Appendix 23c: 2009 Pharmacological clinical evidence forest plots[1]

[1] Each study included in this appendix is referred to by a study ID, with studies included in the previous guideline in lower case and new studies in upper case (primary author and date or study number for unpublished trials).

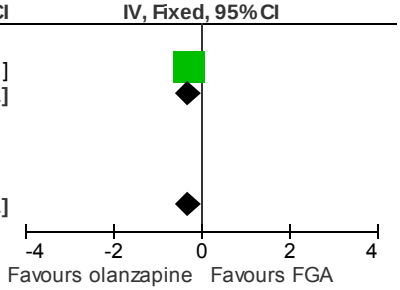
Table 1: Studies included in the initial treatment review

Treatment	versus Comparator		
	HAL	**QUE**	**RIS**
OLZ	Jones 1998 [54weeks, N=44] DEHAAN2003 [6weeks, N=24] LIEBERMAN2003A [24weeks, N=263]	MCEVOY2007A [52weeks, N=267]	Jones 1998 [54weeks, N=42] MCEVOY2007A [52weeks, N=266] VANNIMWEGEN2008 [6weeks, N=138]
RIS	Emsley1995 [6weeks, N=183] Jones 1998 [54weeks, N=44] LEE2007 [24weeks, N=20] MOLLER2008 [8weeks, N=296] SCHOOLER2005 [104weeks, N=559]	MCEVOY2007A [52weeks, N=267]	

1 Olanzapine versus haloperidol (critical outcomes)

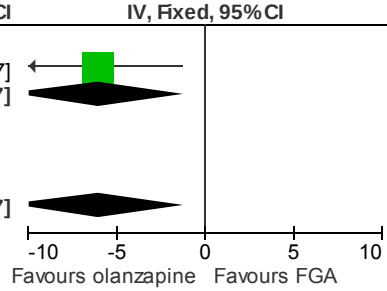
1.1 Global state: 1. Severity score (CGI)

Study or Subgroup	Olanzapine Mean	SD	Total	FGA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 vs. haloperidol (medium-term)								
LIEBERMAN2003A	3.24	1.18	127	3.54	1.18	127	100.0%	-0.30 [-0.59, -0.01]
Subtotal (95% CI)			**127**			**127**	**100.0%**	**-0.30 [-0.59, -0.01]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.03 (P = 0.04)								
Total (95% CI)			**127**			**127**	**100.0%**	**-0.30 [-0.59, -0.01]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.03 (P = 0.04)								
Test for subgroup differences: Not applicable								



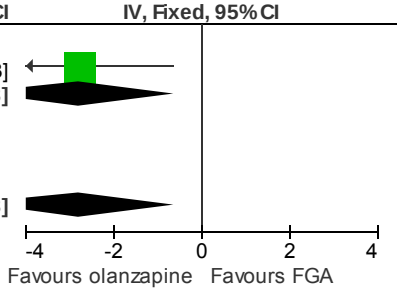
1.2 Mental state: 1. PANSS total (endpoint)

Study or Subgroup	Olanzapine Mean	SD	Total	FGA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.2.1 vs. haloperidol (medium-term) - PANSS total score								
LIEBERMAN2003A	59.33	19.41	126	65.4	19.42	125	100.0%	-6.07 [-10.87, -1.27]
Subtotal (95% CI)			**126**			**125**	**100.0%**	**-6.07 [-10.87, -1.27]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.48 (P = 0.01)								
Total (95% CI)			**126**			**125**	**100.0%**	**-6.07 [-10.87, -1.27]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.48 (P = 0.01)								
Test for subgroup differences: Not applicable								



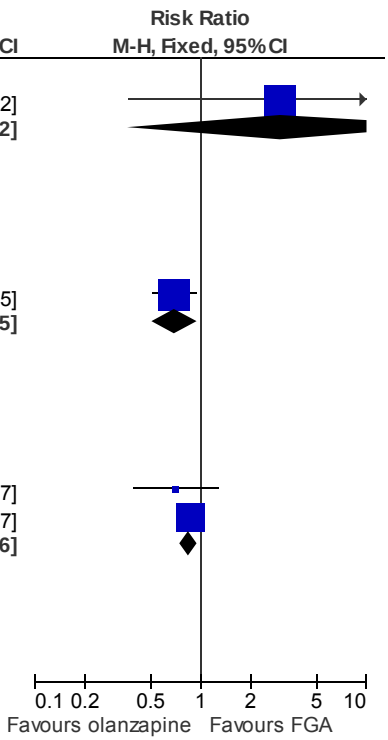
1.3 Mental state: 2. Depression (endpoint)

Study or Subgroup	Olanzapine Mean	SD	Total	FGA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.3.1 vs. haloperidol (medium-term) - Montgomery-Asberg Depression Score								
LIEBERMAN2003A	8.49	8.68	125	11.27	8.68	126	100.0%	-2.78 [-4.93, -0.63]
Subtotal (95% CI)			**125**			**126**	**100.0%**	**-2.78 [-4.93, -0.63]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.54 (P = 0.01)								
Total (95% CI)			**125**			**126**	**100.0%**	**-2.78 [-4.93, -0.63]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.54 (P = 0.01)								
Test for subgroup differences: Not applicable								



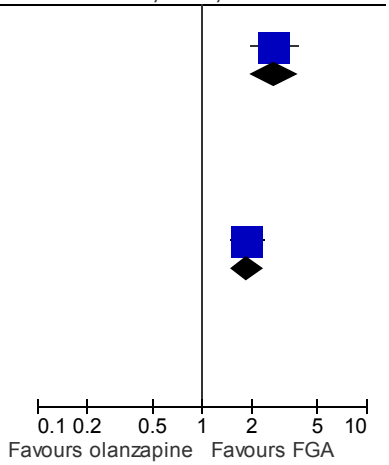
1.4 Leaving the study early: 1. Any reason

Study or Subgroup	Olanzapine Events	Olanzapine Total	FGA Events	FGA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 vs. haloperidol (short-term: <12 weeks)						
DEHAAN2003	3	12	1	12	100.0%	3.00 [0.36, 24.92]
Subtotal (95% CI)		**12**		**12**	**100.0%**	**3.00 [0.36, 24.92]**
Total events	3		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						
1.4.2 vs. haloperidol (medium-term: 12-51 weeks)						
LIEBERMAN2003A	42	131	61	132	100.0%	0.69 [0.51, 0.95]
Subtotal (95% CI)		**131**		**132**	**100.0%**	**0.69 [0.51, 0.95]**
Total events	42		61			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.31 (P = 0.02)						
1.4.3 vs. haloperidol (long-term: >51 weeks)						
Jones1998	9	21	14	23	10.4%	0.70 [0.39, 1.27]
LIEBERMAN2003A	100	131	116	132	89.6%	0.87 [0.77, 0.97]
Subtotal (95% CI)		**152**		**155**	**100.0%**	**0.85 [0.76, 0.96]**
Total events	109		130			
Heterogeneity: Chi² = 0.51, df = 1 (P = 0.47); I² = 0%						
Test for overall effect: Z = 2.67 (P = 0.007)						



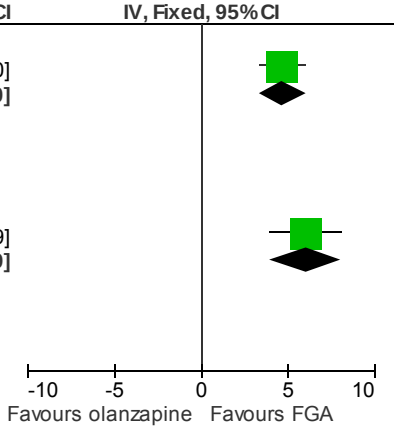
1.5 AE: 1. Metabolic SEs - weight gain

Study or Subgroup	Olanzapine Events	Olanzapine Total	FGA Events	FGA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.5.1 vs. haloperidol (short-term) - >7% increase in body weight from baseline						
LIEBERMAN2003A	81	131	30	132	100.0%	2.72 [1.93, 3.83]
Subtotal (95% CI)		**131**		**132**	**100.0%**	**2.72 [1.93, 3.83]**
Total events	81		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.73 (P < 0.00001)						
1.5.2 vs. haloperidol (long-term: 2 yrs) - >7% increase in body weight from baseline						
LIEBERMAN2003A	95	131	51	132	100.0%	1.88 [1.48, 2.38]
Subtotal (95% CI)		**131**		**132**	**100.0%**	**1.88 [1.48, 2.38]**
Total events	95		51			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.15 (P < 0.00001)						



1.6 AE: 1. Metabolic SEs - weight gain (change from baseline)

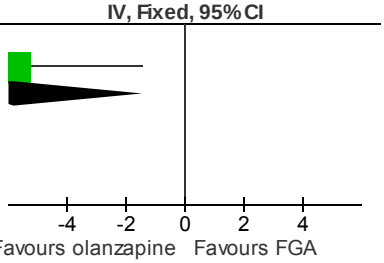
Study or Subgroup	Olanzapine Mean	SD	Total	FGA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.6.1 vs. haloperidol (medium-term)								
LIEBERMAN2003A	7.3	6.13	124	2.64	4.54	124	100.0%	4.66 [3.32, 6.00]
Subtotal (95% CI)			**124**			**124**	**100.0%**	**4.66 [3.32, 6.00]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 6.80 (P < 0.00001)								
1.6.2 vs. haloperidol (long-term)								
LIEBERMAN2003A	10.2	9.6	124	4.2	7	124	100.0%	6.00 [3.91, 8.09]
Subtotal (95% CI)			**124**			**124**	**100.0%**	**6.00 [3.91, 8.09]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.62 (P < 0.00001)								



Test for subgroup differences: Chi² = 1.12, df = 1 (P = 0.29), I² = 10.5%

1.7 AE: 1. Metabolic SEs - prolactin (ng/ml) (change from baseline)

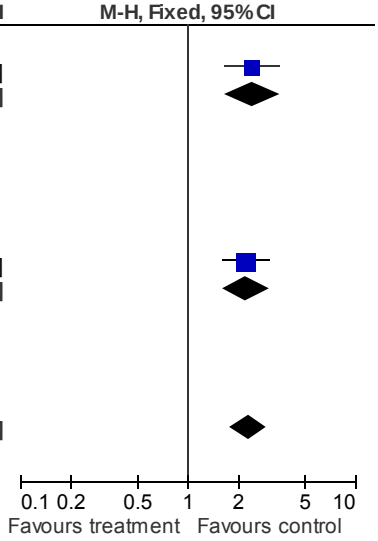
Study or Subgroup	Olanzapine Mean	SD	Total	FGA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.7.1 vs. haloperidol (medium-term)								
LIEBERMAN2003A	1.15	18.6	109	6.92	14.35	120	100.0%	-5.77 [-10.10, -1.44]
Subtotal (95% CI)			**109**			**120**	**100.0%**	**-5.77 [-10.10, -1.44]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.61 (P = 0.009)								



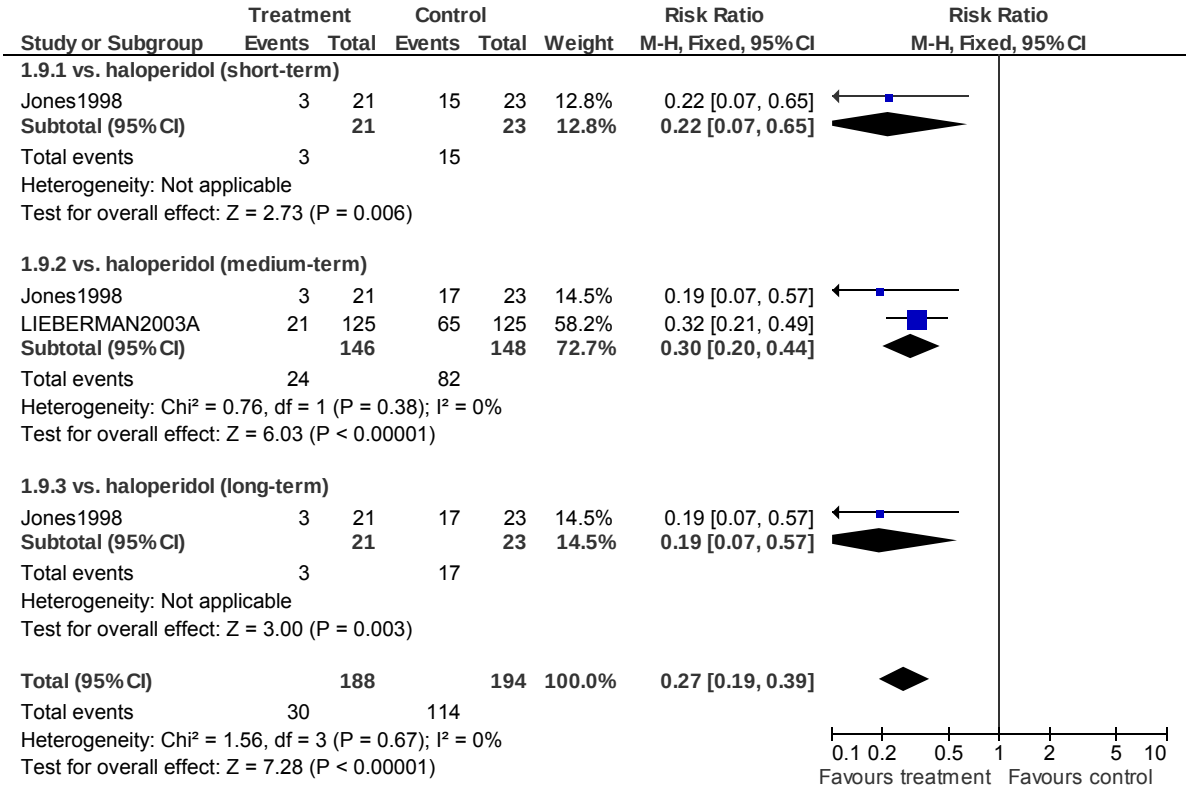
Test for subgroup differences: Not applicable

1.8 AE: 1. Metabolic SEs - abnormal liver enzyme levels

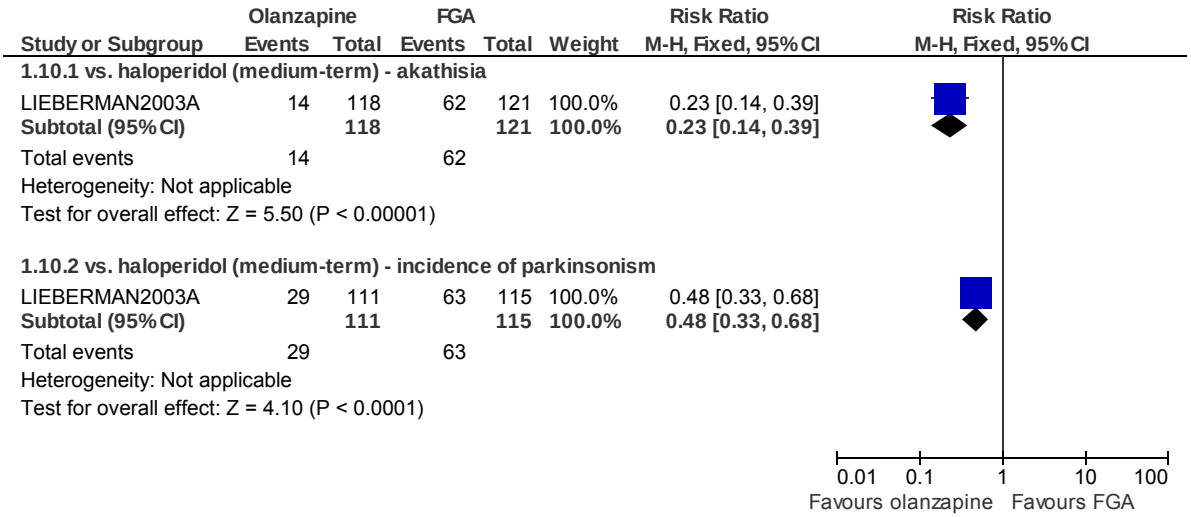
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.8.1 vs haloperidol (SGOT levels - long-term)						
LIEBERMAN2003A	54	100	26	116	44.1%	2.41 [1.64, 3.54]
Subtotal (95% CI)		**100**		**116**	**44.1%**	**2.41 [1.64, 3.54]**
Total events	54		26			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.49 (P < 0.00001)						
1.8.2 vs haloperidol (SGPT levels - long-term)						
LIEBERMAN2003A	63	100	33	116	55.9%	2.21 [1.60, 3.07]
Subtotal (95% CI)		**100**		**116**	**55.9%**	**2.21 [1.60, 3.07]**
Total events	63		33			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.79 (P < 0.00001)						
Total (95% CI)		**200**		**232**	**100.0%**	**2.30 [1.79, 2.95]**
Total events	117		59			
Heterogeneity: Chi² = 0.11, df = 1 (P = 0.74); I² = 0%						
Test for overall effect: Z = 6.57 (P < 0.00001)						



1.9 AE: 2. Neurologic SEs - Use of anticholinergic medication

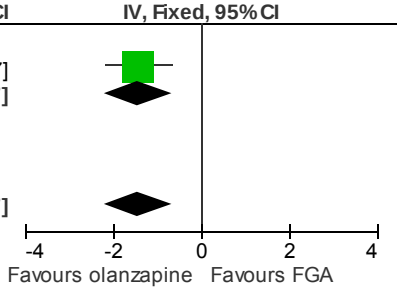


1.10 AE: 2. Neurologic SEs (treatment-emergent)



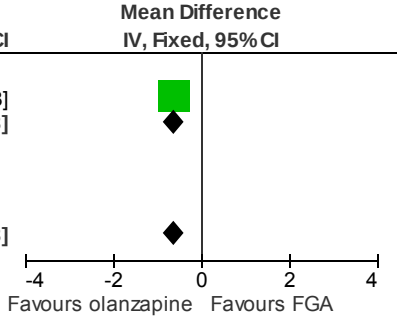
1.11 AE: 2. Neurologic SEs - treatment-emergent EPS (change from baseline)

Study or Subgroup	Olanzapine Mean	SD	Total	FGA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.11.1 vs. haloperidol (medium-term) - SAS								
LIEBERMAN2003A	0	3.01	124	1.44	3.15	124	100.0%	-1.44 [-2.21, -0.67]
Subtotal (95% CI)			**124**			**124**	**100.0%**	**-1.44 [-2.21, -0.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.68 (P = 0.0002)								
Total (95% CI)			**124**			**124**	**100.0%**	**-1.44 [-2.21, -0.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.68 (P = 0.0002)								
Test for subgroup differences: Not applicable								



1.12 AE: 2. Neurologic SEs - treatment-emergent akathisia (change from baseline)

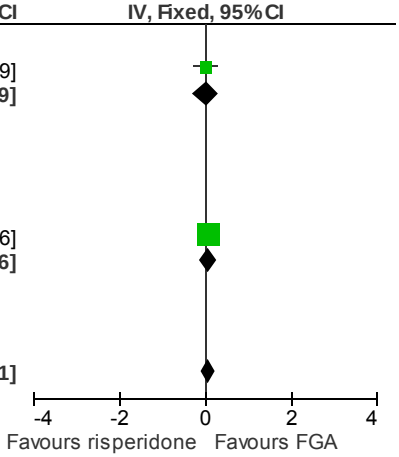
Study or Subgroup	Olanzapine Mean	SD	Total	FGA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.12.1 vs. haloperidol (medium-term) - BAS								
LIEBERMAN2003A	-0.13	0.86	125	0.5	1.14	125	100.0%	-0.63 [-0.88, -0.38]
Subtotal (95% CI)			**125**			**125**	**100.0%**	**-0.63 [-0.88, -0.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.93 (P < 0.00001)								
Total (95% CI)			**125**			**125**	**100.0%**	**-0.63 [-0.88, -0.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.93 (P < 0.00001)								
Test for subgroup differences: Not applicable								



2 Risperidone versus haloperidol (critical outcomes)

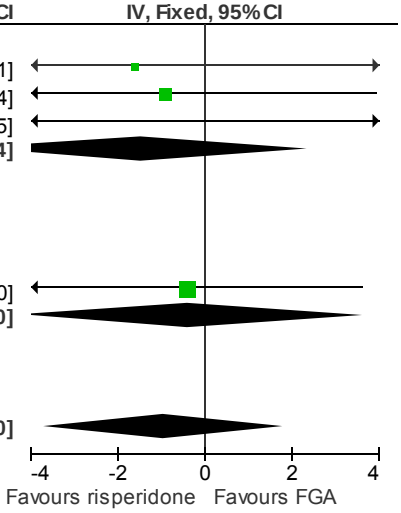
2.1 Global state: 1. Severity score (CGI)

Study or Subgroup	Risperidone Mean	SD	Total	FGA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.1.1 vs. haloperidol (short-term)								
MOLLER2008	3.9	1.2	143	3.9	1.3	146	31.3%	0.00 [-0.29, 0.29]
Subtotal (95% CI)			**143**			**146**	**31.3%**	**0.00 [-0.29, 0.29]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
2.1.2 vs. haloperidol (long-term)								
SCHOOLER2005	2.69	1.14	263	2.62	1.14	264	68.7%	0.07 [-0.12, 0.26]
Subtotal (95% CI)			**263**			**264**	**68.7%**	**0.07 [-0.12, 0.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.70 (P = 0.48)								
Total (95% CI)			**406**			**410**	**100.0%**	**0.05 [-0.11, 0.21]**
Heterogeneity: Chi² = 0.16, df = 1 (P = 0.69); I² = 0%								
Test for overall effect: Z = 0.58 (P = 0.56)								
Test for subgroup differences: Chi² = 0.16, df = 1 (P = 0.69), I² = 0%								



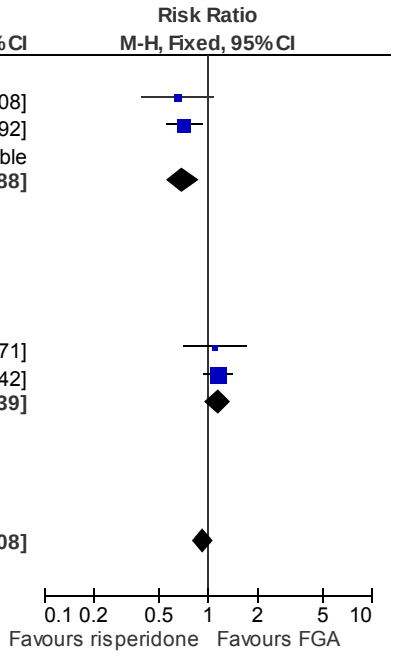
2.2 Mental state: 1. PANSS total (endpoint/change)

Study or Subgroup	Risperidone Mean	SD	Total	FGA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.2.1 vs. haloperidol (short-term) - PANSS total score								
Emsley1995	-30.9	24.75	98	-29.3	24.75	84	14.6%	-1.60 [-8.81, 5.61]
MOLLER2008	56.6	19.7	143	57.5	22.2	146	32.5%	-0.90 [-5.74, 3.94]
LEE2007	63.6	10.75	10	68.1	15.81	10	5.4%	-4.50 [-16.35, 7.35]
Subtotal (95% CI)			**251**			**240**	**52.6%**	**-1.47 [-5.27, 2.34]**
Heterogeneity: Chi² = 0.31, df = 2 (P = 0.86); I² = 0%								
Test for overall effect: Z = 0.76 (P = 0.45)								
2.2.2 vs. haloperidol (long-term) - PANSS total score								
SCHOOLER2005	-21	23.72	264	-20.6	23.23	264	47.4%	-0.40 [-4.40, 3.60]
Subtotal (95% CI)			**264**			**264**	**47.4%**	**-0.40 [-4.40, 3.60]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.20 (P = 0.84)								
Total (95% CI)			**515**			**504**	**100.0%**	**-0.96 [-3.72, 1.80]**
Heterogeneity: Chi² = 0.45, df = 3 (P = 0.93); I² = 0%								
Test for overall effect: Z = 0.68 (P = 0.50)								
Test for subgroup differences: Chi² = 0.14, df = 1 (P = 0.71), I² = 0%								



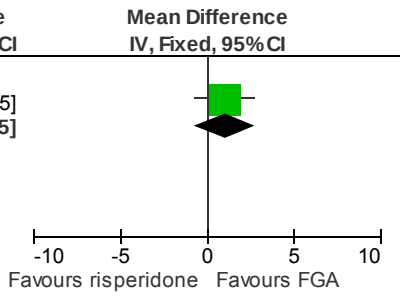
2.3 Leaving the study early: 1. Any reason

Study or Subgroup	Risperidone Events	Total	FGA Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.3.1 vs. haloperidol (short-term)						
Emsley1995	20	99	26	84	12.7%	0.65 [0.39, 1.08]
MOLLER2008	55	143	79	146	35.4%	0.71 [0.55, 0.92]
LEE2007	0	10	0	10		Not estimable
Subtotal (95% CI)		**252**		**240**	**48.1%**	**0.70 [0.55, 0.88]**
Total events	75		105			
Heterogeneity: Chi² = 0.09, df = 1 (P = 0.77); I² = 0%						
Test for overall effect: Z = 3.10 (P = 0.002)						
2.3.2 vs. haloperidol (long-term)						
Jones1998	14	21	14	23	6.1%	1.10 [0.70, 1.71]
SCHOOLER2005	117	278	101	277	45.8%	1.15 [0.94, 1.42]
Subtotal (95% CI)		**299**		**300**	**51.9%**	**1.15 [0.95, 1.39]**
Total events	131		115			
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.83); I² = 0%						
Test for overall effect: Z = 1.41 (P = 0.16)						
Total (95% CI)		**551**		**540**	**100.0%**	**0.93 [0.80, 1.08]**
Total events	206		220			
Heterogeneity: Chi² = 10.81, df = 3 (P = 0.01); I² = 72%						
Test for overall effect: Z = 0.98 (P = 0.33)						



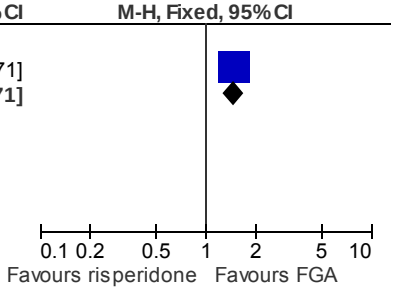
2.4 AE: 1. Metabolic SEs - weight gain - Endpoint

Study or Subgroup	Risperidone Mean	SD	Total	FGA Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.4.1 vs. haloperidol (long-term)								
SCHOOLER2005	7.5	9.29	211	6.5	8.86	204	100.0%	1.00 [-0.75, 2.75]
Subtotal (95% CI)			**211**			**204**	**100.0%**	**1.00 [-0.75, 2.75]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.12 (P = 0.26)								
Test for subgroup differences: Not applicable								



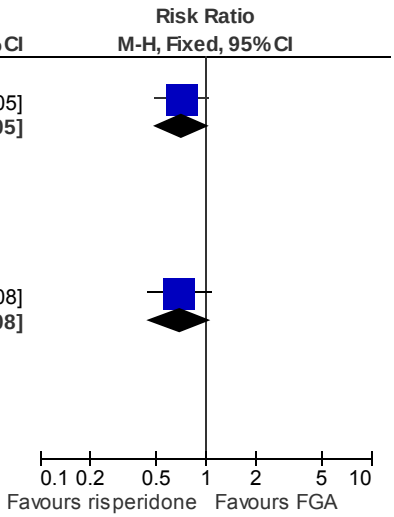
2.5 AE: 1. Metabolic SEs - prolactin related problems

Study or Subgroup	Risperidone Events	Total	FGA Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.5.1 vs. haloperidol (long-term) - abnormal prolactin levels						
SCHOOLER2005	189	256	124	249	100.0%	1.48 [1.28, 1.71]
Subtotal (95% CI)		**256**		**249**	**100.0%**	**1.48 [1.28, 1.71]**
Total events	189		124			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.34 (P < 0.00001)						

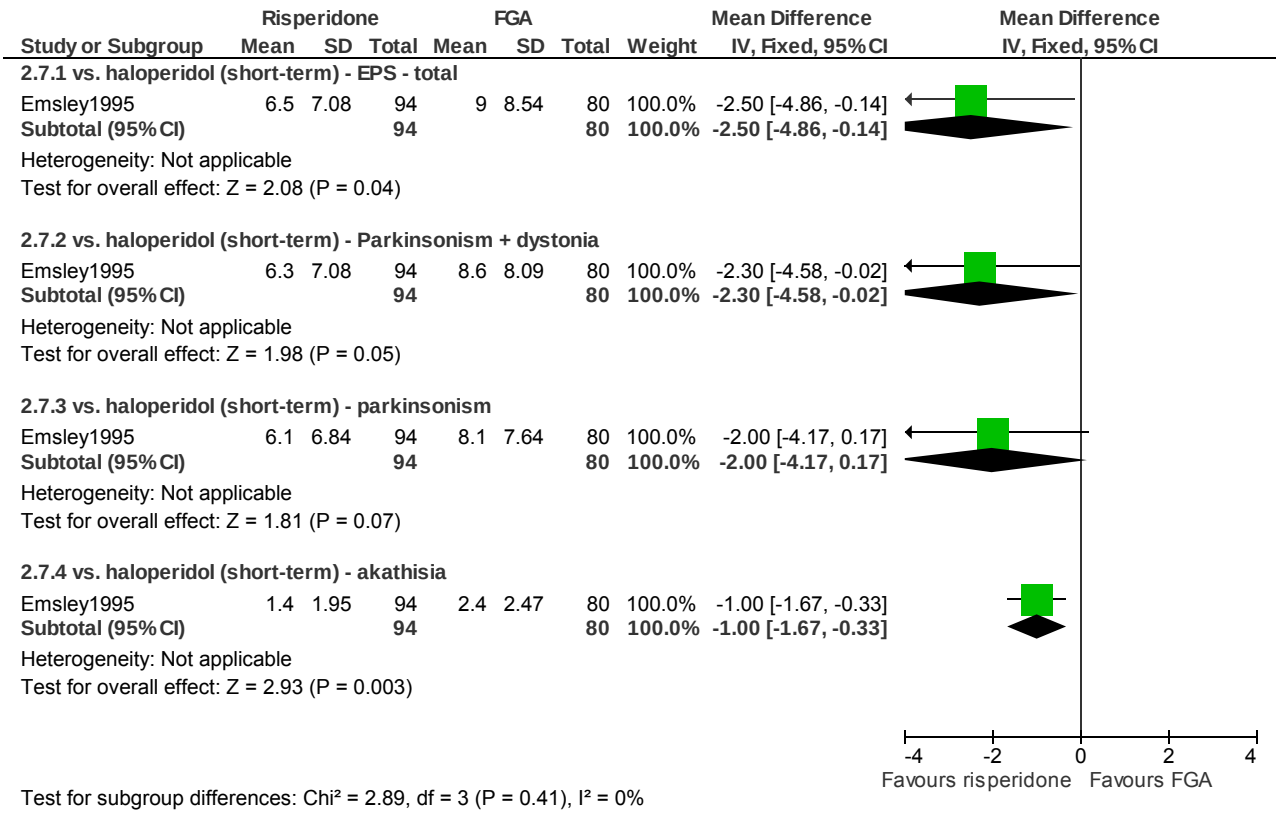


2.6 AE: 2. Neurologic SEs (treatment-emergent)

Study or Subgroup	Risperidone Events	Total	FGA Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.6.1 vs. haloperidol (short-term) - EPS (SAS >0)						
MOLLER2008	33	143	47	146	100.0%	0.72 [0.49, 1.05]
Subtotal (95% CI)		**143**		**146**	**100.0%**	**0.72 [0.49, 1.05]**
Total events	33		47			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.71 (P = 0.09)						
2.6.2 vs. haloperidol (short-term) - akathisia						
MOLLER2008	25	143	37	146	100.0%	0.69 [0.44, 1.08]
Subtotal (95% CI)		**143**		**146**	**100.0%**	**0.69 [0.44, 1.08]**
Total events	25		37			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.61 (P = 0.11)						

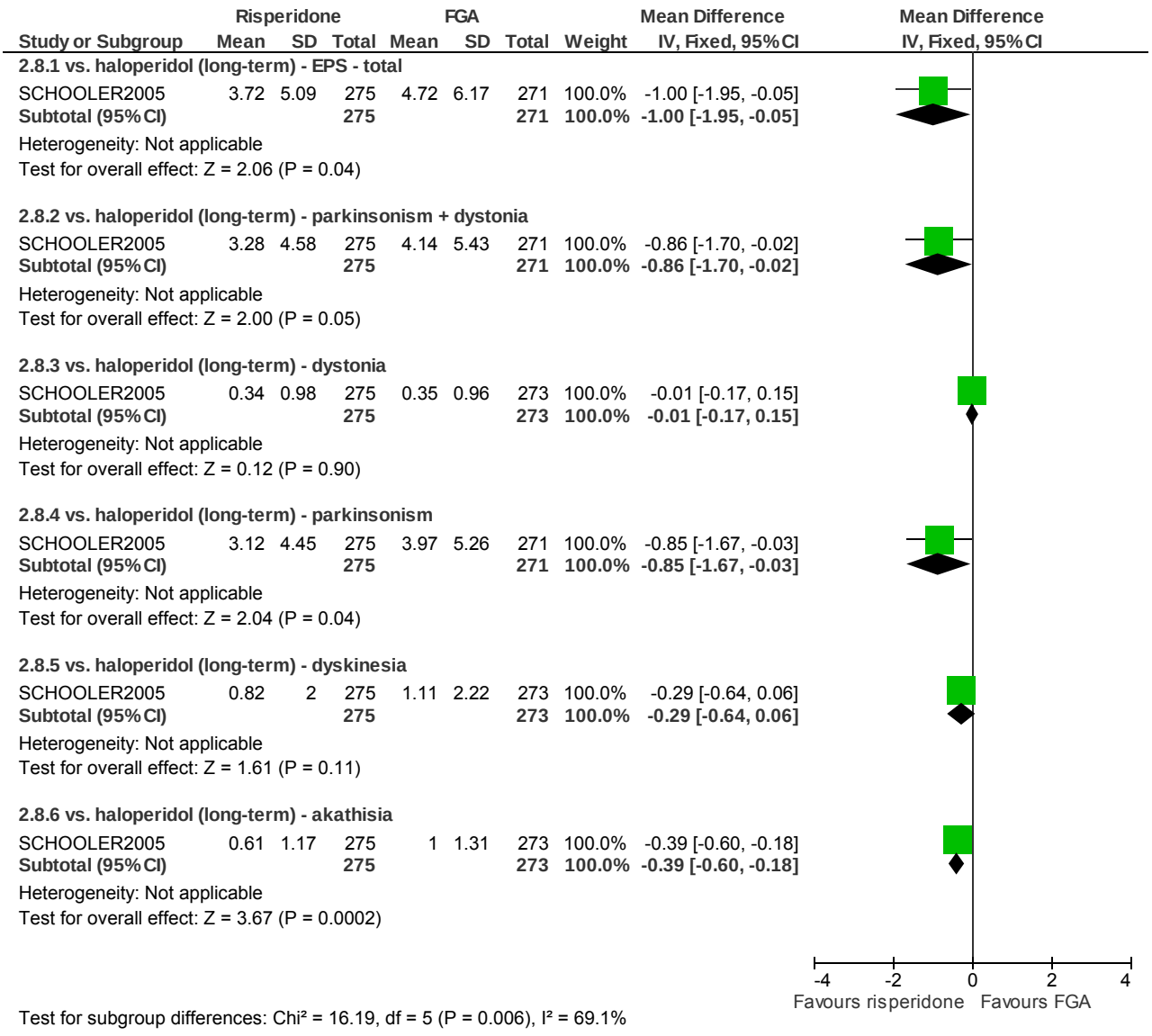


2.7 AE: 2. Neurologic SEs - Change from baseline (ESRS)



Test for subgroup differences: Chi² = 2.89, df = 3 (P = 0.41), I² = 0%

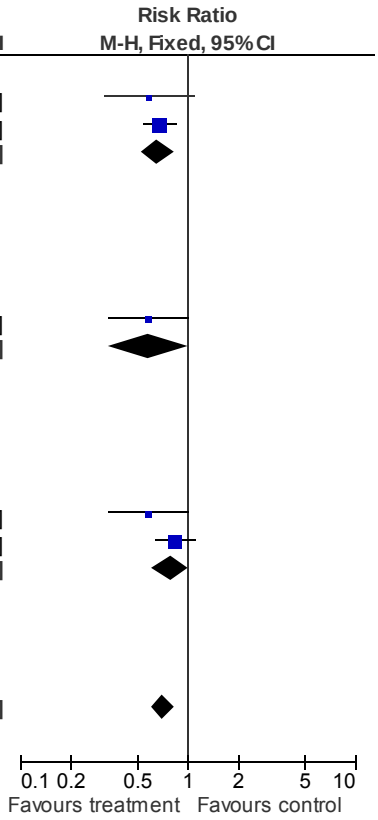
2.8 AE: 2. Neurologic SEs - Change from baseline (ESRS)



Test for subgroup differences: Chi² = 16.19, df = 5 (P = 0.006), I² = 69.1%

2.9 AE: 2. Neurologic SEs - Use of anticholinergic medication

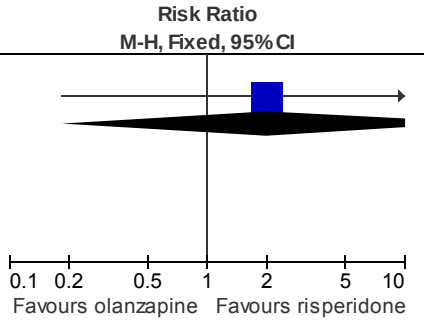
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.9.1 vs. haloperidol (short-term)						
Jones1998	8	21	15	23	8.1%	0.58 [0.31, 1.09]
Emsley1995	50	99	63	84	38.4%	0.67 [0.53, 0.85]
Subtotal (95% CI)		**120**		**107**	**46.5%**	**0.66 [0.53, 0.82]**
Total events	58		78			
Heterogeneity: Chi² = 0.18, df = 1 (P = 0.67); I² = 0%						
Test for overall effect: Z = 3.76 (P = 0.0002)						
2.9.2 vs. haloperidol (medium-term)						
Jones1998	9	21	17	23	9.2%	0.58 [0.33, 1.01]
Subtotal (95% CI)		**21**		**23**	**9.2%**	**0.58 [0.33, 1.01]**
Total events	9		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.94 (P = 0.05)						
2.9.3 vs. haloperidol (long-term)						
Jones1998	9	21	17	23	9.2%	0.58 [0.33, 1.01]
SCHOOLER2005	48	116	68	137	35.2%	0.83 [0.63, 1.10]
Subtotal (95% CI)		**137**		**160**	**44.3%**	**0.78 [0.61, 1.00]**
Total events	57		85			
Heterogeneity: Chi² = 1.34, df = 1 (P = 0.25); I² = 26%						
Test for overall effect: Z = 1.97 (P = 0.05)						
Total (95% CI)		**278**		**290**	**100.0%**	**0.71 [0.60, 0.83]**
Total events	124		180			
Heterogeneity: Chi² = 2.91, df = 4 (P = 0.57); I² = 0%						
Test for overall effect: Z = 4.34 (P < 0.0001)						



3 Olanzapine versus risperidone (critical outcomes)

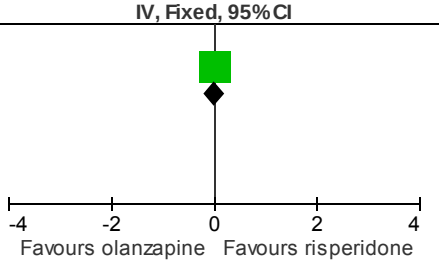
3.1 Mortality

Study or Subgroup	Olanzapine Events	Total	Risperidone Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 Suicide, suicide ideation or attempt (long-term)						
MCEVOY2007A	2	133	1	133	100.0%	2.00 [0.18, 21.79]
Subtotal (95% CI)		**133**		**133**	**100.0%**	**2.00 [0.18, 21.79]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.57 (P = 0.57)						



3.2 Global state: 1. Severity score - Change from baseline (CGI)

Study or Subgroup	Olanzapine Mean	SD	Total	Risperidone Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.2.1 vs. risperidone (medium-term)								
MCEVOY2007A	-0.9	0.65	85	-0.9	0.65	86	100.0%	0.00 [-0.19, 0.19]
Subtotal (95% CI)			**85**			**86**	**100.0%**	**0.00 [-0.19, 0.19]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								



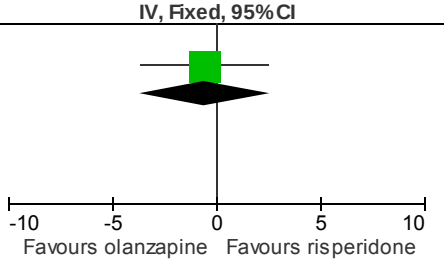
Test for subgroup differences: Not applicable

3.3 Mental state: 1. PANSS total score (change from baseline)

Study or Subgroup	Olanzapine Mean	SD	Total	Risperidone Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95%CI
3.3.1 vs. risperidone (medium-term)								
MCEVOY2007A	-14.3	10.33	85	-13.7	10.39	86	100.0%	-0.60 [-3.71, 2.51]
Subtotal (95%CI)			**85**			**86**	**100.0%**	**-0.60 [-3.71, 2.51]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.38 (P = 0.70)



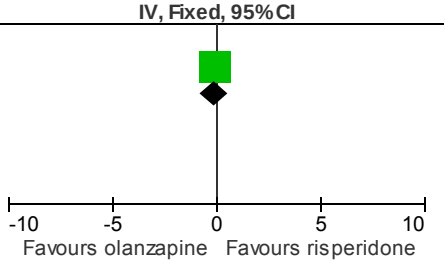
Test for subgroup differences: Not applicable

3.4 Mental state: 4. Depression (change from baseline: Calgary Depression Scale for Schizophrenia score)

Study or Subgroup	Olanzapine Mean	SD	Total	Risperidone Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95%CI
3.4.1 vs. risperidone (medium-term)								
MCEVOY2007A	-1.1	2.12	85	-1	2.23	86	100.0%	-0.10 [-0.75, 0.55]
Subtotal (95%CI)			**85**			**86**	**100.0%**	**-0.10 [-0.75, 0.55]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.30 (P = 0.76)



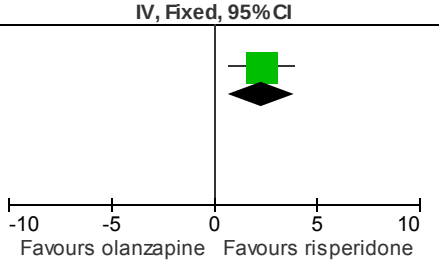
Test for subgroup differences: Not applicable

3.5 Psychosocial functioning: 1. Change from baseline (HC QoL Scale, social subscale) - sign changed

Study or Subgroup	Olanzapine Mean	SD	Total	Risperidone Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95%CI
3.5.1 vs. risperidone (medium-term)								
MCEVOY2007A	1.1	5.35	85	-1.2	5.47	86	100.0%	2.30 [0.68, 3.92]
Subtotal (95%CI)			**85**			**86**	**100.0%**	**2.30 [0.68, 3.92]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.78 (P = 0.005)



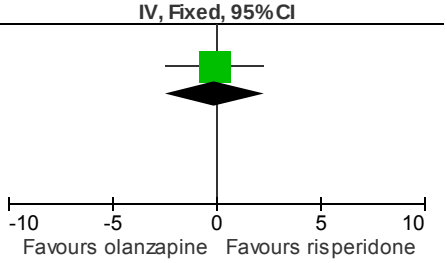
Test for subgroup differences: Not applicable

3.6 Psychosocial functioning: 1. Change from baseline (HC QoL Scale, vocational subscale) - sign changed

Study or Subgroup	Olanzapine Mean	SD	Total	Risperidone Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95%CI
3.6.1 vs. risperidone (medium-term)								
MCEVOY2007A	-1.6	7.84	85	-1.5	7.98	86	100.0%	-0.10 [-2.47, 2.27]
Subtotal (95%CI)			**85**			**86**	**100.0%**	**-0.10 [-2.47, 2.27]**

Heterogeneity: Not applicable

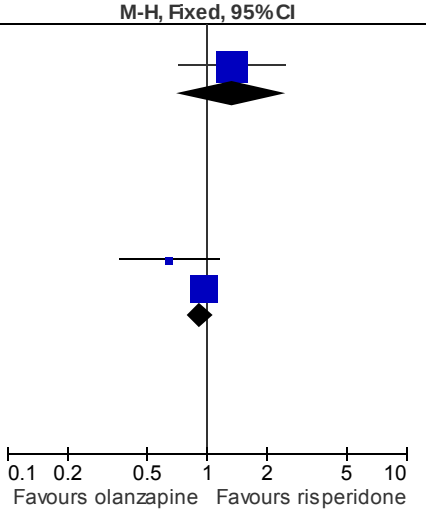
Test for overall effect: Z = 0.08 (P = 0.93)



Test for subgroup differences: Not applicable

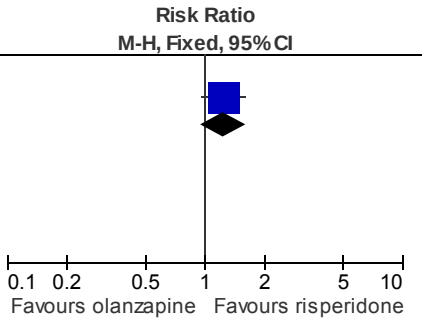
3.7 Leaving the study early: 1. Any reason

Study or Subgroup	Olanzapine Events	Olanzapine Total	Risperidone Events	Risperidone Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.7.1 vs. risperidone (short-term)						
VANNIMWEGEN2008	17	66	14	72	100.0%	1.32 [0.71, 2.47]
Subtotal (95% CI)		**66**		**72**	**100.0%**	**1.32 [0.71, 2.47]**
Total events	17		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.88 (P = 0.38)						
3.7.2 vs. risperidone (long-term)						
Jones1998	9	21	14	21	12.8%	0.64 [0.36, 1.15]
MCEVOY2007A	91	133	95	133	87.2%	0.96 [0.82, 1.12]
Subtotal (95% CI)		**154**		**154**	**100.0%**	**0.92 [0.79, 1.07]**
Total events	100		109			
Heterogeneity: Chi² = 1.74, df = 1 (P = 0.19); I² = 42%						
Test for overall effect: Z = 1.10 (P = 0.27)						



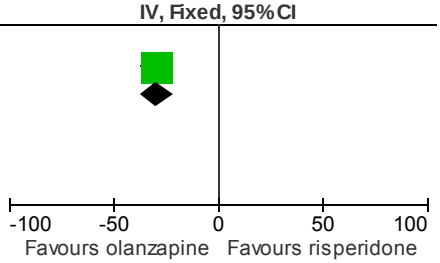
3.8 AE: 1. Metabolic SEs - weight gain (at least moderate in severity)

Study or Subgroup	Olanzapine Events	Olanzapine Total	Risperidone Events	Risperidone Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.8.1 Weight gain (long-term)						
MCEVOY2007A	68	133	55	133	100.0%	1.24 [0.95, 1.61]
Subtotal (95% CI)		**133**		**133**	**100.0%**	**1.24 [0.95, 1.61]**
Total events	68		55			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.59 (P = 0.11)						



3.9 AE: 1. Metabolic SEs - prolactin level (change from baseline)

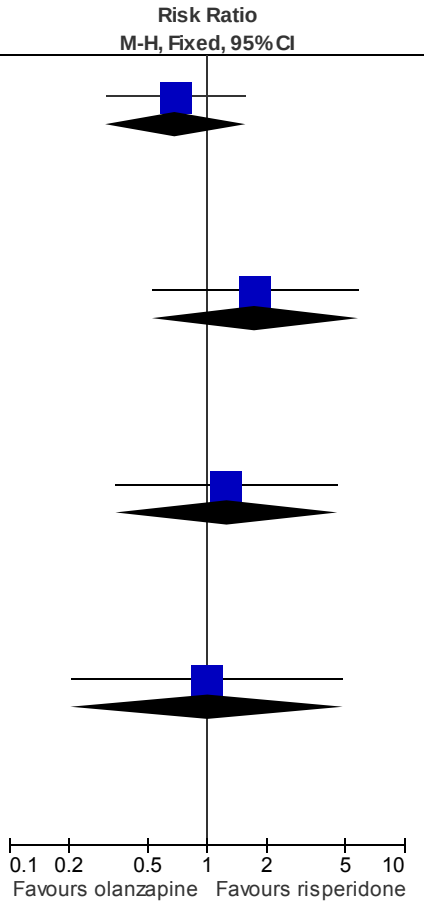
Study or Subgroup	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Risperidone Mean	Risperidone SD	Risperidone Total	Weight	Mean Difference IV, Fixed, 95% CI
3.9.1 vs. risperidone (medium-term)								
MCEVOY2007A	-16.4	25.45	85	13.3	26.89	86	100.0%	-29.70 [-37.55, -21.85]
Subtotal (95% CI)			**85**			**86**	**100.0%**	**-29.70 [-37.55, -21.85]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 7.42 (P < 0.00001)								



Test for subgroup differences: Not applicable

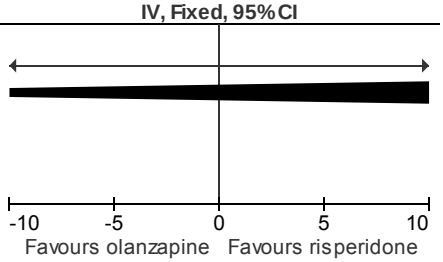
3.10 AE: 1. Metabolic SEs - prolactin related problems (at least moderate in severity)

Study or Subgroup	Olanzapine Events	Olanzapine Total	Risperidone Events	Risperidone Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.10.1 Gynecomastia (long-term)						
MCEVOY2007A	9	133	13	133	100.0%	0.69 [0.31, 1.56]
Subtotal (95% CI)		**133**		**133**	**100.0%**	**0.69 [0.31, 1.56]**
Total events	9		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.88 (P = 0.38)						
3.10.2 Urinary hesitancy (long-term)						
MCEVOY2007A	7	133	4	133	100.0%	1.75 [0.52, 5.84]
Subtotal (95% CI)		**133**		**133**	**100.0%**	**1.75 [0.52, 5.84]**
Total events	7		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.91 (P = 0.36)						
3.10.3 Incontinence or nocturia (long-term)						
MCEVOY2007A	5	133	4	133	100.0%	1.25 [0.34, 4.55]
Subtotal (95% CI)		**133**		**133**	**100.0%**	**1.25 [0.34, 4.55]**
Total events	5		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.34 (P = 0.74)						
3.10.4 Galactorrhea (long-term)						
MCEVOY2007A	3	133	3	133	100.0%	1.00 [0.21, 4.87]
Subtotal (95% CI)		**133**		**133**	**100.0%**	**1.00 [0.21, 4.87]**
Total events	3		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						



3.11 AE: 1. Metabolic SEs - fasting triglycerides level (mg/dl) (change from baseline)

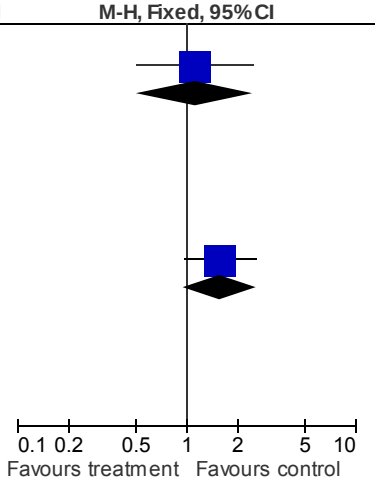
Study or Subgroup	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Risperidone Mean	Risperidone SD	Risperidone Total	Weight	Mean Difference IV, Fixed, 95% CI
3.11.1 vs. risperidone (medium-term)								
MCEVOY2007A	32.3	108.51	85	18.2	118.8	86	100.0%	14.10 [-20.00, 48.20]
Subtotal (95% CI)			**85**			**86**	**100.0%**	**14.10 [-20.00, 48.20]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.81 (P = 0.42)								



Test for subgroup differences: Not applicable

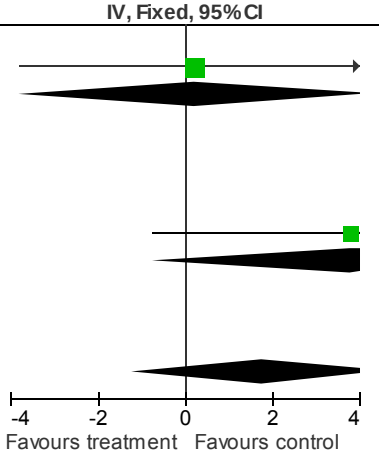
3.12 AE: 1. Metabolic SEs - fasting triglycerides level (>= 150 mg/dl)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.12.1 vs. risperidone (medium-term)						
MCEVOY2007A	11	85	10	86	100.0%	1.11 [0.50, 2.48]
Subtotal (95% CI)		**85**		**86**	**100.0%**	**1.11 [0.50, 2.48]**
Total events	11		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.26 (P = 0.79)						
3.12.2 vs. risperidone (long-term)						
MCEVOY2007A	22	37	14	37	100.0%	1.57 [0.96, 2.57]
Subtotal (95% CI)		**37**		**37**	**100.0%**	**1.57 [0.96, 2.57]**
Total events	22		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.80 (P = 0.07)						



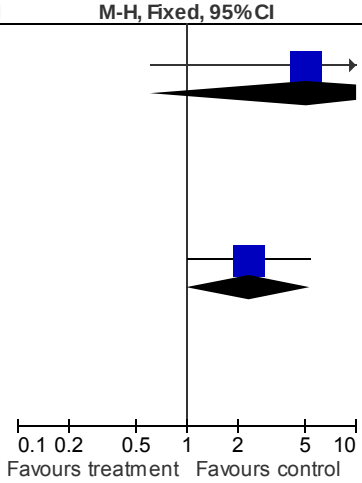
3.13 AE: 1. Metabolic SEs - fasting glucose level (mg/dl) (change from baseline)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.13.1 vs. risperidone (medium-term)								
MCEVOY2007A	1.7	12.82	85	1.5	13.91	86	56.4%	0.20 [-3.81, 4.21]
Subtotal (95% CI)			**85**			**86**	**56.4%**	**0.20 [-3.81, 4.21]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.10 (P = 0.92)								
3.13.2 vs. risperidone (long-term)								
MCEVOY2007A	8.6	9.67	37	4.8	10.34	37	43.6%	3.80 [-0.76, 8.36]
Subtotal (95% CI)			**37**			**37**	**43.6%**	**3.80 [-0.76, 8.36]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.63 (P = 0.10)								
Total (95% CI)			**122**			**123**	**100.0%**	**1.77 [-1.24, 4.78]**
Heterogeneity: Chi² = 1.35, df = 1 (P = 0.25); I² = 26%								
Test for overall effect: Z = 1.15 (P = 0.25)								
Test for subgroup differences: Chi² = 1.35, df = 1 (P = 0.25), I² = 25.9%								



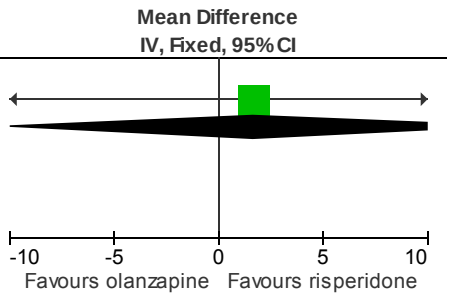
3.14 AE: 1. Metabolic SEs - fasting glucose level (>= 100 mg/dl)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.14.1 vs. risperidone (medium-term)						
MCEVOY2007A	5	85	1	86	100.0%	5.06 [0.60, 42.40]
Subtotal (95% CI)		**85**		**86**	**100.0%**	**5.06 [0.60, 42.40]**
Total events	5		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.49 (P = 0.14)						
3.14.2 vs. risperidone (long-term)						
MCEVOY2007A	14	37	6	37	100.0%	2.33 [1.01, 5.41]
Subtotal (95% CI)		**37**		**37**	**100.0%**	**2.33 [1.01, 5.41]**
Total events	14		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.98 (P = 0.05)						



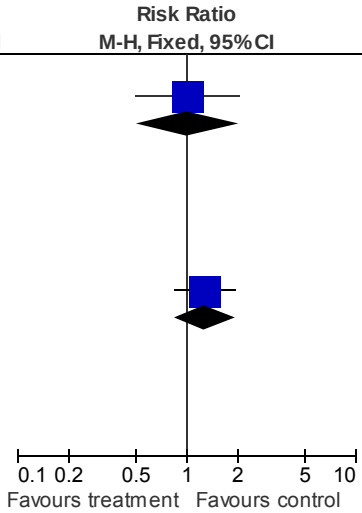
3.15 AE: 1. Metabolic SEs - fasting total cholesterol level (mg/dl) (change from baseline)

Study or Subgroup	Olanzapine Mean	SD	Total	Risperidone Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.15.1 vs. risperidone (medium-term)								
MCEVOY2007A	8.9	42.59	85	7.2	46.55	86	100.0%	1.70 [-11.67, 15.07]
Subtotal (95% CI)			**85**			**86**	**100.0%**	**1.70 [-11.67, 15.07]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.25 (P = 0.80)								
Test for subgroup differences: Not applicable								



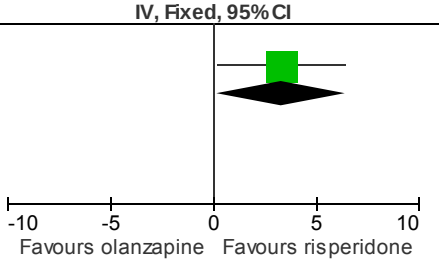
3.16 AE: 1. Metabolic SEs - fasting total cholesterol level (>= 200 mg/dl)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.16.1 vs. risperidone (medium-term)						
MCEVOY2007A	13	85	13	86	100.0%	1.01 [0.50, 2.05]
Subtotal (95% CI)		**85**		**86**	**100.0%**	**1.01 [0.50, 2.05]**
Total events	13		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.03 (P = 0.97)						
3.16.2 vs. risperidone (long-term)						
MCEVOY2007A	23	37	18	37	100.0%	1.28 [0.84, 1.94]
Subtotal (95% CI)		**37**		**37**	**100.0%**	**1.28 [0.84, 1.94]**
Total events	23		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.16 (P = 0.25)						



3.17 AE: 1. Metabolic SEs - fasting high-density lipoprotein cholesterol level (mg/dl) (change from baseline)

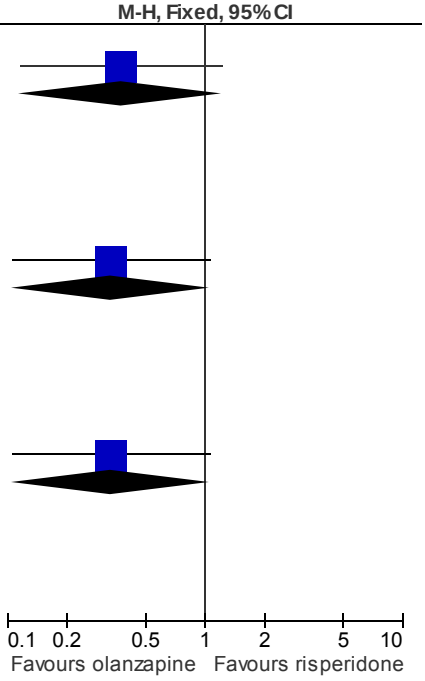
Study or Subgroup	Olanzapine Mean	SD	Total	Risperidone Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.17.1 vs. risperidone (medium-term)								
MCEVOY2007A	3.8	9.96	85	0.5	10.94	86	100.0%	3.30 [0.16, 6.44]
Subtotal (95% CI)			**85**			**86**	**100.0%**	**3.30 [0.16, 6.44]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.06 (P = 0.04)								



Test for subgroup differences: Not applicable

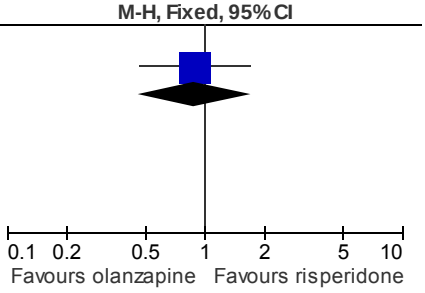
3.18 AE: 2. Neurologic SEs - Use of anticholinergic medication

Study or Subgroup	Olanzapine Events	Total	Risperidone Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.18.1 vs. haloperidol (short-term)						
Jones1998	3	21	8	21	100.0%	0.38 [0.12, 1.22]
Subtotal (95% CI)		**21**		**21**	**100.0%**	**0.38 [0.12, 1.22]**
Total events	3		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.63 (P = 0.10)						
3.18.2 vs. haloperidol (medium-term)						
Jones1998	3	21	9	21	100.0%	0.33 [0.10, 1.06]
Subtotal (95% CI)		**21**		**21**	**100.0%**	**0.33 [0.10, 1.06]**
Total events	3		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.86 (P = 0.06)						
3.18.3 vs. haloperidol (long-term)						
Jones1998	3	21	9	21	100.0%	0.33 [0.10, 1.06]
Subtotal (95% CI)		**21**		**21**	**100.0%**	**0.33 [0.10, 1.06]**
Total events	3		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.86 (P = 0.06)						



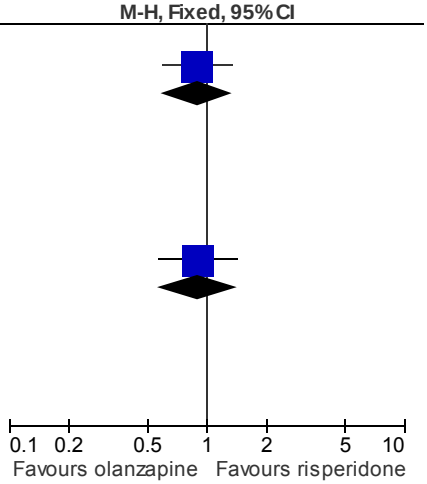
3.19 AE: 1. Metabolic SEs - other (at least moderate in severity) (long-term)

Study or Subgroup	Olanzapine Events	Total	Risperidone Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.19.1 Orthostatic faintness						
MCEVOY2007A	15	133	17	133	100.0%	0.88 [0.46, 1.69]
Subtotal (95% CI)		**133**		**133**	**100.0%**	**0.88 [0.46, 1.69]**
Total events	15		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.38 (P = 0.71)						



3.20 AE: 2. Neurologic SEs (treatment-emergent - at least moderate in severity)

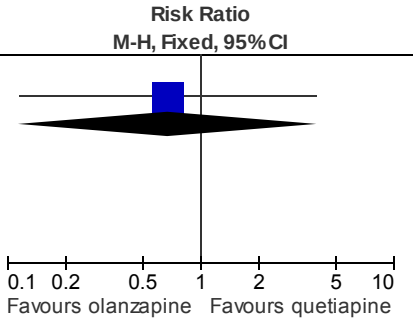
Study or Subgroup	Olanzapine Events	Olanzapine Total	Risperidone Events	Risperidone Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.20.1 Akinesia (long-term)						
MCEVOY2007A	32	133	36	133	100.0%	0.89 [0.59, 1.34]
Subtotal (95% CI)		**133**		**133**	**100.0%**	**0.89 [0.59, 1.34]**
Total events	32		36			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.56 (P = 0.57)						
3.20.2 Akathisia (long-term)						
MCEVOY2007A	27	133	30	133	100.0%	0.90 [0.57, 1.43]
Subtotal (95% CI)		**133**		**133**	**100.0%**	**0.90 [0.57, 1.43]**
Total events	27		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.45 (P = 0.65)						



4 Olanzapine versus quetiapine (critical outcomes)

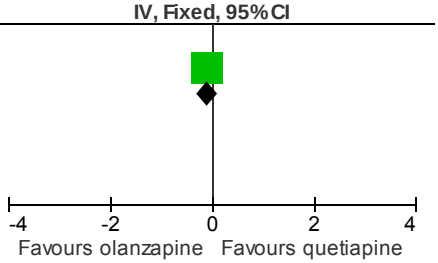
4.1 Mortality

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.1.1 Suicide, suicide ideation or attempt (long-term)						
MCEVOY2007A	2	133	3	134	100.0%	0.67 [0.11, 3.96]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**0.67 [0.11, 3.96]**
Total events	2		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.44 (P = 0.66)						



4.2 Global state: 1. Severity score - Change from baseline (CGI)

Study or Subgroup	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Mean Difference IV, Fixed, 95% CI
4.2.1 vs. quetiapine (medium-term)								
MCEVOY2007A	-0.9	0.65	85	-0.8	0.69	96	100.0%	-0.10 [-0.30, 0.10]
Subtotal (95% CI)			**85**			**96**	**100.0%**	**-0.10 [-0.30, 0.10]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.00 (P = 0.32)								



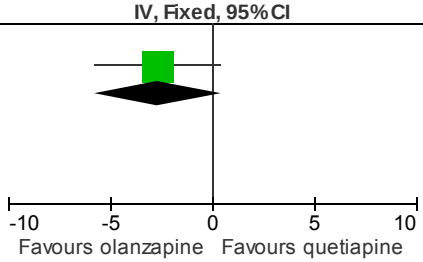
Test for subgroup differences: Not applicable

4.3 Mental state: 1. PANSS total score (change from baseline)

Study or Subgroup	Olanzapine Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.3.1 vs. quetiapine (medium-term)								
MCEVOY2007A	-14.3	10.33	85	-11.6	10.88	96	100.0%	-2.70 [-5.79, 0.39]
Subtotal (95% CI)			**85**			**96**	**100.0%**	**-2.70 [-5.79, 0.39]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.71 (P = 0.09)



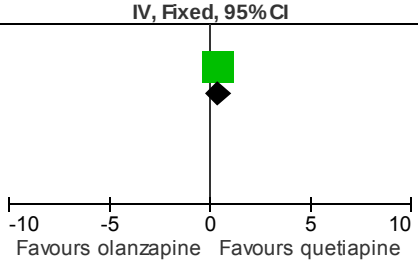
Test for subgroup differences: Not applicable

4.4 Mental state: 4. Depression (change from baseline: Calgary Depression Scale for Schizophrenia score)

Study or Subgroup	Olanzapine Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.4.1 vs. quetiapine (medium-term)								
MCEVOY2007A	-1.1	2.12	85	-1.5	2.25	96	100.0%	0.40 [-0.24, 1.04]
Subtotal (95% CI)			**85**			**96**	**100.0%**	**0.40 [-0.24, 1.04]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.23 (P = 0.22)



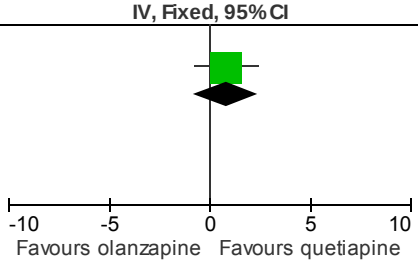
Test for subgroup differences: Not applicable

4.5 Psychosocial functioning: 1. Change from baseline (HC QoL Scale, social subscale) - sign changed

Study or Subgroup	Olanzapine Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.5.1 vs. quetiapine (medium-term)								
MCEVOY2007A	1.1	5.35	85	0.3	5.68	96	100.0%	0.80 [-0.81, 2.41]
Subtotal (95% CI)			**85**			**96**	**100.0%**	**0.80 [-0.81, 2.41]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.98 (P = 0.33)



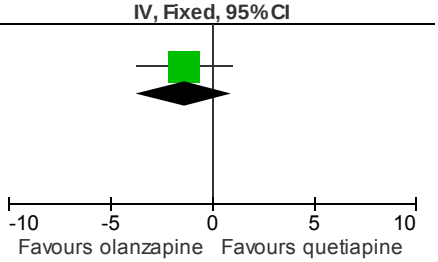
Test for subgroup differences: Not applicable

4.6 Psychosocial functioning: 1. Change from baseline (HC QoL Scale, vocational subscale) - sign changed

Study or Subgroup	Olanzapine Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.6.1 vs. quetiapine (medium-term)								
MCEVOY2007A	-1.6	7.84	85	-0.2	8.33	96	100.0%	-1.40 [-3.76, 0.96]
Subtotal (95% CI)			**85**			**96**	**100.0%**	**-1.40 [-3.76, 0.96]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.16 (P = 0.24)



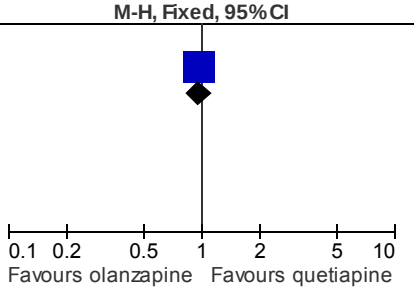
Test for subgroup differences: Not applicable

4.7 Leaving the study early: 1. Any reason

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.7.1 vs. quetiapine (long-term)						
MCEVOY2007A	91	133	95	134	100.0%	0.97 [0.82, 1.13]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**0.97 [0.82, 1.13]**
Total events	91		95			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.44 (P = 0.66)

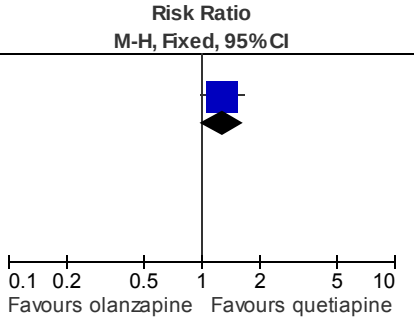


4.8 AE: 1. Metabolic SEs - weight gain (at least moderate in severity)

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.8.1 Weight gain (long-term)						
MCEVOY2007A	68	133	54	134	100.0%	1.27 [0.97, 1.65]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**1.27 [0.97, 1.65]**
Total events	68		54			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.76 (P = 0.08)



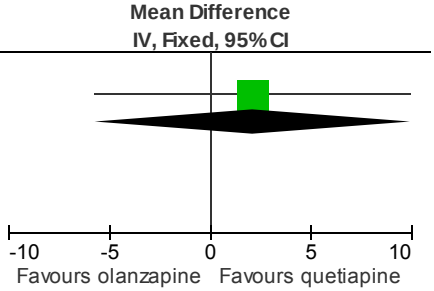
4.9 AE: 1. Metabolic SEs - prolactin level (change from baseline)

Study or Subgroup	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Mean Difference IV, Fixed, 95% CI
4.9.1 vs. quetiapine (medium-term)								
MCEVOY2007A	-16.4	25.45	85	-18.5	28.61	96	100.0%	2.10 [-5.78, 9.98]
Subtotal (95% CI)			**85**			**96**	**100.0%**	**2.10 [-5.78, 9.98]**

Heterogeneity: Not applicable

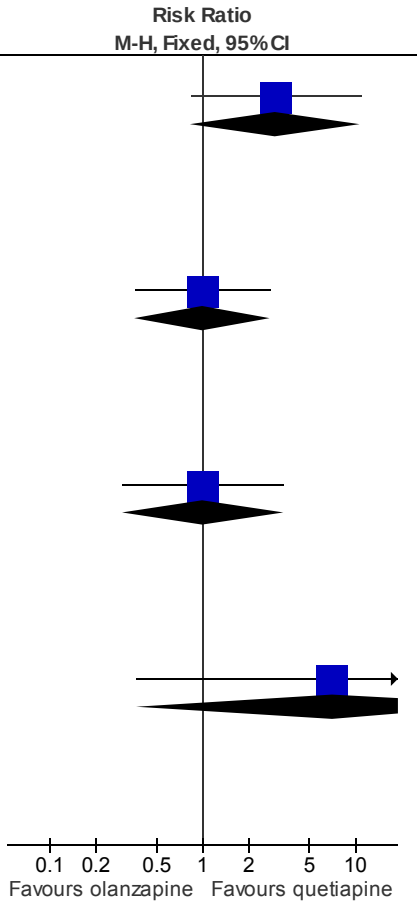
Test for overall effect: Z = 0.52 (P = 0.60)

Test for subgroup differences: Not applicable



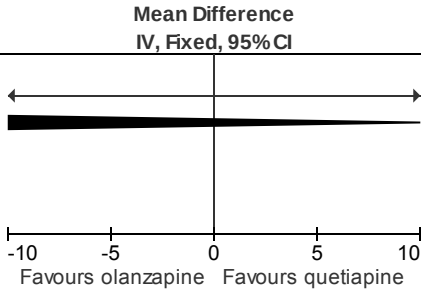
4.10 AE: 1. Metabolic SEs - prolactin related SEs (at least moderate in severity)

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.10.1 Gynecomastia (long-term)						
MCEVOY2007A	9	133	3	134	100.0%	3.02 [0.84, 10.92]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**3.02 [0.84, 10.92]**
Total events	9		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.69 (P = 0.09)						
4.10.2 Urinary hesitancy (long-term)						
MCEVOY2007A	7	133	7	134	100.0%	1.01 [0.36, 2.79]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**1.01 [0.36, 2.79]**
Total events	7		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						
4.10.3 Incontinence or nocturia (long-term)						
MCEVOY2007A	5	133	5	134	100.0%	1.01 [0.30, 3.40]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**1.01 [0.30, 3.40]**
Total events	5		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						
4.10.4 Galactorrhea (long-term)						
MCEVOY2007A	3	133	0	134	100.0%	7.05 [0.37, 135.22]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**7.05 [0.37, 135.22]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (P = 0.19)						



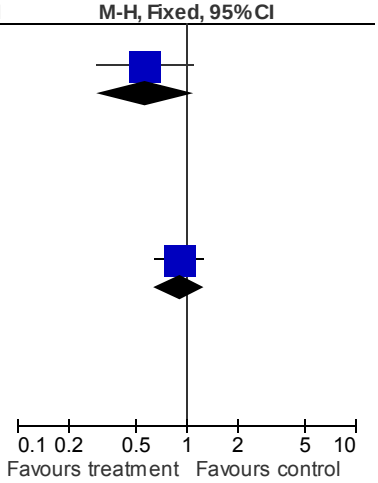
4.11 AE: 1. Metabolic SEs - fasting triglycerides level (mg/dl) (change from baseline)

Study or Subgroup	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Mean Difference IV, Fixed, 95% CI
4.11.1 vs. quetiapine (medium-term)								
MCEVOY2007A	32.3	108.51	85	52.9	119.14	96	100.0%	-20.60 [-53.77, 12.57]
Subtotal (95% CI)			**85**			**96**	**100.0%**	**-20.60 [-53.77, 12.57]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.22 (P = 0.22)								
Test for subgroup differences: Not applicable								



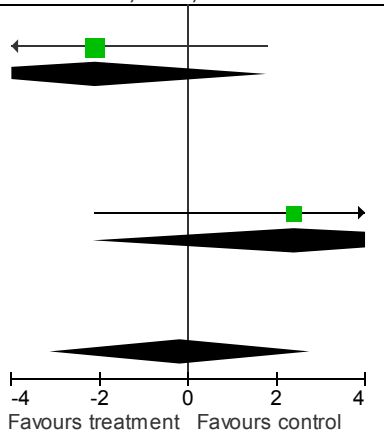
4.12 AE: 1. Metabolic SEs - fasting triglycerides level (>= 150 mg/dl)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.12.1 vs. quetiapine (medium-term)						
MCEVOY2007A	11	85	22	96	100.0%	0.56 [0.29, 1.10]
Subtotal (95% CI)		**85**		**96**	**100.0%**	**0.56 [0.29, 1.10]**
Total events	11		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.69 (P = 0.09)						
4.12.2 vs. quetiapine (long-term)						
MCEVOY2007A	22	37	29	44	100.0%	0.90 [0.64, 1.27]
Subtotal (95% CI)		**37**		**44**	**100.0%**	**0.90 [0.64, 1.27]**
Total events	22		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.55)						



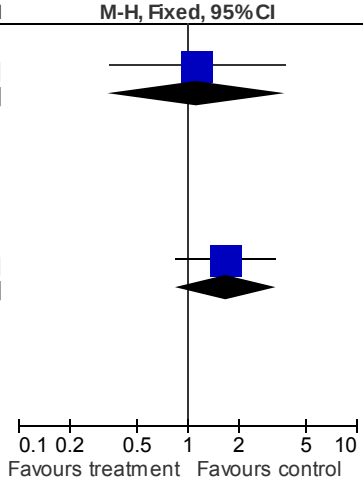
4.13 AE: 1. Metabolic SEs - fasting glucose level (mg/dl) (change from baseline)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.13.1 vs. quetiapine (medium-term)								
MCEVOY2007A	1.7	12.82	85	3.8	13.91	96	57.4%	-2.10 [-5.99, 1.79]
Subtotal (95% CI)			**85**			**96**	**57.4%**	**-2.10 [-5.99, 1.79]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.06 (P = 0.29)								
4.13.2 vs. quetiapine (long-term)								
MCEVOY2007A	8.6	9.67	37	6.2	11.08	44	42.6%	2.40 [-2.12, 6.92]
Subtotal (95% CI)			**37**			**44**	**42.6%**	**2.40 [-2.12, 6.92]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.04 (P = 0.30)								
Total (95% CI)			**122**			**140**	**100.0%**	**-0.18 [-3.13, 2.77]**
Heterogeneity: Chi² = 2.19, df = 1 (P = 0.14); I² = 54%								
Test for overall effect: Z = 0.12 (P = 0.90)								
Test for subgroup differences: Chi² = 2.19, df = 1 (P = 0.14), I² = 54.2%								



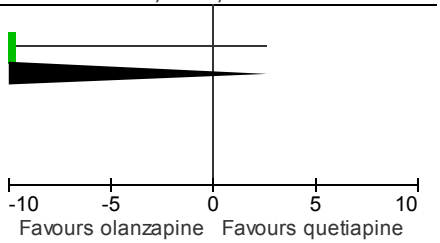
4.14 AE: 1. Metabolic SEs - fasting glucose level (>= 100 mg/dl)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.14.1 vs. quetiapine (medium-term)						
MCEVOY2007A	5	85	5	96	100.0%	1.13 [0.34, 3.77]
Subtotal (95% CI)		**85**		**96**	**100.0%**	**1.13 [0.34, 3.77]**
Total events	5		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.20 (P = 0.84)						
4.14.2 vs. quetiapine (long-term)						
MCEVOY2007A	14	37	10	44	100.0%	1.66 [0.84, 3.30]
Subtotal (95% CI)		**37**		**44**	**100.0%**	**1.66 [0.84, 3.30]**
Total events	14		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.46 (P = 0.14)						



4.15 AE: 1. Metabolic SEs - fasting total cholesterol level (mg/dl) (change from baseline)

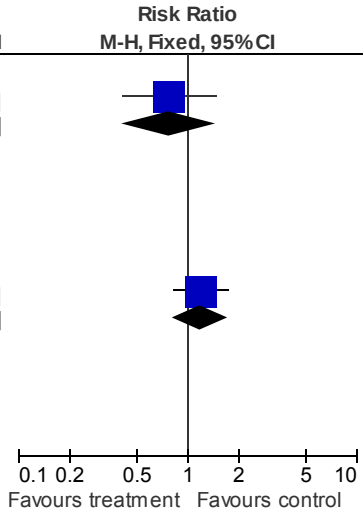
Study or Subgroup	Olanzapine Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.15.1 vs. quetiapine (medium-term)								
MCEVOY2007A	8.9	42.59	85	19.3	46.83	96	100.0%	-10.40 [-23.43, 2.63]
Subtotal (95% CI)			**85**			**96**	**100.0%**	**-10.40 [-23.43, 2.63]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.56 (P = 0.12)								



Test for subgroup differences: Not applicable

4.16 AE: 1. Metabolic SEs - fasting total cholesterol level (>= 200 mg/dl)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.16.1 vs. quetiapine (medium-term)						
MCEVOY2007A	13	85	19	96	100.0%	0.77 [0.41, 1.47]
Subtotal (95% CI)		**85**		**96**	**100.0%**	**0.77 [0.41, 1.47]**
Total events	13		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						
4.16.2 vs. quetiapine (long-term)						
MCEVOY2007A	23	37	23	44	100.0%	1.19 [0.81, 1.74]
Subtotal (95% CI)		**37**		**44**	**100.0%**	**1.19 [0.81, 1.74]**
Total events	23		23			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.90 (P = 0.37)						

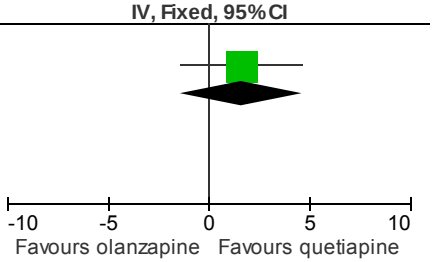


4.17 AE: 1. Metabolic SEs - fasting high-density lipoprotein cholesterol level (mg/dl) (change from baseline)

Study or Subgroup	Olanzapine Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.17.1 vs. quetiapine (medium-term)								
MCEVOY2007A	3.8	9.96	85	2.2	10.97	96	100.0%	1.60 [-1.45, 4.65]
Subtotal (95% CI)			**85**			**96**	**100.0%**	**1.60 [-1.45, 4.65]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.03 (P = 0.30)



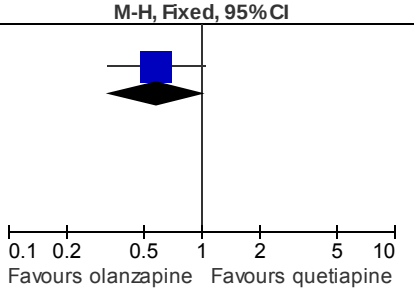
Test for subgroup differences: Not applicable

4.18 AE: 1. Metabolic SEs - other (at least moderate in severity)

Study or Subgroup	Olanzapine Events	Total	Quetiapine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.18.1 Orthostatic faintness (long-term)						
MCEVOY2007A	15	133	26	134	100.0%	0.58 [0.32, 1.05]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**0.58 [0.32, 1.05]**
Total events	15		26			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.81 (P = 0.07)



4.19 AE: 2. Neurologic SEs (treatment-emergent - at least moderate in severity)

Study or Subgroup	Olanzapine Events	Total	Quetiapine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.19.1 Akinesia (long-term)						
MCEVOY2007A	32	133	33	134	100.0%	0.98 [0.64, 1.49]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**0.98 [0.64, 1.49]**
Total events	32		33			

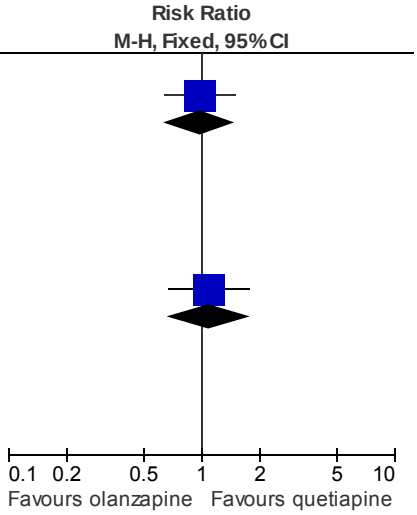
Heterogeneity: Not applicable

Test for overall effect: Z = 0.11 (P = 0.91)

4.19.2 Akathisia (long-term)						
MCEVOY2007A	27	133	25	134	100.0%	1.09 [0.67, 1.77]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**1.09 [0.67, 1.77]**
Total events	27		25			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.34 (P = 0.73)



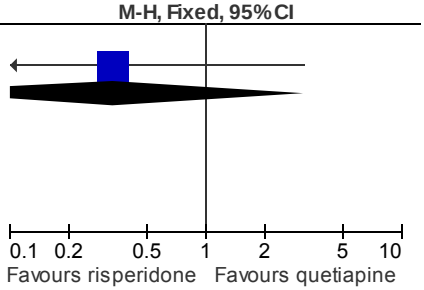
5 Risperidone versus quetiapine (critical outcomes)

5.1 Mortality

Study or Subgroup	Risperidone Events	Risperidone Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.1.1 Suicide, suicide ideation or attempt (long-term)						
MCEVOY2007A	1	133	3	134	100.0%	0.34 [0.04, 3.19]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**0.34 [0.04, 3.19]**
Total events	1		3			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.95 (P = 0.34)



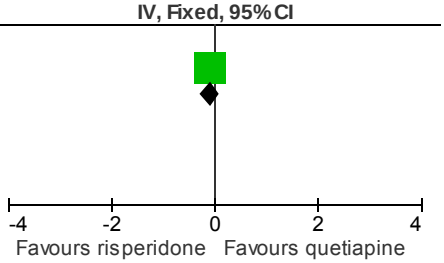
5.2 Global state: 1. Severity score - Change from baseline (CGI)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Mean Difference IV, Fixed, 95% CI
5.2.1 vs. quetiapine (medium-term)								
MCEVOY2007A	-0.9	0.65	86	-0.8	0.69	96	100.0%	-0.10 [-0.29, 0.09]
Subtotal (95% CI)			**86**			**96**	**100.0%**	**-0.10 [-0.29, 0.09]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.01 (P = 0.31)

Test for subgroup differences: Not applicable



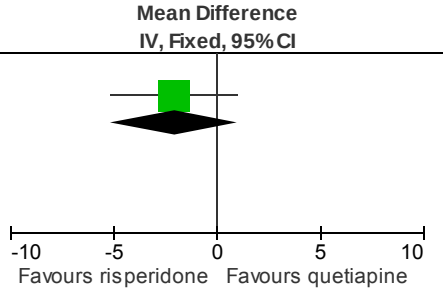
5.3 Mental state: 1. PANSS total score (change from baseline)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Mean Difference IV, Fixed, 95% CI
5.3.1 vs. quetiapine (medium-term)								
MCEVOY2007A	-13.7	10.39	86	-11.6	10.88	96	100.0%	-2.10 [-5.19, 0.99]
Subtotal (95% CI)			**86**			**96**	**100.0%**	**-2.10 [-5.19, 0.99]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.33 (P = 0.18)

Test for subgroup differences: Not applicable



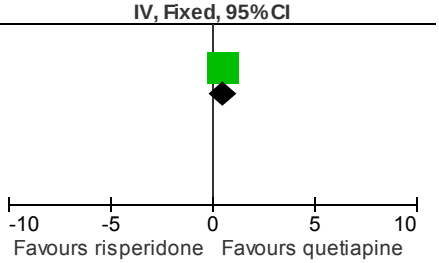
5.4 Mental state: 4. Depression (change from baseline: Calgary Depression Scale for Schizophrenia score)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Mean Difference IV, Fixed, 95% CI
5.4.1 vs. quetiapine (medium-term)								
MCEVOY2007A	-1	2.23	86	-1.5	2.25	96	100.0%	0.50 [-0.15, 1.15]
Subtotal (95% CI)			**86**			**96**	**100.0%**	**0.50 [-0.15, 1.15]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.50 (P = 0.13)

Test for subgroup differences: Not applicable

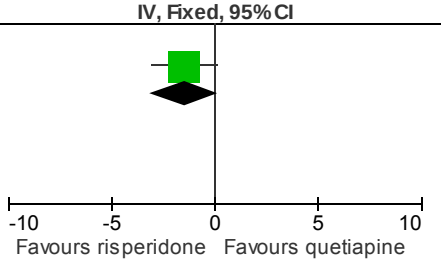


5.5 Psychosocial functioning: 1. Change from baseline (HC QoL Scale, social subscale) - sign changed

Study or Subgroup	Risperidone Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.5.1 vs. quetiapine (medium-term)								
MCEVOY2007A	-1.2	5.47	86	0.3	5.68	96	100.0%	-1.50 [-3.12, 0.12]
Subtotal (95% CI)			**86**			**96**	**100.0%**	**-1.50 [-3.12, 0.12]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.81 (P = 0.07)



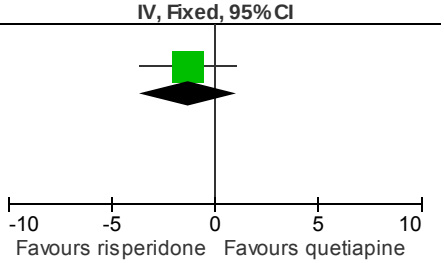
Test for subgroup differences: Not applicable

5.6 Psychosocial functioning: 1. Change from baseline (HC QoL Scale, vocational subscale) - sign changed

Study or Subgroup	Risperidone Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.6.1 vs. quetiapine (medium-term)								
MCEVOY2007A	-1.5	7.98	86	-0.2	8.33	96	100.0%	-1.30 [-3.67, 1.07]
Subtotal (95% CI)			**86**			**96**	**100.0%**	**-1.30 [-3.67, 1.07]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.07 (P = 0.28)



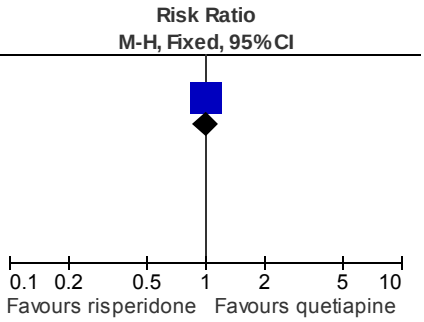
Test for subgroup differences: Not applicable

5.7 Leaving the study early: 1. Any reason

Study or Subgroup	Risperidone Events	Total	Quetiapine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.7.1 vs. quetiapine (long-term)						
MCEVOY2007A	95	133	95	134	100.0%	1.01 [0.86, 1.17]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**1.01 [0.86, 1.17]**
Total events	95		95			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.10 (P = 0.92)

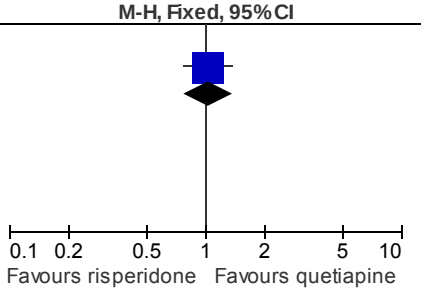


5.8 AE: 1. Metabolic SEs - weight gain (at least moderate in severity)

Study or Subgroup	Risperidone Events	Total	Quetiapine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.8.1 Weight gain (long-term)						
MCEVOY2007A	55	133	54	134	100.0%	1.03 [0.77, 1.37]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**1.03 [0.77, 1.37]**
Total events	55		54			

Heterogeneity: Not applicable

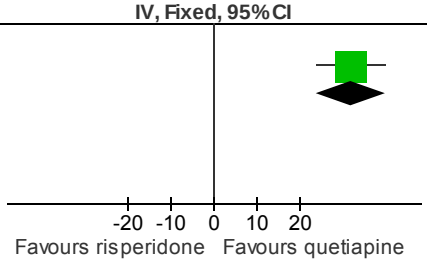
Test for overall effect: Z = 0.18 (P = 0.86)



5.9 AE: 1. Metabolic SEs - prolactin level (change from baseline)

Study or Subgroup	Risperidone Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.9.1 vs. quetiapine (medium-term)								
MCEVOY2007A	13.3	26.89	86	-18.5	28.61	96	100.0%	31.80 [23.73, 39.87]
Subtotal (95% CI)			**86**			**96**	**100.0%**	**31.80 [23.73, 39.87]**

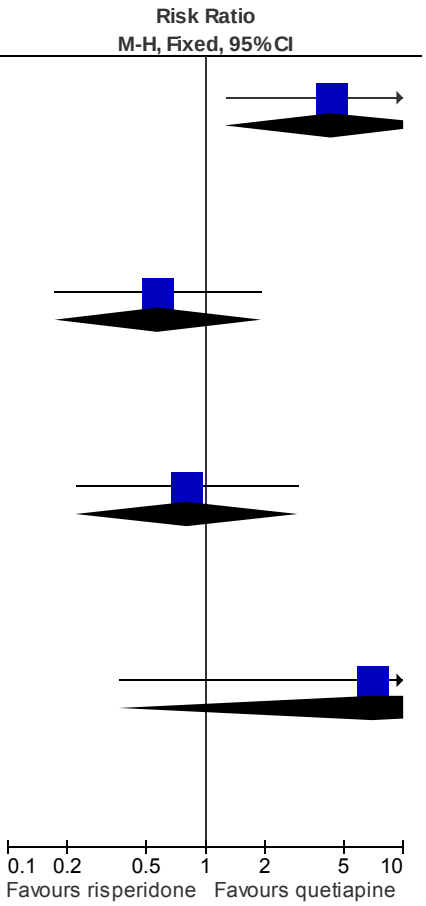
Heterogeneity: Not applicable
Test for overall effect: Z = 7.73 (P < 0.00001)



Test for subgroup differences: Not applicable

5.10 AE: 1. Metabolic SEs - prolactin related SEs (at least moderate in severity)

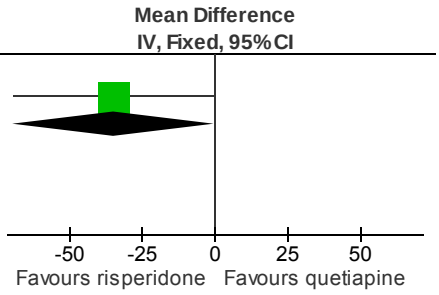
Study or Subgroup	Risperidone Events	Total	Quetiapine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.10.1 Gynecomastia (long-term)						
MCEVOY2007A	13	133	3	134	100.0%	4.37 [1.27, 14.97]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**4.37 [1.27, 14.97]**
Total events	13		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.34 (P = 0.02)						
5.10.2 Urinary hesitancy (long-term)						
MCEVOY2007A	4	133	7	134	100.0%	0.58 [0.17, 1.92]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**0.58 [0.17, 1.92]**
Total events	4		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.90 (P = 0.37)						
5.10.3 Incontinence or nocturia (long-term)						
MCEVOY2007A	4	133	5	134	100.0%	0.81 [0.22, 2.94]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**0.81 [0.22, 2.94]**
Total events	4		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.33 (P = 0.74)						
5.10.4 Galactorrhea (long-term)						
MCEVOY2007A	3	133	0	134	100.0%	7.05 [0.37, 135.22]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**7.05 [0.37, 135.22]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (P = 0.19)						



5.11 AE: 1. Metabolic SEs - fasting triglycerides level (mg/dl) (change from baseline)

Study or Subgroup	Risperidone Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.11.1 vs. quetiapine (medium-term)								
MCEVOY2007A	18.2	118.8	86	52.9	119.14	96	100.0%	-34.70 [-69.32, -0.08]
Subtotal (95% CI)			**86**			**96**	**100.0%**	**-34.70 [-69.32, -0.08]**

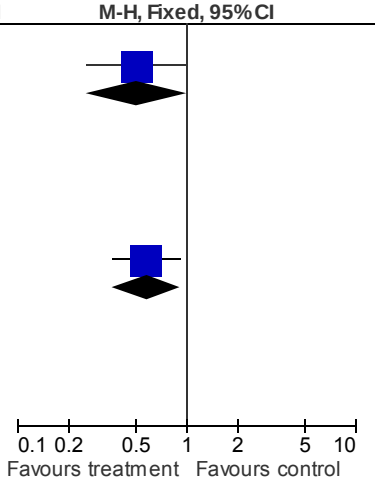
Heterogeneity: Not applicable
Test for overall effect: Z = 1.96 (P = 0.05)



Test for subgroup differences: Not applicable

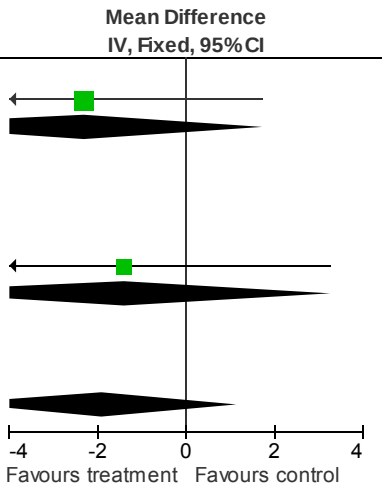
5.12 AE: 1. Metabolic SEs - fasting triglycerides level (>= 150 mg/dl)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.12.1 vs. quetiapine (medium-term)						
MCEVOY2007A	10	86	22	96	100.0%	0.51 [0.25, 1.01]
Subtotal (95% CI)		**86**		**96**	**100.0%**	**0.51 [0.25, 1.01]**
Total events	10		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.93 (P = 0.05)						
5.12.2 vs. quetiapine (long-term)						
MCEVOY2007A	14	37	29	44	100.0%	0.57 [0.36, 0.91]
Subtotal (95% CI)		**37**		**44**	**100.0%**	**0.57 [0.36, 0.91]**
Total events	14		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.34 (P = 0.02)						



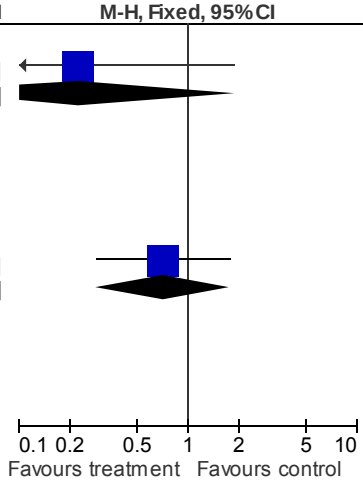
5.13 AE: 1. Metabolic SEs - fasting glucose level (mg/dl) (change from baseline)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
5.13.1 vs. quetiapine (medium-term)								
MCEVOY2007A	1.5	13.91	86	3.8	13.91	96	57.1%	-2.30 [-6.35, 1.75]
Subtotal (95% CI)			**86**			**96**	**57.1%**	**-2.30 [-6.35, 1.75]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.11 (P = 0.27)								
5.13.2 vs. quetiapine (long-term)								
MCEVOY2007A	4.8	10.34	37	6.2	11.08	44	42.9%	-1.40 [-6.07, 3.27]
Subtotal (95% CI)			**37**			**44**	**42.9%**	**-1.40 [-6.07, 3.27]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.59 (P = 0.56)								
Total (95% CI)			**123**			**140**	**100.0%**	**-1.91 [-4.97, 1.15]**
Heterogeneity: Chi² = 0.08, df = 1 (P = 0.78); I² = 0%								
Test for overall effect: Z = 1.23 (P = 0.22)								
Test for subgroup differences: Chi² = 0.08, df = 1 (P = 0.78), I² = 0%								



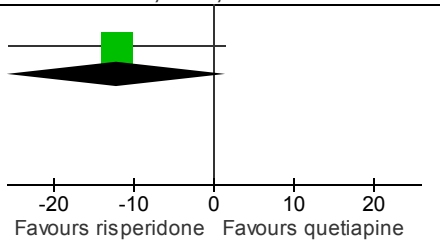
5.14 AE: 1. Metabolic SEs - fasting glucose level (>= 100 mg/dl)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.14.1 vs. quetiapine (medium-term)						
MCEVOY2007A	1	86	5	96	100.0%	0.22 [0.03, 1.87]
Subtotal (95% CI)		**86**		**96**	**100.0%**	**0.22 [0.03, 1.87]**
Total events	1		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.38 (P = 0.17)						
5.14.2 vs. quetiapine (long-term)						
MCEVOY2007A	6	37	10	44	100.0%	0.71 [0.29, 1.78]
Subtotal (95% CI)		**37**		**44**	**100.0%**	**0.71 [0.29, 1.78]**
Total events	6		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.72 (P = 0.47)						



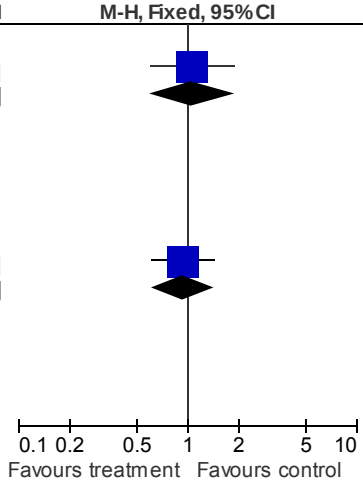
5.15 AE: 1. Metabolic SEs - fasting total cholesterol level (mg/dl) (change from baseline)

Study or Subgroup	Risperidone Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.15.1 vs. quetiapine (medium-term)								
MCEVOY2007A	7.2	46.55	86	19.3	46.83	96	100.0%	-12.10 [-25.68, 1.48]
Subtotal (95% CI)			**86**			**96**	**100.0%**	**-12.10 [-25.68, 1.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.75 (P = 0.08)								
Test for subgroup differences: Not applicable								



5.16 AE: 1. Metabolic SEs - fasting total cholesterol level (>= 200 mg/dl)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.16.1 vs. quetiapine (medium-term)						
MCEVOY2007A	18	86	19	96	100.0%	1.06 [0.59, 1.88]
Subtotal (95% CI)		**86**		**96**	**100.0%**	**1.06 [0.59, 1.88]**
Total events	18		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.19 (P = 0.85)						
5.16.2 vs. quetiapine (long-term)						
MCEVOY2007A	18	37	23	44	100.0%	0.93 [0.60, 1.44]
Subtotal (95% CI)		**37**		**44**	**100.0%**	**0.93 [0.60, 1.44]**
Total events	18		23			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.32 (P = 0.75)						

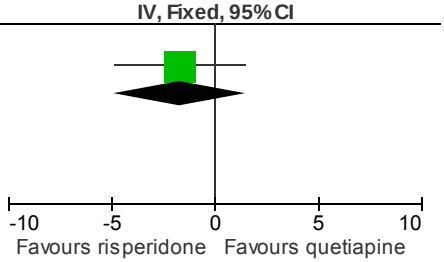


5.17 AE: 1. Metabolic SEs - fasting high-density lipoprotein cholesterol level (mg/dl) (change from baseline)

Study or Subgroup	Risperidone Mean	SD	Total	Quetiapine Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.17.1 vs. quetiapine (medium-term)								
MCEVOY2007A	0.5	10.94	86	2.2	10.97	96	100.0%	-1.70 [-4.89, 1.49]
Subtotal (95% CI)			**86**			**96**	**100.0%**	**-1.70 [-4.89, 1.49]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.05 (P = 0.30)



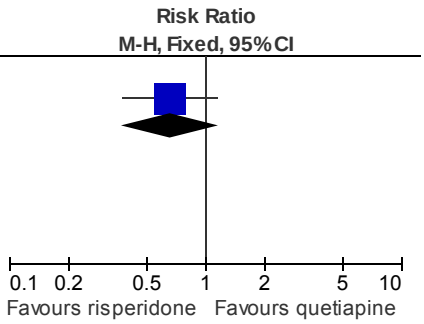
Test for subgroup differences: Not applicable

5.18 AE: 1. Metabolic SEs - other (at least moderate in severity)

Study or Subgroup	Risperidone Events	Total	Quetiapine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.18.1 Orthostatic faintness (long-term)						
MCEVOY2007A	17	133	26	134	100.0%	0.66 [0.38, 1.16]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**0.66 [0.38, 1.16]**
Total events	17		26			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.45 (P = 0.15)



5.19 AE: 2. Neurologic SEs (treatment-emergent - at least moderate in severity)

Study or Subgroup	Risperidone Events	Total	Quetiapine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.19.1 Akinesia (long-term)						
MCEVOY2007A	36	133	33	134	100.0%	1.10 [0.73, 1.65]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**1.10 [0.73, 1.65]**
Total events	36		33			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.46 (P = 0.65)

5.19.2 Akathisia (long-term)						
MCEVOY2007A	30	133	25	134	100.0%	1.21 [0.75, 1.94]
Subtotal (95% CI)		**133**		**134**	**100.0%**	**1.21 [0.75, 1.94]**
Total events	30		25			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.79 (P = 0.43)

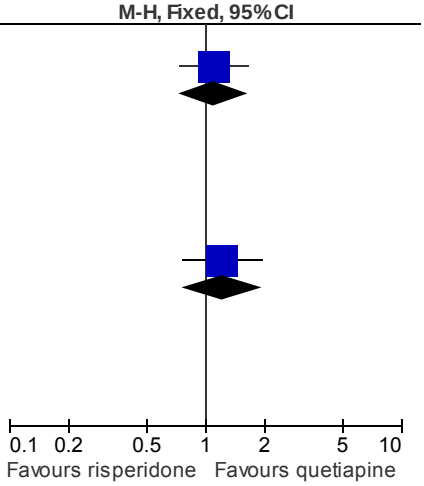


Table 2: Studies included in the acute treatment review (SGA versus FGA)

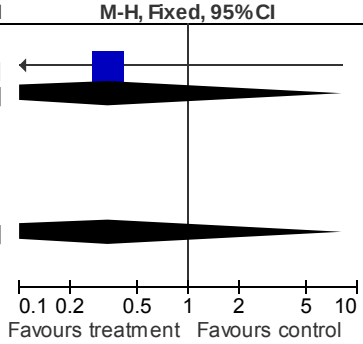
Treatment	versus Comparator					
	CHL	**FLUPE**	**FLUPH**	**HAL**	**PER**	**ZUC**
AMI		Hillert 1994 [6weeks, N=132]		Carriere 2000 [16weeks, N=199] Delcker 1990 [6weeks, N=41] Moller 1997 [6weeks, N=322] Puech 1998 [4weeks, N=319] Ziegler 1989 [4weeks, N=40]		
ARI				KANE2002 [4 weeks, N=414] KASPER2003 [52weeks, N=1294]		
OLZ	Loza 1999 [6weeks, N=41]	HGBL 1997 [4weeks, N=46]	Jakovljevic 1999 [6weeks, N=60]	Beasley 1996a [6weeks, N=138] Beasley 1997 [6weeks, N=170] HGCJ 1999 (HK) [14weeks, N=31] HGCU 1998 (Taiwan) [14weeks, N=54] KONGSAKON2006 [24weeks, N=281] Malyarov 1999 [26weeks, N=33] Reams 1998 [6weeks, N=59] ROSENHECK2003 [52weeks, N=309] Tollefson 1997 [6weeks, N=1996]	Naukkarinen 1999 [26weeks, N=46] Szafranski 1999 [18weeks, N=56]	
QUE	Link 1994 [6weeks, N=201]			Arvanitis 1996 [6weeks, N=310] ATMACA2002 [6weeks, N=35] Fleischhacker 1996 [6weeks, N=448] Purdon 2000 [26weeks, N=25]		

RIS				Blin 1996 [4weeks, N=41] Ceskova 1993 [8weeks, N=62] Cetin 1999 [6weeks, N=70] Chouinard 1993a [8weeks, N=113] Claus 1991 [12weeks, N=44] Janicak 1999 [6weeks, N=61] Liu 2000 [12weeks, N=38] Malyarov 1999 [26weeks, N=28] Marder 1994 [8weeks, N=322] Mesotten 1991 [8weeks, N=60] Min 1993 [8weeks, N=35] Muller-Siecheneder 1998 [6weeks, N=123] Peuskens 1995 [8weeks, N=1362] ZHANG2001 [12weeks, N=78]	Hoyberg 1993 [8weeks, N=107]	Huttunen 1995 [8weeks, N=98]
SER				Hale 2000 [8weeks, N=617]		
ZOT	Cooper 1999a [8weeks, N=106]			Barnas 1987 [7weeks, N=30] Fleischhacker 1989 [6weeks, N=40] Klieser 1996 [4weeks, N=65] Petit 1996 [8weeks, N=126] Knoll CTR (StudyZT4002) [26weeks, N=125]	Dieterle 1999 [4weeks, N=40]	

1 Amisulpride versus FGA (phase: acute treatment) (critical outcomes)

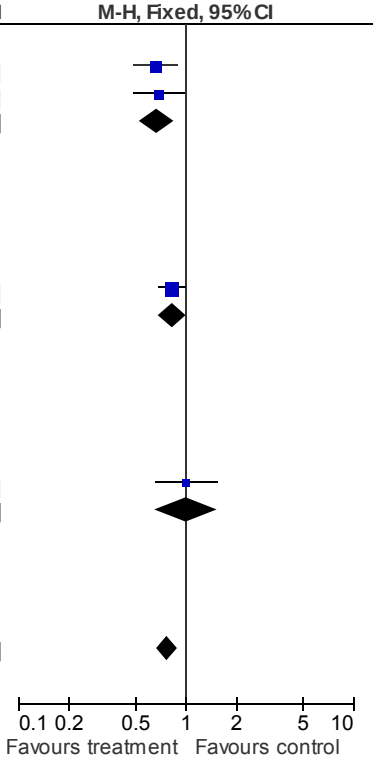
1.1 Mortality: 1. Suicide

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 vs. HAL						
Moller 1997	0	95	1	96	100.0%	0.34 [0.01, 8.17]
Subtotal (95% CI)		**95**		**96**	**100.0%**	**0.34 [0.01, 8.17]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.67 (P = 0.50)						
Total (95% CI)		**95**		**96**	**100.0%**	**0.34 [0.01, 8.17]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.67 (P = 0.50)						



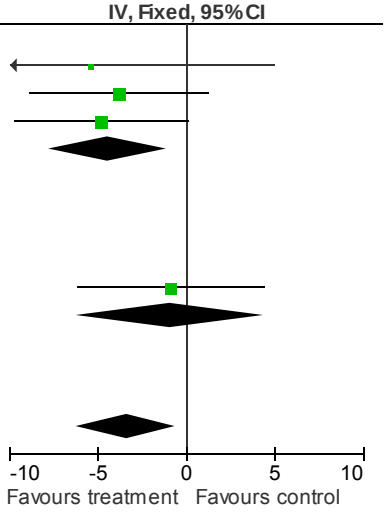
1.2 Global state: 2. Non-response (CGI) (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 vs. HAL (short-term)						
Moller 1997	36	94	55	94	27.9%	0.65 [0.48, 0.89]
Puech 1998	58	194	28	64	21.4%	0.68 [0.48, 0.97]
Subtotal (95% CI)		**288**		**158**	**49.2%**	**0.67 [0.53, 0.84]**
Total events	94		83			
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.86); I² = 0%						
Test for overall effect: Z = 3.43 (P = 0.0006)						
1.2.2 vs. HAL (medium-term)						
Carriere 2000	58	94	79	105	37.8%	0.82 [0.68, 1.00]
Subtotal (95% CI)		**94**		**105**	**37.8%**	**0.82 [0.68, 1.00]**
Total events	58		79			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.01 (P = 0.04)						
1.2.3 vs. other FGA (short-term)						
Hillert 1994	27	70	24	62	12.9%	1.00 [0.65, 1.53]
Subtotal (95% CI)		**70**		**62**	**12.9%**	**1.00 [0.65, 1.53]**
Total events	27		24			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.99)						
Total (95% CI)		**452**		**325**	**100.0%**	**0.77 [0.66, 0.89]**
Total events	179		186			
Heterogeneity: Chi² = 3.31, df = 3 (P = 0.35); I² = 9%						
Test for overall effect: Z = 3.58 (P = 0.0003)						



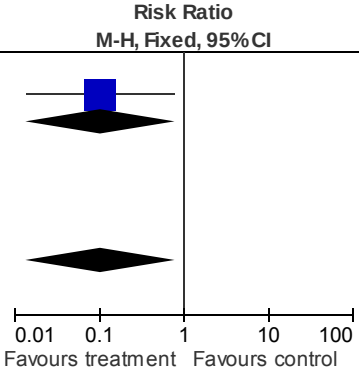
1.3 Mental state: 1. BPRS total (endpoint/change) (short-to-medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
1.3.1 vs. HAL								
Carriere 2000	-27.3	36.65	91	-21.9	36.65	103	7.5%	-5.40 [-15.73, 4.93]
Moller 1997	40.4	18.7	94	44.2	16.8	94	31.0%	-3.80 [-8.88, 1.28]
Puech 1998	35.2	12.7	63	40	15.1	61	33.1%	-4.80 [-9.72, 0.12]
Subtotal (95% CI)			**248**			**258**	**71.5%**	**-4.43 [-7.77, -1.09]**
Heterogeneity: Chi² = 0.11, df = 2 (P = 0.94); I² = 0%								
Test for overall effect: Z = 2.60 (P = 0.009)								
1.3.2 vs. other FGA								
Hillert 1994	32.4	15.4	70	33.3	15.6	62	28.5%	-0.90 [-6.20, 4.40]
Subtotal (95% CI)			**70**			**62**	**28.5%**	**-0.90 [-6.20, 4.40]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.33 (P = 0.74)								
Total (95% CI)			**318**			**320**	**100.0%**	**-3.42 [-6.25, -0.60]**
Heterogeneity: Chi² = 1.33, df = 3 (P = 0.72); I² = 0%								
Test for overall effect: Z = 2.37 (P = 0.02)								
Test for subgroup differences: Chi² = 1.22, df = 1 (P = 0.27), I² = 17.9%								



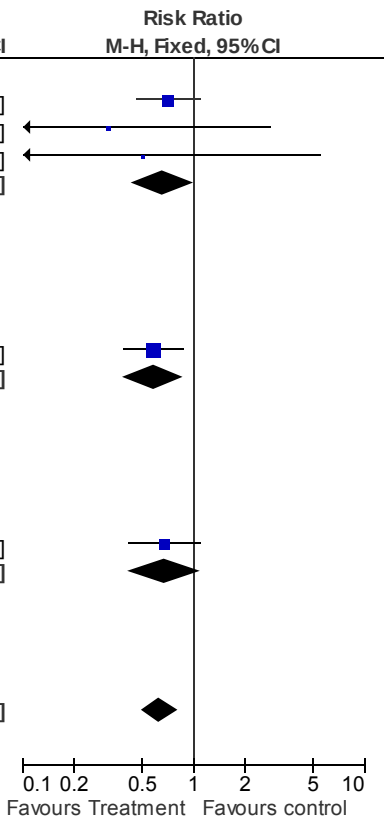
1.4 Mental state: 2. Depression (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 vs. HAL						
Carriere 2000	1	94	11	105	100.0%	0.10 [0.01, 0.77]
Subtotal (95% CI)		**94**		**105**	**100.0%**	**0.10 [0.01, 0.77]**
Total events	1		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.21 (P = 0.03)						
Total (95% CI)		**94**		**105**	**100.0%**	**0.10 [0.01, 0.77]**
Total events	1		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.21 (P = 0.03)						



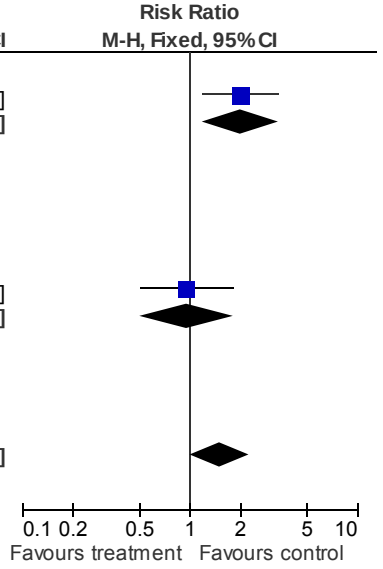
1.5 Leaving the study early: 1. Any reason (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.5.1 vs. HAL (short-term)						
Puech 1998	45	194	21	64	29.6%	0.71 [0.46, 1.09]
Delcker 1990	1	21	3	20	2.9%	0.32 [0.04, 2.80]
Moller 1997	1	95	2	96	1.9%	0.51 [0.05, 5.48]
Subtotal (95% CI)		**310**		**180**	**34.4%**	**0.66 [0.44, 1.01]**
Total events	47		26			
Heterogeneity: Chi² = 0.57, df = 2 (P = 0.75); I² = 0%						
Test for overall effect: Z = 1.91 (P = 0.06)						
1.5.2 vs. HAL (medium-term)						
Carriere 2000	24	94	46	105	40.8%	0.58 [0.39, 0.88]
Subtotal (95% CI)		**94**		**105**	**40.8%**	**0.58 [0.39, 0.88]**
Total events	24		46			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.60 (P = 0.009)						
1.5.3 vs. other FGA (short-term)						
Hillert 1994	19	70	25	62	24.9%	0.67 [0.41, 1.10]
Subtotal (95% CI)		**70**		**62**	**24.9%**	**0.67 [0.41, 1.10]**
Total events	19		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.59 (P = 0.11)						
Total (95% CI)		**474**		**347**	**100.0%**	**0.63 [0.49, 0.81]**
Total events	90		97			
Heterogeneity: Chi² = 0.89, df = 4 (P = 0.93); I² = 0%						
Test for overall effect: Z = 3.57 (P = 0.0004)						



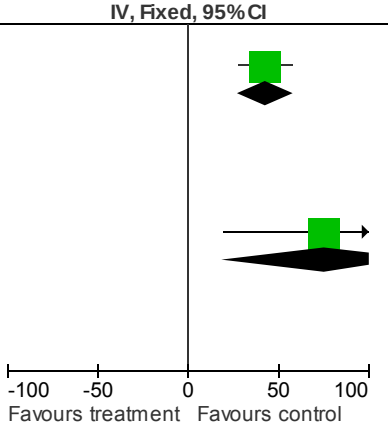
1.6 AE: 1. Metabolic SEs - weight gain (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 vs. HAL (medium-term)						
Carriere 2000	30	91	17	103	51.8%	2.00 [1.18, 3.37]
Subtotal (95% CI)		**91**		**103**	**51.8%**	**2.00 [1.18, 3.37]**
Total events	30		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.59 (P = 0.010)						
1.6.2 vs. other FGA (short-term)						
Hillert 1994	15	70	14	62	48.2%	0.95 [0.50, 1.81]
Subtotal (95% CI)		**70**		**62**	**48.2%**	**0.95 [0.50, 1.81]**
Total events	15		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.16 (P = 0.87)						
Total (95% CI)		**161**		**165**	**100.0%**	**1.49 [1.00, 2.22]**
Total events	45		31			
Heterogeneity: Chi² = 3.09, df = 1 (P = 0.08); I² = 68%						
Test for overall effect: Z = 1.96 (P = 0.05)						



1.7 AE: 1. Metabolic SEs - prolactin-related (short term)

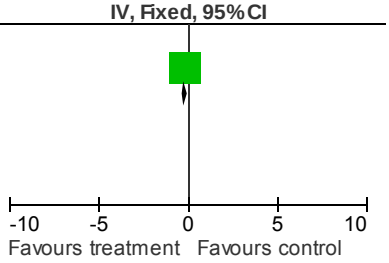
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.7.1 vs. other FGA: Prolactin levels - men								
Hillert 1994	68.8	27.5	18	26.1	17	17	100.0%	42.70 [27.64, 57.76]
Subtotal (95% CI)			**18**			**17**	**100.0%**	**42.70 [27.64, 57.76]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.56 (P < 0.00001)								
1.7.2 vs. other FGA: Prolactin levels - women								
Hillert 1994	165.5	87.3	11	90.2	39.3	12	100.0%	75.30 [19.12, 131.48]
Subtotal (95% CI)			**11**			**12**	**100.0%**	**75.30 [19.12, 131.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.63 (P = 0.009)								



Test for subgroup differences: Chi² = 1.21, df = 1 (P = 0.27), I² = 17.1%

1.8 AE: 2. Neurologic SEs (<500 mg/day amisulpride) (short-term)

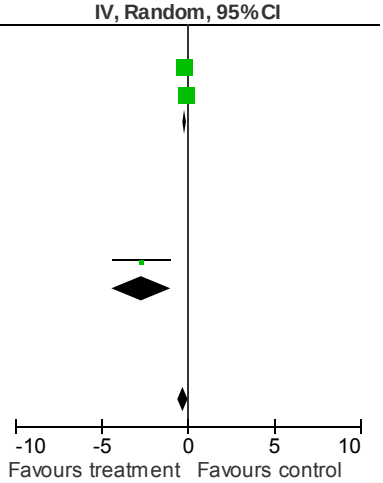
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.8.1 vs. HAL: Simpson Angus Scale endpoint scores								
Puech 1998	0.2	0.33	62	0.4	0.49	61	100.0%	-0.20 [-0.35, -0.05]
Subtotal (95% CI)			**62**			**61**	**100.0%**	**-0.20 [-0.35, -0.05]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.65 (P = 0.008)								



Test for subgroup differences: Not applicable

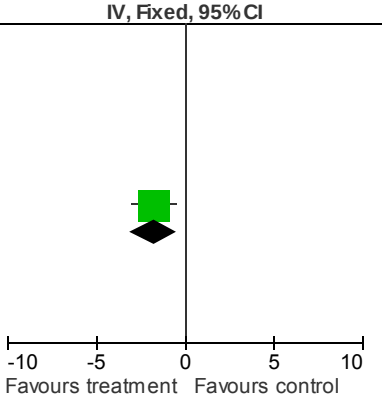
1.9 AE: 2. Neurologic SEs (>500 mg/day amisulpride) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.9.1 vs. HAL: Simpson Angus Scale endpoint/change scores								
Moller 1997	0.4	0.51	93	0.63	0.59	93	48.7%	-0.23 [-0.39, -0.07]
Puech 1998	0.26	0.45	63	0.4	0.49	61	48.1%	-0.14 [-0.31, 0.03]
Subtotal (95% CI)			**156**			**154**	**96.8%**	**-0.19 [-0.30, -0.07]**
Heterogeneity: Tau² = 0.00; Chi² = 0.59, df = 1 (P = 0.44); I² = 0%								
Test for overall effect: Z = 3.20 (P = 0.001)								
1.9.2 vs. other FGA: Simpson Angus Scale change scores								
Hillert 1994	1.1	3.7	70	3.8	5.9	62	3.2%	-2.70 [-4.41, -0.99]
Subtotal (95% CI)			**70**			**62**	**3.2%**	**-2.70 [-4.41, -0.99]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.10 (P = 0.002)								
Total (95% CI)			**226**			**216**	**100.0%**	**-0.27 [-0.58, 0.05]**
Heterogeneity: Tau² = 0.05; Chi² = 8.90, df = 2 (P = 0.01); I² = 78%								
Test for overall effect: Z = 1.66 (P = 0.10)								



1.10 AE: 2. Neurologic SEs - EPS (>500 mg/day amisulpride) (short-term)

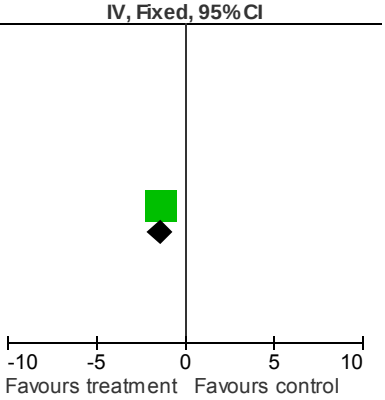
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.10.1 vs. HAL: AIMS change scores								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
1.10.2 vs. other FGA: AIMS change scores								
Hillert 1994	0	2.8	70	1.8	4.4	62	100.0%	-1.80 [-3.08, -0.52]
Subtotal (95% CI)			**70**			**62**	**100.0%**	**-1.80 [-3.08, -0.52]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.76 (P = 0.006)								



Test for subgroup differences: Not applicable

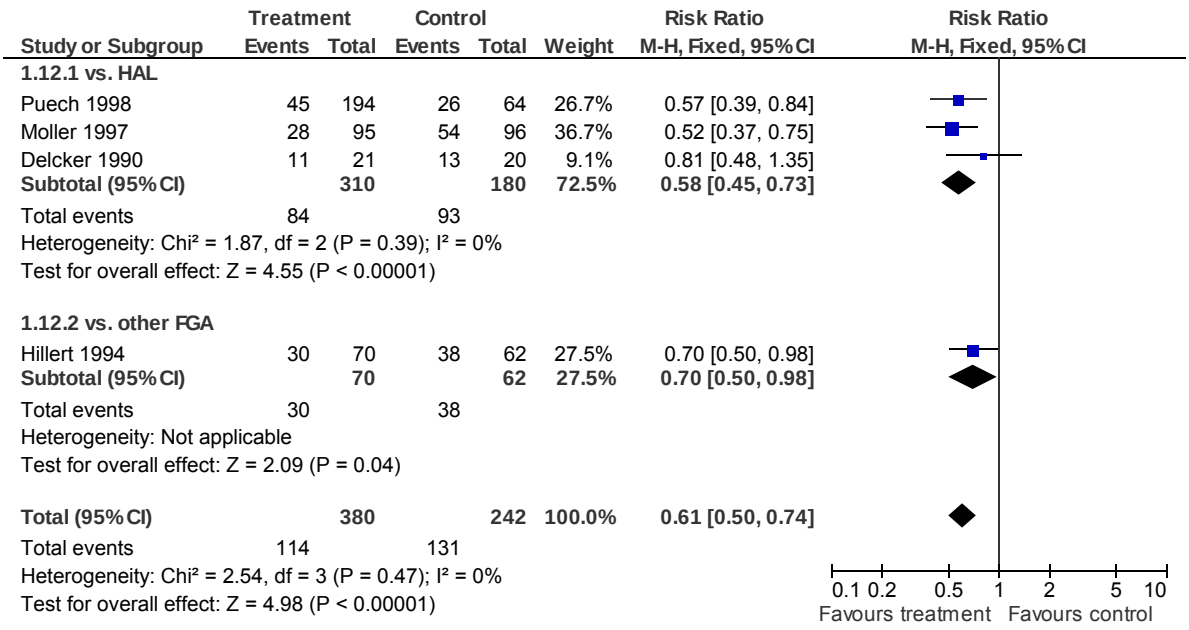
1.11 AE: 2. Neurologic SEs - akathisia (>500 mg/day amisulpride) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.11.1 vs. HAL: Barnes Akathisia Scale change scores								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
1.11.2 vs. other FGA: Barnes Akathisia Scale change scores								
Hillert 1994	0.2	1.9	70	1.6	2.4	62	100.0%	-1.40 [-2.14, -0.66]
Subtotal (95% CI)			**70**			**62**	**100.0%**	**-1.40 [-2.14, -0.66]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.68 (P = 0.0002)								

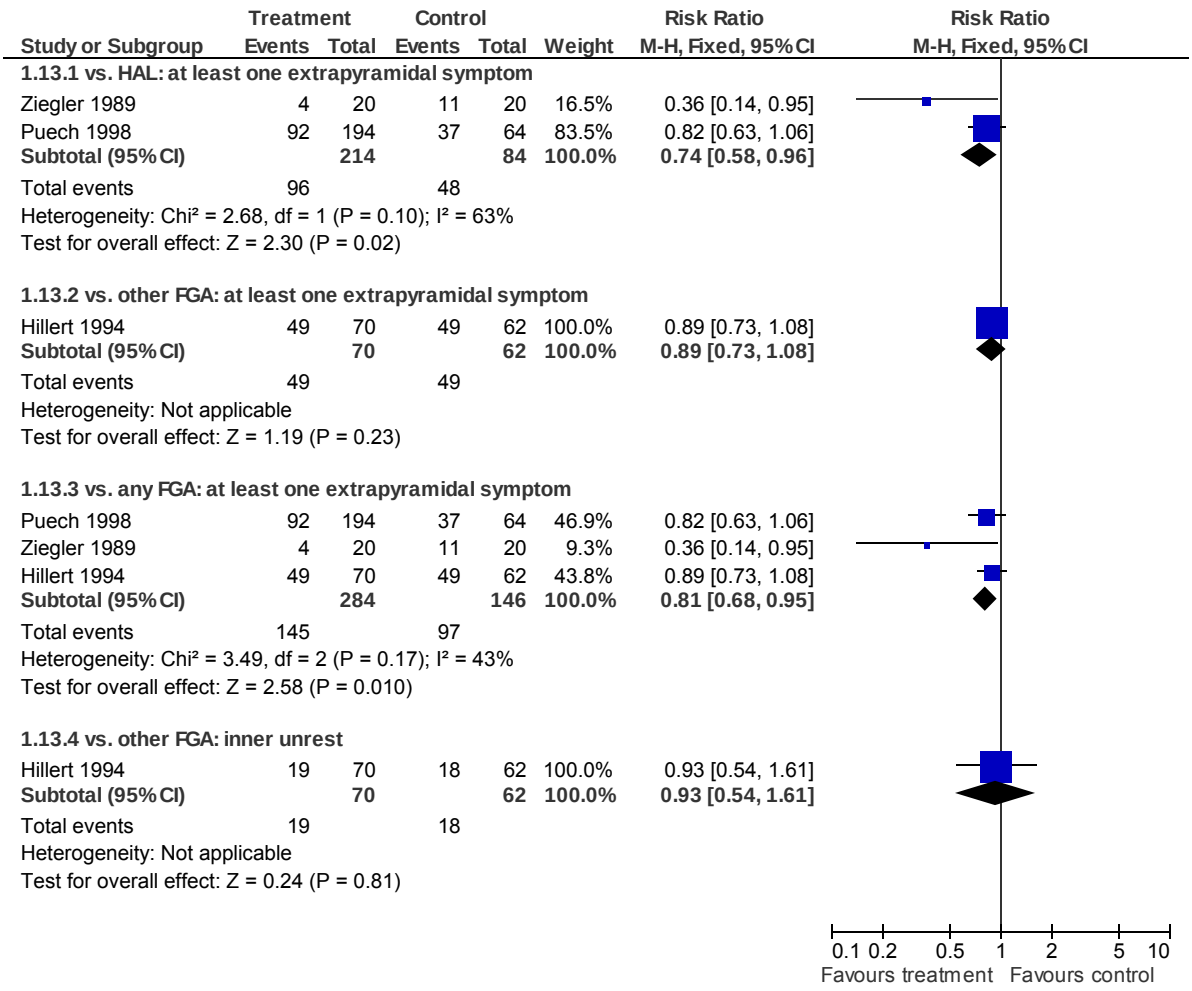


Test for subgroup differences: Not applicable

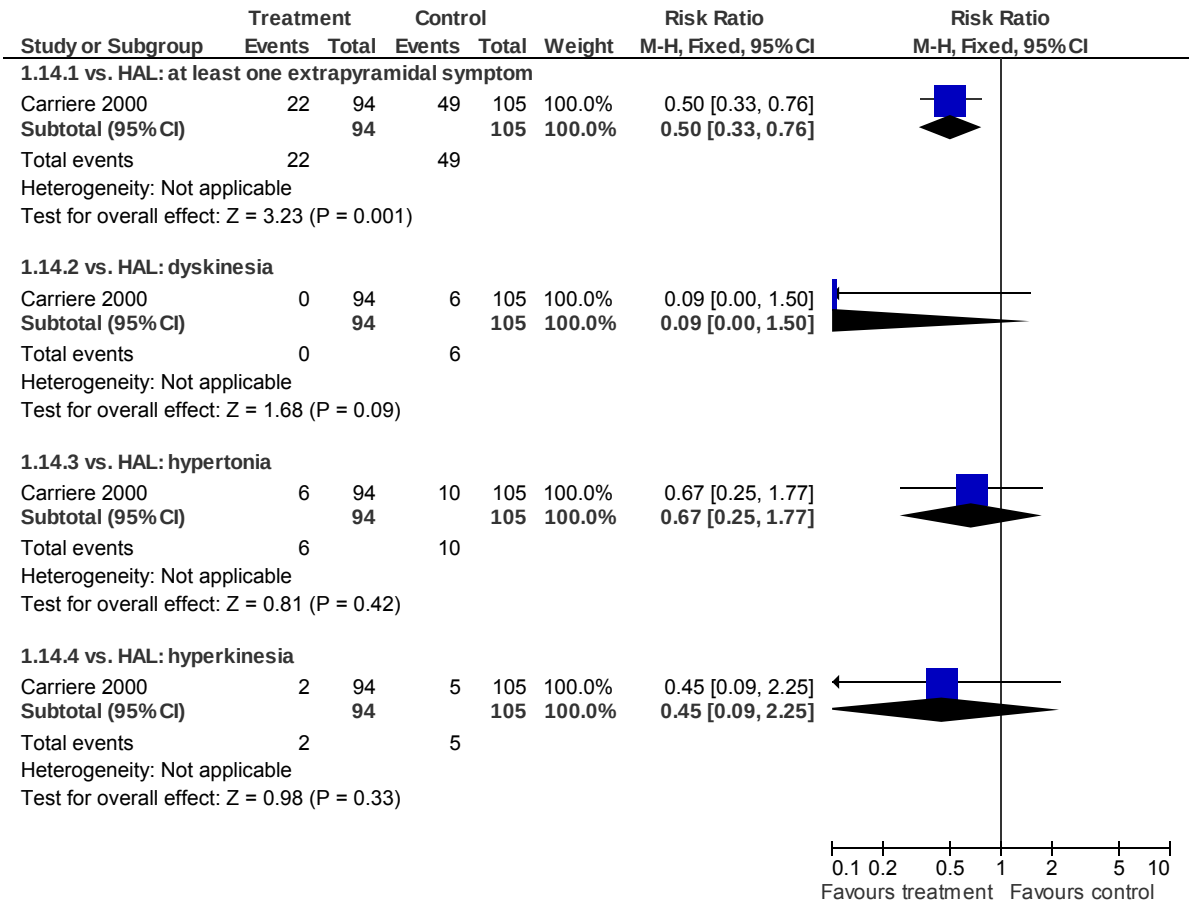
1.12 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)



1.13 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



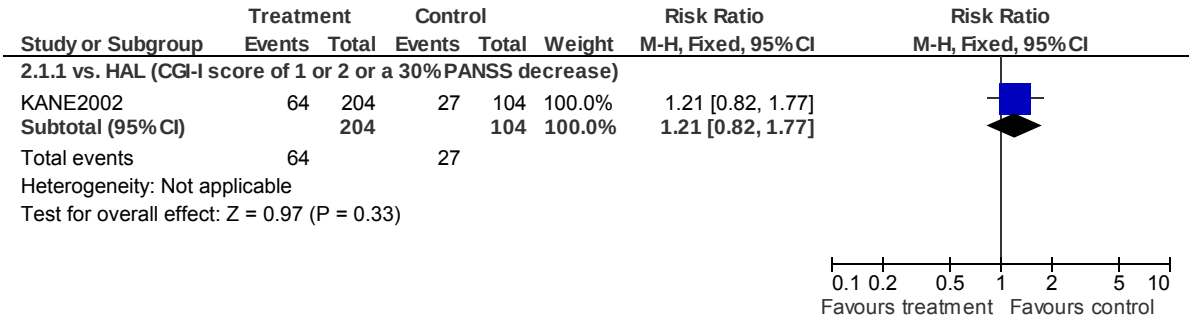
1.14 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)



Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.14.1 vs. HAL: at least one extrapyramidal symptom						
Carriere 2000	22	94	49	105	100.0%	0.50 [0.33, 0.76]
Subtotal (95% CI)		**94**		**105**	**100.0%**	**0.50 [0.33, 0.76]**
Total events	22		49			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.23 (P = 0.001)						
1.14.2 vs. HAL: dyskinesia						
Carriere 2000	0	94	6	105	100.0%	0.09 [0.00, 1.50]
Subtotal (95% CI)		**94**		**105**	**100.0%**	**0.09 [0.00, 1.50]**
Total events	0		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.68 (P = 0.09)						
1.14.3 vs. HAL: hypertonia						
Carriere 2000	6	94	10	105	100.0%	0.67 [0.25, 1.77]
Subtotal (95% CI)		**94**		**105**	**100.0%**	**0.67 [0.25, 1.77]**
Total events	6		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.81 (P = 0.42)						
1.14.4 vs. HAL: hyperkinesia						
Carriere 2000	2	94	5	105	100.0%	0.45 [0.09, 2.25]
Subtotal (95% CI)		**94**		**105**	**100.0%**	**0.45 [0.09, 2.25]**
Total events	2		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.33)						

2 Aripiprazole versus FGA (phase: acute treatment) (critical outcomes)

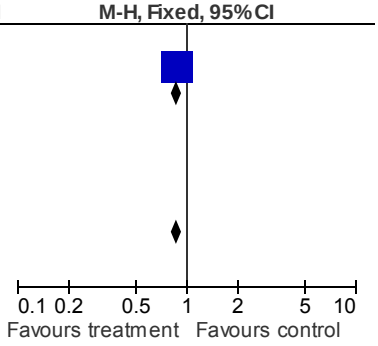
2.1 Global state: 3. No important clinical response by 6-8 weeks



Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 vs. HAL (CGI-I score of 1 or 2 or a 30% PANSS decrease)						
KANE2002	64	204	27	104	100.0%	1.21 [0.82, 1.77]
Subtotal (95% CI)		**204**		**104**	**100.0%**	**1.21 [0.82, 1.77]**
Total events	64		27			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						

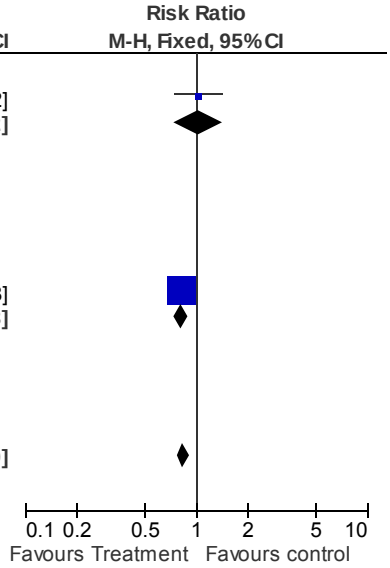
2.2 Mental state: 1. Non-remission (RSWG criteria) (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 vs. HAL						
KASPER2003	577	853	336	430	100.0%	0.87 [0.81, 0.93]
Subtotal (95% CI)		**853**		**430**	**100.0%**	**0.87 [0.81, 0.93]**
Total events	577		336			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.14 (P < 0.0001)						
Total (95% CI)		**853**		**430**	**100.0%**	**0.87 [0.81, 0.93]**
Total events	577		336			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.14 (P < 0.0001)						



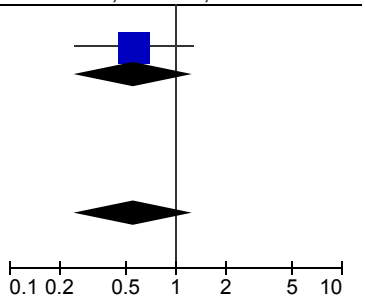
2.3 Leaving the study early: 1. Any reason (short-to-long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.3.1 vs. HAL (short-term)						
KANE2002	42	102	42	104	9.4%	1.02 [0.73, 1.42]
Subtotal (95% CI)		**102**		**104**	**9.4%**	**1.02 [0.73, 1.42]**
Total events	42		42			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.12 (P = 0.91)						
2.3.2 vs. HAL (long-term)						
KASPER2003	486	853	302	430	90.6%	0.81 [0.75, 0.88]
Subtotal (95% CI)		**853**		**430**	**90.6%**	**0.81 [0.75, 0.88]**
Total events	486		302			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.84 (P < 0.00001)						
Total (95% CI)		**955**		**534**	**100.0%**	**0.83 [0.76, 0.90]**
Total events	528		344			
Heterogeneity: Chi² = 1.79, df = 1 (P = 0.18); I² = 44%						
Test for overall effect: Z = 4.36 (P < 0.0001)						



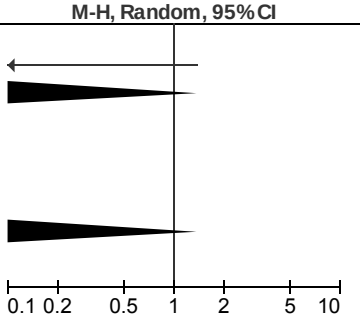
2.4 AE: 1. Metabolic SEs - Weight gain (>= 7% increase from baseline) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.4.1 vs. HAL						
KANE2002	11	203	10	103	100.0%	0.56 [0.25, 1.27]
Subtotal (95% CI)		**203**		**103**	**100.0%**	**0.56 [0.25, 1.27]**
Total events	11		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.39 (P = 0.16)						
Total (95% CI)		**203**		**103**	**100.0%**	**0.56 [0.25, 1.27]**
Total events	11		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.39 (P = 0.16)						



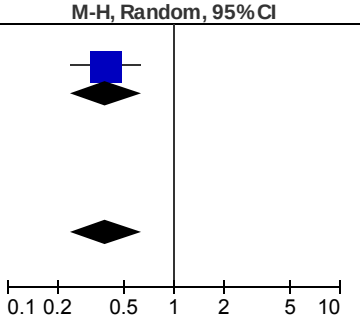
2.5 AE: 1. Metabolic SEs - Clinically sig. increase in QTc interval (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.5.1 vs. HAL						
KANE2002	0	203	3	103	100.0%	0.07 [0.00, 1.40]
Subtotal (95% CI)		**203**		**103**	**100.0%**	**0.07 [0.00, 1.40]**
Total events	0		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.74 (P = 0.08)						
Total (95% CI)		**203**		**103**	**100.0%**	**0.07 [0.00, 1.40]**
Total events	0		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.74 (P = 0.08)						



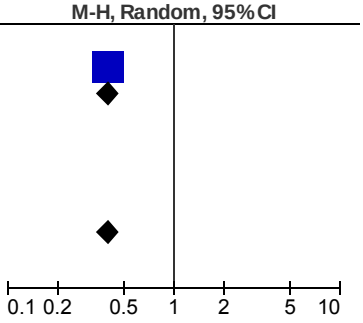
2.6 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.6.1 vs. HAL						
KANE2002	23	203	30	103	100.0%	0.39 [0.24, 0.63]
Subtotal (95% CI)		**203**		**103**	**100.0%**	**0.39 [0.24, 0.63]**
Total events	23		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.79 (P = 0.0002)						
Total (95% CI)		**203**		**103**	**100.0%**	**0.39 [0.24, 0.63]**
Total events	23		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.79 (P = 0.0002)						



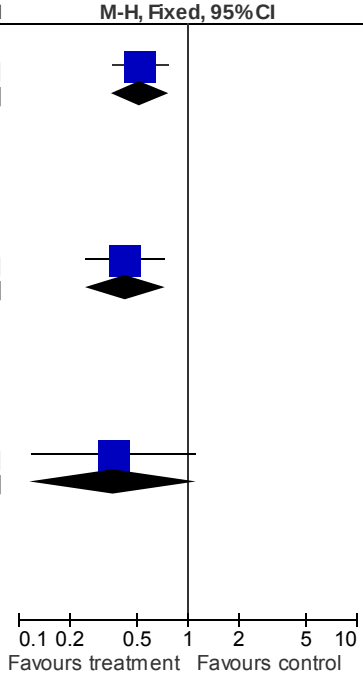
2.7 AE: 2. Neurologic SEs - Use of anticholinergic medication (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.7.1 vs. HAL						
KASPER2003	196	853	245	430	100.0%	0.40 [0.35, 0.47]
Subtotal (95% CI)		**853**		**430**	**100.0%**	**0.40 [0.35, 0.47]**
Total events	196		245			
Heterogeneity: Not applicable						
Test for overall effect: Z = 12.04 (P < 0.00001)						
Total (95% CI)		**853**		**430**	**100.0%**	**0.40 [0.35, 0.47]**
Total events	196		245			
Heterogeneity: Not applicable						
Test for overall effect: Z = 12.04 (P < 0.00001)						



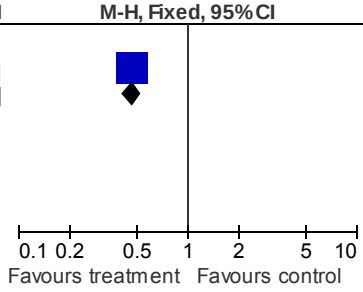
2.8 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.8.1 vs. HAL: EPS						
KANE2002	38	203	37	103	100.0%	0.52 [0.35, 0.77]
Subtotal (95% CI)		**203**		**103**	**100.0%**	**0.52 [0.35, 0.77]**
Total events	38		37			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.31 (P = 0.0009)						
2.8.2 vs. HAL: akathisia						
KANE2002	20	203	24	103	100.0%	0.42 [0.25, 0.73]
Subtotal (95% CI)		**203**		**103**	**100.0%**	**0.42 [0.25, 0.73]**
Total events	20		24			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.10 (P = 0.002)						
2.8.3 vs. HAL: tremor						
KANE2002	5	203	7	103	100.0%	0.36 [0.12, 1.11]
Subtotal (95% CI)		**203**		**103**	**100.0%**	**0.36 [0.12, 1.11]**
Total events	5		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.77 (P = 0.08)						



2.9 AE: 2. Neurologic SEs (treatment-emergent) (long-term)

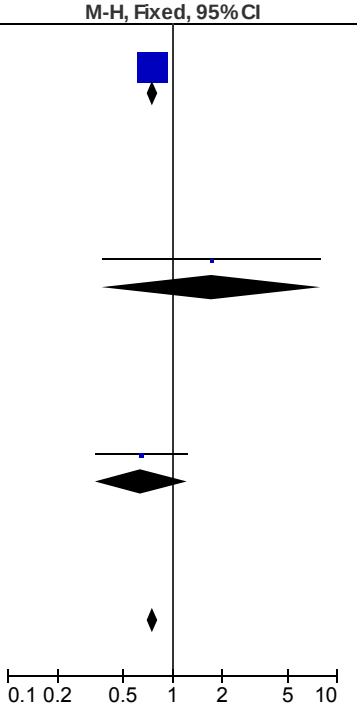
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.9.1 vs. HAL: EPS related						
KASPER2003	230	853	249	430	100.0%	0.47 [0.41, 0.53]
Subtotal (95% CI)		**853**		**430**	**100.0%**	**0.47 [0.41, 0.53]**
Total events	230		249			
Heterogeneity: Not applicable						
Test for overall effect: Z = 10.96 (P < 0.00001)						



3 Olanzapine versus FGA (phase: acute treatment) (critical outcomes)

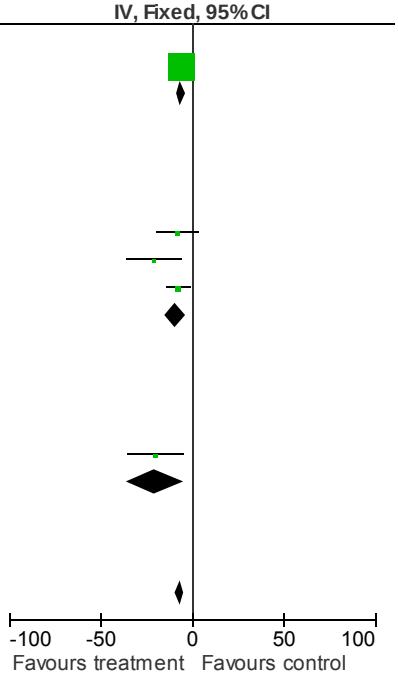
3.1 Global state: 1. No important clinical response (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 vs. HAL (short-term)						
Tollefson 1997	718	1336	471	660	97.5%	0.75 [0.70, 0.81]
Subtotal (95% CI)		**1336**		**660**	**97.5%**	**0.75 [0.70, 0.81]**
Total events	718		471			
Heterogeneity: Not applicable						
Test for overall effect: Z = 8.01 (P < 0.00001)						
3.1.2 vs. other FGA (short-term)						
HGBL 1997	4	15	2	13	0.3%	1.73 [0.38, 7.98]
Subtotal (95% CI)		**15**		**13**	**0.3%**	**1.73 [0.38, 7.98]**
Total events	4		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.71 (P = 0.48)						
3.1.3 vs. other FGA (medium-term)						
Jakovljevic 1999	9	27	14	27	2.2%	0.64 [0.34, 1.23]
Subtotal (95% CI)		**27**		**27**	**2.2%**	**0.64 [0.34, 1.23]**
Total events	9		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.34 (P = 0.18)						
Total (95% CI)		**1378**		**700**	**100.0%**	**0.75 [0.70, 0.81]**
Total events	731		487			
Heterogeneity: Chi² = 1.38, df = 2 (P = 0.50); I² = 0%						
Test for overall effect: Z = 8.00 (P < 0.00001)						



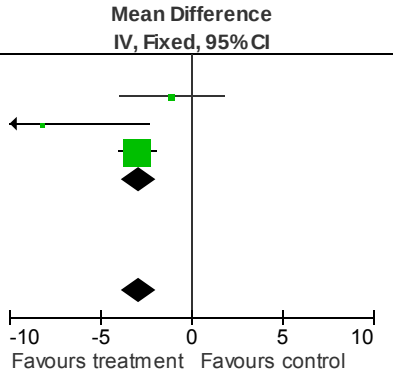
3.2 Mental state: 1. PANSS total (endpoint/change from baseline) (short-to-medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.2.1 vs. HAL (short-term)								
Tollefson 1997	72.41	23.5	1312	78.73	22.92	636	84.8%	-6.32 [-8.51, -4.13]
Subtotal (95% CI)			**1312**			**636**	**84.8%**	**-6.32 [-8.51, -4.13]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.66 (P < 0.00001)								
3.2.2 vs. HAL (medium-term)								
HGCU (Taiwan) 1998	61.92	19.32	24	70.11	23.66	28	3.0%	-8.19 [-19.88, 3.50]
HGCJ (HK) 1999	57.25	17.25	16	78.43	23.71	14	1.8%	-21.18 [-36.20, -6.16]
KONGSAKON2006	-44.6	27.82	139	-36.7	28.57	123	8.7%	-7.90 [-14.75, -1.05]
Subtotal (95% CI)			**179**			**165**	**13.4%**	**-9.74 [-15.24, -4.24]**
Heterogeneity: Chi² = 2.57, df = 2 (P = 0.28); I² = 22%								
Test for overall effect: Z = 3.47 (P = 0.0005)								
3.2.3 vs. other FGA (medium-term)								
Jakovljevic 1999	57	23.6	27	77.4	33.4	27	1.7%	-20.40 [-35.83, -4.97]
Subtotal (95% CI)			**27**			**27**	**1.7%**	**-20.40 [-35.83, -4.97]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.59 (P = 0.010)								
Total (95% CI)			**1518**			**828**	**100.0%**	**-7.02 [-9.04, -5.00]**
Heterogeneity: Chi² = 6.80, df = 4 (P = 0.15); I² = 41%								
Test for overall effect: Z = 6.83 (P < 0.00001)								
Test for subgroup differences: Chi² = 4.23, df = 2 (P = 0.12), I² = 52.7%								

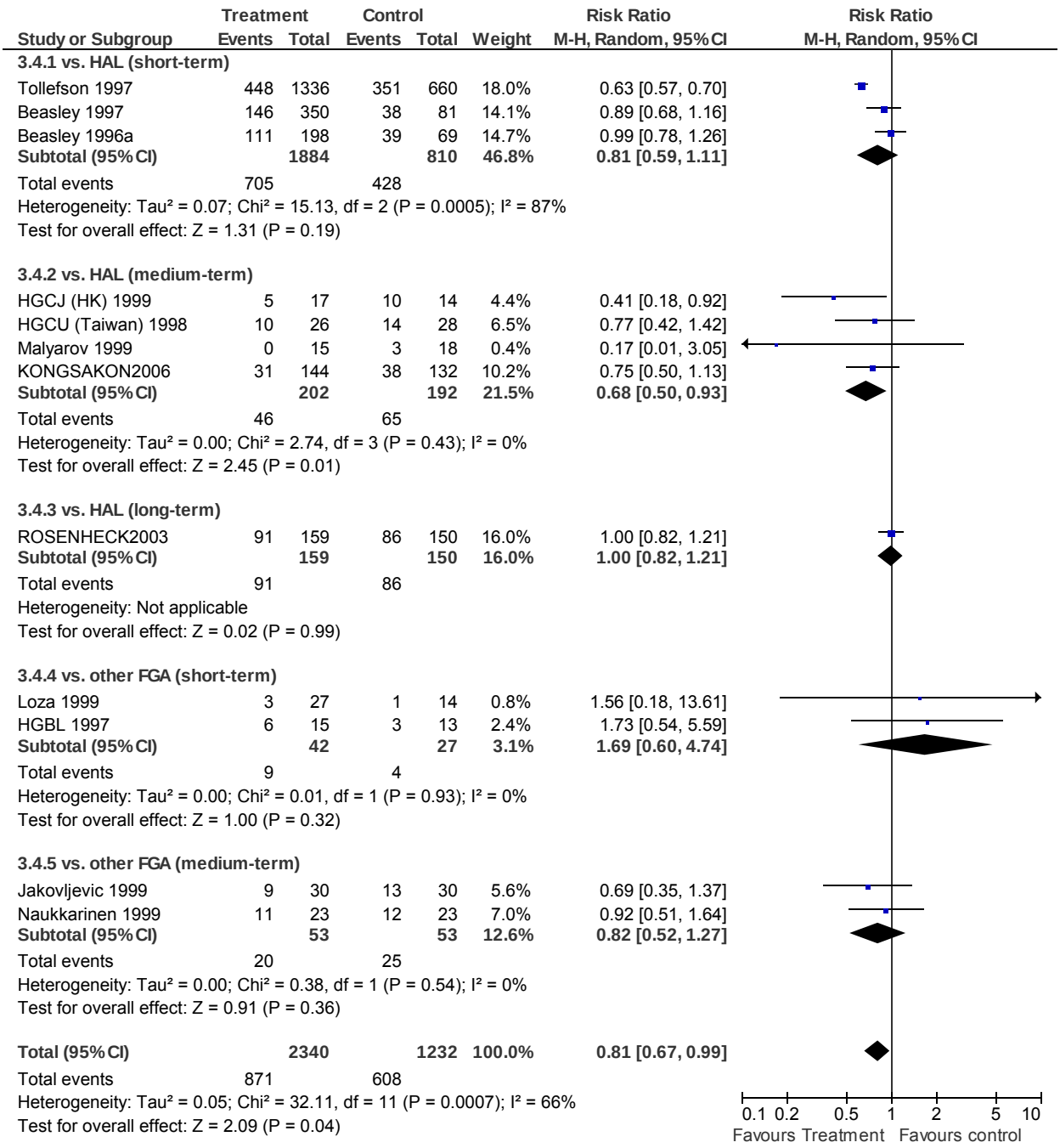


3.3 Mental state:2. Depression (MADRS, endpoint, high-poor) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.3.1 vs. HAL								
HGCU (Taiwan) 1998	3.67	5.43	24	4.79	5.14	28	11.5%	-1.12 [-4.01, 1.77]
HGCJ (HK) 1999	4.06	4.39	16	12.29	10.56	14	2.7%	-8.23 [-14.17, -2.29]
Tollefson 1997	10.65	8.3	1053	13.64	9.82	428	85.8%	-2.99 [-4.05, -1.93]
Subtotal (95% CI)			**1093**			**470**	**100.0%**	**-2.92 [-3.90, -1.94]**
Heterogeneity: Chi² = 4.58, df = 2 (P = 0.10); I² = 56%								
Test for overall effect: Z = 5.84 (P < 0.00001)								
Total (95% CI)			**1093**			**470**	**100.0%**	**-2.92 [-3.90, -1.94]**
Heterogeneity: Chi² = 4.58, df = 2 (P = 0.10); I² = 56%								
Test for overall effect: Z = 5.84 (P < 0.00001)								
Test for subgroup differences: Not applicable								

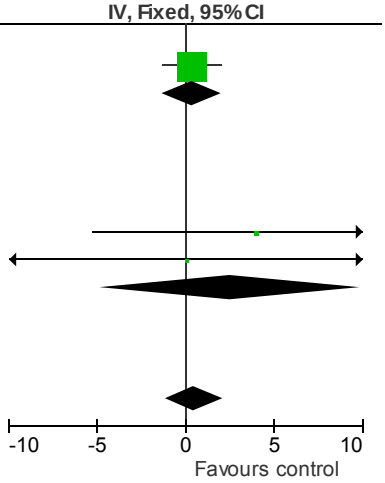


3.4 Leaving the study early: 1. Any reason (short-to-long-term)



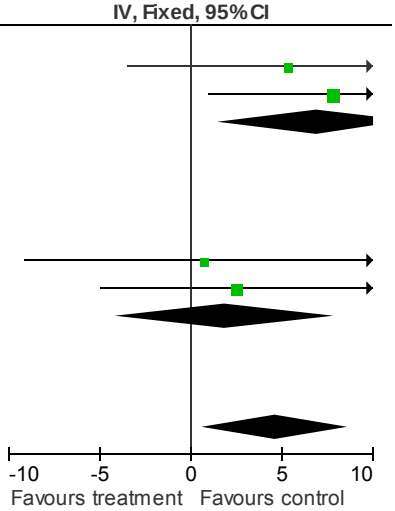
3.5 AE: 1. Metabolic SEs - weight (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.5.1 vs. HAL								
Tollefson 1997	78.3	17.02	1303	77.95	17.92	633	95.0%	0.35 [-1.32, 2.02]
Subtotal (95% CI)			**1303**			**633**	**95.0%**	**0.35 [-1.32, 2.02]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.41 (P = 0.68)								
3.5.2 vs. other FGA								
Loza 1999	73.19	13.47	27	69.21	14.86	14	3.1%	3.98 [-5.32, 13.28]
HGBL 1997	74.57	13.09	14	74.5	17.16	12	1.9%	0.07 [-11.82, 11.96]
Subtotal (95% CI)			**41**			**26**	**5.0%**	**2.50 [-4.83, 9.82]**
Heterogeneity: Chi² = 0.26, df = 1 (P = 0.61); I² = 0%								
Test for overall effect: Z = 0.67 (P = 0.50)								
Total (95% CI)			**1344**			**659**	**100.0%**	**0.46 [-1.18, 2.09]**
Heterogeneity: Chi² = 0.57, df = 2 (P = 0.75); I² = 0%								
Test for overall effect: Z = 0.55 (P = 0.58)								
Test for subgroup differences: Chi² = 0.31, df = 1 (P = 0.58), I² = 0%								



