.0%**	**1.60 [-2.50, 5.70]**

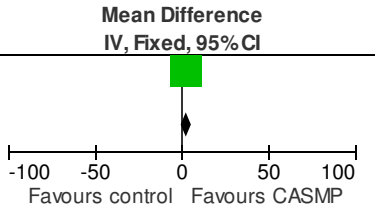
Heterogeneity: Not applicable
Test for overall effect: Z = 0.77 (P = 0.44)



3.3 Bodily pain (SF-36) (change scores) (range 0-100)

Study or Subgroup	CASMP Mean	CASMP SD	CASMP Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
McGillion 2008	4.4	8.7	57	2.1	9.2	60	100.0%	2.30 [-0.94, 5.54]
Total (95% CI)			**57**			**60**	**100.0%**	**2.30 [-0.94, 5.54]**

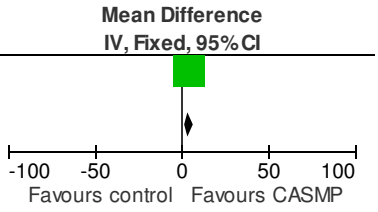
Heterogeneity: Not applicable
Test for overall effect: Z = 1.39 (P = 0.16)



3.4 General Health (SF-36) (change scores) (0-100)

Study or Subgroup	CASMP Mean	CASMP SD	CASMP Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
McGillion 2008	2.27	7.7	57	-1.6	6.4	60	100.0%	3.87 [1.30, 6.44]
Total (95% CI)			**57**			**60**	**100.0%**	**3.87 [1.30, 6.44]**

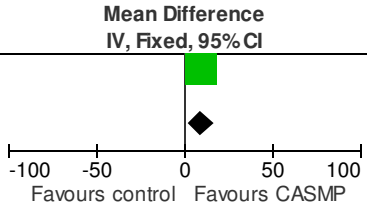
Heterogeneity: Not applicable
Test for overall effect: Z = 2.95 (P = 0.003)



3.5 Angina frequency (SAQ) (range 0-100- higher scores better functioning) (change scores)

Study or Subgroup	CASMP Mean	CASMP SD	CASMP Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
McGillion 2008	11.4	23.7	57	2.2	18.4	60	100.0%	9.20 [1.48, 16.92]
Total (95% CI)			**57**			**60**	**100.0%**	**9.20 [1.48, 16.92]**

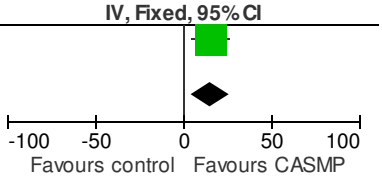
Heterogeneity: Not applicable
Test for overall effect: Z = 2.34 (P = 0.02)



3.6 Angina stability (SAQ) (range 0-100) (change scores)

	CASMP			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
McGillion 2008	18	35	57	2.9	24.4	60	100.0%	15.10 [4.11, 26.09]	
Total (95% CI)			**57**			**60**	**100.0%**	**15.10 [4.11, 26.09]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.69 (P = 0.007)



3.7 Disease perception (SAQ) (range 0-100) (change scores)

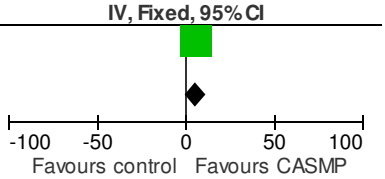
	CASMP			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
McGillion 2008	9.9	23.5	57	3.3	19.1	60	100.0%	6.60 [-1.18, 14.38]	
Total (95% CI)			**57**			**60**	**100.0%**	**6.60 [-1.18, 14.38]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.66 (P = 0.10)

3.8 Physical limitation (SAQ) (range 0-100) (change scores)

	CASMP			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
McGillion 2008	7.1	16.5	57	1.6	15.1	60	100.0%	5.50 [-0.24, 11.24]	
Total (95% CI)			**57**			**60**	**100.0%**	**5.50 [-0.24, 11.24]**	

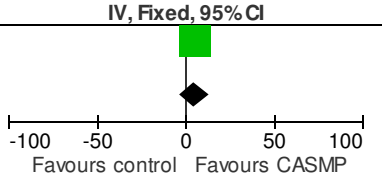
Heterogeneity: Not applicable
Test for overall effect: Z = 1.88 (P = 0.06)



3.9 Treatment satisfaction (SAQ) (range 0-100) (change scores)

	CASMP			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
McGillion 2008	9.7	24.6	57	4.8	18.7	60	100.0%	4.90 [-3.05, 12.85]	
Total (95% CI)			**57**			**60**	**100.0%**	**4.90 [-3.05, 12.85]**	

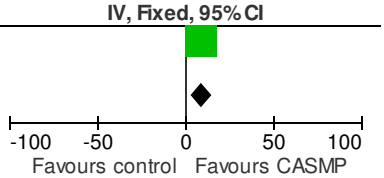
Heterogeneity: Not applicable
Test for overall effect: Z = 1.21 (P = 0.23)



3.10 Self-Efficay Scale (range scores 10- 100 -higher scores better) (change scores)

	CASMP			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
McGillion 2008	8.4	17.6	57	-0.2	14.4	60	100.0%	8.60 [2.76, 14.44]	
Total (95% CI)			**57**			**60**	**100.0%**	**8.60 [2.76, 14.44]**	

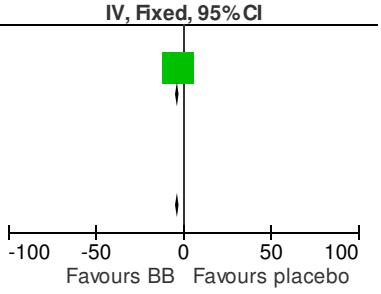
Heterogeneity: Not applicable
Test for overall effect: Z = 2.88 (P = 0.004)



1 beta blocker vs placebo

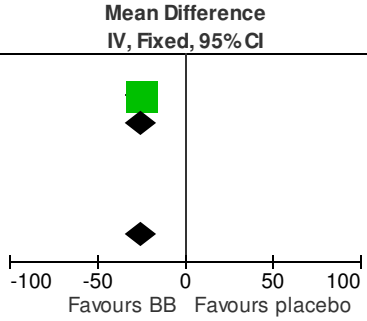
1.1 ischemic episodes

Study or Subgroup	beta blocker Mean	SD	Total	placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 propanolol vs placebo								
Bugiardini 1989	0.7	0.6	16	3.9	1.8	16	100.0%	-3.20 [-4.13, -2.27]
Subtotal (95% CI)			**16**			**16**	**100.0%**	**-3.20 [-4.13, -2.27]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 6.75 (P < 0.00001)								
Total (95% CI)			**16**			**16**	**100.0%**	**-3.20 [-4.13, -2.27]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 6.75 (P < 0.00001)								
Test for subgroup differences: Not applicable								



