APPENDIX 14: CLINICAL EVIDENCE FOREST PLOTS

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14a: RECOGNITION AND AT RISK STATE OF PSYCHOSIS IN CHILDREN AND YOUNG PEOPLE

Pharmacological Interventions

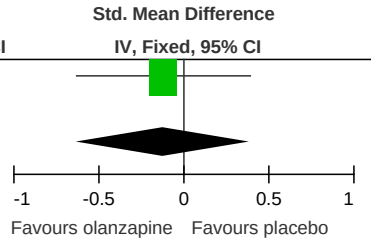
1. Children and young people 25 years and younger: olanzapine versus placebo: 52 weeks post-treatment efficacy outcomes

1.1 Mental state: Change in mean total symptoms (PANSS)

	olanzapine			placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGLASHAN2003	-4.5	22.12	30	-1.83	21.65	29	100.0%	-0.12 [-0.63, 0.39]
Total (95% CI)			**30**			**29**	**100.0%**	**-0.12 [-0.63, 0.39]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.46 (P = 0.64)

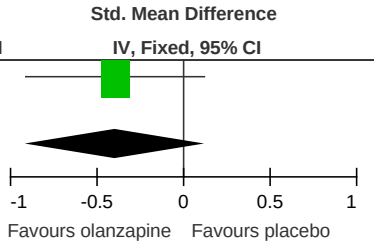


1.2 Mental state: Change in mean positive symptoms (SAPS)

	Olanzapine			placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGLASHAN2003	-1.63	5.65	30	0.86	6.74	29	100.0%	-0.40 [-0.91, 0.12]
Total (95% CI)			**30**			**29**	**100.0%**	**-0.40 [-0.91, 0.12]**

Heterogeneity: Not applicable

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

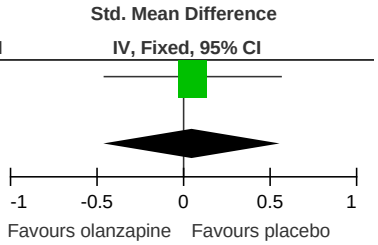


1.3 Mental state: change in negative symptoms (SANS)

	olanzapine			placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGLASHAN2003	-0.43	6.55	30	-0.76	5.66	29	100.0%	0.05 [-0.46, 0.56]
Total (95% CI)			**30**			**29**	**100.0%**	**0.05 [-0.46, 0.56]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.20 (P = 0.84)

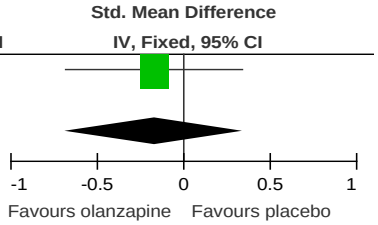


1.4 Change in global state: severity (CGI-S)

	experimental			control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGLASHAN2003	-0.1	1.06	30	0.1	1.23	29	100.0%	-0.17 [-0.68, 0.34]
Total (95% CI)			**30**			**29**	**100.0%**	**-0.17 [-0.68, 0.34]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.66 (P = 0.51)

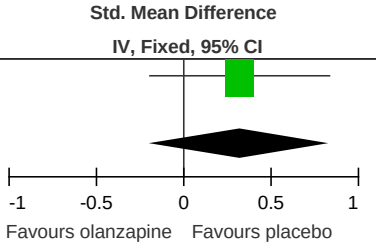


1.5 Mental state: change in depression symptoms (MADRS)

	olanzapine			placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGLASHAN2003	0.27	9.01	30	-2.59	8.6	29	100.0%	0.32 [-0.19, 0.83]
Total (95% CI)			**30**			**29**	**100.0%**	**0.32 [-0.19, 0.83]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.22 (P = 0.22)

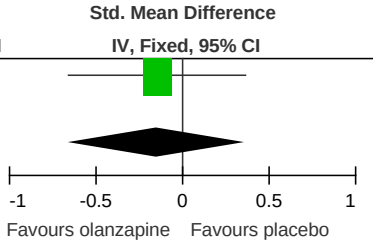


1.6 Mental state: change in mania (YMRS)

	olanzapine			placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGLASHAN2003	0.37	5.74	30	1.21	5.48	29	100.0%	-0.15 [-0.66, 0.36]
Total (95% CI)			**30**			**29**	**100.0%**	**-0.15 [-0.66, 0.36]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.57 (P = 0.57)

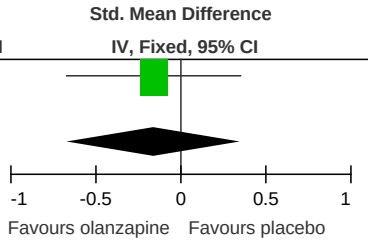


1.7 Change in psychosocial functioning (GAF)

	olanzapine			placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGLASHAN2003	-8.23	15.31	30	-5.93	12.85	29	100.0%	-0.16 [-0.67, 0.35]
Total (95% CI)			**30**			**29**	**100.0%**	**-0.16 [-0.67, 0.35]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.61 (P = 0.54)

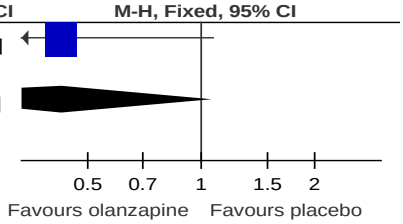


1.8 Transition to psychosis (presence of psychosis scale [author developed measure])

	olanzapine		placebo			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
MCGLASHAN2003	5	31	11	29	100.0%	0.43 [0.17, 1.08]
Total (95% CI)		**31**		**29**	**100.0%**	**0.43 [0.17, 1.08]**
Total events	5		11			

Heterogeneity: Not applicable

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



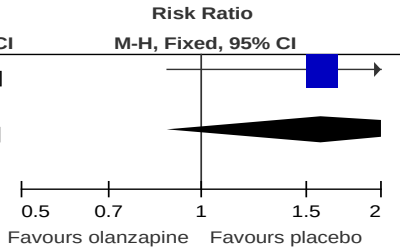
2. Children and young people 25 years and younger: olanzapine versus placebo: 52 weeks post-treatment side effect outcomes

2.1 Leaving the study early for any reason

Study or Subgroup	olanzapine Events	olanzapine Total	placebo Events	placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MCGLASHAN2003	17	31	10	29	100.0%	1.59 [0.88, 2.88]
Total (95% CI)		**31**		**29**	**100.0%**	**1.59 [0.88, 2.88]**
Total events	17		10			

Heterogeneity: Not applicable

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



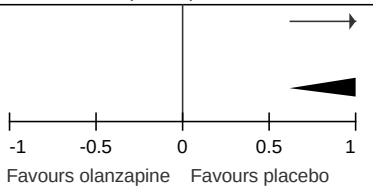
3. Children and young people 25 years and younger: olanzapine versus placebo: 52 weeks post-treatment side effect outcomes

3.1 Side effects: mean change in weight (kg)

Study or Subgroup	olanzapine Mean	olanzapine SD	olanzapine Total	placebo Mean	placebo SD	placebo Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCGLASHAN2003	8.79	9.05	30	0.3	4.24	29	100.0%	1.18 [0.62, 1.73]
Total (95% CI)			**30**			**29**	**100.0%**	**1.18 [0.62, 1.73]**

Heterogeneity: Not applicable

Test for overall effect: Z = 4.16 (P < 0.0001)

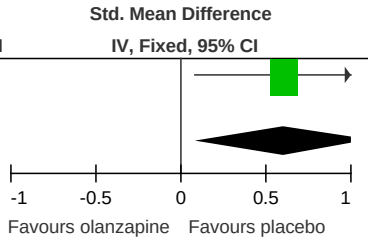


3.2 Side effects: mean change in sitting pulse (beats/min)

Study or Subgroup	olanzapine Mean	olanzapine SD	olanzapine Total	placebo Mean	placebo SD	placebo Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCGLASHAN2003	9.03	15.25	30	-0.24	14.98	29	100.0%	0.61 [0.08, 1.13]
Total (95% CI)			**30**			**29**	**100.0%**	**0.61 [0.08, 1.13]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.27 (P = 0.02)

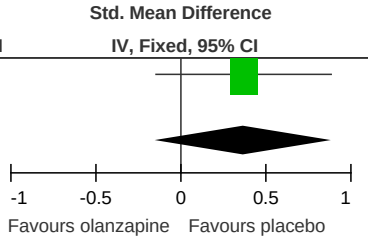


3.3 Side effects: mean change in standing pulse (beats/min)

Study or Subgroup	olanzapine Mean	olanzapine SD	olanzapine Total	placebo Mean	placebo SD	placebo Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCGLASHAN2003	9.5	17.56	30	2.62	19.22	29	100.0%	0.37 [-0.15, 0.88]
Total (95% CI)			**30**			**29**	**100.0%**	**0.37 [-0.15, 0.88]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.40 (P = 0.16)



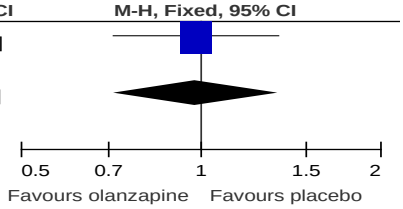
4. Children and young people 25 years and younger: olanzapine versus placebo: 104 week's follow-up (change scores from post-treatment until follow-up when no treatment was received)

4.1 Leaving the study early for any reason

Study or Subgroup	olanzapine Events	olanzapine Total	placebo Events	placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MCGLASHAN2003	22	31	21	29	100.0%	0.98 [0.71, 1.35]
Total (95% CI)		**31**		**29**	**100.0%**	**0.98 [0.71, 1.35]**
Total events	22		21			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.12 (P = 0.90)



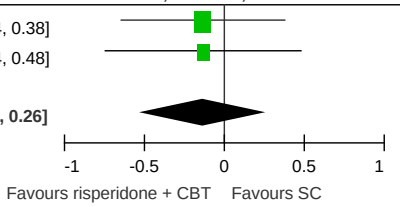
5. Children and young people 25 years and younger: risperidone + CBT versus supportive counselling: post-treatment efficacy outcomes

5.1 Mental state: mean endpoint total symptoms (BPRS)

Study or Subgroup	Favours risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
MCGORRY2002	15.6	8.3	31	16.9	10.9	28	58.9%	-0.13 [-0.64, 0.38]
PHILLIPS2009	14	9.3	24	15.3	10.1	18	41.1%	-0.13 [-0.74, 0.48]
Total (95% CI)			**55**			**46**	**100.0%**	**-0.13 [-0.53, 0.26]**

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%

Test for overall effect: Z = 0.66 (P = 0.51)

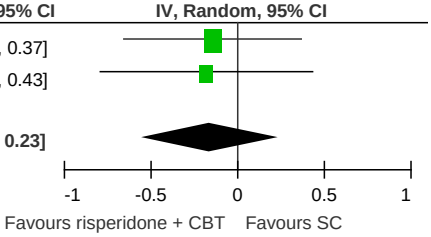


5.2 Mental state: mean endpoint positive symptoms (BPRS psychotic subscale)

Study or Subgroup	risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
MCGORRY2002	3.1	3.2	31	3.6	3.6	28	58.9%	-0.15 [-0.66, 0.37]
PHILLIPS2009	2.6	2.5	24	3.1	3	18	41.1%	-0.18 [-0.79, 0.43]
Total (95% CI)			**55**			**46**	**100.0%**	**-0.16 [-0.55, 0.23]**

Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.93); I² = 0%

Test for overall effect: Z = 0.80 (P = 0.43)

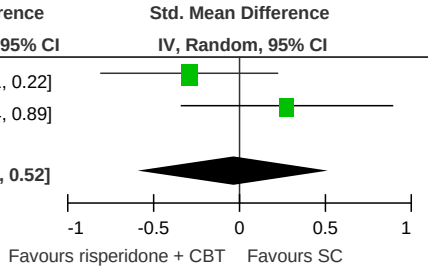


5.3 Mental state: mean endpoint negative symptoms (SANS, SOPS Negative)

Study or Subgroup	risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
MCGORRY2002	15.5	11.5	31	20.1	19	28	54.6%	-0.29 [-0.81, 0.22]
PHILLIPS2009	17.8	13.8	24	13.9	13.9	18	45.4%	0.28 [-0.34, 0.89]
Total (95% CI)			**55**			**46**	**100.0%**	**-0.03 [-0.59, 0.52]**

Heterogeneity: Tau² = 0.08; Chi² = 1.94, df = 1 (P = 0.16); I² = 48%

Test for overall effect: Z = 0.12 (P = 0.90)

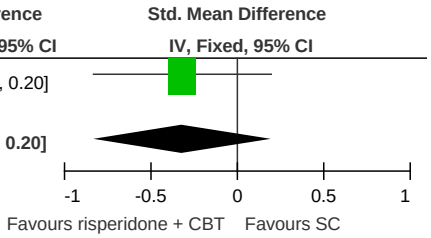


5.4 Mental state: mean endpoint depression symptoms (HAM-D)

Study or Subgroup	risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCGORRY2002	13.8	8.3	31	16.9	10.9	28	100.0%	-0.32 [-0.83, 0.20]
Total (95% CI)			**31**			**28**	**100.0%**	**-0.32 [-0.83, 0.20]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.21 (P = 0.23)

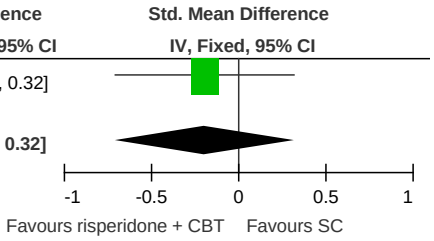


5.5 Mental state: mean endpoint mania symptoms (YMRS)

Study or Subgroup	risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCGORRY2002	1.5	2.8	31	2.2	4.2	28	100.0%	-0.20 [-0.71, 0.32]
Total (95% CI)			**31**			**28**	**100.0%**	**-0.20 [-0.71, 0.32]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.75 (P = 0.45)

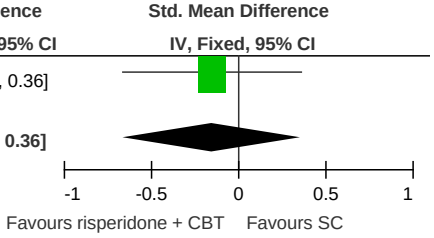


5.6 Mental state: mean endpoint anxiety symptoms (HAM-A)

Study or Subgroup	risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCGORRY2002	10.1	5.6	31	11.2	8.5	28	100.0%	-0.15 [-0.66, 0.36]
Total (95% CI)			**31**			**28**	**100.0%**	**-0.15 [-0.66, 0.36]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.58 (P = 0.56)

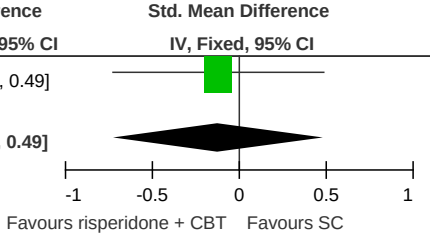


5.7 Mean endpoint psychosocial functioning (GAF)

Study or Subgroup	risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
PHILLIPS2009	-86.8	17.7	25	-84.4	22	18	100.0%	-0.12 [-0.73, 0.49]
Total (95% CI)			**25**			**18**	**100.0%**	**-0.12 [-0.73, 0.49]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.39 (P = 0.70)

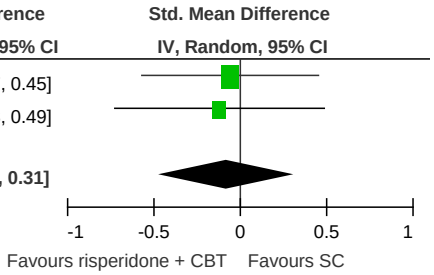


5.8 Mean endpoint quality of life (QLS)

Study or Subgroup	risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
MCGORRY2002	-71	21.4	31	-69.6	26	28	58.5%	-0.06 [-0.57, 0.45]
PHILLIPS2009	-86.8	17.7	25	-84.4	22	18	41.5%	-0.12 [-0.73, 0.49]
Total (95% CI)			**56**			**46**	**100.0%**	**-0.08 [-0.47, 0.31]**

Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.88); I² = 0%

Test for overall effect: Z = 0.42 (P = 0.67)

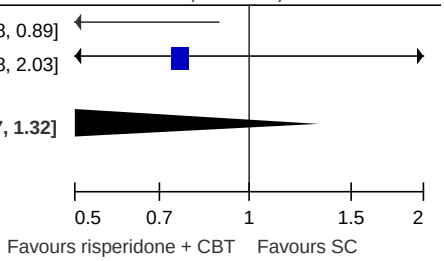


5.9 Transition to psychosis (a predetermined threshold of positive symptoms, CAARMS)

	risperidone + CBT		SC			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
MCGORRY2002	3	31	10	28	44.7%	0.27 [0.08, 0.89]	
PHILLIPS2009	7	43	6	28	55.3%	0.76 [0.28, 2.03]	
Total (95% CI)		**74**		**56**	**100.0%**	**0.48 [0.17, 1.32]**	
Total events	10		16				

Heterogeneity: Tau² = 0.23; Chi² = 1.75, df = 1 (P = 0.19); I² = 43%

Test for overall effect: Z = 1.43 (P = 0.15)



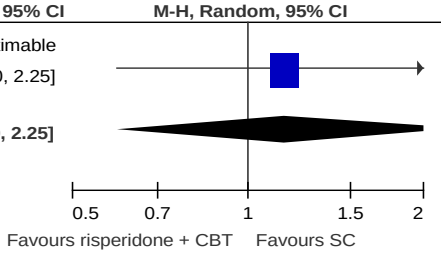
6. Children and young people 25 years and younger: risperidone + CBT versus supportive counselling: post-treatment side effect outcomes

6.1 Leaving the study early for any reason

	risperidone + CBT		SC			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
MCGORRY2002	0	31	0	28		Not estimable	
PHILLIPS2009	16	43	9	28	100.0%	1.16 [0.60, 2.25]	
Total (95% CI)		**74**		**56**	**100.0%**	**1.16 [0.60, 2.25]**	
Total events	16		9				

Heterogeneity: Not applicable

Test for overall effect: Z = 0.43 (P = 0.67)

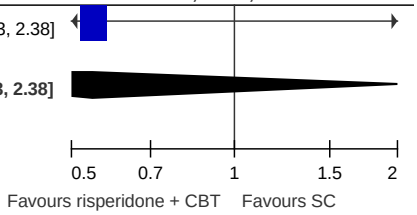


6.2 Extra pyramidal symptoms (mean endpoint UKU scores)

	risperidone + CBT		Supportive Counselling			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
PHILLIPS2009	2	10	4	11	100.0%	0.55 [0.13, 2.38]	
Total (95% CI)		**10**		**11**	**100.0%**	**0.55 [0.13, 2.38]**	
Total events	2		4				

Heterogeneity: Not applicable

Test for overall effect: Z = 0.80 (P = 0.42)



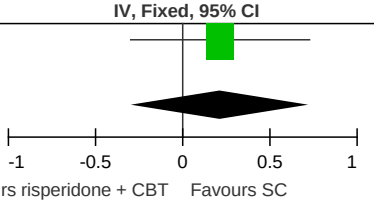
7. Children and young people 25 years and younger: risperidone + CBT versus supportive counselling: 52 week's follow-up efficacy outcomes

7.1 Mental state: Mean endpoint total symptoms (BPRS)

	risperidone + CBT			SC				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
MCGORRY2002	17	9	31	15	9.4	28	100.0%	0.21 [-0.30, 0.73]	
Total (95% CI)			**31**			**28**	**100.0%**	**0.21 [-0.30, 0.73]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.82 (P = 0.41)

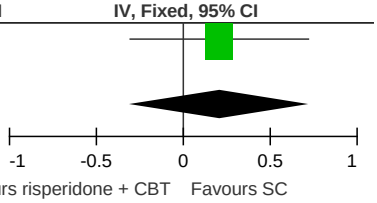


7.2 Mental state: mean endpoint positive symptoms (BPRS psychotic subscale)

	risperidone + CBT			SC				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
MCGORRY2002	3.8	3.6	31	3.1	3	28	100.0%	0.21 [-0.30, 0.72]	
Total (95% CI)			**31**			**28**	**100.0%**	**0.21 [-0.30, 0.72]**	

Heterogeneity: Not applicable

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

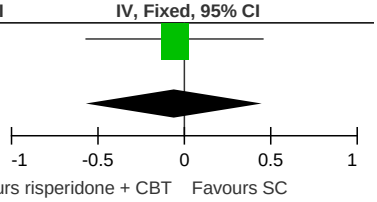


7.3 Mental state: mean endpoint negative symptoms (SANS)

	risperidone + CBT			SC				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
MCGORRY2002	16.8	14.3	31	17.6	13.4	28	100.0%	-0.06 [-0.57, 0.45]	
Total (95% CI)			**31**			**28**	**100.0%**	**-0.06 [-0.57, 0.45]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.22 (P = 0.83)

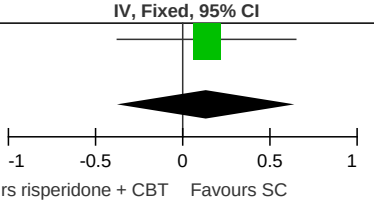


7.4 Mental state: mean endpoint depression symptoms (HAM-D)

	risperidone + CBT			SC				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
MCGORRY2002	12.2	8.8	31	11	8.5	28	100.0%	0.14 [-0.37, 0.65]	
Total (95% CI)			**31**			**28**	**100.0%**	**0.14 [-0.37, 0.65]**	

Heterogeneity: Not applicable

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

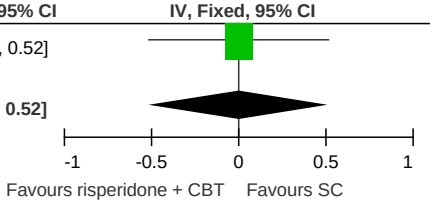


7.5 Mental state: mean endpoint mania symptoms (YMRS)

Study or Subgroup	risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCGORRY2002	1.7	3.7	30	1.7	3.2	28	100.0%	0.00 [-0.52, 0.52]
Total (95% CI)			**30**			**28**	**100.0%**	**0.00 [-0.52, 0.52]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)

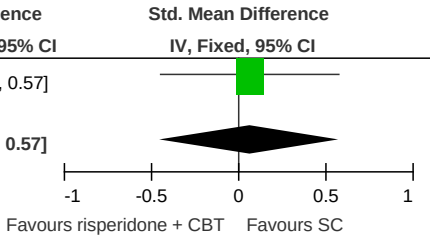


7.6 Mental state: mean endpoint anxiety symptoms (HAM-A)

Study or Subgroup	risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCGORRY2002	11.5	9.3	31	10.9	9.4	28	100.0%	0.06 [-0.45, 0.57]
Total (95% CI)			**31**			**28**	**100.0%**	**0.06 [-0.45, 0.57]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.24 (P = 0.81)

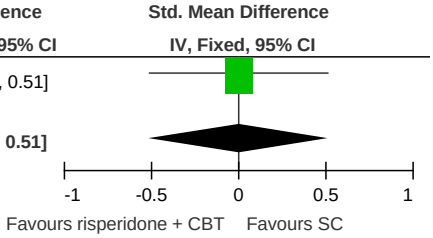


7.7 Mean endpoint psychosocial functioning (GAF)

Study or Subgroup	risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCGORRY2002	-63.5	11.3	31	-63.5	9.1	28	100.0%	0.00 [-0.51, 0.51]
Total (95% CI)			**31**			**28**	**100.0%**	**0.00 [-0.51, 0.51]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)

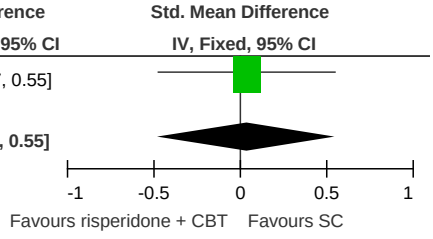


7.8 Mean endpoint quality of life (QLS)

Study or Subgroup	risperidone + CBT Mean	SD	Total	SC Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCGORRY2002	-76.3	22.7	31	-77.1	20.2	28	100.0%	0.04 [-0.47, 0.55]
Total (95% CI)			**31**			**28**	**100.0%**	**0.04 [-0.47, 0.55]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.14 (P = 0.89)

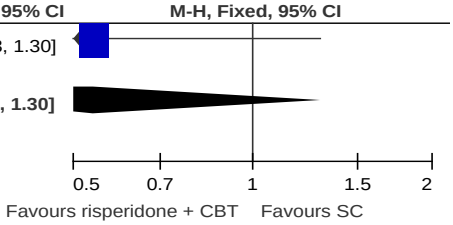


1.1 Transition to psychosis (assessed using a categorical model, to the predetermined threshold of positive psychotic symptoms)

Study or Subgroup	risperidone + CBT Events	Total	SC Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MCGORRY2002	6	31	10	28	100.0%	0.54 [0.23, 1.30]
Total (95% CI)		**31**		**28**	**100.0%**	**0.54 [0.23, 1.30]**
Total events	6		10			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.37 (P = 0.17)



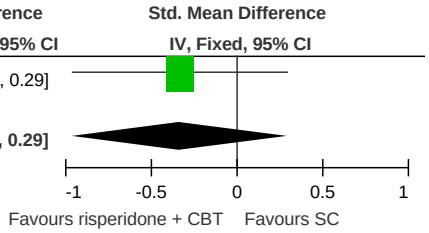
8. Children and young people 25 years and younger: risperidone + CBT versus supportive counselling: 156-208 week's follow-up efficacy outcomes

8.1 Mental state: mean endpoint total symptoms (BPRS)

	risperidone + CBT			SC				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGORRY2002	22.47	11.28	17	26.33	11.39	24	100.0%	-0.33 [-0.96, 0.29]
Total (95% CI)			**17**			**24**	**100.0%**	**-0.33 [-0.96, 0.29]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.04 (P = 0.30)

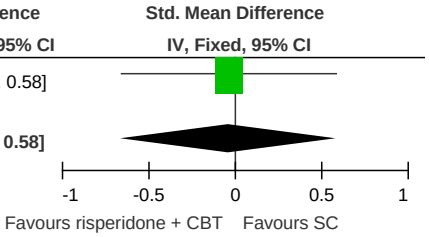


8.2 Mental state: mean endpoint positive symptoms (BPRS psychotic subscale)

	risperidone + CBT			SC				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGORRY2002	4.65	2.67	17	4.75	2.61	24	100.0%	-0.04 [-0.66, 0.58]
Total (95% CI)			**17**			**24**	**100.0%**	**-0.04 [-0.66, 0.58]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.12 (P = 0.91)

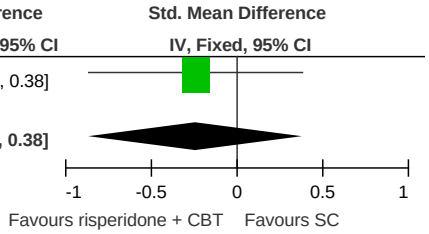


8.3 Mental state: mean endpoint negative symptoms (SANS)

	risperidone + CBT			SC				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGORRY2002	27	22.84	17	31.74	16.25	24	100.0%	-0.24 [-0.87, 0.38]
Total (95% CI)			**17**			**24**	**100.0%**	**-0.24 [-0.87, 0.38]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.76 (P = 0.45)

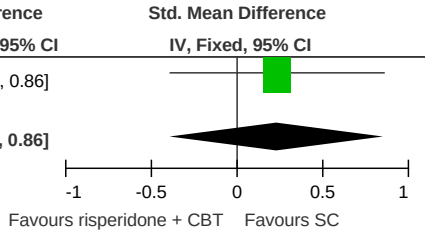


8.4 Mental state: mean endpoint depression symptoms (HAM-D)

	risperidone + CBT			SC				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGORRY2002	25.82	13.42	17	22.91	11.25	24	100.0%	0.23 [-0.39, 0.86]
Total (95% CI)			**17**			**24**	**100.0%**	**0.23 [-0.39, 0.86]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.74 (P = 0.46)

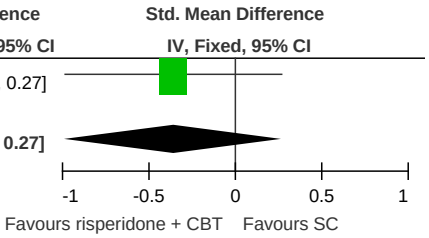


8.5 Mental state: mean endpoint mania symptoms (YMRS)

	risperidone + CBT			SC				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGORRY2002	7.18	8.55	17	10.43	9.13	24	100.0%	-0.36 [-0.98, 0.27]
Total (95% CI)			**17**			**24**	**100.0%**	**-0.36 [-0.98, 0.27]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.12 (P = 0.26)

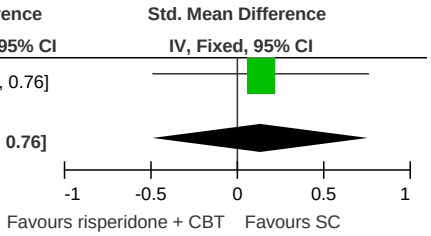


8.6 Mental state: mean endpoint anxiety symptoms (HAM-A)

	risperidone + CBT			SC				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGORRY2002	18.82	10.29	17	17.52	8.78	24	100.0%	0.14 [-0.49, 0.76]
Total (95% CI)			**17**			**24**	**100.0%**	**0.14 [-0.49, 0.76]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.43 (P = 0.67)

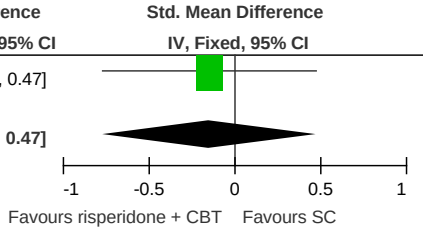


8.7 Mean endpoint psychosocial functioning (GAF)

	risperidone + CBT			SC				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGORRY2002	-59.88	15.89	17	-57.48	15.72	24	100.0%	-0.15 [-0.77, 0.47]
Total (95% CI)			**17**			**24**	**100.0%**	**-0.15 [-0.77, 0.47]**

Heterogeneity: Not applicable

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

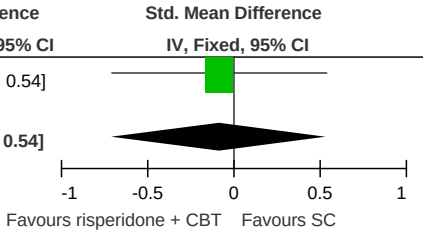


8.8 Mean endpoint quality of life (QLS)

	risperidone + CBT			SC				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCGORRY2002	-80.53	24.43	17	-78.5	22.74	24	100.0%	-0.08 [-0.71, 0.54]
Total (95% CI)			**17**			**24**	**100.0%**	**-0.08 [-0.71, 0.54]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.27 (P = 0.79)

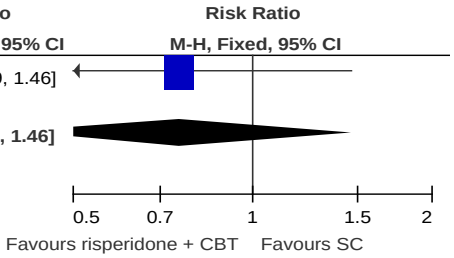


8.9 Transition to psychosis (assessed using a categorical model, to the predetermined threshold of positive psychotic symptoms)

	risperidone + CBT		SC			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
MCGORRY2002	10	31	12	28	100.0%	0.75 [0.39, 1.46]
Total (95% CI)		**31**		**28**	**100.0%**	**0.75 [0.39, 1.46]**
Total events	10		12			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.84 (P = 0.40)

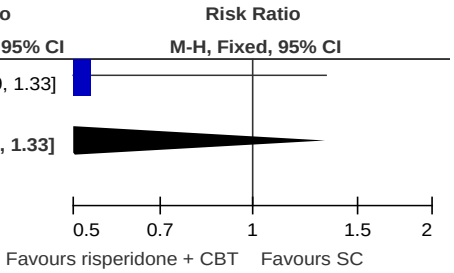


8.10 Number of participants requiring hospitalization

	risperidone + CBT		SC			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
MCGORRY2002	5	24	7	17	100.0%	0.51 [0.19, 1.33]
Total (95% CI)		**24**		**17**	**100.0%**	**0.51 [0.19, 1.33]**
Total events	5		7			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.38 (P = 0.17)



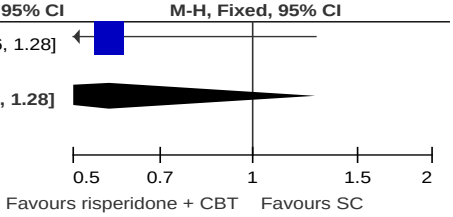
9. Children and young people 25 years and younger: risperidone + CBT versus supportive counselling: 156-208 week's follow-up side effect outcomes

9.1 Leaving the study early for any reason

Study or Subgroup	risperidone + CBT Events	risperidone + CBT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MCGORRY2002	7	31	11	28	100.0%	0.57 [0.26, 1.28]
Total (95% CI)		**31**		**28**	**100.0%**	**0.57 [0.26, 1.28]**
Total events	7		11			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.36 (P = 0.17)



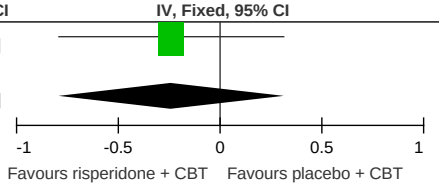
10. Children and young people 25 years and older: risperidone + CBT versus placebo + CBT: 52 weeks post-treatment efficacy outcomes

10.1 Mental state: mean endpoint total symptoms (BPRS)

Study or Subgroup	risperidone + CBT Mean	SD	Total	placebo + CBT Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
PHILLIPS2009	14	9.3	24	16.5	11.1	27	100.0%	-0.24 [-0.79, 0.31]
Total (95% CI)			**24**			**27**	**100.0%**	**-0.24 [-0.79, 0.31]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.85 (P = 0.40)

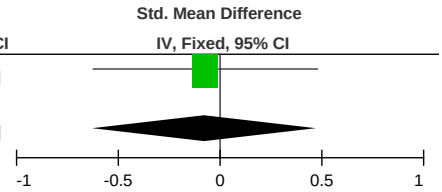


10.2 Mental state: mean endpoint positive symptoms (BPRS psychotic subscale)

Study or Subgroup	risperidone + CBT Mean	SD	Total	placebo + CBT Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
PHILLIPS2009	2.6	2.5	24	2.8	2.9	27	100.0%	-0.07 [-0.62, 0.48]
Total (95% CI)			**24**			**27**	**100.0%**	**-0.07 [-0.62, 0.48]**

Heterogeneity: Not applicable

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

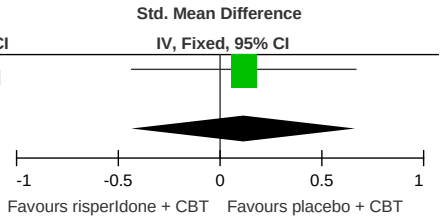


10.3 Mental state: mean endpoint negative symptoms (SANS)

Study or Subgroup	risperidone + CBT Mean	SD	Total	placebo + CBT Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
PHILLIPS2009	17.8	13.8	24	16.3	11.6	27	100.0%	0.12 [-0.43, 0.67]
Total (95% CI)			**24**			**27**	**100.0%**	**0.12 [-0.43, 0.67]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.41 (P = 0.68)

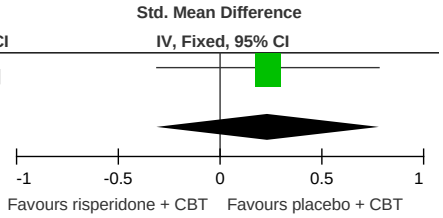


10.4 Mean endpoint psychosocial functioning (GAF)

	risperidone + CBT			placebo + CBT				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
PHILLIPS2009	-64.8	9	26	-66.8	7.7	26	100.0%	0.24 [-0.31, 0.78]
Total (95% CI)			**26**			**26**	**100.0%**	**0.24 [-0.31, 0.78]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.84 (P = 0.40)

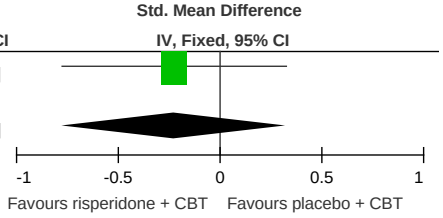


10.5 Mean endpoint quality of life (QLS)

	risperidone + CBT			placebo + CBT				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
PHILLIPS2009	-86.8	17.7	25	-81.1	30.3	26	100.0%	-0.23 [-0.78, 0.33]
Total (95% CI)			**25**			**26**	**100.0%**	**-0.23 [-0.78, 0.33]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.80 (P = 0.42)

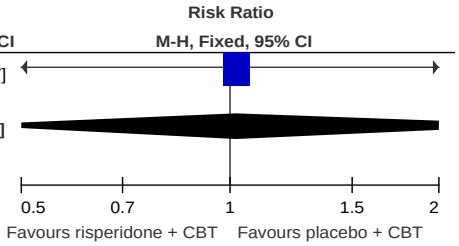


10.6 Transition to psychosis (CAARMS)

	risperidone + CBT		placebo + CBT			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
PHILLIPS2009	7	43	7	44	100.0%	1.02 [0.39, 2.67]
Total (95% CI)		**43**		**44**	**100.0%**	**1.02 [0.39, 2.67]**
Total events	7		7			

Heterogeneity: Not applicable

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



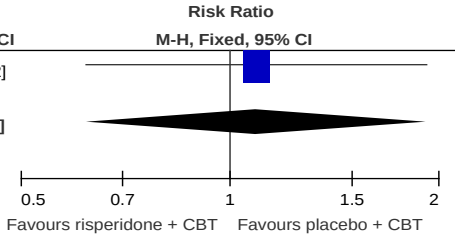
11. Children and young people 25 years and younger: risperidone + CBT versus placebo + CBT: 52 weeks post-treatment side effect outcomes

11.1 Leaving the study early for any reason

	risperidone + CBT		placebo + CBT			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
PHILLIPS2009	16	43	15	44	100.0%	1.09 [0.62, 1.92]
Total (95% CI)		**43**		**44**	**100.0%**	**1.09 [0.62, 1.92]**
Total events	16		15			

Heterogeneity: Not applicable

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

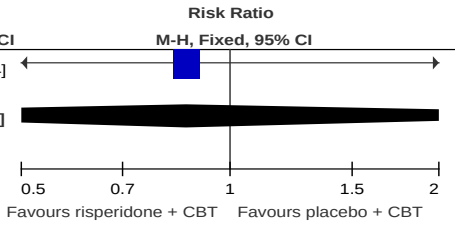


11.2 Extra pyramidal symptoms (mean endpoint UKU scores)

	risperidone + CBT		placebo + CBT			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
PHILLIPS2009	2	10	3	13	100.0%	0.87 [0.18, 4.24]
Total (95% CI)		**10**		**13**	**100.0%**	**0.87 [0.18, 4.24]**
Total events	2		3			

Heterogeneity: Not applicable

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



Dietary Interventions

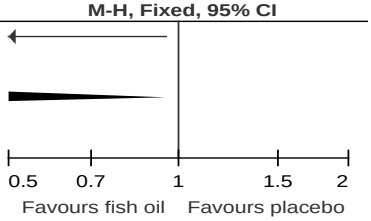
12. Children and young people 25 years and younger: omega-3 fatty acids versus placebo: 12 weeks post-treatment efficacy outcomes

12.1 Transition to psychosis (DSM-IV)

Study or Subgroup	Fish oil Events	Fish oil Total	placebo Events	placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
AMMINGER2010	1	38	8	38	100.0%	0.13 [0.02, 0.95]
Total (95% CI)		**38**		**38**	**100.0%**	**0.13 [0.02, 0.95]**
Total events	1		8			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.01 (P = 0.04)



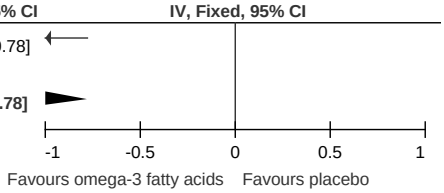
13. Omega-3 fatty acids versus placebo: 52 week's follow-up efficacy outcomes

13.1 Mental state: mean endpoint total symptoms (PANSS)

Study or Subgroup	omega-3 fatty acids Mean	omega-3 fatty acids SD	omega-3 fatty acids Total	placebo Mean	placebo SD	placebo Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
AMMINGER2010	-15.7	11.09	41	-4.4	5.87	40	100.0%	-1.26 [-1.74, -0.78]
Total (95% CI)			**41**			**40**	**100.0%**	**-1.26 [-1.74, -0.78]**

Heterogeneity: Not applicable

Test for overall effect: Z = 5.15 (P < 0.00001)

