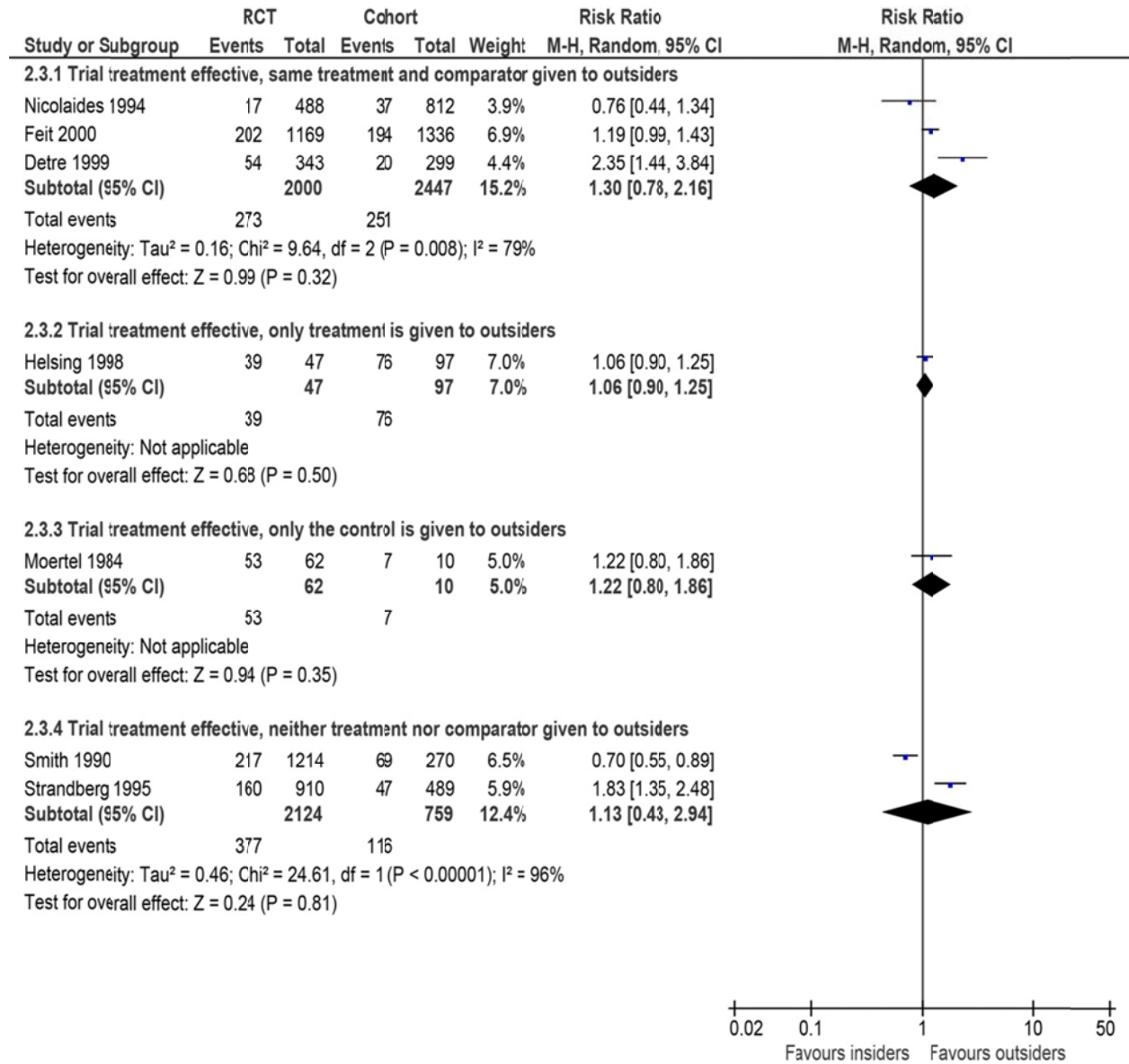**Appendix 2 (as supplied by the authors):** Meta-analyses for randomized controlled trials (RCTs) with mortality as an outcome, without randomization of potential participants as "insiders" (participating in the RCT) v. "outsiders" (not participating in the RCT); subgroups are based on effectiveness of trial treatment. Values less than 1.0 indicate that being an "insider" is favoured. CASS = Coronary Artery Surgery Study, CI = confidence interval. For reference details, see the reference list in the main article.