1.2 ischemic duration (min)

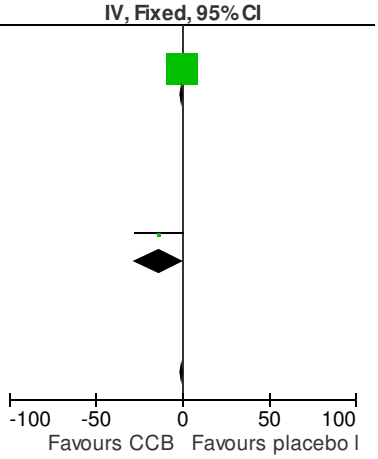
Study or Subgroup	beta blocker Mean	SD	Total	placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.2.1 propanolol vs placebo								
Bugiardini 1989	4	5	16	29	18	16	100.0%	-25.00 [-34.15, -15.85]
Subtotal (95% CI)			**16**			**16**	**100.0%**	**-25.00 [-34.15, -15.85]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.35 (P < 0.00001)								
Total (95% CI)			**16**			**16**	**100.0%**	**-25.00 [-34.15, -15.85]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.35 (P < 0.00001)								
Test for subgroup differences: Not applicable								



2 calcium channel blockers vs placebo

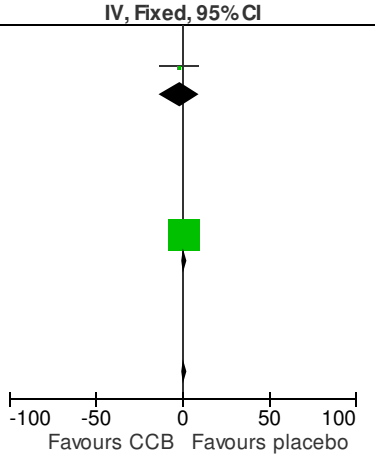
2.1 ischemic episodes

Study or Subgroup	calcium channel blockers Mean	SD	Total	placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.1.1 verapamil vs placebo								
Bugiardini 1989	3.4	1.7	16	3.9	1.8	16	99.3%	-0.50 [-1.71, 0.71]
Subtotal (95% CI)			**16**			**16**	**99.3%**	**-0.50 [-1.71, 0.71]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.81 (P = 0.42)								
2.1.2 verapamil or nifedipine vs placebo								
Cannon 1985	21	21	22	35	27	22	0.7%	-14.00 [-28.29, 0.29]
Subtotal (95% CI)			**22**			**22**	**0.7%**	**-14.00 [-28.29, 0.29]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.92 (P = 0.05)								
Total (95% CI)			**38**			**38**	**100.0%**	**-0.60 [-1.81, 0.61]**
Heterogeneity: Chi² = 3.40, df = 1 (P = 0.07); I² = 71%								
Test for overall effect: Z = 0.97 (P = 0.33)								
Test for subgroup differences: Chi² = 3.40, df = 1 (P = 0.07), I² = 70.6%								



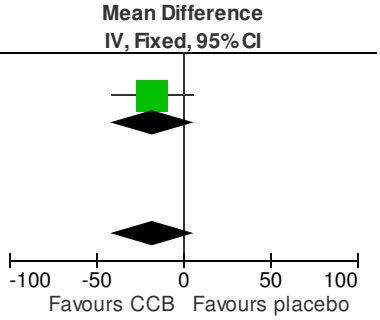
2.2 ischemia duration (min)

Study or Subgroup	calcium channel blockers Mean	SD	Total	placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.2.1 verapamil vs placebo								
Bugiardini 1989	27	15	16	29	18	16	1.3%	-2.00 [-13.48, 9.48]
Subtotal (95% CI)			**16**			**16**	**1.3%**	**-2.00 [-13.48, 9.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.34 (P = 0.73)								
2.2.2 verapamil or nifedipine vs placebo								
Cannon 1985	4.63	2.15	22	3.85	2.27	22	98.7%	0.78 [-0.53, 2.09]
Subtotal (95% CI)			**22**			**22**	**98.7%**	**0.78 [-0.53, 2.09]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.17 (P = 0.24)								
Total (95% CI)			**38**			**38**	**100.0%**	**0.74 [-0.55, 2.04]**
Heterogeneity: Chi² = 0.22, df = 1 (P = 0.64); I² = 0%								
Test for overall effect: Z = 1.12 (P = 0.26)								
Test for subgroup differences: Chi² = 0.22, df = 1 (P = 0.64), I² = 0%								



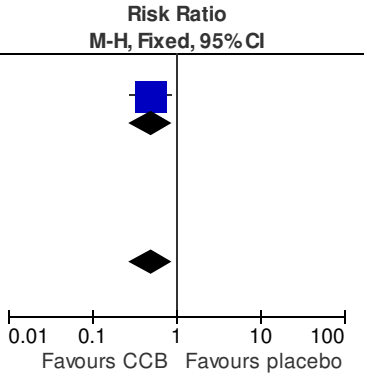
2.3 Nitroglycerin tablets consumption

Study or Subgroup	calcium channel blockers Mean	SD	Total	placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.3.1 verapamil or nifedipine vs placebo								
Cannon 1985	23	27	22	41	50	22	100.0%	-18.00 [-41.74, 5.74]
Subtotal (95% CI)			**22**			**22**	**100.0%**	**-18.00 [-41.74, 5.74]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.49 (P = 0.14)								
Total (95% CI)			**22**			**22**	**100.0%**	**-18.00 [-41.74, 5.74]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.49 (P = 0.14)								
Test for subgroup differences: Not applicable								



2.4 presence of chest pain during exercise

Study or Subgroup	calcium channel blockers Events	Total	placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.4.1 verapamil or nifedipine vs placebo						
Cannon 1985	9	25	16	22	100.0%	0.49 [0.28, 0.89]
Subtotal (95% CI)		**25**		**22**	**100.0%**	**0.49 [0.28, 0.89]**
Total events	9		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.37 (P = 0.02)						
Total (95% CI)		**25**		**22**	**100.0%**	**0.49 [0.28, 0.89]**
Total events	9		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.37 (P = 0.02)						
Test for subgroup differences: Not applicable						