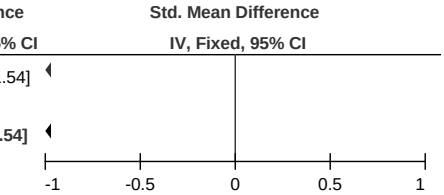


13.2 Mental state: mean endpoint positive symptoms (SAPS)

Study or Subgroup	omega-3 fatty acids Mean	omega-3 fatty acids SD	omega-3 fatty acids Total	placebo Mean	placebo SD	placebo Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
AMMINGER2010	-4.4	1.68	41	-1.5	0.98	40	100.0%	-2.08 [-2.63, -1.54]
Total (95% CI)			**41**			**40**	**100.0%**	**-2.08 [-2.63, -1.54]**

Heterogeneity: Not applicable

Test for overall effect: Z = 7.48 (P < 0.00001)

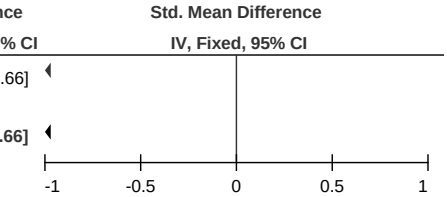


13.3 Mental state: mean endpoint negative symptoms (SANS)

Study or Subgroup	omega-3 fatty acids Mean	omega-3 fatty acids SD	omega-3 fatty acids Total	placebo Mean	placebo SD	placebo Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
AMMINGER2010	-3.9	1.78	41	-0.8	0.8	40	100.0%	-2.22 [-2.77, -1.66]
Total (95% CI)			**41**			**40**	**100.0%**	**-2.22 [-2.77, -1.66]**

Heterogeneity: Not applicable

Test for overall effect: Z = 7.77 (P < 0.00001)

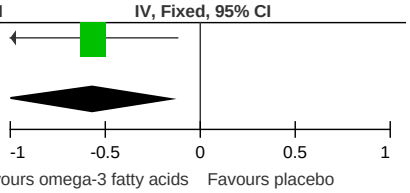


13.4 Mental state: mean endpoint depression symptoms (MADRS)

	omega-3 fatty acids			placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
AMMINGER2010	-8.1	5.41	41	-5.3	4.37	40	100.0%	-0.56 [-1.01, -0.12]
Total (95% CI)			**41**			**40**	**100.0%**	**-0.56 [-1.01, -0.12]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.48 (P = 0.01)

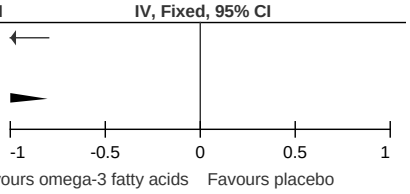


13.5 Mean endpoint psychosocial functioning (GAF)

	omega-3 fatty acids			placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
AMMINGER2010	-17.7	9.68	41	-7.2	6.17	40	100.0%	-1.28 [-1.76, -0.80]
Total (95% CI)			**41**			**40**	**100.0%**	**-1.28 [-1.76, -0.80]**

Heterogeneity: Not applicable

Test for overall effect: Z = 5.22 (P < 0.00001)

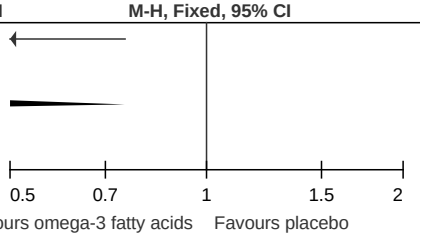


13.6 Transition to psychosis (DSM-IV)

	omega-3 fatty acids		placebo			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
AMMINGER2010	2	41	11	40	100.0%	0.18 [0.04, 0.75]
Total (95% CI)		**41**		**40**	**100.0%**	**0.18 [0.04, 0.75]**
Total events	2		11			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.35 (P = 0.02)



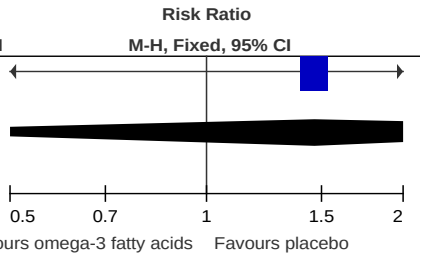
14. Children and young people 25 years and younger: omega-3 fatty acids versus placebo: 52 week's follow-up side effect outcomes

14.1 Leaving the study early for any reason

	omega-3 fatty acids		placebo			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
AMMINGER2010	3	41	2	40	100.0%	1.46 [0.26, 8.30]
Total (95% CI)		**41**		**40**	**100.0%**	**1.46 [0.26, 8.30]**
Total events	3		2			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.43 (P = 0.67)



Psychological interventions

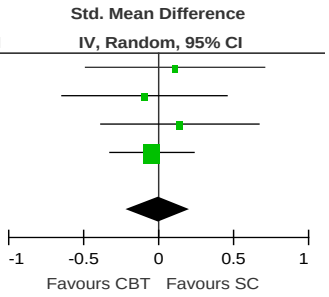
15. Combined children and young people 18 years and younger with 25 years and younger: CBT versus supportive counselling: post-treatment efficacy outcomes

15.1 Mental state: mean endpoint total symptoms (BPRS, SOPS, PANSS, CAARMS severity)

	CBT			SC				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
PHILLIPS2009	16.5	11.1	27	15.3	10.1	18	12.5%	0.11 [-0.49, 0.71]
ADDINGTON2011	5.8	5.508176	27	6.3	4.850258	24	14.7%	-0.09 [-0.64, 0.46]
MORRISON2004	49.4667	15.11322	35	47.4	13.12631	23	16.0%	0.14 [-0.38, 0.67]
MORRISON2011	17.89	16.5	97	18.69	19.34	99	56.8%	-0.04 [-0.32, 0.24]
Total (95% CI)			**186**			**164**	**100.0%**	**-0.00 [-0.21, 0.21]**

Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 3 (P = 0.89); I² = 0%

Test for overall effect: Z = 0.02 (P = 0.98)

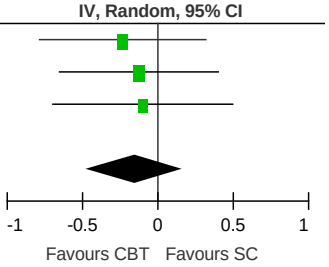


15.2 Mental state: mean endpoint positive symptoms (BPRS positive, SOPS positive, PANSS positive)

	CBT			SC				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
ADDINGTON2011	6.4	5.2	27	7.6	4.9	24	33.9%	-0.23 [-0.79, 0.32]
MORRISON2004	10.5417	3.05001	35	10.9286	2.99908	23	37.2%	-0.13 [-0.65, 0.40]
PHILLIPS2009	2.8	2.9	27	3.1	3	18	29.0%	-0.10 [-0.70, 0.50]
Total (95% CI)			**89**			**65**	**100.0%**	**-0.15 [-0.48, 0.17]**

Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 2 (P = 0.94); I² = 0%

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

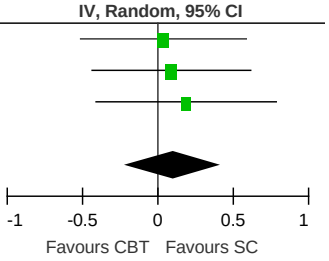


15.3 Mental state: mean endpoint negative symptoms (SOPS negative, PANSS negative)

	CBT			SC				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
ADDINGTON2011	5.2	5.8	27	5	4.8	24	34.0%	0.04 [-0.51, 0.59]
MORRISON2004	12.2917	5.53628	35	11.8182	4.64367	23	37.2%	0.09 [-0.44, 0.62]
PHILLIPS2009	16.3	11.6	27	13.9	13.9	18	28.8%	0.19 [-0.41, 0.79]
Total (95% CI)			**89**			**65**	**100.0%**	**0.10 [-0.22, 0.42]**

Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 2 (P = 0.93); I² = 0%

Test for overall effect: Z = 0.61 (P = 0.54)

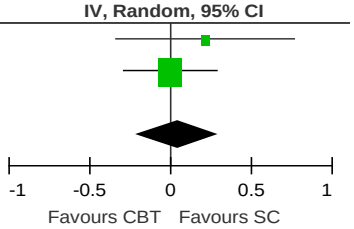


15.4 Mental state: mean endpoint depression symptoms (BDI-PC, CDSS)

	CBT			SC				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
ADDINGTON2011	2.9	4	27	2.1	3.3	24	21.4%	0.21 [-0.34, 0.77]
MORRISON2011	5.6	4.72	92	5.61	4.79	93	78.6%	-0.00 [-0.29, 0.29]
Total (95% CI)			**119**			**117**	**100.0%**	**0.04 [-0.21, 0.30]**

Heterogeneity: Tau² = 0.00; Chi² = 0.46, df = 1 (P = 0.50); I² = 0%

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

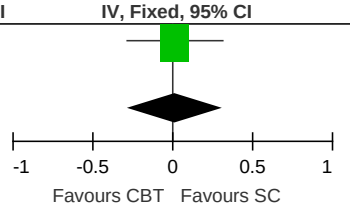


15.5 Mental state: mean endpoint social anxiety symptoms (SIAS)

	CBT			SC				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**
MORRISON2011	30.85	17.98	82	30.6	16.91	90	100.0%	0.01 [-0.28, 0.31]
Total (95% CI)			**82**			**90**	**100.0%**	**0.01 [-0.28, 0.31]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.09 (P = 0.93)

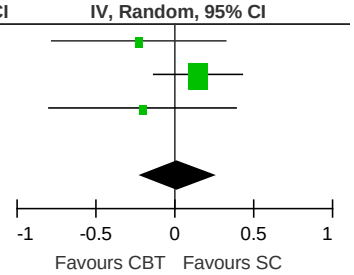


15.6 Mean endpoint psychosocial functioning (GAF)

	CBT			SC				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
ADDINGTON2011	-64.2	14.4	27	-61.3	9.9	24	18.7%	-0.23 [-0.78, 0.32]
MORRISON2011	-59.3	16.21	97	-61.61	15.04	98	65.0%	0.15 [-0.13, 0.43]
PHILLIPS2009	-66.8	7.7	26	-64.6	13.6	19	16.3%	-0.20 [-0.80, 0.39]
Total (95% CI)			**150**			**141**	**100.0%**	**0.02 [-0.22, 0.26]**

Heterogeneity: Tau² = 0.00; Chi² = 2.11, df = 2 (P = 0.35); I² = 5%

Test for overall effect: Z = 0.16 (P = 0.87)

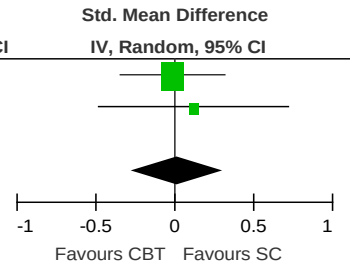


15.7 Mean endpoint quality of life (MANSA, QLS)

	CBT			SC				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
MORRISON2011	-53.17	12.38	75	-53	11.45	66	76.8%	-0.01 [-0.34, 0.32]
PHILLIPS2009	-81.1	30.3	26	-84.4	22	18	23.2%	0.12 [-0.48, 0.72]
Total (95% CI)			**101**			**84**	**100.0%**	**0.02 [-0.27, 0.31]**

Heterogeneity: Tau² = 0.00; Chi² = 0.14, df = 1 (P = 0.70); I² = 0%

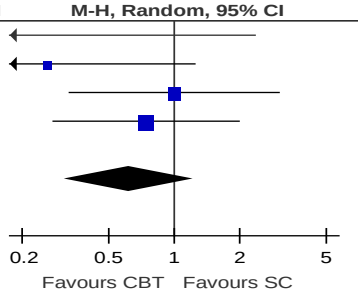
Test for overall effect: Z = 0.11 (P = 0.91)



1.2 Transition to psychosis (DSM-IV, PANSS, CAARMS, PANSS)

Study or Subgroup	CBT Events	CBT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Random, 95% CI
ADDINGTON2011	0	27	3	24	5.3%	0.13 [0.01, 2.35]
MORRISON2004	2	35	5	23	18.2%	0.26 [0.06, 1.24]
MORRISON2011	6	144	6	144	34.1%	1.00 [0.33, 3.03]
PHILLIPS2009	7	44	6	28	42.4%	0.74 [0.28, 1.98]
Total (95% CI)		**250**		**219**	**100.0%**	**0.62 [0.31, 1.22]**
Total events	15		20			

Heterogeneity: Tau² = 0.03; Chi² = 3.19, df = 3 (P = 0.36); I² = 6%
Test for overall effect: Z = 1.38 (P = 0.17)

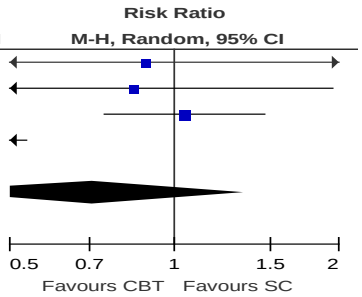


16. Combined children and young people 18 years and younger, with 25 years and younger: CBT versus supportive counselling: post-treatment side effect outcomes

16.1 Leaving the study early for any reason

Study or Subgroup	CBT Events	CBT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Random, 95% CI
ADDINGTON2011	8	27	8	24	21.2%	0.89 [0.39, 2.00]
MORRISON2004	9	35	7	23	20.8%	0.84 [0.37, 1.95]
MORRISON2011	47	144	45	144	29.6%	1.04 [0.75, 1.46]
PHILLIPS2009	15	44	27	28	28.4%	0.35 [0.23, 0.54]
Total (95% CI)		**250**		**219**	**100.0%**	**0.71 [0.38, 1.34]**
Total events	79		87			

Heterogeneity: Tau² = 0.33; Chi² = 16.73, df = 3 (P = 0.0008); I² = 82%
Test for overall effect: Z = 1.05 (P = 0.29)

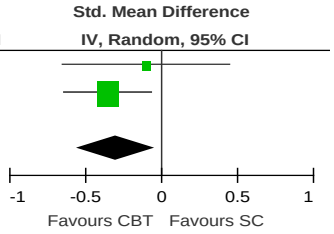


17. Combined children and young 18 years and younger, with 25 years and younger: CBT versus supportive counselling: 52 week's follow-up efficacy outcomes

17.1 Mental state: mean endpoint total symptoms (SOPS, CAARMS severity)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	SC Mean	SC SD	SC Total	Weight	Std. Mean Difference IV, Random, 95% CI
ADDINGTON2011	4.8	5.355838	27	5.35	5.169623	24	21.5%	-0.10 [-0.65, 0.45]
MORRISON2011	14.88	15.54	95	20.84	17.75	93	78.5%	-0.36 [-0.64, -0.07]
Total (95% CI)			**122**			**117**	**100.0%**	**-0.30 [-0.56, -0.05]**

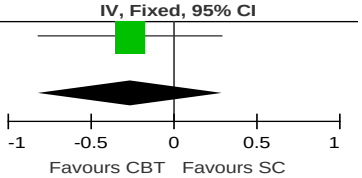
Heterogeneity: Tau² = 0.00; Chi² = 0.64, df = 1 (P = 0.42); I² = 0%
Test for overall effect: Z = 2.31 (P = 0.02)



17.2 Mental state: mean endpoint positive symptoms (SOPS positive)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	SC Mean	SC SD	SC Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
ADDINGTON2011	5.2	5.6	27	6.6	4.7	24	100.0%	-0.27 [-0.82, 0.29]
Total (95% CI)			**27**			**24**	**100.0%**	**-0.27 [-0.82, 0.29]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.94 (P = 0.35)

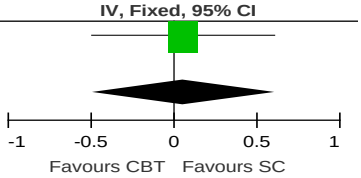


17.3 Mental state: mean endpoint negative symptoms (SOPS negative)

	CBT			SC				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
ADDINGTON2011	4.4	5.1	27	4.1	5.6	24	100.0%	0.06 [-0.49, 0.61]	
Total (95% CI)			**27**			**24**	**100.0%**	**0.06 [-0.49, 0.61]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.20 (P = 0.84)

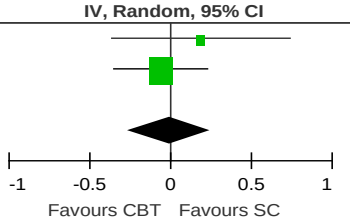


17.4 Mental state: mean endpoint depression symptoms (CDSS, BDI-PC)

	CBT			SC				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
ADDINGTON2011	3.3	4.6	27	2.5	3.7	24	21.7%	0.19 [-0.36, 0.74]	
MORRISON2011	5.41	5.12	93	5.72	4.92	90	78.3%	-0.06 [-0.35, 0.23]	
Total (95% CI)			**120**			**114**	**100.0%**	**-0.01 [-0.26, 0.25]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.61, df = 1 (P = 0.43); I² = 0%

Test for overall effect: Z = 0.06 (P = 0.95)

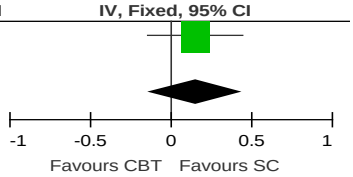


17.5 Mental state: mean endpoint social anxiety symptoms (SIAS)

	CBT			SC				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
MORRISON2011	32.51	17.08	91	29.99	16.6	87	100.0%	0.15 [-0.15, 0.44]	
Total (95% CI)			**91**			**87**	**100.0%**	**0.15 [-0.15, 0.44]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.99 (P = 0.32)

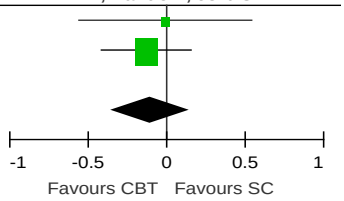


17.6 Mean endpoint psychosocial functioning (GAF)

	CBT			SC				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
ADDINGTON2011	-62.7	12.3	27	-62.6	10.2	24	21.2%	-0.01 [-0.56, 0.54]	
MORRISON2011	-60.74	16.69	95	-58.59	16.23	94	78.8%	-0.13 [-0.42, 0.16]	
Total (95% CI)			**122**			**118**	**100.0%**	**-0.10 [-0.36, 0.15]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%

Test for overall effect: Z = 0.81 (P = 0.42)

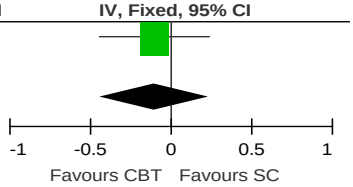


17.7 Mean endpoint quality of life (MANSA)

	CBT			SC				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
MORRISON2011	53.38	12.6	66	54.65	11.75	68	100.0%	-0.10 [-0.44, 0.24]	
Total (95% CI)			**66**			**68**	**100.0%**	**-0.10 [-0.44, 0.24]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.60 (P = 0.55)

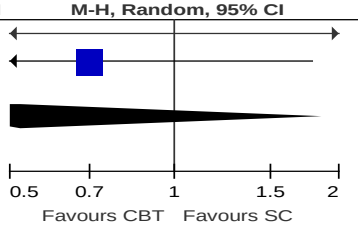


17.8 Transition to psychosis (DSM-IV, PANSS)

Study or Subgroup	CBT Events	CBT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Random, 95% CI
ADDINGTON2011	0	27	3	24	16.9%	0.13 [0.01, 2.35]
MORRISON2011	7	144	10	144	83.1%	0.70 [0.27, 1.79]
Total (95% CI)		**171**		**168**	**100.0%**	**0.52 [0.15, 1.87]**
Total events	7		13			

Heterogeneity: Tau² = 0.28; Chi² = 1.23, df = 1 (P = 0.27); I² = 19%

Test for overall effect: Z = 0.99 (P = 0.32)



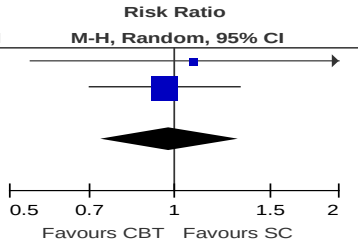
18. Combined children and young people 18 years and younger, with 25 years and younger: CBT versus supportive counselling: 52 week's follow-up side effect outcomes

18.1 Leaving the study early for any reason

Study or Subgroup	CBT Events	CBT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Random, 95% CI
ADDINGTON2011	11	27	9	24	17.5%	1.09 [0.55, 2.16]
MORRISON2011	49	144	51	144	82.5%	0.96 [0.70, 1.32]
Total (95% CI)		**171**		**168**	**100.0%**	**0.98 [0.74, 1.31]**
Total events	60		60			

Heterogeneity: Tau² = 0.00; Chi² = 0.10, df = 1 (P = 0.75); I² = 0%

Test for overall effect: Z = 0.13 (P = 0.90)



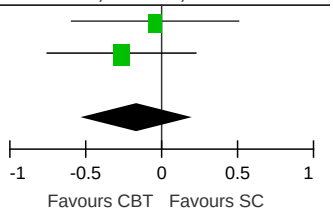
19. CBT versus supportive counselling: follow-up of 78 weeks or more

19.1 Mental state: mean endpoint total symptoms (SOPS, CAARMS severity)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	SC Mean	SC SD	SC Total	Weight	Std. Mean Difference IV, Random, 95% CI
ADDINGTON2011	4.5	4.452527	27	4.7	4.738143	24	44.2%	-0.04 [-0.59, 0.51]
MORRISON2011	13.94	16.07	34	18.84	20.52	31	55.8%	-0.26 [-0.75, 0.22]
Total (95% CI)			**61**			**55**	**100.0%**	**-0.17 [-0.53, 0.20]**

Heterogeneity: Tau² = 0.00; Chi² = 0.35, df = 1 (P = 0.56); I² = 0%

Test for overall effect: Z = 0.89 (P = 0.37)

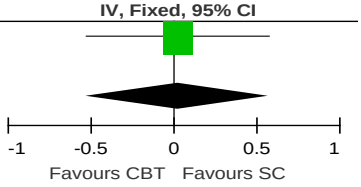


19.2 Mental state: mean endpoint positive symptoms (SOPS positive)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	SC Mean	SC SD	SC Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
ADDINGTON2011	4.6	4.6	27	4.5	4.1	24	100.0%	0.02 [-0.53, 0.57]
Total (95% CI)			**27**			**24**	**100.0%**	**0.02 [-0.53, 0.57]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.08 (P = 0.94)

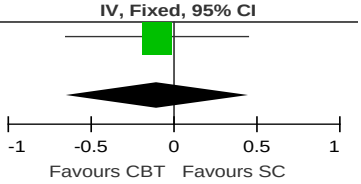


19.3 Mental state: mean endpoint negative symptoms (SOPS negative)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	SC Mean	SC SD	SC Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
ADDINGTON2011	4.4	4.3	27	4.9	5.3	24	100.0%	-0.10 [-0.65, 0.45]
Total (95% CI)			**27**			**24**	**100.0%**	**-0.10 [-0.65, 0.45]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.37 (P = 0.71)

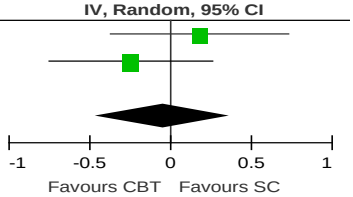


19.4 Mental state: mean endpoint depression symptoms (CDSS, BDI-PC)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	SC Mean	SC SD	SC Total	Weight	Std. Mean Difference IV, Random, 95% CI
ADDINGTON2011	2.6	3.5	27	1.9	4.2	24	46.5%	0.18 [-0.37, 0.73]
MORRISON2011	4.85	4.49	33	6	4.77	28	53.5%	-0.25 [-0.75, 0.26]
Total (95% CI)			**60**			**52**	**100.0%**	**-0.05 [-0.46, 0.37]**

Heterogeneity: Tau² = 0.02; Chi² = 1.24, df = 1 (P = 0.27); I² = 19%

Test for overall effect: Z = 0.23 (P = 0.82)

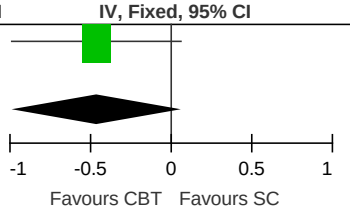


19.5 Mental state: mean endpoint social anxiety symptoms (SIAS)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	SC Mean	SC SD	SC Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MORRISON2011	27.81	17.3	32	36.42	19.48	26	100.0%	-0.46 [-0.99, 0.06]
Total (95% CI)			**32**			**26**	**100.0%**	**-0.46 [-0.99, 0.06]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.73 (P = 0.08)

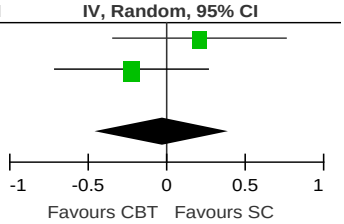


19.6 Mean endpoint psychosocial functioning (GAF)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	SC Mean	SC SD	SC Total	Weight	Std. Mean Difference IV, Random, 95% CI
ADDINGTON2011	-60.2	17.9	27	-63.4	11	24	45.5%	0.21 [-0.34, 0.76]
MORRISON2011	-64.12	17.71	34	-60.19	16.88	31	54.5%	-0.22 [-0.71, 0.26]
Total (95% CI)			**61**			**55**	**100.0%**	**-0.03 [-0.45, 0.40]**

Heterogeneity: Tau² = 0.02; Chi² = 1.33, df = 1 (P = 0.25); I² = 25%

Test for overall effect: Z = 0.13 (P = 0.90)

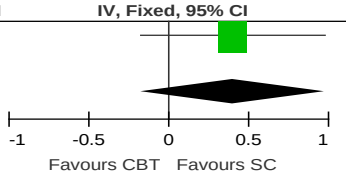


19.7 Mean endpoint quality of life (MANSA)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	SC Mean	SC SD	SC Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MORRISON2011	56.78	10.55	27	52.33	11.32	21	100.0%	0.40 [-0.17, 0.98]
Total (95% CI)			**27**			**21**	**100.0%**	**0.40 [-0.17, 0.98]**

Heterogeneity: Not applicable

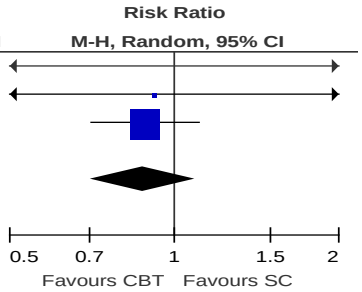
Test for overall effect: Z = 1.37 (P = 0.17)



19.8 Transition to psychosis (DSM-IV, PANSS)

Study or Subgroup	CBT Events	CBT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Random, 95% CI
ADDINGTON2011	0	27	3	24	0.6%	0.13 [0.01, 2.35]
MORRISON2004	7	35	5	23	4.7%	0.92 [0.33, 2.55]
MORRISON2011	69	144	78	144	94.7%	0.88 [0.70, 1.11]
Total (95% CI)		**206**		**191**	**100.0%**	**0.88 [0.70, 1.09]**
Total events	76		86			

Heterogeneity: Tau² = 0.00; Chi² = 1.74, df = 2 (P = 0.42); I² = 0%
Test for overall effect: Z = 1.17 (P = 0.24)

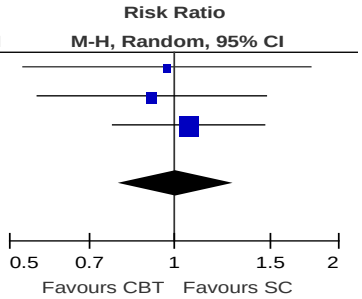


20. Combined children and young people 18 years and younger, with 25 years and younger: CBT versus supportive counselling: follow-up of 78 weeks or more, side effect outcomes

20.1 Leaving the study early for any reason

Study or Subgroup	CBT Events	CBT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Random, 95% CI
ADDINGTON2011	12	27	11	24	16.2%	0.97 [0.53, 1.78]
MORRISON2004	18	35	13	23	25.6%	0.91 [0.56, 1.47]
MORRISON2011	51	144	48	144	58.2%	1.06 [0.77, 1.46]
Total (95% CI)		**206**		**191**	**100.0%**	**1.01 [0.79, 1.28]**
Total events	81		72			

Heterogeneity: Tau² = 0.00; Chi² = 0.30, df = 2 (P = 0.86); I² = 0%
Test for overall effect: Z = 0.05 (P = 0.96)

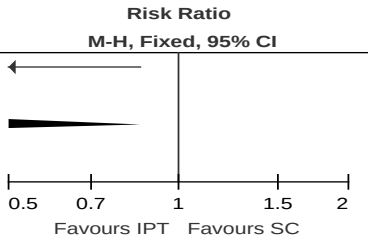


21. Children and young people 25 years and younger: integrated psychological therapies (IPT) versus supportive counselling: 52 weeks post-treatment efficacy outcomes

21.1 Transition to psychosis (PANSS)

Study or Subgroup	IPT Events	IPT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BECHDOLF2012	2	54	11	59	100.0%	0.20 [0.05, 0.86]
Total (95% CI)		**54**		**59**	**100.0%**	**0.20 [0.05, 0.86]**
Total events	2		11			

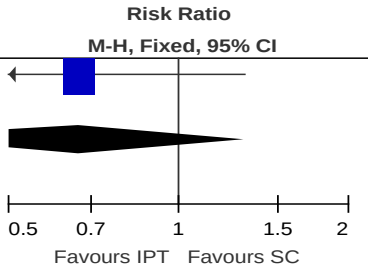
Heterogeneity: Not applicable
Test for overall effect: Z = 2.17 (P = 0.03)



21.2 Transition to psychosis (assuming drop outs transitioned; PANSS)

Study or Subgroup	IPT Events	IPT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BECHDOLF2012	11	63	17	65	100.0%	0.67 [0.34, 1.31]
Total (95% CI)		**63**		**65**	**100.0%**	**0.67 [0.34, 1.31]**
Total events	11		17			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.17 (P = 0.24)



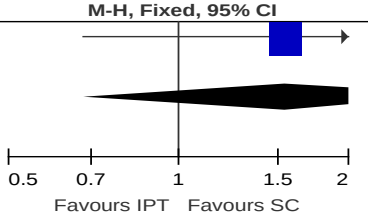
22. Children and young people 25 years and younger: integrated psychological therapies (IPT) versus supportive counselling: 52 weeks post-treatment side effect outcomes

22.1 Leaving the study early for any reason

Study or Subgroup	IPT Events	IPT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BECHDOLF2012	12	63	8	65	100.0%	1.55 [0.68, 3.53]
Total (95% CI)		**63**		**65**	**100.0%**	**1.55 [0.68, 3.53]**
Total events	12		8			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.04 (P = 0.30)



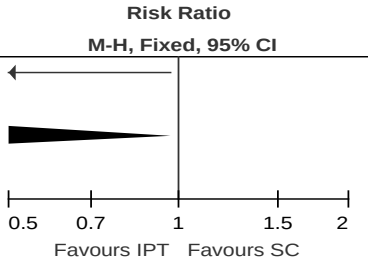
23. Children and young people 25 years and younger: integrated psychological therapies (IPT) versus supportive counselling: 104 week's follow-up efficacy outcomes

23.1 Transition to psychosis / sub threshold psychosis (PANSS)

Study or Subgroup	IPT Events	IPT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BECHDOLF2012	4	54	13	59	100.0%	0.34 [0.12, 0.97]
Total (95% CI)		**54**		**59**	**100.0%**	**0.34 [0.12, 0.97]**
Total events	4		13			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.02 (P = 0.04)

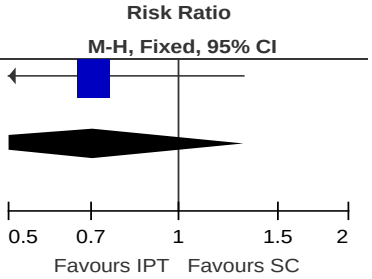


23.2 Transition to psychosis / sub threshold psychosis (assuming drop outs transitioned; PANSS)

Study or Subgroup	IPT Events	IPT Total	SC Events	SC Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BECHDOLF2012	13	63	19	65	100.0%	0.71 [0.38, 1.31]
Total (95% CI)		**63**		**65**	**100.0%**	**0.71 [0.38, 1.31]**
Total events	13		19			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.11 (P = 0.27)



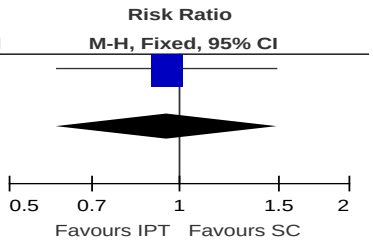
24. Children and young people 25 years and younger: integrated psychological therapies (IPT) versus supportive counselling: 104 week's follow-up side effect outcomes

24.1 Leaving the study early for any reason

	IPT		SC			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
BECHDOLF2012	23	63	25	65	100.0%	0.95 [0.61, 1.49]
Total (95% CI)		**63**		**65**	**100.0%**	**0.95 [0.61, 1.49]**
Total events	23		25			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.23 (P = 0.82)



14b: PSYCHOLOGICAL INTERVENTIONS

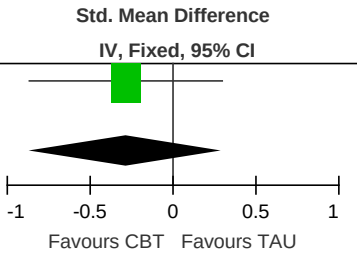
1. Children and young people 25 years and younger: CBT versus treatment as usual: 26 weeks post-treatment

1.1 Mental state: depression (CDSS)

	CBT			TAU				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
JACKSON2009	3.9	3.5	22	4.9	3.4	24	100.0%	-0.29 [-0.87, 0.30]
Total (95% CI)			**22**			**24**	**100.0%**	**-0.29 [-0.87, 0.30]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.96 (P = 0.34)

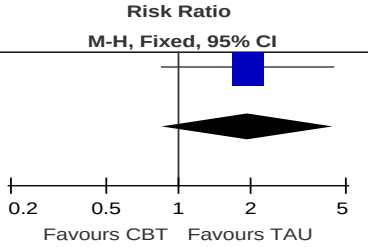


1.2 Leaving the study early for any reason

	CBT		TAU			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
JACKSON2009	14	36	6	30	100.0%	1.94 [0.85, 4.43]
Total (95% CI)		**36**		**30**	**100.0%**	**1.94 [0.85, 4.43]**
Total events	14		6			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.58 (P = 0.11)



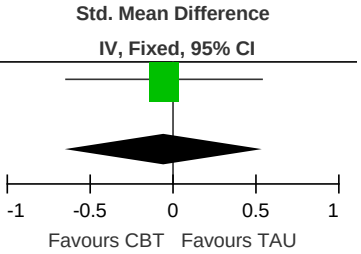
2. Children and young people 25 years and younger: CBT versus treatment as usual: 52 week's follow-up

2.1 Mental state: depression (CDSS)

	CBT			TAU				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
JACKSON2009	3.7	3.9	22	3.9	3.3	22	100.0%	-0.05 [-0.65, 0.54]
Total (95% CI)			**22**			**22**	**100.0%**	**-0.05 [-0.65, 0.54]**

Heterogeneity: Not applicable

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

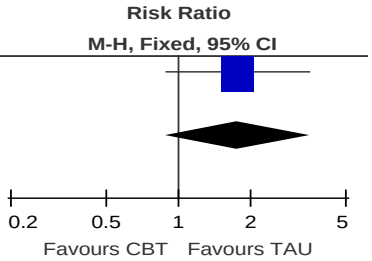


2.2 Leaving the study early for any reason

	CBT		TAU			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
JACKSON2009	17	36	8	30	100.0%	1.77 [0.89, 3.52]
Total (95% CI)		**36**		**30**	**100.0%**	**1.77 [0.89, 3.52]**
Total events	17		8			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.63 (P = 0.10)



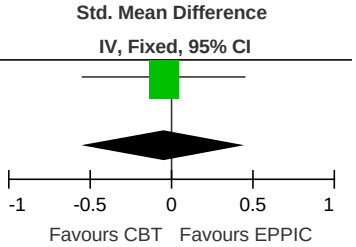
3. Children and young people 25 years and younger: CBT versus EPPIC[1] treatment as usual: 14 weeks post-treatment

3.1 Mental state: positive symptoms (BPRS psychotic subscale)

	CBT			EPPIC TAU				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
JACKSON2008	7.45	4.05	31	7.65	4.03	31	100.0%	-0.05 [-0.55, 0.45]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.05 [-0.55, 0.45]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.19 (P = 0.85)

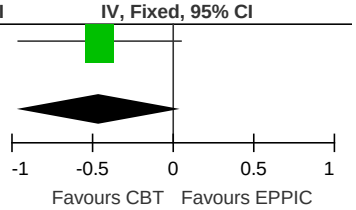


3.2 Mental state: negative symptoms (SANS)

	CBT			EPPIC TAU				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
JACKSON2008	17.67	9.43	31	22.88	12.87	31	100.0%	-0.46 [-0.96, 0.05]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.46 [-0.96, 0.05]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.77 (P = 0.08)

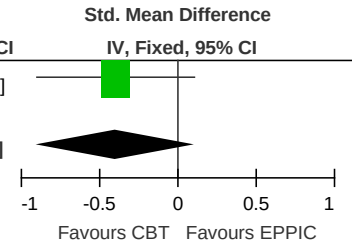


3.3 Functioning: social (SOFAS)

	CBT			EPPIC TAU				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
JACKSON2008	-62.69	13.81	31	-57.6	11.37	31	100.0%	-0.40 [-0.90, 0.11]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.40 [-0.90, 0.11]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.55 (P = 0.12)

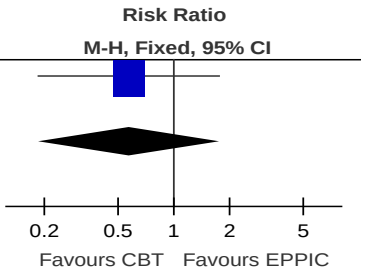


3.4 Leaving the study early for any reason

	CBT		EPPIC TAU			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
JACKSON2008	4	31	7	31	100.0%	0.57 [0.19, 1.76]
Total (95% CI)		**31**		**31**	**100.0%**	**0.57 [0.19, 1.76]**
Total events	4		7			

Heterogeneity: Not applicable

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



[1] Early Psychosis Prevention and Intervention Centre, Australia

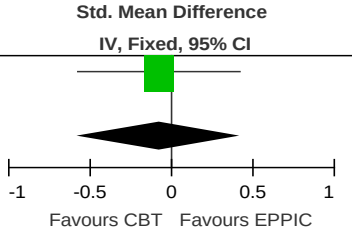
4. Children and young people 25 years and younger: CBT versus EPPIC[1] treatment as usual: 52 week's follow-up

4.1 Mental state: positive symptoms (BPRS psychotic subscale)

	CBT			EPPIC TAU				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
JACKSON2008	7.2	4.08	31	7.55	4.76	31	100.0%	-0.08 [-0.58, 0.42]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.08 [-0.58, 0.42]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.31 (P = 0.76)

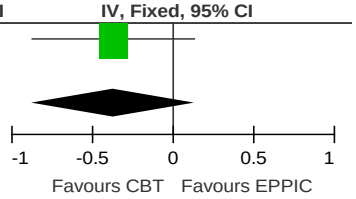


4.2 Mental state: negative symptoms (SANS)

	CBT			EPPIC TAU				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
JACKSON2008	14.66	10.9	31	19.55	14.79	31	100.0%	-0.37 [-0.87, 0.13]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.37 [-0.87, 0.13]**

Heterogeneity: Not applicable

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

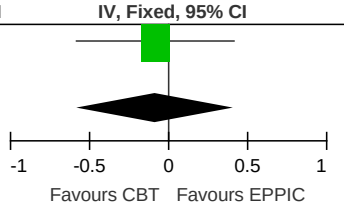


4.3 Functioning: social (SOFAS)

	CBT			EPPIC TAU				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
JACKSON2008	-64.21	15.18	31	-62.91	15.18	31	100.0%	-0.08 [-0.58, 0.41]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.08 [-0.58, 0.41]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.33 (P = 0.74)

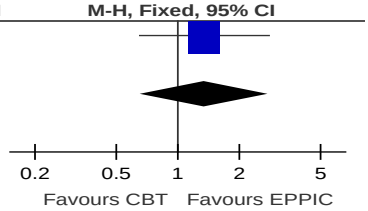


4.4 Relapse: number of participants hospitalised

	CBT		EPPIC TAU			
Study or Subgroup	Events	Total	Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
JACKSON2008	12	30	8	27	100.0%	1.35 [0.65, 2.80]
Total (95% CI)		**30**		**27**	**100.0%**	**1.35 [0.65, 2.80]**
Total events	12		8			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.81 (P = 0.42)

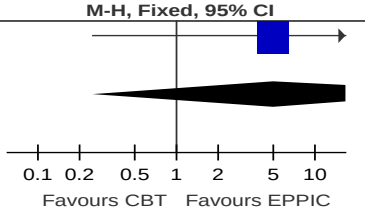


4.5 Mortality: number of suicides

Study or Subgroup	CBT Events	CBT Total	EPPIC TAU Events	EPPIC TAU Total	Weight	Risk Ratio M-H, Fixed, 95% CI
JACKSON2008	2	31	0	31	100.0%	5.00 [0.25, 100.08]
Total (95% CI)		**31**		**31**	**100.0%**	**5.00 [0.25, 100.08]**
Total events	2		0			