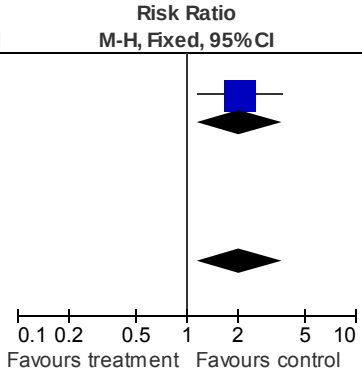
3.6 AE: 1. Metabolic SEs - weight (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.6.1 vs. HAL								
HGCJ (HK) 1999	64.71	13.67	16	59.36	11.08	14	20.6%	5.35 [-3.51, 14.21]
HGCU (Taiwan) 1998	70.85	11.87	24	63.05	13.15	27	34.3%	7.80 [0.93, 14.67]
Subtotal (95% CI)			**40**			**41**	**54.9%**	**6.88 [1.45, 12.31]**
Heterogeneity: Chi² = 0.18, df = 1 (P = 0.67); I² = 0%								
Test for overall effect: Z = 2.48 (P = 0.01)								
3.6.2 vs. other FGA								
Naukkarinen 1999	79.31	12.34	23	78.59	20.84	23	16.5%	0.72 [-9.18, 10.62]
Jakovljevic 1999	78.18	14.02	30	75.65	15.36	29	28.6%	2.53 [-4.98, 10.04]
Subtotal (95% CI)			**53**			**52**	**45.1%**	**1.87 [-4.11, 7.85]**
Heterogeneity: Chi² = 0.08, df = 1 (P = 0.78); I² = 0%								
Test for overall effect: Z = 0.61 (P = 0.54)								
Total (95% CI)			**93**			**93**	**100.0%**	**4.62 [0.60, 8.64]**
Heterogeneity: Chi² = 1.74, df = 3 (P = 0.63); I² = 0%								
Test for overall effect: Z = 2.25 (P = 0.02)								
Test for subgroup differences: Chi² = 1.48, df = 1 (P = 0.22), I² = 32.4%								



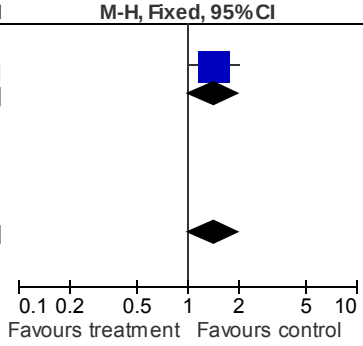
3.7 AE: 1. Metabolic SEs - weight gain (>=7% increase from baseline) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.7.1 vs. HAL						
KONGSAKON2006	32	113	13	94	100.0%	2.05 [1.14, 3.67]
Subtotal (95% CI)		**113**		**94**	**100.0%**	**2.05 [1.14, 3.67]**
Total events	32		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.41 (P = 0.02)						
Total (95% CI)		**113**		**94**	**100.0%**	**2.05 [1.14, 3.67]**
Total events	32		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.41 (P = 0.02)						



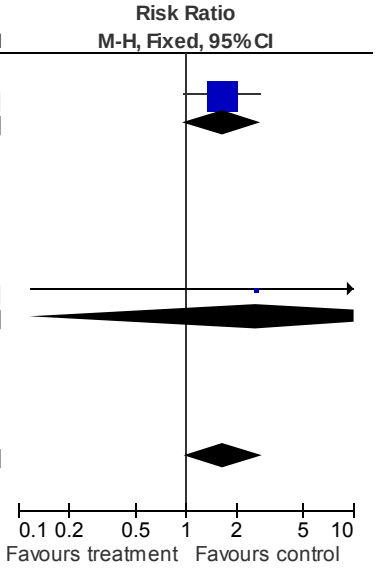
3.8 AE: 1. Metabolic SEs - weight gain (>=7% increase from baseline) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.8.1 vs. HAL						
KONGSAKON2006	51	113	30	94	100.0%	1.41 [0.99, 2.02]
Subtotal (95% CI)		**113**		**94**	**100.0%**	**1.41 [0.99, 2.02]**
Total events	51		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.89 (P = 0.06)						
Total (95% CI)		**113**		**94**	**100.0%**	**1.41 [0.99, 2.02]**
Total events	51		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.89 (P = 0.06)						



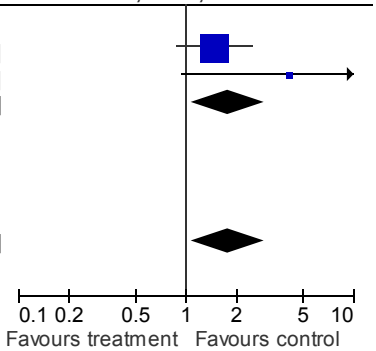
3.9 AE: 1. Metabolic SEs - weight gain (related to study drug) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.9.1 vs. HAL						
ROSENHECK2003	29	105	17	101	97.0%	1.64 [0.96, 2.80]
Subtotal (95% CI)		**105**		**101**	**97.0%**	**1.64 [0.96, 2.80]**
Total events	29		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.82 (P = 0.07)						
3.9.2 vs. other FGA						
HGBL 1997	1	15	0	13	3.0%	2.63 [0.12, 59.40]
Subtotal (95% CI)		**15**		**13**	**3.0%**	**2.63 [0.12, 59.40]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.61 (P = 0.54)						
Total (95% CI)		**120**		**114**	**100.0%**	**1.67 [0.99, 2.82]**
Total events	30		17			
Heterogeneity: Chi² = 0.08, df = 1 (P = 0.77); I² = 0%						
Test for overall effect: Z = 1.91 (P = 0.06)						



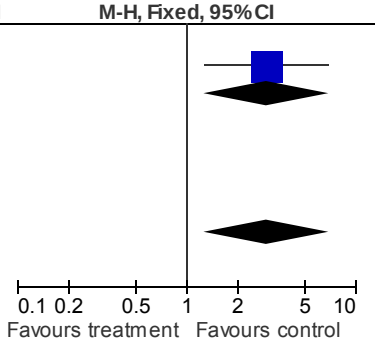
3.10 AE: 1. Metabolic SEs - weight gain (related to study drug) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.10.1 vs. HAL						
ROSENHECK2003	29	92	16	75	89.0%	1.48 [0.87, 2.51]
KONGSAKON2006	10	113	2	94	11.0%	4.16 [0.93, 18.52]
Subtotal (95% CI)		**205**		**169**	**100.0%**	**1.77 [1.08, 2.92]**
Total events	39		18			
Heterogeneity: Chi² = 1.71, df = 1 (P = 0.19); I² = 41%						
Test for overall effect: Z = 2.25 (P = 0.02)						
Total (95% CI)		**205**		**169**	**100.0%**	**1.77 [1.08, 2.92]**
Total events	39		18			
Heterogeneity: Chi² = 1.71, df = 1 (P = 0.19); I² = 41%						
Test for overall effect: Z = 2.25 (P = 0.02)						



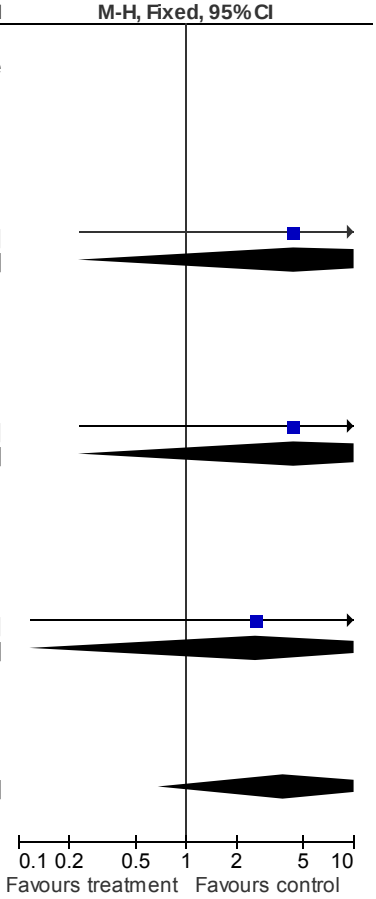
3.11 AE: 1. Metabolic SEs - weight gain (related to study drug) (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.11.1 vs. HAL						
ROSENHECK2003	21	85	6	72	100.0%	2.96 [1.27, 6.95]
Subtotal (95% CI)		**85**		**72**	**100.0%**	**2.96 [1.27, 6.95]**
Total events	21		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.50 (P = 0.01)						
Total (95% CI)		**85**		**72**	**100.0%**	**2.96 [1.27, 6.95]**
Total events	21		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.50 (P = 0.01)						



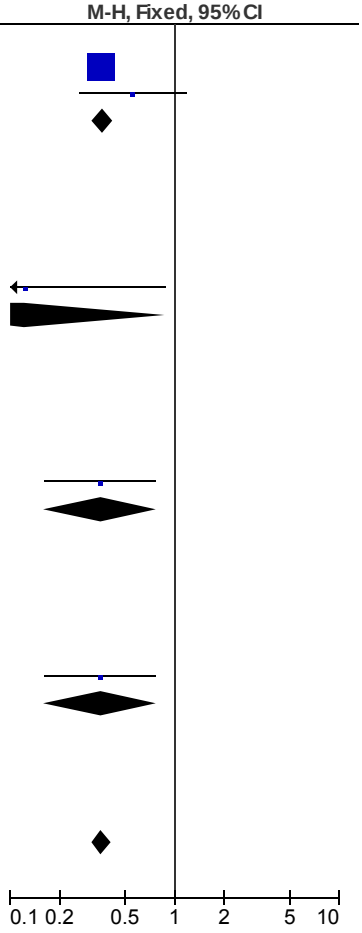
3.12 AE: 1. Metabolic SEs - treatment emergent (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.12.1 vs. HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
3.12.2 versus other FGA: Liver function test abnormal						
HGBL 1997	2	15	0	13	33.3%	4.38 [0.23, 83.62]
Subtotal (95% CI)		**15**		**13**	**33.3%**	**4.38 [0.23, 83.62]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.33)						
3.12.3 versus other FGA: SGPT increased						
HGBL 1997	2	15	0	13	33.3%	4.38 [0.23, 83.62]
Subtotal (95% CI)		**15**		**13**	**33.3%**	**4.38 [0.23, 83.62]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.33)						
3.12.4 versus other FGA: SGOT increased						
HGBL 1997	1	15	0	13	33.3%	2.63 [0.12, 59.40]
Subtotal (95% CI)		**15**		**13**	**33.3%**	**2.63 [0.12, 59.40]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.61 (P = 0.54)						
Total (95% CI)		**45**		**39**	**100.0%**	**3.79 [0.67, 21.31]**
Total events	5		0			
Heterogeneity: Chi² = 0.07, df = 2 (P = 0.96); I² = 0%						
Test for overall effect: Z = 1.51 (P = 0.13)						



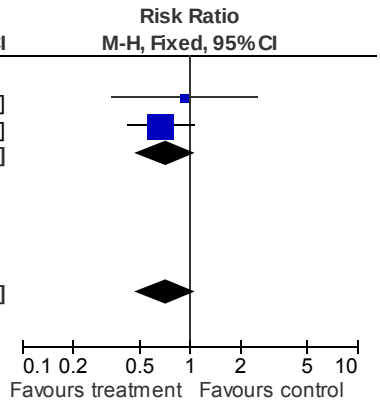
3.13 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.13.1 vs. HAL (short-term)						
Tollefson 1997	228	1336	315	660	87.9%	0.36 [0.31, 0.41]
KONGSAKON2006	10	113	15	94	3.4%	0.55 [0.26, 1.18]
Subtotal (95% CI)		**1449**		**754**	**91.3%**	**0.36 [0.32, 0.42]**
Total events	238		330			
Heterogeneity: Chi² = 1.27, df = 1 (P = 0.26); I² = 21%						
Test for overall effect: Z = 14.09 (P < 0.00001)						
3.13.2 vs. other FGA (short-term)						
HGBL 1997	1	15	7	13	1.6%	0.12 [0.02, 0.88]
Subtotal (95% CI)		**15**		**13**	**1.6%**	**0.12 [0.02, 0.88]**
Total events	1		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.09 (P = 0.04)						
3.13.3 vs. other FGA (medium-term)						
Jakovljevic 1999	6	30	17	30	3.5%	0.35 [0.16, 0.77]
Subtotal (95% CI)		**30**		**30**	**3.5%**	**0.35 [0.16, 0.77]**
Total events	6		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.61 (P = 0.009)						
3.13.4 vs. other FGA (medium-term)						
Jakovljevic 1999	6	30	17	30	3.5%	0.35 [0.16, 0.77]
Subtotal (95% CI)		**30**		**30**	**3.5%**	**0.35 [0.16, 0.77]**
Total events	6		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.61 (P = 0.009)						
Total (95% CI)		**1524**		**827**	**100.0%**	**0.36 [0.31, 0.41]**
Total events	251		371			
Heterogeneity: Chi² = 2.42, df = 4 (P = 0.66); I² = 0%						
Test for overall effect: Z = 14.73 (P < 0.00001)						

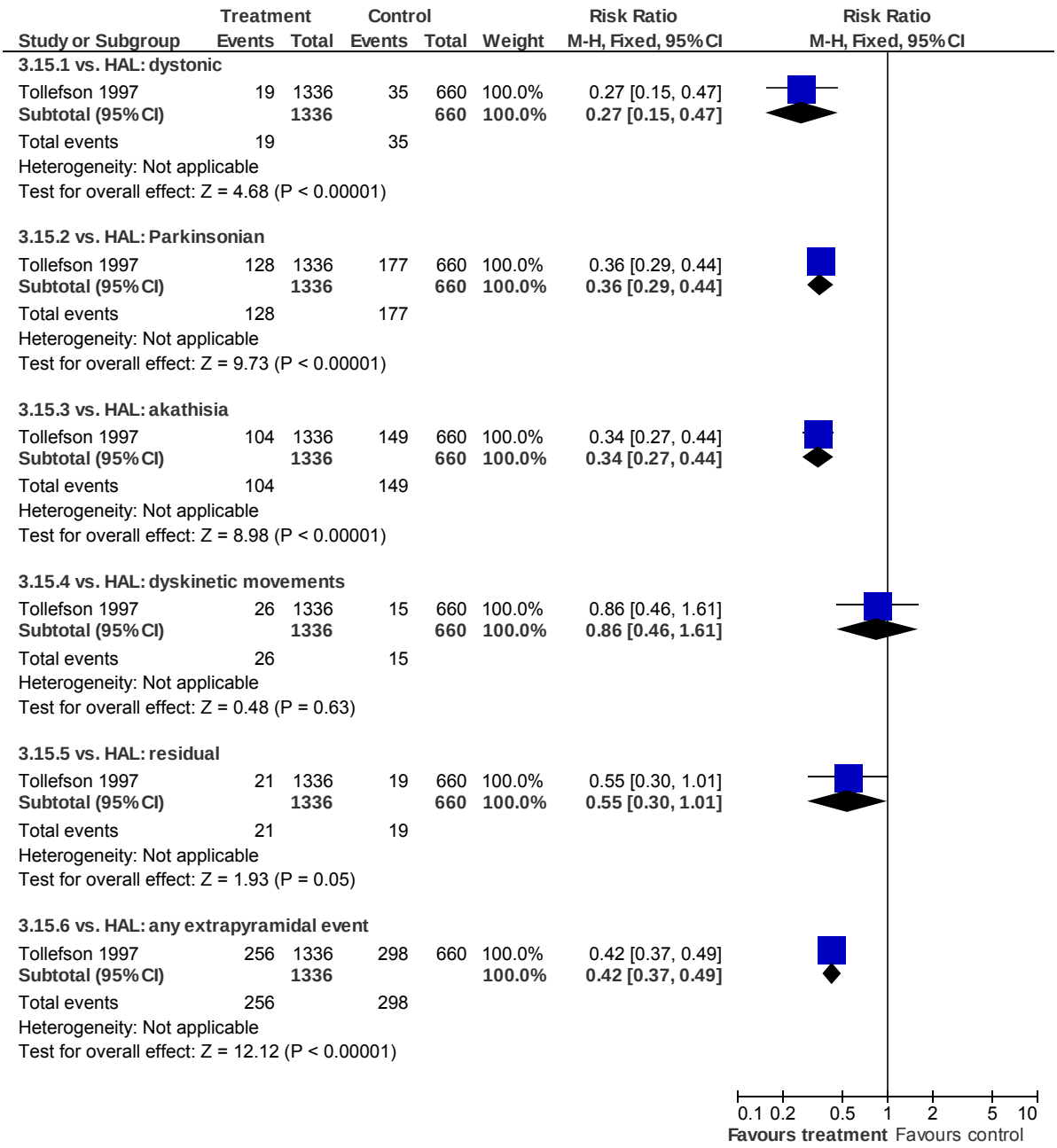


3.14 AE: 2. Neurologic SEs - Use of anticholinergic medication (long-term)

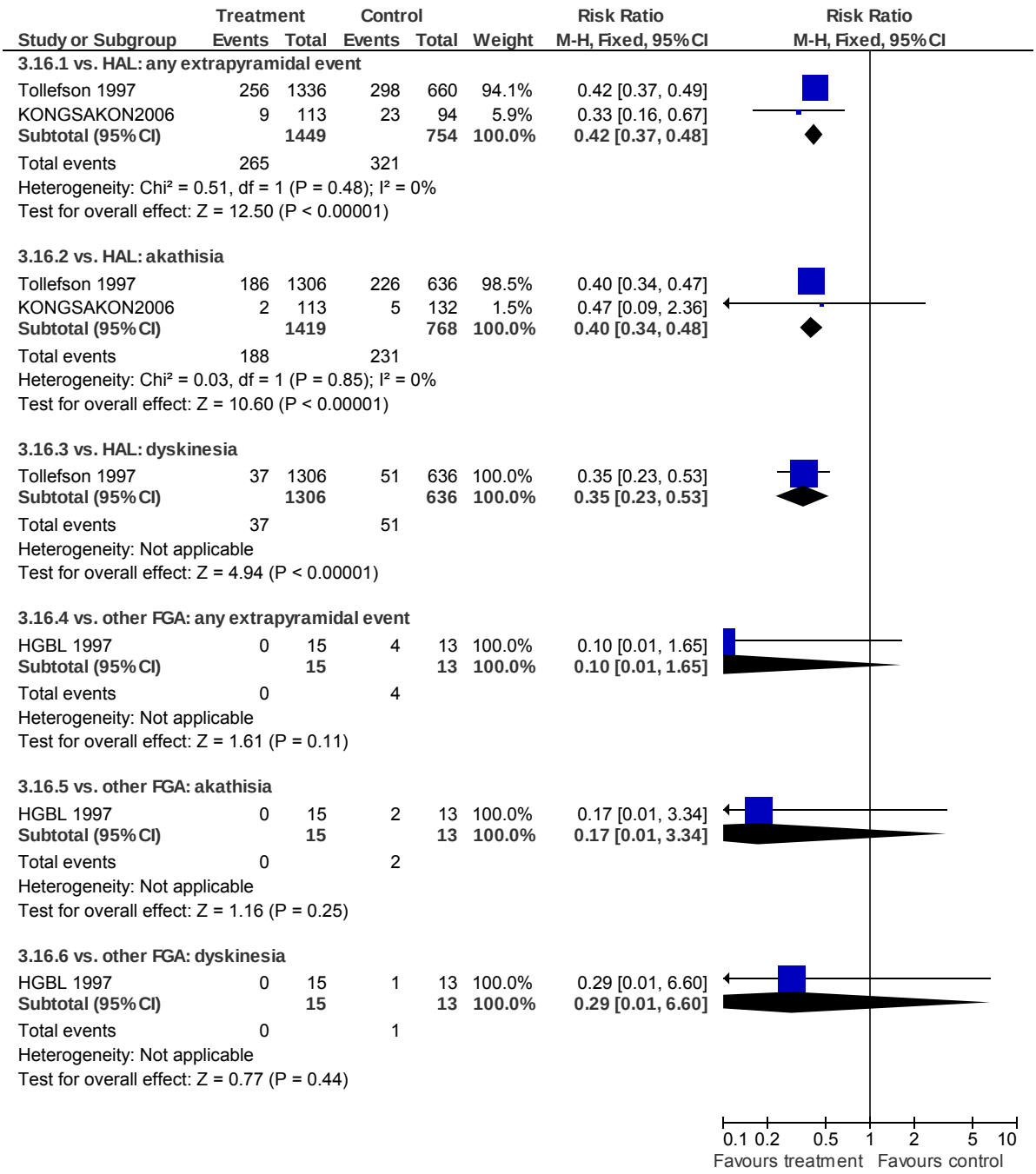
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.14.1 vs. HAL						
ROSENHECK2003	7	92	7	85	18.2%	0.92 [0.34, 2.52]
KONGSAKON2006	24	113	30	94	81.8%	0.67 [0.42, 1.06]
Subtotal (95% CI)		**205**		**179**	**100.0%**	**0.71 [0.47, 1.08]**
Total events	31		37			
Heterogeneity: Chi² = 0.34, df = 1 (P = 0.56); I² = 0%						
Test for overall effect: Z = 1.58 (P = 0.11)						
Total (95% CI)		**205**		**179**	**100.0%**	**0.71 [0.47, 1.08]**
Total events	31		37			
Heterogeneity: Chi² = 0.34, df = 1 (P = 0.56); I² = 0%						
Test for overall effect: Z = 1.58 (P = 0.11)						



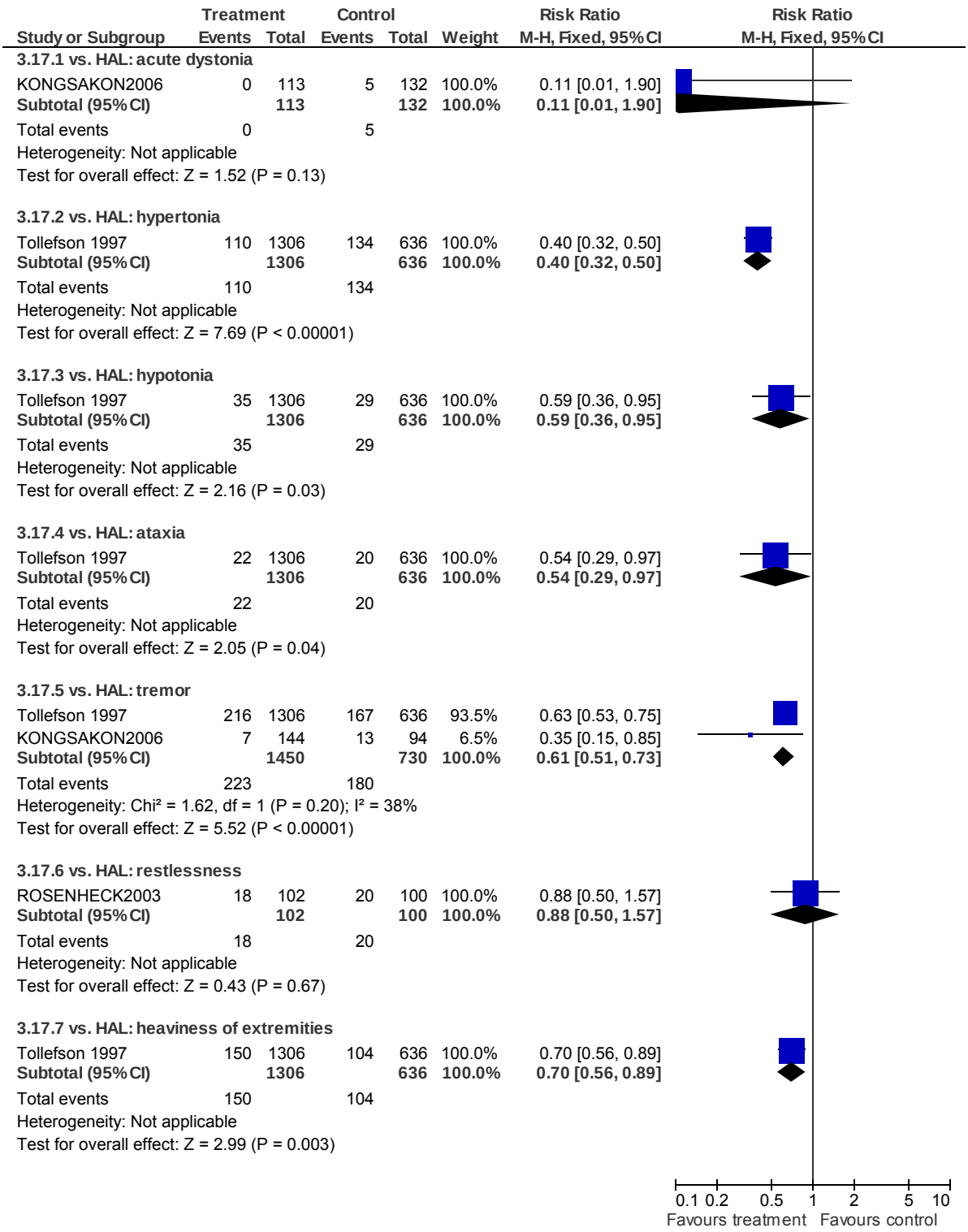
3.15 AE: 2. Neurologic SEs (treatment-emergent: COSTART) (short-term)



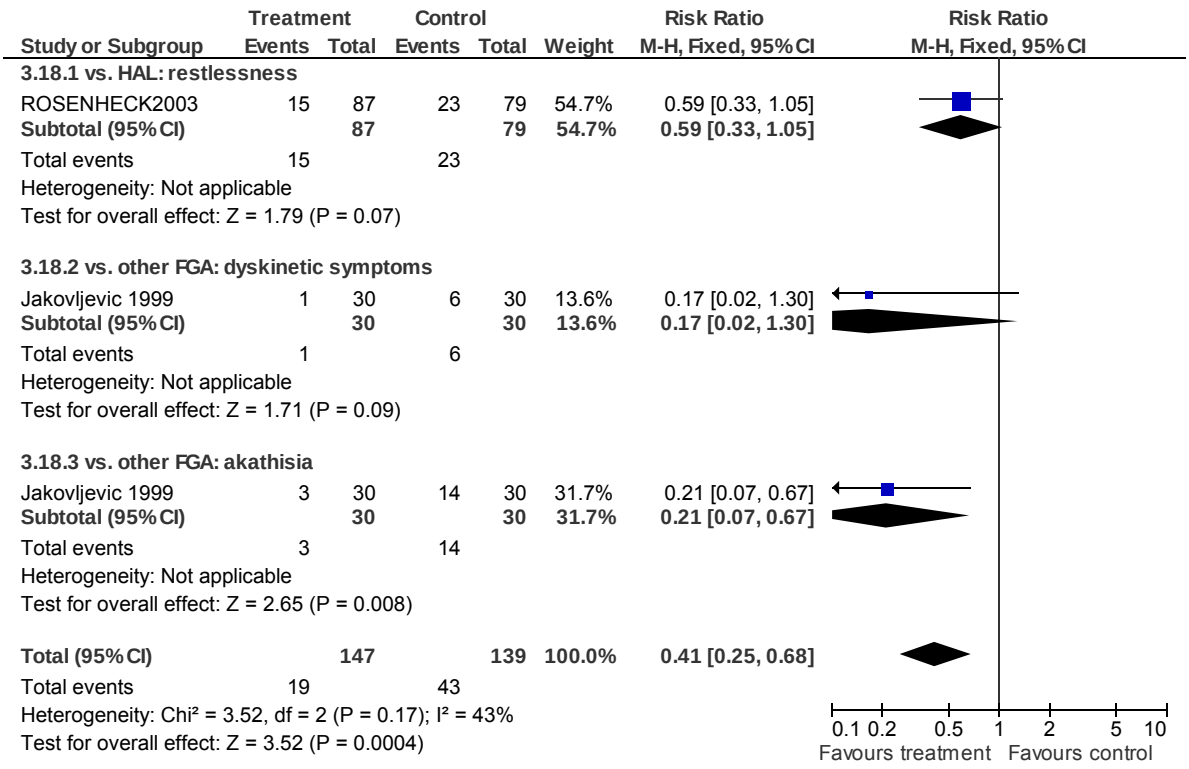
3.16 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



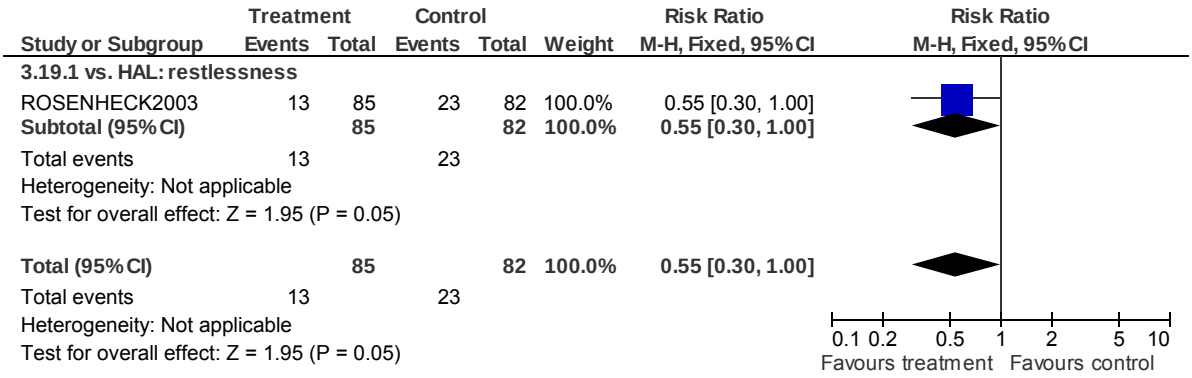
3.17 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



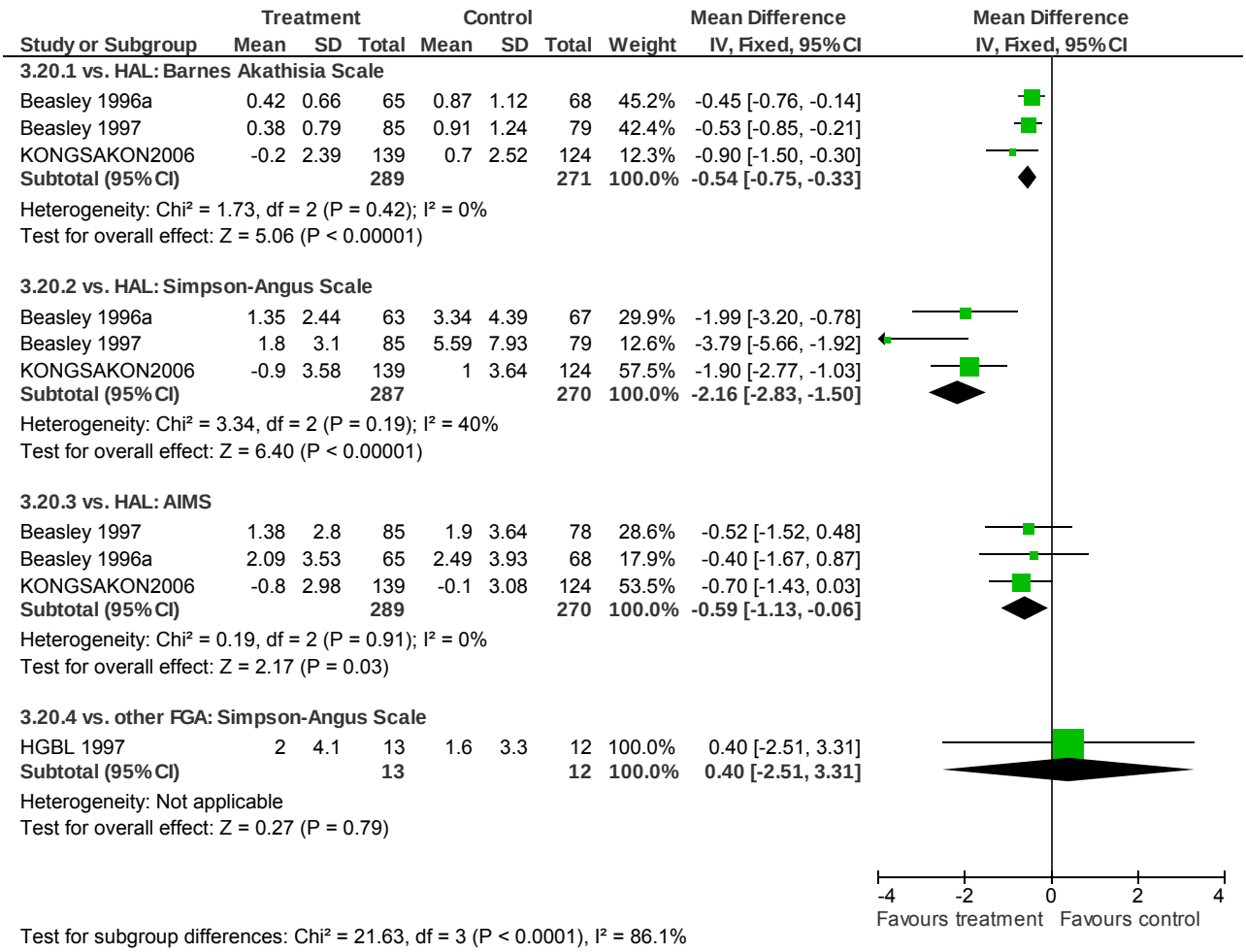
3.18 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)



3.19 AE: 2. Neurologic SEs (treatment-emergent) (long-term)

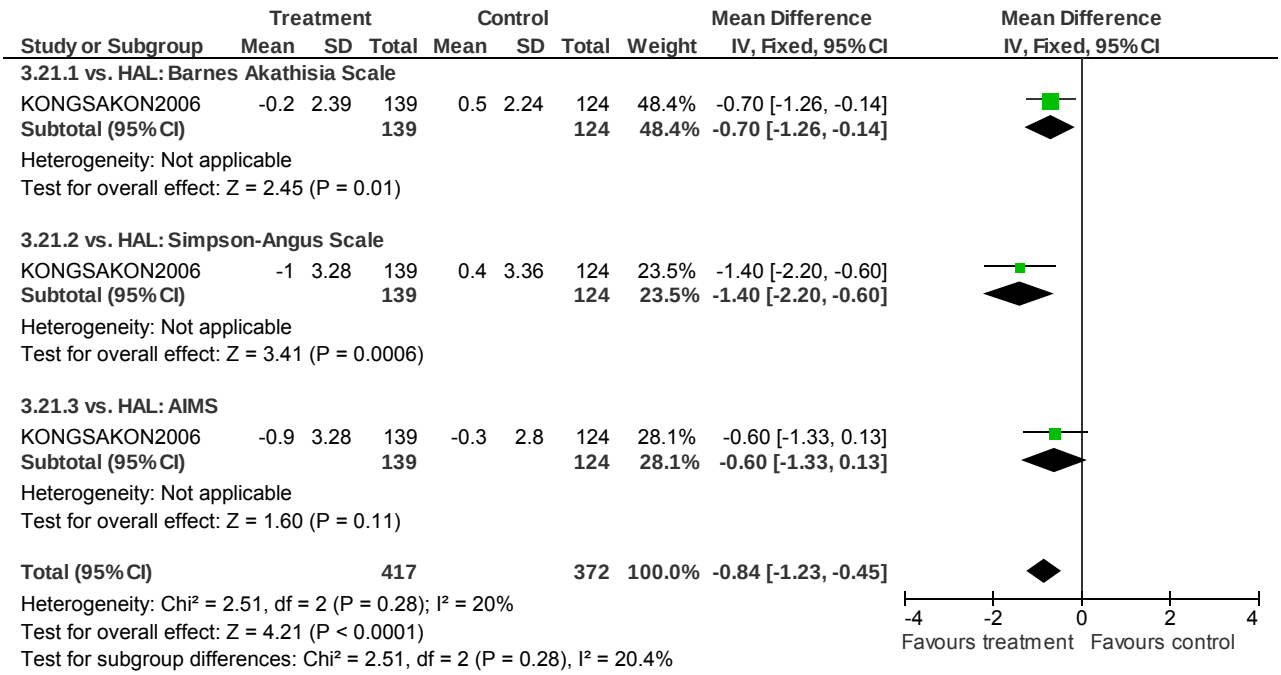


3.20 AE: 2. Neurologic SEs (treatment-emergent) (endpoint/change from baseline) (short-term)



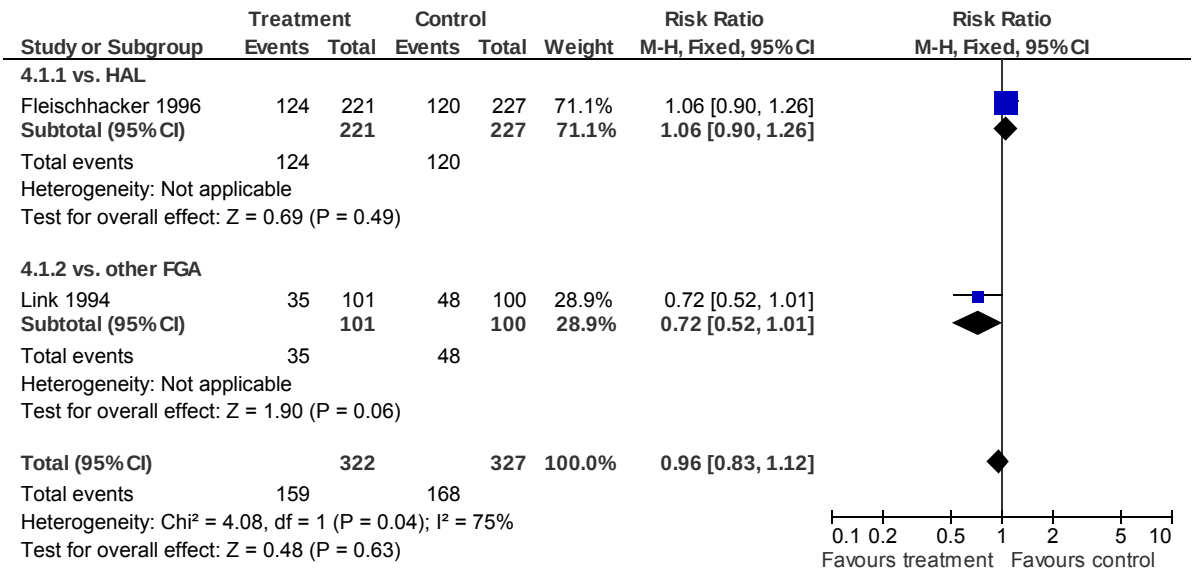
Test for subgroup differences: Chi² = 21.63, df = 3 (P < 0.0001), I² = 86.1%

3.21 AE: 2. Neurologic SEs (treatment-emergent) (change from baseline) (medium-term)



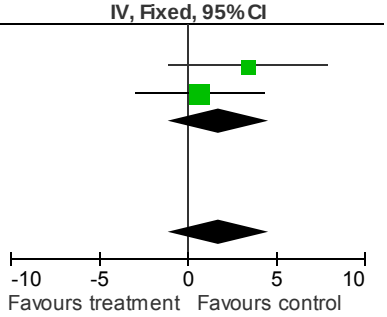
4 Quetiapine versus FGA (phase: acute treatment) (critical outcomes)

4.1 Global state: 2. Not improved to a clinically important degree (CGI) (short-term)



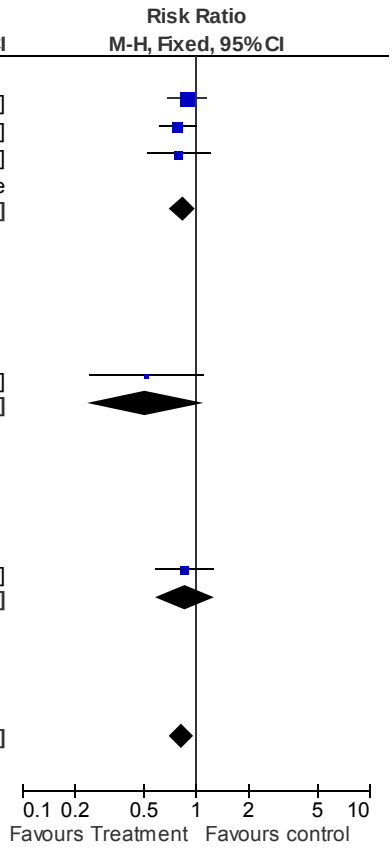
4.2 Mental state: 1. PANSS total (endpoint/change from baseline) (short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
4.2.1 vs. HAL								
Fleischhacker 1996	-18.7	24.07	218	-22.1	24.12	219	39.7%	3.40 [-1.12, 7.92]
ATMACA2002	75.08	5.65	18	74.43	5.42	17	60.3%	0.65 [-3.02, 4.32]
Subtotal (95% CI)			**236**			**236**	**100.0%**	**1.74 [-1.11, 4.59]**
Heterogeneity: Chi² = 0.86, df = 1 (P = 0.35); I² = 0%								
Test for overall effect: Z = 1.20 (P = 0.23)								
Total (95% CI)			**236**			**236**	**100.0%**	**1.74 [-1.11, 4.59]**
Heterogeneity: Chi² = 0.86, df = 1 (P = 0.35); I² = 0%								
Test for overall effect: Z = 1.20 (P = 0.23)								
Test for subgroup differences: Not applicable								



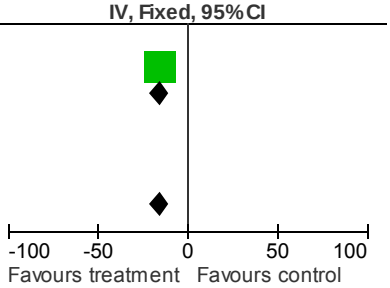
4.3 Leaving the study early: 1. Any reason (short-to-medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.3.1 vs. HAL (short-term)						
Fleischhacker 1996	69	221	80	227	37.8%	0.89 [0.68, 1.15]
Arvanitis 1996	80	157	34	52	24.5%	0.78 [0.61, 1.00]
Kudo 1999	26	90	33	90	15.8%	0.79 [0.52, 1.20]
ATMACA2002	0	18	0	17		Not estimable
Subtotal (95% CI)		**486**		**386**	**78.2%**	**0.83 [0.70, 0.99]**
Total events	175		147			
Heterogeneity: Chi² = 0.55, df = 2 (P = 0.76); I² = 0%						
Test for overall effect: Z = 2.07 (P = 0.04)						
4.3.2 vs. HAL (medium-term)						
Purdon 2000	5	13	9	12	4.5%	0.51 [0.24, 1.10]
Subtotal (95% CI)		**13**		**12**	**4.5%**	**0.51 [0.24, 1.10]**
Total events	5		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.72 (P = 0.09)						
4.3.3 vs. other FGA (short-term)						
Link 1994	31	101	36	100	17.3%	0.85 [0.58, 1.26]
Subtotal (95% CI)		**101**		**100**	**17.3%**	**0.85 [0.58, 1.26]**
Total events	31		36			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.80 (P = 0.43)						
Total (95% CI)		**600**		**498**	**100.0%**	**0.82 [0.70, 0.96]**
Total events	211		192			
Heterogeneity: Chi² = 2.03, df = 4 (P = 0.73); I² = 0%						
Test for overall effect: Z = 2.48 (P = 0.01)						



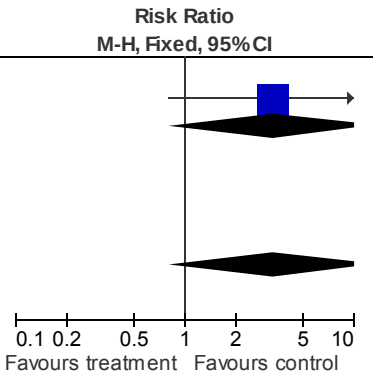
4.4 AE: 1. Metabolic SEs - prolactin levels (ng/mL) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.4.1 vs. HAL								
ATMACA2002	15.74	4.83	18	31.41	10.19	17	100.0%	-15.67 [-21.00, -10.34]
Subtotal (95% CI)			**18**			**17**	**100.0%**	**-15.67 [-21.00, -10.34]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.76 (P < 0.00001)								
Total (95% CI)			**18**			**17**	**100.0%**	**-15.67 [-21.00, -10.34]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.76 (P < 0.00001)								
Test for subgroup differences: Not applicable								

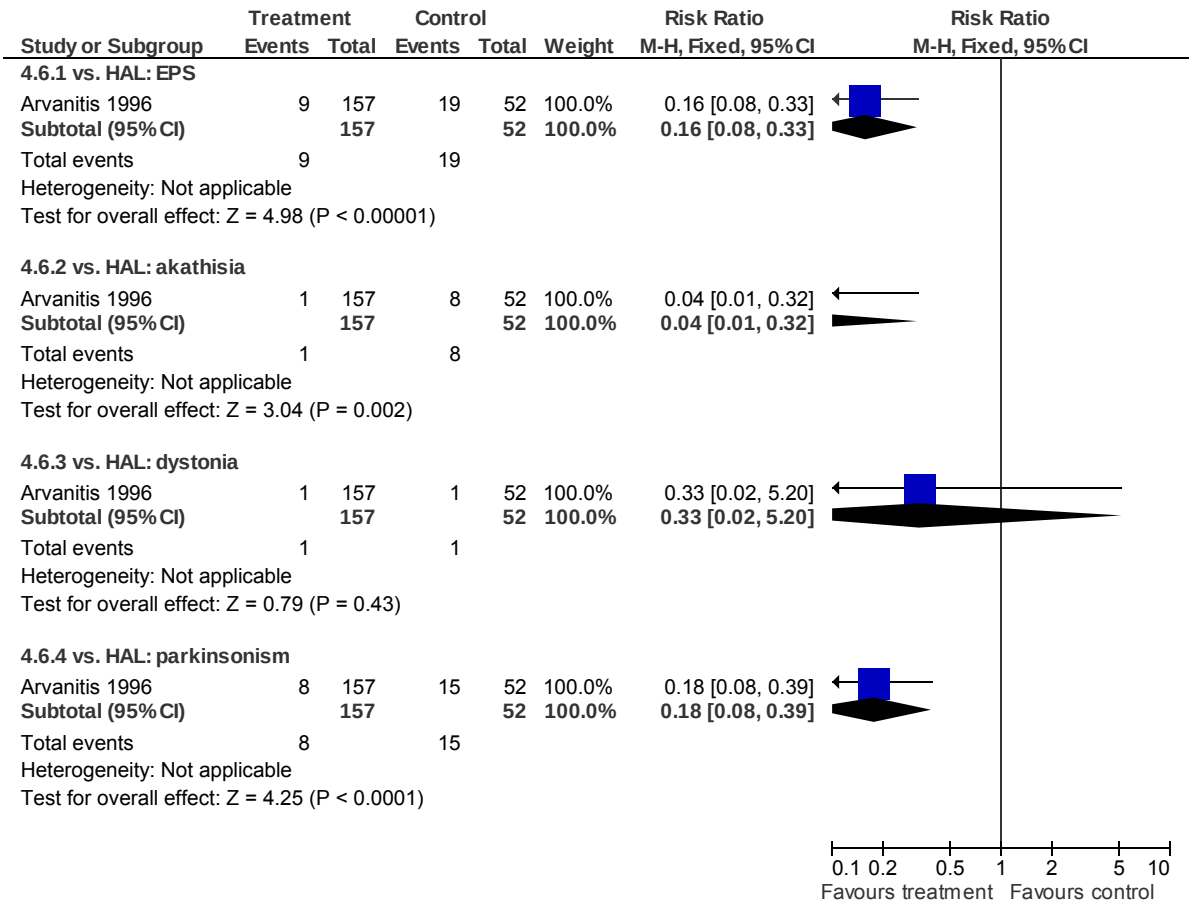


4.5 AE: 1. Metabolic SEs - weight gain (>=7% increase from baseline) (short-term)

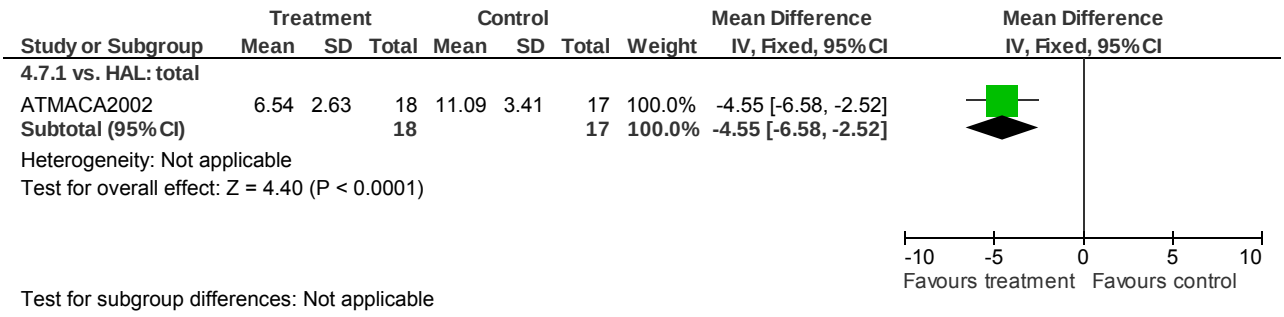
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.5.1 vs. HAL						
Arvanitis 1996	20	157	2	52	100.0%	3.31 [0.80, 13.69]
Subtotal (95% CI)		**157**		**52**	**100.0%**	**3.31 [0.80, 13.69]**
Total events	20		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.65 (P = 0.10)						
Total (95% CI)		**157**		**52**	**100.0%**	**3.31 [0.80, 13.69]**
Total events	20		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.65 (P = 0.10)						



4.6 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



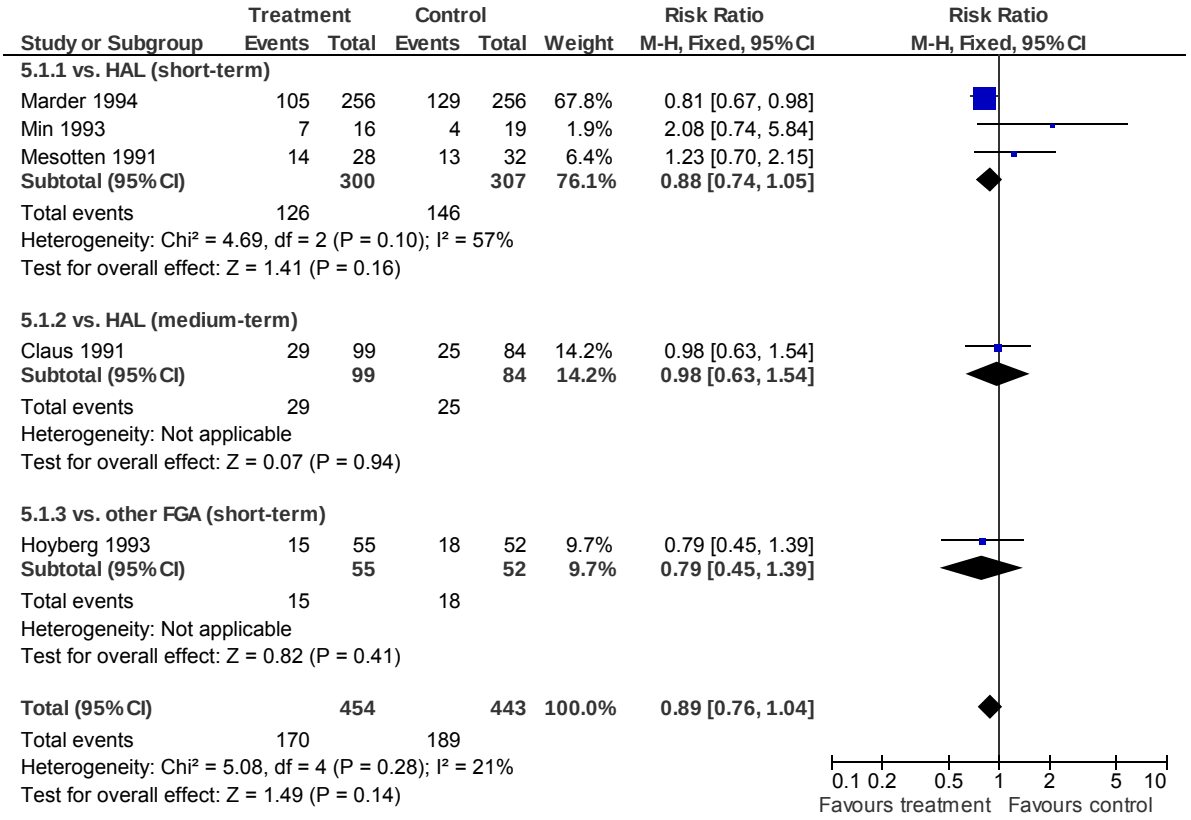
4.7 AE: 2. Neurologic SEs - change in ESRS (high score = poor) (short-term)



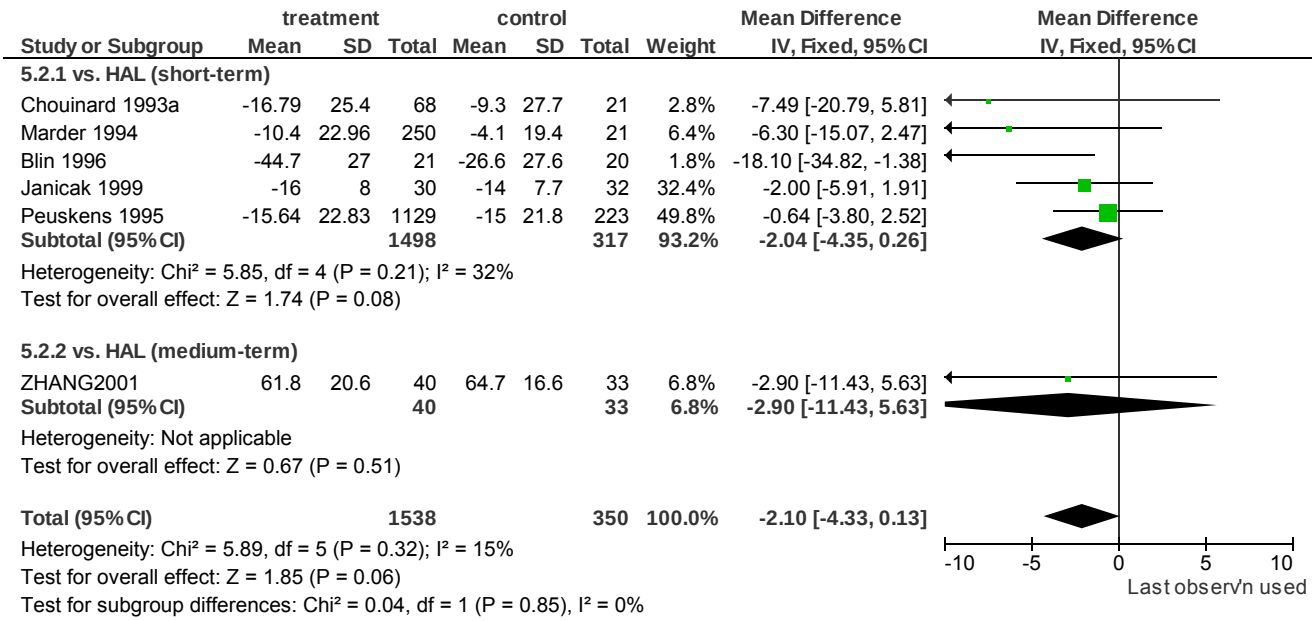
Test for subgroup differences: Not applicable

5 Risperidone versus FGA (phase: acute treatment) (critical outcomes)

5.1 Global state: 2. Not improved to a clinically important degree (CGI) (short-to-medium-term)

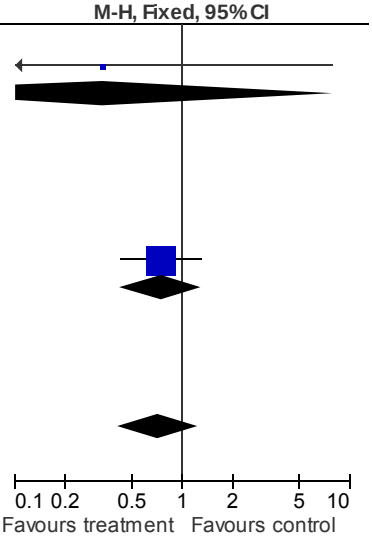


5.2 Mental state: 1. PANSS total (endpoint/change from baseline) (short-to-medium-term)

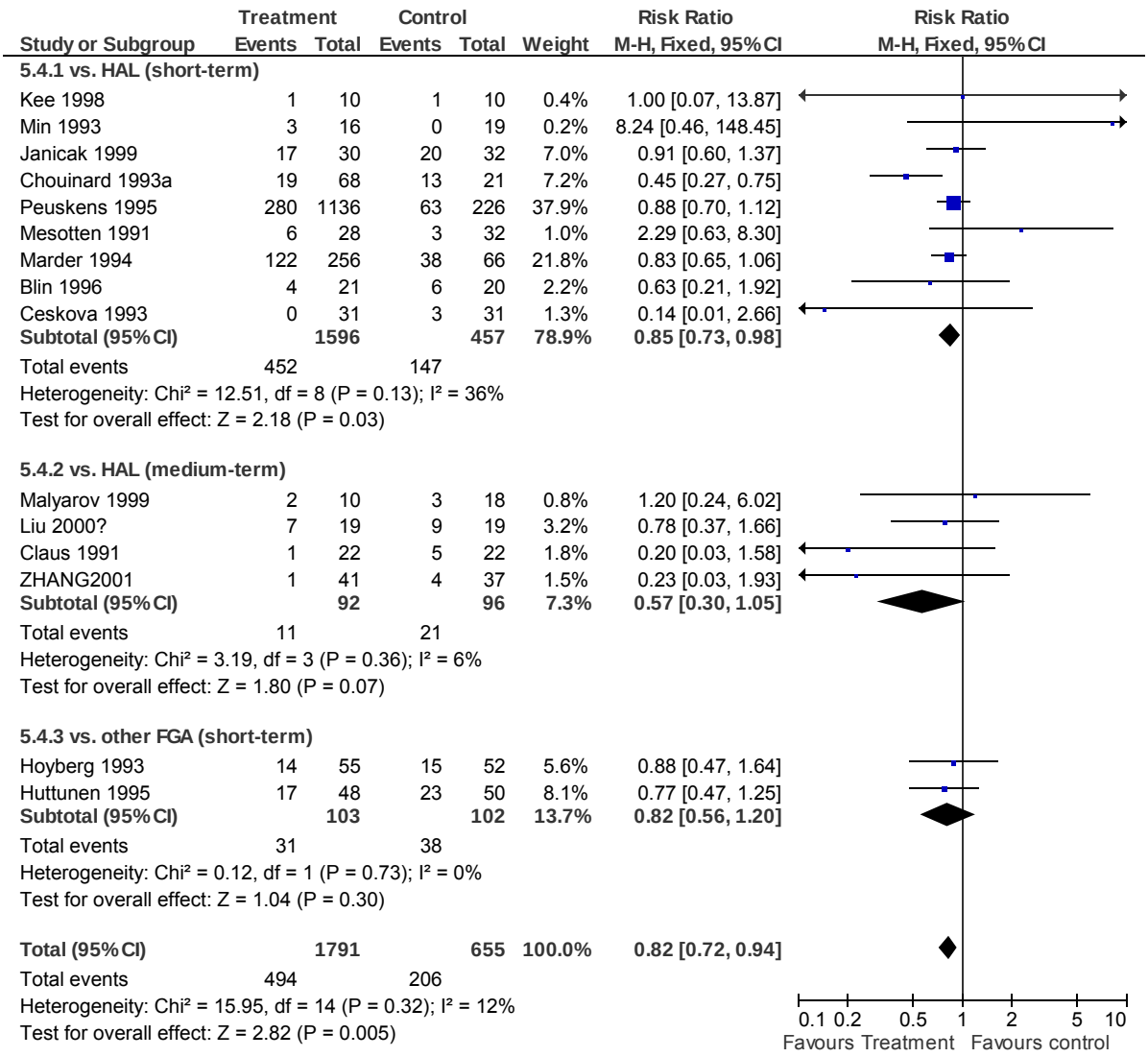


5.3 Mental state: 3. Depression (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.3.1 vs. HAL						
Ceskova 1993	0	31	1	31	7.1%	0.33 [0.01, 7.88]
Subtotal (95% CI)		**31**		**31**	**7.1%**	**0.33 [0.01, 7.88]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
5.3.2 vs. other FGA						
Hoyberg 1993	15	55	19	52	92.9%	0.75 [0.43, 1.31]
Subtotal (95% CI)		**55**		**52**	**92.9%**	**0.75 [0.43, 1.31]**
Total events	15		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						
Total (95% CI)		**86**		**83**	**100.0%**	**0.72 [0.41, 1.25]**
Total events	15		20			
Heterogeneity: Chi² = 0.25, df = 1 (P = 0.62); I² = 0%						
Test for overall effect: Z = 1.18 (P = 0.24)						

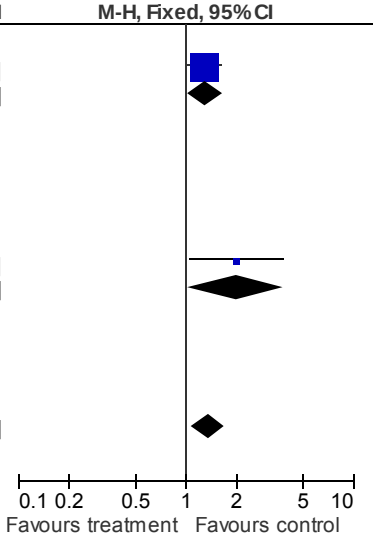


5.4 Leaving the study early: 1. Any reason (short-to-medium-term)



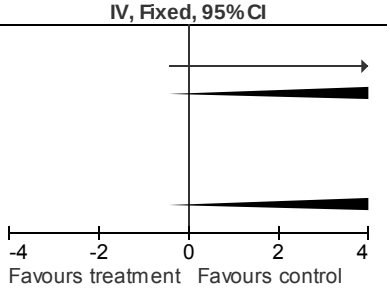
5.5 AE: 1. Metabolic SEs - weight gain (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.5.1 vs. HAL						
Peuskens 1995	369	1136	57	226	90.2%	1.29 [1.01, 1.64]
Subtotal (95% CI)		**1136**		**226**	**90.2%**	**1.29 [1.01, 1.64]**
Total events	369		57			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.07 (P = 0.04)						
5.5.2 vs. other FGA						
Hoyberg 1993	21	55	10	52	9.8%	1.99 [1.04, 3.81]
Subtotal (95% CI)		**55**		**52**	**9.8%**	**1.99 [1.04, 3.81]**
Total events	21		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.07 (P = 0.04)						
Total (95% CI)		**1191**		**278**	**100.0%**	**1.36 [1.08, 1.70]**
Total events	390		67			
Heterogeneity: Chi² = 1.50, df = 1 (P = 0.22); I² = 33%						
Test for overall effect: Z = 2.66 (P = 0.008)						



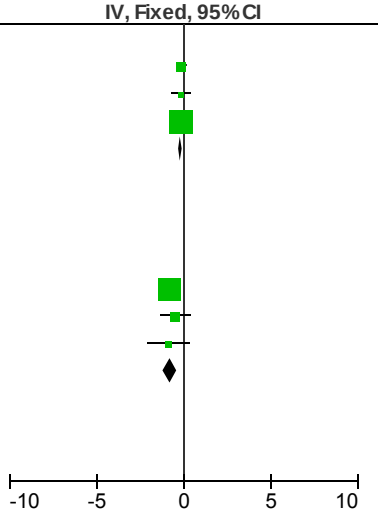
5.6 AE: 1. Metabolic side-effect - Serum Prolactin (endpt mean) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.6.1 versus HAL								
ZHANG2001	29.8	19.2	40	22.4	14.9	33	100.0%	7.40 [-0.43, 15.23]
Subtotal (95% CI)			**40**			**33**	**100.0%**	**7.40 [-0.43, 15.23]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.85 (P = 0.06)								
Total (95% CI)			**40**			**33**	**100.0%**	**7.40 [-0.43, 15.23]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.85 (P = 0.06)								
Test for subgroup differences: Not applicable								



5.7 AE: 2. Neurologic SEs - change in CGI (high score = poor) (short-term)

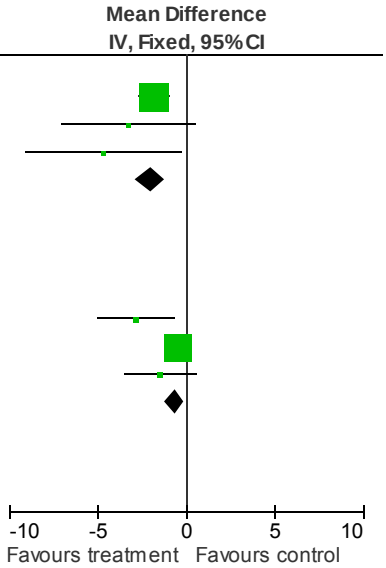
Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
5.7.1 vs. HAL: severity of dyskinesia								
Marder 1994	0.42	1.2	252	0.6	1.1	62	21.3%	-0.18 [-0.49, 0.13]
Chouinard 1993a	0.2	1	68	0.4	1.2	21	6.4%	-0.20 [-0.77, 0.37]
Peuskens 1995	0.29	1.1	1128	0.5	1.19	223	72.3%	-0.21 [-0.38, -0.04]
Subtotal (95% CI)			**1448**			**306**	**100.0%**	**-0.20 [-0.35, -0.06]**
Heterogeneity: Chi² = 0.03, df = 2 (P = 0.99); I² = 0%								
Test for overall effect: Z = 2.77 (P = 0.006)								
5.7.2 vs. HAL: severity of parkinsonism								
Marder 1994	0.55	1.27	252	1.4	1.8	62	68.8%	-0.85 [-1.32, -0.38]
Chouinard 1993a	0.79	1.39	92	1.3	1.9	21	20.9%	-0.51 [-1.37, 0.35]
Blin 1996	1.2	2.1	21	2.1	1.9	20	10.3%	-0.90 [-2.12, 0.32]
Subtotal (95% CI)			**365**			**103**	**100.0%**	**-0.78 [-1.18, -0.39]**
Heterogeneity: Chi² = 0.50, df = 2 (P = 0.78); I² = 0%								
Test for overall effect: Z = 3.90 (P < 0.0001)								



Test for subgroup differences: Chi² = 7.39, df = 1 (P = 0.007), I² = 86.5%

5.8 AE: 2. Neurologic SEs - change in ESRS (high score = poor) (short-term)

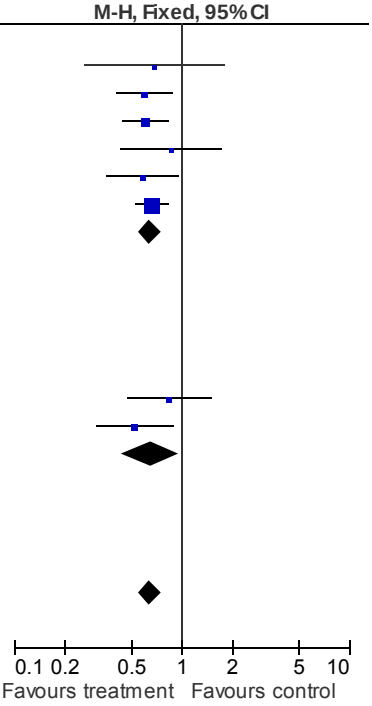
Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
5.8.1 vs. HAL: severity of parkinsonism								
Peuskens 1995	2.33	5.28	1130	4.2	6.27	223	91.5%	-1.87 [-2.75, -0.99]
Blin 1996	2.6	4.4	21	5.9	7.5	20	4.9%	-3.30 [-7.09, 0.49]
Chouinard 1993a	3.92	9.6	68	8.6	8.9	21	3.6%	-4.68 [-9.12, -0.24]
Subtotal (95% CI)			**1219**			**264**	**100.0%**	**-2.04 [-2.88, -1.20]**
Heterogeneity: Chi² = 1.93, df = 2 (P = 0.38); I² = 0%								
Test for overall effect: Z = 4.76 (P < 0.00001)								
5.8.2 vs. HAL: total								
Marder 1994	2.52	5.5	252	5.4	8.4	62	5.9%	-2.88 [-5.08, -0.68]
Peuskens 1995	2.23	3.74	1130	2.7	4.03	223	87.3%	-0.47 [-1.04, 0.10]
Blin 1996	1.8	3.5	21	3.3	3.2	20	6.8%	-1.50 [-3.55, 0.55]
Subtotal (95% CI)			**1403**			**305**	**100.0%**	**-0.68 [-1.22, -0.15]**
Heterogeneity: Chi² = 4.98, df = 2 (P = 0.08); I² = 60%								
Test for overall effect: Z = 2.50 (P = 0.01)								



Test for subgroup differences: Chi² = 7.15, df = 1 (P = 0.008), I² = 86.0%

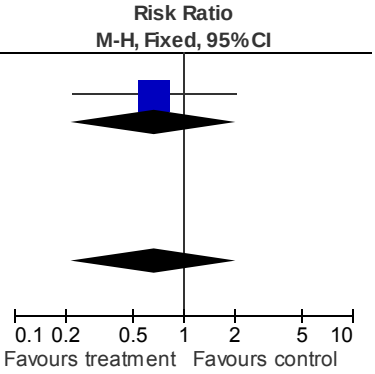
5.9 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.9.1 vs. HAL						
Blin 1996	5	21	7	20	2.7%	0.68 [0.26, 1.80]
Chouinard 1993a	29	68	15	21	8.5%	0.60 [0.41, 0.88]
Marder 1994	72	256	31	66	18.4%	0.60 [0.43, 0.83]
Mesotten 1991	9	28	12	32	4.2%	0.86 [0.43, 1.73]
Janicak 1999	12	30	22	32	7.9%	0.58 [0.35, 0.96]
Peuskens 1995	224	1136	68	226	42.3%	0.66 [0.52, 0.83]
Subtotal (95% CI)		**1539**		**397**	**84.0%**	**0.64 [0.55, 0.75]**
Total events	351		155			
Heterogeneity: Chi² = 1.16, df = 5 (P = 0.95); I² = 0%						
Test for overall effect: Z = 5.57 (P < 0.00001)						
5.9.2 vs. other FGA						
Hoyberg 1993	15	55	17	52	6.5%	0.83 [0.47, 1.49]
Huttunen 1995	13	48	26	50	9.5%	0.52 [0.30, 0.89]
Subtotal (95% CI)		**103**		**102**	**16.0%**	**0.65 [0.44, 0.96]**
Total events	28		43			
Heterogeneity: Chi² = 1.36, df = 1 (P = 0.24); I² = 27%						
Test for overall effect: Z = 2.17 (P = 0.03)						
Total (95% CI)		**1642**		**499**	**100.0%**	**0.64 [0.56, 0.74]**
Total events	379		198			
Heterogeneity: Chi² = 2.53, df = 7 (P = 0.92); I² = 0%						
Test for overall effect: Z = 5.96 (P < 0.00001)						

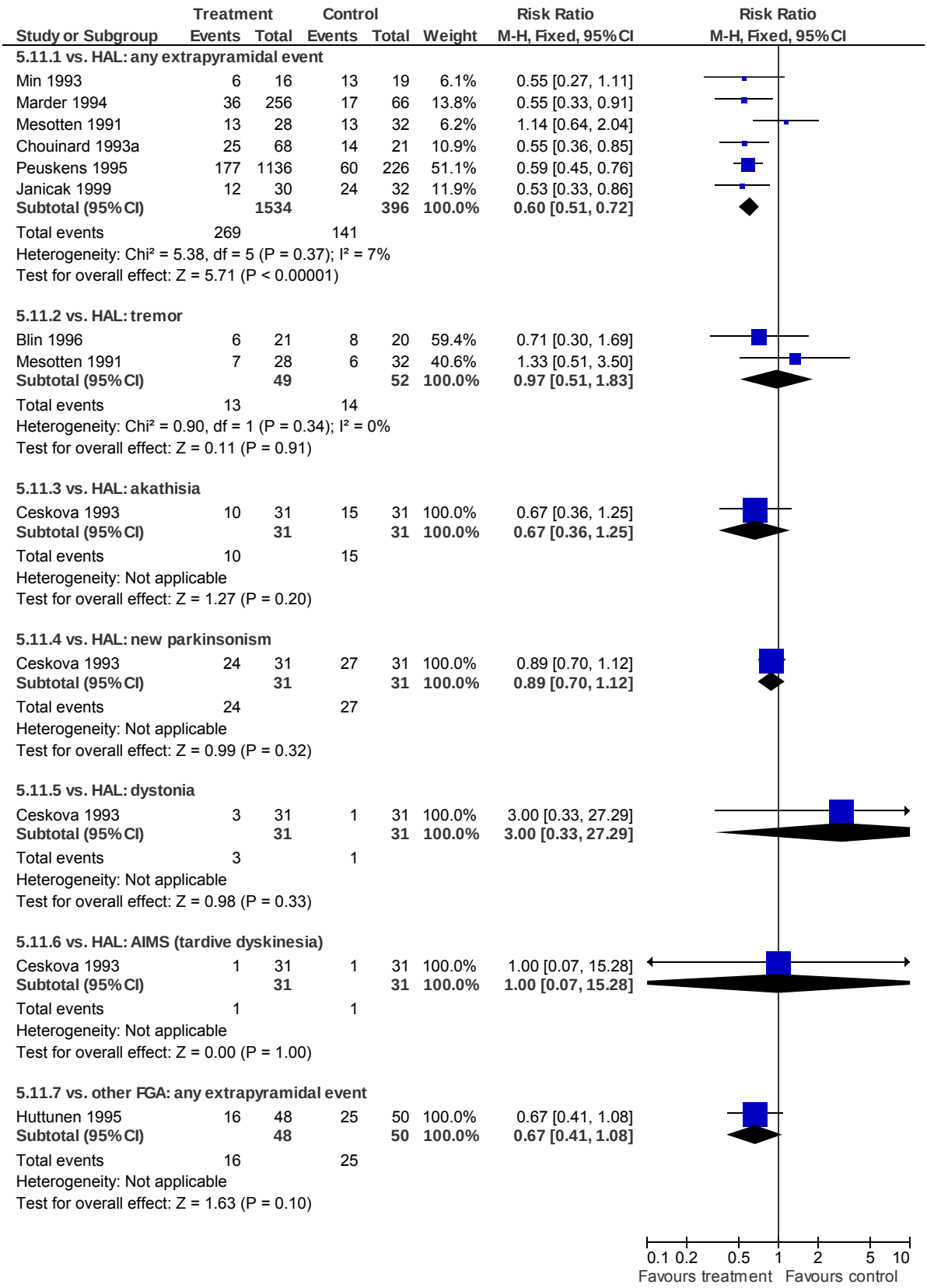


5.10 AE: 2. Neurologic SEs - Use of anticholinergic medication (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.10.1 vs. HAL						
Claus 1991	4	22	6	22	100.0%	0.67 [0.22, 2.04]
Subtotal (95% CI)		**22**		**22**	**100.0%**	**0.67 [0.22, 2.04]**
Total events	4		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.71 (P = 0.48)						
Total (95% CI)		**22**		**22**	**100.0%**	**0.67 [0.22, 2.04]**
Total events	4		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.71 (P = 0.48)						



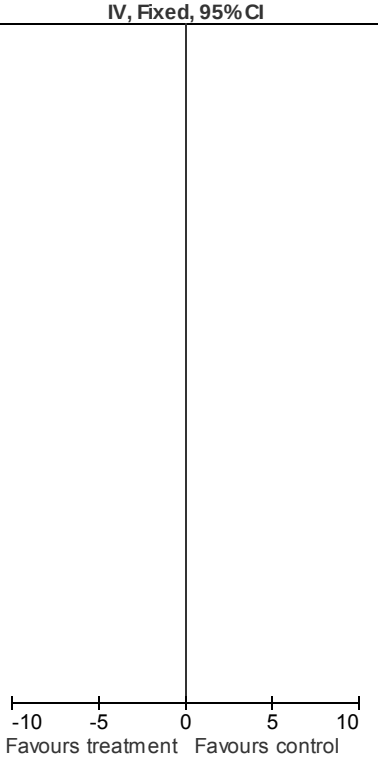
5.11 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



6 Sertindole versus HAL (phase: acute treatment) (critical outcomes)

6.1 Global state: 1. CGI-Severity endpoint score (short-term)

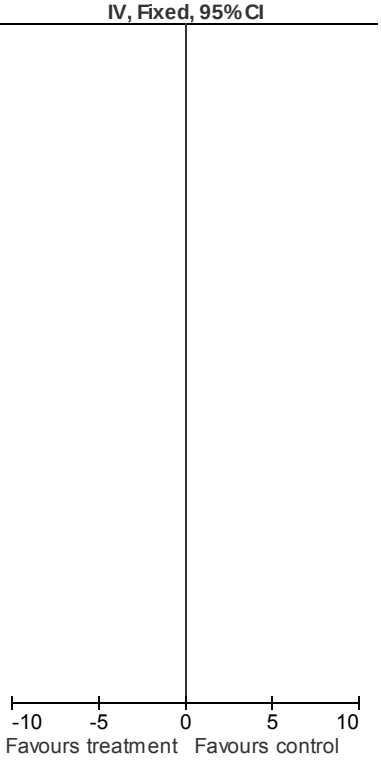
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.1.1 sertindole 8mg								
Hale 2000	3.1	0	120	3	0	125		Not estimable
Subtotal (95% CI)			**120**			**125**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
6.1.2 sertindole 16mg								
Hale 2000	3	0	127	3	0	125		Not estimable
Subtotal (95% CI)			**127**			**125**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
6.1.3 sertindole 20mg								
Hale 2000	3.1	0	128	3	0	125		Not estimable
Subtotal (95% CI)			**128**			**125**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
6.1.4 sertindole 24mg								
Hale 2000	3	0	117	3	0	125		Not estimable
Subtotal (95% CI)			**117**			**125**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								



Test for subgroup differences: Not applicable

6.2 Mental state: 1. PANSS total endpoint score (short-term)

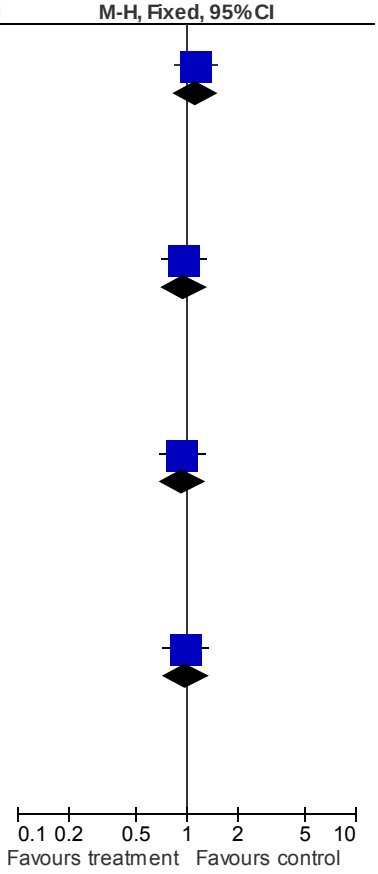
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.2.1 sertindole 8mg								
Hale 2000	51.5	0	120	46.6	0	125		Not estimable
Subtotal (95% CI)			**120**			**125**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
6.2.2 sertindole 16mg								
Hale 2000	48.3	0	127	46.6	0	125		Not estimable
Subtotal (95% CI)			**127**			**125**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
6.2.3 sertindole 20mg								
Hale 2000	50	0	128	46.6	0	125		Not estimable
Subtotal (95% CI)			**128**			**125**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
6.2.4 sertindole 24mg								
Hale 2000	47.9	0	117	46.6	0	125		Not estimable
Subtotal (95% CI)			**117**			**125**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								



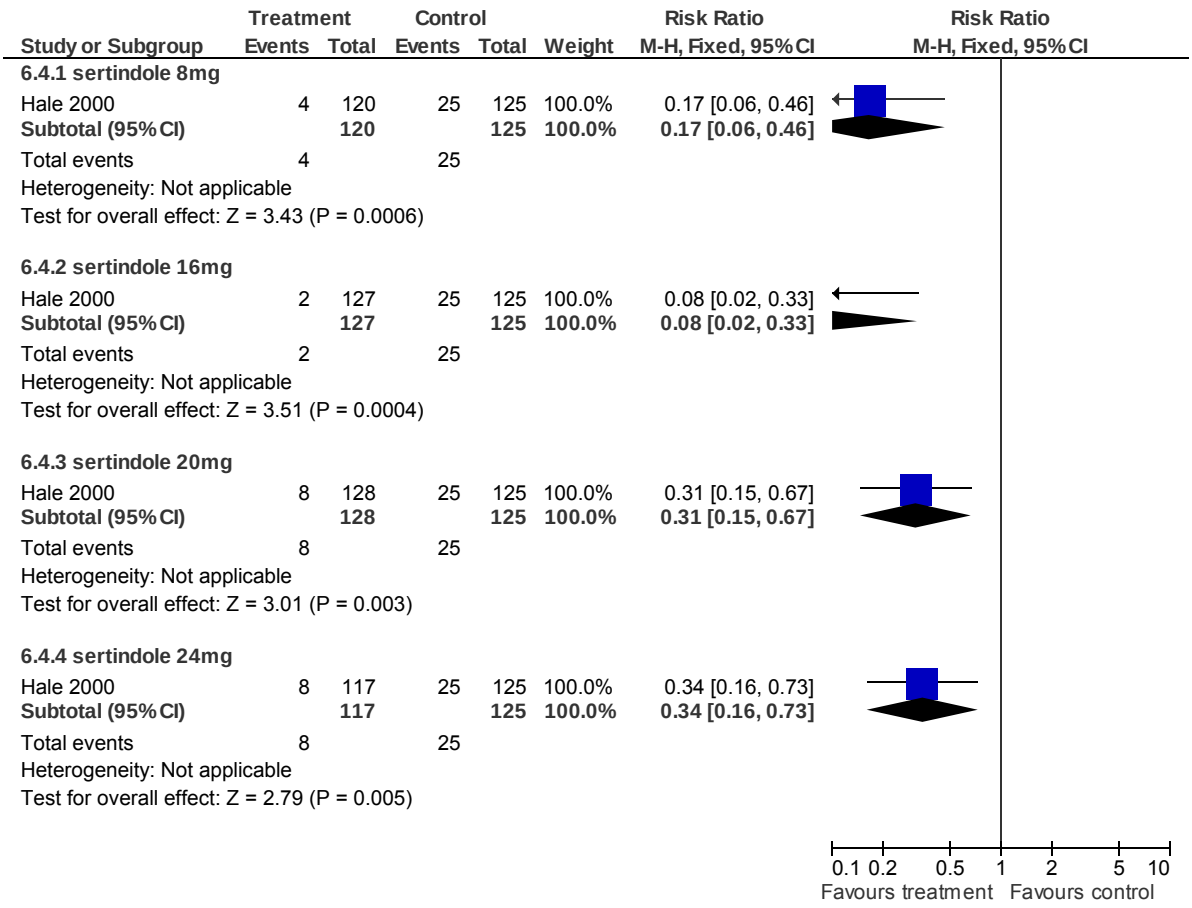
Test for subgroup differences: Not applicable

6.3 Leaving study early: 1. Any reason (short-term)

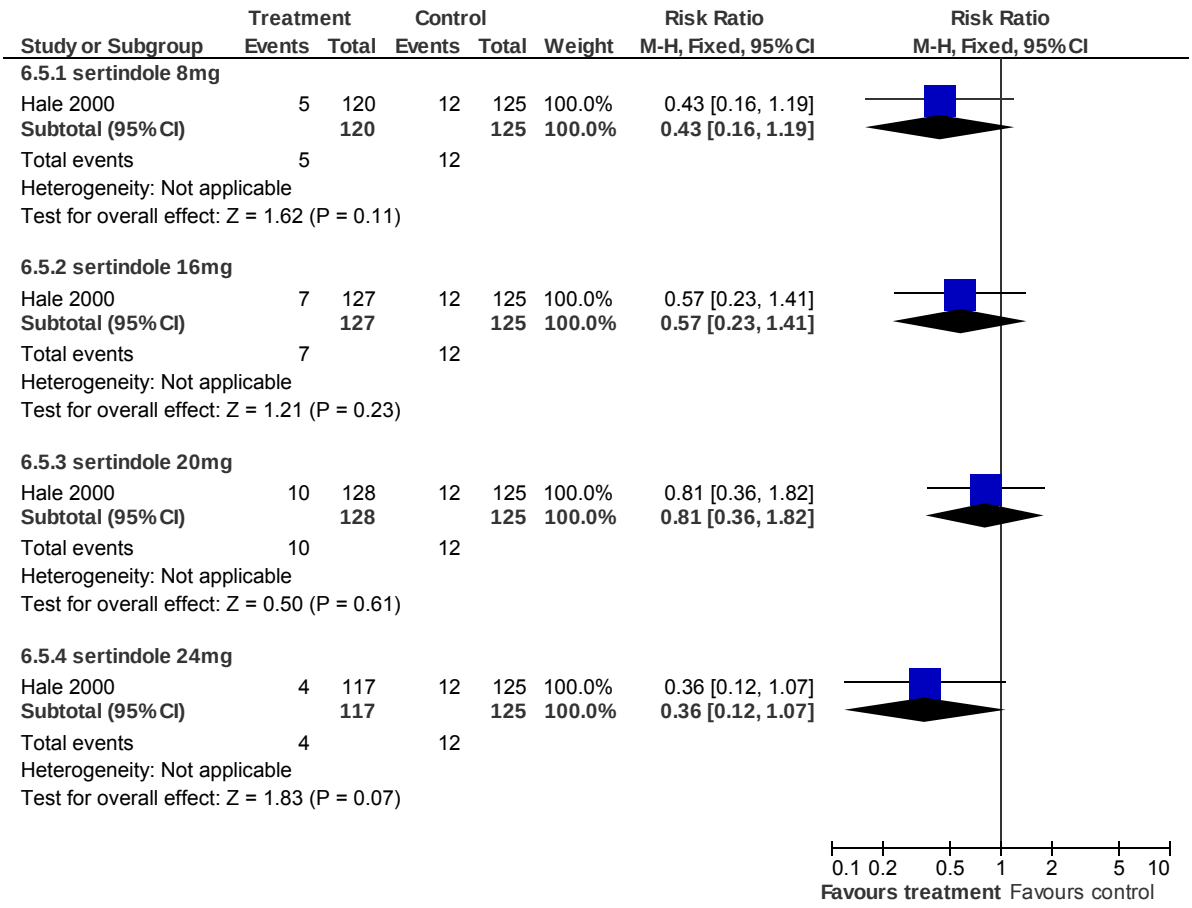
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.3.2 sertindole 8mg						
Hale 2000	53	120	49	125	100.0%	1.13 [0.84, 1.52]
Subtotal (95% CI)		**120**		**125**	**100.0%**	**1.13 [0.84, 1.52]**
Total events	53		49			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						
6.3.3 sertindole 16mg						
Hale 2000	48	127	49	125	100.0%	0.96 [0.71, 1.32]
Subtotal (95% CI)		**127**		**125**	**100.0%**	**0.96 [0.71, 1.32]**
Total events	48		49			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.23 (P = 0.82)						
6.3.4 sertindole 20mg						
Hale 2000	47	128	49	125	100.0%	0.94 [0.68, 1.28]
Subtotal (95% CI)		**128**		**125**	**100.0%**	**0.94 [0.68, 1.28]**
Total events	47		49			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.41 (P = 0.68)						
6.3.5 sertindole 24mg						
Hale 2000	45	117	49	125	100.0%	0.98 [0.71, 1.35]
Subtotal (95% CI)		**117**		**125**	**100.0%**	**0.98 [0.71, 1.35]**
Total events	45		49			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.12 (P = 0.91)						



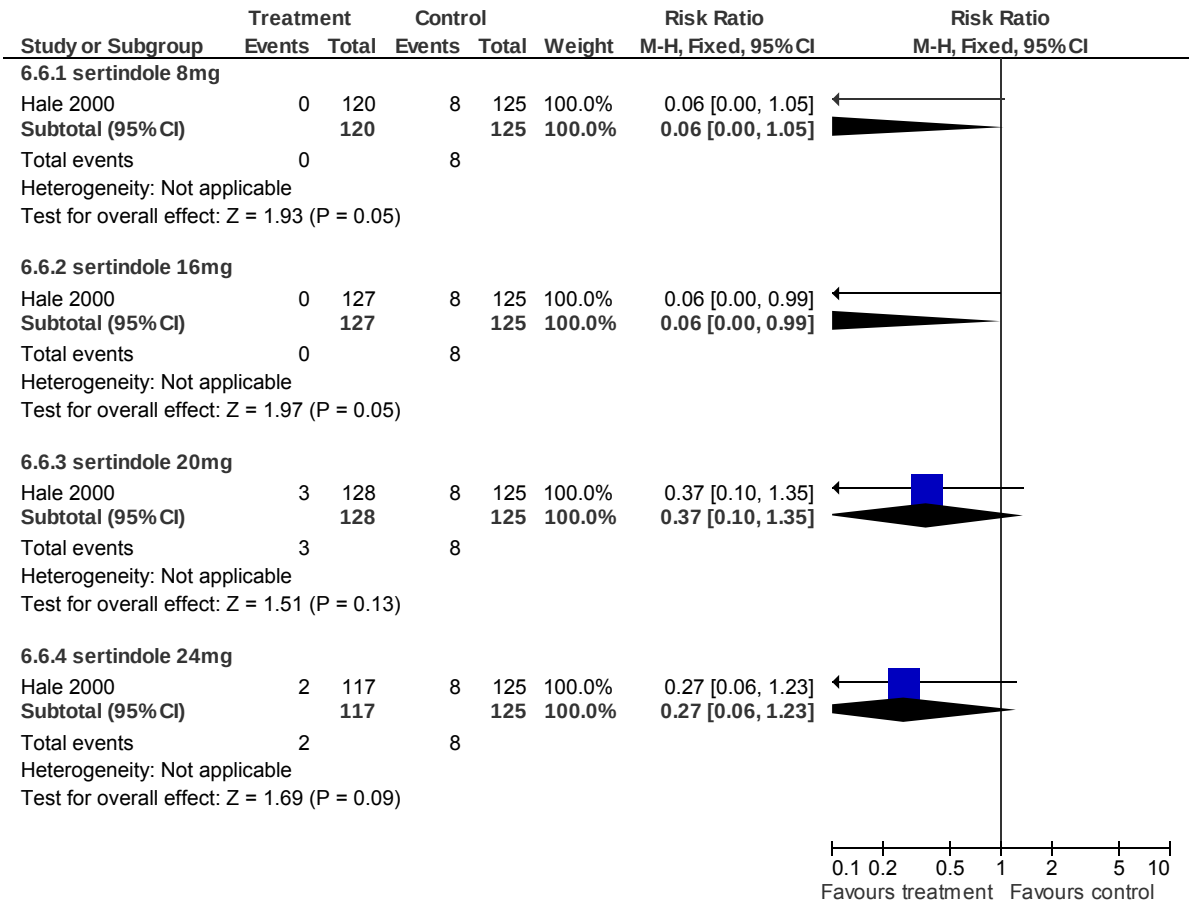
6.4 AE: 2. Neurologic SEs - Akathisia (short-term)



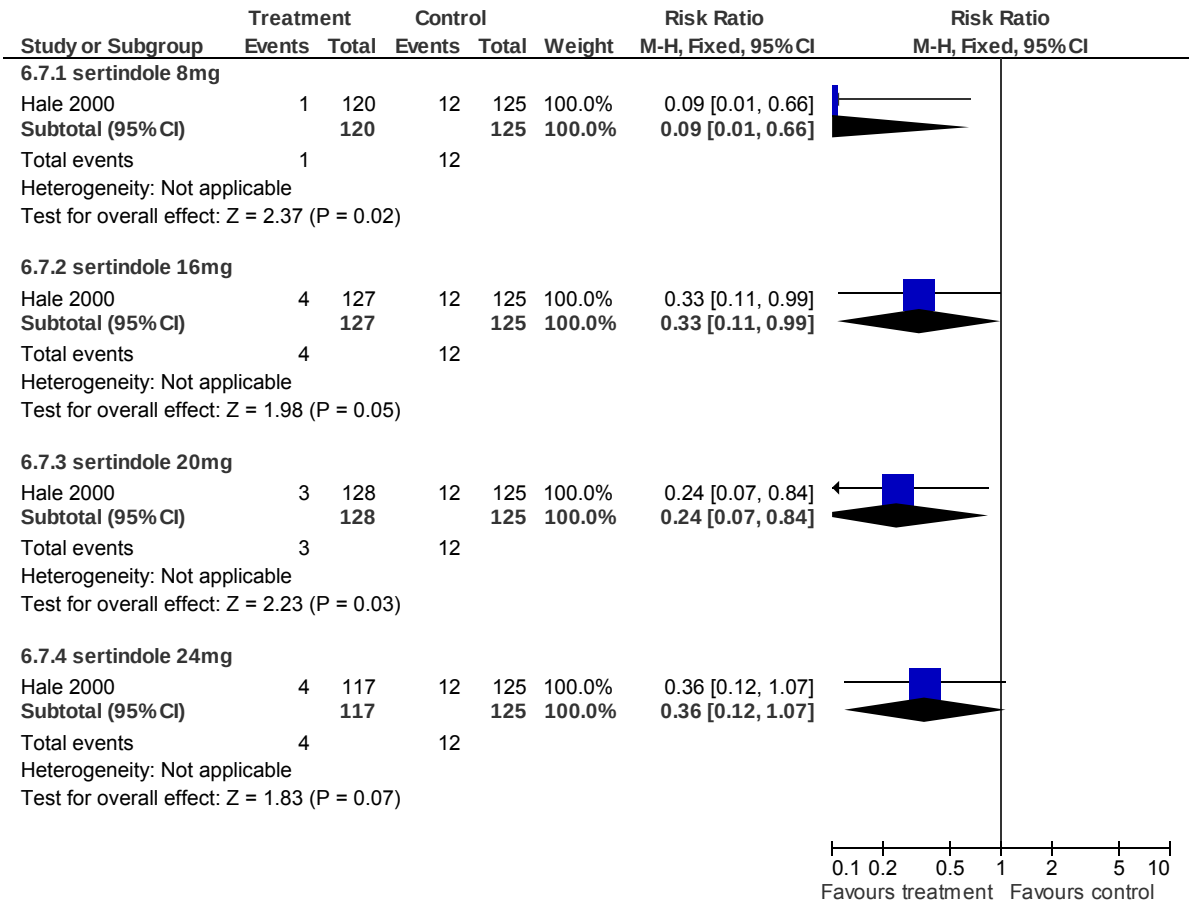
6.5 AE: 2. Neurologic SEs - Asthenia (short-term)



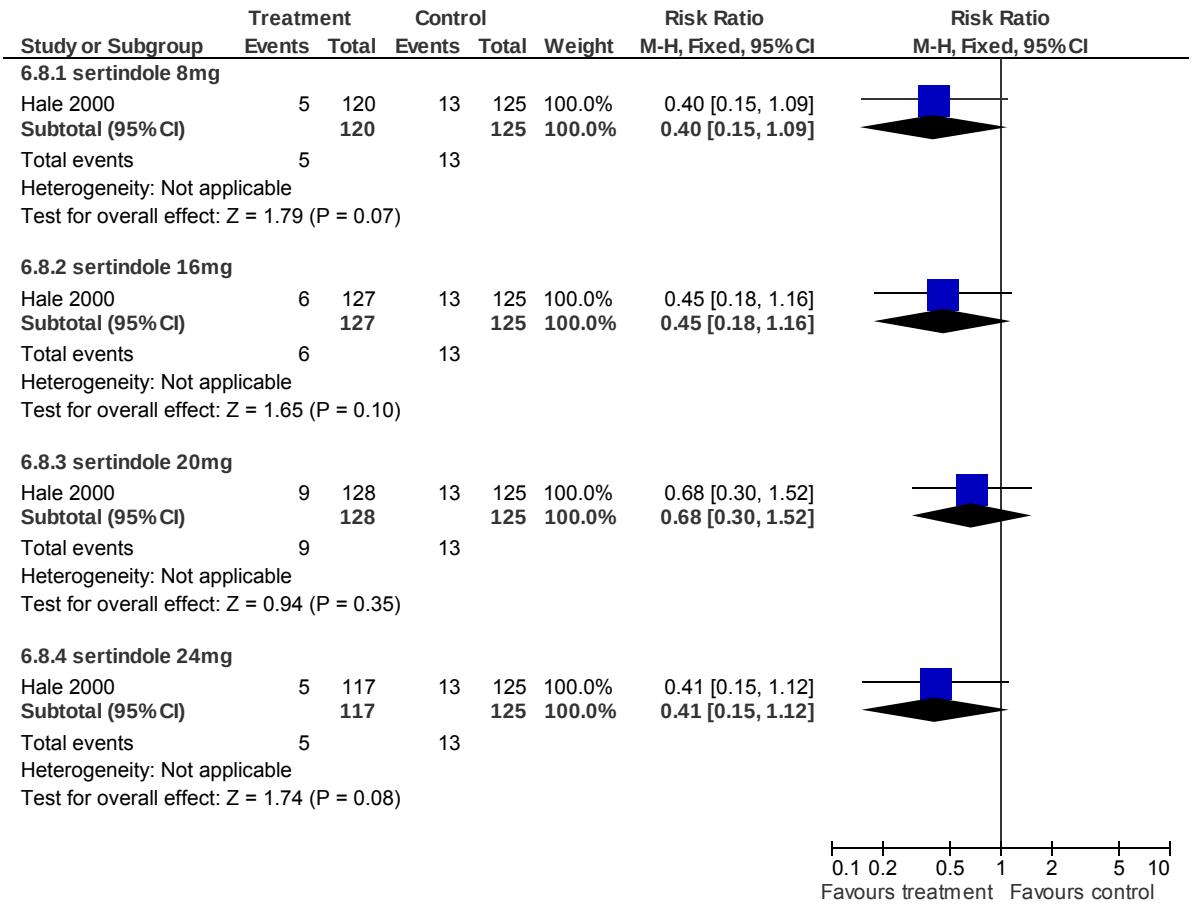
6.6 AE: 2. Neurologic SEs - Dystonia (short-term)



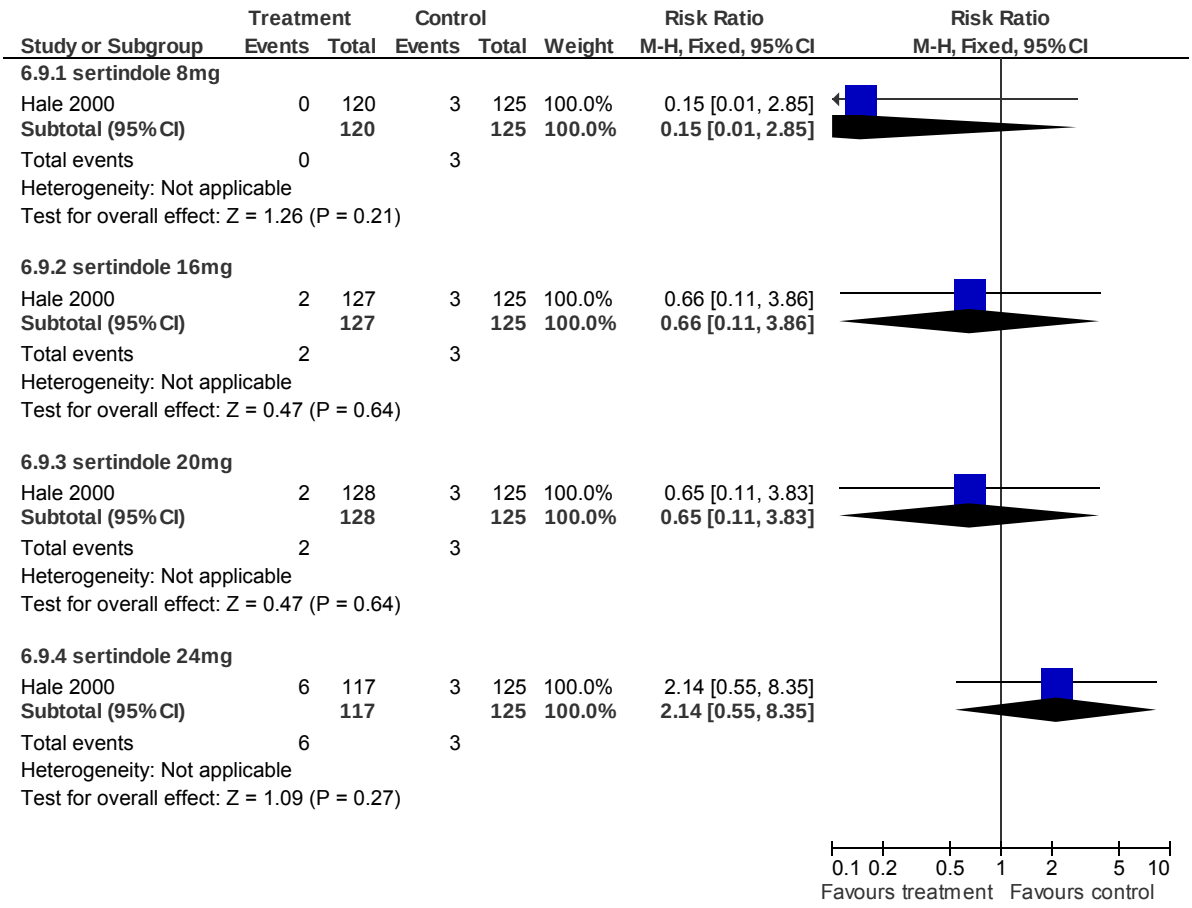
6.7 AE: 2. Neurologic SEs - Extrapyramidal syndrome (short-term)



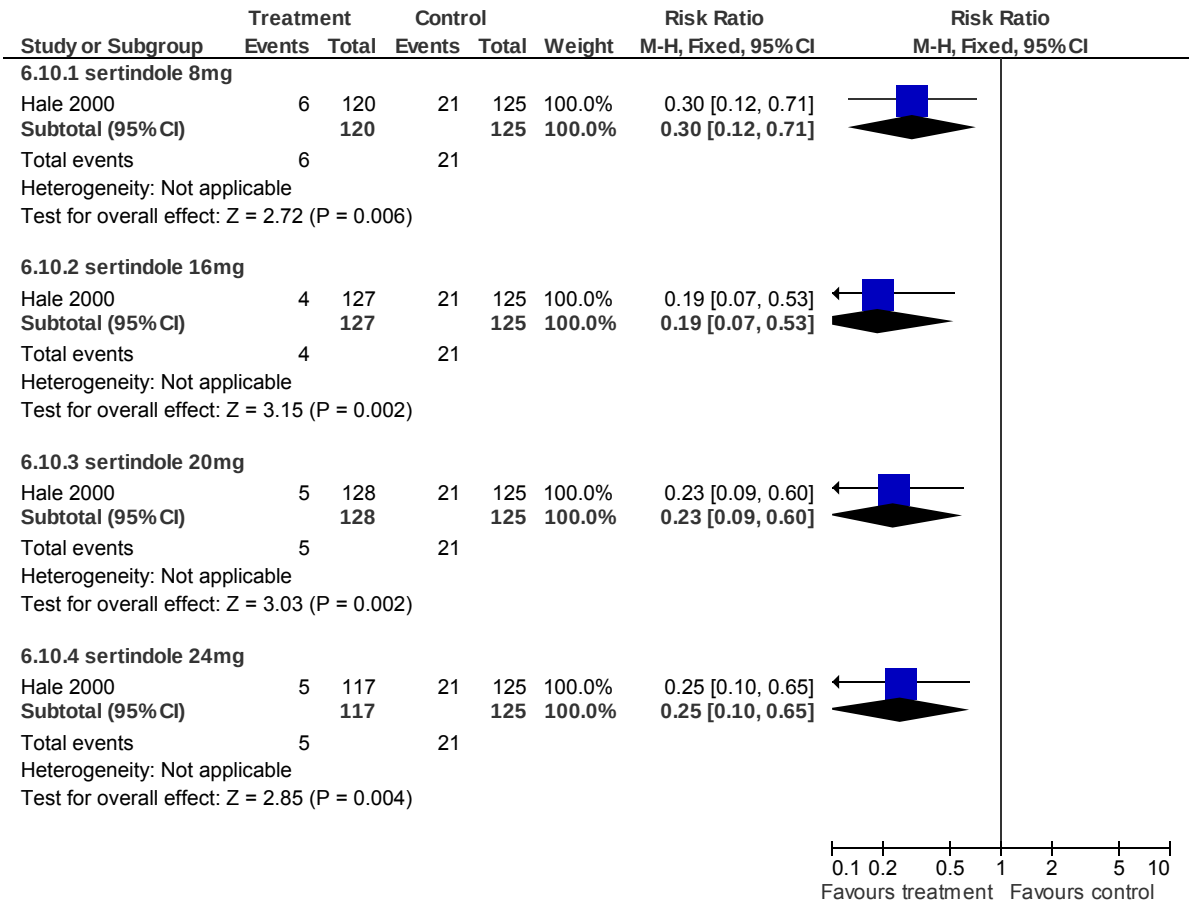
6.8 AE: 2. Neurologic SEs - Hypertonia (short-term)



6.9 AE: 2. Neurologic SEs - Hypokinesia (short-term)



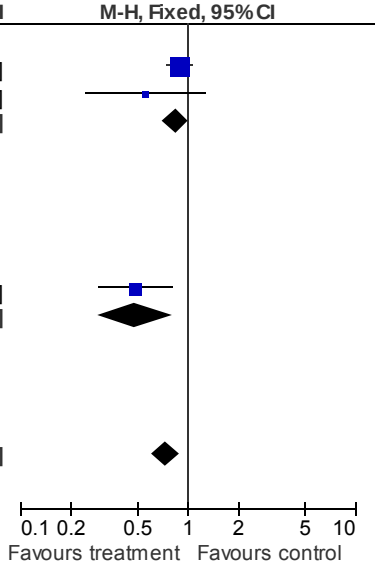
6.10 AE: 2. Neurologic SEs - Tremor (short-term)



7 Zotepine versus FGA (phase: acute treatment) (critical outcomes)

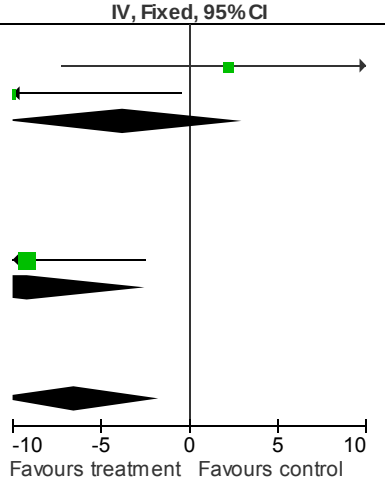
7.1 Global state: 2. Not improved to a clinically important degree (CGI?) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.1.1 vs. HAL						
Petit 1996	47	63	53	63	58.2%	0.89 [0.74, 1.06]
Barnas 1987	5	15	9	15	9.9%	0.56 [0.24, 1.27]
Subtotal (95% CI)		**78**		**78**	**68.1%**	**0.84 [0.70, 1.01]**
Total events	52		62			
Heterogeneity: Chi² = 1.32, df = 1 (P = 0.25); I² = 24%						
Test for overall effect: Z = 1.86 (P = 0.06)						
7.1.2 vs. other FGA						
Cooper 1999a	14	53	29	53	31.9%	0.48 [0.29, 0.81]
Subtotal (95% CI)		**53**		**53**	**31.9%**	**0.48 [0.29, 0.81]**
Total events	14		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.79 (P = 0.005)						
Total (95% CI)		**131**		**131**	**100.0%**	**0.73 [0.60, 0.88]**
Total events	66		91			
Heterogeneity: Chi² = 7.64, df = 2 (P = 0.02); I² = 74%						
Test for overall effect: Z = 3.31 (P = 0.0009)						

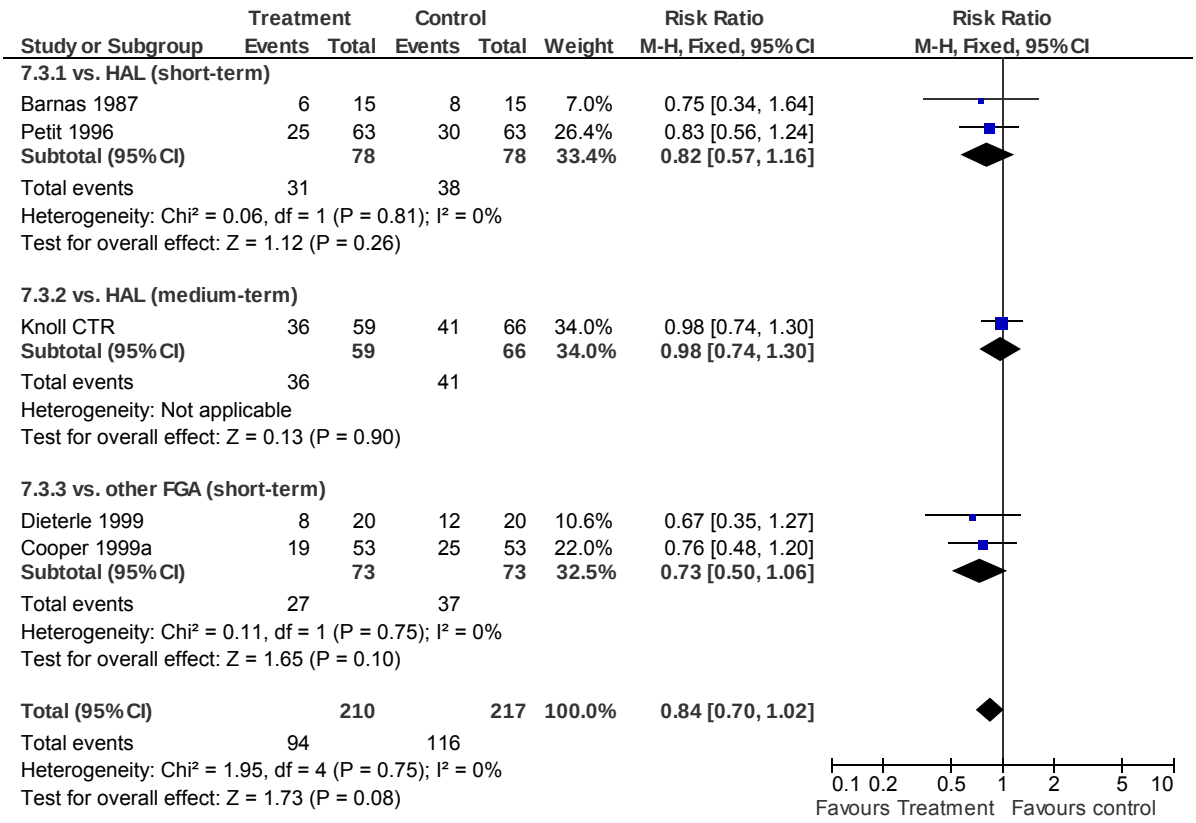


7.2 Mental state: 1. BPRS total (endpoint, high=poor) (short-term)

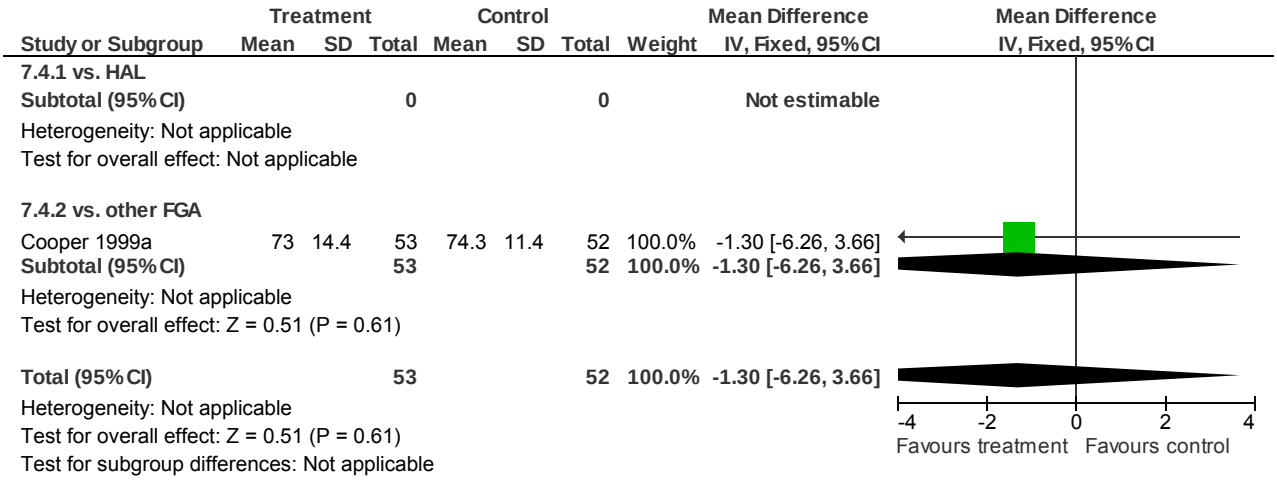
Study or Subgroup	treatment Mean	SD	Total	control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.2.1 vs. HAL								
Klieser 1996	40.6	18.6	20	38.4	16.3	45	25.6%	2.20 [-7.24, 11.64]
Barnas 1987	39.7	14.9	15	49.8	12	15	24.3%	-10.10 [-19.78, -0.42]
Subtotal (95% CI)			**35**			**60**	**49.9%**	**-3.80 [-10.55, 2.96]**
Heterogeneity: Chi² = 3.18, df = 1 (P = 0.07); I² = 69%								
Test for overall effect: Z = 1.10 (P = 0.27)								
7.2.2 vs. other FGA								
Cooper 1999a	43.4	13.8	53	52.6	20.7	52	50.1%	-9.20 [-15.94, -2.46]
Subtotal (95% CI)			**53**			**52**	**50.1%**	**-9.20 [-15.94, -2.46]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.67 (P = 0.007)								
Total (95% CI)			**88**			**112**	**100.0%**	**-6.50 [-11.28, -1.73]**
Heterogeneity: Chi² = 4.41, df = 2 (P = 0.11); I² = 55%								
Test for overall effect: Z = 2.67 (P = 0.008)								
Test for subgroup differences: Chi² = 1.23, df = 1 (P = 0.27), I² = 18.8%								



7.3 Leaving the study early: 1. Any reason (short-to-medium-term)

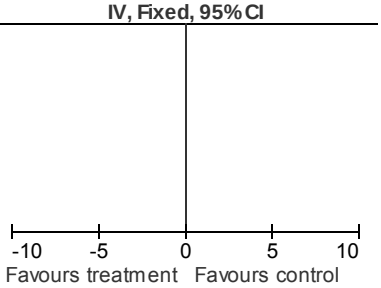


7.4 AE: 1. Metabolic SEs - weight change (short-term)



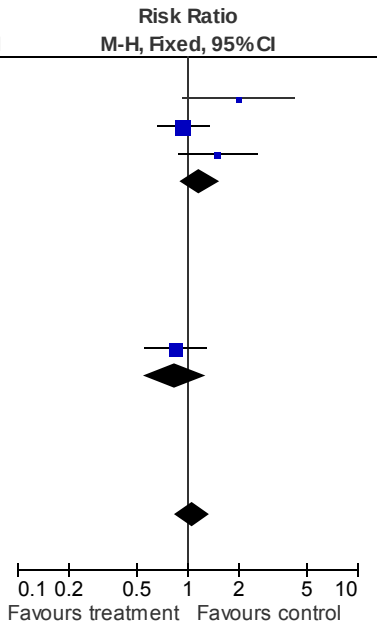
7.5 AE: 1. Metabolic SEs - weight change from baseline (kg) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.5.1 vs. HAL								
Knoll CTR	2.5	0	59	0.5	0	66		Not estimable
Subtotal (95% CI)			**59**			**66**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Total (95% CI)			**59**			**66**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



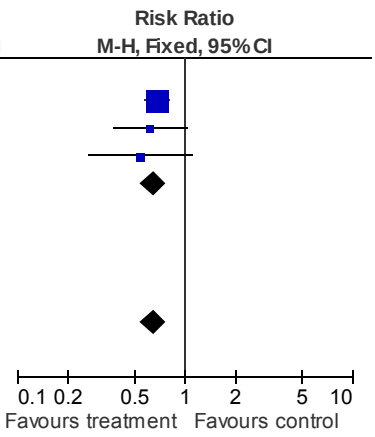
7.6 AE: 1. Metabolic SEs - treatment emergent (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.6.1 vs. HAL: liver function abnormalities						
Fleischhacker 1989	12	20	6	20	8.3%	2.00 [0.94, 4.27]
Petit 1996	30	63	32	63	44.4%	0.94 [0.66, 1.34]
Barnas 1987	12	15	8	15	11.1%	1.50 [0.88, 2.57]
Subtotal (95% CI)		**98**		**98**	**63.9%**	**1.17 [0.89, 1.55]**
Total events	54		46			
Heterogeneity: Chi² = 4.23, df = 2 (P = 0.12); I² = 53%						
Test for overall effect: Z = 1.14 (P = 0.26)						
7.6.2 vs. other FGA: liver function abnormalities						
Cooper 1999a	22	53	26	53	36.1%	0.85 [0.56, 1.29]
Subtotal (95% CI)		**53**		**53**	**36.1%**	**0.85 [0.56, 1.29]**
Total events	22		26			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.78 (P = 0.44)						
Total (95% CI)		**151**		**151**	**100.0%**	**1.06 [0.84, 1.33]**
Total events	76		72			
Heterogeneity: Chi² = 5.86, df = 3 (P = 0.12); I² = 49%						
Test for overall effect: Z = 0.46 (P = 0.65)						



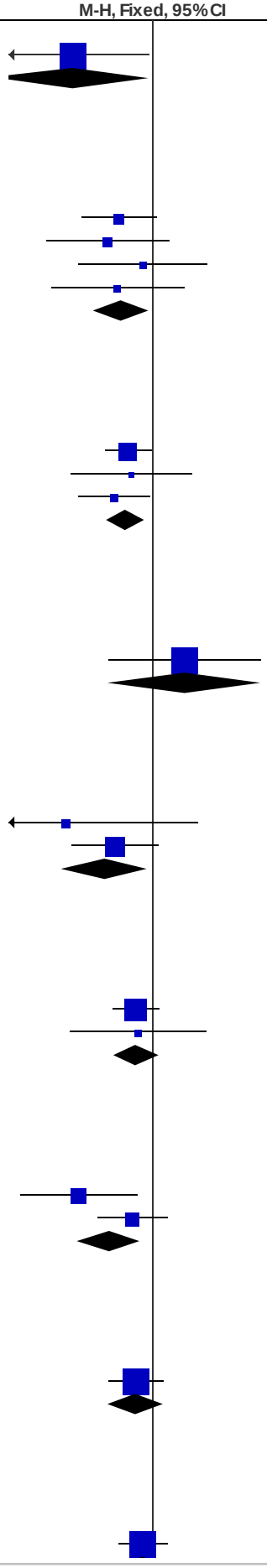
7.7 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.7.1 vs. HAL						
Petit 1996	42	63	62	63	68.6%	0.68 [0.57, 0.81]
Barnas 1987	8	15	13	15	14.4%	0.62 [0.37, 1.03]
Klieser 1996	6	20	25	45	17.0%	0.54 [0.26, 1.11]
Subtotal (95% CI)		**98**		**123**	**100.0%**	**0.65 [0.54, 0.77]**
Total events	56		100			
Heterogeneity: Chi² = 0.56, df = 2 (P = 0.76); I² = 0%						
Test for overall effect: Z = 4.71 (P < 0.00001)						
Total (95% CI)		**98**		**123**	**100.0%**	**0.65 [0.54, 0.77]**
Total events	56		100			
Heterogeneity: Chi² = 0.56, df = 2 (P = 0.76); I² = 0%						
Test for overall effect: Z = 4.71 (P < 0.00001)						



7.8 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.8.1 vs. HAL: any extrapyramidal event						
Knoll CTR	3	59	12	66	100.0%	0.28 [0.08, 0.94]
Subtotal (95% CI)		**59**		**66**	**100.0%**	**0.28 [0.08, 0.94]**
Total events	3		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.05 (P = 0.04)						
7.8.2 vs. HAL: tremor						
Barnas 1987	7	15	12	15	32.4%	0.58 [0.32, 1.06]
Knoll CTR	5	59	12	69	29.8%	0.49 [0.18, 1.30]
Petit 1996	6	63	7	63	18.9%	0.86 [0.31, 2.41]
Fleischhacker 1989	4	20	7	20	18.9%	0.57 [0.20, 1.65]
Subtotal (95% CI)		**157**		**167**	**100.0%**	**0.60 [0.39, 0.94]**
Total events	22		38			
Heterogeneity: Chi² = 0.65, df = 3 (P = 0.89); I² = 0%						
Test for overall effect: Z = 2.22 (P = 0.03)						
7.8.3 vs. HAL: akathisia						
Petit 1996	25	63	37	63	64.9%	0.68 [0.47, 0.98]
Fleischhacker 1989	5	20	7	20	12.3%	0.71 [0.27, 1.88]
Barnas 1987	7	15	13	15	22.8%	0.54 [0.30, 0.96]
Subtotal (95% CI)		**98**		**98**	**100.0%**	**0.65 [0.48, 0.88]**
Total events	37		57			
Heterogeneity: Chi² = 0.49, df = 2 (P = 0.78); I² = 0%						
Test for overall effect: Z = 2.83 (P = 0.005)						
7.8.4 vs. HAL: asthenia						
Knoll CTR	6	59	4	66	100.0%	1.68 [0.50, 5.66]
Subtotal (95% CI)		**59**		**66**	**100.0%**	**1.68 [0.50, 5.66]**
Total events	6		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.83 (P = 0.40)						
7.8.5 vs. HAL: dystonia						
Fleischhacker 1989	1	20	4	20	26.7%	0.25 [0.03, 2.05]
Barnas 1987	6	15	11	15	73.3%	0.55 [0.27, 1.09]
Subtotal (95% CI)		**35**		**35**	**100.0%**	**0.47 [0.24, 0.93]**
Total events	7		15			
Heterogeneity: Chi² = 0.53, df = 1 (P = 0.46); I² = 0%						
Test for overall effect: Z = 2.18 (P = 0.03)						
7.8.6 vs. HAL: dyskinesia						
Petit 1996	26	63	34	63	83.7%	0.76 [0.53, 1.11]
Knoll CTR	5	59	7	66	16.3%	0.80 [0.27, 2.38]
Subtotal (95% CI)		**122**		**129**	**100.0%**	**0.77 [0.54, 1.10]**
Total events	31		41			
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.94); I² = 0%						
Test for overall effect: Z = 1.42 (P = 0.15)						
7.8.7 vs. HAL: rigidity						
Fleischhacker 1989	4	20	13	20	54.2%	0.31 [0.12, 0.78]
Barnas 1987	8	15	11	15	45.8%	0.73 [0.41, 1.28]
Subtotal (95% CI)		**35**		**35**	**100.0%**	**0.50 [0.30, 0.83]**
Total events	12		24			
Heterogeneity: Chi² = 2.74, df = 1 (P = 0.10); I² = 63%						
Test for overall effect: Z = 2.69 (P = 0.007)						
7.8.8 vs. other FGA: akathisia						
Cooper 1999a	20	53	26	53	100.0%	0.77 [0.49, 1.20]
Subtotal (95% CI)		**53**		**53**	**100.0%**	**0.77 [0.49, 1.20]**
Total events	20		26			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.16 (P = 0.24)						
7.8.9 vs. other FGA: asthenia						
Cooper 1999a	24	53	28	53	100.0%	0.86 [0.58, 1.27]



Subtotal (95% CI)	**53**	**53**	**100.0%**	**0.86 [0.58, 1.27]**	
Total events	24	28			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.77 (P = 0.44)

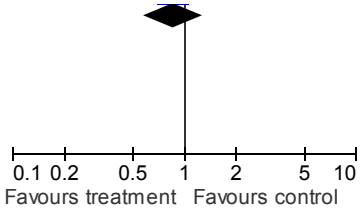


Table 3: Studies included in the acute treatment review (SGA versus SGA)

Treatment	versus Comparator								
	AMI	**ARI**	**OLZ**	**PAL**	**QUE**	**RIS**	**SER**	**ZIP**	**ZOT**
AMI			MARTIN2002 [24weeks, N=377] WAGNER2005 [8weeks, N=52]			Fleurot 1997 [8weeks, N=228] HWANG2003 [6weeks, N=47] Lecrubier 2000 [26weeks, N=310]			
ARI						CHAN2007 [4weeks, N=83] POTKIN2003A [4weeks, N=404]		ZIMBROFF2007 [4weeks, N=256]	
OLZ	MARTIN2002 [24weeks, N=377] WAGNER2005 [8weeks, N=52]			DAVIDSON2007 (9 mg) [6weeks, N=618] KANE2007A [6weeks, N=250] MARDER2007 (6 mg) [6weeks, N=222]	RIEDEL2007B [8weeks, N=52]	Conley 2001 [8weeks, N=377] Gureje 1998 [30weeks, N=65] Malyarov 1999 [26weeks, N=25] Tran 1997 [28weeks, N=339] S036 [6weeks,		BREIER2005 [28weeks, N=548] R-0548 (SIMPSON2004) [6weeks, N=269]	

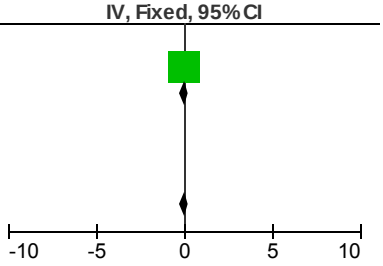
						N=122]			
PAL			DAVIDSON2007 (9 mg) [6weeks, N=618] KANE2007A [6weeks, N=250] MARDER2007 (6 mg) [6weeks, N=222]						
QUE			RIEDEL2007B [8weeks, N=52]			ZHONG2006 [8weeks, N=673]			
RIS	Fleurot 1997 [8weeks, N=228] HWANG2003 [6weeks, N=47] Lecrubier 2000 [26weeks, N=310] HWANG2003 [6weeks, N=47]	CHAN2007 [4weeks, N=83] POTKIN2003A [4weeks, N=404]	Conley 2001 [8weeks, N=377] Gureje 1998 [30weeks, N=65] Malyarov 1999 [26weeks, N=25] Tran 1997 [28weeks, N=339] S036 [6weeks,		ZHONG2006 [8weeks, N=673]		AZORIN2006 [12weeks, N=187]	128–302 (ADDINGTON2004) [8weeks, N=296]	Klieser 1996 [4weeks, N=59]

			N=122]						
SER						AZORIN2006 [12weeks, N=187]			
ZIP			BREIER2005 [28weeks, N=548] R-0548 (SIMPSON2004) [6weeks, N=269]			128–302 (ADDINGTON2004) [8weeks, N=296]			
ZOT						Klieser 1996 [4weeks, N=59]			

1 Aripiprazole versus Ziprasidone (phase: acute treatment) (critical outcomes)

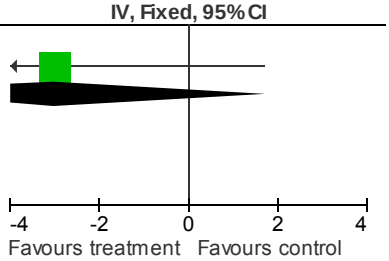
1.1 Global state: 1. CGI-S (change)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 Short-term								
ZIMBROFF2007	-1.15	1.01	126	-1.12	0.99	121	100.0%	-0.03 [-0.28, 0.22]
Subtotal (95% CI)			**126**			**121**	**100.0%**	**-0.03 [-0.28, 0.22]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.24 (P = 0.81)								
Total (95% CI)			**126**			**121**	**100.0%**	**-0.03 [-0.28, 0.22]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.24 (P = 0.81)								
Test for subgroup differences: Not applicable								



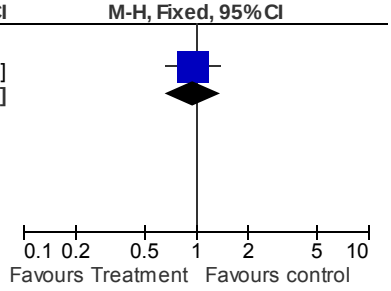
1.2 Mental state: 1. PANSS total (Change)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.2.1 Short-term								
ZIMBROFF2007	-24.6	19.08	126	-21.6	18.7	121	100.0%	-3.00 [-7.71, 1.71]
Subtotal (95% CI)			**126**			**121**	**100.0%**	**-3.00 [-7.71, 1.71]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.25 (P = 0.21)								
Test for subgroup differences: Not applicable								



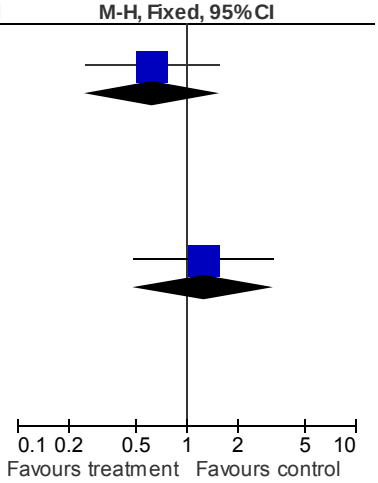
1.3 Leaving the study early: 1. Any reason

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 Short-term						
ZIMBROFF2007	39	129	40	127	100.0%	0.96 [0.67, 1.39]
Subtotal (95% CI)		**129**		**127**	**100.0%**	**0.96 [0.67, 1.39]**
Total events	39		40			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.22 (P = 0.83)						



1.4 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 Extrapyramidal syndrome						
ZIMBROFF2007	7	128	11	125	100.0%	0.62 [0.25, 1.55]
Subtotal (95% CI)		**128**		**125**	**100.0%**	**0.62 [0.25, 1.55]**
Total events	7		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						
1.4.2 Akathisia						
ZIMBROFF2007	9	128	7	125	100.0%	1.26 [0.48, 3.27]
Subtotal (95% CI)		**128**		**125**	**100.0%**	**1.26 [0.48, 3.27]**
Total events	9		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.47 (P = 0.64)						

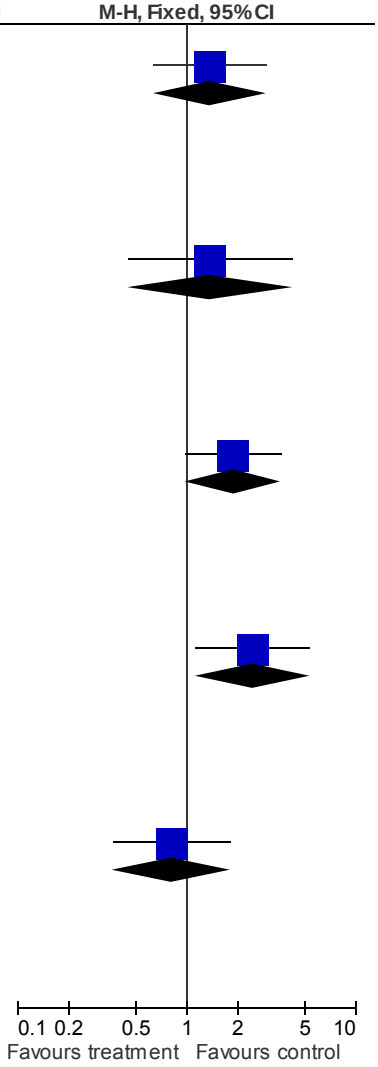


1.5 AE: 2. Neurologic SEs - AIMS Change

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.5.1 Short-term								
ZIMBROFF2007	-0.4	1.13	128	0	1.12	125	100.0%	-0.40 [-0.68, -0.12]
Subtotal (95% CI)			**128**			**125**	**100.0%**	**-0.40 [-0.68, -0.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.83 (P = 0.005)								
Total (95% CI)			**128**			**125**	**100.0%**	**-0.40 [-0.68, -0.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.83 (P = 0.005)								
Test for subgroup differences: Not applicable								

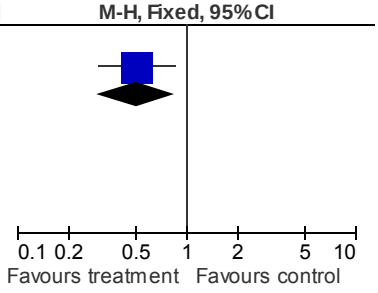
1.6 AE: 5. Gastrointestinal SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 Constipation						
ZIMBROFF2007	14	128	10	125	100.0%	1.37 [0.63, 2.96]
Subtotal (95% CI)		**128**		**125**	**100.0%**	**1.37 [0.63, 2.96]**
Total events	14		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						
1.6.2 Diarrhea						
ZIMBROFF2007	7	128	5	125	100.0%	1.37 [0.45, 4.19]
Subtotal (95% CI)		**128**		**125**	**100.0%**	**1.37 [0.45, 4.19]**
Total events	7		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.55 (P = 0.58)						
1.6.3 Dyspepsia						
ZIMBROFF2007	23	128	12	125	100.0%	1.87 [0.97, 3.60]
Subtotal (95% CI)		**128**		**125**	**100.0%**	**1.87 [0.97, 3.60]**
Total events	23		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.88 (P = 0.06)						
1.6.4 Nausea						
ZIMBROFF2007	20	128	8	125	100.0%	2.44 [1.12, 5.34]
Subtotal (95% CI)		**128**		**125**	**100.0%**	**2.44 [1.12, 5.34]**
Total events	20		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.24 (P = 0.03)						
1.6.5 Vomiting						
ZIMBROFF2007	10	128	12	125	100.0%	0.81 [0.36, 1.82]
Subtotal (95% CI)		**128**		**125**	**100.0%**	**0.81 [0.36, 1.82]**
Total events	10		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.50 (P = 0.61)						



1.7 AE: 6. Sedation (short-term)

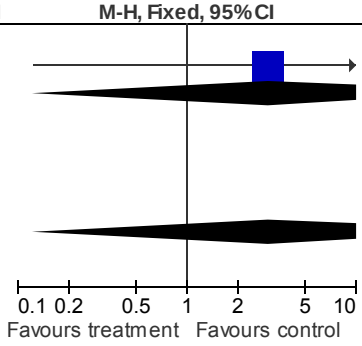
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.7.1 Day time sleepiness - increase (somnolence)						
ZIMBROFF2007	17	128	33	125	100.0%	0.50 [0.30, 0.86]
Subtotal (95% CI)		**128**		**125**	**100.0%**	**0.50 [0.30, 0.86]**
Total events	17		33			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.54 (P = 0.01)						



2 Olanzapine versus Amisulpride (phase: acute treatment) (critical outcomes)

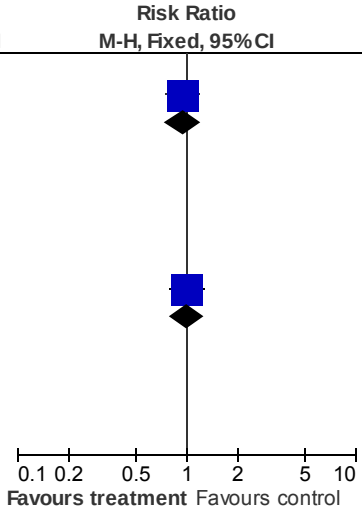
2.1 Mortality (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 Suicide						
MARTIN2002	1	188	0	189	100.0%	3.02 [0.12, 73.56]
Subtotal (95% CI)		**188**		**189**	**100.0%**	**3.02 [0.12, 73.56]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
Total (95% CI)		**188**		**189**	**100.0%**	**3.02 [0.12, 73.56]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						



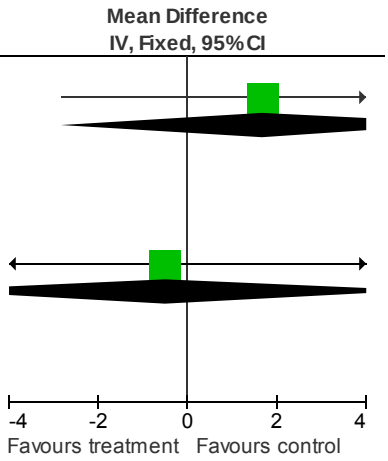
2.2 Global state: 1. Not improved (CGI)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 Short-term						
MARTIN2002	76	188	81	189	100.0%	0.94 [0.74, 1.20]
Subtotal (95% CI)		**188**		**189**	**100.0%**	**0.94 [0.74, 1.20]**
Total events	76		81			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.48 (P = 0.63)						
2.2.2 Medium-term						
MARTIN2002	78	188	78	189	100.0%	1.01 [0.79, 1.28]
Subtotal (95% CI)		**188**		**189**	**100.0%**	**1.01 [0.79, 1.28]**
Total events	78		78			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.04 (P = 0.97)						



2.3 Mental state: 1. PANSS total (Change)

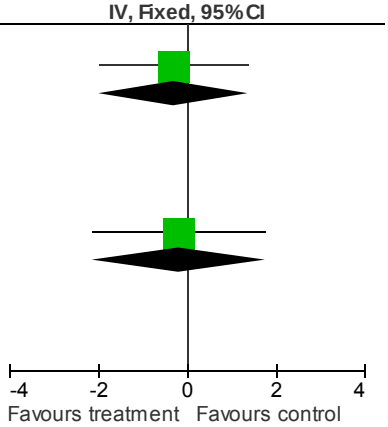
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.3.1 Short-term								
MARTIN2002	-23.9	22.4	186	-25.6	22.1	186	100.0%	1.70 [-2.82, 6.22]
Subtotal (95% CI)			**186**			**186**	**100.0%**	**1.70 [-2.82, 6.22]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.74 (P = 0.46)								
2.3.2 Medium-term								
MARTIN2002	-27.3	25.7	186	-26.8	26.6	186	100.0%	-0.50 [-5.82, 4.82]
Subtotal (95% CI)			**186**			**186**	**100.0%**	**-0.50 [-5.82, 4.82]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.18 (P = 0.85)								



Test for subgroup differences: Chi² = 0.38, df = 1 (P = 0.54), I² = 0%

2.4 Mental state: 2. Depression MADRS (change) (short-term)

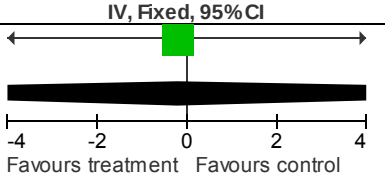
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.4.1 Short-term								
MARTIN2002	-6.3	7.7	186	-6	8.8	186	100.0%	-0.30 [-1.98, 1.38]
Subtotal (95% CI)			**186**			**186**	**100.0%**	**-0.30 [-1.98, 1.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.35 (P = 0.73)								
2.4.2 Medium-term								
MARTIN2002	-6.3	8.7	185	-6.1	10.4	186	100.0%	-0.20 [-2.15, 1.75]
Subtotal (95% CI)			**185**			**186**	**100.0%**	**-0.20 [-2.15, 1.75]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.20 (P = 0.84)								



Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.94), I² = 0%

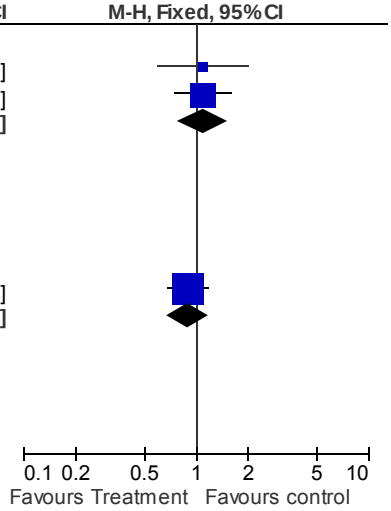
2.5 Psychosocial functioning: 1. Mean improvement % (SOFAS; signs reversed) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
MARTIN2002	-30.2	49.5	177	-30	54.3	182	100.0%	-0.20 [-10.94, 10.54]
Total (95% CI)			**177**			**182**	**100.0%**	**-0.20 [-10.94, 10.54]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.04 (P = 0.97)								



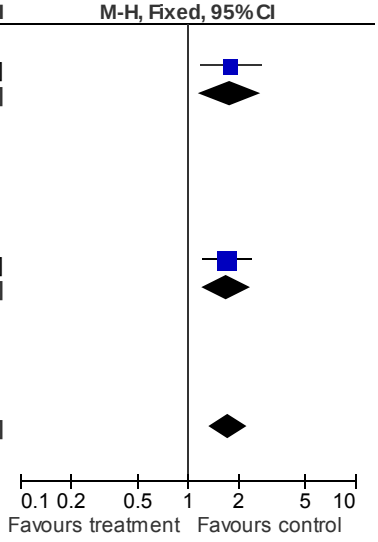
2.6 Leaving the study early: 1. Any reason

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.6.1 Short-term						
WAGNER2005	12	26	11	26	22.0%	1.09 [0.59, 2.01]
MARTIN2002	42	188	39	189	78.0%	1.08 [0.74, 1.59]
Subtotal (95% CI)		**214**		**215**	**100.0%**	**1.08 [0.78, 1.51]**
Total events	54		50			
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² = 0%						
Test for overall effect: Z = 0.48 (P = 0.63)						
2.6.2 Medium-term						
MARTIN2002	61	188	69	189	100.0%	0.89 [0.67, 1.17]
Subtotal (95% CI)		**188**		**189**	**100.0%**	**0.89 [0.67, 1.17]**
Total events	61		69			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.83 (P = 0.41)						



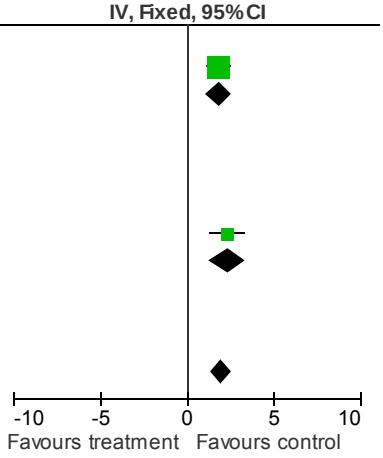
2.7 AE: 1. Metabolic SEs - Weight gain (>=7% increase from baseline)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.7.1 Short-term						
MARTIN2002	48	188	27	189	40.8%	1.79 [1.17, 2.74]
Subtotal (95% CI)		**188**		**189**	**40.8%**	**1.79 [1.17, 2.74]**
Total events	48		27			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.67 (P = 0.008)						
2.7.2 Medium-term						
MARTIN2002	66	186	39	186	59.2%	1.69 [1.20, 2.38]
Subtotal (95% CI)		**186**		**186**	**59.2%**	**1.69 [1.20, 2.38]**
Total events	66		39			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.04 (P = 0.002)						
Total (95% CI)		**374**		**375**	**100.0%**	**1.73 [1.33, 2.26]**
Total events	114		66			
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0%						
Test for overall effect: Z = 4.04 (P < 0.0001)						



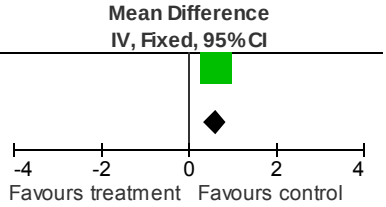
2.8 AE: 1. Metabolic SEs - Weight change from baseline (kg)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.8.1 Short-term								
MARTIN2002	2.7	3.9	186	0.9	3.2	186	67.2%	1.80 [1.08, 2.52]
Subtotal (95% CI)			**186**			**186**	**67.2%**	**1.80 [1.08, 2.52]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.87 (P < 0.00001)								
2.8.2 Medium-term								
MARTIN2002	3.9	5.3	186	1.6	4.9	186	32.8%	2.30 [1.26, 3.34]
Subtotal (95% CI)			**186**			**186**	**32.8%**	**2.30 [1.26, 3.34]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.35 (P < 0.0001)								
Total (95% CI)			**372**			**372**	**100.0%**	**1.96 [1.37, 2.56]**
Heterogeneity: Chi² = 0.60, df = 1 (P = 0.44); I² = 0%								
Test for overall effect: Z = 6.48 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.60, df = 1 (P = 0.44), I² = 0%								



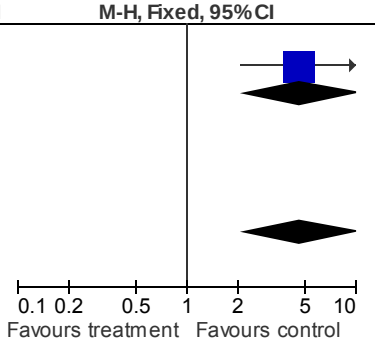
2.9 AE: 1. Metabolic SEs - BMI (change) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
MARTIN2002	0.9	1.3	186	0.3	1.1	186	100.0%	0.60 [0.36, 0.84]
Total (95% CI)			**186**			**186**	**100.0%**	**0.60 [0.36, 0.84]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.81 (P < 0.00001)								



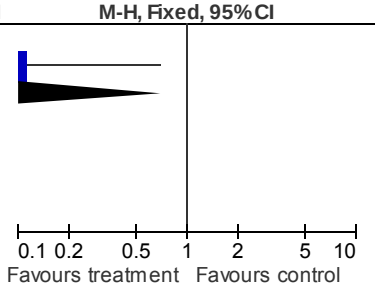
2.10 AE: 1. Metabolic SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.10.1 Increased liver transaminase levels						
MARTIN2002	32	188	7	189	100.0%	4.60 [2.08, 10.15]
Subtotal (95% CI)		**188**		**189**	**100.0%**	**4.60 [2.08, 10.15]**
Total events	32		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.77 (P = 0.0002)						
Total (95% CI)		**188**		**189**	**100.0%**	**4.60 [2.08, 10.15]**
Total events	32		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.77 (P = 0.0002)						



2.11 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

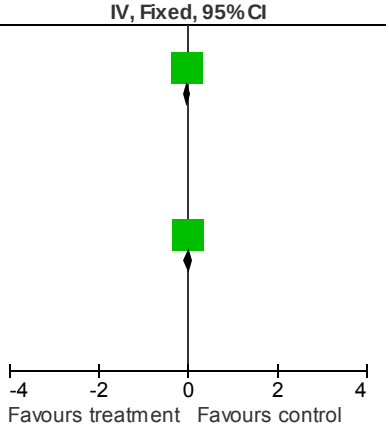
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.11.1 Extrapyramidal disorder						
MARTIN2002	1	188	11	189	100.0%	0.09 [0.01, 0.70]
Subtotal (95% CI)		**188**		**189**	**100.0%**	**0.09 [0.01, 0.70]**
Total events	1		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.30 (P = 0.02)						



2.12 AE: 2. Neurologic SEs - Simpson-Angus Scale (endpt)

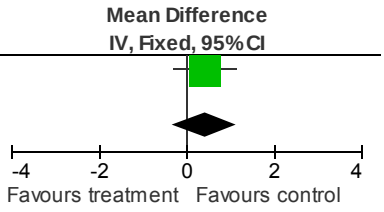
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.12.1 Short-term								
MARTIN2002	0.21	0.36	186	0.24	0.4	186	100.0%	-0.03 [-0.11, 0.05]
Subtotal (95% CI)			**186**			**186**	**100.0%**	**-0.03 [-0.11, 0.05]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.76 (P = 0.45)								
2.12.2 Medium-term								
MARTIN2002	-0.1	0.4	185	-0.1	0.4	186	100.0%	0.00 [-0.08, 0.08]
Subtotal (95% CI)			**185**			**186**	**100.0%**	**0.00 [-0.08, 0.08]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								

Test for subgroup differences: Chi² = 0.27, df = 1 (P = 0.60), I² = 0%



2.13 AE: 2. Neurologic SEs - AIMS Change (medium-term)

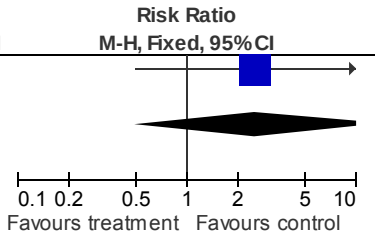
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
MARTIN2002	-0.5	3.6	175	-0.9	3.4	186	100.0%	0.40 [-0.32, 1.12]
Total (95% CI)			**175**			**186**	**100.0%**	**0.40 [-0.32, 1.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.08 (P = 0.28)								



2.14 AE: 2. Neurologic SEs - Barnes Akathisia Scale (moderate/marked) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MARTIN2002	5	185	2	186	100.0%	2.51 [0.49, 12.79]
Total (95% CI)		**185**		**186**	**100.0%**	**2.51 [0.49, 12.79]**
Total events	5		2			

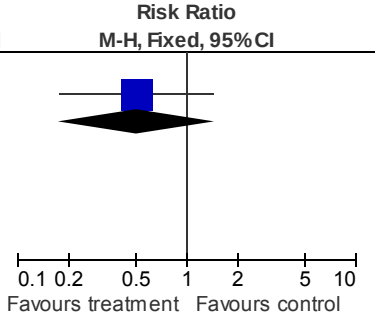
Heterogeneity: Not applicable
Test for overall effect: Z = 1.11 (P = 0.27)



2.15 AE: 5. Gastrointestinal SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.15.1 Constipation						
MARTIN2002	5	188	10	189	100.0%	0.50 [0.18, 1.44]
Subtotal (95% CI)		**188**		**189**	**100.0%**	**0.50 [0.18, 1.44]**
Total events	5		10			

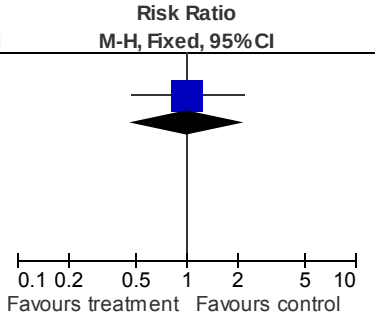
Heterogeneity: Not applicable
Test for overall effect: Z = 1.28 (P = 0.20)



2.16 AE: 6. Sedation (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.16.1 Day time sleepiness - increase (somnolence)						
MARTIN2002	12	188	12	189	100.0%	1.01 [0.46, 2.18]
Subtotal (95% CI)		**188**		**189**	**100.0%**	**1.01 [0.46, 2.18]**
Total events	12		12			

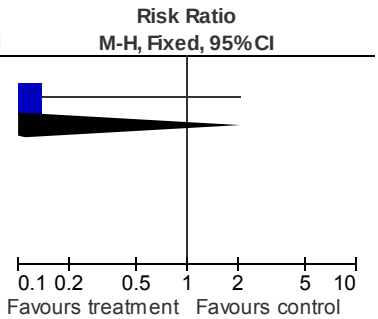
Heterogeneity: Not applicable
Test for overall effect: Z = 0.01 (P = 0.99)



2.17 AE: 8. Menstrual problems (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.17.1 Amenorrhoea						
MARTIN2002	0	188	4	189	100.0%	0.11 [0.01, 2.06]
Subtotal (95% CI)		**188**		**189**	**100.0%**	**0.11 [0.01, 2.06]**
Total events	0		4			

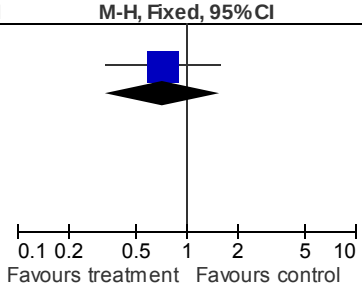
Heterogeneity: Not applicable
Test for overall effect: Z = 1.47 (P = 0.14)



2.18 AE: 9. Other SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.18.1 Insomnia						
MARTIN2002	10	188	14	189	100.0%	0.72 [0.33, 1.58]
Subtotal (95% CI)		**188**		**189**	**100.0%**	**0.72 [0.33, 1.58]**
Total events	10		14			

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

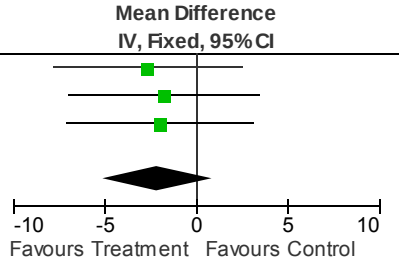


3 Olanzapine versus Paliperidone (phase: acute treatment) (critical outcomes)

3.1 Mental state: 1. PANSS total (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
MARDER2007	-18.4	19.9	105	-15.7	18.9	111	33.3%	-2.70 [-7.88, 2.48]
DAVIDSON2007	-18.1	20.3	126	-16.3	21.8	123	32.6%	-1.80 [-7.04, 3.44]
KANE2007A	-19.9	19	128	-17.9	22.2	123	34.1%	-2.00 [-7.12, 3.12]
Total (95% CI)			**359**			**357**	**100.0%**	**-2.17 [-5.16, 0.82]**

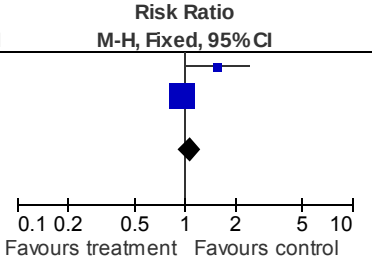
Heterogeneity: Chi² = 0.06, df = 2 (P = 0.97); I² = 0%
Test for overall effect: Z = 1.42 (P = 0.16)



3.2 Mental state: 2. Non-response (<50% improvement in PANSS) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MARDER2007	35	110	23	112	18.9%	1.55 [0.98, 2.44]
KANE2007A	95	128	96	123	81.1%	0.95 [0.83, 1.09]
Total (95% CI)		**238**		**235**	**100.0%**	**1.06 [0.92, 1.23]**
Total events	130		119			

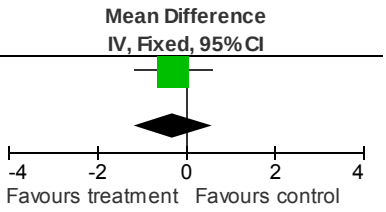
Heterogeneity: Chi² = 5.14, df = 1 (P = 0.02); I² = 81%
Test for overall effect: Z = 0.82 (P = 0.41)



3.3 Mental state: 3. Depression (PANSS anxiety/depression factor scores)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
DAVIDSON2007	-2.2	3.4	126	-1.9	3.7	123	100.0%	-0.30 [-1.18, 0.58]
Total (95% CI)			**126**			**123**	**100.0%**	**-0.30 [-1.18, 0.58]**

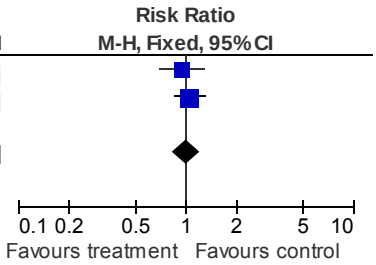
Heterogeneity: Not applicable
Test for overall effect: Z = 0.67 (P = 0.51)



3.4 Psychosocial functioning: 1. No response (PSP scale)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KANE2007A	48	128	49	123	43.7%	0.94 [0.69, 1.29]
MARDER2007	67	110	65	112	56.3%	1.05 [0.84, 1.30]
Total (95% CI)		**238**		**235**	**100.0%**	**1.00 [0.84, 1.20]**
Total events	115		114			

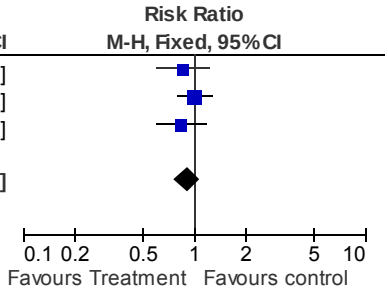
Heterogeneity: Chi² = 0.33, df = 1 (P = 0.57); I² = 0%
Test for overall effect: Z = 0.02 (P = 0.98)



3.5 Leaving the study early: 1. Any reason (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KANE2007A	38	128	43	123	28.9%	0.85 [0.59, 1.22]
MARDER2007	60	110	61	112	39.8%	1.00 [0.79, 1.27]
DAVIDSON2007	40	128	47	125	31.3%	0.83 [0.59, 1.17]
Total (95% CI)		**366**		**360**	**100.0%**	**0.90 [0.76, 1.08]**
Total events	138		151			

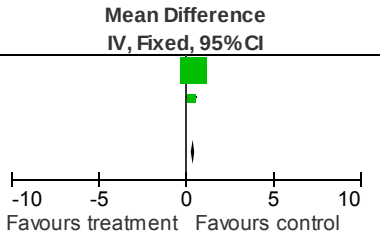
Heterogeneity: Chi² = 1.04, df = 2 (P = 0.59); I² = 0%
Test for overall effect: Z = 1.13 (P = 0.26)



3.6 AE: 1. Metabolic SEs - BMI (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
KANE2007A	0.5	0.1	122	0.1	0.8	118	82.1%	0.40 [0.25, 0.55]
DAVIDSON2007	0.8	1.32	114	0.5	1.08	118	17.9%	0.30 [-0.01, 0.61]
Total (95% CI)			**236**			**236**	**100.0%**	**0.38 [0.25, 0.51]**