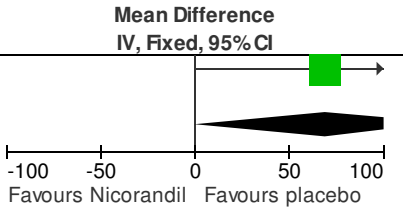


3 Nicorandil vs placebo

3.3 Time to 1mm ST-segment depression (sec)

Study or Subgroup	nicorandil Mean	SD	Total	placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Chen 1997	342	104	13	273	72	13	100.0%	69.00 [0.24, 137.76]
Total (95% CI)			**13**			**13**	**100.0%**	**69.00 [0.24, 137.76]**

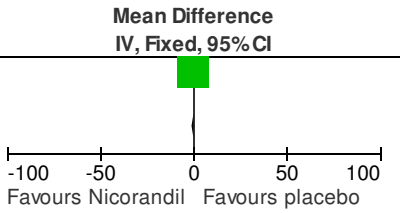
Heterogeneity: Not applicable
Test for overall effect: Z = 1.97 (P = 0.05)



3.4 maximum ST-segment depression (mm)

Study or Subgroup	nicorandil Mean	SD	Total	placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Chen 1997	1.5	0.6	13	1.9	0.9	13	100.0%	-0.40 [-0.99, 0.19]
Total (95% CI)			**13**			**13**	**100.0%**	**-0.40 [-0.99, 0.19]**

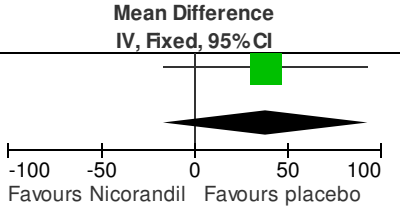
Heterogeneity: Not applicable
Test for overall effect: Z = 1.33 (P = 0.18)



3.5 Total exercise duration (sec)

Study or Subgroup	nicorandil Mean	SD	Total	placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Chen 1997	443	78	13	405	64	13	100.0%	38.00 [-16.85, 92.85]
Total (95% CI)			**13**			**13**	**100.0%**	**38.00 [-16.85, 92.85]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.36 (P = 0.17)



4 beta blockers vs calcium channel blockers in patients with pressure-rate product variation <1050

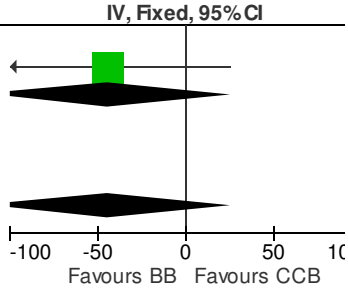
4.1 exercise duration (sec)

Study or Subgroup	beta blockers Mean	SD	Total	calcium channel blockers Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.1.1 acebutolol vs verapamil in patients with pressure-rate product variation >1050								
Romeo 1988	318	101	15	362	93	15	100.0%	-44.00 [-113.48, 25.48]
Subtotal (95% CI)			**15**			**15**	**100.0%**	**-44.00 [-113.48, 25.48]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.24 (P = 0.21)

Total (95% CI)			**15**			**15**	**100.0%**	**-44.00 [-113.48, 25.48]**

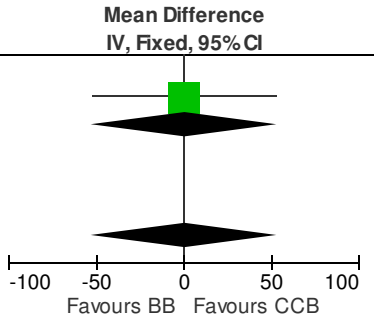
Heterogeneity: Not applicable
Test for overall effect: Z = 1.24 (P = 0.21)
Test for subgroup differences: Not applicable



5 beta blockers vs calcium channel blockers in patients with pressure-rate product variation >1050

5.1 exercise duration (sec)

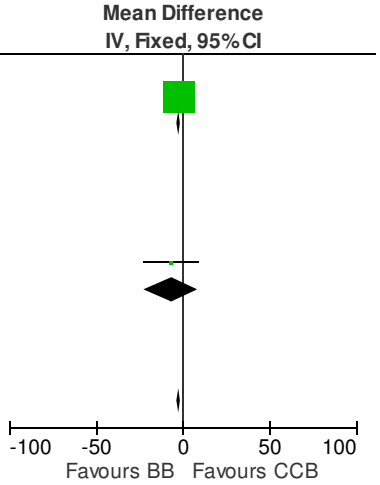
Study or Subgroup	beta blockers Mean	SD	Total	calcium channel blockers Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.1.1 acebutolol vs verapamil in patients with pressure-rate product variation <1050								
Romeo 1988	288	66	15	288	80	15	100.0%	0.00 [-52.48, 52.48]
Subtotal (95% CI)			**15**			**15**	**100.0%**	**0.00 [-52.48, 52.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Total (95% CI)			**15**			**15**	**100.0%**	**0.00 [-52.48, 52.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Test for subgroup differences: Not applicable								



6 Beta blockers vs calcium channel blockers

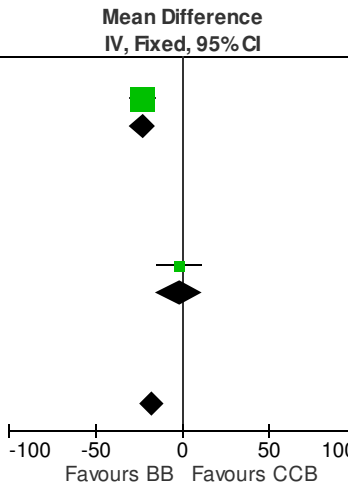
6.1 Number of anginal episodes (per 4 weeks per patient)