Heterogeneity: Not applicable

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



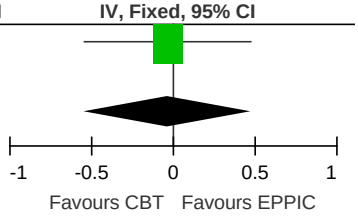
5. Children and young people 25 years and younger: CBT versus EPPIC[2] treatment as usual in acutely suicidal participants: 10 weeks post-treatment

5.1 Quality of life (QLS)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	EPPIC TAU Mean	EPPIC TAU SD	EPPIC TAU Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
POWER2003	2.3	3.1	27	2.4	2.5	33	100.0%	-0.04 [-0.54, 0.47]
Total (95% CI)			**27**			**33**	**100.0%**	**-0.04 [-0.54, 0.47]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.14 (P = 0.89)

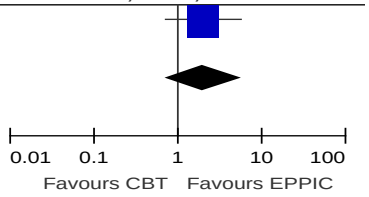


5.2 Leaving the study early for any reason

Study or Subgroup	CBT Events	CBT Total	EPPIC TAU Events	EPPIC TAU Total	Weight	Risk Ratio M-H, Fixed, 95% CI
POWER2003	10	31	4	25	100.0%	2.02 [0.72, 5.66]
Total (95% CI)		**31**		**25**	**100.0%**	**2.02 [0.72, 5.66]**
Total events	10		4			

Heterogeneity: Not applicable

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

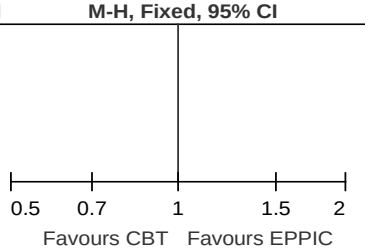


5.3 Mortality: number of suicides (assuming drop outs did not commit suicide)

Study or Subgroup	CBT Events	CBT Total	EPPIC TAU Events	EPPIC TAU Total	Weight	Risk Ratio M-H, Fixed, 95% CI
POWER2003	0	31	0	25		Not estimable
Total (95% CI)		**31**		**25**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable

Test for overall effect: Not applicable



[2] Early Psychosis Prevention and Intervention Centre, Australia

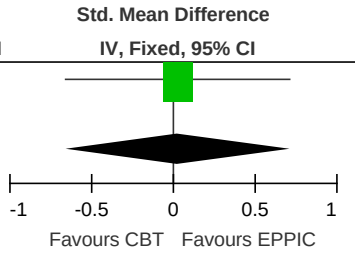
6. Children and young people 25 years and younger CBT versus EPPIC[3] treatment as usual in acutely suicidal participants: 36 week's follow-up

6.1 Quality of life (QLS)

	CBT			EPPIC TAU				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
POWER2003	2.3	3.5	15	2.2	3.9	18	100.0%	0.03 [-0.66, 0.71]
Total (95% CI)			**15**			**18**	**100.0%**	**0.03 [-0.66, 0.71]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.07 (P = 0.94)

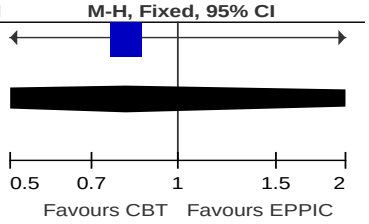


6.2 Mortality: number of suicides (assuming drop outs did not commit suicide)

	CBT		EPPIC TAU			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
POWER2003	1	31	1	25	100.0%	0.81 [0.05, 12.26]
Total (95% CI)		**31**		**25**	**100.0%**	**0.81 [0.05, 12.26]**
Total events	1		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.15 (P = 0.88)



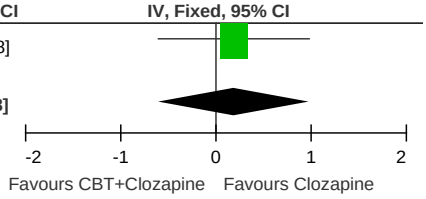
7. Children and young people 25 years and younger CBT + clozapine versus clozapine: 12 weeks post-treatment

7.1 Mental state: positive symptoms (BPRS psychotic subscale)

	CBT+Clozapine			Clozapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
EDWARDS2011	9.1	4.2	11	8.4	3.1	14	100.0%	0.19 [-0.60, 0.98]
Total (95% CI)			**11**			**14**	**100.0%**	**0.19 [-0.60, 0.98]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.46 (P = 0.64)

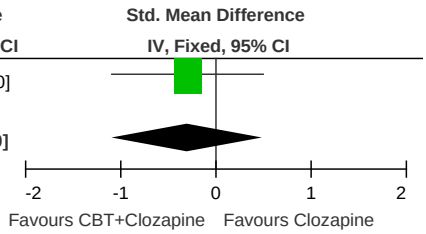


7.2 Mental state: negative symptoms (SANS)

	CBT+Clozapine			Clozapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
EDWARDS2011	26.5	12.1	11	29.4	6.6	14	100.0%	-0.30 [-1.09, 0.50]
Total (95% CI)			**11**			**14**	**100.0%**	**-0.30 [-1.09, 0.50]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.74 (P = 0.46)



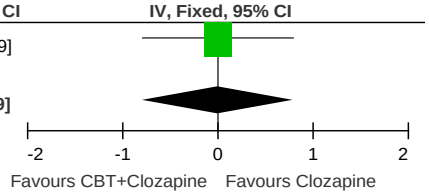
[3] [3] Early Psychosis Prevention and Intervention Centre, Australia

7.3 Global state (CGI)

Study or Subgroup	CBT+Clozapine Mean	SD	Total	Clozapine Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
EDWARDS2011	3.6	1.4	11	3.6	0.9	14	100.0%	0.00 [-0.79, 0.79]
Total (95% CI)			**11**			**14**	**100.0%**	**0.00 [-0.79, 0.79]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)

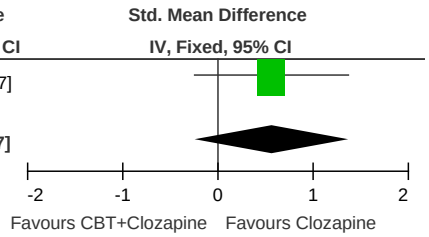


7.4 Mental state: depression symptoms (BDI)

Study or Subgroup	CBT+Clozapine Mean	SD	Total	Clozapine Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
EDWARDS2011	22.5	9.6	11	18.1	5.5	14	100.0%	0.56 [-0.25, 1.37]
Total (95% CI)			**11**			**14**	**100.0%**	**0.56 [-0.25, 1.37]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.37 (P = 0.17)

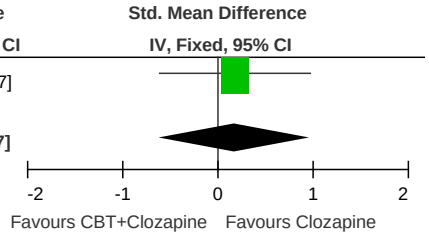


7.5 Functioning: social (SOFAS)

Study or Subgroup	CBT+Clozapine Mean	SD	Total	Clozapine Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
EDWARDS2011	-52.1	11.1	11	-54	9.6	14	100.0%	0.18 [-0.61, 0.97]
Total (95% CI)			**11**			**14**	**100.0%**	**0.18 [-0.61, 0.97]**

Heterogeneity: Not applicable

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

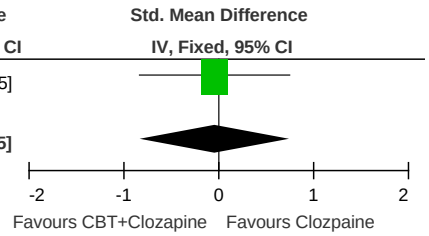


7.6 Quality of life (QLS)

Study or Subgroup	CBT+Clozapine Mean	SD	Total	Clozapine Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
EDWARDS2011	-59.3	11.9	11	-58.8	10.4	14	100.0%	-0.04 [-0.83, 0.75]
Total (95% CI)			**11**			**14**	**100.0%**	**-0.04 [-0.83, 0.75]**

Heterogeneity: Not applicable

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



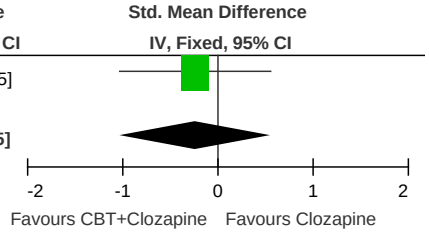
8. Children and young people 25 years and younger: CBT + clozapine versus clozapine: 24 week's follow-up

8.1 Mental state: positive symptoms (BPRS psychotic subscale)

	CBT+Clozapine			Clozapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
EDWARDS2011	7.9	4	11	8.7	2.5	14	100.0%	-0.24 [-1.03, 0.55]
Total (95% CI)			**11**			**14**	**100.0%**	**-0.24 [-1.03, 0.55]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.59 (P = 0.55)

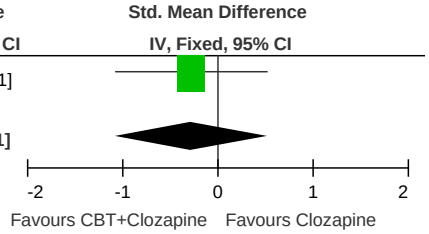


8.2 Mental state: negative symptoms (SANS)

	CBT+Clozapine			Clozapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
EDWARDS2011	24.9	12.2	11	27.8	8	14	100.0%	-0.28 [-1.07, 0.51]
Total (95% CI)			**11**			**14**	**100.0%**	**-0.28 [-1.07, 0.51]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.69 (P = 0.49)

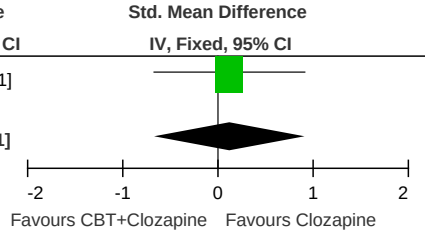


8.3 Global state (CGI)

	CBT+Clozapine			Clozapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
EDWARDS2011	3.5	0.8	11	3.4	0.8	14	100.0%	0.12 [-0.67, 0.91]
Total (95% CI)			**11**			**14**	**100.0%**	**0.12 [-0.67, 0.91]**

Heterogeneity: Not applicable

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

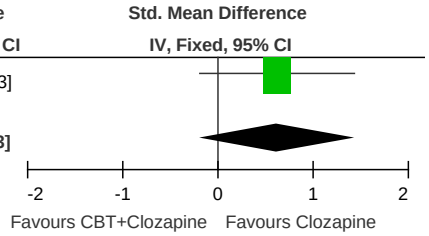


8.4 Mental state: depression symptoms (BDI)

	CBT+Clozapine			Clozapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
EDWARDS2011	22.6	7.6	11	18.6	4.9	14	100.0%	0.62 [-0.19, 1.43]
Total (95% CI)			**11**			**14**	**100.0%**	**0.62 [-0.19, 1.43]**

Heterogeneity: Not applicable

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

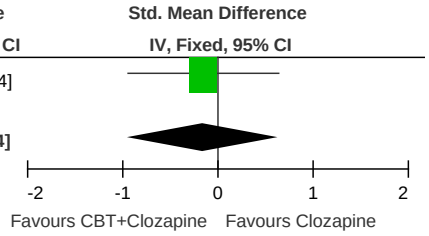


8.5 Functioning: social (SOFAS)

Study or Subgroup	CBT+Clozapine Mean	SD	Total	Clozapine Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
EDWARDS2011	-55.4	10.5	11	-53.8	9.8	14	100.0%	-0.15 [-0.94, 0.64]
Total (95% CI)			**11**			**14**	**100.0%**	**-0.15 [-0.94, 0.64]**

Heterogeneity: Not applicable

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

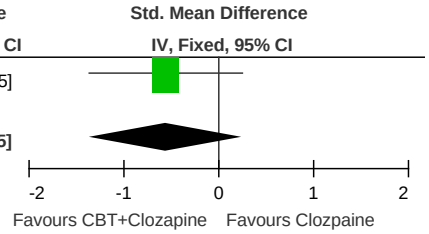


8.6 Quality of life (QLS)

Study or Subgroup	CBT+Clozapine Mean	SD	Total	Clozapine Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
EDWARDS2011	-63.3	16.1	11	-54.5	14.6	14	100.0%	-0.56 [-1.36, 0.25]
Total (95% CI)			**11**			**14**	**100.0%**	**-0.56 [-1.36, 0.25]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.35 (P = 0.18)

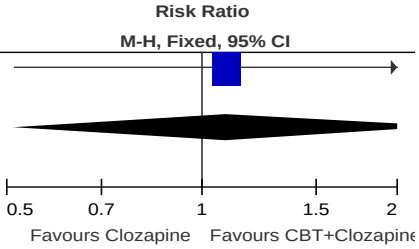


8.7 Remission (score of "mild" or less on each of the three items of the BPRS-P and a CGI severity item rating of "mild" or less; assuming drop outs did not achieve remission)

Study or Subgroup	CBT+Clozapine Events	Total	Clozapine Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
EDWARDS2011	6	11	7	14	100.0%	1.09 [0.51, 2.31]
Total (95% CI)		**11**		**14**	**100.0%**	**1.09 [0.51, 2.31]**
Total events	6		7			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.23 (P = 0.82)



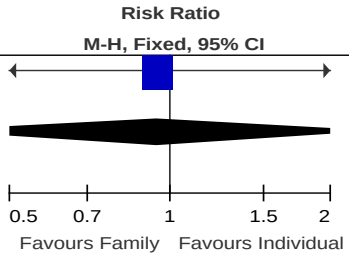
9. Children and young people 25 years and younger: individual CBT versus family CBT: 52 weeks post-randomisation

9.1 Relapse: number of participants (BPRS; assuming drop outs relapsed)

Study or Subgroup	CBT (Family) Events	Total	CBT (Individual) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
LINZEN1996	6	39	6	37	100.0%	0.95 [0.34, 2.68]
Total (95% CI)		**39**		**37**	**100.0%**	**0.95 [0.34, 2.68]**
Total events	6		6			

Heterogeneity: Not applicable

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



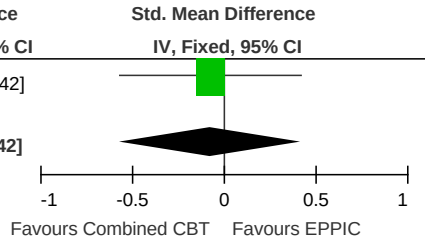
10. Children and young people 25 years and younger: individual and family CBT versus EPPIC[14] treatment as usual: 30.33 weeks post-treatment

10.1 Mental state: total symptoms (BPRS)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	EPPIC TAU Mean	EPPIC TAU SD	EPPIC TAU Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
GLEESON2009	34.3	8.4	31	35	9.8	32	100.0%	-0.08 [-0.57, 0.42]
Total (95% CI)			**31**			**32**	**100.0%**	**-0.08 [-0.57, 0.42]**

Heterogeneity: Not applicable

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

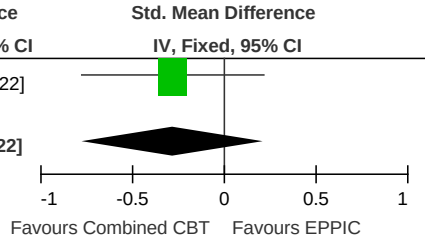


10.2 Mental state: positive symptoms (BPRS psychotic subscale)

Study or Subgroup	CBT Mean	CBT SD	CBT Total	EPPIC TAU Mean	EPPIC TAU SD	EPPIC TAU Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
GLEESON2009	5.7	2.2	31	6.5	3.3	32	100.0%	-0.28 [-0.78, 0.22]
Total (95% CI)			**31**			**32**	**100.0%**	**-0.28 [-0.78, 0.22]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.11 (P = 0.27)

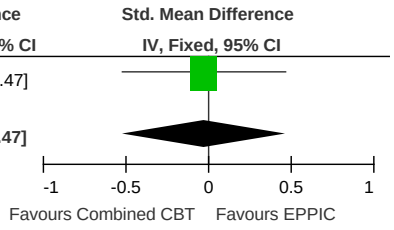


10.3 Mental state: negative symptoms (SANS)

Study or Subgroup	CBT(individual & family) Mean	CBT(individual & family) SD	CBT(individual & family) Total	EPPIC TAU Mean	EPPIC TAU SD	EPPIC TAU Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
GLEESON2009	4.2	3.4	31	4.3	3.7	32	100.0%	-0.03 [-0.52, 0.47]
Total (95% CI)			**31**			**32**	**100.0%**	**-0.03 [-0.52, 0.47]**

Heterogeneity: Not applicable

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

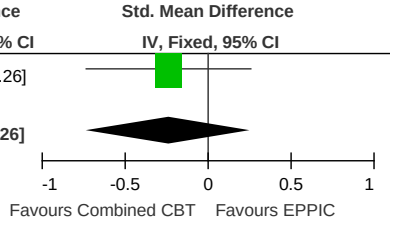


10.4 Mental state: depression symptoms (MADRS)

Study or Subgroup	CBT(individual & family) Mean	CBT(individual & family) SD	CBT(individual & family) Total	EPPIC TAU Mean	EPPIC TAU SD	EPPIC TAU Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
GLEESON2009	8.3	9	31	10.8	11.5	32	100.0%	-0.24 [-0.73, 0.26]
Total (95% CI)			**31**			**32**	**100.0%**	**-0.24 [-0.73, 0.26]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.94 (P = 0.35)



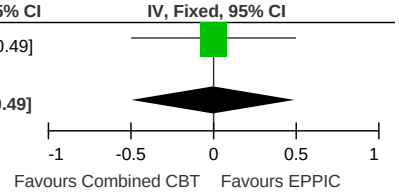
[4] Early Psychosis Prevention and Intervention Centre, Australia

10.5 Quality of life (WHOQLA-abbreviated version)

Study or Subgroup	CBT(individual & family) Mean	SD	Total	EPPIC TAU Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
GLEESON2009	3.6	0.8	31	3.6	1.1	32	100.0%	0.00 [-0.49, 0.49]
Total (95% CI)			**31**			**32**	**100.0%**	**0.00 [-0.49, 0.49]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)

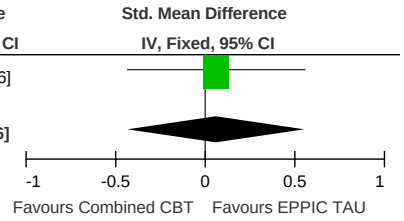


10.6 Functioning: social (SOFAS)

Study or Subgroup	CBT(individual & family) Mean	SD	Total	EPPIC TAU Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
GLEESON2009	-63.8	15.7	31	-64.8	16.5	32	100.0%	0.06 [-0.43, 0.56]
Total (95% CI)			**31**			**32**	**100.0%**	**0.06 [-0.43, 0.56]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.24 (P = 0.81)

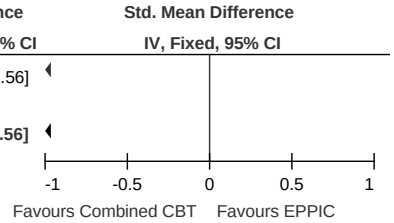


10.7 Relapse: time in days (BPRS)

Study or Subgroup	CBT(individual & family) Mean	SD	Total	EPPIC TAU Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
GLEESON2009	-273.25	9.2	38	-241	10.35	38	100.0%	-3.26 [-3.96, -2.56]
Total (95% CI)			**38**			**38**	**100.0%**	**-3.26 [-3.96, -2.56]**

Heterogeneity: Not applicable

Test for overall effect: Z = 9.17 (P < 0.00001)

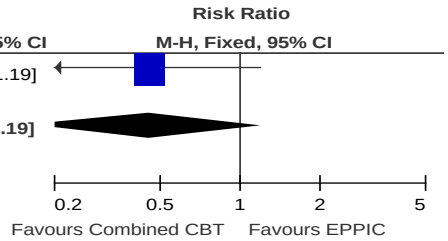


10.8 Relapse: number of participants (BPRS; assuming drop outs relapsed)

Study or Subgroup	Favours CBT Events	Total	EPPIC TAU Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
GLEESON2009	5	41	11	41	100.0%	0.45 [0.17, 1.19]
Total (95% CI)		**41**		**41**	**100.0%**	**0.45 [0.17, 1.19]**
Total events	5		11			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.60 (P = 0.11)

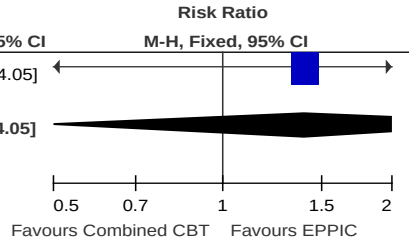


10.9 Leaving the study early for any reason

Study or Subgroup	CBT(individual & family) Events	Total	EPPIC TAU Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
GLEESON2009	7	41	5	41	100.0%	1.40 [0.48, 4.05]
Total (95% CI)		**41**		**41**	**100.0%**	**1.40 [0.48, 4.05]**
Total events	7		5			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.62 (P = 0.53)



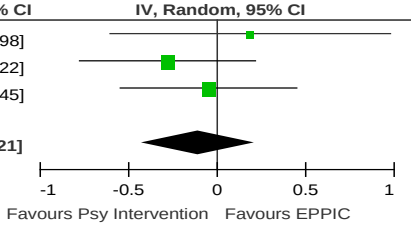
11. Children and young people 25 years and younger: any psychological intervention versus EPPIC[5] treatment as usual: post-treatment

11.1 Mental state: positive symptoms

Study or Subgroup	Psy intervention Mean	SD	Total	EPPIC TAU Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
EDWARDS2011	9.1	4.2	11	8.4	3.1	14	16.5%	0.19 [-0.60, 0.98]
GLEESON2009	5.7	2.2	31	6.5	3.3	32	41.9%	-0.28 [-0.78, 0.22]
JACKSON2008	7.45	4.05	31	7.65	4.03	31	41.6%	-0.05 [-0.55, 0.45]
Total (95% CI)			**73**			**77**	**100.0%**	**-0.11 [-0.43, 0.21]**

Heterogeneity: Tau² = 0.00; Chi² = 1.05, df = 2 (P = 0.59); I² = 0%

Test for overall effect: Z = 0.65 (P = 0.51)

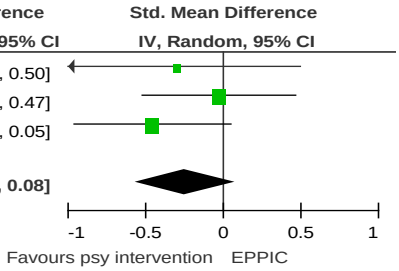


11.2 Mental state: negative symptoms

Study or Subgroup	Psy intervention Mean	SD	Total	EPPIC TAU Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
EDWARDS2011	26.5	12.1	11	29.4	6.6	14	16.5%	-0.30 [-1.09, 0.50]
GLEESON2009	4.2	3.4	31	4.3	3.7	32	42.7%	-0.03 [-0.52, 0.47]
JACKSON2008	17.67	9.43	31	22.88	12.87	31	40.9%	-0.46 [-0.96, 0.05]
Total (95% CI)			**73**			**77**	**100.0%**	**-0.25 [-0.57, 0.08]**

Heterogeneity: Tau² = 0.00; Chi² = 1.43, df = 2 (P = 0.49); I² = 0%

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

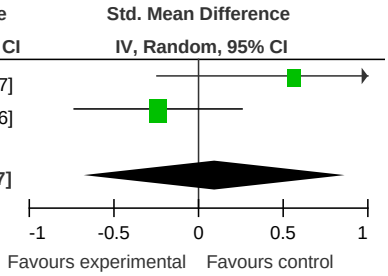


11.3 Mental state: depression symptoms

Study or Subgroup	Psy intervention Mean	SD	Total	EPPIC TAU Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
EDWARDS2011	22.5	9.6	11	18.1	5.5	14	41.8%	0.56 [-0.25, 1.37]
GLEESON2009	8.3	9	31	10.8	11.5	32	58.2%	-0.24 [-0.73, 0.26]
Total (95% CI)			**42**			**46**	**100.0%**	**0.10 [-0.68, 0.87]**

Heterogeneity: Tau² = 0.20; Chi² = 2.75, df = 1 (P = 0.10); I² = 64%

Test for overall effect: Z = 0.24 (P = 0.81)

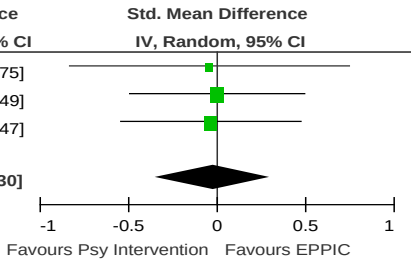


11.4 Quality of life

Study or Subgroup	Psy intervention Mean	SD	Total	EPPIC TAU Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
EDWARDS2011	-59.3	11.9	11	-58.8	10.4	14	16.8%	-0.04 [-0.83, 0.75]
GLEESON2009	3.6	0.8	31	3.6	1.1	32	42.8%	0.00 [-0.49, 0.49]
POWER2003	2.3	3.1	27	2.4	2.5	33	40.4%	-0.04 [-0.54, 0.47]
Total (95% CI)			**69**			**79**	**100.0%**	**-0.02 [-0.34, 0.30]**

Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 2 (P = 0.99); I² = 0%

Test for overall effect: Z = 0.13 (P = 0.90)



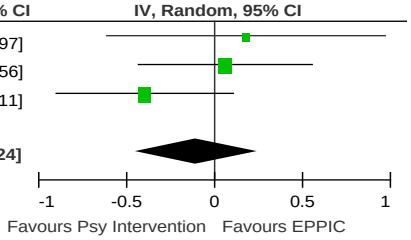
[5] Early Psychosis Prevention and Intervention Centre, Australia

11.5 Functioning: social

Study or Subgroup	Psy intervention Mean	SD	Total	EPPIC TAU Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
EDWARDS2011	-52.1	11.1	11	-54	9.6	14	17.7%	0.18 [-0.61, 0.97]
GLEESON2009	-63.8	15.7	31	-64.8	16.5	32	41.8%	0.06 [-0.43, 0.56]
JACKSON2008	-62.69	13.81	31	-57.6	11.37	31	40.5%	-0.40 [-0.90, 0.11]
Total (95% CI)			**73**			**77**	**100.0%**	**-0.10 [-0.45, 0.24]**

Heterogeneity: Tau² = 0.01; Chi² = 2.23, df = 2 (P = 0.33); I² = 10%

Test for overall effect: Z = 0.59 (P = 0.55)

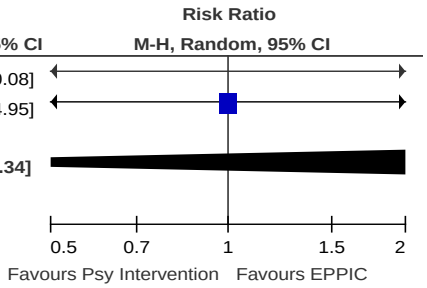


11.6 Mortality: number of suicides (assuming drop outs did not commit suicide)

Study or Subgroup	Psy intervention Events	Total	EPPIC TAU Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
JACKSON2008	2	31	0	31	44.9%	5.00 [0.25, 100.08]
POWER2003	1	21	1	21	55.1%	1.00 [0.07, 14.95]
Total (95% CI)		**52**		**52**	**100.0%**	**2.06 [0.28, 15.34]**
Total events	3		1			

Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 1 (P = 0.43); I² = 0%

Test for overall effect: Z = 0.71 (P = 0.48)

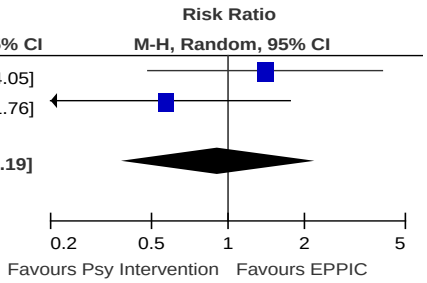


11.7 Leaving the study early for any reason

Study or Subgroup	Psy intervention Events	Total	EPPIC TAU Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
GLEESON2009	7	41	5	41	52.1%	1.40 [0.48, 4.05]
JACKSON2008	4	31	7	31	47.9%	0.57 [0.19, 1.76]
Total (95% CI)		**72**		**72**	**100.0%**	**0.91 [0.38, 2.19]**
Total events	11		12			

Heterogeneity: Tau² = 0.09; Chi² = 1.29, df = 1 (P = 0.26); I² = 22%

Test for overall effect: Z = 0.21 (P = 0.84)



14c: PHARMACOLOGICAL INTERVENTIONS

14ci: Treatment of first episode psychosis

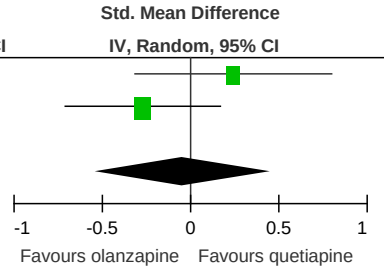
1. Combined of first episode psychosis children and young people 18 years and younger with 25 years and younger: olanzapine versus quetiapine: post-treatment efficacy outcomes

1.1 Mental state: total symptoms (PANSS) (mean endpoint: ARANGO2009, mean change: MCEVOY2007)

	Olanzapine			Quetipaine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
ARANGO2009	71.62	17.33	26	67.29	17.86	24	44.2%	0.24 [-0.31, 0.80]
MCEVOY2007	-18.4	9.73	37	-15.6	10.68	44	55.8%	-0.27 [-0.71, 0.17]
Total (95% CI)			**63**			**68**	**100.0%**	**-0.04 [-0.54, 0.46]**

Heterogeneity: Tau² = 0.07; Chi² = 2.01, df = 1 (P = 0.16); I² = 50%

Test for overall effect: Z = 0.17 (P = 0.86)

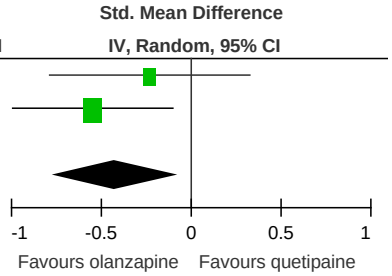


1.2 Mental state: positive symptoms (SAPS) (mean endpoint: ARANGO2009, mean change: MCEVOY2007)

	Olanzapine			Quetipaine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
ARANGO2009	14.04	4.75	26	15.08	4.07	24	39.0%	-0.23 [-0.79, 0.33]
MCEVOY2007	-7.1	3.1	37	-5.3	3.38	44	61.0%	-0.55 [-0.99, -0.10]
Total (95% CI)			**63**			**68**	**100.0%**	**-0.42 [-0.77, -0.08]**

Heterogeneity: Tau² = 0.00; Chi² = 0.76, df = 1 (P = 0.38); I² = 0%

Test for overall effect: Z = 2.39 (P = 0.02)

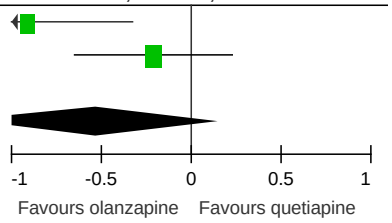


1.3 Mental state: negative symptoms (SANS) (mean endpoint: ARANGO2009, mean change: MCEVOY2007)

	Olanzapine			Quetipaine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
ARANGO2009	16.29	5.15	24	22.15	7.24	26	46.0%	-0.91 [-1.50, -0.33]
MCEVOY2007	-3.5	3.1	37	-2.8	3.45	44	54.0%	-0.21 [-0.65, 0.23]
Total (95% CI)			**61**			**70**	**100.0%**	**-0.53 [-1.22, 0.15]**

Heterogeneity: Tau² = 0.18; Chi² = 3.54, df = 1 (P = 0.06); I² = 72%

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

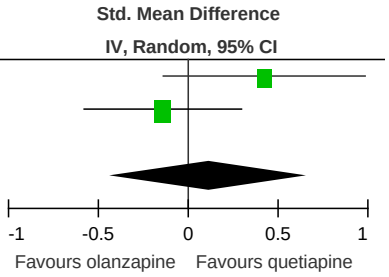


1.4 Global state: severity (CGI-S) (mean endpoint: ARANGO2009, mean change: MCEVOY2007)

	Olanzapine			Quetipaine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
ARANGO2009	3.54	1.3	26	2.96	1.4	24	44.9%	0.42 [-0.14, 0.98]
MCEVOY2007	-1.3	0.67	37	-1.2	0.73	44	55.1%	-0.14 [-0.58, 0.30]
Total (95% CI)			**63**			**68**	**100.0%**	**0.11 [-0.44, 0.66]**

Heterogeneity: Tau² = 0.09; Chi² = 2.41, df = 1 (P = 0.12); I² = 59%

Test for overall effect: Z = 0.40 (P = 0.69)

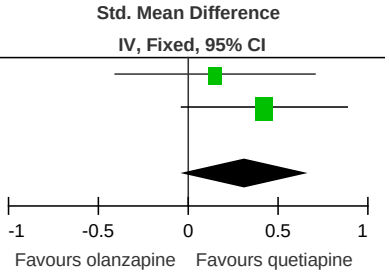


1.5 Mental state: depression (HAM-D, CDSS) (mean endpoint: ARANGO2009, mean change: MCEVOY2007)

	Olanzapine			Quetipaine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
ARANGO2009	9.12	7.91	26	8	6.7	24	40.8%	0.15 [-0.41, 0.71]
MCEVOY2007	-1.2	2.01	37	-2.1	2.19	37	59.2%	0.42 [-0.04, 0.88]
Total (95% CI)			**63**			**61**	**100.0%**	**0.31 [-0.04, 0.67]**

Heterogeneity: Chi² = 0.55, df = 1 (P = 0.46); I² = 0%

Test for overall effect: Z = 1.72 (P = 0.08)

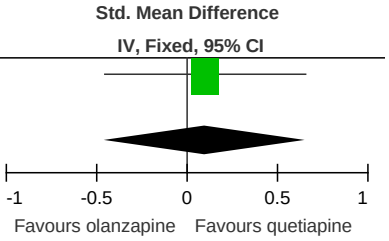


1.6 Mental state: mean endpoint mania (YMRS)

	Olanzapine			Quetipaine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
ARANGO2009	6.34	9.62	26	5.5	6.39	24	100.0%	0.10 [-0.45, 0.66]
Total (95% CI)			**26**			**24**	**100.0%**	**0.10 [-0.45, 0.66]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.35 (P = 0.72)

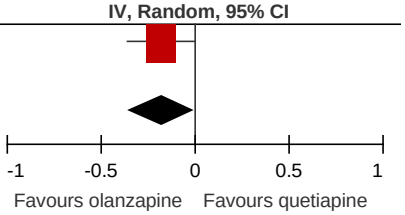


1.7 Mean change in quality of life (QLS)

				Std. Mean Difference
Study or Subgroup	Std. Mean Difference	SE	Weight	IV, Random, 95% CI
MCEVOY2007	-0.18	0.091837	100.0%	-0.18 [-0.36, -0.00]
Total (95% CI)			**100.0%**	**-0.18 [-0.36, -0.00]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.96 (P = 0.05)



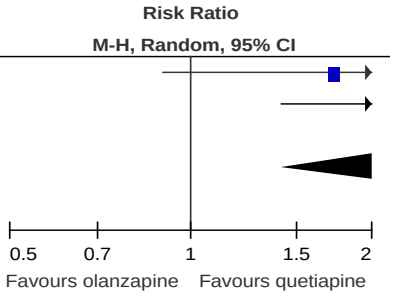
2. Combined of first episode psychosis children and young people 18 years and younger with 25 years and younger: olanzapine versus quetiapine: post-treatment side effect outcomes

2.1 Side effects: weight gain (kg, not defined: ARANGO2009; number of participants with weight (lbs) gain of 7% or greater: MCEVOY2007)

	Olanzapine		Quetiapine			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
ARANGO2009	15	26	8	24	32.1%	1.73 [0.90, 3.33]
MCEVOY2007	28	37	15	44	67.9%	2.22 [1.42, 3.48]
Total (95% CI)		**63**		**68**	**100.0%**	**2.05 [1.41, 2.97]**
Total events	43		23			

Heterogeneity: Tau² = 0.00; Chi² = 0.38, df = 1 (P = 0.54); I² = 0%

Test for overall effect: Z = 3.80 (P = 0.0001)

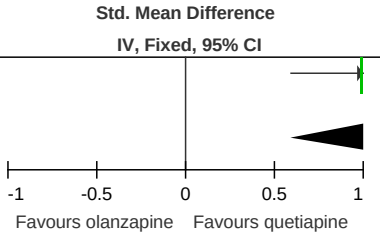


2.2 Side effects: mean change in weight (lbs)

	Olanzapine			Quetiapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	24.4	10.64	37	12.49	11.48	44	100.0%	1.06 [0.59, 1.53]
Total (95% CI)			**37**			**44**	**100.0%**	**1.06 [0.59, 1.53]**

Heterogeneity: Not applicable

Test for overall effect: Z = 4.45 (P < 0.00001)

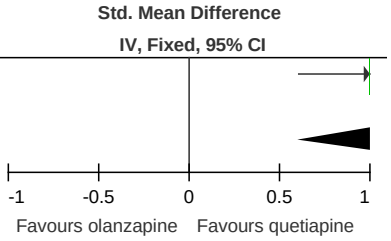


2.3 Side effects: mean change in BMI (kg/m2)

	Olanzapine			Quetiapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	3.7	1.58	37	1.9	1.72	44	100.0%	1.08 [0.61, 1.54]
Total (95% CI)			**37**			**44**	**100.0%**	**1.08 [0.61, 1.54]**

Heterogeneity: Not applicable

Test for overall effect: Z = 4.49 (P < 0.00001)

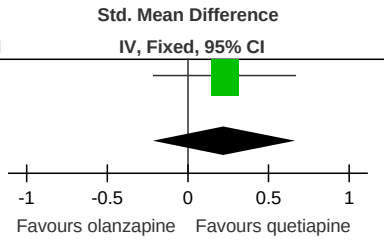


2.4 Side effects: mean change in fasting serum glucose level (mg/dl)

	Olanzapine			Quetiapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	8.6	9.67	37	6.2	11.08	44	100.0%	0.23 [-0.21, 0.67]
Total (95% CI)			**37**			**44**	**100.0%**	**0.23 [-0.21, 0.67]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.02 (P = 0.31)

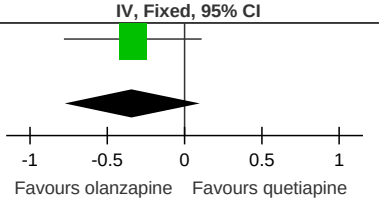


2.5 Side effects: mean change in fasting total cholesterol (mg/dl)

	Olanzapine			Quetiapine				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
MCEVOY2007	15.7	26.16	37	25.2	29.58	44	100.0%	-0.34 [-0.78, 0.11]	
Total (95% CI)			**37**			**44**	**100.0%**	**-0.34 [-0.78, 0.11]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 1.49 (P = 0.14)

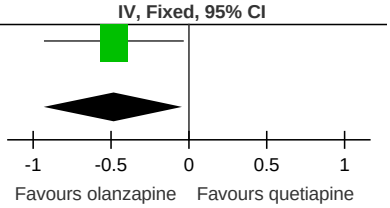


2.6 Side effects: mean change in fasting high-density lipoprotein cholesterol (mg/dl)

	Olanzapine			Quetiapine				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
MCEVOY2007	-6.5	5.54	37	-3.6	6.3	44	100.0%	-0.48 [-0.93, -0.04]	
Total (95% CI)			**37**			**44**	**100.0%**	**-0.48 [-0.93, -0.04]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 2.13 (P = 0.03)

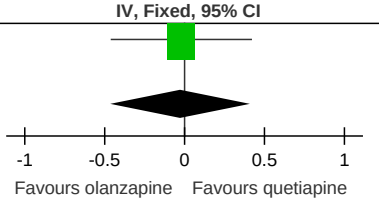


2.7 Side effects: mean change in fasting triglycerides (mg/dl)

	Olanzapine			Quetiapine				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
MCEVOY2007	66.4	78.47	37	68.1	88.69	44	100.0%	-0.02 [-0.46, 0.42]	
Total (95% CI)			**37**			**44**	**100.0%**	**-0.02 [-0.46, 0.42]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.09 (P = 0.93)

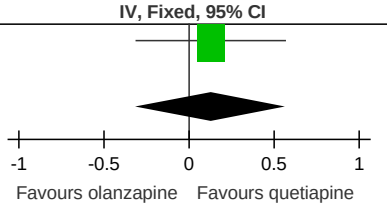


2.8 Side effects: mean change in systolic BP (mmHg)

	Olanzapine			Quetiapine				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
MCEVOY2007	8.5	7.42	37	7.5	8.03	44	100.0%	0.13 [-0.31, 0.57]	
Total (95% CI)			**37**			**44**	**100.0%**	**0.13 [-0.31, 0.57]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.57 (P = 0.57)