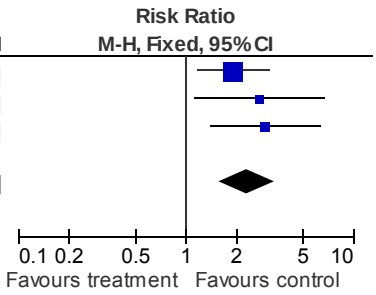
Heterogeneity: Chi² = 0.33, df = 1 (P = 0.57); I² = 0%
Test for overall effect: Z = 5.68 (P < 0.00001)



3.7 AE: 1. Metabolic SEs - Weight gain (>= 7% increase from baseline)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
DAVIDSON2007	37	127	19	124	57.8%	1.90 [1.16, 3.12]
KANE2007A	17	128	6	123	18.4%	2.72 [1.11, 6.68]
MARDER2007	23	109	8	112	23.7%	2.95 [1.38, 6.32]
Total (95% CI)		**364**		**359**	**100.0%**	**2.30 [1.58, 3.35]**
Total events	77		33			

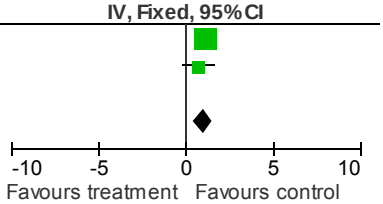
Heterogeneity: Chi² = 1.12, df = 2 (P = 0.57); I² = 0%
Test for overall effect: Z = 4.34 (P < 0.0001)



3.8 AE: 1. Metabolic SEs - Weight gain from baseline (kg) (short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
KANE2007A	1.3	2.8	123	0.2	2.4	118	66.0%	1.10 [0.44, 1.76]
DAVIDSON2007	2.2	3.94	115	1.5	3.14	118	34.0%	0.70 [-0.22, 1.62]
Total (95% CI)			**238**			**236**	**100.0%**	**0.96 [0.43, 1.50]**

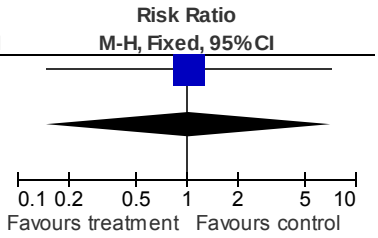
Heterogeneity: Chi² = 0.48, df = 1 (P = 0.49); I² = 0%
Test for overall effect: Z = 3.54 (P = 0.0004)



3.9 AE: 1. Metabolic SEs - Glucose-related AEs (incl. hyperglycemia, hypoglycemia, diabetes)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MARDER2007	2	109	2	112	100.0%	1.03 [0.15, 7.17]
Total (95% CI)		**109**		**112**	**100.0%**	**1.03 [0.15, 7.17]**
Total events	2		2			

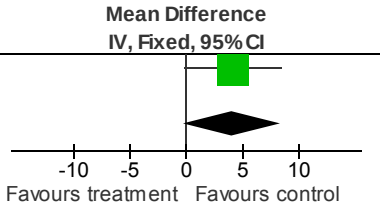
Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.98)



3.10 AE: 1. Metabolic SEs - Plasma levels of aspartate aminotransferase (change) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
MARDER2007	3.6	19	105	-0.5	12.7	111	100.0%	4.10 [-0.23, 8.43]
Total (95% CI)			**105**			**111**	**100.0%**	**4.10 [-0.23, 8.43]**

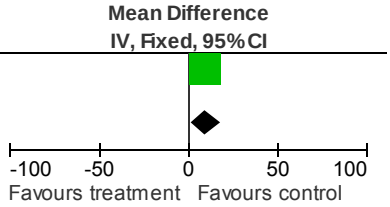
Heterogeneity: Not applicable
Test for overall effect: Z = 1.85 (P = 0.06)



3.11 AE: 1. Metabolic SEs - Plasma levels of alanine aminotransferase (change from baseline) (short term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
MARDER2007	7.6	37.3	105	-1.7	22.1	111	100.0%	9.30 [1.07, 17.53]
Total (95% CI)			**105**			**111**	**100.0%**	**9.30 [1.07, 17.53]**

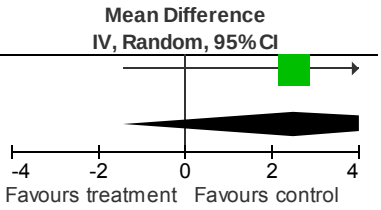
Heterogeneity: Not applicable
Test for overall effect: Z = 2.21 (P = 0.03)



3.12 AE: 1. Metabolic SEs - Insulin (change) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
KANE2007A	1.5	15	115	-1	14.6	104	100.0%	2.50 [-1.42, 6.42]
Total (95% CI)			**115**			**104**	**100.0%**	**2.50 [-1.42, 6.42]**

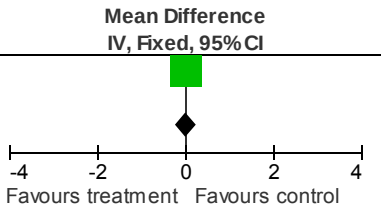
Heterogeneity: Not applicable
Test for overall effect: Z = 1.25 (P = 0.21)



3.13 AE: 1. Metabolic SEs - Glucose (change) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KANE2007A	0	0.89	127	0	0.96	114	100.0%	0.00 [-0.23, 0.23]
Total (95% CI)			**127**			**114**	**100.0%**	**0.00 [-0.23, 0.23]**

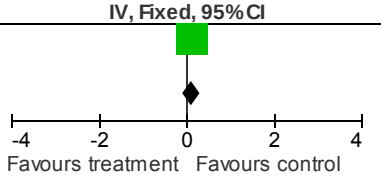
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



3.14 AE: 1. Metabolic SEs - LDL(change, mmol/L) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KANE2007A	0.1	0.7	122	0	0.7	111	100.0%	0.10 [-0.08, 0.28]
Total (95% CI)			**122**			**111**	**100.0%**	**0.10 [-0.08, 0.28]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.09 (P = 0.28)



3.15 AE: 1. Metabolic SEs - HDL (change, mmol/L) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KANE2007A	0	0.2	124	0	0.2	112	100.0%	0.00 [-0.05, 0.05]
Total (95% CI)			**124**			**112**	**100.0%**	**0.00 [-0.05, 0.05]**

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

3.16 AE: 1. Metabolic SEs - Cholesterol (change, mmol/L) (short-term)

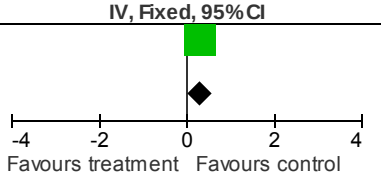
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KANE2007A	0.2	0.8	126	-0.1	0.8	112	100.0%	0.30 [0.10, 0.50]
Total (95% CI)			**126**			**112**	**100.0%**	**0.30 [0.10, 0.50]**

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

3.17 AE: 1. Metabolic SEs - Triclyerides (change, mmol/L) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KANE2007A	0.1	1.2	126	-0.2	0.9	112	100.0%	0.30 [0.03, 0.57]
Total (95% CI)			**126**			**112**	**100.0%**	**0.30 [0.03, 0.57]**

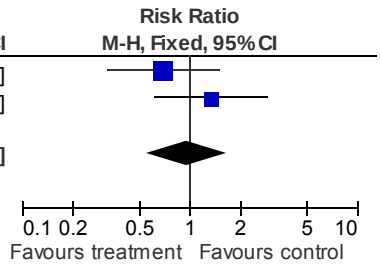
Heterogeneity: Not applicable
Test for overall effect: Z = 2.20 (P = 0.03)



3.18 AE: 2. Neurologic SEs - Needing additional anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KANE2007A	10	128	14	123	59.1%	0.69 [0.32, 1.49]
MARDER2007	13	109	10	112	40.9%	1.34 [0.61, 2.92]
Total (95% CI)		**237**		**235**	**100.0%**	**0.95 [0.55, 1.64]**
Total events	23		24			

Heterogeneity: Chi² = 1.41, df = 1 (P = 0.23); I² = 29%
Test for overall effect: Z = 0.18 (P = 0.86)

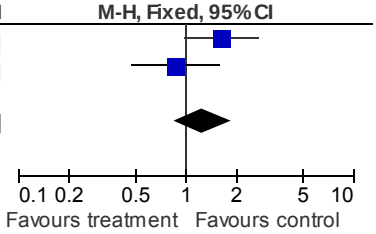


3.19 AE: 2. Neurologic SEs - Akathisia (not absent by BARS) (short-term)

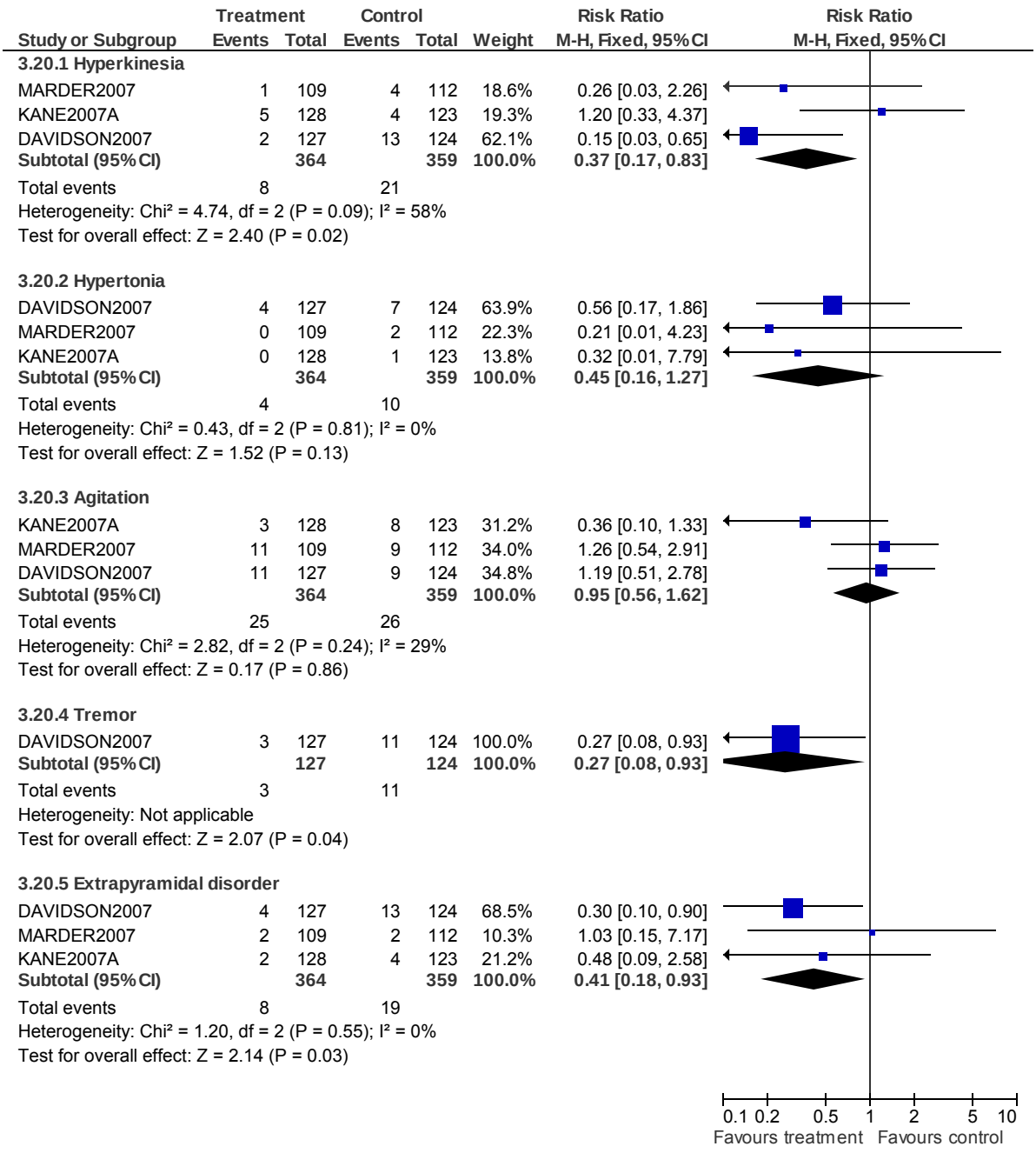
	Treatment		Control			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**	**M-H, Fixed, 95% CI**
DAVIDSON2007	31	124	19	124	50.3%	1.63 [0.98, 2.73]	
MARDER2007	16	109	19	112	49.7%	0.87 [0.47, 1.59]	
Total (95% CI)		**233**		**236**	**100.0%**	**1.25 [0.85, 1.84]**	
Total events	47		38				

Heterogeneity: Chi² = 2.43, df = 1 (P = 0.12); I² = 59%

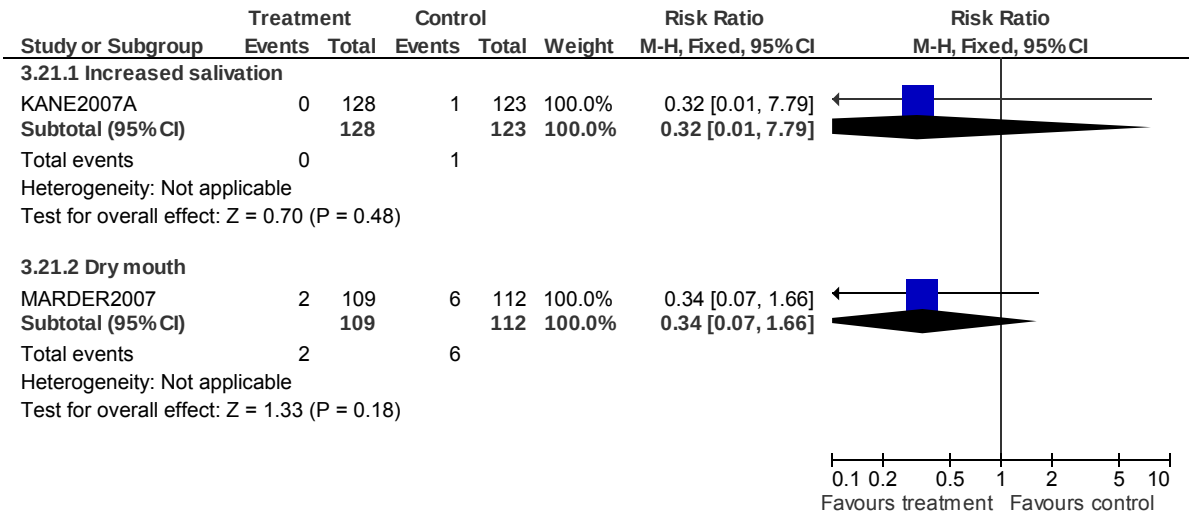
Test for overall effect: Z = 1.13 (P = 0.26)



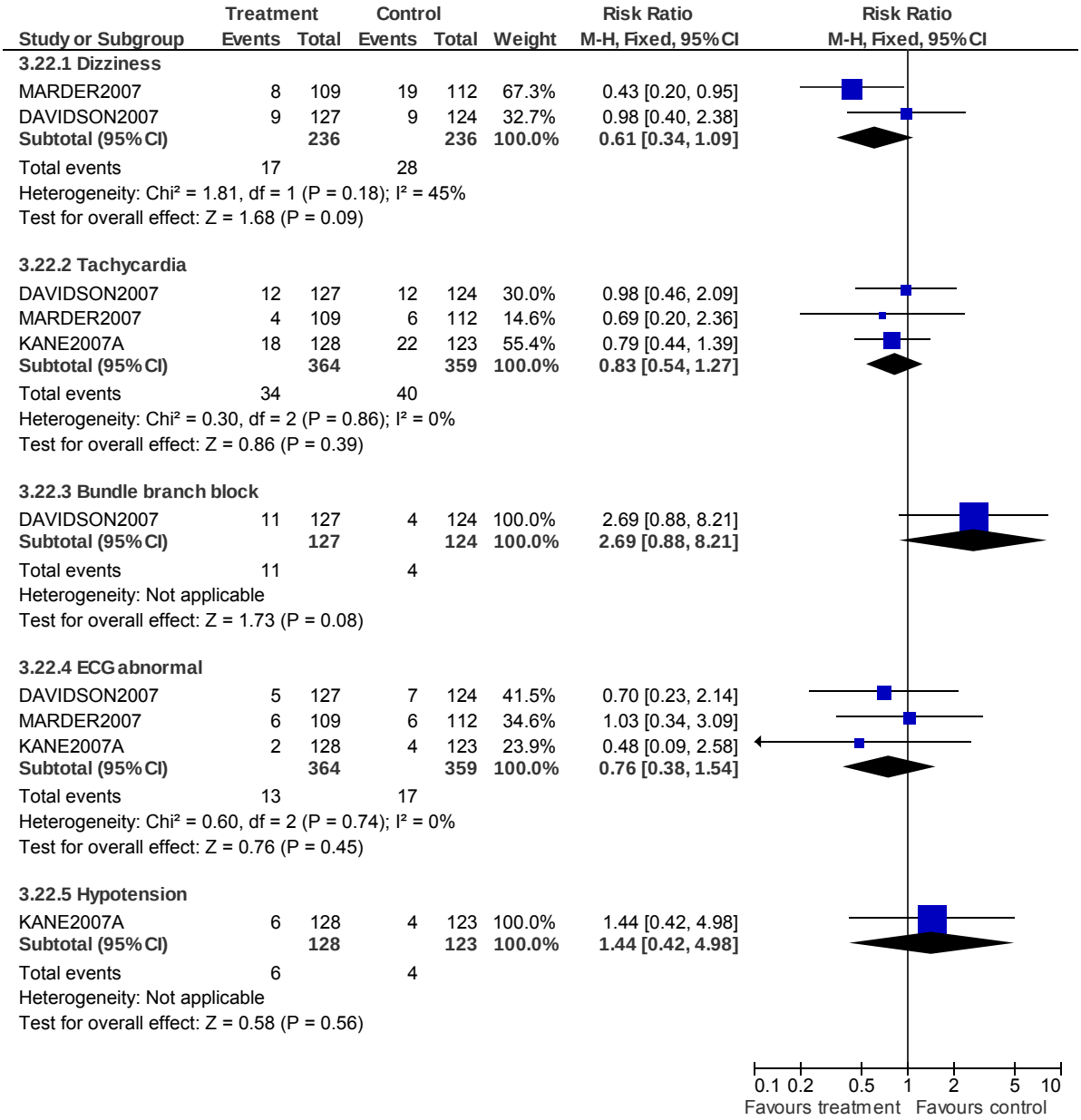
3.20 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



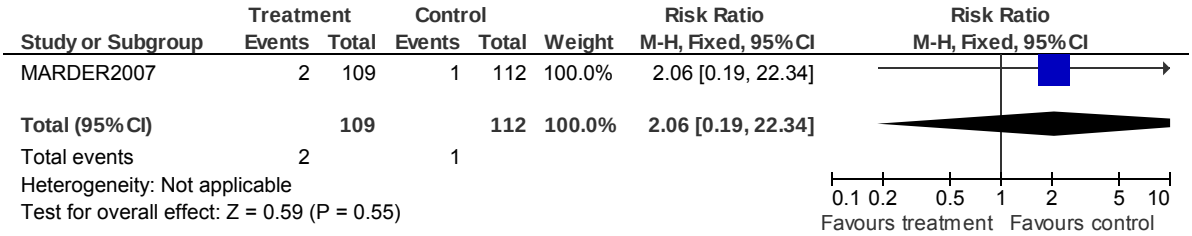
3.21 AE: 3. Autonomic SEs (short-term)



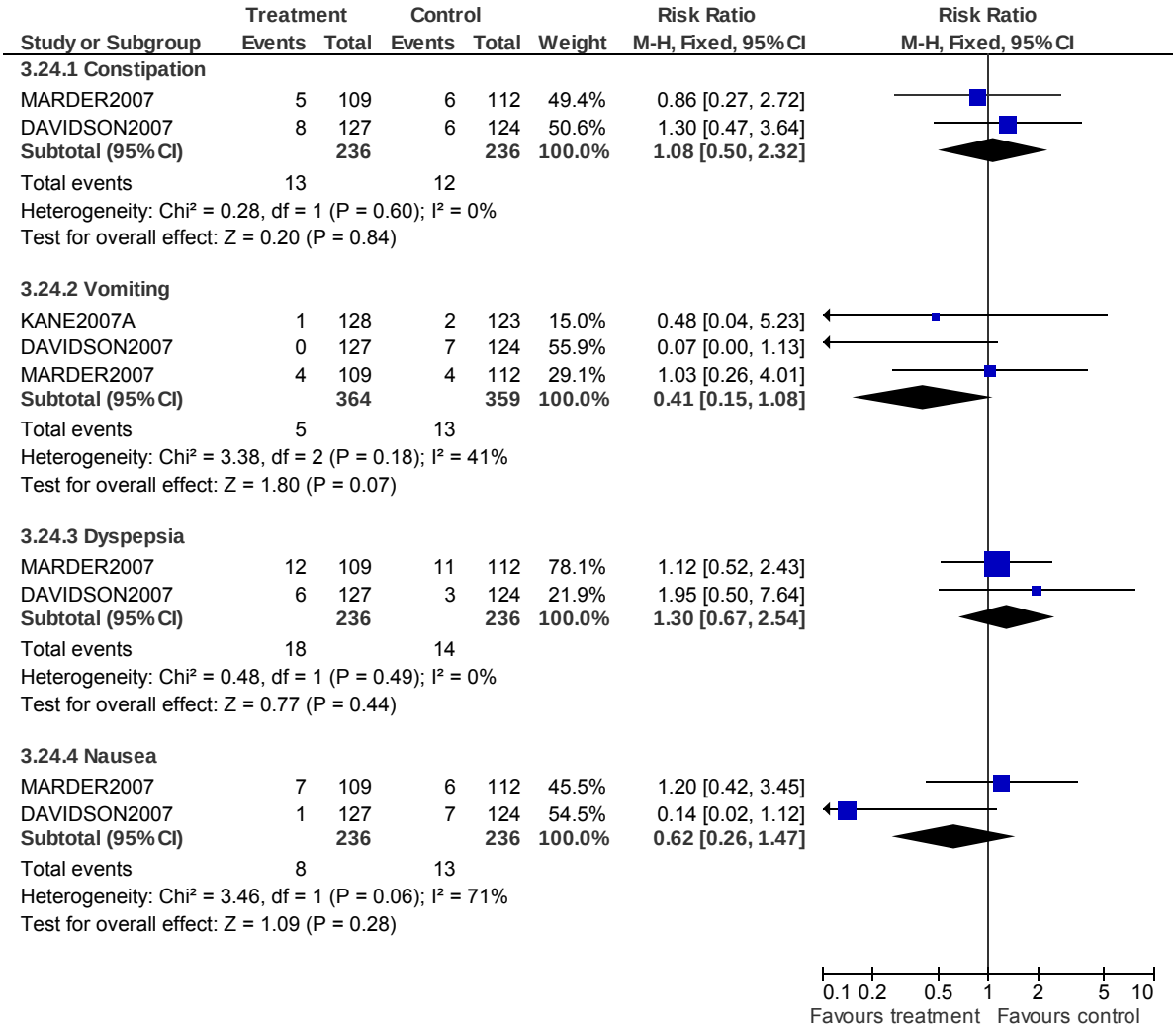
3.22 AE: 4. Cardiovascular SEs (short-term)



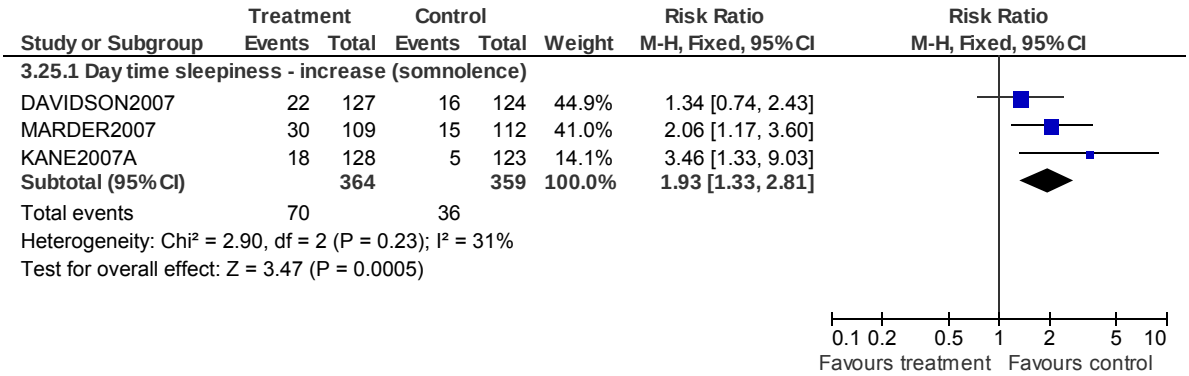
3.23 AE: 4. Cardiovascular SEs - Prolonged max postbaseline QTcLD (short-term)



3.24 AE: 5. Gastrointestinal SEs (short-term)

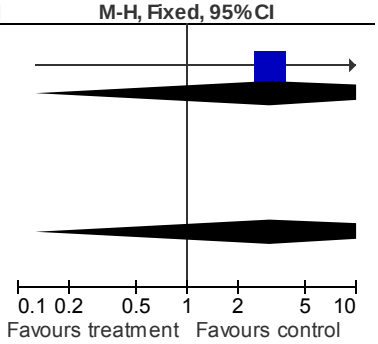


3.25 AE: 6. Sedation (short-term)

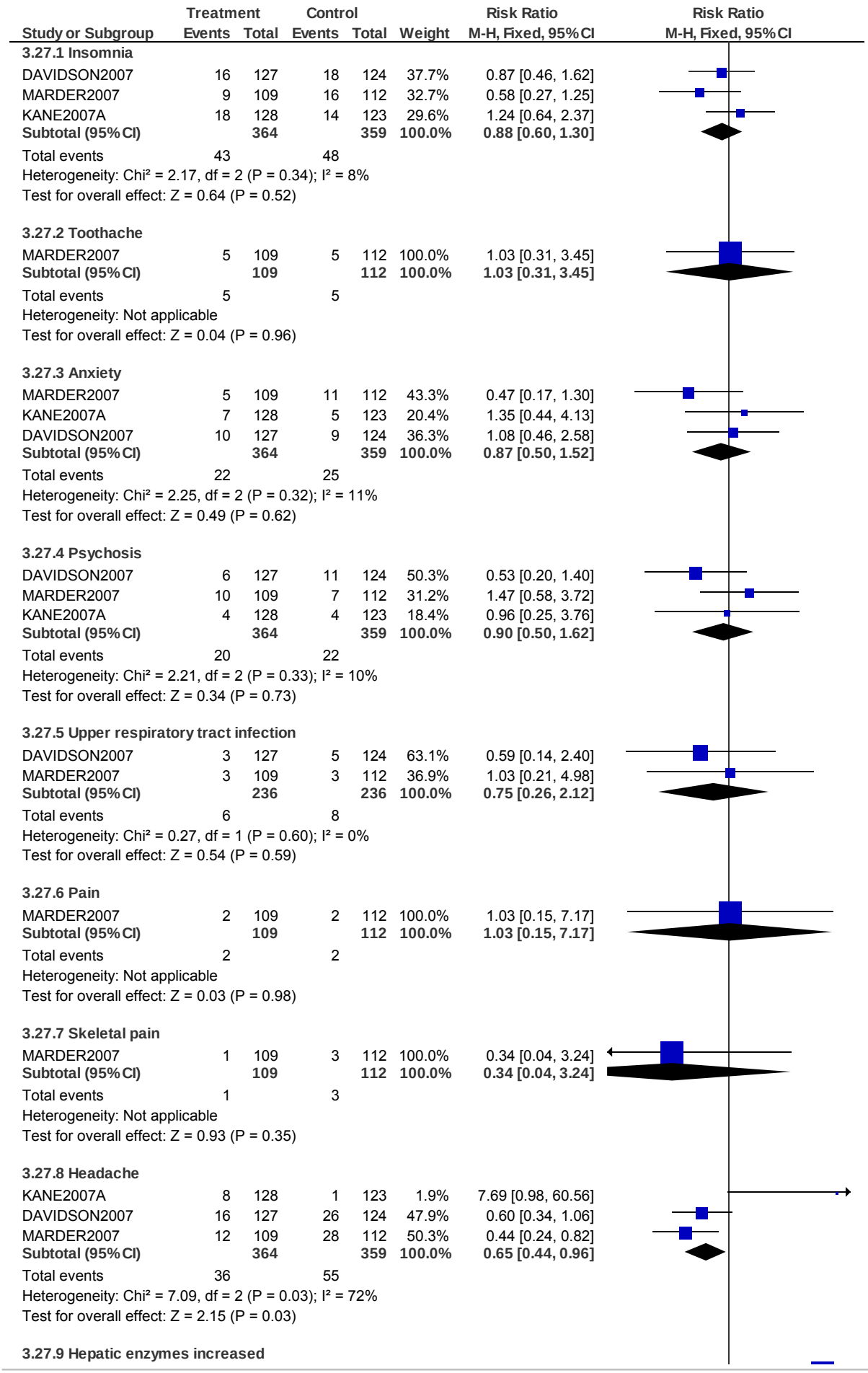


3.26 AE: 9. Dermatological system (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.26.1 Rash						
MARDER2007	1	109	0	112	100.0%	3.08 [0.13, 74.84]
Subtotal (95% CI)		**109**		**112**	**100.0%**	**3.08 [0.13, 74.84]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
Total (95% CI)		**109**		**112**	**100.0%**	**3.08 [0.13, 74.84]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						

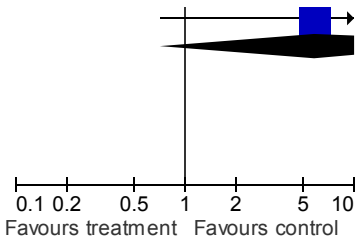


3.27 AE: 10. Other SEs (short-term)



DAVIDSON2007	6	127	1	124	100.0%	5.86 [0.72, 47.96]	
Subtotal (95% CI)		**127**		**124**	**100.0%**	**5.86 [0.72, 47.96]**	
Total events	6		1				

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

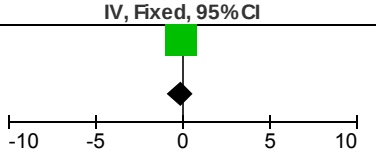


4 Olanzapine versus Quetiapine (phase: acute treatment) (critical outcomes)

4.1 Global state: 1. CGI-S (endpoint, high=poor) (short-term)

	Treatment			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
RIEDEL2007B	3.94	1.2	17	4.06	1	16	100.0%	-0.12 [-0.87, 0.63]	
Total (95% CI)			**17**			**16**	**100.0%**	**-0.12 [-0.87, 0.63]**	

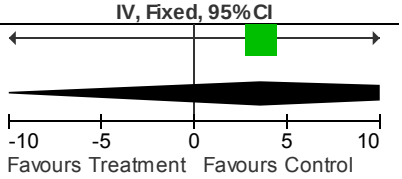
Heterogeneity: Not applicable
Test for overall effect: Z = 0.31 (P = 0.75)



4.2 Mental state: 1. PANSS total (endpt mean lower=better) (short-term)

	Treatment			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
RIEDEL2007B	-17.88	20.71	17	-21.5	23.39	16	100.0%	3.62 [-11.49, 18.73]	
Total (95% CI)			**17**			**16**	**100.0%**	**3.62 [-11.49, 18.73]**	

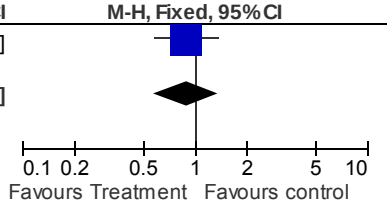
Heterogeneity: Not applicable
Test for overall effect: Z = 0.47 (P = 0.64)



4.3 Leaving the study early: 1. Any reason (short-term)

	Treatment		Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
RIEDEL2007B	15	26	17	26	100.0%	0.88 [0.57, 1.36]	
Total (95% CI)		**26**		**26**	**100.0%**	**0.88 [0.57, 1.36]**	
Total events	15		17				

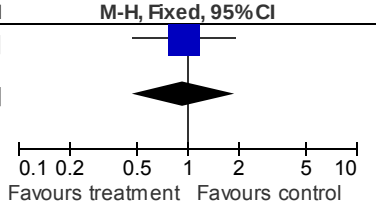
Heterogeneity: Not applicable
Test for overall effect: Z = 0.57 (P = 0.57)



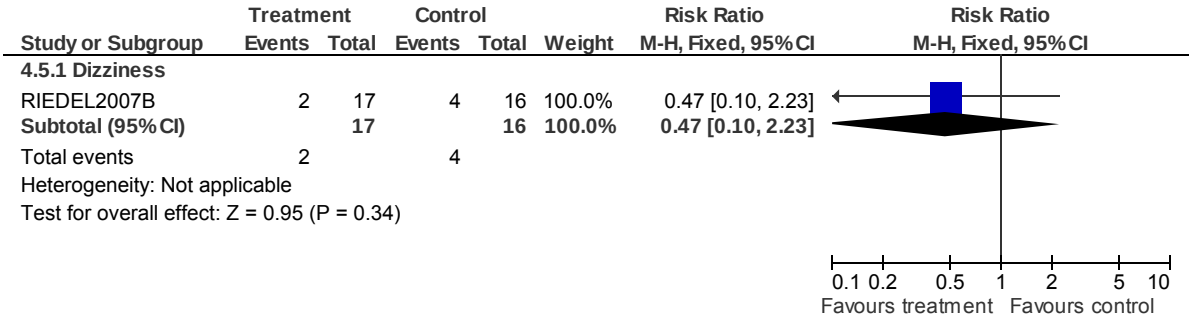
4.4 AE: 1. Metabolic SEs - Weight gain (> 7% increase from baseline) (short-term)

	Treatment		Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
RIEDEL2007B	8	17	8	16	100.0%	0.94 [0.47, 1.90]	
Total (95% CI)		**17**		**16**	**100.0%**	**0.94 [0.47, 1.90]**	
Total events	8		8				

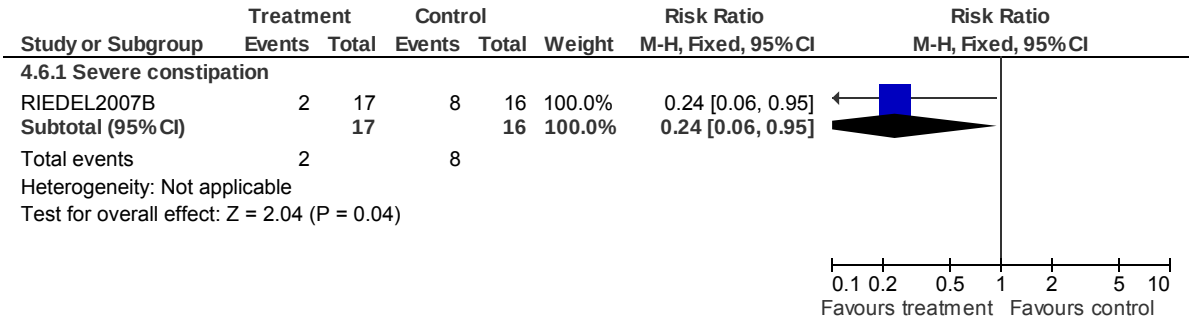
Heterogeneity: Not applicable
Test for overall effect: Z = 0.17 (P = 0.87)



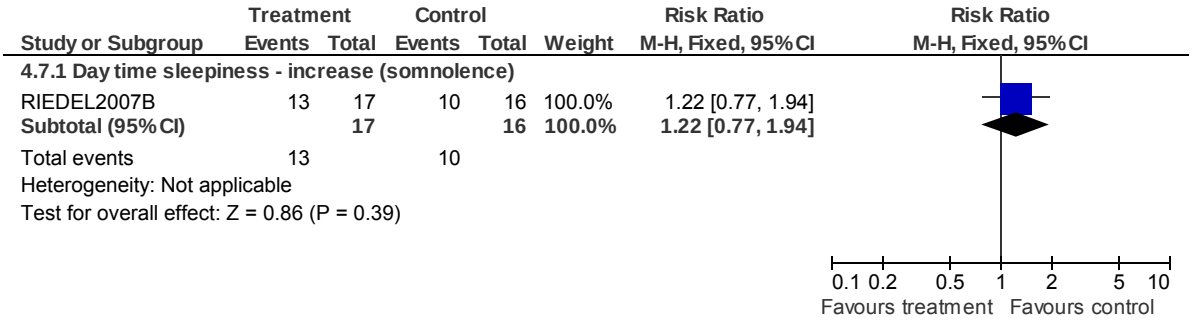
4.5 AE: 4. Cardiovascular SEs (short-term)



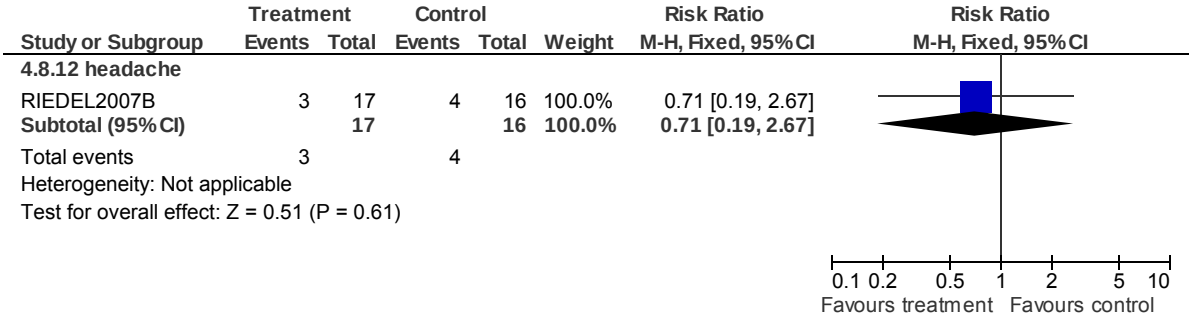
4.6 AE: 5. Gastrointestinal SEs (short-term)



4.7 AE: 6. Sedation (short-term)



4.8 AE: 9. Other SEs (short-term)



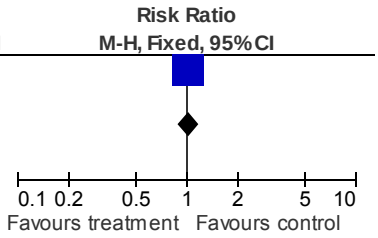
5 Olanzapine versus Risperidone (phase: acute treatment) (critical outcomes)

5.1 Global state: 1. Not improved (CGI) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Conley 2001	131	189	128	188	100.0%	1.02 [0.89, 1.17]
Total (95% CI)		**189**		**188**	**100.0%**	**1.02 [0.89, 1.17]**
Total events	131		128			

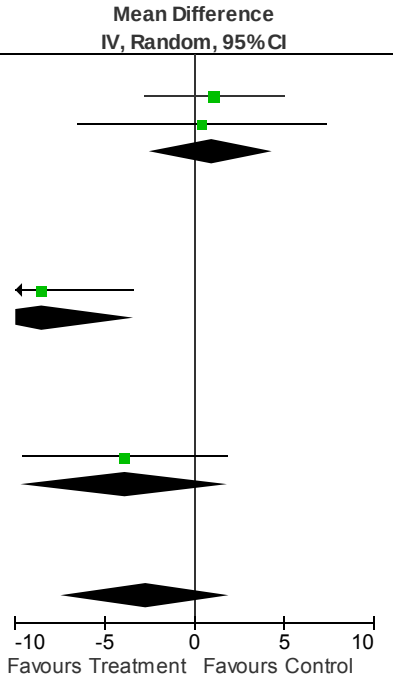
Heterogeneity: Not applicable

Test for overall effect: Z = 0.26 (P = 0.80)



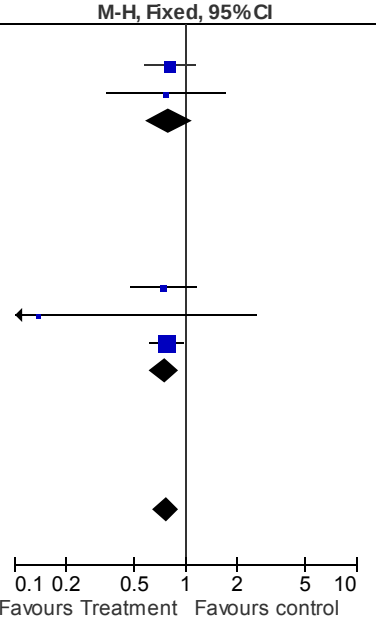
5.2 Mental state: 1. PANSS/BPRS total (endpoint, high=poor)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
5.2.1 Short-term (PANSS)								
Conley 2001	65.8	16.8	144	64.7	16.6	134	29.6%	1.10 [-2.83, 5.03]
Study S036	48.8	20.1	62	48.4	18.7	58	20.6%	0.40 [-6.54, 7.34]
Subtotal (95% CI)			**206**			**192**	**50.2%**	**0.93 [-2.49, 4.35]**
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.86); I² = 0%								
Test for overall effect: Z = 0.53 (P = 0.59)								
5.2.2 Medium-term (PANSS)								
Tran 1997	62.28	25.04	166	70.81	22.57	165	25.8%	-8.53 [-13.67, -3.39]
Subtotal (95% CI)			**166**			**165**	**25.8%**	**-8.53 [-13.67, -3.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.26 (P = 0.001)								
5.2.3 Medium-term (BPRS)								
Gureje 1998	15.5	14.2	32	19.4	8.2	30	24.0%	-3.90 [-9.63, 1.83]
Subtotal (95% CI)			**32**			**30**	**24.0%**	**-3.90 [-9.63, 1.83]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.33 (P = 0.18)								
Total (95% CI)			**404**			**387**	**100.0%**	**-2.73 [-7.43, 1.97]**
Heterogeneity: Tau² = 15.38; Chi² = 9.41, df = 3 (P = 0.02); I² = 68%								
Test for overall effect: Z = 1.14 (P = 0.25)								



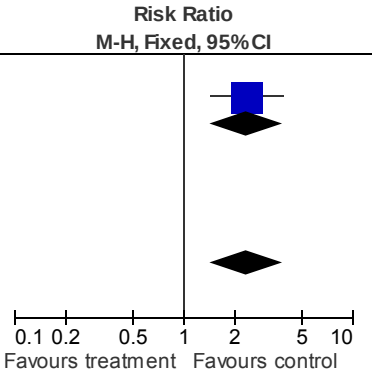
5.3 Leaving the study early: 1. Any reason

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.3.1 Short-term						
Conley 2001	43	189	53	188	29.9%	0.81 [0.57, 1.14]
Study S036	9	63	11	59	6.4%	0.77 [0.34, 1.72]
Subtotal (95% CI)		**252**		**247**	**36.4%**	**0.80 [0.58, 1.10]**
Total events	52		64			
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.91); I² = 0%						
Test for overall effect: Z = 1.37 (P = 0.17)						
5.3.2 Medium-term						
Gureje 1998	15	32	21	33	11.7%	0.74 [0.47, 1.16]
Malyarov 1999	0	15	2	10	1.7%	0.14 [0.01, 2.60]
Tran 1997	70	172	88	167	50.3%	0.77 [0.61, 0.97]
Subtotal (95% CI)		**219**		**210**	**63.6%**	**0.75 [0.61, 0.92]**
Total events	85		111			
Heterogeneity: Chi² = 1.35, df = 2 (P = 0.51); I² = 0%						
Test for overall effect: Z = 2.76 (P = 0.006)						
Total (95% CI)		**471**		**457**	**100.0%**	**0.77 [0.64, 0.91]**
Total events	137		175			
Heterogeneity: Chi² = 1.43, df = 4 (P = 0.84); I² = 0%						
Test for overall effect: Z = 2.96 (P = 0.003)						



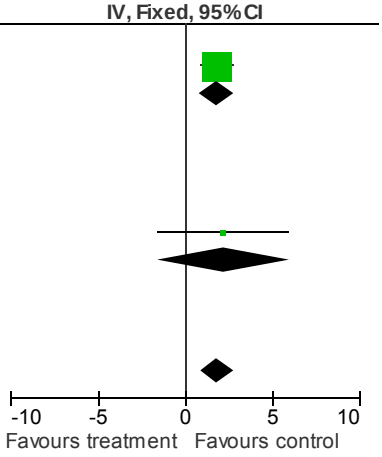
5.4 AE: 1. Metabolic SEs - Weight gain (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.4.1 Increase of >=7% body weight						
Conley 2001	44	161	18	155	100.0%	2.35 [1.42, 3.89]
Subtotal (95% CI)		**161**		**155**	**100.0%**	**2.35 [1.42, 3.89]**
Total events	44		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.34 (P = 0.0008)						
Total (95% CI)		**161**		**155**	**100.0%**	**2.35 [1.42, 3.89]**
Total events	44		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.34 (P = 0.0008)						



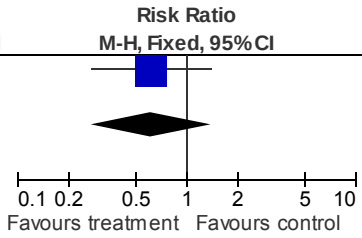
5.5 AE: 1. Metabolic SEs - Weight change from baseline (kg)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.5.1 Short-term								
Conley 2001	3.27	5.08	161	1.48	3.54	155	93.9%	1.79 [0.83, 2.75]
Subtotal (95% CI)			**161**			**155**	**93.9%**	**1.79 [0.83, 2.75]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.65 (P = 0.0003)								
5.5.2 Medium-term								
Tran 1997	80.85	19.39	166	78.69	15.51	165	6.1%	2.16 [-1.62, 5.94]
Subtotal (95% CI)			**166**			**165**	**6.1%**	**2.16 [-1.62, 5.94]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.12 (P = 0.26)								
Total (95% CI)			**327**			**320**	**100.0%**	**1.81 [0.88, 2.75]**
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.85); I² = 0%								
Test for overall effect: Z = 3.81 (P = 0.0001)								
Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.85), I² = 0%								



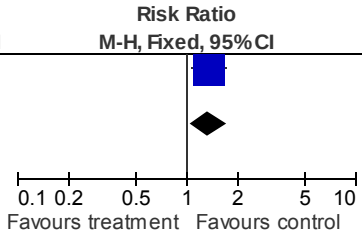
5.6 AE: 1. Metabolic SEs - Alanine transaminase (out of normal range) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Study S036	8	63	12	58	100.0%	0.61 [0.27, 1.39]
Total (95% CI)		**63**		**58**	**100.0%**	**0.61 [0.27, 1.39]**
Total events	8		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.17 (P = 0.24)						



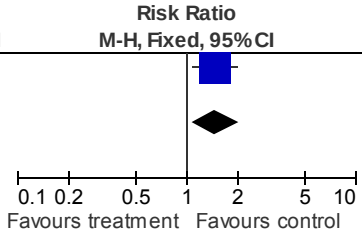
5.7 AE: 1. Metabolic SEs - LDL-C (>5% increase) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Conley 2001	94	162	52	120	100.0%	1.34 [1.05, 1.71]
Total (95% CI)		**162**		**120**	**100.0%**	**1.34 [1.05, 1.71]**
Total events	94		52			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.36 (P = 0.02)						



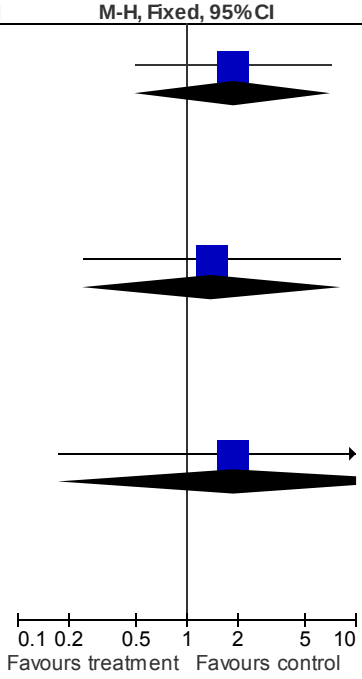
5.8 AE: 1. Metabolic SEs - Tryglycerides (>10% increase) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Conley 2001	63	138	41	132	100.0%	1.47 [1.08, 2.01]
Total (95% CI)		**138**		**132**	**100.0%**	**1.47 [1.08, 2.01]**
Total events	63		41			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.41 (P = 0.02)						



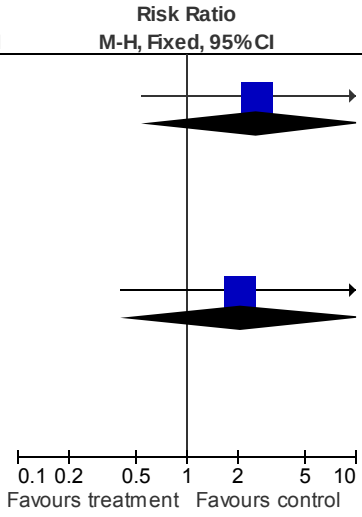
5.9 AE: 1. Metabolic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.9.1 Abnormal liver function						
Study S036	6	63	3	59	100.0%	1.87 [0.49, 7.15]
Subtotal (95% CI)		**63**		**59**	**100.0%**	**1.87 [0.49, 7.15]**
Total events	6		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.92 (P = 0.36)						
5.9.2 GI symptoms						
Study S036	3	63	2	59	100.0%	1.40 [0.24, 8.11]
Subtotal (95% CI)		**63**		**59**	**100.0%**	**1.40 [0.24, 8.11]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.38 (P = 0.70)						
5.9.3 Hyperglycemia						
Study S036	2	63	1	59	100.0%	1.87 [0.17, 20.12]
Subtotal (95% CI)		**63**		**59**	**100.0%**	**1.87 [0.17, 20.12]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.52 (P = 0.60)						



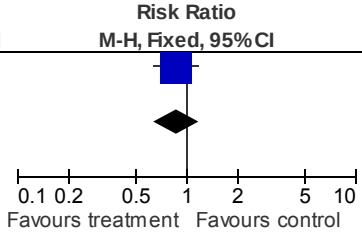
5.10 AE: 1. Metabolic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.10.1 Weight gain						
Gureje 1998	5	32	2	33	100.0%	2.58 [0.54, 12.34]
Subtotal (95% CI)		**32**		**33**	**100.0%**	**2.58 [0.54, 12.34]**
Total events	5		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.19 (P = 0.24)						
5.10.2 Increased appetite						
Gureje 1998	4	32	2	33	100.0%	2.06 [0.41, 10.49]
Subtotal (95% CI)		**32**		**33**	**100.0%**	**2.06 [0.41, 10.49]**
Total events	4		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.87 (P = 0.38)						



5.11 AE: 2. Neurologic SEs - Needing additional anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Conley 2001	53	189	61	188	100.0%	0.86 [0.64, 1.18]
Total (95% CI)		**189**		**188**	**100.0%**	**0.86 [0.64, 1.18]**
Total events	53		61			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.93 (P = 0.35)						

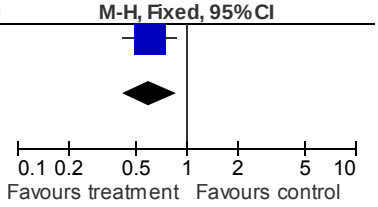


5.12 AE: 2. Neurologic SEs - Needing additional anticholinergic medication (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Tran 1997	34	172	55	167	100.0%	0.60 [0.41, 0.87]
Total (95% CI)		**172**		**167**	**100.0%**	**0.60 [0.41, 0.87]**
Total events	34		55			

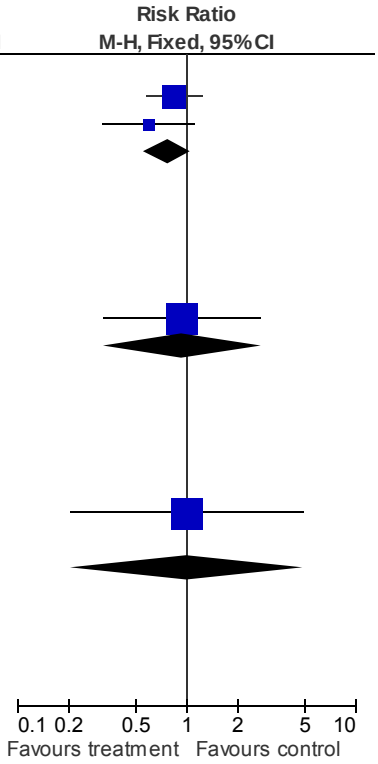
Heterogeneity: Not applicable

Test for overall effect: Z = 2.70 (P = 0.007)



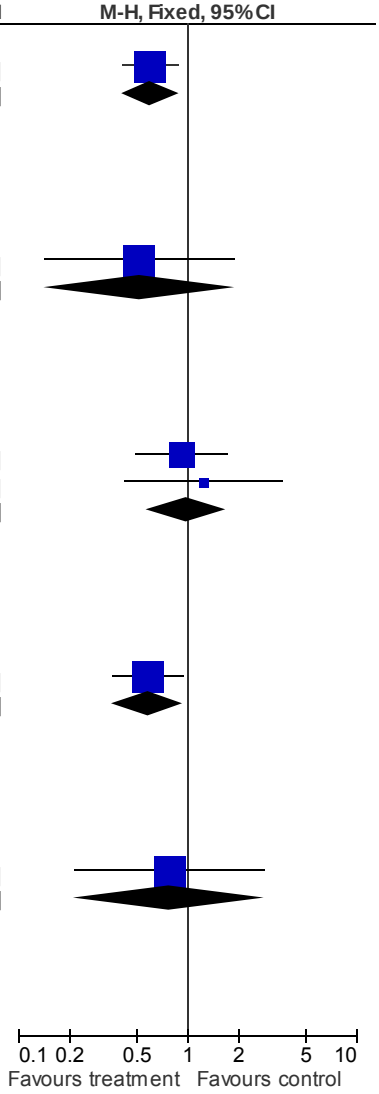
5.13 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.13.1 Any extrapyramidal event						
Conley 2001	38	189	45	188	69.7%	0.84 [0.57, 1.23]
Study S036	12	63	19	59	30.3%	0.59 [0.32, 1.11]
Subtotal (95% CI)		**252**		**247**	**100.0%**	**0.76 [0.55, 1.06]**
Total events	50		64			
Heterogeneity: Chi² = 0.87, df = 1 (P = 0.35); I² = 0%						
Test for overall effect: Z = 1.62 (P = 0.11)						
5.13.2 Restlessness						
Study S036	6	63	6	59	100.0%	0.94 [0.32, 2.74]
Subtotal (95% CI)		**63**		**59**	**100.0%**	**0.94 [0.32, 2.74]**
Total events	6		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.12 (P = 0.90)						
5.13.3 Agitation						
Conley 2001	3	189	3	188	100.0%	0.99 [0.20, 4.87]
Study S036	0	63	0	59		Not estimable
Subtotal (95% CI)		**252**		**247**	**100.0%**	**0.99 [0.20, 4.87]**
Total events	3		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						



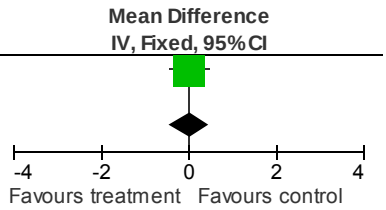
5.14 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.14.1 Any extrapyramidal event						
Tran 1997	32	172	52	167	100.0%	0.60 [0.41, 0.88]
Subtotal (95% CI)		**172**		**167**	**100.0%**	**0.60 [0.41, 0.88]**
Total events	32		52			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.62 (P = 0.009)						
5.14.2 Asthenia						
Gureje 1998	3	32	6	33	100.0%	0.52 [0.14, 1.89]
Subtotal (95% CI)		**32**		**33**	**100.0%**	**0.52 [0.14, 1.89]**
Total events	3		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.00 (P = 0.32)						
5.14.3 Akathisia						
Tran 1997	17	172	18	167	78.8%	0.92 [0.49, 1.72]
Gureje 1998	6	32	5	33	21.2%	1.24 [0.42, 3.65]
Subtotal (95% CI)		**204**		**200**	**100.0%**	**0.99 [0.57, 1.69]**
Total events	23		23			
Heterogeneity: Chi² = 0.22, df = 1 (P = 0.64); I² = 0%						
Test for overall effect: Z = 0.05 (P = 0.96)						
5.14.4 New parkinsonism						
Tran 1997	22	172	37	167	100.0%	0.58 [0.36, 0.94]
Subtotal (95% CI)		**172**		**167**	**100.0%**	**0.58 [0.36, 0.94]**
Total events	22		37			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.23 (P = 0.03)						
5.14.5 Dyskinetic movements						
Tran 1997	4	172	5	167	100.0%	0.78 [0.21, 2.84]
Subtotal (95% CI)		**172**		**167**	**100.0%**	**0.78 [0.21, 2.84]**
Total events	4		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.38 (P = 0.70)						



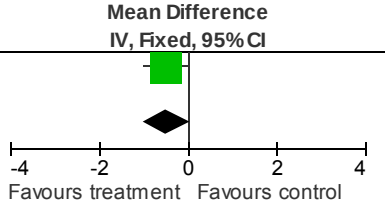
5.15 AE: 2. Neurologic SEs - Barnes Akathisia Scale (BAS; endpt mean) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Study S036	0.5	1.2	58	0.5	1.3	52	100.0%	0.00 [-0.47, 0.47]
Total (95% CI)			**58**			**52**	**100.0%**	**0.00 [-0.47, 0.47]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								



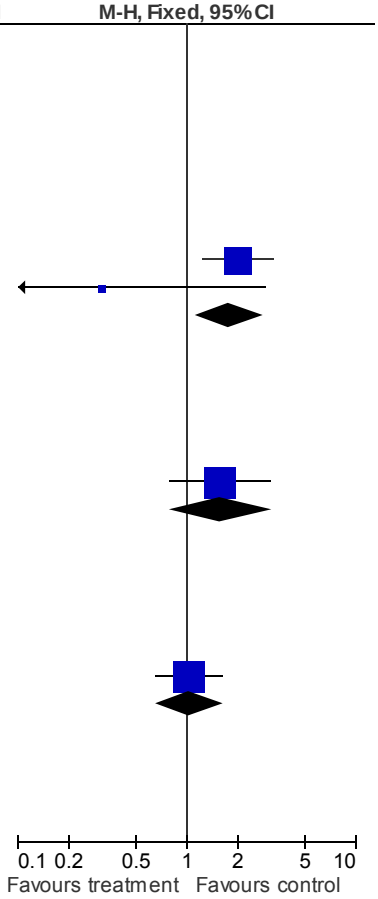
5.16 AE: 2. Neurologic SEs - Simpson-Angus Scale (SAS; endpt mean) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Study S036	0.2	0.7	58	0.7	1.8	52	100.0%	-0.50 [-1.02, 0.02]
Total (95% CI)			**58**			**52**	**100.0%**	**-0.50 [-1.02, 0.02]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.88 (P = 0.06)								



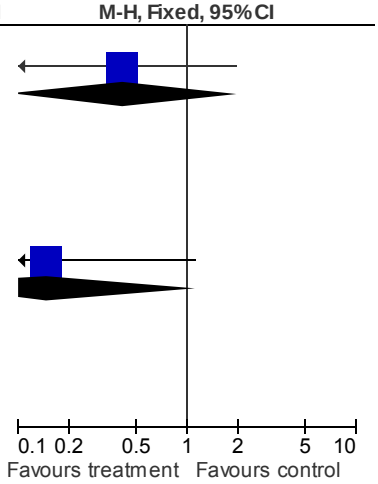
5.17 AE: 3. Autonomic SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.17.1 Sweating						
Study S036	0	63	0	59		Not estimable
Subtotal (95% CI)		**63**		**59**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
5.17.2 Dry mouth						
Conley 2001	42	189	21	188	87.2%	1.99 [1.23, 3.23]
Study S036	1	63	3	59	12.8%	0.31 [0.03, 2.92]
Subtotal (95% CI)		**252**		**247**	**100.0%**	**1.77 [1.12, 2.82]**
Total events	43		24			
Heterogeneity: Chi² = 2.54, df = 1 (P = 0.11); I² = 61%						
Test for overall effect: Z = 2.43 (P = 0.02)						
5.17.3 Vision abnormalities						
Conley 2001	19	189	12	188	100.0%	1.57 [0.79, 3.15]
Subtotal (95% CI)		**189**		**188**	**100.0%**	**1.57 [0.79, 3.15]**
Total events	19		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.28 (P = 0.20)						
5.17.4 Rhinitis						
Conley 2001	31	189	30	188	100.0%	1.03 [0.65, 1.63]
Subtotal (95% CI)		**189**		**188**	**100.0%**	**1.03 [0.65, 1.63]**
Total events	31		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.12 (P = 0.91)						



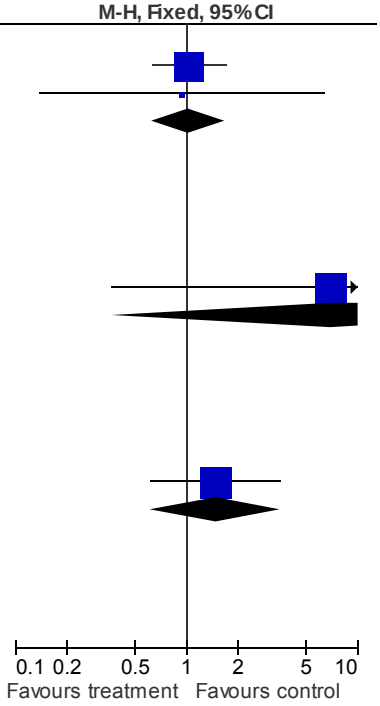
5.18 AE: 3. Autonomic SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.18.1 Increased salivation						
Gureje 1998	2	32	5	33	100.0%	0.41 [0.09, 1.97]
Subtotal (95% CI)		**32**		**33**	**100.0%**	**0.41 [0.09, 1.97]**
Total events	2		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.11 (P = 0.27)						
5.18.2 Rhinitis						
Gureje 1998	1	32	7	33	100.0%	0.15 [0.02, 1.13]
Subtotal (95% CI)		**32**		**33**	**100.0%**	**0.15 [0.02, 1.13]**
Total events	1		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.84 (P = 0.07)						



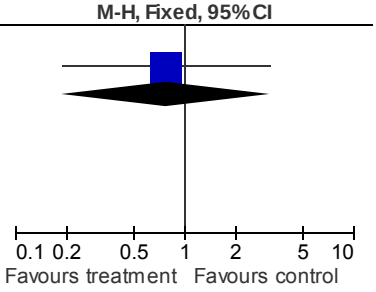
5.19 AE: 4. Cardiovascular SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.19.1 Dizziness						
Conley 2001	27	189	26	188	92.7%	1.03 [0.63, 1.70]
Study S036	2	63	2	59	7.3%	0.94 [0.14, 6.44]
Subtotal (95% CI)		**252**		**247**	**100.0%**	**1.03 [0.63, 1.66]**
Total events	29		28			
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.92); I² = 0%						
Test for overall effect: Z = 0.10 (P = 0.92)						
5.19.2 Cardiovascular symptoms						
Conley 2001	3	189	0	188	100.0%	6.96 [0.36, 133.88]
Subtotal (95% CI)		**189**		**188**	**100.0%**	**6.96 [0.36, 133.88]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.29 (P = 0.20)						
5.19.3 Cardiovascular syndrome						
Study S036	11	63	7	59	100.0%	1.47 [0.61, 3.54]
Subtotal (95% CI)		**63**		**59**	**100.0%**	**1.47 [0.61, 3.54]**
Total events	11		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.86 (P = 0.39)						



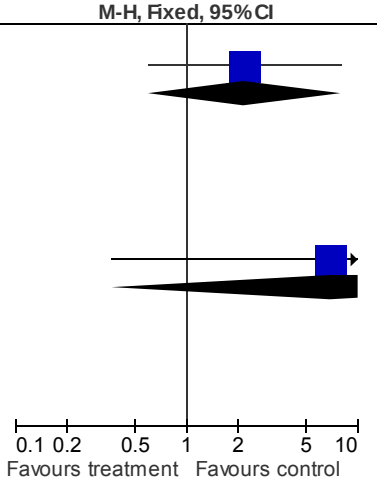
5.20 AE: 4. Cardiovascular SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.20.1 Dizziness						
Gureje 1998	3	32	4	33	100.0%	0.77 [0.19, 3.19]
Subtotal (95% CI)		**32**		**33**	**100.0%**	**0.77 [0.19, 3.19]**
Total events	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.36 (P = 0.72)						



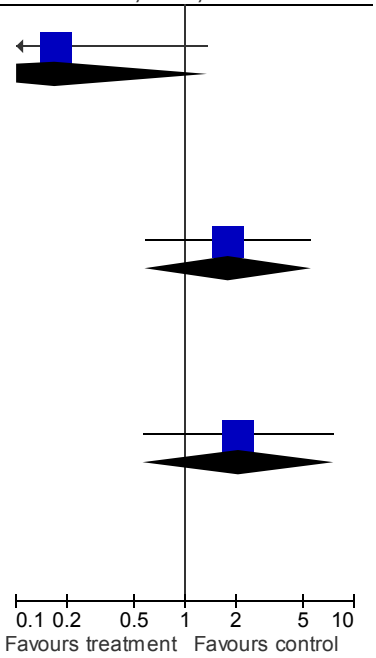
5.21 AE: 5. Gastrointestinal SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.21.1 Constipation						
Study S036	7	63	3	59	100.0%	2.19 [0.59, 8.06]
Subtotal (95% CI)		**63**		**59**	**100.0%**	**2.19 [0.59, 8.06]**
Total events	7		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.17 (P = 0.24)						
5.21.2 Gastrointestinal disorders						
Conley 2001	3	189	0	188	100.0%	6.96 [0.36, 133.88]
Subtotal (95% CI)		**189**		**188**	**100.0%**	**6.96 [0.36, 133.88]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.29 (P = 0.20)						



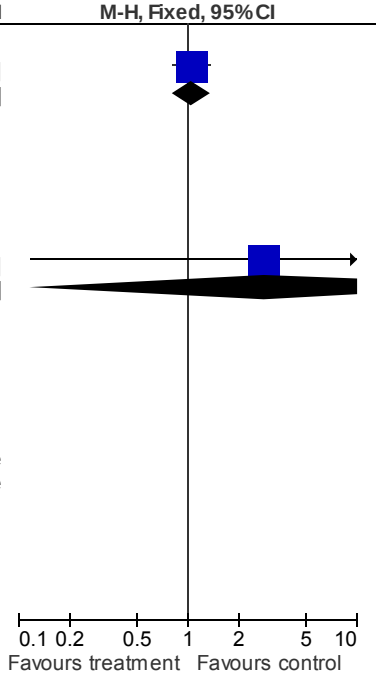
5.22 AE: 5. Gastrointestinal SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.22.1 Constipation						
Gureje 1998	1	32	6	33	100.0%	0.17 [0.02, 1.35]
Subtotal (95% CI)		**32**		**33**	**100.0%**	**0.17 [0.02, 1.35]**
Total events	1		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.68 (P = 0.09)						
5.22.2 Vomiting						
Gureje 1998	7	32	4	33	100.0%	1.80 [0.58, 5.58]
Subtotal (95% CI)		**32**		**33**	**100.0%**	**1.80 [0.58, 5.58]**
Total events	7		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.03 (P = 0.31)						
5.22.3 Abdominal pain						
Gureje 1998	6	32	3	33	100.0%	2.06 [0.56, 7.55]
Subtotal (95% CI)		**32**		**33**	**100.0%**	**2.06 [0.56, 7.55]**
Total events	6		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.09 (P = 0.27)						



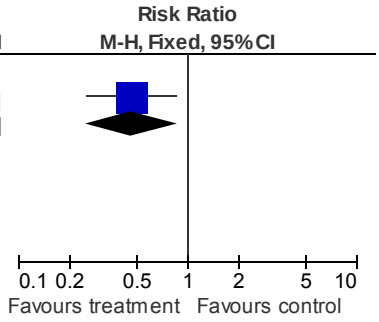
5.23 AE: 6. Sedation (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.23.1 Day time sleepiness - increase (somnolence)						
Conley 2001	73	189	69	188	100.0%	1.05 [0.81, 1.36]
Subtotal (95% CI)		**189**		**188**	**100.0%**	**1.05 [0.81, 1.36]**
Total events	73		69			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.38 (P = 0.70)						
5.23.2 Lethargy						
Study S036	1	63	0	59	100.0%	2.81 [0.12, 67.71]
Subtotal (95% CI)		**63**		**59**	**100.0%**	**2.81 [0.12, 67.71]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.64 (P = 0.52)						
5.23.3 Fatigue						
Study S036	0	63	0	59		Not estimable
Subtotal (95% CI)		**63**		**59**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



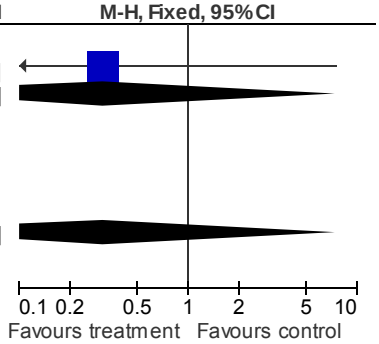
5.24 AE: 6. Sedation (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.24.1 Day time sleepiness - increase (somnolence)						
Gureje 1998	9	32	20	33	100.0%	0.46 [0.25, 0.86]
Subtotal (95% CI)		**32**		**33**	**100.0%**	**0.46 [0.25, 0.86]**
Total events	9		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.43 (P = 0.01)						

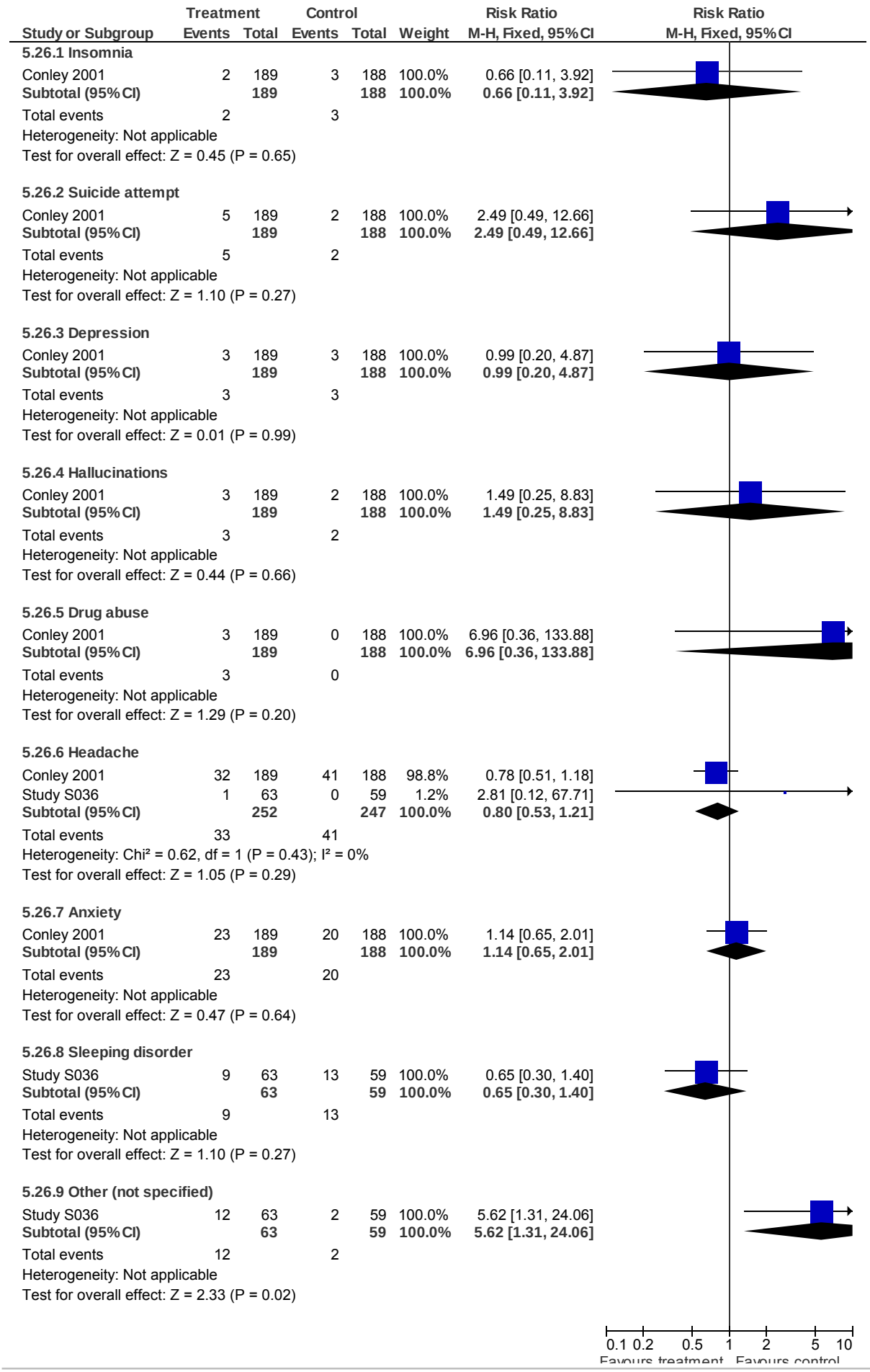


5.25 AE: 9. Dermatological system (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.25.1 Rash						
Study S036	0	63	1	59	100.0%	0.31 [0.01, 7.52]
Subtotal (95% CI)		**63**		**59**	**100.0%**	**0.31 [0.01, 7.52]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.72 (P = 0.47)						
Total (95% CI)		**63**		**59**	**100.0%**	**0.31 [0.01, 7.52]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.72 (P = 0.47)						

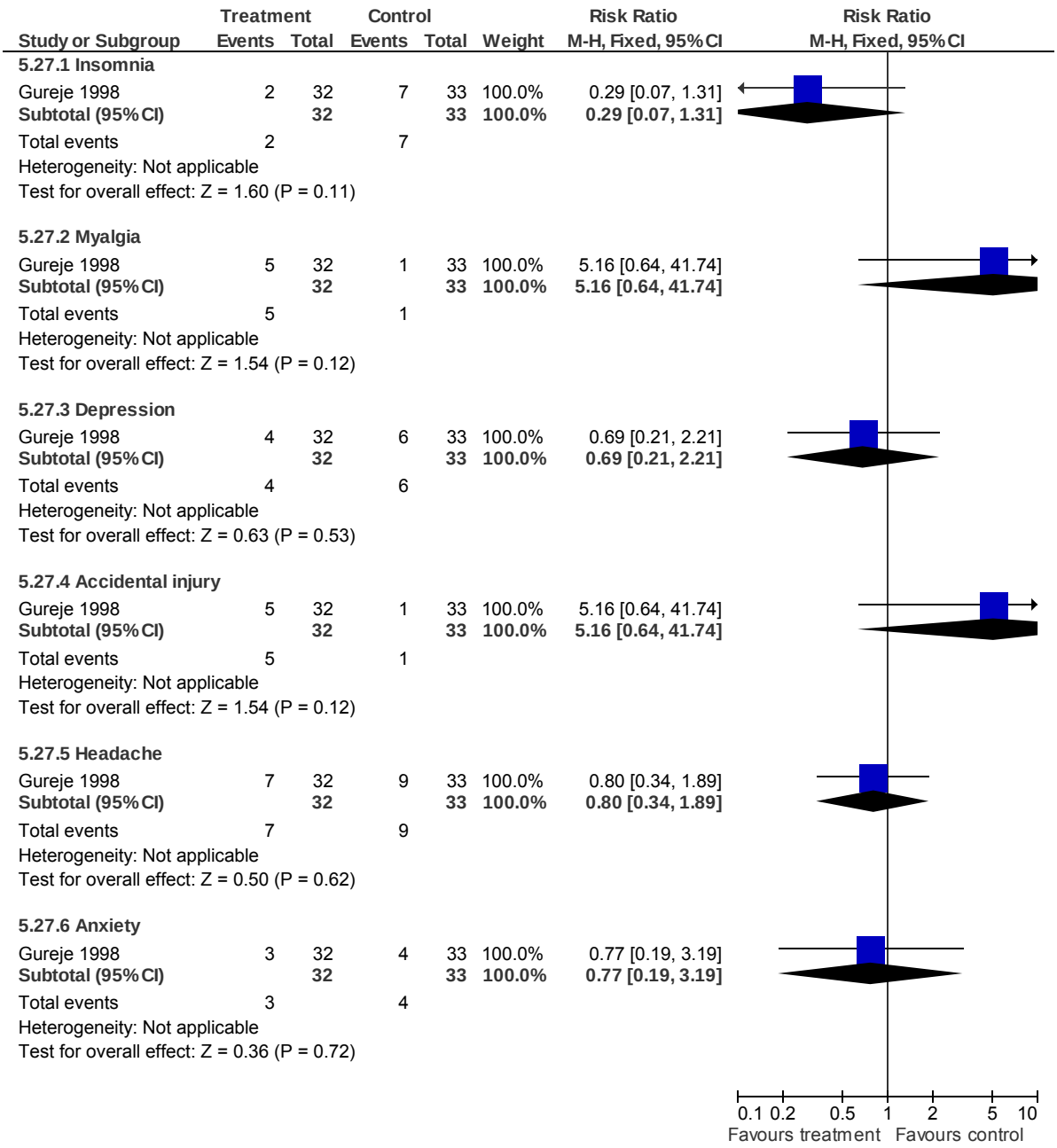


5.26 AE: 10. Other SEs (short-term)



Favours treatment
Favours control

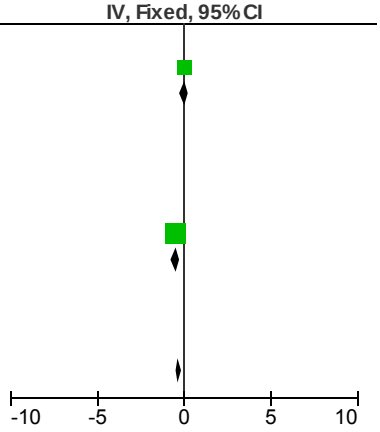
5.27 AE: 10. Other SEs (medium-term)



6 Olanzapine versus Ziprasidone (phase: acute treatment) (critical outcomes)

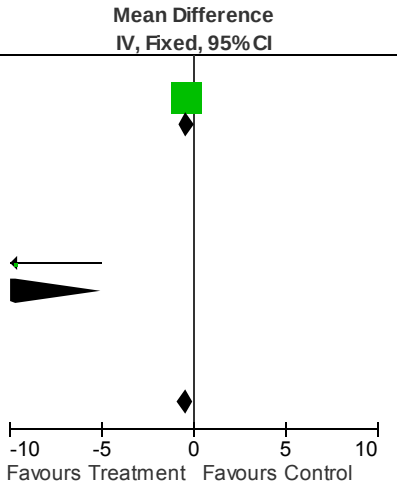
6.1 Global state: 1. CGI-S (endpoint/change)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.1.1 Short-term								
Study R-0548	3.6	1.3	133	3.6	1.17	136	39.3%	0.00 [-0.30, 0.30]
Subtotal (95% CI)			**133**			**136**	**39.3%**	**0.00 [-0.30, 0.30]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
6.1.2 Medium-term								
BREIER2005	-1.6	1.4	268	-1.1	1.4	263	60.7%	-0.50 [-0.74, -0.26]
Subtotal (95% CI)			**268**			**263**	**60.7%**	**-0.50 [-0.74, -0.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.11 (P < 0.0001)								
Total (95% CI)			**401**			**399**	**100.0%**	**-0.30 [-0.49, -0.12]**
Heterogeneity: Chi² = 6.66, df = 1 (P = 0.010); I² = 85%								
Test for overall effect: Z = 3.20 (P = 0.001)								
Test for subgroup differences: Chi² = 6.66, df = 1 (P = 0.010), I² = 85.0%								



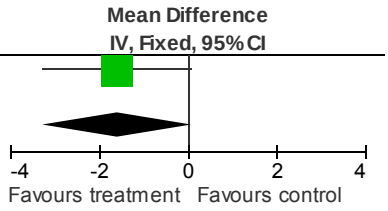
6.2 Mental state: 1. PANSS total (change from baseline)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.2.1 Short-term								
Study R-0548	-19.41	1.75	133	-19.02	1.87	136	99.2%	-0.39 [-0.82, 0.04]
Subtotal (95% CI)			**133**			**136**	**99.2%**	**-0.39 [-0.82, 0.04]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.77 (P = 0.08)								
6.2.2 Medium-term								
BREIER2005	-35.7	26.5	268	-26	28.3	261	0.8%	-9.70 [-14.37, -5.03]
Subtotal (95% CI)			**268**			**261**	**0.8%**	**-9.70 [-14.37, -5.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.07 (P < 0.0001)								
Total (95% CI)			**401**			**397**	**100.0%**	**-0.47 [-0.90, -0.04]**
Heterogeneity: Chi² = 15.11, df = 1 (P = 0.0001); I² = 93%								
Test for overall effect: Z = 2.13 (P = 0.03)								
Test for subgroup differences: Chi² = 15.11, df = 1 (P = 0.0001), I² = 93.4%								



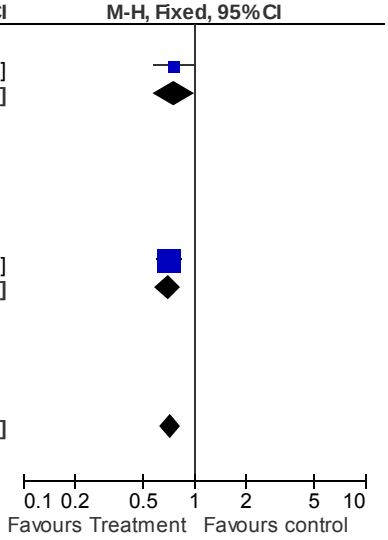
6.3 Mental state: 3. Depression (Montgomery-Asberg Dep Rating Scale) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
BREIER2005	-7.1	10	270	-5.5	9.8	260	100.0%	-1.60 [-3.29, 0.09]
Total (95% CI)			**270**			**260**	**100.0%**	**-1.60 [-3.29, 0.09]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.86 (P = 0.06)								



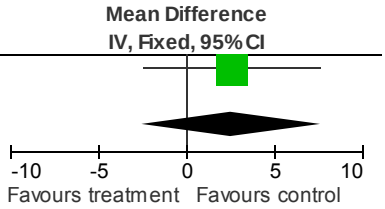
6.4 Leaving the study early: 1. Any reason (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.4.1 Short-term						
Study R-0548	49	133	66	136	29.3%	0.76 [0.57, 1.01]
Subtotal (95% CI)		**133**		**136**	**29.3%**	**0.76 [0.57, 1.01]**
Total events	49		66			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.92 (P = 0.06)						
6.4.2 Medium-term						
BREIER2005	112	277	156	271	70.7%	0.70 [0.59, 0.84]
Subtotal (95% CI)		**277**		**271**	**70.7%**	**0.70 [0.59, 0.84]**
Total events	112		156			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.94 (P < 0.0001)						
Total (95% CI)		**410**		**407**	**100.0%**	**0.72 [0.62, 0.83]**
Total events	161		222			
Heterogeneity: Chi² = 0.21, df = 1 (P = 0.65); I² = 0%						
Test for overall effect: Z = 4.33 (P < 0.0001)						



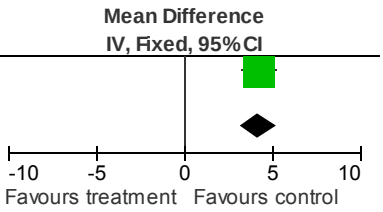
6.5 AE: 1. Metabolic SEs - Weight (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Study R-0548	88	20.43	133	85.5	21.77	136	100.0%	2.50 [-2.54, 7.54]
Total (95% CI)			**133**			**136**	**100.0%**	**2.50 [-2.54, 7.54]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.97 (P = 0.33)								

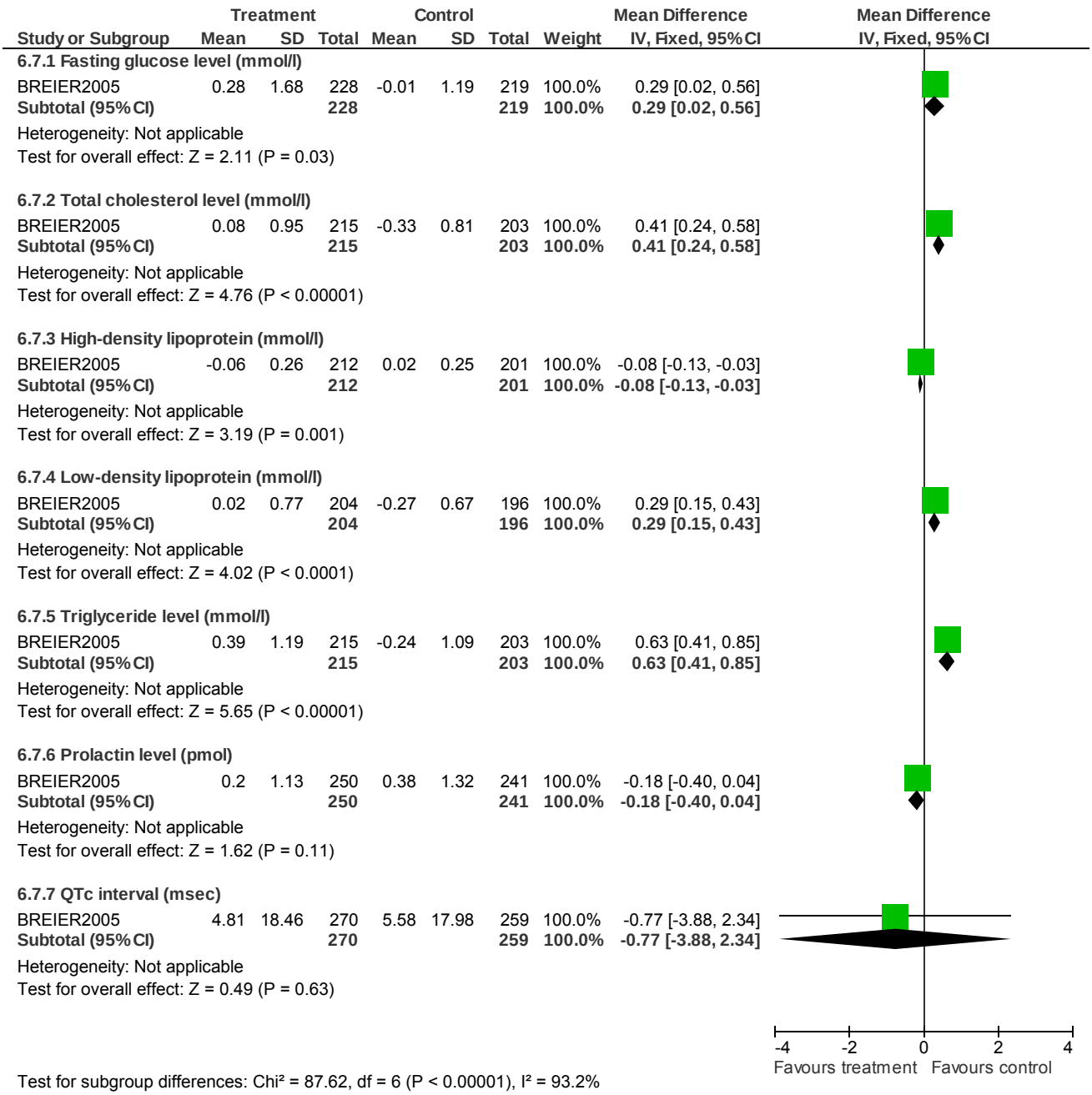


6.6 AE: 1. Metabolic SEs - Weight (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
BREIER2005	3.06	6.87	269	-1.12	4.7	260	100.0%	4.18 [3.18, 5.18]
Total (95% CI)			**269**			**260**	**100.0%**	**4.18 [3.18, 5.18]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 8.19 (P < 0.00001)								



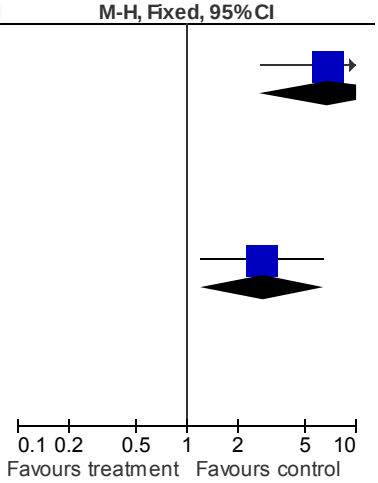
6.7 AE: 1. Metabolic SEs - Various (medium-term)



Test for subgroup differences: Chi² = 87.62, df = 6 (P < 0.00001), I² = 93.2%

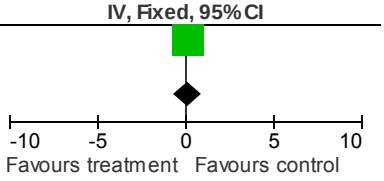
6.8 AE: 1. Metabolic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.8.1 Weight increase						
BREIER2005	35	277	5	271	100.0%	6.85 [2.72, 17.22]
Subtotal (95% CI)		**277**		**271**	**100.0%**	**6.85 [2.72, 17.22]**
Total events	35		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.09 (P < 0.0001)						
6.8.2 Appetite increase						
BREIER2005	20	277	7	271	100.0%	2.80 [1.20, 6.50]
Subtotal (95% CI)		**277**		**271**	**100.0%**	**2.80 [1.20, 6.50]**
Total events	20		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.39 (P = 0.02)						



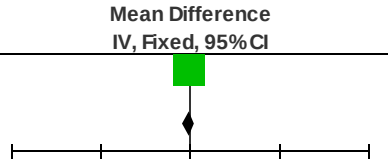
6.9 AE: 2. Neurologic SEs - Involuntary Movement Scale (AIMS; short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Study R-0548	1.4	3.39	133	1.3	2.86	136	100.0%	0.10 [-0.65, 0.85]
Total (95% CI)			**133**			**136**	**100.0%**	**0.10 [-0.65, 0.85]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.26 (P = 0.79)								



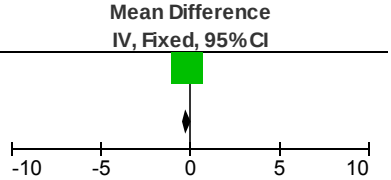
6.10 AE: 2. Neurologic SEs - Involuntary Movement Scale (AIMS; medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
BREIER2005	-0.53	2.14	270	-0.45	2.14	261	100.0%	-0.08 [-0.44, 0.28]
Total (95% CI)			**270**			**261**	**100.0%**	**-0.08 [-0.44, 0.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.43 (P = 0.67)								



6.11 AE: 2. Neurologic SEs - Barnes Akathisia Scale (BAS; short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Study R-0548	0.5	0.86	133	0.7	1.04	136	100.0%	-0.20 [-0.43, 0.03]
Total (95% CI)			**133**			**136**	**100.0%**	**-0.20 [-0.43, 0.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.72 (P = 0.09)								

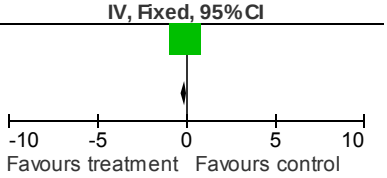


6.12 AE: 2. Neurologic SEs - Barnes Akathisia Scale (BAS; medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95%CI
BREIER2005	-0.21	0.8	270	-0.1	0.85	260	100.0%	-0.11 [-0.25, 0.03]
Total (95%CI)			**270**			**260**	**100.0%**	**-0.11 [-0.25, 0.03]**

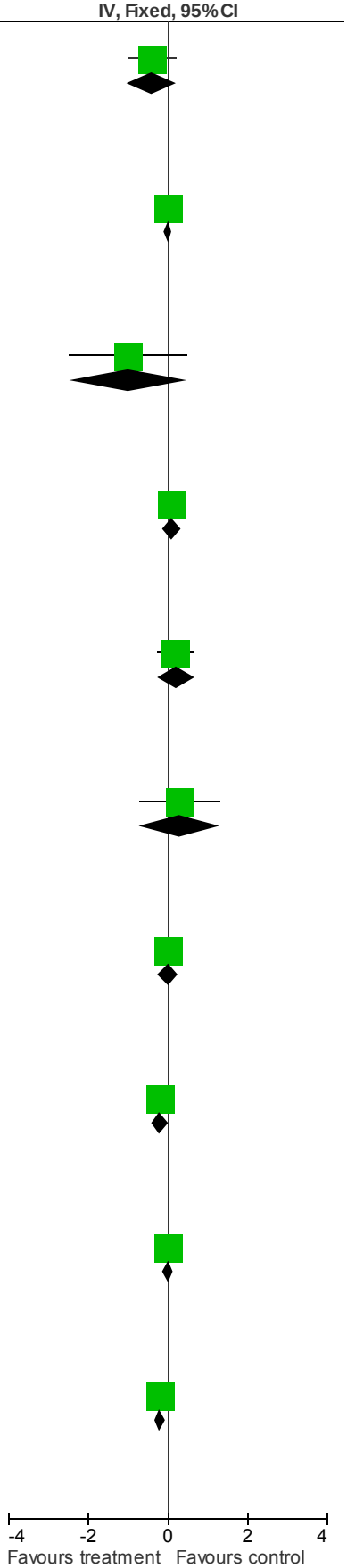
Heterogeneity: Not applicable

Test for overall effect: Z = 1.53 (P = 0.13)



6.13 AE: 2. Neurologic SEs - Extrapyramidal side effect rating scales (ESRS) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.13.1 Behavioural								
Study R-0548	1.4	2.72	133	1.8	2.37	136	100.0%	-0.40 [-1.01, 0.21]
Subtotal (95% CI)			**133**			**136**	**100.0%**	**-0.40 [-1.01, 0.21]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.28 (P = 0.20)								
6.13.2 Dizziness								
Study R-0548	0.1	0.3	133	0.1	0.39	136	100.0%	0.00 [-0.08, 0.08]
Subtotal (95% CI)			**133**			**136**	**100.0%**	**0.00 [-0.08, 0.08]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
6.13.3 Parkinsonism								
Study R-0548	3.3	6.05	133	4.3	6.34	136	100.0%	-1.00 [-2.48, 0.48]
Subtotal (95% CI)			**133**			**136**	**100.0%**	**-1.00 [-2.48, 0.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.32 (P = 0.19)								
6.13.4 Acute dystonia								
Study R-0548	0.1	1.44	133	0	0.09	136	100.0%	0.10 [-0.15, 0.35]
Subtotal (95% CI)			**133**			**136**	**100.0%**	**0.10 [-0.15, 0.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.80 (P = 0.42)								
6.13.5 Chronic/ tardive dystonia								
Study R-0548	0.4	2.5	133	0.2	1.19	136	100.0%	0.20 [-0.27, 0.67]
Subtotal (95% CI)			**133**			**136**	**100.0%**	**0.20 [-0.27, 0.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.83 (P = 0.40)								
6.13.6 Dyskinesia								
Study R-0548	1.7	4.67	133	1.4	3.72	136	100.0%	0.30 [-0.71, 1.31]
Subtotal (95% CI)			**133**			**136**	**100.0%**	**0.30 [-0.71, 1.31]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.58 (P = 0.56)								
6.13.7 Severity of dyskinesia								
Study R-0548	0.5	1.18	133	0.5	1.09	136	100.0%	0.00 [-0.27, 0.27]
Subtotal (95% CI)			**133**			**136**	**100.0%**	**0.00 [-0.27, 0.27]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
6.13.8 Severity of parkinsonism								
Study R-0548	0.4	0.82	133	0.6	0.97	136	100.0%	-0.20 [-0.41, 0.01]
Subtotal (95% CI)			**133**			**136**	**100.0%**	**-0.20 [-0.41, 0.01]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.83 (P = 0.07)								
6.13.9 Severity of dystonia								
Study R-0548	0.1	0.66	133	0.1	0.55	136	100.0%	0.00 [-0.15, 0.15]
Subtotal (95% CI)			**133**			**136**	**100.0%**	**0.00 [-0.15, 0.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
6.13.10 Stage of parkinsonism								
Study R-0548	0.1	0.41	133	0.3	0.71	136	100.0%	-0.20 [-0.34, -0.06]
Subtotal (95% CI)			**133**			**136**	**100.0%**	**-0.20 [-0.34, -0.06]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.84 (P = 0.005)								



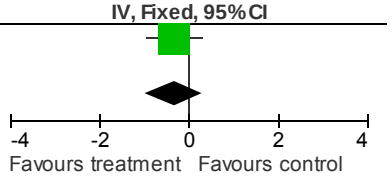
Test for subgroup differences: Chi² = 14.18, df = 9 (P = 0.12), I² = 36.5%

6.14 AE: 2. Neurologic SEs - Simpson-Angus Rating Scale (SAS) (medium-term)

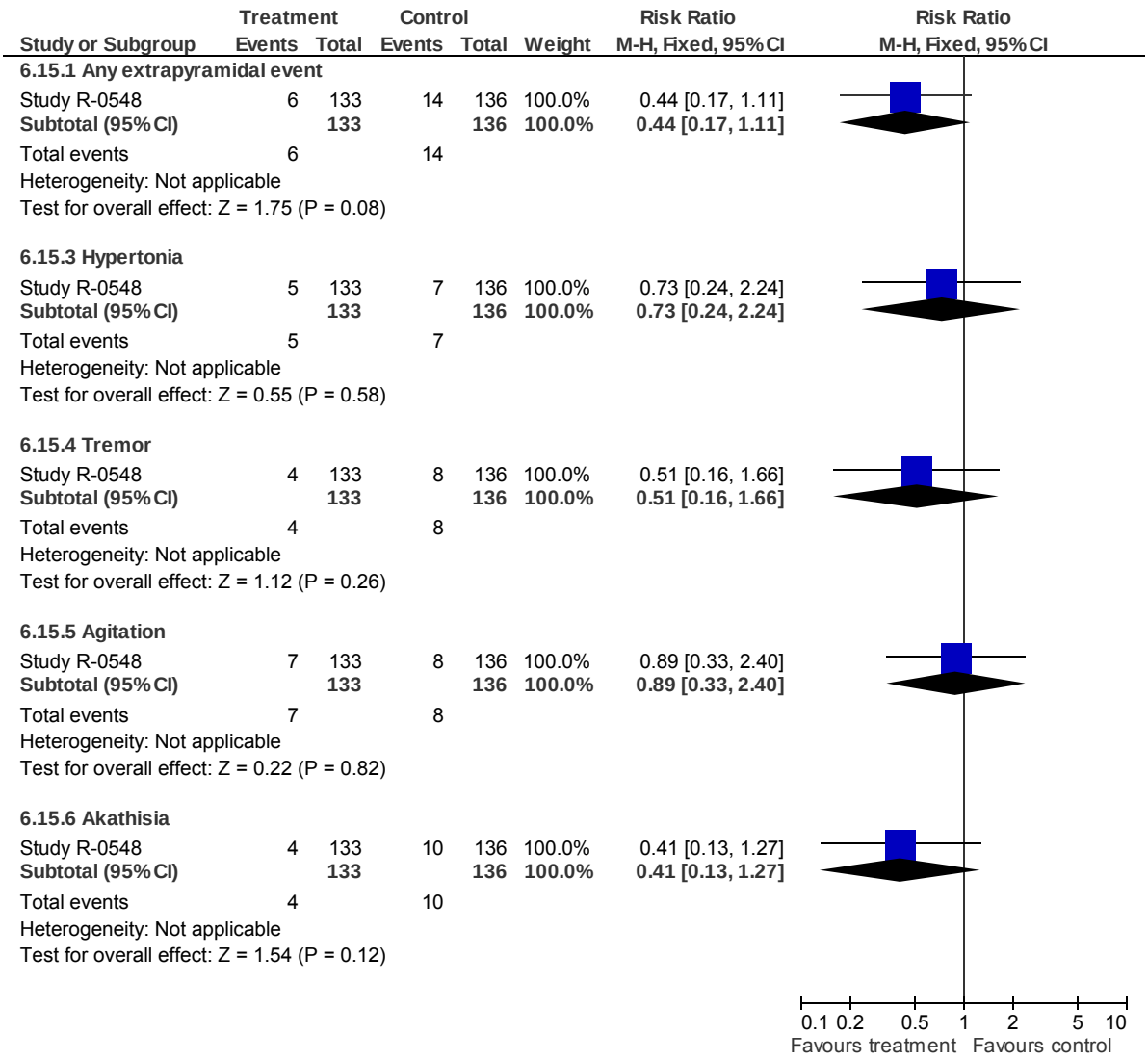
	Treatment			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
BREIER2005	-1.16	3.31	268	-0.82	4.07	260	100.0%	-0.34 [-0.97, 0.29]	
Total (95% CI)			**268**			**260**	**100.0%**	**-0.34 [-0.97, 0.29]**	

Heterogeneity: Not applicable

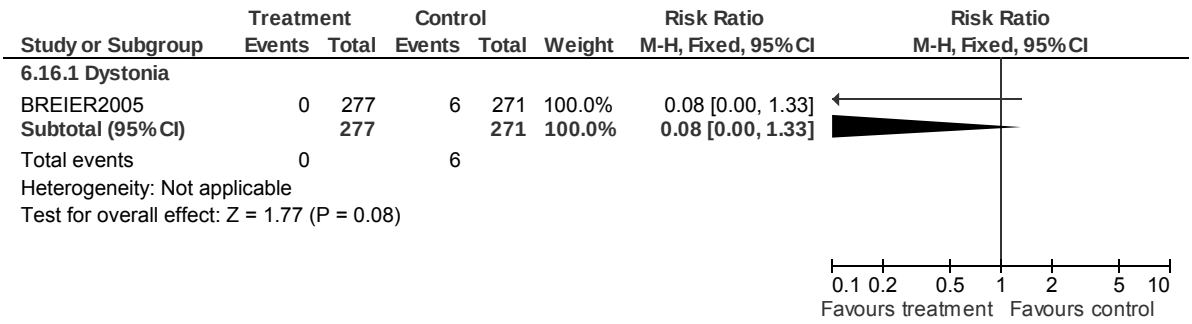
Test for overall effect: Z = 1.05 (P = 0.29)



6.15 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



6.16 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

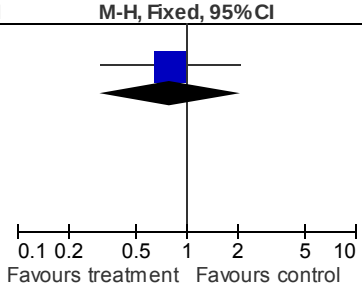


6.17 AE: 3. Autonomic SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.17.2 Dry mouth						
Study R-0548	7	133	9	136	100.0%	0.80 [0.31, 2.07]
Subtotal (95% CI)		**133**		**136**	**100.0%**	**0.80 [0.31, 2.07]**
Total events	7		9			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.47 (P = 0.64)

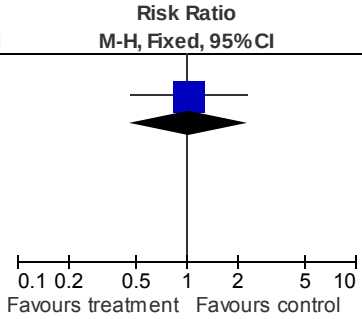


6.18 AE: 4. Cardiovascular SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.18.1 Dizziness						
Study R-0548	11	133	11	136	100.0%	1.02 [0.46, 2.28]
Subtotal (95% CI)		**133**		**136**	**100.0%**	**1.02 [0.46, 2.28]**
Total events	11		11			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.05 (P = 0.96)

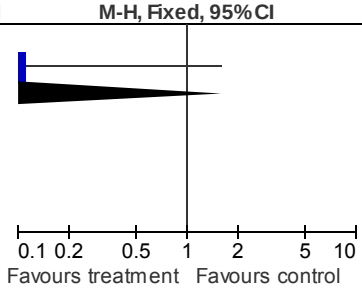


6.19 AE: 4. Cardiovascular SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.19.1 Hypotension						
BREIER2005	0	277	5	271	100.0%	0.09 [0.00, 1.60]
Subtotal (95% CI)		**277**		**271**	**100.0%**	**0.09 [0.00, 1.60]**
Total events	0		5			

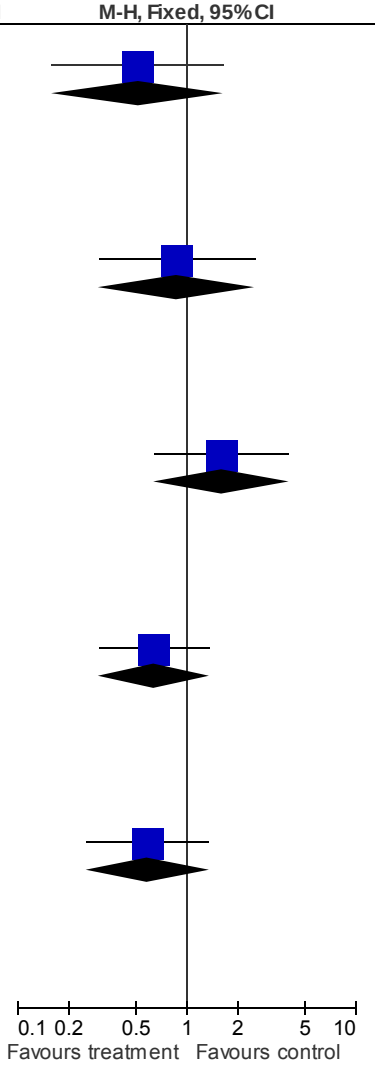
Heterogeneity: Not applicable

Test for overall effect: Z = 1.64 (P = 0.10)



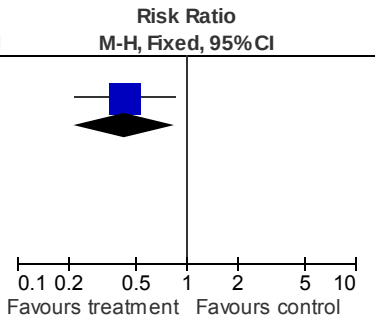
6.20 AE: 5. Gastrointestinal SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.20.1 Constipation						
Study R-0548	4	133	8	136	100.0%	0.51 [0.16, 1.66]
Subtotal (95% CI)		**133**		**136**	**100.0%**	**0.51 [0.16, 1.66]**
Total events	4		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.12 (P = 0.26)						
6.20.2 Vomiting						
Study R-0548	6	133	7	136	100.0%	0.88 [0.30, 2.54]
Subtotal (95% CI)		**133**		**136**	**100.0%**	**0.88 [0.30, 2.54]**
Total events	6		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.24 (P = 0.81)						
6.20.3 Diarrhoea						
Study R-0548	11	133	7	136	100.0%	1.61 [0.64, 4.02]
Subtotal (95% CI)		**133**		**136**	**100.0%**	**1.61 [0.64, 4.02]**
Total events	11		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.01 (P = 0.31)						
6.20.4 Dyspepsia						
Study R-0548	10	133	16	136	100.0%	0.64 [0.30, 1.36]
Subtotal (95% CI)		**133**		**136**	**100.0%**	**0.64 [0.30, 1.36]**
Total events	10		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.17 (P = 0.24)						
6.20.5 Nausea						
Study R-0548	8	133	14	136	100.0%	0.58 [0.25, 1.35]
Subtotal (95% CI)		**133**		**136**	**100.0%**	**0.58 [0.25, 1.35]**
Total events	8		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.26 (P = 0.21)						



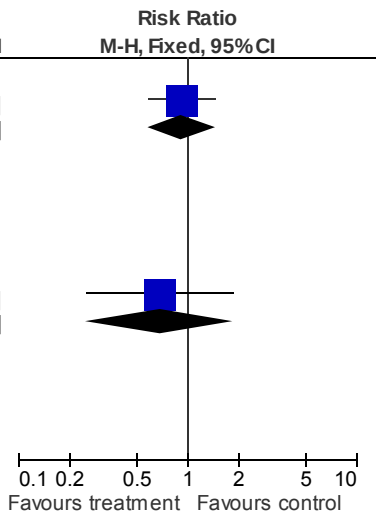
6.21 AE: 5. Gastrointestinal SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.21.1 Vomiting						
BREIER2005	11	277	25	271	100.0%	0.43 [0.22, 0.86]
Subtotal (95% CI)		**277**		**271**	**100.0%**	**0.43 [0.22, 0.86]**
Total events	11		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.40 (P = 0.02)						

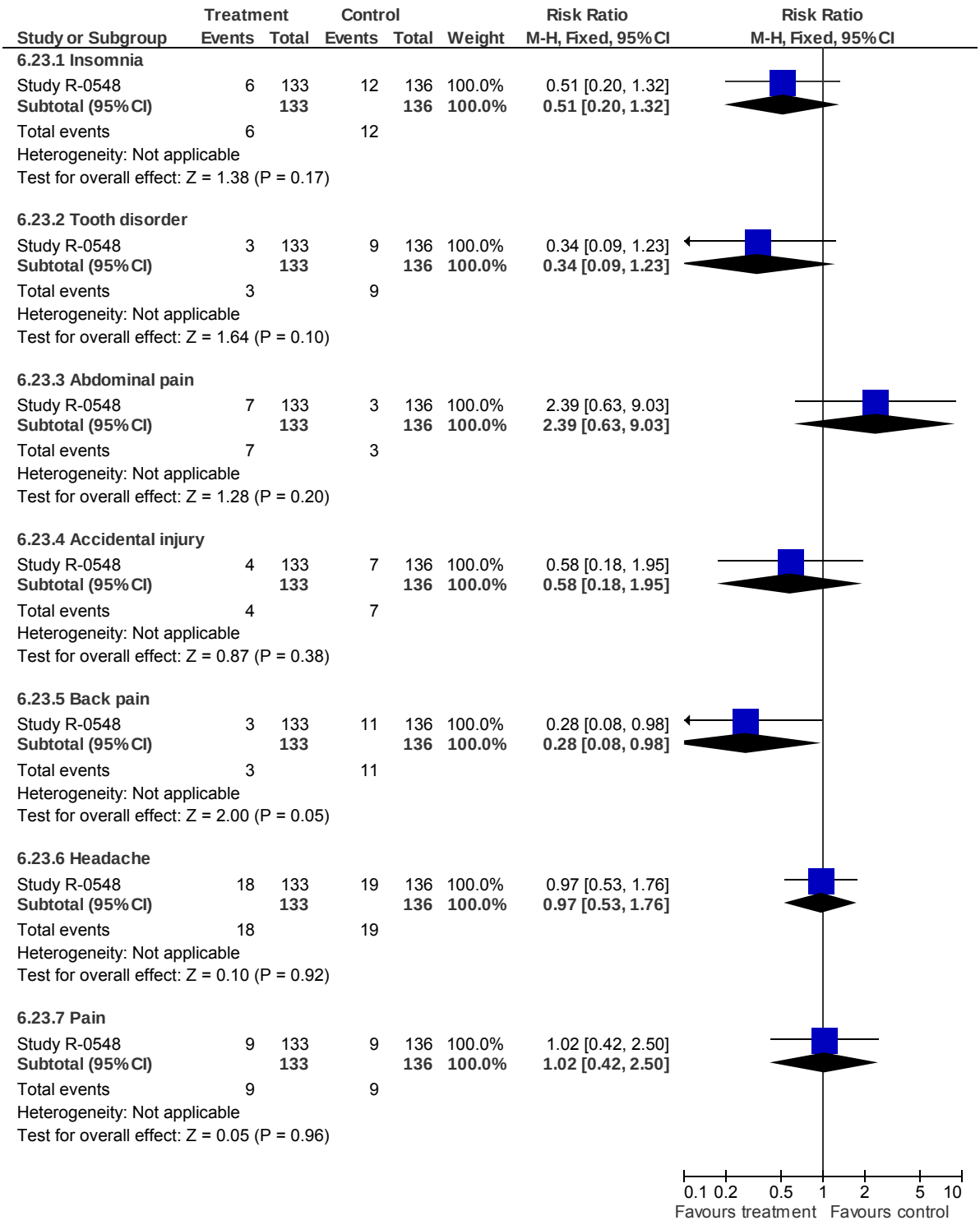


6.22 AE: 6. Sedation (short-term)

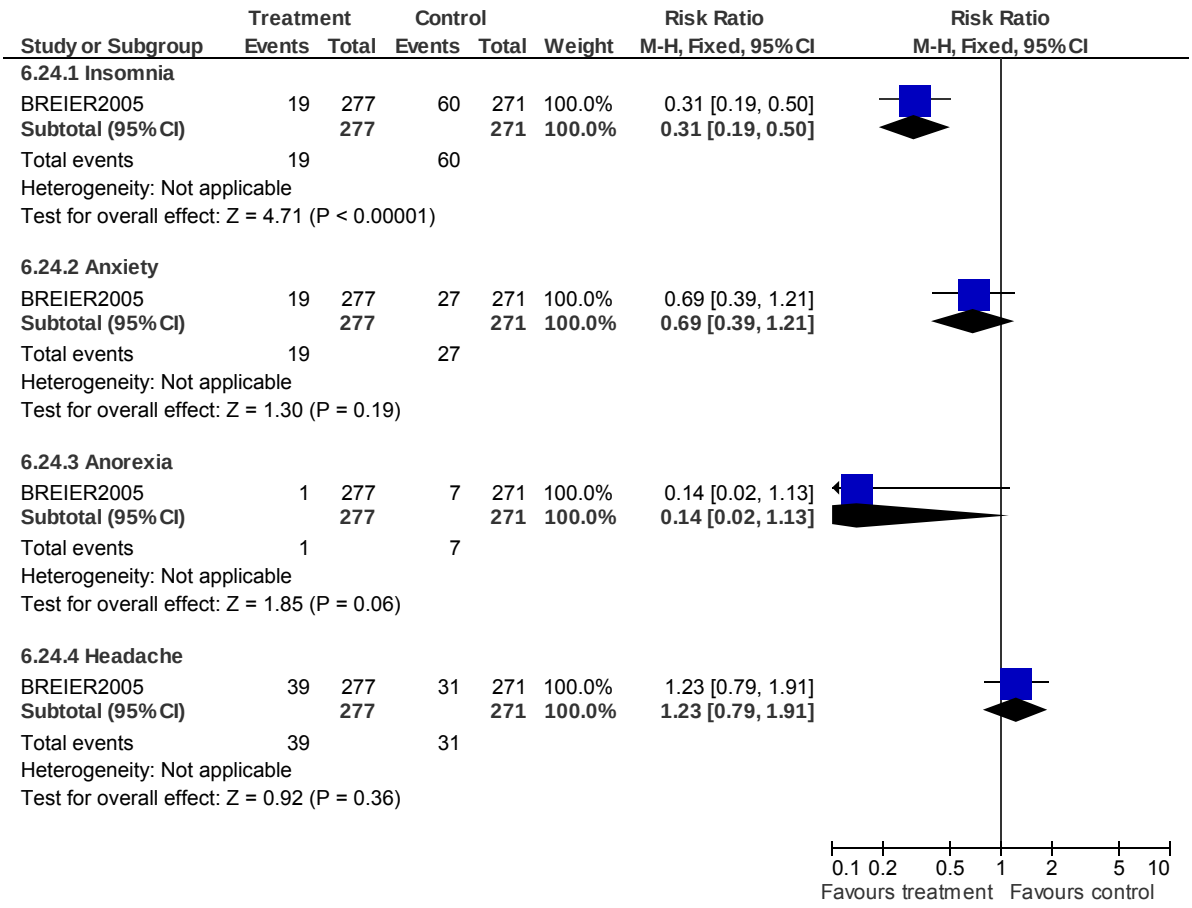
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.22.1 Day time sleepiness - increase (somnolence)						
Study R-0548	27	133	30	136	100.0%	0.92 [0.58, 1.46]
Subtotal (95% CI)		**133**		**136**	**100.0%**	**0.92 [0.58, 1.46]**
Total events	27		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.35 (P = 0.72)						
6.22.2 Asthenia						
Study R-0548	6	133	9	136	100.0%	0.68 [0.25, 1.86]
Subtotal (95% CI)		**133**		**136**	**100.0%**	**0.68 [0.25, 1.86]**
Total events	6		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.75 (P = 0.45)						



6.23 AE: 9. Other SEs (short-term)



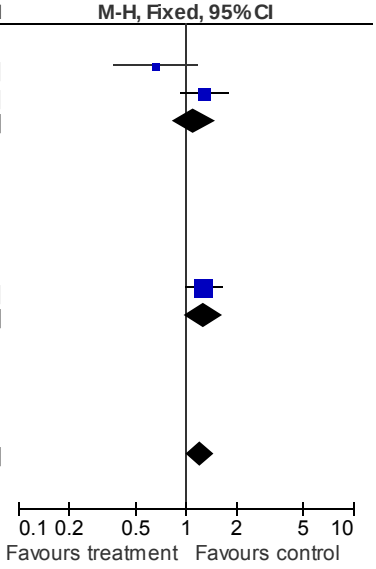
6.24 AE: 9. Other SEs (medium-term)



7 Risperidone versus Amisulpride (phase: acute treatment) (critical outcomes)

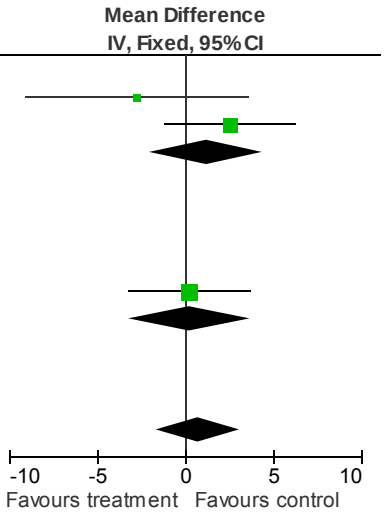
7.1 Global state: 1. Non-response (CGI) (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.1.1 Short-term						
HWANG2003	10	25	14	23	13.0%	0.66 [0.37, 1.18]
Fleurot 1997	48	113	38	115	33.5%	1.29 [0.92, 1.80]
Subtotal (95% CI)		**138**		**138**	**46.5%**	**1.11 [0.83, 1.48]**
Total events	58		52			
Heterogeneity: Chi² = 3.85, df = 1 (P = 0.05); I² = 74%						
Test for overall effect: Z = 0.71 (P = 0.48)						
7.1.2 Medium-term						
Lecrubier 2000	78	158	59	152	53.5%	1.27 [0.99, 1.64]
Subtotal (95% CI)		**158**		**152**	**53.5%**	**1.27 [0.99, 1.64]**
Total events	78		59			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.85 (P = 0.06)						
Total (95% CI)		**296**		**290**	**100.0%**	**1.20 [0.99, 1.45]**
Total events	136		111			
Heterogeneity: Chi² = 4.48, df = 2 (P = 0.11); I² = 55%						
Test for overall effect: Z = 1.84 (P = 0.07)						



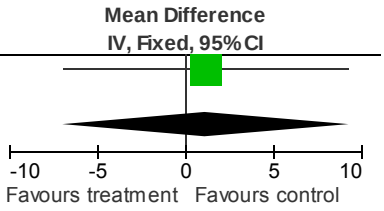
7.9 Mental state: 1. BPRS total (change from baseline)

Study or Subgroup	treatment Mean	SD	Total	control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.9.1 Short-term								
HWANG2003	-17.7	11.5	25	-14.9	10.7	22	13.9%	-2.80 [-9.15, 3.55]
Fleurot 1997	-15.2	13.9	113	-17.7	14.9	115	40.0%	2.50 [-1.24, 6.24]
Subtotal (95% CI)			**138**			**137**	**53.8%**	**1.13 [-2.09, 4.36]**
Heterogeneity: Chi² = 1.99, df = 1 (P = 0.16); I² = 50%								
Test for overall effect: Z = 0.69 (P = 0.49)								
7.9.2 Medium-term								
Lecrubier 2000	-19.6	12.6	123	-19.8	15	121	46.2%	0.20 [-3.28, 3.68]
Subtotal (95% CI)			**123**			**121**	**46.2%**	**0.20 [-3.28, 3.68]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.11 (P = 0.91)								
Total (95% CI)			**261**			**258**	**100.0%**	**0.70 [-1.66, 3.07]**
Heterogeneity: Chi² = 2.14, df = 2 (P = 0.34); I² = 6%								
Test for overall effect: Z = 0.58 (P = 0.56)								
Test for subgroup differences: Chi² = 0.15, df = 1 (P = 0.70), I² = 0%								



7.12 Psychosocial functioning: 1. SOFAS (Change from baseline) (short-term)(signs reversed)

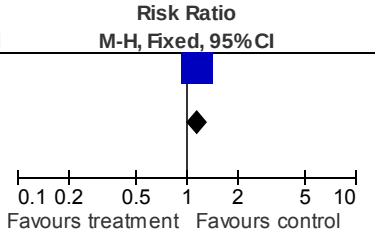
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
HWANG2003	-10	14.5	25	-11.1	13.9	22	100.0%	1.10 [-7.03, 9.23]
Total (95% CI)			**25**			**22**	**100.0%**	**1.10 [-7.03, 9.23]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.27 (P = 0.79)								



7.13 Psychosocial functioning: 2. No response (social functioning, <50% improvement on SOFA) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lecrubier 2000	122	158	102	152	100.0%	1.15 [1.00, 1.32]
Total (95% CI)		**158**		**152**	**100.0%**	**1.15 [1.00, 1.32]**
Total events	122		102			

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



7.14 Leaving the study early: 1. Any reason (short-to-medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.14.1 Short-term						
Fleurot 1997	32	113	37	113	38.7%	0.86 [0.58, 1.28]
HWANG2003	0	25	3	23	3.8%	0.13 [0.01, 2.42]
Subtotal (95% CI)		**138**		**136**	**42.5%**	**0.80 [0.54, 1.18]**
Total events	32		40			

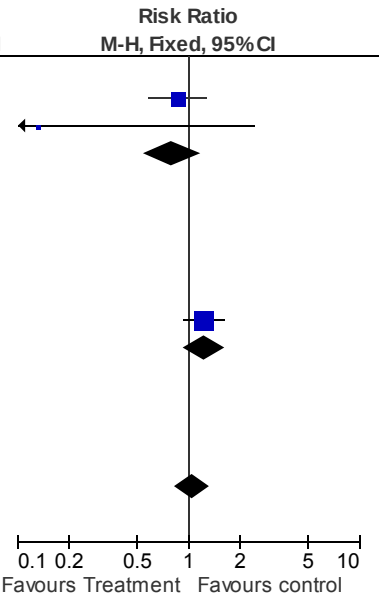
Heterogeneity: Chi² = 1.63, df = 1 (P = 0.20); I² = 38%
Test for overall effect: Z = 1.13 (P = 0.26)

7.14.2 Medium-term						
Lecrubier 2000	69	158	54	152	57.5%	1.23 [0.93, 1.62]
Subtotal (95% CI)		**158**		**152**	**57.5%**	**1.23 [0.93, 1.62]**
Total events	69		54			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.46 (P = 0.15)

Total (95% CI)		**296**		**288**	**100.0%**	**1.05 [0.84, 1.31]**
Total events	101		94			

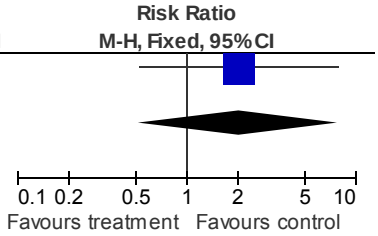
Heterogeneity: Chi² = 4.13, df = 2 (P = 0.13); I² = 52%
Test for overall effect: Z = 0.40 (P = 0.69)



7.25 AE: 1. Metabolic SEs - Weight gain (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fleurot 1997	6	113	3	114	100.0%	2.02 [0.52, 7.87]
Total (95% CI)		**113**		**114**	**100.0%**	**2.02 [0.52, 7.87]**
Total events	6		3			

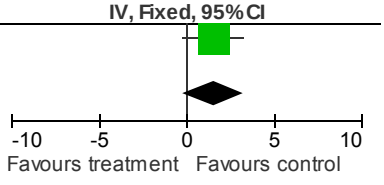
Heterogeneity: Not applicable
Test for overall effect: Z = 1.01 (P = 0.31)



7.27 AE: 1. Metabolic SEs - Weight change from baseline (kg) (short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
HWANG2003	1.6	2.8	25	0.1	3.3	22	100.0%	1.50 [-0.26, 3.26]
Total (95% CI)			**25**			**22**	**100.0%**	**1.50 [-0.26, 3.26]**

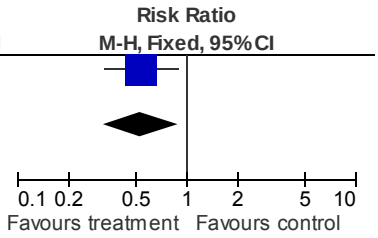
Heterogeneity: Not applicable
Test for overall effect: Z = 1.67 (P = 0.10)



7.28 AE: 1. Metabolic SEs - Weight gain (>7% from baseline) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lecrubier 2000	18	100	32	95	100.0%	0.53 [0.32, 0.89]
Total (95% CI)		**100**		**95**	**100.0%**	**0.53 [0.32, 0.89]**
Total events	18		32			

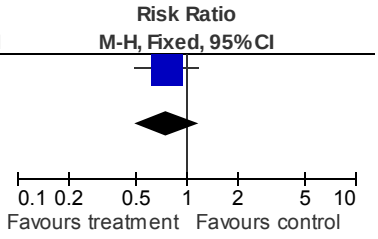
Heterogeneity: Not applicable
Test for overall effect: Z = 2.43 (P = 0.01)



7.33 AE: 2. Neurologic SEs - Needing additional anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Fleurot 1997	26	113	35	115	100.0%	0.76 [0.49, 1.17]
Total (95% CI)		**113**		**115**	**100.0%**	**0.76 [0.49, 1.17]**
Total events	26		35			

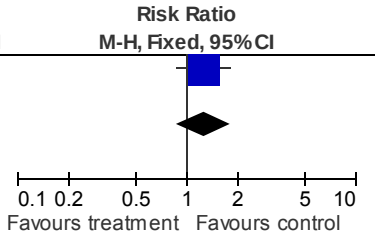
Heterogeneity: Not applicable
Test for overall effect: Z = 1.26 (P = 0.21)



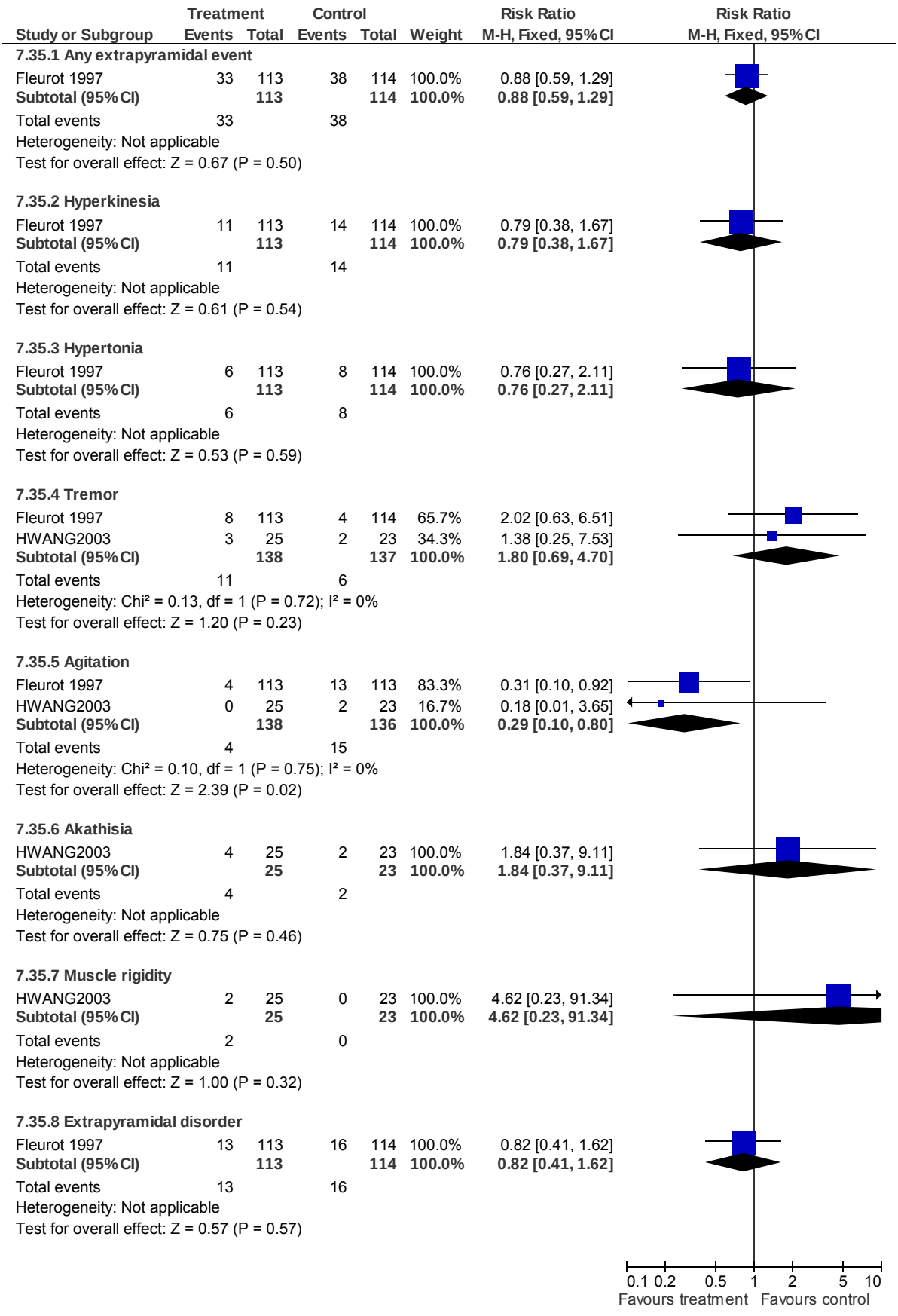
7.34 AE: 2. Neurologic SEs - Needing additional anticholinergic medication (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lecrubier 2000	47	158	36	152	100.0%	1.26 [0.87, 1.82]
Total (95% CI)		**158**		**152**	**100.0%**	**1.26 [0.87, 1.82]**
Total events	47		36			

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

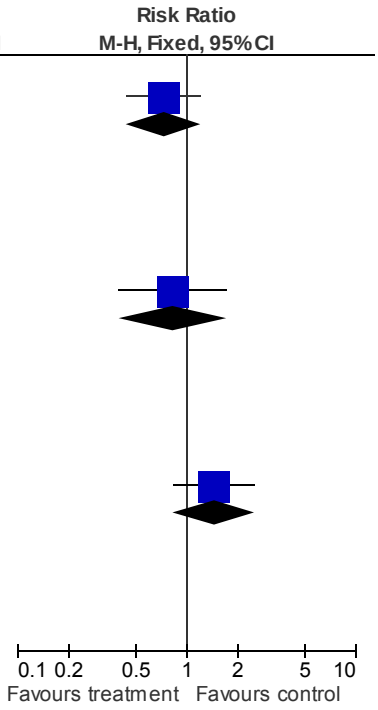


7.35 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



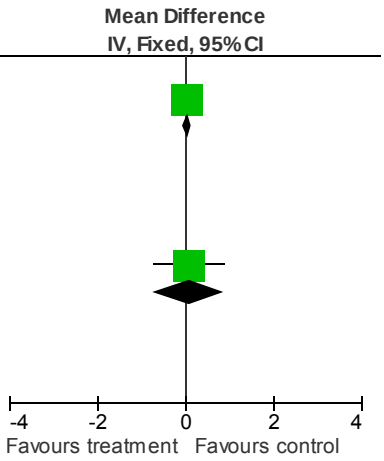
7.36 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.36.2 Hyperkinesia						
Lecrubier 2000	22	158	29	152	100.0%	0.73 [0.44, 1.21]
Subtotal (95% CI)		**158**		**152**	**100.0%**	**0.73 [0.44, 1.21]**
Total events	22		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.22 (P = 0.22)						
7.36.5 Agitation						
Lecrubier 2000	12	158	14	152	100.0%	0.82 [0.39, 1.73]
Subtotal (95% CI)		**158**		**152**	**100.0%**	**0.82 [0.39, 1.73]**
Total events	12		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.51 (P = 0.61)						
7.36.8 Extrapyramidal disorder						
Lecrubier 2000	27	158	18	152	100.0%	1.44 [0.83, 2.51]
Subtotal (95% CI)		**158**		**152**	**100.0%**	**1.44 [0.83, 2.51]**
Total events	27		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (P = 0.19)						



7.37 AE: 2. Neurologic SEs - SAS/ AIMS (change) (medium-term)

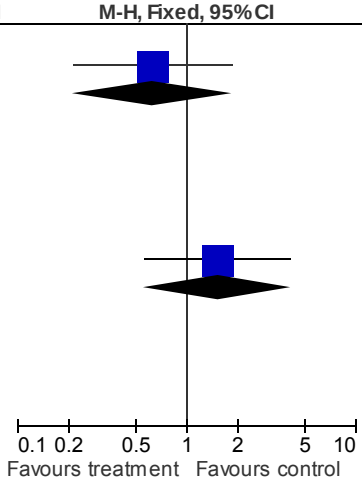
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.37.1 Simpson-Angus Scale								
Lecrubier 2000	-0.07	0.41	158	-0.1	0.45	152	100.0%	0.03 [-0.07, 0.13]
Subtotal (95% CI)			**158**			**152**	**100.0%**	**0.03 [-0.07, 0.13]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.61 (P = 0.54)								
7.37.2 Involuntary Movement Scale								
Lecrubier 2000	-0.1	4.1	158	-0.16	3.17	152	100.0%	0.06 [-0.75, 0.87]
Subtotal (95% CI)			**158**			**152**	**100.0%**	**0.06 [-0.75, 0.87]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.14 (P = 0.89)								



Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.94), I² = 0%

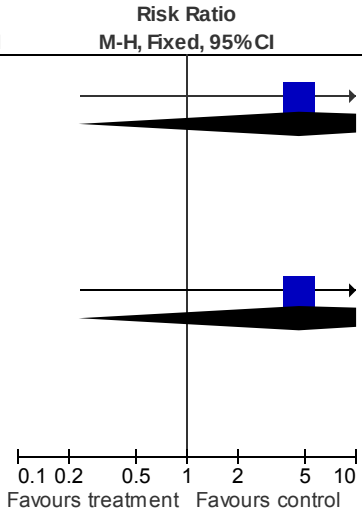
7.38 AE: 3. Autonomic SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.38.1 Salivation - increased						
Fleurot 1997	5	113	8	114	100.0%	0.63 [0.21, 1.87]
Subtotal (95% CI)		**113**		**114**	**100.0%**	**0.63 [0.21, 1.87]**
Total events	5		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.83 (P = 0.41)						
7.38.2 Rhinitis						
Fleurot 1997	9	113	6	114	100.0%	1.51 [0.56, 4.11]
Subtotal (95% CI)		**113**		**114**	**100.0%**	**1.51 [0.56, 4.11]**
Total events	9		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.81 (P = 0.42)						



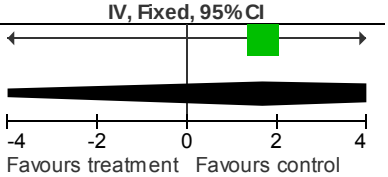
7.39 AE: 4. Cardiovascular SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.39.1 Dizziness						
HWANG2003	2	25	0	23	100.0%	4.62 [0.23, 91.34]
Subtotal (95% CI)		**25**		**23**	**100.0%**	**4.62 [0.23, 91.34]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.00 (P = 0.32)						
7.39.3 Palpitations						
HWANG2003	2	25	0	23	100.0%	4.62 [0.23, 91.34]
Subtotal (95% CI)		**25**		**23**	**100.0%**	**4.62 [0.23, 91.34]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.00 (P = 0.32)						



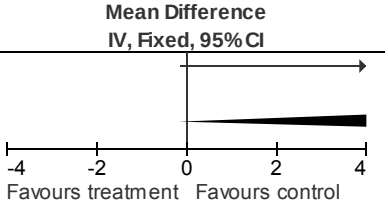
7.40 AE: 4. Cardiovascular - systolic blood pressue (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
HWANG2003	-5.9	16.4	25	-7.6	13.2	22	100.0%	1.70 [-6.77, 10.17]
Total (95% CI)			**25**			**22**	**100.0%**	**1.70 [-6.77, 10.17]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.39 (P = 0.69)								



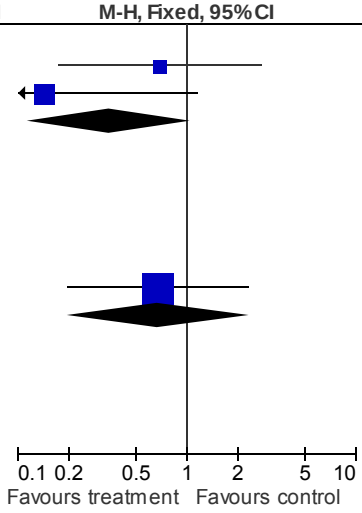
7.41 AE: 4. Cardiovascular - heart rate (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
HWANG2003	1.7	13.1	25	-6.1	14.5	22	100.0%	7.80 [-0.14, 15.74]
Total (95% CI)			**25**			**22**	**100.0%**	**7.80 [-0.14, 15.74]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.92 (P = 0.05)								



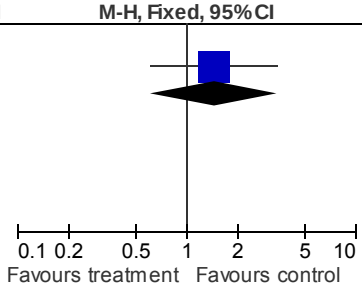
7.42 AE: 5. Gastrointestinal SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.42.1 Constipation						
HWANG2003	3	25	4	23	37.4%	0.69 [0.17, 2.76]
Fleurot 1997	1	113	7	114	62.6%	0.14 [0.02, 1.15]
Subtotal (95% CI)		**138**		**137**	**100.0%**	**0.35 [0.11, 1.06]**
Total events	4		11			
Heterogeneity: Chi² = 1.63, df = 1 (P = 0.20); I² = 39%						
Test for overall effect: Z = 1.86 (P = 0.06)						
7.42.2 Vomiting						
Fleurot 1997	4	113	6	114	100.0%	0.67 [0.19, 2.32]
Subtotal (95% CI)		**113**		**114**	**100.0%**	**0.67 [0.19, 2.32]**
Total events	4		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.63 (P = 0.53)						

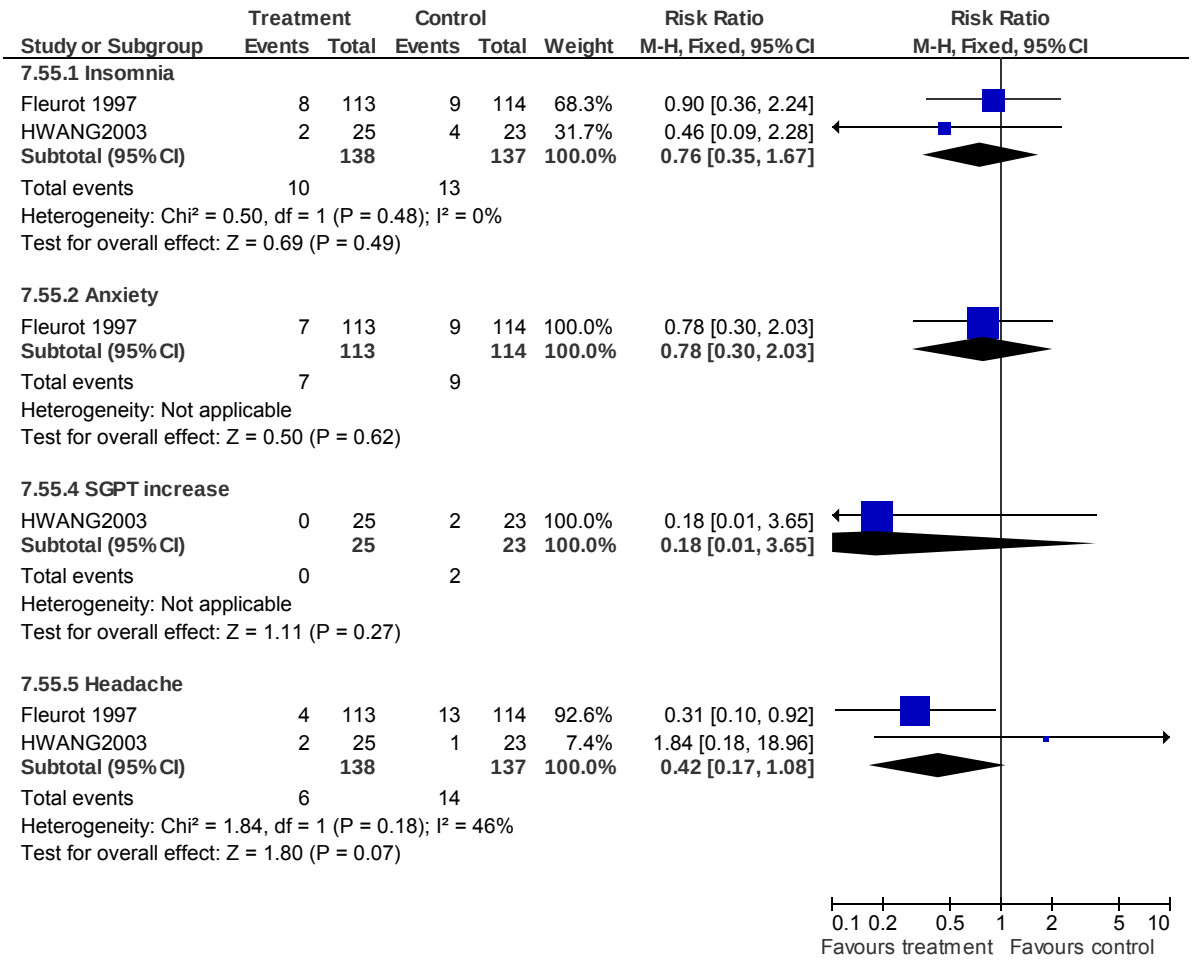


7.45 AE: 6. Sedation (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.45.1 Somnolence						
Lecrubier 2000	12	158	8	152	100.0%	1.44 [0.61, 3.43]
Subtotal (95% CI)		**158**		**152**	**100.0%**	**1.44 [0.61, 3.43]**
Total events	12		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.83 (P = 0.41)						

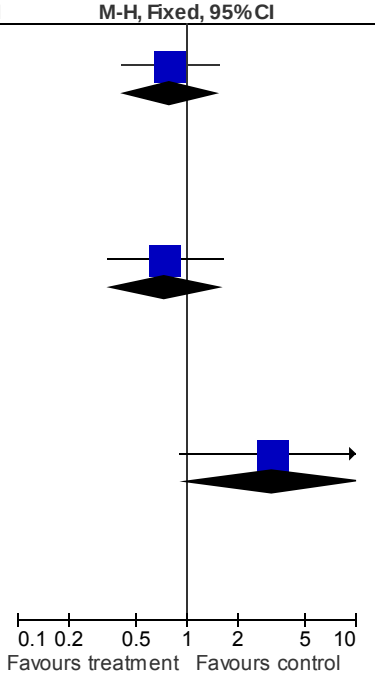


7.55 AE: 7. Other SEs (short-term)



7.56 AE: 7. Other SEs (medium-term)

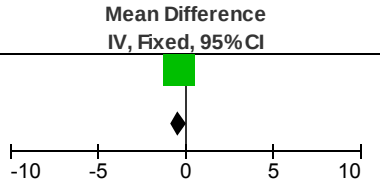
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.56.1 Insomnia						
Lecrubier 2000	14	158	17	152	100.0%	0.79 [0.40, 1.55]
Subtotal (95% CI)		**158**		**152**	**100.0%**	**0.79 [0.40, 1.55]**
Total events	14		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
7.56.2 Anxiety						
Lecrubier 2000	10	158	13	152	100.0%	0.74 [0.33, 1.64]
Subtotal (95% CI)		**158**		**152**	**100.0%**	**0.74 [0.33, 1.64]**
Total events	10		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.74 (P = 0.46)						
7.56.5 Depression						
Lecrubier 2000	10	158	3	152	100.0%	3.21 [0.90, 11.43]
Subtotal (95% CI)		**158**		**152**	**100.0%**	**3.21 [0.90, 11.43]**
Total events	10		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.80 (P = 0.07)						



8 Risperidone versus Aripiprazole (phase: acute treatment) (critical outcomes)

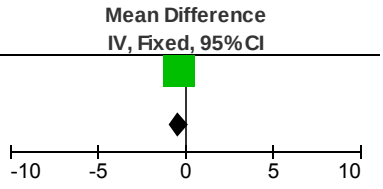
8.1 Global state: 1. CGI-S (Change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
CHAN2007	-1.6	1	34	-1.2	1.1	49	100.0%	-0.40 [-0.86, 0.06]
Total (95% CI)			**34**			**49**	**100.0%**	**-0.40 [-0.86, 0.06]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.72 (P = 0.09)								



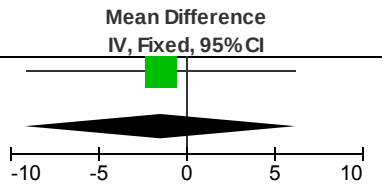
8.2 Global state: 1. CGI-I (Change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
CHAN2007	2.6	1.1	34	3	1.5	49	100.0%	-0.40 [-0.96, 0.16]
Total (95% CI)			**34**			**49**	**100.0%**	**-0.40 [-0.96, 0.16]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.40 (P = 0.16)								



8.3 Mental state: 1. PANSS total (change from baseline) (short-term)

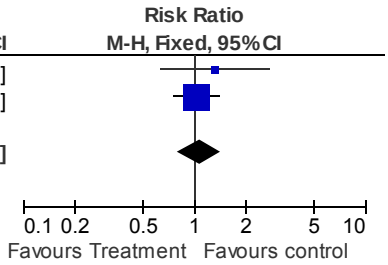
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
CHAN2007	-21.1	17.1	34	-19.6	18.1	49	100.0%	-1.50 [-9.16, 6.16]
Total (95% CI)			**34**			**49**	**100.0%**	**-1.50 [-9.16, 6.16]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.38 (P = 0.70)								



8.4 Leaving the study early: 1. Any reason (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
CHAN2007	10	34	11	49	15.6%	1.31 [0.63, 2.74]
POTKIN2003A	37	99	74	202	84.4%	1.02 [0.75, 1.40]
Total (95% CI)		**133**		**251**	**100.0%**	**1.07 [0.80, 1.42]**
Total events	47		85			

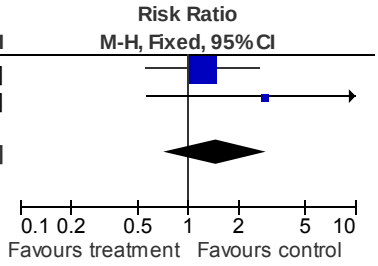
Heterogeneity: Chi² = 0.38, df = 1 (P = 0.54); I² = 0%
Test for overall effect: Z = 0.43 (P = 0.67)



8.5 AE: 1. Metabolic SEs - Weight gain (>= 7% increase from baseline) (chort-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
POTKIN2003A	9	99	15	201	85.8%	1.22 [0.55, 2.69]
CHAN2007	4	34	2	49	14.2%	2.88 [0.56, 14.86]
Total (95% CI)		**133**		**250**	**100.0%**	**1.45 [0.72, 2.93]**
Total events	13		17			

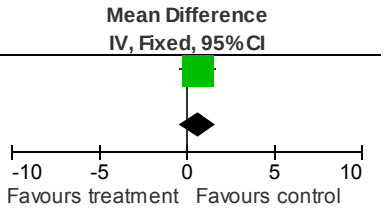
Heterogeneity: Chi² = 0.86, df = 1 (P = 0.35); I² = 0%
Test for overall effect: Z = 1.05 (P = 0.30)



8.6 AE: 1. Metabolic SEs - Weight gain (short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
CHAN2007	1.5	2.5	34	0.9	2.2	49	100.0%	0.60 [-0.44, 1.64]
Total (95% CI)			**34**			**49**	**100.0%**	**0.60 [-0.44, 1.64]**

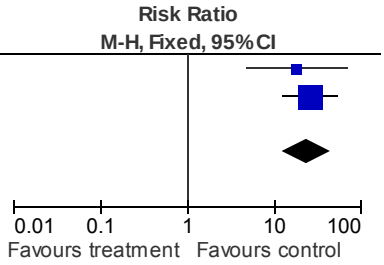
Heterogeneity: Not applicable
Test for overall effect: Z = 1.13 (P = 0.26)



8.7 AE: 1. Metabolic SEs - Prolactin change (increased level above 23-25 ng/mL) (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
CHAN2007	26	28	2	39	26.6%	18.11 [4.68, 70.11]
POTKIN2003A	89	99	7	201	73.4%	25.81 [12.43, 53.61]
Total (95% CI)		**127**		**240**	**100.0%**	**23.77 [12.51, 45.13]**
Total events	115		9			

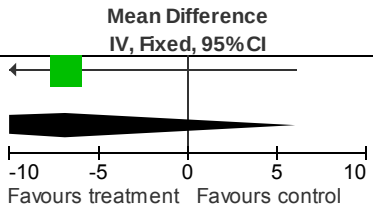
Heterogeneity: Chi² = 0.20, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 9.68 (P < 0.00001)



8.8 AE: 1. Metabolic SEs - Fasting glucose (change from baseline, mg/dL) (short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
CHAN2007	-2.7	27.6	34	4.1	32	49	100.0%	-6.80 [-19.70, 6.10]
Total (95% CI)			**34**			**49**	**100.0%**	**-6.80 [-19.70, 6.10]**

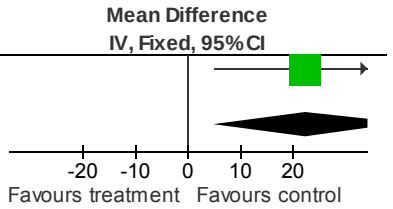
Heterogeneity: Not applicable
Test for overall effect: Z = 1.03 (P = 0.30)



8.9 AE: 1. Metabolic SEs - Total cholesterol (change from baseline, mg/dL) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
CHAN2007	19.2	27.9	34	-3.1	52.3	49	100.0%	22.30 [4.91, 39.69]
Total (95% CI)			**34**			**49**	**100.0%**	**22.30 [4.91, 39.69]**

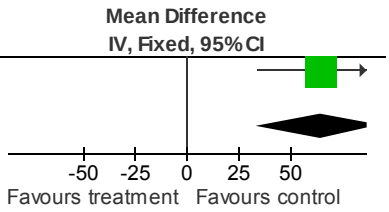
Heterogeneity: Not applicable
Test for overall effect: Z = 2.51 (P = 0.01)



8.10 AE: 1. Metabolic SEs - Serum prolactin (Change from baseline, mg/dL) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
CHAN2007	55.4	42.3	34	-9	96.4	49	100.0%	64.40 [33.89, 94.91]
Total (95% CI)			**34**			**49**	**100.0%**	**64.40 [33.89, 94.91]**

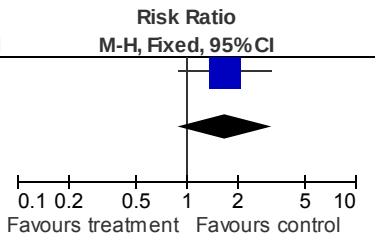
Heterogeneity: Not applicable
Test for overall effect: Z = 4.14 (P < 0.0001)



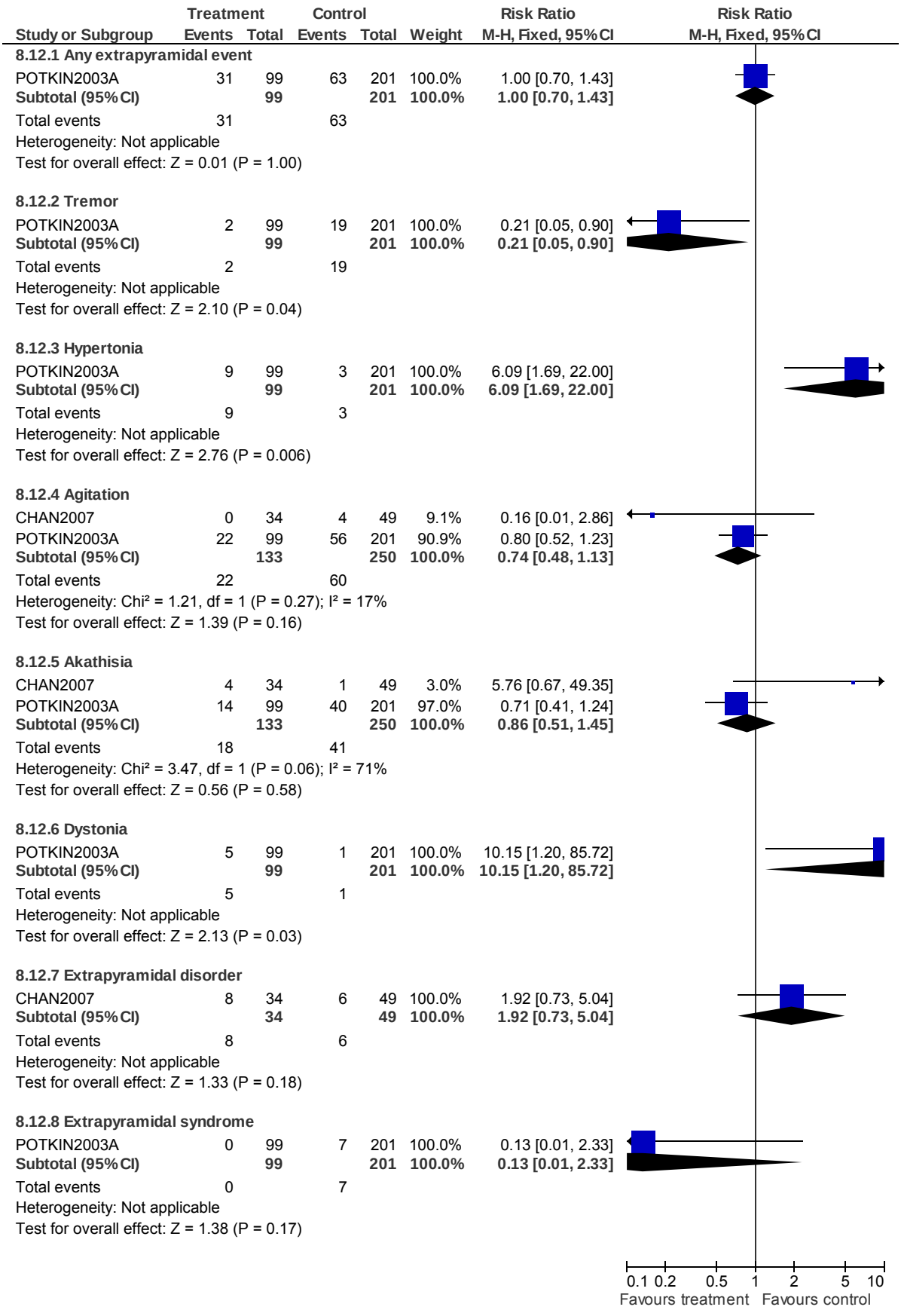
8.11 AE: 2. Neurologic SEs - Needing additional anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
CHAN2007	14	34	12	49	100.0%	1.68 [0.89, 3.17]
Total (95% CI)		**34**		**49**	**100.0%**	**1.68 [0.89, 3.17]**
Total events	14		12			

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



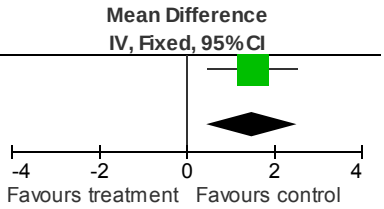
8.12 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



8.13 AE: 2. Neurologic SEs - Simpson-Angus Scale (SAS; change from baseline) (short-term)

	Treatment			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
CHAN2007	1.3	2.4	34	-0.2	2.3	49	100.0%	1.50 [0.47, 2.53]
Total (95% CI)			**34**			**49**	**100.0%**	**1.50 [0.47, 2.53]**

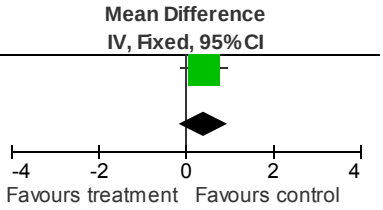
Heterogeneity: Not applicable
Test for overall effect: Z = 2.85 (P = 0.004)



8.14 AE: 2. Neurologic SEs - Barnes Akathisia Scale (BAS; change from baseline) (short-term)

	Treatment			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
CHAN2007	0.5	1.4	34	0.1	1	49	100.0%	0.40 [-0.15, 0.95]
Total (95% CI)			**34**			**49**	**100.0%**	**0.40 [-0.15, 0.95]**

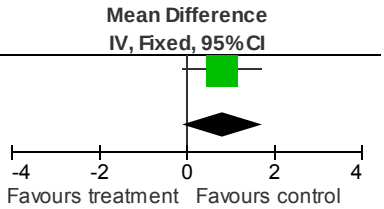
Heterogeneity: Not applicable
Test for overall effect: Z = 1.43 (P = 0.15)