Study or Subgroup	beta blockers Mean	SD	Total	calcium channel blockers Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.1.1 propanolol vs verapamil								
Bugiardini 1989	0.7	0.6	16	3.4	1.7	16	99.7%	-2.70 [-3.58, -1.82]
Subtotal (95% CI)			**16**			**16**	**99.7%**	**-2.70 [-3.58, -1.82]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.99 (P < 0.00001)								
6.1.2 atenolol vs amlodipine								
Lanza 1999	15	13	10	22	22	10	0.3%	-7.00 [-22.84, 8.84]
Subtotal (95% CI)			**10**			**10**	**0.3%**	**-7.00 [-22.84, 8.84]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.87 (P = 0.39)								
Total (95% CI)			**26**			**26**	**100.0%**	**-2.71 [-3.60, -1.83]**
Heterogeneity: Chi² = 0.28, df = 1 (P = 0.60); I² = 0%								
Test for overall effect: Z = 6.03 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.28, df = 1 (P = 0.60), I² = 0%								



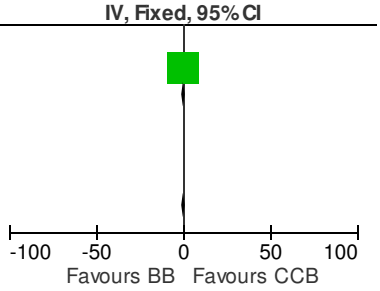
6.2 Chest pain episodes duration (min)

Study or Subgroup	beta blockers Mean	SD	Total	calcium channel blockers Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.2.1 propanolol vs verapamil								
Bugiardini 1989	4	5	16	27	15	16	74.6%	-23.00 [-30.75, -15.25]
Subtotal (95% CI)			**16**			**16**	**74.6%**	**-23.00 [-30.75, -15.25]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.82 (P < 0.00001)								
6.2.2 atenolol vs amlodipine								
Lanza 1999	14	13	10	16	17	10	25.4%	-2.00 [-15.26, 11.26]
Subtotal (95% CI)			**10**			**10**	**25.4%**	**-2.00 [-15.26, 11.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.30 (P = 0.77)								
Total (95% CI)			**26**			**26**	**100.0%**	**-17.66 [-24.35, -10.97]**
Heterogeneity: Chi² = 7.18, df = 1 (P = 0.007); I² = 86%								
Test for overall effect: Z = 5.17 (P < 0.00001)								
Test for subgroup differences: Chi² = 7.18, df = 1 (P = 0.007), I² = 86.1%								



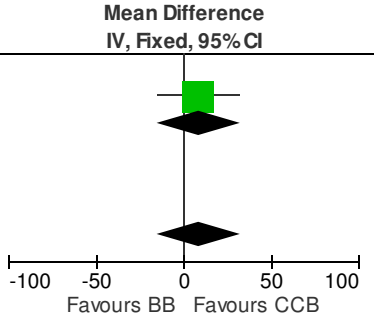
6.3 severity of chest pain (scale 1-5)

Study or Subgroup	beta blockers Mean	SD	Total	calcium channel blockers Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.3.1 atenolol vs amlodipine								
Lanza 1999	2.5	1.2	10	2.7	1	10	100.0%	-0.20 [-1.17, 0.77]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**-0.20 [-1.17, 0.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.40 (P = 0.69)								
Total (95% CI)			**10**			**10**	**100.0%**	**-0.20 [-1.17, 0.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.40 (P = 0.69)								
Test for subgroup differences: Not applicable								



6.4 quality of life (scale 0-100 mm)

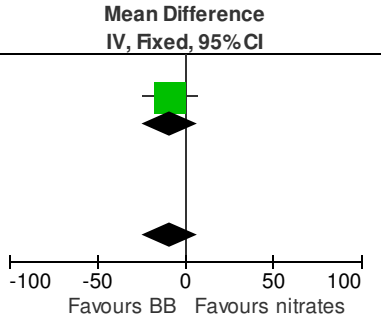
Study or Subgroup	beta blockers Mean	SD	Total	calcium channel blockers Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.4.1 atenolol vs amlodipine								
Lanza 1999	59	29	10	51	25	10	100.0%	8.00 [-15.73, 31.73]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**8.00 [-15.73, 31.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.66 (P = 0.51)								
Total (95% CI)			**10**			**10**	**100.0%**	**8.00 [-15.73, 31.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.66 (P = 0.51)								
Test for subgroup differences: Not applicable								



7 beta blockers vs nitrates

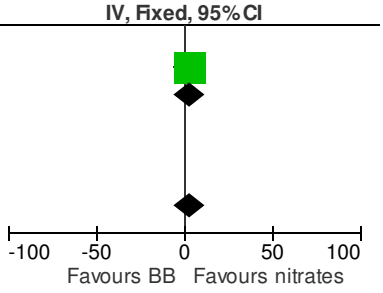
7.1 Number of anginal episodes (per 4 weeks per patient)

Study or Subgroup	beta blockers Mean	SD	Total	nitrates Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.1.1 atenolol vs ISMN								
Lanza 1999	15	13	10	24	22	10	100.0%	-9.00 [-24.84, 6.84]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**-9.00 [-24.84, 6.84]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.11 (P = 0.27)								
Total (95% CI)			**10**			**10**	**100.0%**	**-9.00 [-24.84, 6.84]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.11 (P = 0.27)								
Test for subgroup differences: Not applicable								



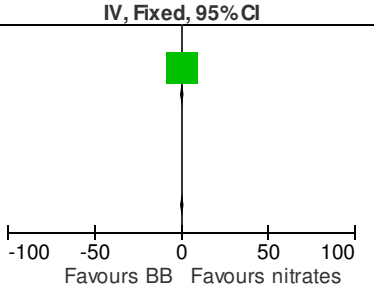
7.2 Chest pain episodes duration (min)

Study or Subgroup	beta blockers Mean	SD	Total	nitrates Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.2.1 atenolol vs ISMN								
Lanza 1999	14	13	10	11	7	10	100.0%	3.00 [-6.15, 12.15]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**3.00 [-6.15, 12.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.64 (P = 0.52)								
Total (95% CI)			**10**			**10**	**100.0%**	**3.00 [-6.15, 12.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.64 (P = 0.52)								
Test for subgroup differences: Not applicable								



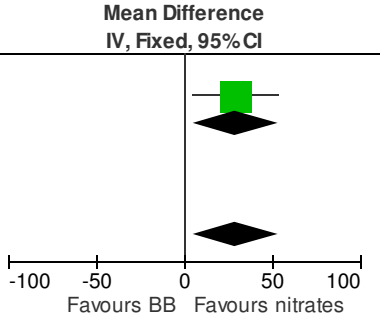
7.3 severity of chest pain (scale 1-5)