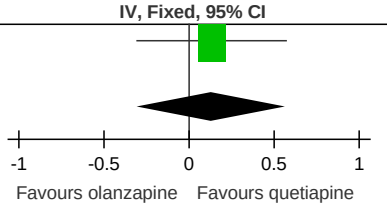


2.9 Side effects: mean change in diastolic BP (mmHg)

	Olanzapine			Quetiapine				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
MCEVOY2007	4.8	4.99	37	4.1	5.44	44	100.0%	0.13 [-0.31, 0.57]	
Total (95% CI)			**37**			**44**	**100.0%**	**0.13 [-0.31, 0.57]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.59 (P = 0.55)

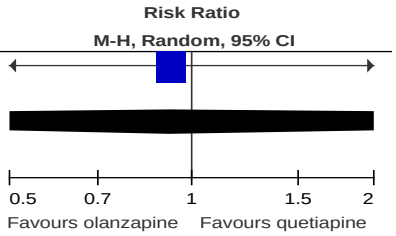


2.10 Side effects: tachycardia

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Random, 95% CI
ARANGO2009	1	26	1	24	100.0%	0.92 [0.06, 13.95]
Total (95% CI)		**26**		**24**	**100.0%**	**0.92 [0.06, 13.95]**
Total events	1		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.06 (P = 0.95)

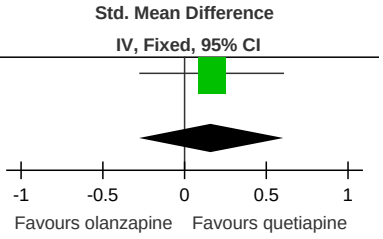


2.11 Side effects: mean change in prolactin level (mg/dl)

Study or Subgroup	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCEVOY2007	-15.9	15.57	37	-18.7	17.64	44	100.0%	0.17 [-0.27, 0.60]
Total (95% CI)			**37**			**44**	**100.0%**	**0.17 [-0.27, 0.60]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.74 (P = 0.46)

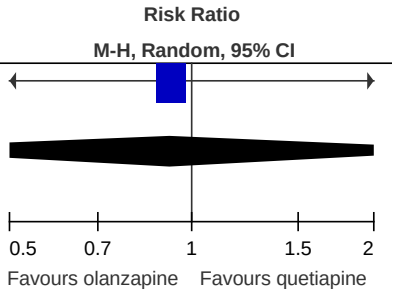


2.12 Side effects: tremor

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Random, 95% CI
ARANGO2009	4	26	4	24	100.0%	0.92 [0.26, 3.29]
Total (95% CI)		**26**		**24**	**100.0%**	**0.92 [0.26, 3.29]**
Total events	4		4			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.12 (P = 0.90)

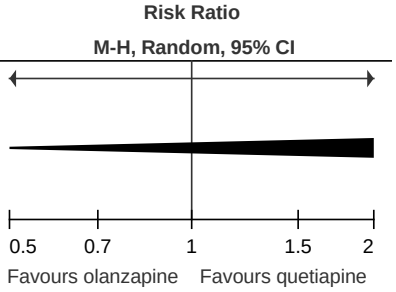


2.13 Side effects: akathesia

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Random, 95% CI
ARANGO2009	3	26	0	24	100.0%	6.48 [0.35, 119.32]
Total (95% CI)		**26**		**24**	**100.0%**	**6.48 [0.35, 119.32]**
Total events	3		0			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.26 (P = 0.21)

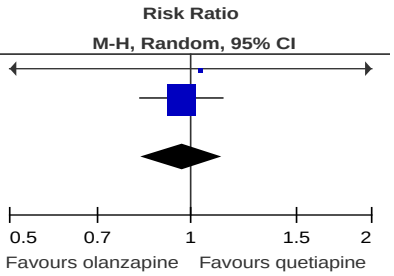


2.14 Leaving the study early for any reason

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetipaine Events	Quetipaine Total	Weight	Risk Ratio M-H, Random, 95% CI
ARANGO2009	9	26	8	24	4.0%	1.04 [0.48, 2.25]
MCEVOY2007	91	133	95	134	96.0%	0.97 [0.82, 1.13]
Total (95% CI)		**159**		**158**	**100.0%**	**0.97 [0.83, 1.13]**
Total events	100		103			

Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.85); I² = 0%

Test for overall effect: Z = 0.41 (P = 0.68)



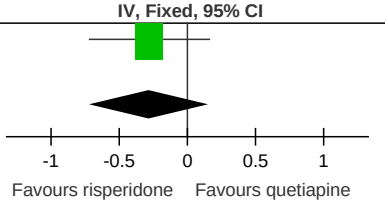
3. Children and young people 25 years and younger: risperidone versus quetiapine: post-treatment efficacy outcomes

3.1 Mental state: mean change in total symptoms (PANSS)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCEVOY2007	-18.5	9.91	37	-15.6	10.68	44	100.0%	-0.28 [-0.72, 0.16]
Total (95% CI)			**37**			**44**	**100.0%**	**-0.28 [-0.72, 0.16]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.24 (P = 0.22)

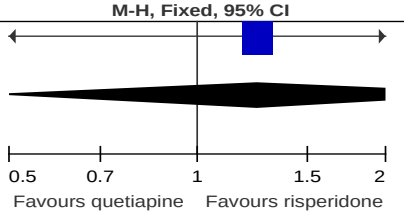


3.2 Mental state: response (number of participants with a 30% reduction PANSS)

Study or Subgroup	Risperidone Events	Risperidone Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SWADI2010	5	11	4	11	100.0%	1.25 [0.45, 3.45]
Total (95% CI)		**11**		**11**	**100.0%**	**1.25 [0.45, 3.45]**
Total events	5		4			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.43 (P = 0.67)

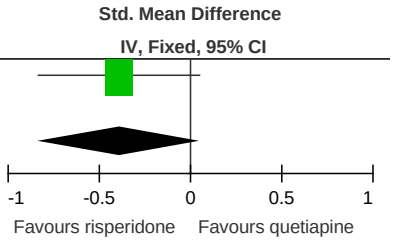


3.3 Mental state: mean change in positive symptoms (SAPS)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCEVOY2007	-6.6	3.16	37	-5.3	3.38	44	100.0%	-0.39 [-0.83, 0.05]
Total (95% CI)			**37**			**44**	**100.0%**	**-0.39 [-0.83, 0.05]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.74 (P = 0.08)

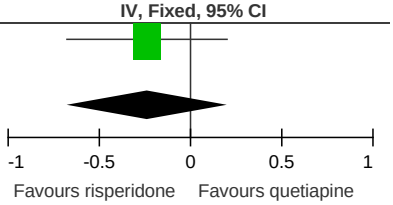


3.4 Mental state: mean change in negative symptoms (SANS)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCEVOY2007	-3.6	3.16	37	-2.8	3.45	44	100.0%	-0.24 [-0.68, 0.20]
Total (95% CI)			**37**			**44**	**100.0%**	**-0.24 [-0.68, 0.20]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.07 (P = 0.29)

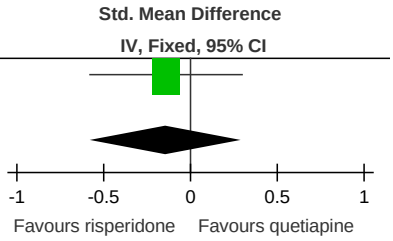


3.5 Mean change in global state: severity (CGI-S)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCEVOY2007	-1.3	0.67	37	-1.2	0.73	44	100.0%	-0.14 [-0.58, 0.30]
Total (95% CI)			**37**			**44**	**100.0%**	**-0.14 [-0.58, 0.30]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.63 (P = 0.53)

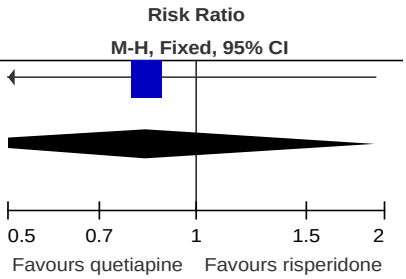


3.6 Global state response (number of participants with a 30% reduction CGI-S)

Study or Subgroup	Risperidone Events	Risperidone Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SWADI2010	5	11	6	11	100.0%	0.83 [0.36, 1.94]
Total (95% CI)		**11**		**11**	**100.0%**	**0.83 [0.36, 1.94]**
Total events	5		6			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.42 (P = 0.67)

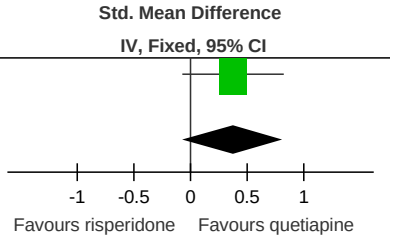


3.7 Mental state: mean change in depression (CDSS)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCEVOY2007	-1.3	2.01	37	-2.1	2.19	44	100.0%	0.38 [-0.07, 0.82]
Total (95% CI)			**37**			**44**	**100.0%**	**0.38 [-0.07, 0.82]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.67 (P = 0.10)

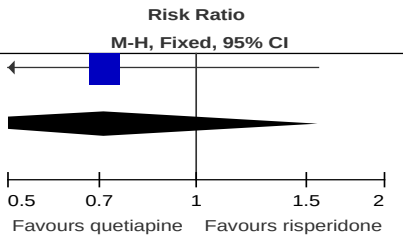


3.8 Mental state: depression response (number of participants with a 30% reduction HAM-D)

Study or Subgroup	Risperidone Events	Risperidone Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SWADI2010	5	11	7	11	100.0%	0.71 [0.33, 1.57]
Total (95% CI)		**11**		**11**	**100.0%**	**0.71 [0.33, 1.57]**
Total events	5		7			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.84 (P = 0.40)

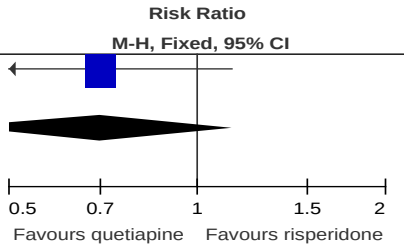


3.9 Mental state: mania response (number of participants with a 30% reduction (YMRS)

Study or Subgroup	Risperidone Events	Risperidone Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SWADI2010	7	11	10	11	100.0%	0.70 [0.43, 1.14]
Total (95% CI)		**11**		**11**	**100.0%**	**0.70 [0.43, 1.14]**
Total events	7		10			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.44 (P = 0.15)

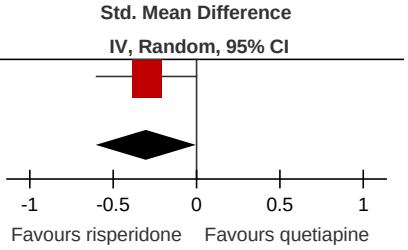


3.10 Mean change in quality of life (QLS)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
MCEVOY2007	-0.3	0.153061	100.0%	-0.30 [-0.60, -0.00]
Total (95% CI)			**100.0%**	**-0.30 [-0.60, -0.00]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.96 (P = 0.05)



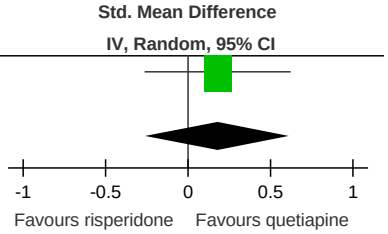
4. Children and young people 25 years and younger: risperidone versus quetiapine: post-treatment side effect outcomes

4.1 Side effects: mean change in weight (lbs)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
MCEVOY2007	14.5	10.58	37	12.49	11.48	44	100.0%	0.18 [-0.26, 0.62]
Total (95% CI)			**37**			**44**	**100.0%**	**0.18 [-0.26, 0.62]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.80 (P = 0.42)

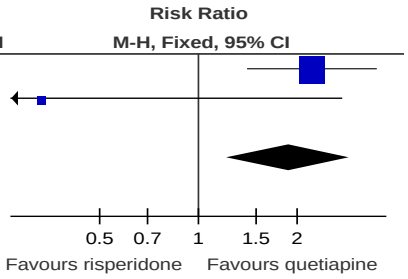


4.2 Side effects: weight gain (number of participants who gained over 7%)

Study or Subgroup	Risperidone Events	Risperidone Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
MCEVOY2007	28	37	15	44	82.0%	2.22 [1.42, 3.48]
SWADI2010	1	11	3	11	18.0%	0.33 [0.04, 2.73]
Total (95% CI)		**48**		**55**	**100.0%**	**1.88 [1.22, 2.89]**
Total events	29		18			

Heterogeneity: Chi² = 3.12, df = 1 (P = 0.08); I² = 68%

Test for overall effect: Z = 2.87 (P = 0.004)

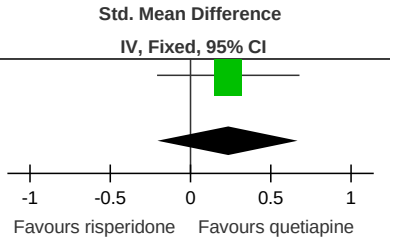


4.3 Side effects: mean change in BMI (kg/m2)

	Risperidone			Quetiapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	2.3	1.64	37	1.9	1.72	44	100.0%	0.24 [-0.20, 0.67]
Total (95% CI)			**37**			**44**	**100.0%**	**0.24 [-0.20, 0.67]**

Heterogeneity: Not applicable

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

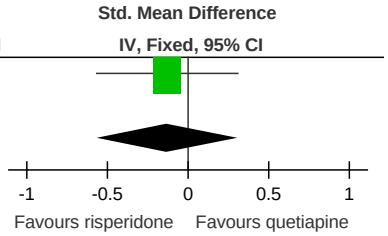


4.4 Side effects: mean change in fasting serum glucose level (mg/dl)

	Risperidone			Quetiapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	4.8	10.34	37	6.2	11.08	44	100.0%	-0.13 [-0.57, 0.31]
Total (95% CI)			**37**			**44**	**100.0%**	**-0.13 [-0.57, 0.31]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.58 (P = 0.56)

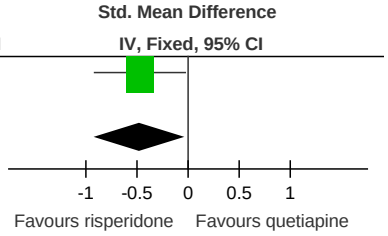


4.5 Side effects: mean change in fasting total cholesterol (mg/dl)

	Risperidone			Quetiapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	11.4	28.28	37	25.2	29.58	44	100.0%	-0.47 [-0.91, -0.03]
Total (95% CI)			**37**			**44**	**100.0%**	**-0.47 [-0.91, -0.03]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.08 (P = 0.04)

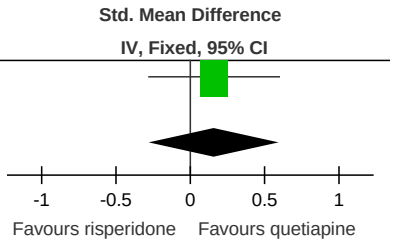


4.6 Side effects: mean change in fasting high-density lipoprotein cholesterol (mg/dl)

	Risperidone			Quetiapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	-2.6	6.02	37	-3.6	6.3	44	100.0%	0.16 [-0.28, 0.60]
Total (95% CI)			**37**			**44**	**100.0%**	**0.16 [-0.28, 0.60]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.72 (P = 0.47)

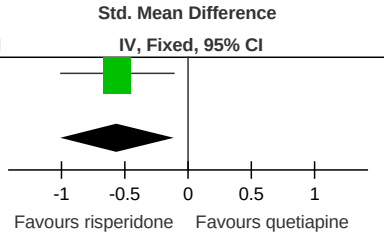


4.7 Side effects: fasting mean change in triglycerides (mg/dl)

	Risperidone			Quetiapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	19.1	84.67	37	68.1	88.69	44	100.0%	-0.56 [-1.00, -0.11]
Total (95% CI)			**37**			**44**	**100.0%**	**-0.56 [-1.00, -0.11]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.45 (P = 0.01)

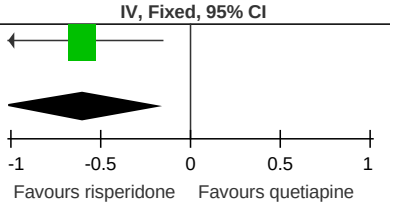


4.8 Side effects: mean change in systolic BP (mm Hg)

	Risperidone			Quetiapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	2.7	7.73	37	7.5	8.03	44	100.0%	-0.60 [-1.05, -0.15]
Total (95% CI)			**37**			**44**	**100.0%**	**-0.60 [-1.05, -0.15]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.64 (P = 0.008)

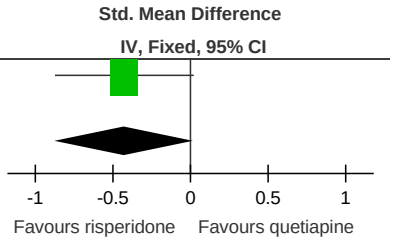


4.9 Side effects: mean change in diastolic BP (mm Hg)

	Risperidone			Quetiapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	1.8	5.23	37	4.1	5.44	44	100.0%	-0.43 [-0.87, 0.02]
Total (95% CI)			**37**			**44**	**100.0%**	**-0.43 [-0.87, 0.02]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.89 (P = 0.06)

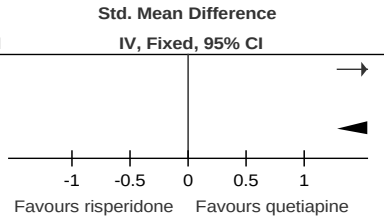


4.10 Side effects: mean change in prolactin level (mg/dl)

	Risperidone			Quetiapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	12.1	15.88	37	-18.7	17.64	44	100.0%	1.81 [1.29, 2.33]
Total (95% CI)			**37**			**44**	**100.0%**	**1.81 [1.29, 2.33]**

Heterogeneity: Not applicable

Test for overall effect: Z = 6.79 (P < 0.00001)

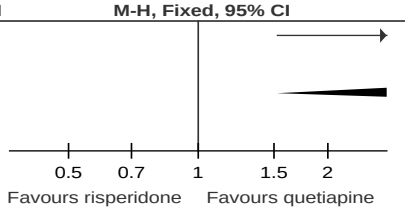


4.11 Side effects: elevated prolactin level (mg/dl)

	Risperidone		Quetiapine			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
SWADI2010	10	11	1	11	100.0%	10.00 [1.53, 65.41]
Total (95% CI)		**11**		**11**	**100.0%**	**10.00 [1.53, 65.41]**
Total events	10		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.40 (P = 0.02)

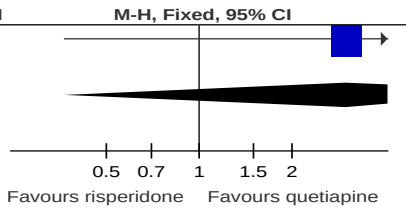


4.12 Side effects: extra pyramidal (number of participants with an AIMS score >2)

	Risperidone		Quetiapine			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
SWADI2010	3	11	1	11	100.0%	3.00 [0.37, 24.58]
Total (95% CI)		**11**		**11**	**100.0%**	**3.00 [0.37, 24.58]**
Total events	3		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.02 (P = 0.31)

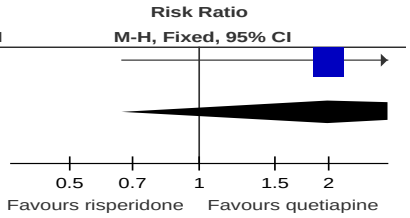


4.13 Side effects: extra pyramidal (number of participants with a SAS score >2)

Study or Subgroup	Risperidone Events	Risperidone Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SWADI2010	6	11	3	11	100.0%	2.00 [0.66, 6.04]
Total (95% CI)		**11**		**11**	**100.0%**	**2.00 [0.66, 6.04]**
Total events	6		3			

Heterogeneity: Not applicable

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

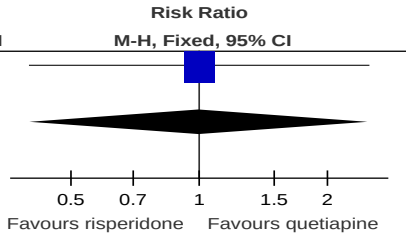


4.14 Side effects: extra pyramidal (number of participants with a BARS score >1)

Study or Subgroup	Risperidone Events	Risperidone Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
SWADI2010	5	11	5	11	100.0%	1.00 [0.40, 2.50]
Total (95% CI)		**11**		**11**	**100.0%**	**1.00 [0.40, 2.50]**
Total events	5		5			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)

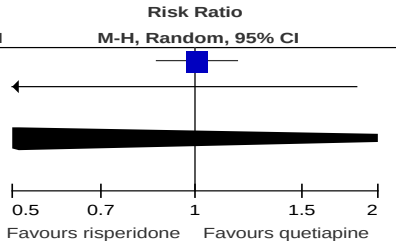


4.15 Leaving the study early for any reason

Study or Subgroup	Risperidone Events	Risperidone Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Random, 95% CI
MCEVOY2007	95	133	95	134	69.4%	1.01 [0.86, 1.17]
SWADI2010	0	11	4	11	30.6%	0.11 [0.01, 1.85]
Total (95% CI)		**144**		**145**	**100.0%**	**0.51 [0.06, 4.08]**
Total events	95		99			

Heterogeneity: Tau² = 1.60; Chi² = 2.56, df = 1 (P = 0.11); I² = 61%

Test for overall effect: Z = 0.63 (P = 0.53)



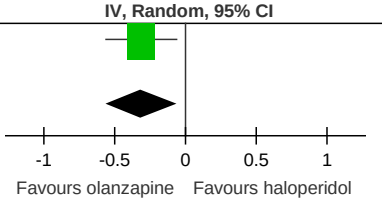
5. Children and young people 25 years and younger: olanzapine versus haloperidol: efficacy outcomes during treatment (at 12 weeks)

5.1 Mental state: mean endpoint total symptoms (PANSS)

Study or Subgroup	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Weight	Std. Mean Difference IV, Random, 95% CI
LIEBERMAN2003	59.33	19.41	126	65.4	19.42	125	100.0%	-0.31 [-0.56, -0.06]
Total (95% CI)			**126**			**125**	**100.0%**	**-0.31 [-0.56, -0.06]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.45 (P = 0.01)

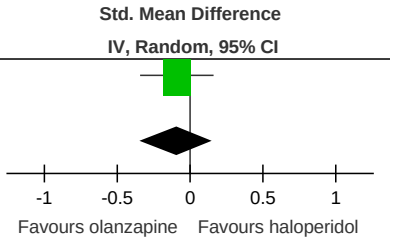


5.2 Mental state: mean endpoint positive symptoms (SAPS)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
LIEBERMAN2003	13.39	5.59	126	13.9	5.59	126	100.0%	-0.09 [-0.34, 0.16]
Total (95% CI)			**126**			**126**	**100.0%**	**-0.09 [-0.34, 0.16]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.72 (P = 0.47)

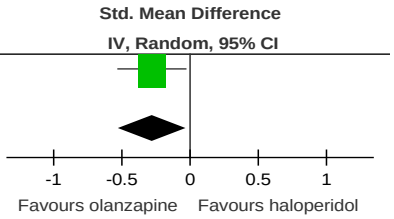


5.3 Mental state: mean endpoint negative symptoms (SANS)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
LIEBERMAN2003	16.64	5.89	126	18.29	5.87	126	100.0%	-0.28 [-0.53, -0.03]
Total (95% CI)			**126**			**126**	**100.0%**	**-0.28 [-0.53, -0.03]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.21 (P = 0.03)

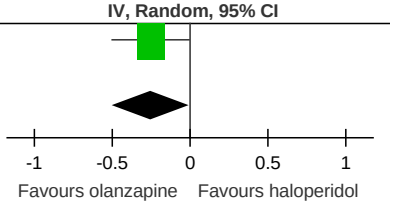


5.4 mean endpoint global state: severity (CGI-S)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
LIEBERMAN2003	3.24	1.18	127	3.54	1.18	127	100.0%	-0.25 [-0.50, -0.01]
Total (95% CI)			**127**			**127**	**100.0%**	**-0.25 [-0.50, -0.01]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.01 (P = 0.04)

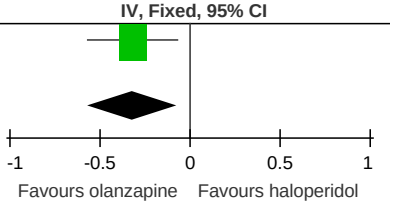


5.5 Mental state: mean endpoint depression (MADRS)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
LIEBERMAN2003	8.49	8.68	125	11.27	8.68	126	100.0%	-0.32 [-0.57, -0.07]
Total (95% CI)			**125**			**126**	**100.0%**	**-0.32 [-0.57, -0.07]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.51 (P = 0.01)



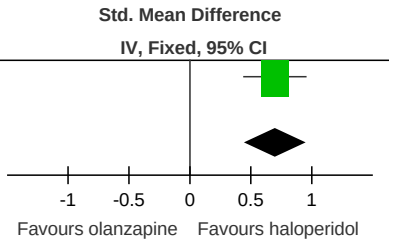
6. Children and young people 25 years and younger: olanzapine versus haloperidol: side effect outcomes during treatment (at 12 weeks)

6.1 Side effects: mean endpoint weight (kg) (104 weeks post-treatment)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
LIEBERMAN2003	10.2	10.1	131	4	7.3	123	100.0%	0.70 [0.44, 0.95]
Total (95% CI)			**131**			**123**	**100.0%**	**0.70 [0.44, 0.95]**

Heterogeneity: Not applicable

Test for overall effect: Z = 5.40 (P < 0.00001)

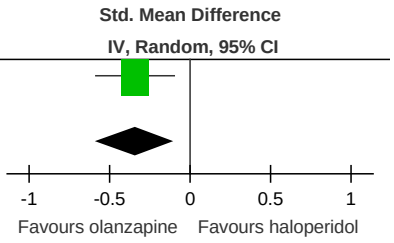


6.2 Side effects: mean endpoint prolactin level (mg/dl)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
LIEBERMAN2003	1.2	18.6	131	6.9	14.4	132	100.0%	-0.34 [-0.59, -0.10]
Total (95% CI)			**131**			**132**	**100.0%**	**-0.34 [-0.59, -0.10]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.75 (P = 0.006)

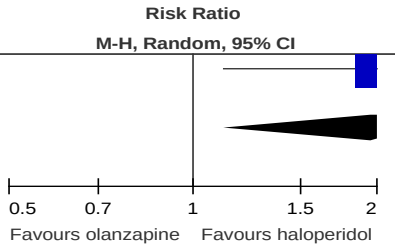


6.3 Leaving the study early for any reason (104 weeks post-treatment)

	Olanzapine		Haloperidol			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
LIEBERMAN2003	31	131	16	132	100.0%	1.95 [1.12, 3.39]
Total (95% CI)		**131**		**132**	**100.0%**	**1.95 [1.12, 3.39]**
Total events	31		16			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.37 (P = 0.02)



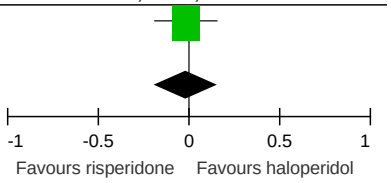
7. Children and young people 25 years and younger: haloperidol versus risperidone: efficacy outcomes post-treatment (time point unclear)

7.1 Mental state: mean change in total symptoms (PANSS)

	Risperidone			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
SCHOOLER2005	-21	23.72	264	-20.6	23.23	264	100.0%	-0.02 [-0.19, 0.15]
Total (95% CI)			**264**			**264**	**100.0%**	**-0.02 [-0.19, 0.15]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.20 (P = 0.85)

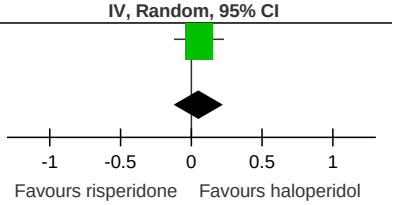


7.2 Mental state: mean change in positive symptoms (SAPS)

	Risperidone			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SCHOOLER2005	-6.6	6.99	264	-7	7.8	264	100.0%	0.05 [-0.12, 0.22]
Total (95% CI)			**264**			**264**	**100.0%**	**0.05 [-0.12, 0.22]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.62 (P = 0.54)

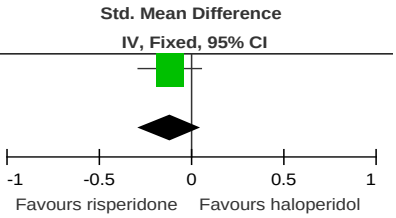


7.3 Mental state: mean change in negative symptoms (SANS)

	Risperidone			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
SCHOOLER2005	-4.8	7.15	264	-4.2	0.44	264	100.0%	-0.12 [-0.29, 0.05]
Total (95% CI)			**264**			**264**	**100.0%**	**-0.12 [-0.29, 0.05]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.36 (P = 0.17)

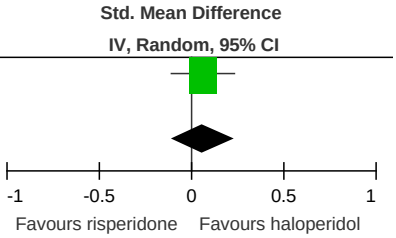


7.4 Mean change in global state: severity (CGI-S)

	Risperidone			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SCHOOLER2005	2.69	1.14	263	2.62	1.14	264	100.0%	0.06 [-0.11, 0.23]
Total (95% CI)			**263**			**264**	**100.0%**	**0.06 [-0.11, 0.23]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.70 (P = 0.48)



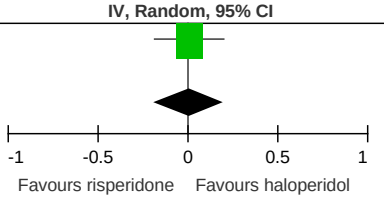
8. Children and young people 25 years and younger: haloperidol versus risperidone: side effect outcomes post-treatment (time point unclear)

8.1 Side effects: mean change in weight (lbs)

	Risperidone			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SCHOOLER2005	7.5	150.94	211	6.5	143.96	204	100.0%	0.01 [-0.19, 0.20]
Total (95% CI)			**211**			**204**	**100.0%**	**0.01 [-0.19, 0.20]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.07 (P = 0.95)

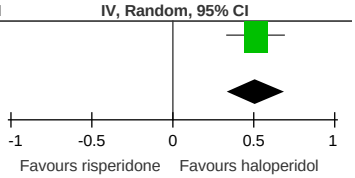


8.2 Side effects: mean change in prolactin level (mg/dl)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Weight	Std. Mean Difference IV, Random, 95% CI
SCHOOLER2005	45.287481	33.76576	258	29.3234538	28.27658	249	100.0%	0.51 [0.33, 0.69]
Total (95% CI)			**258**			**249**	**100.0%**	**0.51 [0.33, 0.69]**

Heterogeneity: Not applicable

Test for overall effect: Z = 5.66 (P < 0.00001)

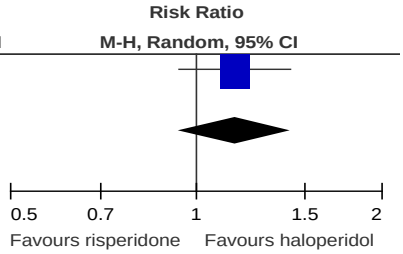


8.3 Leaving the study early for any reason

Study or Subgroup	Risperidone Events	Risperidone Total	Haloperidol Events	Haloperidol Total	Weight	Risk Ratio M-H, Random, 95% CI
SCHOOLER2005	117	278	101	277	100.0%	1.15 [0.94, 1.42]
Total (95% CI)		**278**		**277**	**100.0%**	**1.15 [0.94, 1.42]**
Total events	117		101			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.35 (P = 0.18)



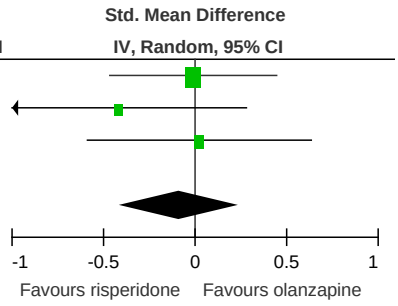
9. Children and young people 25 years and younger: risperidone versus olanzapine: post-treatment efficacy outcomes

9.1 Mental state: mean change in total symptoms (PANSS)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
MCEVOY2007	-18.5	9.91	37	-18.4	9.73	37	50.5%	-0.01 [-0.47, 0.45]
SIKICH2008	-35	22.4	21	-25.6	21	13	21.4%	-0.42 [-1.12, 0.28]
VANBRUGGEN2003	-15	2.6	24	-15.1	5.6	18	28.1%	0.02 [-0.59, 0.63]
Total (95% CI)			**82**			**68**	**100.0%**	**-0.09 [-0.41, 0.24]**

Heterogeneity: Tau² = 0.00; Chi² = 1.10, df = 2 (P = 0.58); I² = 0%

Test for overall effect: Z = 0.53 (P = 0.59)

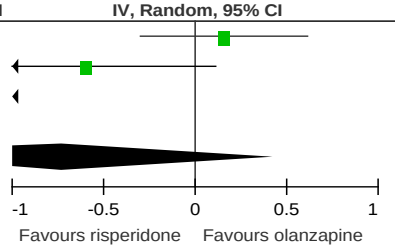


9.2 Mental state: mean change in positive symptoms (SAPS, CPRS-positive)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
MCEVOY2007	-6.6	3.16	37	-7.1	3.1	37	35.1%	0.16 [-0.30, 0.61]
SIKICH2008	-13.3	7.7	21	-9	5.8	13	32.6%	-0.60 [-1.30, 0.11]
VANBRUGGEN2003	-5.5	1.2	24	-3.2	1.3	18	32.3%	-1.81 [-2.55, -1.08]
Total (95% CI)			**82**			**68**	**100.0%**	**-0.72 [-1.87, 0.43]**

Heterogeneity: Tau² = 0.93; Chi² = 20.23, df = 2 (P < 0.0001); I² = 90%

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

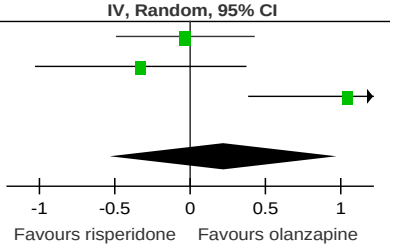


9.3 Mental state: mean change in negative symptoms (SANS)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
MCEVOY2007	-3.6	3.16	37	-3.5	3.1	37	36.7%	-0.03 [-0.49, 0.42]
SIKICH2008	-6.7	4.8	21	-4.7	7.5	13	31.1%	-0.33 [-1.02, 0.37]
VANBRUGGEN2003	-2.4	1.4	24	-4.3	2.2	18	32.1%	1.04 [0.39, 1.70]
Total (95% CI)			**82**			**68**	**100.0%**	**0.22 [-0.53, 0.98]**

Heterogeneity: Tau² = 0.35; Chi² = 9.57, df = 2 (P = 0.008); I² = 79%

Test for overall effect: Z = 0.58 (P = 0.56)

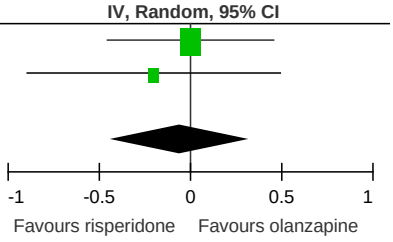


9.4 Mean change in global state: severity (CGI-S)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
MCEVOY2007	-1.3	0.67	37	-1.3	0.67	37	69.8%	0.00 [-0.46, 0.46]
SIKICH2008	-2.2	1.1	21	-1.9	1.9	13	30.2%	-0.20 [-0.90, 0.49]
Total (95% CI)			**58**			**50**	**100.0%**	**-0.06 [-0.44, 0.32]**

Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 1 (P = 0.63); I² = 0%

Test for overall effect: Z = 0.31 (P = 0.75)

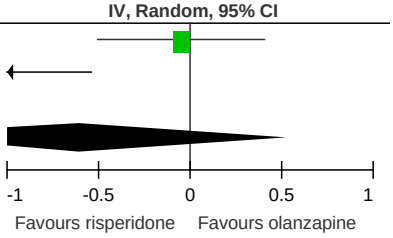


9.5 Mental state: mean change in depression (CDSS, PANSS-depression)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
MCEVOY2007	-1.3	2.01	37	-1.2	2.01	37	52.3%	-0.05 [-0.50, 0.41]
VANBRUGGEN2003	0.7	1	24	2.1	1.3	18	47.7%	-1.21 [-1.88, -0.54]
Total (95% CI)			**61**			**55**	**100.0%**	**-0.60 [-1.74, 0.53]**

Heterogeneity: Tau² = 0.59; Chi² = 7.88, df = 1 (P = 0.005); I² = 87%

Test for overall effect: Z = 1.04 (P = 0.30)

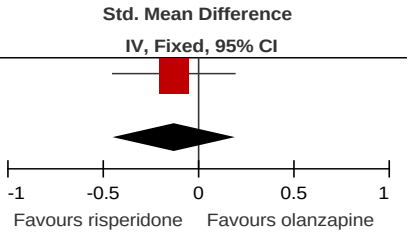


9.6 Mean change in quality of life (QLS)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
MCEVOY2007	-0.13	0.163265	100.0%	-0.13 [-0.45, 0.19]
Total (95% CI)			**100.0%**	**-0.13 [-0.45, 0.19]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.80 (P = 0.43)

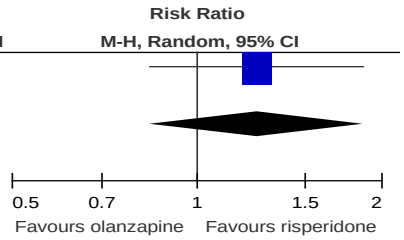


9.7 Response (number of participants achieving mild or better on the SADS-C+PD positive symptom items plus a CGI rating of much improved or very much improved)

Study or Subgroup	Risperidone Events	Risperidone Total	Olanzapine Events	Olanzapine Total	Weight	Risk Ratio M-H, Random, 95% CI
ROBINSON2006	30	60	24	60	100.0%	1.25 [0.84, 1.86]
Total (95% CI)		**60**		**60**	**100.0%**	**1.25 [0.84, 1.86]**
Total events	30		24			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.09 (P = 0.27)

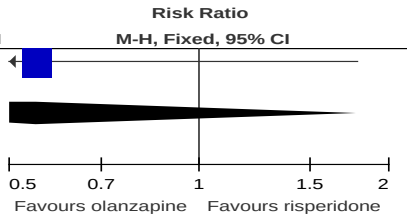


9.8 Remission (PANSS)

Study or Subgroup	Risperidone Events	Risperidone Total	Olanzapine Events	Olanzapine Total	Weight	Risk Ratio M-H, Fixed, 95% CI
VANBRUGGEN2003	4	26	5	18	100.0%	0.55 [0.17, 1.78]
Total (95% CI)		**26**		**18**	**100.0%**	**0.55 [0.17, 1.78]**
Total events	4		5			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.99 (P = 0.32)



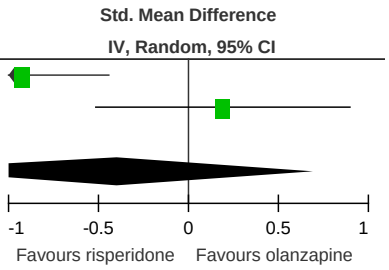
10. Children and young people 25 years and younger: risperidone versus olanzapine: post-treatment side effect outcomes

10.1 Side effects: mean change in weight (kg, lbs)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
MCEVOY2007	14.5	10.58	37	24.4	10.64	37	52.8%	-0.92 [-1.40, -0.44]
VANBRUGGEN2003	4.5	5.2	16	3.6	3.8	15	47.2%	0.19 [-0.51, 0.90]
Total (95% CI)			**53**			**52**	**100.0%**	**-0.40 [-1.49, 0.69]**

Heterogeneity: Tau² = 0.53; Chi² = 6.54, df = 1 (P = 0.01); I² = 85%

Test for overall effect: Z = 0.71 (P = 0.48)

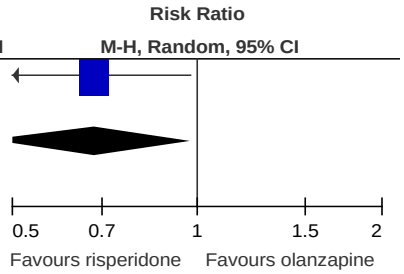


10.2 Side effects: weight gain (number of participants who gained ≥ 7%)

Study or Subgroup	Risperidone Events	Risperidone Total	Olanzapine Events	Olanzapine Total	Weight	Risk Ratio M-H, Random, 95% CI
MCEVOY2007	19	37	28	37	100.0%	0.68 [0.47, 0.98]
Total (95% CI)		**37**		**37**	**100.0%**	**0.68 [0.47, 0.98]**
Total events	19		28			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.09 (P = 0.04)