8.15 AE: 2. Neurologic SEs - Involuntary Movement Scale (AIMS; change from baseline) (short-term)

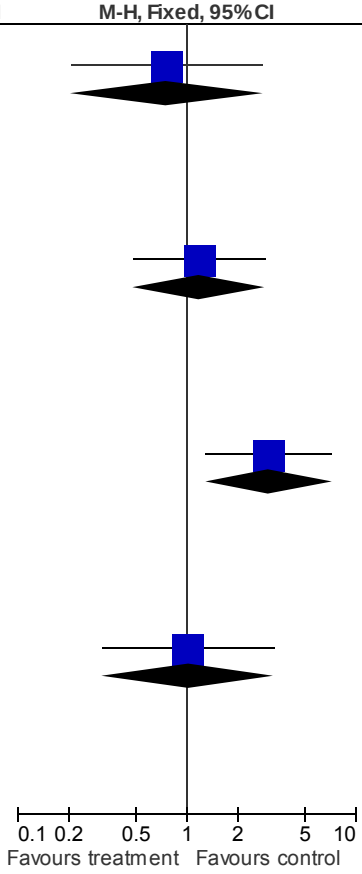
	Treatment			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
CHAN2007	0.4	1.7	34	-0.4	2.5	49	100.0%	0.80 [-0.10, 1.70]
Total (95% CI)			**34**			**49**	**100.0%**	**0.80 [-0.10, 1.70]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.74 (P = 0.08)



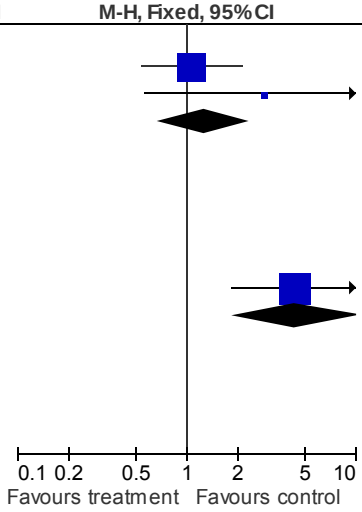
8.16 AE: 3. Autonomic SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.16.1 Increased salivation						
POTKIN2003A	3	99	8	201	100.0%	0.76 [0.21, 2.81]
Subtotal (95% CI)		**99**		**201**	**100.0%**	**0.76 [0.21, 2.81]**
Total events	3		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.41 (P = 0.68)						
8.16.2 Dry mouth						
POTKIN2003A	7	99	12	201	100.0%	1.18 [0.48, 2.91]
Subtotal (95% CI)		**99**		**201**	**100.0%**	**1.18 [0.48, 2.91]**
Total events	7		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.37 (P = 0.71)						
8.16.3 Rhinitis						
POTKIN2003A	12	99	8	201	100.0%	3.05 [1.29, 7.21]
Subtotal (95% CI)		**99**		**201**	**100.0%**	**3.05 [1.29, 7.21]**
Total events	12		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.53 (P = 0.01)						
8.16.4 Blurred vision						
POTKIN2003A	4	99	8	201	100.0%	1.02 [0.31, 3.29]
Subtotal (95% CI)		**99**		**201**	**100.0%**	**1.02 [0.31, 3.29]**
Total events	4		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.03 (P = 0.98)						



8.17 AE: 4. Cardiovascular SEs (short-term)

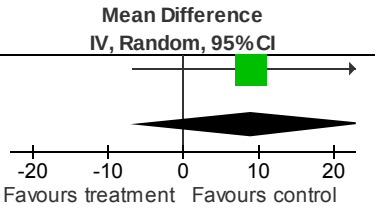
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.17.1 Dizziness / lightheadedness						
POTKIN2003A	11	99	21	201	89.4%	1.06 [0.53, 2.12]
CHAN2007	4	34	2	49	10.6%	2.88 [0.56, 14.86]
Subtotal (95% CI)		**133**		**250**	**100.0%**	**1.26 [0.67, 2.35]**
Total events	15		23			
Heterogeneity: Chi² = 1.21, df = 1 (P = 0.27); I² = 17%						
Test for overall effect: Z = 0.71 (P = 0.47)						
8.17.2 Tachycardia						
POTKIN2003A	15	99	7	201	100.0%	4.35 [1.83, 10.33]
Subtotal (95% CI)		**99**		**201**	**100.0%**	**4.35 [1.83, 10.33]**
Total events	15		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.33 (P = 0.0009)						



8.18 AE: 4. Cardiovascular SEs - QTc prolongation (Change in QTc interval ms) (short-term)

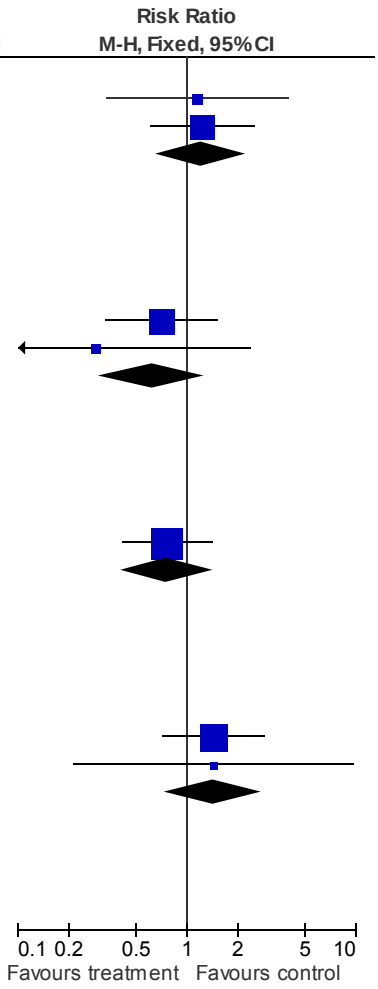
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
CHAN2007	8	34	34	-1	39	49	100.0%	9.00 [-6.81, 24.81]
Total (95% CI)			**34**			**49**	**100.0%**	**9.00 [-6.81, 24.81]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.12 (P = 0.26)



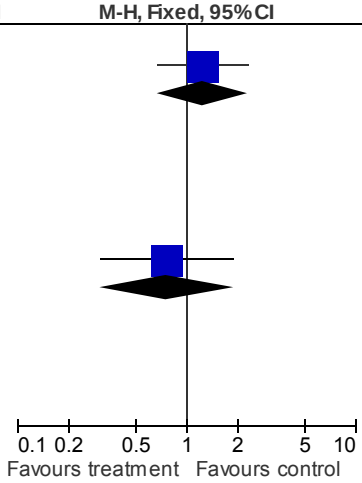
8.19 AE: 5. Gastrointestinal SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.19.1 Constipation						
CHAN2007	4	34	5	49	25.6%	1.15 [0.33, 3.98]
POTKIN2003A	11	99	18	201	74.4%	1.24 [0.61, 2.52]
Subtotal (95% CI)		**133**		**250**	**100.0%**	**1.22 [0.66, 2.26]**
Total events	15		23			
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.92); I² = 0%						
Test for overall effect: Z = 0.63 (P = 0.53)						
8.19.2 Vomiting						
POTKIN2003A	8	99	23	201	78.7%	0.71 [0.33, 1.52]
CHAN2007	1	34	5	49	21.3%	0.29 [0.04, 2.36]
Subtotal (95% CI)		**133**		**250**	**100.0%**	**0.62 [0.30, 1.26]**
Total events	9		28			
Heterogeneity: Chi² = 0.62, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 1.32 (P = 0.19)						
8.19.3 Dyspepsia						
POTKIN2003A	12	99	32	201	100.0%	0.76 [0.41, 1.41]
Subtotal (95% CI)		**99**		**201**	**100.0%**	**0.76 [0.41, 1.41]**
Total events	12		32			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.86 (P = 0.39)						
8.19.4 Nausea						
POTKIN2003A	12	99	17	201	87.3%	1.43 [0.71, 2.88]
CHAN2007	2	34	2	49	12.7%	1.44 [0.21, 9.74]
Subtotal (95% CI)		**133**		**250**	**100.0%**	**1.43 [0.74, 2.77]**
Total events	14		19			
Heterogeneity: Chi² = 0.00, df = 1 (P = 1.00); I² = 0%						
Test for overall effect: Z = 1.08 (P = 0.28)						



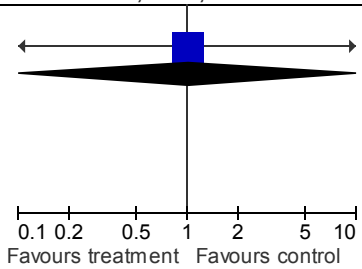
8.20 AE: 6. Sedation (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.20.1 Day time sleepiness - increase (somnolence)						
POTKIN2003A	14	99	23	201	100.0%	1.24 [0.67, 2.30]
Subtotal (95% CI)		**99**		**201**	**100.0%**	**1.24 [0.67, 2.30]**
Total events	14		23			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.67 (P = 0.50)						
8.20.2 Asthenia						
POTKIN2003A	6	99	16	201	100.0%	0.76 [0.31, 1.89]
Subtotal (95% CI)		**99**		**201**	**100.0%**	**0.76 [0.31, 1.89]**
Total events	6		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.56)						



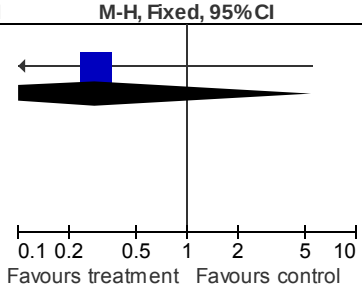
8.21 AE: 7. Sexual dysfunction (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.21.1 Vaginitis						
POTKIN2003A	1	99	2	201	100.0%	1.02 [0.09, 11.06]
Subtotal (95% CI)		**99**		**201**	**100.0%**	**1.02 [0.09, 11.06]**
Total events	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						



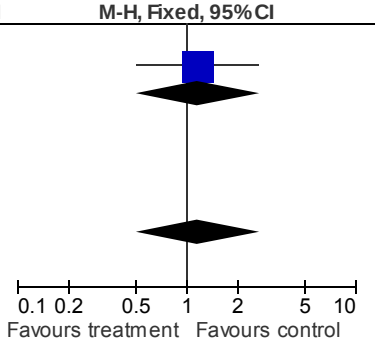
8.22 AE: 8. Menstrual problems (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.22.1 Dysmenorrhea						
POTKIN2003A	0	99	3	201	100.0%	0.29 [0.02, 5.53]
Subtotal (95% CI)		**99**		**201**	**100.0%**	**0.29 [0.02, 5.53]**
Total events	0		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.82 (P = 0.41)						

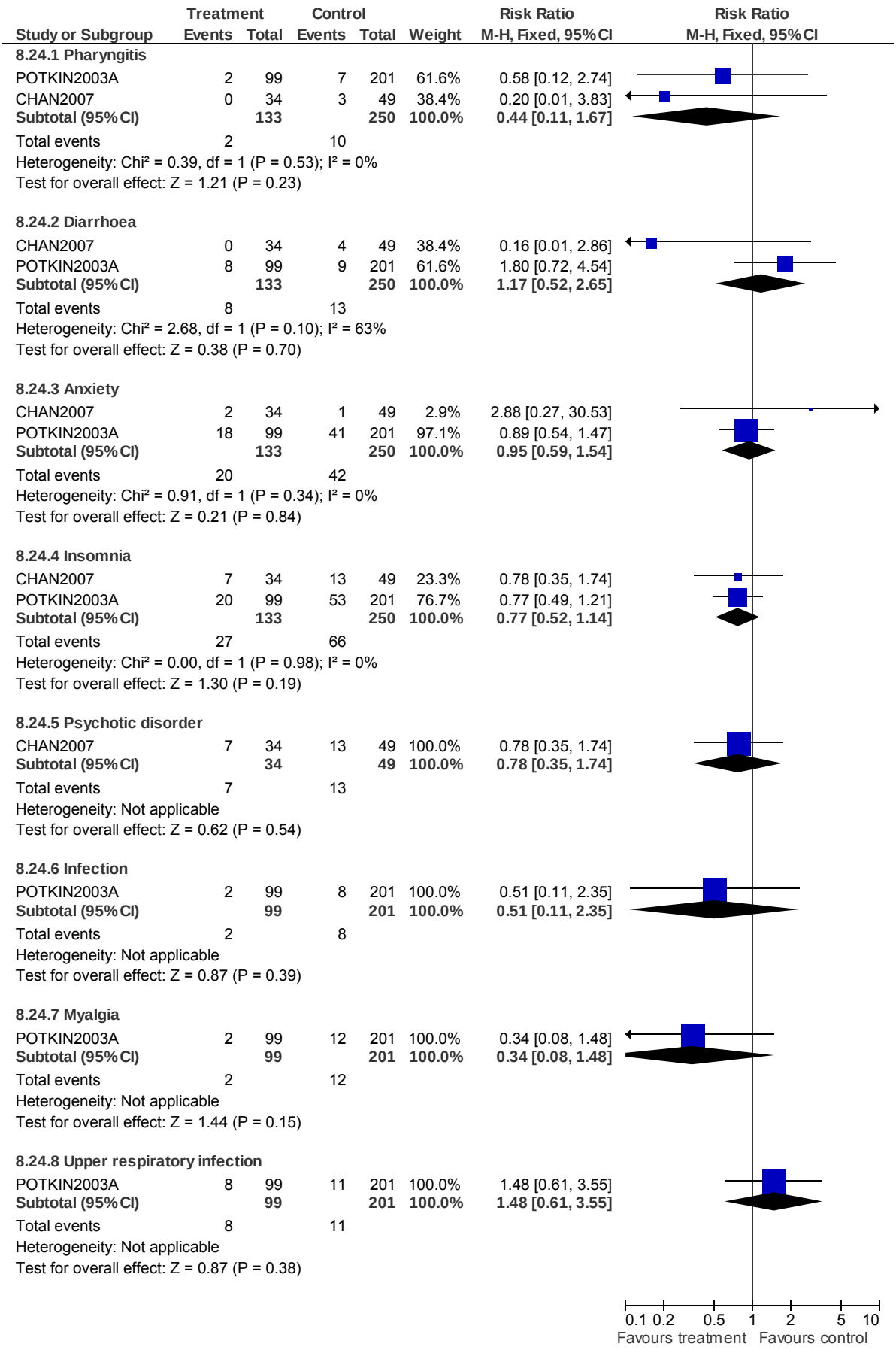


8.23 AE: 9. Dermatological system (short-term)

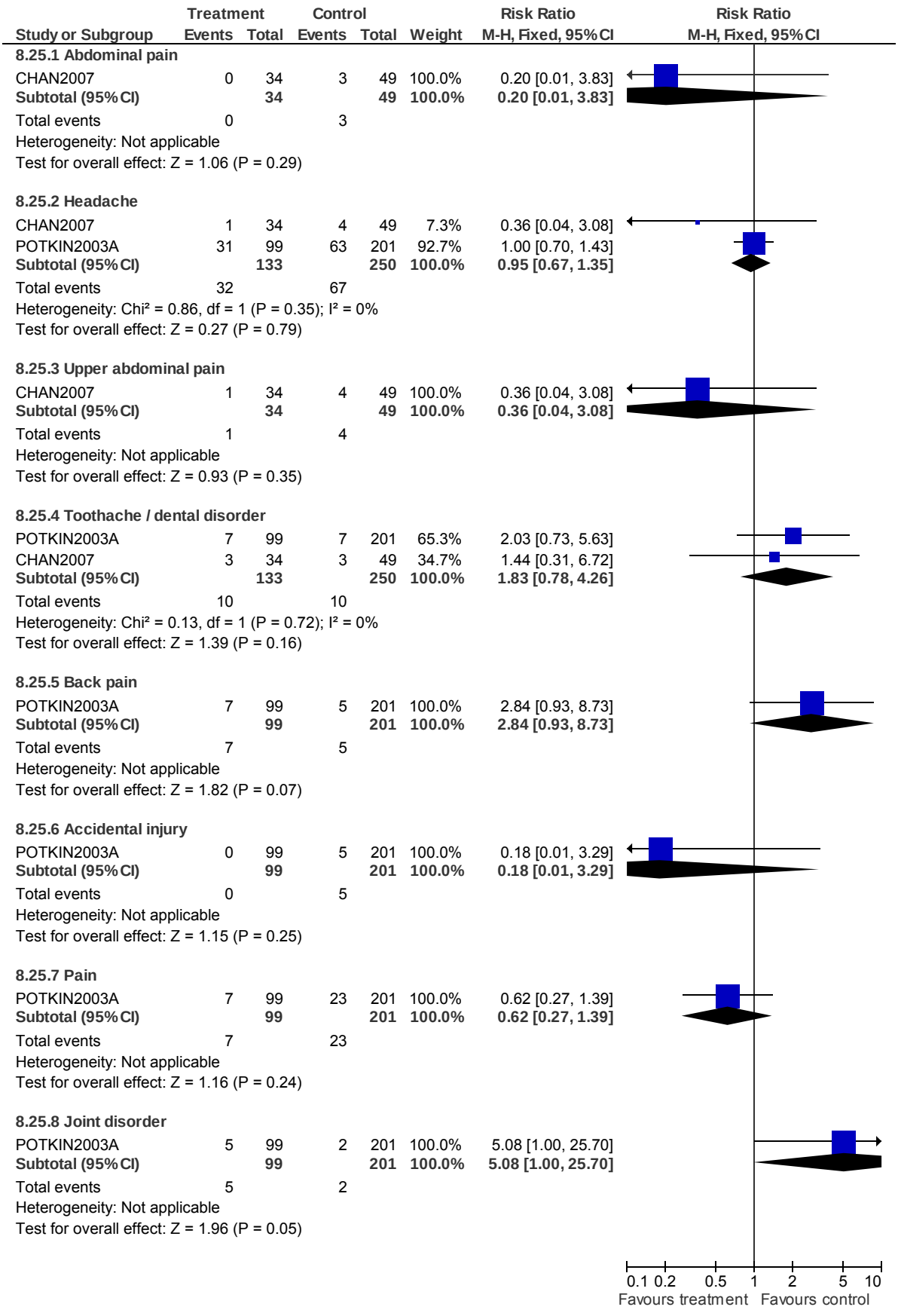
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
8.23.1 Skin rash						
POTKIN2003A	8	99	14	201	100.0%	1.16 [0.50, 2.67]
Subtotal (95% CI)		**99**		**201**	**100.0%**	**1.16 [0.50, 2.67]**
Total events	8		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.35 (P = 0.73)						
Total (95% CI)		**99**		**201**	**100.0%**	**1.16 [0.50, 2.67]**
Total events	8		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.35 (P = 0.73)						



8.24 AE: 10. Other SEs (short-term)



8.25 AE: 10. Other SEs - pain & injury (short-term)

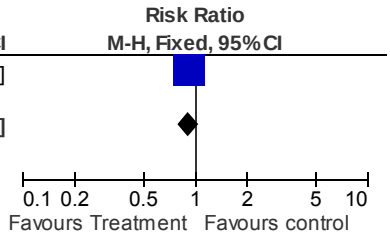


9 Risperidone versus Quetiapine (phase: acute treatment) (critical outcomes)

9.1 Leaving the study early: 1. Any reason (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ZHONG2006	167	335	184	338	100.0%	0.92 [0.79, 1.06]
Total (95% CI)		**335**		**338**	**100.0%**	**0.92 [0.79, 1.06]**
Total events	167		184			

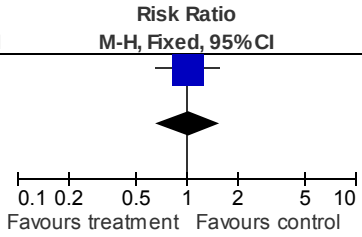
Heterogeneity: Not applicable
Test for overall effect: Z = 1.19 (P = 0.23)



9.2 AE: 1. Metabolic SEs - Weight gain (>= 7% increase from baseline)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ZHONG2006	35	334	35	338	100.0%	1.01 [0.65, 1.58]
Total (95% CI)		**334**		**338**	**100.0%**	**1.01 [0.65, 1.58]**
Total events	35		35			

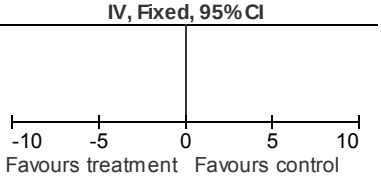
Heterogeneity: Not applicable
Test for overall effect: Z = 0.05 (P = 0.96)



9.3 AE: 1. Metabolic SEs - Weight gain (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
ZHONG2006	2.12	0	334	1.64	0	338		Not estimable
Total (95% CI)			**334**			**338**		**Not estimable**

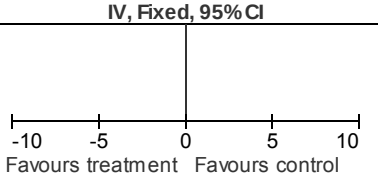
Heterogeneity: Not applicable
Test for overall effect: Not applicable



9.4 AE: 1. Metabolic SEs - Prolactin levels (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
ZHONG2006	35.5	0	334	-11.5	0	338		Not estimable
Total (95% CI)			**334**			**338**		**Not estimable**

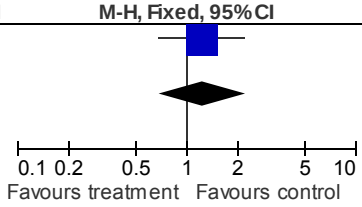
Heterogeneity: Not applicable
Test for overall effect: Not applicable



9.5 AE: 2. Neurologic SEs - Needing additional anticholinergic medication (short-term)

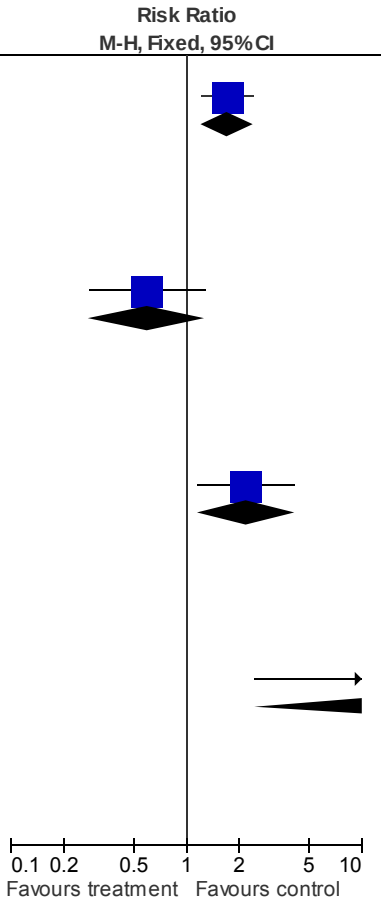
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ZHONG2006	23	334	19	338	100.0%	1.23 [0.68, 2.21]
Total (95% CI)		**334**		**338**	**100.0%**	**1.23 [0.68, 2.21]**
Total events	23		19			

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



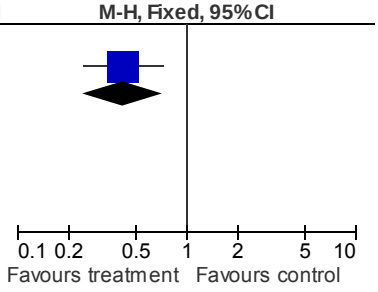
9.6 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.6.1 Any extrapyramidal event						
ZHONG2006	73	334	43	338	100.0%	1.72 [1.22, 2.43]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**1.72 [1.22, 2.43]**
Total events	73		43			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.07 (P = 0.002)						
9.6.2 Agitation						
ZHONG2006	10	334	17	338	100.0%	0.60 [0.28, 1.28]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**0.60 [0.28, 1.28]**
Total events	10		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.33 (P = 0.18)						
9.6.3 Akathisia						
ZHONG2006	28	334	13	338	100.0%	2.18 [1.15, 4.13]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**2.18 [1.15, 4.13]**
Total events	28		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.39 (P = 0.02)						
9.6.4 Dystonia						
ZHONG2006	18	334	1	338	100.0%	18.22 [2.45, 135.68]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**18.22 [2.45, 135.68]**
Total events	18		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.83 (P = 0.005)						



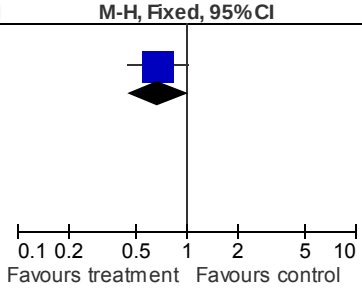
9.7 AE: 3. Autonomic SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.7.1 Dry mouth						
ZHONG2006	17	334	41	338	100.0%	0.42 [0.24, 0.72]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**0.42 [0.24, 0.72]**
Total events	17		41			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.12 (P = 0.002)						



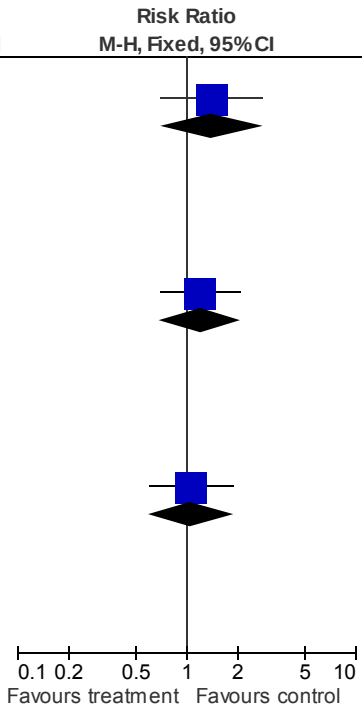
9.8 AE: 4. Cardiovascular SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.8.1 Dizziness						
ZHONG2006	32	334	48	338	100.0%	0.67 [0.44, 1.03]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**0.67 [0.44, 1.03]**
Total events	32		48			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.83 (P = 0.07)						



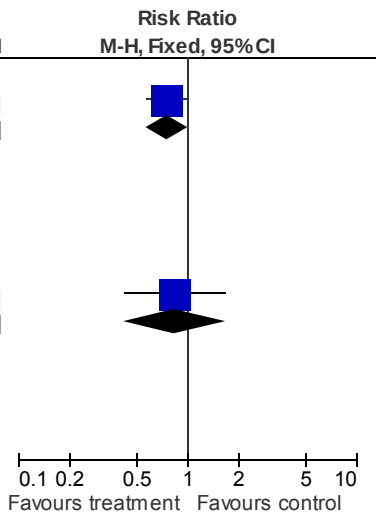
9.9 AE: 5. Gastrointestinal SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.9.1 Vomiting						
ZHONG2006	18	334	13	338	100.0%	1.40 [0.70, 2.81]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**1.40 [0.70, 2.81]**
Total events	18		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						
9.9.2 Dyspepsia						
ZHONG2006	26	334	22	338	100.0%	1.20 [0.69, 2.07]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**1.20 [0.69, 2.07]**
Total events	26		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.64 (P = 0.52)						
9.9.3 Nausea						
ZHONG2006	22	334	21	338	100.0%	1.06 [0.59, 1.89]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**1.06 [0.59, 1.89]**
Total events	22		21			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.20 (P = 0.84)						

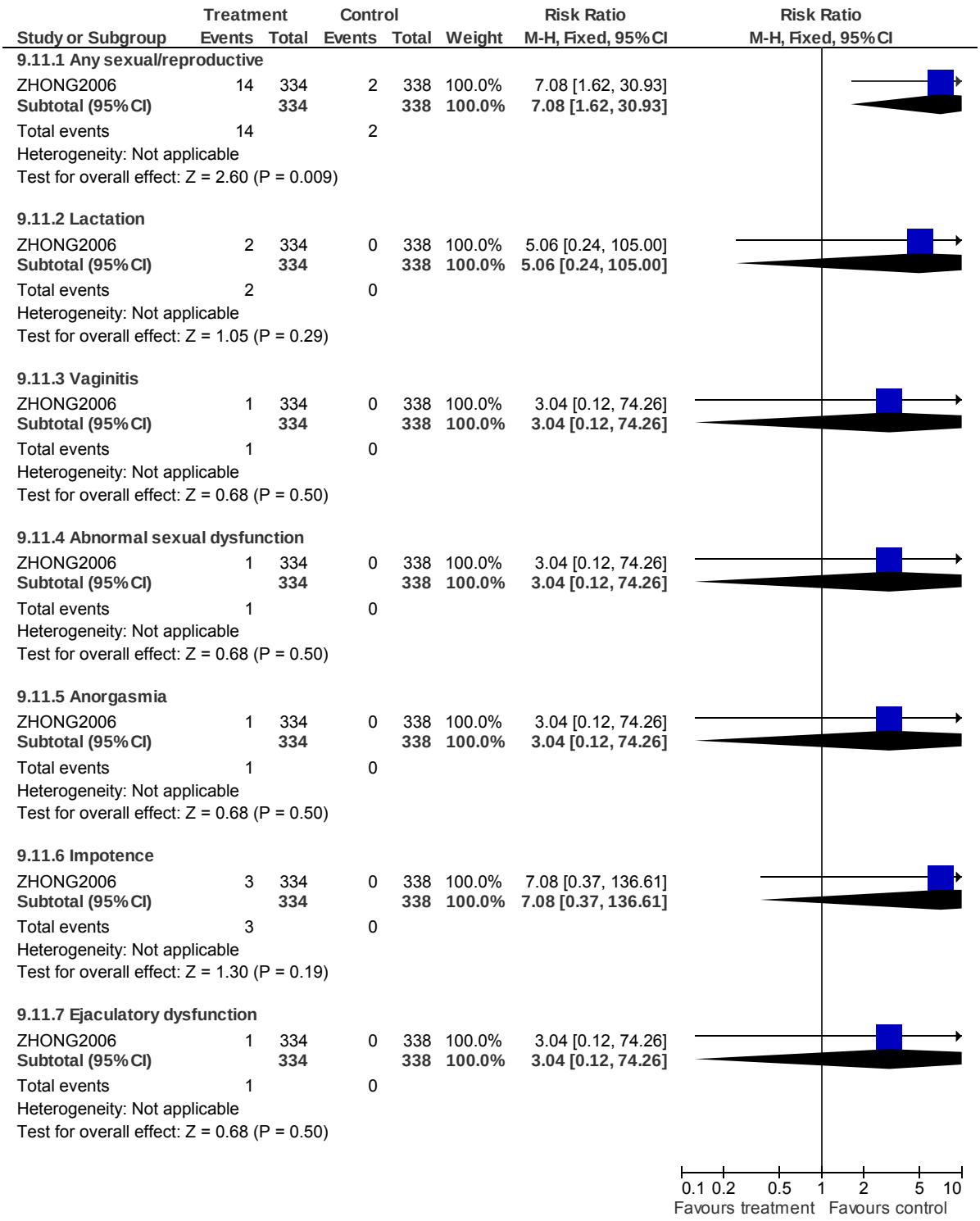


9.10 AE: 6. Sedation (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.10.1 Day time sleepiness - increase (somnolence)						
ZHONG2006	66	334	89	338	100.0%	0.75 [0.57, 0.99]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**0.75 [0.57, 0.99]**
Total events	66		89			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.01 (P = 0.04)						
9.10.2 Asthenia						
ZHONG2006	14	334	17	338	100.0%	0.83 [0.42, 1.66]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**0.83 [0.42, 1.66]**
Total events	14		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.52 (P = 0.61)						

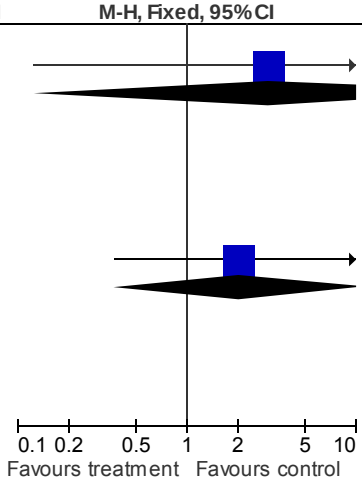


9.11 AE: 7. Sexual dysfunction (short-term)



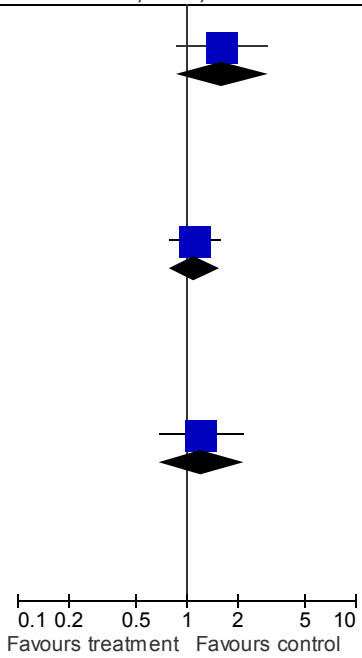
9.12 AE: 8. Menstrual problems (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.12.1 Menorrhagia						
ZHONG2006	1	334	0	338	100.0%	3.04 [0.12, 74.26]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**3.04 [0.12, 74.26]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
9.12.2 Dysmenorrhea						
ZHONG2006	4	334	2	338	100.0%	2.02 [0.37, 10.98]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**2.02 [0.37, 10.98]**
Total events	4		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.82 (P = 0.41)						



9.13 AE: 9. Other SEs (short-term)

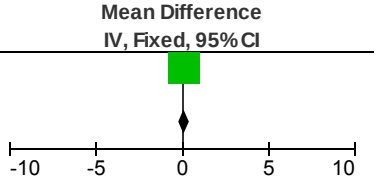
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.13.1 Pharyngitis						
ZHONG2006	24	334	15	338	100.0%	1.62 [0.86, 3.03]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**1.62 [0.86, 3.03]**
Total events	24		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.51 (P = 0.13)						
9.13.2 Headache						
ZHONG2006	56	334	51	338	100.0%	1.11 [0.78, 1.57]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**1.11 [0.78, 1.57]**
Total events	56		51			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.55)						
9.13.3 Pain						
ZHONG2006	24	334	20	338	100.0%	1.21 [0.68, 2.16]
Subtotal (95% CI)		**334**		**338**	**100.0%**	**1.21 [0.68, 2.16]**
Total events	24		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.66 (P = 0.51)						



10 Risperidone versus Sertindole (phase: acute treatment) (critical outcomes)

10.1 Global state: 1. CGI-S (change from baseline) (medium-term)

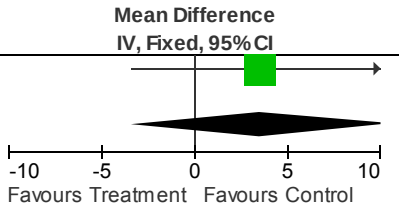
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
AZORIN2006	-1.3	1	82	-1.4	1.2	90	100.0%	0.10 [-0.23, 0.43]
Total (95% CI)			**82**			**90**	**100.0%**	**0.10 [-0.23, 0.43]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.60 (P = 0.55)								



10.2 Mental state: 1. PANSS total (Change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
AZORIN2006	-25.8	22.4	82	-29.3	23.9	90	100.0%	3.50 [-3.42, 10.42]
Total (95% CI)			**82**			**90**	**100.0%**	**3.50 [-3.42, 10.42]**

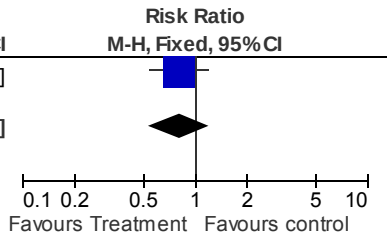
Heterogeneity: Not applicable
Test for overall effect: Z = 0.99 (P = 0.32)



10.3 Leaving the study early: 1. Any reason (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
AZORIN2006	28	89	38	97	100.0%	0.80 [0.54, 1.19]
Total (95% CI)		**89**		**97**	**100.0%**	**0.80 [0.54, 1.19]**
Total events	28		38			

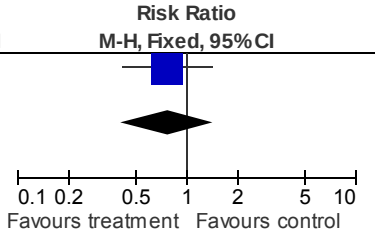
Heterogeneity: Not applicable
Test for overall effect: Z = 1.09 (P = 0.28)



10.4 AE: 1. Metabolic SEs - Weight gain (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
AZORIN2006	14	89	20	97	100.0%	0.76 [0.41, 1.42]
Total (95% CI)		**89**		**97**	**100.0%**	**0.76 [0.41, 1.42]**
Total events	14		20			

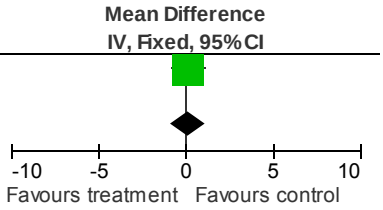
Heterogeneity: Not applicable
Test for overall effect: Z = 0.86 (P = 0.39)



10.5 AE: 2. Neurologic SEs - AIMS (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
AZORIN2006	-0.7	3.3	74	-0.8	3	82	100.0%	0.10 [-0.89, 1.09]
Total (95% CI)			**74**			**82**	**100.0%**	**0.10 [-0.89, 1.09]**

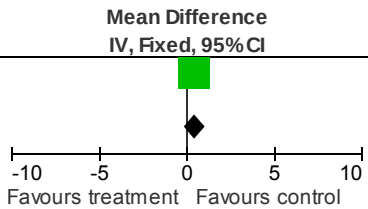
Heterogeneity: Not applicable
Test for overall effect: Z = 0.20 (P = 0.84)



10.6 AE: 2. Neurologic SEs - Barnes Akathisia Scale (BAS; medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
AZORIN2006	-0.1	2.2	86	-0.5	1.8	93	100.0%	0.40 [-0.19, 0.99]
Total (95% CI)			**86**			**93**	**100.0%**	**0.40 [-0.19, 0.99]**

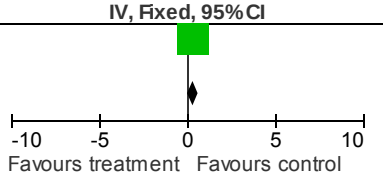
Heterogeneity: Not applicable
Test for overall effect: Z = 1.33 (P = 0.19)



10.7 AE: 1. Neurologic SEs - Simpson-Angus Scale (SAS; change from baseline) (medium-term)

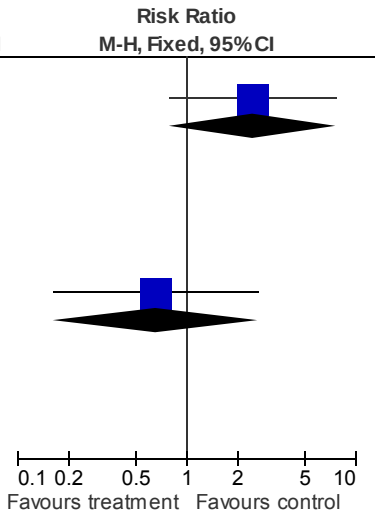
Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
AZORIN2006	-0.2	3.5	86	-1.1	3	93	100.0%	0.28 [-0.02, 0.57]
Total (95% CI)			**86**			**93**	**100.0%**	**0.28 [-0.02, 0.57]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.83 (P = 0.07)



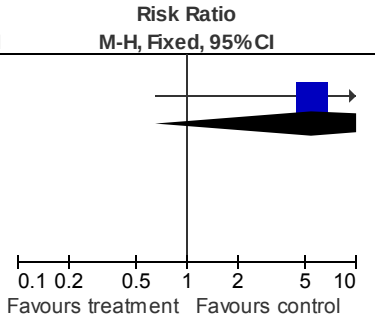
10.8 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.8.1 Any extrapyramidal event						
AZORIN2006	9	89	4	97	100.0%	2.45 [0.78, 7.68]
Subtotal (95% CI)		**89**		**97**	**100.0%**	**2.45 [0.78, 7.68]**
Total events	9		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.54 (P = 0.12)						
10.8.2 Tremor						
AZORIN2006	3	89	5	97	100.0%	0.65 [0.16, 2.66]
Subtotal (95% CI)		**89**		**97**	**100.0%**	**0.65 [0.16, 2.66]**
Total events	3		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.59 (P = 0.55)						



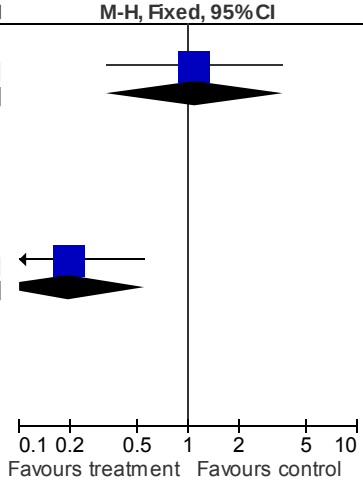
10.9 AE: 3. Autonomic SEs (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.9.1 Salivation - increased						
AZORIN2006	5	89	1	97	100.0%	5.45 [0.65, 45.75]
Subtotal (95% CI)		**89**		**97**	**100.0%**	**5.45 [0.65, 45.75]**
Total events	5		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.56 (P = 0.12)						



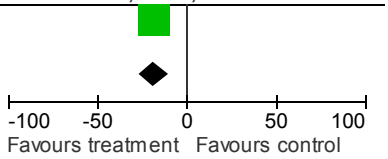
10.10 AE: 4. Cardiovascular SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.10.1 Low blood pressure (hypotension)						
AZORIN2006	5	89	5	97	100.0%	1.09 [0.33, 3.64]
Subtotal (95% CI)		**89**		**97**	**100.0%**	**1.09 [0.33, 3.64]**
Total events	5		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.14 (P = 0.89)						
10.10.2 QT prolongation						
AZORIN2006	4	89	22	97	100.0%	0.20 [0.07, 0.55]
Subtotal (95% CI)		**89**		**97**	**100.0%**	**0.20 [0.07, 0.55]**
Total events	4		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.09 (P = 0.002)						



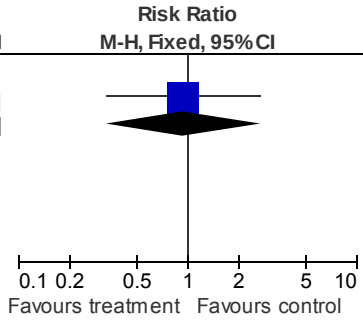
10.11 AE: 4. Cardiovascular SEs - QTc (Endpoint) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
AZORIN2006	411	27	83	429.6	29.1	91	100.0%	-18.60 [-26.94, -10.26]
Total (95% CI)			**83**			**91**	**100.0%**	**-18.60 [-26.94, -10.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.37 (P < 0.0001)								



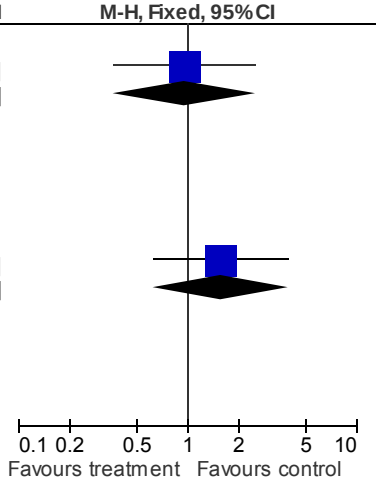
10.12 AE: 5. Gastrointestinal SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.12.1 Constipation						
AZORIN2006	6	89	7	97	100.0%	0.93 [0.33, 2.67]
Subtotal (95% CI)		**89**		**97**	**100.0%**	**0.93 [0.33, 2.67]**
Total events	6		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.13 (P = 0.90)						



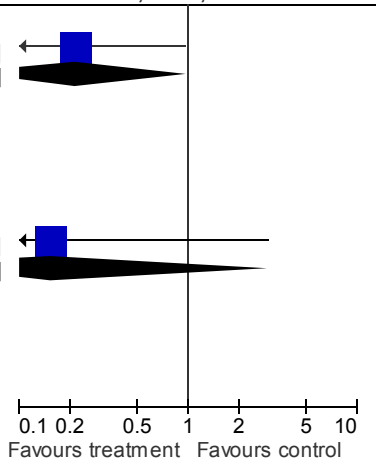
10.13 AE: 6. Sedation (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.13.1 Day time sleepiness - increase (somnolence)						
AZORIN2006	7	89	8	97	100.0%	0.95 [0.36, 2.52]
Subtotal (95% CI)		**89**		**97**	**100.0%**	**0.95 [0.36, 2.52]**
Total events	7		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.10 (P = 0.92)						
10.13.2 Asthenia						
AZORIN2006	10	89	7	97	100.0%	1.56 [0.62, 3.91]
Subtotal (95% CI)		**89**		**97**	**100.0%**	**1.56 [0.62, 3.91]**
Total events	10		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.94 (P = 0.35)						



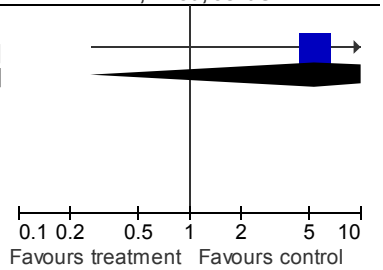
10.14 AE: 7. Sexual dysfunction (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.14.1 Ejaculation abnormal						
AZORIN2006	2	89	10	97	100.0%	0.22 [0.05, 0.97]
Subtotal (95% CI)		**89**		**97**	**100.0%**	**0.22 [0.05, 0.97]**
Total events	2		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.00 (P = 0.05)						
10.14.2 Erectile dysfunction						
AZORIN2006	0	89	3	97	100.0%	0.16 [0.01, 2.97]
Subtotal (95% CI)		**89**		**97**	**100.0%**	**0.16 [0.01, 2.97]**
Total events	0		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.24 (P = 0.22)						

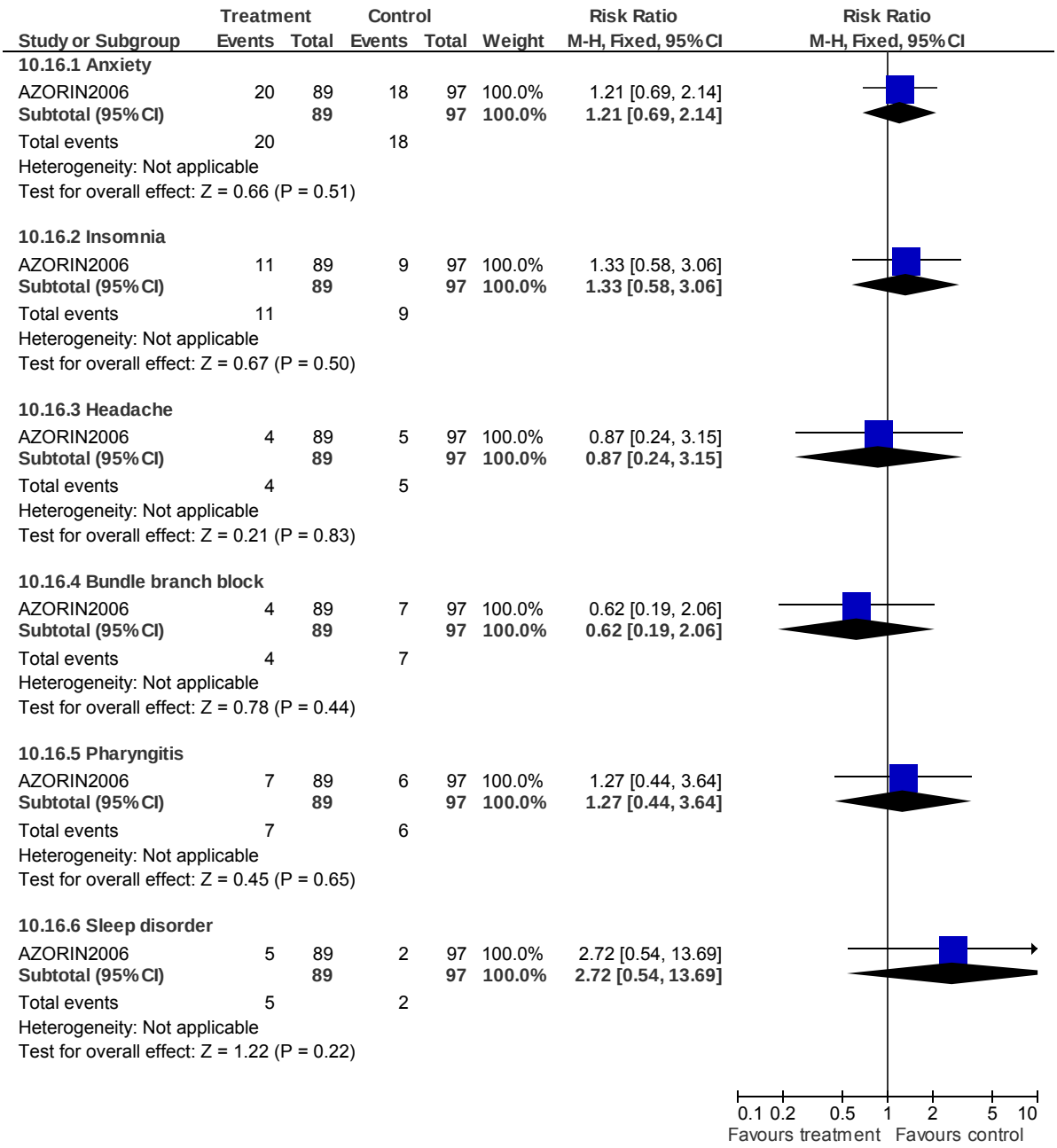


10.15 AE: 8. Menstrual problems (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.15.1 Amenorrhea						
AZORIN2006	2	89	0	97	100.0%	5.44 [0.26, 111.88]
Subtotal (95% CI)		**89**		**97**	**100.0%**	**5.44 [0.26, 111.88]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.10 (P = 0.27)						

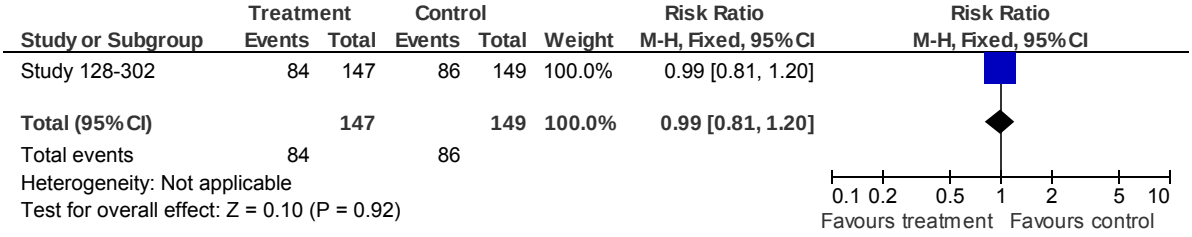


10.16 AE: 9. Other SEs (medium-term)



11 Risperidone versus Ziprasidone (phase: acute treatment) (critical outcomes)

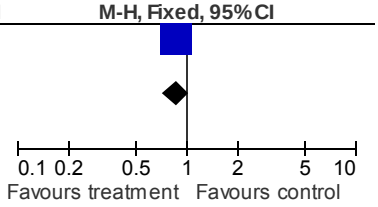
11.1 Global state: 1. No clinically important response (CGI-I) (short-term)



11.2 Mental state: 1. Non-response (<30% improvement in PANSS) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Study 128-302	84	147	99	149	100.0%	0.86 [0.72, 1.03]
Total (95% CI)		**147**		**149**	**100.0%**	**0.86 [0.72, 1.03]**
Total events	84		99			

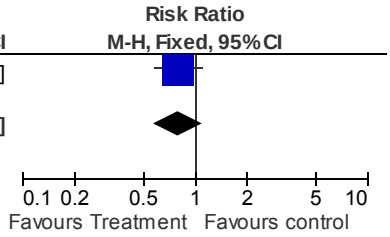
Heterogeneity: Not applicable
Test for overall effect: Z = 1.64 (P = 0.10)



11.3 Leaving the study early: 1. Any reason (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Study 128-302	43	147	55	149	100.0%	0.79 [0.57, 1.10]
Total (95% CI)		**147**		**149**	**100.0%**	**0.79 [0.57, 1.10]**
Total events	43		55			

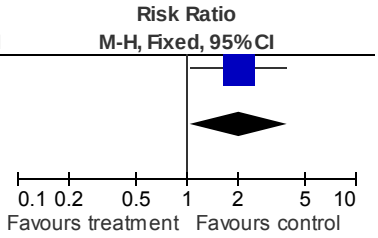
Heterogeneity: Not applicable
Test for overall effect: Z = 1.39 (P = 0.16)



11.4 AE: 1. Metabolic SEs - Weight gain (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Study 128-302	24	147	12	149	100.0%	2.03 [1.05, 3.90]
Total (95% CI)		**147**		**149**	**100.0%**	**2.03 [1.05, 3.90]**
Total events	24		12			

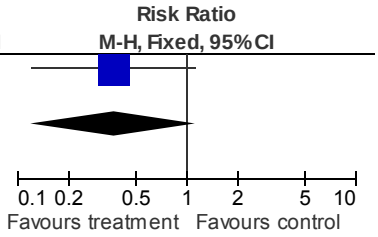
Heterogeneity: Not applicable
Test for overall effect: Z = 2.12 (P = 0.03)



11.5 AE: 1. Metabolic SEs - Weight loss (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Study 128-302	4	147	11	149	100.0%	0.37 [0.12, 1.13]
Total (95% CI)		**147**		**149**	**100.0%**	**0.37 [0.12, 1.13]**
Total events	4		11			

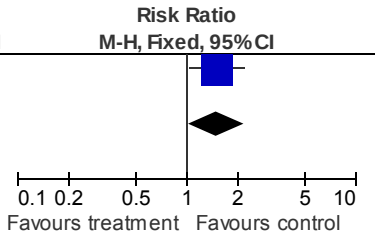
Heterogeneity: Not applicable
Test for overall effect: Z = 1.74 (P = 0.08)



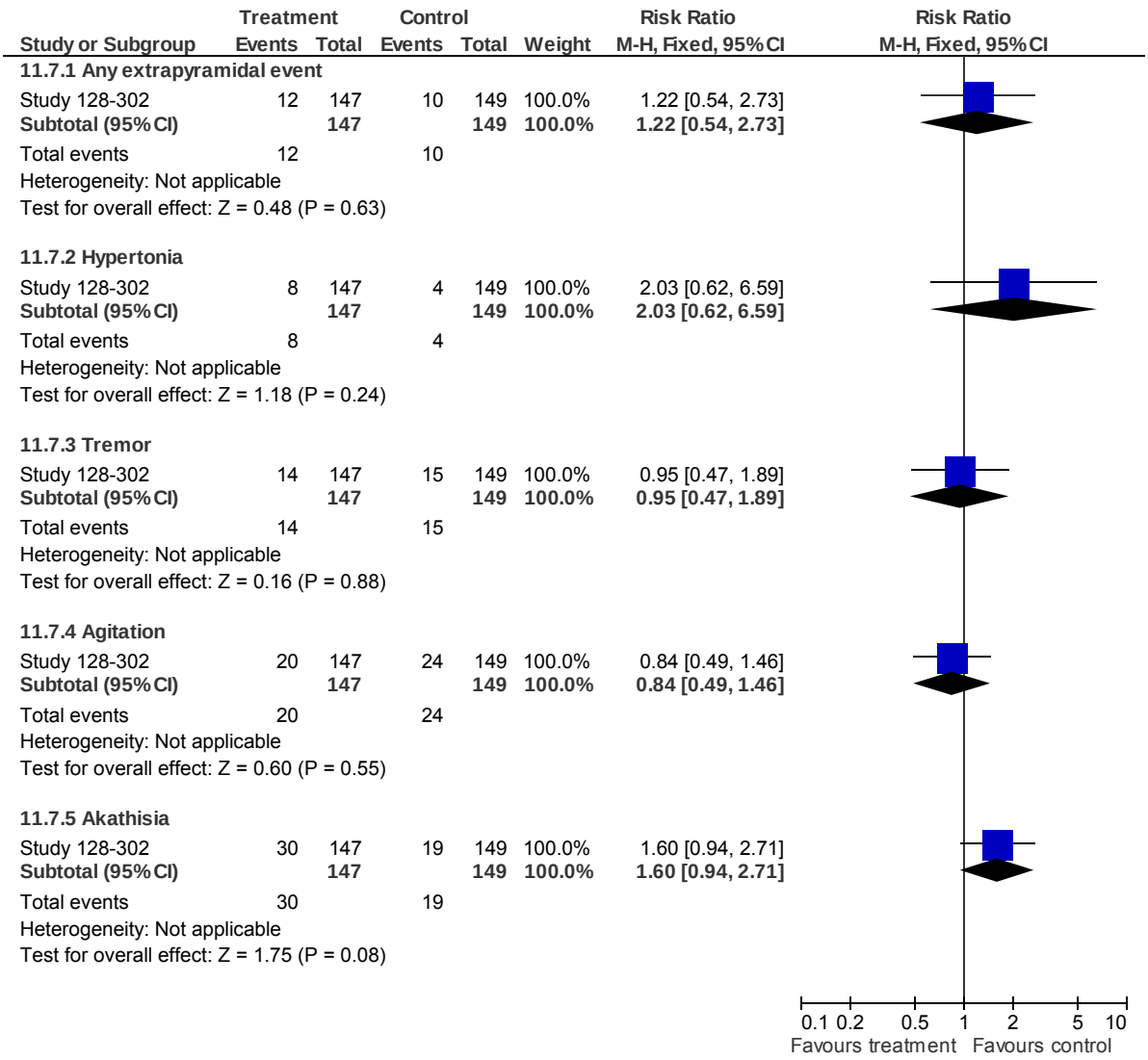
11.6 AE: 2. Neurologic SEs - Needing additional anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Study 128-302	49	147	33	149	100.0%	1.51 [1.03, 2.20]
Total (95% CI)		**147**		**149**	**100.0%**	**1.51 [1.03, 2.20]**
Total events	49		33			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.12 (P = 0.03)

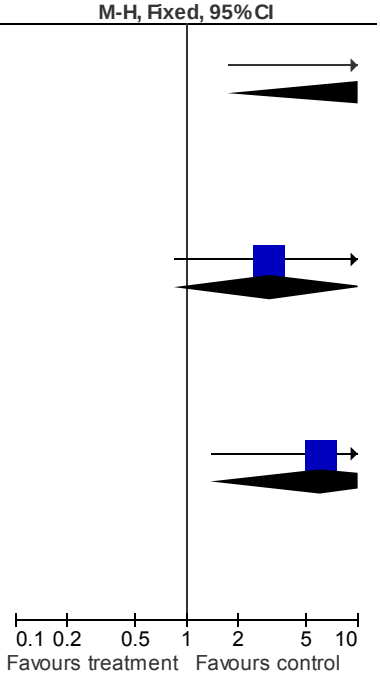


11.7 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



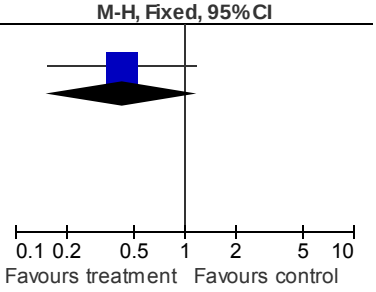
11.8 AE: 3. Autonomic SEs (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
11.8.1 Salivation - increased						
Study 128-302	13	147	1	149	100.0%	13.18 [1.75, 99.45]
Subtotal (95% CI)		**147**		**149**	**100.0%**	**13.18 [1.75, 99.45]**
Total events	13		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.50 (P = 0.01)						
11.8.2 Dry mouth						
Study 128-302	9	147	3	149	100.0%	3.04 [0.84, 11.01]
Subtotal (95% CI)		**147**		**149**	**100.0%**	**3.04 [0.84, 11.01]**
Total events	9		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.69 (P = 0.09)						
11.8.3 Vision abnormalities						
Study 128-302	12	147	2	149	100.0%	6.08 [1.39, 26.70]
Subtotal (95% CI)		**147**		**149**	**100.0%**	**6.08 [1.39, 26.70]**
Total events	12		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.39 (P = 0.02)						

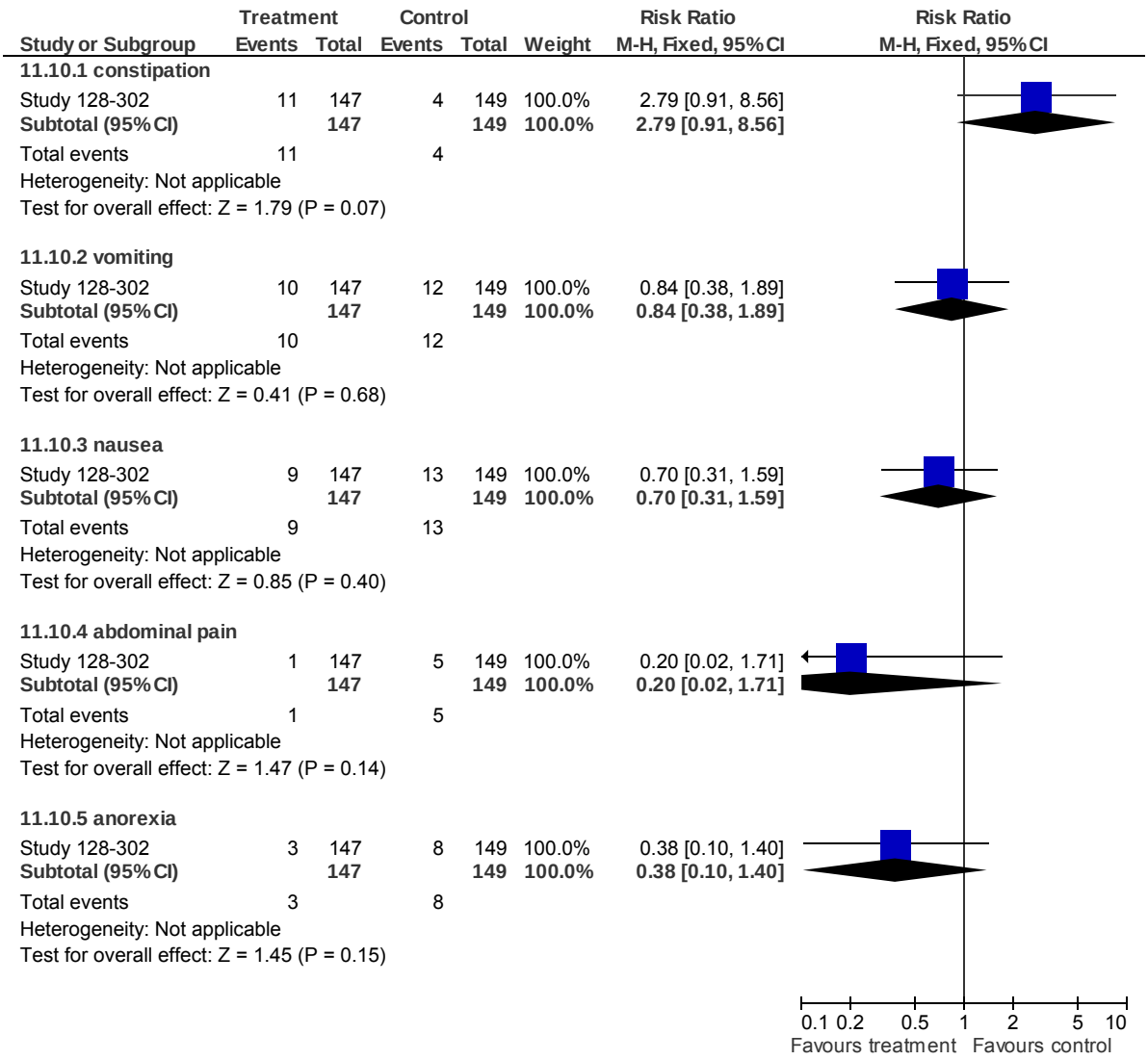


11.9 AE: 4. Cardiovascular SEs (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
11.9.1 Dizziness						
Study 128-302	5	147	12	149	100.0%	0.42 [0.15, 1.17]
Subtotal (95% CI)		**147**		**149**	**100.0%**	**0.42 [0.15, 1.17]**
Total events	5		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.66 (P = 0.10)						

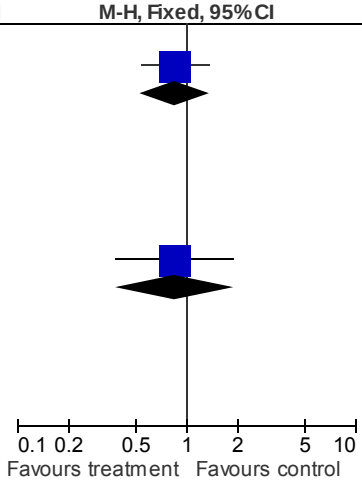


11.10 AE: 5. Gastrointestinal SEs (short-term)



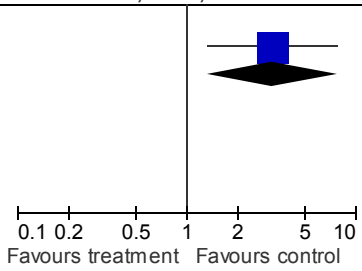
11.11 AE: 6. Sedation (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
11.11.1 Day time sleepiness - increase (somnolence)						
Study 128-302	26	147	31	149	100.0%	0.85 [0.53, 1.36]
Subtotal (95% CI)		**147**		**149**	**100.0%**	**0.85 [0.53, 1.36]**
Total events	26		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
11.11.2 Asthenia						
Study 128-302	10	147	12	149	100.0%	0.84 [0.38, 1.89]
Subtotal (95% CI)		**147**		**149**	**100.0%**	**0.84 [0.38, 1.89]**
Total events	10		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.41 (P = 0.68)						

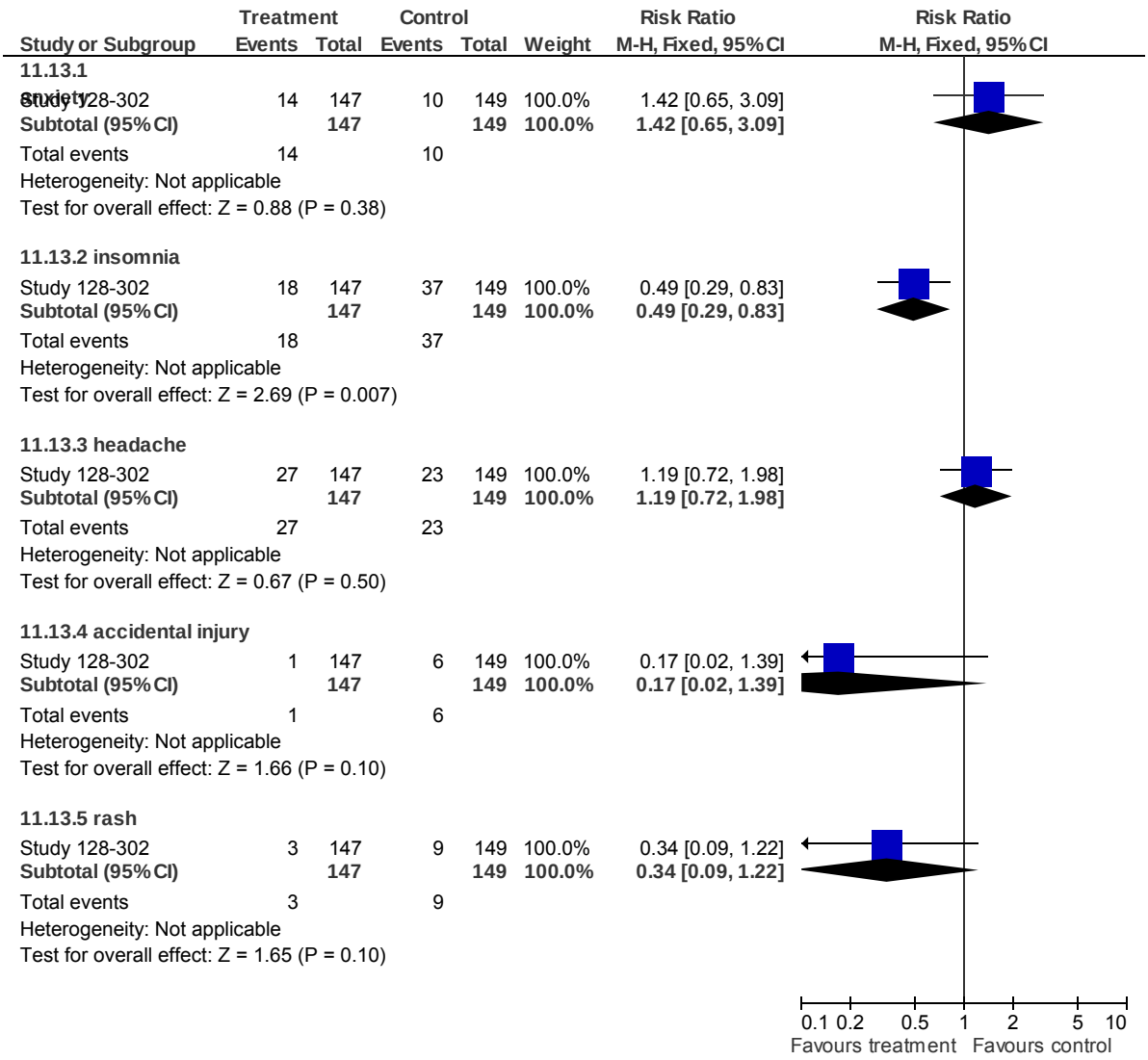


11.12 AE: 8. Menstrual problems (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
11.12.1 urogenital adverse events						
Study 128-302	19	147	6	149	100.0%	3.21 [1.32, 7.81]
Subtotal (95% CI)		**147**		**149**	**100.0%**	**3.21 [1.32, 7.81]**
Total events	19		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.57 (P = 0.01)						

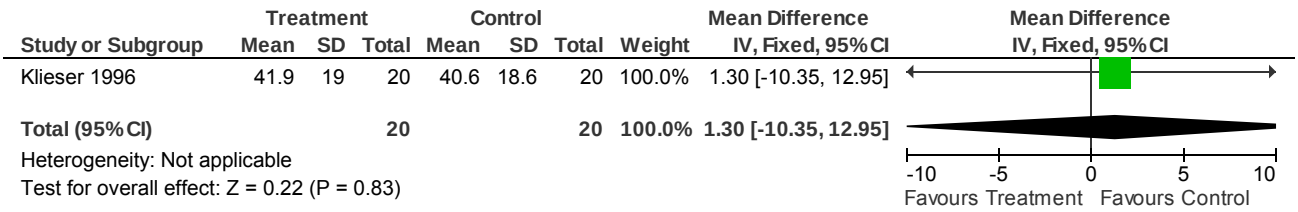


11.13 AE: 9. Other SEs (short-term)



12 Risperidone versus Zotepine (phase: acute treatment) (critical outcomes)

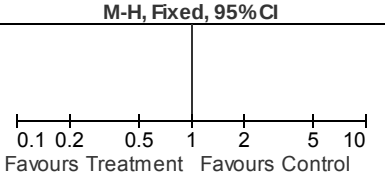
12.1 Mental state: 1. BPRS endpoint score (high = poor)



12.2 Leaving the study early: 1. Any reason

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Total (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			

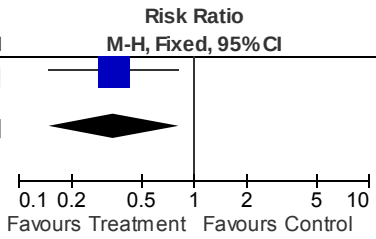
Heterogeneity: Not applicable
Test for overall effect: Not applicable



12.3 AE: 1. Neurologic SEs - needing additional anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Klieser 1996	12	115	6	20	100.0%	0.35 [0.15, 0.82]
Total (95% CI)		**115**		**20**	**100.0%**	**0.35 [0.15, 0.82]**
Total events	12		6			

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



12.4 AE: 1. Neurologic SEs - parkinsonism (Simpson-Angus Scale endpoint, high = poor)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Klieser 1996	2.6	5.3	20	0.1	2.4	20	100.0%	2.50 [-0.05, 5.05]
Total (95% CI)			**20**			**20**	**100.0%**	**2.50 [-0.05, 5.05]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.92 (P = 0.05)

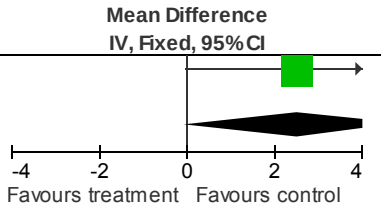


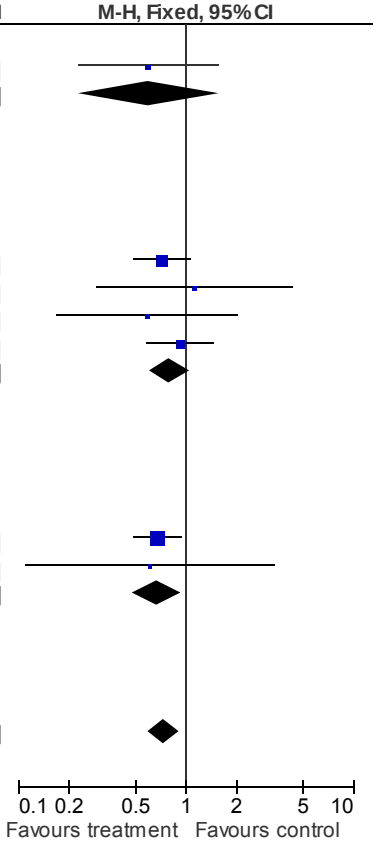
Table 4: Studies included in the relapse prevention review

Treatment	versus Comparator				
	Placebo	**HAL**	**OLZ**	**RIS**	**ZIP**
AMI	LOO1997 [26weeks, N=141]	Speller 1997 [52weeks, N=60]			
ARI	PIGOTT2003 [26weeks, N=310]				
OLZ	BEASLEY2000 [42weeks, N=326] DELLVA1997 (study 1) [46weeks, N=58] DELLVA1997 (study 2) [46weeks, N=62]	STUDY-S029 [52weeks, N=275] Tran 1998a [52weeks, N=55] Tran 1998b [52weeks, N=62] Tran 1998c [22–84weeks, N=690]		Tran 1997 [28weeks, N=339]	SIMPSON2005 [28weeks, N=126]
PAL	KRAMER2007 [up to 46weeks, N=207]				
RIS		Csernansky 2000 [52weeks, N=365] MARDER2003 [104weeks, N=63]	Tran 1997 [28weeks, N=339]		
ZIP	ARATO2002 [52weeks, N=277]		SIMPSON2005 [28weeks, N=126]		
ZOT	COOPER2000 [26weeks, N=119]				

1 SGA versus Haloperidol - raw relapse rates

1.1 Relapse rates

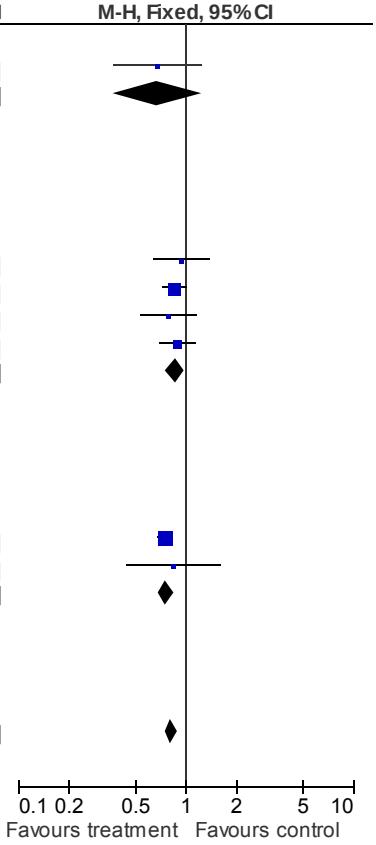
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Amisulpride vs haloperidol						
Speller1997	5	29	9	31	5.5%	0.59 [0.23, 1.56]
Subtotal (95% CI)		**29**		**31**	**5.5%**	**0.59 [0.23, 1.56]**
Total events	5		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.05 (P = 0.29)						
1.1.2 Olanzapine vs haloperidol						
Tran1998c	71	534	29	156	28.5%	0.72 [0.48, 1.06]
Tran1998a	10	45	2	10	2.1%	1.11 [0.29, 4.31]
Tran1998b	6	48	3	14	3.0%	0.58 [0.17, 2.04]
S029	28	141	29	134	18.9%	0.92 [0.58, 1.46]
Subtotal (95% CI)		**768**		**314**	**52.4%**	**0.80 [0.60, 1.06]**
Total events	115		63			
Heterogeneity: Chi² = 1.12, df = 3 (P = 0.77); I² = 0%						
Test for overall effect: Z = 1.57 (P = 0.12)						
1.1.3 Risperidone vs haloperidol						
Csernansky2000	41	177	65	188	40.0%	0.67 [0.48, 0.93]
MARDER2003	2	33	3	30	2.0%	0.61 [0.11, 3.38]
Subtotal (95% CI)		**210**		**218**	**42.0%**	**0.67 [0.48, 0.92]**
Total events	43		68			
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.91); I² = 0%						
Test for overall effect: Z = 2.43 (P = 0.02)						
Total (95% CI)		**1007**		**563**	**100.0%**	**0.73 [0.59, 0.90]**
Total events	163		140			
Heterogeneity: Chi² = 1.92, df = 6 (P = 0.93); I² = 0%						
Test for overall effect: Z = 2.94 (P = 0.003)						



2 SGA versus Haloperidol - overall treatment failure

2.1 Relapse or leaving early for any other reason

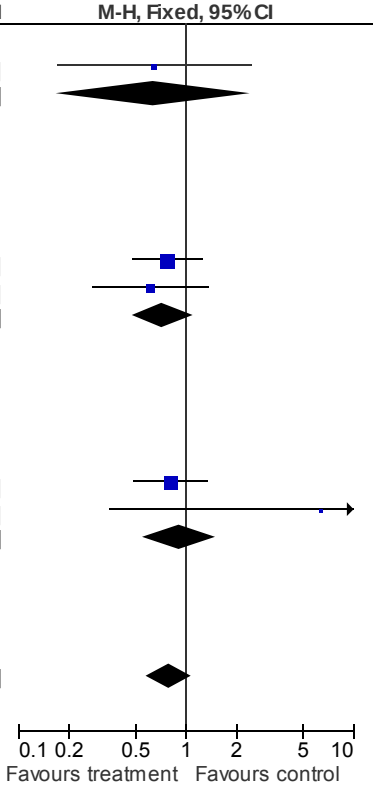
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 Amisulpride vs haloperidol						
Speller1997	10	29	16	31	3.6%	0.67 [0.36, 1.23]
Subtotal (95% CI)		**29**		**31**	**3.6%**	**0.67 [0.36, 1.23]**
Total events	10		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (P = 0.19)						
2.1.2 Olanzapine vs haloperidol						
Tran1998b	32	48	10	14	3.6%	0.93 [0.63, 1.37]
Tran1998c	251	534	86	156	31.1%	0.85 [0.72, 1.01]
Tran1998a	28	45	8	10	3.1%	0.78 [0.53, 1.14]
S029	63	141	68	134	16.3%	0.88 [0.69, 1.13]
Subtotal (95% CI)		**768**		**314**	**54.0%**	**0.86 [0.76, 0.98]**
Total events	374		172			
Heterogeneity: Chi² = 0.48, df = 3 (P = 0.92); I² = 0%						
Test for overall effect: Z = 2.29 (P = 0.02)						
2.1.3 Risperidone vs haloperidol						
Csernansky2000	123	177	174	188	39.4%	0.75 [0.68, 0.83]
MARDER2003	11	33	12	30	2.9%	0.83 [0.43, 1.60]
Subtotal (95% CI)		**210**		**218**	**42.3%**	**0.76 [0.68, 0.84]**
Total events	134		186			
Heterogeneity: Chi² = 0.10, df = 1 (P = 0.75); I² = 0%						
Test for overall effect: Z = 5.02 (P < 0.00001)						
Total (95% CI)		**1007**		**563**	**100.0%**	**0.81 [0.74, 0.88]**
Total events	518		374			
Heterogeneity: Chi² = 3.74, df = 6 (P = 0.71); I² = 0%						
Test for overall effect: Z = 4.80 (P < 0.00001)						



3 SGA versus Haloperidol - leaving the study early due to adverse events

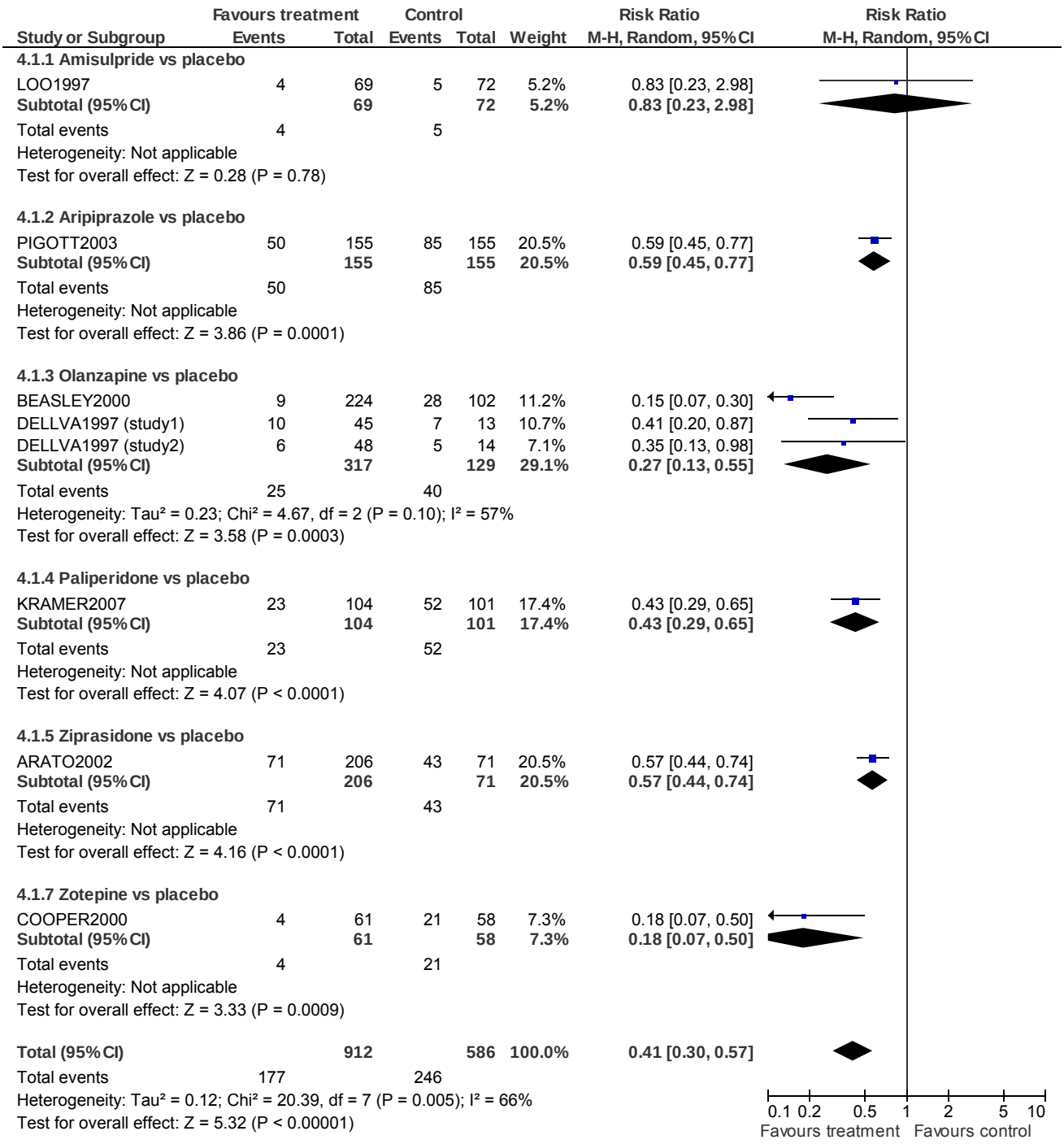
3.1 Leaving the study early due to adverse events

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 Amisulpride vs haloperidol						
Speller1997	3	29	5	31	6.1%	0.64 [0.17, 2.45]
Subtotal (95% CI)		**29**		**31**	**6.1%**	**0.64 [0.17, 2.45]**
Total events	3		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.65 (P = 0.52)						
3.1.2 Olanzapine vs haloperidol						
Tran1998a+b+c	54	627	20	180	39.4%	0.78 [0.48, 1.26]
S029	9	141	14	134	18.2%	0.61 [0.27, 1.36]
Subtotal (95% CI)		**768**		**314**	**57.6%**	**0.72 [0.48, 1.10]**
Total events	63		34			
Heterogeneity: Chi² = 0.25, df = 1 (P = 0.62); I² = 0%						
Test for overall effect: Z = 1.53 (P = 0.13)						
3.1.3 Risperidone vs haloperidol						
Csernansky2000	22	177	29	188	35.6%	0.81 [0.48, 1.35]
MARDER2003	3	33	0	30	0.7%	6.38 [0.34, 118.69]
Subtotal (95% CI)		**210**		**218**	**36.3%**	**0.91 [0.55, 1.49]**
Total events	25		29			
Heterogeneity: Chi² = 1.92, df = 1 (P = 0.17); I² = 48%						
Test for overall effect: Z = 0.38 (P = 0.70)						
Total (95% CI)		**1007**		**563**	**100.0%**	**0.79 [0.58, 1.07]**
Total events	91		68			
Heterogeneity: Chi² = 2.45, df = 4 (P = 0.65); I² = 0%						
Test for overall effect: Z = 1.53 (P = 0.13)						



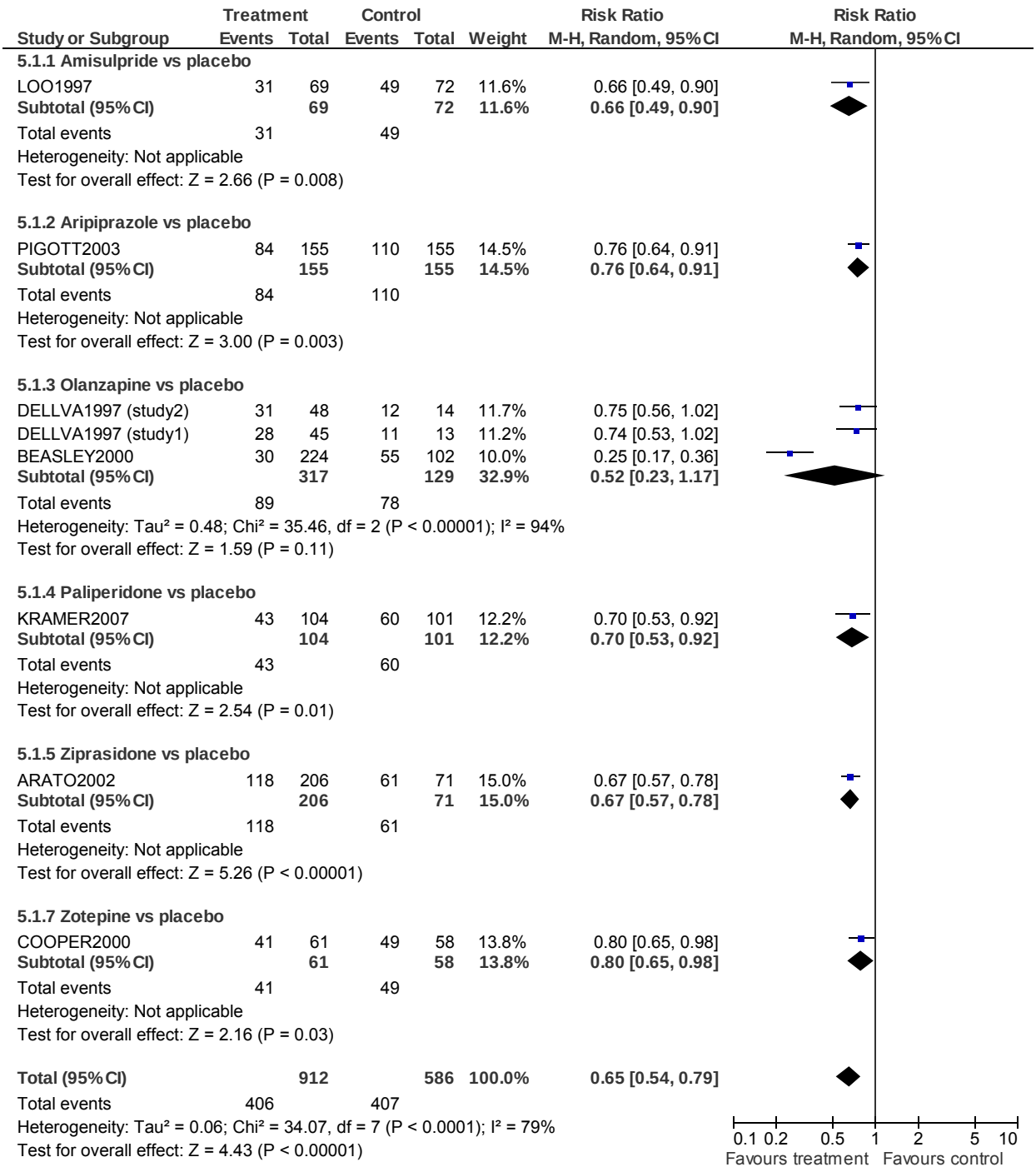
4 SGA versus Placebo - raw relapse rates

4.1 Relapse rates

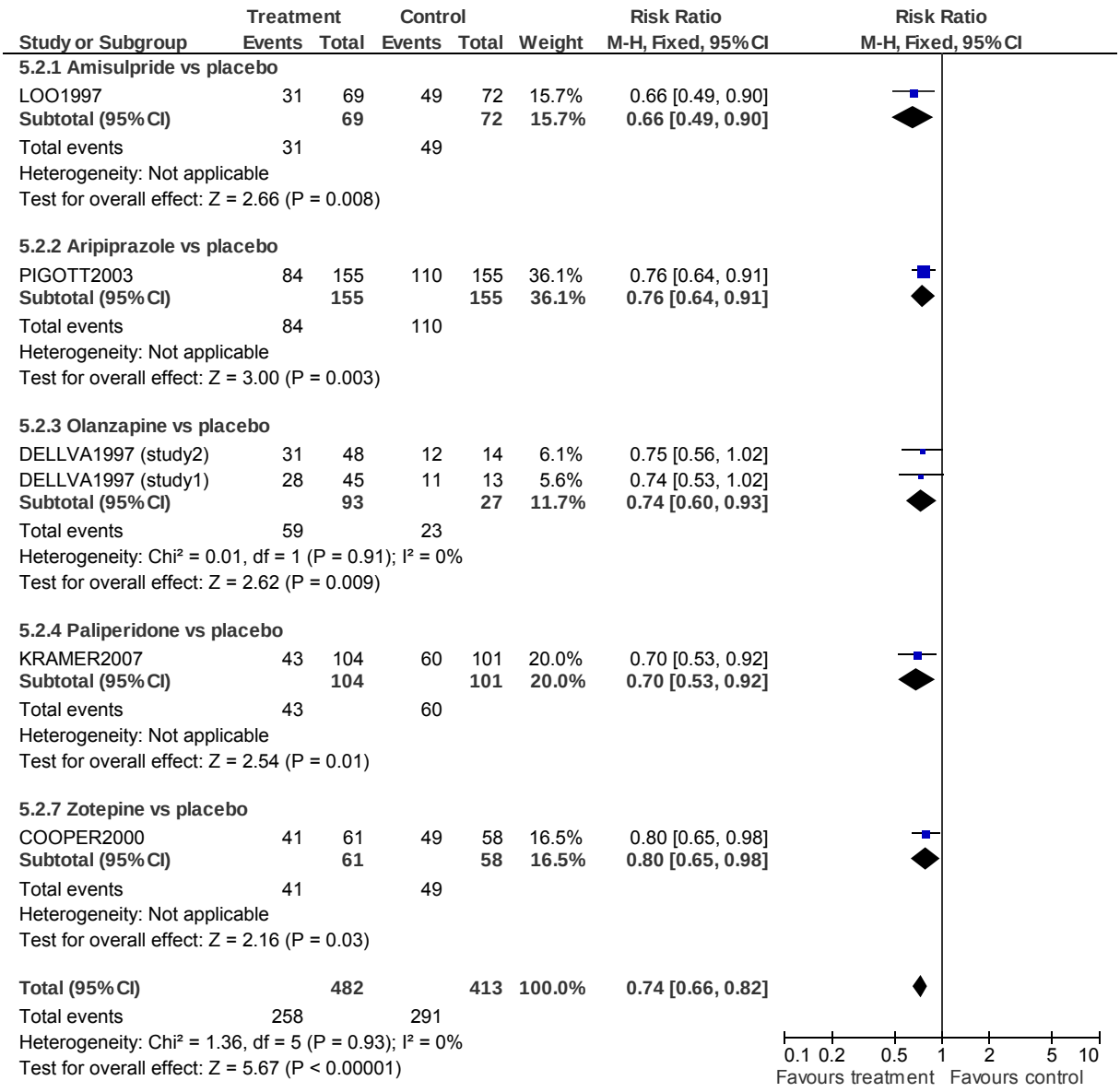


5 SGA versus Placebo - overall treatment failure

5.1 Relapse or leaving early for any other reason

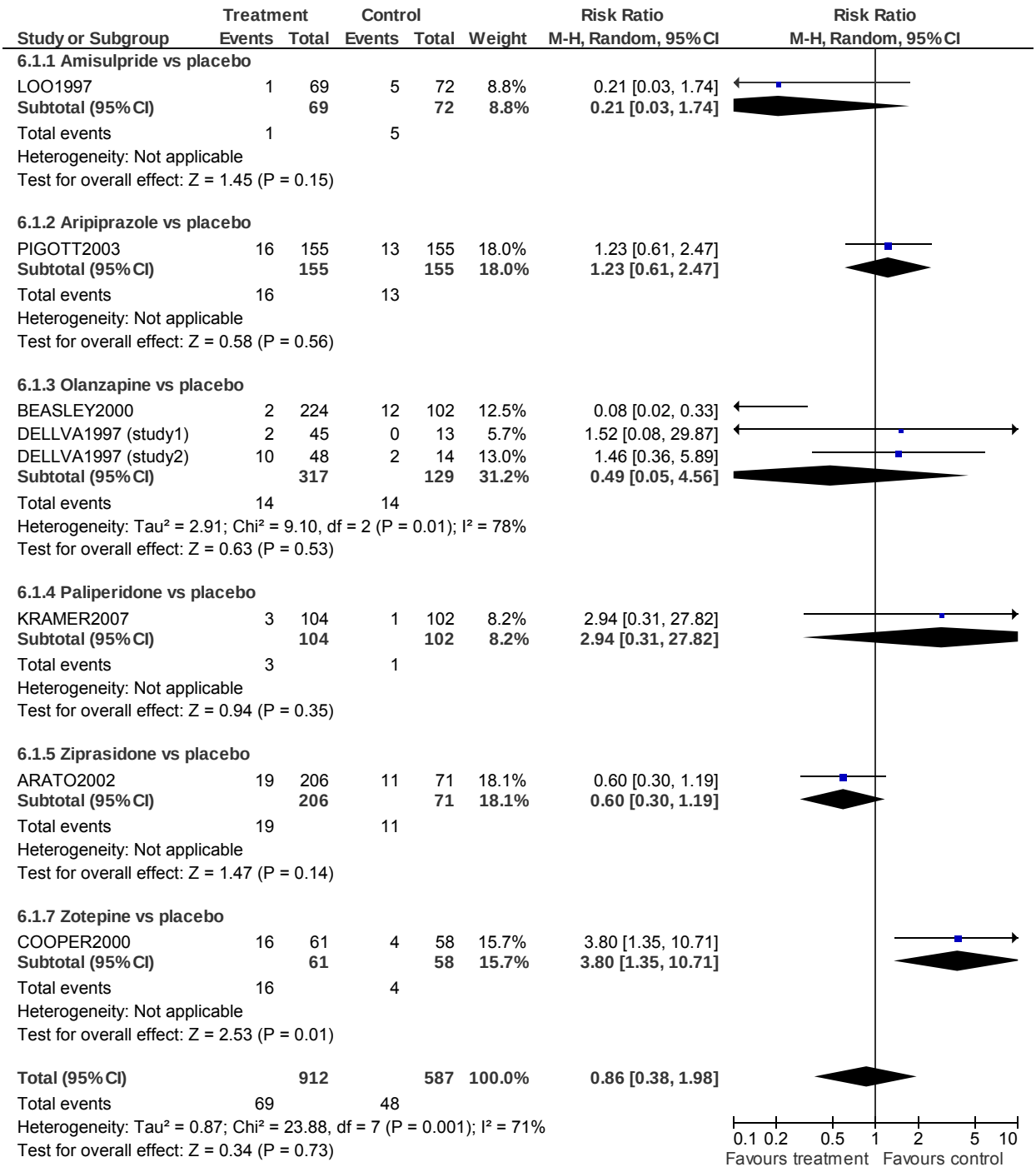


5.2 Relapse or leaving early for any other reason (sensitivity analysis: excl. Beasley2000)



6 SGA versus Placebo - leaving the study early due to adverse events

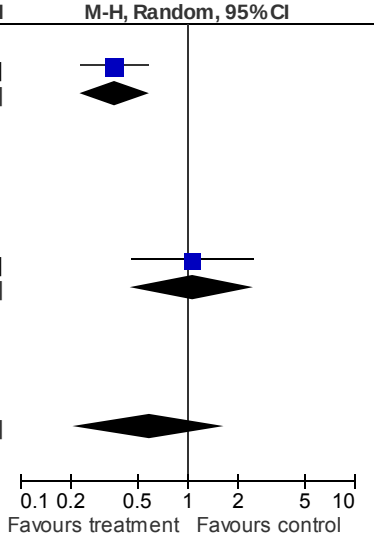
6.1 Number leaving early



7 SGA versus SGA - raw relapse rates

7.1 Relapse rates

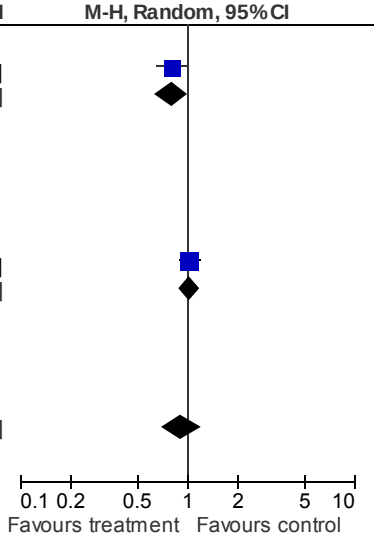
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
7.1.1 Olanzapine vs risperidone						
Tran1997	20	172	53	167	55.6%	0.37 [0.23, 0.59]
Subtotal (95% CI)		**172**		**167**	**55.6%**	**0.37 [0.23, 0.59]**
Total events	20		53			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.20 (P < 0.0001)						
7.1.2 Olanzapine vs ziprasidone						
SIMPSON2005	11	71	8	55	44.4%	1.07 [0.46, 2.47]
Subtotal (95% CI)		**71**		**55**	**44.4%**	**1.07 [0.46, 2.47]**
Total events	11		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.15 (P = 0.88)						
Total (95% CI)		**243**		**222**	**100.0%**	**0.59 [0.21, 1.67]**
Total events	31		61			
Heterogeneity: Tau² = 0.45; Chi² = 4.73, df = 1 (P = 0.03); I² = 79%						
Test for overall effect: Z = 1.00 (P = 0.32)						



8 SGA versus SGA - overall treatment failure

8.1 Relapse or leaving early for any other reason

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
8.1.1 Olanzapine vs risperidone						
Tran1997	73	172	88	167	45.6%	0.81 [0.64, 1.01]
Subtotal (95% CI)		**172**		**167**	**45.6%**	**0.81 [0.64, 1.01]**
Total events	73		88			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.88 (P = 0.06)						
8.1.2 Olanzapine vs ziprasidone						
SIMPSON2005	61	71	46	55	54.4%	1.03 [0.88, 1.19]
Subtotal (95% CI)		**71**		**55**	**54.4%**	**1.03 [0.88, 1.19]**
Total events	61		46			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.35 (P = 0.73)						
Total (95% CI)		**243**		**222**	**100.0%**	**0.92 [0.69, 1.22]**
Total events	134		134			
Heterogeneity: Tau² = 0.03; Chi² = 4.38, df = 1 (P = 0.04); I² = 77%						
Test for overall effect: Z = 0.58 (P = 0.56)						



9 SGA versus SGA - leaving the study early due to adverse events

9.1 Leaving the study early due to adverse events

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.1.1 Olanzapine vs risperidone						
Tran1997	17	172	17	167	75.4%	0.97 [0.51, 1.84]
Subtotal (95% CI)		**172**		**167**	**75.4%**	**0.97 [0.51, 1.84]**
Total events	17		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.09 (P = 0.93)						
9.1.2 Olanzapine vs ziprasidone						
SIMPSON2005	6	71	5	55	24.6%	0.93 [0.30, 2.89]
Subtotal (95% CI)		**71**		**55**	**24.6%**	**0.93 [0.30, 2.89]**
Total events	6		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.13 (P = 0.90)						
Total (95% CI)		**243**		**222**	**100.0%**	**0.96 [0.55, 1.67]**
Total events	23		22			
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.95); I² = 0%						
Test for overall effect: Z = 0.14 (P = 0.89)						

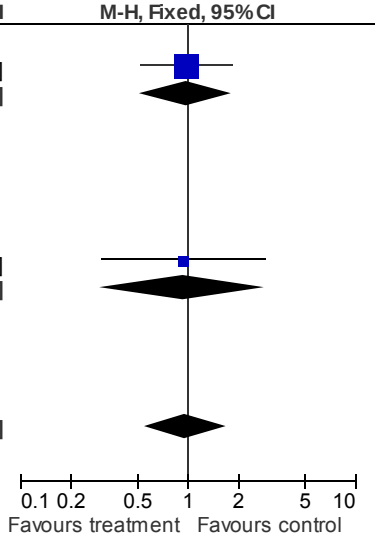


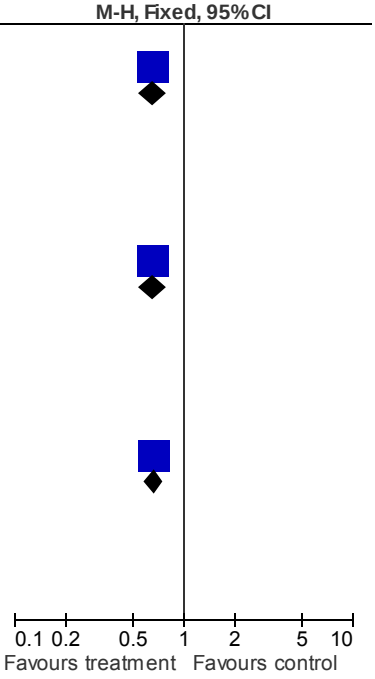
Table 5: Studies included in the review of long-acting injectable risperidone

Treatment	versus Comparator	
	Placebo	Oral RIS
Long-acting risperidone injection	KANE2003 [12weeks, N=400]	CHUE2005 [12weeks, N=642]

1 Long-acting risperidone versus placebo

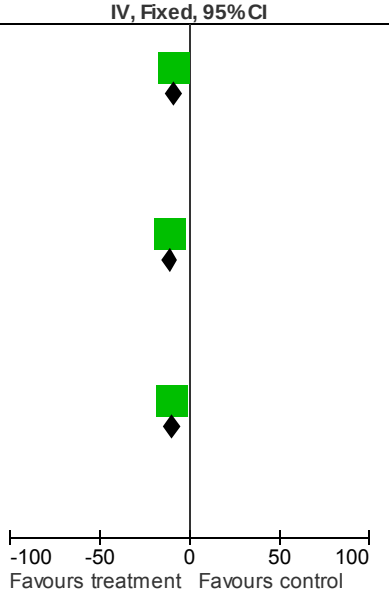
1.1 Global state: 1. No important clinical response (<20% improvement on PANSS total) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 25 mg vs placebo						
KANE2003	55	99	83	98	100.0%	0.66 [0.54, 0.80]
Subtotal (95% CI)		**99**		**98**	**100.0%**	**0.66 [0.54, 0.80]**
Total events	55		83			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.23 (P < 0.0001)						
1.1.2 50 mg vs placebo						
KANE2003	57	103	83	98	100.0%	0.65 [0.54, 0.79]
Subtotal (95% CI)		**103**		**98**	**100.0%**	**0.65 [0.54, 0.79]**
Total events	57		83			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.33 (P < 0.0001)						
1.1.3 75 mg vs placebo						
KANE2003	66	100	98	98	100.0%	0.66 [0.57, 0.76]
Subtotal (95% CI)		**100**		**98**	**100.0%**	**0.66 [0.57, 0.76]**
Total events	66		98			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.73 (P < 0.00001)						



1.2 Mental state: 1. PANSS total (change from baseline) (medium-term)

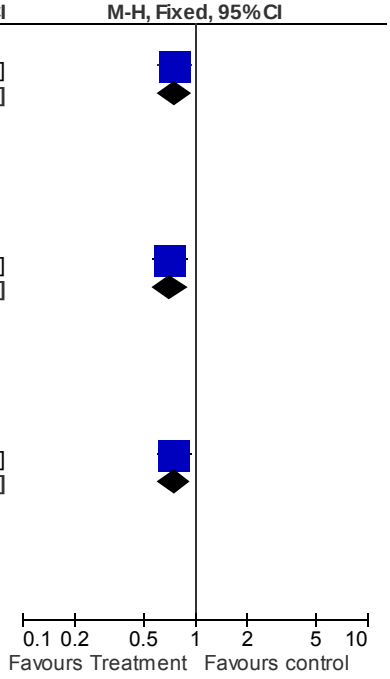
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.2.1 25 mg vs placebo								
KANE2003	-6.2	16.9	93	2.6	16.9	92	100.0%	-8.80 [-13.67, -3.93]
Subtotal (95% CI)			**93**			**92**	**100.0%**	**-8.80 [-13.67, -3.93]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.54 (P = 0.0004)								
1.2.2 50 mg vs placebo								
KANE2003	-8.5	16.9	98	2.6	16.9	92	100.0%	-11.10 [-15.91, -6.29]
Subtotal (95% CI)			**98**			**92**	**100.0%**	**-11.10 [-15.91, -6.29]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.52 (P < 0.00001)								
1.2.3 75 mg vs placebo								
KANE2003	-7.4	16.9	87	2.6	16.9	92	100.0%	-10.00 [-14.95, -5.05]
Subtotal (95% CI)			**87**			**92**	**100.0%**	**-10.00 [-14.95, -5.05]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.96 (P < 0.0001)								



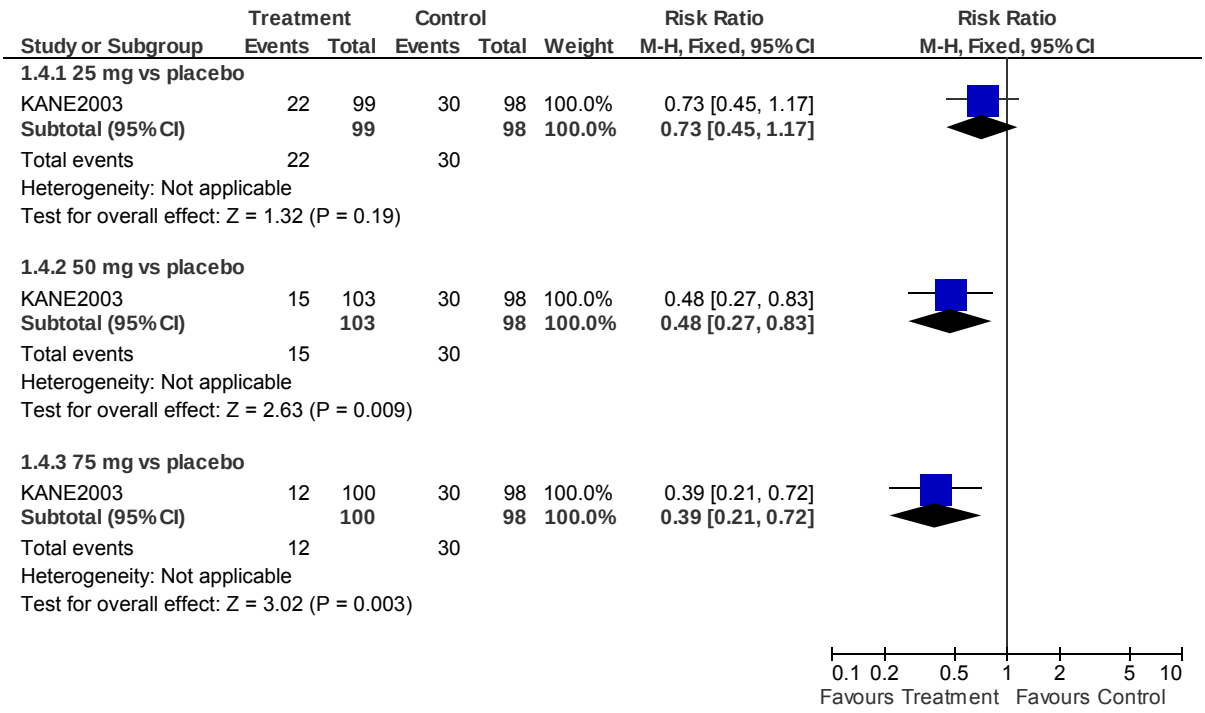
Test for subgroup differences: Chi² = 0.43, df = 2 (P = 0.80), I² = 0%

1.3 Leaving the study early: 1. Any reason (medium-term)

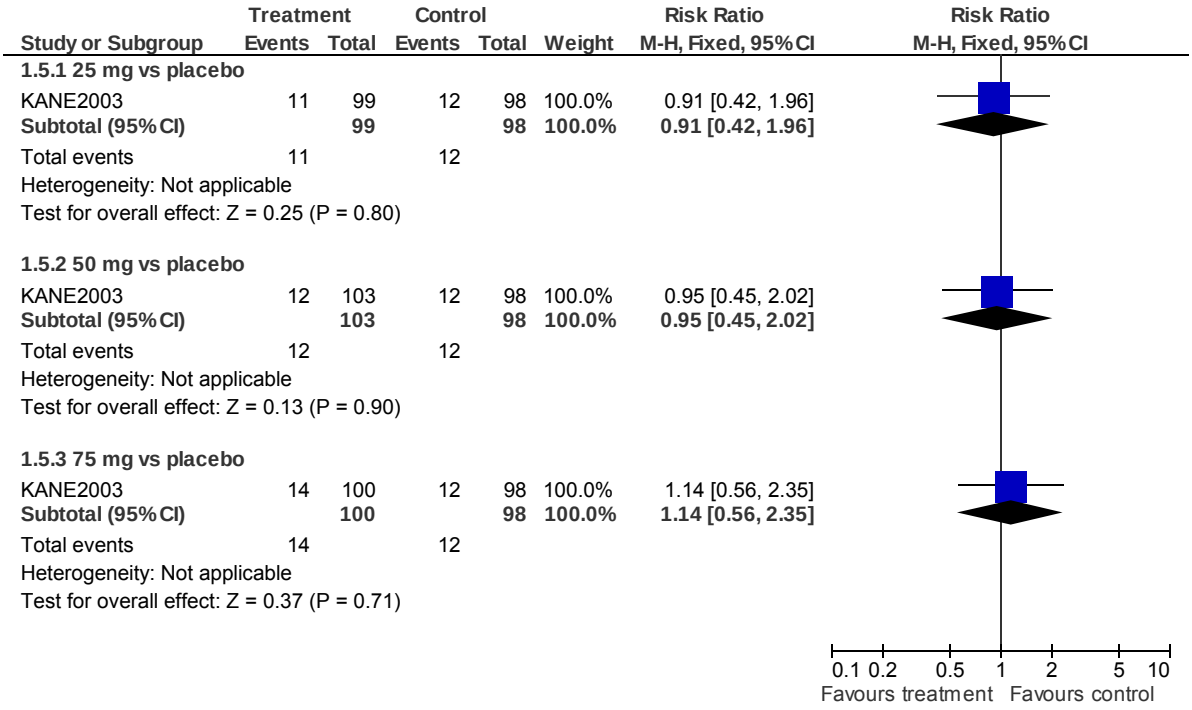
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 25 mg vs placebo						
KANE2003	52	99	68	98	100.0%	0.76 [0.60, 0.95]
Subtotal (95% CI)		**99**		**98**	**100.0%**	**0.76 [0.60, 0.95]**
Total events	52		68			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.38 (P = 0.02)						
1.3.2 50 mg vs placebo						
KANE2003	51	103	68	98	100.0%	0.71 [0.56, 0.90]
Subtotal (95% CI)		**103**		**98**	**100.0%**	**0.71 [0.56, 0.90]**
Total events	51		68			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.81 (P = 0.005)						
1.3.3 75 mg vs placebo						
KANE2003	52	100	68	98	100.0%	0.75 [0.60, 0.94]
Subtotal (95% CI)		**100**		**98**	**100.0%**	**0.75 [0.60, 0.94]**
Total events	52		68			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.46 (P = 0.01)						



1.4 Leaving the study early: 2. Due to lack of efficacy (medium-term)



1.5 Leaving the study early: 3: Adverse event (medium-term)



1.6 AE: 1. Metabolic SEs - weight gain at endpoint (medium-term)

1.6.1 25 mg vs placebo

Study ID	LAI risperidone	Placebo
KANE2003	0.5 kg	-1.4 kg

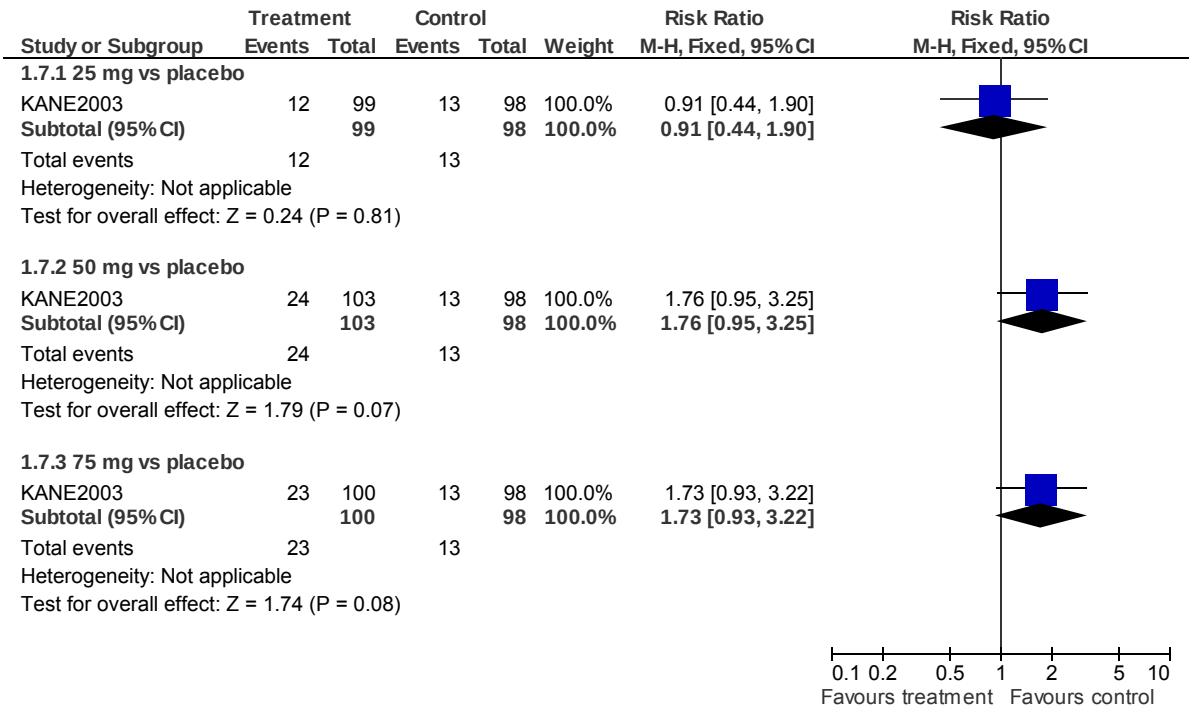
1.6.2 50 mg vs placebo

Study ID	LAI risperidone	Placebo
KANE2003	1.2 kg	-1.4 kg

1.6.3 75 mg vs placebo

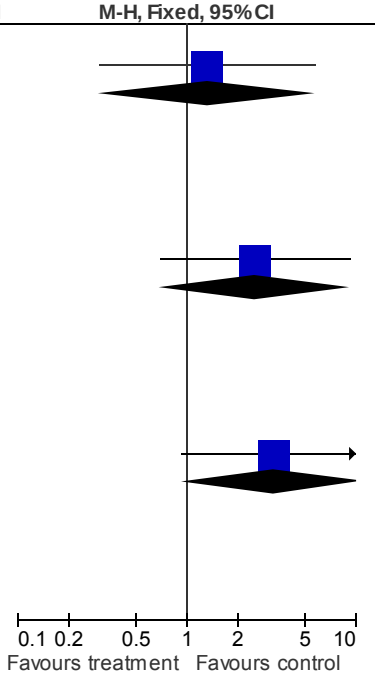
Study ID	LAI risperidone	Placebo
KANE2003	1.9 kg	-1.4 kg

1.7 AE: 2. Neurologic SEs - Use of anticholinergic medication (medium-term)



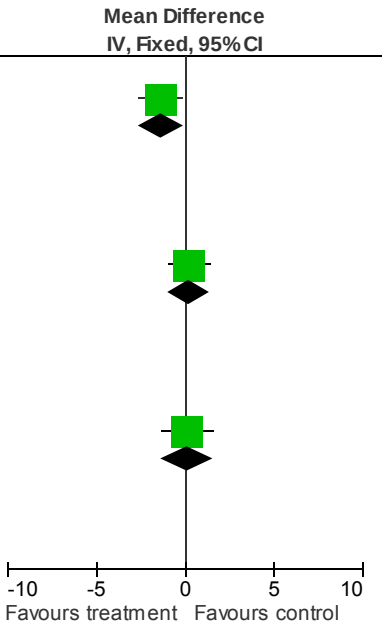
1.8 AE: 2. Neurologic SEs - Extrapyramidal disorder (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.8.1 25 mg vs placebo						
KANE2003	4	99	3	98	100.0%	1.32 [0.30, 5.74]
Subtotal (95% CI)		**99**		**98**	**100.0%**	**1.32 [0.30, 5.74]**
Total events	4		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.37 (P = 0.71)						
1.8.2 50 mg vs placebo						
KANE2003	8	103	3	98	100.0%	2.54 [0.69, 9.29]
Subtotal (95% CI)		**103**		**98**	**100.0%**	**2.54 [0.69, 9.29]**
Total events	8		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.41 (P = 0.16)						
1.8.3 75 mg vs placebo						
KANE2003	10	100	3	98	100.0%	3.27 [0.93, 11.51]
Subtotal (95% CI)		**100**		**98**	**100.0%**	**3.27 [0.93, 11.51]**
Total events	10		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.84 (P = 0.07)						



1.9 AE: 2. Neurologic SEs - ESRS total (medium-term)

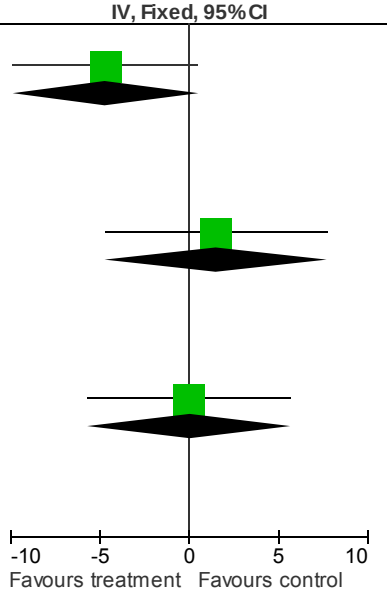
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.9.1 25 mg vs placebo								
KANE2003	-1.5	4	97	-0.1	4.8	93	100.0%	-1.40 [-2.66, -0.14]
Subtotal (95% CI)			**97**			**93**	**100.0%**	**-1.40 [-2.66, -0.14]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.18 (P = 0.03)								
1.9.2 50 mg vs placebo								
KANE2003	0.1	3.6	98	-0.1	4.8	93	100.0%	0.20 [-1.01, 1.41]
Subtotal (95% CI)			**98**			**93**	**100.0%**	**0.20 [-1.01, 1.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.32 (P = 0.75)								
1.9.3 75 mg vs placebo								
KANE2003	0	5.3	90	-0.1	4.8	93	100.0%	0.10 [-1.37, 1.57]
Subtotal (95% CI)			**90**			**93**	**100.0%**	**0.10 [-1.37, 1.57]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.13 (P = 0.89)								



Test for subgroup differences: Chi² = 3.82, df = 2 (P = 0.15), I² = 47.6%

1.10 AE: 3. Pain at injection site (patient rating) (first injection)

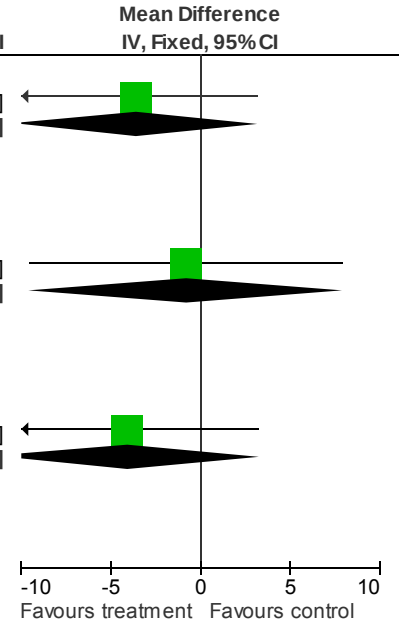
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.10.1 25 mg vs placebo								
KANE2003	12	15.8	97	16.7	20.7	96	100.0%	-4.70 [-9.90, 0.50]
Subtotal (95% CI)			**97**			**96**	**100.0%**	**-4.70 [-9.90, 0.50]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.77 (P = 0.08)								
1.10.2 50 mg vs placebo								
KANE2003	18.2	24	102	16.7	20.7	96	100.0%	1.50 [-4.73, 7.73]
Subtotal (95% CI)			**102**			**96**	**100.0%**	**1.50 [-4.73, 7.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.47 (P = 0.64)								
1.10.3 75 mg vs placebo								
KANE2003	16.7	20	100	16.7	20.7	96	100.0%	0.00 [-5.70, 5.70]
Subtotal (95% CI)			**100**			**96**	**100.0%**	**0.00 [-5.70, 5.70]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								



Test for subgroup differences: Chi² = 2.61, df = 2 (P = 0.27), I² = 23.4%

1.11 AE: 3. Pain at injection site (patient rating) (sixth injection)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.11.1 25 mg vs placebo								
KANE2003	9	10.3	44	12.6	17.4	32	100.0%	-3.60 [-10.35, 3.15]
Subtotal (95% CI)			**44**			**32**	**100.0%**	**-3.60 [-10.35, 3.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.04 (P = 0.30)								
1.11.2 50 mg vs placebo								
KANE2003	11.8	21.2	43	12.6	17.4	32	100.0%	-0.80 [-9.55, 7.95]
Subtotal (95% CI)			**43**			**32**	**100.0%**	**-0.80 [-9.55, 7.95]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.18 (P = 0.86)								
1.11.3 75 mg vs placebo								
KANE2003	8.5	14.4	45	12.6	17.4	32	100.0%	-4.10 [-11.45, 3.25]
Subtotal (95% CI)			**45**			**32**	**100.0%**	**-4.10 [-11.45, 3.25]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.09 (P = 0.27)								



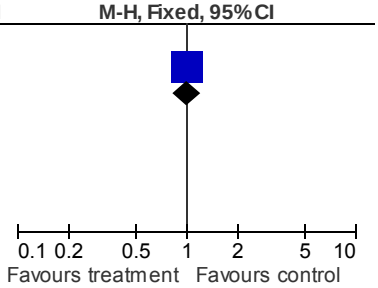
Test for subgroup differences: Chi² = 0.36, df = 2 (P = 0.84), I² = 0%

2 Long-acting risperidone versus oral risperidone

2.1 Global state: 1. No important clinical response (moderate or severe on CGI at endpoint) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 vs oral risperidone						
CHUE2005	134	319	135	321	100.0%	1.00 [0.83, 1.20]
Subtotal (95% CI)		**319**		**321**	**100.0%**	**1.00 [0.83, 1.20]**
Total events	134		135			

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



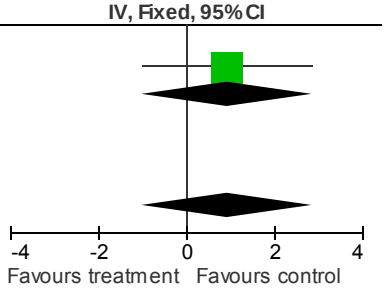
2.2 Mental state: 1. PANSS total (change from baseline)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
2.2.1 vs oral risperidone								
CHUE2005	-5.4	11.42	266	-6.3	11.61	275	100.0%	0.90 [-1.04, 2.84]
Subtotal (95% CI)			**266**			**275**	**100.0%**	**0.90 [-1.04, 2.84]**

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

Total (95% CI)			**266**			**275**	**100.0%**	**0.90 [-1.04, 2.84]**

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



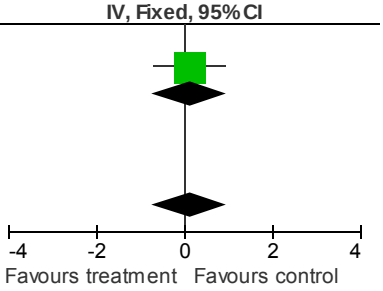
2.3 Mental state: 1. PANSS negative symptoms (change from baseline)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
2.3.1 vs oral risperidone								
CHUE2005	-1.5	4.89	266	-1.6	4.97	275	100.0%	0.10 [-0.73, 0.93]
Subtotal (95% CI)			**266**			**275**	**100.0%**	**0.10 [-0.73, 0.93]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)

Total (95% CI)			**266**			**275**	**100.0%**	**0.10 [-0.73, 0.93]**

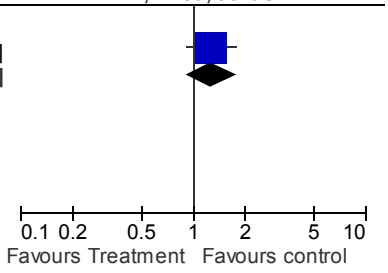
Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)
Test for subgroup differences: Not applicable



2.4 Leaving the study early: 1. Any reason (medium-term)

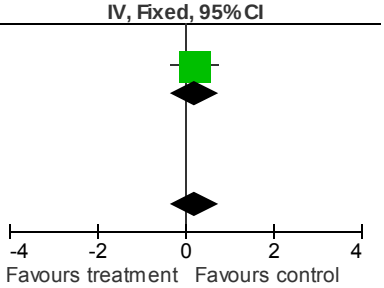
Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.4.1 vs oral risperidone						
CHUE2005	63	319	50	321	100.0%	1.27 [0.90, 1.78]
Subtotal (95% CI)		**319**		**321**	**100.0%**	**1.27 [0.90, 1.78]**
Total events	63		50			

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



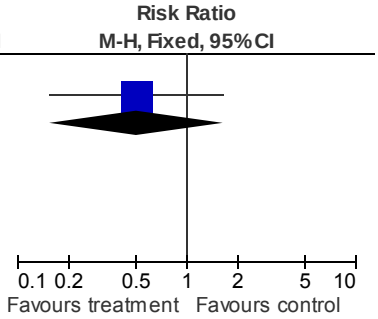
2.5 AE: 1. Metabolic SEs - Weight gain (change from baseline)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.5.1 vs oral risperidone								
CHUE2005	0.5	3.57	319	0.3	3.58	321	100.0%	0.20 [-0.35, 0.75]
Subtotal (95% CI)			**319**			**321**	**100.0%**	**0.20 [-0.35, 0.75]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.71 (P = 0.48)								
Total (95% CI)			**319**			**321**	**100.0%**	**0.20 [-0.35, 0.75]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.71 (P = 0.48)								
Test for subgroup differences: Not applicable								



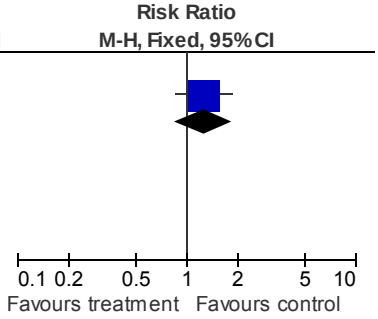
2.6 AE: 1. Metabolic SEs - Potentially attributable to prolactin elevation (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.6.1 vs oral risperidone						
CHUE2005	4	319	8	321	100.0%	0.50 [0.15, 1.65]
Subtotal (95% CI)		**319**		**321**	**100.0%**	**0.50 [0.15, 1.65]**
Total events	4		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.13 (P = 0.26)						



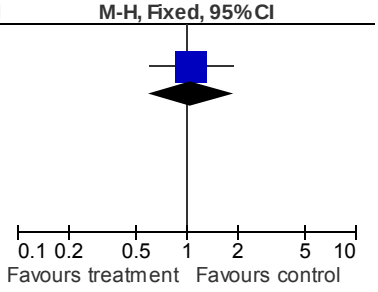
2.7 AE: 2. Neurologic SEs - Use of anticholinergic medication (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.7.1 vs oral risperidone						
CHUE2005	49	319	39	321	100.0%	1.26 [0.86, 1.87]
Subtotal (95% CI)		**319**		**321**	**100.0%**	**1.26 [0.86, 1.87]**
Total events	49		39			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.18 (P = 0.24)						



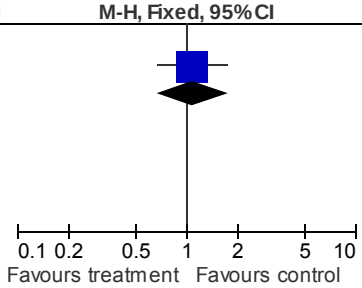
2.8 AE: 2. Neurologic SEs - Movement disorder-related AEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.8.1 vs oral risperidone						
CHUE2005	22	319	21	321	100.0%	1.05 [0.59, 1.88]
Subtotal (95% CI)		**319**		**321**	**100.0%**	**1.05 [0.59, 1.88]**
Total events	22		21			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.18 (P = 0.86)						



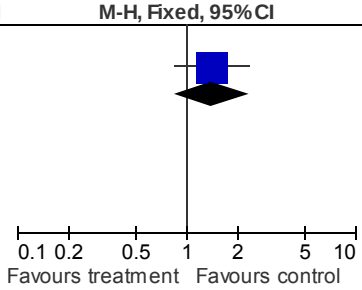
2.9 AE: 3. Other SEs - Insomnia (medium-term)

	Treatment		Control			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**	**M-H, Fixed, 95% CI**
2.9.1 vs oral risperidone							
CHUE2005	31	319	29	321	100.0%	1.08 [0.66, 1.74]	
Subtotal (95% CI)		**319**		**321**	**100.0%**	**1.08 [0.66, 1.74]**	
Total events	31		29				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.30 (P = 0.77)							



2.10 AE: 3. Other SEs - Anxiety (medium-term)

	Treatment		Control			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**	**M-H, Fixed, 95% CI**
2.10.1 vs oral risperidone							
CHUE2005	32	319	23	321	100.0%	1.40 [0.84, 2.34]	
Subtotal (95% CI)		**319**		**321**	**100.0%**	**1.40 [0.84, 2.34]**	
Total events	32		23				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.29 (P = 0.20)							



2.11 AE: 3. Other SEs - Headache (medium-term)

	Treatment		Control			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**	**M-H, Fixed, 95% CI**
2.11.1 vs oral risperidone							
CHUE2005	26	319	23	321	100.0%	1.14 [0.66, 1.95]	
Subtotal (95% CI)		**319**		**321**	**100.0%**	**1.14 [0.66, 1.95]**	
Total events	26		23				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.47 (P = 0.64)							

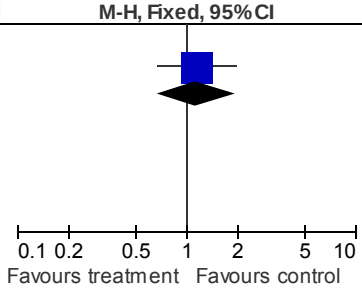


Table 6: Studies included in the review of antipsychotic medication for people whose illness has not responded adequately to treatment

Treatment	versus Comparator									
	CHL	**CLZ**	**FLUPHEN**	**HAL**	**OLZ**	**PER**	**QUE**	**RIS**	**ZIP**	**ZOT**
ARI						KANE2007B [6weeks, N=300]				
CLZ	Claghorn 1987 [4–8weeks, N=151] Hong 1997 [12weeks, N=40] Kane 1988 [6weeks, N=268]			Buchanan1998 [10weeks, N=75] Klieser 1989 [6weeks, N=32] Rosenheck 1997 [52weeks, N=423] VOLAVKA2002 [14weeks, N=77]	Beuzen 1998 [18weeks, N=180] Bitter 1999 [18weeks, N=150] Oliemeulen 2000 [8weeks, N=36] VOLAVKA2002 [14weeks, N=79] MELTZER2008 [26weeks, N=40]			Anand 1998 [12weeks, N=273] Bondolfi 1998 [8weeks, N=86] Breier 1999 [6weeks, N=29] Chowdhury 1999 [16weeks, N=60] VOLAVKA2002 [14weeks, N=81]		Meyer-Lindberg 1996 [6weeks, N=50]
OLZ	Conley 1998a [8weeks, N=84]	Beuzen 1998 [18weeks, N=180] Bitter 1999 [18weeks, N=150] Oliemeulen 2000 [8weeks, N=36] VOLAVKA2		Altamura 1999 [14weeks, N=28] Breier 2000 [6weeks, N=526] BUCHANAN2005 [16weeks, N=63]				VOLAVKA2002 [14weeks, N=80]	KINON2006A [24weeks, N=394]	

		002 [14weeks, N=79] MELTZER2008 [26weeks, N=40]								
QUE			CONLEY 2005 [12weeks, N=25]	Emsley 1999 [8weeks, N=288]				CONLEY2005 [12weeks, N=25]		
RIS		Anand 1998 [12weeks, N=273] Bondolfi 1998 [8weeks, N=86] Breier 1999 [6weeks, N=29] Chowdhury 1999 [16weeks, N=60] VOLAVKA2002 [14weeks, N=81]	CONLEY 2005 [12weeks, N=26]	Heck 2000 [6weeks, N=77] Kern 1998/1999 [8weeks, N=64] SEE1999 [5weeks, N=20]	VOLAVKA2002 [14weeks, N=80]		CONLEY2005 [12weeks, N=25]			
ZIP					KINON2006A [24weeks, N=394]					

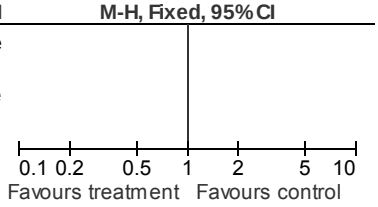
ZOT		Meyer-Lindberg 1996 [6weeks, N=50]								

1 Aripiprazole vs. FGA (in people whose illness has not responded adequately to treatment)

1.1 Mortality (short-term)

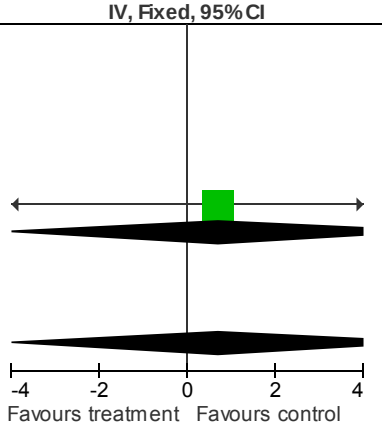
Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KANE2007B	0	154	0	146		Not estimable
Total (95% CI)		**154**		**146**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable



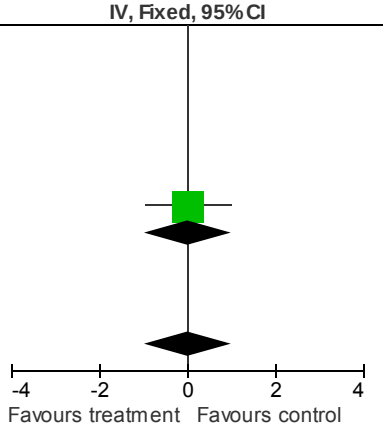
1.2 Mental state: 1. PANSS total (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
1.2.1 vs HAL								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
1.2.2 vs other FGA								
KANE2007B	-9.8	21.38	150	-10.5	21.25	144	100.0%	0.70 [-4.17, 5.57]
Subtotal (95% CI)			**150**			**144**	**100.0%**	**0.70 [-4.17, 5.57]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.28 (P = 0.78)								
Total (95% CI)			**150**			**144**	**100.0%**	**0.70 [-4.17, 5.57]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.28 (P = 0.78)								
Test for subgroup differences: Not applicable								



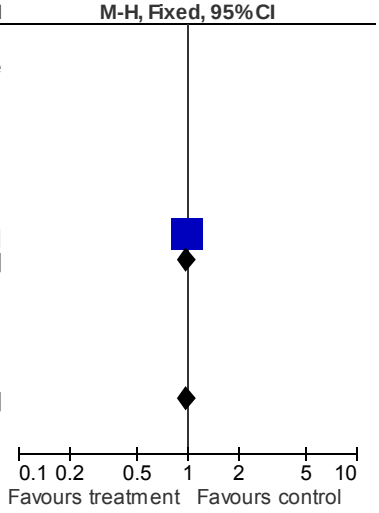
1.3 Mental state: 1. BPRS total (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
1.3.1 vs HAL								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
1.3.2 vs other FGA								
KANE2007B	-2	4.34	150	-2	4.25	144	100.0%	0.00 [-0.98, 0.98]
Subtotal (95% CI)			**150**			**144**	**100.0%**	**0.00 [-0.98, 0.98]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Total (95% CI)			**150**			**144**	**100.0%**	**0.00 [-0.98, 0.98]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Test for subgroup differences: Not applicable								



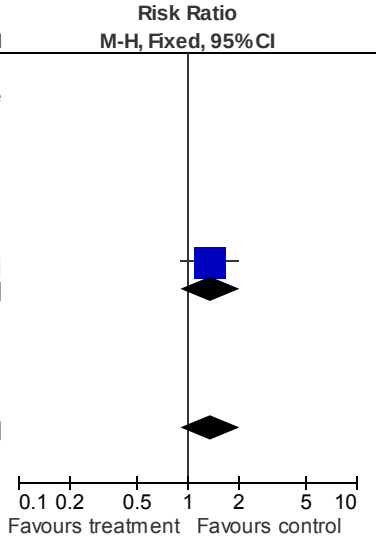
1.4 Mental state: 2. Non-response (<30% improvement on PANSS or CGI-I >2) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 vs HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.4.2 vs other FGA						
KANE2007B	114	154	110	146	100.0%	0.98 [0.86, 1.12]
Subtotal (95% CI)		**154**		**146**	**100.0%**	**0.98 [0.86, 1.12]**
Total events	114		110			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.26 (P = 0.79)						
Total (95% CI)		**154**		**146**	**100.0%**	**0.98 [0.86, 1.12]**
Total events	114		110			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.26 (P = 0.79)						



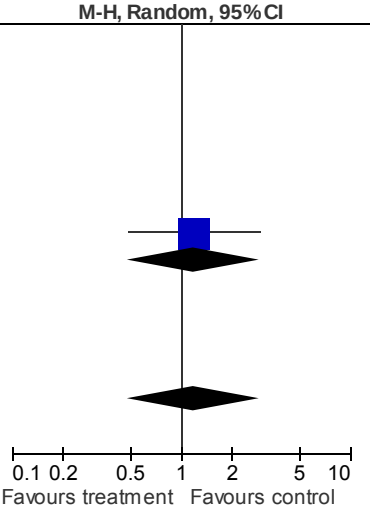
1.5 Leaving the study early: 1. Any reason (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.5.1 vs HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.5.2 vs other FGA						
KANE2007B	44	154	31	146	100.0%	1.35 [0.90, 2.01]
Subtotal (95% CI)		**154**		**146**	**100.0%**	**1.35 [0.90, 2.01]**
Total events	44		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.45 (P = 0.15)						
Total (95% CI)		**154**		**146**	**100.0%**	**1.35 [0.90, 2.01]**
Total events	44		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.45 (P = 0.15)						



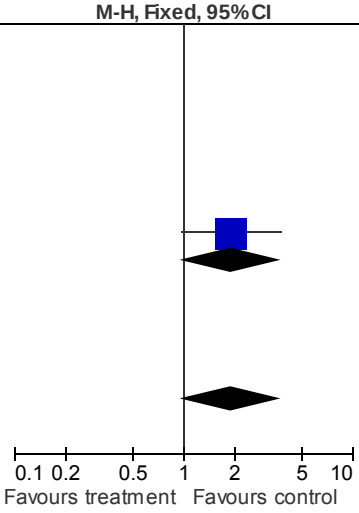
1.6 Leaving the study early: 2. Due to lack of efficacy (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.6.1 vs HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.6.2 vs other FGA						
KANE2007B	10	154	8	146	100.0%	1.19 [0.48, 2.92]
Subtotal (95% CI)		**154**		**146**	**100.0%**	**1.19 [0.48, 2.92]**
Total events	10		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.37 (P = 0.71)						
Total (95% CI)		**154**		**146**	**100.0%**	**1.19 [0.48, 2.92]**
Total events	10		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.37 (P = 0.71)						

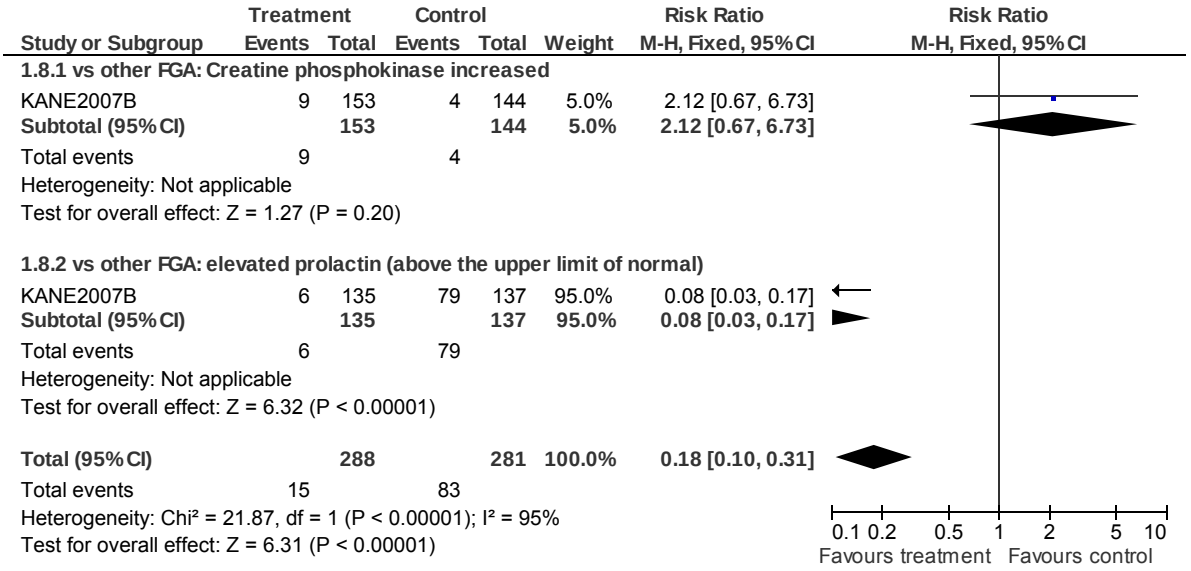


1.7 Leaving the study early: 3: Adverse event (short-term)

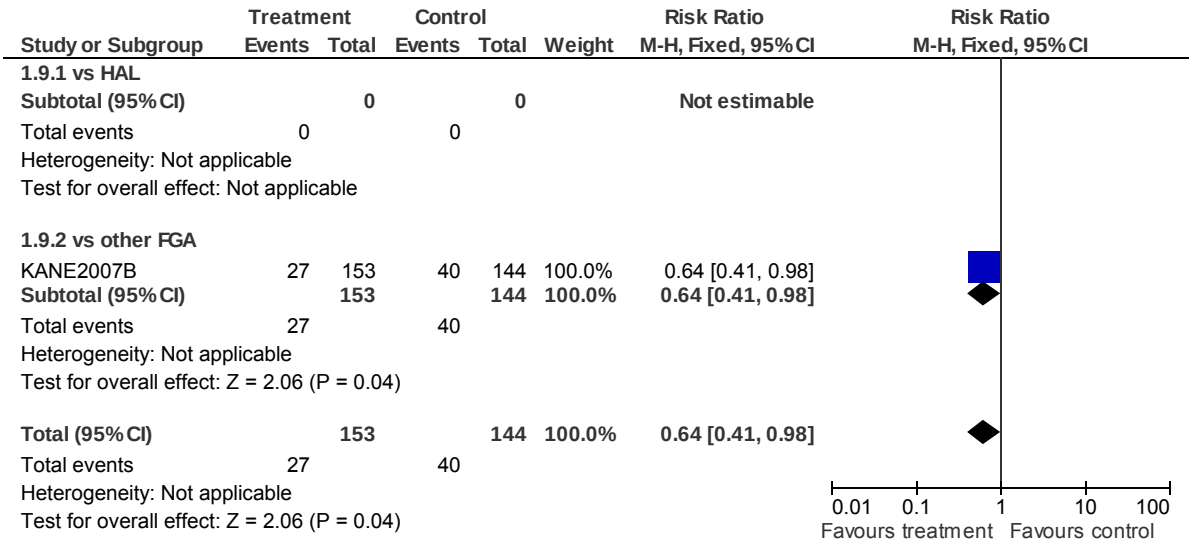
Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.7.1 vs HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.7.2 vs other FGA						
KANE2007B	22	154	11	146	100.0%	1.90 [0.95, 3.77]
Subtotal (95% CI)		**154**		**146**	**100.0%**	**1.90 [0.95, 3.77]**
Total events	22		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.82 (P = 0.07)						
Total (95% CI)		**154**		**146**	**100.0%**	**1.90 [0.95, 3.77]**
Total events	22		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.82 (P = 0.07)						



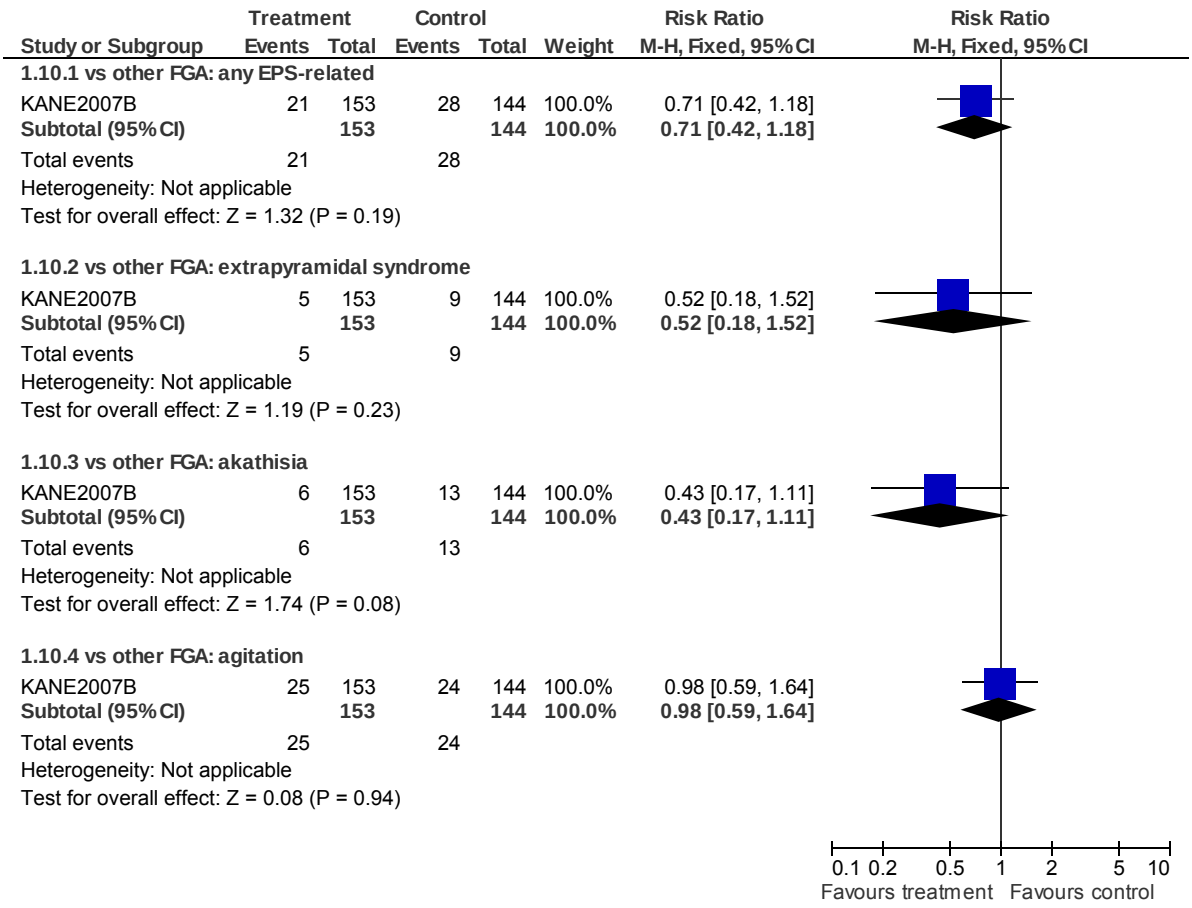
1.8 AE: 1. Metabolic SEs (treatment-emergent) (short-term)



1.9 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)



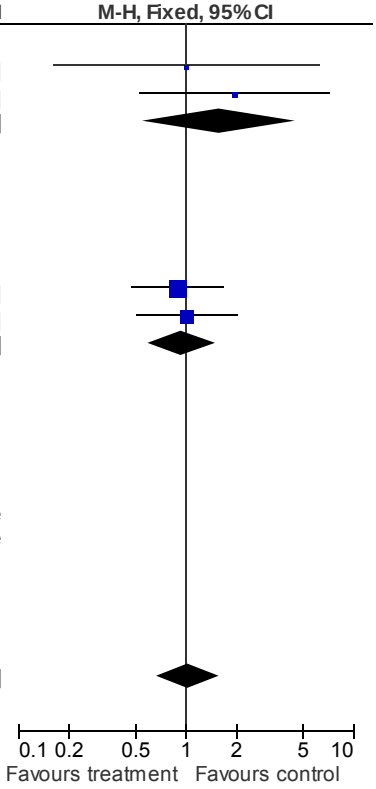
1.10 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



2 Clozapine vs. FGA (in people whose illness has not responded adequately to treatment)

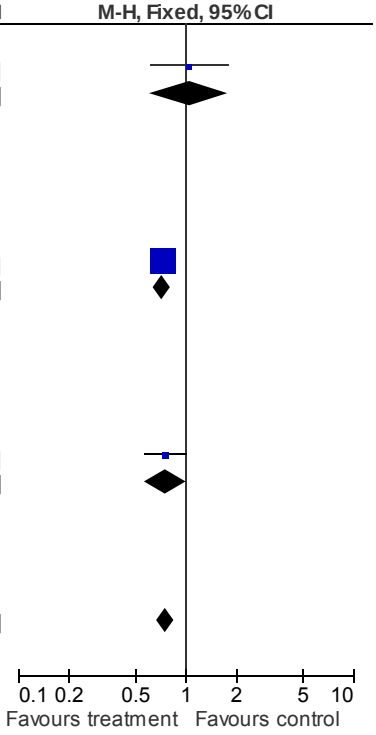
2.1 Global state: 1. Relapse (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 vs HAL (short-term)						
Klieser 1989	2	16	2	16	5.6%	1.00 [0.16, 6.25]
Buchanan 1998	6	38	3	37	8.5%	1.95 [0.53, 7.22]
Subtotal (95% CI)		**54**		**53**	**14.1%**	**1.57 [0.55, 4.51]**
Total events	8		5			
Heterogeneity: Chi² = 0.34, df = 1 (P = 0.56); I² = 0%						
Test for overall effect: Z = 0.84 (P = 0.40)						
2.1.2 vs other FGA (short-term)						
Kane 1988	15	126	19	142	49.9%	0.89 [0.47, 1.68]
Claghorn 1987	13	75	13	76	36.1%	1.01 [0.50, 2.04]
Subtotal (95% CI)		**201**		**218**	**85.9%**	**0.94 [0.59, 1.51]**
Total events	28		32			
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.79); I² = 0%						
Test for overall effect: Z = 0.25 (P = 0.80)						
2.1.3 vs other FGA (medium-term)						
Hong 1997	0	21	0	19		Not estimable
Subtotal (95% CI)		**21**		**19**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**276**		**290**	**100.0%**	**1.03 [0.67, 1.58]**
Total events	36		37			
Heterogeneity: Chi² = 1.12, df = 3 (P = 0.77); I² = 0%						
Test for overall effect: Z = 0.14 (P = 0.89)						



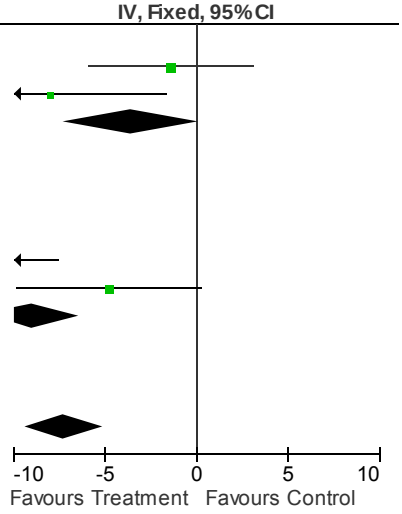
2.2 Global state: 2. Not improved (CGI) (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 vs HAL (short-term)						
Buchanan 1998	12	21	11	20	7.1%	1.04 [0.60, 1.79]
Subtotal (95% CI)		**21**		**20**	**7.1%**	**1.04 [0.60, 1.79]**
Total events	12		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.14 (P = 0.89)						
2.2.2 vs other FGA (short-term)						
Kane 1988	88	126	137	142	81.0%	0.72 [0.64, 0.82]
Subtotal (95% CI)		**126**		**142**	**81.0%**	**0.72 [0.64, 0.82]**
Total events	88		137			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.32 (P < 0.00001)						
2.2.3 vs other FGA (medium-term)						
Hong 1997	15	21	18	19	11.9%	0.75 [0.56, 1.01]
Subtotal (95% CI)		**21**		**19**	**11.9%**	**0.75 [0.56, 1.01]**
Total events	15		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.91 (P = 0.06)						
Total (95% CI)		**168**		**181**	**100.0%**	**0.75 [0.67, 0.84]**
Total events	115		166			
Heterogeneity: Chi² = 1.73, df = 2 (P = 0.42); I² = 0%						
Test for overall effect: Z = 5.11 (P < 0.00001)						



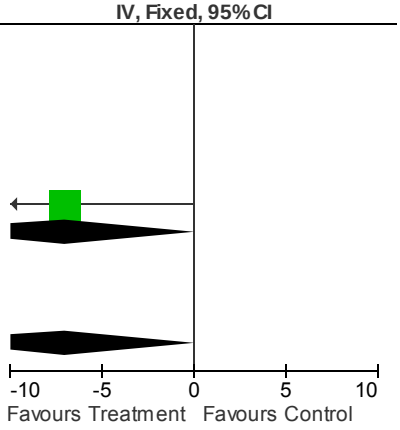
2.3 Mental state: 1. BPRS total (endpoint, high=poor) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.3.1 vs HAL								
Buchanan 1998	35.6	10.6	38	37	9.4	37	21.9%	-1.40 [-5.93, 3.13]
Klieser 1989	36	6	15	44	11	15	11.2%	-8.00 [-14.34, -1.66]
Subtotal (95% CI)			**53**			**52**	**33.1%**	**-3.63 [-7.32, 0.06]**
Heterogeneity: Chi² = 2.75, df = 1 (P = 0.10); I² = 64%								
Test for overall effect: Z = 1.93 (P = 0.05)								
2.3.2 vs other FGA								
Kane 1988	45.1	13	126	55.67	12	139	49.3%	-10.57 [-13.59, -7.55]
Claghorn 1987	35.52	14.64	62	40.3	14.24	63	17.6%	-4.78 [-9.84, 0.28]
Subtotal (95% CI)			**188**			**202**	**66.9%**	**-9.05 [-11.64, -6.45]**
Heterogeneity: Chi² = 3.70, df = 1 (P = 0.05); I² = 73%								
Test for overall effect: Z = 6.84 (P < 0.00001)								
Total (95% CI)			**241**			**254**	**100.0%**	**-7.25 [-9.38, -5.13]**
Heterogeneity: Chi² = 12.01, df = 3 (P = 0.007); I² = 75%								
Test for overall effect: Z = 6.70 (P < 0.00001)								
Test for subgroup differences: Chi² = 5.55, df = 1 (P = 0.02), I² = 82.0%								