Study or Subgroup	beta blockers Mean	SD	Total	nitrates Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.3.1 atenolol vs ISMN								
Lanza 1999	2.5	1.2	10	2.3	1.2	10	100.0%	0.20 [-0.85, 1.25]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**0.20 [-0.85, 1.25]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.37 (P = 0.71)								
Total (95% CI)			**10**			**10**	**100.0%**	**0.20 [-0.85, 1.25]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.37 (P = 0.71)								
Test for subgroup differences: Not applicable								



7.4 quality of life (scale 0-100 mm)

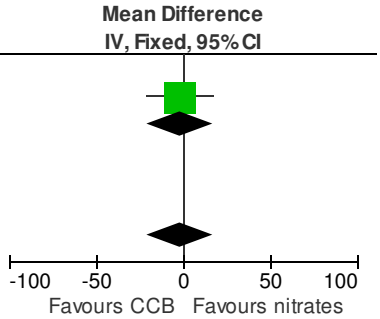
Study or Subgroup	beta blockers Mean	SD	Total	nitrates Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.4.1 atenolol vs ISMN								
Lanza 1999	59	29	10	30	27	10	100.0%	29.00 [4.44, 53.56]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**29.00 [4.44, 53.56]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.31 (P = 0.02)								
Total (95% CI)			**10**			**10**	**100.0%**	**29.00 [4.44, 53.56]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.31 (P = 0.02)								
Test for subgroup differences: Not applicable								



8 Calcium channel blockers vs nitrates

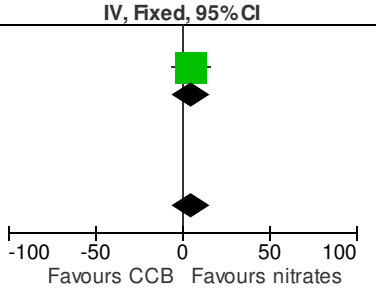
8.1 Number of anginal episodes (per 4 weeks per patient)

Study or Subgroup	calcium channel blockers Mean	SD	Total	nitrates Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
8.1.1 amlodipine vs ISMN								
Lanza 1999	22	22	10	24	22	10	100.0%	-2.00 [-21.28, 17.28]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**-2.00 [-21.28, 17.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.20 (P = 0.84)								
Total (95% CI)			**10**			**10**	**100.0%**	**-2.00 [-21.28, 17.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.20 (P = 0.84)								
Test for subgroup differences: Not applicable								



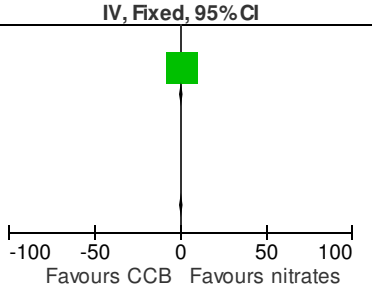
8.2 Chest pain episodes duration (min)

Study or Subgroup	calcium channel blockers Mean	SD	Total	nitrates Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
8.2.1 amlodipine vs ISMN								
Lanza 1999	16	17	10	11	7	10	100.0%	5.00 [-6.39, 16.39]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**5.00 [-6.39, 16.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.86 (P = 0.39)								
Total (95% CI)			**10**			**10**	**100.0%**	**5.00 [-6.39, 16.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.86 (P = 0.39)								
Test for subgroup differences: Not applicable								



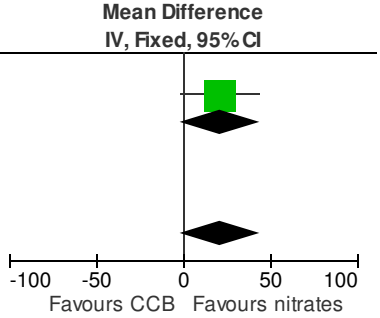
8.3 severity of chest pain (scale 1-5)

Study or Subgroup	calcium channel blockers Mean	SD	Total	nitrates Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
8.3.1 amlodipine vs ISMN								
Lanza 1999	2.7	1	10	2.3	1.2	10	100.0%	0.40 [-0.57, 1.37]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**0.40 [-0.57, 1.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.81 (P = 0.42)								
Total (95% CI)			**10**			**10**	**100.0%**	**0.40 [-0.57, 1.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.81 (P = 0.42)								
Test for subgroup differences: Not applicable								



8.4 quality of life (scale 0-100 mm)

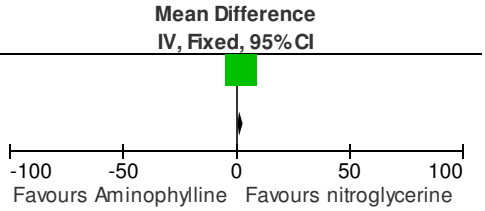
Study or Subgroup	calcium channel blockers Mean	SD	Total	nitrates Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
8.4.1 amlodipine vs ISMN								
Lanza 1999	51	25	10	30	27	10	100.0%	21.00 [-1.81, 43.81]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**21.00 [-1.81, 43.81]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.80 (P = 0.07)								
Total (95% CI)			**10**			**10**	**100.0%**	**21.00 [-1.81, 43.81]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.80 (P = 0.07)								
Test for subgroup differences: Not applicable								



9 Aminophylline vs Nitroglycerine

9.1 Time to 1mm ST depression

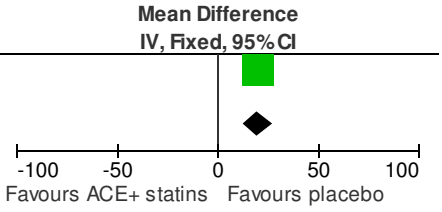
Study or Subgroup	Aminophylline Mean	SD	Total	Nitroglycerine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Radice 1996	5.5	1.6	20	3.6	1.7	20	100.0%	1.90 [0.88, 2.92]
Total (95% CI)			**20**			**20**	**100.0%**	**1.90 [0.88, 2.92]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.64 (P = 0.0003)								