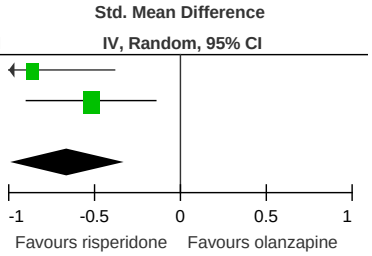


10.3 Side effects: BMI (kg/m2) (mean change: MCEVOY2007, mean endpoint: ROBINSON2006)

	Risperidone			Olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
MCEVOY2007	2.3	1.64	37	3.7	1.58	37	40.3%	-0.86 [-1.34, -0.38]
ROBINSON2006	26.7	2.863513	56	28.2	2.863513	56	59.7%	-0.52 [-0.90, -0.14]
Total (95% CI)			**93**			**93**	**100.0%**	**-0.66 [-0.98, -0.33]**

Heterogeneity: Tau² = 0.01; Chi² = 1.20, df = 1 (P = 0.27); I² = 17%

Test for overall effect: Z = 3.94 (P < 0.0001)

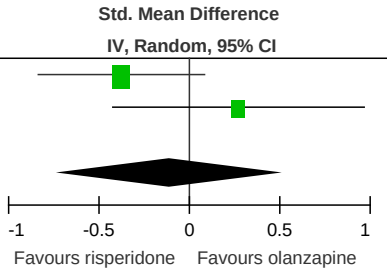


10.4 Side effects: mean change in fasting serum glucose level (mg/dl)

	Risperidone			Olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
MCEVOY2007	4.8	10.34	37	8.6	9.67	37	58.4%	-0.38 [-0.84, 0.08]
SIKICH2008	85.2	6.9	21	82.8	10.9	13	41.6%	0.27 [-0.42, 0.97]
Total (95% CI)			**58**			**50**	**100.0%**	**-0.11 [-0.73, 0.52]**

Heterogeneity: Tau² = 0.12; Chi² = 2.32, df = 1 (P = 0.13); I² = 57%

Test for overall effect: Z = 0.33 (P = 0.74)

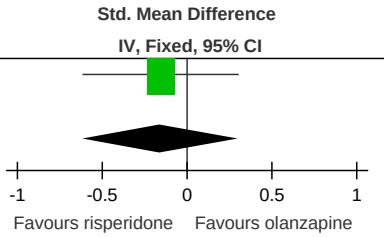


10.5 Side effects: mean change in fasting total cholesterol (mg/dl)

	Risperidone			Olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	11.4	28.28	37	15.7	26.16	37	100.0%	-0.16 [-0.61, 0.30]
Total (95% CI)			**37**			**37**	**100.0%**	**-0.16 [-0.61, 0.30]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.67 (P = 0.50)

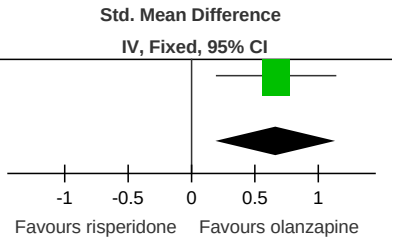


10.6 Side effects: mean change in fasting high-density lipoprotein cholesterol (mg/dl)

	Risperidone			Olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	-2.6	6.02	37	-6.5	5.54	37	100.0%	0.67 [0.20, 1.14]
Total (95% CI)			**37**			**37**	**100.0%**	**0.67 [0.20, 1.14]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.79 (P = 0.005)

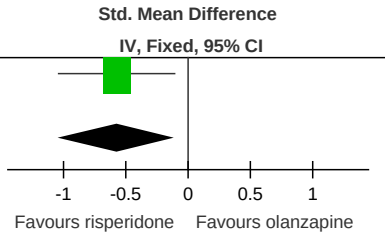


10.7 Side effects: mean change in fasting triglycerides (mg/dl)

	Risperidone			Olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
MCEVOY2007	19.1	84.67	37	66.4	78.47	37	100.0%	-0.57 [-1.04, -0.11]
Total (95% CI)			**37**			**37**	**100.0%**	**-0.57 [-1.04, -0.11]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.41 (P = 0.02)

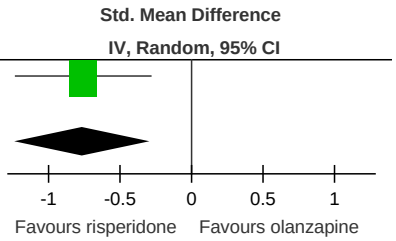


10.8 Side effects: mean change in systolic BP (mm Hg)

	Risperidone			Olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
MCEVOY2007	2.7	7.73	37	8.5	7.42	37	100.0%	-0.76 [-1.23, -0.28]
Total (95% CI)			**37**			**37**	**100.0%**	**-0.76 [-1.23, -0.28]**

Heterogeneity: Not applicable

Test for overall effect: Z = 3.14 (P = 0.002)

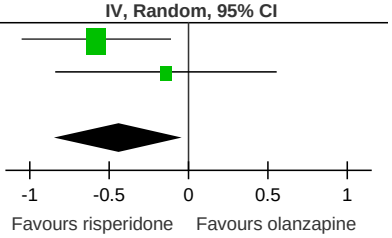


10.9 Side effects: mean change in diastolic BP (mm Hg)

	Risperidone			Olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
MCEVOY2007	1.8	5.23	37	4.8	4.99	37	67.8%	-0.58 [-1.05, -0.12]
SIKICH2008	67.6	7.9	21	68.8	8.8	13	32.2%	-0.14 [-0.83, 0.55]
Total (95% CI)			**58**			**50**	**100.0%**	**-0.44 [-0.84, -0.04]**

Heterogeneity: Tau² = 0.01; Chi² = 1.06, df = 1 (P = 0.30); I² = 6%

Test for overall effect: Z = 2.14 (P = 0.03)

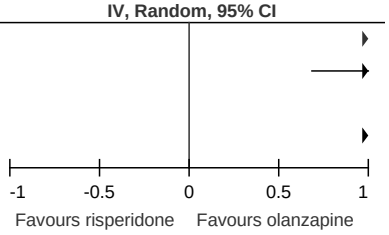


10.10 Side effects: mean change in prolactin level (mg/ml)

	Risperidone			Olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
MCEVOY2007	12.1	15.88	37	-15.9	15.57	37	67.8%	1.76 [1.22, 2.30]
SIKICH2008	48.9	26.5	21	16.5	7.9	13	32.2%	1.47 [0.69, 2.26]
Total (95% CI)			**58**			**50**	**100.0%**	**1.67 [1.22, 2.11]**

Heterogeneity: Tau² = 0.00; Chi² = 0.36, df = 1 (P = 0.55); I² = 0%

Test for overall effect: Z = 7.34 (P < 0.00001)

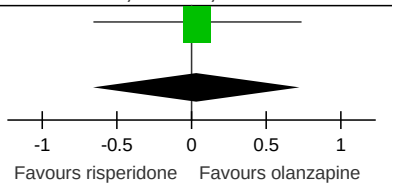


10.11 Side effects: extra pyramidal (mean change in AIMS scores)

	Risperidone			Olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SIKICH2008	1	18.7	21	0.4	1.1	13	100.0%	0.04 [-0.65, 0.73]
Total (95% CI)			**21**			**13**	**100.0%**	**0.04 [-0.65, 0.73]**

Heterogeneity: Not applicable

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

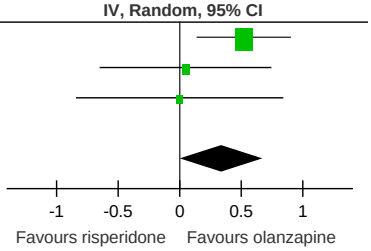


10.12 Side effects: extra pyramidal (SAS scores)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
ROBINSON2006	1.4	0.381802	56	1.2	0.381802	56	62.9%	0.52 [0.14, 0.90]
SIKICH2008	1.2	2.3	21	1.1	1.6	13	21.8%	0.05 [-0.64, 0.74]
VANBRUGGEN2003	2.9	4.1	11	2.9	3.6	11	15.3%	0.00 [-0.84, 0.84]
Total (95% CI)			**88**			**80**	**100.0%**	**0.34 [0.00, 0.67]**

Heterogeneity: Tau² = 0.01; Chi² = 2.19, df = 2 (P = 0.33); I² = 9%

Test for overall effect: Z = 1.97 (P = 0.05)

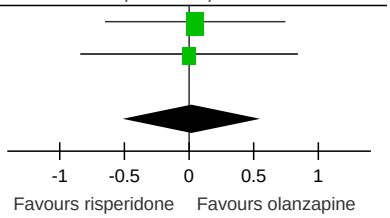


10.13 Side effects: extra pyramidal (SAS scores) sensitivity analysis (taking out ROBINSON2006)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
SIKICH2008	1.2	2.3	21	1.1	1.6	13	59.3%	0.05 [-0.64, 0.74]
VANBRUGGEN2003	2.9	4.1	11	2.9	3.6	11	40.7%	0.00 [-0.84, 0.84]
Total (95% CI)			**32**			**24**	**100.0%**	**0.03 [-0.50, 0.56]**

Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.93); I² = 0%

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

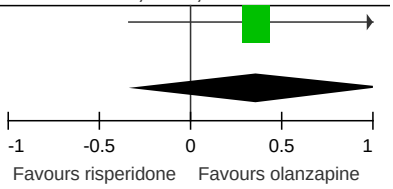


10.14 Side effects: extra pyramidal (mean change in BARS scores)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
SIKICH2008	1.1	1.8	21	0.5	1.3	13	100.0%	0.36 [-0.34, 1.06]
Total (95% CI)			**21**			**13**	**100.0%**	**0.36 [-0.34, 1.06]**

Heterogeneity: Not applicable

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

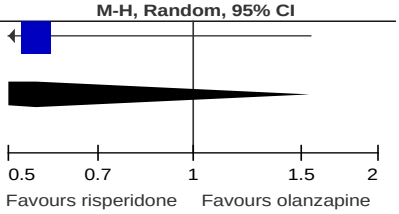


10.15 Side effects: parkinsonism

Study or Subgroup	Risperidone Events	Risperidone Total	Olanzapine Events	Olanzapine Total	Weight	Risk Ratio M-H, Random, 95% CI
ROBINSON2006	5	56	9	56	100.0%	0.56 [0.20, 1.55]
Total (95% CI)		**56**		**56**	**100.0%**	**0.56 [0.20, 1.55]**
Total events	5		9			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.12 (P = 0.26)

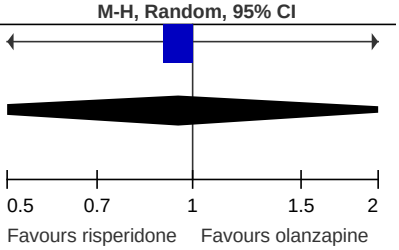


10.16 Side effects: akathesia

Study or Subgroup	Risperidone Events	Risperidone Total	Olanzapine Events	Olanzapine Total	Weight	Risk Ratio M-H, Random, 95% CI
VANBRUGGEN2003	6	19	4	12	100.0%	0.95 [0.34, 2.68]
Total (95% CI)		**19**		**12**	**100.0%**	**0.95 [0.34, 2.68]**
Total events	6		4			

Heterogeneity: Not applicable

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

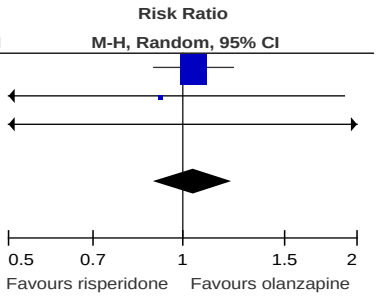


10.17 Leaving the study early for any reason

Study or Subgroup	Favours risperidone Events	Favours risperidone Total	Olanzapine Events	Olanzapine Total	Weight	Risk Ratio M-H, Random, 95% CI
MCEVOY2007	95	133	91	133	95.3%	1.04 [0.89, 1.22]
ROBINSON2006	11	56	12	56	4.5%	0.92 [0.44, 1.90]
VANBRUGGEN2003	2	26	0	18	0.3%	3.52 [0.18, 69.21]
Total (95% CI)		**215**		**207**	**100.0%**	**1.04 [0.89, 1.21]**
Total events	108		103			

Heterogeneity: Tau² = 0.00; Chi² = 0.76, df = 2 (P = 0.68); I² = 0%

Test for overall effect: Z = 0.52 (P = 0.61)



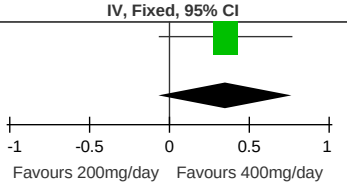
11. Children and young people 25 years and younger: quetiapine (200 mg/day) versus quetiapine (400 mg/day): post-treatment efficacy outcomes

11.1 Mental state: mean endpoint total symptoms (PANSS)

Study or Subgroup	Quetiapine 200mg/day Mean	SD	Total	Quetiapine 400mg/day Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
BERGER2008	51.2	11	46	47.1	12.1	45	100.0%	0.35 [-0.06, 0.77]
Total (95% CI)			**46**			**45**	**100.0%**	**0.35 [-0.06, 0.77]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.66 (P = 0.10)

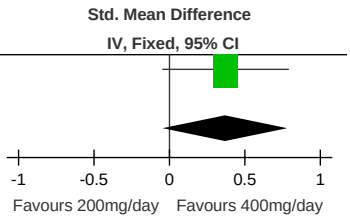


11.2 Mental state: mean endpoint positive symptoms (BPRS-psychotic)

Study or Subgroup	Quetiapine 200mg/day Mean	SD	Total	Quetiapine 400mg/day Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
BERGER2008	11.9	3.7	46	10.6	3.2	45	100.0%	0.37 [-0.04, 0.79]
Total (95% CI)			**46**			**45**	**100.0%**	**0.37 [-0.04, 0.79]**

Heterogeneity: Not applicable

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

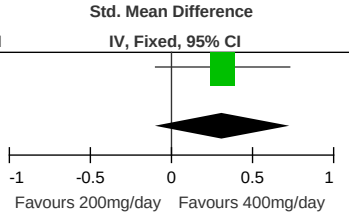


11.3 Mental state: mean endpoint negative symptoms (SANS)

	Quetiapine 200mg/day			Quetiapine 400mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
BERGER2008	31.1	17.2	46	26.1	14	45	100.0%	0.32 [-0.10, 0.73]
Total (95% CI)			**46**			**45**	**100.0%**	**0.32 [-0.10, 0.73]**

Heterogeneity: Not applicable

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

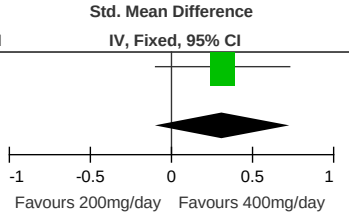


11.4 Mean endpoint global state: severity (CGI-S)

	Quetiapine 200mg/day			Quetiapine 400mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
BERGER2008	31.1	17.2	46	26.1	14	45	100.0%	0.32 [-0.10, 0.73]
Total (95% CI)			**46**			**45**	**100.0%**	**0.32 [-0.10, 0.73]**

Heterogeneity: Not applicable

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

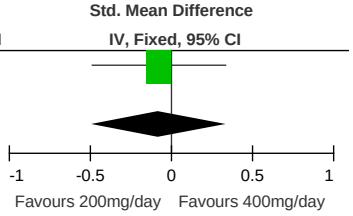


11.5 Mental state: mean endpoint depression (CDSS)

	Quetiapine 200mg/day			Quetiapine 400mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
BERGER2008	5.5	3.5	46	5.8	4.2	45	100.0%	-0.08 [-0.49, 0.33]
Total (95% CI)			**46**			**45**	**100.0%**	**-0.08 [-0.49, 0.33]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.37 (P = 0.71)

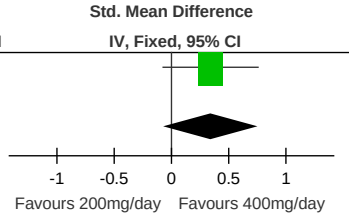


11.6 Mental state: mean endpoint mania (YMRS)

	Quetiapine 200mg/day			Quetiapine 400mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
BERGER2008	8.9	7.1	46	6.4	7.4	45	100.0%	0.34 [-0.07, 0.76]
Total (95% CI)			**46**			**45**	**100.0%**	**0.34 [-0.07, 0.76]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.62 (P = 0.11)

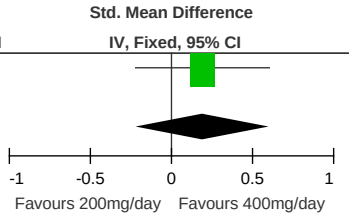


11.7 Mean endpoint psychosocial functioning (GAF)

	Quetiapine 200mg/day			Quetiapine 400mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
BERGER2008	-52.9	13.9	46	-55.3	10.7	45	100.0%	0.19 [-0.22, 0.60]
Total (95% CI)			**46**			**45**	**100.0%**	**0.19 [-0.22, 0.60]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.91 (P = 0.36)

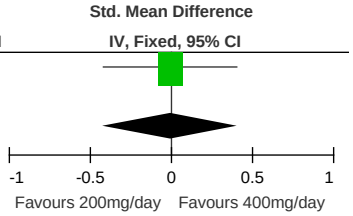


11.8 Mean endpoint social functioning (SOFAS)

	Quetiapine 200mg/day			Quetiapine 400mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
BERGER2008	-53.8	13.2	46	-53.7	10.3	45	100.0%	-0.01 [-0.42, 0.40]
Total (95% CI)			**46**			**45**	**100.0%**	**-0.01 [-0.42, 0.40]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.04 (P = 0.97)

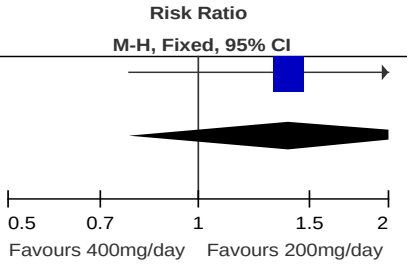


11.9 Response (BPRS)

	200mg/day		400mg/day			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
BERGER2008	20	69	15	72	100.0%	1.39 [0.78, 2.49]
Total (95% CI)		**69**		**72**	**100.0%**	**1.39 [0.78, 2.49]**
Total events	20		15			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.11 (P = 0.27)

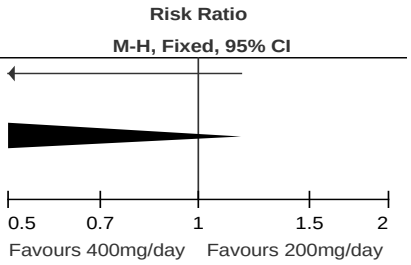


11.10 Remission (BPRS)

	200mg/day		400mg/day			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
BERGER2008	5	69	12	72	100.0%	0.43 [0.16, 1.17]
Total (95% CI)		**69**		**72**	**100.0%**	**0.43 [0.16, 1.17]**
Total events	5		12			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.65 (P = 0.10)



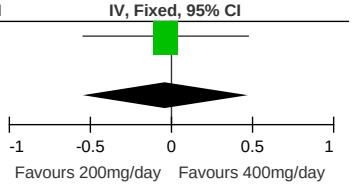
12. Children and young people 25 years and younger: quetiapine (200 mg/day) versus quetiapine (400 mg/day): post-treatment efficacy outcomes

12.1 Side effects: Mean endpoint weight (kg)

	Quetiapine 200mg/day			Quetiapine 400mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
BERGER2008	2.3	3.1	27	2.4	2.5	33	100.0%	-0.04 [-0.54, 0.47]
Total (95% CI)			**27**			**33**	**100.0%**	**-0.04 [-0.54, 0.47]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.14 (P = 0.89)

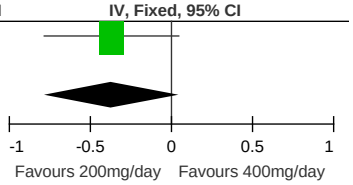


12.2 Side effects: extra pyramidal (mean endpoint UKU scores)

	Quetiapine 200mg/day			Quetiapine 400mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
BERGER2008	0.2	0.6	46	0.6	1.4	45	100.0%	-0.37 [-0.78, 0.04]
Total (95% CI)			**46**			**45**	**100.0%**	**-0.37 [-0.78, 0.04]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.75 (P = 0.08)

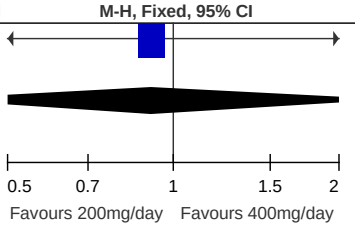


12.3 Leaving the study early for any reason

	Quetiapine 200mg/day		Quetiapine 400mg/day			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
BERGER2008	7	69	8	72	100.0%	0.91 [0.35, 2.38]
Total (95% CI)		**69**		**72**	**100.0%**	**0.91 [0.35, 2.38]**
Total events	7		8			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.19 (P = 0.85)



14cii: Treatment of the acute episode

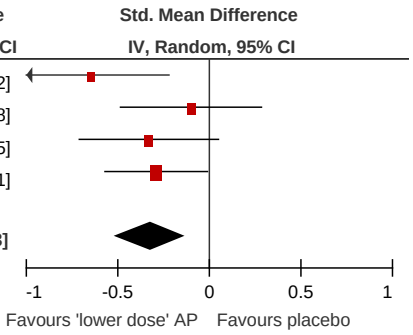
1. 'Lower dose' antipsychotic versus placebo: post-treatment efficacy outcomes

1.1 Mental state: total symptoms (PANSS, BPRS)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
KRYZHANOVSKAYA2009B	-0.64602096	0.21713	18.5%	-0.65 [-1.07, -0.22]
SINGH2011	-0.1	0.196429	22.0%	-0.10 [-0.48, 0.28]
AstraZenecaD1441C00112	-0.33	0.193878	22.5%	-0.33 [-0.71, 0.05]
FINDLING2008	-0.29	0.142857	37.0%	-0.29 [-0.57, -0.01]
Total (95% CI)			**100.0%**	**-0.32 [-0.52, -0.13]**

Heterogeneity: Tau² = 0.01; Chi² = 3.56, df = 3 (P = 0.31); I² = 16%

Test for overall effect: Z = 3.25 (P = 0.001)

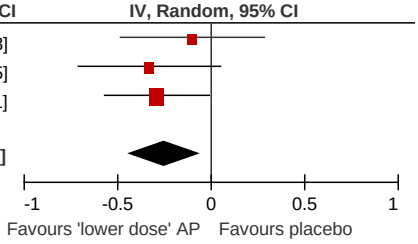


1.2 Mental state: mean change in total symptoms (PANSS) sensitivity analysis (taking KRYZHANOVSKAYA2009B out of the analysis)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
SINGH2011	-0.1	0.196429	25.5%	-0.10 [-0.48, 0.28]
AstraZenecaD1441C00112	-0.33	0.193878	26.2%	-0.33 [-0.71, 0.05]
FINDLING2008	-0.29	0.142857	48.3%	-0.29 [-0.57, -0.01]
Total (95% CI)			**100.0%**	**-0.25 [-0.45, -0.06]**

Heterogeneity: Tau² = 0.00; Chi² = 0.83, df = 2 (P = 0.66); I² = 0%

Test for overall effect: Z = 2.54 (P = 0.01)

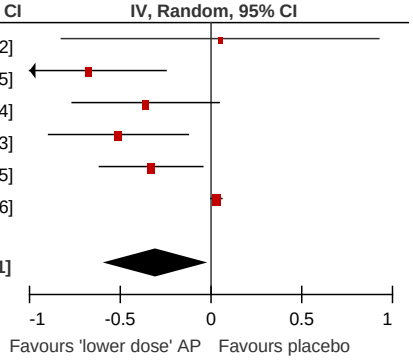


1.3 Mental state: positive symptoms (PANSS Positive)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
PAILLERE-MARTINOT1995	0.05	0.446429	7.5%	0.05 [-0.82, 0.92]
KRYZHANOVSKAYA2009B	-0.67393376	0.2175373	15.8%	-0.67 [-1.10, -0.25]
AstraZenecaD1441C00112	-0.36	0.206633	16.4%	-0.36 [-0.76, 0.04]
HASS2009B	-0.51	0.196429	16.9%	-0.51 [-0.89, -0.13]
FINDLING2008	-0.33	0.145408	19.5%	-0.33 [-0.61, -0.05]
SINGH2011	0.03	0.01531	23.9%	0.03 [-0.00, 0.06]
Total (95% CI)			**100.0%**	**-0.30 [-0.59, -0.01]**

Heterogeneity: Tau² = 0.09; Chi² = 27.04, df = 5 (P < 0.0001); I² = 82%

Test for overall effect: Z = 2.06 (P = 0.04)

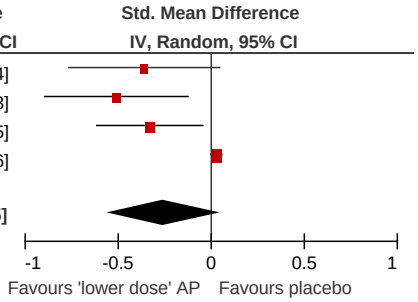


1.4 Mental State: mean change in positive symptoms (PANSS positive) sensitivity analysis (taking out KRYZHANOVSKAYA2009B and PALLIERE-MARTINOT1995)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
AstraZenecaD1441C00112	-0.36	0.206633	20.6%	-0.36 [-0.76, 0.04]
HASS2009B	-0.51	0.196429	21.4%	-0.51 [-0.89, -0.13]
FINDLING2008	-0.33	0.145408	25.4%	-0.33 [-0.61, -0.05]
SINGH2011	0.03	0.01531	32.6%	0.03 [-0.00, 0.06]
Total (95% CI)			**100.0%**	**-0.26 [-0.56, 0.05]**

Heterogeneity: Tau² = 0.07; Chi² = 16.88, df = 3 (P = 0.0007); I² = 82%

Test for overall effect: Z = 1.67 (P = 0.10)

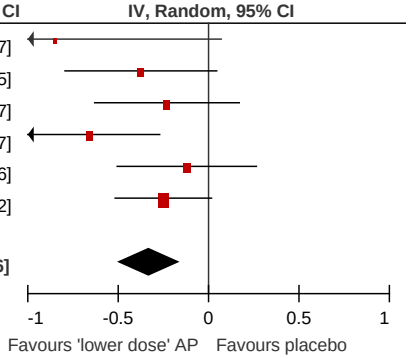


1.5 Mental state: negative symptoms (PANSS negative)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
PAILLERE-MARTINOT1995	-0.85	0.469388	3.4%	-0.85 [-1.77, 0.07]
KRYZHANOVSKAYA2009B	-0.37443458	0.21403956	14.9%	-0.37 [-0.79, 0.05]
AstraZenecaD1441C00112	-0.23	0.204082	16.2%	-0.23 [-0.63, 0.17]
HASS2009B	-0.66	0.19898	16.9%	-0.66 [-1.05, -0.27]
SINGH2011	-0.12	0.196429	17.3%	-0.12 [-0.50, 0.26]
FINDLING2008	-0.25	0.135969	31.4%	-0.25 [-0.52, 0.02]
Total (95% CI)			**100.0%**	**-0.33 [-0.50, -0.16]**

Heterogeneity: Tau² = 0.01; Chi² = 5.75, df = 5 (P = 0.33); I² = 13%

Test for overall effect: Z = 3.78 (P = 0.0002)

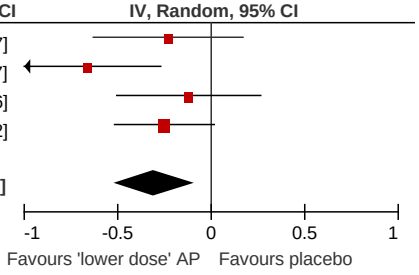


1.6 Mental state: mean change in negative symptoms (PANSS negative) sensitivity analysis (taking out KRYZHANOVSKAYA2009B and PALLIERE-MARTINOT1995)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
AstraZenecaD1441C00112	-0.23	0.204082	20.9%	-0.23 [-0.63, 0.17]
HASS2009B	-0.66	0.19898	21.7%	-0.66 [-1.05, -0.27]
SINGH2011	-0.12	0.196429	22.1%	-0.12 [-0.50, 0.26]
FINDLING2008	-0.25	0.135969	35.4%	-0.25 [-0.52, 0.02]
Total (95% CI)			**100.0%**	**-0.31 [-0.52, -0.09]**

Heterogeneity: Tau² = 0.01; Chi² = 4.37, df = 3 (P = 0.22); I² = 31%

Test for overall effect: Z = 2.82 (P = 0.005)

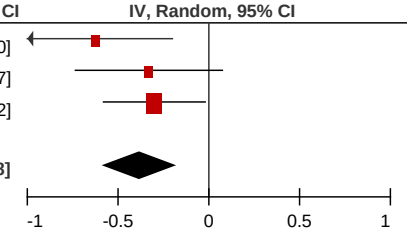


1.7 Global state: severity (CGI-S)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
KRYZHANOVSKAYA2009B	-0.62570375	0.21684355	22.7%	-0.63 [-1.05, -0.20]
AstraZenecaD1441C00112	-0.33	0.206633	25.0%	-0.33 [-0.73, 0.07]
FINDLING2008	-0.3	0.142857	52.3%	-0.30 [-0.58, -0.02]
Total (95% CI)			**100.0%**	**-0.38 [-0.58, -0.18]**

Heterogeneity: Tau² = 0.00; Chi² = 1.66, df = 2 (P = 0.44); I² = 0%

Test for overall effect: Z = 3.69 (P = 0.0002)

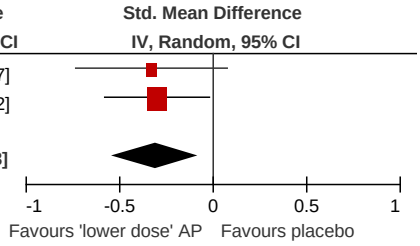


1.8 Mean change in global state: severity (CGI-S) sensitivity analysis (taking out KRYZHANOVSKAYA2009B)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
AstraZenecaD1441C00112	-0.33	0.206633	32.3%	-0.33 [-0.73, 0.07]
FINDLING2008	-0.3	0.142857	67.7%	-0.30 [-0.58, -0.02]
Total (95% CI)			**100.0%**	**-0.31 [-0.54, -0.08]**

Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.90); I² = 0%

Test for overall effect: Z = 2.64 (P = 0.008)

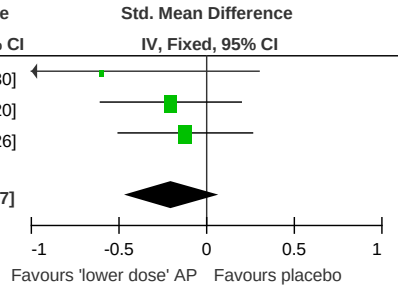


1.9 Mental state: depression (positive and negative syndrome scale; MADRS)

Study or Subgroup	Low dose AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
PAILLERE-MARTINOT1995	7.6	4.1	10	10.9	6.2	10	8.7%	-0.60 [-1.50, 0.30]
AstraZenecaD1441C00112	-2.96	2.31	54	-2.47	2.47	43	43.5%	-0.20 [-0.61, 0.20]
SINGH2011	-1.4	2.22	54	-1.1	2.69	51	47.8%	-0.12 [-0.50, 0.26]
Total (95% CI)			**118**			**104**	**100.0%**	**-0.20 [-0.46, 0.07]**

Heterogeneity: Chi² = 0.93, df = 2 (P = 0.63); I² = 0%

Test for overall effect: Z = 1.47 (P = 0.14)

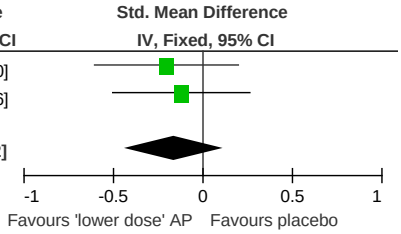


1.10 Mean change in depression (Positive and Negative Syndrome Scale; PANSS anxiety and depression; MADRS) sensitivity analysis (taking out PALLIERE-MARTINOT1995)

Study or Subgroup	Low dose AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
AstraZenecaD1441C00112	-2.96	2.31	54	-2.47	2.47	43	47.6%	-0.20 [-0.61, 0.20]
SINGH2011	-1.4	2.22	54	-1.1	2.69	51	52.4%	-0.12 [-0.50, 0.26]
Total (95% CI)			**108**			**94**	**100.0%**	**-0.16 [-0.44, 0.12]**

Heterogeneity: Chi² = 0.09, df = 1 (P = 0.77); I² = 0%

Test for overall effect: Z = 1.14 (P = 0.26)

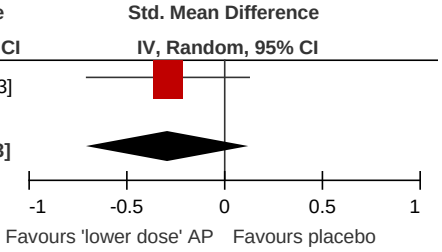


1.11 Mean change in quality of life (QLS)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
FINDLING2008	-0.29	0.2121	100.0%	-0.29 [-0.71, 0.13]
Total (95% CI)			**100.0%**	**-0.29 [-0.71, 0.13]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.37 (P = 0.17)

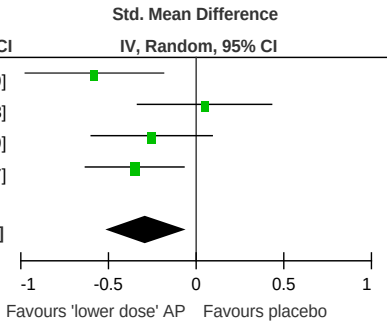


1.12 Mean change in psychosocial functioning (CGAS)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
HASS2009B	-16.9	16	51	-7.9	14.8	52	21.5%	-0.58 [-0.97, -0.19]
SINGH2011	-4.4	10.72	54	-5	13.82	51	22.3%	0.05 [-0.33, 0.43]
AstraZenecaD1441C00112	-13.04	12.34	65	-9.89	12.41	65	25.2%	-0.25 [-0.60, 0.09]
FINDLING2008	-14.7	14.92	99	-9.8	12.87	98	31.1%	-0.35 [-0.63, -0.07]
Total (95% CI)			**269**			**266**	**100.0%**	**-0.29 [-0.52, -0.06]**

Heterogeneity: Tau² = 0.02; Chi² = 5.29, df = 3 (P = 0.15); I² = 43%

Test for overall effect: Z = 2.43 (P = 0.01)

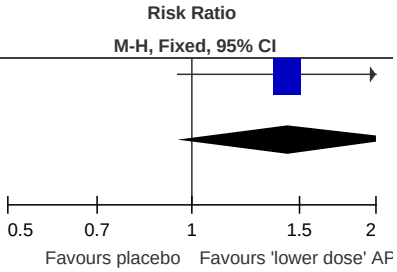


1.13 Response (CGI-I)

Study or Subgroup	Placebo Events	Total	'Lower dose' AP Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
AstraZenecaD1441C00112	33	55	18	43	100.0%	1.43 [0.95, 2.17]
Total (95% CI)		**55**		**43**	**100.0%**	**1.43 [0.95, 2.17]**
Total events	33		18			

Heterogeneity: Not applicable

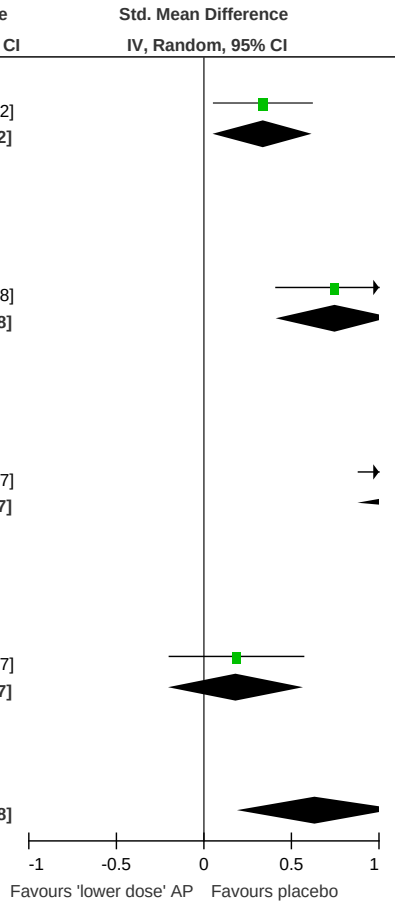
Test for overall effect: Z = 1.71 (P = 0.09)



2. 'Lower dose' antipsychotic versus placebo: post-treatment side effect outcomes

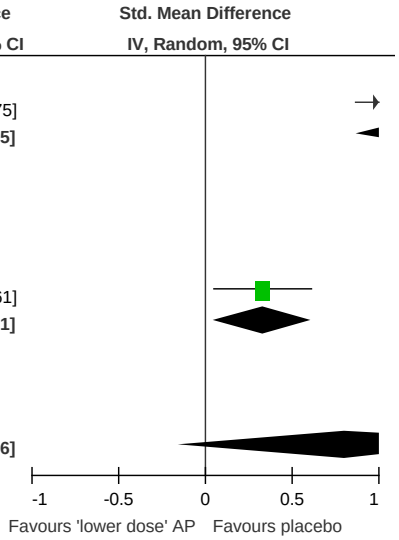
2.1 Side effects: weight (kg) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A; AZD1441C00112; SINGH2011)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.1.1 Aripriprazole 10mg/day								
FINDLING2008A	0	2.1	99	-0.8	2.6	98	26.8%	0.34 [0.06, 0.62]
Subtotal (95% CI)			**99**			**98**	**26.8%**	**0.34 [0.06, 0.62]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.35 (P = 0.02)								
2.1.2 Quetiapine 400mg/day								
AstraZenecaD1441C00112	1.9	2.47	73	-0.1	2.84	73	25.6%	0.75 [0.41, 1.08]
Subtotal (95% CI)			**73**			**73**	**25.6%**	**0.75 [0.41, 1.08]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.36 (P < 0.0001)								
2.1.3 Olanzapine 11mg/day								
KRYZHANOVSKAYA2009B	4.3	3.3	72	0.1	2.8	35	23.1%	1.33 [0.88, 1.77]
Subtotal (95% CI)			**72**			**35**	**23.1%**	**1.33 [0.88, 1.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.87 (P < 0.00001)								
2.1.4 Paliperidone 1.5mg/day								
SINGH2011	0.3	1.52	54	0	1.68	51	24.5%	0.19 [-0.20, 0.57]
Subtotal (95% CI)			**54**			**51**	**24.5%**	**0.19 [-0.20, 0.57]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.95 (P = 0.34)								
Total (95% CI)			**298**			**257**	**100.0%**	**0.63 [0.19, 1.08]**
Heterogeneity: Tau² = 0.17; Chi² = 18.73, df = 3 (P = 0.0003); I² = 84%								
Test for overall effect: Z = 2.80 (P = 0.005)								
Test for subgroup differences: Chi² = 18.73, df = 3 (P = 0.0003), I² = 84.0%								



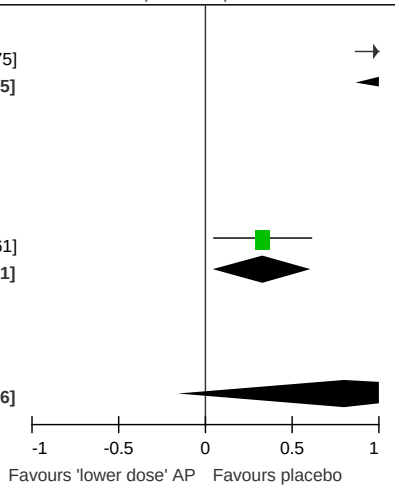
2.2 Side effects: BMI(kg/m2) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.2.1 Olanzapine 11mg/day								
KRYZHANOVSKAYA2009B	1.4	1.2	72	-0.1	1	35	48.4%	1.31 [0.87, 1.75]
Subtotal (95% CI)			**72**			**35**	**48.4%**	**1.31 [0.87, 1.75]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.80 (P < 0.00001)								
2.2.2 Aripriprazole 10mg/day								
FINDLING2008A	0	0.8	99	-0.3	1	98	51.6%	0.33 [0.05, 0.61]
Subtotal (95% CI)			**99**			**98**	**51.6%**	**0.33 [0.05, 0.61]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.30 (P = 0.02)								
Total (95% CI)			**171**			**133**	**100.0%**	**0.80 [-0.15, 1.76]**
Heterogeneity: Tau² = 0.44; Chi² = 13.39, df = 1 (P = 0.0003); I² = 93%								
Test for overall effect: Z = 1.65 (P = 0.10)								
Test for subgroup differences: Chi² = 13.39, df = 1 (P = 0.0003), I² = 92.5%								