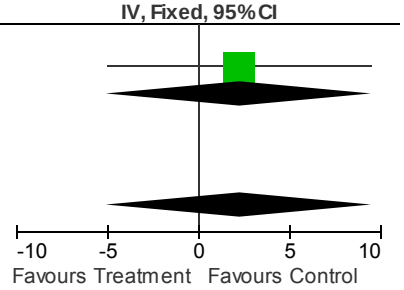
2.4 Mental state: 1. BPRS total (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.4.1 vs HAL								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
2.4.2 vs other FGA								
Hong 1997	45	12	19	52	10	19	100.0%	-7.00 [-14.02, 0.02]
Subtotal (95% CI)			**19**			**19**	**100.0%**	**-7.00 [-14.02, 0.02]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.95 (P = 0.05)								
Total (95% CI)			**19**			**19**	**100.0%**	**-7.00 [-14.02, 0.02]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.95 (P = 0.05)								
Test for subgroup differences: Not applicable								



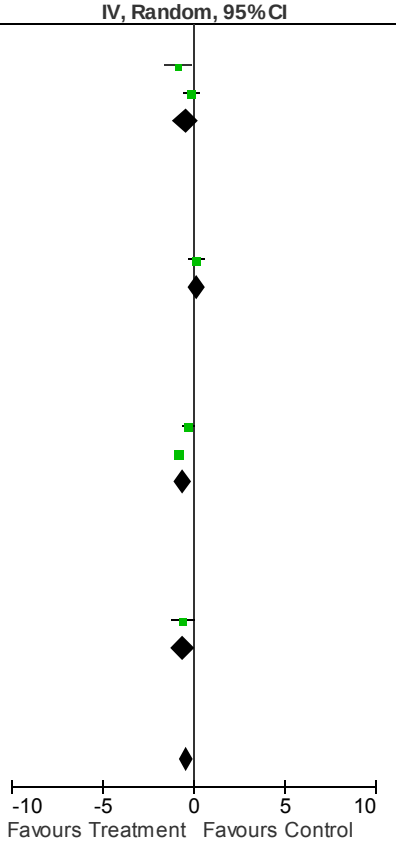
2.5 Mental state: 1. PANSS total (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.5.1 vs HAL								
VOLAVKA2002	90.9	15.8	40	88.7	16.6	37	100.0%	2.20 [-5.05, 9.45]
Subtotal (95% CI)			**40**			**37**	**100.0%**	**2.20 [-5.05, 9.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.59 (P = 0.55)								
Total (95% CI)			**40**			**37**	**100.0%**	**2.20 [-5.05, 9.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.59 (P = 0.55)								
Test for subgroup differences: Not applicable								



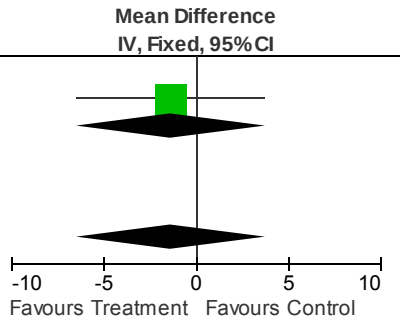
2.6 Mental state: 1. BPRS/PANSS total (endpoint, high=poor) (short-to-medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.6.1 vs HAL (short-term)								
Klieser 1989	36	6	15	44	11	15	11.4%	-0.88 [-1.63, -0.12]
Buchanan 1998	35.6	10.6	38	37	9.4	37	17.2%	-0.14 [-0.59, 0.32]
Subtotal (95% CI)			**53**			**52**	**28.6%**	**-0.44 [-1.16, 0.27]**
Heterogeneity: Tau² = 0.17; Chi² = 2.72, df = 1 (P = 0.10); I² = 63%								
Test for overall effect: Z = 1.22 (P = 0.22)								
2.6.2 vs HAL (medium-term)								
VOLAVKA2002	90.9	15.8	40	88.7	16.6	37	17.3%	0.13 [-0.31, 0.58]
Subtotal (95% CI)			**40**			**37**	**17.3%**	**0.13 [-0.31, 0.58]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.59 (P = 0.56)								
2.6.3 vs other FGA (short-term)								
Claghorn 1987	35.52	14.64	62	40.3	14.24	63	19.4%	-0.33 [-0.68, 0.02]
Kane 1988	45.1	13	126	55.67	12	139	21.5%	-0.84 [-1.10, -0.59]
Subtotal (95% CI)			**188**			**202**	**40.8%**	**-0.60 [-1.11, -0.10]**
Heterogeneity: Tau² = 0.11; Chi² = 5.42, df = 1 (P = 0.02); I² = 82%								
Test for overall effect: Z = 2.34 (P = 0.02)								
2.6.4 vs other FGA (medium-term)								
Hong 1997	45	12	19	52	10	19	13.2%	-0.62 [-1.27, 0.03]
Subtotal (95% CI)			**19**			**19**	**13.2%**	**-0.62 [-1.27, 0.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.86 (P = 0.06)								
Total (95% CI)			**300**			**310**	**100.0%**	**-0.43 [-0.78, -0.08]**
Heterogeneity: Tau² = 0.13; Chi² = 19.35, df = 5 (P = 0.002); I² = 74%								
Test for overall effect: Z = 2.38 (P = 0.02)								



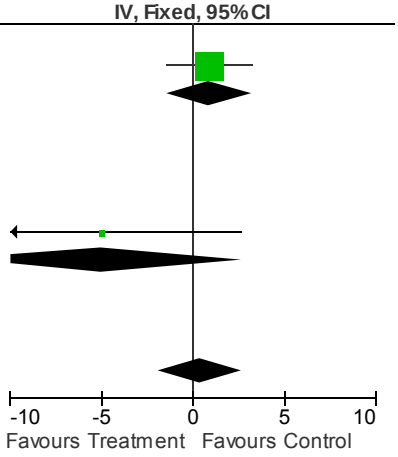
2.7 Mental state: 2. Negative symptoms (endpoint, high=poor) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.7.1 vs HAL								
Buchanan 1998	27	11.5	38	28.4	11.1	37	100.0%	-1.40 [-6.51, 3.71]
Subtotal (95% CI)			**38**			**37**	**100.0%**	**-1.40 [-6.51, 3.71]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.54 (P = 0.59)								
Total (95% CI)			**38**			**37**	**100.0%**	**-1.40 [-6.51, 3.71]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.54 (P = 0.59)								
Test for subgroup differences: Not applicable								



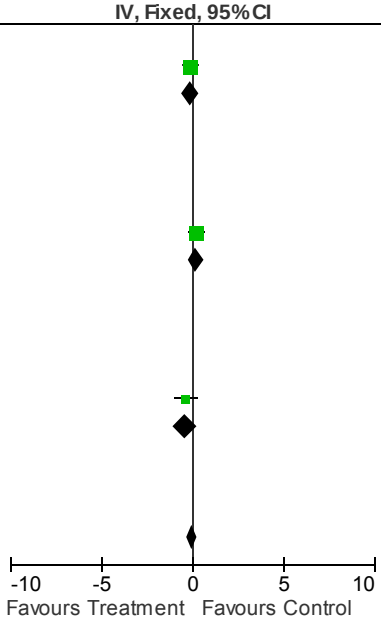
2.8 Mental state: 2. PANSS negative score (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.8.1 vs HAL								
VOLAVKA2002	23.5	4.9	40	22.6	5.6	37	91.3%	0.90 [-1.46, 3.26]
Subtotal (95% CI)			**40**			**37**	**91.3%**	**0.90 [-1.46, 3.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.75 (P = 0.45)								
2.8.2 vs other FGA								
Hong 1997	33	13	19	38	11	19	8.7%	-5.00 [-12.66, 2.66]
Subtotal (95% CI)			**19**			**19**	**8.7%**	**-5.00 [-12.66, 2.66]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.28 (P = 0.20)								
Total (95% CI)			**59**			**56**	**100.0%**	**0.39 [-1.87, 2.64]**
Heterogeneity: Chi² = 2.08, df = 1 (P = 0.15); I² = 52%								
Test for overall effect: Z = 0.34 (P = 0.74)								
Test for subgroup differences: Chi² = 2.08, df = 1 (P = 0.15), I² = 52.0%								



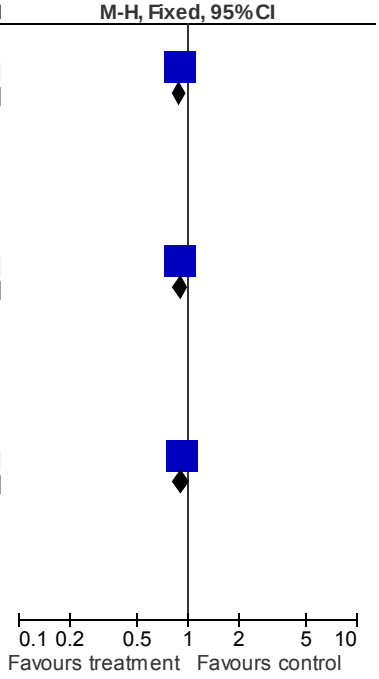
2.9 Mental state: 2. Negative symptoms (endpoint, high=poor) (short-to-medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.9.1 vs HAL (short-term)								
Buchanan 1998	27	11.5	38	28.4	11.1	37	39.7%	-0.12 [-0.58, 0.33]
Subtotal (95% CI)			**38**			**37**	**39.7%**	**-0.12 [-0.58, 0.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.53 (P = 0.60)								
2.9.2 vs HAL (medium-term)								
VOLAVKA2002	23.5	4.9	40	22.6	5.6	37	40.6%	0.17 [-0.28, 0.62]
Subtotal (95% CI)			**40**			**37**	**40.6%**	**0.17 [-0.28, 0.62]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.74 (P = 0.46)								
2.9.3 vs other FGA (medium-term)								
Hong 1997	33	13	19	38	11	19	19.7%	-0.41 [-1.05, 0.24]
Subtotal (95% CI)			**19**			**19**	**19.7%**	**-0.41 [-1.05, 0.24]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.24 (P = 0.22)								
Total (95% CI)			**97**			**93**	**100.0%**	**-0.06 [-0.35, 0.23]**
Heterogeneity: Chi² = 2.20, df = 2 (P = 0.33); I² = 9%								
Test for overall effect: Z = 0.41 (P = 0.68)								
Test for subgroup differences: Chi² = 2.20, df = 2 (P = 0.33), I² = 9.1%								



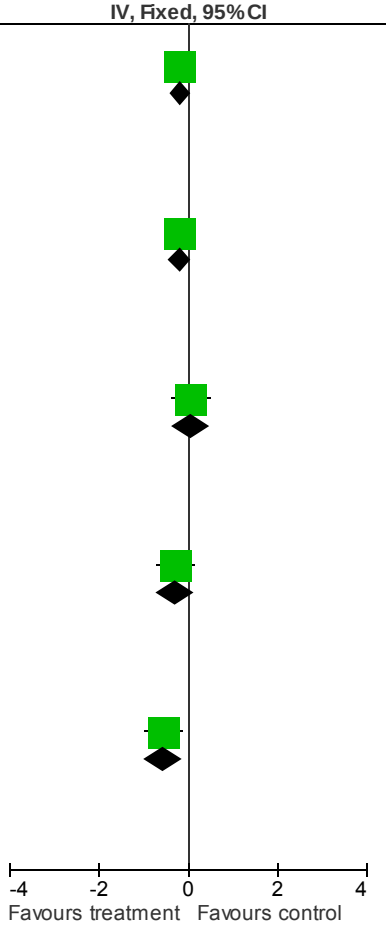
2.10 Mental state: 3. Non-response (20% or less improvement on PANSS) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.10.1 vs HAL (short-term)						
Rosenheck 1997	161	205	192	218	100.0%	0.89 [0.82, 0.97]
Subtotal (95% CI)		**205**		**218**	**100.0%**	**0.89 [0.82, 0.97]**
Total events	161		192			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.59 (P = 0.010)						
2.10.2 vs HAL (medium-term)						
Rosenheck 1997	143	205	169	218	100.0%	0.90 [0.80, 1.01]
Subtotal (95% CI)		**205**		**218**	**100.0%**	**0.90 [0.80, 1.01]**
Total events	143		169			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.80 (P = 0.07)						
2.10.3 vs HAL (long-term)						
Rosenheck 1997	144	205	167	218	100.0%	0.92 [0.82, 1.03]
Subtotal (95% CI)		**205**		**218**	**100.0%**	**0.92 [0.82, 1.03]**
Total events	144		167			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.47 (P = 0.14)						



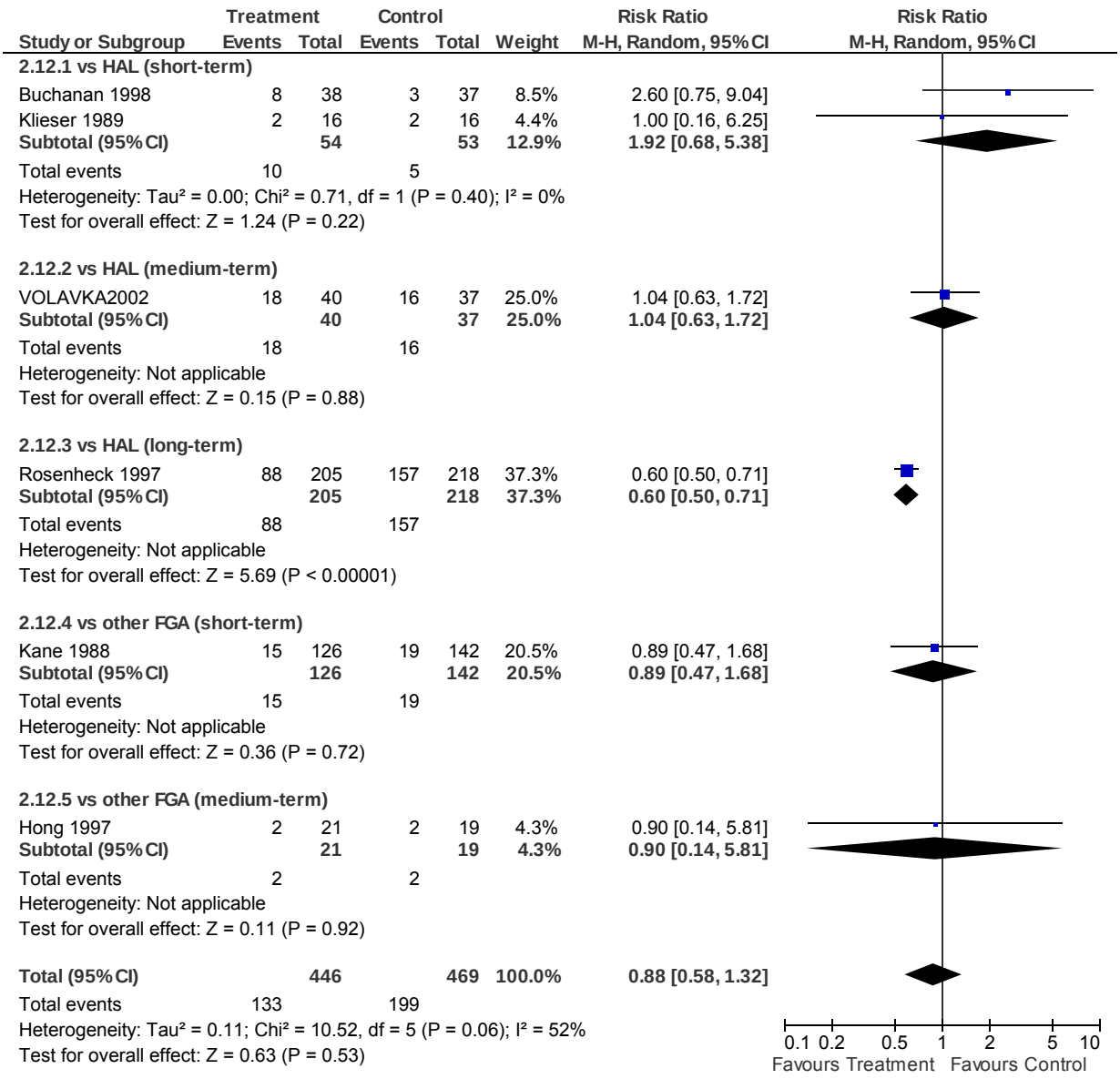
2.11 Cognitive functioning: 1. Global & domain scores (Z score change) (medium-term) (sign changed)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.11.1 vs HAL: Global score								
VOLAVKA2002	-0.15	0.39	24	0.04	0.44	25	100.0%	-0.19 [-0.42, 0.04]
Subtotal (95% CI)			**24**			**25**	**100.0%**	**-0.19 [-0.42, 0.04]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.60 (P = 0.11)								
2.11.2 vs HAL: General executive & perceptual organisation								
VOLAVKA2002	-0.08	0.39	24	0.11	0.53	25	100.0%	-0.19 [-0.45, 0.07]
Subtotal (95% CI)			**24**			**25**	**100.0%**	**-0.19 [-0.45, 0.07]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.43 (P = 0.15)								
2.11.3 vs HAL: Declarative verbal learning & memory								
VOLAVKA2002	0.15	0.72	24	0.09	0.84	25	100.0%	0.06 [-0.38, 0.50]
Subtotal (95% CI)			**24**			**25**	**100.0%**	**0.06 [-0.38, 0.50]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.27 (P = 0.79)								
2.11.4 vs HAL: Processing speed & attention								
VOLAVKA2002	-0.48	0.82	24	-0.19	0.71	25	100.0%	-0.29 [-0.72, 0.14]
Subtotal (95% CI)			**24**			**25**	**100.0%**	**-0.29 [-0.72, 0.14]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.32 (P = 0.19)								
2.11.5 vs HAL: Simple motor functioning								
VOLAVKA2002	-0.6	0.72	24	-0.05	0.81	25	100.0%	-0.55 [-0.98, -0.12]
Subtotal (95% CI)			**24**			**25**	**100.0%**	**-0.55 [-0.98, -0.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.51 (P = 0.01)								

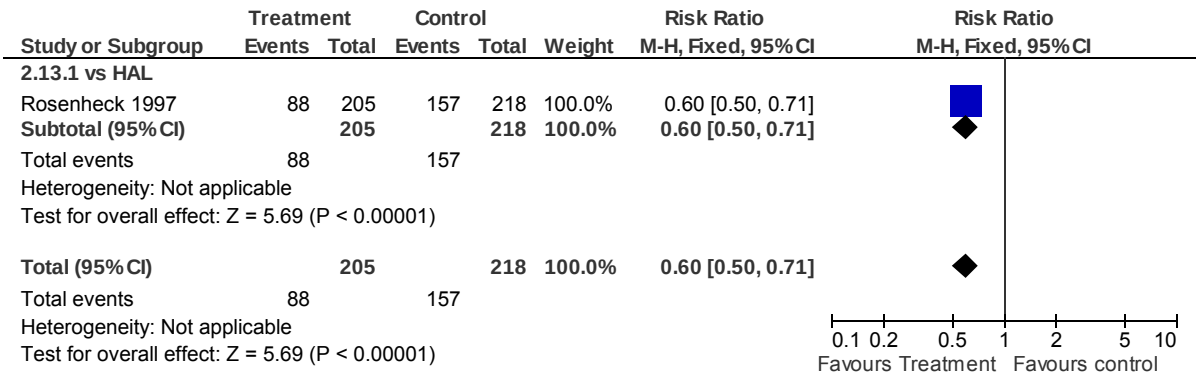


Test for subgroup differences: Chi² = 4.06, df = 4 (P = 0.40), I² = 1.5%

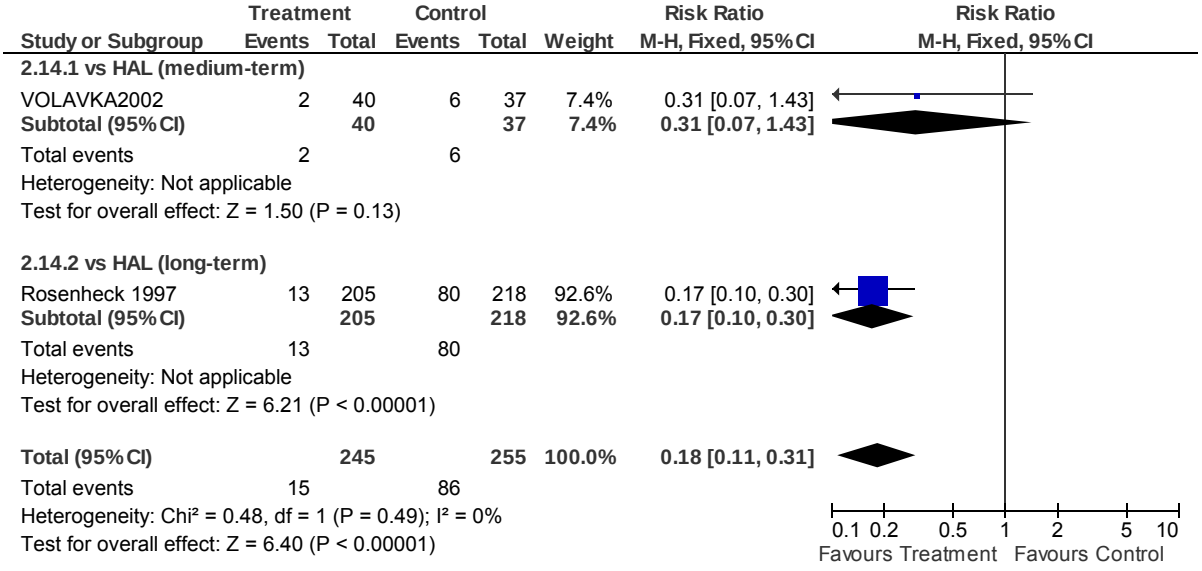
2.12 Leaving the study early: 1. Any reason (short-to-medium-term)



2.13 Leaving the study early: 1. Any reason (long-term)

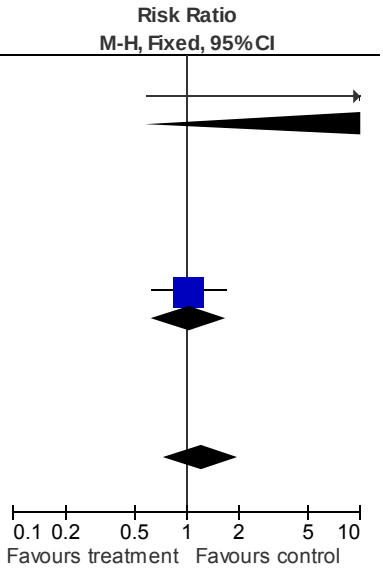


2.14 Leaving the study early: 2. Due to lack of efficacy (medium-to-long-term)



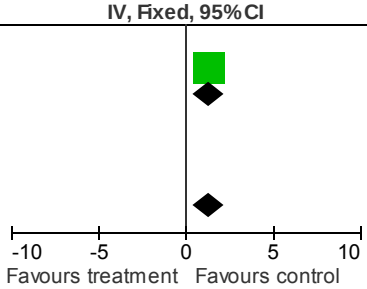
2.15 Leaving the study early: 3: Adverse event (medium-to-long-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.15.1 vs HAL (medium-term)						
VOLAVKA2002	5	40	0	37	1.9%	10.20 [0.58, 178.24]
Subtotal (95% CI)		**40**		**37**	**1.9%**	**10.20 [0.58, 178.24]**
Total events	5		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.59 (P = 0.11)						
2.15.2 vs HAL (long-term)						
Rosenheck 1997	26	205	27	218	98.1%	1.02 [0.62, 1.69]
Subtotal (95% CI)		**205**		**218**	**98.1%**	**1.02 [0.62, 1.69]**
Total events	26		27			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.09 (P = 0.93)						
Total (95% CI)		**245**		**255**	**100.0%**	**1.20 [0.74, 1.95]**
Total events	31		27			
Heterogeneity: Chi² = 2.53, df = 1 (P = 0.11); I² = 61%						
Test for overall effect: Z = 0.75 (P = 0.46)						



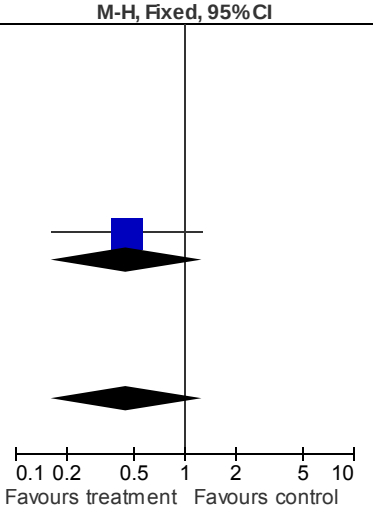
2.16 AE: 1. Metabolic SEs - BMI (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
2.16.1 vs HAL								
VOLAVKA2002	1.4	1.9	38	0.1	2	36	100.0%	1.30 [0.41, 2.19]
Subtotal (95% CI)			**38**			**36**	**100.0%**	**1.30 [0.41, 2.19]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.86 (P = 0.004)								
Total (95% CI)			**38**			**36**	**100.0%**	**1.30 [0.41, 2.19]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.86 (P = 0.004)								
Test for subgroup differences: Not applicable								



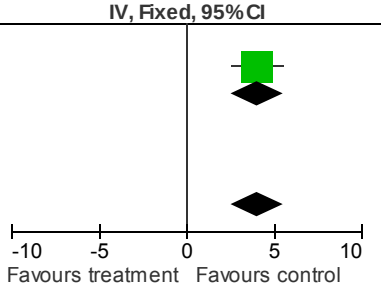
2.17 AE: 1. Metabolic SEs - Weight gain (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.17.1 vs HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
2.17.2 vs other FGA						
Hong 1997	4	21	8	19	100.0%	0.45 [0.16, 1.26]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**0.45 [0.16, 1.26]**
Total events	4		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.51 (P = 0.13)						
Total (95% CI)		**21**		**19**	**100.0%**	**0.45 [0.16, 1.26]**
Total events	4		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.51 (P = 0.13)						



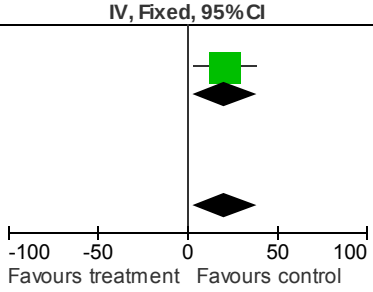
2.18 AE: 1. Metabolic SEs - Weight change from baseline (kg) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.18.1 vs HAL								
VOLAVKA2002	4.2	4.7	38	0.2	0.2	36	100.0%	4.00 [2.50, 5.50]
Subtotal (95% CI)			**38**			**36**	**100.0%**	**4.00 [2.50, 5.50]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.24 (P < 0.00001)								
Total (95% CI)			**38**			**36**	**100.0%**	**4.00 [2.50, 5.50]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.24 (P < 0.00001)								
Test for subgroup differences: Not applicable								

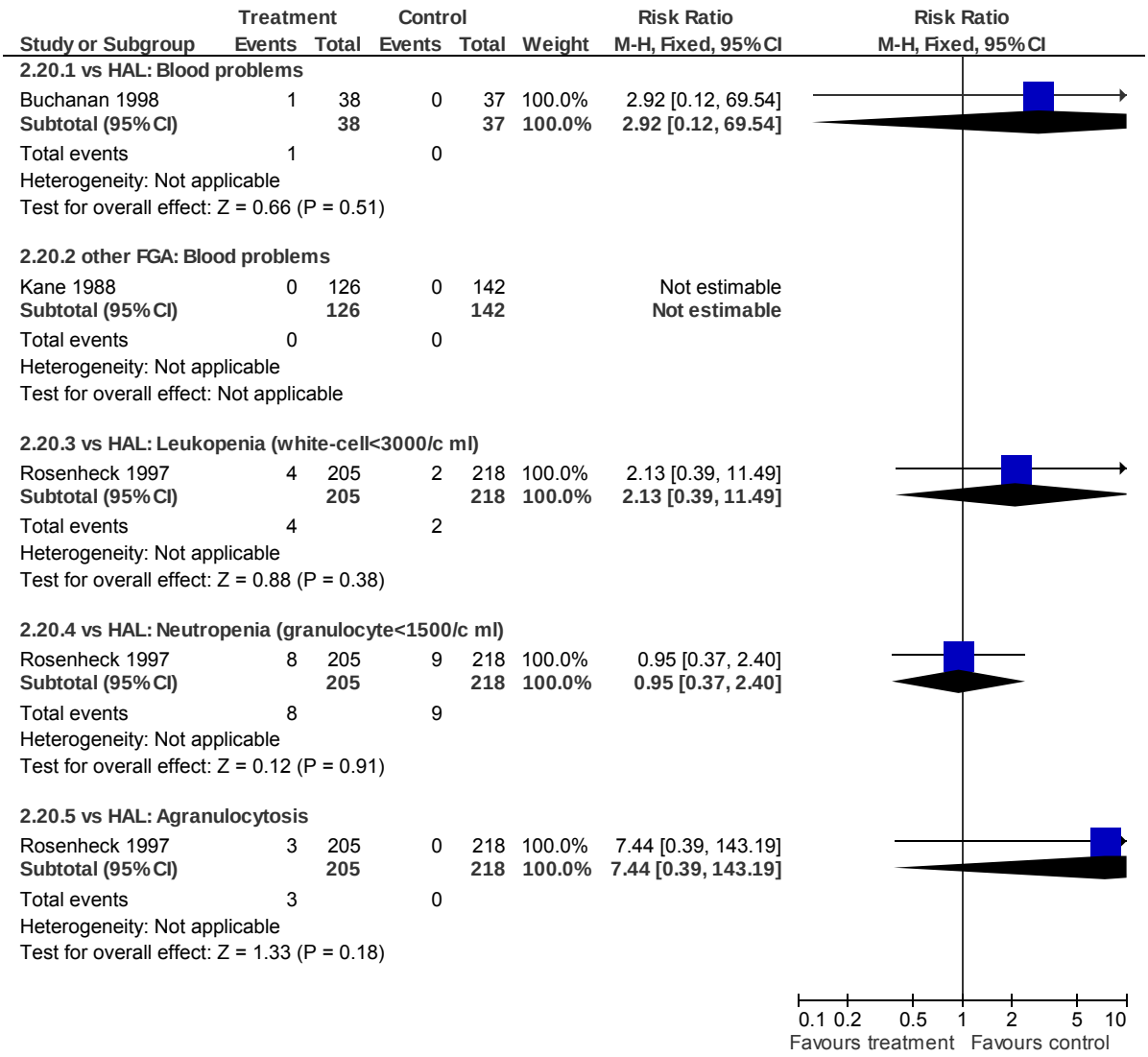


2.19 AE: 1. Metabolic SEs - Cholestrol mg/dL (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.19.1 vs HAL								
VOLAVKA2002	16.3	39.6	28	-4.4	25.2	25	100.0%	20.70 [3.02, 38.38]
Subtotal (95% CI)			**28**			**25**	**100.0%**	**20.70 [3.02, 38.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.29 (P = 0.02)								
Total (95% CI)			**28**			**25**	**100.0%**	**20.70 [3.02, 38.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.29 (P = 0.02)								
Test for subgroup differences: Not applicable								

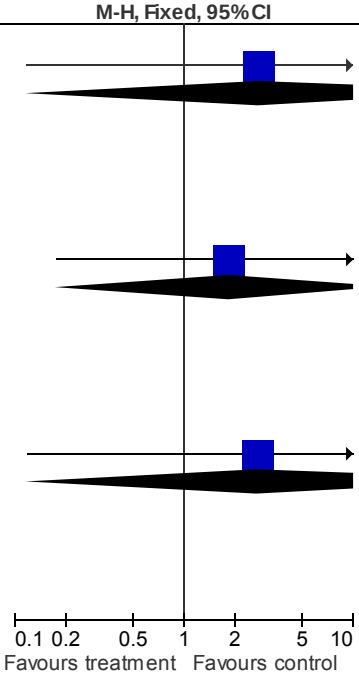


2.20 AE: 1. Metabolic SEs (treatment-emergent) (short-term)



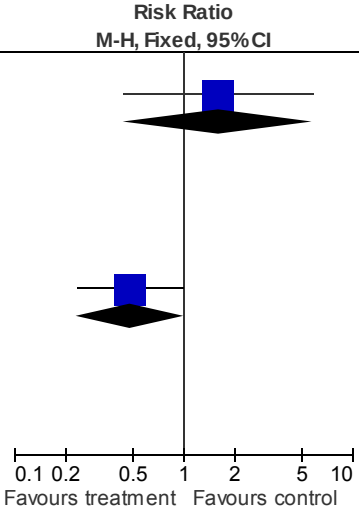
2.21 AE: 1. Metabolic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.21.1 vs HAL: Agranulocytosis						
VOLAVKA2002	1	40	0	37	100.0%	2.78 [0.12, 66.20]
Subtotal (95% CI)		**40**		**37**	**100.0%**	**2.78 [0.12, 66.20]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.63 (P = 0.53)						
2.21.2 vs HAL: Neutropenia						
VOLAVKA2002	2	40	1	37	100.0%	1.85 [0.17, 19.56]
Subtotal (95% CI)		**40**		**37**	**100.0%**	**1.85 [0.17, 19.56]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.51 (P = 0.61)						
2.21.3 vs other FGA: Blood problems						
Hong 1997	1	21	0	19	100.0%	2.73 [0.12, 63.19]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**2.73 [0.12, 63.19]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.63 (P = 0.53)						



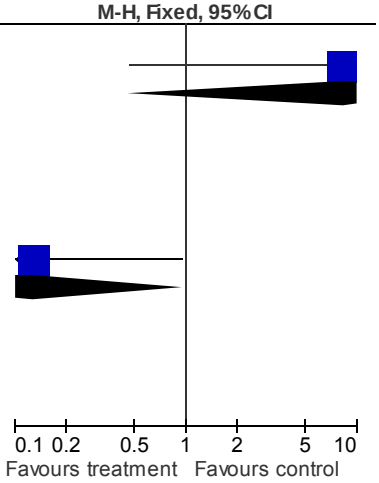
2.22 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.22.1 vs HAL: Movement disorder						
Buchanan 1998	5	21	3	20	100.0%	1.59 [0.44, 5.79]
Subtotal (95% CI)		**21**		**20**	**100.0%**	**1.59 [0.44, 5.79]**
Total events	5		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.70 (P = 0.48)						
2.22.2 vs other FGA: Movement disorder						
Claghorn 1987	9	75	19	76	100.0%	0.48 [0.23, 0.99]
Subtotal (95% CI)		**75**		**76**	**100.0%**	**0.48 [0.23, 0.99]**
Total events	9		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.98 (P = 0.05)						



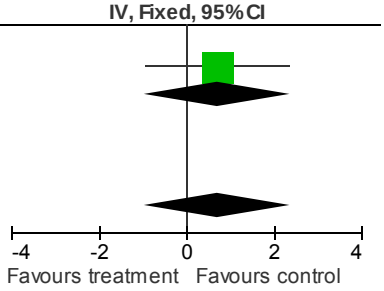
2.23 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.23.1 vs HAL: Seizures						
VOLAVKA2002	4	40	0	37	100.0%	8.34 [0.46, 149.82]
Subtotal (95% CI)		**40**		**37**	**100.0%**	**8.34 [0.46, 149.82]**
Total events	4		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.44 (P = 0.15)						
2.23.2 vs other FGA: Movement disorder						
Hong 1997	1	21	7	19	100.0%	0.13 [0.02, 0.96]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**0.13 [0.02, 0.96]**
Total events	1		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.00 (P = 0.05)						

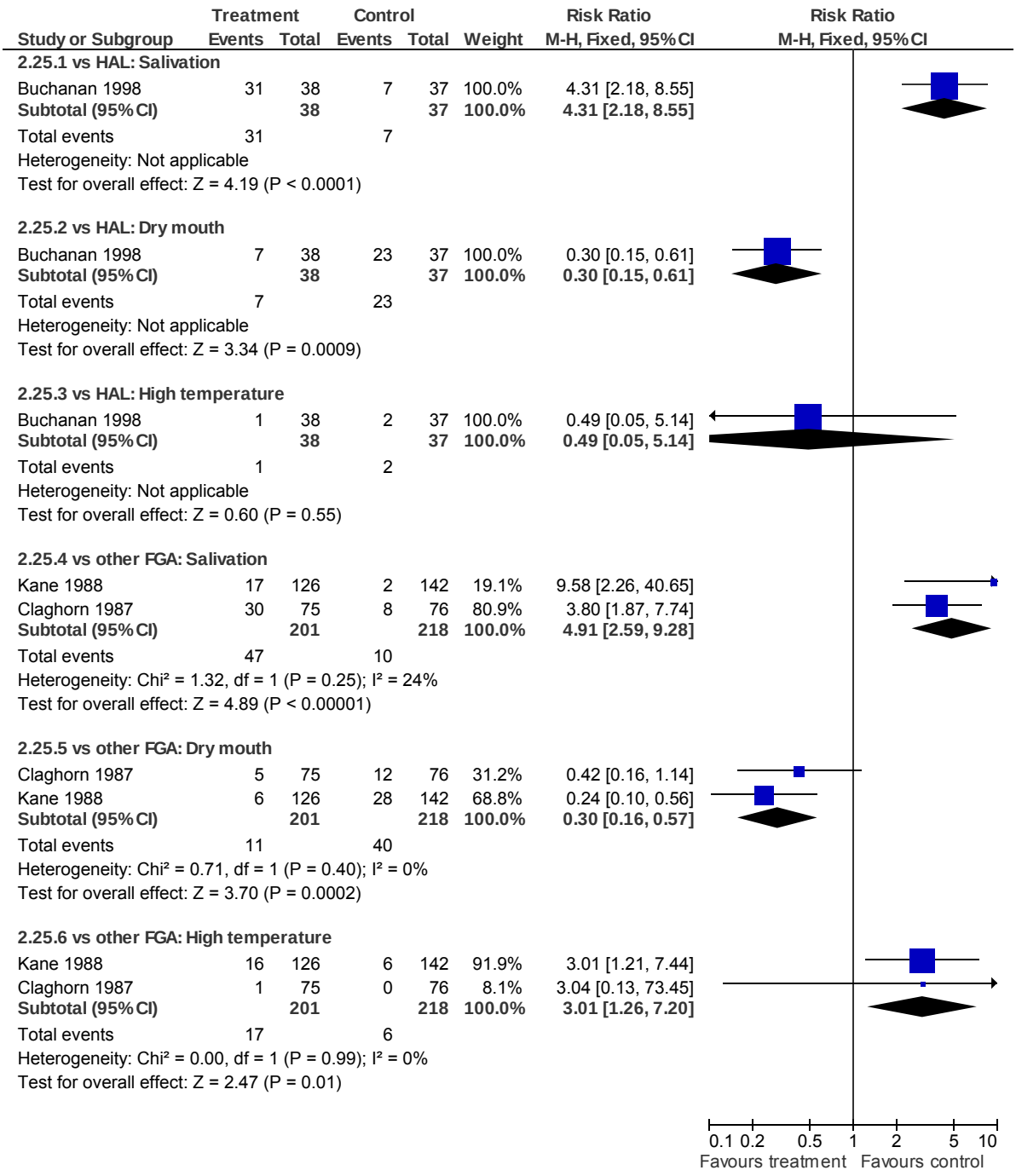


2.24 AE: 2. Neurologic SEs - Extrapyramidal Symptom Rating Scale (endpt mean) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.24.1 vs HAL								
VOLAVKA2002	5.1	3.8	40	4.4	3.6	37	100.0%	0.70 [-0.95, 2.35]
Subtotal (95% CI)			**40**			**37**	**100.0%**	**0.70 [-0.95, 2.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.83 (P = 0.41)								
Total (95% CI)			**40**			**37**	**100.0%**	**0.70 [-0.95, 2.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.83 (P = 0.41)								
Test for subgroup differences: Not applicable								

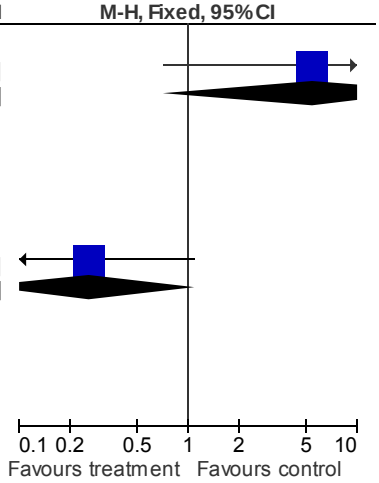


2.25 AE: 3. Autonomic SEs (short-term)



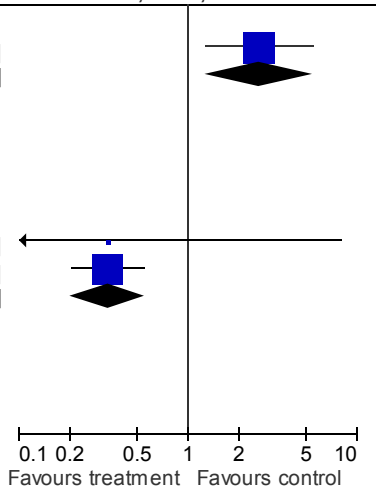
2.26 AE: 3. Autonomic SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.26.1 vs other FGA: Salivation						
Hong 1997	6	21	1	19	100.0%	5.43 [0.72, 41.09]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**5.43 [0.72, 41.09]**
Total events	6		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.64 (P = 0.10)						
2.26.2 vs other FGA: Dry mouth						
Hong 1997	2	21	7	19	100.0%	0.26 [0.06, 1.10]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**0.26 [0.06, 1.10]**
Total events	2		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.84 (P = 0.07)						



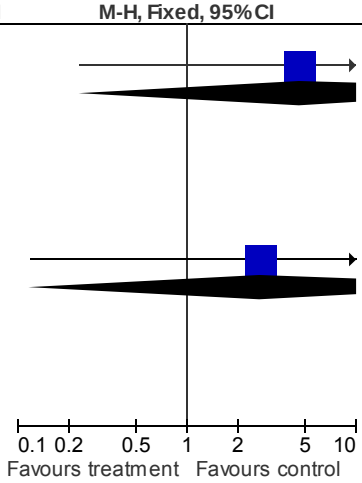
2.27 AE: 4. Cardiovascular SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.27.1 vs HAL: Dizziness/low blood pressure						
Buchanan 1998	19	38	7	37	100.0%	2.64 [1.26, 5.53]
Subtotal (95% CI)		**38**		**37**	**100.0%**	**2.64 [1.26, 5.53]**
Total events	19		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.58 (P = 0.010)						
2.27.2 vs other FGA: Dizziness/low blood pressure						
Claghorn 1987	0	75	1	76	2.9%	0.34 [0.01, 8.16]
Kane 1988	16	126	54	142	97.1%	0.33 [0.20, 0.55]
Subtotal (95% CI)		**201**		**218**	**100.0%**	**0.33 [0.20, 0.55]**
Total events	16		55			
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.99); I² = 0%						
Test for overall effect: Z = 4.32 (P < 0.0001)						



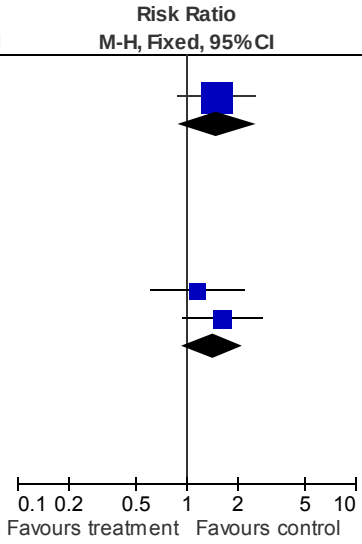
2.28 AE: 4. Cardiovascular SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.28.1 vs HAL: Hypertension						
VOLAVKA2002	2	40	0	37	100.0%	4.63 [0.23, 93.46]
Subtotal (95% CI)		**40**		**37**	**100.0%**	**4.63 [0.23, 93.46]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.00 (P = 0.32)						
2.28.2 vs other FGA: Dizziness/ low blood pressure						
Hong 1997	1	21	0	19	100.0%	2.73 [0.12, 63.19]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**2.73 [0.12, 63.19]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.63 (P = 0.53)						



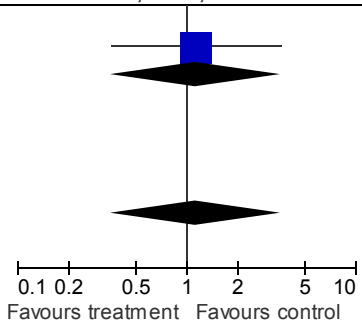
2.29 AE: 6. Sedation (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.29.1 vs HAL: Day time sleepiness - increase (somnolence)						
Buchanan 1998	20	38	13	37	100.0%	1.50 [0.88, 2.55]
Subtotal (95% CI)		**38**		**37**	**100.0%**	**1.50 [0.88, 2.55]**
Total events	20		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.49 (P = 0.14)						
2.29.2 vs other FGA: Day time sleepiness - increase (somnolence)						
Claghorn 1987	16	75	14	76	45.1%	1.16 [0.61, 2.20]
Kane 1988	26	126	18	142	54.9%	1.63 [0.94, 2.82]
Subtotal (95% CI)		**201**		**218**	**100.0%**	**1.42 [0.93, 2.15]**
Total events	42		32			
Heterogeneity: Chi² = 0.62, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 1.63 (P = 0.10)						



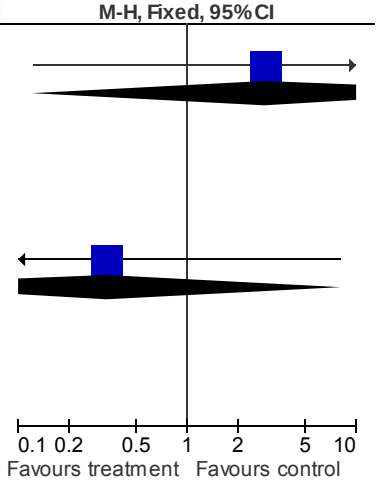
2.30 AE: 6. Sedation (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.30.1 vs other FGA: Day time sleepiness - increase (somnolence)						
Hong 1997	5	21	4	19	100.0%	1.13 [0.35, 3.60]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**1.13 [0.35, 3.60]**
Total events	5		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.84)						
Total (95% CI)		**21**		**19**	**100.0%**	**1.13 [0.35, 3.60]**
Total events	5		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.84)						



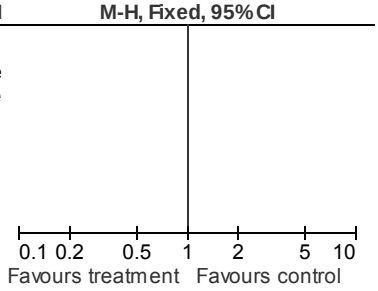
2.31 AE: 10. Other SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.31.1 vs HAL: Fits						
Buchanan 1998	1	38	0	37	100.0%	2.92 [0.12, 69.54]
Subtotal (95% CI)		**38**		**37**	**100.0%**	**2.92 [0.12, 69.54]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.66 (P = 0.51)						
2.31.2 vs other FGA: Fits						
Claghorn 1987	0	75	1	76	100.0%	0.34 [0.01, 8.16]
Subtotal (95% CI)		**75**		**76**	**100.0%**	**0.34 [0.01, 8.16]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.67 (P = 0.50)						



2.32 AE: 10. Other SEs (medium-term)

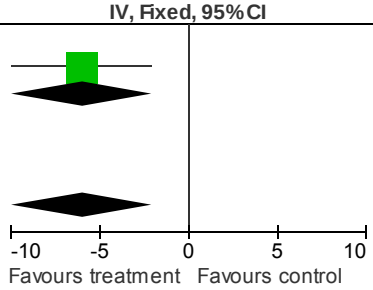
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.32.1 vs other FGA: Fits						
Hong 1997	0	21	0	19		Not estimable
Subtotal (95% CI)		**21**		**19**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



3 Olanzapine vs. FGA (in people whose illness has not responded adequately to treatment)

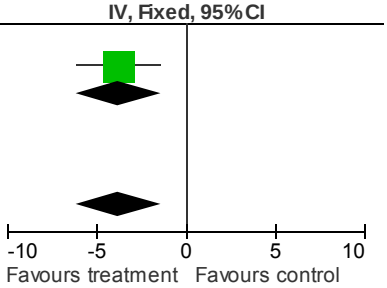
3.1 Mental state: 1. PANSS total (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.1.1 vs HAL								
Breier 2000	-19.4	23	344	-13.4	20.9	172	100.0%	-6.00 [-9.96, -2.04]
Subtotal (95% CI)			**344**			**172**	**100.0%**	**-6.00 [-9.96, -2.04]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.97 (P = 0.003)								
Total (95% CI)			**344**			**172**	**100.0%**	**-6.00 [-9.96, -2.04]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.97 (P = 0.003)								
Test for subgroup differences: Not applicable								



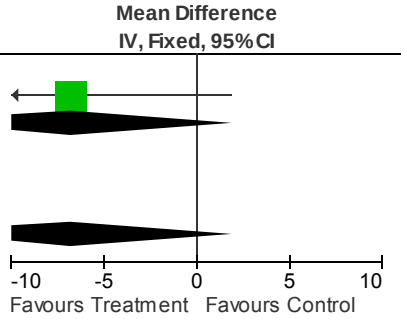
3.2 Mental state: 1. BPRS total (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.2.1 vs HAL								
Breier 2000	-11.7	13.5	344	-7.9	12.6	172	100.0%	-3.80 [-6.16, -1.44]
Subtotal (95% CI)			**344**			**172**	**100.0%**	**-3.80 [-6.16, -1.44]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.15 (P = 0.002)								
Total (95% CI)			**344**			**172**	**100.0%**	**-3.80 [-6.16, -1.44]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.15 (P = 0.002)								
Test for subgroup differences: Not applicable								



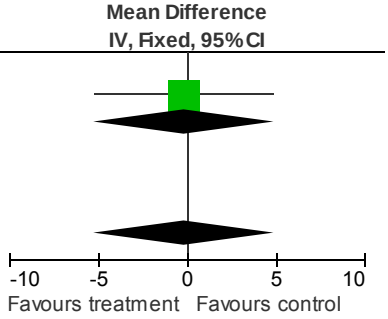
3.3 Mental state: 1. PANSS total (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.3.1 vs HAL								
VOLAVKA2002	81.9	21.8	39	88.7	16.6	37	100.0%	-6.80 [-15.48, 1.88]
Subtotal (95% CI)			**39**			**37**	**100.0%**	**-6.80 [-15.48, 1.88]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.53 (P = 0.12)								
Total (95% CI)			**39**			**37**	**100.0%**	**-6.80 [-15.48, 1.88]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.53 (P = 0.12)								
Test for subgroup differences: Not applicable								



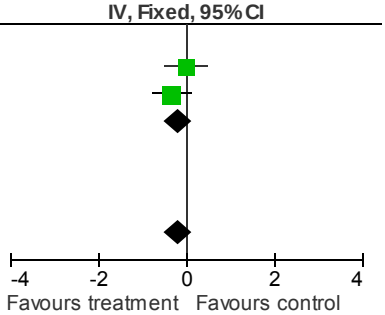
3.4 Mental state: 1. BPRS total (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.4.1 vs HAL								
BUCHANAN2005	33.4	9.9	29	33.6	10.6	34	100.0%	-0.20 [-5.27, 4.87]
Subtotal (95% CI)			**29**			**34**	**100.0%**	**-0.20 [-5.27, 4.87]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.08 (P = 0.94)								
Total (95% CI)			**29**			**34**	**100.0%**	**-0.20 [-5.27, 4.87]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.08 (P = 0.94)								
Test for subgroup differences: Not applicable								



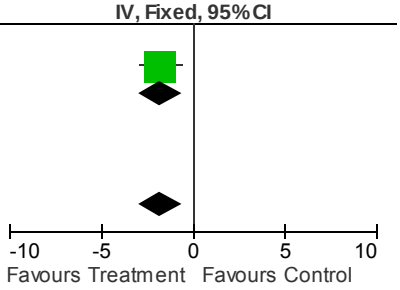
3.5 Mental state: 1. BPRS/PANSS total (endpoint) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
3.5.1 vs HAL (medium-term)								
BUCHANAN2005	33.4	9.9	29	33.6	10.6	34	45.6%	-0.02 [-0.51, 0.48]
VOLAVKA2002	81.9	21.8	39	88.7	16.6	37	54.4%	-0.35 [-0.80, 0.11]
Subtotal (95% CI)			**68**			**71**	**100.0%**	**-0.20 [-0.53, 0.14]**
Heterogeneity: Chi² = 0.91, df = 1 (P = 0.34); I² = 0%								
Test for overall effect: Z = 1.16 (P = 0.25)								
Total (95% CI)			**68**			**71**	**100.0%**	**-0.20 [-0.53, 0.14]**
Heterogeneity: Chi² = 0.91, df = 1 (P = 0.34); I² = 0%								
Test for overall effect: Z = 1.16 (P = 0.25)								
Test for subgroup differences: Not applicable								



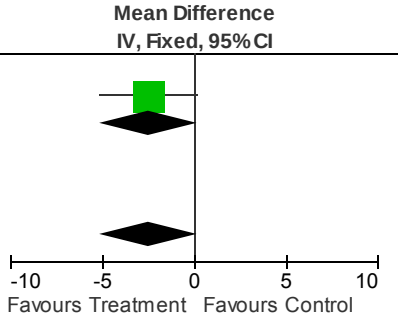
3.6 Mental state: 2. PANSS negative score (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.6.1 vs HAL								
Breier 2000	-4.7	6.6	344	-2.9	6.4	172	100.0%	-1.80 [-2.98, -0.62]
Subtotal (95% CI)			**344**			**172**	**100.0%**	**-1.80 [-2.98, -0.62]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.98 (P = 0.003)								
Total (95% CI)			**344**			**172**	**100.0%**	**-1.80 [-2.98, -0.62]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.98 (P = 0.003)								
Test for subgroup differences: Not applicable								



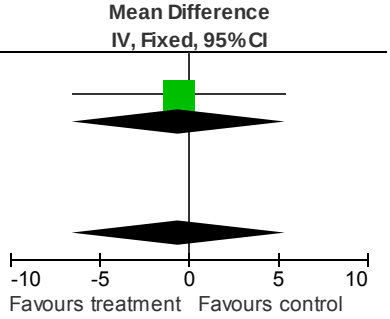
3.7 Mental state: 2. PANSS negative score (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.7.1 vs HAL								
VOLAVKA2002	20.1	6.3	39	22.6	5.6	37	100.0%	-2.50 [-5.18, 0.18]
Subtotal (95% CI)			**39**			**37**	**100.0%**	**-2.50 [-5.18, 0.18]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.83 (P = 0.07)								
Total (95% CI)			**39**			**37**	**100.0%**	**-2.50 [-5.18, 0.18]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.83 (P = 0.07)								
Test for subgroup differences: Not applicable								



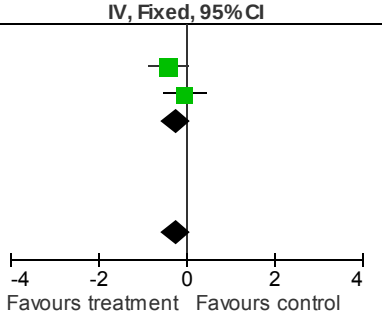
3.8 Mental state: 2. SANS score (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.8.1 vs HAL								
BUCHANAN2005	29.6	12.4	29	30.2	11.6	34	100.0%	-0.60 [-6.56, 5.36]
Subtotal (95% CI)			**29**			**34**	**100.0%**	**-0.60 [-6.56, 5.36]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.20 (P = 0.84)								
Total (95% CI)			**29**			**34**	**100.0%**	**-0.60 [-6.56, 5.36]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.20 (P = 0.84)								
Test for subgroup differences: Not applicable								



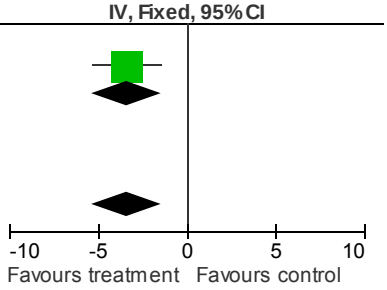
3.9 Mental state: 2. PANSS negative score/SANS (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
3.9.1 vs HAL								
VOLAVKA2002	20.1	6.3	39	22.6	5.6	37	54.3%	-0.41 [-0.87, 0.04]
BUCHANAN2005	29.6	12.4	29	30.2	11.6	34	45.7%	-0.05 [-0.54, 0.45]
Subtotal (95% CI)			**68**			**71**	**100.0%**	**-0.25 [-0.58, 0.09]**
Heterogeneity: Chi² = 1.13, df = 1 (P = 0.29); I² = 12%								
Test for overall effect: Z = 1.45 (P = 0.15)								
Total (95% CI)			**68**			**71**	**100.0%**	**-0.25 [-0.58, 0.09]**
Heterogeneity: Chi² = 1.13, df = 1 (P = 0.29); I² = 12%								
Test for overall effect: Z = 1.45 (P = 0.15)								
Test for subgroup differences: Not applicable								



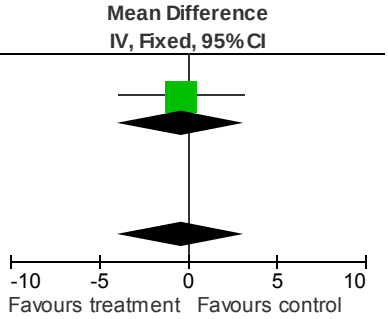
3.10 Mental state: 3. Depression (MADRS) (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.10.1 vs HAL								
Breier 2000	-5.7	8.2	268	-2.3	9.3	115	100.0%	-3.40 [-5.36, -1.44]
Subtotal (95% CI)			**268**			**115**	**100.0%**	**-3.40 [-5.36, -1.44]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.39 (P = 0.0007)								
Total (95% CI)			**268**			**115**	**100.0%**	**-3.40 [-5.36, -1.44]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.39 (P = 0.0007)								
Test for subgroup differences: Not applicable								



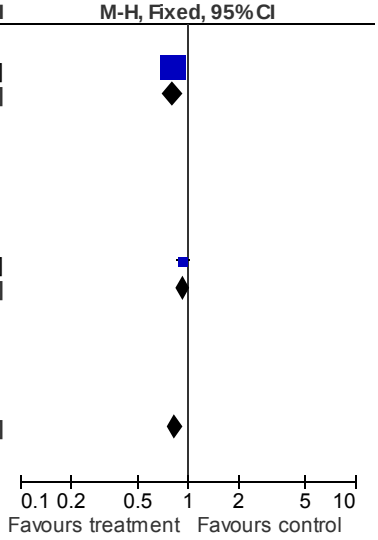
3.11 Mental state: 3. Depression (HDRS) (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.11.1 vs HAL								
BUCHANAN2005	9.4	6.2	29	9.8	8.2	34	100.0%	-0.40 [-3.96, 3.16]
Subtotal (95% CI)			**29**			**34**	**100.0%**	**-0.40 [-3.96, 3.16]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.22 (P = 0.83)								
Total (95% CI)			**29**			**34**	**100.0%**	**-0.40 [-3.96, 3.16]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.22 (P = 0.83)								
Test for subgroup differences: Not applicable								



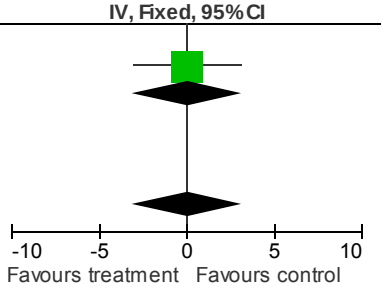
3.12 Mental state: 4. Non-response (<20% improvement on any scale) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.12.1 vs HAL						
Breier 2000	185	352	113	174	78.1%	0.81 [0.70, 0.94]
Subtotal (95% CI)		**352**		**174**	**78.1%**	**0.81 [0.70, 0.94]**
Total events	185		113			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.81 (P = 0.005)						
3.12.2 vs other FGA						
Conley 1998a	39	42	42	42	21.9%	0.93 [0.85, 1.02]
Subtotal (95% CI)		**42**		**42**	**21.9%**	**0.93 [0.85, 1.02]**
Total events	39		42			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.52 (P = 0.13)						
Total (95% CI)		**394**		**216**	**100.0%**	**0.84 [0.74, 0.94]**
Total events	224		155			
Heterogeneity: Chi² = 5.03, df = 1 (P = 0.02); I² = 80%						
Test for overall effect: Z = 3.05 (P = 0.002)						



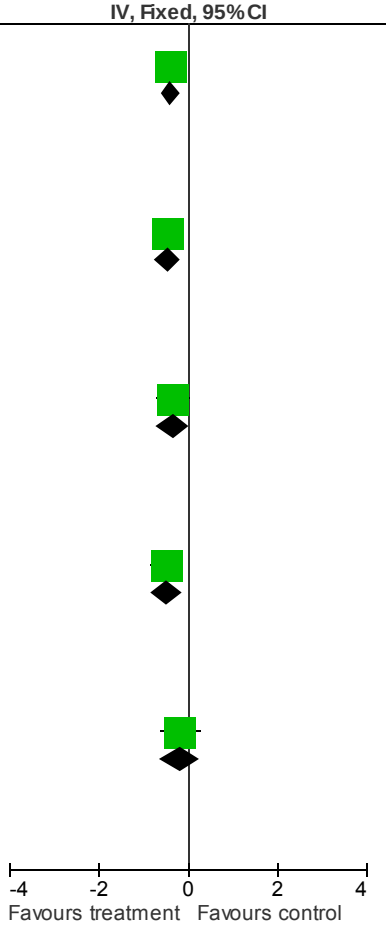
3.13 Social functioning: 1. Level of Functioning Scale (endpoint) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.13.1 vs HAL								
BUCHANAN2005	18.1	5.7	26	18.1	5.9	28	100.0%	0.00 [-3.09, 3.09]
Subtotal (95% CI)			**26**			**28**	**100.0%**	**0.00 [-3.09, 3.09]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Total (95% CI)			**26**			**28**	**100.0%**	**0.00 [-3.09, 3.09]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Test for subgroup differences: Not applicable								



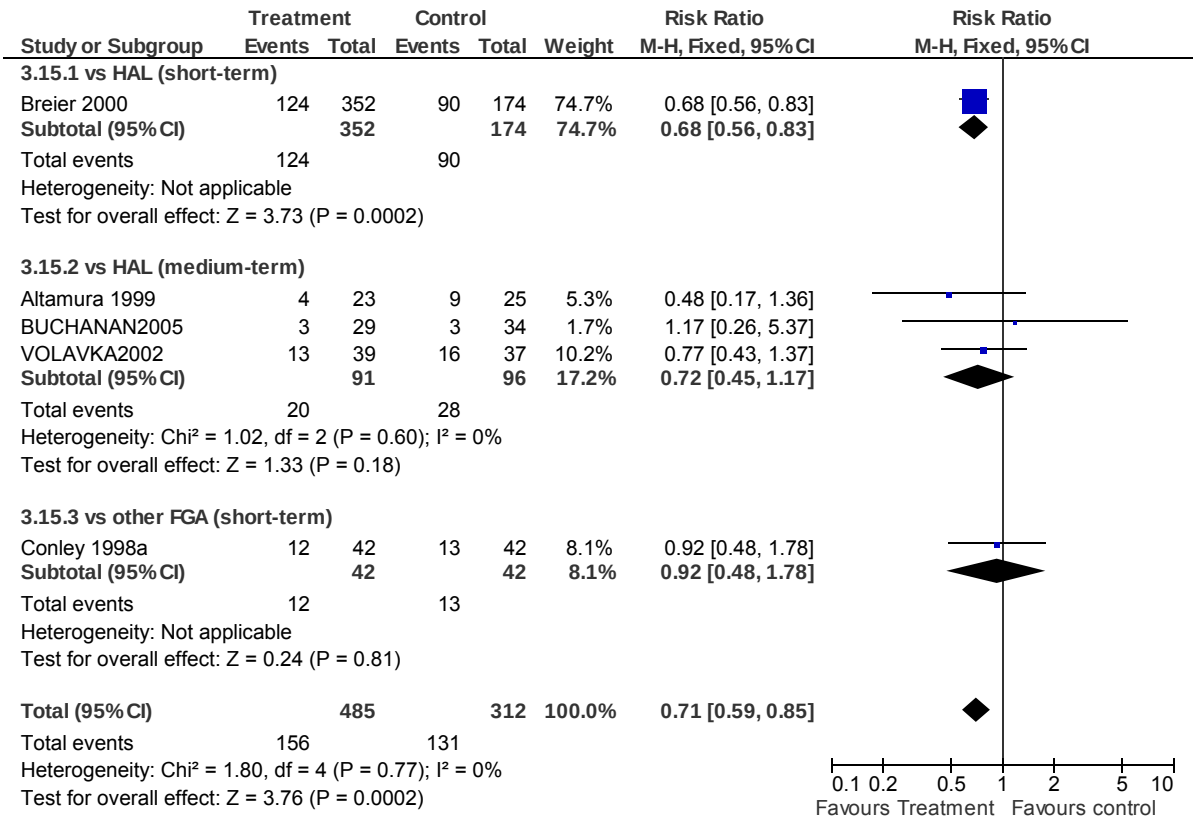
3.14 Cognitive functioning: 1. Global & domain scores (Z score change) (medium-term) (sign changed)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.14.1 vs HAL: Global score								
VOLAVKA2002	-0.35	0.38	26	0.04	0.44	25	100.0%	-0.39 [-0.62, -0.16]
Subtotal (95% CI)			**26**			**25**	**100.0%**	**-0.39 [-0.62, -0.16]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.38 (P = 0.0007)								
3.14.2 vs HAL: General executive & perceptual organisation								
VOLAVKA2002	-0.34	0.53	26	0.11	0.53	25	100.0%	-0.45 [-0.74, -0.16]
Subtotal (95% CI)			**26**			**25**	**100.0%**	**-0.45 [-0.74, -0.16]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.03 (P = 0.002)								
3.14.3 vs HAL: Declarative verbal learning & memory								
VOLAVKA2002	-0.25	0.48	26	0.09	0.84	25	100.0%	-0.34 [-0.72, 0.04]
Subtotal (95% CI)			**26**			**25**	**100.0%**	**-0.34 [-0.72, 0.04]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.77 (P = 0.08)								
3.14.4 vs HAL: Processing speed & attention								
VOLAVKA2002	-0.68	0.61	26	-0.19	0.71	25	100.0%	-0.49 [-0.85, -0.13]
Subtotal (95% CI)			**26**			**25**	**100.0%**	**-0.49 [-0.85, -0.13]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.64 (P = 0.008)								
3.14.5 vs HAL: Simple motor functioning								
VOLAVKA2002	-0.24	0.84	26	-0.05	0.81	25	100.0%	-0.19 [-0.64, 0.26]
Subtotal (95% CI)			**26**			**25**	**100.0%**	**-0.19 [-0.64, 0.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.82 (P = 0.41)								



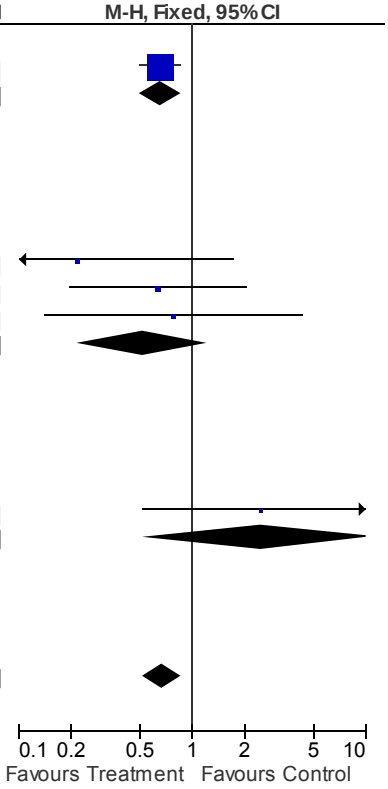
Test for subgroup differences: Chi² = 1.27, df = 4 (P = 0.87), I² = 0%

3.15 Leaving the study early: 1. Any reason (short-to-medium-term)



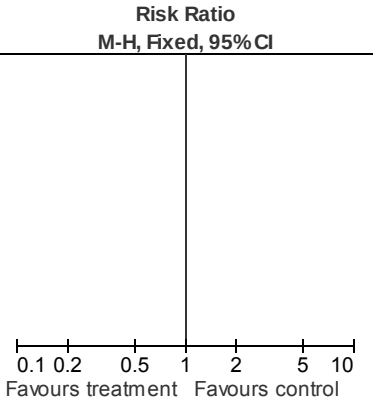
3.16 Leaving the study early: 2. Due to lack of efficacy (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.16.1 vs HAL (short-term)						
Breier 2000	82	352	62	174	84.1%	0.65 [0.50, 0.86]
Subtotal (95% CI)		**352**		**174**	**84.1%**	**0.65 [0.50, 0.86]**
Total events	82		62			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.03 (P = 0.002)						
3.16.2 vs HAL (medium-term)						
Altamura 1999	1	23	5	25	4.9%	0.22 [0.03, 1.72]
VOLAVKA2002	4	39	6	37	6.2%	0.63 [0.19, 2.06]
BUCHANAN2005	2	29	3	34	2.8%	0.78 [0.14, 4.36]
Subtotal (95% CI)		**91**		**96**	**13.9%**	**0.52 [0.22, 1.23]**
Total events	7		14			
Heterogeneity: Chi² = 1.01, df = 2 (P = 0.60); I² = 0%						
Test for overall effect: Z = 1.50 (P = 0.13)						
3.16.3 vs other FGA (short-term)						
Conley 1998a	5	42	2	42	2.0%	2.50 [0.51, 12.17]
Subtotal (95% CI)		**42**		**42**	**2.0%**	**2.50 [0.51, 12.17]**
Total events	5		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.13 (P = 0.26)						
Total (95% CI)		**485**		**312**	**100.0%**	**0.67 [0.52, 0.87]**
Total events	94		78			
Heterogeneity: Chi² = 3.86, df = 4 (P = 0.42); I² = 0%						
Test for overall effect: Z = 3.01 (P = 0.003)						



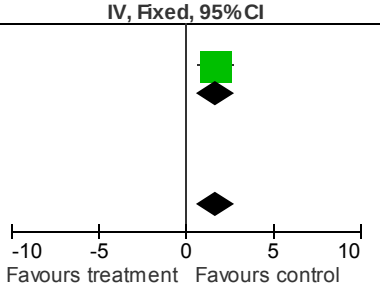
3.17 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.17.1 vs HAL						
BUCHANAN2005	0	29	0	34		Not estimable
VOLAVKA2002	0	39	0	37		Not estimable
Subtotal (95% CI)		**68**		**71**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**68**		**71**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



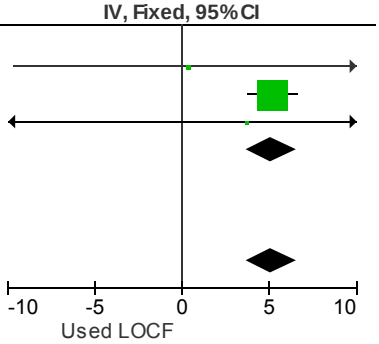
3.18 AE: 1. Metabolic SEs - BMI (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.18.1 vs HAL								
VOLAVKA2002	1.8	2.6	38	0.1	2	36	100.0%	1.70 [0.65, 2.75]
Subtotal (95% CI)			**38**			**36**	**100.0%**	**1.70 [0.65, 2.75]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.16 (P = 0.002)								
Total (95% CI)			**38**			**36**	**100.0%**	**1.70 [0.65, 2.75]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.16 (P = 0.002)								
Test for subgroup differences: Not applicable								



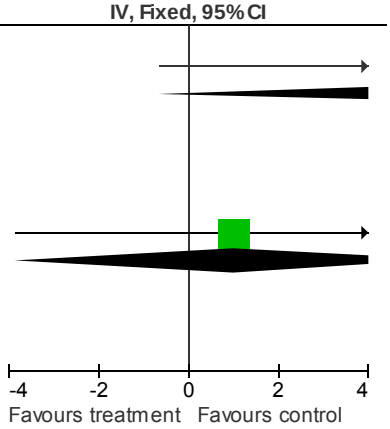
3.19 AE: 1. Metabolic SEs - weight (kg) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.19.1 vs HAL: weight increase								
Altamura 1999	79.57	16.54	22	79.22	18.59	25	2.1%	0.35 [-9.69, 10.39]
VOLAVKA2002	5.4	4.6	38	0.2	0.2	36	97.5%	5.20 [3.74, 6.66]
BUCHANAN2005	196.1	37	27	192.4	44.1	31	0.5%	3.70 [-17.18, 24.58]
Subtotal (95% CI)			**87**			**92**	**100.0%**	**5.09 [3.65, 6.54]**
Heterogeneity: Chi² = 0.89, df = 2 (P = 0.64); I² = 0%								
Test for overall effect: Z = 6.91 (P < 0.00001)								
Total (95% CI)			**87**			**92**	**100.0%**	**5.09 [3.65, 6.54]**
Heterogeneity: Chi² = 0.89, df = 2 (P = 0.64); I² = 0%								
Test for overall effect: Z = 6.91 (P < 0.00001)								
Test for subgroup differences: Not applicable								



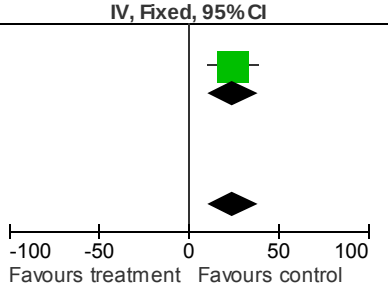
3.20 AE: 1. Metabolic SEs - blood pressure (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.20.1 vs HAL: Systolic								
BUCHANAN2005	130.2	14.6	28	122.5	18.4	32	100.0%	7.70 [-0.66, 16.06]
Subtotal (95% CI)			**28**			**32**	**100.0%**	**7.70 [-0.66, 16.06]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.81 (P = 0.07)								
3.20.2 vs HAL: Diastolic								
BUCHANAN2005	79.6	10.3	28	78.6	8.8	32	100.0%	1.00 [-3.88, 5.88]
Subtotal (95% CI)			**28**			**32**	**100.0%**	**1.00 [-3.88, 5.88]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.40 (P = 0.69)								
Test for subgroup differences: Chi² = 1.84, df = 1 (P = 0.17), I² = 45.6%								



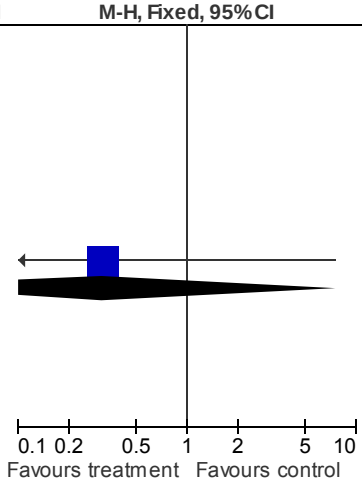
3.21 AE: 1. Metabolic SEs - Cholestrol mg/dL (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.21.1 vs HAL								
VOLAVKA2002	20.1	26.8	26	-4.4	25.2	25	100.0%	24.50 [10.23, 38.77]
Subtotal (95% CI)			**26**			**25**	**100.0%**	**24.50 [10.23, 38.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.36 (P = 0.0008)								
Total (95% CI)			**26**			**25**	**100.0%**	**24.50 [10.23, 38.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.36 (P = 0.0008)								
Test for subgroup differences: Not applicable								

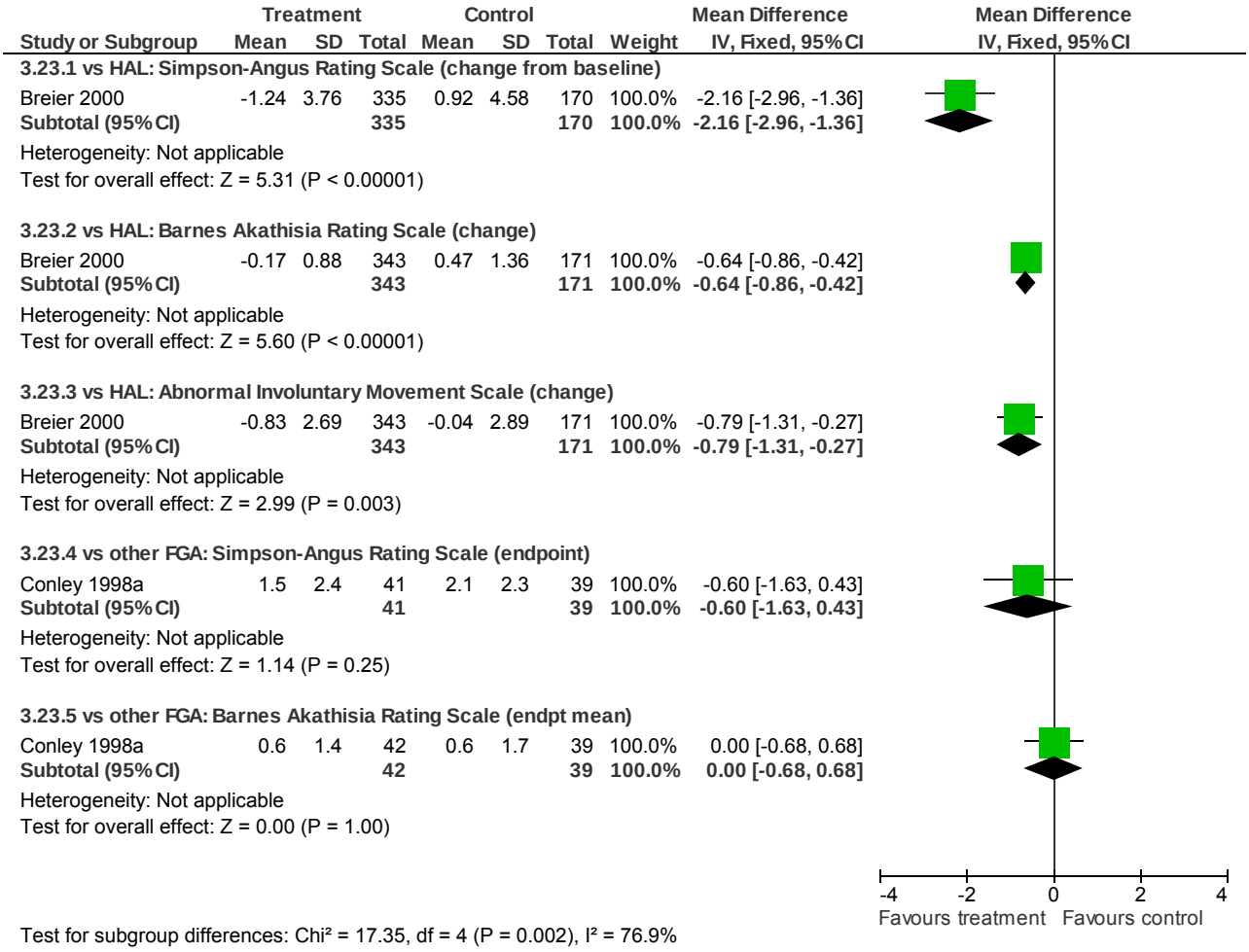


3.22 AE: 1. Metabolic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.22.1 vs HAL: Agranulocytosis						
VOLAVKA2002	0	39	0	37		Not estimable
Subtotal (95% CI)		**39**		**37**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
3.22.2 vs HAL: Neutropenia						
VOLAVKA2002	0	39	1	37	100.0%	0.32 [0.01, 7.54]
Subtotal (95% CI)		**39**		**37**	**100.0%**	**0.32 [0.01, 7.54]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.71 (P = 0.48)						

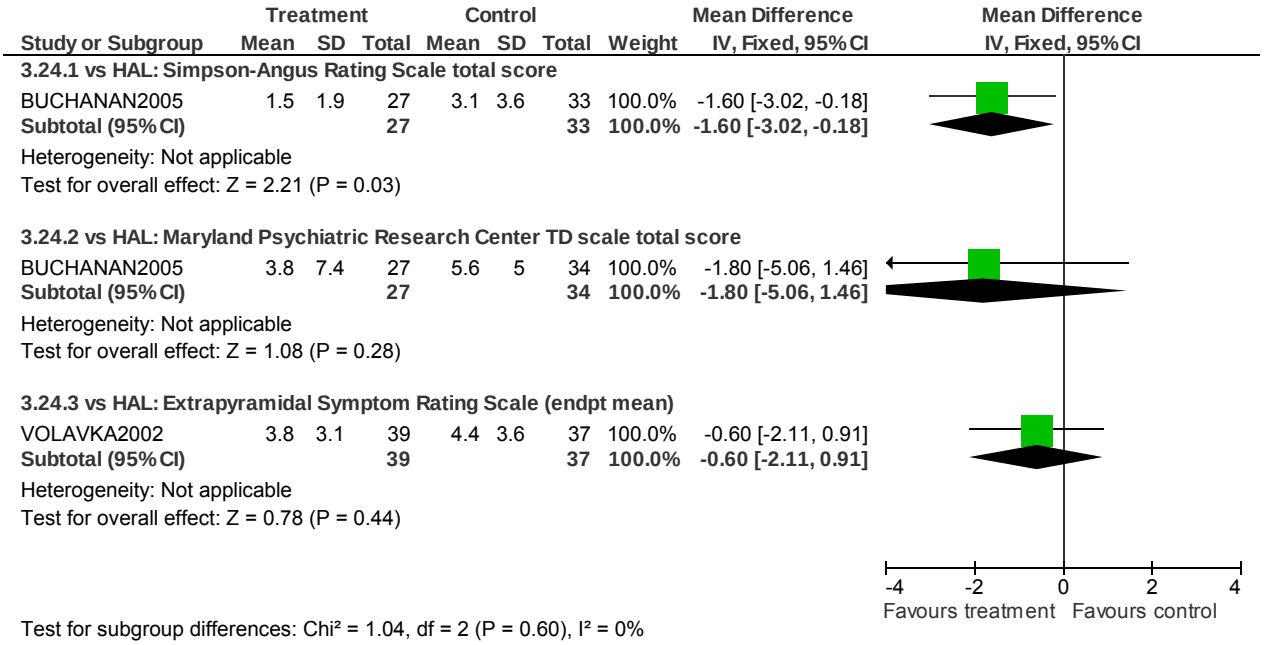


3.23 AE: 2 Neurologic SEs (treatment-emergent) (short-term)



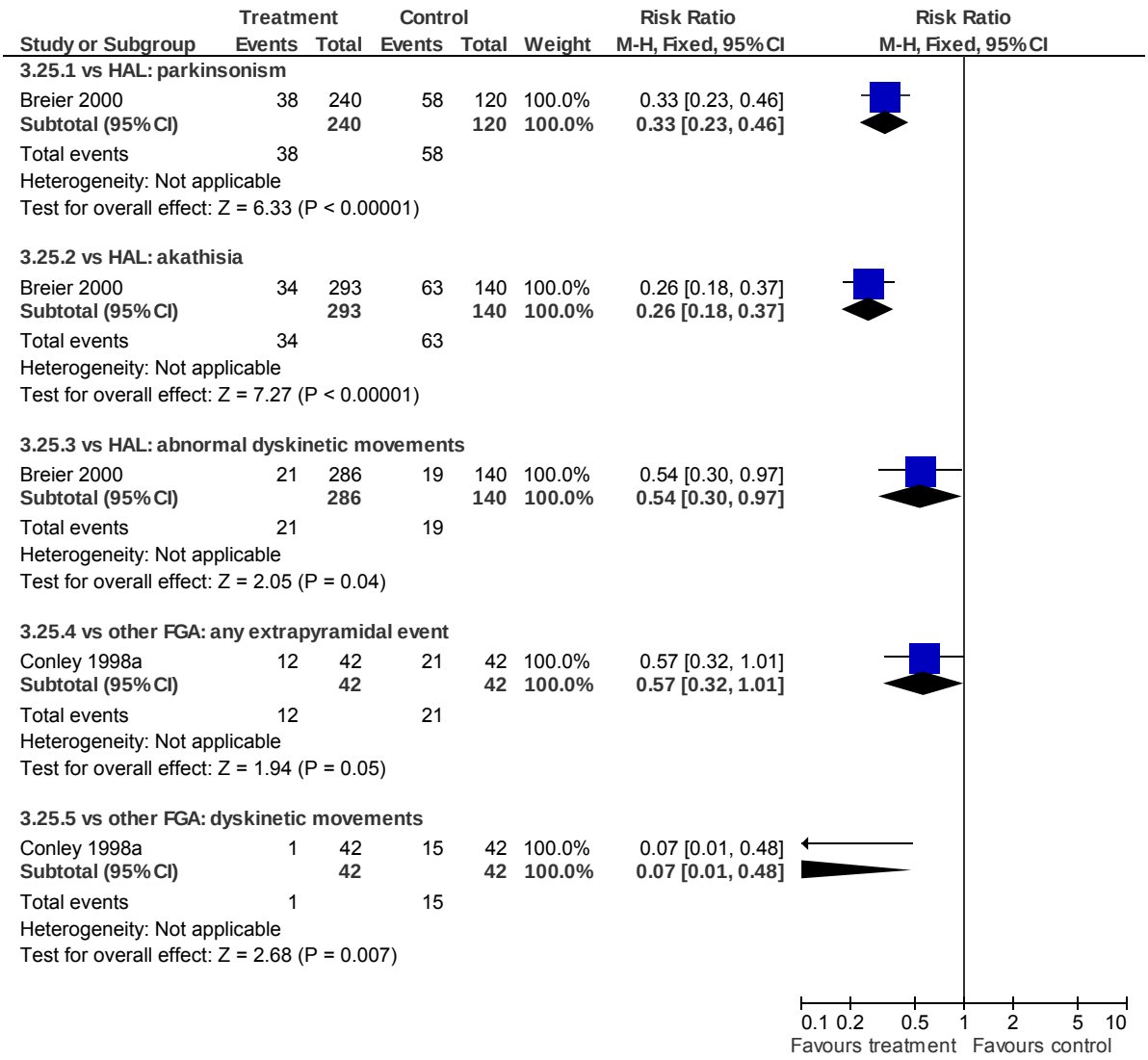
Test for subgroup differences: Chi² = 17.35, df = 4 (P = 0.002), I² = 76.9%

3.24 AE: 2 Neurologic SEs (treatment-emergent) (medium-term)

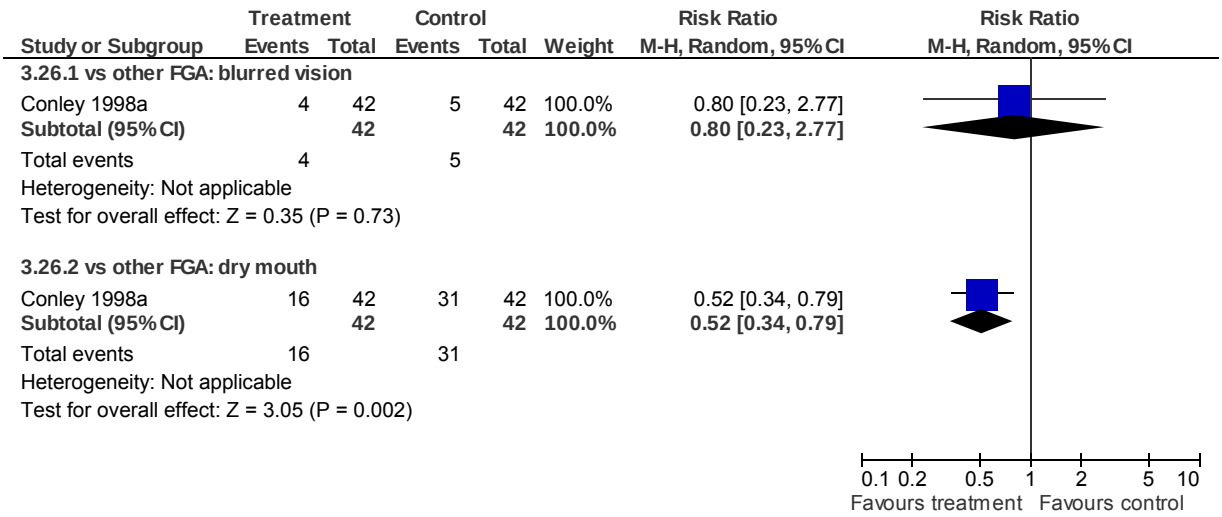


Test for subgroup differences: Chi² = 1.04, df = 2 (P = 0.60), I² = 0%

3.25 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

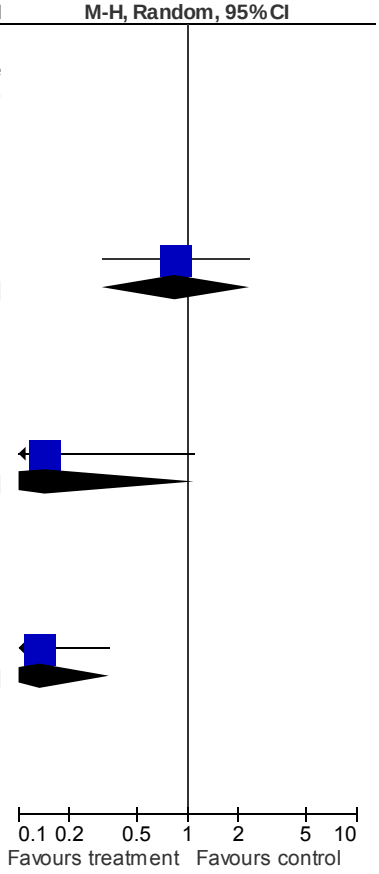


3.26 AE: 3. Autonomic SEs (short-term)



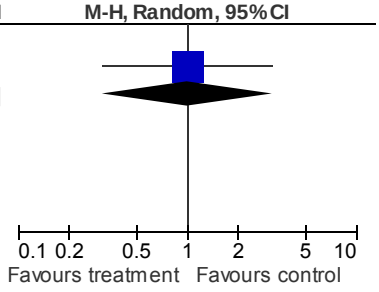
3.27 AE: 4. Cardiovascular SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
3.27.1 vs HAL: hypertension						
VOLAVKA2002	0	40	0	37		Not estimable
Subtotal (95% CI)		**40**		**37**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
3.27.2 vs other FGA: dizziness						
Conley 1998a	6	42	7	42	100.0%	0.86 [0.31, 2.34]
Subtotal (95% CI)		**42**		**42**	**100.0%**	**0.86 [0.31, 2.34]**
Total events	6		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.30 (P = 0.76)						
3.27.3 vs other FGA: palpitations						
Conley 1998a	1	42	7	42	100.0%	0.14 [0.02, 1.11]
Subtotal (95% CI)		**42**		**42**	**100.0%**	**0.14 [0.02, 1.11]**
Total events	1		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.86 (P = 0.06)						
3.27.4 vs other FGA: orthostatic changes						
Conley 1998a	4	42	30	42	100.0%	0.13 [0.05, 0.35]
Subtotal (95% CI)		**42**		**42**	**100.0%**	**0.13 [0.05, 0.35]**
Total events	4		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.15 (P < 0.0001)						



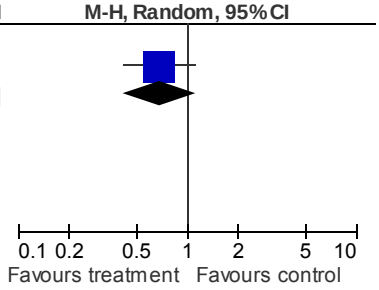
3.28 AE: 5. Gastrointestinal SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
3.28.1 vs other FGA: nausea						
Conley 1998a	5	42	5	42	100.0%	1.00 [0.31, 3.20]
Subtotal (95% CI)		**42**		**42**	**100.0%**	**1.00 [0.31, 3.20]**
Total events	5		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						



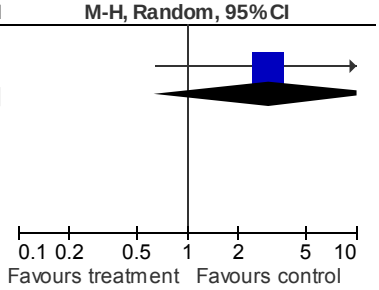
3.29 AE: 6. Sedation (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
3.29.1 vs other FGA: drowsiness						
Conley 1998a	15	42	22	42	100.0%	0.68 [0.41, 1.12]
Subtotal (95% CI)		**42**		**42**	**100.0%**	**0.68 [0.41, 1.12]**
Total events	15		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.51 (P = 0.13)						



3.30 AE: 7. Other SEs (short-term)

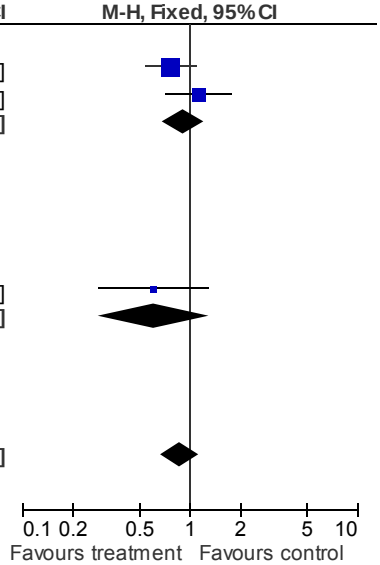
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
3.30.1 vs other FGA: difficulty in getting to sleep						
Conley 1998a	6	42	2	42	100.0%	3.00 [0.64, 14.02]
Subtotal (95% CI)		**42**		**42**	**100.0%**	**3.00 [0.64, 14.02]**
Total events	6		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.40 (P = 0.16)						



4 Quetiapine vs. FGA (in people whose illness has not responded adequately to treatment)

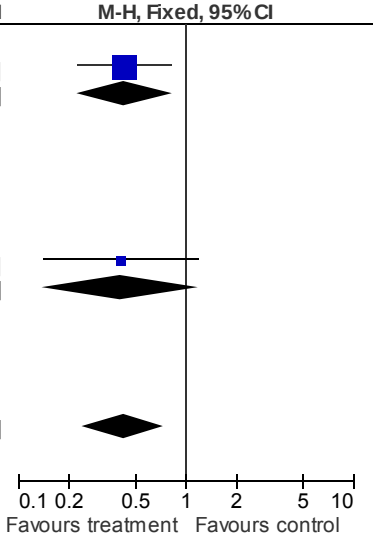
4.5 Leaving the study early: 1. Any reason (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.5.1 vs HAL (short-term)						
Murasaki 1999	34	100	43	97	54.5%	0.77 [0.54, 1.09]
Emsley 1999	31	143	28	145	34.7%	1.12 [0.71, 1.77]
Subtotal (95% CI)		**243**		**242**	**89.2%**	**0.91 [0.68, 1.20]**
Total events	65		71			
Heterogeneity: Chi² = 1.71, df = 1 (P = 0.19); I² = 41%						
Test for overall effect: Z = 0.70 (P = 0.49)						
4.5.3 vs other FGA (medium-term)						
CONLEY2005	5	12	9	13	10.8%	0.60 [0.28, 1.29]
Subtotal (95% CI)		**12**		**13**	**10.8%**	**0.60 [0.28, 1.29]**
Total events	5		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.31 (P = 0.19)						
Total (95% CI)		**255**		**255**	**100.0%**	**0.87 [0.67, 1.14]**
Total events	70		80			
Heterogeneity: Chi² = 2.60, df = 2 (P = 0.27); I² = 23%						
Test for overall effect: Z = 1.01 (P = 0.31)						



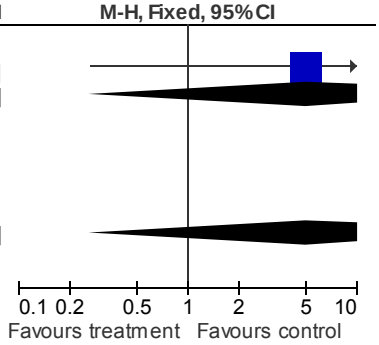
4.6 Leaving the study early: 2. Due to lack of efficacy (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.6.1 vs HAL (short-term)						
Murasaki 1999	11	100	25	97	76.8%	0.43 [0.22, 0.82]
Subtotal (95% CI)		**100**		**97**	**76.8%**	**0.43 [0.22, 0.82]**
Total events	11		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.56 (P = 0.01)						
4.6.3 vs other FGA (medium-term)						
CONLEY2005	3	12	8	13	23.2%	0.41 [0.14, 1.18]
Subtotal (95% CI)		**12**		**13**	**23.2%**	**0.41 [0.14, 1.18]**
Total events	3		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.65 (P = 0.10)						
Total (95% CI)		**112**		**110**	**100.0%**	**0.42 [0.24, 0.74]**
Total events	14		33			
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.94); I² = 0%						
Test for overall effect: Z = 3.02 (P = 0.002)						



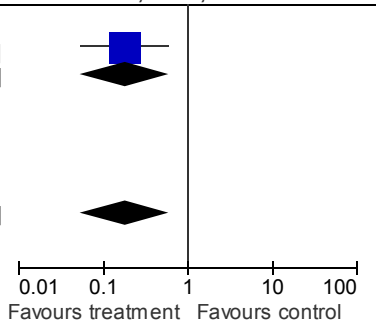
4.7 Leaving the study early: 3: Adverse event (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.7.3 vs other FGA (medium-term)						
CONLEY2005	2	13	0	13	100.0%	5.00 [0.26, 95.02]
Subtotal (95% CI)		**13**		**13**	**100.0%**	**5.00 [0.26, 95.02]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.07 (P = 0.28)						
Total (95% CI)		**13**		**13**	**100.0%**	**5.00 [0.26, 95.02]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.07 (P = 0.28)						



4.9 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)

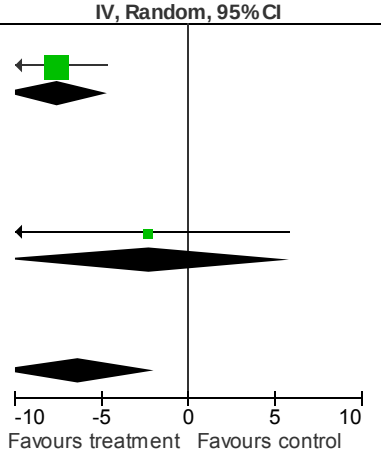
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.9.1 vs HAL						
Emsley 1999	3	143	17	145	100.0%	0.18 [0.05, 0.60]
Subtotal (95% CI)		**143**		**145**	**100.0%**	**0.18 [0.05, 0.60]**
Total events	3		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.80 (P = 0.005)						
Total (95% CI)		**143**		**145**	**100.0%**	**0.18 [0.05, 0.60]**
Total events	3		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.80 (P = 0.005)						



5 Risperidone vs. FGA (in people whose illness has not responded adequately to treatment)

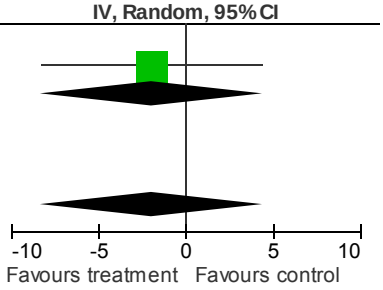
5.1 Mental state: 1. PANSS total (short-to-medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
5.1.1 vs HAL (short-term)								
SEE1999	59.95	3.05	10	67.55	3.62	10	76.8%	-7.60 [-10.53, -4.67]
Subtotal (95% CI)			**10**			**10**	**76.8%**	**-7.60 [-10.53, -4.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.08 (P < 0.00001)								
5.1.2 vs HAL (medium-term)								
VOLAVKA2002	86.4	20.1	41	88.7	16.6	37	23.2%	-2.30 [-10.45, 5.85]
Subtotal (95% CI)			**41**			**37**	**23.2%**	**-2.30 [-10.45, 5.85]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.55 (P = 0.58)								
Total (95% CI)			**51**			**47**	**100.0%**	**-6.37 [-10.76, -1.99]**
Heterogeneity: Tau² = 4.27; Chi² = 1.44, df = 1 (P = 0.23); I² = 30%								
Test for overall effect: Z = 2.85 (P = 0.004)								



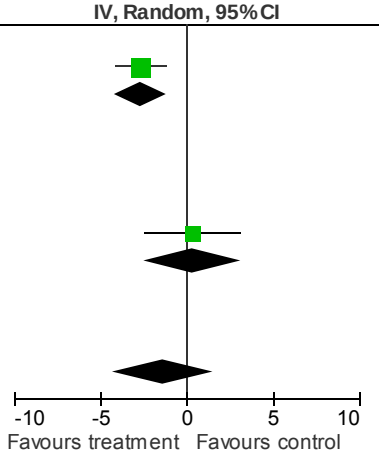
5.2 Mental state: 1. BPRS total (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
5.2.1 vs HAL (short-term)								
Kern 1998	57.3	12.35	29	59.3	12.35	29	100.0%	-2.00 [-8.36, 4.36]
Subtotal (95% CI)			**29**			**29**	**100.0%**	**-2.00 [-8.36, 4.36]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.62 (P = 0.54)								
Total (95% CI)			**29**			**29**	**100.0%**	**-2.00 [-8.36, 4.36]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.62 (P = 0.54)								



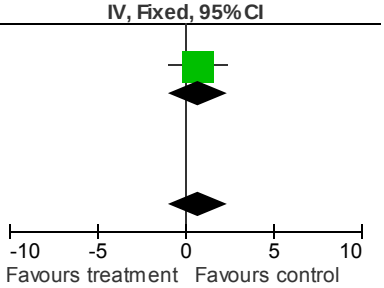
5.3 Mental state: 2. PANSS negative symptoms (short-to-medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
5.3.1 vs HAL (short-term)								
SEE1999	19.2	1.57	10	21.9	1.85	10	57.9%	-2.70 [-4.20, -1.20]
Subtotal (95% CI)			**10**			**10**	**57.9%**	**-2.70 [-4.20, -1.20]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.52 (P = 0.0004)								
5.3.2 vs HAL (medium-term)								
VOLAVKA2002	22.9	6.9	41	22.6	5.6	37	42.1%	0.30 [-2.48, 3.08]
Subtotal (95% CI)			**41**			**37**	**42.1%**	**0.30 [-2.48, 3.08]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.21 (P = 0.83)								
Total (95% CI)			**51**			**47**	**100.0%**	**-1.44 [-4.34, 1.47]**
Heterogeneity: Tau² = 3.20; Chi² = 3.46, df = 1 (P = 0.06); I² = 71%								
Test for overall effect: Z = 0.97 (P = 0.33)								



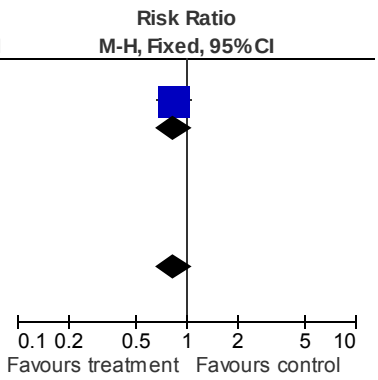
5.4 Mental state: 2. BPRS negative symptoms (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.4.1 vs HAL								
Kern 1998	9.4	3.28	29	8.7	3.28	29	100.0%	0.70 [-0.99, 2.39]
Subtotal (95% CI)			**29**			**29**	**100.0%**	**0.70 [-0.99, 2.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.81 (P = 0.42)								
Total (95% CI)			**29**			**29**	**100.0%**	**0.70 [-0.99, 2.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.81 (P = 0.42)								
Test for subgroup differences: Not applicable								

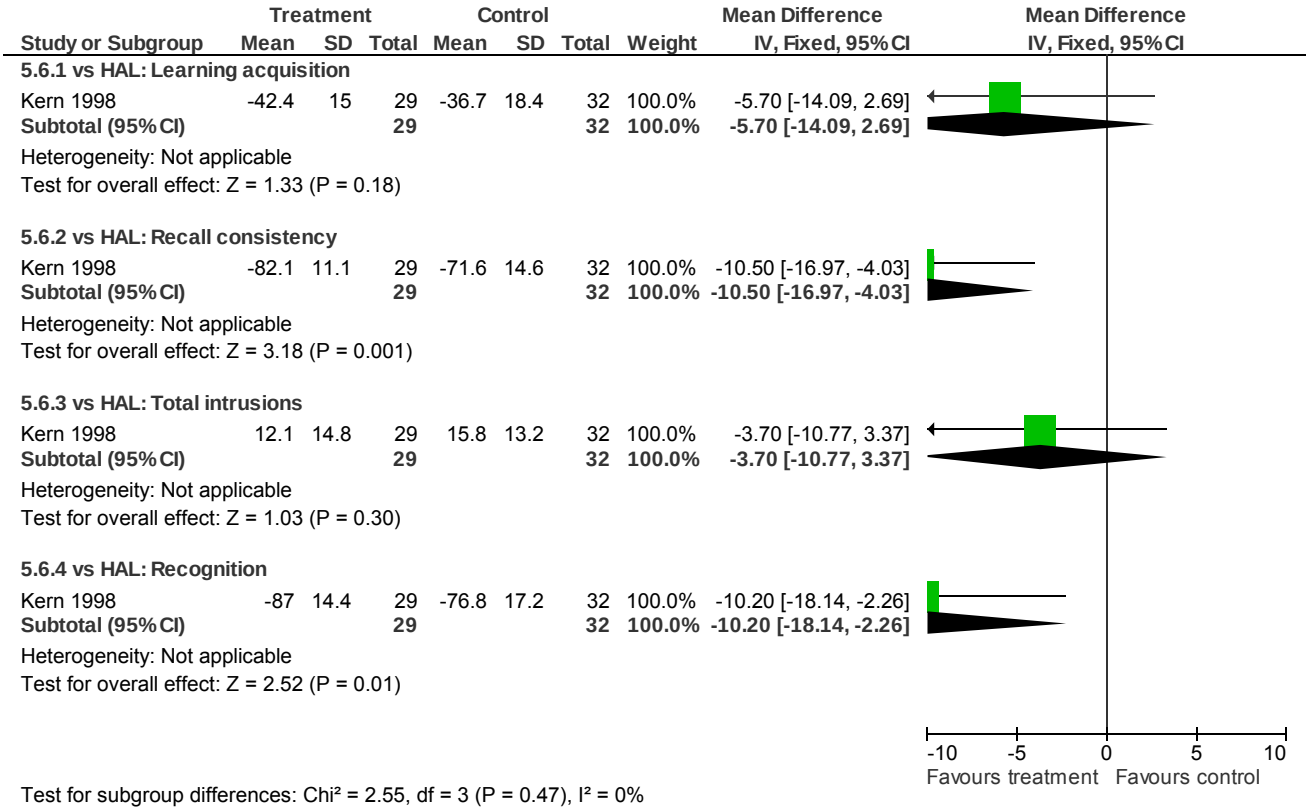


5.5 Mental state: 4. Non-response (<20% improvement in BPRS & CGI 3 or more & BPRS > 35) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.5.1 vs HAL						
Kern 1998	25	34	29	33	100.0%	0.84 [0.66, 1.06]
Subtotal (95% CI)		**34**		**33**	**100.0%**	**0.84 [0.66, 1.06]**
Total events	25		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.47 (P = 0.14)						
Total (95% CI)		**34**		**33**	**100.0%**	**0.84 [0.66, 1.06]**
Total events	25		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.47 (P = 0.14)						



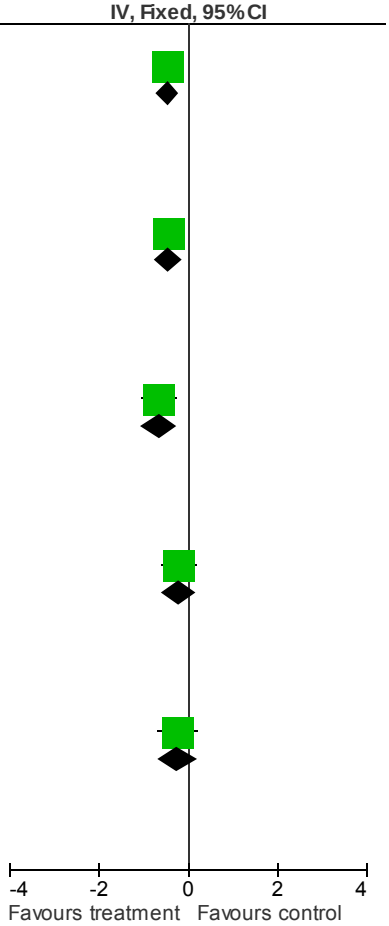
5.6 Cognitive functioning: 1. CVLT (short-term)



Test for subgroup differences: Chi² = 2.55, df = 3 (P = 0.47), I² = 0%

5.7 Cognitive functioning: 1. Global & domain scores (Z score change) (medium-term) (sign changed)

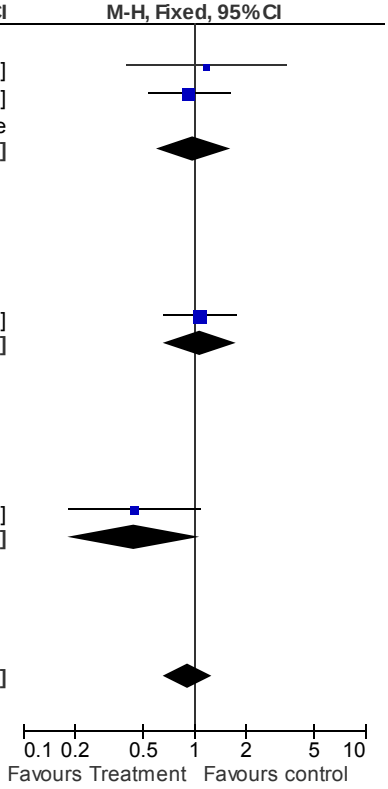
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.7.1 vs HAL: Global score								
VOLAVKA2002	-0.42	0.48	26	0.04	0.44	25	100.0%	-0.46 [-0.71, -0.21]
Subtotal (95% CI)			**26**			**25**	**100.0%**	**-0.46 [-0.71, -0.21]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.57 (P = 0.0004)								
5.7.2 vs HAL: General executive & perceptual organisation								
VOLAVKA2002	-0.33	0.59	26	0.11	0.53	25	100.0%	-0.44 [-0.75, -0.13]
Subtotal (95% CI)			**26**			**25**	**100.0%**	**-0.44 [-0.75, -0.13]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.80 (P = 0.005)								
5.7.3 vs HAL: Declarative verbal learning & memory								
VOLAVKA2002	-0.57	0.59	26	0.09	0.84	25	100.0%	-0.66 [-1.06, -0.26]
Subtotal (95% CI)			**26**			**25**	**100.0%**	**-0.66 [-1.06, -0.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.24 (P = 0.001)								
5.7.4 vs HAL: Processing speed & attention								
VOLAVKA2002	-0.4	0.73	26	-0.19	0.71	25	100.0%	-0.21 [-0.61, 0.19]
Subtotal (95% CI)			**26**			**25**	**100.0%**	**-0.21 [-0.61, 0.19]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.04 (P = 0.30)								
5.7.5 vs HAL: Simple motor functioning								
VOLAVKA2002	-0.29	0.84	26	-0.05	0.81	25	100.0%	-0.24 [-0.69, 0.21]
Subtotal (95% CI)			**26**			**25**	**100.0%**	**-0.24 [-0.69, 0.21]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.04 (P = 0.30)								



Test for subgroup differences: Chi² = 3.19, df = 4 (P = 0.53), I² = 0%

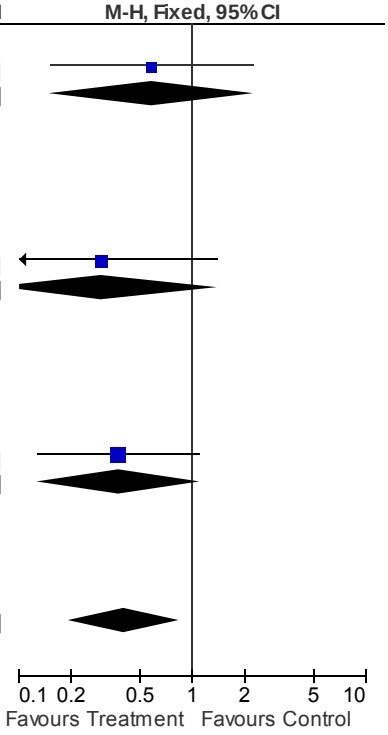
5.8 Leaving the study early: 1. Any reason (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.8.1 vs HAL (short-term)						
Kern 1998	6	34	5	33	10.9%	1.16 [0.39, 3.45]
Heck 2000	15	40	15	37	33.5%	0.93 [0.53, 1.62]
SEE1999	0	10	0	10		Not estimable
Subtotal (95% CI)		**84**		**80**	**44.4%**	**0.98 [0.60, 1.62]**
Total events	21		20			
Heterogeneity: Chi² = 0.14, df = 1 (P = 0.71); I² = 0%						
Test for overall effect: Z = 0.06 (P = 0.95)						
5.8.2 vs HAL (medium-term)						
VOLAVKA2002	19	41	16	37	36.2%	1.07 [0.65, 1.76]
Subtotal (95% CI)		**41**		**37**	**36.2%**	**1.07 [0.65, 1.76]**
Total events	19		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.27 (P = 0.78)						
5.8.3 vs other FGA (medium-term)						
CONLEY2005	4	13	9	13	19.4%	0.44 [0.18, 1.08]
Subtotal (95% CI)		**13**		**13**	**19.4%**	**0.44 [0.18, 1.08]**
Total events	4		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.78 (P = 0.07)						
Total (95% CI)		**138**		**130**	**100.0%**	**0.91 [0.66, 1.26]**
Total events	44		45			
Heterogeneity: Chi² = 3.10, df = 3 (P = 0.38); I² = 3%						
Test for overall effect: Z = 0.56 (P = 0.58)						



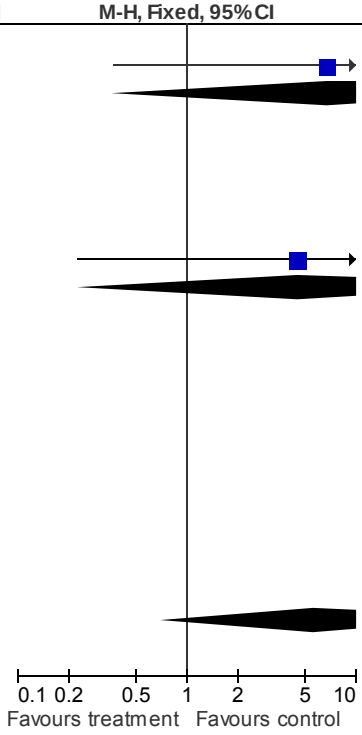
5.9 Leaving the study early: 2. Due to lack of efficacy (short-to-medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.9.1 vs HAL (short-term)						
Kern 1998	3	34	5	33	26.2%	0.58 [0.15, 2.24]
Subtotal (95% CI)		**34**		**33**	**26.2%**	**0.58 [0.15, 2.24]**
Total events	3		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						
5.9.2 vs HAL (medium-term)						
VOLAVKA2002	2	41	6	37	32.5%	0.30 [0.06, 1.40]
Subtotal (95% CI)		**41**		**37**	**32.5%**	**0.30 [0.06, 1.40]**
Total events	2		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.53 (P = 0.13)						
5.9.3 vs other FGA (medium-term)						
CONLEY2005	3	13	8	13	41.3%	0.38 [0.13, 1.11]
Subtotal (95% CI)		**13**		**13**	**41.3%**	**0.38 [0.13, 1.11]**
Total events	3		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.78 (P = 0.08)						
Total (95% CI)		**88**		**83**	**100.0%**	**0.41 [0.19, 0.85]**
Total events	8		19			
Heterogeneity: Chi² = 0.44, df = 2 (P = 0.80); I² = 0%						
Test for overall effect: Z = 2.39 (P = 0.02)						



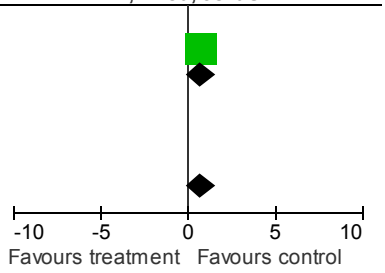
5.10 Leaving the study early: 3: Adverse event (short-to-medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.10.1 vs HAL (short-term)						
Kern 1998	3	34	0	33	49.1%	6.80 [0.36, 126.76]
Subtotal (95% CI)		**34**		**33**	**49.1%**	**6.80 [0.36, 126.76]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.28 (P = 0.20)						
5.10.2 vs HAL (medium-term)						
VOLAVKA2002	2	41	0	37	50.9%	4.52 [0.22, 91.27]
Subtotal (95% CI)		**41**		**37**	**50.9%**	**4.52 [0.22, 91.27]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.32)						
5.10.3 vs other FGA (medium-term)						
CONLEY2005	0	13	0	13		Not estimable
Subtotal (95% CI)		**13**		**13**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**88**		**83**	**100.0%**	**5.64 [0.70, 45.56]**
Total events	5		0			
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.85); I² = 0%						
Test for overall effect: Z = 1.62 (P = 0.10)						



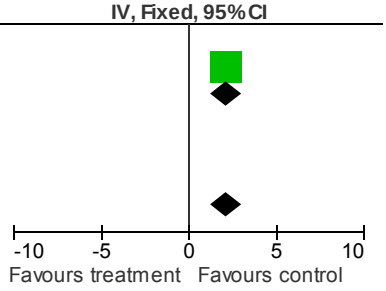
5.11 AE: 1. Metabolic SEs - BMI (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
5.11.1 vs HAL								
VOLAVKA2002	0.8	1.7	39	0.1	2	36	100.0%	0.70 [-0.14, 1.54]
Subtotal (95% CI)			**39**			**36**	**100.0%**	**0.70 [-0.14, 1.54]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.63 (P = 0.10)								
Total (95% CI)			**39**			**36**	**100.0%**	**0.70 [-0.14, 1.54]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.63 (P = 0.10)								
Test for subgroup differences: Not applicable								



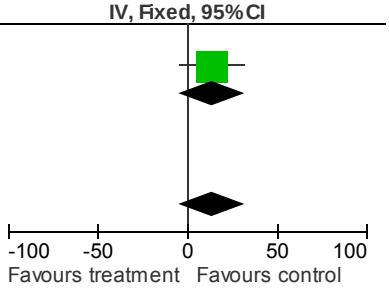
5.12 AE: 1. Metabolic SEs - weight change from baseline (kg) (medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
5.12.1 vs HAL								
VOLAVKA2002	2.3	2.8	39	0.2	0.2	36	100.0%	2.10 [1.22, 2.98]
Subtotal (95% CI)			**39**			**36**	**100.0%**	**2.10 [1.22, 2.98]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.67 (P < 0.00001)								
Total (95% CI)			**39**			**36**	**100.0%**	**2.10 [1.22, 2.98]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.67 (P < 0.00001)								
Test for subgroup differences: Not applicable								



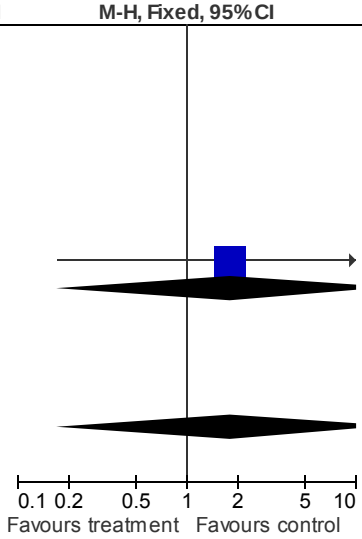
5.13 AE: 1. Metabolic SEs - Cholestrol mg/dL (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.13.1 vs HAL								
VOLAVKA2002	9.2	36.7	22	-4.4	25.2	25	100.0%	13.60 [-4.64, 31.84]
Subtotal (95% CI)			**22**			**25**	**100.0%**	**13.60 [-4.64, 31.84]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.46 (P = 0.14)								
Total (95% CI)			**22**			**25**	**100.0%**	**13.60 [-4.64, 31.84]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.46 (P = 0.14)								
Test for subgroup differences: Not applicable								



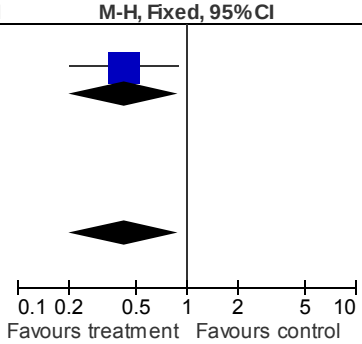
5.14 AE: 1. Metabolic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.14.1 vs HAL: Agranulocytosis						
VOLAVKA2002	0	41	0	37		Not estimable
Subtotal (95% CI)		**41**		**37**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
5.14.2 vs HAL: Neutropenia						
VOLAVKA2002	2	41	1	37	100.0%	1.80 [0.17, 19.10]
Subtotal (95% CI)		**41**		**37**	**100.0%**	**1.80 [0.17, 19.10]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.49 (P = 0.62)						
Total (95% CI)		**82**		**74**	**100.0%**	**1.80 [0.17, 19.10]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.49 (P = 0.62)						



5.15 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.15.1 vs HAL						
Kern 1998	7	34	16	33	100.0%	0.42 [0.20, 0.90]
Subtotal (95% CI)		**34**		**33**	**100.0%**	**0.42 [0.20, 0.90]**
Total events	7		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.24 (P = 0.02)						
Total (95% CI)		**34**		**33**	**100.0%**	**0.42 [0.20, 0.90]**
Total events	7		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.24 (P = 0.02)						

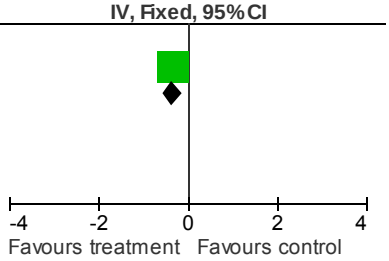


5.16 AE: 2. Neurologic SEs - Any rating scale (treatment-emergent) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.16.1 vs HAL: Simpson-Angus Rating Scale total score								
SEE1999	1.5	0.21	10	1.85	0.24	10	100.0%	-0.35 [-0.55, -0.15]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**-0.35 [-0.55, -0.15]**

Heterogeneity: Not applicable

Test for overall effect: Z = 3.47 (P = 0.0005)



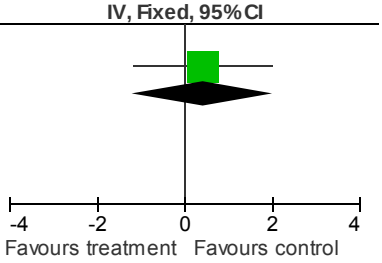
Test for subgroup differences: Not applicable

5.17 AE: 2. Neurologic SEs - Any rating scale (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
5.17.1 vs HAL: Extrapyramidal Symptom Rating Scale (endpt mean)								
VOLAVKA2002	4.8	3.6	41	4.4	3.6	37	100.0%	0.40 [-1.20, 2.00]
Subtotal (95% CI)			**41**			**37**	**100.0%**	**0.40 [-1.20, 2.00]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.49 (P = 0.62)



Test for subgroup differences: Not applicable

5.18 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.18.1 vs HAL						
Heck 2000	11	40	10	37	100.0%	1.02 [0.49, 2.11]
Subtotal (95% CI)		**40**		**37**	**100.0%**	**1.02 [0.49, 2.11]**
Total events	11		10			

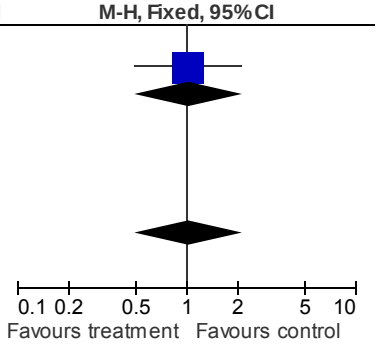
Heterogeneity: Not applicable

Test for overall effect: Z = 0.05 (P = 0.96)

Total (95% CI)		**40**		**37**	**100.0%**	**1.02 [0.49, 2.11]**
Total events	11		10			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.05 (P = 0.96)



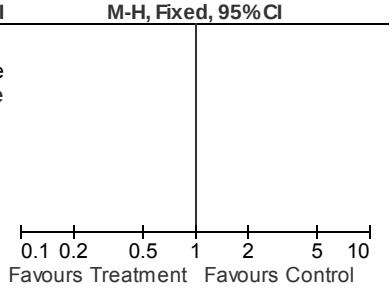
6 Clozapine vs. Olanzapine (in people whose illness has not responded adequately to treatment)

6.1 Mortality (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.1.1 suicides						
Beuzen 1998	0	90	0	90		Not estimable
Subtotal (95% CI)		**90**		**90**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable

Test for overall effect: Not applicable

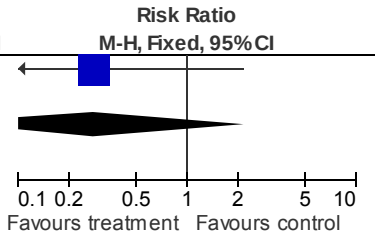


6.2 Global state: 1. Relapse (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Oliemeulen 2000	1	15	5	21	100.0%	0.28 [0.04, 2.16]
Total (95% CI)		**15**		**21**	**100.0%**	**0.28 [0.04, 2.16]**
Total events	1		5			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.22 (P = 0.22)

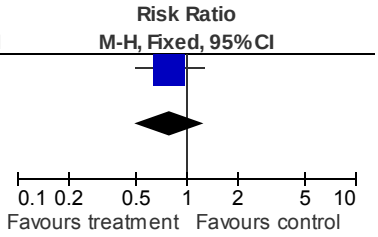


6.3 Global state: 1. Relapse (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Beuzen 1998	22	90	28	90	100.0%	0.79 [0.49, 1.26]
Total (95% CI)		**90**		**90**	**100.0%**	**0.79 [0.49, 1.26]**
Total events	22		28			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.99 (P = 0.32)



6.4 Global state: 1. Relapse (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.4.1 Short-term						
Oliemeulen 2000	1	15	5	21	13.0%	0.28 [0.04, 2.16]
Subtotal (95% CI)		**15**		**21**	**13.0%**	**0.28 [0.04, 2.16]**
Total events	1		5			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.22 (P = 0.22)

6.4.2 Medium-term						
Beuzen 1998	22	90	28	90	87.0%	0.79 [0.49, 1.26]
Subtotal (95% CI)		**90**		**90**	**87.0%**	**0.79 [0.49, 1.26]**
Total events	22		28			

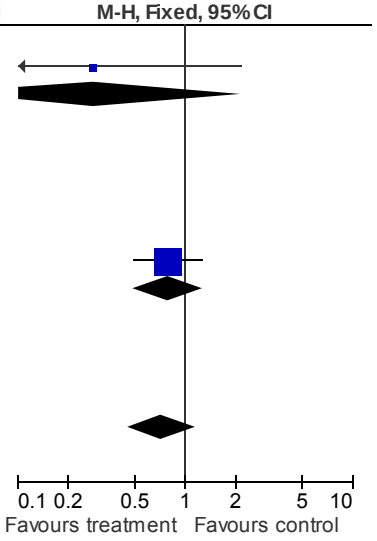
Heterogeneity: Not applicable

Test for overall effect: Z = 0.99 (P = 0.32)

Total (95% CI)		**105**		**111**	**100.0%**	**0.72 [0.45, 1.14]**
Total events	23		33			

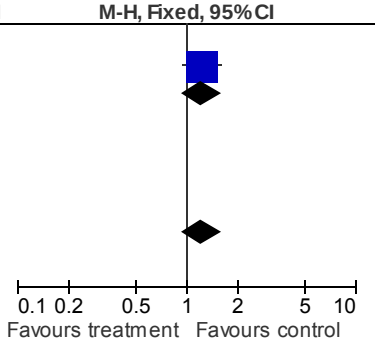
Heterogeneity: Chi² = 0.95, df = 1 (P = 0.33); I² = 0%

Test for overall effect: Z = 1.39 (P = 0.16)



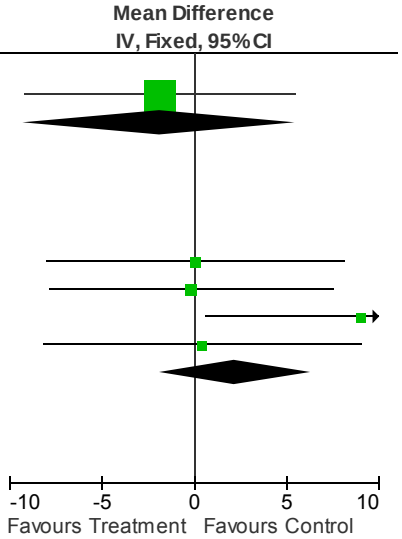
6.5 Global state: 2. Non-response (CGI) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.5.1 Medium-term						
Beuzen 1998	55	90	45	90	100.0%	1.22 [0.94, 1.59]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**1.22 [0.94, 1.59]**
Total events	55		45			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.49 (P = 0.14)						
Total (95% CI)		**90**		**90**	**100.0%**	**1.22 [0.94, 1.59]**
Total events	55		45			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.49 (P = 0.14)						



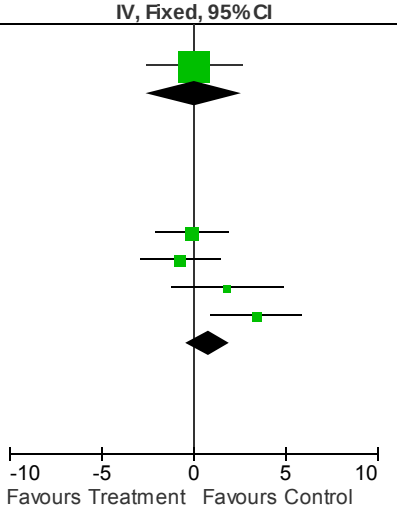
6.6 Mental state: 1. PANSS total (endpoint/change) (short-to-medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.6.1 Short-term								
MELTZER2008	84	12.83	21	85.9	10.9	19	100.0%	-1.90 [-9.26, 5.46]
Subtotal (95% CI)			**21**			**19**	**100.0%**	**-1.90 [-9.26, 5.46]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.51 (P = 0.61)								
6.6.2 Medium-term								
Beuzen 1998	82.6	29.06	89	82.57	25.7	87	25.6%	0.03 [-8.07, 8.13]
Bitter 1999	-37.9	23.4	70	-37.7	23.1	70	28.3%	-0.20 [-7.90, 7.50]
VOLAVKA2002	90.9	15.8	40	81.9	21.8	39	23.7%	9.00 [0.59, 17.41]
MELTZER2008	72.1	15.58	21	71.7	12.2	19	22.5%	0.40 [-8.23, 9.03]
Subtotal (95% CI)			**220**			**215**	**100.0%**	**2.17 [-1.92, 6.27]**
Heterogeneity: Chi² = 3.32, df = 3 (P = 0.34); I² = 10%								
Test for overall effect: Z = 1.04 (P = 0.30)								
Test for subgroup differences: Chi² = 0.90, df = 1 (P = 0.34), I² = 0%								



6.7 Mental state: 2. PANSS negative score (endpoint/change) (short-to-medium-term)

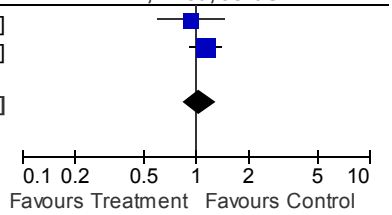
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.7.1 Short-term								
MELTZER2008	22.1	4.58	21	22.1	3.92	19	100.0%	0.00 [-2.64, 2.64]
Subtotal (95% CI)			**21**			**19**	**100.0%**	**0.00 [-2.64, 2.64]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
6.7.2 Medium-term								
Bitter 1999	-7.7	6.1	70	-7.6	6	70	34.3%	-0.10 [-2.10, 1.90]
Beuzen 1998	22.01	7.61	89	22.76	7.19	87	28.8%	-0.75 [-2.94, 1.44]
MELTZER2008	20.9	5.5	21	19.1	4.36	19	14.7%	1.80 [-1.26, 4.86]
VOLAVKA2002	23.5	4.9	40	20.1	6.3	39	22.2%	3.40 [0.91, 5.89]
Subtotal (95% CI)			**220**			**215**	**100.0%**	**0.77 [-0.41, 1.94]**
Heterogeneity: Chi² = 7.29, df = 3 (P = 0.06); I² = 59%								
Test for overall effect: Z = 1.28 (P = 0.20)								



Test for subgroup differences: Chi² = 0.27, df = 1 (P = 0.60), I² = 0%

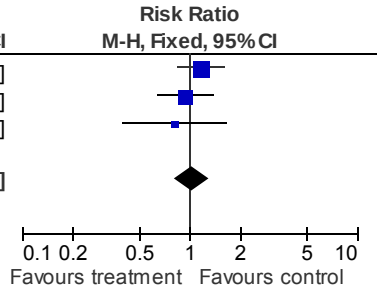
6.8 Mental state: 3. Non-response (< 20% change on BPRS/PANSS) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Oliemeulen 2000	10	15	15	21	42.7%	0.93 [0.60, 1.46]
MELTZER2008	20	21	16	19	57.3%	1.13 [0.91, 1.40]
Total (95% CI)		**36**		**40**	**100.0%**	**1.05 [0.84, 1.31]**
Total events	30		31			
Heterogeneity: Chi² = 0.74, df = 1 (P = 0.39); I² = 0%						
Test for overall effect: Z = 0.40 (P = 0.69)						



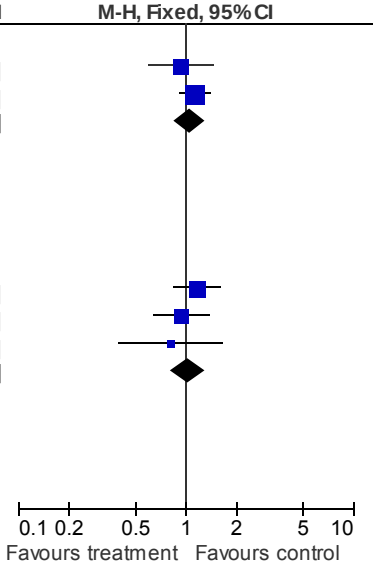
6.9 Mental state: 3. Non-response (<20-30% improvement in PANSS) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Beuzen 1998	43	90	37	90	47.4%	1.16 [0.84, 1.61]
Bitter 1999	29	74	32	76	40.5%	0.93 [0.63, 1.37]
MELTZER2008	8	21	9	19	12.1%	0.80 [0.39, 1.66]
Total (95% CI)		**185**		**185**	**100.0%**	**1.03 [0.81, 1.30]**
Total events	80		78			
Heterogeneity: Chi² = 1.23, df = 2 (P = 0.54); I² = 0%						
Test for overall effect: Z = 0.21 (P = 0.84)						



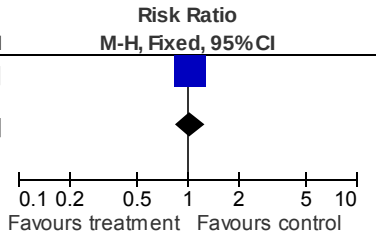
6.10 Mental state: 3. Non-response (<20-30% improvement in PANSS) (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.10.1 Short-term						
Oliemeulen 2000	10	15	15	21	42.7%	0.93 [0.60, 1.46]
MELTZER2008	20	21	16	19	57.3%	1.13 [0.91, 1.40]
Subtotal (95% CI)		**36**		**40**	**100.0%**	**1.05 [0.84, 1.31]**
Total events	30		31			
Heterogeneity: Chi² = 0.74, df = 1 (P = 0.39); I² = 0%						
Test for overall effect: Z = 0.40 (P = 0.69)						
6.10.2 Medium-term						
Beuzen 1998	43	90	37	90	47.4%	1.16 [0.84, 1.61]
Bitter 1999	29	74	32	76	40.5%	0.93 [0.63, 1.37]
MELTZER2008	8	21	9	19	12.1%	0.80 [0.39, 1.66]
Subtotal (95% CI)		**185**		**185**	**100.0%**	**1.03 [0.81, 1.30]**
Total events	80		78			
Heterogeneity: Chi² = 1.23, df = 2 (P = 0.54); I² = 0%						
Test for overall effect: Z = 0.21 (P = 0.84)						



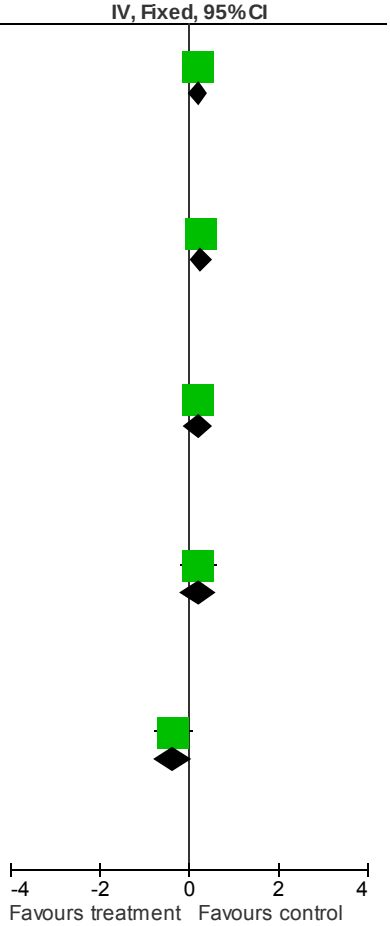
6.11 Mental state: 3. Non-response (<50% improvement in PANSS) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bitter 1999	54	74	54	76	100.0%	1.03 [0.84, 1.25]
Total (95% CI)		**74**		**76**	**100.0%**	**1.03 [0.84, 1.25]**
Total events	54		54			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.26 (P = 0.79)						



6.12 Cognitive functioning: 1. Global & domain scores (Z score change) (medium-term) (sign changed)

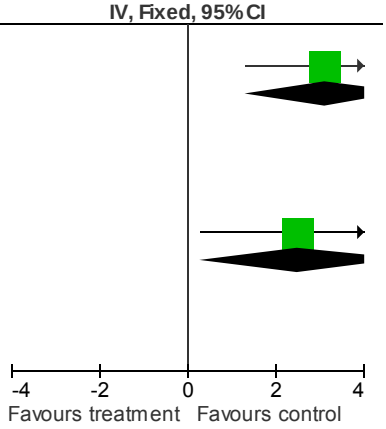
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.12.1 Global score								
VOLAVKA2002	-0.15	0.39	24	-0.35	0.38	26	100.0%	0.20 [-0.01, 0.41]
Subtotal (95% CI)			**24**			**26**	**100.0%**	**0.20 [-0.01, 0.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.83 (P = 0.07)								
6.12.2 General executive & perceptual organisation								
VOLAVKA2002	-0.08	0.39	24	-0.34	0.53	26	100.0%	0.26 [0.00, 0.52]
Subtotal (95% CI)			**24**			**26**	**100.0%**	**0.26 [0.00, 0.52]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.99 (P = 0.05)								
6.12.3 Declarative verbal learning & memory								
VOLAVKA2002	0.15	0.72	24	-0.05	0.48	26	100.0%	0.20 [-0.14, 0.54]
Subtotal (95% CI)			**24**			**26**	**100.0%**	**0.20 [-0.14, 0.54]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.15 (P = 0.25)								
6.12.4 Processing speed & attention								
VOLAVKA2002	-0.48	0.82	24	-0.68	0.61	26	100.0%	0.20 [-0.20, 0.60]
Subtotal (95% CI)			**24**			**26**	**100.0%**	**0.20 [-0.20, 0.60]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.97 (P = 0.33)								
6.12.5 Simple motor functioning								
VOLAVKA2002	-0.6	0.72	24	-0.24	0.85	26	100.0%	-0.36 [-0.80, 0.08]
Subtotal (95% CI)			**24**			**26**	**100.0%**	**-0.36 [-0.80, 0.08]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.62 (P = 0.11)								



Test for subgroup differences: Chi² = 6.28, df = 4 (P = 0.18), I² = 36.3%

6.13 Cognitive functioning: 1. Cognitive measures with sig. differences (endpoint; signs converted) (medium-term)

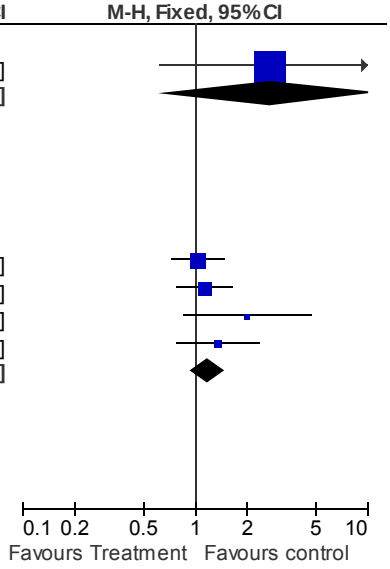
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.13.1 WISC-R Mazes								
MELTZER2008	-15.4	3.21	21	-18.5	2.62	19	100.0%	3.10 [1.29, 4.91]
Subtotal (95% CI)			**21**			**19**	**100.0%**	**3.10 [1.29, 4.91]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.36 (P = 0.0008)								
6.13.2 Verbal List Learning - Delayed Recall								
MELTZER2008	-4.7	4.12	21	-7.2	3.05	19	100.0%	2.50 [0.27, 4.73]
Subtotal (95% CI)			**21**			**19**	**100.0%**	**2.50 [0.27, 4.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.19 (P = 0.03)								



Test for subgroup differences: Chi² = 0.17, df = 1 (P = 0.68), I² = 0%

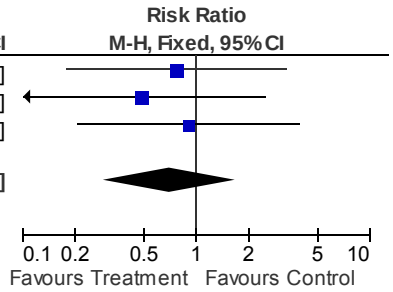
6.14 Leaving the study early: 1. Any reason (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.14.1 Short-term						
MELTZER2008	6	21	2	19	100.0%	2.71 [0.62, 11.87]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**2.71 [0.62, 11.87]**
Total events	6		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.33 (P = 0.18)						
6.14.2 Medium-term						
Beuzen 1998	37	90	36	90	42.8%	1.03 [0.72, 1.46]
Bitter 1999	33	74	30	76	35.2%	1.13 [0.78, 1.65]
MELTZER2008	11	21	5	19	6.2%	1.99 [0.85, 4.68]
VOLAVKA2002	18	40	13	39	15.7%	1.35 [0.77, 2.37]
Subtotal (95% CI)		**225**		**224**	**100.0%**	**1.17 [0.94, 1.47]**
Total events	99		84			
Heterogeneity: Chi² = 2.28, df = 3 (P = 0.52); I² = 0%						
Test for overall effect: Z = 1.40 (P = 0.16)						



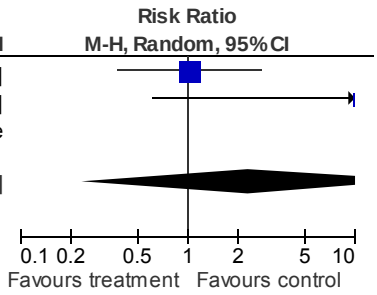
6.15 Leaving the study early: 2. Due to lack of efficacy (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bitter 1999	3	74	4	76	35.4%	0.77 [0.18, 3.32]
VOLAVKA2002	2	40	4	39	36.3%	0.49 [0.09, 2.51]
MELTZER2008	3	21	3	19	28.3%	0.90 [0.21, 3.96]
Total (95% CI)		**135**		**134**	**100.0%**	**0.71 [0.29, 1.69]**
Total events	8		11			
Heterogeneity: Chi² = 0.32, df = 2 (P = 0.85); I² = 0%						
Test for overall effect: Z = 0.78 (P = 0.43)						



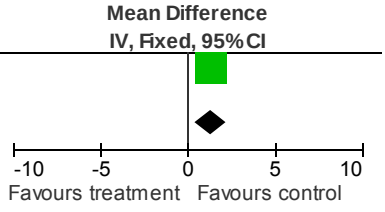
6.16 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Bitter 1999	7	74	7	76	65.3%	1.03 [0.38, 2.78]
VOLAVKA2002	5	40	0	39	34.7%	10.73 [0.61, 187.79]
MELTZER2008	0	21	0	19		Not estimable
Total (95% CI)		**135**		**134**	**100.0%**	**2.32 [0.23, 23.31]**
Total events	12		7			
Heterogeneity: Tau² = 1.86; Chi² = 2.56, df = 1 (P = 0.11); I² = 61%						
Test for overall effect: Z = 0.71 (P = 0.48)						



6.17 AE: 1. Metabolic SEs - BMI (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	1.4	1.9	38	0.1	2	36	100.0%	1.30 [0.41, 2.19]
Total (95% CI)			**38**			**36**	**100.0%**	**1.30 [0.41, 2.19]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.86 (P = 0.004)								

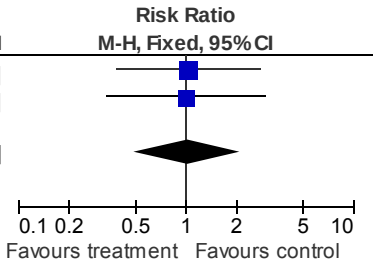


6.18 AE: 1. Metabolic SEs - No. with weight gain (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bitter 1999	7	74	7	76	53.5%	1.03 [0.38, 2.78]
Beuzen 1998	6	90	6	90	46.5%	1.00 [0.34, 2.98]
Total (95% CI)		**164**		**166**	**100.0%**	**1.01 [0.49, 2.12]**
Total events	13		13			

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.97); I² = 0%

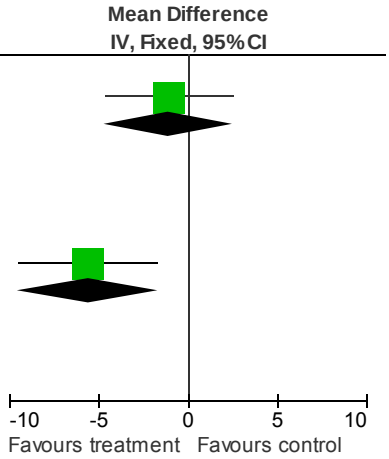
Test for overall effect: Z = 0.04 (P = 0.97)



6.19 AE: 1. Metabolic SEs - Weight at endpoint (kg) (medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
6.19.1 Short-term								
MELTZER2008	92.35	6.24	21	93.44	5.34	19	100.0%	-1.09 [-4.68, 2.50]
Subtotal (95% CI)			**21**			**19**	**100.0%**	**-1.09 [-4.68, 2.50]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.60 (P = 0.55)								
6.19.2 Medium-term								
MELTZER2008	92.81	6.86	21	98.43	5.73	19	100.0%	-5.62 [-9.52, -1.72]
Subtotal (95% CI)			**21**			**19**	**100.0%**	**-5.62 [-9.52, -1.72]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.82 (P = 0.005)								

Test for subgroup differences: Chi² = 2.80, df = 1 (P = 0.09), I² = 64.3%

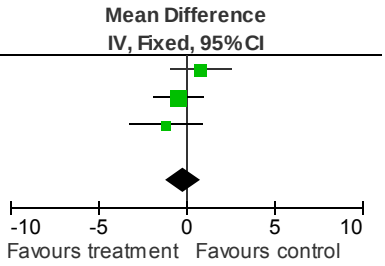


6.20 AE: 1. Metabolic SEs - Weight change from baseline (kg) (medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Bitter 1999	4.1	5.6	74	3.3	5.3	76	31.7%	0.80 [-0.95, 2.55]
Beuzen 1998	1.8	5	90	2.3	4.9	90	46.2%	-0.50 [-1.95, 0.95]
VOLAVKA2002	4.2	4.7	38	5.4	4.6	38	22.1%	-1.20 [-3.29, 0.89]
Total (95% CI)			**202**			**204**	**100.0%**	**-0.24 [-1.23, 0.74]**

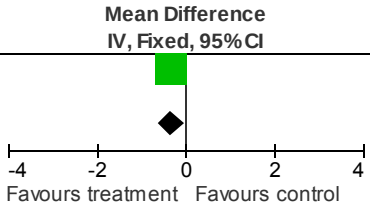
Heterogeneity: Chi² = 2.30, df = 2 (P = 0.32); I² = 13%

Test for overall effect: Z = 0.48 (P = 0.63)



6.21 AE: 1. Metabolic SEs - Urinary pH (change from baseline) (medium-term)

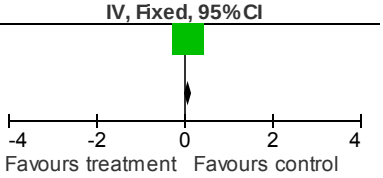
Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Bitter 1999	-0.12	0.77	67	0.22	1	67	100.0%	-0.34 [-0.64, -0.04]
Total (95% CI)			**67**			**67**	**100.0%**	**-0.34 [-0.64, -0.04]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.21 (P = 0.03)								



6.22 AE: 1. Metabolic SEs - Phosphate (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bitter 1999	0.06	0.21	70	-0.01	0.2	67	100.0%	0.07 [0.00, 0.14]
Total (95% CI)			**70**			**67**	**100.0%**	**0.07 [0.00, 0.14]**

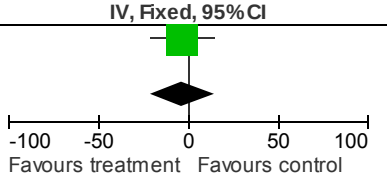
Heterogeneity: Not applicable
Test for overall effect: Z = 2.00 (P = 0.05)



6.23 AE: 1. Metabolic SEs - Cholestrol mg/dL (change from baseline) (medium-term)

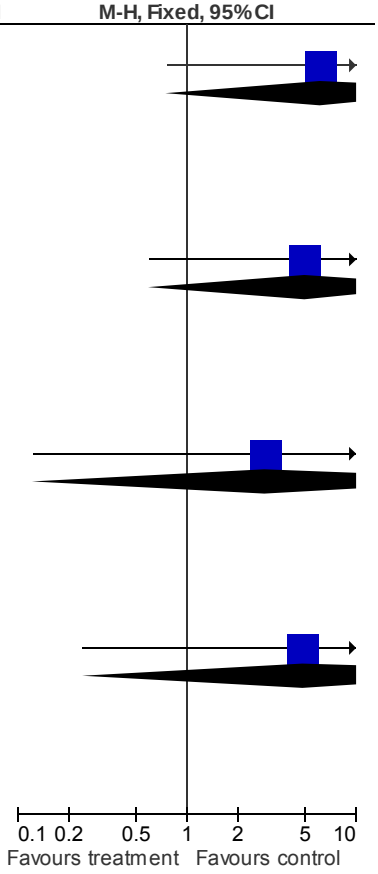
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	16.3	39.6	28	20.1	26.8	26	100.0%	-3.80 [-21.72, 14.12]
Total (95% CI)			**28**			**26**	**100.0%**	**-3.80 [-21.72, 14.12]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.42 (P = 0.68)



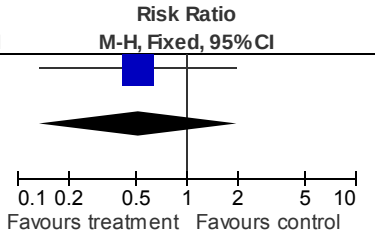
6.24 AE: 1. Metabolic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.24.1 Abnormally elevated alkaline phosphatase levels						
Bitter 1999	6	74	1	76	100.0%	6.16 [0.76, 49.95]
Subtotal (95% CI)		**74**		**76**	**100.0%**	**6.16 [0.76, 49.95]**
Total events	6		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.70 (P = 0.09)						
6.24.2 White blood cell problems						
Beuzen 1998	5	90	1	90	100.0%	5.00 [0.60, 41.95]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**5.00 [0.60, 41.95]**
Total events	5		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.48 (P = 0.14)						
6.24.3 Agranulocytosis						
VOLAVKA2002	1	40	0	39	100.0%	2.93 [0.12, 69.74]
Subtotal (95% CI)		**40**		**39**	**100.0%**	**2.93 [0.12, 69.74]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.66 (P = 0.51)						
6.24.4 Neutropenia						
VOLAVKA2002	2	40	0	39	100.0%	4.88 [0.24, 98.47]
Subtotal (95% CI)		**40**		**39**	**100.0%**	**4.88 [0.24, 98.47]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.03 (P = 0.30)						



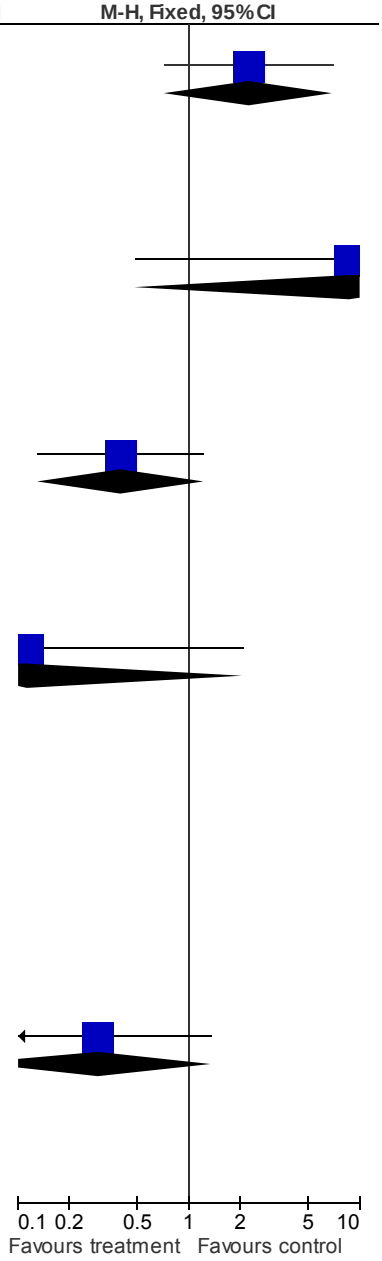
6.25 AE: 2. Neurologic SEs - Use of anticholinergic medication (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bitter 1999	3	74	6	76	100.0%	0.51 [0.13, 1.98]
Total (95% CI)		**74**		**76**	**100.0%**	**0.51 [0.13, 1.98]**
Total events	3		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						



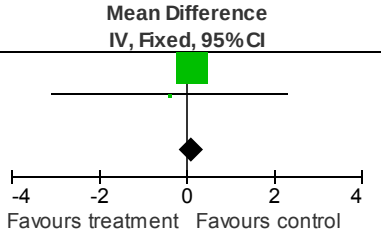
6.26 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.26.1 Any extrapyramidal event						
Beuzen 1998	9	90	4	90	100.0%	2.25 [0.72, 7.04]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**2.25 [0.72, 7.04]**
Total events	9		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.39 (P = 0.16)						
6.26.2 Seizures						
VOLAVKA2002	4	40	0	39	100.0%	8.78 [0.49, 157.85]
Subtotal (95% CI)		**40**		**39**	**100.0%**	**8.78 [0.49, 157.85]**
Total events	4		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.47 (P = 0.14)						
6.26.3 Agitation						
Beuzen 1998	4	90	10	90	100.0%	0.40 [0.13, 1.23]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**0.40 [0.13, 1.23]**
Total events	4		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.60 (P = 0.11)						
6.26.4 Akathisia						
Bitter 1999	0	74	4	76	100.0%	0.11 [0.01, 2.08]
Subtotal (95% CI)		**74**		**76**	**100.0%**	**0.11 [0.01, 2.08]**
Total events	0		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.46 (P = 0.14)						
6.26.5 New parkinsonism						
Bitter 1999	0	74	0	76		Not estimable
Subtotal (95% CI)		**74**		**76**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
6.26.6 Dyskinetic movements						
Bitter 1999	2	74	7	76	100.0%	0.29 [0.06, 1.37]
Subtotal (95% CI)		**74**		**76**	**100.0%**	**0.29 [0.06, 1.37]**
Total events	2		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.56 (P = 0.12)						



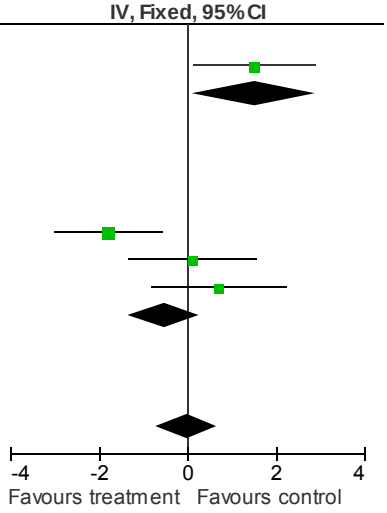
6.27 AE: 2. Neurologic SEs - Hillside or Barnes Akathisia Scale (change) (medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Beuzen 1998	-0.3	0.9	88	-0.4	1	84	98.9%	0.10 [-0.18, 0.38]
Bitter 1999	-2.7	7.1	69	-2.3	8.9	68	1.1%	-0.40 [-3.10, 2.30]
Total (95% CI)			**157**			**152**	**100.0%**	**0.09 [-0.19, 0.38]**
Heterogeneity: Chi² = 0.13, df = 1 (P = 0.72); I² = 0%								
Test for overall effect: Z = 0.65 (P = 0.51)								