10 Angiotensin-Converting Enzyme Inhibitors and statins vs placebo

10.1 Seattle Angina Questionnaire angina frequency score

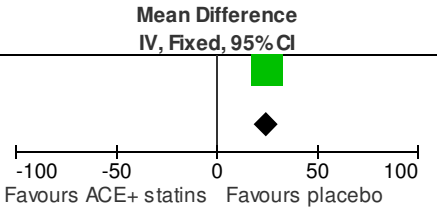
Study or Subgroup	ACE + statins Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Pizzi 2004	82.1	13.8	22	62.4	10.5	23	100.0%	19.70 [12.51, 26.89]
Total (95% CI)			**22**			**23**	**100.0%**	**19.70 [12.51, 26.89]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.37 (P < 0.00001)								



10.2 Seattle Angina Questionnaire Quality of life score

	ACE + statins			Placebo				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Pizzi 2004	86.5	11.7	22	61.9	9.4	23	100.0%	24.60 [18.38, 30.82]
Total (95% CI)			**22**			**23**	**100.0%**	**24.60 [18.38, 30.82]**

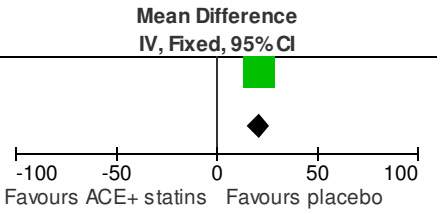
Heterogeneity: Not applicable
Test for overall effect: Z = 7.75 (P < 0.00001)



10.3 Seattle Angina Questionnaire summary score

	ACE + statins			Placebo				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Pizzi 2004	84.2	9.8	22	63.3	8.6	23	100.0%	20.90 [15.50, 26.30]
Total (95% CI)			**22**			**23**	**100.0%**	**20.90 [15.50, 26.30]**

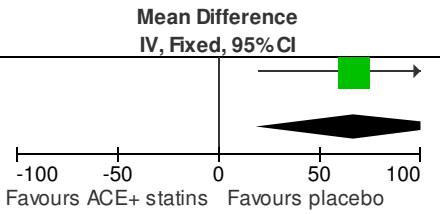
Heterogeneity: Not applicable
Test for overall effect: Z = 7.59 (P < 0.00001)



10.4 Peak exercise time (s)

	ACE + statins			Placebo				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Pizzi 2004	555.6	84.6	22	488.4	79.2	23	100.0%	67.20 [19.27, 115.13]
Total (95% CI)			**22**			**23**	**100.0%**	**67.20 [19.27, 115.13]**

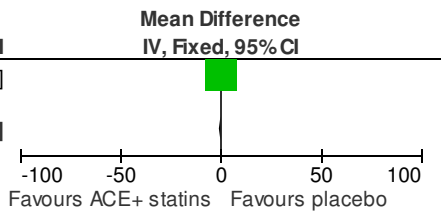
Heterogeneity: Not applicable
Test for overall effect: Z = 2.75 (P = 0.006)



10.5 ST depression (mV)

	ACE + statins			Placebo				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Pizzi 2004	0.12	0.3	22	0.21	0.8	23	100.0%	-0.09 [-0.44, 0.26]
Total (95% CI)			**22**			**23**	**100.0%**	**-0.09 [-0.44, 0.26]**

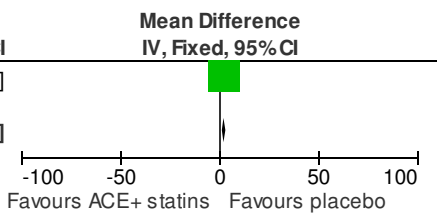
Heterogeneity: Not applicable
Test for overall effect: Z = 0.50 (P = 0.61)



10.6 Flow-mediated Dilation of brachial artery (%)

	ACE + statins			Placebo				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Pizzi 2004	4.2	1.7	22	2.3	1.2	23	100.0%	1.90 [1.04, 2.76]
Total (95% CI)			**22**			**23**	**100.0%**	**1.90 [1.04, 2.76]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.31 (P < 0.0001)

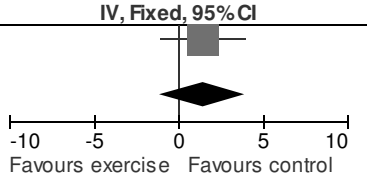


1 Exercise programme + symptom monitoring versus symptoms monitoring only

1.1 HADS total (8 week follow up)

Study or Subgroup	Exercise + monitoring Mean	SD	Total	Monitoring only Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Asbury 2008	11.5	5.7	32	10.1	4.6	32	100.0%	1.40 [-1.14, 3.94]
Total (95% CI)			**32**			**32**	**100.0%**	**1.40 [-1.14, 3.94]**

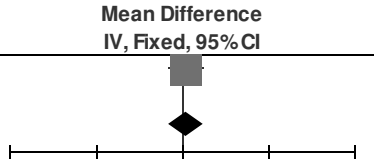
Heterogeneity: Not applicable
Test for overall effect: Z = 1.08 (P = 0.28)



1.2 SF-36 physical functioning (8 week follow up)

Study or Subgroup	Exercise + monitoring Mean	SD	Total	Monitoring only Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Asbury 2008	62.1	19.7	32	60.3	22.2	32	100.0%	1.80 [-8.48, 12.08]
Total (95% CI)			**32**			**32**	**100.0%**	**1.80 [-8.48, 12.08]**

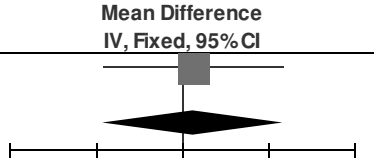
Heterogeneity: Not applicable
Test for overall effect: Z = 0.34 (P = 0.73)



1.3 SF-36 pain (8 week follow up)

Study or Subgroup	Exercise + monitoring Mean	SD	Total	Monitoring only Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Asbury 2008	58.7	22.3	32	57.4	20.3	32	100.0%	1.30 [-9.15, 11.75]
Total (95% CI)			**32**			**32**	**100.0%**	**1.30 [-9.15, 11.75]**

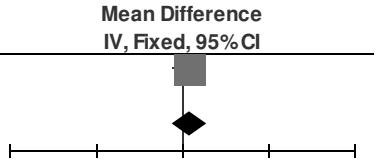
Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)



1.4 SF-36 general health (8 week follow up)

Study or Subgroup	Exercise + monitoring Mean	SD	Total	Monitoring only Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Asbury 2008	58.2	16.4	32	54.3	22.9	32	100.0%	3.90 [-5.86, 13.66]
Total (95% CI)			**32**			**32**	**100.0%**	**3.90 [-5.86, 13.66]**