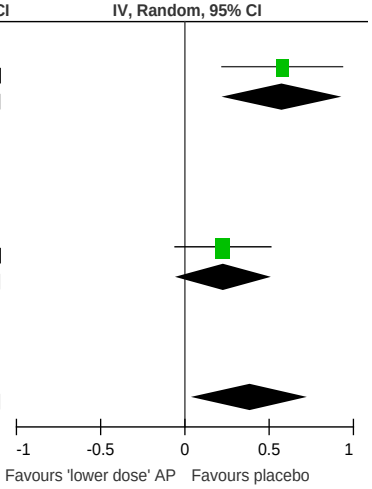
2.3 Side effects: fasting serum glucose level (mg/dl) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A; AZD1441C00112; SINGH2011)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.2.1 Olanzapine 11mg/day								
KRYZHANOVSKAYA2009B	1.4	1.2	72	-0.1	1	35	48.4%	1.31 [0.87, 1.75]
Subtotal (95% CI)			**72**			**35**	**48.4%**	**1.31 [0.87, 1.75]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.80 (P < 0.00001)								
2.2.2 Aripriprazole 10mg/day								
FINDLING2008A	0	0.8	99	-0.3	1	98	51.6%	0.33 [0.05, 0.61]
Subtotal (95% CI)			**99**			**98**	**51.6%**	**0.33 [0.05, 0.61]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.30 (P = 0.02)								
Total (95% CI)			**171**			**133**	**100.0%**	**0.80 [-0.15, 1.76]**
Heterogeneity: Tau² = 0.44; Chi² = 13.39, df = 1 (P = 0.0003); I² = 93%								
Test for overall effect: Z = 1.65 (P = 0.10)								
Test for subgroup differences: Chi² = 13.39, df = 1 (P = 0.0003), I² = 92.5%								



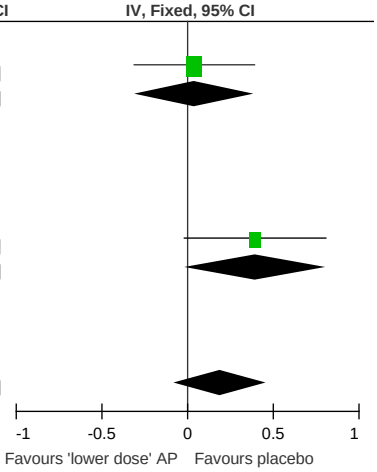
2.4 Side effects: mean change in fasting total cholesterol (mg/dl)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.5.1 Quetiapine 400mg/day								
AstraZenecaD1441C00112	7.8226	28.8231	62	-8.0635	25.74745	63	45.0%	0.58 [0.22, 0.94]
Subtotal (95% CI)			**62**			**63**	**45.0%**	**0.58 [0.22, 0.94]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.16 (P = 0.002)								
2.5.2 Aripriprazole 10mg/day								
FINDLING2008A	-5.01	23.28	95	-10.38	24.08	96	55.0%	0.23 [-0.06, 0.51]
Subtotal (95% CI)			**95**			**96**	**55.0%**	**0.23 [-0.06, 0.51]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.56 (P = 0.12)								
Total (95% CI)			**157**			**159**	**100.0%**	**0.38 [0.04, 0.73]**
Heterogeneity: Tau² = 0.03; Chi² = 2.28, df = 1 (P = 0.13); I² = 56%								
Test for overall effect: Z = 2.19 (P = 0.03)								
Test for subgroup differences: Chi² = 2.28, df = 1 (P = 0.13), I² = 56.1%								



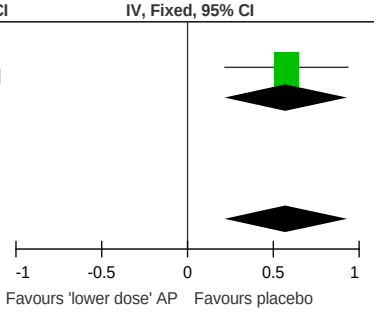
2.5 Side effects: mean change in fasting high-density lipoprotein cholesterol (mg/dl)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.7.1 Quetiapine 400mg/day								
AstraZenecaD1441C00112	2.8226	9.24267	62	2.4603	8.95297	63	58.1%	0.04 [-0.31, 0.39]
Subtotal (95% CI)			**62**			**63**	**58.1%**	**0.04 [-0.31, 0.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.22 (P = 0.82)								
2.7.2 Aripriprazole 10mg/day								
FINDLING2008A	-0.13	6.99	47	-6.09	20.23	45	41.9%	0.39 [-0.02, 0.81]
Subtotal (95% CI)			**47**			**45**	**41.9%**	**0.39 [-0.02, 0.81]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.87 (P = 0.06)								
Total (95% CI)			**109**			**108**	**100.0%**	**0.19 [-0.08, 0.46]**
Heterogeneity: Chi² = 1.64, df = 1 (P = 0.20); I² = 39%								
Test for overall effect: Z = 1.38 (P = 0.17)								
Test for subgroup differences: Chi² = 1.64, df = 1 (P = 0.20), I² = 39.2%								



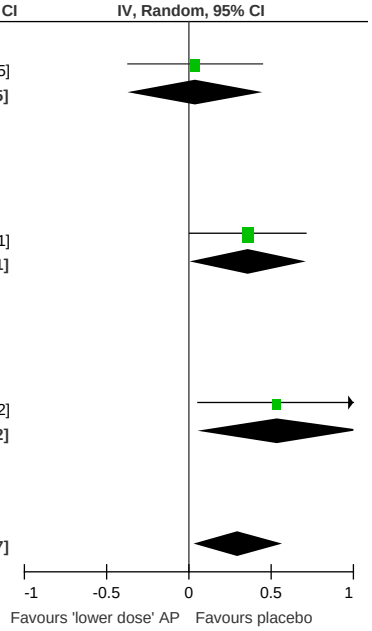
2.6 Side effects: mean change in fasting low-density lipoprotein cholesterol (mg/dl)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.10.1 Quetiapine 400mg/day								
AstraZenecaD1441C00112	8.6613	22.73579	62	-3.8889	20.505	63	100.0%	0.58 [0.22, 0.93]
Subtotal (95% CI)			**62**			**63**	**100.0%**	**0.58 [0.22, 0.93]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.16 (P = 0.002)								
Total (95% CI)			**62**			**63**	**100.0%**	**0.58 [0.22, 0.93]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.16 (P = 0.002)								
Test for subgroup differences: Not applicable								



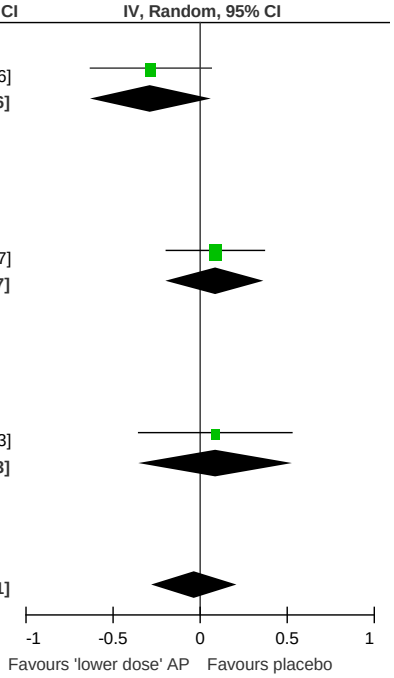
2.7 Side effects: fasting triglycerides (mg/dl) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A; AZD1441C00112)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.11.1 Aripriprazole 10mg/day								
FINDLING2008A	-4.53	48.72	47	-6.51	53.82	45	33.2%	0.04 [-0.37, 0.45]
Subtotal (95% CI)			**47**			**45**	**33.2%**	**0.04 [-0.37, 0.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.18 (P = 0.85)								
2.11.2 Quetiapine 400mg/day								
AstraZenecaD1441C00112	9.6613	64.77172	62	-8.0635	25.74745	63	41.1%	0.36 [0.00, 0.71]
Subtotal (95% CI)			**62**			**63**	**41.1%**	**0.36 [0.00, 0.71]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.99 (P = 0.05)								
2.11.3 Olanzpaine 11mg/day								
KRYZHANOVSKAYA2009B	41.6	75.3	55	4.4	51.4	25	25.7%	0.54 [0.05, 1.02]
Subtotal (95% CI)			**55**			**25**	**25.7%**	**0.54 [0.05, 1.02]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.18 (P = 0.03)								
Total (95% CI)			**164**			**133**	**100.0%**	**0.30 [0.03, 0.57]**
Heterogeneity: Tau² = 0.01; Chi² = 2.60, df = 2 (P = 0.27); I² = 23%								
Test for overall effect: Z = 2.17 (P = 0.03)								
Test for subgroup differences: Chi² = 2.60, df = 2 (P = 0.27), I² = 23.1%								



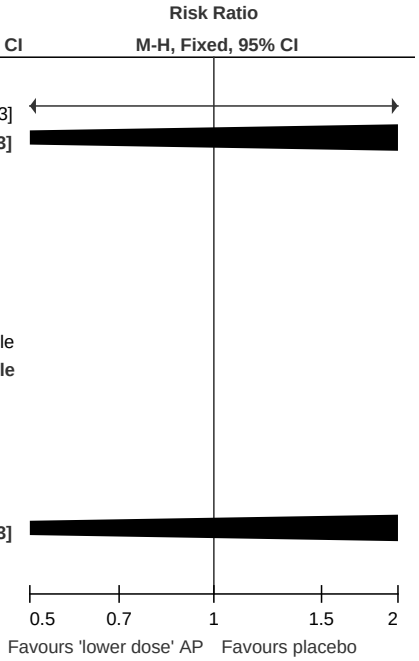
2.8 Side effects: QTcB interval (msec) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A; AZD1441C00112)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.13.1 Quetiapine 400mg/day								
AstraZenecaD1441C00112	-4.88	26.39	64	2.63	26.46	65	33.3%	-0.28 [-0.63, 0.06]
Subtotal (95% CI)			**64**			**65**	**33.3%**	**-0.28 [-0.63, 0.06]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.60 (P = 0.11)								
2.13.2 Aripriprazole 10mg/day								
FINDLING2008A	0	14	98	-1.3	15.6	96	43.1%	0.09 [-0.19, 0.37]
Subtotal (95% CI)			**98**			**96**	**43.1%**	**0.09 [-0.19, 0.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.61 (P = 0.54)								
2.13.3 Olanzapine 11mg/day								
KRYZHANOVSKAYA2009B	-0.5	19	63	-2.1	16.3	29	23.6%	0.09 [-0.35, 0.53]
Subtotal (95% CI)			**63**			**29**	**23.6%**	**0.09 [-0.35, 0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.39 (P = 0.70)								
Total (95% CI)			**225**			**190**	**100.0%**	**-0.04 [-0.28, 0.21]**
Heterogeneity: Tau² = 0.02; Chi² = 2.98, df = 2 (P = 0.23); I² = 33%								
Test for overall effect: Z = 0.29 (P = 0.77)								
Test for subgroup differences: Chi² = 2.98, df = 2 (P = 0.23), I² = 32.8%								



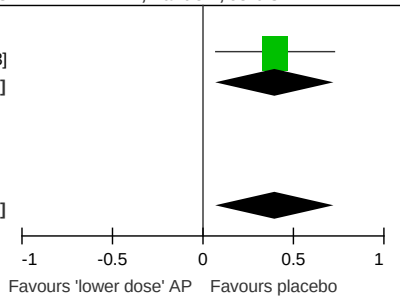
2.9 Side effects: QTcB interval (msec) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A; AZD1441C00112)

Study or Subgroup	'Lower dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.15.1 Quetiapine 400mg/day						
AstraZenecaD1441C00112	1	73	0	75	100.0%	3.08 [0.13, 74.43]
Subtotal (95% CI)		**73**		**75**	**100.0%**	**3.08 [0.13, 74.43]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
2.15.2 Paliperidone 1.5mg/day						
SINGH2011	0	54	0	51		Not estimable
Subtotal (95% CI)		**54**		**51**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**127**		**126**	**100.0%**	**3.08 [0.13, 74.43]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
Test for subgroup differences: Not applicable						



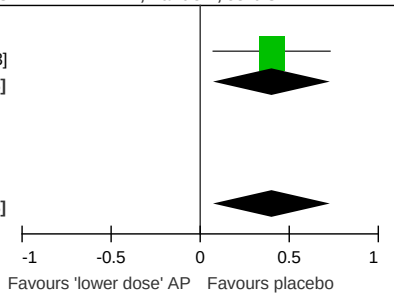
2.10 Side effects: mean change in systolic BP (mm Hg)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.17.1 Quetiapine 400mg/day								
AstraZenecaD1441C00112	2.3	10.78	73	-1.7	9.1	73	100.0%	0.40 [0.07, 0.73]
Subtotal (95% CI)			**73**			**73**	**100.0%**	**0.40 [0.07, 0.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.39 (P = 0.02)								
Total (95% CI)			**73**			**73**	**100.0%**	**0.40 [0.07, 0.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.39 (P = 0.02)								
Test for subgroup differences: Not applicable								



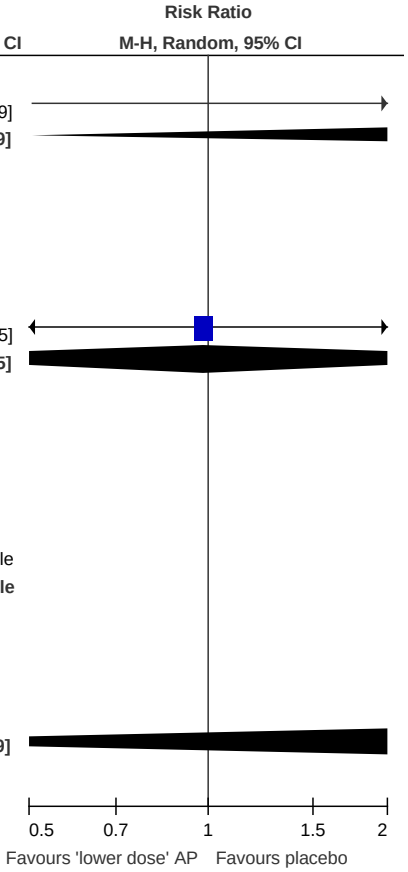
2.11 Side effects: mean change in diastolic BP (mm Hg)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.19.1 Quetiapine 400mg/day								
AstraZenecaD1441C00112	2.1	8.65	73	-1.2	7.68	73	100.0%	0.40 [0.07, 0.73]
Subtotal (95% CI)			**73**			**73**	**100.0%**	**0.40 [0.07, 0.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.40 (P = 0.02)								
Total (95% CI)			**73**			**73**	**100.0%**	**0.40 [0.07, 0.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.40 (P = 0.02)								
Test for subgroup differences: Not applicable								



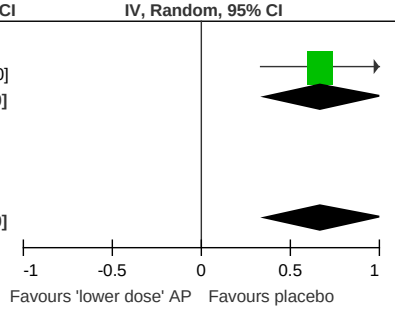
2.12 Side effects: tachycardia

Study or Subgroup	'Lower dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.21.1 Quetiapine 400mg/day						
AstraZenecaD1441C00112	4	73	0	75	35.7%	9.24 [0.51, 168.69]
Subtotal (95% CI)		**73**		**75**	**35.7%**	**9.24 [0.51, 168.69]**
Total events	4		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.50 (P = 0.13)						
2.21.2 Risperidone 1-3mg/day						
HAAS2009B	3	55	3	54	64.3%	0.98 [0.21, 4.65]
Subtotal (95% CI)		**55**		**54**	**64.3%**	**0.98 [0.21, 4.65]**
Total events	3		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.98)						
2.21.3 Paliperidone 1.5mg/day						
SINGH2011	0	54	0	51		Not estimable
Subtotal (95% CI)		**54**		**51**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**182**		**180**	**100.0%**	**2.19 [0.24, 19.69]**
Total events	7		3			
Heterogeneity: Tau² = 1.33; Chi² = 1.94, df = 1 (P = 0.16); I² = 48%						
Test for overall effect: Z = 0.70 (P = 0.49)						
Test for subgroup differences: Chi² = 1.78, df = 1 (P = 0.18), I² = 43.8%						



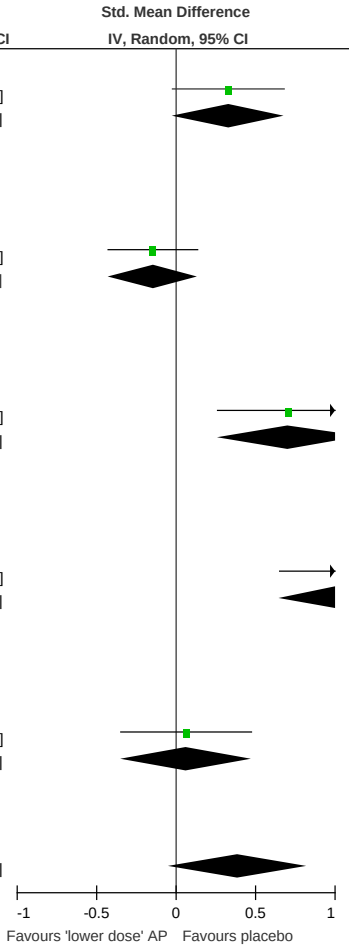
2.13 Side effects: mean change in standing pulse (beats/min)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.23.1 Quetiapine 400mg/day								
AstraZenecaD1441C00112	6.3	13.12	73	-2.5	13.14	73	100.0%	0.67 [0.33, 1.00]
Subtotal (95% CI)			**73**			**73**	**100.0%**	**0.67 [0.33, 1.00]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.92 (P < 0.0001)								
Total (95% CI)			**73**			**73**	**100.0%**	**0.67 [0.33, 1.00]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.92 (P < 0.0001)								
Test for subgroup differences: Not applicable								



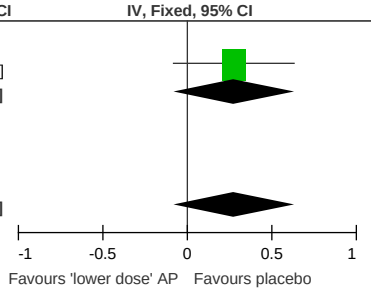
2.14 Side effects: prolactin level (mg/dl) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A; AZD1441C00112; HAAS2009B; SINGH2011)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.25.1 Quetiapine 400mg/day								
AstraZenecaD1441C00112	-10.5476	16.12225	63	-18.2467	28.7495	63	20.5%	0.33 [-0.02, 0.68]
Subtotal (95% CI)			**63**			**63**	**20.5%**	**0.33 [-0.02, 0.68]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.83 (P = 0.07)								
2.25.2 Aripriprazole 10mg/day								
FINDLING2008A	-11.93	23.29	98	-8.45	24.23	96	21.5%	-0.15 [-0.43, 0.14]
Subtotal (95% CI)			**98**			**96**	**21.5%**	**-0.15 [-0.43, 0.14]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.01 (P = 0.31)								
2.25.3 Olanzapine 11mg/day								
KRYZHANOVSKAYA2009B	8.8	17.9	64	-3.3	14.8	30	18.9%	0.71 [0.26, 1.15]
Subtotal (95% CI)			**64**			**30**	**18.9%**	**0.71 [0.26, 1.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.11 (P = 0.002)								
2.25.4 Risperidone 1-3mg/day								
HAAS2009B	25.5	32.859	55	-5.31111	24.55995	54	19.7%	1.05 [0.65, 1.45]
Subtotal (95% CI)			**55**			**54**	**19.7%**	**1.05 [0.65, 1.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.14 (P < 0.00001)								
2.25.5 Paliperidone 1.5mg/day								
SINGH2011	25.211373	32.335753	51	23.252683	28.565498	41	19.5%	0.06 [-0.35, 0.47]
Subtotal (95% CI)			**51**			**41**	**19.5%**	**0.06 [-0.35, 0.47]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.30 (P = 0.76)								
Total (95% CI)			**331**			**284**	**100.0%**	**0.39 [-0.05, 0.83]**
Heterogeneity: Tau² = 0.21; Chi² = 27.63, df = 4 (P < 0.0001); I² = 86%								
Test for overall effect: Z = 1.75 (P = 0.08)								
Test for subgroup differences: Chi² = 27.63, df = 4 (P < 0.0001), I² = 85.5%								



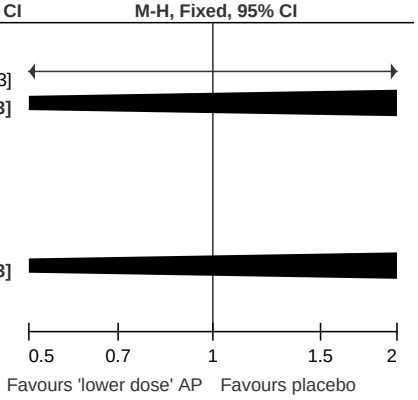
2.15 Side effects: mean change in insulin level (mg/dl)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.27.1 Quetiapine 400mg/day								
AstraZenecaD1441C00112	4.2742	19.25938	62	-1.0333	19.05742	60	100.0%	0.28 [-0.08, 0.63]
Subtotal (95% CI)			**62**			**60**	**100.0%**	**0.28 [-0.08, 0.63]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.51 (P = 0.13)								
Total (95% CI)			**62**			**60**	**100.0%**	**0.28 [-0.08, 0.63]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.51 (P = 0.13)								
Test for subgroup differences: Not applicable								



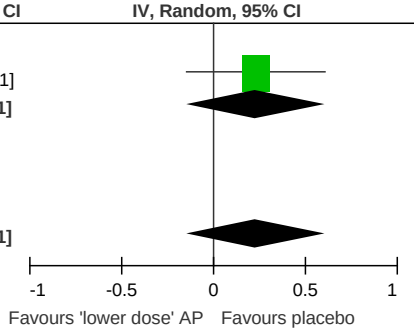
2.16 Side effects: extra pyramidal disorder

Study or Subgroup	'Lower dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.29.1 Quetiapine 400mg/day						
AstraZenecaD1441C00112	1	73	0	75	100.0%	3.08 [0.13, 74.43]
Subtotal (95% CI)		**73**		**75**	**100.0%**	**3.08 [0.13, 74.43]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
Total (95% CI)		**73**		**75**	**100.0%**	**3.08 [0.13, 74.43]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
Test for subgroup differences: Not applicable						



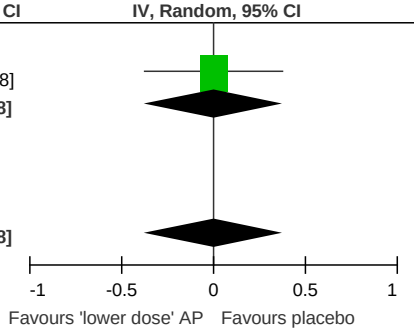
2.17 Side effects: extra pyramidal (mean difference in AIMS scores)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.31.1 Risperidone 1-3mg/day								
HAAS2009B	0.1	2	55	-0.3	1.4	54	100.0%	0.23 [-0.15, 0.61]
Subtotal (95% CI)			**55**			**54**	**100.0%**	**0.23 [-0.15, 0.61]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.20 (P = 0.23)								
Total (95% CI)			**55**			**54**	**100.0%**	**0.23 [-0.15, 0.61]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.20 (P = 0.23)								
Test for subgroup differences: Not applicable								



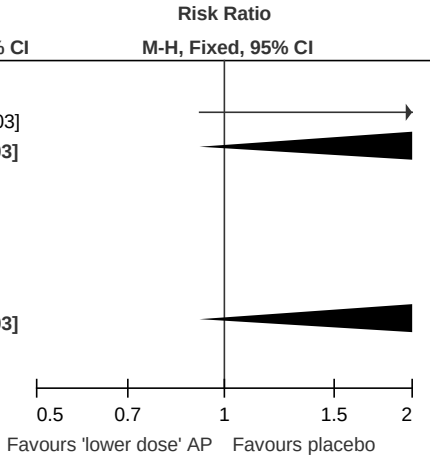
2.18 Side effects: extra pyramidal (mean difference in SAS scores)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.33.1 Risperidone 1-3mg/day								
HAAS2009B	0	0.2	55	0	0.1	54	100.0%	0.00 [-0.38, 0.38]
Subtotal (95% CI)			**55**			**54**	**100.0%**	**0.00 [-0.38, 0.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Total (95% CI)			**55**			**54**	**100.0%**	**0.00 [-0.38, 0.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Test for subgroup differences: Not applicable								



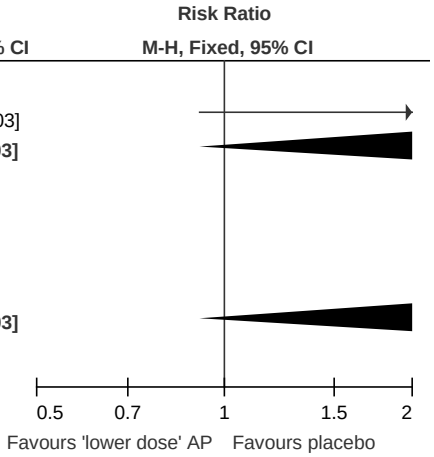
2.19 Side effects: parkinsonism

	'Lower dose' AP		Placebo			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**
2.35.1 Aripriprazole 10mg/day						
FINDLING2008A	15	100	7	100	100.0%	2.14 [0.91, 5.03]
Subtotal (95% CI)		**100**		**100**	**100.0%**	**2.14 [0.91, 5.03]**
Total events	15		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.75 (P = 0.08)						
Total (95% CI)		**100**		**100**	**100.0%**	**2.14 [0.91, 5.03]**
Total events	15		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.75 (P = 0.08)						
Test for subgroup differences: Not applicable						



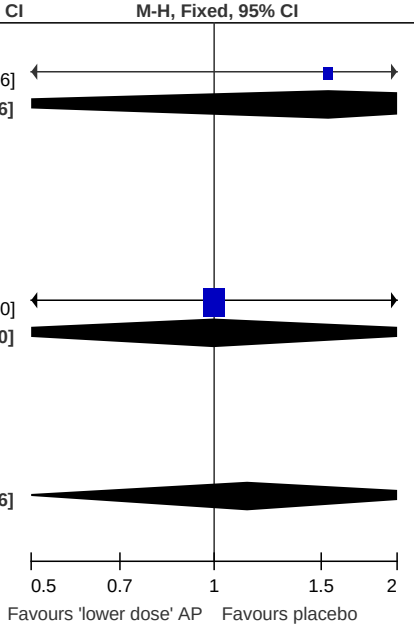
2.20 Side effects: tremor

	'Lower dose' AP		Placebo			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**
2.35.1 Aripriprazole 10mg/day						
FINDLING2008A	15	100	7	100	100.0%	2.14 [0.91, 5.03]
Subtotal (95% CI)		**100**		**100**	**100.0%**	**2.14 [0.91, 5.03]**
Total events	15		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.75 (P = 0.08)						
Total (95% CI)		**100**		**100**	**100.0%**	**2.14 [0.91, 5.03]**
Total events	15		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.75 (P = 0.08)						
Test for subgroup differences: Not applicable						



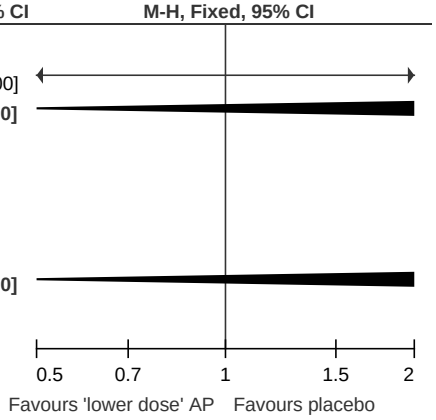
2.21 Side effects: akathesia

Study or Subgroup	'Lower dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.39.1 Quetiapine 400mg/day						
AstraZenecaD1441C00112	3	73	2	75	24.7%	1.54 [0.27, 8.96]
Subtotal (95% CI)		**73**		**75**	**24.7%**	**1.54 [0.27, 8.96]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.48 (P = 0.63)						
2.39.2 Aripriprazole 10mg/day						
FINDLING2008A	6	100	6	100	75.3%	1.00 [0.33, 3.00]
Subtotal (95% CI)		**100**		**100**	**75.3%**	**1.00 [0.33, 3.00]**
Total events	6		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**173**		**175**	**100.0%**	**1.13 [0.45, 2.86]**
Total events	9		8			
Heterogeneity: Chi² = 0.17, df = 1 (P = 0.68); I² = 0%						
Test for overall effect: Z = 0.27 (P = 0.79)						
Test for subgroup differences: Chi² = 0.17, df = 1 (P = 0.68), I² = 0%						



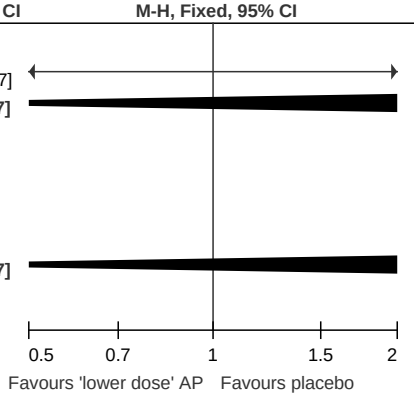
2.22 Side effects: dystonia

Study or Subgroup	'Lower dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.41.1 Aripriprazole 10mg/day						
FINDLING2008A	4	100	0	100	100.0%	9.00 [0.49, 165.00]
Subtotal (95% CI)		**100**		**100**	**100.0%**	**9.00 [0.49, 165.00]**
Total events	4		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.48 (P = 0.14)						
Total (95% CI)		**100**		**100**	**100.0%**	**9.00 [0.49, 165.00]**
Total events	4		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.48 (P = 0.14)						
Test for subgroup differences: Not applicable						



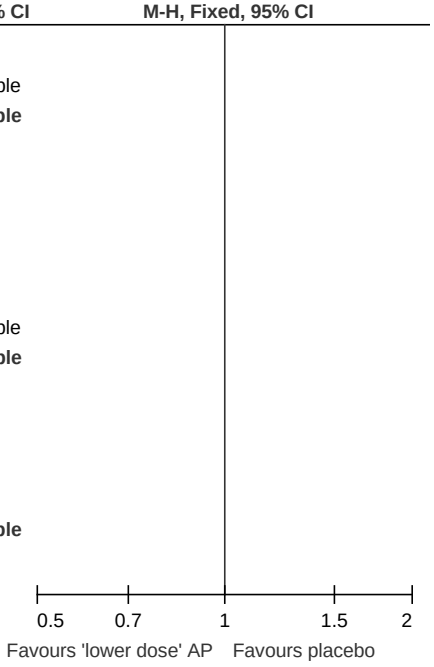
2.23 Side effects: dyskenesia

Study or Subgroup	'Lower dose' AP Events	'Lower dose' AP Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.45.1 Quetiapine 400mg/day						
AstraZenecaD1441C00112	2	73	0	75	100.0%	5.14 [0.25, 105.17]
Subtotal (95% CI)		**73**		**75**	**100.0%**	**5.14 [0.25, 105.17]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.06 (P = 0.29)						
Total (95% CI)		**73**		**75**	**100.0%**	**5.14 [0.25, 105.17]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.06 (P = 0.29)						
Test for subgroup differences: Not applicable						



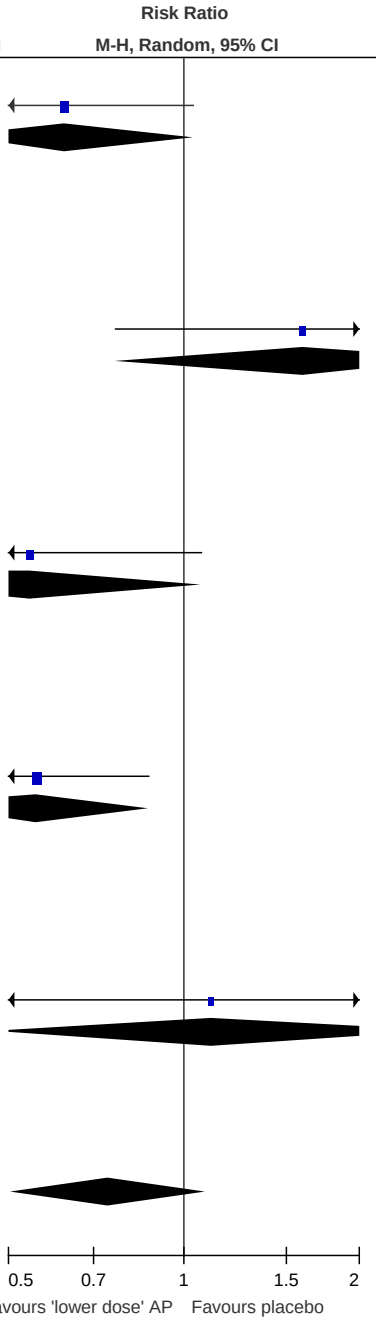
2.24 Side effects: mortality (including suicide)

Study or Subgroup	'Lower dose' AP Events	'Lower dose' AP Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.47.1 Aripriprazole 10mg/day						
FINDLING2008A	0	100	0	100		Not estimable
Subtotal (95% CI)		**100**		**100**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
2.47.2 Risperidone 1-3mg/day						
HAAS2009B	0	55	0	54		Not estimable
Subtotal (95% CI)		**55**		**54**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**155**		**154**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



2.25 Leaving the study early for any reason

Study or Subgroup	'Lower dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.49.1 Quetiapine 400mg/day						
AstraZenecaD1441C00112	17	73	28	75	24.7%	0.62 [0.37, 1.04]
Subtotal (95% CI)		**73**		**75**	**24.7%**	**0.62 [0.37, 1.04]**
Total events	17		28			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.82 (P = 0.07)						
2.49.2 Aripriprazole 10mg/day						
FINDLING2008A	16	100	10	100	16.7%	1.60 [0.76, 3.35]
Subtotal (95% CI)		**100**		**100**	**16.7%**	**1.60 [0.76, 3.35]**
Total events	16		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.25 (P = 0.21)						
2.49.3 Risperidone 1-3mg/day						
HAAS2009B	10	55	18	54	18.6%	0.55 [0.28, 1.07]
Subtotal (95% CI)		**55**		**54**	**18.6%**	**0.55 [0.28, 1.07]**
Total events	10		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.76 (P = 0.08)						
2.49.4 Olanzapine 11mg/day						
KRYZHANOVSKAYA2009B	23	72	20	35	27.6%	0.56 [0.36, 0.87]
Subtotal (95% CI)		**72**		**35**	**27.6%**	**0.56 [0.36, 0.87]**
Total events	23		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.57 (P = 0.01)						
2.49.5 Amisulpride 50-100mg/day						
PALLIERE-MARTINOT1995	6	14	5	13	12.5%	1.11 [0.45, 2.78]
Subtotal (95% CI)		**14**		**13**	**12.5%**	**1.11 [0.45, 2.78]**
Total events	6		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.23 (P = 0.82)						
Total (95% CI)		**314**		**277**	**100.0%**	**0.74 [0.51, 1.09]**
Total events	72		81			
Heterogeneity: Tau² = 0.09; Chi² = 7.60, df = 4 (P = 0.11); I² = 47%						
Test for overall effect: Z = 1.52 (P = 0.13)						
Test for subgroup differences: Chi² = 7.50, df = 4 (P = 0.11), I² = 46.6%						



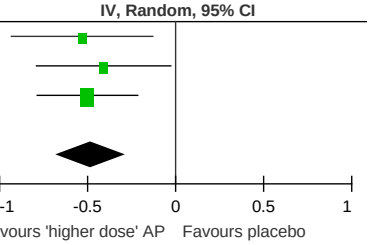
3. 'Higher dose' antipsychotic versus placebo: post-treatment efficacy outcomes

3.1 Mental state: mean change in total symptoms (PANSS)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
SINGH2011	-17.3	14.33	48	-7.9	20.15	51	24.5%	-0.53 [-0.93, -0.13]
AstraZenecaD1441C00112	-28.44	13.52	55	-19.15	29.12	53	27.1%	-0.41 [-0.79, -0.03]
FINDLING2008	-28.6	8.86	97	-21.2	18.81	98	48.4%	-0.50 [-0.79, -0.22]
Total (95% CI)			**200**			**202**	**100.0%**	**-0.48 [-0.68, -0.28]**

Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 2 (P = 0.90); I² = 0%

Test for overall effect: Z = 4.77 (P < 0.00001)

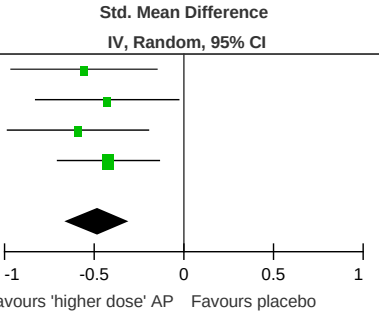


3.2 Mental state: mean change in positive symptoms (SAPS)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
AstraZenecaD1441C00112	-9.34	4.35	55	-6.51	5.82	43	19.4%	-0.56 [-0.96, -0.15]
SINGH2011	-6	5.39	48	-3.3	7	51	20.1%	-0.43 [-0.83, -0.03]
HASS2009B	-6.5	5.4	50	-3	6.3	54	20.7%	-0.59 [-0.98, -0.20]
FINDLING2008	-8.1	5.91	97	-5.6	5.94	98	39.8%	-0.42 [-0.70, -0.14]
Total (95% CI)			**250**			**246**	**100.0%**	**-0.48 [-0.66, -0.30]**

Heterogeneity: Tau² = 0.00; Chi² = 0.67, df = 3 (P = 0.88); I² = 0%

Test for overall effect: Z = 5.29 (P < 0.00001)

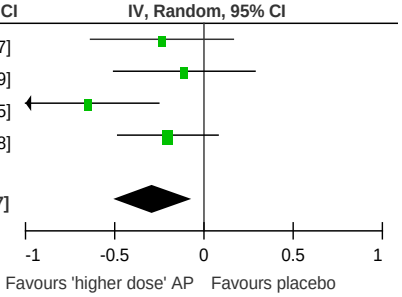


3.3 Mental state: mean change in negative symptoms (SANS)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
AstraZenecaD1441C00112	-6.21	4.58	55	-5.09	4.9	43	21.7%	-0.24 [-0.64, 0.17]
SINGH2011	-2.4	5.56	47	-1.8	5.3	51	22.0%	-0.11 [-0.51, 0.29]
HASS2009B	-4.9	4.9	50	-1.9	4.3	54	22.1%	-0.65 [-1.04, -0.25]
FINDLING2008	-6.6	5.91	97	-5.4	5.94	98	34.2%	-0.20 [-0.48, 0.08]
Total (95% CI)			**249**			**246**	**100.0%**	**-0.29 [-0.51, -0.07]**

Heterogeneity: Tau² = 0.02; Chi² = 4.38, df = 3 (P = 0.22); I² = 32%

Test for overall effect: Z = 2.57 (P = 0.01)

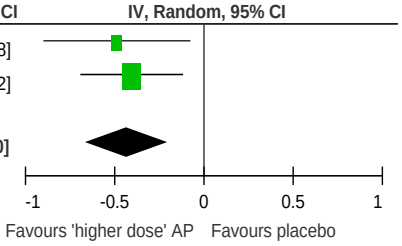


3.4 Mean change in global state: severity (CGI-S)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
AstraZenecaD1441C00112	-1.28	0.87	55	-0.81	1.06	42	32.6%	-0.49 [-0.90, -0.08]
FINDLING2008	-1.3	0.98	97	-0.9	0.99	98	67.4%	-0.40 [-0.69, -0.12]
Total (95% CI)			**152**			**140**	**100.0%**	**-0.43 [-0.66, -0.20]**

Heterogeneity: Tau² = 0.00; Chi² = 0.11, df = 1 (P = 0.74); I² = 0%

Test for overall effect: Z = 3.63 (P = 0.0003)

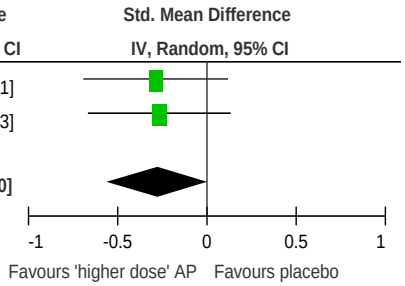


3.5 Mean change in depression (PANSS depression, PANSS anxiety and depression)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
AstraZenecaD1441C00112	-3.16	2.31	55	-2.47	2.47	43	49.4%	-0.29 [-0.69, 0.11]
SINGH2011	-1.9	3.25	48	-1.1	2.69	51	50.6%	-0.27 [-0.66, 0.13]
Total (95% CI)			**103**			**94**	**100.0%**	**-0.28 [-0.56, 0.00]**

Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.94); I² = 0%

Test for overall effect: Z = 1.93 (P = 0.05)