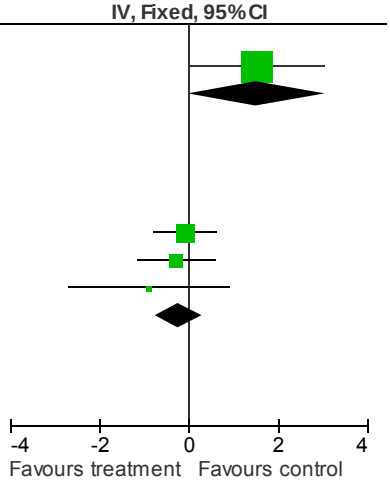
6.28 AE: 2. Neurologic SEs - Simpson-Angus Scale (SAS; change/endpoint) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.28.1 Short-term								
MELTZER2008	2.5	2.29	21	1	2.18	19	25.0%	1.50 [0.11, 2.89]
Subtotal (95% CI)			**21**			**19**	**25.0%**	**1.50 [0.11, 2.89]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.12 (P = 0.03)								
6.28.2 Medium-term								
Beuzen 1998	-3.2	4.8	88	-1.4	3.3	84	31.9%	-1.80 [-3.03, -0.57]
Bitter 1999	-2.9	3.9	70	-3	4.8	69	22.7%	0.10 [-1.36, 1.56]
MELTZER2008	2.3	2.75	21	1.6	2.18	19	20.5%	0.70 [-0.83, 2.23]
Subtotal (95% CI)			**179**			**172**	**75.0%**	**-0.54 [-1.34, 0.26]**
Heterogeneity: Chi² = 7.32, df = 2 (P = 0.03); I² = 73%								
Test for overall effect: Z = 1.33 (P = 0.18)								
Total (95% CI)			**200**			**191**	**100.0%**	**-0.03 [-0.73, 0.66]**
Heterogeneity: Chi² = 13.59, df = 3 (P = 0.004); I² = 78%								
Test for overall effect: Z = 0.09 (P = 0.92)								
Test for subgroup differences: Chi² = 6.27, df = 1 (P = 0.01), I² = 84.1%								



6.29 AE: 2. Neurologic SEs - Abnormal Involuntary Movement Scale (AIMS; change/endpoint) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.29.1 Short-term								
MELTZER2008	2	2.75	21	0.5	2.18	19	100.0%	1.50 [-0.03, 3.03]
Subtotal (95% CI)			**21**			**19**	**100.0%**	**1.50 [-0.03, 3.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.92 (P = 0.05)								
6.29.2 Medium-term								
Beuzen 1998	-0.8	2.2	88	-0.7	2.5	84	55.8%	-0.10 [-0.81, 0.61]
Bitter 1999	-0.9	2.8	70	-0.6	2.5	69	35.7%	-0.30 [-1.18, 0.58]
MELTZER2008	1.4	3.21	21	2.3	2.62	19	8.5%	-0.90 [-2.71, 0.91]
Subtotal (95% CI)			**179**			**172**	**100.0%**	**-0.24 [-0.77, 0.29]**
Heterogeneity: Chi² = 0.68, df = 2 (P = 0.71); I² = 0%								
Test for overall effect: Z = 0.89 (P = 0.37)								
Test for subgroup differences: Chi² = 4.43, df = 1 (P = 0.04), I² = 77.4%								

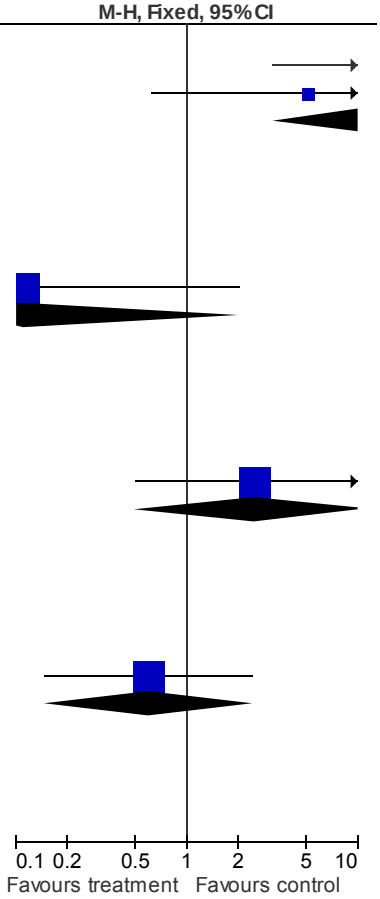


6.30 AE: 2. Neurologic SEs - Extrapyramidal Symptom Rating Scale (endpt mean) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	5.1	3.8	40	3.8	3.1	39	100.0%	1.30 [-0.23, 2.83]
Total (95% CI)			**40**			**39**	**100.0%**	**1.30 [-0.23, 2.83]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.67 (P = 0.10)								

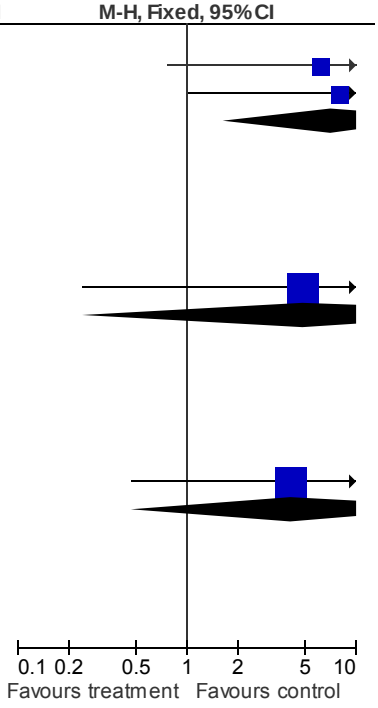
6.31 AE: 3. Autonomic SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.31.1 Hypersalivation						
Beuzen 1998	26	90	2	90	67.0%	13.00 [3.18, 53.15]
Bitter 1999	5	74	1	76	33.0%	5.14 [0.61, 42.91]
Subtotal (95% CI)		**164**		**166**	**100.0%**	**10.40 [3.25, 33.30]**
Total events	31		3			
Heterogeneity: Chi² = 0.52, df = 1 (P = 0.47); I² = 0%						
Test for overall effect: Z = 3.94 (P < 0.0001)						
6.31.2 Dry mouth						
Beuzen 1998	0	90	4	90	100.0%	0.11 [0.01, 2.03]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**0.11 [0.01, 2.03]**
Total events	0		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.48 (P = 0.14)						
6.31.3 Sweating						
Beuzen 1998	5	90	2	90	100.0%	2.50 [0.50, 12.55]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**2.50 [0.50, 12.55]**
Total events	5		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.11 (P = 0.27)						
6.31.4 Rhinitis						
Beuzen 1998	3	90	5	90	100.0%	0.60 [0.15, 2.44]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**0.60 [0.15, 2.44]**
Total events	3		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.71 (P = 0.47)						



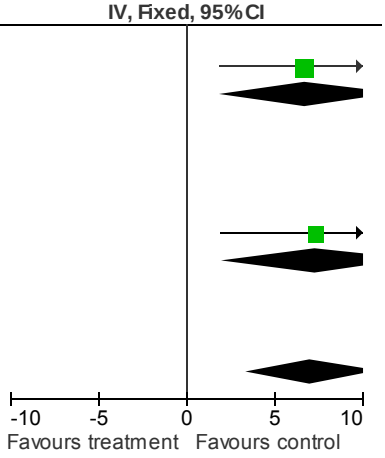
6.32 AE: 4. Cardiovascular SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.32.1 Dizziness						
Bitter 1999	6	74	1	76	49.7%	6.16 [0.76, 49.95]
Beuzen 1998	8	90	1	90	50.3%	8.00 [1.02, 62.66]
Subtotal (95% CI)		**164**		**166**	**100.0%**	**7.09 [1.64, 30.72]**
Total events	14		2			
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.86); I² = 0%						
Test for overall effect: Z = 2.62 (P = 0.009)						
6.32.2 Hypertension						
VOLAVKA2002	2	40	0	39	100.0%	4.88 [0.24, 98.47]
Subtotal (95% CI)		**40**		**39**	**100.0%**	**4.88 [0.24, 98.47]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.03 (P = 0.30)						
6.32.3 Postural hypotension						
Bitter 1999	4	74	1	76	100.0%	4.11 [0.47, 35.90]
Subtotal (95% CI)		**74**		**76**	**100.0%**	**4.11 [0.47, 35.90]**
Total events	4		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.28 (P = 0.20)						



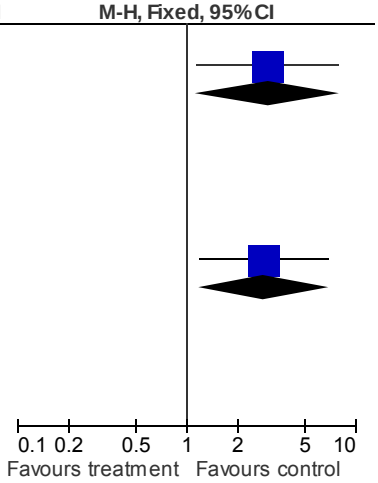
6.33 AE: 4. Cardiovascular SEs - heart rate (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
6.33.1 Supine								
Bitter 1999	11.1	15.1	72	4.4	15	75	54.9%	6.70 [1.83, 11.57]
Subtotal (95% CI)			**72**			**75**	**54.9%**	**6.70 [1.83, 11.57]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.70 (P = 0.007)								
6.33.2 Standing								
Bitter 1999	12.7	16.2	72	5.4	17	75	45.1%	7.30 [1.93, 12.67]
Subtotal (95% CI)			**72**			**75**	**45.1%**	**7.30 [1.93, 12.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.67 (P = 0.008)								
Total (95% CI)			**144**			**150**	**100.0%**	**6.97 [3.37, 10.58]**
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.87); I² = 0%								
Test for overall effect: Z = 3.79 (P = 0.0002)								
Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.87), I² = 0%								



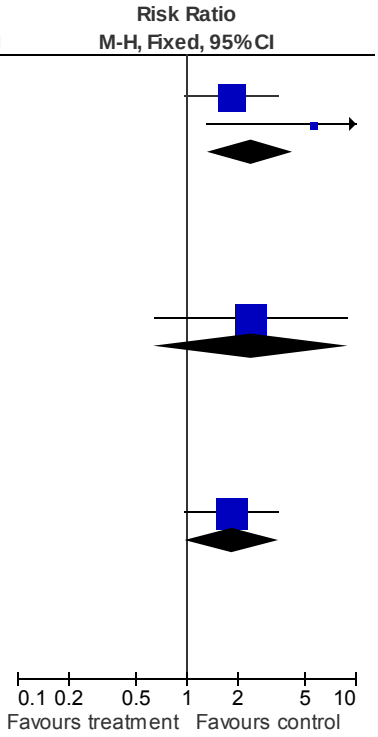
6.34 AE: 5. Gastrointestinal SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.34.1 Nausea/ vomiting						
Beuzen 1998	15	90	5	90	100.0%	3.00 [1.14, 7.91]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**3.00 [1.14, 7.91]**
Total events	15		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.22 (P = 0.03)						
6.34.2 Constipation						
Beuzen 1998	17	90	6	90	100.0%	2.83 [1.17, 6.86]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**2.83 [1.17, 6.86]**
Total events	17		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.31 (P = 0.02)						

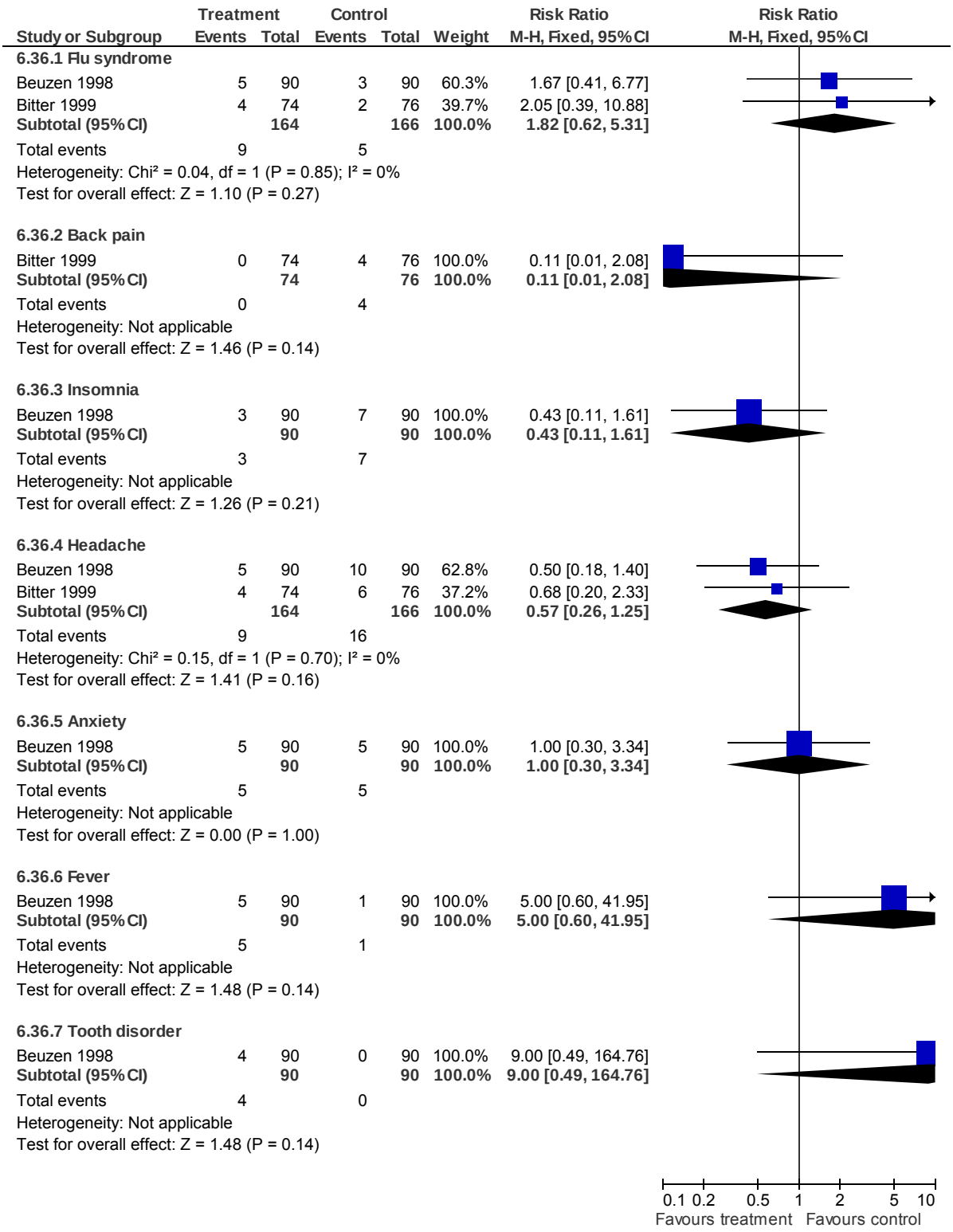


6.35 AE: 6. Sedation (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.35.1 Day time sleepiness - increase (somnolence)						
Beuzen 1998	22	90	12	90	85.9%	1.83 [0.97, 3.48]
Bitter 1999	11	74	2	76	14.1%	5.65 [1.30, 24.62]
Subtotal (95% CI)		**164**		**166**	**100.0%**	**2.37 [1.33, 4.24]**
Total events	33		14			
Heterogeneity: $Chi^2 = 1.96$, df = 1 (P = 0.16); $I^2 = 49\%$						
Test for overall effect: Z = 2.92 (P = 0.004)						
6.35.2 Asthenia						
Bitter 1999	7	74	3	76	100.0%	2.40 [0.64, 8.92]
Subtotal (95% CI)		**74**		**76**	**100.0%**	**2.40 [0.64, 8.92]**
Total events	7		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.30 (P = 0.19)						
6.35.3 Too much sleep (hypersomnia)						
Beuzen 1998	22	90	12	90	100.0%	1.83 [0.97, 3.48]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**1.83 [0.97, 3.48]**
Total events	22		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.86 (P = 0.06)						



6.36 AE: 10. Other SEs (medium-term)

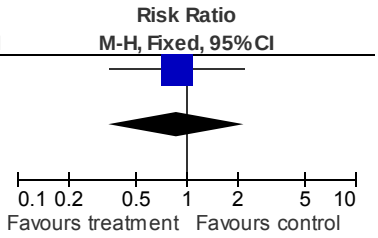


7 Clozapine vs. Risperidone (in people whose illness has not responded adequately to treatment)

7.1 Global state: 1. Relapse (or deterioration in mental state) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bondolfi 1998	7	43	8	43	100.0%	0.88 [0.35, 2.20]
Total (95% CI)		**43**		**43**	**100.0%**	**0.88 [0.35, 2.20]**
Total events	7		8			

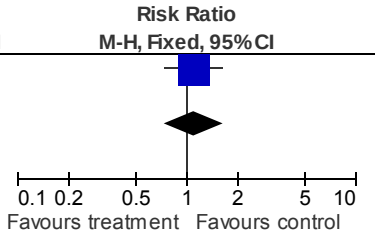
Heterogeneity: Not applicable
Test for overall effect: Z = 0.28 (P = 0.78)



7.2 Global state: 1. Relapse (or deterioration in mental state) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Anand 1998	38	138	34	135	100.0%	1.09 [0.73, 1.63]
Total (95% CI)		**138**		**135**	**100.0%**	**1.09 [0.73, 1.63]**
Total events	38		34			

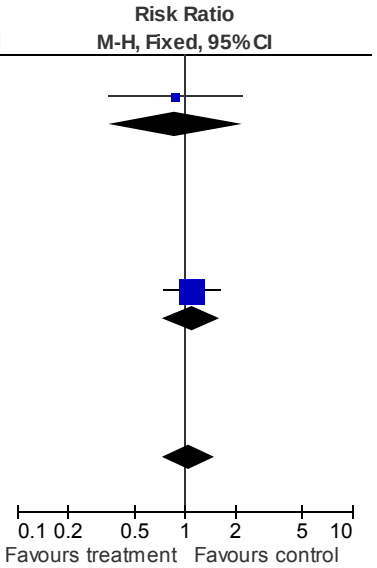
Heterogeneity: Not applicable
Test for overall effect: Z = 0.44 (P = 0.66)



7.3 Global state: 1. Relapse (or deterioration in mental state) (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.3.1 Short-term						
Bondolfi 1998	7	43	8	43	18.9%	0.88 [0.35, 2.20]
Subtotal (95% CI)		**43**		**43**	**18.9%**	**0.88 [0.35, 2.20]**
Total events	7		8			
7.3.2 Medium-term						
Anand 1998	38	138	34	135	81.1%	1.09 [0.73, 1.63]
Subtotal (95% CI)		**138**		**135**	**81.1%**	**1.09 [0.73, 1.63]**
Total events	38		34			
Total (95% CI)		**181**		**178**	**100.0%**	**1.05 [0.73, 1.52]**
Total events	45		42			

Heterogeneity: Chi² = 0.19, df = 1 (P = 0.66); I² = 0%
Test for overall effect: Z = 0.27 (P = 0.78)

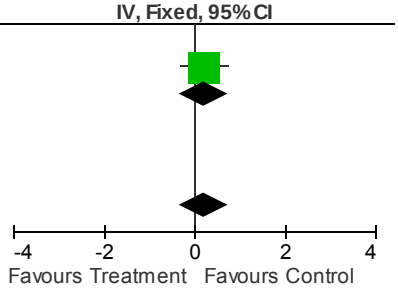


7.4 Global state: 2. CGI (endpoint; high = poor) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.4.1 short term								
Bondolfi 1998	3.1	1.3	43	2.9	1.2	43	100.0%	0.20 [-0.33, 0.73]
Subtotal (95% CI)			**43**			**43**	**100.0%**	**0.20 [-0.33, 0.73]**
Total (95% CI)			**43**			**43**	**100.0%**	**0.20 [-0.33, 0.73]**

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

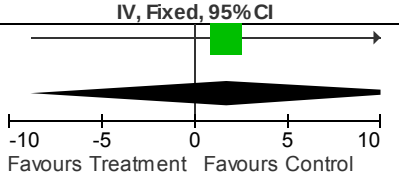
Heterogeneity: Not applicable
Test for overall effect: Z = 0.74 (P = 0.46)
Test for subgroup differences: Not applicable



7.5 Mental state: 1. PANSS total (endpoint, high=poor) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bondolfi 1998	78.9	25.5	43	77.2	24.3	43	100.0%	1.70 [-8.83, 12.23]
Total (95% CI)			**43**			**43**	**100.0%**	**1.70 [-8.83, 12.23]**

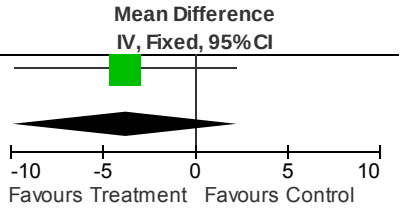
Heterogeneity: Not applicable
Test for overall effect: Z = 0.32 (P = 0.75)



7.6 Mental state: 1. BPRS total (endpoint, high=poor) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Breier 1999	32	6.37	14	35.8	9.89	15	100.0%	-3.80 [-9.82, 2.22]
Total (95% CI)			**14**			**15**	**100.0%**	**-3.80 [-9.82, 2.22]**

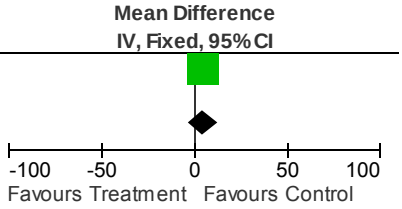
Heterogeneity: Not applicable
Test for overall effect: Z = 1.24 (P = 0.22)



7.7 Mental state: 1. PANSS total (endpoint, high=poor) (medium-term)

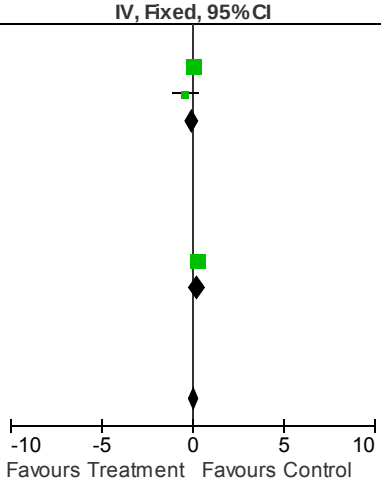
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	90.9	15.8	40	86.4	20.1	41	100.0%	4.50 [-3.36, 12.36]
Total (95% CI)			**40**			**41**	**100.0%**	**4.50 [-3.36, 12.36]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.12 (P = 0.26)



7.8 Mental state: 1. BPRS/PANSS total (endpoint, high=poor) (short-to-medium-term)

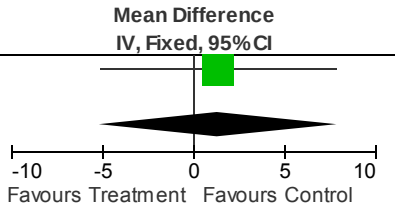
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
7.8.1 Short-term								
Bondolfi 1998	78.9	25.5	43	77.2	24.3	43	44.2%	0.07 [-0.36, 0.49]
Breier 1999	32	6.37	14	35.8	9.89	15	14.5%	-0.44 [-1.18, 0.30]
Subtotal (95% CI)			**57**			**58**	**58.7%**	**-0.06 [-0.42, 0.31]**
Heterogeneity: Chi² = 1.37, df = 1 (P = 0.24); I² = 27%								
Test for overall effect: Z = 0.31 (P = 0.76)								
7.8.2 Medium-term								
VOLAVKA2002	90.9	15.8	40	86.4	20.1	41	41.3%	0.25 [-0.19, 0.68]
Subtotal (95% CI)			**40**			**41**	**41.3%**	**0.25 [-0.19, 0.68]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.10 (P = 0.27)								
Total (95% CI)			**97**			**99**	**100.0%**	**0.07 [-0.21, 0.35]**
Heterogeneity: Chi² = 2.46, df = 2 (P = 0.29); I² = 19%								
Test for overall effect: Z = 0.47 (P = 0.64)								
Test for subgroup differences: Chi² = 1.09, df = 1 (P = 0.30), I² = 8.2%								



7.9 Mental state: 2. SANS (endpoint, high=poor) (short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Breier 1999	48.93	8.43	14	47.6	9.42	15	100.0%	1.33 [-5.17, 7.83]
Total (95% CI)			**14**			**15**	**100.0%**	**1.33 [-5.17, 7.83]**

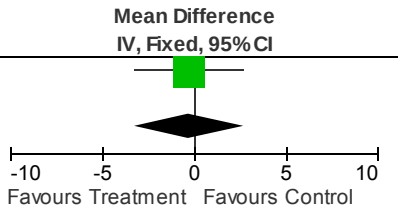
Heterogeneity: Not applicable
Test for overall effect: Z = 0.40 (P = 0.69)



7.10 Mental state: 2. PANSS negative score (endpoint, high=poor) (short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Bondolfi 1998	21.2	6.9	43	21.5	7.2	43	100.0%	-0.30 [-3.28, 2.68]
Total (95% CI)			**43**			**43**	**100.0%**	**-0.30 [-3.28, 2.68]**

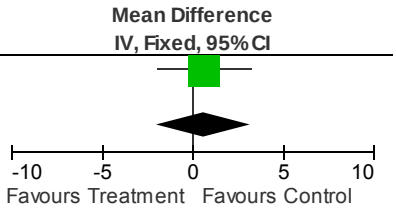
Heterogeneity: Not applicable
Test for overall effect: Z = 0.20 (P = 0.84)



7.11 Mental state: 2. PANSS negative score (endpoint, high=poor) (medium-term)

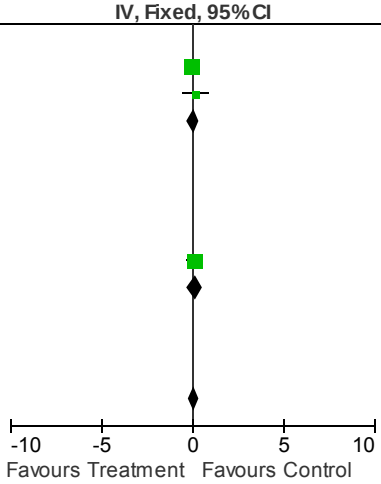
Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	23.5	4.9	40	22.9	6.9	41	100.0%	0.60 [-2.00, 3.20]
Total (95% CI)			**40**			**41**	**100.0%**	**0.60 [-2.00, 3.20]**

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



7.12 Mental state: 2. SANS/PANSS negative score (endpoint, high=poor) (short-to-medium-term)

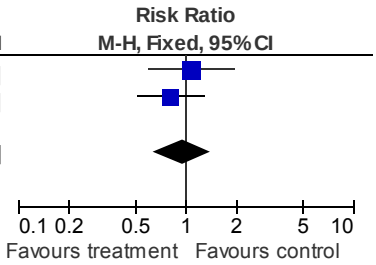
Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
7.12.1 Short-term								
Bondolfi 1998	21.2	6.9	43	21.5	7.2	43	43.9%	-0.04 [-0.46, 0.38]
Breier 1999	48.93	8.43	14	47.6	9.42	15	14.8%	0.14 [-0.59, 0.87]
Subtotal (95% CI)			**57**			**58**	**58.7%**	**0.00 [-0.36, 0.37]**
Heterogeneity: Chi² = 0.19, df = 1 (P = 0.66); I² = 0%								
Test for overall effect: Z = 0.03 (P = 0.98)								
7.12.2 Medium-term								
VOLAVKA2002	23.5	4.9	40	22.9	6.9	41	41.3%	0.10 [-0.34, 0.53]
Subtotal (95% CI)			**40**			**41**	**41.3%**	**0.10 [-0.34, 0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.45 (P = 0.66)								
Total (95% CI)			**97**			**99**	**100.0%**	**0.04 [-0.24, 0.32]**
Heterogeneity: Chi² = 0.29, df = 2 (P = 0.86); I² = 0%								
Test for overall effect: Z = 0.31 (P = 0.76)								
Test for subgroup differences: Chi² = 0.11, df = 1 (P = 0.75), I² = 0%								



7.13 Mental state: 4. Non-response (<20% improvement in BPRS/PANSS) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bondolfi 1998	15	43	14	43	54.7%	1.07 [0.59, 1.94]
Breier 1999	9	14	12	15	45.3%	0.80 [0.50, 1.28]
Total (95% CI)		**57**		**58**	**100.0%**	**0.95 [0.64, 1.41]**
Total events	24		26			

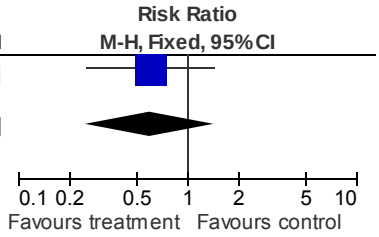
Heterogeneity: Chi² = 0.66, df = 1 (P = 0.42); I² = 0%
Test for overall effect: Z = 0.25 (P = 0.80)



7.14 Mental state: 4. Non-response (<20% improvement in PANSS positive subscale) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chowdhury 1999	6	30	10	30	100.0%	0.60 [0.25, 1.44]
Total (95% CI)		**30**		**30**	**100.0%**	**0.60 [0.25, 1.44]**
Total events	6		10			

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



7.15 Mental state: 4. Non-response (<20% improvement in BPRS/PANSS total/positive subscale) (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.15.1 Short-term						
Bondolfi 1998	15	43	14	43	39.3%	1.07 [0.59, 1.94]
Breier 1999	9	14	12	15	32.6%	0.80 [0.50, 1.28]
Subtotal (95% CI)		**57**		**58**	**71.9%**	**0.95 [0.64, 1.41]**
Total events	24		26			

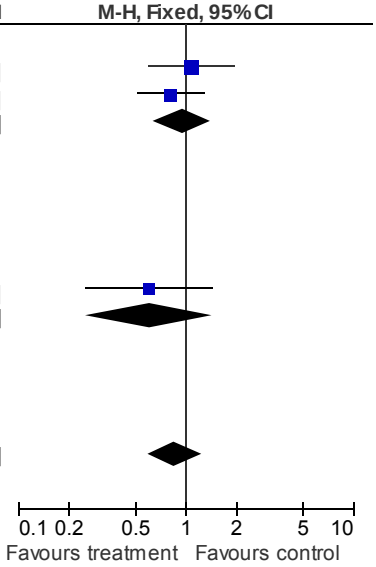
Heterogeneity: Chi² = 0.66, df = 1 (P = 0.42); I² = 0%
Test for overall effect: Z = 0.25 (P = 0.80)

7.15.2 Medium-term						
Chowdhury 1999	6	30	10	30	28.1%	0.60 [0.25, 1.44]
Subtotal (95% CI)		**30**		**30**	**28.1%**	**0.60 [0.25, 1.44]**
Total events	6		10			

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

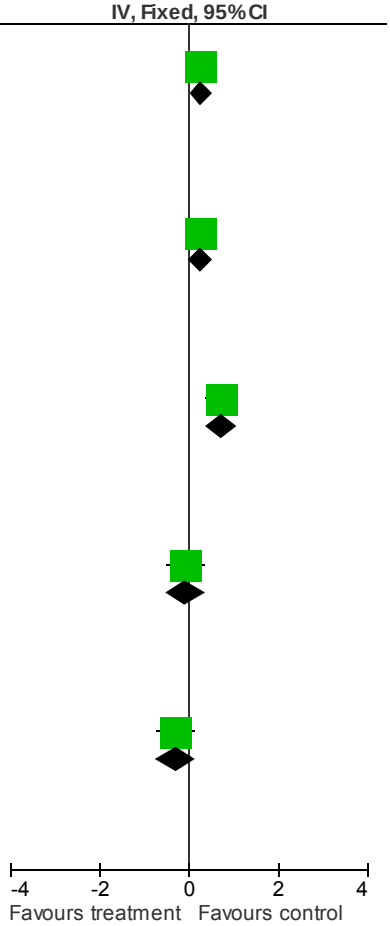
Total (95% CI)		**87**		**88**	**100.0%**	**0.85 [0.59, 1.23]**
Total events	30		36			

Heterogeneity: Chi² = 1.25, df = 2 (P = 0.54); I² = 0%
Test for overall effect: Z = 0.86 (P = 0.39)



7.16 Cognitive functioning: 1. Global & domain scores (Z score change) (medium-term) (sign changed)

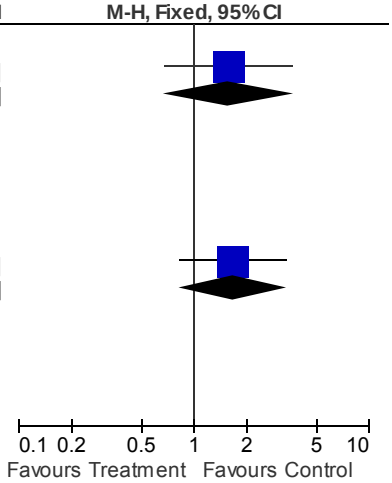
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.16.1 Global score								
VOLAVKA2002	-0.15	0.39	24	-0.42	0.48	26	100.0%	0.27 [0.03, 0.51]
Subtotal (95% CI)			**24**			**26**	**100.0%**	**0.27 [0.03, 0.51]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.19 (P = 0.03)								
7.16.2 General executive & perceptual organisation								
VOLAVKA2002	-0.08	0.39	24	-0.33	0.59	26	100.0%	0.25 [-0.03, 0.53]
Subtotal (95% CI)			**24**			**26**	**100.0%**	**0.25 [-0.03, 0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.78 (P = 0.08)								
7.16.3 Declarative verbal learning & memory								
VOLAVKA2002	0.15	0.72	24	-0.57	0.59	26	100.0%	0.72 [0.35, 1.09]
Subtotal (95% CI)			**24**			**26**	**100.0%**	**0.72 [0.35, 1.09]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.85 (P = 0.0001)								
7.16.4 Processing speed & attention								
VOLAVKA2002	-0.48	0.82	24	-0.4	0.73	26	100.0%	-0.08 [-0.51, 0.35]
Subtotal (95% CI)			**24**			**26**	**100.0%**	**-0.08 [-0.51, 0.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.36 (P = 0.72)								
7.16.5 Simple motor functioning								
VOLAVKA2002	-0.6	0.72	24	-0.29	0.84	26	100.0%	-0.31 [-0.74, 0.12]
Subtotal (95% CI)			**24**			**26**	**100.0%**	**-0.31 [-0.74, 0.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.40 (P = 0.16)								



Test for subgroup differences: Chi² = 14.95, df = 4 (P = 0.005), I² = 73.2%

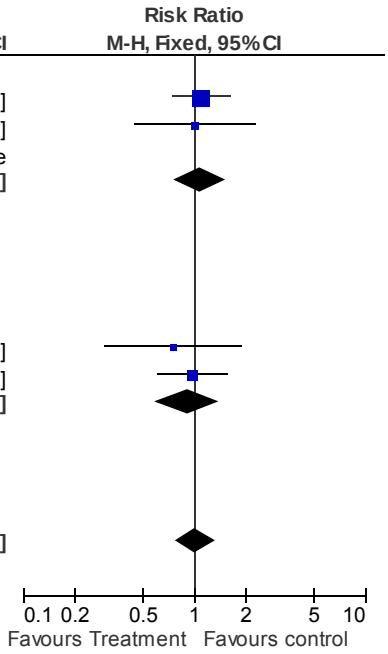
7.17 Cognitive functioning: 2. Problem with cognitive function (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.17.1 Concentration difficulties						
Bondolfi 1998	11	43	7	43	100.0%	1.57 [0.67, 3.67]
Subtotal (95% CI)		**43**		**43**	**100.0%**	**1.57 [0.67, 3.67]**
Total events	11		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.04 (P = 0.30)						
7.17.2 Memory problems						
Bondolfi 1998	15	43	9	43	100.0%	1.67 [0.82, 3.39]
Subtotal (95% CI)		**43**		**43**	**100.0%**	**1.67 [0.82, 3.39]**
Total events	15		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.41 (P = 0.16)						



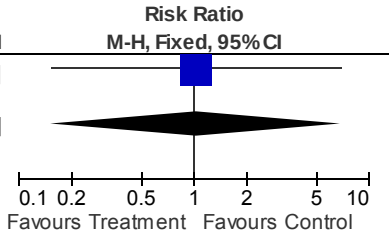
7.18 Leaving the study early: 1. Any reason (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.18.1 Short-term						
Anand 1998	38	138	34	135	49.0%	1.09 [0.73, 1.63]
Bondolfi 1998	9	43	9	43	12.8%	1.00 [0.44, 2.27]
Breier 1999	0	14	0	15		Not estimable
Subtotal (95% CI)		**195**		**193**	**61.8%**	**1.07 [0.75, 1.54]**
Total events	47		43			
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.85); I² = 0%						
Test for overall effect: Z = 0.39 (P = 0.70)						
7.18.2 Medium-term						
Chowdhury 1999	6	30	8	30	11.4%	0.75 [0.30, 1.90]
VOLAVKA2002	18	40	19	41	26.8%	0.97 [0.60, 1.56]
Subtotal (95% CI)		**70**		**71**	**38.2%**	**0.90 [0.59, 1.39]**
Total events	24		27			
Heterogeneity: Chi² = 0.24, df = 1 (P = 0.62); I² = 0%						
Test for overall effect: Z = 0.46 (P = 0.65)						
Total (95% CI)		**265**		**264**	**100.0%**	**1.01 [0.77, 1.33]**
Total events	71		70			
Heterogeneity: Chi² = 0.57, df = 3 (P = 0.90); I² = 0%						
Test for overall effect: Z = 0.07 (P = 0.95)						



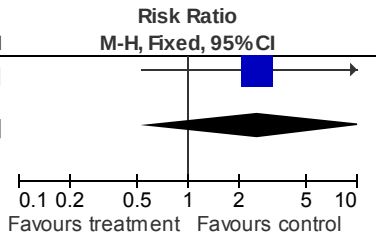
7.19 Leaving the study early: 2. Due to lack of efficacy (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
VOLAVKA2002	2	40	2	41	100.0%	1.02 [0.15, 6.93]
Total (95% CI)		**40**		**41**	**100.0%**	**1.02 [0.15, 6.93]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.03 (P = 0.98)						



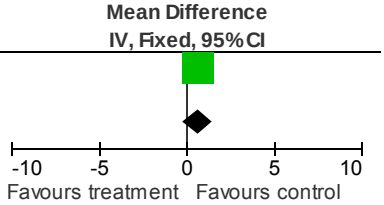
7.20 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
VOLAVKA2002	5	40	2	41	100.0%	2.56 [0.53, 12.45]
Total (95% CI)		**40**		**41**	**100.0%**	**2.56 [0.53, 12.45]**
Total events	5		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.17 (P = 0.24)						



7.21 AE: 1. Metabolic SEs - BMI (change from baseline) (medium-term)

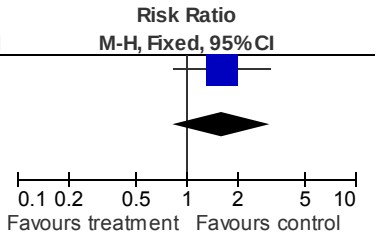
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	1.4	1.9	38	0.8	1.7	39	100.0%	0.60 [-0.21, 1.41]
Total (95% CI)			**38**			**39**	**100.0%**	**0.60 [-0.21, 1.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.46 (P = 0.14)								



7.22 AE: 1. Metabolic SEs - Weight gain (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bondolfi 1998	16	43	10	43	100.0%	1.60 [0.82, 3.12]
Total (95% CI)		**43**		**43**	**100.0%**	**1.60 [0.82, 3.12]**
Total events	16		10			

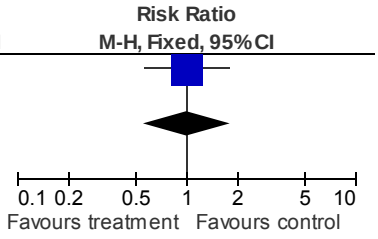
Heterogeneity: Not applicable
Test for overall effect: Z = 1.38 (P = 0.17)



7.23 AE: 1. Metabolic SEs - Weight gain (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chowdhury 1999	13	30	13	30	100.0%	1.00 [0.56, 1.78]
Total (95% CI)		**30**		**30**	**100.0%**	**1.00 [0.56, 1.78]**
Total events	13		13			

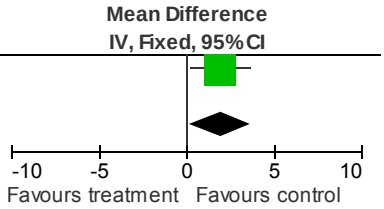
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



7.24 AE: 1. Metabolic SEs - Weight change from baseline (kg) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	4.2	4.7	38	2.3	2.8	39	100.0%	1.90 [0.17, 3.63]
Total (95% CI)			**38**			**39**	**100.0%**	**1.90 [0.17, 3.63]**

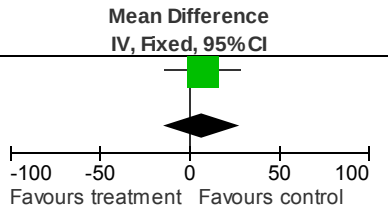
Heterogeneity: Not applicable
Test for overall effect: Z = 2.15 (P = 0.03)



7.25 AE: 1. Metabolic SEs - Cholestrol mg/dL (change from baseline) (medium-term)

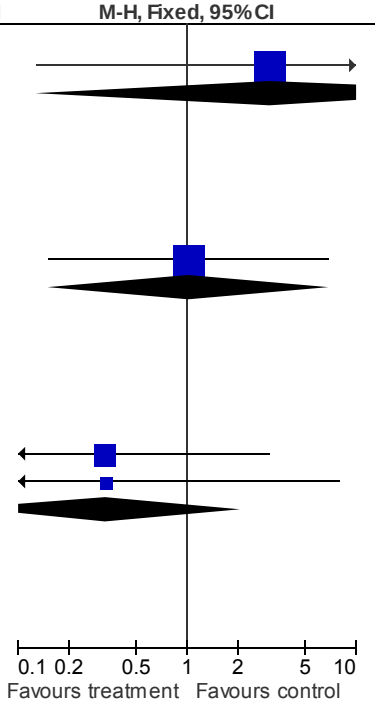
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	16.3	39.6	28	9.2	36.7	22	100.0%	7.10 [-14.12, 28.32]
Total (95% CI)			**28**			**22**	**100.0%**	**7.10 [-14.12, 28.32]**

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



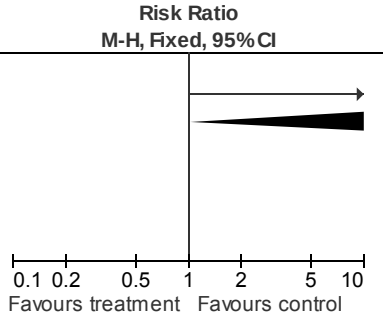
7.26 AE: 1. Metabolic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.26.1 Agranulocytosis						
VOLAVKA2002	1	40	0	41	100.0%	3.07 [0.13, 73.28]
Subtotal (95% CI)		**40**		**41**	**100.0%**	**3.07 [0.13, 73.28]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
7.26.2 Neutropenia						
VOLAVKA2002	2	40	2	41	100.0%	1.02 [0.15, 6.93]
Subtotal (95% CI)		**40**		**41**	**100.0%**	**1.02 [0.15, 6.93]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.03 (P = 0.98)						
7.26.3 White blood cell problems						
Anand 1998	1	138	3	135	66.9%	0.33 [0.03, 3.10]
Bondolfi 1998	0	43	1	43	33.1%	0.33 [0.01, 7.96]
Subtotal (95% CI)		**181**		**178**	**100.0%**	**0.33 [0.05, 2.06]**
Total events	1		4			
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.99); I² = 0%						
Test for overall effect: Z = 1.19 (P = 0.23)						



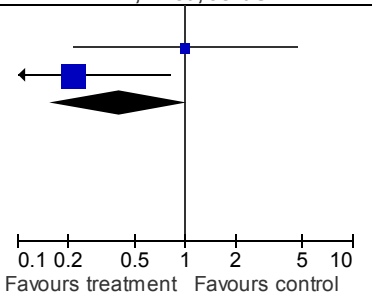
7.27 AE: 1. Metabolic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.27.1 Leucocytosis						
Chowdhury 1999	8	30	0	30	100.0%	17.00 [1.03, 281.91]
Subtotal (95% CI)		**30**		**30**	**100.0%**	**17.00 [1.03, 281.91]**
Total events	8		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.98 (P = 0.05)						



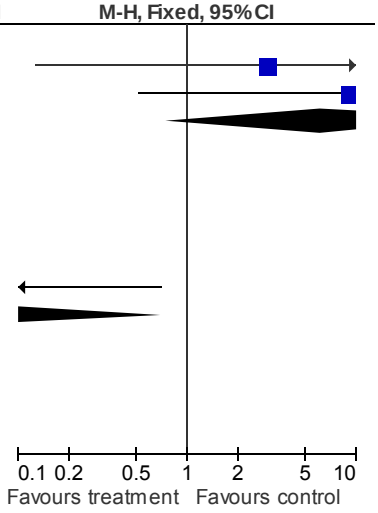
7.28 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.28.1 EPS						
Bondolfi 1998	3	43	3	43	23.7%	1.00 [0.21, 4.68]
Breier 1999	2	14	10	15	76.3%	0.21 [0.06, 0.81]
Subtotal (95% CI)		**57**		**58**	**100.0%**	**0.40 [0.16, 1.03]**
Total events	5		13			
Heterogeneity: Chi² = 2.20, df = 1 (P = 0.14); I² = 54%						
Test for overall effect: Z = 1.90 (P = 0.06)						



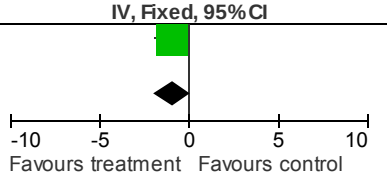
7.29 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.29.1 Seizures						
Chowdhury 1999	1	30	0	30	50.3%	3.00 [0.13, 70.83]
VOLAVKA2002	4	40	0	41	49.7%	9.22 [0.51, 165.87]
Subtotal (95% CI)		**70**		**71**	**100.0%**	**6.09 [0.75, 49.24]**
Total events	5		0			
Heterogeneity: Chi² = 0.27, df = 1 (P = 0.60); I² = 0%						
Test for overall effect: Z = 1.69 (P = 0.09)						
7.29.2 Akathisia						
Chowdhury 1999	0	30	11	30	100.0%	0.04 [0.00, 0.71]
Subtotal (95% CI)		**30**		**30**	**100.0%**	**0.04 [0.00, 0.71]**
Total events	0		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.20 (P = 0.03)						



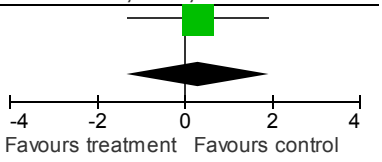
7.30 AE: 1. Neurologic SEs - Simpson-Angus Rating Scale (short-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Breier 1999	11.36	1.08	14	12.33	1.63	15	100.0%	-0.97 [-1.97, 0.03]
Total (95% CI)			**14**			**15**	**100.0%**	**-0.97 [-1.97, 0.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.90 (P = 0.06)								



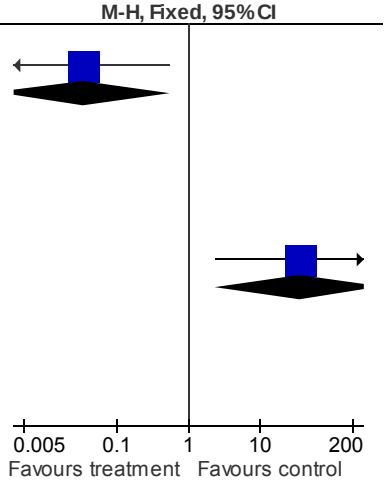
7.31 AE: 2. Neurologic SEs - Extrapyramidal Symptom Rating Scale (endpt mean) (medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	5.1	3.8	40	4.8	3.6	41	100.0%	0.30 [-1.31, 1.91]
Total (95% CI)			**40**			**41**	**100.0%**	**0.30 [-1.31, 1.91]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.36 (P = 0.72)								



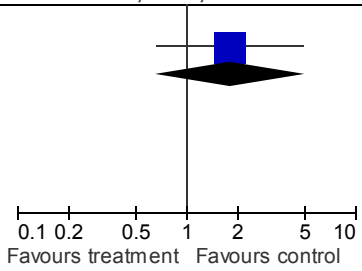
7.32 AE: 3. Autonomic SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.32.1 Dry mouth						
Chowdhury 1999	0	30	14	30	100.0%	0.03 [0.00, 0.55]
Subtotal (95% CI)		**30**		**30**	**100.0%**	**0.03 [0.00, 0.55]**
Total events	0		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.38 (P = 0.02)						
7.32.2 Too much (hypersalivation)						
Chowdhury 1999	18	30	0	30	100.0%	37.00 [2.33, 587.26]
Subtotal (95% CI)		**30**		**30**	**100.0%**	**37.00 [2.33, 587.26]**
Total events	18		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.56 (P = 0.01)						



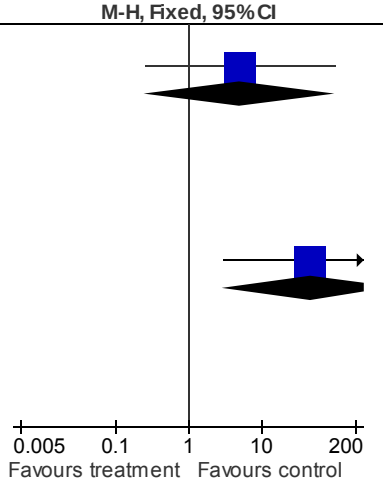
7.33 AE: 4. Cardiovascular SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.33.1 Orthostatic dizziness						
Bondolfi 1998	9	43	5	43	100.0%	1.80 [0.66, 4.93]
Subtotal (95% CI)		**43**		**43**	**100.0%**	**1.80 [0.66, 4.93]**
Total events	9		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.14 (P = 0.25)						



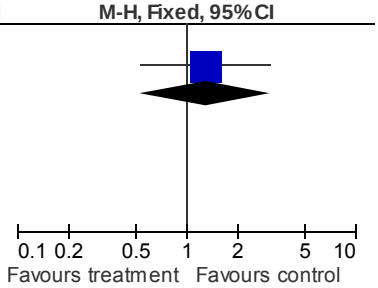
7.34 AE: 4. Cardiovascular SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.34.1 Hypertension						
VOLAVKA2002	2	40	0	41	100.0%	5.12 [0.25, 103.47]
Subtotal (95% CI)		**40**		**41**	**100.0%**	**5.12 [0.25, 103.47]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.07 (P = 0.29)						
7.34.2 Tachycardia						
Chowdhury 1999	23	30	0	30	100.0%	47.00 [2.99, 740.03]
Subtotal (95% CI)		**30**		**30**	**100.0%**	**47.00 [2.99, 740.03]**
Total events	23		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.74 (P = 0.006)						



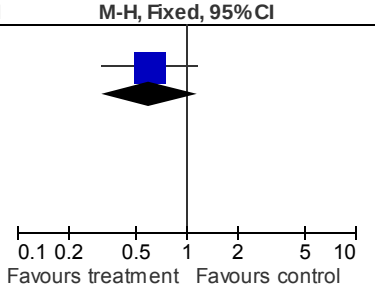
7.35 AE: 5. Gastrointestinal SEs (short-term)

	Treatment		Control			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**	**M-H, Fixed, 95% CI**
7.35.1 Nausea/vomiting							
Bondolfi 1998	9	43	7	43	100.0%	1.29 [0.53, 3.14]	
Subtotal (95% CI)		**43**		**43**	**100.0%**	**1.29 [0.53, 3.14]**	
Total events	9		7				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.55 (P = 0.58)							

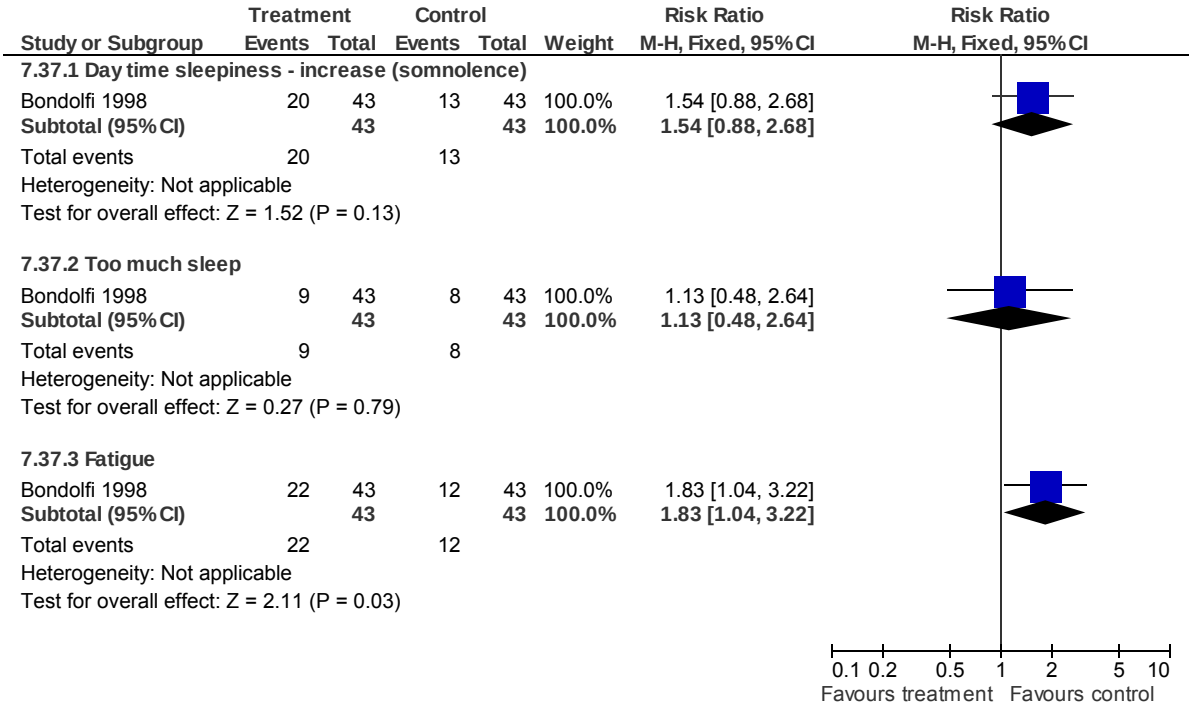


7.36 AE: 5. Gastrointestinal SEs (medium-term)

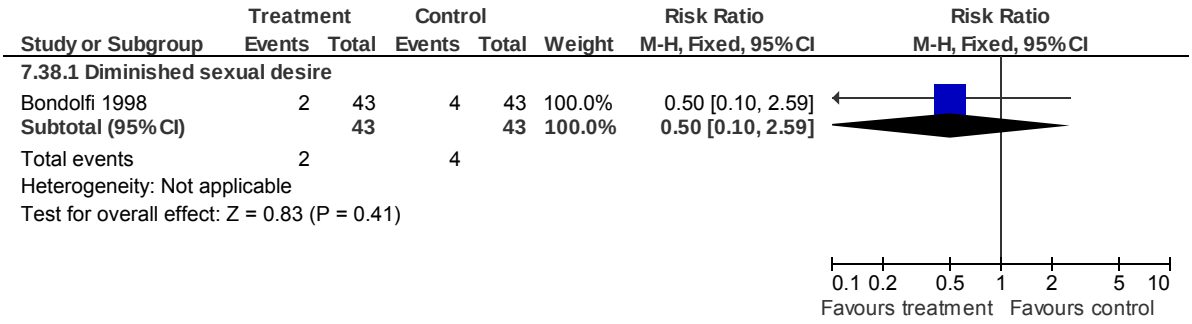
	Treatment		Control			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**	**M-H, Fixed, 95% CI**
7.36.1 Constipation							
Chowdhury 1999	9	30	15	30	100.0%	0.60 [0.31, 1.15]	
Subtotal (95% CI)		**30**		**30**	**100.0%**	**0.60 [0.31, 1.15]**	
Total events	9		15				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.53 (P = 0.13)							



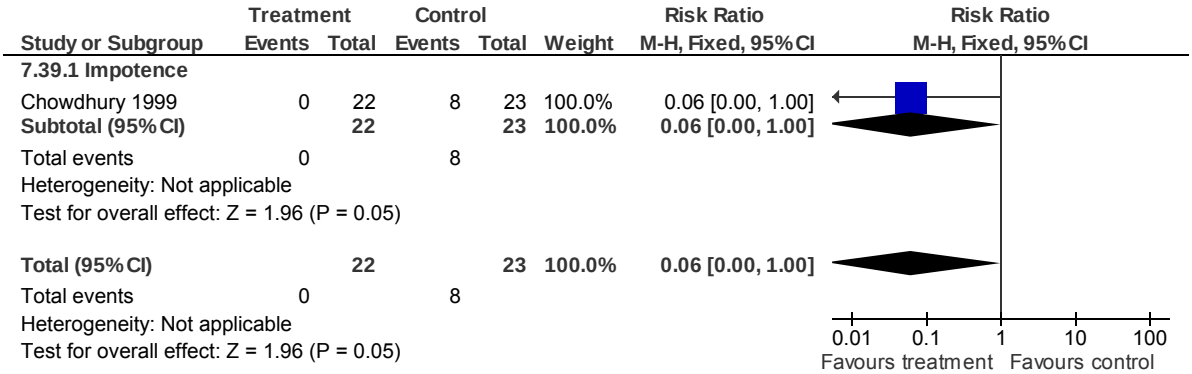
7.37 AE: 6. Sedation (short-term)



7.38 AE: 7. Sexual dysfunction (short-term)



7.39 AE: 7: Sexual dysfunction (medium-term)

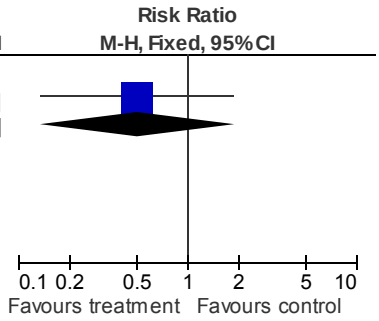


7.40 AE: 10. Other SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.40.1 Insomnia						
Bondolfi 1998	3	43	6	43	100.0%	0.50 [0.13, 1.87]
Subtotal (95% CI)		**43**		**43**	**100.0%**	**0.50 [0.13, 1.87]**
Total events	3		6			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.03 (P = 0.30)

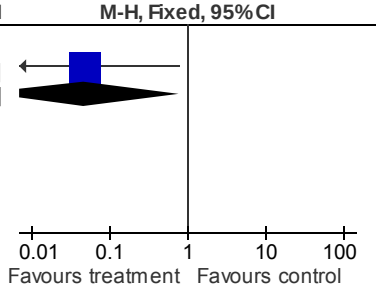


7.41 AE: 10. Other SEs (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.41.1 Insomnia						
Chowdhury 1999	0	30	10	30	100.0%	0.05 [0.00, 0.78]
Subtotal (95% CI)		**30**		**30**	**100.0%**	**0.05 [0.00, 0.78]**
Total events	0		10			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.14 (P = 0.03)



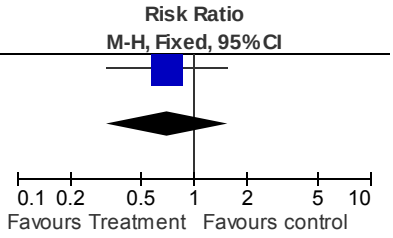
8 Clozapine vs. Zotepine (in people whose illness has not responded adequately to treatment)

8.1 Leaving the study early: 1. Any reason (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Meyer-Lindberg 1996	7	25	10	25	100.0%	0.70 [0.32, 1.54]
Total (95% CI)		**25**		**25**	**100.0%**	**0.70 [0.32, 1.54]**
Total events	7		10			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.88 (P = 0.38)



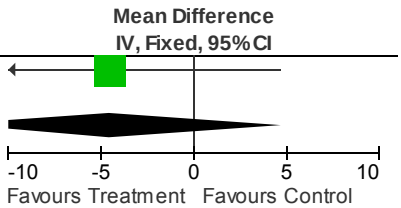
9 Olanzapine vs. Risperidone (in people whose illness has not responded adequately to treatment)

9.1 Mental state: 1. PANSS total (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	81.9	21.8	39	86.4	20.1	41	100.0%	-4.50 [-13.70, 4.70]
Total (95% CI)			**39**			**41**	**100.0%**	**-4.50 [-13.70, 4.70]**

Heterogeneity: Not applicable

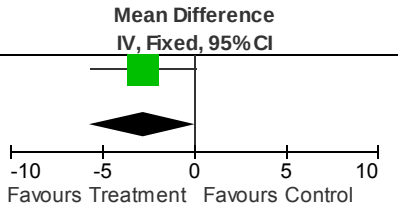
Test for overall effect: Z = 0.96 (P = 0.34)



9.2 Mental state: 2. PANSS negative score (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	20.1	6.3	39	22.9	6.9	41	100.0%	-2.80 [-5.69, 0.09]
Total (95% CI)			**39**			**41**	**100.0%**	**-2.80 [-5.69, 0.09]**

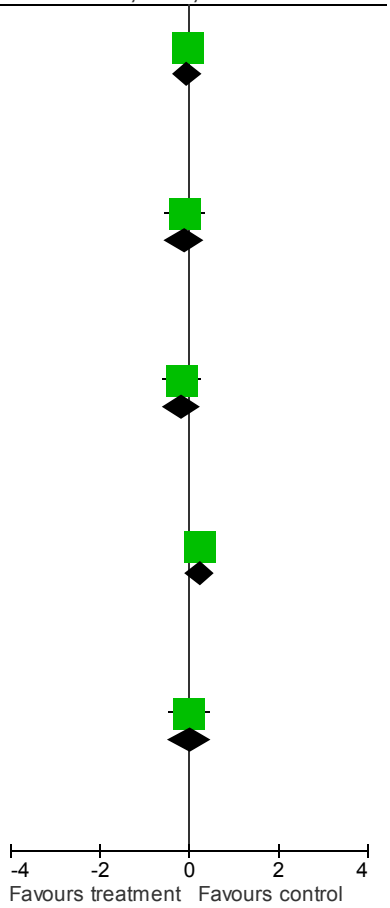
Heterogeneity: Not applicable
Test for overall effect: Z = 1.90 (P = 0.06)



9.3 Cognitive functioning: 1. Global & domain scores (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
9.3.1 Global score								
VOLAVKA2002	0.25	0.59	26	0.29	0.68	26	100.0%	-0.04 [-0.39, 0.31]
Subtotal (95% CI)			**26**			**26**	**100.0%**	**-0.04 [-0.39, 0.31]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.23 (P = 0.82)								
9.3.2 General executive & perceptual organisation								
VOLAVKA2002	0.22	0.82	26	0.33	0.83	26	100.0%	-0.11 [-0.56, 0.34]
Subtotal (95% CI)			**26**			**26**	**100.0%**	**-0.11 [-0.56, 0.34]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.48 (P = 0.63)								
9.3.3 Declarative verbal learning & memory								
VOLAVKA2002	0.2	0.65	26	0.37	0.9	26	100.0%	-0.17 [-0.60, 0.26]
Subtotal (95% CI)			**26**			**26**	**100.0%**	**-0.17 [-0.60, 0.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.78 (P = 0.43)								
9.3.4 Processing speed & attention								
VOLAVKA2002	0.55	0.62	26	0.31	0.62	26	100.0%	0.24 [-0.10, 0.58]
Subtotal (95% CI)			**26**			**26**	**100.0%**	**0.24 [-0.10, 0.58]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.40 (P = 0.16)								
9.3.5 Simple motor functioning								
VOLAVKA2002	0.19	0.75	26	0.19	0.96	26	100.0%	0.00 [-0.47, 0.47]
Subtotal (95% CI)			**26**			**26**	**100.0%**	**0.00 [-0.47, 0.47]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								

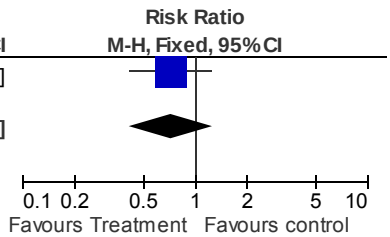
Test for subgroup differences: Chi² = 2.83, df = 4 (P = 0.59), I² = 0%



9.4 Leaving the study early: 1. Any reason (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
VOLAVKA2002	13	39	19	41	100.0%	0.72 [0.41, 1.25]
Total (95% CI)		**39**		**41**	**100.0%**	**0.72 [0.41, 1.25]**
Total events	13		19			

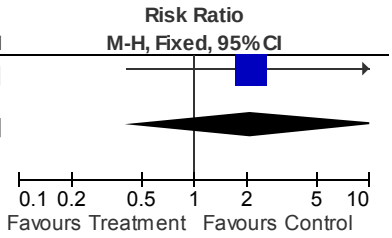
Heterogeneity: Not applicable
Test for overall effect: Z = 1.17 (P = 0.24)



9.5 Leaving the study early: 2. Due to lack of efficacy (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
VOLAVKA2002	4	39	2	41	100.0%	2.10 [0.41, 10.84]
Total (95% CI)		**39**		**41**	**100.0%**	**2.10 [0.41, 10.84]**
Total events	4		2			

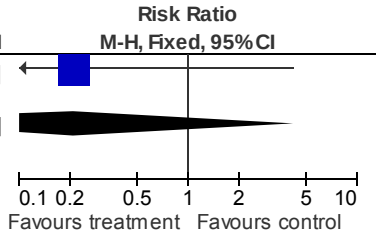
Heterogeneity: Not applicable
Test for overall effect: Z = 0.89 (P = 0.37)



9.6 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
VOLAVKA2002	0	39	2	41	100.0%	0.21 [0.01, 4.24]
Total (95% CI)		**39**		**41**	**100.0%**	**0.21 [0.01, 4.24]**
Total events	0		2			

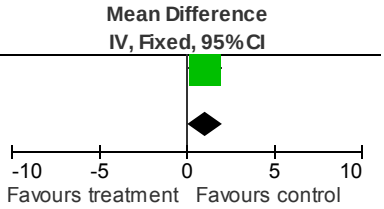
Heterogeneity: Not applicable
Test for overall effect: Z = 1.02 (P = 0.31)



9.7 AE: 1. Metabolic SEs - BMI (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	1.8	2.6	38	0.8	1.7	39	100.0%	1.00 [0.02, 1.98]
Total (95% CI)			**38**			**39**	**100.0%**	**1.00 [0.02, 1.98]**

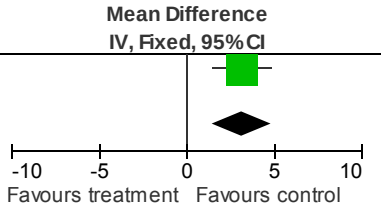
Heterogeneity: Not applicable
Test for overall effect: Z = 1.99 (P = 0.05)



9.8 AE: 1. Metabolic SEs - Weight change from baseline (kg) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	5.4	4.6	38	2.3	2.8	39	100.0%	3.10 [1.39, 4.81]
Total (95% CI)			**38**			**39**	**100.0%**	**3.10 [1.39, 4.81]**

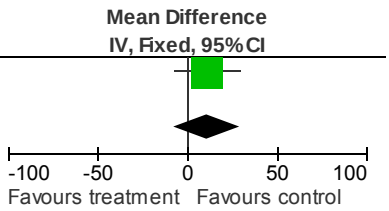
Heterogeneity: Not applicable
Test for overall effect: Z = 3.56 (P = 0.0004)



9.9 AE: 1. Metabolic SEs - Cholestrol mg/dL (change from baseline) (medium-term)

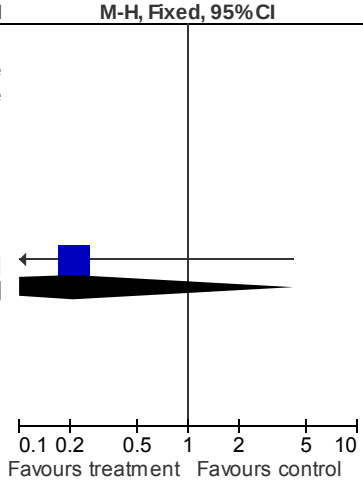
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
VOLAVKA2002	20.1	26.8	26	9.2	36.7	22	100.0%	10.90 [-7.57, 29.37]
Total (95% CI)			**26**			**22**	**100.0%**	**10.90 [-7.57, 29.37]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.16 (P = 0.25)



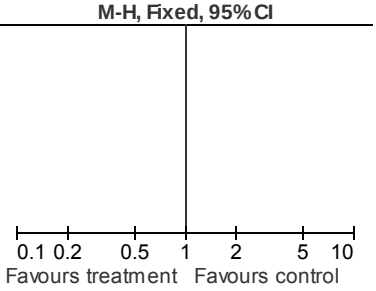
9.10 AE: 1. Metabolic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.10.1 Agranulocytosis						
VOLAVKA2002	0	39	0	41		Not estimable
Subtotal (95% CI)		**39**		**41**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
9.10.2 Neutropenia						
VOLAVKA2002	0	39	2	41	100.0%	0.21 [0.01, 4.24]
Subtotal (95% CI)		**39**		**41**	**100.0%**	**0.21 [0.01, 4.24]**
Total events	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						



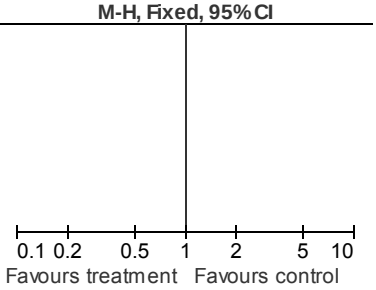
9.11 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.11.1 Seizures						
VOLAVKA2002	0	39	0	41		Not estimable
Subtotal (95% CI)		**39**		**41**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



9.12 AE: 4. Cardiovascular SEs (medium-term)

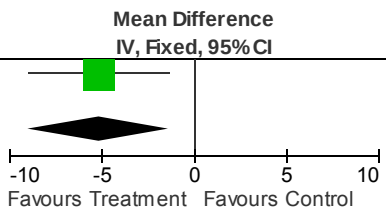
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
9.12.1 Hypertension						
VOLAVKA2002	0	39	0	41		Not estimable
Subtotal (95% CI)		**39**		**41**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



10 Olanzapine vs. Ziprasidone (in people whose illness has not responded adequately to treatment)

10.1 Mental state: 1. PANSS total (change from baseline) (medium-term)

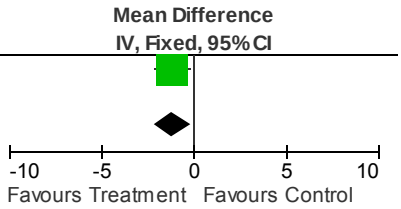
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006A	-13.5	19.35	202	-8.3	19.35	192	100.0%	-5.20 [-9.02, -1.38]
Total (95% CI)			**202**			**192**	**100.0%**	**-5.20 [-9.02, -1.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.67 (P = 0.008)								



10.2 Mental state: 2. Depression - Calgary Depression Scale for Schizophrenia (CDSS; change) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006A	-6	4.97	202	-4.8	4.97	192	100.0%	-1.20 [-2.18, -0.22]
Total (95% CI)			**202**			**192**	**100.0%**	**-1.20 [-2.18, -0.22]**

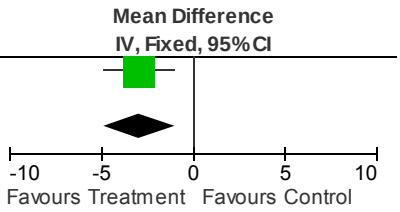
Heterogeneity: Not applicable
Test for overall effect: Z = 2.40 (P = 0.02)



10.3 Mental state: 2. Depression (MADRS; change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006A	-12.1	9.8	202	-9.15	9.8	192	100.0%	-2.95 [-4.89, -1.01]
Total (95% CI)			**202**			**192**	**100.0%**	**-2.95 [-4.89, -1.01]**

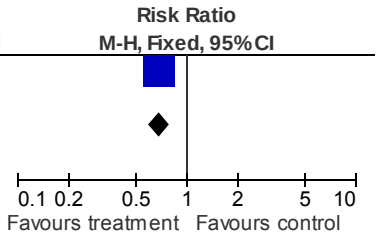
Heterogeneity: Not applicable
Test for overall effect: Z = 2.99 (P = 0.003)



10.4 Psychosocial functioning: 1. No response (< 5 point improvement on GAF) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KINON2006A	111	202	127	158	100.0%	0.68 [0.59, 0.79]
Total (95% CI)		**202**		**158**	**100.0%**	**0.68 [0.59, 0.79]**
Total events	111		127			

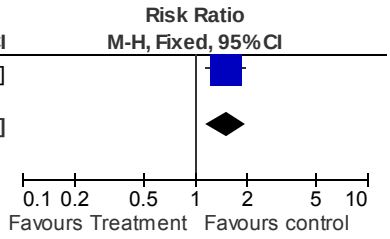
Heterogeneity: Not applicable
Test for overall effect: Z = 5.08 (P < 0.00001)



10.5 Leaving the study early: 1. Any reason (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KINON2006A	90	202	57	192	100.0%	1.50 [1.15, 1.96]
Total (95% CI)		**202**		**192**	**100.0%**	**1.50 [1.15, 1.96]**
Total events	90		57			

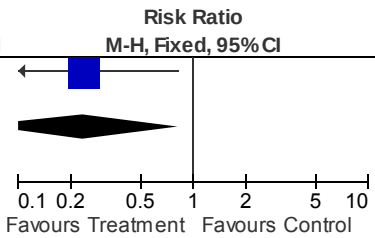
Heterogeneity: Not applicable
Test for overall effect: Z = 2.99 (P = 0.003)



10.6 Leaving the study early: 2. Due to lack of efficacy (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KINON2006A	3	202	12	192	100.0%	0.24 [0.07, 0.83]
Total (95% CI)		**202**		**192**	**100.0%**	**0.24 [0.07, 0.83]**
Total events	3		12			

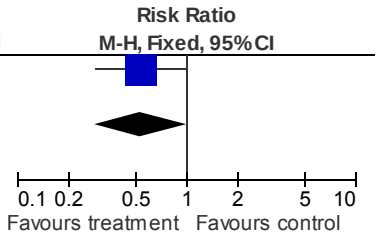
Heterogeneity: Not applicable
Test for overall effect: Z = 2.25 (P = 0.02)



10.7 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KINON2006A	14	202	25	192	100.0%	0.53 [0.29, 0.99]
Total (95% CI)		**202**		**192**	**100.0%**	**0.53 [0.29, 0.99]**
Total events	14		25			

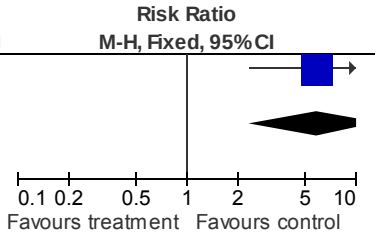
Heterogeneity: Not applicable
Test for overall effect: Z = 1.98 (P = 0.05)



10.8 AE: 1. Metabolic SEs - Weight gain (>=7% from baseline) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KINON2006A	31	202	5	192	100.0%	5.89 [2.34, 14.84]
Total (95% CI)		**202**		**192**	**100.0%**	**5.89 [2.34, 14.84]**
Total events	31		5			

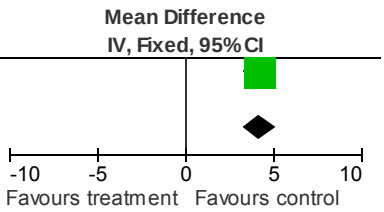
Heterogeneity: Not applicable
Test for overall effect: Z = 3.76 (P = 0.0002)



10.9 AE: 1. Metabolic SEs - Weight change from baseline (kg) (medium-term)

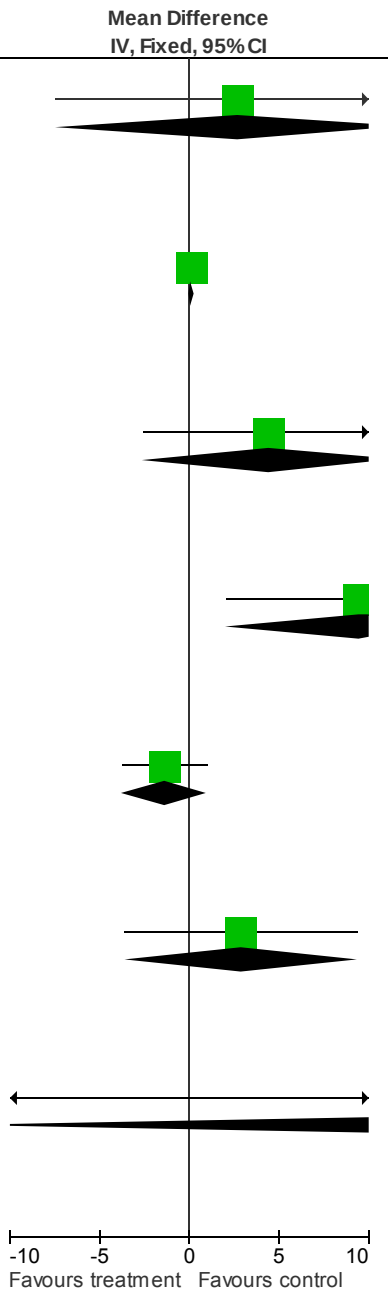
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006A	2.53	4.91	194	-1.65	4.16	182	100.0%	4.18 [3.26, 5.10]
Total (95% CI)			**194**			**182**	**100.0%**	**4.18 [3.26, 5.10]**

Heterogeneity: Not applicable
Test for overall effect: Z = 8.92 (P < 0.00001)



10.10 AE: 1. Metabolic SEs - Various (change from baseline) (medium-term)

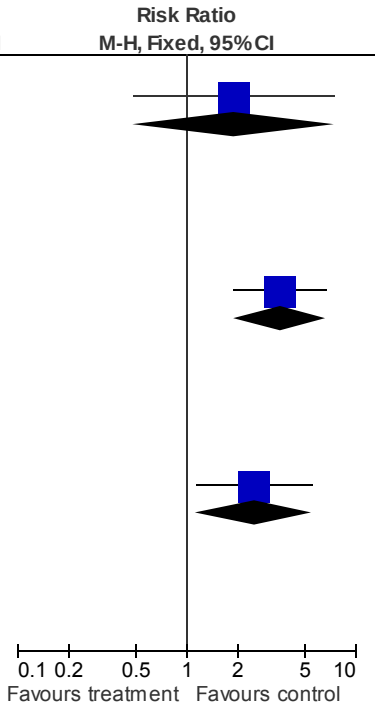
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
10.10.1 Fasting glucose (mg/dL)								
KINON2006A	2.85	37.84	117	0.14	36.25	90	100.0%	2.71 [-7.44, 12.86]
Subtotal (95% CI)			**117**			**90**	**100.0%**	**2.71 [-7.44, 12.86]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.52 (P = 0.60)								
10.10.2 HgbA1c (%)								
KINON2006A	0.06	0.76	169	-0.06	0.76	146	100.0%	0.12 [-0.05, 0.29]
Subtotal (95% CI)			**169**			**146**	**100.0%**	**0.12 [-0.05, 0.29]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.40 (P = 0.16)								
10.10.3 Prolactin (ng/dL)								
KINON2006A	-2.74	27.79	168	-7.19	34.51	145	100.0%	4.45 [-2.57, 11.47]
Subtotal (95% CI)			**168**			**145**	**100.0%**	**4.45 [-2.57, 11.47]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.24 (P = 0.21)								
10.10.4 Cholestrol (mg/dL)								
KINON2006A	-2.27	33.92	172	-11.7	33.18	146	100.0%	9.43 [2.04, 16.82]
Subtotal (95% CI)			**172**			**146**	**100.0%**	**9.43 [2.04, 16.82]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.50 (P = 0.01)								
10.10.5 HDL cholesterol-dextran precipitate (mg/dL)								
KINON2006A	-1.87	11.74	167	-0.5	9.63	144	100.0%	-1.37 [-3.75, 1.01]
Subtotal (95% CI)			**167**			**144**	**100.0%**	**-1.37 [-3.75, 1.01]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.13 (P = 0.26)								
10.10.6 LDL cholesterol (mg/dL)								
KINON2006A	-4.41	26.59	156	-7.3	28.79	129	100.0%	2.89 [-3.60, 9.38]
Subtotal (95% CI)			**156**			**129**	**100.0%**	**2.89 [-3.60, 9.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.87 (P = 0.38)								
10.10.7 Triglycerides(mg/dL)								
KINON2006A	13.59	192.7	172	-9.47	130.1	146	100.0%	23.06 [-12.64, 58.76]
Subtotal (95% CI)			**172**			**146**	**100.0%**	**23.06 [-12.64, 58.76]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.27 (P = 0.21)								



Test for subgroup differences: Chi² = 11.60, df = 6 (P = 0.07), I² = 48.3%

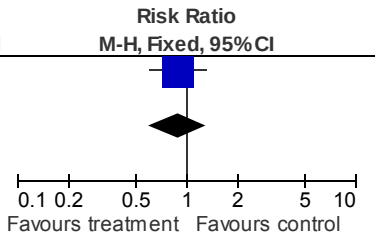
10.11 AE: 1. Metabolic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.11.1 Abnormal vital signs or QTc interval						
KINON2006A	6	202	3	192	100.0%	1.90 [0.48, 7.49]
Subtotal (95% CI)		**202**		**192**	**100.0%**	**1.90 [0.48, 7.49]**
Total events	6		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.92 (P = 0.36)						
10.11.2 Weight gain						
KINON2006A	41	202	11	192	100.0%	3.54 [1.88, 6.69]
Subtotal (95% CI)		**202**		**192**	**100.0%**	**3.54 [1.88, 6.69]**
Total events	41		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.90 (P < 0.0001)						
10.11.3 Increased appetite						
KINON2006A	21	202	8	192	100.0%	2.50 [1.13, 5.50]
Subtotal (95% CI)		**202**		**192**	**100.0%**	**2.50 [1.13, 5.50]**
Total events	21		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.27 (P = 0.02)						



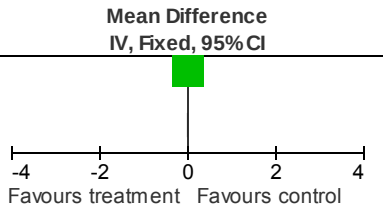
10.12 AE: 2. Neurologic SEs - Use of anticholinergic medication (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KINON2006A	38	202	41	192	100.0%	0.88 [0.59, 1.31]
Total (95% CI)		**202**		**192**	**100.0%**	**0.88 [0.59, 1.31]**
Total events	38		41			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.63 (P = 0.53)						



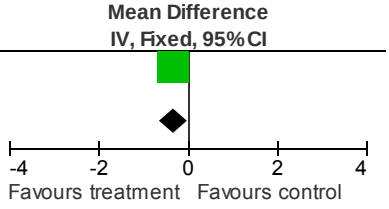
10.13 AE: 2. Neurologic SEs - Barnes Akathisia Scale (BAS; change) (medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006A	-0.12	0.01	202	-0.12	0.01	192	100.0%	0.00 [-0.00, 0.00]
Total (95% CI)			**202**			**192**	**100.0%**	**0.00 [-0.00, 0.00]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								



10.14 AE: 2. Neurologic SEs - Simpson-Angus Scale (SAS; change) (medium-term)

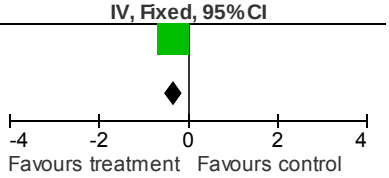
Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006A	-0.37	1.61	202	-0.03	1.61	192	100.0%	-0.34 [-0.66, -0.02]
Total (95% CI)			**202**			**192**	**100.0%**	**-0.34 [-0.66, -0.02]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.10 (P = 0.04)								



10.15 AE: 2. Neurologic SEs - Abnormal Involuntary Movement Scale (AIMS; change) (medium-term)

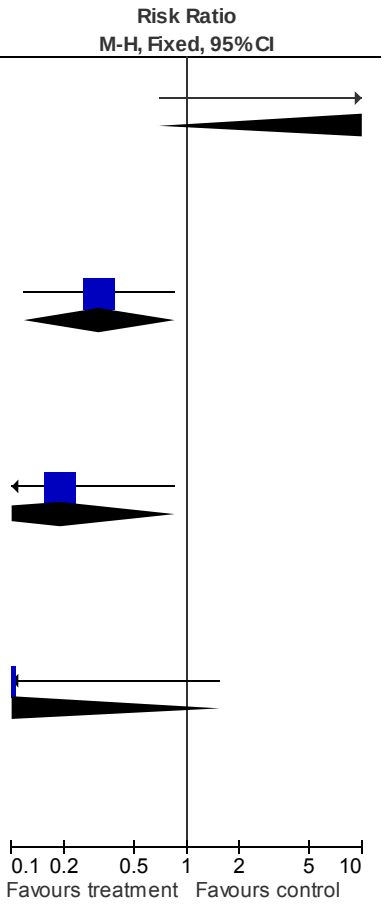
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006A	-0.68	1.02	202	-0.34	1.02	192	100.0%	-0.34 [-0.54, -0.14]
Total (95% CI)			**202**			**192**	**100.0%**	**-0.34 [-0.54, -0.14]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.31 (P = 0.0009)



10.16 AE: 10. Other SEs (medium-term)

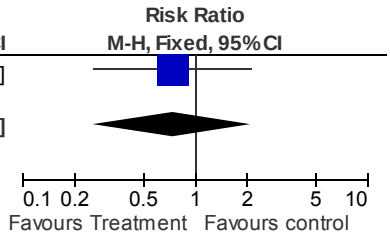
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
10.16.1 Peripheral edema						
KINON2006A	6	202	0	192	100.0%	12.36 [0.70, 217.92]
Subtotal (95% CI)		**202**		**192**	**100.0%**	**12.36 [0.70, 217.92]**
Total events	6		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.72 (P = 0.09)						
10.16.2 Psychosis						
KINON2006A	5	202	15	192	100.0%	0.32 [0.12, 0.85]
Subtotal (95% CI)		**202**		**192**	**100.0%**	**0.32 [0.12, 0.85]**
Total events	5		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.27 (P = 0.02)						
10.16.3 Decreased appetite						
KINON2006A	2	202	10	192	100.0%	0.19 [0.04, 0.86]
Subtotal (95% CI)		**202**		**192**	**100.0%**	**0.19 [0.04, 0.86]**
Total events	2		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.16 (P = 0.03)						
10.16.4 Influenza & migraine						
KINON2006A	0	202	5	192	100.0%	0.09 [0.00, 1.55]
Subtotal (95% CI)		**202**		**192**	**100.0%**	**0.09 [0.00, 1.55]**
Total events	0		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.66 (P = 0.10)						



11 Risperidone vs. Quetiapine (in people whose illness has not responded adequately to treatment)

11.1 Leaving the study early: 1. Any reason (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
CONLEY2005	4	13	5	12	100.0%	0.74 [0.26, 2.12]
Total (95% CI)		**13**		**12**	**100.0%**	**0.74 [0.26, 2.12]**
Total events	4		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.56 (P = 0.57)						

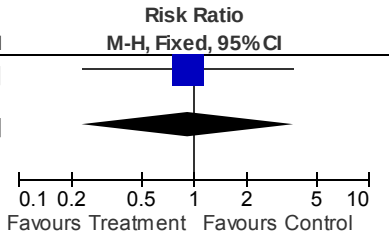


11.2 Leaving the study early: 2. Due to lack of efficacy (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
CONLEY2005	3	13	3	12	100.0%	0.92 [0.23, 3.72]
Total (95% CI)		**13**		**12**	**100.0%**	**0.92 [0.23, 3.72]**
Total events	3		3			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.11 (P = 0.91)



11.3 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
CONLEY2005	0	13	2	12	100.0%	0.19 [0.01, 3.52]
Total (95% CI)		**13**		**12**	**100.0%**	**0.19 [0.01, 3.52]**
Total events	0		2			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.12 (P = 0.26)

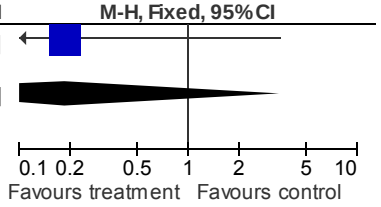


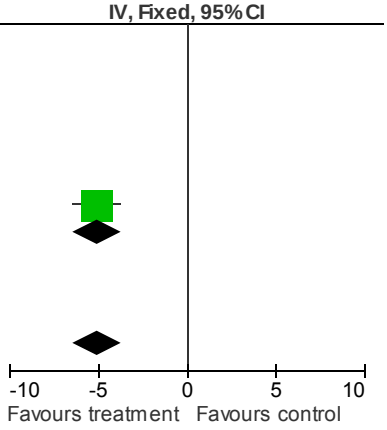
Table 7: Studies included in the review of antipsychotic medication for people with persistent negative symptoms

Treatment	versus Comparator							
	AMI	**FLUP**	**FLUPHEN**	**HAL**	**OLZ**	**QUE**	**RIS**	**ZIP**
AMI			Boyer 1990 [6weeks, N=62]	Speller 1997 [52weeks, N=60]	Lecrubier 1999 [LECRUBIER2006] (OLZ) [26weeks, N=140]			Study 128-305 [OLIE2006] [12weeks, N=123]
OLZ	Lecrubier 1999 [LECRUBIER2006] [26weeks, N=140]			LINDENMAYER2007 [12weeks, N=35]		KINON2006B [26weeks, N=346] SIROTA2006 [12weeks, N=40]		
QUE				Murasaki 1999 [8weeks, N=197]	KINON2006B [26weeks, N=346] SIROTA2006 [12weeks, N=40]		RIEDEL2005 [12weeks, N=44]	
RIS		RUHRMANN2007 [25weeks, N=153]				RIEDEL2005 [12weeks, N=44]		

1 Amisulpride versus FGA (phase: persistent negative symptoms)

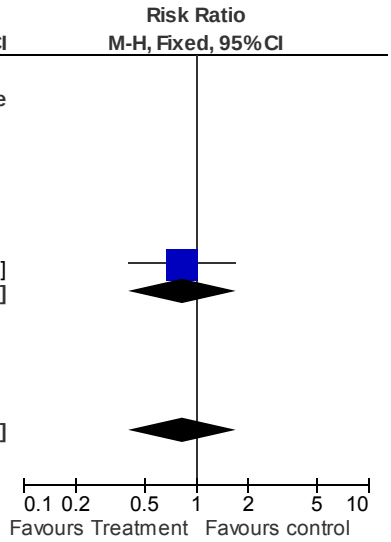
1.1 Mental state: 1. BPRS total endpoint scores (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 vs HAL								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
1.1.2 vs other FGA								
Boyer 1990	37.2	3.1	32	42.3	2.2	25	100.0%	-5.10 [-6.48, -3.72]
Subtotal (95% CI)			**32**			**25**	**100.0%**	**-5.10 [-6.48, -3.72]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 7.26 (P < 0.00001)								
Total (95% CI)			**32**			**25**	**100.0%**	**-5.10 [-6.48, -3.72]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 7.26 (P < 0.00001)								
Test for subgroup differences: Not applicable								



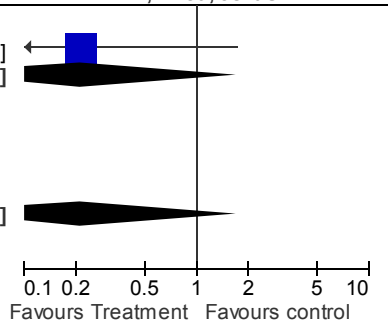
1.2 Leaving the study early: 1. Any reason (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 vs HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.2.2 vs other FGA						
Boyer 1990	10	34	10	28	100.0%	0.82 [0.40, 1.69]
Subtotal (95% CI)		**34**		**28**	**100.0%**	**0.82 [0.40, 1.69]**
Total events	10		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.53 (P = 0.60)						
Total (95% CI)		**34**		**28**	**100.0%**	**0.82 [0.40, 1.69]**
Total events	10		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.53 (P = 0.60)						



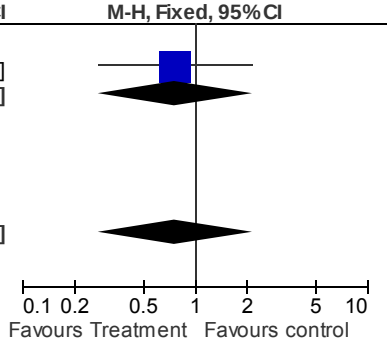
1.3 Leaving the study early: 1. Any reason (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 vs HAL						
Speller 1997	1	29	5	31	100.0%	0.21 [0.03, 1.72]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.21 [0.03, 1.72]**
Total events	1		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.45 (P = 0.15)						
Total (95% CI)		**29**		**31**	**100.0%**	**0.21 [0.03, 1.72]**
Total events	1		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.45 (P = 0.15)						



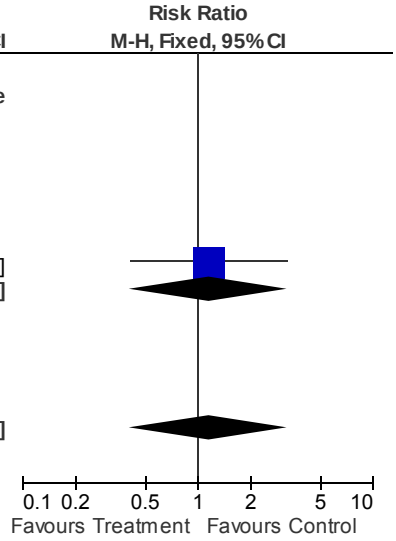
1.4 Leaving the study early: 1. Any reason (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 vs HAL						
Speller 1997	5	29	7	31	100.0%	0.76 [0.27, 2.14]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.76 [0.27, 2.14]**
Total events	5		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.51 (P = 0.61)						
Total (95% CI)		**29**		**31**	**100.0%**	**0.76 [0.27, 2.14]**
Total events	5		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.51 (P = 0.61)						



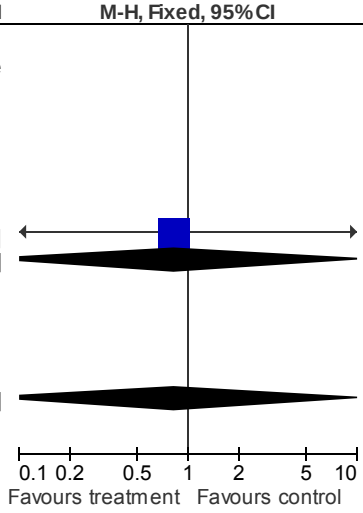
1.5 Leaving the study early: 2. Due to lack of efficacy (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.5.1 vs HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.5.2 vs other FGA						
Boyer 1990	7	34	5	28	100.0%	1.15 [0.41, 3.24]
Subtotal (95% CI)		**34**		**28**	**100.0%**	**1.15 [0.41, 3.24]**
Total events	7		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.27 (P = 0.79)						
Total (95% CI)		**34**		**28**	**100.0%**	**1.15 [0.41, 3.24]**
Total events	7		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.27 (P = 0.79)						



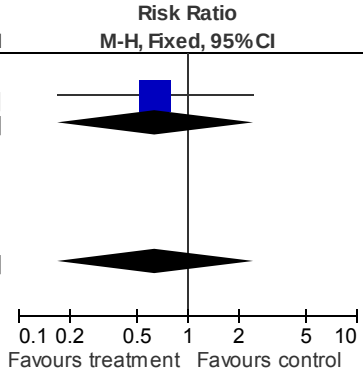
1.6 Leaving the study early: 3: Adverse event (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 vs HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.6.2 vs other FGA						
Boyer 1990	1	34	1	28	100.0%	0.82 [0.05, 12.58]
Subtotal (95% CI)		**34**		**28**	**100.0%**	**0.82 [0.05, 12.58]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.14 (P = 0.89)						
Total (95% CI)		**34**		**28**	**100.0%**	**0.82 [0.05, 12.58]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.14 (P = 0.89)						



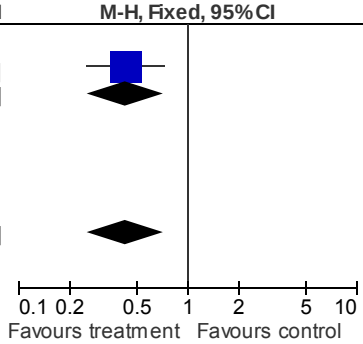
1.7 Leaving the study early: 3: Adverse event (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.7.1 vs HAL						
Speller 1997	3	29	5	31	100.0%	0.64 [0.17, 2.45]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.64 [0.17, 2.45]**
Total events	3		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.65 (P = 0.52)						
Total (95% CI)		**29**		**31**	**100.0%**	**0.64 [0.17, 2.45]**
Total events	3		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.65 (P = 0.52)						



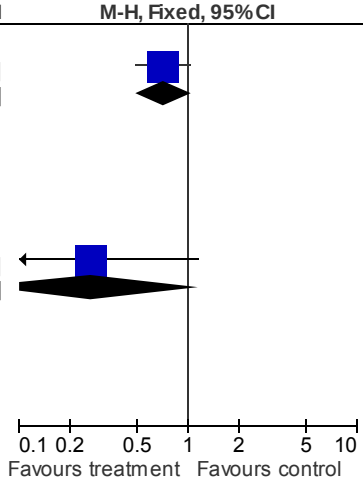
1.8 AE: 2. Neurologic SEs - Use of anticholinergic medication (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.8.1 vs HAL						
Speller 1997	10	29	25	31	100.0%	0.43 [0.25, 0.73]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.43 [0.25, 0.73]**
Total events	10		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.14 (P = 0.002)						
Total (95% CI)		**29**		**31**	**100.0%**	**0.43 [0.25, 0.73]**
Total events	10		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.14 (P = 0.002)						



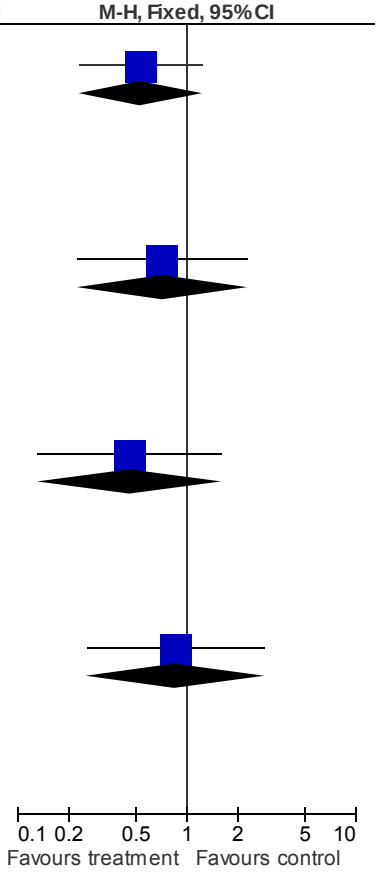
1.9 AE: 2. Neurologic SEs (treatment-emergent) (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.9.1 vs HAL: parkinsonian side-effects						
Speller 1997	16	29	24	31	100.0%	0.71 [0.49, 1.04]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.71 [0.49, 1.04]**
Total events	16		24			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.75 (P = 0.08)						
1.9.2 vs HAL: akathisia						
Speller 1997	2	29	8	31	100.0%	0.27 [0.06, 1.16]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.27 [0.06, 1.16]**
Total events	2		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.77 (P = 0.08)						



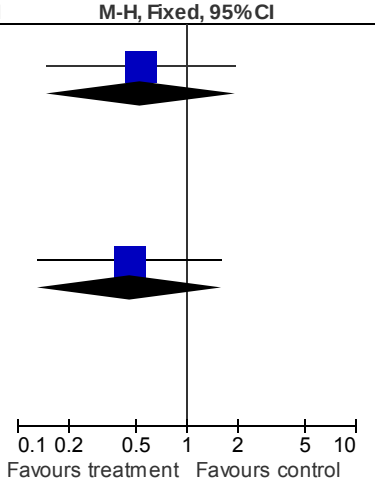
1.10 AE: 3. Autonomic SEs (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.10.1 vs HAL: dry mouth						
Speller 1997	6	29	12	31	100.0%	0.53 [0.23, 1.24]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.53 [0.23, 1.24]**
Total events	6		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.46 (P = 0.14)						
1.10.2 vs HAL: blurred vision						
Speller 1997	4	29	6	31	100.0%	0.71 [0.22, 2.27]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.71 [0.22, 2.27]**
Total events	4		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.57 (P = 0.57)						
1.10.3 vs HAL: nasal stuffiness						
Speller 1997	3	29	7	31	100.0%	0.46 [0.13, 1.61]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.46 [0.13, 1.61]**
Total events	3		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.22 (P = 0.22)						
1.10.4 vs HAL: sweating						
Speller 1997	4	29	5	31	100.0%	0.86 [0.25, 2.88]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.86 [0.25, 2.88]**
Total events	4		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.25 (P = 0.80)						



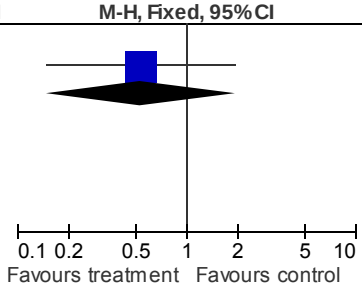
1.11 AE: 4. Cardiovascular SEs (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.11.1 vs HAL: dizziness						
Speller 1997	3	29	6	31	100.0%	0.53 [0.15, 1.94]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.53 [0.15, 1.94]**
Total events	3		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						
1.11.2 vs HAL: palpitations						
Speller 1997	3	29	7	31	100.0%	0.46 [0.13, 1.61]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.46 [0.13, 1.61]**
Total events	3		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.22 (P = 0.22)						



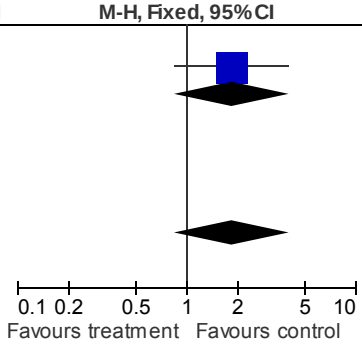
1.12 AE: 5. Gastrointestinal SEs (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.12.1 vs HAL: constipation						
Speller 1997	3	29	6	31	100.0%	0.53 [0.15, 1.94]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.53 [0.15, 1.94]**
Total events	3		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						



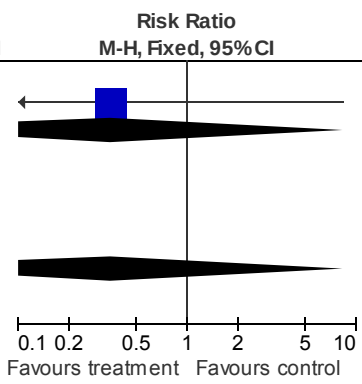
1.13 AE: 6. Sedation (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.13.1 vs HAL: Drowsiness						
Speller 1997	12	29	7	31	100.0%	1.83 [0.84, 4.01]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**1.83 [0.84, 4.01]**
Total events	12		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.52 (P = 0.13)						
Total (95% CI)		**29**		**31**	**100.0%**	**1.83 [0.84, 4.01]**
Total events	12		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.52 (P = 0.13)						



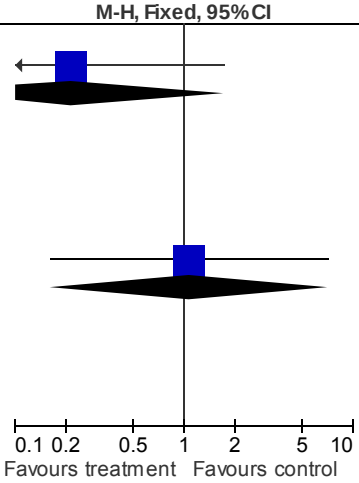
1.14 AE: 8. Menstrual problems (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.14.1 vs HAL: galactorrhoea/ menstrual disturbance						
Speller 1997	0	29	1	31	100.0%	0.36 [0.02, 8.39]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.36 [0.02, 8.39]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.64 (P = 0.52)						
Total (95% CI)		**29**		**31**	**100.0%**	**0.36 [0.02, 8.39]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.64 (P = 0.52)						



1.15 AE: 9. Other SEs (long-term)

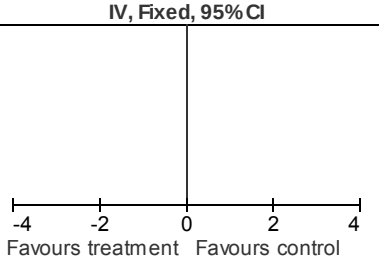
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.15.1 vs HAL: insomnia						
Speller 1997	1	29	5	31	100.0%	0.21 [0.03, 1.72]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.21 [0.03, 1.72]**
Total events	1		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.45 (P = 0.15)						
1.15.2 vs HAL: urinary retention						
Speller 1997	2	29	2	31	100.0%	1.07 [0.16, 7.10]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**1.07 [0.16, 7.10]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.07 (P = 0.94)						



2 Quetiapine versus FGA (phase: persistent negative symptoms)

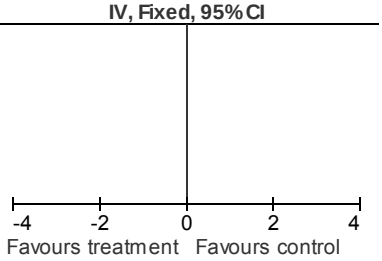
2.1 Mental state: 1. PANSS total (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.1.1 vs HAL								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Total (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



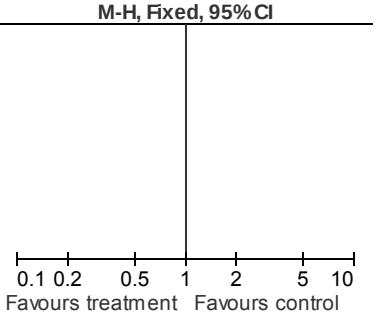
2.2 Mental state: 1. BPRS total (change from baseline) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.2.1 vs HAL								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Total (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



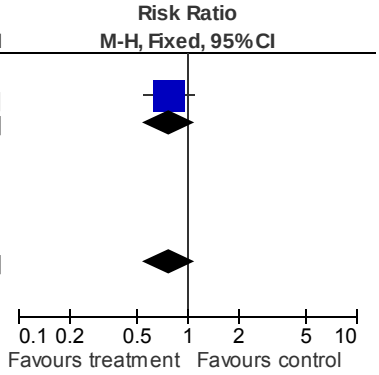
2.3 Mental state: 2. Non-response (<30% improvement on PANSS or CGI-I >2) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.3.1 vs HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



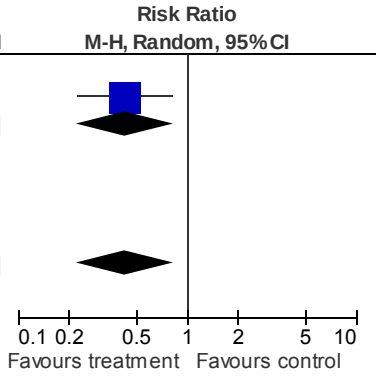
2.4 Leaving the study early: 1. Any reason (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.4.1 vs HAL						
Murasaki 1999	34	100	43	97	100.0%	0.77 [0.54, 1.09]
Subtotal (95% CI)		**100**		**97**	**100.0%**	**0.77 [0.54, 1.09]**
Total events	34		43			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.47 (P = 0.14)						
Total (95% CI)		**100**		**97**	**100.0%**	**0.77 [0.54, 1.09]**
Total events	34		43			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.47 (P = 0.14)						



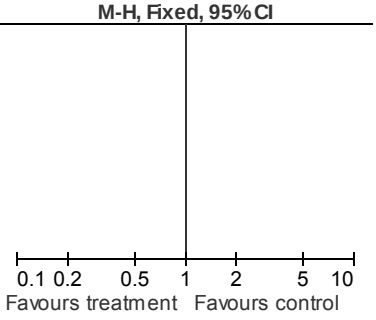
2.5 Leaving the study early: 2. Due to lack of efficacy (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.5.1 vs HAL						
Murasaki 1999	11	100	25	97	100.0%	0.43 [0.22, 0.82]
Subtotal (95% CI)		**100**		**97**	**100.0%**	**0.43 [0.22, 0.82]**
Total events	11		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.56 (P = 0.01)						
Total (95% CI)		**100**		**97**	**100.0%**	**0.43 [0.22, 0.82]**
Total events	11		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.56 (P = 0.01)						



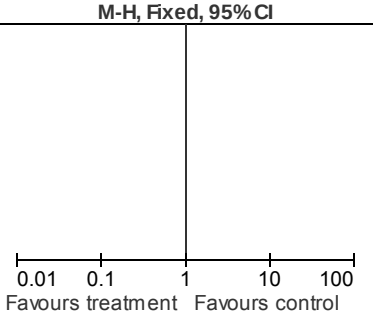
2.6 Leaving the study early: 3: Adverse event (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.6.1 vs HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



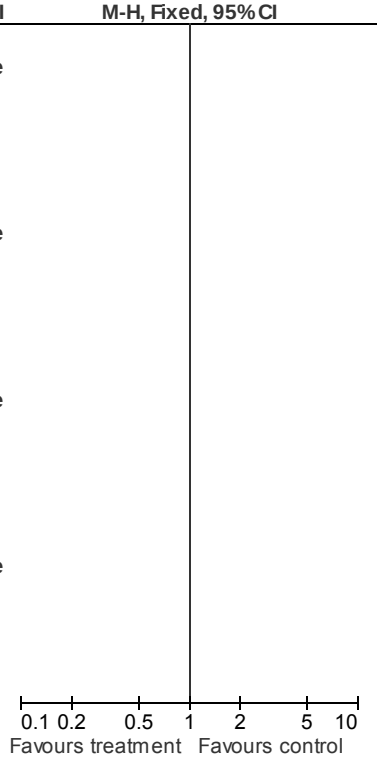
2.7 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.7.1 vs HAL						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



2.8 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

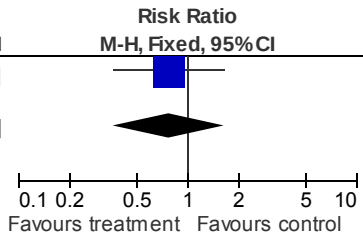
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.8.1 vs other FGA: any EPS-related						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
2.8.2 vs other FGA: extrapyramidal syndrome						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
2.8.3 vs other FGA: akathisia						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
2.8.4 vs other FGA: agitation						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



3 Risperidone versus FGA (flupentixol) (phase: persistent negative symptoms)

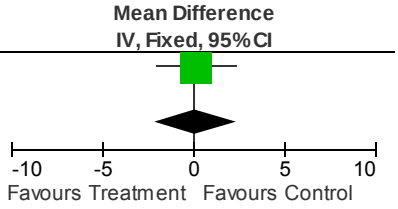
3.1 Global state: 1. Relapse (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RUHRMANN2007	10	72	13	72	100.0%	0.77 [0.36, 1.64]
Total (95% CI)		**72**		**72**	**100.0%**	**0.77 [0.36, 1.64]**
Total events	10		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						



3.2 Mental state: 1. PANSS negative score (endpoint, high=poor) (medium-term)

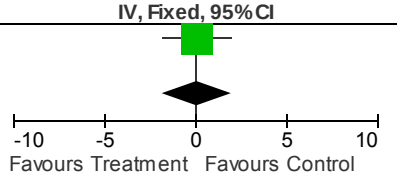
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
RUHRMANN2007	15.4	6.89	72	15.31	6.62	72	100.0%	0.09 [-2.12, 2.30]
Total (95% CI)			**72**			**72**	**100.0%**	**0.09 [-2.12, 2.30]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.08 (P = 0.94)								



3.3 Mental state: 2. PANSS depressive/anxiety component (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
RUHRMANN2007	13.76	6.06	72	13.71	5.62	72	100.0%	0.05 [-1.86, 1.96]
Total (95% CI)			**72**			**72**	**100.0%**	**0.05 [-1.86, 1.96]**

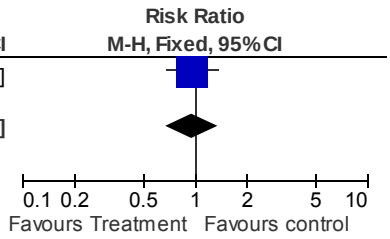
Heterogeneity: Not applicable
Test for overall effect: Z = 0.05 (P = 0.96)



3.4 Leaving the study early: 1. Any reason (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RUHRMANN2007	34	77	35	76	100.0%	0.96 [0.68, 1.36]
Total (95% CI)		**77**		**76**	**100.0%**	**0.96 [0.68, 1.36]**
Total events	34		35			

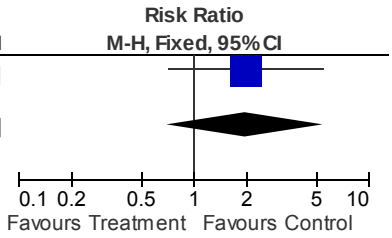
Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)



3.5 Leaving the study early: 2. Due to lack of efficacy (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RUHRMANN2007	10	77	5	76	100.0%	1.97 [0.71, 5.51]
Total (95% CI)		**77**		**76**	**100.0%**	**1.97 [0.71, 5.51]**
Total events	10		5			

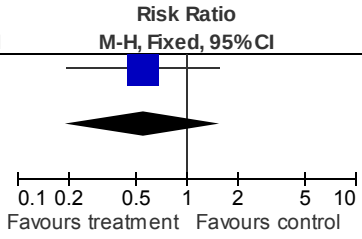
Heterogeneity: Not applicable
Test for overall effect: Z = 1.30 (P = 0.19)



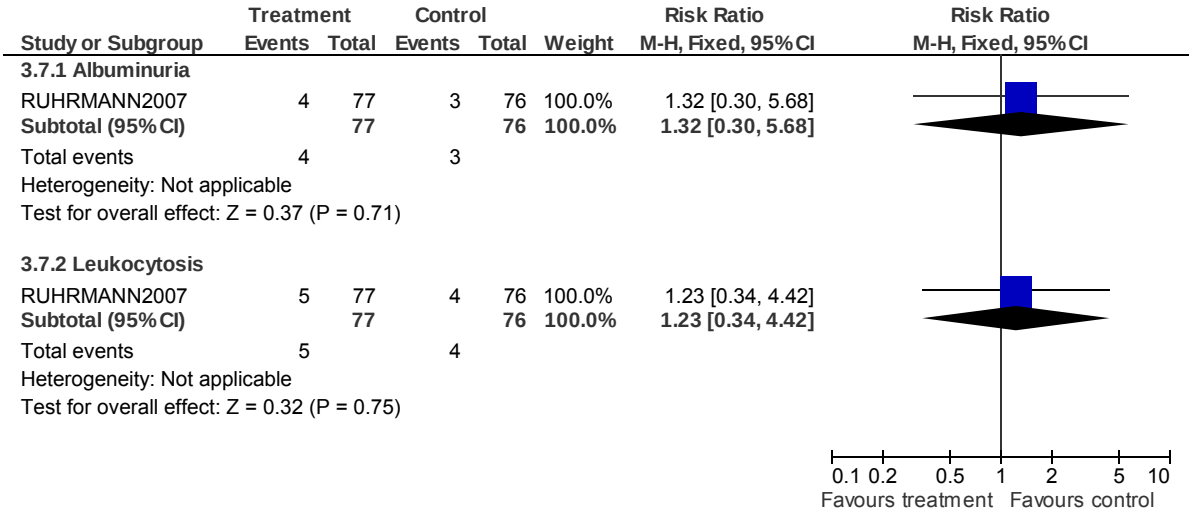
3.6 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RUHRMANN2007	5	77	9	76	100.0%	0.55 [0.19, 1.56]
Total (95% CI)		**77**		**76**	**100.0%**	**0.55 [0.19, 1.56]**
Total events	5		9			

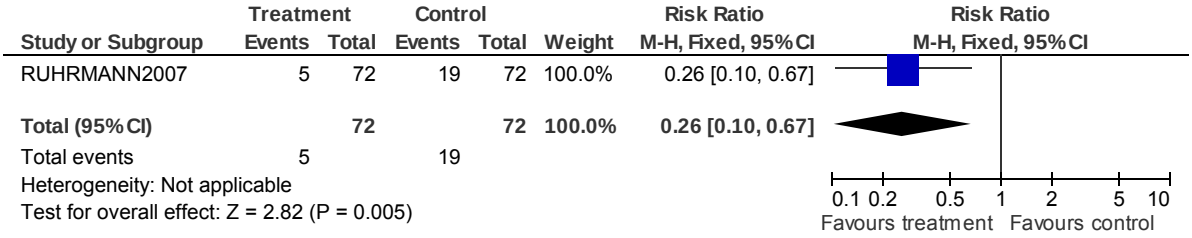
Heterogeneity: Not applicable
Test for overall effect: Z = 1.13 (P = 0.26)



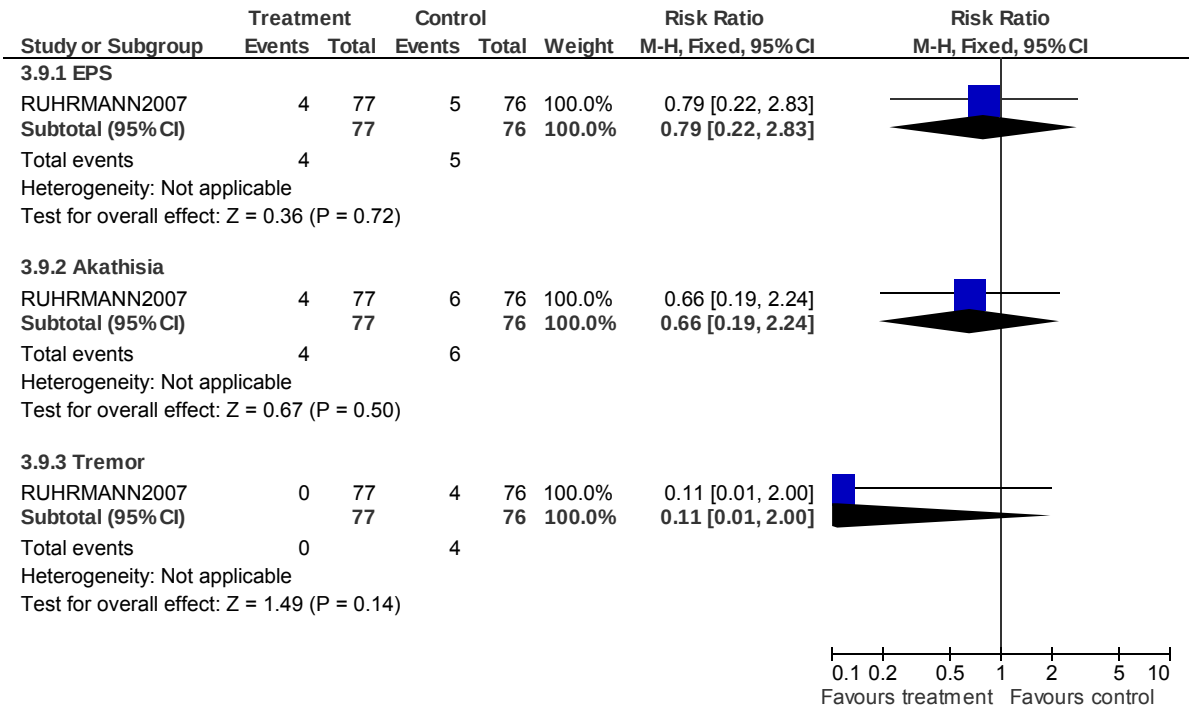
3.7 AE: 1. Metabolic SEs (treatment-emergent) (short-term)



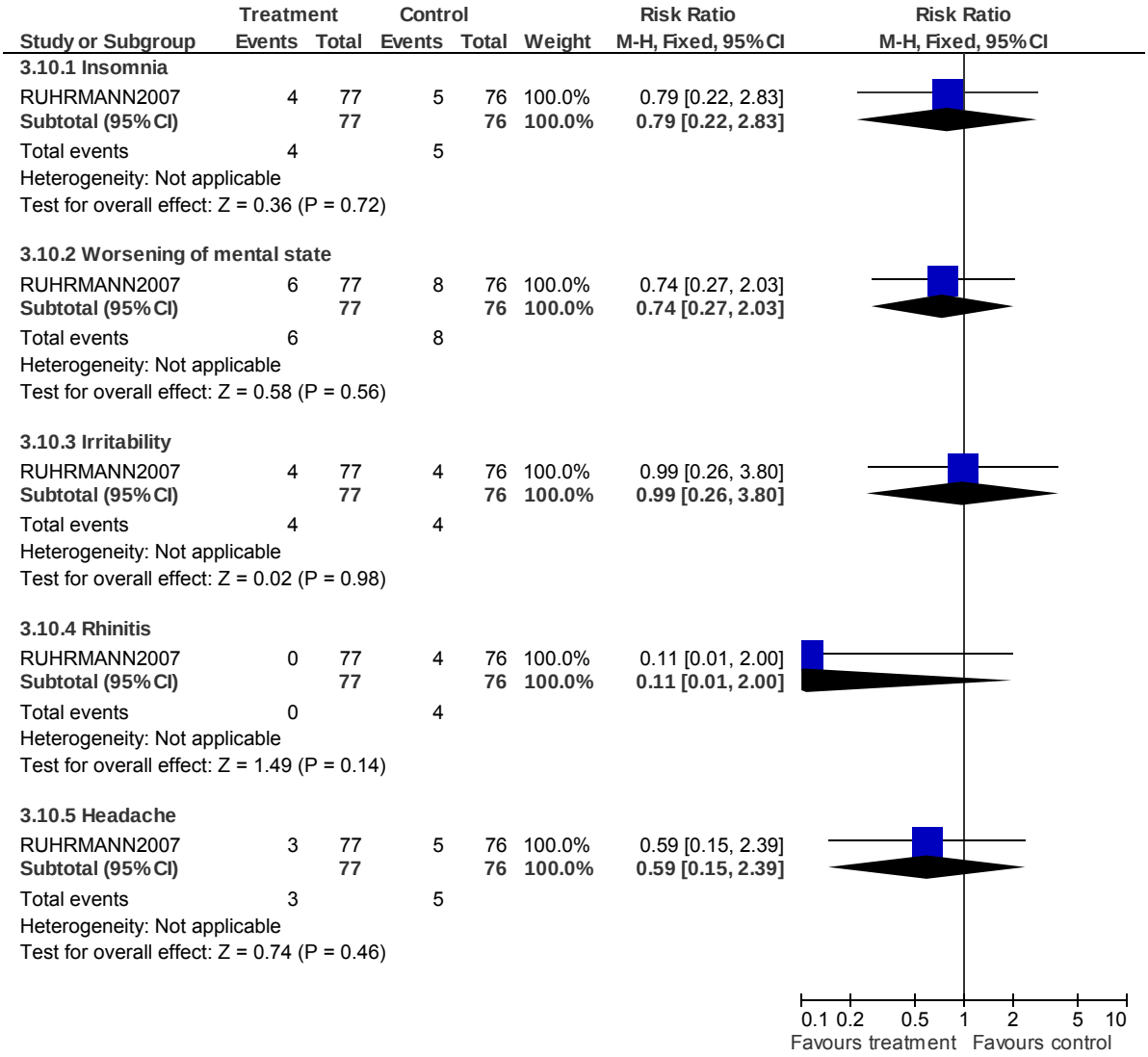
3.8 AE: 2. Neurologic SEs - Use of anticholinergic medication (medium-term)



3.9 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)



3.10 AE: 10. Other SEs (medium-term)



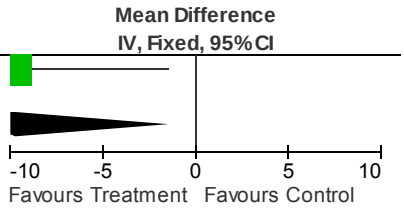
4 Olanzapine versus Amisulpride (phase: persistent negative symptoms)

4.1 Global state: 1. Relapse (medium-term)

4.2 Mental state: 1. PANSS total (change from baseline) (Medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lecrubier 1999	-23.4	24.4	70	-13.7	25.4	70	100.0%	-9.70 [-17.95, -1.45]
Total (95% CI)			**70**			**70**	**100.0%**	**-9.70 [-17.95, -1.45]**

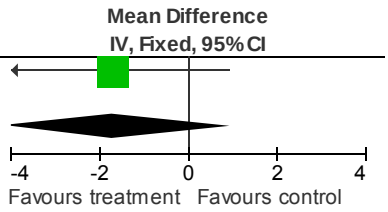
Heterogeneity: Not applicable
Test for overall effect: Z = 2.30 (P = 0.02)



4.3 Mental state: 2. PANSS negative score (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lecrubier 1999	-8.7	8	70	-7	7.8	70	100.0%	-1.70 [-4.32, 0.92]
Total (95% CI)			**70**			**70**	**100.0%**	**-1.70 [-4.32, 0.92]**

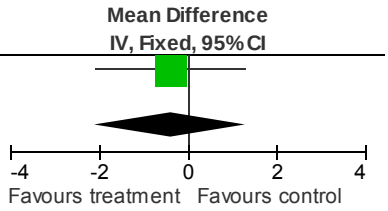
Heterogeneity: Not applicable
Test for overall effect: Z = 1.27 (P = 0.20)



4.4 Mental state: 2. SANS summary score (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lecrubier 1999	-4.7	5.3	70	-4.3	4.9	70	100.0%	-0.40 [-2.09, 1.29]
Total (95% CI)			**70**			**70**	**100.0%**	**-0.40 [-2.09, 1.29]**

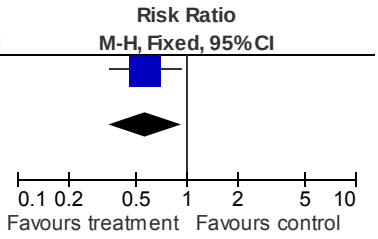
Heterogeneity: Not applicable
Test for overall effect: Z = 0.46 (P = 0.64)



4.5 Mental state: 3. Non-response (<20% improvement in SANS & <10% improvement in PANSS) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lecrubier 1999	17	70	30	70	100.0%	0.57 [0.35, 0.93]
Total (95% CI)		**70**		**70**	**100.0%**	**0.57 [0.35, 0.93]**
Total events	17		30			

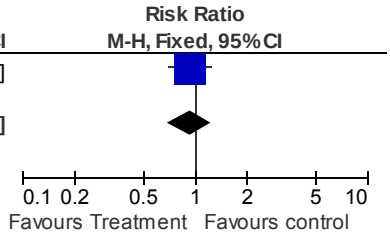
Heterogeneity: Not applicable
Test for overall effect: Z = 2.25 (P = 0.02)



4.6 Leaving the study early: 1. Any reason (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lecrubier 1999	38	70	41	70	100.0%	0.93 [0.69, 1.24]
Total (95% CI)		**70**		**70**	**100.0%**	**0.93 [0.69, 1.24]**
Total events	38		41			

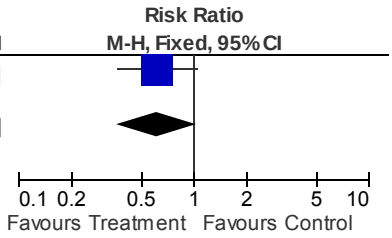
Heterogeneity: Not applicable
Test for overall effect: Z = 0.51 (P = 0.61)



4.7 Leaving the study early: 2. Due to lack of efficacy (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lecrubier 1999	16	70	26	70	100.0%	0.62 [0.36, 1.04]
Total (95% CI)		**70**		**70**	**100.0%**	**0.62 [0.36, 1.04]**
Total events	16		26			

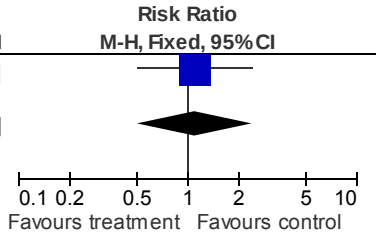
Heterogeneity: Not applicable
Test for overall effect: Z = 1.80 (P = 0.07)



4.8 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lecrubier 1999	11	70	10	70	100.0%	1.10 [0.50, 2.42]
Total (95% CI)		**70**		**70**	**100.0%**	**1.10 [0.50, 2.42]**
Total events	11		10			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)



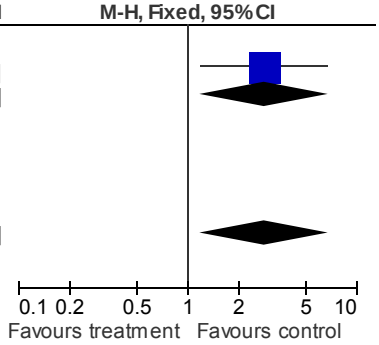
4.9 AE: 1. Metabolic SEs - Weight gain

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.9.1 Treatment-emergent weight gain						
Lecrubier 1999	17	70	6	70	100.0%	2.83 [1.19, 6.76]
Subtotal (95% CI)		**70**		**70**	**100.0%**	**2.83 [1.19, 6.76]**
Total events	17		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.35 (P = 0.02)

Total (95% CI)		**70**		**70**	**100.0%**	**2.83 [1.19, 6.76]**
Total events	17		6			

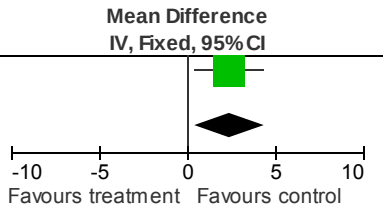
Heterogeneity: Not applicable
Test for overall effect: Z = 2.35 (P = 0.02)



4.10 AE: 1. Metabolic SEs - Weight change from baseline (kg) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Lecrubier 1999	2.56	5.88	70	0.21	5.99	70	100.0%	2.35 [0.38, 4.32]
Total (95% CI)			**70**			**70**	**100.0%**	**2.35 [0.38, 4.32]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.34 (P = 0.02)

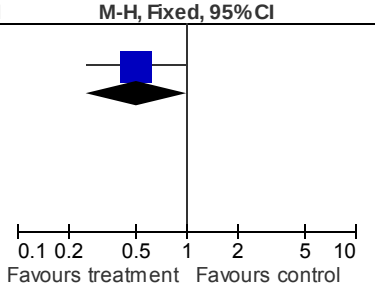


4.11 AE: 2. Neurologic SEs (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.11.1 Agitation						
Lecrubier 1999	10	70	20	70	100.0%	0.50 [0.25, 0.99]
Subtotal (95% CI)		**70**		**70**	**100.0%**	**0.50 [0.25, 0.99]**
Total events	10		20			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.99 (P = 0.05)



4.12 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.12.1 EPS						
Lecrubier 1999	14	70	18	70	100.0%	0.78 [0.42, 1.44]
Subtotal (95% CI)		**70**		**70**	**100.0%**	**0.78 [0.42, 1.44]**
Total events	14		18			

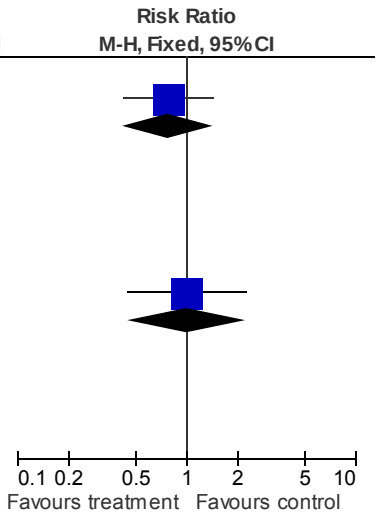
Heterogeneity: Not applicable

Test for overall effect: Z = 0.80 (P = 0.42)

4.12.2 Akathisia						
Lecrubier 1999	10	70	10	70	100.0%	1.00 [0.44, 2.25]
Subtotal (95% CI)		**70**		**70**	**100.0%**	**1.00 [0.44, 2.25]**
Total events	10		10			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)



4.13 AE: 5. Gastrointestinal SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.13.1 Nausea						
Lecrubier 1999	2	70	4	70	100.0%	0.50 [0.09, 2.64]
Subtotal (95% CI)		**70**		**70**	**100.0%**	**0.50 [0.09, 2.64]**
Total events	2		4			

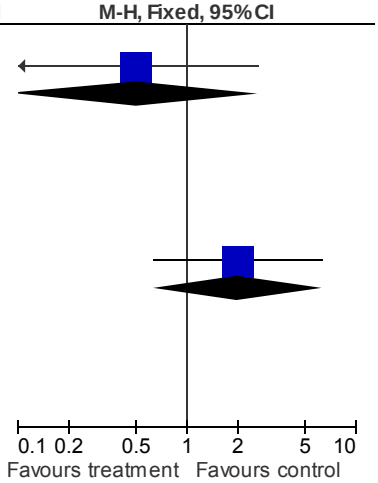
Heterogeneity: Not applicable

Test for overall effect: Z = 0.82 (P = 0.41)

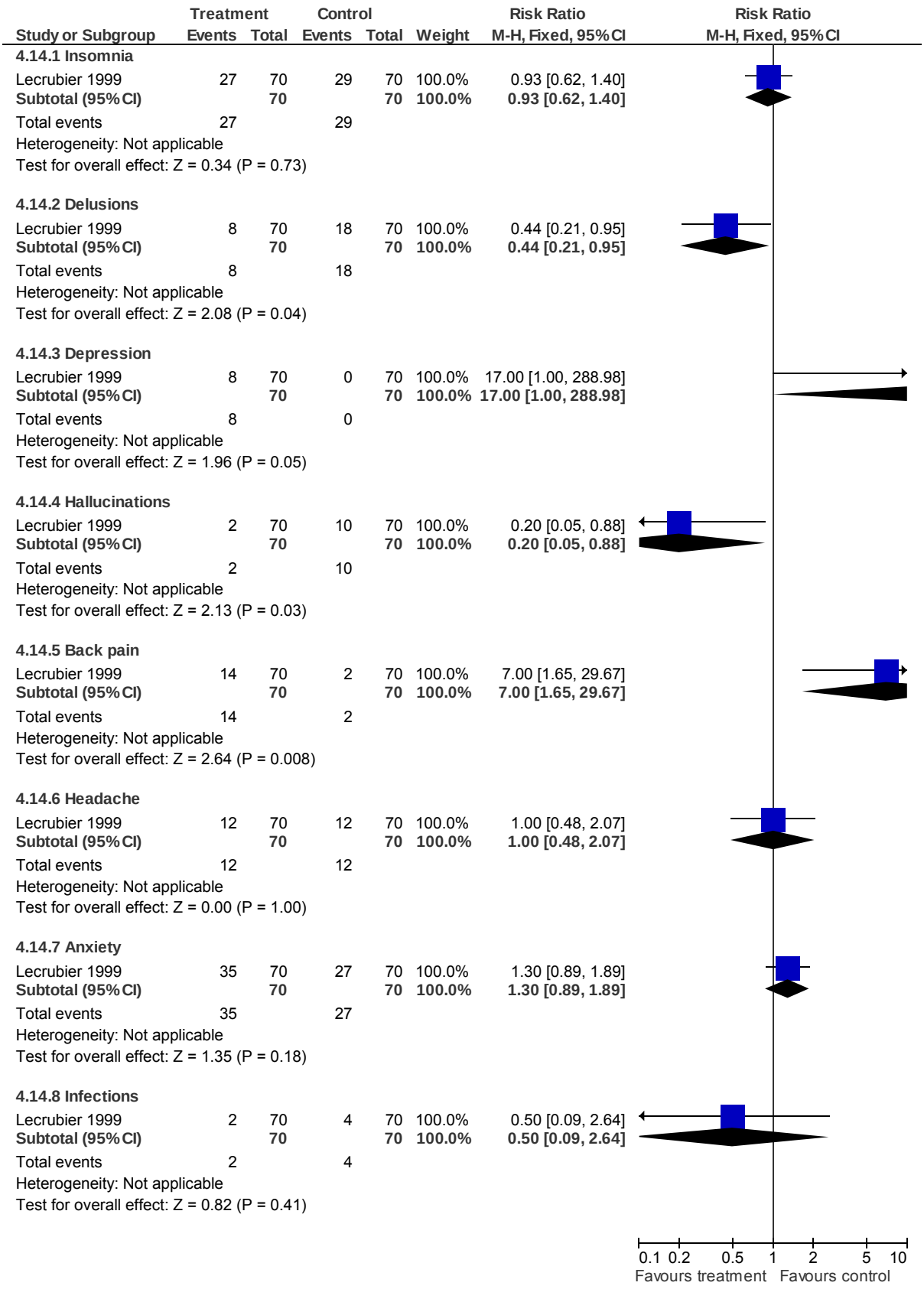
4.13.2 Vomiting						
Lecrubier 1999	8	70	4	70	100.0%	2.00 [0.63, 6.34]
Subtotal (95% CI)		**70**		**70**	**100.0%**	**2.00 [0.63, 6.34]**
Total events	8		4			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.18 (P = 0.24)



4.14 AE: 10. Other SEs (medium-term)

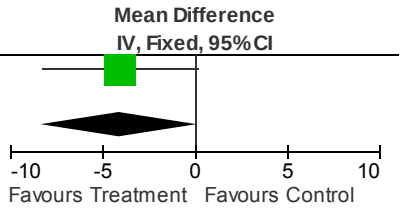


5 Olanzapine versus Quetiapine (phase: persistent negative symptoms)

5.1 Mental state: 1. PANSS total (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006B	-11.3	18.3	166	-7.2	21.2	169	100.0%	-4.10 [-8.34, 0.14]
Total (95% CI)			**166**			**169**	**100.0%**	**-4.10 [-8.34, 0.14]**

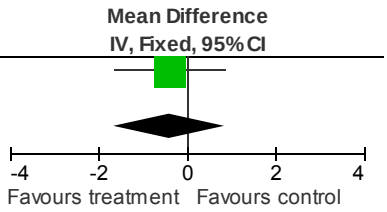
Heterogeneity: Not applicable
Test for overall effect: Z = 1.90 (P = 0.06)



5.2 Mental state: 2. PANSS negative score (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006B	-4	5.8	167	-3.6	6	169	100.0%	-0.40 [-1.66, 0.86]
Total (95% CI)			**167**			**169**	**100.0%**	**-0.40 [-1.66, 0.86]**

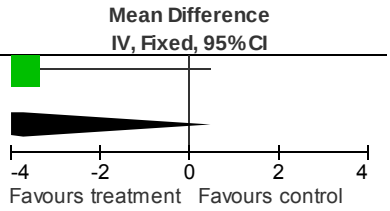
Heterogeneity: Not applicable
Test for overall effect: Z = 0.62 (P = 0.53)



5.3 Mental state: 2. SANS total (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006B	-12	18.9	166	-8.3	20.1	169	100.0%	-3.70 [-7.88, 0.48]
Total (95% CI)			**166**			**169**	**100.0%**	**-3.70 [-7.88, 0.48]**

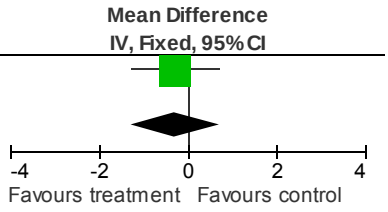
Heterogeneity: Not applicable
Test for overall effect: Z = 1.74 (P = 0.08)



5.4 Mental state: 3. Calgary Depression Scale (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006B	-1.7	4.5	165	-1.4	4.8	169	100.0%	-0.30 [-1.30, 0.70]
Total (95% CI)			**165**			**169**	**100.0%**	**-0.30 [-1.30, 0.70]**

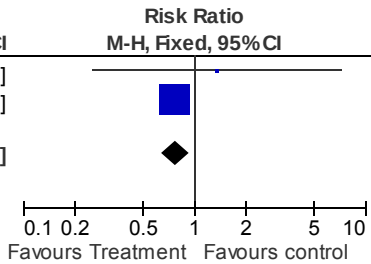
Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)



5.5 Leaving the study early: 1. Any reason (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SIROTA2006	3	21	2	19	1.9%	1.36 [0.25, 7.27]
KINON2006B	81	171	109	175	98.1%	0.76 [0.63, 0.92]
Total (95% CI)		**192**		**194**	**100.0%**	**0.77 [0.64, 0.94]**
Total events	84		111			

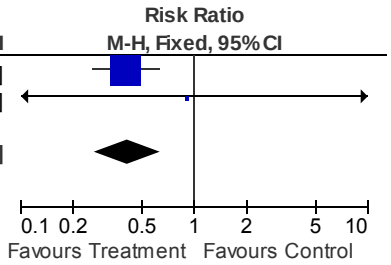
Heterogeneity: Chi² = 0.46, df = 1 (P = 0.50); I² = 0%
Test for overall effect: Z = 2.60 (P = 0.009)



5.6 Leaving the study early: 2. Due to lack of efficacy (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
KINON2006B	22	171	56	175	98.1%	0.40 [0.26, 0.63]
SIROTA2006	1	21	1	19	1.9%	0.90 [0.06, 13.48]
Total (95% CI)		**192**		**194**	**100.0%**	**0.41 [0.27, 0.64]**
Total events	23		57			

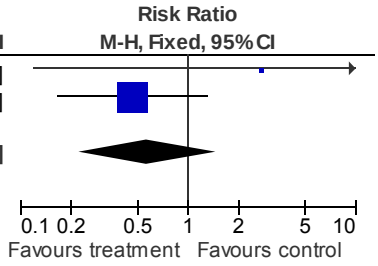
Heterogeneity: Chi² = 0.34, df = 1 (P = 0.56); I² = 0%
Test for overall effect: Z = 3.97 (P < 0.0001)



5.7 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SIROTA2006	1	21	0	19	4.6%	2.73 [0.12, 63.19]
KINON2006B	5	171	11	175	95.4%	0.47 [0.17, 1.31]
Total (95% CI)		**192**		**194**	**100.0%**	**0.57 [0.22, 1.47]**
Total events	6		11			

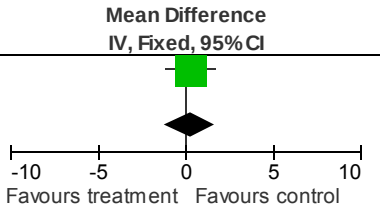
Heterogeneity: Chi² = 1.10, df = 1 (P = 0.29); I² = 9%
Test for overall effect: Z = 1.17 (P = 0.24)



5.8 AE: 1. Metabolic SEs - BMI (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006B	0.36	9.5	171	0.12	1.57	175	100.0%	0.24 [-1.20, 1.68]
Total (95% CI)			**171**			**175**	**100.0%**	**0.24 [-1.20, 1.68]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.33 (P = 0.74)



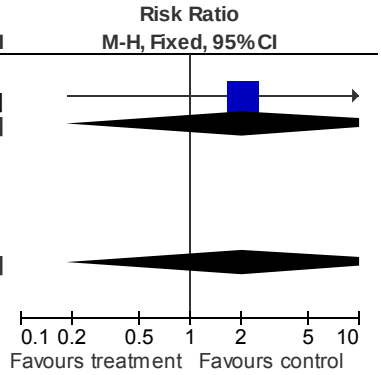
5.9 AE: 1. Metabolic SEs - Weight gain

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.9.1 Treatment-emergent weight gain						
KINON2006B	2	171	1	175	100.0%	2.05 [0.19, 22.36]
Subtotal (95% CI)		**171**		**175**	**100.0%**	**2.05 [0.19, 22.36]**
Total events	2		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)

Total (95% CI)		**171**		**175**	**100.0%**	**2.05 [0.19, 22.36]**
Total events	2		1			

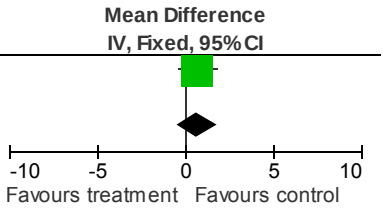
Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.56)



5.10 AE: 1. Metabolic SEs - Weight change from baseline (kg) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
KINON2006B	1.03	5.78	171	0.39	4.74	175	100.0%	0.64 [-0.48, 1.76]
Total (95% CI)			**171**			**175**	**100.0%**	**0.64 [-0.48, 1.76]**

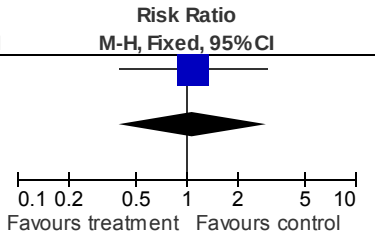
Heterogeneity: Not applicable
Test for overall effect: Z = 1.12 (P = 0.26)



5.11 AE: 2. Neurologic SEs - Use of anticholinergic medication (medium-term)

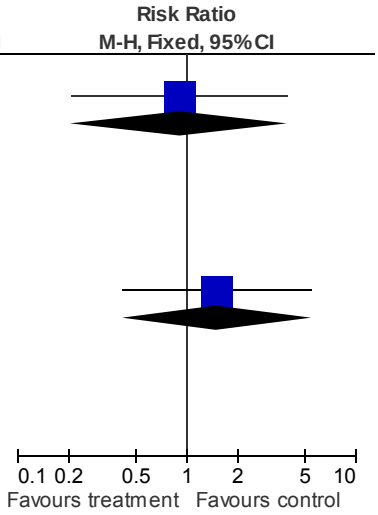
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SIROTA2006	6	21	5	19	100.0%	1.09 [0.39, 2.99]
Total (95% CI)		**21**		**19**	**100.0%**	**1.09 [0.39, 2.99]**
Total events	6		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.16 (P = 0.87)



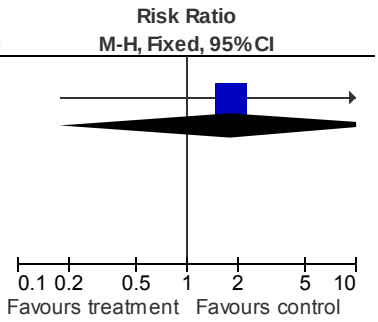
5.12 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.12.1 Akathisia						
SIROTA2006	3	21	3	19	100.0%	0.90 [0.21, 3.96]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**0.90 [0.21, 3.96]**
Total events	3		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.13 (P = 0.89)						
5.12.2 New parkinsonism						
SIROTA2006	5	21	3	19	100.0%	1.51 [0.42, 5.48]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**1.51 [0.42, 5.48]**
Total events	5		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.62 (P = 0.53)						



5.13 AE: 5. Gastrointestinal SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.13.1 Abdominal pain						
SIROTA2006	2	21	1	19	100.0%	1.81 [0.18, 18.39]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**1.81 [0.18, 18.39]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.50 (P = 0.62)						

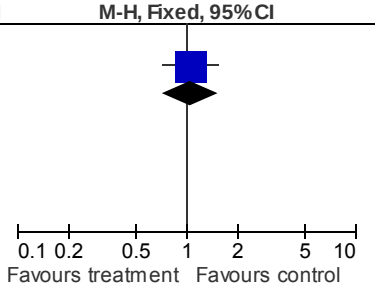


5.14 AE: 6. Sedation (short-term)

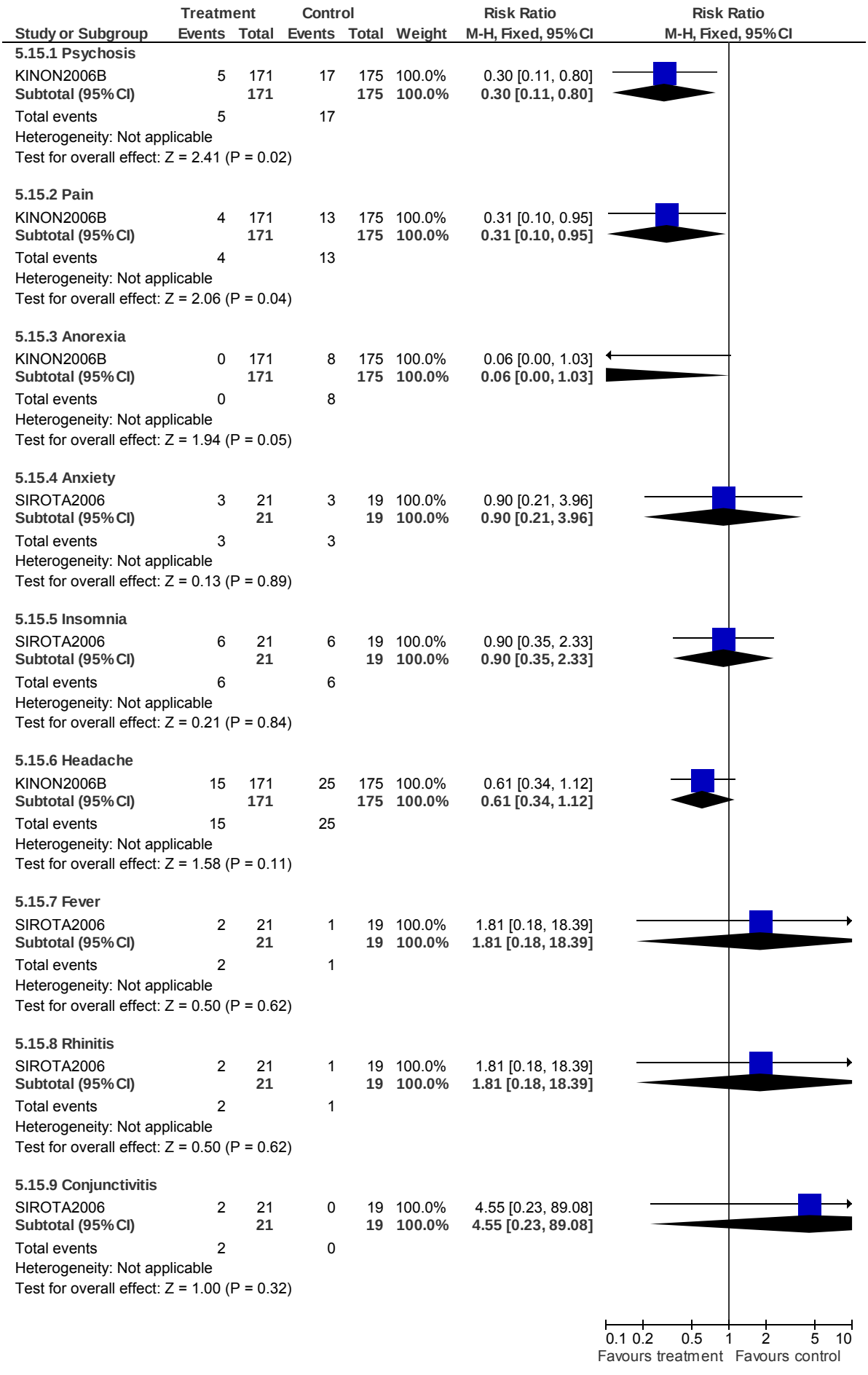
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.14.1 Day time sleepiness - increase (somnolence)						
KINON2006B	41	171	40	175	100.0%	1.05 [0.72, 1.54]
Subtotal (95% CI)		**171**		**175**	**100.0%**	**1.05 [0.72, 1.54]**
Total events	41		40			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.25 (P = 0.81)



5.15 AE: 10. Other SEs (medium-term)

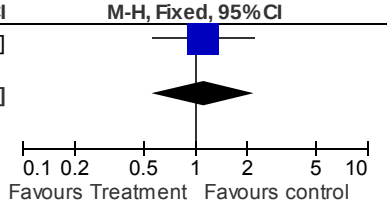


6 Risperidone versus Quetiapine (phase: persistent negative symptoms)

6.1 Leaving the study early: 1. Any reason (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RIEDEL2005	10	22	9	22	100.0%	1.11 [0.56, 2.19]
Total (95% CI)		**22**		**22**	**100.0%**	**1.11 [0.56, 2.19]**
Total events	10		9			

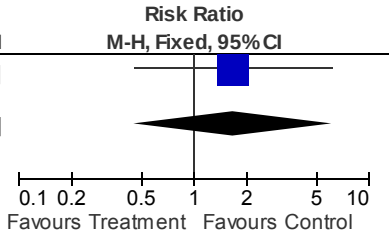
Heterogeneity: Not applicable
Test for overall effect: Z = 0.30 (P = 0.76)



6.2 Leaving the study early: 2. Due to lack of efficacy (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RIEDEL2005	5	22	3	22	100.0%	1.67 [0.45, 6.14]
Total (95% CI)		**22**		**22**	**100.0%**	**1.67 [0.45, 6.14]**
Total events	5		3			

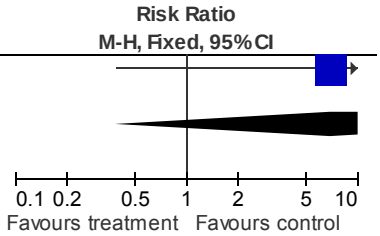
Heterogeneity: Not applicable
Test for overall effect: Z = 0.77 (P = 0.44)



6.3 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RIEDEL2005	3	22	0	22	100.0%	7.00 [0.38, 128.02]
Total (95% CI)		**22**		**22**	**100.0%**	**7.00 [0.38, 128.02]**
Total events	3		0			

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



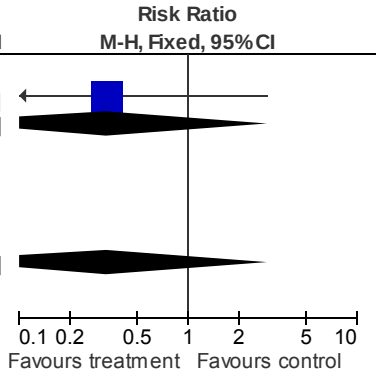
6.4 AE: 1. Metabolic SEs - Weight gain

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.4.1 Increase of >=7% body weight						
RIEDEL2005	1	22	3	22	100.0%	0.33 [0.04, 2.96]
Subtotal (95% CI)		**22**		**22**	**100.0%**	**0.33 [0.04, 2.96]**
Total events	1		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.99 (P = 0.32)

Total (95% CI)		**22**		**22**	**100.0%**	**0.33 [0.04, 2.96]**
Total events	1		3			

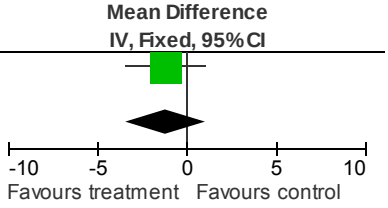
Heterogeneity: Not applicable
Test for overall effect: Z = 0.99 (P = 0.32)



6.5 AE: 1. Metabolic SEs - Weight change from baseline (kg) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
RIEDEL2005	1.72	3.57	22	2.93	4.02	22	100.0%	-1.21 [-3.46, 1.04]
Total (95% CI)			**22**			**22**	**100.0%**	**-1.21 [-3.46, 1.04]**

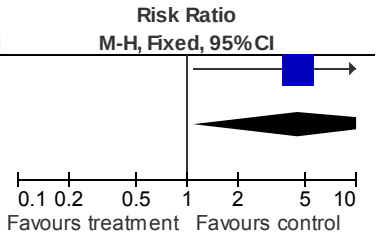
Heterogeneity: Not applicable
Test for overall effect: Z = 1.06 (P = 0.29)



6.6 AE: 2. Neurologic SEs - Use of anticholinergic medication (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
RIEDEL2005	9	22	2	22	100.0%	4.50 [1.09, 18.50]
Total (95% CI)		**22**		**22**	**100.0%**	**4.50 [1.09, 18.50]**
Total events	9		2			

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



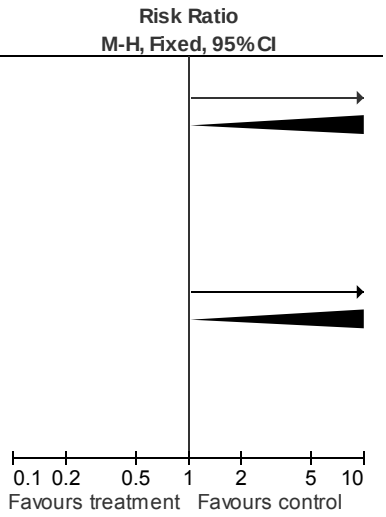
6.7 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.7.1 Akathisia						
RIEDEL2005	8	22	0	22	100.0%	17.00 [1.04, 277.61]
Subtotal (95% CI)		**22**		**22**	**100.0%**	**17.00 [1.04, 277.61]**
Total events	8		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.99 (P = 0.05)