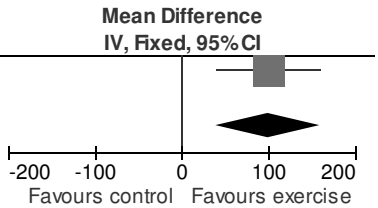
Heterogeneity: Not applicable
Test for overall effect: Z = 0.78 (P = 0.43)



1.5 Shuttle walk test (m) (8 week follow up)

Study or Subgroup	Exercise + monitoring Mean	SD	Total	Monitoring only Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Asbury 2008	426.6	133	32	326.8	111	32	100.0%	99.80 [39.78, 159.82]
Total (95% CI)			**32**			**32**	**100.0%**	**99.80 [39.78, 159.82]**

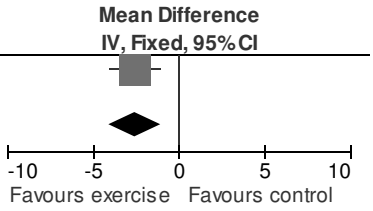
Heterogeneity: Not applicable
Test for overall effect: Z = 3.26 (P = 0.001)



1.6 Symptom frequency (8 week follow up)

Study or Subgroup	Exercise + monitoring Mean	SD	Total	Monitoring only Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Asbury 2008	2	2.1	32	4.6	3.8	32	100.0%	-2.60 [-4.10, -1.10]
Total (95% CI)			**32**			**32**	**100.0%**	**-2.60 [-4.10, -1.10]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.39 (P = 0.0007)

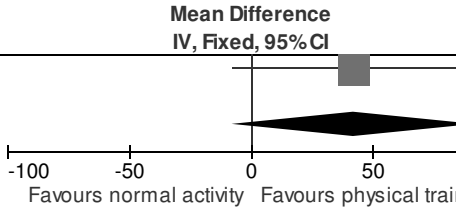


2 Physical training versus normal activity

2.1 Distance walked (m) (8 week follow up)

Study or Subgroup	Physical training Mean	SD	Total	Normal activity Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tyni-Lenne 2002	587	49	7	545	46	7	100.0%	42.00 [-7.79, 91.79]
Total (95% CI)			**7**			**7**	**100.0%**	**42.00 [-7.79, 91.79]**

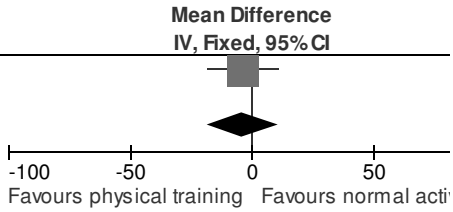
Heterogeneity: Not applicable
Test for overall effect: Z = 1.65 (P = 0.10)



2.2 Peak heart rate (bpm) (8 week follow up)

Study or Subgroup	Physical training Mean	SD	Total	Normal activity Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tyni-Lenne 2002	102	17	7	106	10	7	100.0%	-4.00 [-18.61, 10.61]
Total (95% CI)			**7**			**7**	**100.0%**	**-4.00 [-18.61, 10.61]**

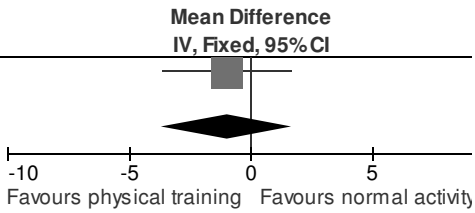
Heterogeneity: Not applicable
Test for overall effect: Z = 0.54 (P = 0.59)



2.3 Exertion (Borg RPE) (8 week follow up)

Study or Subgroup	Physical training Mean	SD	Total	Normal activity Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tyni-Lenne 2002	13	3	7	14	2	7	100.0%	-1.00 [-3.67, 1.67]
Total (95% CI)			**7**			**7**	**100.0%**	**-1.00 [-3.67, 1.67]**

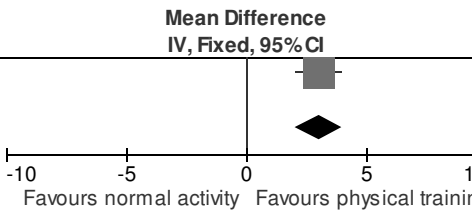
Heterogeneity: Not applicable
Test for overall effect: Z = 0.73 (P = 0.46)



2.4 Pain onset (min) after exercise (8 week follow up)

Study or Subgroup	Physical training Mean	SD	Total	Normal activity Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Eriksson 2000	6	1	7	3	1	10	100.0%	3.00 [2.03, 3.97]
Total (95% CI)			**7**			**10**	**100.0%**	**3.00 [2.03, 3.97]**

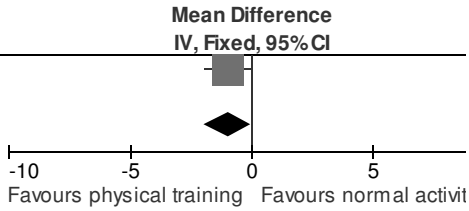
Heterogeneity: Not applicable
Test for overall effect: Z = 6.09 (P < 0.00001)



2.5 Max pain (Borg CR-10) (8 week follow up)

Study or Subgroup	Physical training Mean	SD	Total	Normal activity Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Eriksson 2000	3	1	7	4	1	10	100.0%	-1.00 [-1.97, -0.03]
Total (95% CI)			**7**			**10**	**100.0%**	**-1.00 [-1.97, -0.03]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.03 (P = 0.04)

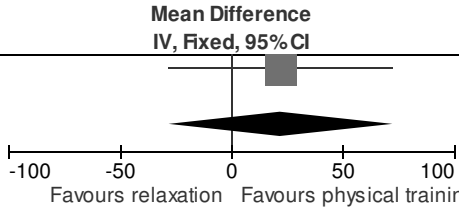


3 Physical training versus relaxation

3.1 Distance walked (m) (8 week follow up)

Study or Subgroup	Physical training Mean	SD	Total	Relaxation Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tyni-Lenne 2002	587	49	7	565	47	7	100.0%	22.00 [-28.30, 72.30]
Total (95% CI)			**7**			**7**	**100.0%**	**22.00 [-28.30, 72.30]**