Study or Subgroup	RCT Events	Total	Cohort Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.3.1 Trial treatment effective, same treatment and comparator given to outsiders						
Nicolaides 1994	17	488	37	812	3.9%	0.76 [0.44, 1.34]
Feit 2000	202	1169	194	1336	6.9%	1.19 [0.99, 1.43]
Detre 1999	54	343	20	299	4.4%	2.35 [1.44, 3.84]
Subtotal (95% CI)		2000		2447	15.2%	1.30 [0.78, 2.16]
Total events	273		251			
Heterogeneity: Tau² = 0.16; Chi² = 9.64, df = 2 (P = 0.008); I² = 79%						
Test for overall effect: Z = 0.99 (P = 0.32)						
2.3.2 Trial treatment effective, only treatment is given to outsiders						
Helsing 1998	39	47	76	97	7.0%	1.06 [0.90, 1.25]
Subtotal (95% CI)		47		97	7.0%	1.06 [0.90, 1.25]
Total events	39		76			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
2.3.3 Trial treatment effective, only the control is given to outsiders						
Moertel 1984	53	62	7	10	5.0%	1.22 [0.80, 1.86]
Subtotal (95% CI)		62		10	5.0%	1.22 [0.80, 1.86]
Total events	53		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.94 (P = 0.35)						
2.3.4 Trial treatment effective, neither treatment nor comparator given to outsiders						
Smith 1990	217	1214	69	270	6.5%	0.70 [0.55, 0.89]
Strandberg 1995	160	910	47	489	5.9%	1.83 [1.35, 2.48]
Subtotal (95% CI)		2124		759	12.4%	1.13 [0.43, 2.94]
Total events	377		116			
Heterogeneity: Tau² = 0.46; Chi² = 24.61, df = 1 (P < 0.00001); I² = 96%						
Test for overall effect: Z = 0.24 (P = 0.81)						

Favours insiders   Favours outsiders

Appendix 2 (continued)

Study or Subgroup	RCT Events	RCT Total	Cohort Events	Cohort Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
2.3.5 Trial treatment ineffective							
Lidbrink 1995	23	20000	42	7785	4.3%	0.21 [0.13, 0.35]	
Boesen 2007	18	258	18	137	3.5%	0.53 [0.29, 0.99]	
van Bergen 1995	42	350	118	587	5.8%	0.60 [0.43, 0.83]	
Clapp 1989	6	115	7	85	1.7%	0.63 [0.22, 1.82]	
Rigg 2000	31	455	23	237	4.2%	0.70 [0.42, 1.18]	
Tanai 2009	71	100	15	19	6.3%	0.90 [0.69, 1.17]	
Woodhouse 1995	182	194	133	145	7.5%	1.02 [0.96, 1.09]	
CASS 1984	65	779	104	1309	6.0%	1.05 [0.78, 1.41]	
Urban 1999	40	55	12	24	4.9%	1.45 [0.94, 2.24]	
Subtotal (95% CI)		22306		10328	44.2%	0.73 [0.50, 1.05]	
Total events	478		472				

Heterogeneity: Tau² = 0.26; Chi² = 101.87, df = 8 (P < 0.00001); I² = 92%
Test for overall effect: Z = 1.70 (P = 0.09)

Study or Subgroup	RCT Events	RCT Total	Cohort Events	Cohort Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
2.3.6 Trial effect, or treatment given unknown							
Marcinczyk 1997	0	54	0	29		Not estimable	
Vind 2009	1	256	4	297	0.5%	0.29 [0.03, 2.58]	
Sesso 2002	165	22071	128	11152	6.6%	0.65 [0.52, 0.82]	
Tenenbaum 2002	423	3122	52	380	6.3%	0.99 [0.76, 1.29]	
Wyse 1991	51	1672	8	318	2.9%	1.21 [0.58, 2.53]	
Subtotal (95% CI)		27175		12176	16.2%	0.83 [0.59, 1.18]	
Total events	640		192				

Heterogeneity: Tau² = 0.06; Chi² = 7.56, df = 3 (P = 0.06); I² = 60%
Test for overall effect: Z = 1.03 (P = 0.30)

Total (95% CI)		53714		25817	100.0%	0.92 [0.78, 1.07]	
Total events	1860		1114				

Heterogeneity: Tau² = 0.09; Chi² = 117.15, df = 19 (P < 0.00001); I² = 84%
Test for overall effect: Z = 1.09 (P = 0.28)
Test for subgroup differences: Chi² = 6.33, df = 5 (P = 0.28), I² = 21.0%

Favours insiders   Favours outsiders
0.02   0.1   1   10   50