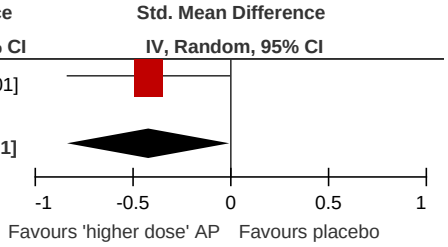


3.6 Mean change in quality of life (QLS)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
FINDLING2008	-0.42	0.211735	100.0%	-0.42 [-0.83, -0.01]
Total (95% CI)			**100.0%**	**-0.42 [-0.83, -0.01]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.98 (P = 0.05)

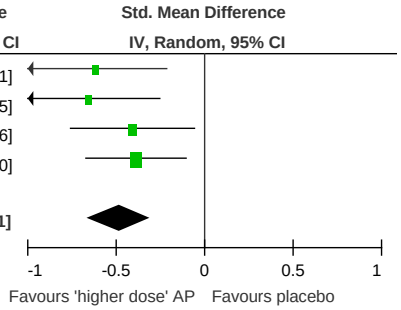


3.7 Mean change in psychosocial functioning (CGAS)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
SINGH2011	-13.1	12.07	48	-5	13.82	51	18.6%	-0.62 [-1.02, -0.21]
HASS2009B	-18.9	18.4	48	-7.9	14.8	52	18.7%	-0.66 [-1.06, -0.25]
AstraZenecaD1441C00112	-14.94	12.22	63	-9.89	12.41	65	24.8%	-0.41 [-0.76, -0.06]
FINDLING2008	-14.8	12.8	97	-9.8	12.87	98	37.9%	-0.39 [-0.67, -0.10]
Total (95% CI)			**256**			**266**	**100.0%**	**-0.49 [-0.66, -0.31]**

Heterogeneity: Tau² = 0.00; Chi² = 1.75, df = 3 (P = 0.63); I² = 0%

Test for overall effect: Z = 5.46 (P < 0.00001)

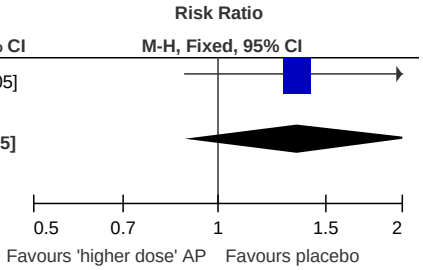


3.8 Response (CGI-I)

Study or Subgroup	'Higher dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
AstraZenecaD1441C00112	31	55	18	43	100.0%	1.35 [0.88, 2.05]
Total (95% CI)		**55**		**43**	**100.0%**	**1.35 [0.88, 2.05]**
Total events	31		18			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.38 (P = 0.17)



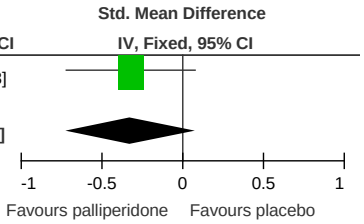
4. Additional (high) dose paliperidone versus placebo: post-treatment efficacy outcomes

4.1 Mental state: mean change in total symptoms (PANSS)

	Palliperidone 6-12mg/day			Placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
SINGH2011	-13.8	15.74	47	-7.9	20.15	51	100.0%	-0.32 [-0.72, 0.08]
Total (95% CI)			**47**			**51**	**100.0%**	**-0.32 [-0.72, 0.08]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.58 (P = 0.11)

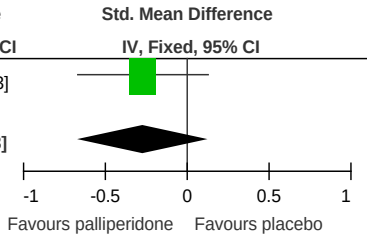


4.2 Mental state: mean change in positive symptoms (SAPS)

	Palliperidone 6-12mg/day			Placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
SINGH2011	-5	5.3	47	-3.3	7	51	100.0%	-0.27 [-0.67, 0.13]
Total (95% CI)			**47**			**51**	**100.0%**	**-0.27 [-0.67, 0.13]**

Heterogeneity: Not applicable

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

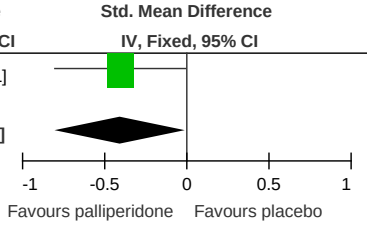


4.3 Mental state: mean change in negative symptoms (SANS)

	Palliperidone 6-12mg/day			Placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
SINGH2011	-3.7	3.85	48	-1.8	5.3	51	100.0%	-0.41 [-0.80, -0.01]
Total (95% CI)			**48**			**51**	**100.0%**	**-0.41 [-0.80, -0.01]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.99 (P = 0.05)

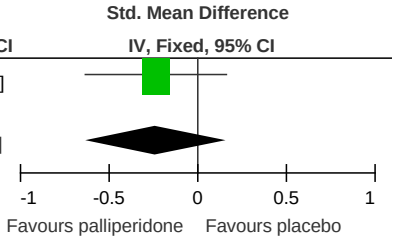


4.4 Mental state: mean change in anxiety and depression (PANSS Anxiety and Depression)

	Palliperidone			Placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
SINGH2011	-1.8	3.19	47	-1.1	2.69	51	100.0%	-0.24 [-0.63, 0.16]
Total (95% CI)			**47**			**51**	**100.0%**	**-0.24 [-0.63, 0.16]**

Heterogeneity: Not applicable

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

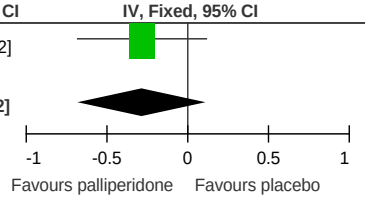


4.5 Mean change in psychosocial functioning (CGAS)

Study or Subgroup	Palliperidone 6-12mg/day Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
SINGH2011	-8.6	11.18	47	-5	13.82	51	100.0%	-0.28 [-0.68, 0.12]
Total (95% CI)			**47**			**51**	**100.0%**	**-0.28 [-0.68, 0.12]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.39 (P = 0.16)



5. 'Higher dose' antipsychotic versus placebo: post-treatment side effect outcomes

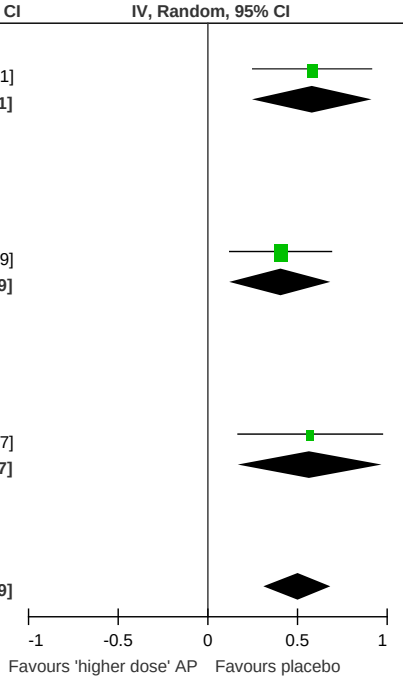
5.1 Side effects: mean change in weight (kg)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.1.1 Quetiapine 800mg/day								
AstraZenecaD1441C00112	1.5	2.63	73	-0.1	2.84	73	32.9%	0.58 [0.25, 0.91]
Subtotal (95% CI)			**73**			**73**	**32.9%**	**0.58 [0.25, 0.91]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.44 (P = 0.0006)								
5.1.2 Aripriprazole 30mg/day								
FINDLING2008A	0.2	2.3	97	-0.8	2.6	98	44.9%	0.41 [0.12, 0.69]
Subtotal (95% CI)			**97**			**98**	**44.9%**	**0.41 [0.12, 0.69]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.80 (P = 0.005)								
5.1.3 Paliperidone 3-6mg/day								
SINGH2011	1.1	2.13	48	0	1.68	51	22.3%	0.57 [0.17, 0.97]
Subtotal (95% CI)			**48**			**51**	**22.3%**	**0.57 [0.17, 0.97]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.78 (P = 0.005)								
Total (95% CI)			**218**			**222**	**100.0%**	**0.50 [0.31, 0.69]**

Heterogeneity: Tau² = 0.00; Chi² = 0.78, df = 2 (P = 0.68); I² = 0%

Test for overall effect: Z = 5.16 (P < 0.00001)

Test for subgroup differences: Chi² = 0.78, df = 2 (P = 0.68), I² = 0%



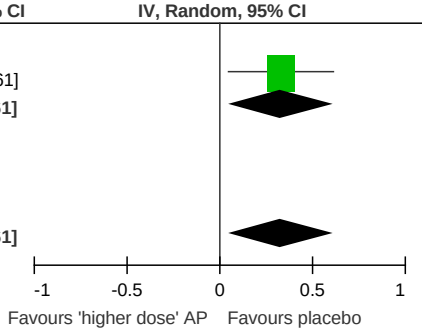
5.2 Side effects: mean change in BMI (kg/m2)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.2.1 Aripriprazole 30mg/day								
FINDLING2008A	0	0.8	97	-0.3	1	98	100.0%	0.33 [0.05, 0.61]
Subtotal (95% CI)			**97**			**98**	**100.0%**	**0.33 [0.05, 0.61]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.29 (P = 0.02)								
Total (95% CI)			**97**			**98**	**100.0%**	**0.33 [0.05, 0.61]**

Heterogeneity: Not applicable

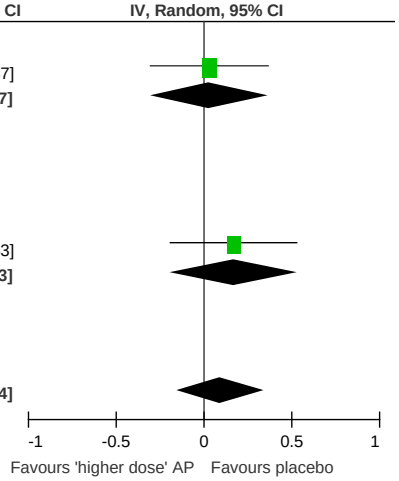
Test for overall effect: Z = 2.29 (P = 0.02)

Test for subgroup differences: Not applicable



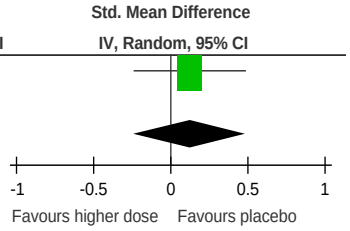
5.3 Side effects: mean change in fasting serum glucose level (mg/dl)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.4.1 Quetiapine 800mg/day								
AstraZenecaD1441C00112	-1.4	9.08	70	-1.7015	10.823	67	53.6%	0.03 [-0.30, 0.37]
Subtotal (95% CI)			**70**			**67**	**53.6%**	**0.03 [-0.30, 0.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.18 (P = 0.86)								
5.4.2 Aripriprazole 30mg/day								
FINDLING2008A	-0.98	10.57	55	-3.15	14.43	65	46.4%	0.17 [-0.19, 0.53]
Subtotal (95% CI)			**55**			**65**	**46.4%**	**0.17 [-0.19, 0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.92 (P = 0.36)								
Total (95% CI)			**125**			**132**	**100.0%**	**0.09 [-0.15, 0.34]**
Heterogeneity: Tau² = 0.00; Chi² = 0.30, df = 1 (P = 0.58); I² = 0%								
Test for overall effect: Z = 0.75 (P = 0.45)								
Test for subgroup differences: Chi² = 0.30, df = 1 (P = 0.58), I² = 0%								



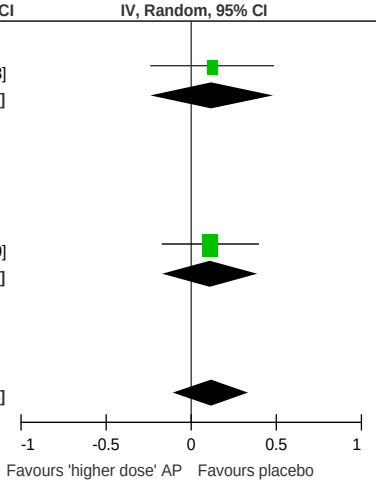
5.4 Side effects: mean change in insulin level (mg/dl)

Study or Subgroup	Higher Dose Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
AstraZenecaD1441C00112	1.2203	17.29567	59	-1.0333	19.05742	60	100.0%	0.12 [-0.24, 0.48]
Total (95% CI)			**59**			**60**	**100.0%**	**0.12 [-0.24, 0.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.67 (P = 0.50)								



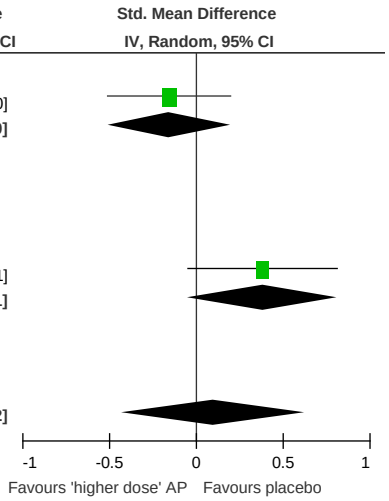
5.5 Side effects: mean change in fasting total cholesterol (mg/dl)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.8.1 Quetiapine 800mg/day								
AstraZenecaD1441C00112	1.2203	17.29567	59	-1.0333	19.05742	60	38.0%	0.12 [-0.24, 0.48]
Subtotal (95% CI)			**59**			**60**	**38.0%**	**0.12 [-0.24, 0.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.67 (P = 0.50)								
5.8.2 Aripriprazole 30mg/day								
FINDLING2008A	-7.43	27.99	98	-10.38	24.08	96	62.0%	0.11 [-0.17, 0.39]
Subtotal (95% CI)			**98**			**96**	**62.0%**	**0.11 [-0.17, 0.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.78 (P = 0.43)								
Total (95% CI)			**157**			**156**	**100.0%**	**0.12 [-0.11, 0.34]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.96); I² = 0%								
Test for overall effect: Z = 1.03 (P = 0.30)								
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.96), I² = 0%								



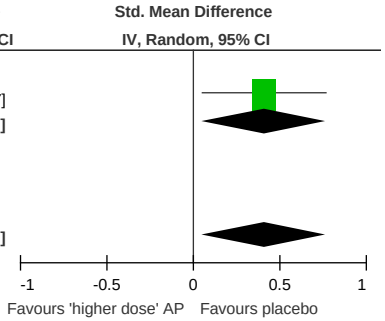
5.6 Side effects: mean change in fasting high-density lipoprotein cholesterol (mg/dl)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.9.1 Quetiapine 800mg/day								
AstraZenecaD1441C00112	0.9667	9.90115	60	2.4603	8.95297	63	52.7%	-0.16 [-0.51, 0.20]
Subtotal (95% CI)			**60**			**63**	**52.7%**	**-0.16 [-0.51, 0.20]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.87 (P = 0.38)								
5.9.2 Aripriprazole 30mg/day								
FINDLING2008A	-0.05	7.92	40	-6.09	20.23	45	47.3%	0.38 [-0.05, 0.81]
Subtotal (95% CI)			**40**			**45**	**47.3%**	**0.38 [-0.05, 0.81]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.74 (P = 0.08)								
Total (95% CI)			**100**			**108**	**100.0%**	**0.10 [-0.43, 0.62]**
Heterogeneity: Tau² = 0.10; Chi² = 3.59, df = 1 (P = 0.06); I² = 72%								
Test for overall effect: Z = 0.36 (P = 0.72)								
Test for subgroup differences: Chi² = 3.59, df = 1 (P = 0.06), I² = 72.2%								



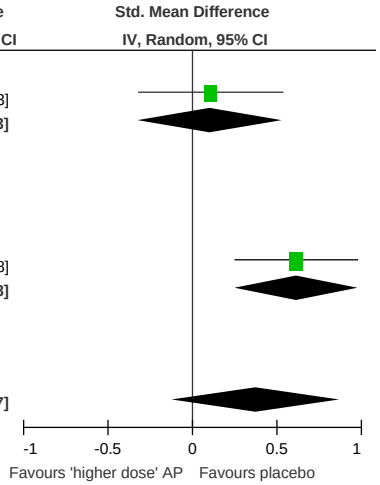
5.7 Side effects: mean change in fasting low-density lipoprotein cholesterol (mg/dl)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.12.1 Quetiapine 800mg/day								
AstraZenecaD1441C00112	4.8167	21.78515	60	-3.8889	20.505	63	100.0%	0.41 [0.05, 0.77]
Subtotal (95% CI)			**60**			**63**	**100.0%**	**0.41 [0.05, 0.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.24 (P = 0.02)								
Total (95% CI)			**60**			**63**	**100.0%**	**0.41 [0.05, 0.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.24 (P = 0.02)								
Test for subgroup differences: Not applicable								



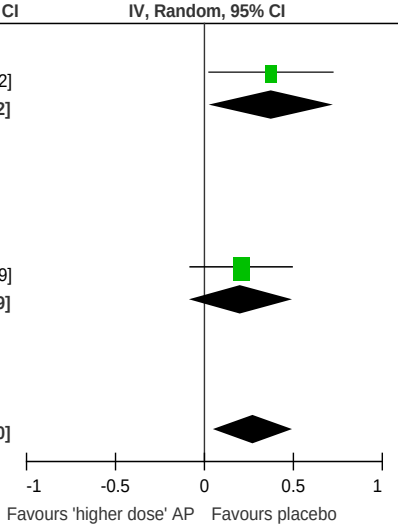
5.8 Side effects: mean change in fasting triglycerides (mg/dl)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.14.1 Aripriprazole 30mg/day								
FINDLING2008A	-0.73	51.85	40	-6.51	53.82	45	47.4%	0.11 [-0.32, 0.53]
Subtotal (95% CI)			**40**			**45**	**47.4%**	**0.11 [-0.32, 0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.50 (P = 0.62)								
5.14.2 Quetiapine 800mg/day								
AstraZenecaD1441C00112	15.5833	47.94357	60	-8.0635	25.74745	63	52.6%	0.61 [0.25, 0.98]
Subtotal (95% CI)			**60**			**63**	**52.6%**	**0.61 [0.25, 0.98]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.33 (P = 0.0009)								
Total (95% CI)			**100**			**108**	**100.0%**	**0.37 [-0.12, 0.87]**
Heterogeneity: Tau² = 0.09; Chi² = 3.15, df = 1 (P = 0.08); I² = 68%								
Test for overall effect: Z = 1.48 (P = 0.14)								
Test for subgroup differences: Chi² = 3.15, df = 1 (P = 0.08), I² = 68.3%								



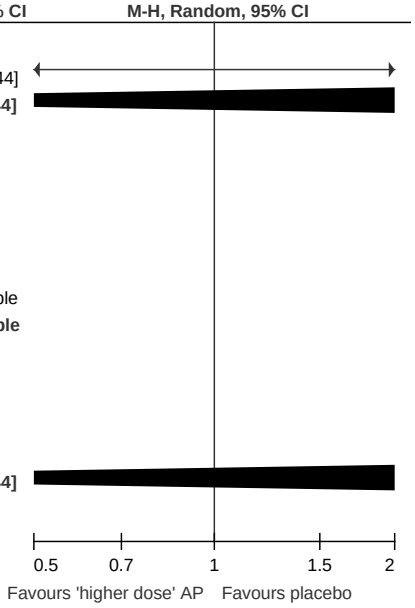
5.9 Side effects: mean change in QTcB interval (msec)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.18.1 Quetiapine 800mg/day								
AstraZenecaD1441C00112	12.97	28.46	64	2.63	26.46	65	40.4%	0.37 [0.03, 0.72]
Subtotal (95% CI)			**64**			**65**	**40.4%**	**0.37 [0.03, 0.72]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.11 (P = 0.04)								
5.18.2 Aripriprazole 30mg/day								
FINDLING2008A	5.4	23.4	92	1.3	15.6	96	59.6%	0.21 [-0.08, 0.49]
Subtotal (95% CI)			**92**			**96**	**59.6%**	**0.21 [-0.08, 0.49]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.41 (P = 0.16)								
Total (95% CI)			**156**			**161**	**100.0%**	**0.27 [0.05, 0.50]**
Heterogeneity: Tau² = 0.00; Chi² = 0.53, df = 1 (P = 0.47); I² = 0%								
Test for overall effect: Z = 2.43 (P = 0.02)								
Test for subgroup differences: Chi² = 0.53, df = 1 (P = 0.47), I² = 0%								



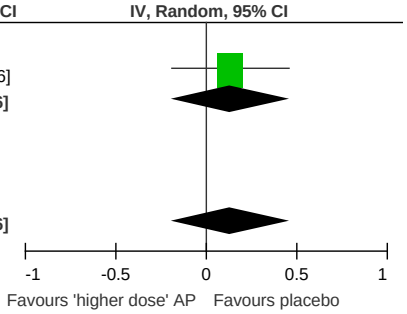
5.10 Side effects: prolonged QT interval (msec)

Study or Subgroup	'Higher dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.19.1 Quetiapine 800mg/day						
AstraZenecaD1441C00112	1	74	0	75	100.0%	3.04 [0.13, 73.44]
Subtotal (95% CI)		**74**		**75**	**100.0%**	**3.04 [0.13, 73.44]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
5.19.2 Paliperidone 3-6mg/day						
SINGH2011	0	48	0	51		Not estimable
Subtotal (95% CI)		**48**		**51**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**122**		**126**	**100.0%**	**3.04 [0.13, 73.44]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
Test for subgroup differences: Not applicable						



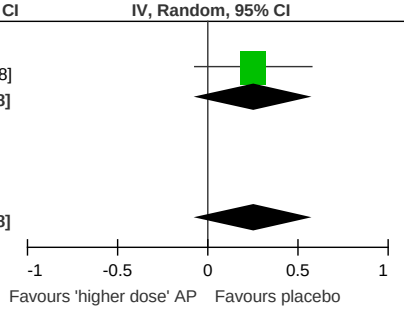
5.11 Side effects: mean change in systolic BP (mm Hg)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.20.1 Quetiapine 800mg/day								
AstraZenecaD1441C00112	-0.4	10.26	74	-1.7	9.1	73	100.0%	0.13 [-0.19, 0.46]
Subtotal (95% CI)			**74**			**73**	**100.0%**	**0.13 [-0.19, 0.46]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.81 (P = 0.42)								
Total (95% CI)			**74**			**73**	**100.0%**	**0.13 [-0.19, 0.46]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.81 (P = 0.42)								
Test for subgroup differences: Not applicable								



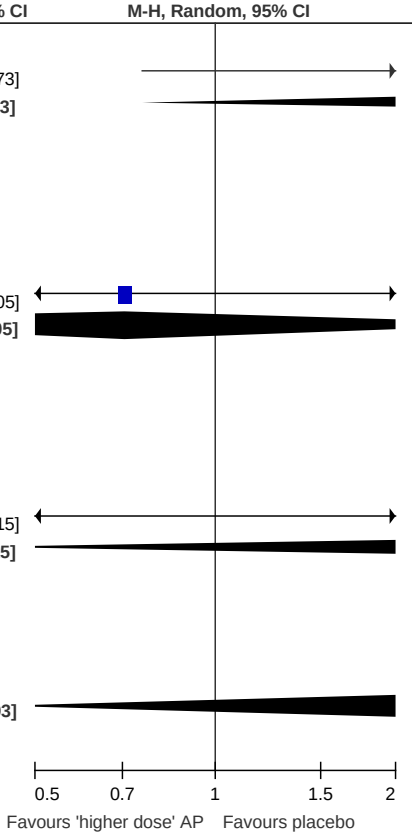
5.12 Side effects: mean change in diastolic BP (mm Hg)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.22.1 Quetiapine 800mg/day								
AstraZenecaD1441C00112	1.1	10.24	74	-1.2	7.68	73	100.0%	0.25 [-0.07, 0.58]
Subtotal (95% CI)			**74**			**73**	**100.0%**	**0.25 [-0.07, 0.58]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.52 (P = 0.13)								
Total (95% CI)			**74**			**73**	**100.0%**	**0.25 [-0.07, 0.58]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.52 (P = 0.13)								
Test for subgroup differences: Not applicable								



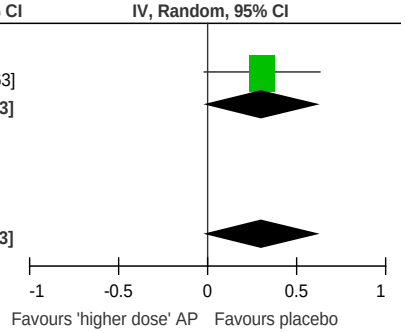
5.13 Side effects: tachycardia

Study or Subgroup	'Higher dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.24.1 Quetiapine 800mg/day						
AstraZenecaD1441C00112	6	74	0	75	28.5%	13.17 [0.76, 229.73]
Subtotal (95% CI)		**74**		**75**	**28.5%**	**13.17 [0.76, 229.73]**
Total events	6		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.77 (P = 0.08)						
5.24.2 Risperidone 4-6mg/day						
HAAS2009B	2	51	3	54	43.9%	0.71 [0.12, 4.05]
Subtotal (95% CI)		**51**		**54**	**43.9%**	**0.71 [0.12, 4.05]**
Total events	2		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.39 (P = 0.70)						
5.24.3 Paliperidone 3-6mg/day						
SINGH2011	3	48	0	51	27.6%	7.43 [0.39, 140.15]
Subtotal (95% CI)		**48**		**51**	**27.6%**	**7.43 [0.39, 140.15]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.34 (P = 0.18)						
Total (95% CI)		**173**		**180**	**100.0%**	**3.11 [0.41, 23.93]**
Total events	11		3			
Heterogeneity: Tau² = 1.67; Chi² = 4.09, df = 2 (P = 0.13); I² = 51%						
Test for overall effect: Z = 1.09 (P = 0.27)						
Test for subgroup differences: Chi² = 3.79, df = 2 (P = 0.15), I² = 47.2%						



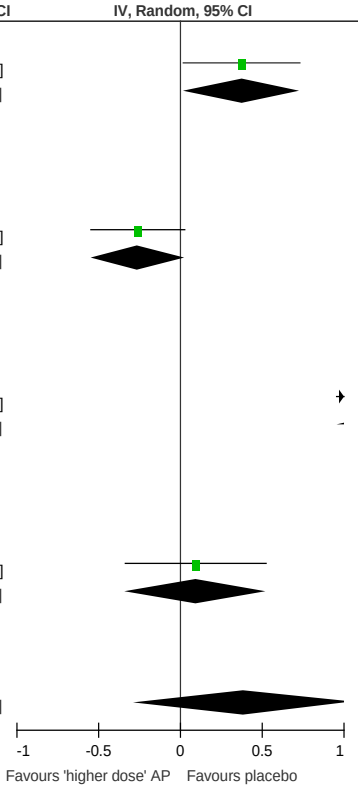
5.14 Side effects: mean change in standing pulse (beats/min)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.26.1 Quetiapine 800mg/day								
AstraZenecaD1441C00112	2.2	17.08	74	-2.5	13.14	73	100.0%	0.31 [-0.02, 0.63]
Subtotal (95% CI)			**74**			**73**	**100.0%**	**0.31 [-0.02, 0.63]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.85 (P = 0.06)								
Total (95% CI)			**74**			**73**	**100.0%**	**0.31 [-0.02, 0.63]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.85 (P = 0.06)								
Test for subgroup differences: Not applicable								



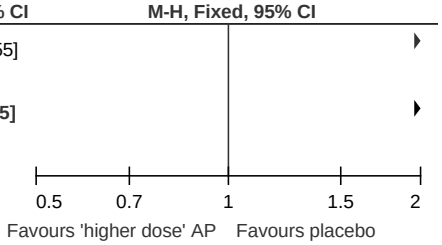
5.15 Side effects: mean change in prolactin (mg/dl)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.28.1 Quetiapine 800mg/day								
AstraZenecaD1441C00112	-7.8333	26.47357	60	-18.2467	28.7495	63	25.2%	0.37 [0.02, 0.73]
Subtotal (95% CI)			**60**			**63**	**25.2%**	**0.37 [0.02, 0.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.06 (P = 0.04)								
5.28.2 Aripriprazole 30mg/day								
FINDLING2008A	-15.14	26.87	92	-8.45	24.23	96	25.9%	-0.26 [-0.55, 0.03]
Subtotal (95% CI)			**92**			**96**	**25.9%**	**-0.26 [-0.55, 0.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.78 (P = 0.08)								
5.28.3 Risperidone 4-6mg/day								
HAAS2009B	40.37255	39.717708	51	-5.31111	24.55995	54	24.5%	1.38 [0.95, 1.81]
Subtotal (95% CI)			**51**			**54**	**24.5%**	**1.38 [0.95, 1.81]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 6.34 (P < 0.00001)								
5.28.4 Paliperidone 3-6mg/day								
SINGH2011	26.647857	42.02895	42	23.252683	28.565498	41	24.4%	0.09 [-0.34, 0.52]
Subtotal (95% CI)			**42**			**41**	**24.4%**	**0.09 [-0.34, 0.52]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.43 (P = 0.67)								
Total (95% CI)			**245**			**254**	**100.0%**	**0.39 [-0.29, 1.06]**
Heterogeneity: Tau² = 0.44; Chi² = 40.07, df = 3 (P < 0.00001); I² = 93%								
Test for overall effect: Z = 1.13 (P = 0.26)								
Test for subgroup differences: Chi² = 40.07, df = 3 (P < 0.00001), I² = 92.5%								



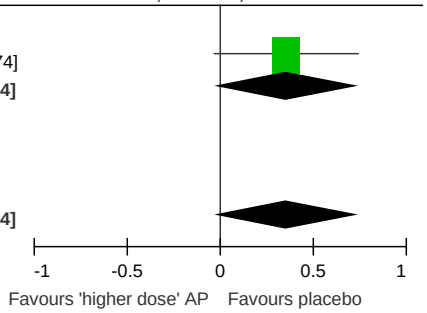
5.16 Side effects: extra pyramidal symptoms

Study or Subgroup	'Higher dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
POOL1976	18	25	1	24	100.0%	17.28 [2.50, 119.55]
Total (95% CI)		**25**		**24**	**100.0%**	**17.28 [2.50, 119.55]**
Total events	18		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.89 (P = 0.004)						



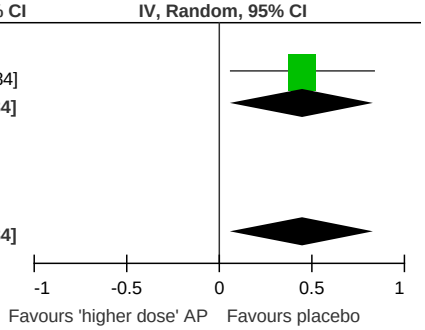
5.17 Side effects: extra pyramidal (mean change in AIMS scores)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.32.1 Risperidone 4-6mg/day								
HAAS2009B	0.2	1.4	51	-0.3	1.4	54	100.0%	0.35 [-0.03, 0.74]
Subtotal (95% CI)			**51**			**54**	**100.0%**	**0.35 [-0.03, 0.74]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.80 (P = 0.07)								
Total (95% CI)			**51**			**54**	**100.0%**	**0.35 [-0.03, 0.74]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.80 (P = 0.07)								
Test for subgroup differences: Not applicable								



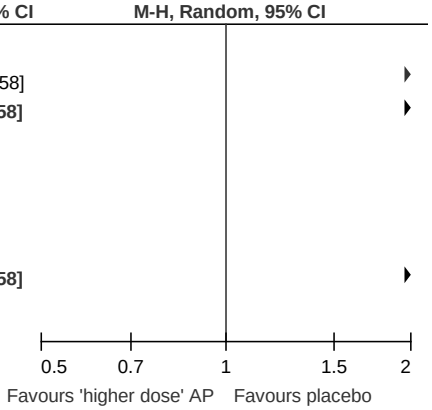
5.18 Side effects: extra pyramidal (mean change in SAS scores)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
5.34.1 Risperidone 4-6mg/day								
HAAS2009B	0.1	0.3	51	0	0.1	54	100.0%	0.45 [0.06, 0.84]
Subtotal (95% CI)			**51**			**54**	**100.0%**	**0.45 [0.06, 0.84]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.27 (P = 0.02)								
Total (95% CI)			**51**			**54**	**100.0%**	**0.45 [0.06, 0.84]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.27 (P = 0.02)								
Test for subgroup differences: Not applicable								



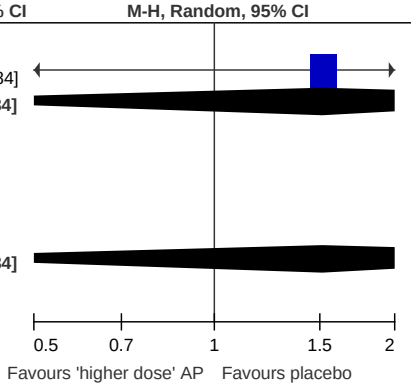
5.19 Side effects: parkinsonism

Study or Subgroup	'Higher dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.36.1 Aripriprazole 30mg/day						
FINDLING2008A	31	100	7	100	100.0%	4.43 [2.05, 9.58]
Subtotal (95% CI)		**100**		**100**	**100.0%**	**4.43 [2.05, 9.58]**
Total events	31		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.78 (P = 0.0002)						
Total (95% CI)		**100**		**100**	**100.0%**	**4.43 [2.05, 9.58]**
Total events	31		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.78 (P = 0.0002)						
Test for subgroup differences: Not applicable						



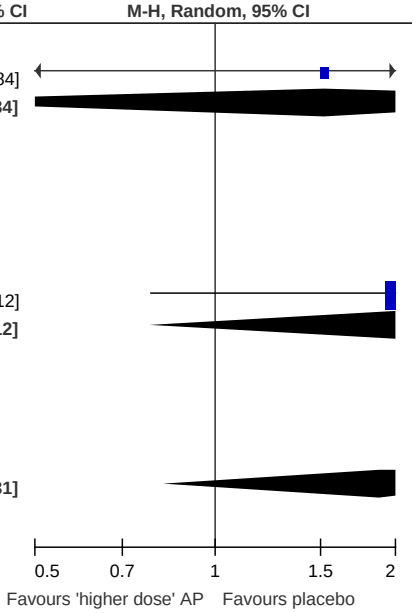
5.20 Side effects: tremour

Study or Subgroup	'Higher dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.38.1 Quetiapine 800mg/day						
AstraZenecaD1441C00112	3	74	2	75	100.0%	1.52 [0.26, 8.84]
Subtotal (95% CI)		**74**		**75**	**100.0%**	**1.52 [0.26, 8.84]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.47 (P = 0.64)						
Total (95% CI)		**74**		**75**	**100.0%**	**1.52 [0.26, 8.84]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.47 (P = 0.64)						
Test for subgroup differences: Not applicable						



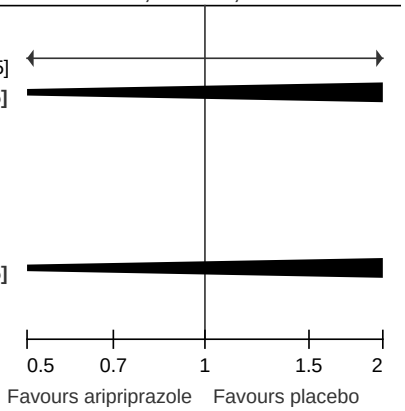
5.21 Side effects: akathesia

Study or Subgroup	'Higher dose' AP Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.40.1 Quetiapine 800mg/day						
AstraZenecaD1441C00112	3	74	2	75	22.2%	1.52 [0.26, 8.84]
Subtotal (95% CI)		**74**		**75**	**22.2%**	**1.52 [0.26, 8.84]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.47 (P = 0.64)						
5.40.2 Aripriprazole 30mg/day						
FINDLING2008A	12	100	6	100	77.8%	2.00 [0.78, 5.12]
Subtotal (95% CI)		**100**		**100**	**77.8%**	**2.00 [0.78, 5.12]**
Total events	12		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.45 (P = 0.15)						
Total (95% CI)		**174**		**175**	**100.0%**	**1.88 [0.82, 4.31]**
Total events	15		8			
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 1 (P = 0.79); I² = 0%						
Test for overall effect: Z = 1.49 (P = 0.14)						
Test for subgroup differences: Chi² = 0.07, df = 1 (P = 0.79), I² = 0%						



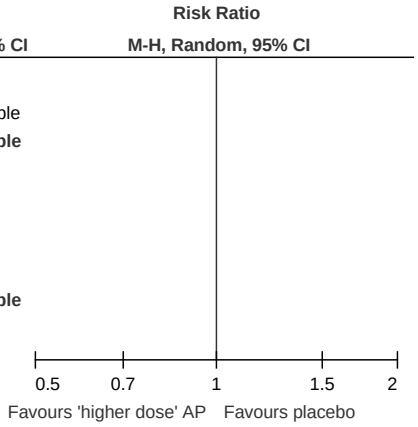
5.22 Side effects: dystonia

Study or Subgroup	Aripriprazole Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.42.1 Aripriprazole 30mg/day						
FINDLING2008A	2	100	0	100	100.0%	5.00 [0.24, 102.85]
Subtotal (95% CI)		**100**		**100**	**100.0%**	**5.00 [0.24, 102.85]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.04 (P = 0.30)						
Total (95% CI)		**100**		**100**	**100.0%**	**5.00 [0.24, 102.85]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.04 (P = 0.30)						
Test for subgroup differences: Not applicable						



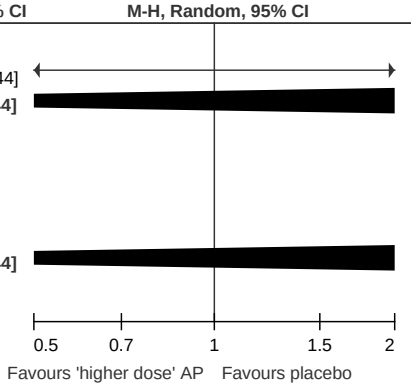
5.23 Side effects: dyskenesia

Study or Subgroup	'Higher dose' AP Events	'Higher dose' AP Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.44.1 Quetiapine 800mg/day						
AstraZenecaD1441C00112	0	74	0	75		Not estimable
Subtotal (95% CI)		**74**		**75**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**74**		**75**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



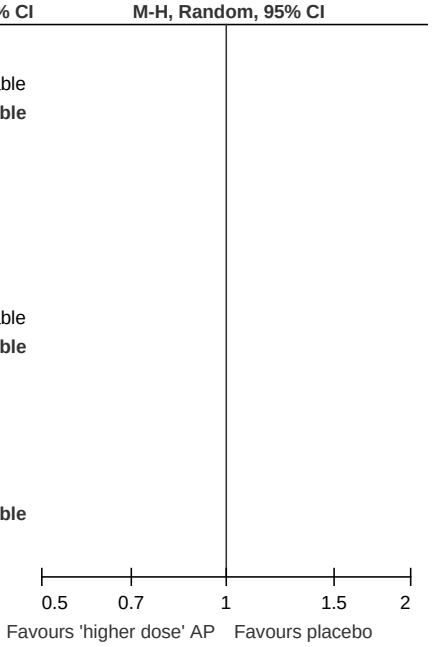
5.24 Side effects: extra pyramidal disorder

Study or Subgroup	'Higher dose' AP Events	'Higher dose' AP Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.46.1 Quetiapine 800mg/day						
AstraZenecaD1441C00112	1	74	0	75	100.0%	3.04 [0.13, 73.44]
Subtotal (95% CI)		**74**		**75**	**100.0%**	**3.04 [0.13, 73.44]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
Total (95% CI)		**74**		**75**	**100.0%**	**3.04 [0.13, 73.44]**
Total events	1		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
Test for subgroup differences: Not applicable						



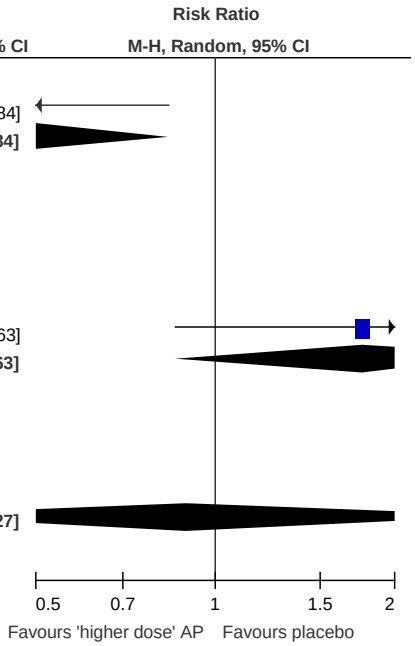
5.25 Side effects: mortality (including suicide)

Study or Subgroup	'Higher dose' AP Events	'Higher dose' AP Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.48.1 Aripriprazole 30mg/day						
FINDLING2008A	0	100	0	100		Not estimable
Subtotal (95% CI)		**100**		**100**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
5.48.2 Risperidone 4-6mg/day						
HAAS2009B	0	51	0	54		Not estimable
Subtotal (95% CI)		**51**		**54**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**151**		**154**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