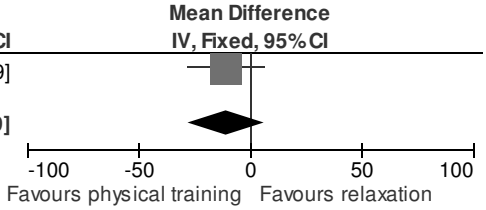
Heterogeneity: Not applicable
Test for overall effect: Z = 0.86 (P = 0.39)



3.2 Peak heart rate (bpm) (8 week follow up)

Study or Subgroup	Physical training Mean	SD	Total	Relaxation Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tyni-Lenne 2002	102	17	7	113	16	7	100.0%	-11.00 [-28.29, 6.29]
Total (95% CI)			**7**			**7**	**100.0%**	**-11.00 [-28.29, 6.29]**

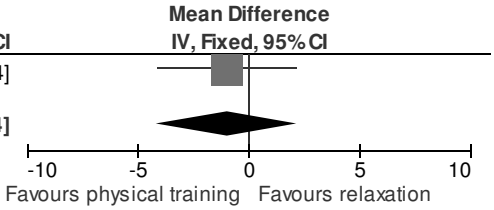
Heterogeneity: Not applicable
Test for overall effect: Z = 1.25 (P = 0.21)



3.3 Exertion (Borg RPE) (8 week follow up)

Study or Subgroup	Physical training Mean	SD	Total	Relaxation Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tyni-Lenne 2002	13	3	7	14	3	7	100.0%	-1.00 [-4.14, 2.14]
Total (95% CI)			**7**			**7**	**100.0%**	**-1.00 [-4.14, 2.14]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.62 (P = 0.53)

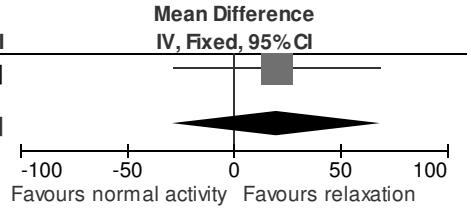


4 Relaxation versus normal activity

4.1 Distance walked (m) (8 week follow up)

Study or Subgroup	Relaxation Mean	SD	Total	Normal activity Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tyni-Lenne 2002	565	47	7	545	46	7	100.0%	20.00 [-28.72, 68.72]
Total (95% CI)			**7**			**7**	**100.0%**	**20.00 [-28.72, 68.72]**

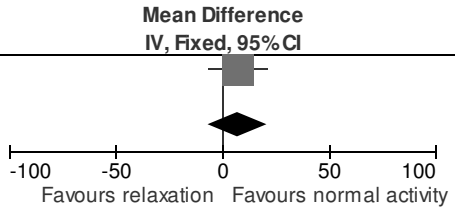
Heterogeneity: Not applicable
Test for overall effect: Z = 0.80 (P = 0.42)



4.2 Peak heart rate (bpm) (8 week follow up)

Study or Subgroup	Relaxation Mean	SD	Total	Normal activity Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tyni-Lenne 2002	113	16	7	106	10	7	100.0%	7.00 [-6.98, 20.98]
Total (95% CI)			**7**			**7**	**100.0%**	**7.00 [-6.98, 20.98]**

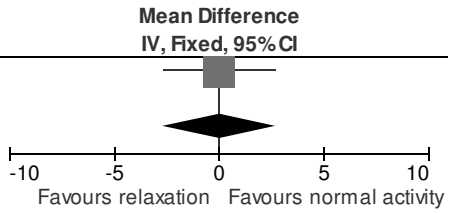
Heterogeneity: Not applicable
Test for overall effect: Z = 0.98 (P = 0.33)



4.3 Exertion (Borg RPE) (8 week follow up)

Study or Subgroup	Relaxation Mean	SD	Total	Normal activity Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tyni-Lenne 2002	14	3	7	14	2	7	100.0%	0.00 [-2.67, 2.67]
Total (95% CI)			**7**			**7**	**100.0%**	**0.00 [-2.67, 2.67]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

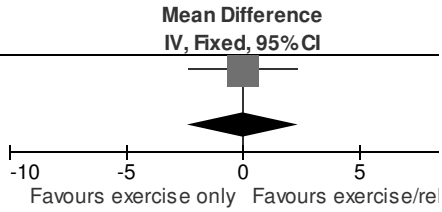


5 Exercise plus relaxation training versus exercise training

5.4 Pain onset (min) after exercise (8 week follow up)

Study or Subgroup	Exercise + relaxation Mean	SD	Total	Exercise only Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Eriksson 2000	6	3	7	6	1	7	100.0%	0.00 [-2.34, 2.34]
Total (95% CI)			**7**			**7**	**100.0%**	**0.00 [-2.34, 2.34]**

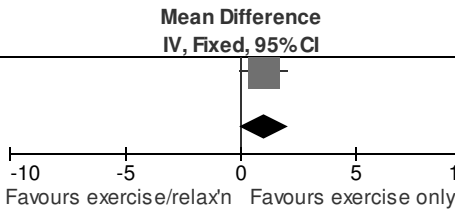
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



5.5 Max pain (Borg CR-10) (8 week follow up)

Study or Subgroup	Exercise/relaxation Mean	SD	Total	Exercise only Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Eriksson 2000	4	1	7	3	1	7	100.0%	1.00 [-0.05, 2.05]
Total (95% CI)			**7**			**7**	**100.0%**	**1.00 [-0.05, 2.05]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.87 (P = 0.06)

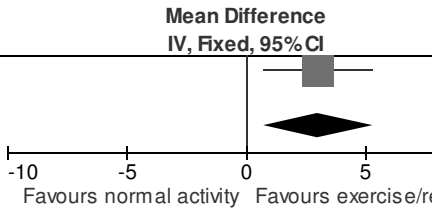


6 Exercise plus relaxation training versus normal activity

6.4 Pain onset (min) after exercise (8 week follow up)

Study or Subgroup	Exercise + relaxation Mean	SD	Total	Normal activity Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Eriksson 2000	6	3	7	3	1	10	100.0%	3.00 [0.69, 5.31]
Total (95% CI)			**7**			**10**	**100.0%**	**3.00 [0.69, 5.31]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.55 (P = 0.01)



6.5 Max pain (Borg CR-10) (8 week follow up)

Study or Subgroup	Exercise/relaxation Mean	SD	Total	Normal activity Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Eriksson 2000	4	1	7	4	1	10	100.0%	0.00 [-0.97, 0.97]
Total (95% CI)			**7**			**10**	**100.0%**	**0.00 [-0.97, 0.97]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)