6.7.2 New parkinsonism						
RIEDEL2005	8	22	0	22	100.0%	17.00 [1.04, 277.61]
Subtotal (95% CI)		**22**		**22**	**100.0%**	**17.00 [1.04, 277.61]**
Total events	8		0			

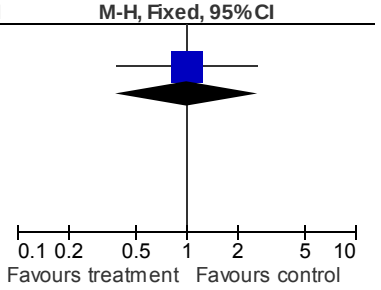
Heterogeneity: Not applicable
Test for overall effect: Z = 1.99 (P = 0.05)



6.8 AE: 4. Cardiovascular SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.8.1 Dizziness						
RIEDEL2005	6	22	6	22	100.0%	1.00 [0.38, 2.62]
Subtotal (95% CI)		**22**		**22**	**100.0%**	**1.00 [0.38, 2.62]**
Total events	6		6			

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

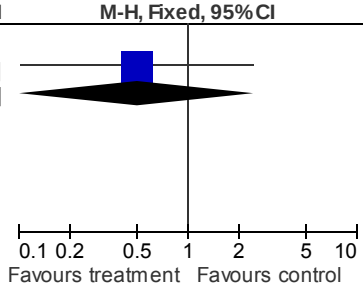


6.9 AE: 5. Gastrointestinal SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.9.1 Nausea						
RIEDEL2005	2	22	4	22	100.0%	0.50 [0.10, 2.45]
Subtotal (95% CI)		**22**		**22**	**100.0%**	**0.50 [0.10, 2.45]**
Total events	2		4			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.85 (P = 0.39)

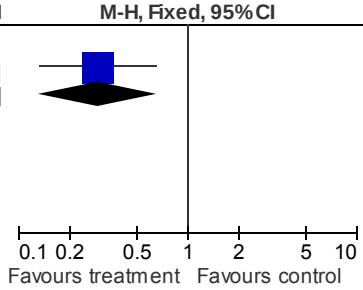


6.10 AE: 6. Sedation (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.10.4 Tiredness						
RIEDEL2005	5	22	17	22	100.0%	0.29 [0.13, 0.66]
Subtotal (95% CI)		**22**		**22**	**100.0%**	**0.29 [0.13, 0.66]**
Total events	5		17			

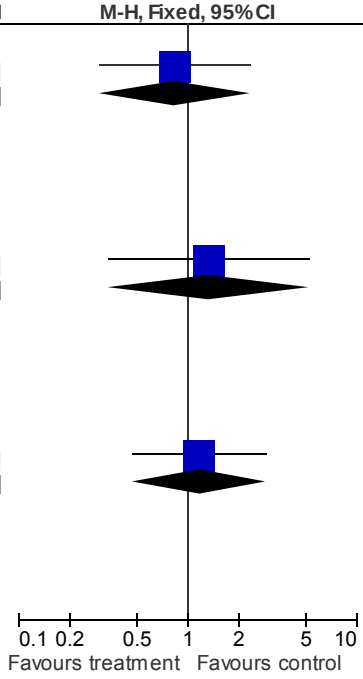
Heterogeneity: Not applicable

Test for overall effect: Z = 2.99 (P = 0.003)



6.11 AE: 10. Other SEs (short-term)

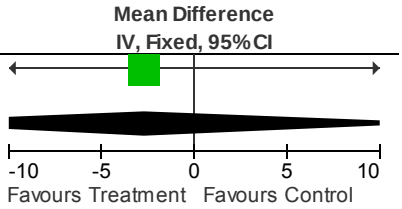
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.11.1 Insomnia						
RIEDEL2005	5	22	6	22	100.0%	0.83 [0.30, 2.33]
Subtotal (95% CI)		**22**		**22**	**100.0%**	**0.83 [0.30, 2.33]**
Total events	5		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.35 (P = 0.73)						
6.11.2 Cold						
RIEDEL2005	4	22	3	22	100.0%	1.33 [0.34, 5.28]
Subtotal (95% CI)		**22**		**22**	**100.0%**	**1.33 [0.34, 5.28]**
Total events	4		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.41 (P = 0.68)						
6.11.3 Headache						
RIEDEL2005	7	22	6	22	100.0%	1.17 [0.47, 2.92]
Subtotal (95% CI)		**22**		**22**	**100.0%**	**1.17 [0.47, 2.92]**
Total events	7		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.33 (P = 0.74)						



7 Amisulpride versus Ziprasidone (phase: persistent negative symptoms)

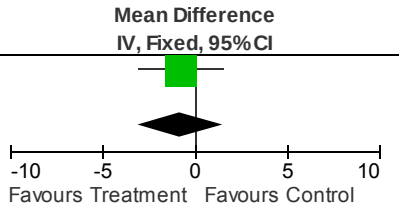
7.1 Mental state: 1. PANSS total (endpoint, high=poor) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
OLIE2006	-14.6	58.17	63	-11.9	19.19	59	100.0%	-2.70 [-17.88, 12.48]
Total (95% CI)			**63**			**59**	**100.0%**	**-2.70 [-17.88, 12.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.35 (P = 0.73)								



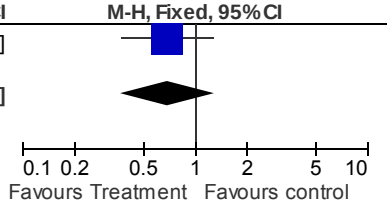
7.2 Mental state: 2. PANSS negative score (change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
OLIE2006	-6.9	6.35	63	-6.1	6.72	59	100.0%	-0.80 [-3.12, 1.52]
Total (95% CI)			**63**			**59**	**100.0%**	**-0.80 [-3.12, 1.52]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.67 (P = 0.50)								



7.3 Leaving the study early: 1. Any reason (medium-term)

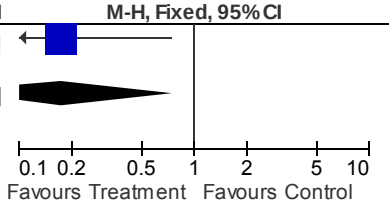
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
OLIE2006	13	63	18	60	100.0%	0.69 [0.37, 1.28]
Total (95% CI)		**63**		**60**	**100.0%**	**0.69 [0.37, 1.28]**
Total events	13		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.18 (P = 0.24)						



7.4 Leaving the study early: 2. Due to lack of efficacy (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
OLIE2006	2	63	11	60	100.0%	0.17 [0.04, 0.75]
Total (95% CI)		**63**		**60**	**100.0%**	**0.17 [0.04, 0.75]**
Total events	2		11			

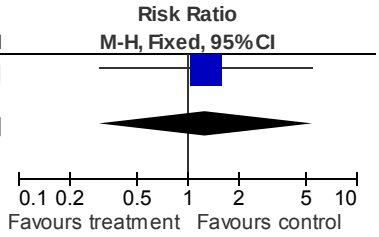
Heterogeneity: Not applicable
Test for overall effect: Z = 2.35 (P = 0.02)



7.5 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
OLIE2006	4	63	3	60	100.0%	1.27 [0.30, 5.44]
Total (95% CI)		**63**		**60**	**100.0%**	**1.27 [0.30, 5.44]**
Total events	4		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.32 (P = 0.75)



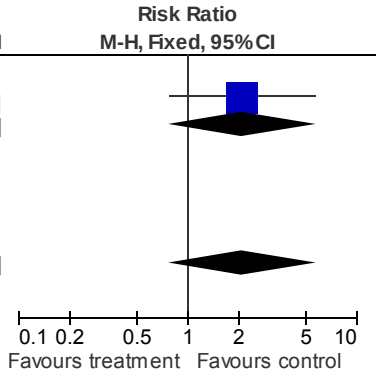
7.6 AE: 1. Metabolic SEs - Weight gain

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.6.1 Increase of >7% body weight						
OLIE2006	11	63	5	60	100.0%	2.10 [0.77, 5.67]
Subtotal (95% CI)		**63**		**60**	**100.0%**	**2.10 [0.77, 5.67]**
Total events	11		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.46 (P = 0.15)

Total (95% CI)		**63**		**60**	**100.0%**	**2.10 [0.77, 5.67]**
Total events	11		5			

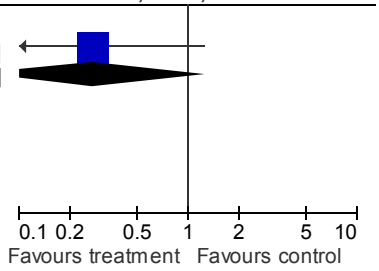
Heterogeneity: Not applicable
Test for overall effect: Z = 1.46 (P = 0.15)



7.7 AE: 1. Metabolic SEs (treatment-emergent) (short-term)

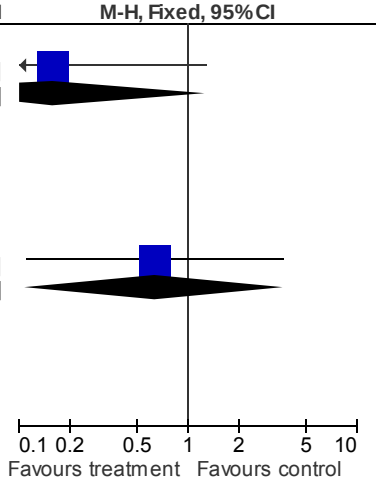
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.7.1 Increase in ketones (>= 1 +)						
OLIE2006	2	63	7	60	100.0%	0.27 [0.06, 1.26]
Subtotal (95% CI)		**63**		**60**	**100.0%**	**0.27 [0.06, 1.26]**
Total events	2		7			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.67 (P = 0.10)



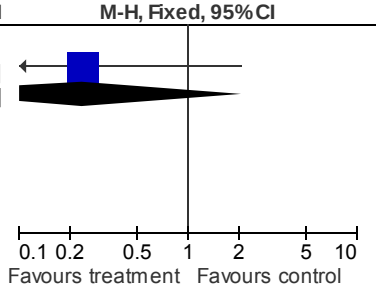
7.8 AE: 2. Neurologic SEs (treatment-emergent) (medium-term)

	Treatment		Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
7.8.1 EPS							
OLIE2006	1	63	6	60	100.0%	0.16 [0.02, 1.28]	
Subtotal (95% CI)		**63**		**60**	**100.0%**	**0.16 [0.02, 1.28]**	
Total events	1		6				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.73 (P = 0.08)							
7.8.2 Akathisia							
OLIE2006	2	63	3	60	100.0%	0.63 [0.11, 3.67]	
Subtotal (95% CI)		**63**		**60**	**100.0%**	**0.63 [0.11, 3.67]**	
Total events	2		3				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.51 (P = 0.61)							



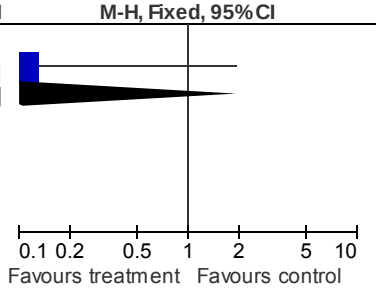
7.9 AE: 3. Autonomic SEs (short-term)

	Treatment		Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
7.9.1 Dry mouth							
OLIE2006	1	63	4	60	100.0%	0.24 [0.03, 2.07]	
Subtotal (95% CI)		**63**		**60**	**100.0%**	**0.24 [0.03, 2.07]**	
Total events	1		4				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.30 (P = 0.19)							



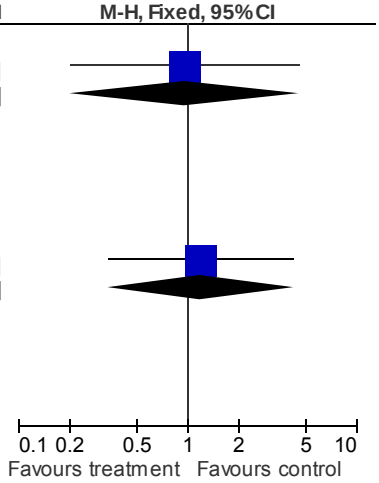
7.10 AE: 4. Cardiovascular SEs (short-term)

	Treatment		Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
7.10.1 Dizziness							
OLIE2006	0	63	4	60	100.0%	0.11 [0.01, 1.93]	
Subtotal (95% CI)		**63**		**60**	**100.0%**	**0.11 [0.01, 1.93]**	
Total events	0		4				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.52 (P = 0.13)							



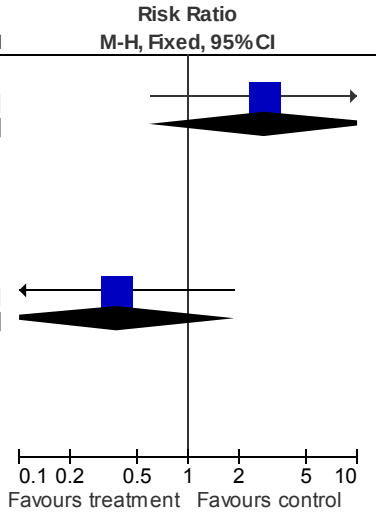
7.11 AE: 5. Gastrointestinal SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.11.1 Nausea						
OLIE2006	3	63	3	60	100.0%	0.95 [0.20, 4.54]
Subtotal (95% CI)		**63**		**60**	**100.0%**	**0.95 [0.20, 4.54]**
Total events	3		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.06 (P = 0.95)						
7.11.2 Vomiting						
OLIE2006	5	63	4	60	100.0%	1.19 [0.34, 4.22]
Subtotal (95% CI)		**63**		**60**	**100.0%**	**1.19 [0.34, 4.22]**
Total events	5		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.27 (P = 0.79)						



7.12 AE: 6. Sedation (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.12.1 Day time sleepiness - increase (somnolence)						
OLIE2006	6	63	2	60	100.0%	2.86 [0.60, 13.61]
Subtotal (95% CI)		**63**		**60**	**100.0%**	**2.86 [0.60, 13.61]**
Total events	6		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.32 (P = 0.19)						
7.12.2 Asthenia						
OLIE2006	2	63	5	60	100.0%	0.38 [0.08, 1.89]
Subtotal (95% CI)		**63**		**60**	**100.0%**	**0.38 [0.08, 1.89]**
Total events	2		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.18 (P = 0.24)						



7.13 AE: 10. Other SEs (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.13.1 Insomnia						
OLIE2006	9	63	10	60	100.0%	0.86 [0.37, 1.96]
Subtotal (95% CI)		**63**		**60**	**100.0%**	**0.86 [0.37, 1.96]**
Total events	9		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.36 (P = 0.72)						
7.13.2 Headache						
OLIE2006	3	63	8	60	100.0%	0.36 [0.10, 1.28]
Subtotal (95% CI)		**63**		**60**	**100.0%**	**0.36 [0.10, 1.28]**
Total events	3		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.58 (P = 0.11)						
7.13.3 Anxiety						
OLIE2006	4	63	5	60	100.0%	0.76 [0.21, 2.70]
Subtotal (95% CI)		**63**		**60**	**100.0%**	**0.76 [0.21, 2.70]**
Total events	4		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.42 (P = 0.67)						

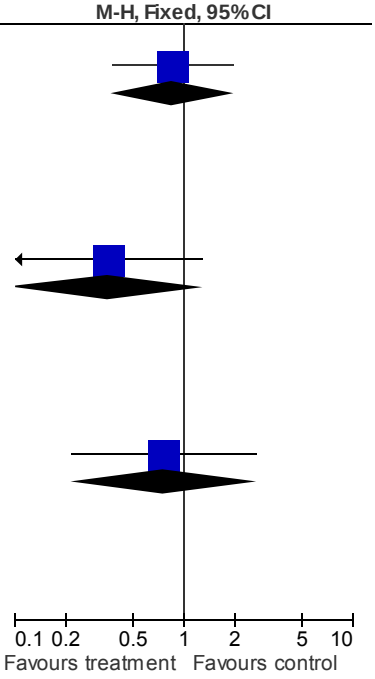


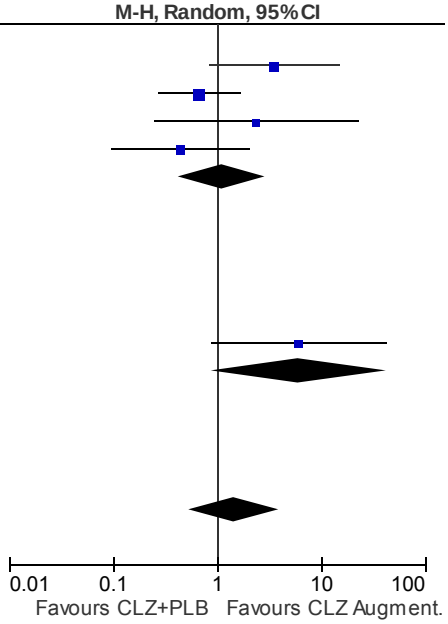
Table 8: Studies included in the augmentation review

Treatment	versus Comparator		
	ARI	RIS	SUL
CLZ	CHANG2008 [8weeks, N=62]	FREUDENREICH2007 [6weeks, N=24] HONER2006 [8weeks, N=68] JOSIASSEN2005 [12weeks, N=40] YAGCIOGLU2005 [6weeks, N=30]	SHILOH1997 [10weeks, N=28]

1 Clozapine augmentation versus clozapine + placebo

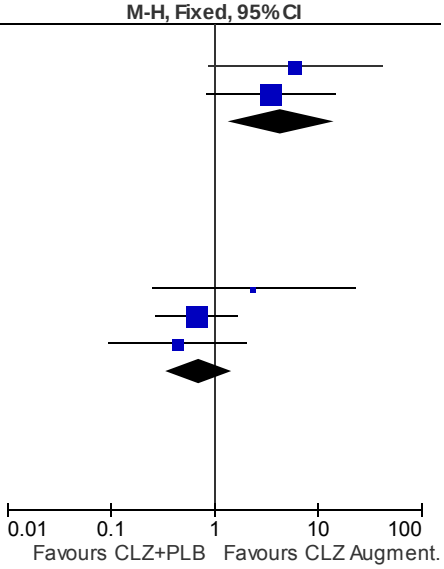
1.1 Number of responders (response defined as >= 20% improvement in BPRS or PANSS) - by augmented drug

Study or Subgroup	CLZ Augment. Events	Total	CLZ PLB Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Clozapine + risperidone						
JOSIASSEN2005	7	20	2	20	21.5%	3.50 [0.83, 14.83]
HONER2006	6	34	9	34	29.4%	0.67 [0.27, 1.67]
FREUDENREICH2007	2	11	1	13	13.0%	2.36 [0.25, 22.70]
YAGCIOGLU2005	2	16	4	14	20.3%	0.44 [0.09, 2.04]
Subtotal (95% CI)		**81**		**81**	**84.2%**	**1.09 [0.42, 2.85]**
Total events	17		16			
Heterogeneity: Tau² = 0.42; Chi² = 5.35, df = 3 (P = 0.15); I² = 44%						
Test for overall effect: Z = 0.18 (P = 0.86)						
1.1.2 Clozapine + sulpride						
SHILOH1997	8	16	1	12	15.8%	6.00 [0.86, 41.73]
Subtotal (95% CI)		**16**		**12**	**15.8%**	**6.00 [0.86, 41.73]**
Total events	8		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.81 (P = 0.07)						
Total (95% CI)		**97**		**93**	**100.0%**	**1.46 [0.54, 3.96]**
Total events	25		17			
Heterogeneity: Tau² = 0.66; Chi² = 8.58, df = 4 (P = 0.07); I² = 53%						
Test for overall effect: Z = 0.74 (P = 0.46)						



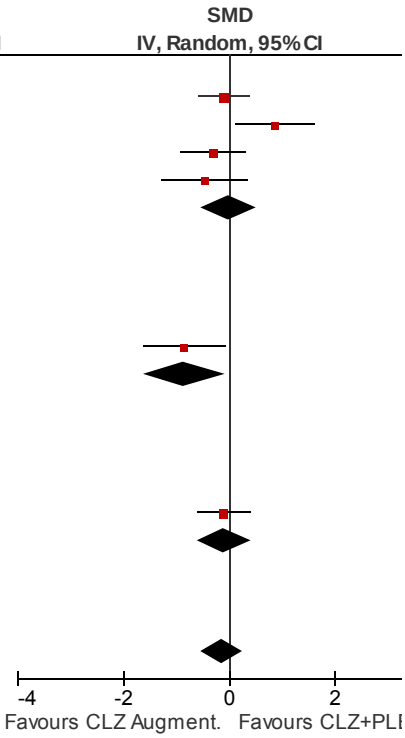
1.2 Number of Responders (response defined as >= 20% improvement in BPRS or PANSS) - by length of treatment

Study or Subgroup	CLZ Augment. Events	Total	CLZ + PLB Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Greater than or equal to 10 weeks						
SHILOH1997	8	16	1	12	36.4%	6.00 [0.86, 41.73]
JOSIASSEN2005	7	20	2	20	63.6%	3.50 [0.83, 14.83]
Subtotal (95% CI)		**36**		**32**	**100.0%**	**4.41 [1.38, 14.07]**
Total events	15		3			
Heterogeneity: Chi² = 0.20, df = 1 (P = 0.66); I² = 0%						
Test for overall effect: Z = 2.51 (P = 0.01)						
1.2.2 Less than 10 weeks						
FREUDENREICH2007	2	11	1	13	6.5%	2.36 [0.25, 22.70]
HONER2006	6	34	9	34	63.5%	0.67 [0.27, 1.67]
YAGCIOGLU2005	2	16	4	14	30.1%	0.44 [0.09, 2.04]
Subtotal (95% CI)		**61**		**61**	**100.0%**	**0.71 [0.34, 1.46]**
Total events	10		14			
Heterogeneity: Chi² = 1.48, df = 2 (P = 0.48); I² = 0%						
Test for overall effect: Z = 0.94 (P = 0.35)						



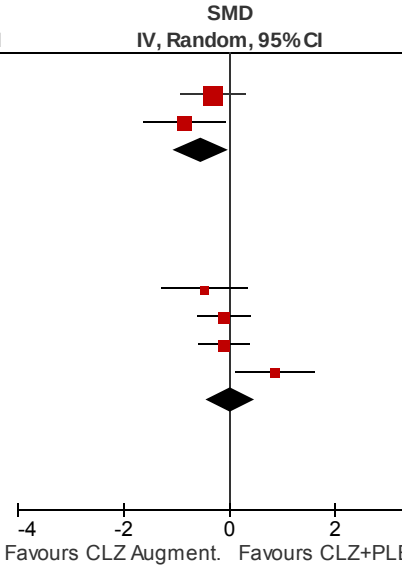
1.3 PANSS or BPRS total score (change from baseline to endpoint)

Study or Subgroup	SMD	SE	CLZ Augment. Total	CLZ + PLB Total	Weight	SMD IV, Random, 95% CI
1.3.1 Clozapine + risperidone						
HONER2006	-0.1	0.2478	32	33	21.0%	-0.10 [-0.59, 0.39]
YAGCIOGLU2005	0.8584	0.3823	16	14	14.4%	0.86 [0.11, 1.61]
JOSIASSEN2005	-0.3061	0.318	20	20	17.3%	-0.31 [-0.93, 0.32]
FREUDENREICH2007	-0.4731	0.4153	11	13	13.1%	-0.47 [-1.29, 0.34]
Subtotal (95% CI)			**79**	**80**	**65.8%**	**-0.02 [-0.53, 0.50]**
Heterogeneity: Tau² = 0.16; Chi² = 7.37, df = 3 (P = 0.06); I² = 59%						
Test for overall effect: Z = 0.06 (P = 0.95)						
1.3.2 Clozapine + sulpride						
SHILOH1997	-0.8551	0.398	16	12	13.8%	-0.86 [-1.64, -0.08]
Subtotal (95% CI)			**16**	**12**	**13.8%**	**-0.86 [-1.64, -0.08]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.15 (P = 0.03)						
1.3.3 Clozapine + amisulpride						
CHANG2008	-0.108	0.2566	29	32	20.5%	-0.11 [-0.61, 0.39]
Subtotal (95% CI)			**29**	**32**	**20.5%**	**-0.11 [-0.61, 0.39]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.42 (P = 0.67)						
Total (95% CI)			**124**	**124**	**100.0%**	**-0.15 [-0.54, 0.23]**
Heterogeneity: Tau² = 0.12; Chi² = 11.01, df = 5 (P = 0.05); I² = 55%						
Test for overall effect: Z = 0.77 (P = 0.44)						



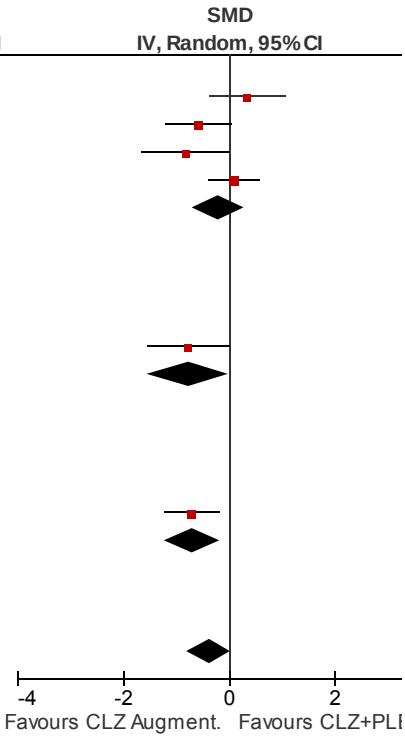
1.4 PANSS or BPRS total (change score) - by length of treatment

Study or Subgroup	SMD	SE	CLZ Augment. Total	CLZ + PLB Total	Weight	SMD IV, Random, 95% CI
1.4.1 Clozapine augmentation >= 10 weeks						
JOSIASSEN2005	-0.3061	0.318	20	20	59.5%	-0.31 [-0.93, 0.32]
SHILOH1997	-0.8551	0.398	16	12	40.5%	-0.86 [-1.64, -0.08]
Subtotal (95% CI)			**36**	**32**	**100.0%**	**-0.53 [-1.06, -0.00]**
Heterogeneity: Tau² = 0.02; Chi² = 1.16, df = 1 (P = 0.28); I² = 14%						
Test for overall effect: Z = 1.96 (P = 0.05)						
1.4.2 Clozapine augmentation < 10 weeks						
FREUDENREICH2007	-0.4731	0.4153	11	13	18.9%	-0.47 [-1.29, 0.34]
CHANG2008	-0.108	0.2566	29	32	29.8%	-0.11 [-0.61, 0.39]
HONER2006	-0.1	0.2478	32	33	30.5%	-0.10 [-0.59, 0.39]
YAGCIOGLU2005	0.8584	0.3823	16	14	20.8%	0.86 [0.11, 1.61]
Subtotal (95% CI)			**88**	**92**	**100.0%**	**0.03 [-0.43, 0.49]**
Heterogeneity: Tau² = 0.12; Chi² = 6.68, df = 3 (P = 0.08); I² = 55%						
Test for overall effect: Z = 0.11 (P = 0.91)						



1.5 PANSS or BPRS negative/SANS (change score)

Study or Subgroup	SMD	SE	CLZ Augment. Total	CLZ + PLB Total	Weight	SMD IV, Random, 95% CI
1.5.1 Clozapine + risperidone						
YAGCIOGLU2005	0.335	0.3685	16	14	15.1%	0.34 [-0.39, 1.06]
JOSIASSEN2005	-0.5949	0.3231	20	20	17.1%	-0.59 [-1.23, 0.04]
FREUDENREICH2007	-0.8333	0.427	11	13	12.9%	-0.83 [-1.67, 0.00]
HONER2006	0.0893	0.2482	32	33	20.8%	0.09 [-0.40, 0.58]
Subtotal (95% CI)			**79**	**80**	**66.0%**	**-0.21 [-0.72, 0.29]**
Heterogeneity: Tau² = 0.15; Chi² = 7.11, df = 3 (P = 0.07); I² = 58%						
Test for overall effect: Z = 0.83 (P = 0.40)						
1.5.2 Clozapine + sulpride						
SHILOH1997	-0.7827	0.3959	16	12	14.1%	-0.78 [-1.56, -0.01]
Subtotal (95% CI)			**16**	**12**	**14.1%**	**-0.78 [-1.56, -0.01]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.98 (P = 0.05)						
1.5.3 Clozapine + amisulpride						
CHANG2008	-0.7122	0.2644	29	32	20.0%	-0.71 [-1.23, -0.19]
Subtotal (95% CI)			**29**	**32**	**20.0%**	**-0.71 [-1.23, -0.19]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.69 (P = 0.007)						
Total (95% CI)			**124**	**124**	**100.0%**	**-0.39 [-0.79, 0.01]**
Heterogeneity: Tau² = 0.14; Chi² = 11.51, df = 5 (P = 0.04); I² = 57%						
Test for overall effect: Z = 1.93 (P = 0.05)						



1.6 PANSS or BPRS negative/SANS (change score) - by length of treatment

Study or Subgroup	SMD	SE	CLZ Augment. Total	CLZ + PLB Total	Weight	SMD IV, Random, 95% CI
1.6.1 Clozapine augmentation >= 10 weeks						
SHILOH1997	-0.7827	0.3959	16	12	40.0%	-0.78 [-1.56, -0.01]
JOSIASSEN2005	-0.5949	0.3231	20	20	60.0%	-0.59 [-1.23, 0.04]
Subtotal (95% CI)			**36**	**32**	**100.0%**	**-0.67 [-1.16, -0.18]**
Heterogeneity: Tau² = 0.00; Chi² = 0.14, df = 1 (P = 0.71); I² = 0%						
Test for overall effect: Z = 2.68 (P = 0.007)						
1.6.2 Clozapine augmentation < 10 weeks						
YAGCIOGLU2005	0.335	0.3685	16	14	22.7%	0.34 [-0.39, 1.06]
HONER2006	0.0893	0.2482	32	33	29.1%	0.09 [-0.40, 0.58]
FREUDENREICH2007	-0.8333	0.427	11	13	20.0%	-0.83 [-1.67, 0.00]
CHANG2008	-0.7122	0.2644	29	32	28.2%	-0.71 [-1.23, -0.19]
Subtotal (95% CI)			**88**	**92**	**100.0%**	**-0.27 [-0.81, 0.28]**
Heterogeneity: Tau² = 0.21; Chi² = 9.31, df = 3 (P = 0.03); I² = 68%						
Test for overall effect: Z = 0.95 (P = 0.34)						

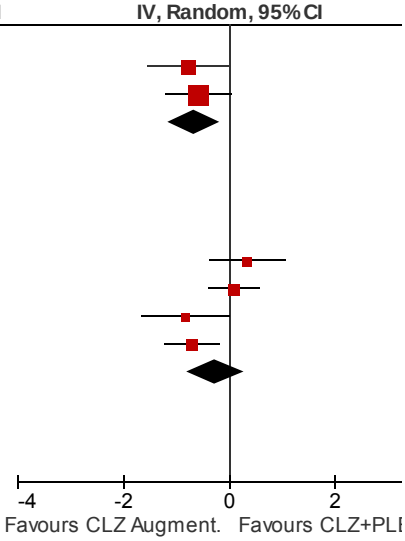


Table 9: Summary of studies included in the overall analysis of side effects

Treatment	Comparator		
	Versus haloperidol (FGA)	**Versus non-haloperidol FGA**	**Versus SGA**
Amisulpride	Carriere2000 [16 weeks] Delcker1990 [6 weeks] Moller1997 [6 weeks] Puech1998 [4 weeks] Speller1997 [52 weeks] Ziegler1989 [4 weeks]	Boyer1990 (fluphenazine) [6 weeks] Hillert1994 (flupentixol) [6 weeks]	Fleurot1997 (risperidone) [8 weeks] HWANG2003 (risperidone) [6 weeks] Lecrubier1999 (olanzapine) [26 weeks] Lecrubier2000 (risperidone) [26 weeks] MARTIN2002 (olanzapine) [24 weeks] WAGNER2005 (olanzapine) [8 weeks]
	k = 6	*k* = 2	*k* = 6
Aripiprazole	KANE2002 [4 weeks] KASPER2003 [52 weeks]	KANE2007B (perphenazine) [6 weeks]	CHAN2007B (risperidone) [4 weeks] MCQUADE2004 (olanzapine) [26 weeks]* POTKIN2003A (risperidone) [4 weeks] ZIMBROFF2007 (ziprasidone) [4 weeks]
	k = 2	*k* = 1	*k* = 4
Clozapine	Buchanan1998 [10 weeks] Rosenheck1997 [52 weeks] Tamminga1994 [52 weeks] VOLAVKA2002 [14 weeks]	Claghorn1987 (chlorpromazine) [4–8 weeks] Hong1997 (chlorpromazine) [12 weeks] Kane1988 (chlorpromazine) [6 weeks] LIEBERMAN2003B [52 weeks]*	Anand1998 (risperidone) [12 weeks] ATMACA2003 (olanzapine/quetiapine/risperidone) [6 weeks]* Beuzen1998 (olanzapine) [18 weeks] Bitter1999 (olanzapine) [18 weeks] Bondolfi1998 (risperidone) [8 weeks] Breier1999 (risperidone) [18 weeks] Chowdhury1999 (risperidone) [16 weeks] MELTZER2003A (olanzapine) [104 weeks]* VOLAVKA2002 (olanzapine/ risperidone) [14 weeks]
	k = 4	*k* = 4	*k* = 9
Olanzapine	Altamura1999 [14 weeks] Beasley1996a [6 weeks] Beasley1997 [6 weeks] Breier2000 [6 weeks] BUCHANAN2005 [16 weeks] HGCJ1999 (HK) [14 weeks]	Conley1998a (chlorpromazine) [8 weeks] HGBL1997 (flupentixol) [4 weeks] Jakovljevic1999 (fluphenazine) [6 weeks] Loza1999 (chlorpromazine) [6 weeks] Naukkarinen1999/HGBJ (perphenazine) [26 weeks]	ATMACA2003 (quetiapine/risperidone) [6 weeks]* Conley 2001 (risperidone) [8 weeks] DAVIDSON2007 (paliperidone) [6 weeks] Gureje1998 (risperidone) [30 weeks] Jones1998 (risperidone) [54 weeks] KANE2007A (paliperidone)

	HGCU1998 (Taiwan) [14 weeks] Jones1998 [54 weeks] KONGSAKON2006 [24 weeks] LIEBERMAN2003A [24 weeks] LINDENMAYER2007 [12 weeks] ROSENHECK2003 [52 weeks] STUDY-S029 [52 weeks] Tollefson1997 [6 weeks] Tran1998a [52 weeks] Tran1998b [52 weeks] Tran1998c [22–84 weeks] VOLAVKA2002 [14 weeks]		[6 weeks] KINON2006B (quetiapine) [26 weeks] Lecrubier1999 (amisulpride) [26 weeks] MARDER2007 (paliperidone) [6 weeks] MARTIN2002 (amisulpride) [24 weeks] MCEVOY2007A (quetiapine/ risperidone) [52 weeks] MCQUADE2004 (aripiprazole) [26 weeks] * RIEDEL2007B (quetiapine) [8 weeks] StudyS036 (risperidone) [6 weeks] SIROTA2006 (quetiapine) [26 weeks] Tran1997 (risperidone) [28 weeks] VANNIMWEGEN2008 (risperidone) [6 weeks] VOLAVKA2002 (risperidone) [14 weeks] WAGNER2005 (amisulpride) [8 weeks]
	k = 18	*k* = 5	*k* = 19
Paliperidone	-	-	DAVIDSON2007 (paliperidone) [6 weeks] KANE2007A (paliperidone) [6 weeks] MARDER2007 (paliperidone) [6 weeks]
			k = 3
Quetiapine	Arvanitis1997 [6 weeks] Emsley1999 [8 weeks] Fleischhacker1996 [6 weeks] Murasaki1999 [8 weeks] Purdon2000 [26 weeks]	CONLEY2005 (fluphenazine) [12 weeks] Link1994 (chlorpromazine) [6 weeks]	ATMACA2003 (clozapine/ olanzapine/ risperidone) [6 weeks] * CONLEY2005 (risperidone) [12 weeks] KINON2006B (olanzapine) [26 weeks] RIEDEL2005 (risperidone) [12 weeks] RIEDEL2007B (olanzapine) [8 weeks] SIROTA2006 (olanzapine) [26 weeks] ZHONG2006 (risperidone) [8 weeks]
	k = 5	*k* = 2	*k* = 7
Risperidone	Blin1996 [4 weeks] Ceskova1993 [8 weeks] Chouinard1993 [8 weeks] Claus1991 [12 weeks] Csernansky1999/ 2000	CONLEY2005 (fluphenazine) [12 weeks] Hoyberg1993 (perphenazine) [8 weeks] Huttunen1995 (zuclopenthixol) [8 weeks] RUHRMANN2007 (flupentixol) [25 weeks]	ATMACA2003 (olanzapine/ quetiapine) [6 weeks] * AZORIN2006 (sertindole) [12 weeks] CHAN2007A (aripiprazole) [4 weeks] Conley2001 (olanzapine) [8 weeks] CONLEY2005 (quetiapine)

	[52 weeks] Emsley1995 [6 weeks] Heck2000 [6 weeks] Janicak1999 [6 weeks] Jones1998 [54 weeks] Kern1998 [8 weeks] LEE2007 [24 weeks] Marder1994 [8 weeks] Mesotten1991 [8 weeks] Min1993 [8 weeks] MOLLER2008 [8 weeks] Peuskens1995 [8 weeks] SCHOOLER2005 [104 weeks] SEE1999 [5 weeks] ZHANG2001 [12 weeks] VOLAVKA2002 [14 weeks]		[12 weeks] Fleurot1997 (amisulpride) [8 weeks] Gureje1998 (olanzapine) [30 weeks] HWANG2003 (amisulpride) [6 weeks] Jones1998 (olanzapine) [54 weeks] Klieser1996 (zotepine) [4 weeks] Lecrubier2000 (amisulpride) [26 weeks] MCEVOY2007A (olanzapine/ quetiapine) [52 weeks] POTKIN2003A (aripiprazole) [4 weeks] RIEDEL2005 (quetiapine) [12 weeks] StudyS036 (olanzapine) [6 weeks] Tran1997 (olanzapine) [28 weeks] VANNIMWEGEN2008 (olanzapine) [6 weeks] VOLAVKA2002 (clozapine/ olanzapine) [14 weeks] ZHONG2006 (quetiapine) [8 weeks]
	k = 20	*k* = 4	*k* = 18
Sertindole	Hale 2000 [8 weeks] Daniel 1998 [52 weeks]*	-	AZORIN2006 (risperidone) [12 weeks]
	k = 2		*k* = 1
Zotepine	Barnas1987 [7 weeks] Fleischhacker1989 [6 weeks] Klieser1996 [4 weeks] KnollCTR (StudyZT4002) [26 weeks] Petit1996 [8 weeks]	Cooper1999a (chlorpromazine) [8 weeks]	Klieser1996 (risperidone) [4 weeks]
	k = 5	*k* = 1	*k* = 1

Note. * Study did not meet the inclusion criteria for any other review reported in this chapter.

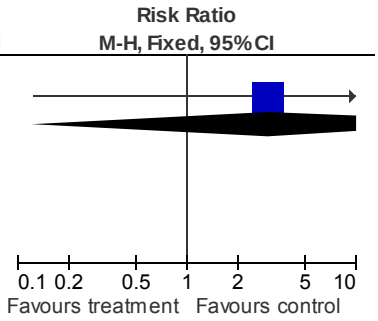
1 Olanzapine versus another antipsychotic drug (overall SE analysis)

1.1 Mortality - Suicide (medium-term)

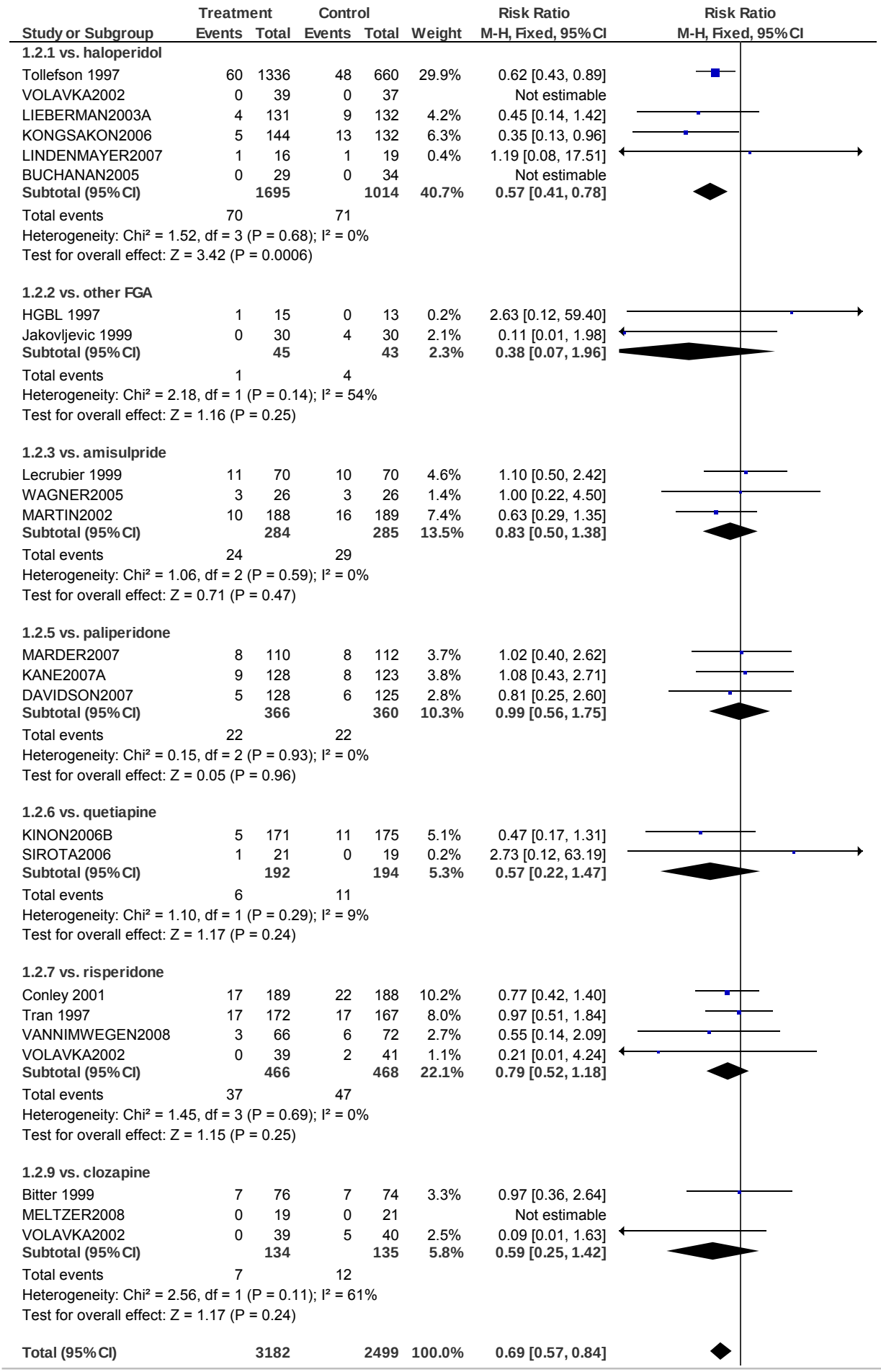
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 vs. amisulpride						
MARTIN2002	1	188	0	189	100.0%	3.02 [0.12, 73.56]
Subtotal (95% CI)		**188**		**189**	**100.0%**	**3.02 [0.12, 73.56]**
Total events	1		0			

Heterogeneity: Not applicable

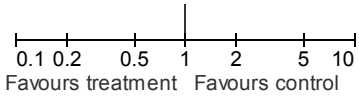
Test for overall effect: Z = 0.68 (P = 0.50)



1.2 Leaving the study early: 3: Adverse event (short-to-medium-term)

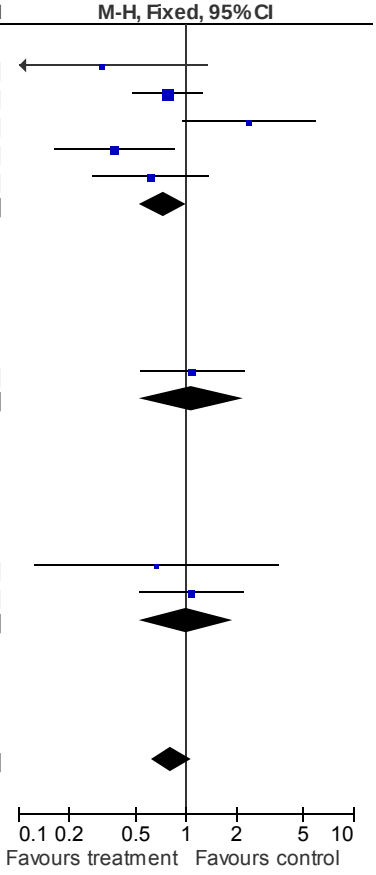


Total events 167 196
Heterogeneity: Chi² = 13.86, df = 19 (P = 0.79); I² = 0%
Test for overall effect: Z = 3.65 (P = 0.0003)

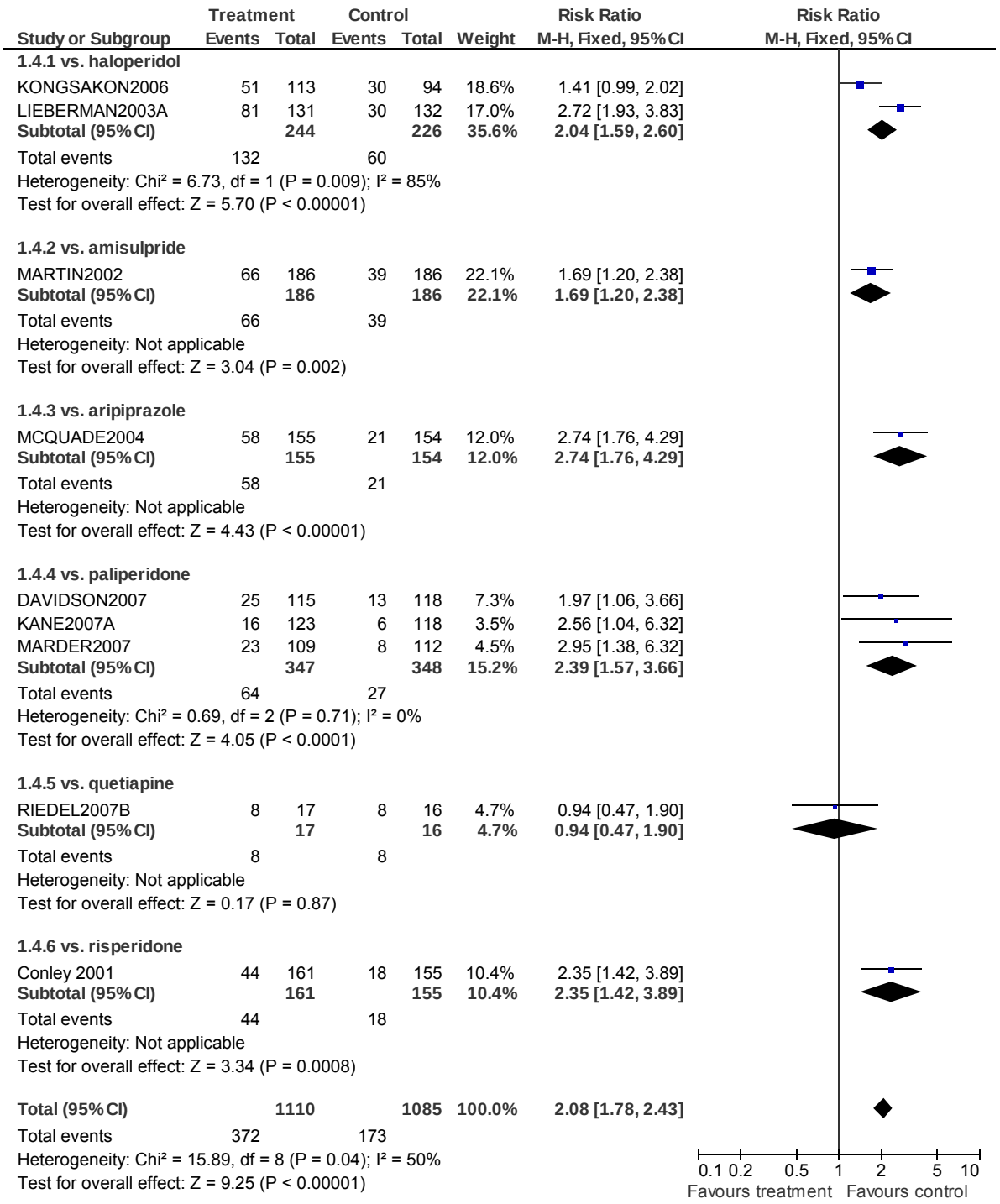


1.3 Leaving the study early: 3: Adverse event (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 vs. haloperidol						
Jones 1998	2	21	7	23	6.3%	0.31 [0.07, 1.34]
Tran 1998a+b+c	54	627	20	180	29.3%	0.78 [0.48, 1.26]
ROSENHECK2003	15	159	6	150	5.8%	2.36 [0.94, 5.92]
LIEBERMAN2003A	7	131	19	132	17.8%	0.37 [0.16, 0.85]
Study S029	9	141	14	134	13.5%	0.61 [0.27, 1.36]
Subtotal (95% CI)		**1079**		**619**	**72.7%**	**0.73 [0.53, 1.01]**
Total events	87		66			
Heterogeneity: Chi² = 10.33, df = 4 (P = 0.04); I² = 61%						
Test for overall effect: Z = 1.89 (P = 0.06)						
1.3.6 vs. quetiapine						
MCEVOY2007A	14	133	13	134	12.2%	1.09 [0.53, 2.22]
Subtotal (95% CI)		**133**		**134**	**12.2%**	**1.09 [0.53, 2.22]**
Total events	14		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.22 (P = 0.82)						
1.3.7 vs. risperidone						
Jones 1998	2	21	3	21	2.8%	0.67 [0.12, 3.59]
MCEVOY2007A	14	133	13	133	12.2%	1.08 [0.53, 2.20]
Subtotal (95% CI)		**154**		**154**	**15.1%**	**1.00 [0.52, 1.93]**
Total events	16		16			
Heterogeneity: Chi² = 0.26, df = 1 (P = 0.61); I² = 0%						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**1366**		**907**	**100.0%**	**0.82 [0.62, 1.07]**
Total events	117		95			
Heterogeneity: Chi² = 12.00, df = 7 (P = 0.10); I² = 42%						
Test for overall effect: Z = 1.49 (P = 0.14)						

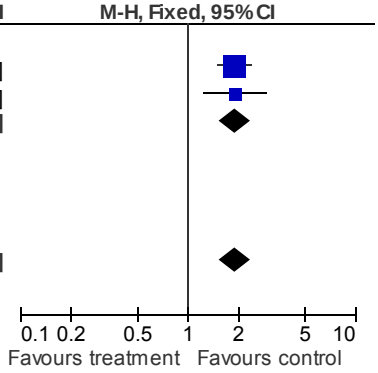


1.4 AE: 1. Metabolic SEs - Weight gain (>=7% increase from baseline) (short-to-medium-term)

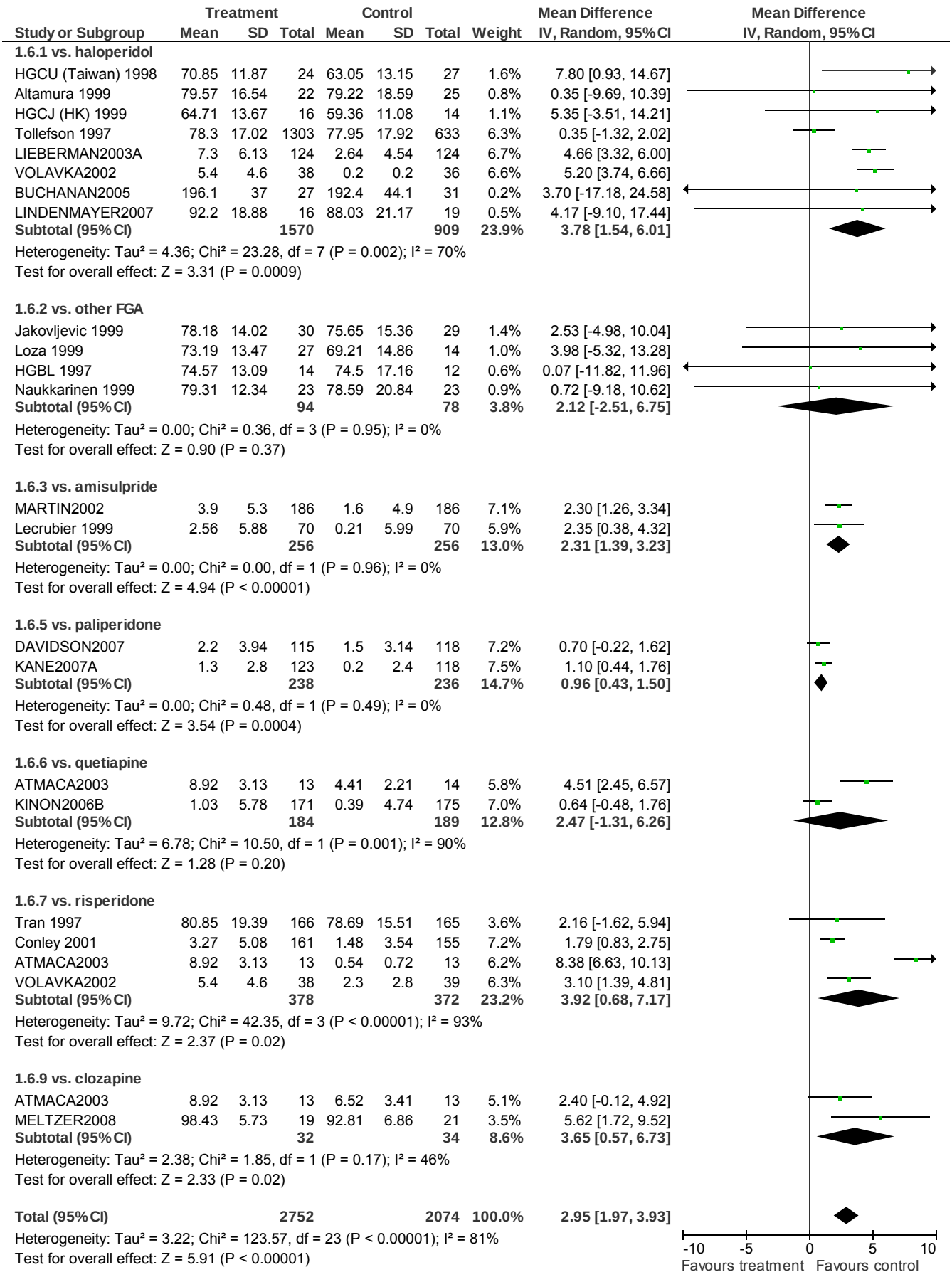


1.5 AE: 1. Metabolic SEs - Weight gain (>=7% increase from baseline) (long-term)

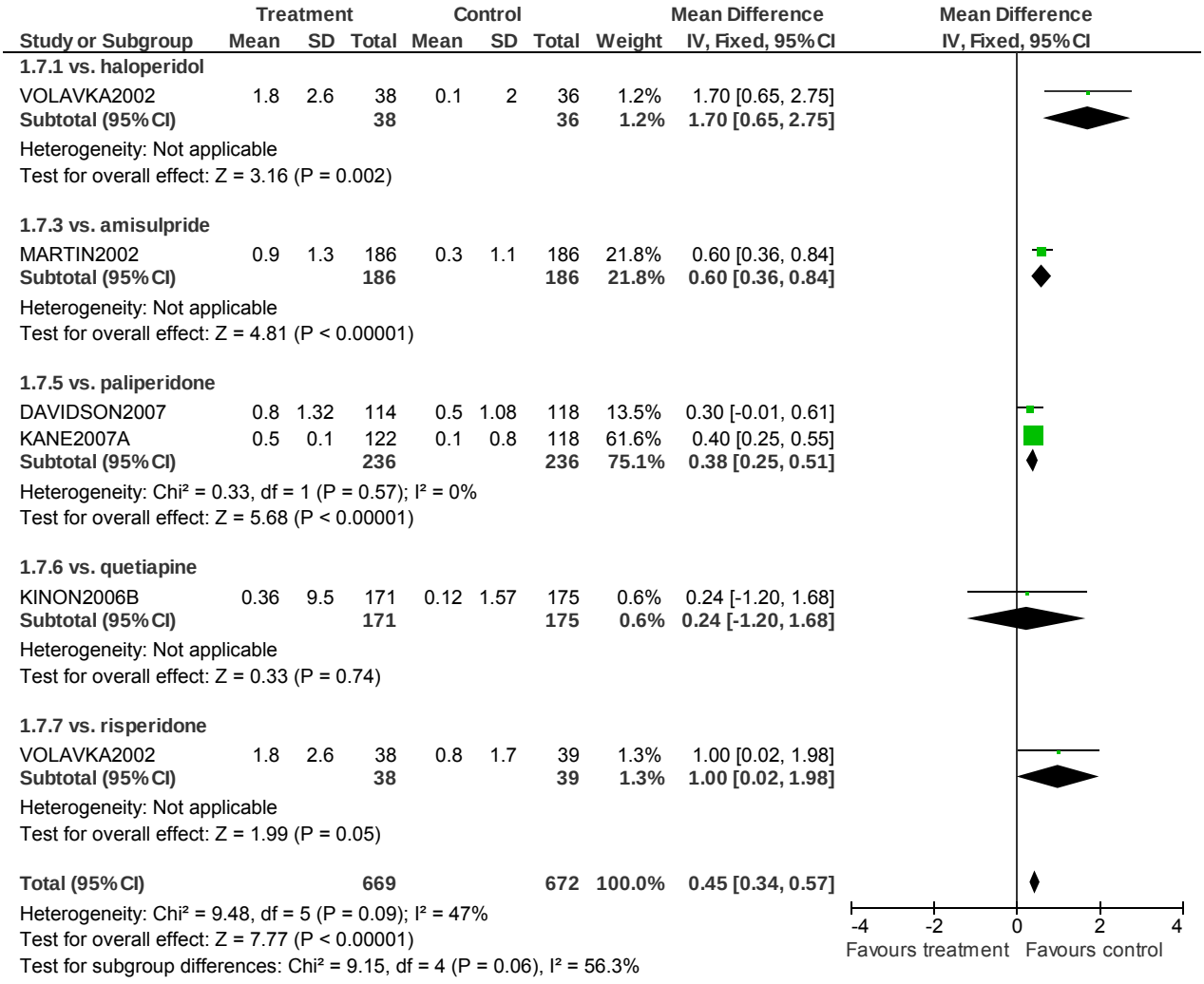
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.5.1 vs. haloperidol						
LIEBERMAN2003A	95	131	51	132	68.3%	1.88 [1.48, 2.38]
Study S029	46	134	23	128	31.7%	1.91 [1.23, 2.96]
Subtotal (95% CI)		**265**		**260**	**100.0%**	**1.89 [1.52, 2.34]**
Total events	141		74			
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.94); I² = 0%						
Test for overall effect: Z = 5.80 (P < 0.00001)						
Total (95% CI)		**265**		**260**	**100.0%**	**1.89 [1.52, 2.34]**
Total events	141		74			
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.94); I² = 0%						
Test for overall effect: Z = 5.80 (P < 0.00001)						



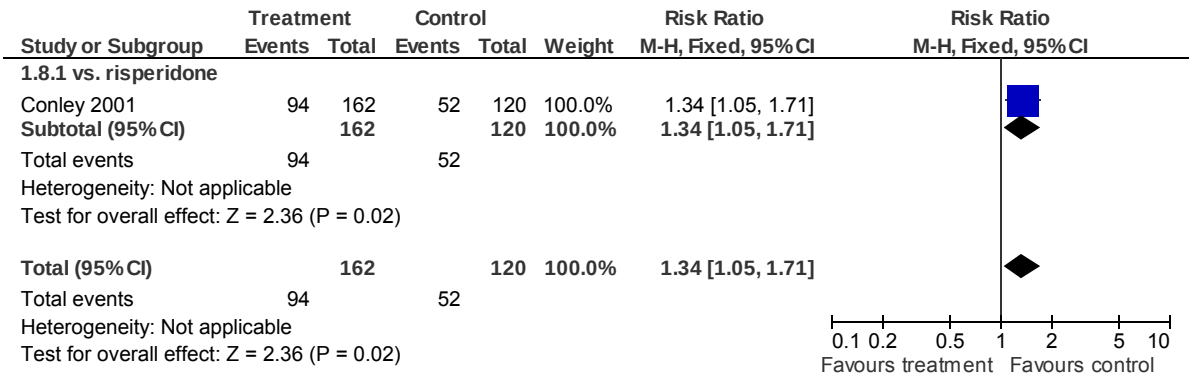
1.6 AE: 1. Metabolic SEs - Weight (endpoint or change; kg) (short-to-medium-term)



1.7 AE: 1. Metabolic SEs - BMI (change) (short-to-medium-term)

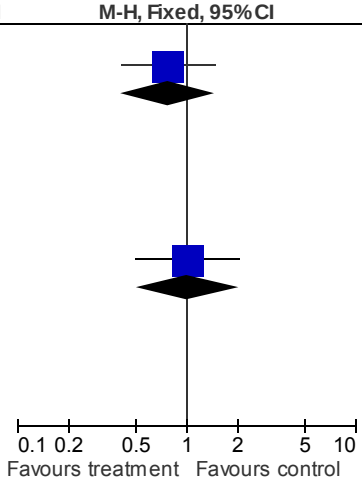


1.8 AE: 1. Metabolic SEs - LDL-C (>5% increase) (short-term)



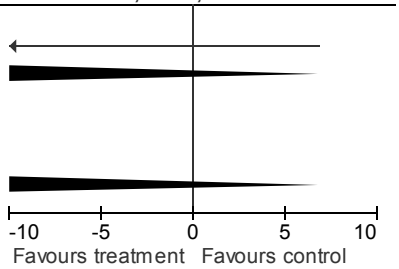
1.9 AE: 1. Metabolic SEs - Fasting total cholesterol level (>= 200 mg/dl) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.9.2 vs. quetiapine						
MCEVOY2007A	13	85	19	96	100.0%	0.77 [0.41, 1.47]
Subtotal (95% CI)		**85**		**96**	**100.0%**	**0.77 [0.41, 1.47]**
Total events	13		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						
1.9.3 vs. risperidone						
MCEVOY2007A	13	85	13	86	100.0%	1.01 [0.50, 2.05]
Subtotal (95% CI)		**85**		**86**	**100.0%**	**1.01 [0.50, 2.05]**
Total events	13		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.03 (P = 0.97)						



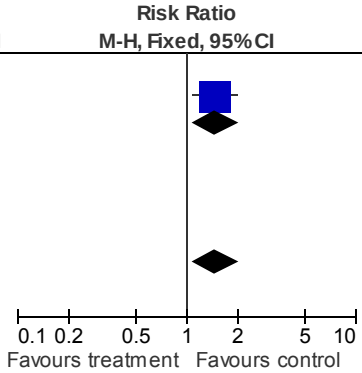
1.10 AE: 1. Metabolic SEs - Cholesterol (mg/dL; endpoint) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.10.1 vs. haloperidol								
LINDENMAYER2007	135.18	46.81	16	156.28	35.62	19	100.0%	-21.10 [-49.08, 6.88]
Subtotal (95% CI)			**16**			**19**	**100.0%**	**-21.10 [-49.08, 6.88]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.48 (P = 0.14)								
Total (95% CI)			**16**			**19**	**100.0%**	**-21.10 [-49.08, 6.88]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.48 (P = 0.14)								
Test for subgroup differences: Not applicable								



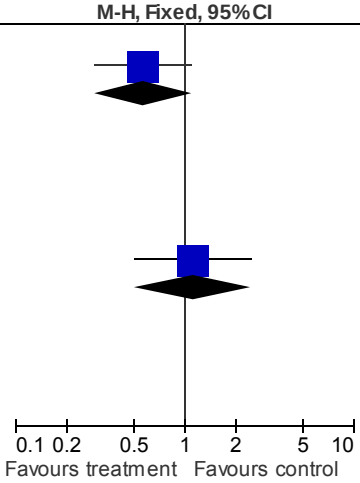
1.11 AE: 1. Metabolic SEs - Triglycerides (>10% increase) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.11.1 vs. risperidone						
Conley 2001	63	138	41	132	100.0%	1.47 [1.08, 2.01]
Subtotal (95% CI)		**138**		**132**	**100.0%**	**1.47 [1.08, 2.01]**
Total events	63		41			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.41 (P = 0.02)						
Total (95% CI)		**138**		**132**	**100.0%**	**1.47 [1.08, 2.01]**
Total events	63		41			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.41 (P = 0.02)						



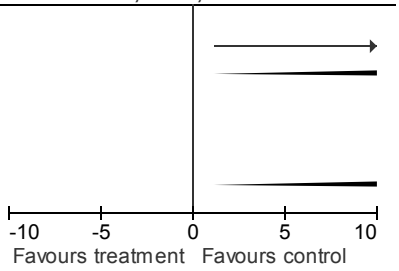
1.12 AE: 1. Metabolic SEs - Fasting triglycerides level (>= 150 mg/dl) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.12.2 vs. quetiapine						
MCEVOY2007A	11	85	22	96	100.0%	0.56 [0.29, 1.10]
Subtotal (95% CI)		**85**		**96**	**100.0%**	**0.56 [0.29, 1.10]**
Total events	11		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.69 (P = 0.09)						
1.12.3 vs. risperidone						
MCEVOY2007A	11	85	10	86	100.0%	1.11 [0.50, 2.48]
Subtotal (95% CI)		**85**		**86**	**100.0%**	**1.11 [0.50, 2.48]**
Total events	11		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.26 (P = 0.79)						



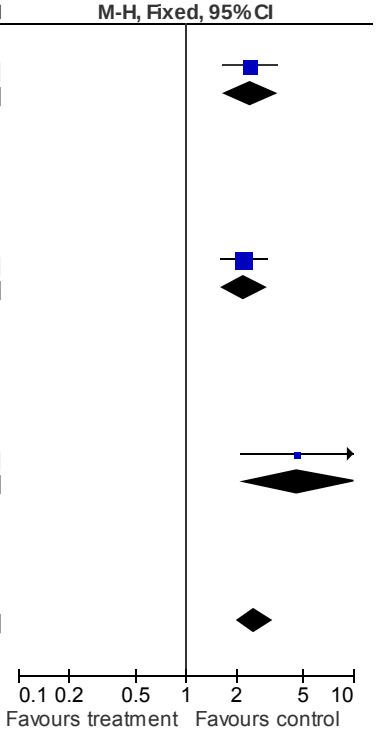
1.13 AE: 1. Metabolic SEs - Triglycerides (mg/dL; endpoint) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.13.1 vs. haloperidol								
LINDENMAYER2007	168.64	32.83	16	126.72	83.25	19	100.0%	41.92 [1.18, 82.66]
Subtotal (95% CI)			**16**			**19**	**100.0%**	**41.92 [1.18, 82.66]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.02 (P = 0.04)								
Total (95% CI)			**16**			**19**	**100.0%**	**41.92 [1.18, 82.66]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.02 (P = 0.04)								
Test for subgroup differences: Not applicable								



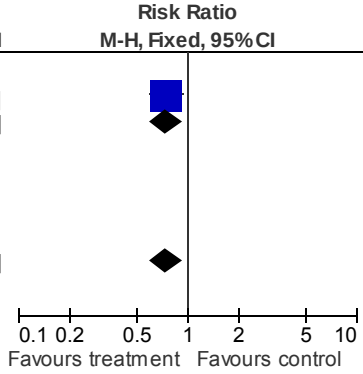
1.14 AE: 1. Metabolic SEs - Abnormal liver enzyme levels

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.14.1 vs. haloperidol (SGOT levels - long-term)						
LIEBERMAN2003A	54	100	26	116	39.1%	2.41 [1.64, 3.54]
Subtotal (95% CI)		**100**		**116**	**39.1%**	**2.41 [1.64, 3.54]**
Total events	54		26			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.49 (P < 0.00001)						
1.14.2 vs. haloperidol (SGPT levels - long-term)						
LIEBERMAN2003A	63	100	33	116	49.6%	2.21 [1.60, 3.07]
Subtotal (95% CI)		**100**		**116**	**49.6%**	**2.21 [1.60, 3.07]**
Total events	63		33			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.79 (P < 0.00001)						
1.14.3 vs. amisulpride (increased liver transaminase levels - short-term)						
MARTIN2002	32	188	7	189	11.3%	4.60 [2.08, 10.15]
Subtotal (95% CI)		**188**		**189**	**11.3%**	**4.60 [2.08, 10.15]**
Total events	32		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.77 (P = 0.0002)						
Total (95% CI)		**388**		**421**	**100.0%**	**2.56 [2.01, 3.26]**
Total events	149		66			
Heterogeneity: Chi² = 2.95, df = 2 (P = 0.23); I² = 32%						
Test for overall effect: Z = 7.64 (P < 0.00001)						



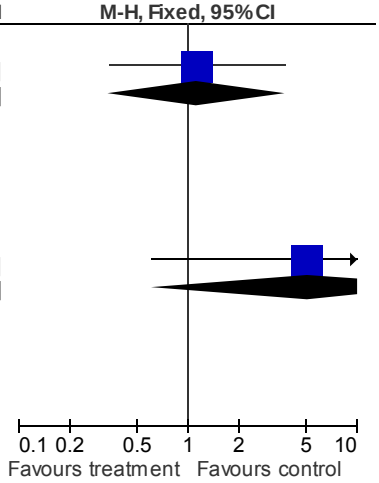
1.15 AE: 1. Metabolic SEs - Abnormal prolactin levels (long-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.15.1 vs. haloperidol						
LIEBERMAN2003A	50	100	78	116	100.0%	0.74 [0.59, 0.94]
Subtotal (95% CI)		**100**		**116**	**100.0%**	**0.74 [0.59, 0.94]**
Total events	50		78			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.49 (P = 0.01)						
Total (95% CI)		**100**		**116**	**100.0%**	**0.74 [0.59, 0.94]**
Total events	50		78			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.49 (P = 0.01)						



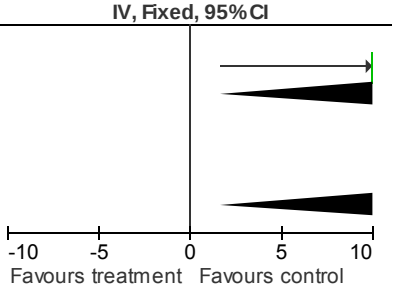
1.16 AE: 1. Metabolic SEs - Fasting glucose level (>= 100 mg/dl) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.16.2 vs. quetiapine						
MCEVOY2007A	5	85	5	96	100.0%	1.13 [0.34, 3.77]
Subtotal (95% CI)		**85**		**96**	**100.0%**	**1.13 [0.34, 3.77]**
Total events	5		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.20 (P = 0.84)						
1.16.3 vs. risperidone						
MCEVOY2007A	5	85	1	86	100.0%	5.06 [0.60, 42.40]
Subtotal (95% CI)		**85**		**86**	**100.0%**	**5.06 [0.60, 42.40]**
Total events	5		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.49 (P = 0.14)						

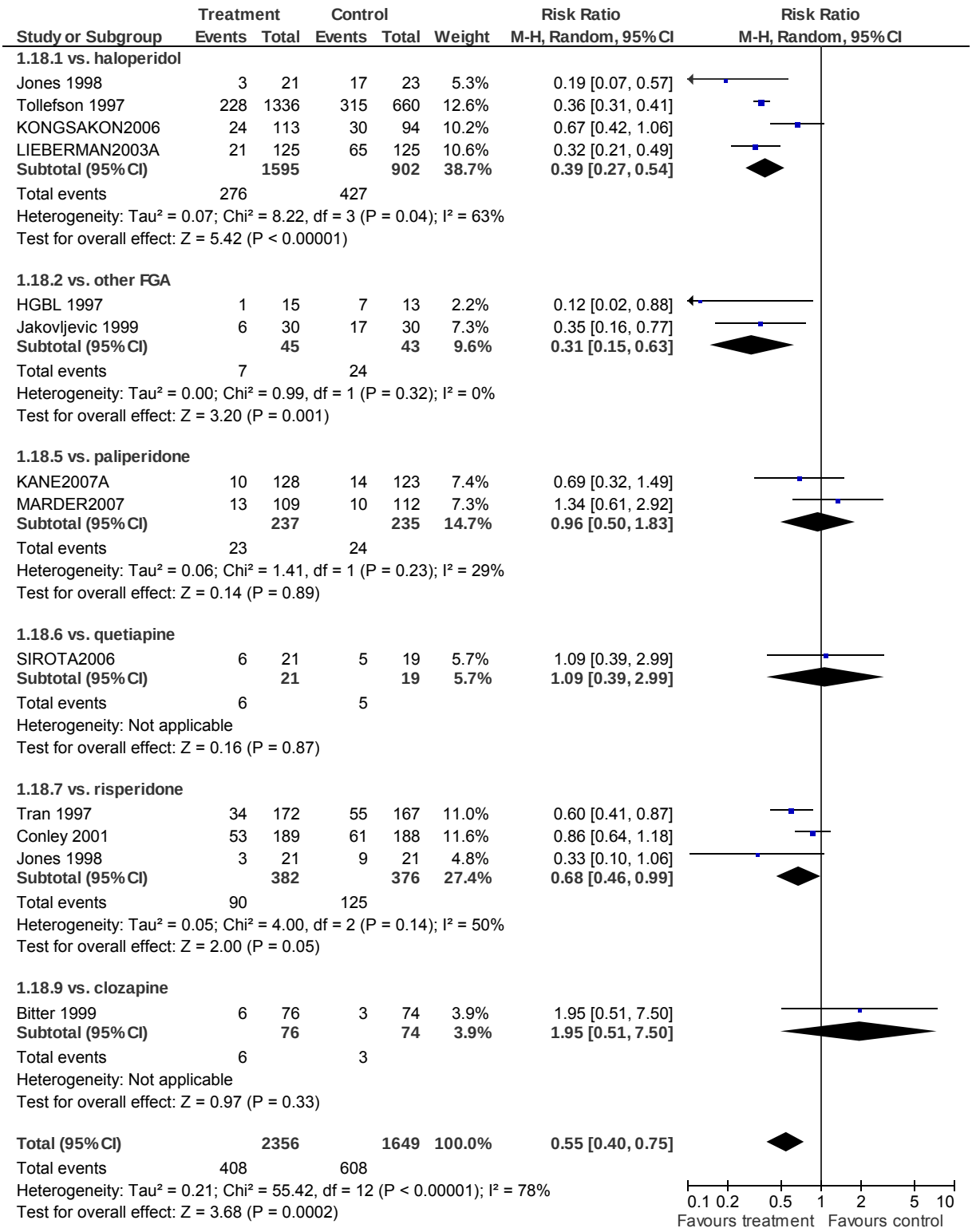


1.17 AE: 1. Metabolic SEs - Glucose (mg/dL; endpoint) (medium-term)

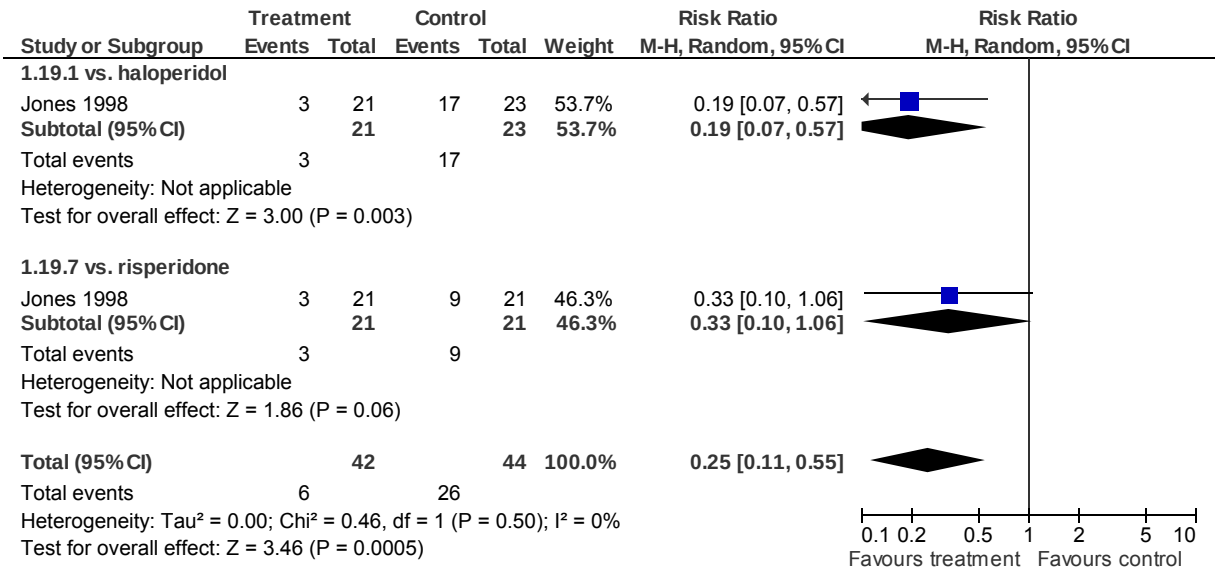
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.17.1 vs. haloperidol								
LINDENMAYER2007	94	17.49	16	83.22	7.16	19	100.0%	10.78 [1.63, 19.93]
Subtotal (95% CI)			**16**			**19**	**100.0%**	**10.78 [1.63, 19.93]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.31 (P = 0.02)								
Total (95% CI)			**16**			**19**	**100.0%**	**10.78 [1.63, 19.93]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.31 (P = 0.02)								
Test for subgroup differences: Not applicable								



1.18 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-to-medium-term)

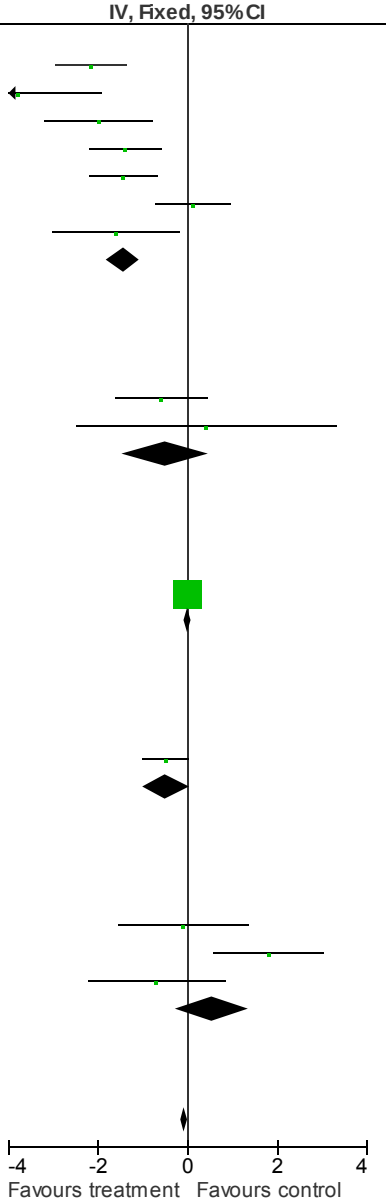


1.19 AE: 2. Neurologic SEs - Use of anticholinergic medication (long-term)

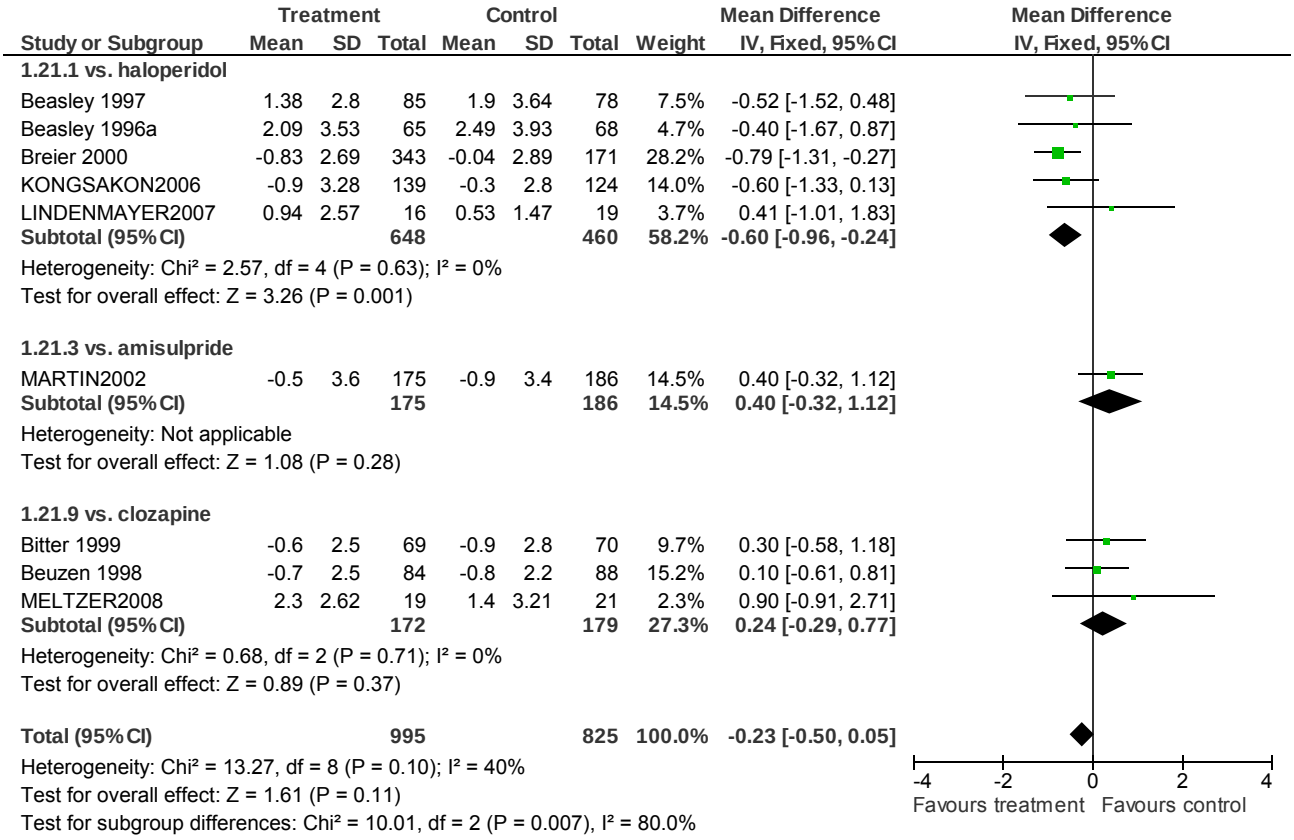


1.20 AE: 2. Neurologic SEs - Simpson-Angus Scale (endpoint/change) (short-to-medium-term)

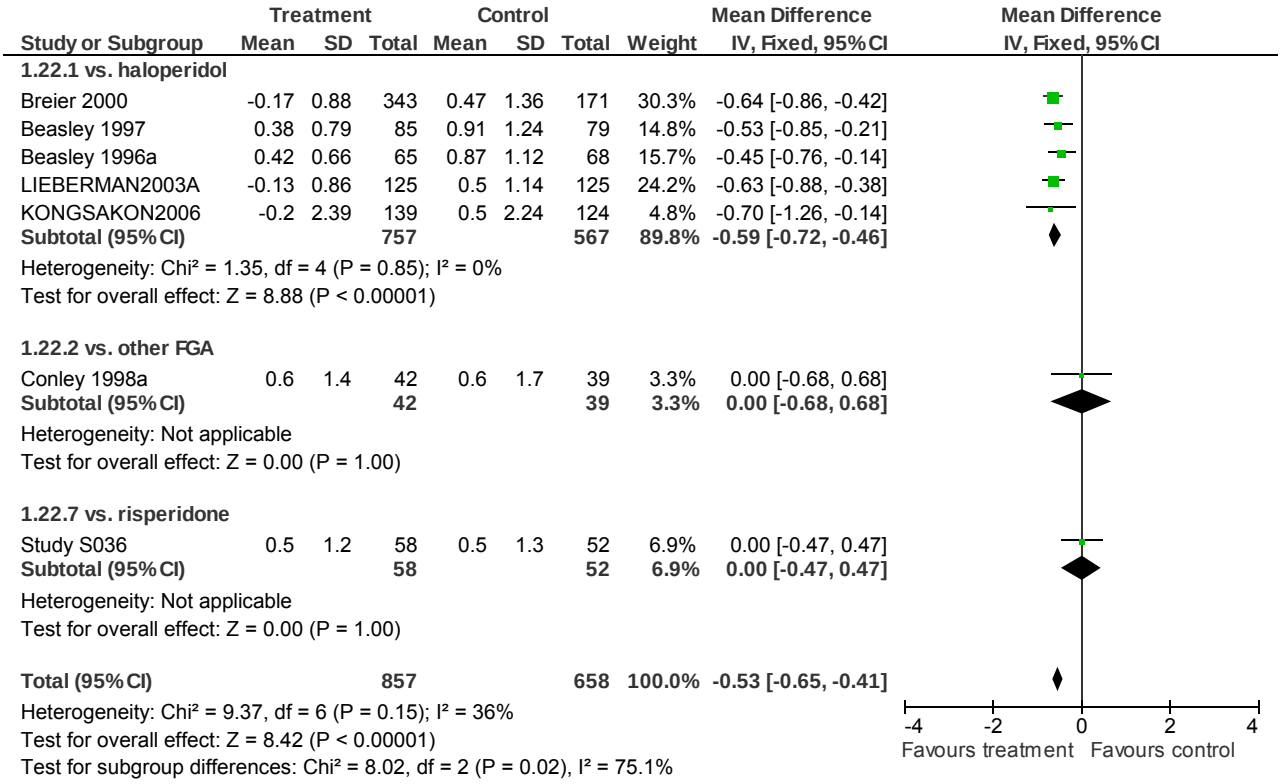
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.20.1 vs. haloperidol								
Breier 2000	-1.24	3.76	335	0.92	4.58	170	1.0%	-2.16 [-2.96, -1.36]
Beasley 1997	1.8	3.1	85	5.59	7.93	79	0.2%	-3.79 [-5.66, -1.92]
Beasley 1996a	1.35	2.44	63	3.34	4.39	67	0.4%	-1.99 [-3.20, -0.78]
KONGSAKON2006	-1	3.28	139	0.4	3.36	124	0.9%	-1.40 [-2.20, -0.60]
LIEBERMAN2003A	0	3.01	124	1.44	3.15	124	1.0%	-1.44 [-2.21, -0.67]
LINDENMAYER2007	1	1.37	16	0.89	1.15	19	0.8%	0.11 [-0.74, 0.96]
BUCHANAN2005	1.5	1.9	27	3.1	3.6	33	0.3%	-1.60 [-3.02, -0.18]
Subtotal (95% CI)			**789**			**616**	**4.7%**	**-1.44 [-1.81, -1.08]**
Heterogeneity: Chi² = 22.91, df = 6 (P = 0.0008); I² = 74%								
Test for overall effect: Z = 7.84 (P < 0.00001)								
1.20.2 vs. other FGA								
Conley 1998a	1.5	2.4	41	2.1	2.3	39	0.6%	-0.60 [-1.63, 0.43]
HGBL 1997	2	4.1	13	1.6	3.3	12	0.1%	0.40 [-2.51, 3.31]
Subtotal (95% CI)			**54**			**51**	**0.6%**	**-0.49 [-1.46, 0.48]**
Heterogeneity: Chi² = 0.40, df = 1 (P = 0.53); I² = 0%								
Test for overall effect: Z = 0.99 (P = 0.32)								
1.20.3 vs. amisulpride								
MARTIN2002	-0.1	0.4	185	-0.1	0.4	186	91.5%	0.00 [-0.08, 0.08]
Subtotal (95% CI)			**185**			**186**	**91.5%**	**0.00 [-0.08, 0.08]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
1.20.7 vs. risperidone								
Study S036	0.2	0.7	58	0.7	1.8	52	2.2%	-0.50 [-1.02, 0.02]
Subtotal (95% CI)			**58**			**52**	**2.2%**	**-0.50 [-1.02, 0.02]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.88 (P = 0.06)								
1.20.9 vs. clozapine								
Bitter 1999	-3	4.8	69	-2.9	3.9	70	0.3%	-0.10 [-1.56, 1.36]
Beuzen 1998	-1.4	3.3	84	-3.2	4.8	88	0.4%	1.80 [0.57, 3.03]
MELTZER2008	1.6	2.18	19	2.3	2.75	21	0.3%	-0.70 [-2.23, 0.83]
Subtotal (95% CI)			**172**			**179**	**0.9%**	**0.54 [-0.26, 1.34]**
Heterogeneity: Chi² = 7.32, df = 2 (P = 0.03); I² = 73%								
Test for overall effect: Z = 1.33 (P = 0.18)								
Total (95% CI)			**1258**			**1084**	**100.0%**	**-0.08 [-0.15, 0.00]**
Heterogeneity: Chi² = 94.76, df = 13 (P < 0.00001); I² = 86%								
Test for overall effect: Z = 1.92 (P = 0.05)								
Test for subgroup differences: Chi² = 64.13, df = 4 (P < 0.00001), I² = 93.8%								



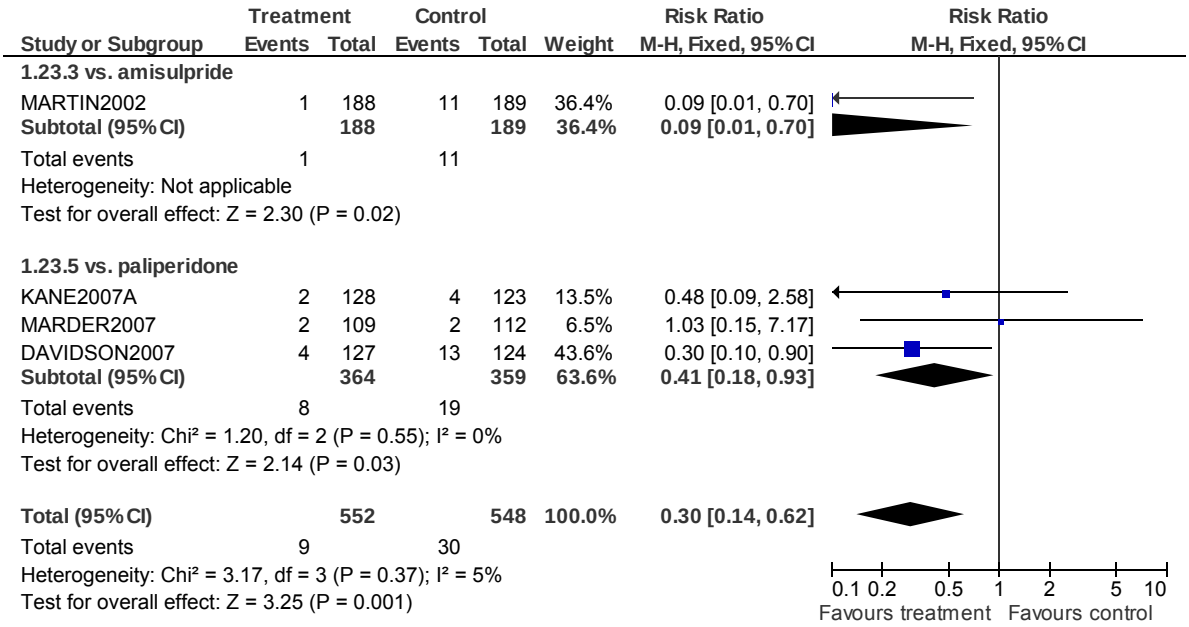
1.21 AE: 2. Neurologic SEs - AIMS (change/endpoint) (medium-term)



1.22 AE: 2. Neurologic SEs - Barnes Akathisia Scale (BAS; endpt mean) (short-term)

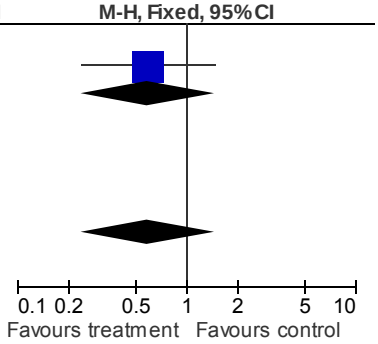


1.23 AE: 2. Neurologic SEs - Extrapyramidal disorder (treatment-emergent) (short-term)

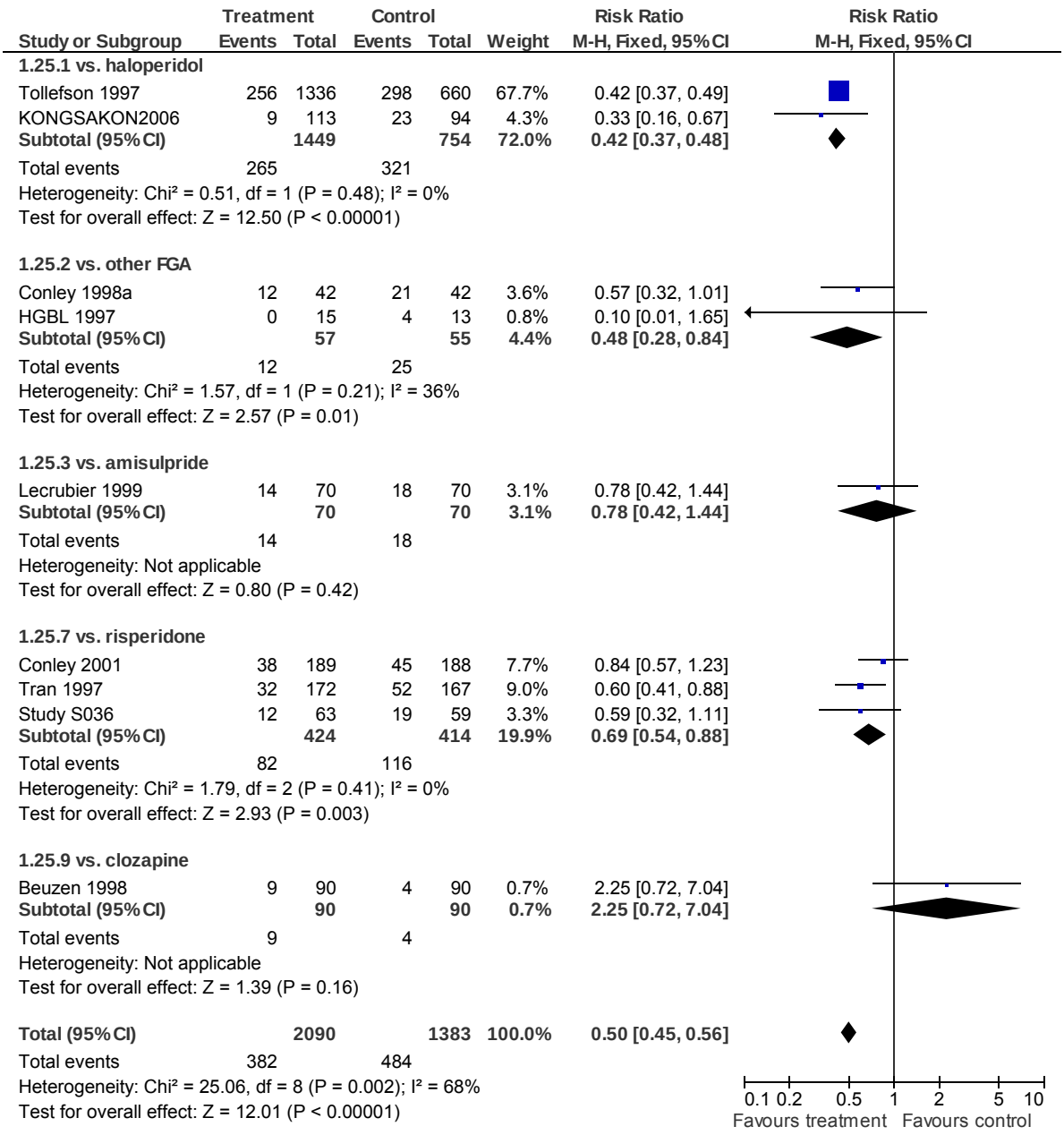


1.24 AE: 2. Neurologic SEs - Extrapyramidal disorder (treatment-emergent) (long-term)

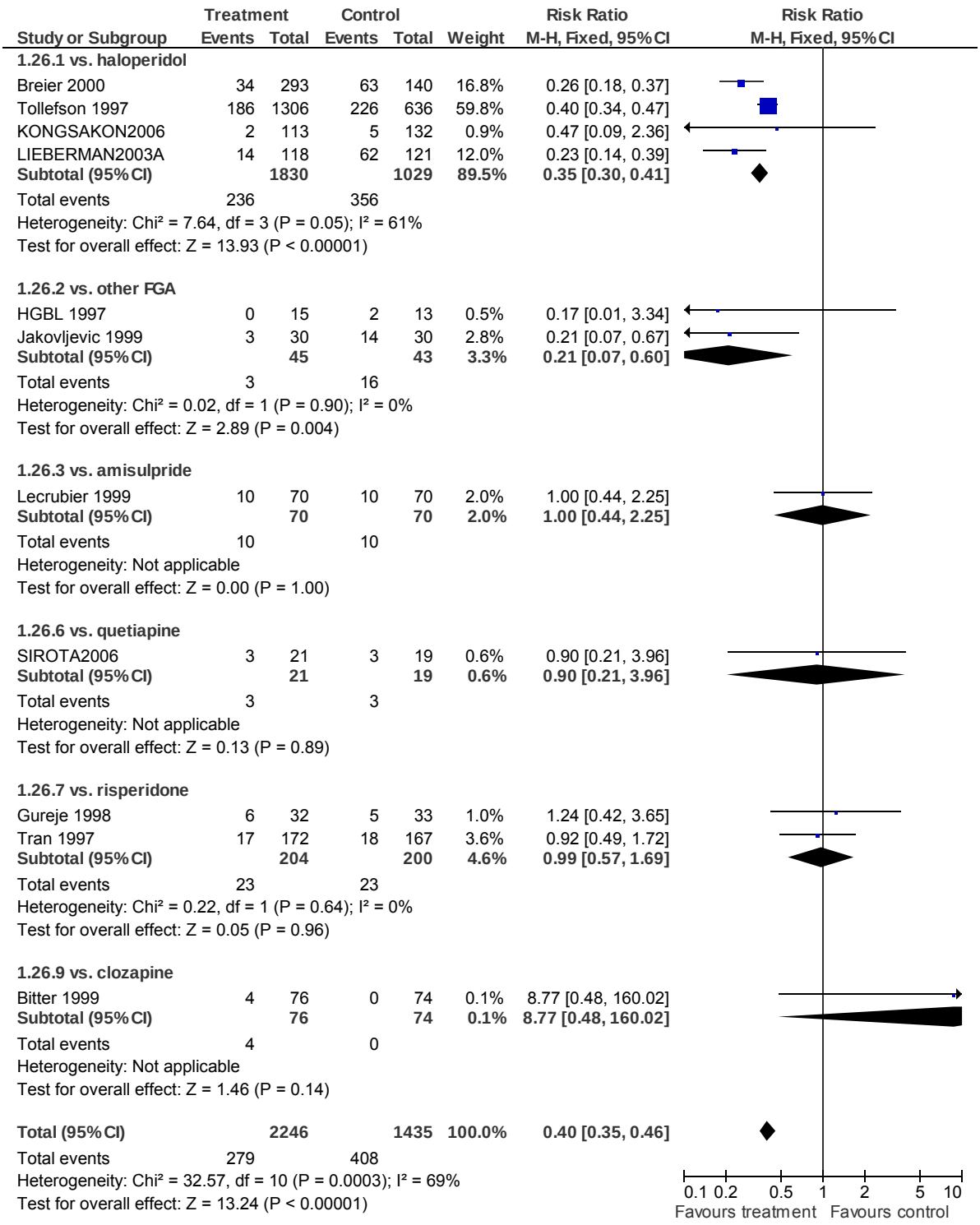
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.24.1 vs. haloperidol						
Study S029	7	144	11	133	100.0%	0.59 [0.23, 1.47]
Subtotal (95% CI)		**144**		**133**	**100.0%**	**0.59 [0.23, 1.47]**
Total events	7		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.13 (P = 0.26)						
Total (95% CI)		**144**		**133**	**100.0%**	**0.59 [0.23, 1.47]**
Total events	7		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.13 (P = 0.26)						



1.25 AE: 2. Neurologic SEs (treatment-emergent) - Any EPS (short-to-medium-term)

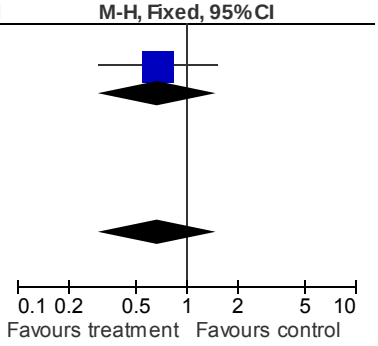


1.26 AE: 2. Neurologic SEs (treatment-emergent) - Akathisia (short-to-medium-term)

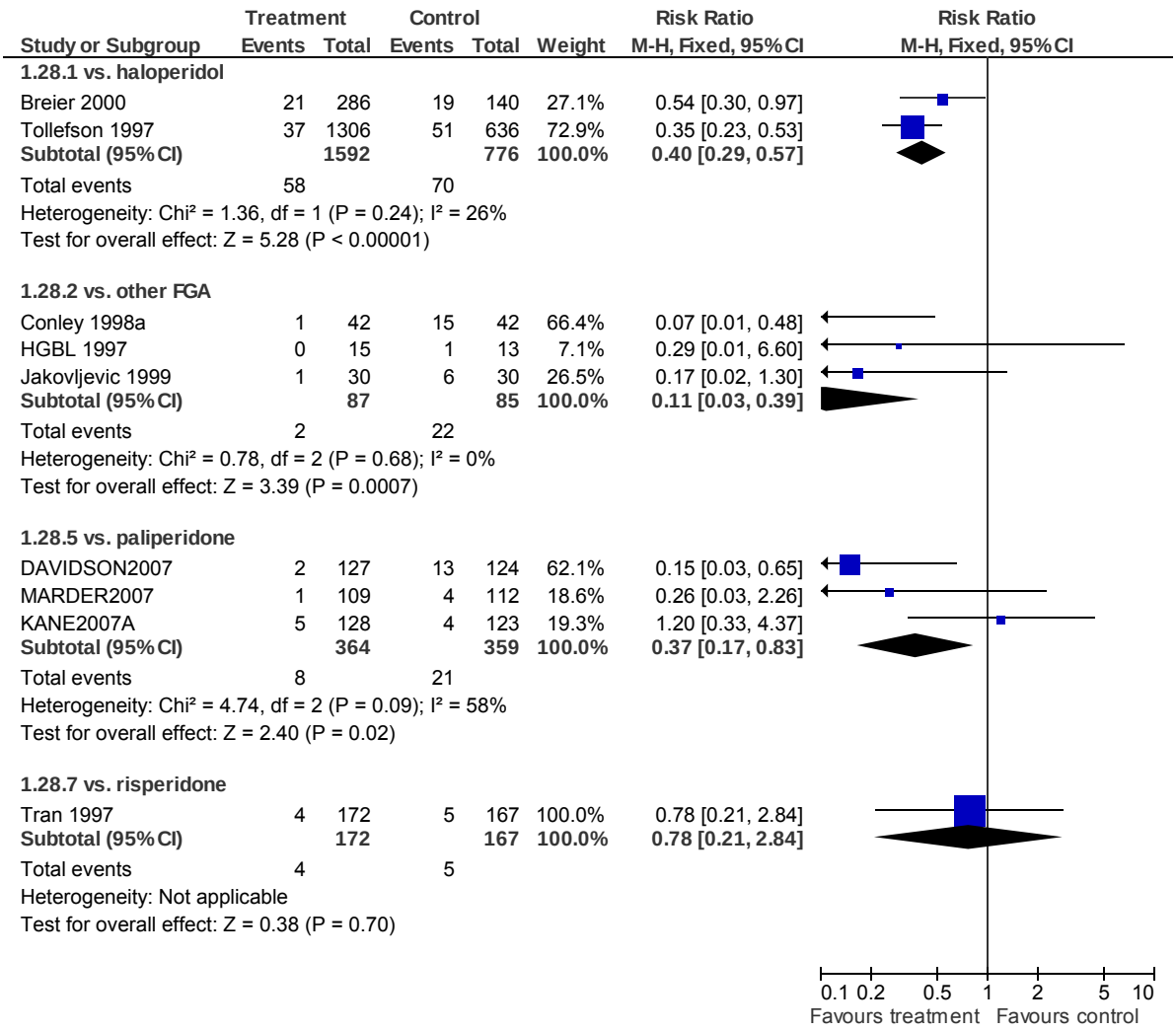


1.27 AE: 2. Neurologic SEs (treatment-emergent) - Akathisia (long-term)

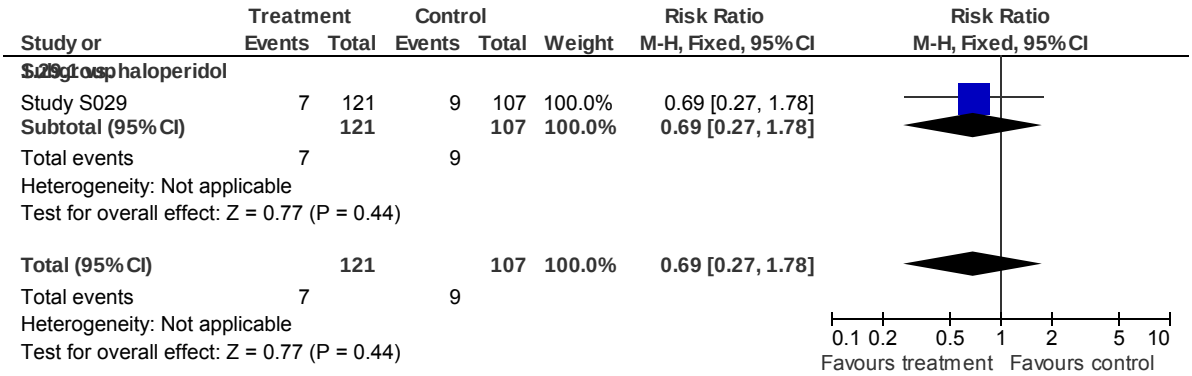
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.27.1 vs. haloperidol						
Study S029	9	121	13	117	100.0%	0.67 [0.30, 1.51]
Subtotal (95% CI)		**121**		**117**	**100.0%**	**0.67 [0.30, 1.51]**
Total events	9		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						
Total (95% CI)		**121**		**117**	**100.0%**	**0.67 [0.30, 1.51]**
Total events	9		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						



1.28 AE: 2. Neurologic SEs (treatment-emergent) - Tardive dyskinesia/dyskinetic movements (short-to-medium

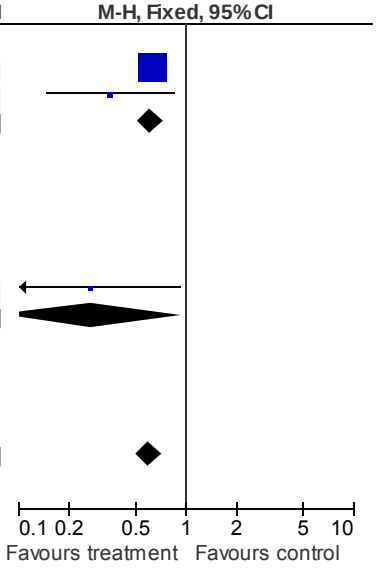


1.29 AE: 2. Neurologic SEs (treatment-emergent) - Dyskinesia (long-term)



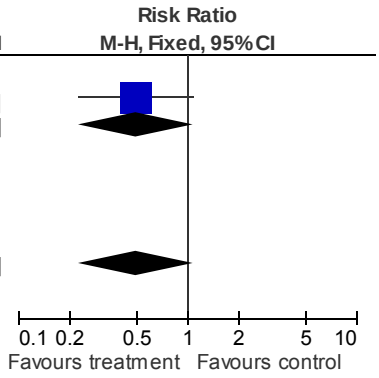
1.30 AE: 2. Neurologic SEs (treatment-emergent) - Tremor (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.30.1 vs. haloperidol						
Tollefson 1997	216	1306	167	636	89.3%	0.63 [0.53, 0.75]
KONGSAKON2006	7	144	13	94	6.3%	0.35 [0.15, 0.85]
Subtotal (95% CI)		**1450**		**730**	**95.6%**	**0.61 [0.51, 0.73]**
Total events	223		180			
Heterogeneity: Chi² = 1.62, df = 1 (P = 0.20); I² = 38%						
Test for overall effect: Z = 5.52 (P < 0.00001)						
1.30.5 vs. paliperidone						
DAVIDSON2007	3	127	11	124	4.4%	0.27 [0.08, 0.93]
Subtotal (95% CI)		**127**		**124**	**4.4%**	**0.27 [0.08, 0.93]**
Total events	3		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.07 (P = 0.04)						
Total (95% CI)		**1577**		**854**	**100.0%**	**0.60 [0.50, 0.71]**
Total events	226		191			
Heterogeneity: Chi² = 3.34, df = 2 (P = 0.19); I² = 40%						
Test for overall effect: Z = 5.85 (P < 0.00001)						



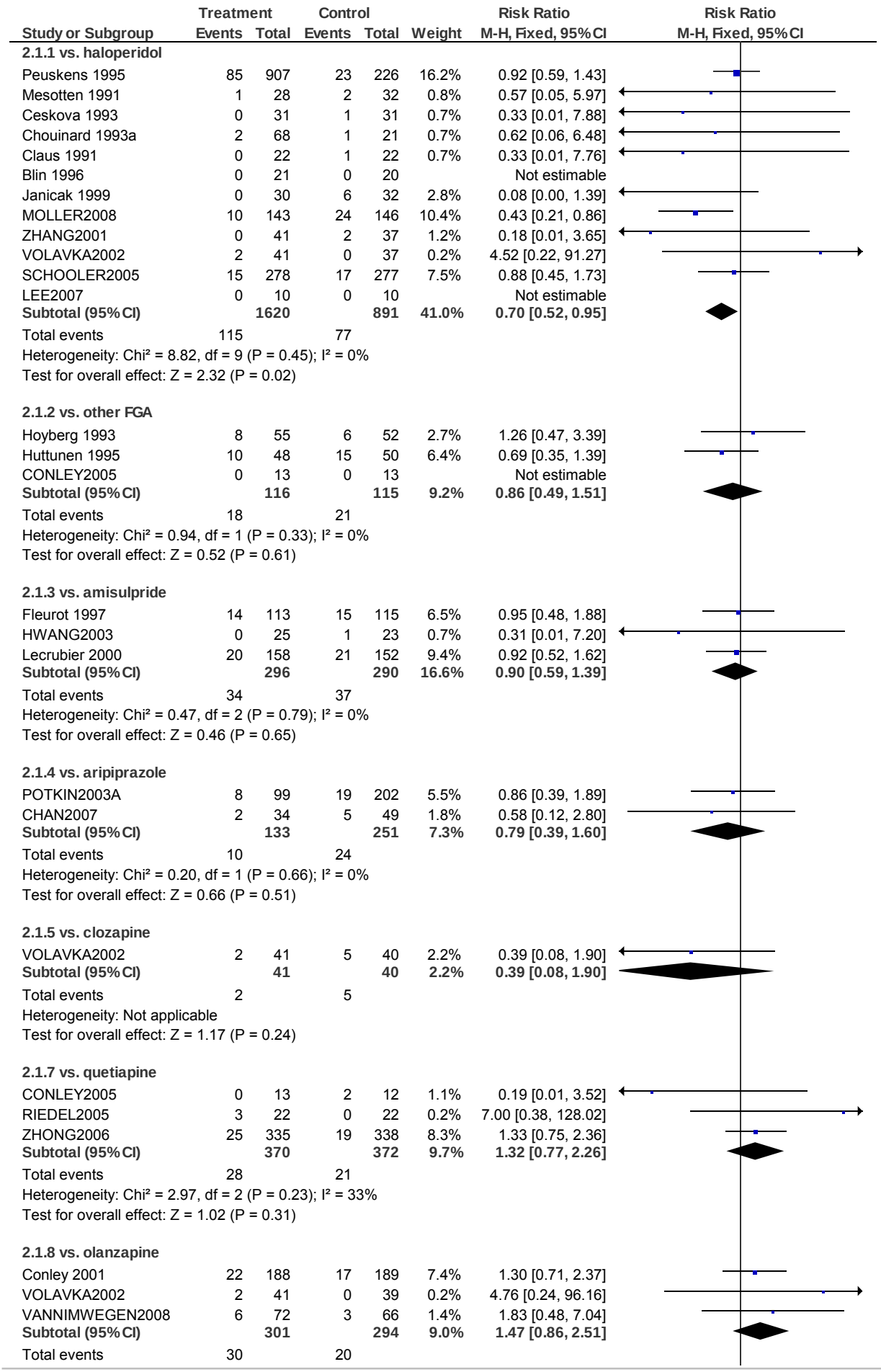
1.31 AE: 2. Neurologic SEs (treatment-emergent) - Parkinsonism (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.31.1 vs. haloperidol						
Study S029	8	76	16	75	100.0%	0.49 [0.22, 1.08]
Subtotal (95% CI)		**76**		**75**	**100.0%**	**0.49 [0.22, 1.08]**
Total events	8		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.76 (P = 0.08)						
Total (95% CI)		**76**		**75**	**100.0%**	**0.49 [0.22, 1.08]**
Total events	8		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.76 (P = 0.08)						



2 Risperidone versus another antipsychotic drug (overall SE analysis)

2.1 Leaving the study early: 3: Adverse event (short-to-medium-term)



Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 vs. haloperidol						
Peuskens 1995	85	907	23	226	16.2%	0.92 [0.59, 1.43]
Mesotten 1991	1	28	2	32	0.8%	0.57 [0.05, 5.97]
Ceskova 1993	0	31	1	31	0.7%	0.33 [0.01, 7.88]
Chouinard 1993a	2	68	1	21	0.7%	0.62 [0.06, 6.48]
Claus 1991	0	22	1	22	0.7%	0.33 [0.01, 7.76]
Blin 1996	0	21	0	20		Not estimable
Janicak 1999	0	30	6	32	2.8%	0.08 [0.00, 1.39]
MOLLER2008	10	143	24	146	10.4%	0.43 [0.21, 0.86]
ZHANG2001	0	41	2	37	1.2%	0.18 [0.01, 3.65]
VOLAVKA2002	2	41	0	37	0.2%	4.52 [0.22, 91.27]
SCHOOLER2005	15	278	17	277	7.5%	0.88 [0.45, 1.73]
LEE2007	0	10	0	10		Not estimable
Subtotal (95% CI)		**1620**		**891**	**41.0%**	**0.70 [0.52, 0.95]**
Total events	115		77			
Heterogeneity: Chi² = 8.82, df = 9 (P = 0.45); I² = 0%						
Test for overall effect: Z = 2.32 (P = 0.02)						
2.1.2 vs. other FGA						
Hoyberg 1993	8	55	6	52	2.7%	1.26 [0.47, 3.39]
Huttunen 1995	10	48	15	50	6.4%	0.69 [0.35, 1.39]
CONLEY2005	0	13	0	13		Not estimable
Subtotal (95% CI)		**116**		**115**	**9.2%**	**0.86 [0.49, 1.51]**
Total events	18		21			
Heterogeneity: Chi² = 0.94, df = 1 (P = 0.33); I² = 0%						
Test for overall effect: Z = 0.52 (P = 0.61)						
2.1.3 vs. amisulpride						
Fleurot 1997	14	113	15	115	6.5%	0.95 [0.48, 1.88]
HWANG2003	0	25	1	23	0.7%	0.31 [0.01, 7.20]
Lecrubier 2000	20	158	21	152	9.4%	0.92 [0.52, 1.62]
Subtotal (95% CI)		**296**		**290**	**16.6%**	**0.90 [0.59, 1.39]**
Total events	34		37			
Heterogeneity: Chi² = 0.47, df = 2 (P = 0.79); I² = 0%						
Test for overall effect: Z = 0.46 (P = 0.65)						
2.1.4 vs. aripiprazole						
POTKIN2003A	8	99	19	202	5.5%	0.86 [0.39, 1.89]
CHAN2007	2	34	5	49	1.8%	0.58 [0.12, 2.80]
Subtotal (95% CI)		**133**		**251**	**7.3%**	**0.79 [0.39, 1.60]**
Total events	10		24			
Heterogeneity: Chi² = 0.20, df = 1 (P = 0.66); I² = 0%						
Test for overall effect: Z = 0.66 (P = 0.51)						
2.1.5 vs. clozapine						
VOLAVKA2002	2	41	5	40	2.2%	0.39 [0.08, 1.90]
Subtotal (95% CI)		**41**		**40**	**2.2%**	**0.39 [0.08, 1.90]**
Total events	2		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.17 (P = 0.24)						
2.1.7 vs. quetiapine						
CONLEY2005	0	13	2	12	1.1%	0.19 [0.01, 3.52]
RIEDEL2005	3	22	0	22	0.2%	7.00 [0.38, 128.02]
ZHONG2006	25	335	19	338	8.3%	1.33 [0.75, 2.36]
Subtotal (95% CI)		**370**		**372**	**9.7%**	**1.32 [0.77, 2.26]**
Total events	28		21			
Heterogeneity: Chi² = 2.97, df = 2 (P = 0.23); I² = 33%						
Test for overall effect: Z = 1.02 (P = 0.31)						
2.1.8 vs. olanzapine						
Conley 2001	22	188	17	189	7.4%	1.30 [0.71, 2.37]
VOLAVKA2002	2	41	0	39	0.2%	4.76 [0.24, 96.16]
VANNIMWEGEN2008	6	72	3	66	1.4%	1.83 [0.48, 7.04]
Subtotal (95% CI)		**301**		**294**	**9.0%**	**1.47 [0.86, 2.51]**
Total events	30		20			

Heterogeneity: Chi² = 0.85, df = 2 (P = 0.65); I² = 0%
Test for overall effect: Z = 1.41 (P = 0.16)

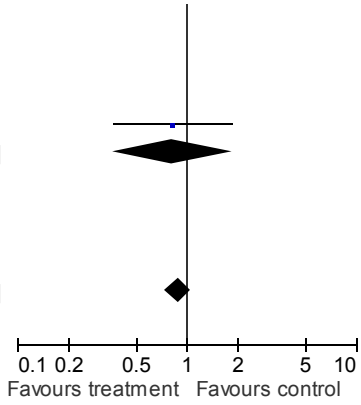
2.1.10 vs. sertindole

AZORIN2006	9	89	12	97	5.0%	0.82 [0.36, 1.85]
Subtotal (95% CI)		**89**		**97**	**5.0%**	**0.82 [0.36, 1.85]**
Total events	9		12			

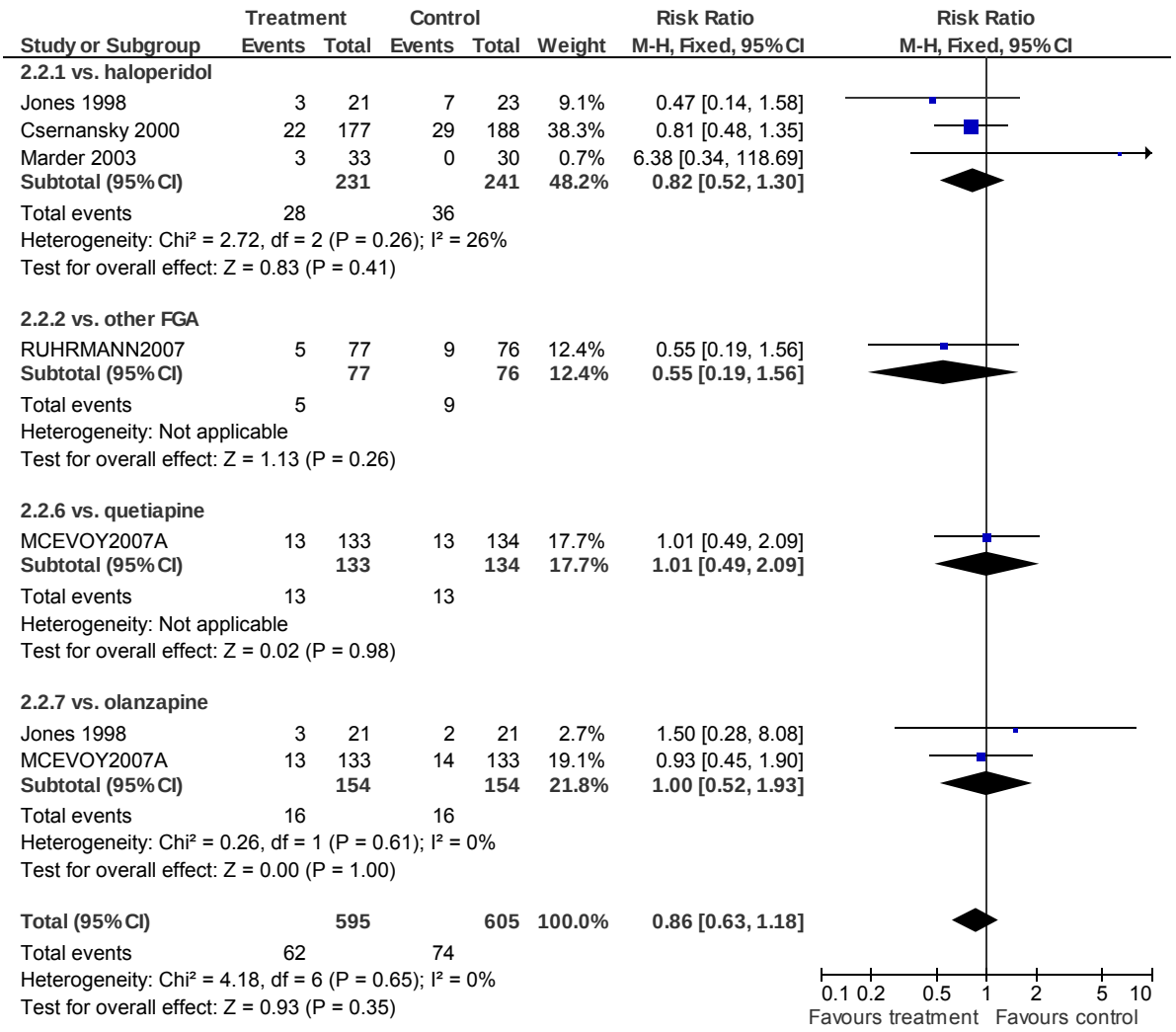
Heterogeneity: Not applicable
Test for overall effect: Z = 0.48 (P = 0.63)

Total (95% CI)		**2966**		**2350**	**100.0%**	**0.88 [0.74, 1.06]**
Total events	246		217			

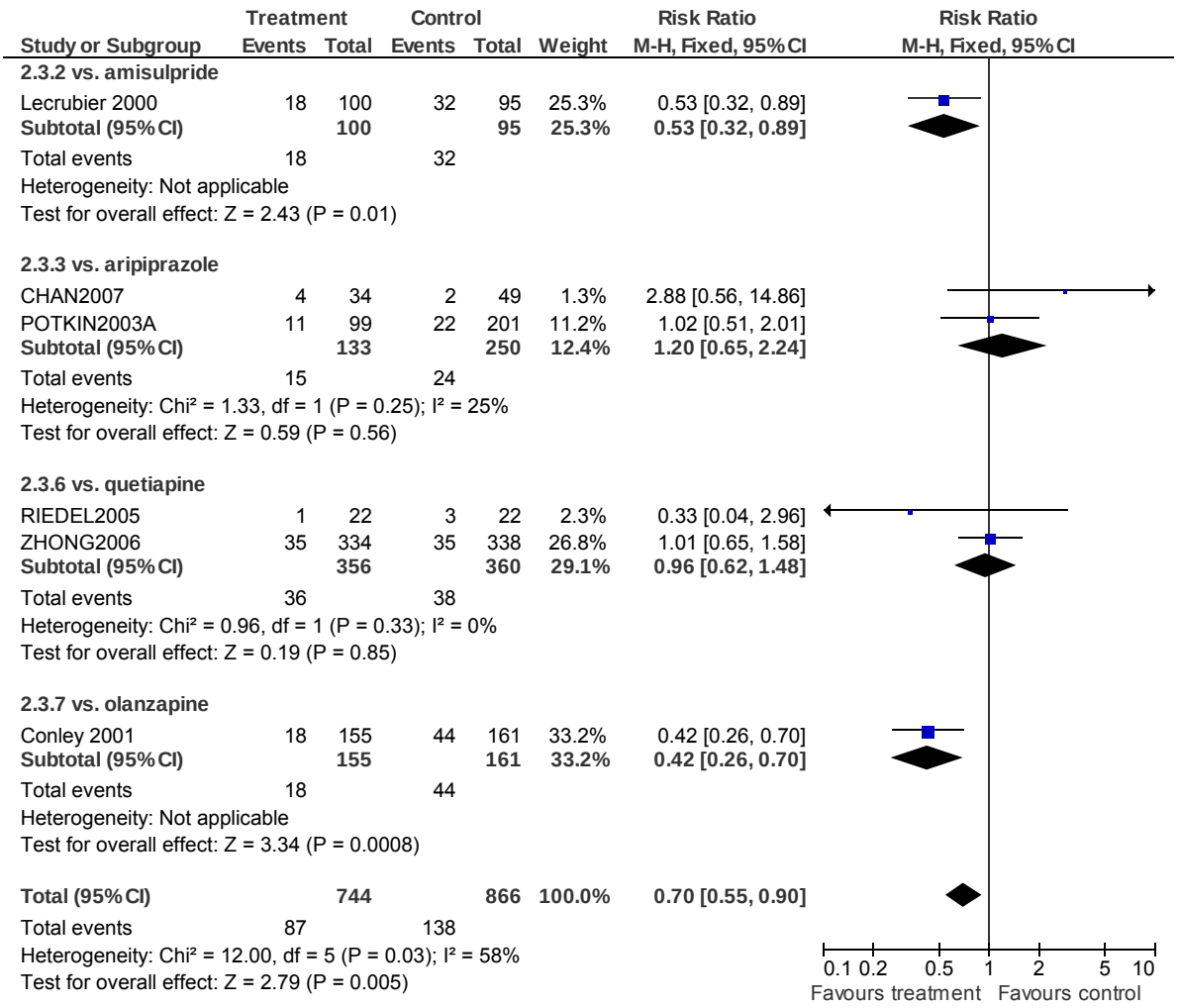
Heterogeneity: Chi² = 21.75, df = 24 (P = 0.59); I² = 0%
Test for overall effect: Z = 1.35 (P = 0.18)



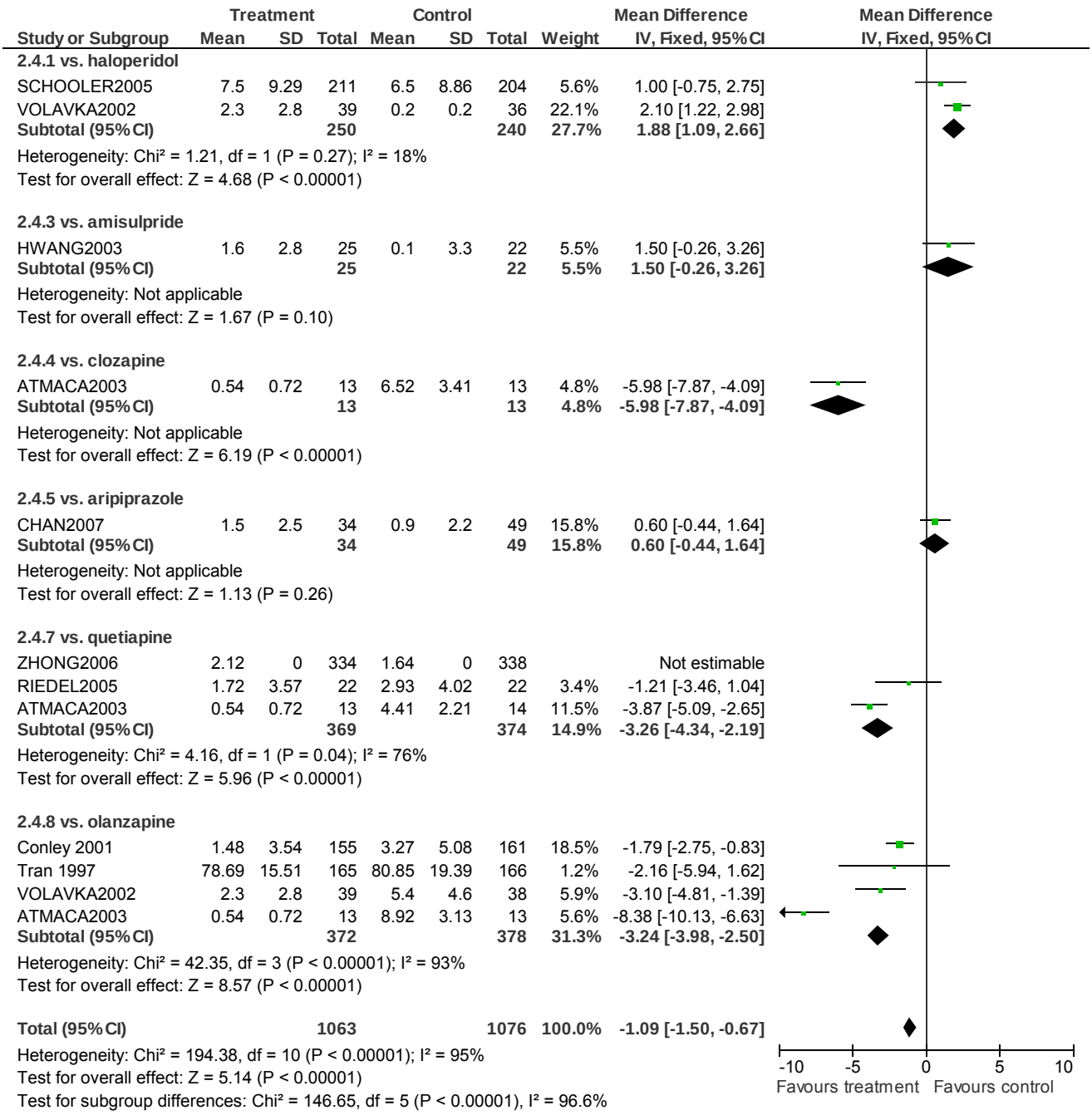
2.2 Leaving the study early: 3: Adverse event (long-term)



2.3 AE: 1. Metabolic SEs - Weight gain (>=7% increase from baseline) (short-to-medium-term)

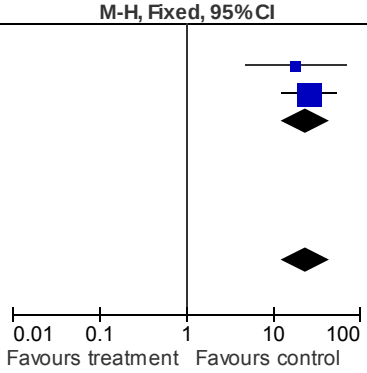


2.4 AE: 1. Metabolic SEs - Weight (endpoint or change; kg) (short-to-medium-term)



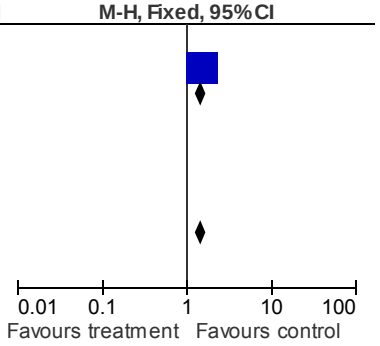
2.5 AE: 1. Metabolic SEs - Abnormal prolactin levels (short-to-medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.5.4 vs. aripiprazole						
CHAN2007	26	28	2	39	26.6%	18.11 [4.68, 70.11]
POTKIN2003A	89	99	7	201	73.4%	25.81 [12.43, 53.61]
Subtotal (95% CI)		**127**		**240**	**100.0%**	**23.77 [12.51, 45.13]**
Total events	115		9			
Heterogeneity: Chi² = 0.20, df = 1 (P = 0.65); I² = 0%						
Test for overall effect: Z = 9.68 (P < 0.00001)						
Total (95% CI)		**127**		**240**	**100.0%**	**23.77 [12.51, 45.13]**
Total events	115		9			
Heterogeneity: Chi² = 0.20, df = 1 (P = 0.65); I² = 0%						
Test for overall effect: Z = 9.68 (P < 0.00001)						



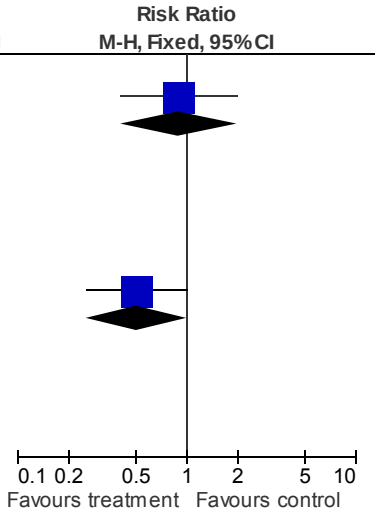
2.6 AE: 1. Metabolic SEs - Abnormal prolactin levels (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.6.1 vs. haloperidol						
SCHOOLER2005	189	256	124	249	100.0%	1.48 [1.28, 1.71]
Subtotal (95% CI)		**256**		**249**	**100.0%**	**1.48 [1.28, 1.71]**
Total events	189		124			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.34 (P < 0.00001)						
Total (95% CI)		**256**		**249**	**100.0%**	**1.48 [1.28, 1.71]**
Total events	189		124			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.34 (P < 0.00001)						



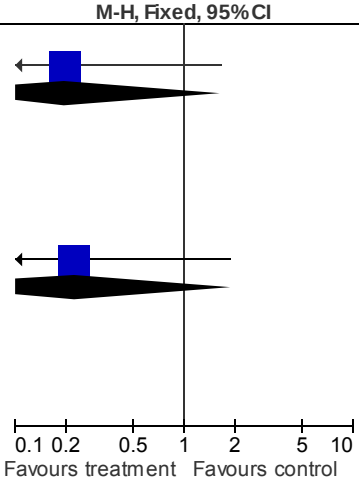
2.7 AE: 1. Metabolic SEs - Fasting triglycerides level (>= 150 mg/dl) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.7.1 vs. olanzapine						
MCEVOY2007A	10	86	11	85	100.0%	0.90 [0.40, 2.00]
Subtotal (95% CI)		**86**		**85**	**100.0%**	**0.90 [0.40, 2.00]**
Total events	10		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.26 (P = 0.79)						
2.7.2 vs. quetiapine						
MCEVOY2007A	10	86	22	96	100.0%	0.51 [0.25, 1.01]
Subtotal (95% CI)		**86**		**96**	**100.0%**	**0.51 [0.25, 1.01]**
Total events	10		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.93 (P = 0.05)						



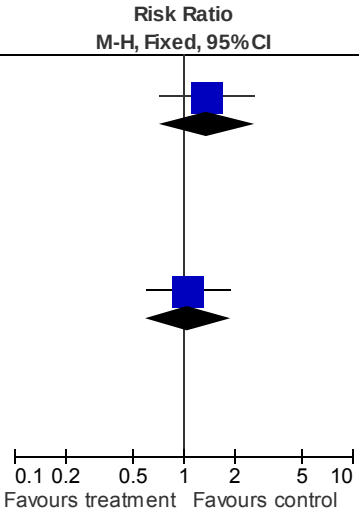
2.8 AE: 1. Metabolic SEs - Fasting glucose level (>= 100 mg/dl) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.8.1 vs. olanzapine						
MCEVOY2007A	1	86	5	85	100.0%	0.20 [0.02, 1.66]
Subtotal (95% CI)		**86**		**85**	**100.0%**	**0.20 [0.02, 1.66]**
Total events	1		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.49 (P = 0.14)						
2.8.2 vs. quetiapine						
MCEVOY2007A	1	86	5	96	100.0%	0.22 [0.03, 1.87]
Subtotal (95% CI)		**86**		**96**	**100.0%**	**0.22 [0.03, 1.87]**
Total events	1		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.38 (P = 0.17)						



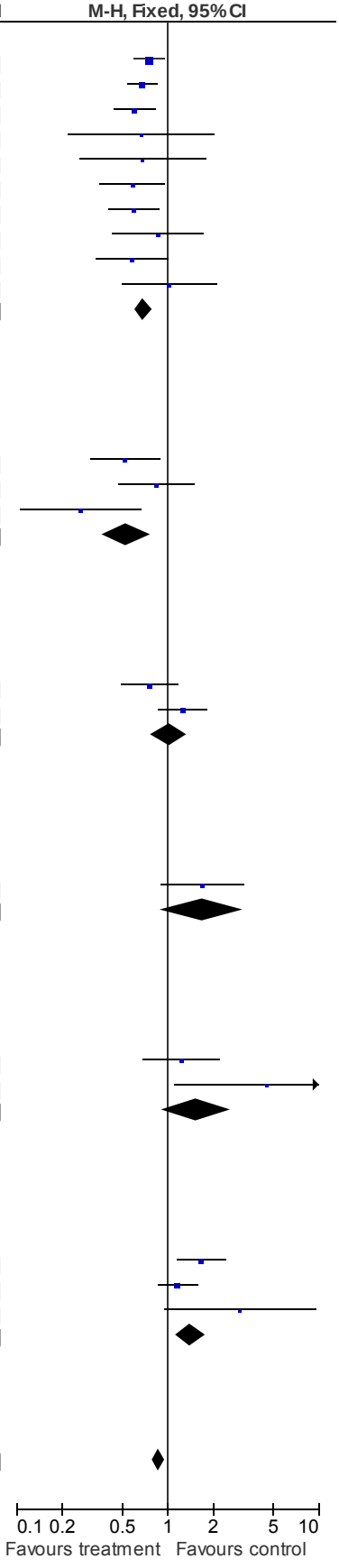
2.9 AE: 1. Metabolic SEs - Fasting total cholesterol level (>= 200 mg/dl) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.9.1 vs. olanzapine						
MCEVOY2007A	18	86	13	85	100.0%	1.37 [0.72, 2.61]
Subtotal (95% CI)		**86**		**85**	**100.0%**	**1.37 [0.72, 2.61]**
Total events	18		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						
2.9.2 vs. quetiapine						
MCEVOY2007A	18	86	19	96	100.0%	1.06 [0.59, 1.88]
Subtotal (95% CI)		**86**		**96**	**100.0%**	**1.06 [0.59, 1.88]**
Total events	18		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.19 (P = 0.85)						



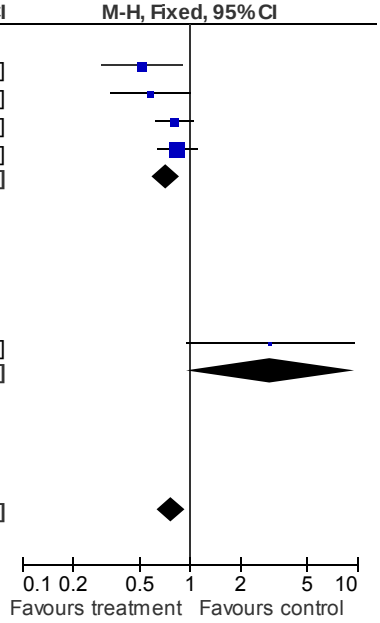
2.10 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-to-medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.10.1 vs. haloperidol						
Peuskens 1995	201	907	67	226	18.7%	0.75 [0.59, 0.95]
Emsley 1995	50	99	63	84	11.9%	0.67 [0.53, 0.85]
Marder 1994	72	256	31	66	8.6%	0.60 [0.43, 0.83]
Claus 1991	4	22	6	22	1.0%	0.67 [0.22, 2.04]
Blin 1996	5	21	7	20	1.3%	0.68 [0.26, 1.80]
Janicak 1999	12	30	22	32	3.7%	0.58 [0.35, 0.96]
Chouinard 1993a	29	68	15	21	4.0%	0.60 [0.41, 0.88]
Mesotten 1991	9	28	12	32	2.0%	0.86 [0.43, 1.73]
Jones 1998	9	21	17	23	2.8%	0.58 [0.33, 1.01]
Heck 2000	11	40	10	37	1.8%	1.02 [0.49, 2.11]
Subtotal (95% CI)		**1492**		**563**	**55.8%**	**0.69 [0.61, 0.78]**
Total events	402		250			
Heterogeneity: Chi² = 4.04, df = 9 (P = 0.91); I² = 0%						
Test for overall effect: Z = 5.80 (P < 0.00001)						
2.10.2 vs. other FGA						
Huttunen 1995	13	48	26	50	4.4%	0.52 [0.30, 0.89]
Hoyberg 1993	15	55	17	52	3.0%	0.83 [0.47, 1.49]
RUHRMANN2007	5	72	19	72	3.3%	0.26 [0.10, 0.67]
Subtotal (95% CI)		**175**		**174**	**10.8%**	**0.53 [0.37, 0.76]**
Total events	33		62			
Heterogeneity: Chi² = 4.52, df = 2 (P = 0.10); I² = 56%						
Test for overall effect: Z = 3.45 (P = 0.0006)						
2.10.3 vs. amisulpride						
Fleurot 1997	26	113	35	115	6.1%	0.76 [0.49, 1.17]
Lecrubier 2000	47	158	36	152	6.4%	1.26 [0.87, 1.82]
Subtotal (95% CI)		**271**		**267**	**12.5%**	**1.01 [0.76, 1.34]**
Total events	73		71			
Heterogeneity: Chi² = 3.01, df = 1 (P = 0.08); I² = 67%						
Test for overall effect: Z = 0.09 (P = 0.93)						
2.10.4 vs. aripiprazole						
CHAN2007	14	34	12	49	1.7%	1.68 [0.89, 3.17]
Subtotal (95% CI)		**34**		**49**	**1.7%**	**1.68 [0.89, 3.17]**
Total events	14		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.60 (P = 0.11)						
2.10.6 vs. quetiapine						
ZHONG2006	23	334	19	338	3.3%	1.23 [0.68, 2.21]
RIEDEL2005	9	22	2	22	0.3%	4.50 [1.09, 18.50]
Subtotal (95% CI)		**356**		**360**	**3.6%**	**1.54 [0.91, 2.61]**
Total events	32		21			
Heterogeneity: Chi² = 2.79, df = 1 (P = 0.09); I² = 64%						
Test for overall effect: Z = 1.60 (P = 0.11)						
2.10.7 vs. olanzapine						
Tran 1997	55	167	34	172	5.8%	1.67 [1.15, 2.41]
Conley 2001	61	188	53	189	9.2%	1.16 [0.85, 1.57]
Jones 1998	9	21	3	21	0.5%	3.00 [0.94, 9.55]
Subtotal (95% CI)		**376**		**382**	**15.6%**	**1.41 [1.12, 1.78]**
Total events	125		90			
Heterogeneity: Chi² = 4.00, df = 2 (P = 0.14); I² = 50%						
Test for overall effect: Z = 2.92 (P = 0.004)						
Total (95% CI)		**2704**		**1795**	**100.0%**	**0.87 [0.79, 0.96]**
Total events	679		506			
Heterogeneity: Chi² = 64.64, df = 20 (P < 0.00001); I² = 69%						
Test for overall effect: Z = 2.79 (P = 0.005)						

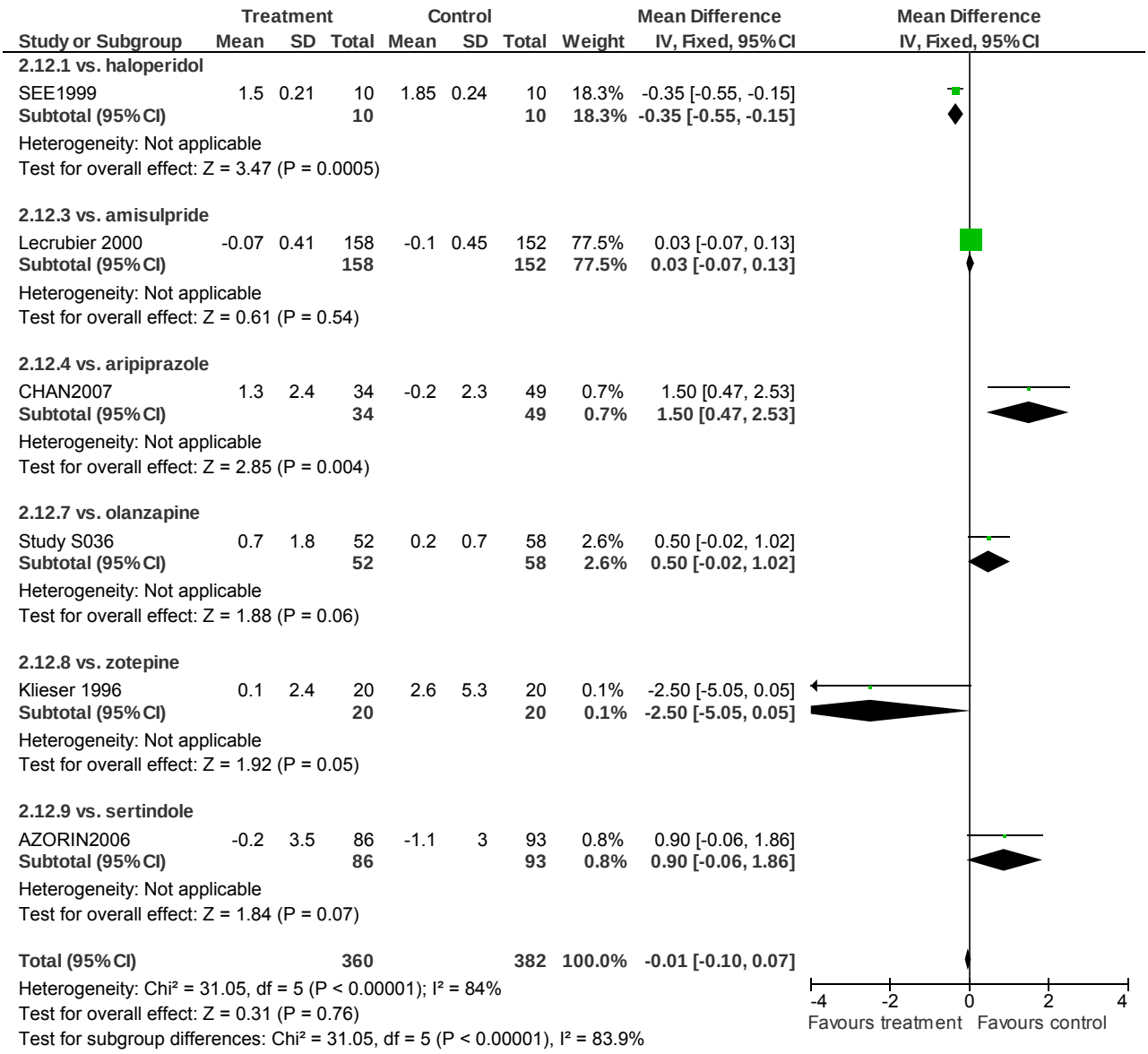


2.11 AE: 2. Neurologic SEs - Use of anticholinergic medication (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.11.1 vs. haloperidol						
Csernansky 2000	16	177	33	188	22.7%	0.51 [0.29, 0.90]
Jones 1998	9	21	17	23	11.5%	0.58 [0.33, 1.01]
Marder 2003	23	33	26	30	19.3%	0.80 [0.62, 1.05]
SCHOOLER2005	48	116	68	137	44.3%	0.83 [0.63, 1.10]
Subtotal (95% CI)		**347**		**378**	**97.9%**	**0.72 [0.60, 0.88]**
Total events	96		144			
Heterogeneity: Chi² = 3.66, df = 3 (P = 0.30); I² = 18%						
Test for overall effect: Z = 3.33 (P = 0.0009)						
2.11.2 vs. olanzapine						
Jones 1998	9	21	3	21	2.1%	3.00 [0.94, 9.55]
Subtotal (95% CI)		**21**		**21**	**2.1%**	**3.00 [0.94, 9.55]**
Total events	9		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.86 (P = 0.06)						
Total (95% CI)		**368**		**399**	**100.0%**	**0.77 [0.64, 0.93]**
Total events	105		147			
Heterogeneity: Chi² = 8.71, df = 4 (P = 0.07); I² = 54%						
Test for overall effect: Z = 2.71 (P = 0.007)						

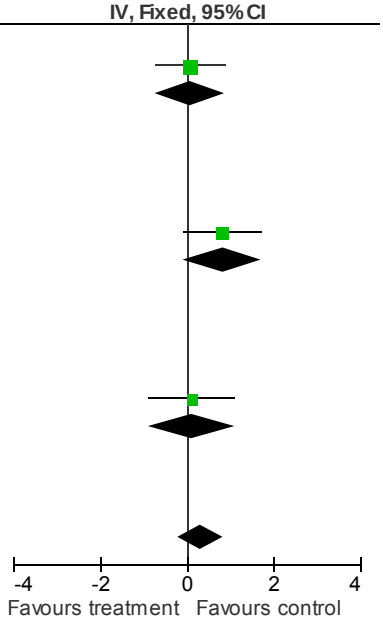


2.12 AE: 2. Neurologic SEs - Simpson-Angus Scale (SAS; endpoint/change) (short-to-medium-term)



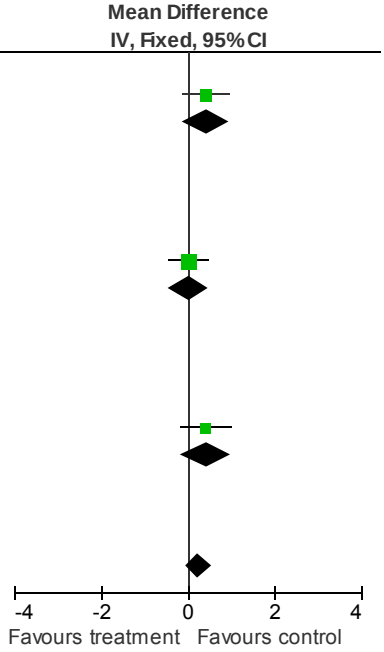
2.13 AE: 2. Neurologic SEs - Involuntary Movement Scale (AIMS; change from baseline) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.13.3 vs. amisulpride								
Lecrubier 2000	-0.1	4.1	158	-0.16	3.17	152	40.3%	0.06 [-0.75, 0.87]
Subtotal (95% CI)			**158**			**152**	**40.3%**	**0.06 [-0.75, 0.87]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.14 (P = 0.89)								
2.13.4 vs. aripiprazole								
CHAN2007	0.4	1.7	34	-0.4	2.5	49	32.7%	0.80 [-0.10, 1.70]
Subtotal (95% CI)			**34**			**49**	**32.7%**	**0.80 [-0.10, 1.70]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.74 (P = 0.08)								
2.13.9 vs. sertindole								
AZORIN2006	-0.7	3.3	74	-0.8	3	82	27.0%	0.10 [-0.89, 1.09]
Subtotal (95% CI)			**74**			**82**	**27.0%**	**0.10 [-0.89, 1.09]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.20 (P = 0.84)								
Total (95% CI)			**266**			**283**	**100.0%**	**0.31 [-0.20, 0.83]**
Heterogeneity: Chi² = 1.66, df = 2 (P = 0.44); I² = 0%								
Test for overall effect: Z = 1.19 (P = 0.24)								
Test for subgroup differences: Chi² = 1.66, df = 2 (P = 0.44), I² = 0%								

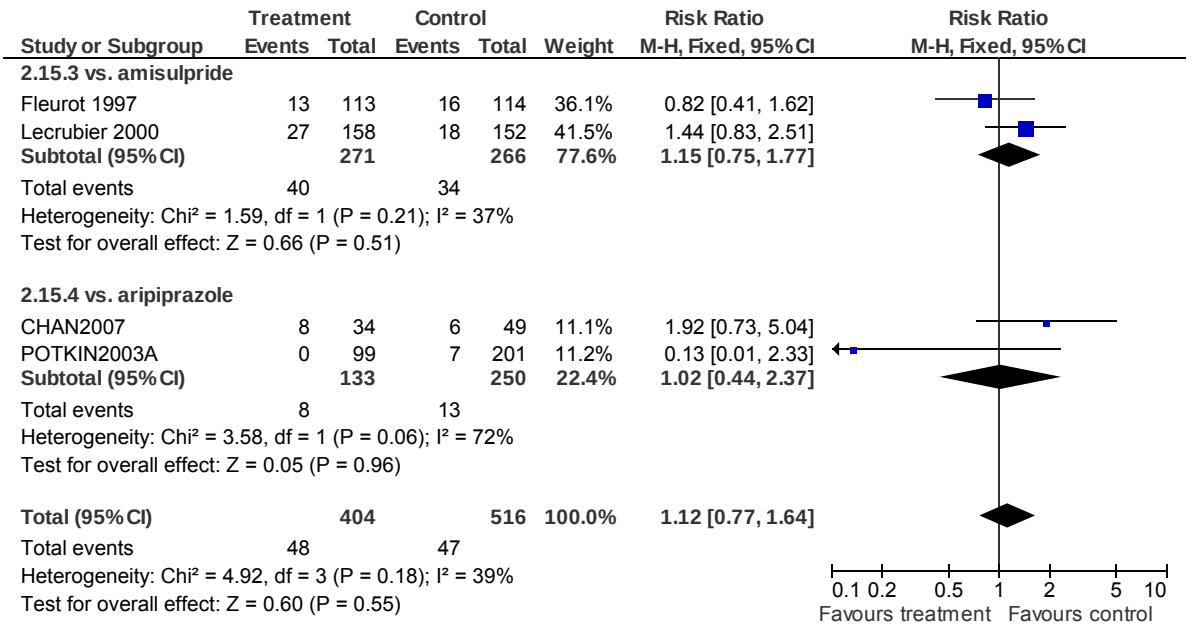


2.14 AE: 2. Neurologic SEs - Barnes Akathisia Scale (BAS; endpt/change) (short-term)

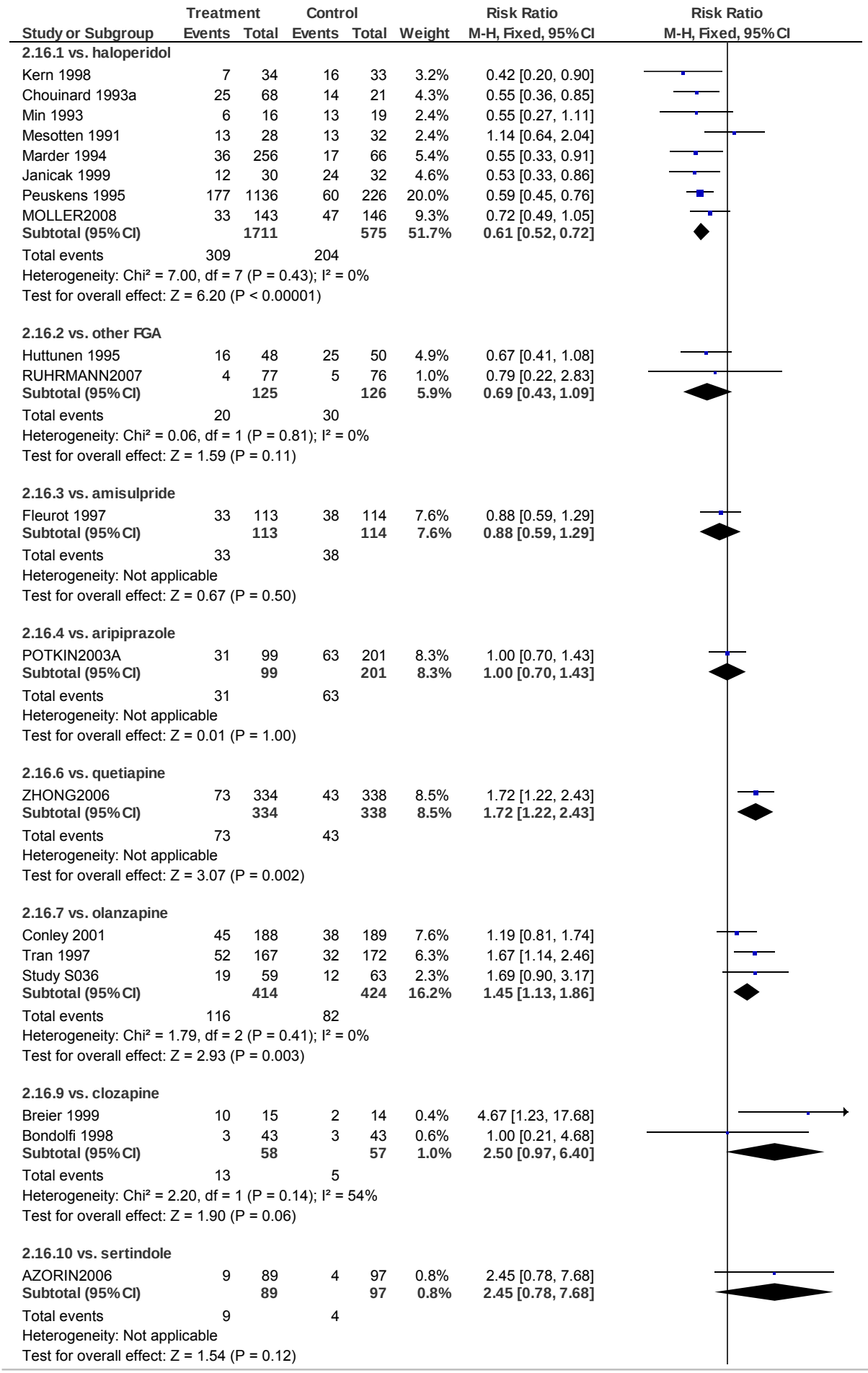
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
2.14.4 vs. aripiprazole								
CHAN2007	0.5	1.4	34	0.1	1	49	31.1%	0.40 [-0.15, 0.95]
Subtotal (95% CI)			**34**			**49**	**31.1%**	**0.40 [-0.15, 0.95]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.43 (P = 0.15)								
2.14.7 vs. olanzapine								
Study S036	0.5	1.3	52	0.5	1.2	58	42.3%	0.00 [-0.47, 0.47]
Subtotal (95% CI)			**52**			**58**	**42.3%**	**0.00 [-0.47, 0.47]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
2.14.9 vs. sertindole								
AZORIN2006	-0.1	2.2	86	-0.5	1.8	93	26.6%	0.40 [-0.19, 0.99]
Subtotal (95% CI)			**86**			**93**	**26.6%**	**0.40 [-0.19, 0.99]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.33 (P = 0.19)								
Total (95% CI)			**172**			**200**	**100.0%**	**0.23 [-0.07, 0.54]**
Heterogeneity: Chi² = 1.61, df = 2 (P = 0.45); I² = 0%								
Test for overall effect: Z = 1.48 (P = 0.14)								
Test for subgroup differences: Chi² = 1.61, df = 2 (P = 0.45), I² = 0%								



2.15 AE: 2. Neurologic SEs - Extrapyramidal disorder/syndrome (treatment-emergent) (short-term)



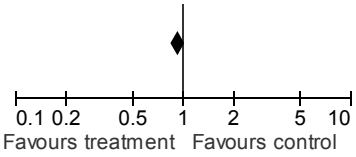
2.16 AE: 2. Neurologic SEs (treatment-emergent) - Any EPS (short-to-medium-term)



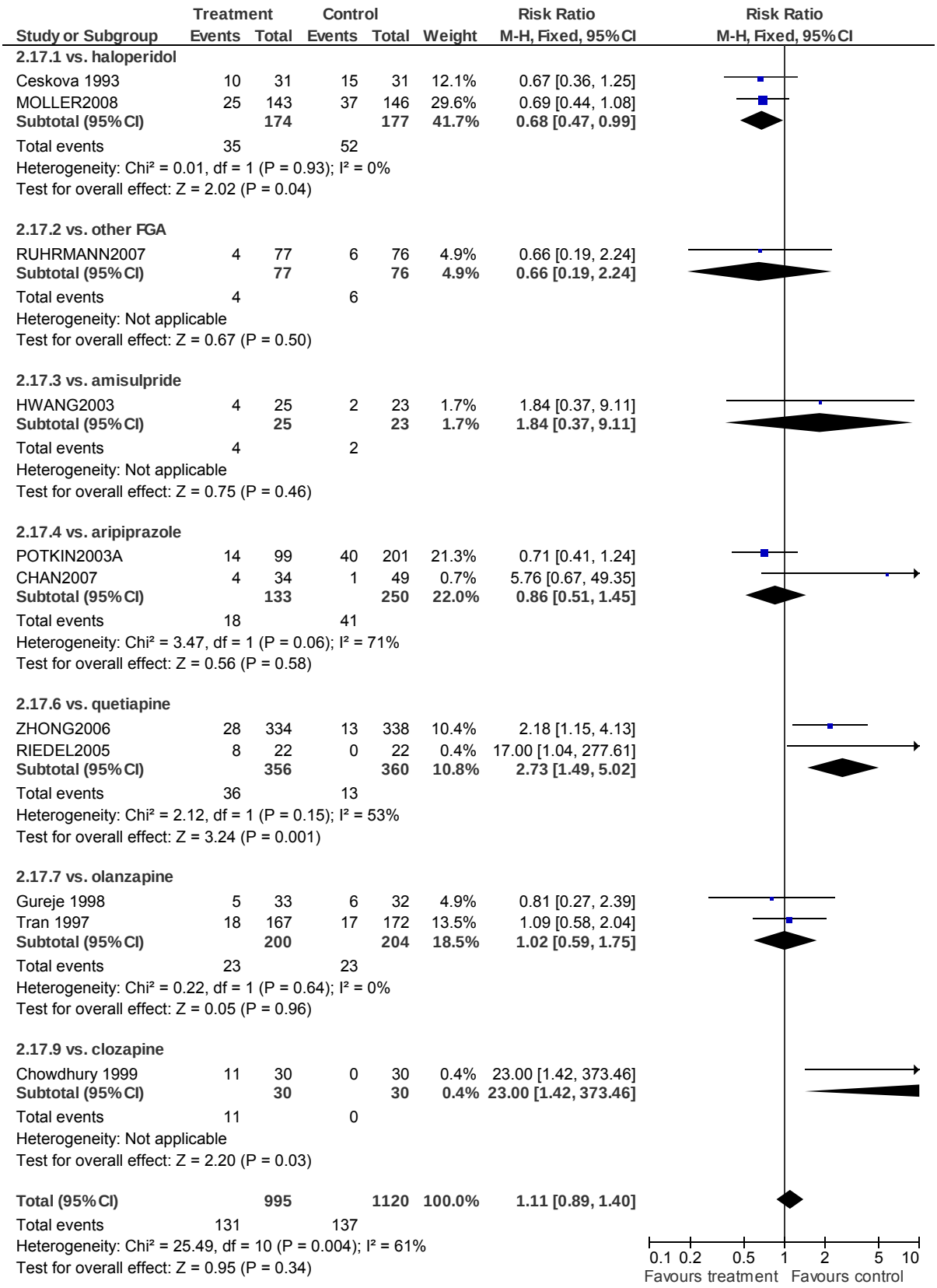
Total (95% CI)		**2943**	**1932**	**100.0%**	**0.93 [0.84, 1.04]**
Total events	604		469		

Heterogeneity: Chi² = 72.79, df = 18 (P < 0.00001); I² = 75%

Test for overall effect: Z = 1.31 (P = 0.19)

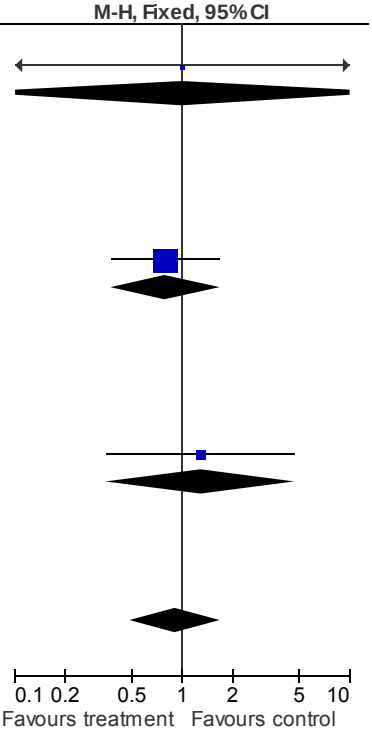


2.17 AE: 2. Neurologic SEs (treatment-emergent) - Akathisia (short-to-medium-term)



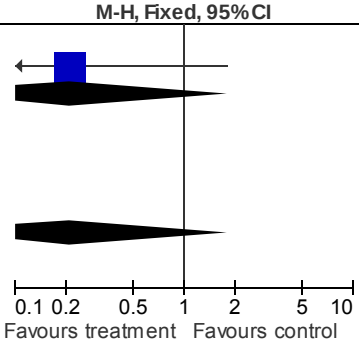
2.18 AE: 2. Neurologic SEs (treatment-emergent) - Tardive dyskinesia/dyskinetic movements (short-to-medium

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.18.1 vs. haloperidol						
Ceskova 1993	1	31	1	31	5.3%	1.00 [0.07, 15.28]
Subtotal (95% CI)		**31**		**31**	**5.3%**	**1.00 [0.07, 15.28]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
2.18.3 vs. amisulpride						
Fleurot 1997	11	113	14	114	73.8%	0.79 [0.38, 1.67]
Subtotal (95% CI)		**113**		**114**	**73.8%**	**0.79 [0.38, 1.67]**
Total events	11		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.61 (P = 0.54)						
2.18.7 vs. olanzapine						
Tran 1997	5	167	4	172	20.9%	1.29 [0.35, 4.71]
Subtotal (95% CI)		**167**		**172**	**20.9%**	**1.29 [0.35, 4.71]**
Total events	5		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.38 (P = 0.70)						
Total (95% CI)		**311**		**317**	**100.0%**	**0.91 [0.48, 1.70]**
Total events	17		19			
Heterogeneity: Chi² = 0.41, df = 2 (P = 0.81); I² = 0%						
Test for overall effect: Z = 0.31 (P = 0.76)						

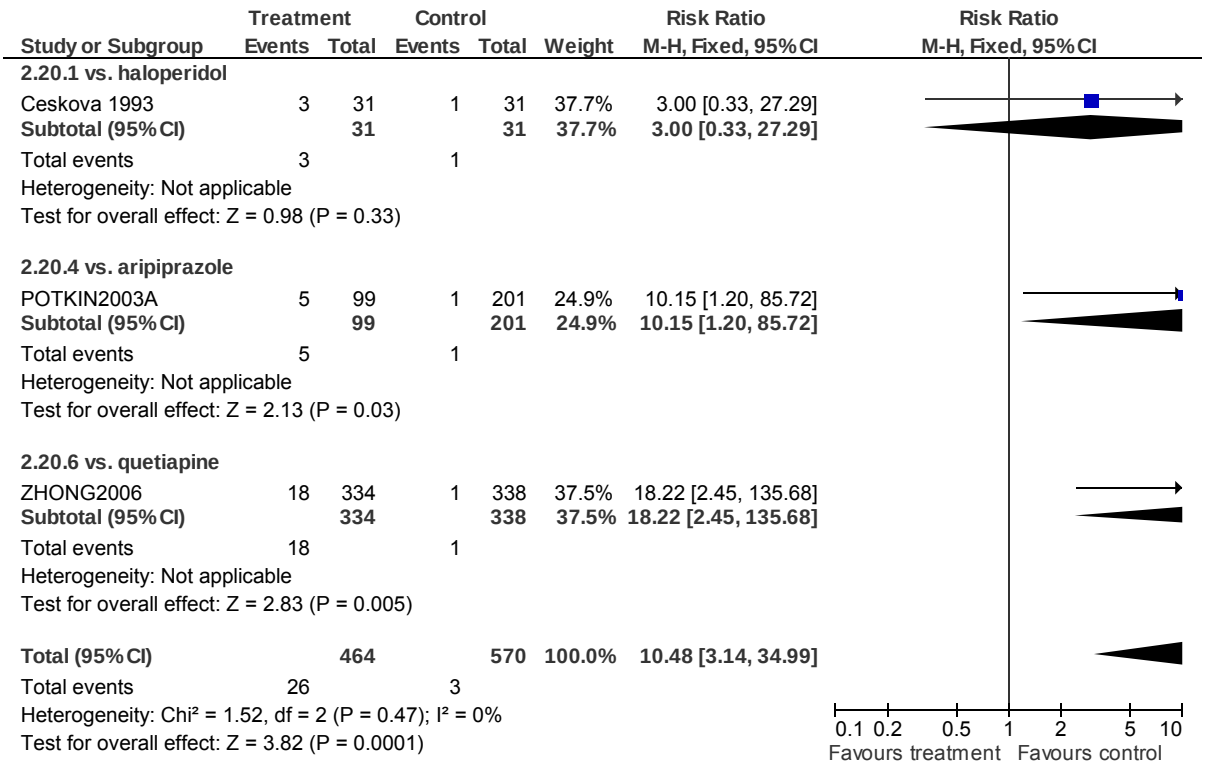


2.19 AE: 2. Neurologic SEs (treatment-emergent) - Tardive dyskinesia (long-term)

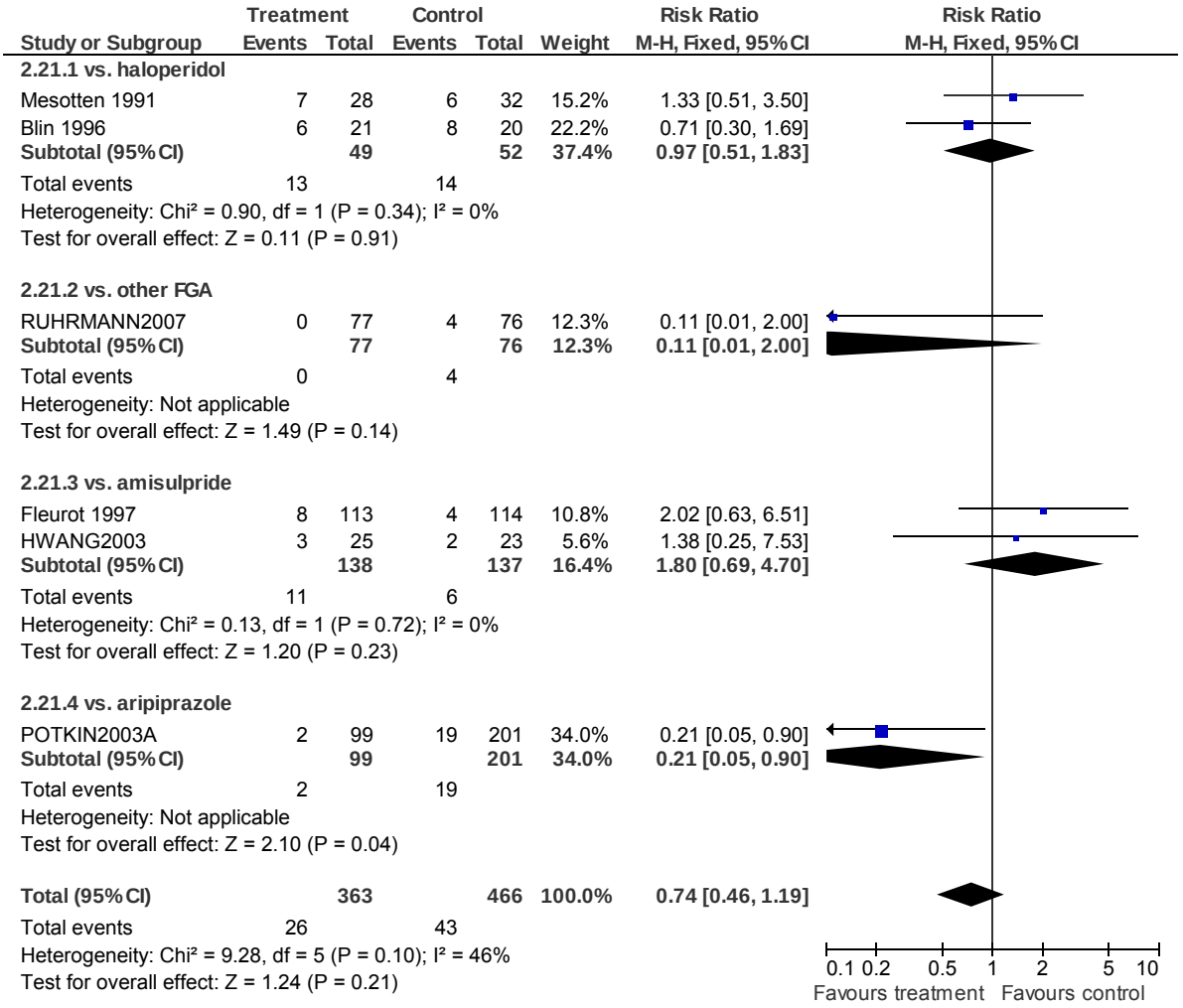
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.19.1 vs. haloperidol						
Csernansky 2000	1	177	5	188	100.0%	0.21 [0.03, 1.80]
Subtotal (95% CI)		**177**		**188**	**100.0%**	**0.21 [0.03, 1.80]**
Total events	1		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.42 (P = 0.16)						
Total (95% CI)		**177**		**188**	**100.0%**	**0.21 [0.03, 1.80]**
Total events	1		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.42 (P = 0.16)						



2.20 AE: 2. Neurologic SEs (treatment-emergent) - Acute dystonia (short-to-medium-term)

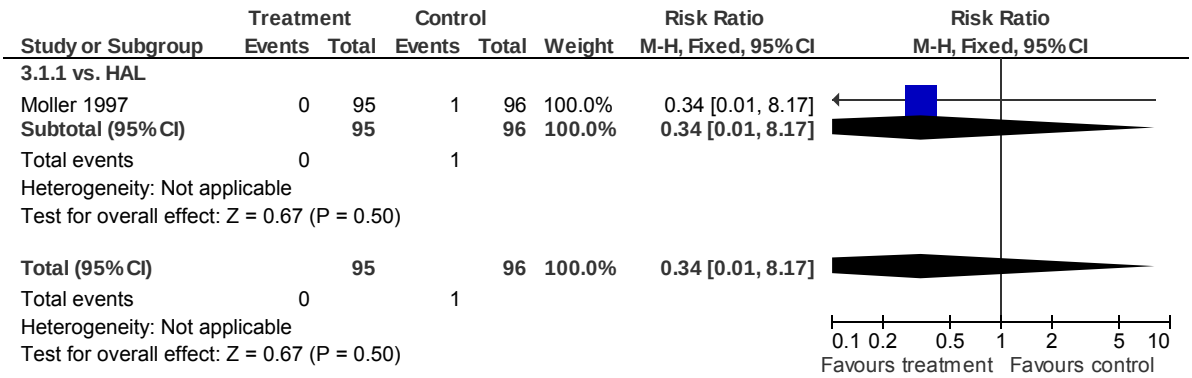


2.21 AE: 2. Neurologic SEs (treatment-emergent) - Tremor (short-to-medium-term)



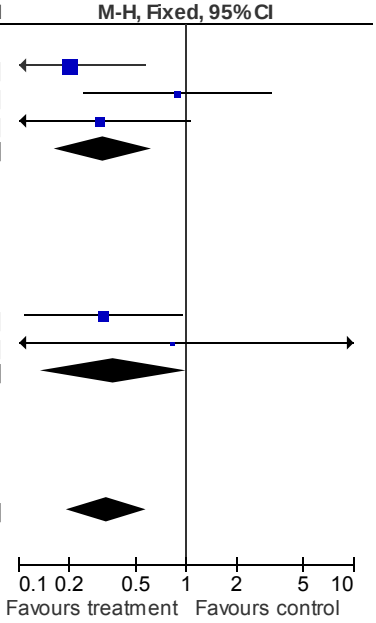
3 Amisulpride versus FGA (overall SE analysis)

3.1 Mortality: 1. Suicide



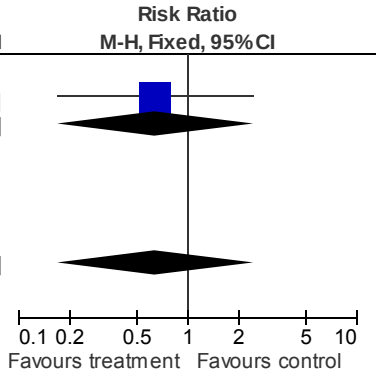
3.2 Leaving the study early: 3: Adverse event (short-to-medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.2.1 vs. HAL						
Carriere 2000	4	94	22	105	43.3%	0.20 [0.07, 0.57]
Puech 1998	8	194	3	64	9.4%	0.88 [0.24, 3.22]
Moller 1997	3	95	10	96	20.7%	0.30 [0.09, 1.07]
Subtotal (95% CI)		**383**		**265**	**73.4%**	**0.32 [0.16, 0.61]**
Total events	15		35			
Heterogeneity: Chi² = 3.10, df = 2 (P = 0.21); I² = 36%						
Test for overall effect: Z = 3.42 (P = 0.0006)						
3.2.4 vs. other FGA						
Hillert 1994	4	70	11	62	24.3%	0.32 [0.11, 0.96]
Boyer 1990	1	34	1	28	2.3%	0.82 [0.05, 12.58]
Subtotal (95% CI)		**104**		**90**	**26.6%**	**0.37 [0.13, 0.99]**
Total events	5		12			
Heterogeneity: Chi² = 0.39, df = 1 (P = 0.53); I² = 0%						
Test for overall effect: Z = 1.97 (P = 0.05)						
Total (95% CI)		**487**		**355**	**100.0%**	**0.33 [0.19, 0.57]**
Total events	20		47			
Heterogeneity: Chi² = 3.50, df = 4 (P = 0.48); I² = 0%						
Test for overall effect: Z = 3.95 (P < 0.0001)						

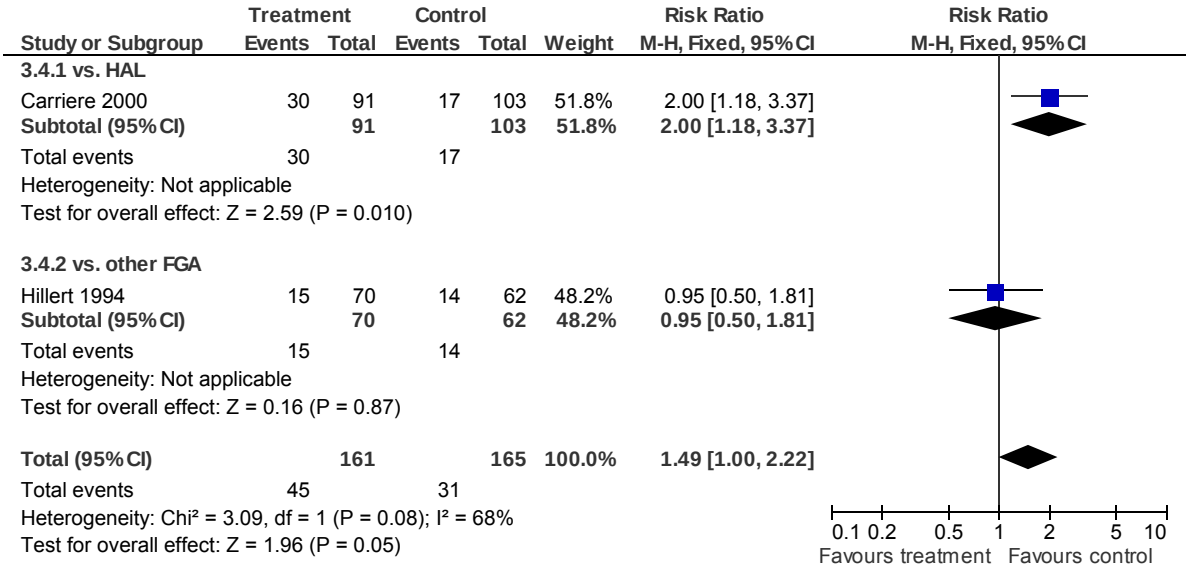


3.3 Leaving the study early: 3: Adverse event (long-term)

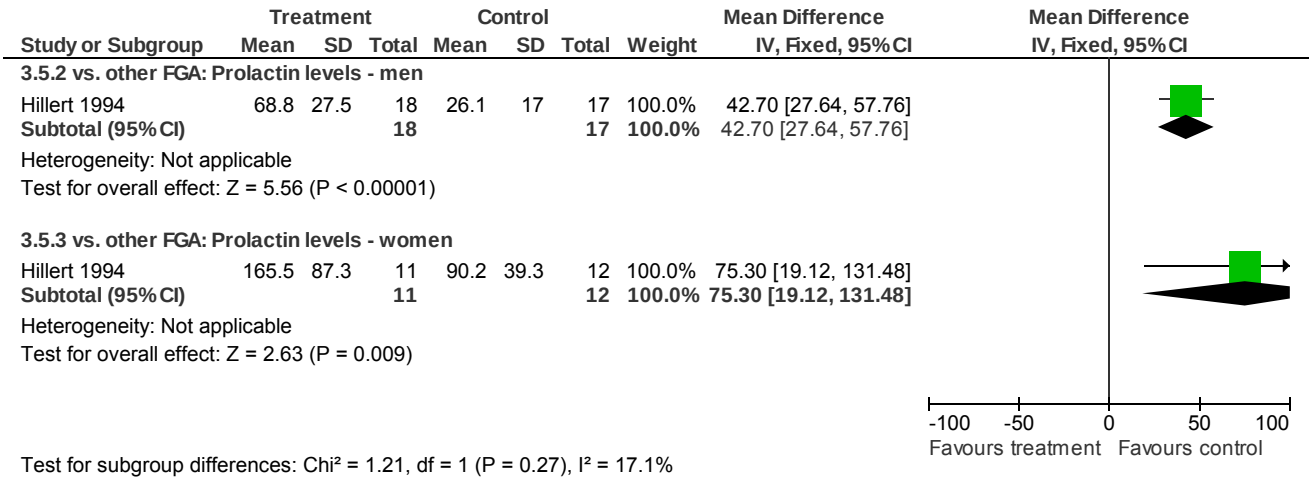
Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.3.1 vs. HAL						
Speller 1997	3	29	5	31	100.0%	0.64 [0.17, 2.45]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.64 [0.17, 2.45]**
Total events	3		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.65 (P = 0.52)						
Total (95% CI)		**29**		**31**	**100.0%**	**0.64 [0.17, 2.45]**
Total events	3		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.65 (P = 0.52)						



3.4 AE: 1. Metabolic SEs - Weight gain (short-to-medium-term)

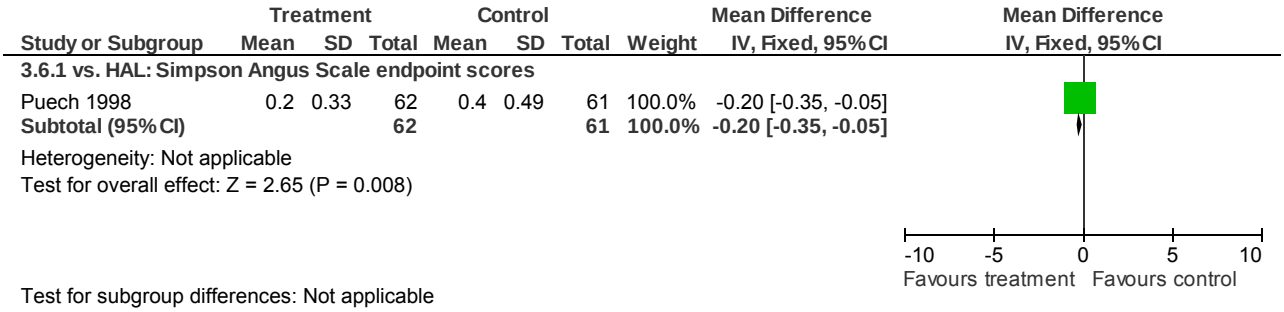


3.5 AE: 1. Metabolic SEs - Prolactin-related (short term)



Test for subgroup differences: Chi² = 1.21, df = 1 (P = 0.27), I² = 17.1%

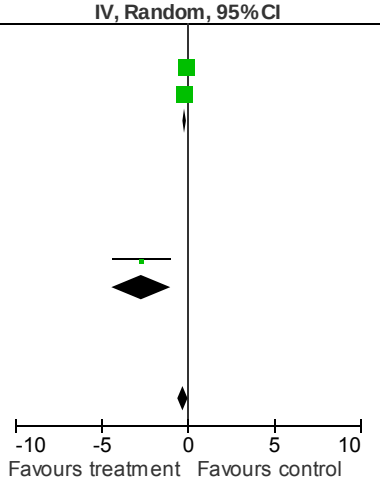
3.6 AE: 2. Neurologic SEs (<500 mg/day amisulpride) (short-term)



Test for subgroup differences: Not applicable

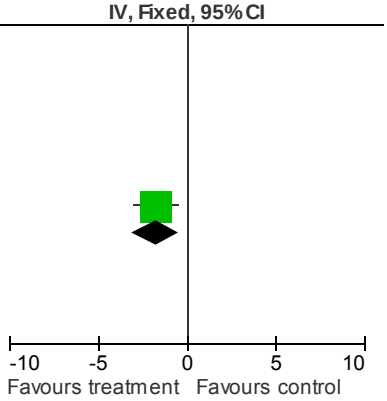
3.7 AE: 2. Neurologic SEs (>500 mg/day amisulpride) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
3.7.1 vs. HAL: Simpson Angus Scale endpoint/change scores								
Puech 1998	0.26	0.45	63	0.4	0.49	61	48.1%	-0.14 [-0.31, 0.03]
Moller 1997	0.4	0.51	93	0.63	0.59	93	48.7%	-0.23 [-0.39, -0.07]
Subtotal (95% CI)			**156**			**154**	**96.8%**	**-0.19 [-0.30, -0.07]**
Heterogeneity: Tau² = 0.00; Chi² = 0.59, df = 1 (P = 0.44); I² = 0%								
Test for overall effect: Z = 3.20 (P = 0.001)								
3.7.2 vs. other FGA: Simpson Angus Scale change scores								
Hillert 1994	1.1	3.7	70	3.8	5.9	62	3.2%	-2.70 [-4.41, -0.99]
Subtotal (95% CI)			**70**			**62**	**3.2%**	**-2.70 [-4.41, -0.99]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.10 (P = 0.002)								
Total (95% CI)			**226**			**216**	**100.0%**	**-0.27 [-0.58, 0.05]**
Heterogeneity: Tau² = 0.05; Chi² = 8.90, df = 2 (P = 0.01); I² = 78%								
Test for overall effect: Z = 1.66 (P = 0.10)								



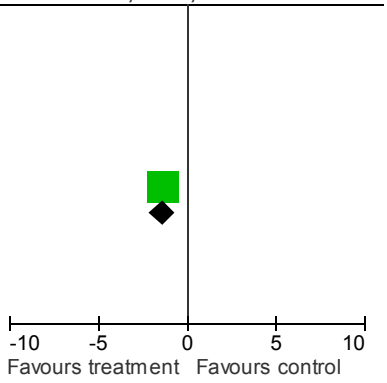
3.8 AE: 2. Neurologic SEs - EPS (>500 mg/day amisulpride) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.8.1 vs. HAL: AIMS change scores								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
3.8.2 vs. other FGA: AIMS change scores								
Hillert 1994	0	2.8	70	1.8	4.4	62	100.0%	-1.80 [-3.08, -0.52]
Subtotal (95% CI)			**70**			**62**	**100.0%**	**-1.80 [-3.08, -0.52]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.76 (P = 0.006)								
Test for subgroup differences: Not applicable								



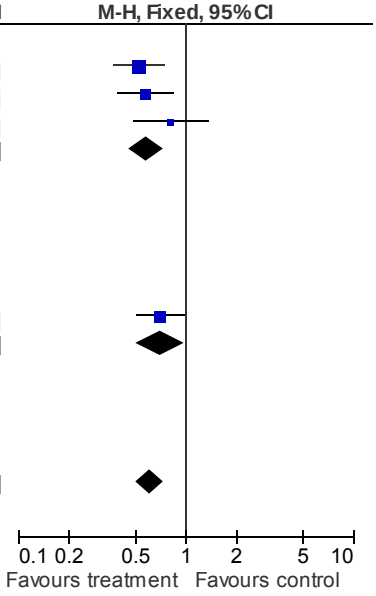
3.9 AE: 2. Neurologic SEs - Akathisia (>500 mg/day amisulpride) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.9.1 vs. HAL: Barnes Akathisia Scale change scores								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
3.9.2 vs. other FGA: Barnes Akathisia Scale change scores								
Hillert 1994	0.2	1.9	70	1.6	2.4	62	100.0%	-1.40 [-2.14, -0.66]
Subtotal (95% CI)			**70**			**62**	**100.0%**	**-1.40 [-2.14, -0.66]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.68 (P = 0.0002)								
Test for subgroup differences: Not applicable								



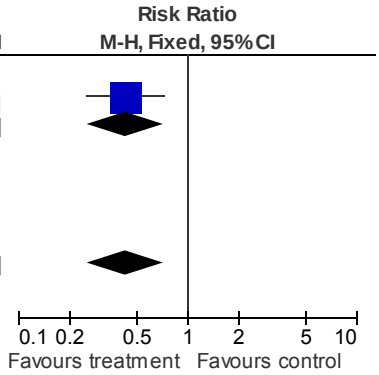
3.10 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.10.1 vs. HAL						
Moller 1997	28	95	54	96	36.7%	0.52 [0.37, 0.75]
Puech 1998	45	194	26	64	26.7%	0.57 [0.39, 0.84]
Delcker 1990	11	21	13	20	9.1%	0.81 [0.48, 1.35]
Subtotal (95% CI)		**310**		**180**	**72.5%**	**0.58 [0.45, 0.73]**
Total events	84		93			
Heterogeneity: Chi² = 1.87, df = 2 (P = 0.39); I² = 0%						
Test for overall effect: Z = 4.55 (P < 0.00001)						
3.10.2 vs. other FGA						
Hillert 1994	30	70	38	62	27.5%	0.70 [0.50, 0.98]
Subtotal (95% CI)		**70**		**62**	**27.5%**	**0.70 [0.50, 0.98]**
Total events	30		38			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.09 (P = 0.04)						
Total (95% CI)		**380**		**242**	**100.0%**	**0.61 [0.50, 0.74]**
Total events	114		131			
Heterogeneity: Chi² = 2.54, df = 3 (P = 0.47); I² = 0%						
Test for overall effect: Z = 4.98 (P < 0.00001)						

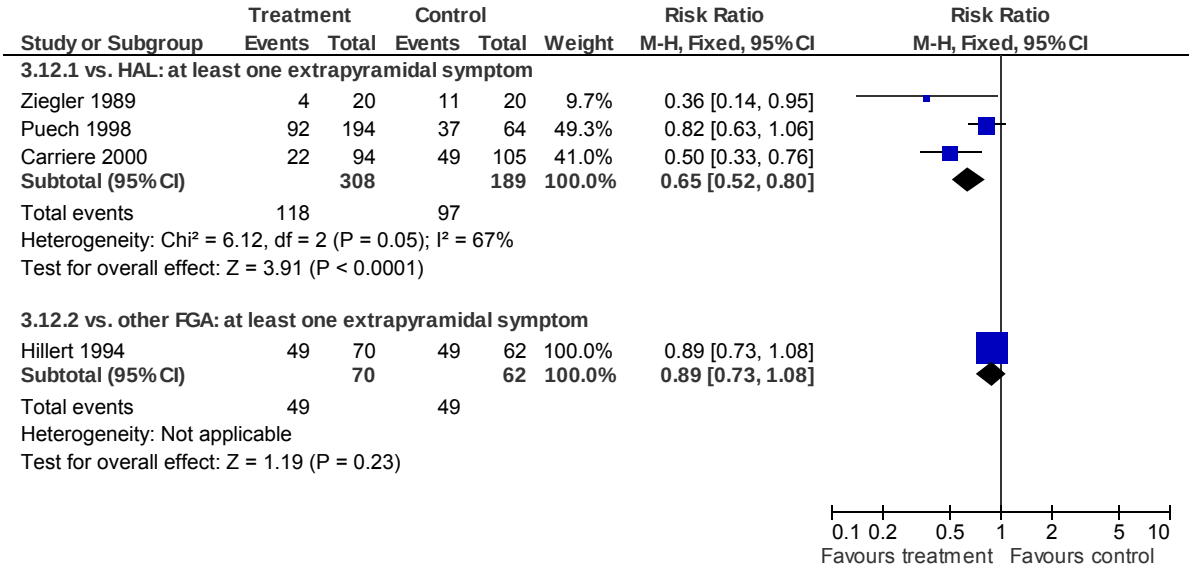


3.11 AE: 2. Neurologic SEs - Use of anticholinergic medication (long-term)

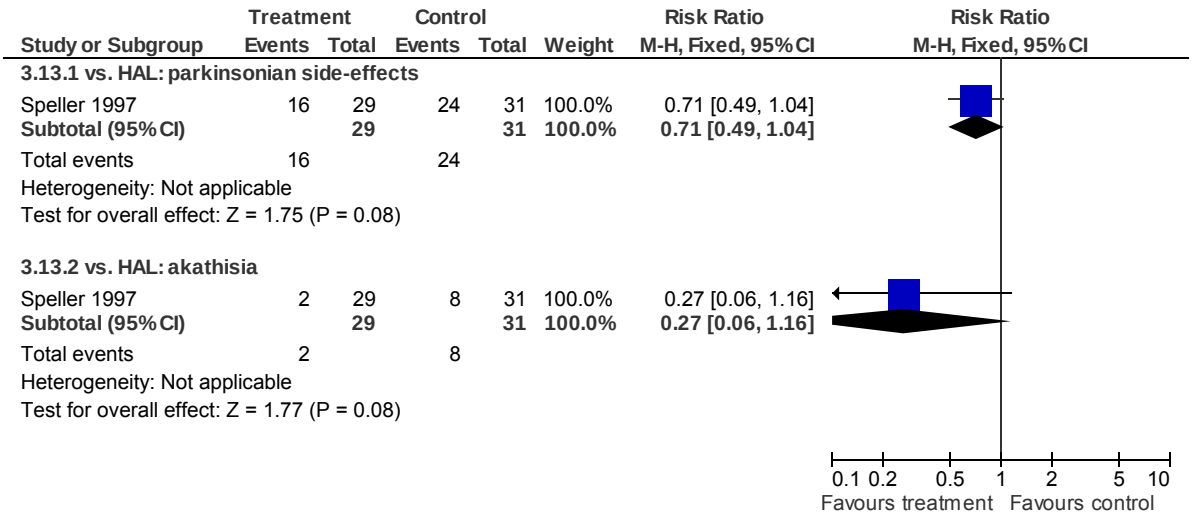
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.11.1 vs. HAL						
Speller 1997	10	29	25	31	100.0%	0.43 [0.25, 0.73]
Subtotal (95% CI)		**29**		**31**	**100.0%**	**0.43 [0.25, 0.73]**
Total events	10		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.14 (P = 0.002)						
Total (95% CI)		**29**		**31**	**100.0%**	**0.43 [0.25, 0.73]**
Total events	10		25			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.14 (P = 0.002)						



3.12 AE: 2. Neurologic SEs (treatment-emergent) (short-term)



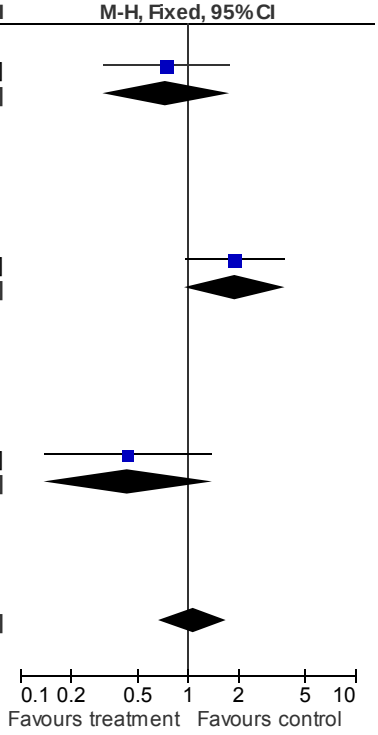
3.13 AE: 2. Neurologic SEs (treatment-emergent) (long-term)



4 Aripiprazole versus another antipsychotic drug (overall SE analysis)

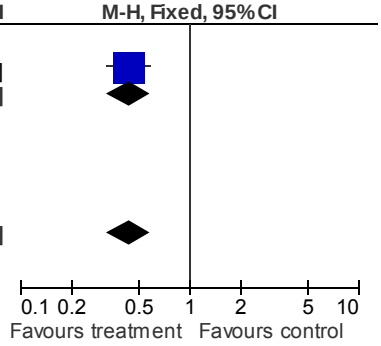
4.1 Leaving the study early: 3: Adverse event (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.1.1 vs. HAL						
KANE2002	8	102	11	104	34.9%	0.74 [0.31, 1.77]
Subtotal (95% CI)		**102**		**104**	**34.9%**	**0.74 [0.31, 1.77]**
Total events	8		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.67 (P = 0.50)						
4.1.2 vs. other FGA						
KANE2007B	22	154	11	146	36.1%	1.90 [0.95, 3.77]
Subtotal (95% CI)		**154**		**146**	**36.1%**	**1.90 [0.95, 3.77]**
Total events	22		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.82 (P = 0.07)						
4.1.3 vs. ziprasidone						
ZIMBROFF2007	4	129	9	127	29.0%	0.44 [0.14, 1.38]
Subtotal (95% CI)		**129**		**127**	**29.0%**	**0.44 [0.14, 1.38]**
Total events	4		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.41 (P = 0.16)						
Total (95% CI)		**385**		**377**	**100.0%**	**1.07 [0.67, 1.71]**
Total events	34		31			
Heterogeneity: Chi² = 5.66, df = 2 (P = 0.06); I² = 65%						
Test for overall effect: Z = 0.29 (P = 0.78)						

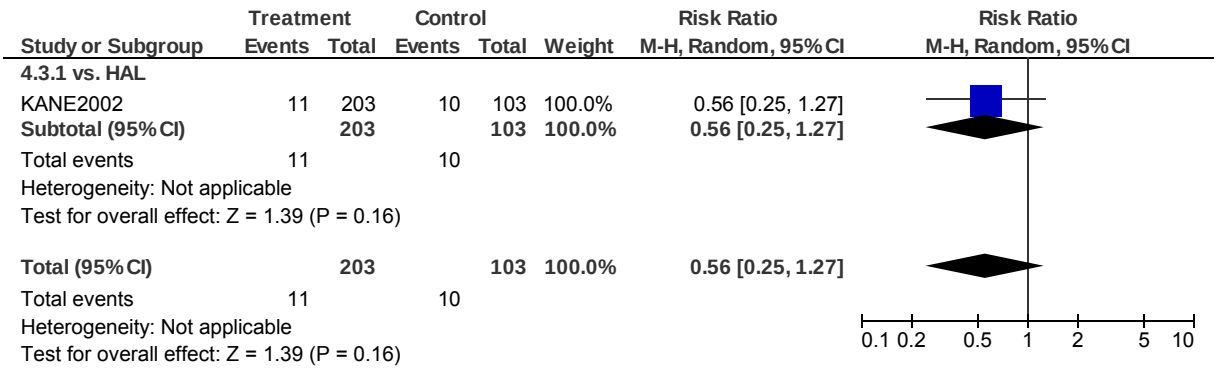


4.2 Leaving the study early: 3: Adverse event (long-term)

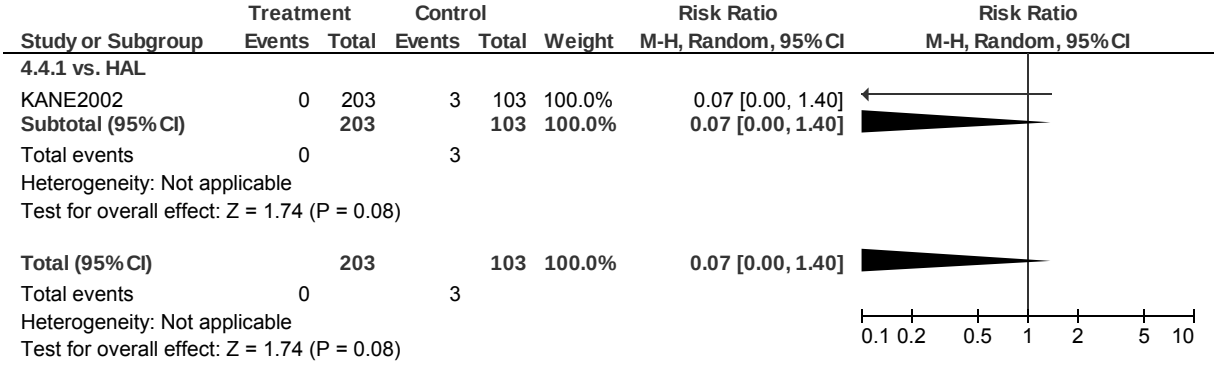
Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.2.1 vs. HAL						
KASPER2003	68	853	79	430	100.0%	0.43 [0.32, 0.59]
Subtotal (95% CI)		**853**		**430**	**100.0%**	**0.43 [0.32, 0.59]**
Total events	68		79			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.40 (P < 0.00001)						
Total (95% CI)		**853**		**430**	**100.0%**	**0.43 [0.32, 0.59]**
Total events	68		79			
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.40 (P < 0.00001)						



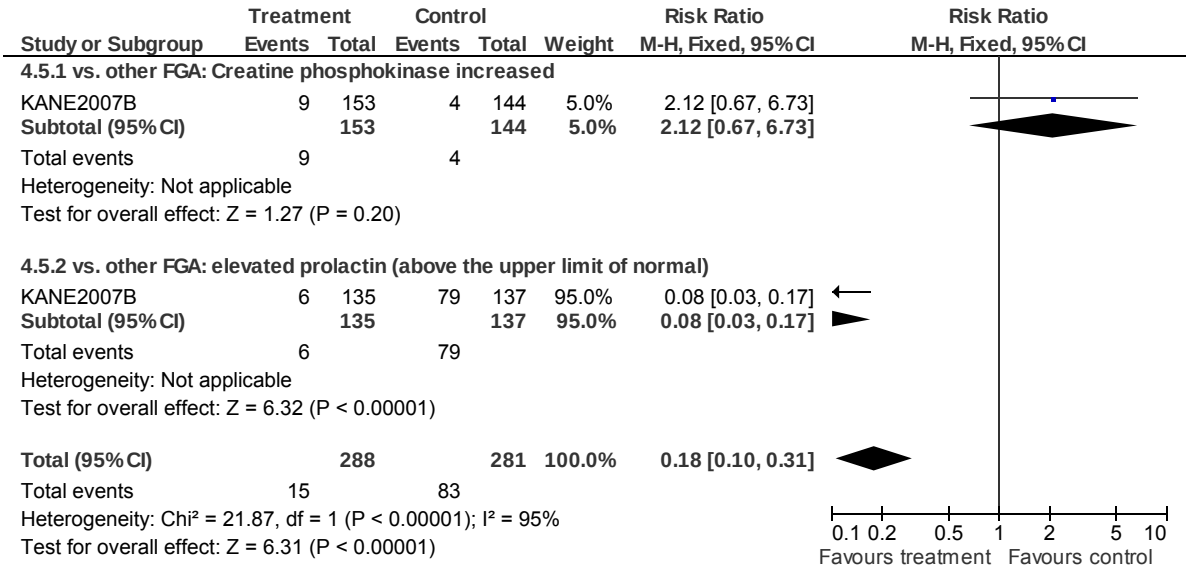
4.3 AE: 1. Metabolic SEs - Weight gain (>= 7% increase from baseline) (short-term)



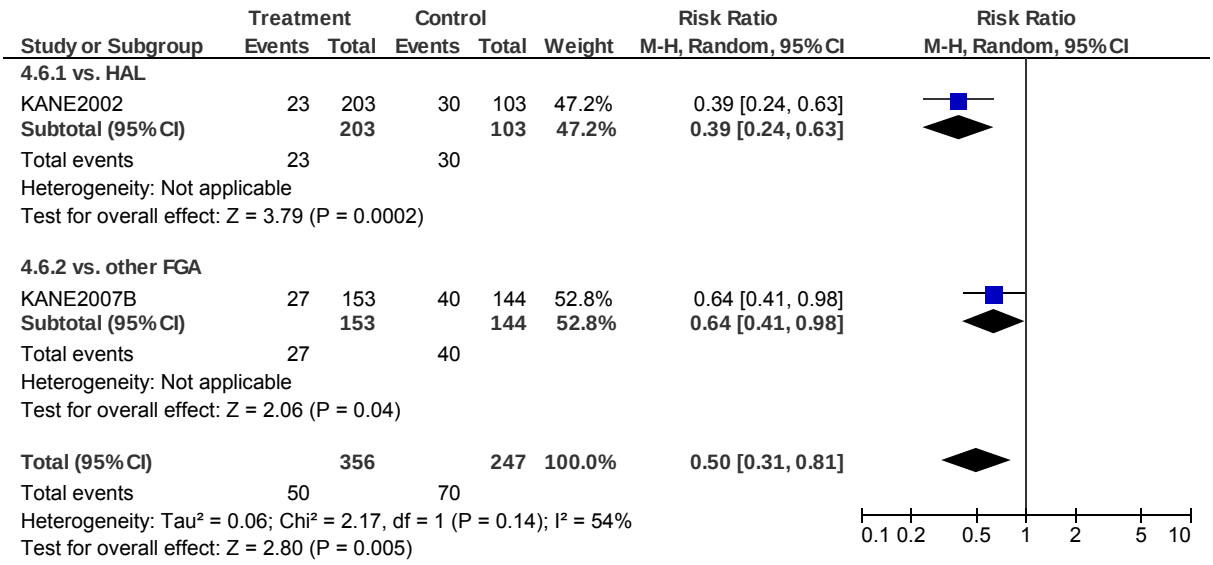
4.4 AE: 1. Metabolic SEs - Clinically sig. increase in QTc interval (short-term)



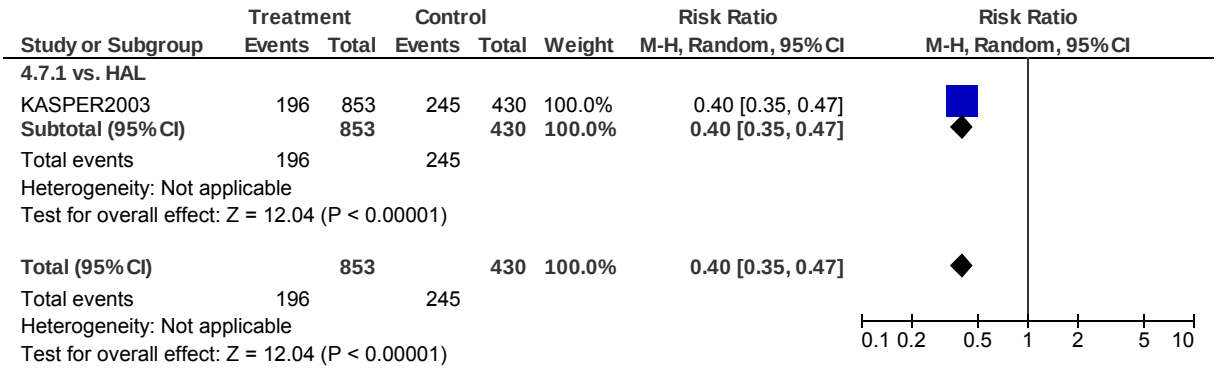
4.5 AE: 1. Metabolic SEs (treatment-emergent) (short-term)



4.6 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)

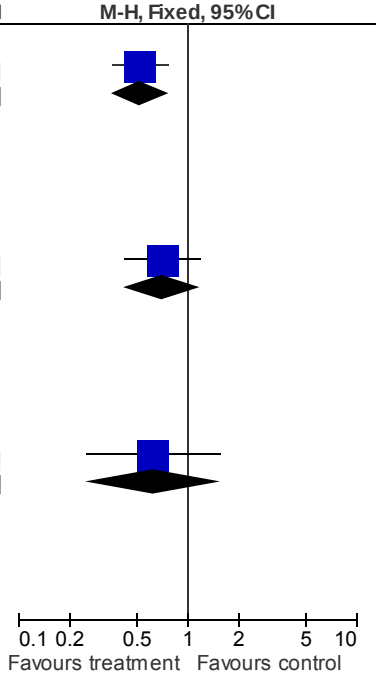


4.7 AE: 2. Neurologic SEs - Use of anticholinergic medication (long-term)



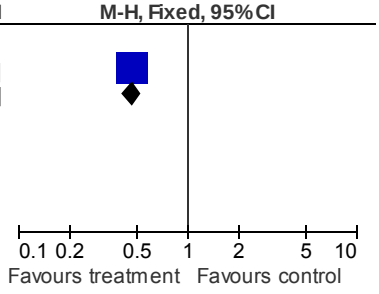
4.8 AE: 2. Neurologic SEs - EPS (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.8.1 vs. HAL: EPS						
KANE2002	38	203	37	103	100.0%	0.52 [0.35, 0.77]
Subtotal (95% CI)		**203**		**103**	**100.0%**	**0.52 [0.35, 0.77]**
Total events	38		37			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.31 (P = 0.0009)						
4.8.2 vs. other FGA: any EPS-related						
KANE2007B	21	153	28	144	100.0%	0.71 [0.42, 1.18]
Subtotal (95% CI)		**153**		**144**	**100.0%**	**0.71 [0.42, 1.18]**
Total events	21		28			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.32 (P = 0.19)						
4.8.3 vs. ziprasidone: Extrapyramidal syndrome						
ZIMBROFF2007	7	128	11	125	100.0%	0.62 [0.25, 1.55]
Subtotal (95% CI)		**128**		**125**	**100.0%**	**0.62 [0.25, 1.55]**
Total events	7		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						

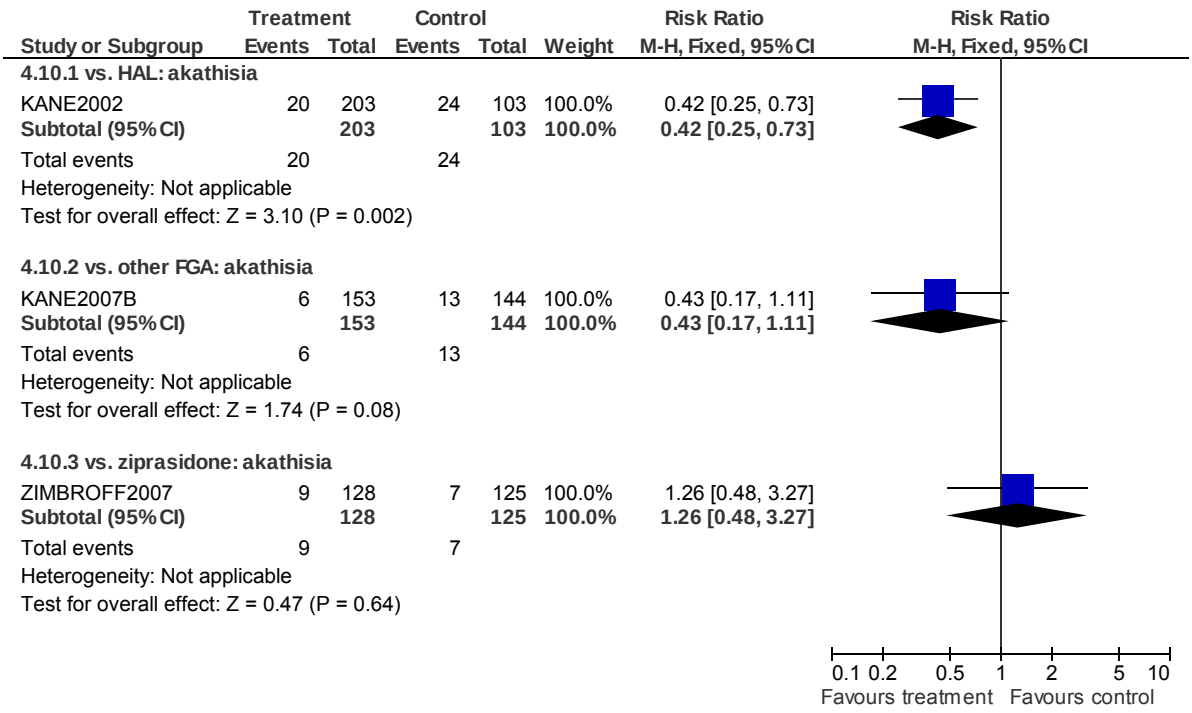


4.9 AE: 2. Neurologic SEs - EPS (treatment-emergent) (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.9.1 vs. HAL: EPS related						
KASPER2003	230	853	249	430	100.0%	0.47 [0.41, 0.53]
Subtotal (95% CI)		**853**		**430**	**100.0%**	**0.47 [0.41, 0.53]**
Total events	230		249			
Heterogeneity: Not applicable						
Test for overall effect: Z = 10.96 (P < 0.00001)						



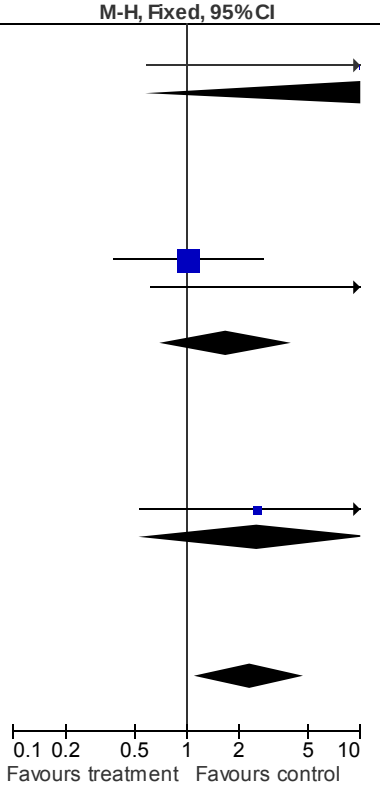
4.10 AE: 2. Neurologic SEs - Akathisia (treatment-emergent) (short-term)



5 Clozapine versus another antipsychotic drug (overall SE analysis)

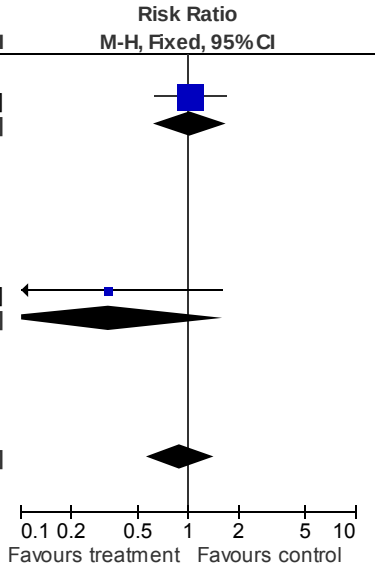
5.1 Leaving the study early: 3: Adverse event (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.1.1 vs. HAL						
VOLAVKA2002	5	40	0	37	5.2%	10.20 [0.58, 178.24]
Subtotal (95% CI)		**40**		**37**	**5.2%**	**10.20 [0.58, 178.24]**
Total events	5		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.59 (P = 0.11)						
5.1.2 vs. OLZ						
Bitter 1999	7	74	7	76	69.7%	1.03 [0.38, 2.78]
VOLAVKA2002	5	40	0	39	5.1%	10.73 [0.61, 187.79]
MELTZER2008	0	21	0	19		Not estimable
Subtotal (95% CI)		**135**		**134**	**74.8%**	**1.69 [0.70, 4.06]**
Total events	12		7			
Heterogeneity: Chi² = 2.56, df = 1 (P = 0.11); I² = 61%						
Test for overall effect: Z = 1.17 (P = 0.24)						
5.1.3 vs. RIS						
VOLAVKA2002	5	40	2	41	19.9%	2.56 [0.53, 12.45]
Subtotal (95% CI)		**40**		**41**	**19.9%**	**2.56 [0.53, 12.45]**
Total events	5		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.17 (P = 0.24)						
Total (95% CI)		**215**		**212**	**100.0%**	**2.31 [1.12, 4.76]**
Total events	22		9			
Heterogeneity: Chi² = 4.69, df = 3 (P = 0.20); I² = 36%						
Test for overall effect: Z = 2.27 (P = 0.02)						



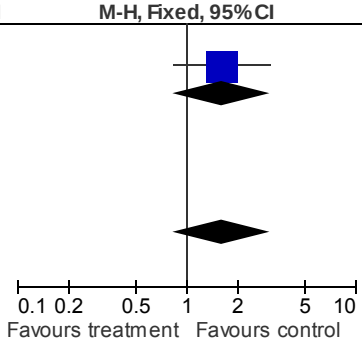
5.2 Leaving the study early: 3: Adverse event (long-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.2.1 vs. HAL						
Rosenheck 1997	26	205	27	218	81.3%	1.02 [0.62, 1.69]
Subtotal (95% CI)		**205**		**218**	**81.3%**	**1.02 [0.62, 1.69]**
Total events	26		27			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.09 (P = 0.93)						
5.2.2 vs. other FGA						
LIEBERMAN2003	2	80	6	80	18.7%	0.33 [0.07, 1.60]
Subtotal (95% CI)		**80**		**80**	**18.7%**	**0.33 [0.07, 1.60]**
Total events	2		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.37 (P = 0.17)						
Total (95% CI)		**285**		**298**	**100.0%**	**0.90 [0.56, 1.44]**
Total events	28		33			
Heterogeneity: Chi² = 1.79, df = 1 (P = 0.18); I² = 44%						
Test for overall effect: Z = 0.46 (P = 0.65)						



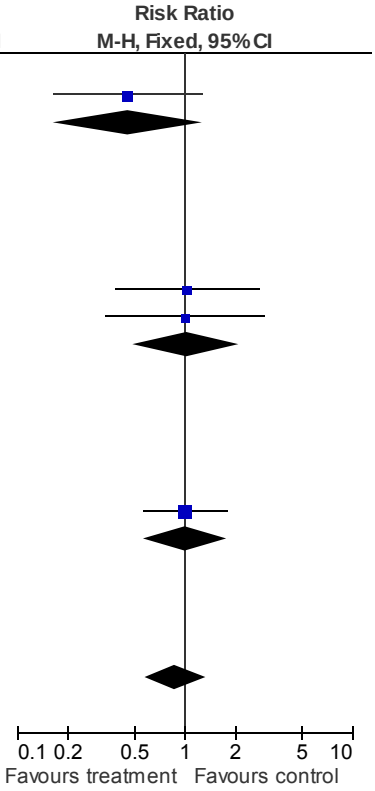
5.3 AE: 1. Metabolic SEs - Weight gain (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.3.4 vs. RIS						
Bondolfi 1998	16	43	10	43	100.0%	1.60 [0.82, 3.12]
Subtotal (95% CI)		**43**		**43**	**100.0%**	**1.60 [0.82, 3.12]**
Total events	16		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.38 (P = 0.17)						
Total (95% CI)		**43**		**43**	**100.0%**	**1.60 [0.82, 3.12]**
Total events	16		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.38 (P = 0.17)						

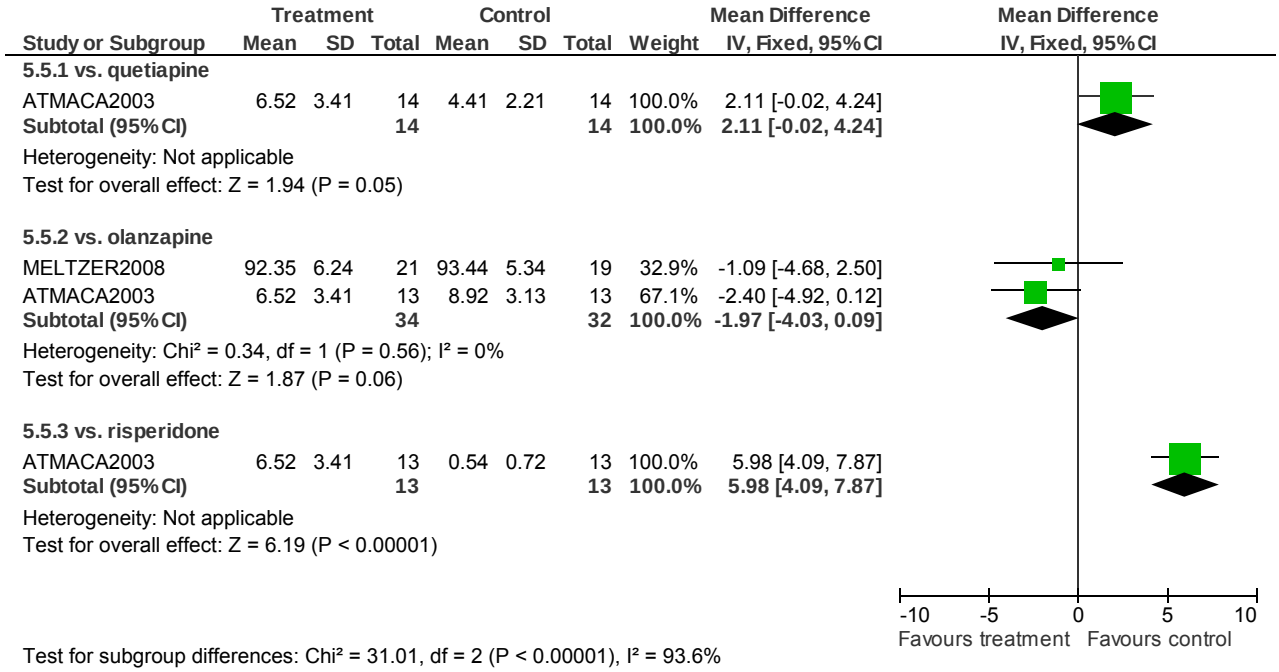


5.4 AE: 1. Metabolic SEs - Weight gain (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.4.2 vs. other FGA						
Hong 1997	4	21	8	19	24.5%	0.45 [0.16, 1.26]
Subtotal (95% CI)		**21**		**19**	**24.5%**	**0.45 [0.16, 1.26]**
Total events	4		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.51 (P = 0.13)						
5.4.3 vs. OLZ						
Bitter 1999	7	74	7	76	20.1%	1.03 [0.38, 2.78]
Beuzen 1998	6	90	6	90	17.5%	1.00 [0.34, 2.98]
Subtotal (95% CI)		**164**		**166**	**37.6%**	**1.01 [0.49, 2.12]**
Total events	13		13			
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.97); I² = 0%						
Test for overall effect: Z = 0.04 (P = 0.97)						
5.4.4 vs. RIS						
Chowdhury 1999	13	30	13	30	37.9%	1.00 [0.56, 1.78]
Subtotal (95% CI)		**30**		**30**	**37.9%**	**1.00 [0.56, 1.78]**
Total events	13		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**215**		**215**	**100.0%**	**0.87 [0.57, 1.33]**
Total events	30		34			
Heterogeneity: Chi² = 1.95, df = 3 (P = 0.58); I² = 0%						
Test for overall effect: Z = 0.64 (P = 0.52)						

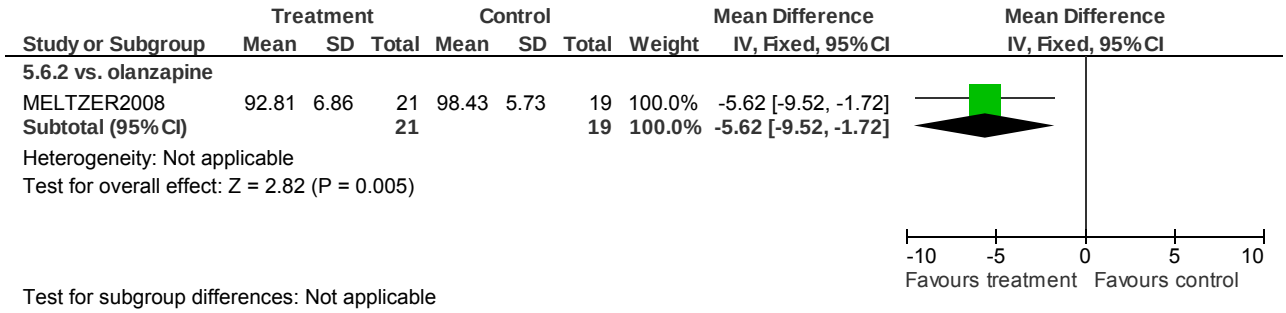


5.5 AE: 1. Metabolic SEs - Weight at endpoint (kg) (short-term)



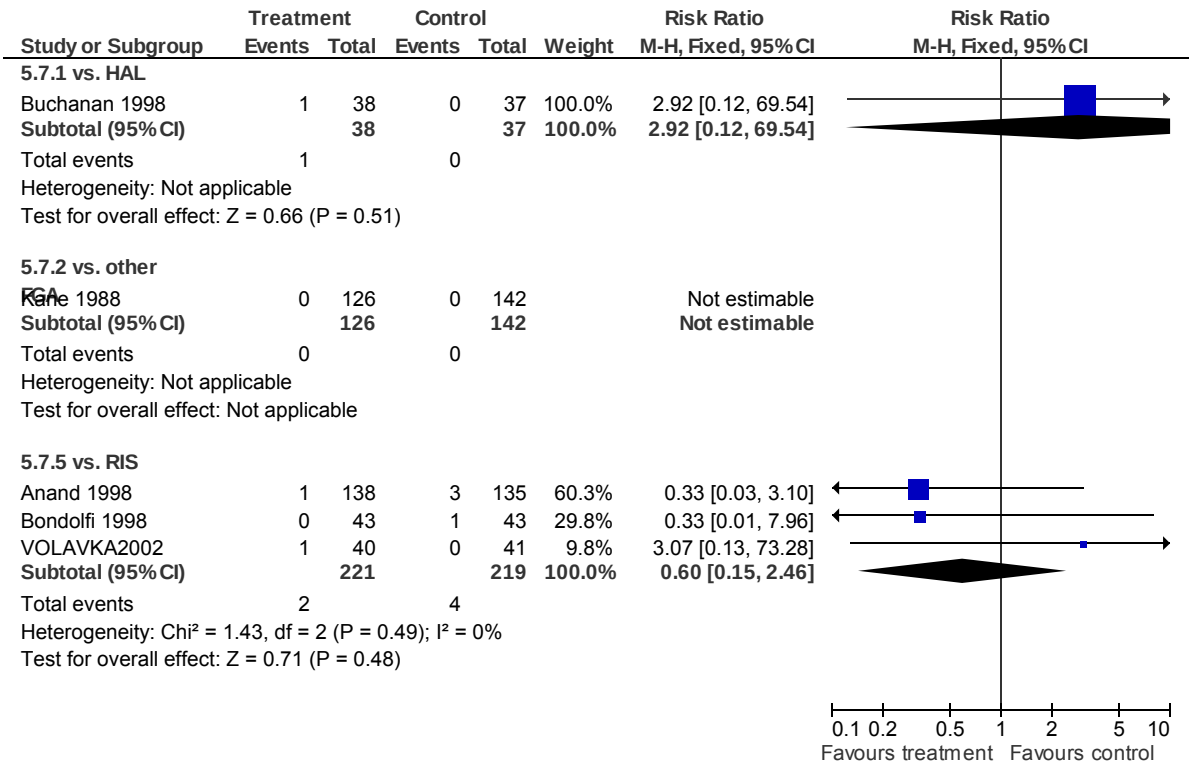
Test for subgroup differences: Chi² = 31.01, df = 2 (P < 0.00001), I² = 93.6%

5.6 AE: 1. Metabolic SEs - Weight at endpoint (kg) (medium-term)



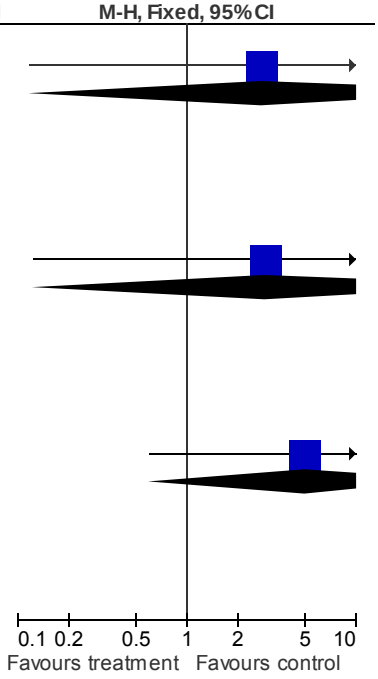
Test for subgroup differences: Not applicable

5.7 AE: 1. Metabolic SEs - Blood problems (treatment-emergent) (short-term)



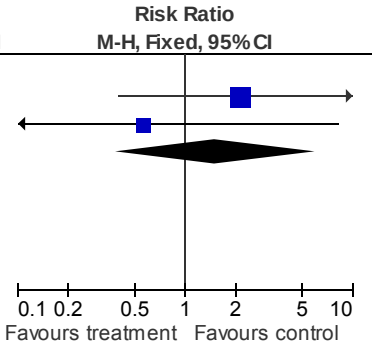
5.8 AE: 1. Metabolic SEs - Blood problems (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.8.1 vs. HAL: Agranulocytosis						
VOLAVKA2002	1	40	0	37	100.0%	2.78 [0.12, 66.20]
Subtotal (95% CI)		**40**		**37**	**100.0%**	**2.78 [0.12, 66.20]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.63 (P = 0.53)						
5.8.2 vs. OLZ: Agranulocytosis						
VOLAVKA2002	1	40	0	39	100.0%	2.93 [0.12, 69.74]
Subtotal (95% CI)		**40**		**39**	**100.0%**	**2.93 [0.12, 69.74]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.66 (P = 0.51)						
5.8.5 vs. OLZ: White blood cell problems						
Beuzen 1998	5	90	1	90	100.0%	5.00 [0.60, 41.95]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**5.00 [0.60, 41.95]**
Total events	5		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.48 (P = 0.14)						



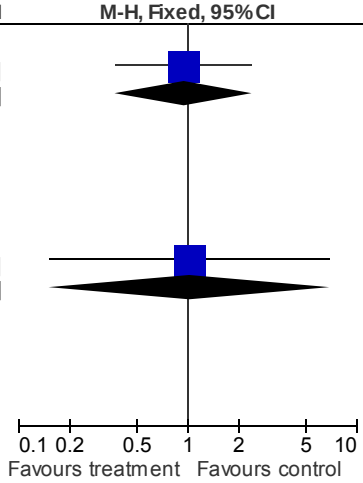
5.9 AE: 1. Metabolic SEs - Blood problems (treatment-emergent) (long-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.9.1 vs. HAL						
Rosenheck 1997	4	205	2	218	60.2%	2.13 [0.39, 11.49]
Tamminga 1994	1	25	1	14	39.8%	0.56 [0.04, 8.28]
Subtotal (95% CI)		**230**		**232**	**100.0%**	**1.50 [0.38, 5.94]**
Total events	5		3			
Heterogeneity: Chi² = 0.68, df = 1 (P = 0.41); I² = 0%						
Test for overall effect: Z = 0.58 (P = 0.56)						



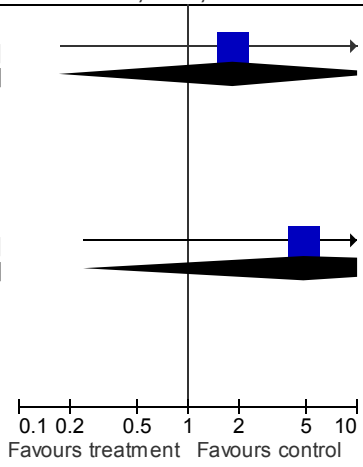
5.10 AE: 1. Metabolic SEs - Neutropenia (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.10.6 vs. HAL: Neutropenia (granulocyte<1500/c ml)						
Rosenheck 1997	8	205	9	218	100.0%	0.95 [0.37, 2.40]
Subtotal (95% CI)		**205**		**218**	**100.0%**	**0.95 [0.37, 2.40]**
Total events	8		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.12 (P = 0.91)						
5.10.7 vs. RIS: Neutropenia						
VOLAVKA2002	2	40	2	41	100.0%	1.02 [0.15, 6.93]
Subtotal (95% CI)		**40**		**41**	**100.0%**	**1.02 [0.15, 6.93]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.03 (P = 0.98)						



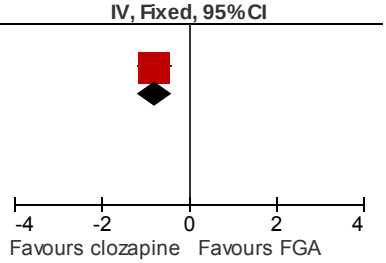
5.11 AE: 1. Metabolic SEs - Neutropenia (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.11.3 vs. HAL: Neutropenia						
VOLAVKA2002	2	40	1	37	100.0%	1.85 [0.17, 19.56]
Subtotal (95% CI)		**40**		**37**	**100.0%**	**1.85 [0.17, 19.56]**
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.51 (P = 0.61)						
5.11.4 vs. OLZ: Neutropenia						
VOLAVKA2002	2	40	0	39	100.0%	4.88 [0.24, 98.47]
		40		**39**	**100.0%**	**4.88 [0.24, 98.47]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.03 (P = 0.30)						



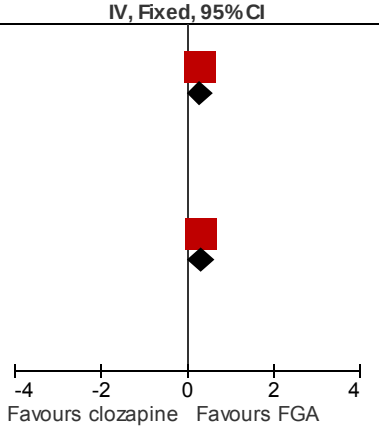
5.12 AE: 1. Metabolic SEs - Prolactin-related problems (long-term)

Study or Subgroup	SMD	SE	Clozapine Total	FGA Total	Weight	SMD IV, Fixed, 95% CI
5.12.1 vs. other FGA - decreased urine production						
LIEBERMAN 2003	-0.8102	0.201	80	80	100.0%	-0.81 [-1.20, -0.42]
Subtotal (95% CI)			**80**	**80**	**100.0%**	**-0.81 [-1.20, -0.42]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.03 (P < 0.0001)						
Test for subgroup differences: Not applicable						



5.13 AE: 1. Metabolic SEs - Clinical parameters (long-term)

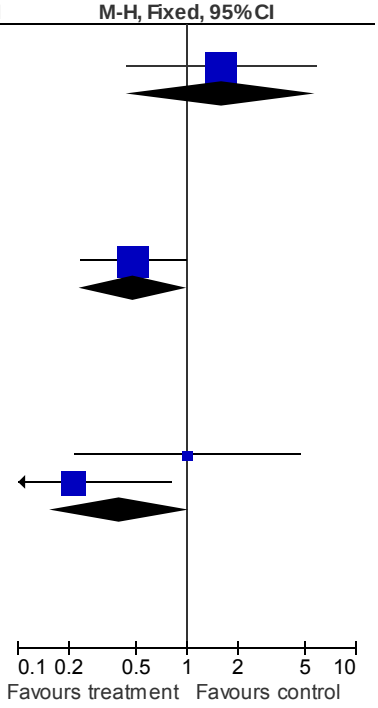
Study or Subgroup	SMD	SE	Clozapine Total	FGA Total	Weight	SMD IV, Fixed, 95% CI
5.13.1 vs. other FGA - EKG heart rate (measured from EKG tracing)						
LIEBERMAN 2003	0.2958	0.1589	80	80	100.0%	0.30 [-0.02, 0.61]
Subtotal (95% CI)			**80**	**80**	**100.0%**	**0.30 [-0.02, 0.61]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.86 (P = 0.06)						
5.13.2 vs. other FGA - EKG QT interval (measured from EKG tracing)						
LIEBERMAN 2003	0.3122	0.159	80	80	100.0%	0.31 [0.00, 0.62]
Subtotal (95% CI)			**80**	**80**	**100.0%**	**0.31 [0.00, 0.62]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.96 (P = 0.05)						



Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.94), I² = 0%

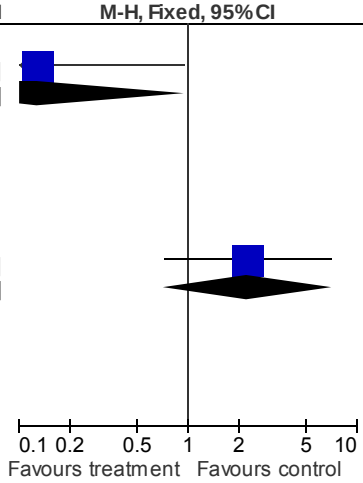
5.14 AE: 2. Neurologic SEs - Movement disorder (treatment-emergent) (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.14.1 vs. HAL: Movement disorder						
Buchanan 1998	5	21	3	20	100.0%	1.59 [0.44, 5.79]
Subtotal (95% CI)		**21**		**20**	**100.0%**	**1.59 [0.44, 5.79]**
Total events	5		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.70 (P = 0.48)						
5.14.2 vs. other FGA: Movement disorder						
Claghorn 1987	9	75	19	76	100.0%	0.48 [0.23, 0.99]
Subtotal (95% CI)		**75**		**76**	**100.0%**	**0.48 [0.23, 0.99]**
Total events	9		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.98 (P = 0.05)						
5.14.3 vs. RIS: EPS						
Bondolfi 1998	3	43	3	43	23.7%	1.00 [0.21, 4.68]
Breier 1999	2	14	10	15	76.3%	0.21 [0.06, 0.81]
Subtotal (95% CI)		**57**		**58**	**100.0%**	**0.40 [0.16, 1.03]**
Total events	5		13			
Heterogeneity: Chi² = 2.20, df = 1 (P = 0.14); I² = 54%						
Test for overall effect: Z = 1.90 (P = 0.06)						



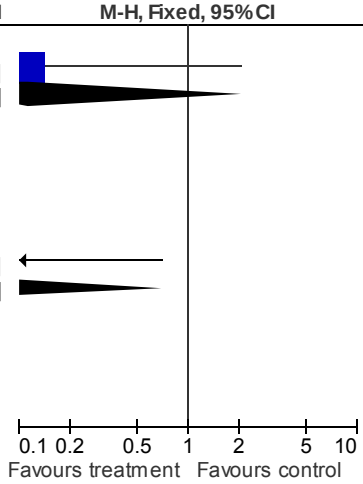
5.15 AE: 2. Neurologic SEs - Movement disorder (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.15.1 vs. other FGA: Movement disorder						
Hong 1997	1	21	7	19	100.0%	0.13 [0.02, 0.96]
Subtotal (95% CI)		**21**		**19**	**100.0%**	**0.13 [0.02, 0.96]**
Total events	1		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.00 (P = 0.05)						
5.15.2 vs. OLZ: Any extrapyramidal event						
Beuzen 1998	9	90	4	90	100.0%	2.25 [0.72, 7.04]
Subtotal (95% CI)		**90**		**90**	**100.0%**	**2.25 [0.72, 7.04]**
Total events	9		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.39 (P = 0.16)						



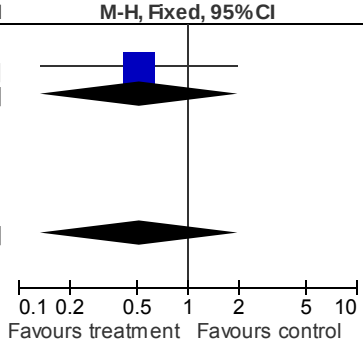
5.16 AE: 2. Neurologic SEs - Akathisia (treatment-emergent) (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.16.7 vs. OLZ						
Bitter 1999	0	74	4	76	100.0%	0.11 [0.01, 2.08]
Subtotal (95% CI)		**74**		**76**	**100.0%**	**0.11 [0.01, 2.08]**
Total events	0		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.46 (P = 0.14)						
5.16.10 vs. RIS						
Chowdhury 1999	0	30	11	30	100.0%	0.04 [0.00, 0.71]
Subtotal (95% CI)		**30**		**30**	**100.0%**	**0.04 [0.00, 0.71]**
Total events	0		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.20 (P = 0.03)						



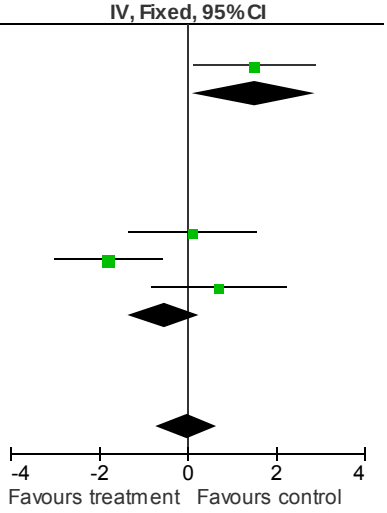
5.17 AE: 2. Neurologic SEs - Needing additional anticholinergic medication (medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
5.17.1 vs. OLZ						
Bitter 1999	3	74	6	76	100.0%	0.51 [0.13, 1.98]
Subtotal (95% CI)		**74**		**76**	**100.0%**	**0.51 [0.13, 1.98]**
Total events	3		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						
Total (95% CI)		**74**		**76**	**100.0%**	**0.51 [0.13, 1.98]**
Total events	3		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						



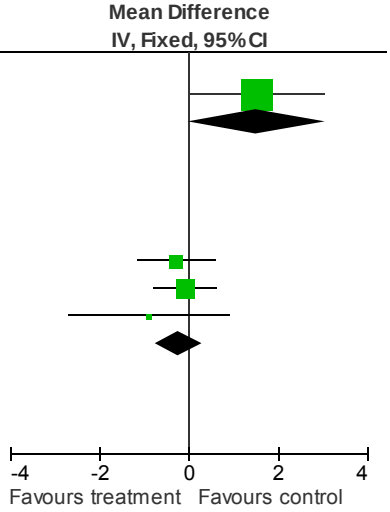
5.18 AE: 2. Neurologic SEs - Simpson-Angus Scale (SAS; change/endpoint) (short-to-medium-term)

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
5.18.1 vs. OLZ (short-term)								
MELTZER2008	2.5	2.29	21	1	2.18	19	25.0%	1.50 [0.11, 2.89]
Subtotal (95% CI)			**21**			**19**	**25.0%**	**1.50 [0.11, 2.89]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.12 (P = 0.03)								
5.18.2 vs. OLZ (medium-term)								
Bitter 1999	-2.9	3.9	70	-3	4.8	69	22.7%	0.10 [-1.36, 1.56]
Beuzen 1998	-3.2	4.8	88	-1.4	3.3	84	31.9%	-1.80 [-3.03, -0.57]
MELTZER2008	2.3	2.75	21	1.6	2.18	19	20.5%	0.70 [-0.83, 2.23]
Subtotal (95% CI)			**179**			**172**	**75.0%**	**-0.54 [-1.34, 0.26]**
Heterogeneity: Chi² = 7.32, df = 2 (P = 0.03); I² = 73%								
Test for overall effect: Z = 1.33 (P = 0.18)								
Total (95% CI)			**200**			**191**	**100.0%**	**-0.03 [-0.73, 0.66]**
Heterogeneity: Chi² = 13.59, df = 3 (P = 0.004); I² = 78%								
Test for overall effect: Z = 0.09 (P = 0.92)								
Test for subgroup differences: Chi² = 6.27, df = 1 (P = 0.01), I² = 84.1%								



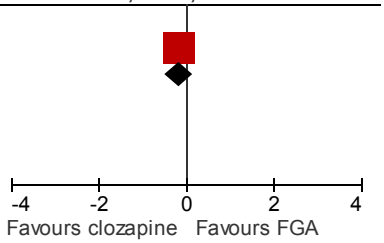
5.19 AE: 2. Neurologic SEs - Abnormal Involuntary Movement Scale (AIMS; change/endpoint) (short-to-medium-

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
5.19.1 vs. OLZ (short-term)								
MELTZER2008	2	2.75	21	0.5	2.18	19	100.0%	1.50 [-0.03, 3.03]
Subtotal (95% CI)						**19**	**100.0%**	**1.50 [-0.03, 3.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.92 (P = 0.05)								
5.19.2 vs. OLZ (medium-term)								
Bitter 1999	-0.9	2.8	70	-0.6	2.5	69	35.7%	-0.30 [-1.18, 0.58]
Beuzen 1998	-0.8	2.2	88	-0.7	2.5	84	55.8%	-0.10 [-0.81, 0.61]
MELTZER2008	1.4	3.21	21	2.3	2.62	19	8.5%	-0.90 [-2.71, 0.91]
Subtotal (95% CI)			**179**			**172**	**100.0%**	**-0.24 [-0.77, 0.29]**
Heterogeneity: Chi² = 0.68, df = 2 (P = 0.71); I² = 0%								
Test for overall effect: Z = 0.89 (P = 0.37)								
Test for subgroup differences: Chi² = 4.43, df = 1 (P = 0.04), I² = 77.4%								



5.20 AE: 2. Neurologic SEs - Simpson-Angus extrapyramidal symptom scale (long-term)

Study or Subgroup	SMD	SE	Clozapine Total	FGA Total	Weight	SMD IV, Fixed, 95% CI
5.20.1 vs. other FGA						
LIEBERMAN 2003	-0.1785	0.1584	80	80	100.0%	-0.18 [-0.49, 0.13]
Subtotal (95% CI)			**80**	**80**	**100.0%**	**-0.18 [-0.49, 0.13]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.13 (P = 0.26)						
Test for subgroup differences: Not applicable						

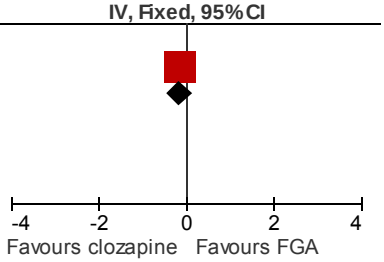


5.21 AE: 2. Neurologic SEs - Simpson-Angus Scale: Parkinsonian (long-term)

Study or Subgroup	SMD	SE	Clozapine Total	FGA Total	Weight	SMD IV, Fixed, 95% CI
5.21.1 vs. other FGA						
LIEBERMAN 2003	-0.1615	0.1583	80	80	100.0%	-0.16 [-0.47, 0.15]
Subtotal (95% CI)			**80**	**80**	**100.0%**	**-0.16 [-0.47, 0.15]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.02 (P = 0.31)



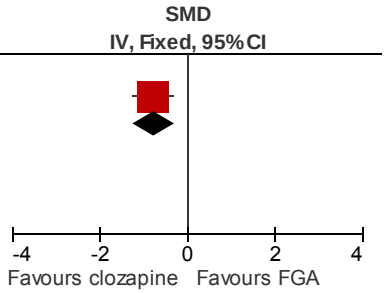
Test for subgroup differences: Not applicable

5.22 AE: 2. Neurologic SEs - Simpson-Angus Extrapyramidal Symptom Scale: dystonia

Study or Subgroup	SMD	SE	Clozapine Total	FGA Total	Weight	SMD IV, Fixed, 95% CI
5.22.1 vs. other FGA						
LIEBERMAN 2003	-0.7868	0.2433	80	80	100.0%	-0.79 [-1.26, -0.31]
Subtotal (95% CI)			**80**	**80**	**100.0%**	**-0.79 [-1.26, -0.31]**

Heterogeneity: Not applicable

Test for overall effect: Z = 3.23 (P = 0.001)



Test for subgroup differences: Not applicable

5.23 AE: 2. Neurologic SEs (only sig. diff presented)

Study or Subgroup	SMD	SE	Clozapine Total	FGA Total	Weight	SMD IV, Fixed, 95% CI
5.23.1 vs. other FGA - tense muscles						
LIEBERMAN 2003	-0.6112	0.2726	80	80	100.0%	-0.61 [-1.15, -0.08]
Subtotal (95% CI)			**80**	**80**	**100.0%**	**-0.61 [-1.15, -0.08]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.24 (P = 0.02)

5.23.2 vs. other FGA - akathisia

LIEBERMAN 2003	-0.4162	0.1599	80	80	100.0%	-0.42 [-0.73, -0.10]
Subtotal (95% CI)			**80**	**80**	**100.0%**	**-0.42 [-0.73, -0.10]**

Heterogeneity: Not applicable

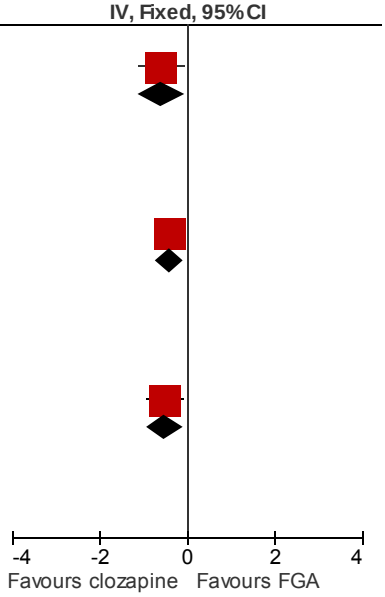
Test for overall effect: Z = 2.60 (P = 0.009)

5.23.3 vs. other FGA - objectively observed restlessness

LIEBERMAN 2003	-0.5191	0.2191	80	80	100.0%	-0.52 [-0.95, -0.09]
Subtotal (95% CI)			**80**	**80**	**100.0%**	**-0.52 [-0.95, -0.09]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.37 (P = 0.02)

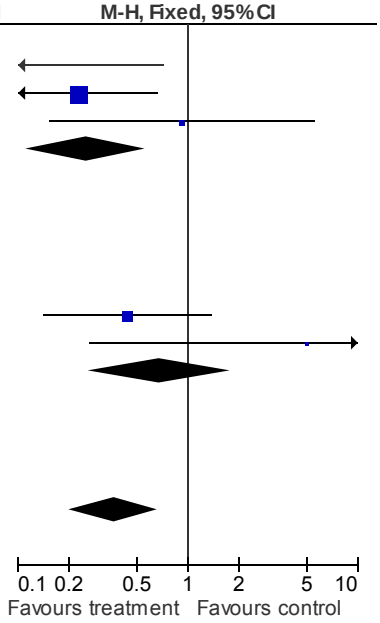


Test for subgroup differences: Chi² = 0.42, df = 2 (P = 0.81), I² = 0%

6 Quetiapine versus FGA (overall SE analysis)

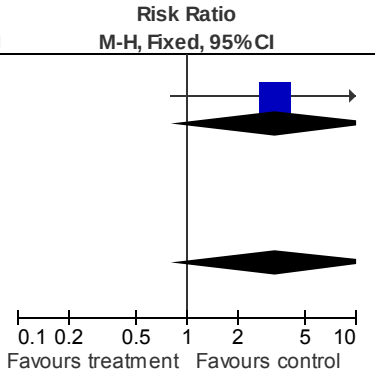
6.1 Leaving the study early: 3: Adverse event (short-to-medium-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.1.1 vs. HAL						
Arvanitis 1997	1	157	4	52	17.0%	0.08 [0.01, 0.72]
Fleischhacker 1996	4	221	18	227	50.2%	0.23 [0.08, 0.66]
Purdon 2000	2	13	2	12	5.9%	0.92 [0.15, 5.56]
Subtotal (95% CI)		**391**		**291**	**73.0%**	**0.25 [0.11, 0.56]**
Total events	7		24			
Heterogeneity: Chi² = 3.06, df = 2 (P = 0.22); I² = 35%						
Test for overall effect: Z = 3.36 (P = 0.0008)						
6.1.3 vs. other FGA						
Link 1994	4	101	9	100	25.6%	0.44 [0.14, 1.38]
CONLEY2005	2	13	0	13	1.4%	5.00 [0.26, 95.02]
Subtotal (95% CI)		**114**		**113**	**27.0%**	**0.68 [0.26, 1.79]**
Total events	6		9			
Heterogeneity: Chi² = 2.32, df = 1 (P = 0.13); I² = 57%						
Test for overall effect: Z = 0.78 (P = 0.43)						
Total (95% CI)		**505**		**404**	**100.0%**	**0.37 [0.20, 0.67]**
Total events	13		33			
Heterogeneity: Chi² = 6.70, df = 4 (P = 0.15); I² = 40%						
Test for overall effect: Z = 3.26 (P = 0.001)						



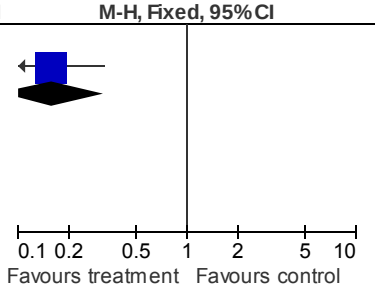
6.2 AE: 1. Metabolic SEs - Weight gain (>=7% increase from baseline) (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.2.1 vs. HAL						
Arvanitis 1997	20	157	2	52	100.0%	3.31 [0.80, 13.69]
Subtotal (95% CI)		**157**		**52**	**100.0%**	**3.31 [0.80, 13.69]**
Total events	20		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.65 (P = 0.10)						
Total (95% CI)		**157**		**52**	**100.0%**	**3.31 [0.80, 13.69]**
Total events	20		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.65 (P = 0.10)						



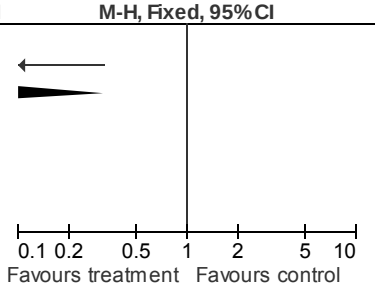
6.3 AE: 2. Neurologic SEs (treatment-emergent) - Any EPS (short-term)

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.3.1 vs. HAL: EPS						
Arvanitis 1997	9	157	19	52	100.0%	0.16 [0.08, 0.33]
Subtotal (95% CI)		**157**		**52**	**100.0%**	**0.16 [0.08, 0.33]**
Total events	9		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.98 (P < 0.00001)						



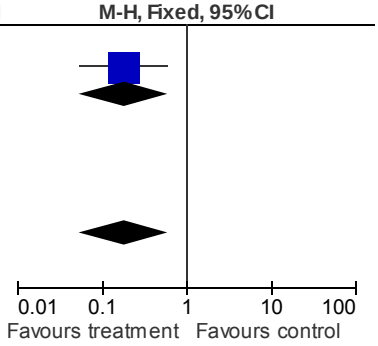
6.4 AE: 2. Neurologic SEs (treatment-emergent) - Akathisia (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.4.3 vs. HAL: akathisia						
Arvanitis 1997	1	157	8	52	100.0%	0.04 [0.01, 0.32]
Subtotal (95% CI)		**157**		**52**	**100.0%**	**0.04 [0.01, 0.32]**
Total events	1		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.04 (P = 0.002)						



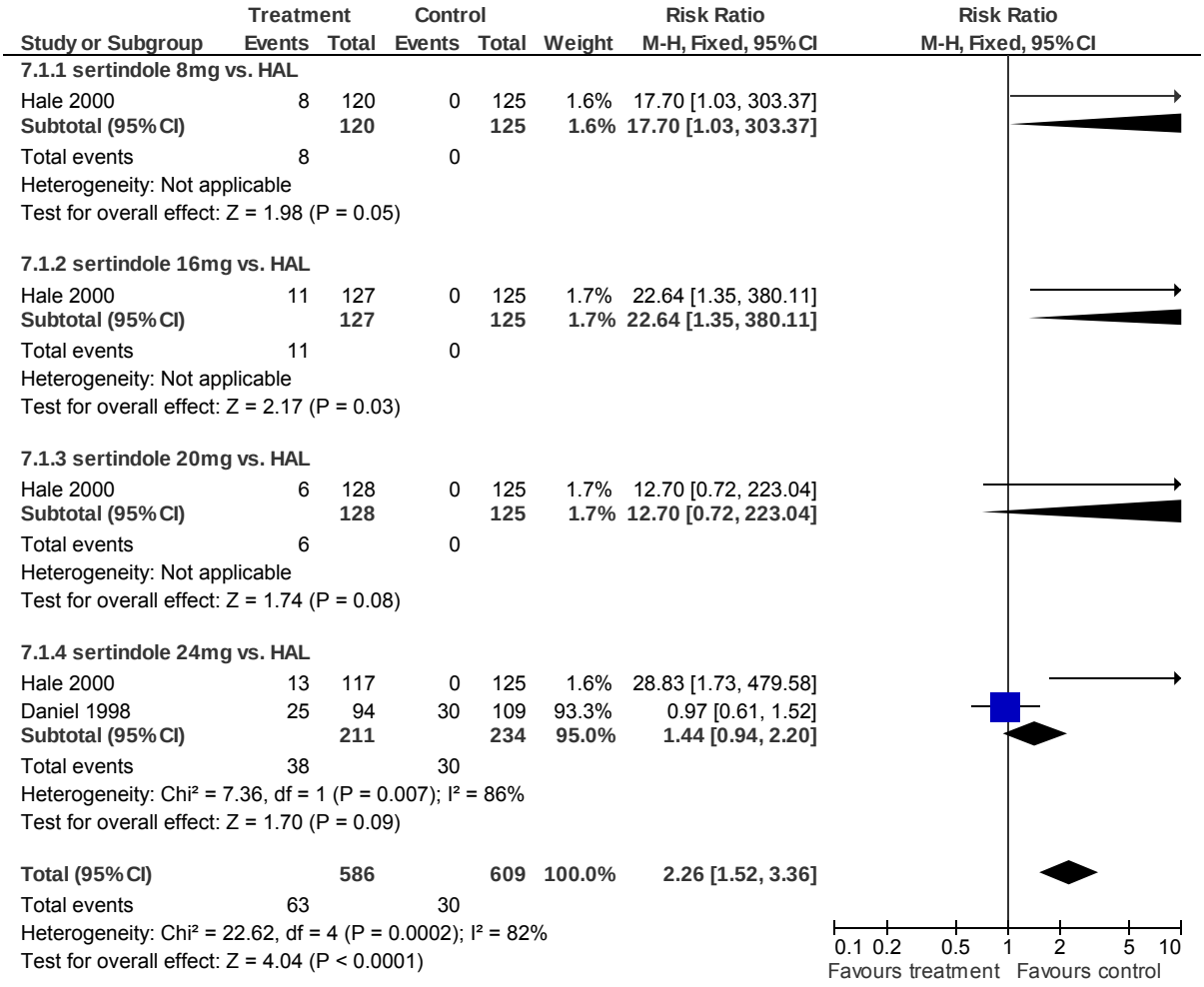
6.5 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
6.5.1 vs. HAL						
Emsley 1999	3	143	17	145	100.0%	0.18 [0.05, 0.60]
Subtotal (95% CI)		**143**		**145**	**100.0%**	**0.18 [0.05, 0.60]**
Total events	3		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.80 (P = 0.005)						
Total (95% CI)		**143**		**145**	**100.0%**	**0.18 [0.05, 0.60]**
Total events	3		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.80 (P = 0.005)						

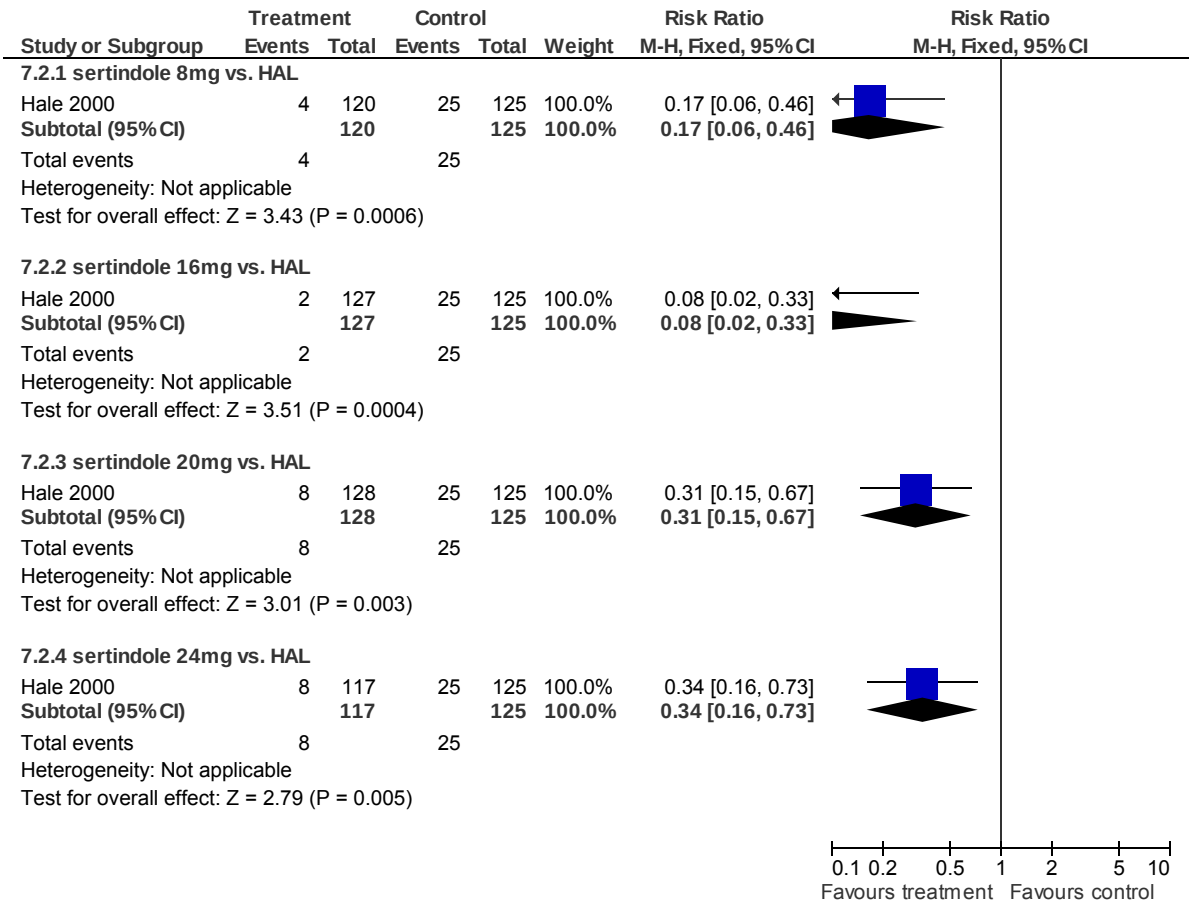


7 Sertindole versus FGA (overall SE analysis)

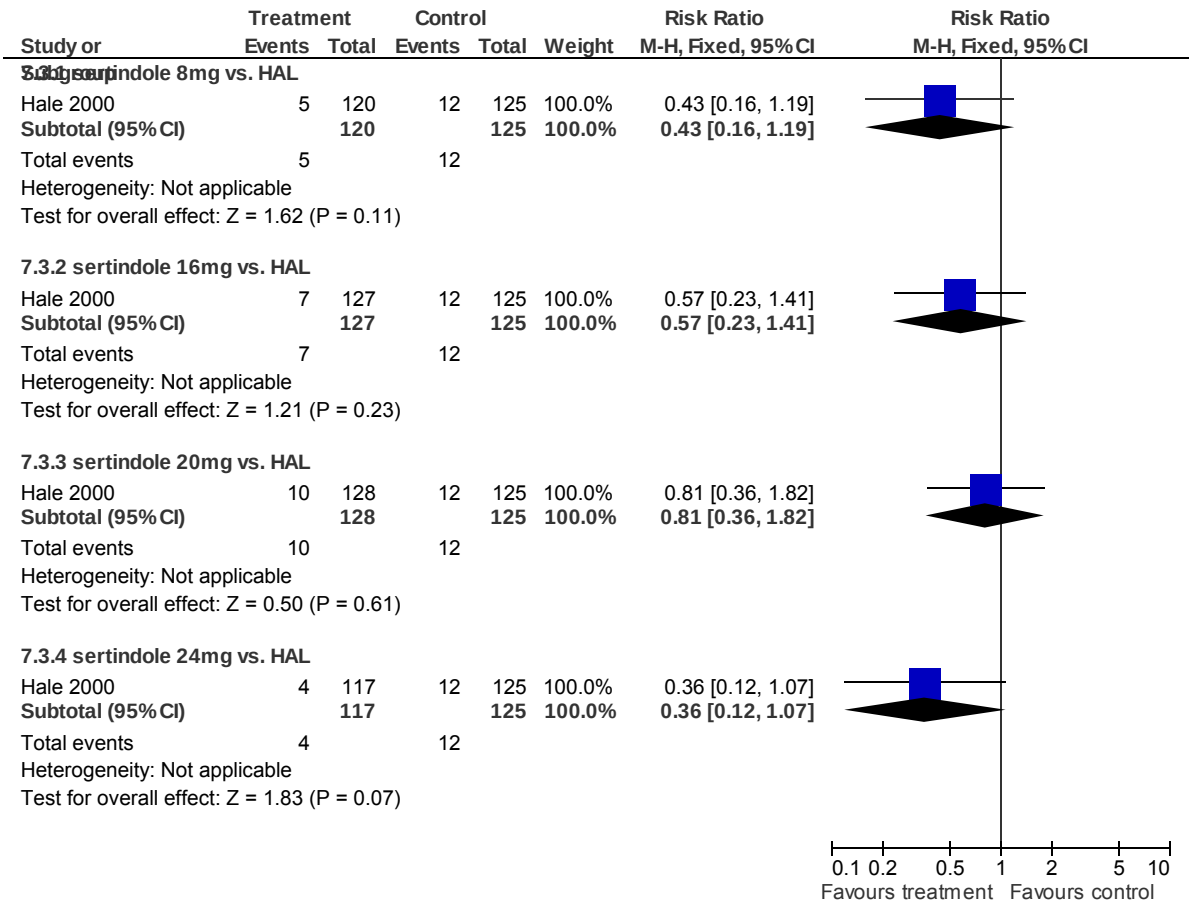
7.1 Leaving the study early: 3: Adverse event (short-term)



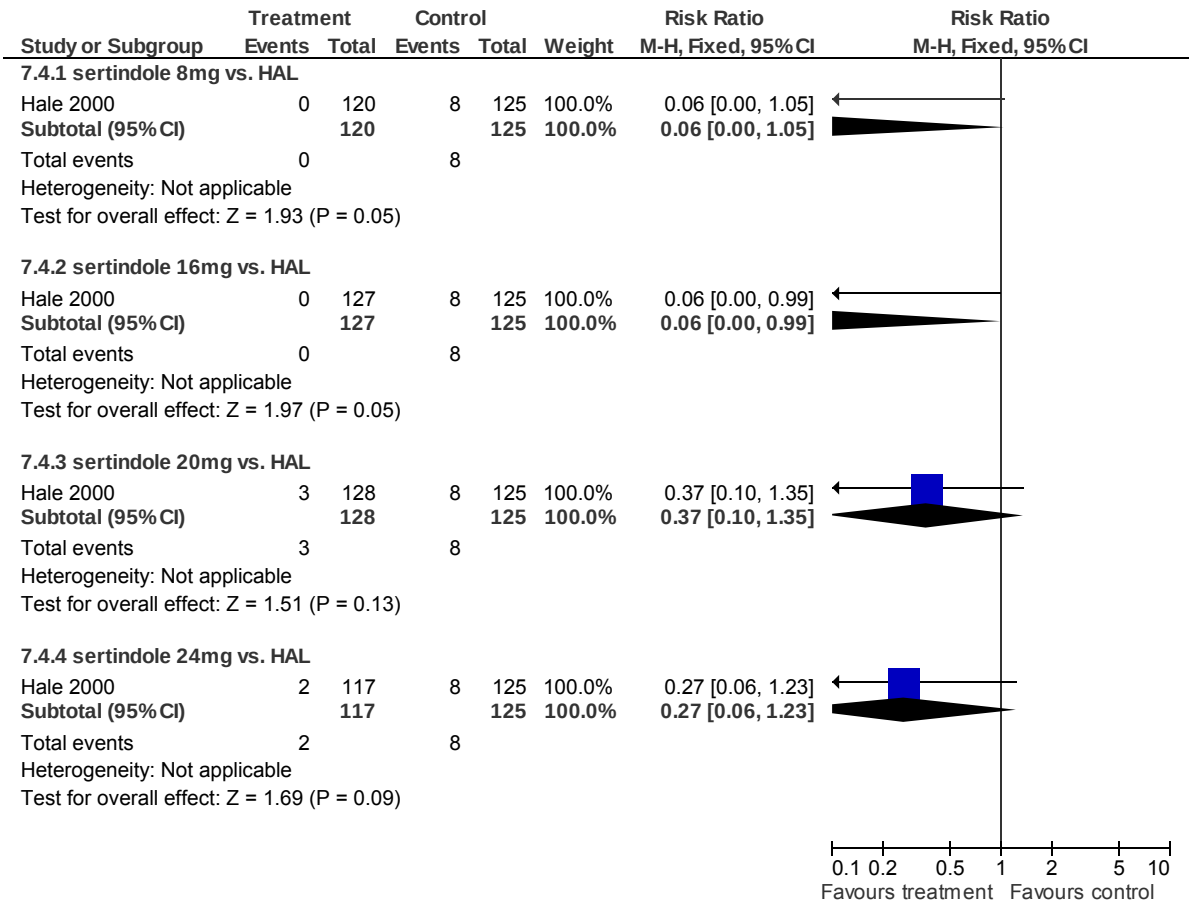
7.2 AE: 2. Neurologic SEs - Akathisia (short-term)



7.3 AE: 2. Neurologic SEs - Asthenia (short-term)

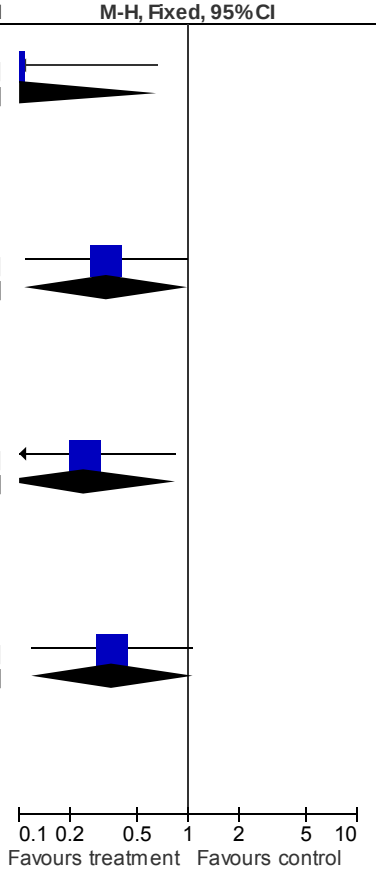


7.4 AE: 2. Neurologic SEs - Dystonia (short-term)

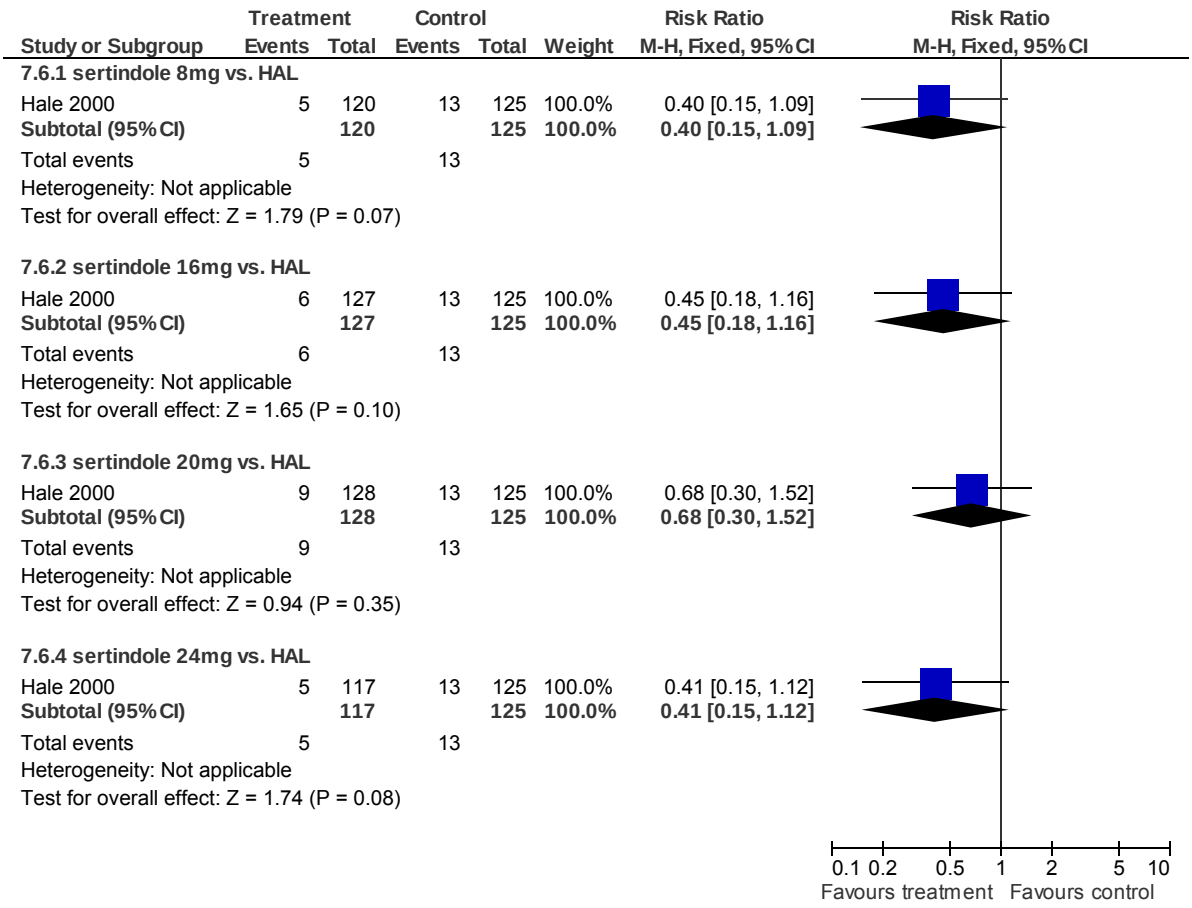


7.5 AE: 2. Neurologic SEs - Extrapyramidal syndrome (short-term)

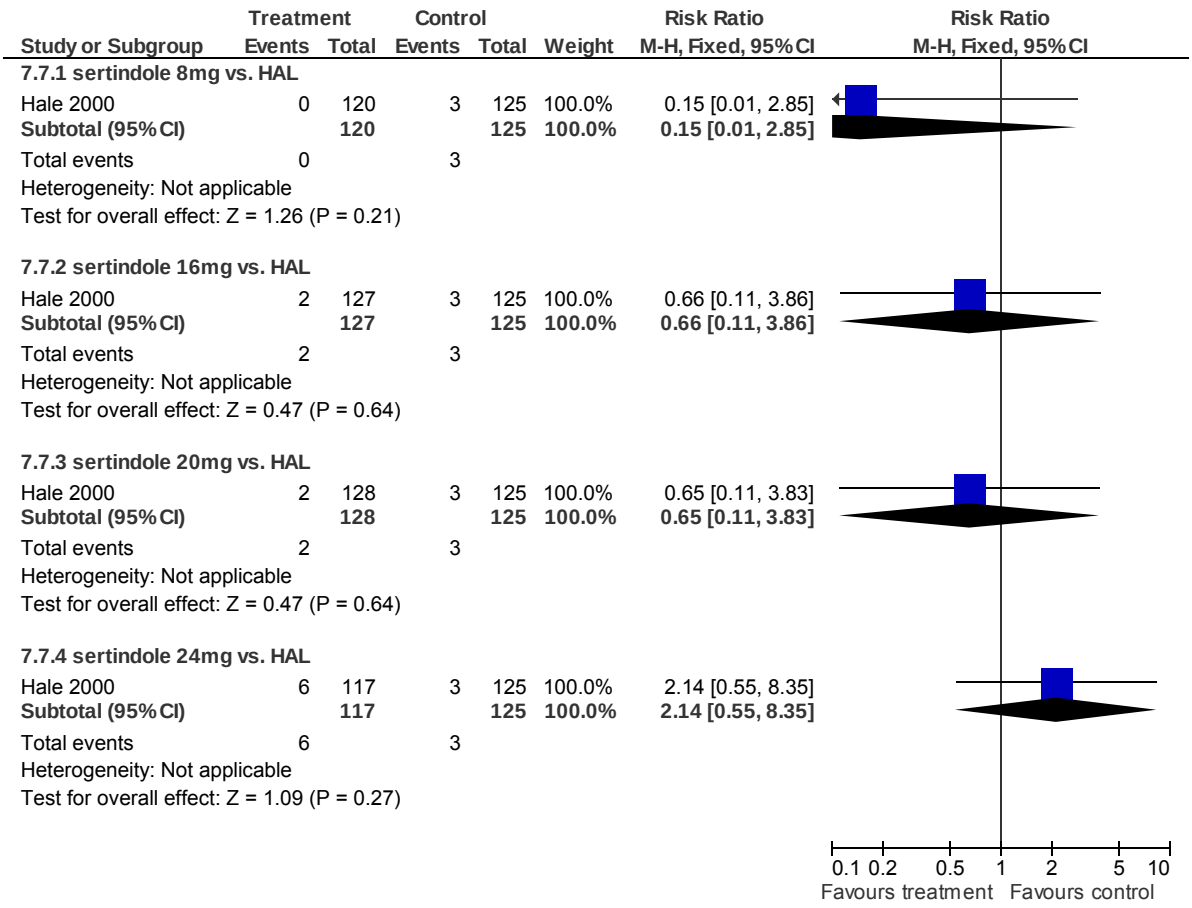
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
7.5.1 sertindole 8mg vs. HAL						
Hale 2000	1	120	12	125	100.0%	0.09 [0.01, 0.66]
Subtotal (95% CI)		**120**		**125**	**100.0%**	**0.09 [0.01, 0.66]**
Total events	1		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.37 (P = 0.02)						
7.5.2 sertindole 16mg vs. HAL						
Hale 2000	4	127	12	125	100.0%	0.33 [0.11, 0.99]
Subtotal (95% CI)		**127**		**125**	**100.0%**	**0.33 [0.11, 0.99]**
Total events	4		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.98 (P = 0.05)						
7.5.3 sertindole 20mg vs. HAL						
Hale 2000	3	128	12	125	100.0%	0.24 [0.07, 0.84]
Subtotal (95% CI)		**128**		**125**	**100.0%**	**0.24 [0.07, 0.84]**
Total events	3		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.23 (P = 0.03)						
7.5.4 sertindole 24mg vs. HAL						
Hale 2000	4	117	12	125	100.0%	0.36 [0.12, 1.07]
Subtotal (95% CI)		**117**		**125**	**100.0%**	**0.36 [0.12, 1.07]**
Total events	4		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.83 (P = 0.07)						



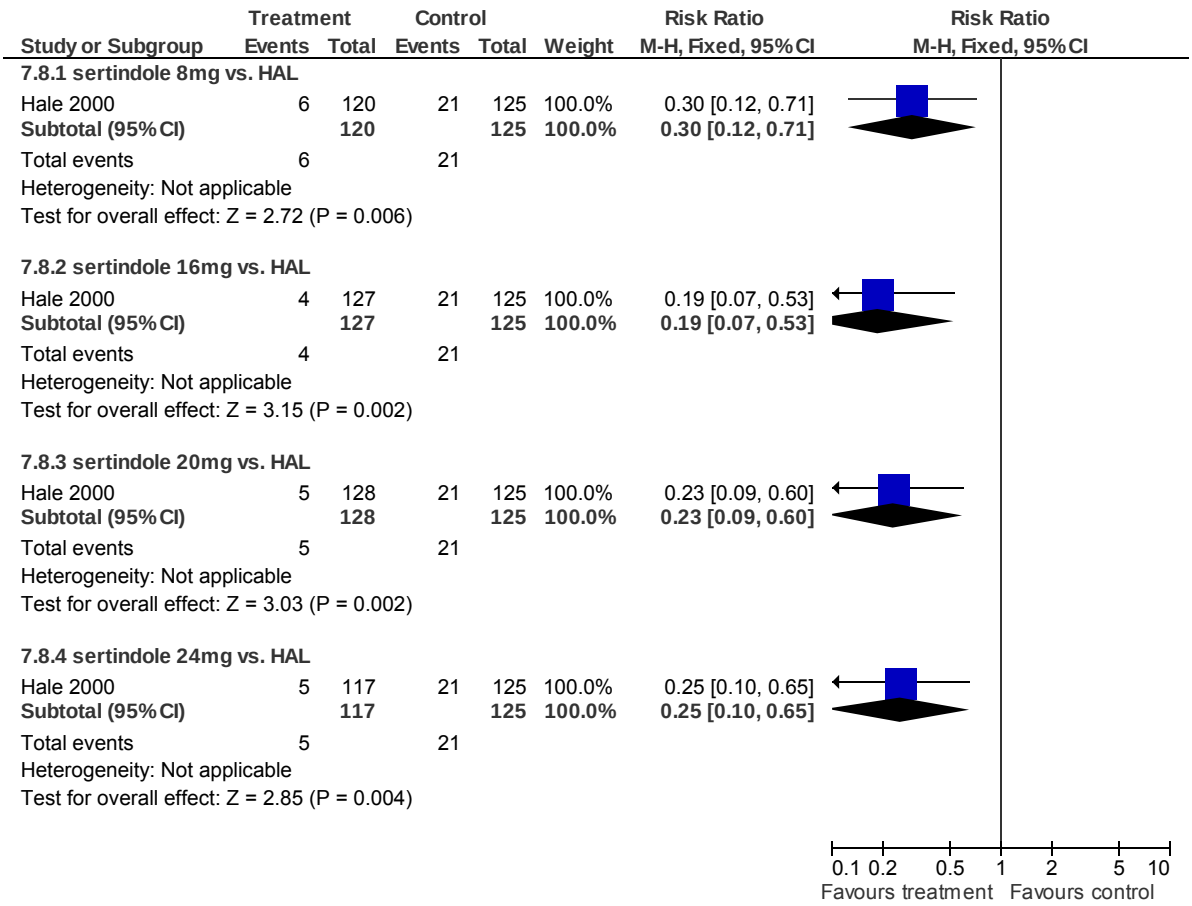
7.6 AE: 2. Neurologic SEs - Hypertonia (short-term)



7.7 AE: 2. Neurologic SEs - Hypokinesia (short-term)

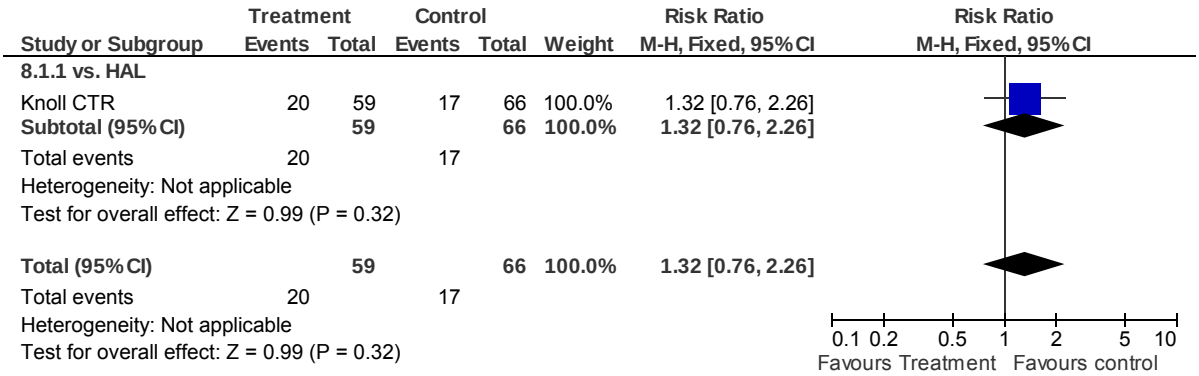


7.8 AE: 2. Neurologic SEs - Tremor (short-term)



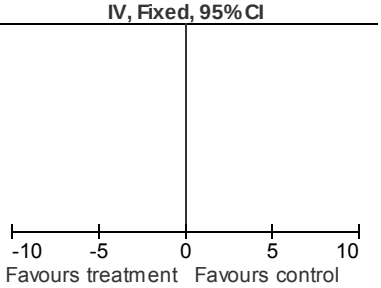
8 Zotepine versus FGA (overall SE analysis)

8.1 Leaving the study early: 3. Due to adverse event (medium-term)



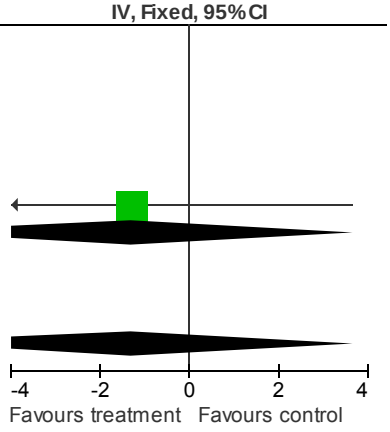
8.2 AE: 1. Metabolic SEs - Weight change from baseline (kg) (medium-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
8.2.1 vs. HAL								
Knoll CTR	2.5	0	59	0.5	0	66		Not estimable
Subtotal (95% CI)			**59**			**66**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Total (95% CI)			**59**			**66**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Not applicable								



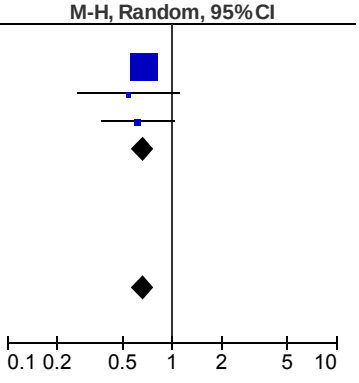
8.3 AE: 1. Metabolic SEs - Weight change (kg) (short-term)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
8.3.1 vs. HAL								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
8.3.2 vs. other FGA								
Cooper 1999a	73	14.4	53	74.3	11.4	52	100.0%	-1.30 [-6.26, 3.66]
Subtotal (95% CI)			**53**			**52**	**100.0%**	**-1.30 [-6.26, 3.66]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.51 (P = 0.61)								
Total (95% CI)			**53**			**52**	**100.0%**	**-1.30 [-6.26, 3.66]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.51 (P = 0.61)								
Test for subgroup differences: Not applicable								

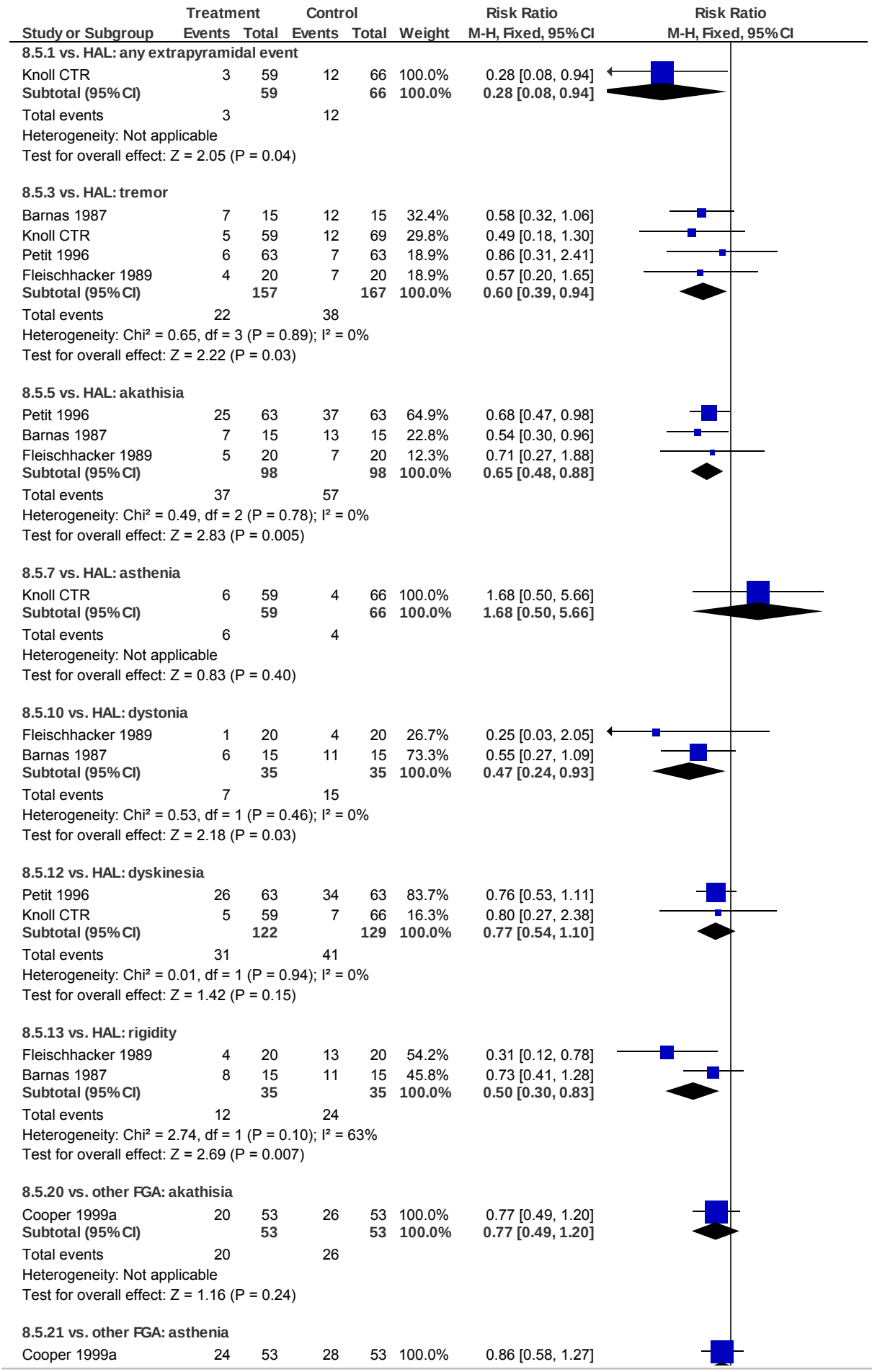


8.4 AE: 2. Neurologic SEs - Use of anticholinergic medication (short-term)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
8.4.1 vs. HAL						
Petit 1996	42	63	62	63	84.7%	0.68 [0.57, 0.81]
Klieser 1996	6	20	25	45	5.2%	0.54 [0.26, 1.11]
Barnas 1987	8	15	13	15	10.1%	0.62 [0.37, 1.03]
Subtotal (95% CI)		**98**		**123**	**100.0%**	**0.66 [0.56, 0.78]**
Total events	56		100			
Heterogeneity: Tau² = 0.00; Chi² = 0.56, df = 2 (P = 0.76); I² = 0%						
Test for overall effect: Z = 4.93 (P < 0.00001)						
Total (95% CI)		**98**		**123**	**100.0%**	**0.66 [0.56, 0.78]**
Total events	56		100			
Heterogeneity: Tau² = 0.00; Chi² = 0.56, df = 2 (P = 0.76); I² = 0%						
Test for overall effect: Z = 4.93 (P < 0.00001)						



8.5 AE: 2. Neurologic SEs - Movement disorders (treatment-emergent) (short-term)



Subtotal (95% CI)	**53**	**53**	**100.0%**	**0.86 [0.58, 1.27]**	
Total events	24	28			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.77 (P = 0.44)

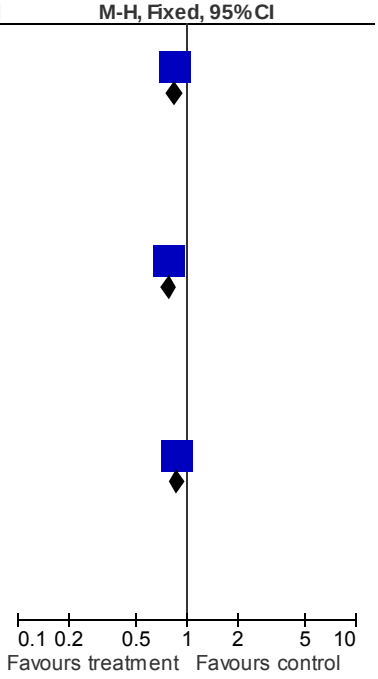
Table 10: Studies included in the review of the effectiveness of antipsychotic drugs

Treatment	versus Comparator		
	versus haloperidol (FGA)	**versus non-haloperidol FGA**	**versus SGA**
SGA		CATIE CUtLASS	CATIE CUtLASS

1 Olanzapine versus another antipsychotic drug

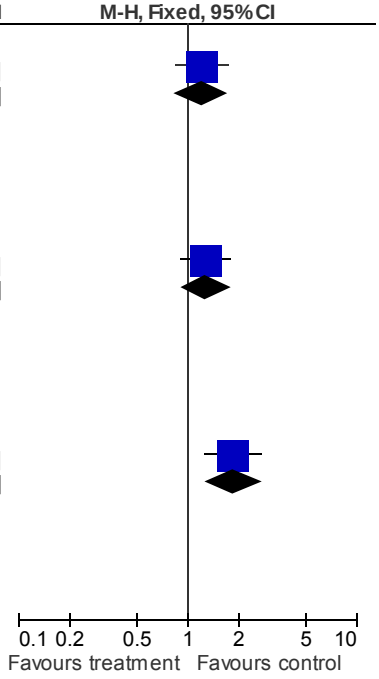
1.1 Discontinuation of treatment for any reason (by 18 months FU)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 vs. perphenazine						
CATIE-phase1	210	336	192	261	100.0%	0.85 [0.76, 0.95]
Subtotal (95% CI)		**336**		**261**	**100.0%**	**0.85 [0.76, 0.95]**
Total events	210		192			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.90 (P = 0.004)						
1.1.2 vs. quetiapine						
CATIE-phase1	210	336	269	337	100.0%	0.78 [0.71, 0.86]
Subtotal (95% CI)		**336**		**337**	**100.0%**	**0.78 [0.71, 0.86]**
Total events	210		269			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.86 (P < 0.00001)						
1.1.3 vs. risperidone						
CATIE-phase1	210	336	245	341	100.0%	0.87 [0.78, 0.97]
Subtotal (95% CI)		**336**		**341**	**100.0%**	**0.87 [0.78, 0.97]**
Total events	210		245			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.57 (P = 0.01)						



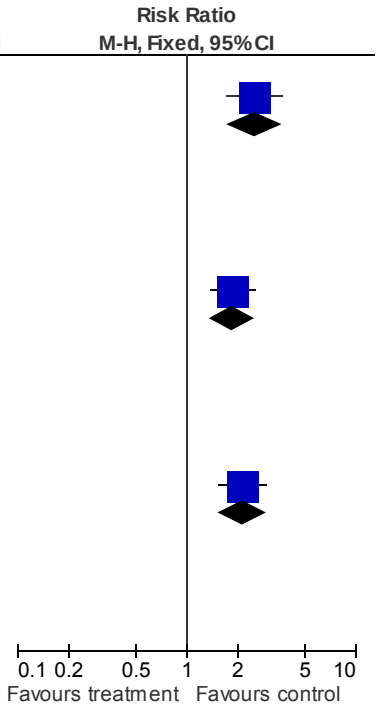
1.2 Discontinuation of treatment owing to intolerability (by 18 months FU)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 vs. perphenazine						
CATIE-phase1	62	336	40	261	100.0%	1.20 [0.84, 1.73]
Subtotal (95% CI)		**336**		**261**	**100.0%**	**1.20 [0.84, 1.73]**
Total events	62		40			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.00 (P = 0.32)						
1.2.2 vs. quetiapine						
CATIE-phase1	62	336	49	337	100.0%	1.27 [0.90, 1.79]
Subtotal (95% CI)		**336**		**337**	**100.0%**	**1.27 [0.90, 1.79]**
Total events	62		49			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.36 (P = 0.17)						
1.2.3 vs. risperidone						
CATIE-phase1	62	336	34	341	100.0%	1.85 [1.25, 2.73]
Subtotal (95% CI)		**336**		**341**	**100.0%**	**1.85 [1.25, 2.73]**
Total events	62		34			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.09 (P = 0.002)						



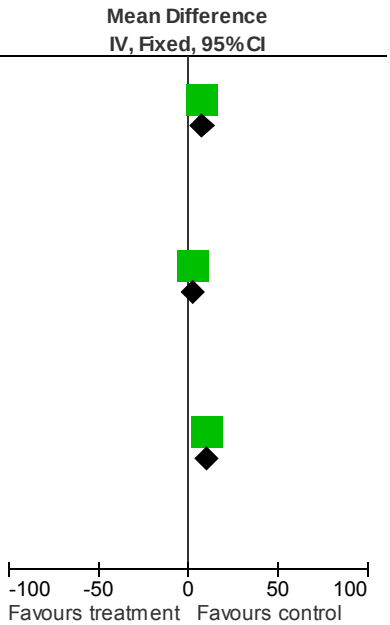
1.3 AE: 1. Metabolic SEs - Weight gain (Increase of >7% body weight) (by 18 months FU)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 vs. perphenazine						
CATIE-phase1	92	307	29	243	100.0%	2.51 [1.71, 3.68]
Subtotal (95% CI)		**307**		**243**	**100.0%**	**2.51 [1.71, 3.68]**
Total events	92		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.72 (P < 0.00001)						
1.3.2 vs. quetiapine						
CATIE-phase1	92	307	49	305	100.0%	1.87 [1.37, 2.54]
Subtotal (95% CI)		**307**		**305**	**100.0%**	**1.87 [1.37, 2.54]**
Total events	92		49			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.96 (P < 0.0001)						
1.3.3 vs. risperidone						
CATIE-phase1	92	307	42	300	100.0%	2.14 [1.54, 2.97]
Subtotal (95% CI)		**307**		**300**	**100.0%**	**2.14 [1.54, 2.97]**
Total events	92		42			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.54 (P < 0.00001)						



1.4 AE: 1. Metabolic SEs - Cholesterol (mg/dl) (by 18 months FU)

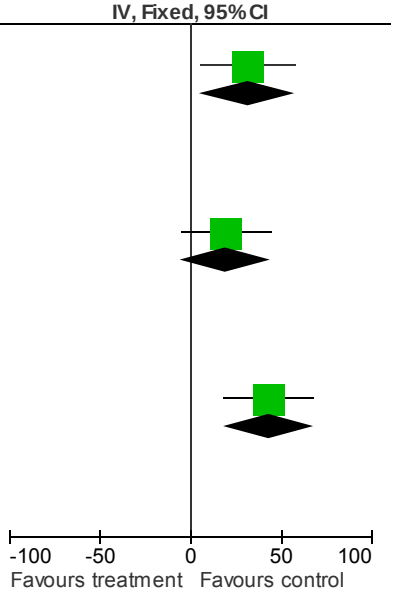
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.4.1 vs. perphenazine								
CATIE-phase1	9.4	40.59	286	1.5	39.31	212	100.0%	7.90 [0.82, 14.98]
Subtotal (95% CI)			**286**			**212**	**100.0%**	**7.90 [0.82, 14.98]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.19 (P = 0.03)								
1.4.2 vs. quetiapine								
CATIE-phase1	9.4	40.59	286	6.6	39.29	268	100.0%	2.80 [-3.85, 9.45]
Subtotal (95% CI)			**286**			**268**	**100.0%**	**2.80 [-3.85, 9.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.82 (P = 0.41)								
1.4.3 vs. risperidone								
CATIE-phase1	9.4	40.59	286	-1.3	38.85	262	100.0%	10.70 [4.05, 17.35]
Subtotal (95% CI)			**286**			**262**	**100.0%**	**10.70 [4.05, 17.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.15 (P = 0.002)								



Test for subgroup differences: Chi² = 2.78, df = 2 (P = 0.25), I² = 28.0%

1.5 AE: 1. Metabolic SEs - Triglycerides (mg/dl) (by 18 months FU)

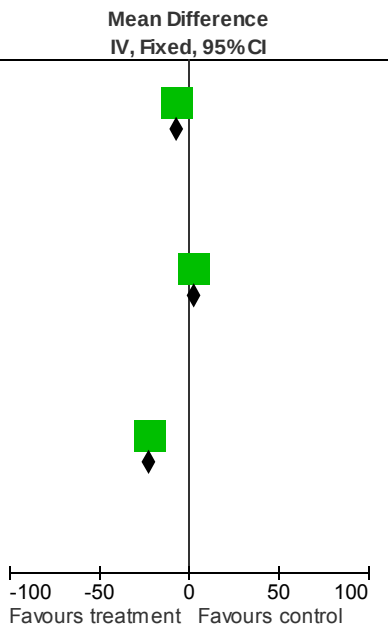
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.5.1 vs. perphenazine								
CATIE-phase1	40.5	150.51	286	9.2	147.06	212	100.0%	31.30 [4.92, 57.68]
Subtotal (95% CI)			**286**			**212**	**100.0%**	**31.30 [4.92, 57.68]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.33 (P = 0.02)								
1.5.2 vs. quetiapine								
CATIE-phase1	40.5	150.51	286	21.2	150.61	268	100.0%	19.30 [-5.79, 44.39]
Subtotal (95% CI)			**286**			**268**	**100.0%**	**19.30 [-5.79, 44.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.51 (P = 0.13)								
1.5.3 vs. risperidone								
CATIE-phase1	40.5	150.51	286	-2.4	147.3	262	100.0%	42.90 [17.95, 67.85]
Subtotal (95% CI)			**286**			**262**	**100.0%**	**42.90 [17.95, 67.85]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.37 (P = 0.0008)								



Test for subgroup differences: Chi² = 1.71, df = 2 (P = 0.43), I² = 0%

1.6 AE: 1. Metabolic SEs - Prolactin (ng/dl) (by 18 months FU)

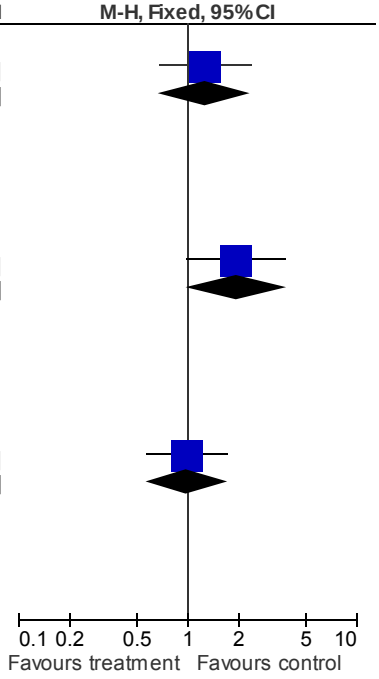
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.6.1 vs. perphenazine								
CATIE-phase1	-8.1	23.68	286	-1.2	23.3	212	100.0%	-6.90 [-11.07, -2.73]
Subtotal (95% CI)			**286**			**212**	**100.0%**	**-6.90 [-11.07, -2.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.24 (P = 0.001)								
1.6.2 vs. quetiapine								
CATIE-phase1	-8.1	23.68	286	-10.6	22.92	268	100.0%	2.50 [-1.38, 6.38]
Subtotal (95% CI)			**286**			**268**	**100.0%**	**2.50 [-1.38, 6.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.26 (P = 0.21)								
1.6.3 vs. risperidone								
CATIE-phase1	-8.1	23.68	286	13.8	22.66	262	100.0%	-21.90 [-25.78, -18.02]
Subtotal (95% CI)			**286**			**262**	**100.0%**	**-21.90 [-25.78, -18.02]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 11.06 (P < 0.00001)								



Test for subgroup differences: Chi² = 77.14, df = 2 (P < 0.00001), I² = 97.4%

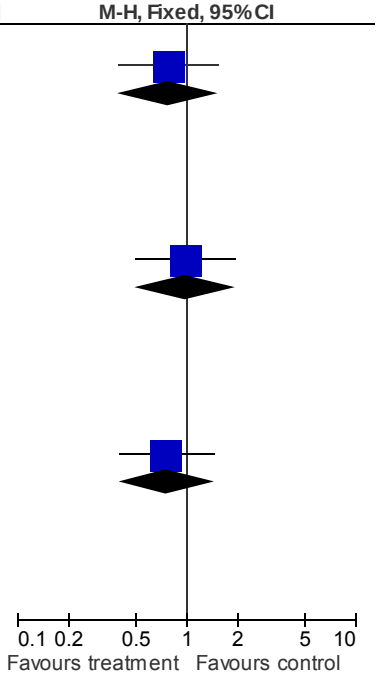
1.7 AE: 2. Neurologic SEs - EPS (treatment-emergent) (by 18 months FU)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.7.1 vs. perphenazine						
CATIE-phase1	23	296	15	243	100.0%	1.26 [0.67, 2.36]
Subtotal (95% CI)		**296**		**243**	**100.0%**	**1.26 [0.67, 2.36]**
Total events	23		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.72 (P = 0.47)						
1.7.2 vs. quetiapine						
CATIE-phase1	23	296	12	298	100.0%	1.93 [0.98, 3.81]
Subtotal (95% CI)		**296**		**298**	**100.0%**	**1.93 [0.98, 3.81]**
Total events	23		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.90 (P = 0.06)						
1.7.3 vs. risperidone						
CATIE-phase1	23	296	23	292	100.0%	0.99 [0.57, 1.72]
Subtotal (95% CI)		**296**		**292**	**100.0%**	**0.99 [0.57, 1.72]**
Total events	23		23			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.05 (P = 0.96)						



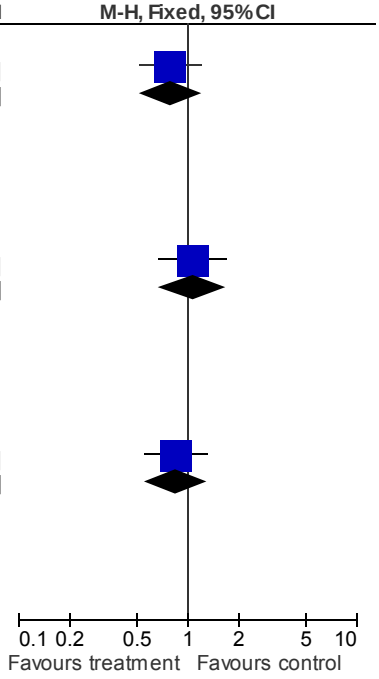
1.8 AE: 2. Neurologic SEs - Akathisia (treatment-emergent) (by 18 months FU)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.8.1 vs. perphenazine						
CATIE-phase1	15	290	16	241	100.0%	0.78 [0.39, 1.54]
Subtotal (95% CI)		**290**		**241**	**100.0%**	**0.78 [0.39, 1.54]**
Total events	15		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.72 (P = 0.47)						
1.8.2 vs. quetiapine						
CATIE-phase1	15	290	16	305	100.0%	0.99 [0.50, 1.96]
Subtotal (95% CI)		**290**		**305**	**100.0%**	**0.99 [0.50, 1.96]**
Total events	15		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.04 (P = 0.97)						
1.8.3 vs. risperidone						
CATIE-phase1	15	290	20	292	100.0%	0.76 [0.39, 1.45]
Subtotal (95% CI)		**290**		**292**	**100.0%**	**0.76 [0.39, 1.45]**
Total events	15		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.85 (P = 0.40)						



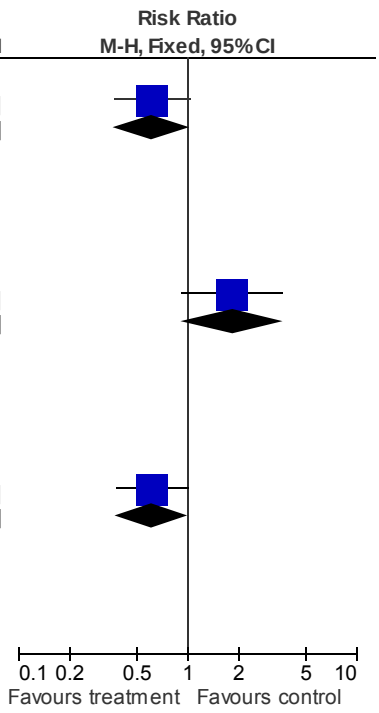
1.9 AE: 2. Neurologic SEs - Parkinsonism (treatment-emergent) (by 18 months FU)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.9.1 vs. perphenazine						
CATIE-phase1	32	236	41	237	100.0%	0.78 [0.51, 1.20]
Subtotal (95% CI)		**236**		**237**	**100.0%**	**0.78 [0.51, 1.20]**
Total events	32		41			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.12 (P = 0.26)						
1.9.2 vs. quetiapine						
CATIE-phase1	32	236	30	236	100.0%	1.07 [0.67, 1.70]
Subtotal (95% CI)		**236**		**236**	**100.0%**	**1.07 [0.67, 1.70]**
Total events	32		30			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.27 (P = 0.79)						
1.9.3 vs. risperidone						
CATIE-phase1	32	236	38	238	100.0%	0.85 [0.55, 1.31]
Subtotal (95% CI)		**236**		**238**	**100.0%**	**0.85 [0.55, 1.31]**
Total events	32		38			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.74 (P = 0.46)						



1.10 AE: 2. Neurologic SEs - Needing additional anticholinergic medication (by 18 months FU)

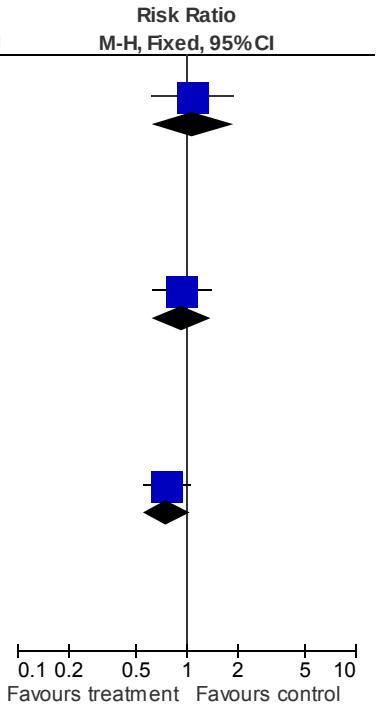
Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.10.1 vs. perphenazine						
CATIE-phase1	25	333	26	212	100.0%	0.61 [0.36, 1.03]
Subtotal (95% CI)		**333**		**212**	**100.0%**	**0.61 [0.36, 1.03]**
Total events	25		26			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.85 (P = 0.07)						
1.10.2 vs. quetiapine						
CATIE-phase1	25	333	11	268	100.0%	1.83 [0.92, 3.65]
Subtotal (95% CI)		**333**		**268**	**100.0%**	**1.83 [0.92, 3.65]**
Total events	25		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.71 (P = 0.09)						
1.10.3 vs. risperidone						
CATIE-phase1	25	333	32	262	100.0%	0.61 [0.37, 1.01]
Subtotal (95% CI)		**333**		**262**	**100.0%**	**0.61 [0.37, 1.01]**
Total events	25		32			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.92 (P = 0.06)						



2 SGA versus FGA

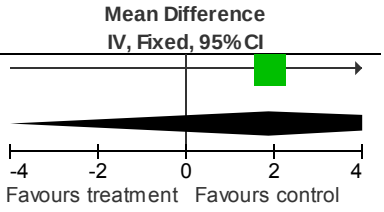
2.2 Leaving the study early: 1. Any reason (by 12 months FU)

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 12-week FU						
CUtLASS-band1	20	109	20	118	100.0%	1.08 [0.62, 1.90]
Subtotal (95% CI)		**109**		**118**	**100.0%**	**1.08 [0.62, 1.90]**
Total events	20		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.28 (P = 0.78)						
2.2.2 26-week FU						
CUtLASS-band1	31	109	36	118	100.0%	0.93 [0.62, 1.40]
Subtotal (95% CI)		**109**		**118**	**100.0%**	**0.93 [0.62, 1.40]**
Total events	31		36			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.34 (P = 0.73)						
2.2.3 52-week FU						
CUtLASS-band1	38	109	54	118	100.0%	0.76 [0.55, 1.05]
Subtotal (95% CI)		**109**		**118**	**100.0%**	**0.76 [0.55, 1.05]**
Total events	38		54			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.65 (P = 0.10)						



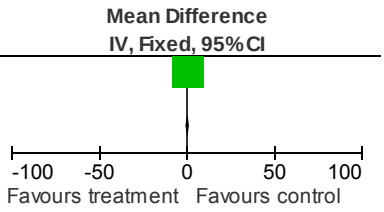
2.3 Quality of Life Scale (high scores = better; signs reversed) (by 12 months FU)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
CUtLASS-band1	-51.3	19.6	85	-53.2	21.2	100	100.0%	1.90 [-3.98, 7.78]
Total (95% CI)			**85**			**100**	**100.0%**	**1.90 [-3.98, 7.78]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.63 (P = 0.53)								



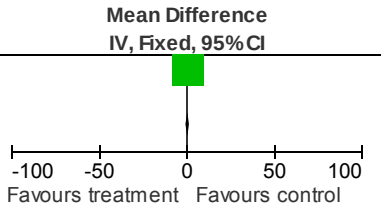
2.4 AE: 1. Neurologic SEs - Simpson-Angus Scale - EPS (by 12 months FU)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
CUtLASS-band1	3.2	3.7	80	3	3.9	94	100.0%	0.20 [-0.93, 1.33]
Total (95% CI)			**80**			**94**	**100.0%**	**0.20 [-0.93, 1.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.35 (P = 0.73)								



2.5 AE: 1. Neurologic SEs - BAS - Akathisia (by 12 months FU)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
CUtLASS-band1	2	2.7	81	1.5	2.4	95	100.0%	0.50 [-0.26, 1.26]
Total (95% CI)			**81**			**95**	**100.0%**	**0.50 [-0.26, 1.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.29 (P = 0.20)								



2.6 AE: 1. Neurologic SEs - AIMS (by 12 months FU)

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
CUtLASS-band1	1.8	3.3	81	2.3	4.5	95	100.0%	-0.50 [-1.66, 0.66]
Total (95% CI)			**81**			**95**	**100.0%**	**-0.50 [-1.66, 0.66]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.85 (P = 0.40)