5.26 Leaving the study early for any reason

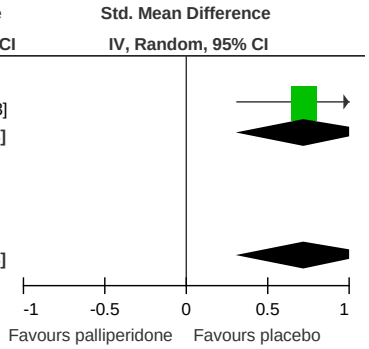
Study or Subgroup	'Higher dose' AP Events	'Higher dose' AP Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
5.50.1 Quetiapine 800mg/day						
AstraZenecaD1441C00112	13	74	28	75	51.4%	0.47 [0.27, 0.84]
Subtotal (95% CI)		**74**		**75**	**51.4%**	**0.47 [0.27, 0.84]**
Total events	13		28			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.57 (P = 0.01)						
5.50.2 Aripriprazole 30mg/day						
FINDLING2008A	18	102	10	100	48.6%	1.76 [0.86, 3.63]
Subtotal (95% CI)		**102**		**100**	**48.6%**	**1.76 [0.86, 3.63]**
Total events	18		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.54 (P = 0.12)						
Total (95% CI)		**176**		**175**	**100.0%**	**0.89 [0.24, 3.27]**
Total events	31		38			
Heterogeneity: Tau² = 0.77; Chi² = 7.91, df = 1 (P = 0.005); I² = 87%						
Test for overall effect: Z = 0.17 (P = 0.87)						
Test for subgroup differences: Chi² = 7.89, df = 1 (P = 0.005), I² = 87.3%						



6. Additional (high) dose paliperidone versus placebo: post-treatment side effect outcomes

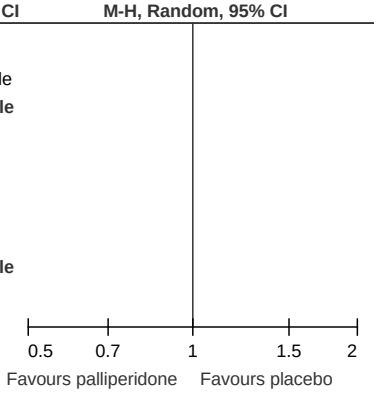
6.1 Side effects: mean change in weight (kg)

	Palliperidone 6-12mg/day			Placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
6.1.4 Paliperidone 6-12mg/day								
SINGH2011	1.4	2.16	47	0	1.68	51	100.0%	0.72 [0.31, 1.13]
Subtotal (95% CI)			**47**			**51**	**100.0%**	**0.72 [0.31, 1.13]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.45 (P = 0.0006)								
Total (95% CI)			**47**			**51**	**100.0%**	**0.72 [0.31, 1.13]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.45 (P = 0.0006)								
Test for subgroup differences: Not applicable								



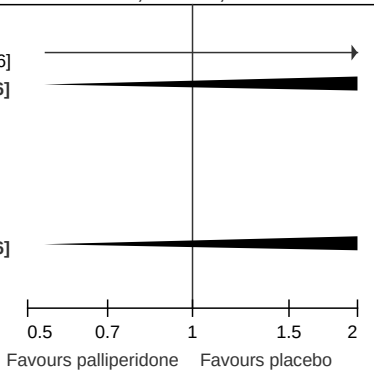
6.2 Side effects: prolonged QT interval

	Palliperidone 6-12mg/day		Placebo			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
6.18.2 Paliperidone 3-6mg/day						
SINGH2011	0	47	0	51		Not estimable
Subtotal (95% CI)		**47**		**51**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**47**		**51**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



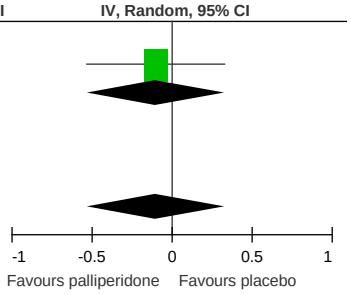
6.3 Side effects: tachycardia

	Palliperidone 6-12mg/day		Placebo			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
6.22.3 Paliperidone 6-12mg/day						
SINGH2011	4	47	0	51	100.0%	9.75 [0.54, 176.36]
Subtotal (95% CI)		**47**		**51**	**100.0%**	**9.75 [0.54, 176.36]**
Total events	4		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.54 (P = 0.12)						
Total (95% CI)		**47**		**51**	**100.0%**	**9.75 [0.54, 176.36]**
Total events	4		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.54 (P = 0.12)						
Test for subgroup differences: Not applicable						



6.4 Side effects: prolactin (mg/dl)

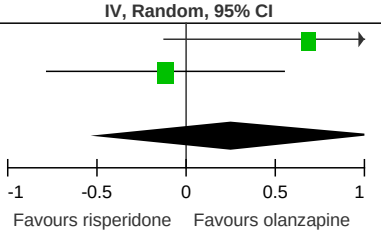
Study or Subgroup	Palliperidone Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
6.24.4 Paliperidone 6-12mg/day								
SINGH2011	20.665714	21.264017	42	23.252683	28.565498	41	100.0%	-0.10 [-0.53, 0.33]
Subtotal (95% CI)			**42**			**41**	**100.0%**	**-0.10 [-0.53, 0.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.46 (P = 0.64)								
Total (95% CI)			**42**			**41**	**100.0%**	**-0.10 [-0.53, 0.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.46 (P = 0.64)								
Test for subgroup differences: Not applicable								



7. Risperidone versus olanzapine: post-treatment efficacy outcomes

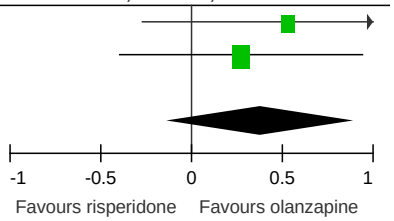
7.1 Mental state: Mean endpoint total symptoms (PANSS, BPRS-C)

Study or Subgroup	Risperidone Mean	SD	Total	Olanzapine Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
MOZES2006	63.46	21.72	13	50.5	13.33	12	45.7%	0.69 [-0.12, 1.50]
SIKICH2004	10	8	19	11	9	16	54.3%	-0.12 [-0.78, 0.55]
Total (95% CI)			**32**			**28**	**100.0%**	**0.25 [-0.53, 1.04]**
Heterogeneity: Tau² = 0.18; Chi² = 2.25, df = 1 (P = 0.13); I² = 56%								
Test for overall effect: Z = 0.63 (P = 0.53)								



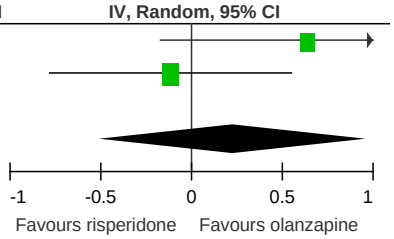
7.2 Mental state: mean endpoint positive symptoms (PANSS Positive, CPRS Positive)

Study or Subgroup	Risperidone Mean	SD	Total	Olanzapine Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
MOZES2006	14	4.31	13	11.53	4.71	12	41.1%	0.53 [-0.27, 1.33]
SIKICH2004	14	12	19	11	9	16	58.9%	0.27 [-0.40, 0.94]
Total (95% CI)			**32**			**28**	**100.0%**	**0.38 [-0.13, 0.89]**
Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 1 (P = 0.63); I² = 0%								
Test for overall effect: Z = 1.45 (P = 0.15)								



7.3 Mental state: mean endpoint negative symptoms (PANSS Negative, CPRS Negative)

Study or Subgroup	Risperidone Mean	SD	Total	Olanzapine Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
MOZES2006	16.53	9.07	13	11.66	4.94	12	45.2%	0.64 [-0.17, 1.45]
SIKICH2004	10	8	19	11	9	16	54.8%	-0.12 [-0.78, 0.55]
Total (95% CI)			**32**			**28**	**100.0%**	**0.22 [-0.51, 0.96]**
Heterogeneity: Tau² = 0.14; Chi² = 1.99, df = 1 (P = 0.16); I² = 50%								
Test for overall effect: Z = 0.60 (P = 0.55)								

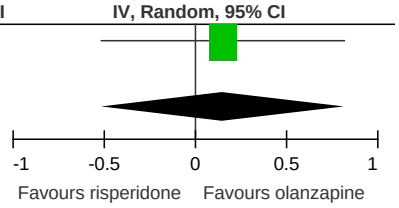


7.4 Mean endpoint global state: severity (CGI-S)

Study or Subgroup	Risperidone Mean	SD	Total	Olanzapine Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
SIKICH2004	3.8	1.3	19	3.6	1.3	16	100.0%	0.15 [-0.52, 0.82]
Total (95% CI)			**19**			**16**	**100.0%**	**0.15 [-0.52, 0.82]**

Heterogeneity: Not applicable

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

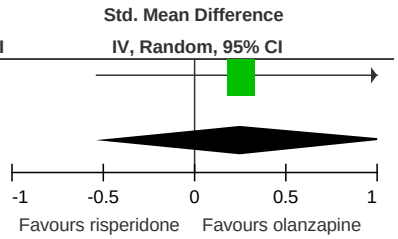


7.5 Mean endpoint psychosocial functioning (CGAS)

Study or Subgroup	Risperidone Mean	SD	Total	Olanzapine Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
MOZES2006	-5.69	2.39	13	-6.25	1.86	12	100.0%	0.25 [-0.54, 1.04]
Total (95% CI)			**13**			**12**	**100.0%**	**0.25 [-0.54, 1.04]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.63 (P = 0.53)



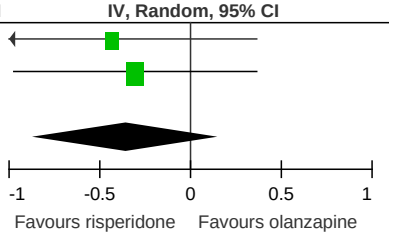
8. Risperidone versus olanzapine: post-treatment side effect outcomes

8.1 Side effects: weight (kg) (mean change: MOZES2006; mean change: SIKICH2004)

Study or Subgroup	Risperidone Mean	SD	Total	Olanzapine Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
MOZES2006	4.45	2.87	13	5.78	3.11	12	41.5%	-0.43 [-1.23, 0.36]
SIKICH2004	66.2	23.4	19	73.9	26.2	16	58.5%	-0.30 [-0.97, 0.36]
Total (95% CI)			**32**			**28**	**100.0%**	**-0.36 [-0.87, 0.16]**

Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.81); I² = 0%

Test for overall effect: Z = 1.37 (P = 0.17)

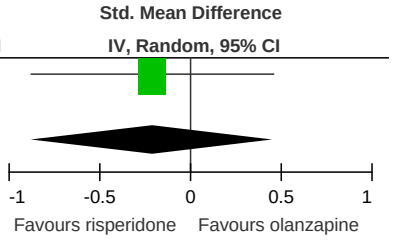


8.2 Side effects: mean endpoint BMI (kg/m2)

Study or Subgroup	Risperidone Mean	SD	Total	Olanzapine Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
SIKICH2004	24.5	6.9	19	25.9	6	16	100.0%	-0.21 [-0.88, 0.46]
Total (95% CI)			**19**			**16**	**100.0%**	**-0.21 [-0.88, 0.46]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.62 (P = 0.54)

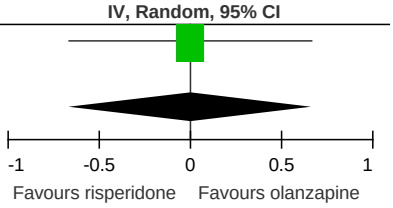


8.3 Side effects: mean endpoint QT Interval (msec)

	Risperidone			Olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SIKICH2004	402	25	19	402	23	16	100.0%	0.00 [-0.67, 0.67]
Total (95% CI)			**19**			**16**	**100.0%**	**0.00 [-0.67, 0.67]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)

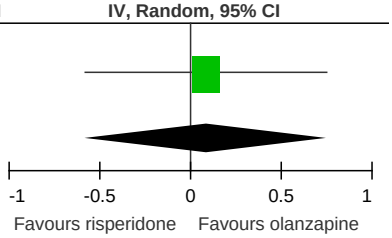


8.4 Side effects: extra pyramidal (mean endpoint SAS scores)

	Risperidone			Olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
MOZES2006	8	13	7	12	0	0		Not estimable
SIKICH2004	2.1	2.2	19	1.9	2.4	16	100.0%	0.09 [-0.58, 0.75]
Total (95% CI)			**26**			**16**	**100.0%**	**0.09 [-0.58, 0.75]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.25 (P = 0.80)

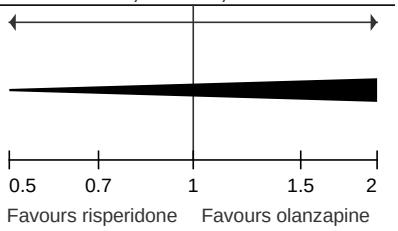


8.5 Side effects: extra pyramidal (mean endpoint BARS scores)

	Risperidone		Olanzapine			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
MOZES2006	3	12	1	13	100.0%	3.25 [0.39, 27.15]
Total (95% CI)		**12**		**13**	**100.0%**	**3.25 [0.39, 27.15]**
Total events	3		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.09 (P = 0.28)

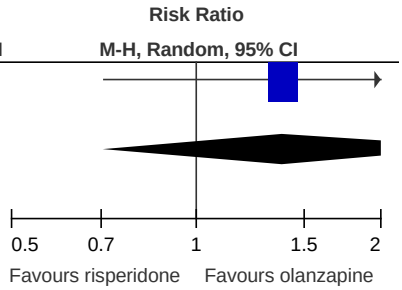


8.6 Side effects: tremor

	Risperidone		Olanzapine			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
MOZES2006	9	13	6	12	100.0%	1.38 [0.71, 2.71]
Total (95% CI)		**13**		**12**	**100.0%**	**1.38 [0.71, 2.71]**
Total events	9		6			

Heterogeneity: Not applicable

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

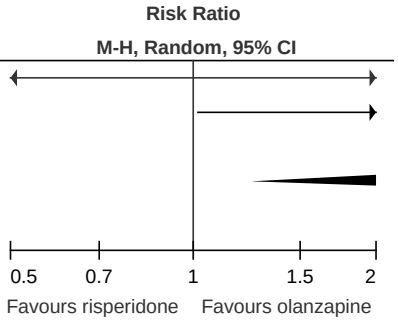


8.7 Leaving the study early for any reason

Study or Subgroup	Risperidone Events	Risperidone Total	Olanzapine Events	Olanzapine Total	Weight	Risk Ratio M-H, Random, 95% CI
MOZES2006	4	13	1	12	30.9%	3.69 [0.48, 28.57]
SIKICH2004	10	20	2	16	69.1%	4.00 [1.02, 15.72]
Total (95% CI)		**33**		**28**	**100.0%**	**3.90 [1.25, 12.17]**
Total events	14		3			

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.95); I² = 0%

Test for overall effect: Z = 2.35 (P = 0.02)



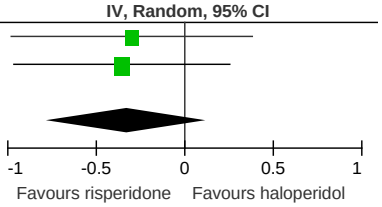
9. Risperidone versus haloperidol: post-treatment efficacy outcomes

9.1 Mental state: mean endpoint total symptoms (BPRS)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Weight	Std. Mean Difference IV, Random, 95% CI
SIKICH2004	27	20	19	33	19	15	44.5%	-0.30 [-0.98, 0.38]
YAO2003/KENNEDY2012	17.82	3.24	21	19.21	4.35	21	55.5%	-0.36 [-0.97, 0.25]
Total (95% CI)			**40**			**36**	**100.0%**	**-0.33 [-0.79, 0.12]**

Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.90); I² = 0%

Test for overall effect: Z = 1.43 (P = 0.15)

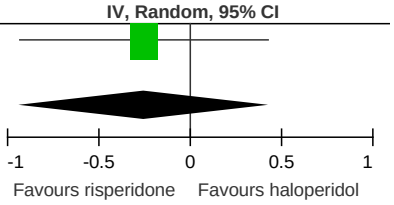


9.2 Mental state: mean endpoint positive symptoms (CPRS-Positive)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Weight	Std. Mean Difference IV, Random, 95% CI
SIKICH2004	14	12	19	17	11	15	100.0%	-0.25 [-0.93, 0.43]
Total (95% CI)			**19**			**15**	**100.0%**	**-0.25 [-0.93, 0.43]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.73 (P = 0.47)

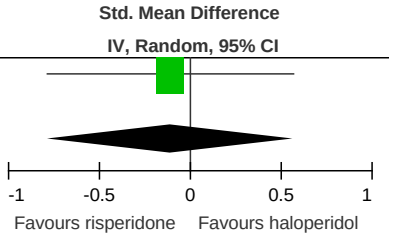


9.3 Mental state: mean endpoint negative symptoms (CPRS-Negative)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Weight	Std. Mean Difference IV, Random, 95% CI
SIKICH2004	10	8	19	11	10	15	100.0%	-0.11 [-0.79, 0.57]
Total (95% CI)			**19**			**15**	**100.0%**	**-0.11 [-0.79, 0.57]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.32 (P = 0.75)

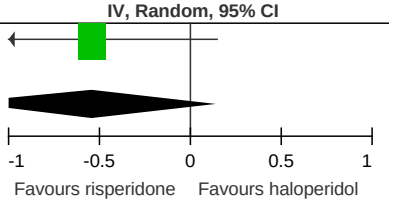


9.4 Mean endpoint global state: severity (CGI-S)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Weight	Std. Mean Difference IV, Random, 95% CI
SIKICH2004	3.8	1.3	19	4.5	1.2	15	100.0%	-0.54 [-1.23, 0.15]
Total (95% CI)			**19**			**15**	**100.0%**	**-0.54 [-1.23, 0.15]**

Heterogeneity: Not applicable

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



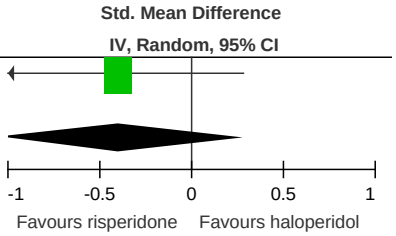
10. Risperidone versus haloperidol: post-treatment side effect outcomes

10.1 Side effects: endpoint mean weight (kg)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Weight	Std. Mean Difference IV, Random, 95% CI
SIKICH2004	66.2	23.4	19	76.1	24.8	15	100.0%	-0.40 [-1.09, 0.28]
Total (95% CI)			**19**			**15**	**100.0%**	**-0.40 [-1.09, 0.28]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.15 (P = 0.25)

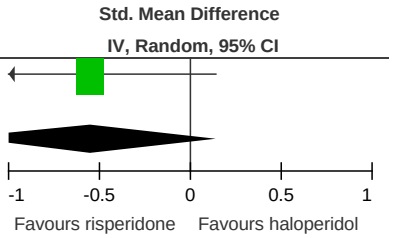


10.2 Side effects: mean endpoint BMI (kg/m2)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Weight	Std. Mean Difference IV, Random, 95% CI
SIKICH2004	22.9	7.3	19	27.6	9.5	15	100.0%	-0.55 [-1.24, 0.14]
Total (95% CI)			**19**			**15**	**100.0%**	**-0.55 [-1.24, 0.14]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.56 (P = 0.12)

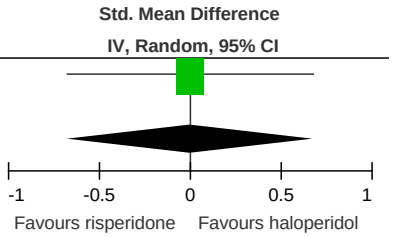


10.3 Side effects: mean endpoint QT interval (msec)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Weight	Std. Mean Difference IV, Random, 95% CI
SIKICH2004	402	25	19	402	16	15	100.0%	0.00 [-0.68, 0.68]
Total (95% CI)			**19**			**15**	**100.0%**	**0.00 [-0.68, 0.68]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)

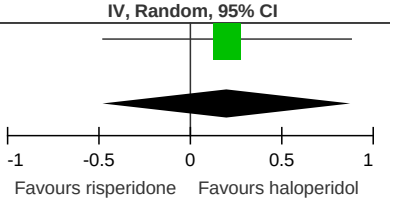


10.4 Side effects: mean endpoint prolactin level (mg/dl)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Weight	Std. Mean Difference IV, Random, 95% CI
SIKICH2004	37.2	19.8	19	32.2	29	15	100.0%	0.20 [-0.48, 0.88]
Total (95% CI)			**19**			**15**	**100.0%**	**0.20 [-0.48, 0.88]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.58 (P = 0.56)

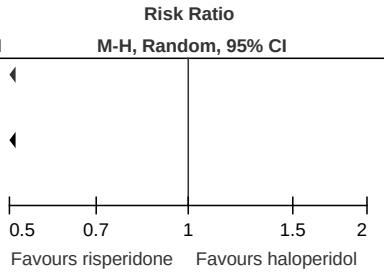


10.5 Side effects: extra pyramidal symptoms

Study or Subgroup	Risperidone Events	Risperidone Total	Haloperidol Events	Haloperidol Total	Weight	Risk Ratio M-H, Random, 95% CI
YAO2003/KENNEDY2012	2	21	21	21	100.0%	0.12 [0.04, 0.37]
Total (95% CI)		**21**		**21**	**100.0%**	**0.12 [0.04, 0.37]**
Total events	2		21			

Heterogeneity: Not applicable

Test for overall effect: Z = 3.61 (P = 0.0003)

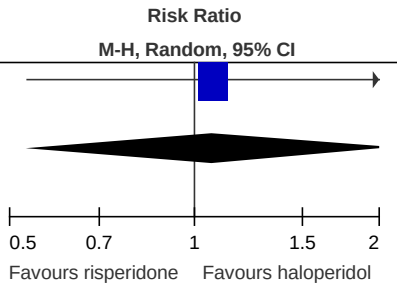


10.6 Leaving the study early for any reason

Study or Subgroup	Risperidone Events	Risperidone Total	Haloperidol Events	Haloperidol Total	Weight	Risk Ratio M-H, Random, 95% CI
SIKICH2004	10	20	7	15	100.0%	1.07 [0.53, 2.15]
Total (95% CI)		**20**		**15**	**100.0%**	**1.07 [0.53, 2.15]**
Total events	10		7			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.19 (P = 0.85)



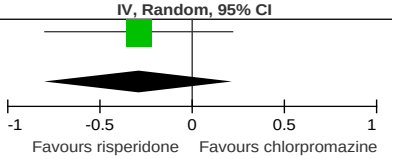
11. Chlorpromazine versus risperidone: post-treatment efficacy outcomes

11.1 Mental state: total symptoms (BPRS)

Study or Subgroup	Risperidone Mean	Risperidone SD	Risperidone Total	Chlorpromazine Mean	Chlorpromazine SD	Chlorpromazine Total	Weight	Std. Mean Difference IV, Random, 95% CI
XIONG2004KENNEDY2012	30.5	5.8	30	32.2	5.8	30	100.0%	-0.29 [-0.80, 0.22]
Total (95% CI)			**30**			**30**	**100.0%**	**-0.29 [-0.80, 0.22]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.11 (P = 0.27)



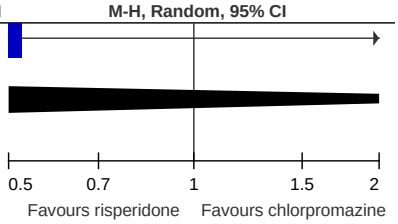
12. Chlorpromazine versus risperidone: post-treatment side effect outcomes

12.1 Side effects: tremor

Study or Subgroup	Risperidone Events	Risperidone Total	Chlopromazine Events	Chlopromazine Total	Weight	Risk Ratio M-H, Random, 95% CI
XIONG2004/KENNEDY2012	1	30	2	30	100.0%	0.50 [0.05, 5.22]
Total (95% CI)		**30**		**30**	**100.0%**	**0.50 [0.05, 5.22]**
Total events	1		2			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.58 (P = 0.56)



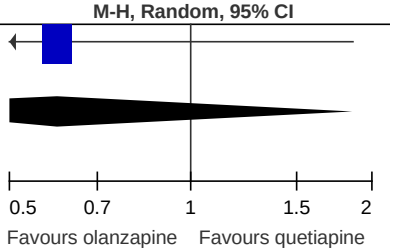
13. Olanzapine versus quetiapine: post-treatment efficacy outcomes

13.1 Response (40% reduction in PANSS total and subscale scores)

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Random, 95% CI
JENSEN2008	3	10	5	10	100.0%	0.60 [0.19, 1.86]
Total (95% CI)		**10**		**10**	**100.0%**	**0.60 [0.19, 1.86]**
Total events	3		5			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.88 (P = 0.38)



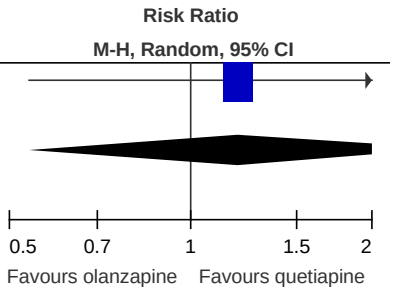
14. Olanzapine versus quetiapine: post-treatment side effect outcomes

14.1 Side effects: weight gain (number of participants with kg gain of >7% from baseline)

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Random, 95% CI
JENSEN2008	6	10	5	10	100.0%	1.20 [0.54, 2.67]
Total (95% CI)		**10**		**10**	**100.0%**	**1.20 [0.54, 2.67]**
Total events	6		5			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.45 (P = 0.66)

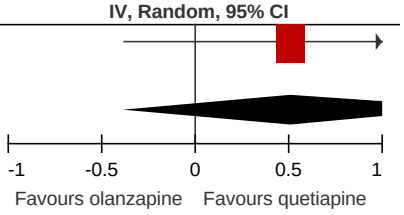


14.2 Side effects: mean endpoint BMI (kg/m2)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
JENSEN2008	0.51	0.454082	100.0%	0.51 [-0.38, 1.40]
Total (95% CI)			**100.0%**	**0.51 [-0.38, 1.40]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.12 (P = 0.26)

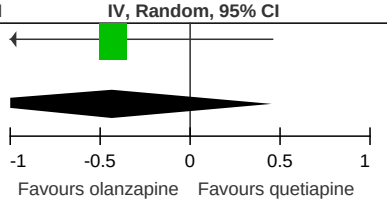


14.3 Side effects: extra pyramidal (mean endpoint SAS scores)

Study or Subgroup	Olanzapine Mean	Olanzapine SD	Olanzapine Total	Quetiapine Mean	Quetiapine SD	Quetiapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
JENSEN2008	0.2	0.41	10	0.5	0.85	10	100.0%	-0.43 [-1.32, 0.46]
Total (95% CI)			**10**			**10**	**100.0%**	**-0.43 [-1.32, 0.46]**

Heterogeneity: Not applicable

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

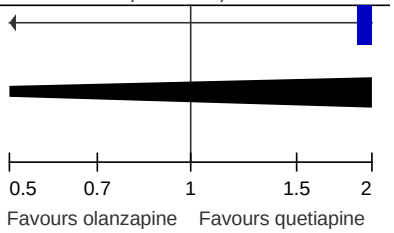


14.4 Side effects: akathesia

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetiapine Events	Quetiapine Total	Weight	Risk Ratio M-H, Random, 95% CI
JENSEN2008	2	10	1	10	100.0%	2.00 [0.21, 18.69]
Total (95% CI)		**10**		**10**	**100.0%**	**2.00 [0.21, 18.69]**
Total events	2		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.61 (P = 0.54)

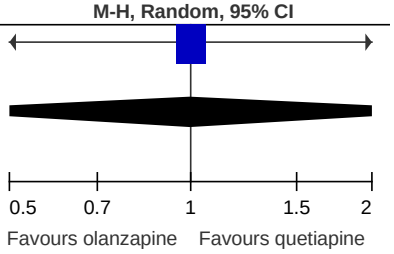


14.5 Leaving the study early for any reason

Study or Subgroup	Olanzapine Events	Olanzapine Total	Quetipaine Events	Quetipaine Total	Weight	Risk Ratio M-H, Random, 95% CI
JENSEN2008	4	10	4	10	100.0%	1.00 [0.34, 2.93]
Total (95% CI)		**10**		**10**	**100.0%**	**1.00 [0.34, 2.93]**
Total events	4		4			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)



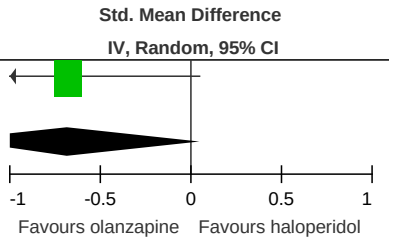
15. Olanzapine versus haloperidol: post-treatment efficacy outcomes

15.1 Mental state: mean endpoint total symptoms (BPRS-C)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SIKICH2004	22	12	16	33	19	15	100.0%	-0.68 [-1.41, 0.05]
Total (95% CI)			**16**			**15**	**100.0%**	**-0.68 [-1.41, 0.05]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.83 (P = 0.07)

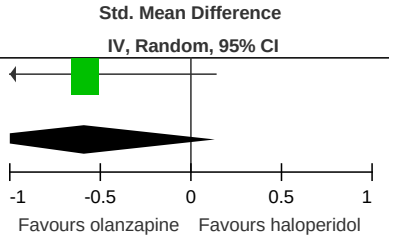


15.2 Mental state: mean endpoint in positive symptoms (CPRS-Positive)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SIKICH2004	11	9	16	17	11	15	100.0%	-0.58 [-1.30, 0.14]
Total (95% CI)			**16**			**15**	**100.0%**	**-0.58 [-1.30, 0.14]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.59 (P = 0.11)

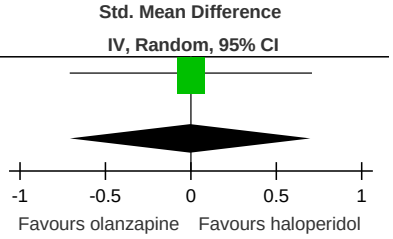


15.3 Mental state: mean endpoint negative symptoms (CPRS-Negative)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SIKICH2004	11	9	16	11	10	15	100.0%	0.00 [-0.70, 0.70]
Total (95% CI)			**16**			**15**	**100.0%**	**0.00 [-0.70, 0.70]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)

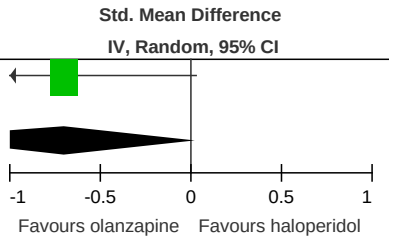


15.4 Mean endpoint in global state: severity (CGI-S)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SIKICH2004	3.6	1.3	16	4.5	1.2	15	100.0%	-0.70 [-1.43, 0.03]
Total (95% CI)			**16**			**15**	**100.0%**	**-0.70 [-1.43, 0.03]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.88 (P = 0.06)



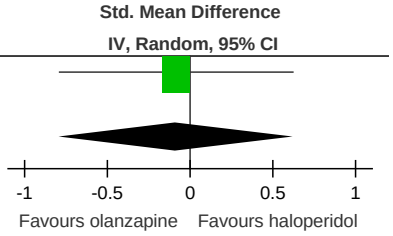
16. Olanzapine versus haloperidol: post-treatment side effect outcomes

16.1 Side effect: mean endpoint in weight (kg)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SIKICH2004	73.9	26.2	16	76.1	24.8	15	100.0%	-0.08 [-0.79, 0.62]
Total (95% CI)			**16**			**15**	**100.0%**	**-0.08 [-0.79, 0.62]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.23 (P = 0.82)

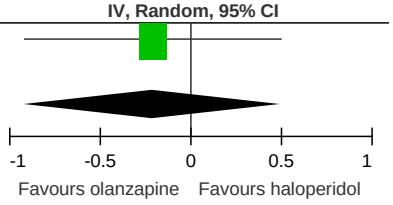


16.2 Side effect: mean endpoint BMI (kg/m2)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SIKICH2004	25.9	6	16	27.6	9.5	15	100.0%	-0.21 [-0.92, 0.50]
Total (95% CI)			**16**			**15**	**100.0%**	**-0.21 [-0.92, 0.50]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.58 (P = 0.56)

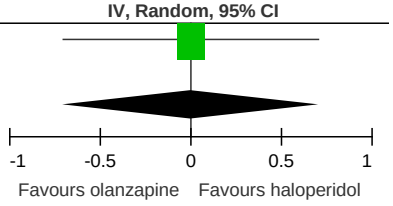


16.3 Side effect: mean endpoint QT interval (msec)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SIKICH2004	402	23	16	402	16	15	100.0%	0.00 [-0.70, 0.70]
Total (95% CI)			**16**			**15**	**100.0%**	**0.00 [-0.70, 0.70]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)

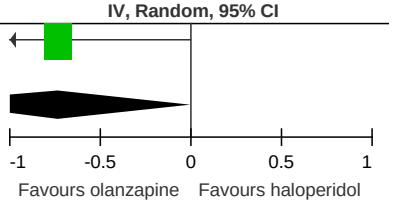


16.4 Side effect: extra pyramidal (mean endpoint in SAS scores)

	Olanzapine			Haloperidol				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SIKICH2004	1.9	2.4	16	5.2	5.8	15	100.0%	-0.73 [-1.46, -0.00]
Total (95% CI)			**16**			**15**	**100.0%**	**-0.73 [-1.46, -0.00]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.97 (P = 0.05)

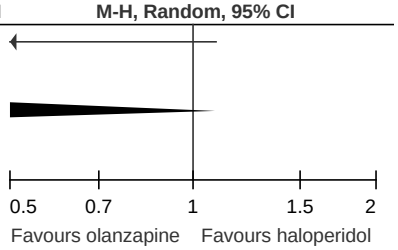


16.5 Leaving the study early for any reason

Study or Subgroup	Olanzapine Events	Olanzapine Total	Haloperidol Events	Haloperidol Total	Weight	Risk Ratio M-H, Random, 95% CI
SIKICH2004	2	16	7	15	100.0%	0.27 [0.07, 1.09]
Total (95% CI)		**16**		**15**	**100.0%**	**0.27 [0.07, 1.09]**
Total events	2		7			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.84 (P = 0.07)



17. 'Lower dose' antipsychotic medication versus 'higher dose' antipsychotic medication: post-treatment efficacy outcomes

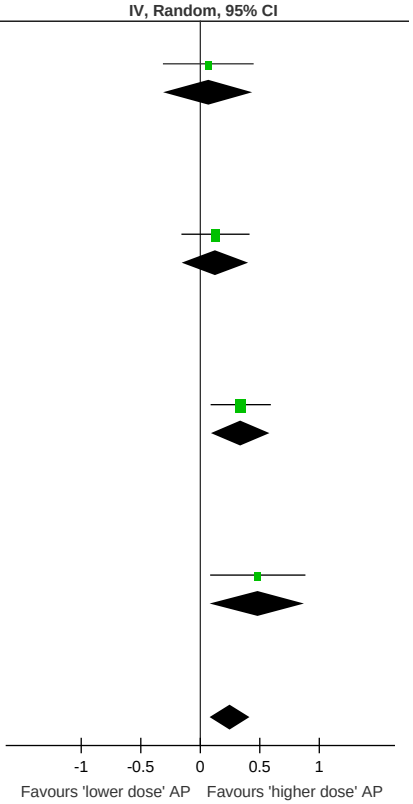
17.1 Mental state: mean change in total symptoms (PANSS)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
17.1.1 Quetiapine 400mg/day versus 800mg/day								
AstraZenecaD1441C00112	-27.31	19.43	54	-28.44	13.52	55	17.8%	0.07 [-0.31, 0.44]
Subtotal (95% CI)			**54**			**55**	**17.8%**	**0.07 [-0.31, 0.44]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.35 (P = 0.73)								
17.1.2 Aripriprazole 10mg/day versus 30mg/day								
FINDLING2008	-26.7	18.9	99	-28.6	8.86	97	29.6%	0.13 [-0.15, 0.41]
Subtotal (95% CI)			**99**			**97**	**29.6%**	**0.13 [-0.15, 0.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.89 (P = 0.37)								
17.1.3 Risperidone 1-3mg/day versus 4-6mg/day								
HAAS2009	80.8	24.33	131	72.8	22.52	124	36.3%	0.34 [0.09, 0.59]
Subtotal (95% CI)			**131**			**124**	**36.3%**	**0.34 [0.09, 0.59]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.69 (P = 0.007)								
17.1.4 Paliperidone 1.5mg/day versus 3-6mg/day								
SINGH2011	-9.8	16.31	54	-17.3	14.33	48	16.3%	0.48 [0.09, 0.88]
Subtotal (95% CI)			**54**			**48**	**16.3%**	**0.48 [0.09, 0.88]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.40 (P = 0.02)								
Total (95% CI)			**338**			**324**	**100.0%**	**0.25 [0.08, 0.42]**

Heterogeneity: Tau² = 0.00; Chi² = 3.49, df = 3 (P = 0.32); I² = 14%

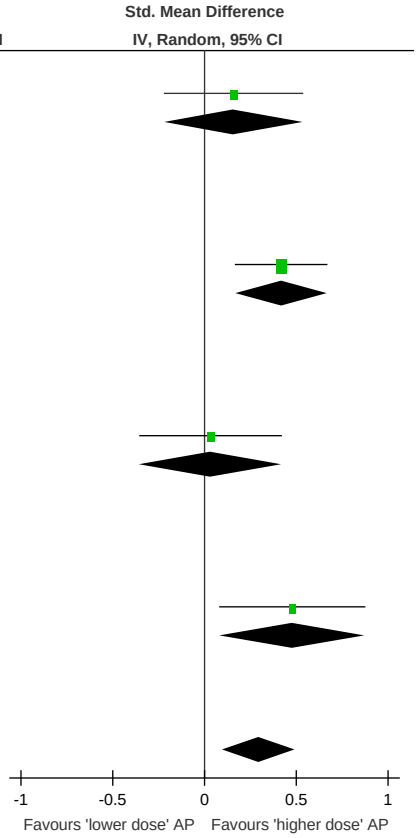
Test for overall effect: Z = 2.95 (P = 0.003)

Test for subgroup differences: Chi² = 3.49, df = 3 (P = 0.32), I² = 13.9%



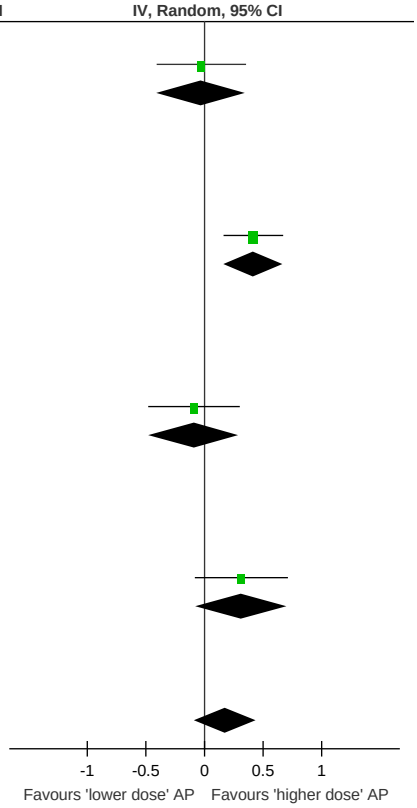
17.2 Mental state: mean change in positive symptoms (PANSS positive)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
17.3.1 Quetiapine 400mg/day versus 800mg/day								
AstraZenecaD1441C00112	-8.56	5.39	54	-9.34	4.35	55	21.4%	0.16 [-0.22, 0.53]
Subtotal (95% CI)			**54**			**55**	**21.4%**	**0.16 [-0.22, 0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.82 (P = 0.41)								
17.3.2 Risperidone 1-3mg/day versus 4-6mg/day								
HAAS2009	-4.8	6.26	131	-7.6	7.11	124	38.1%	0.42 [0.17, 0.67]
Subtotal (95% CI)			**131**			**124**	**38.1%**	**0.42 [0.17, 0.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.30 (P = 0.0010)								
17.3.3 Risperidone 0.15-0.6mg/day versus 1.5-6.0mg/day								
HASS2009B	-6.3	6.5	54	-6.5	5.4	50	20.6%	0.03 [-0.35, 0.42]
Subtotal (95% CI)			**54**			**50**	**20.6%**	**0.03 [-0.35, 0.42]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.17 (P = 0.87)								
17.3.4 Paliperidone 1.5mg/day versus 3-6mg/day								
SINGH2011	-3.1	6.53	54	-6	5.39	48	19.8%	0.48 [0.08, 0.87]
Subtotal (95% CI)			**54**			**48**	**19.8%**	**0.48 [0.08, 0.87]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.37 (P = 0.02)								
Total (95% CI)			**293**			**277**	**100.0%**	**0.29 [0.10, 0.49]**
Heterogeneity: Tau² = 0.01; Chi² = 4.03, df = 3 (P = 0.26); I² = 26%								
Test for overall effect: Z = 2.93 (P = 0.003)								
Test for subgroup differences: Chi² = 4.03, df = 3 (P = 0.26), I² = 25.6%								



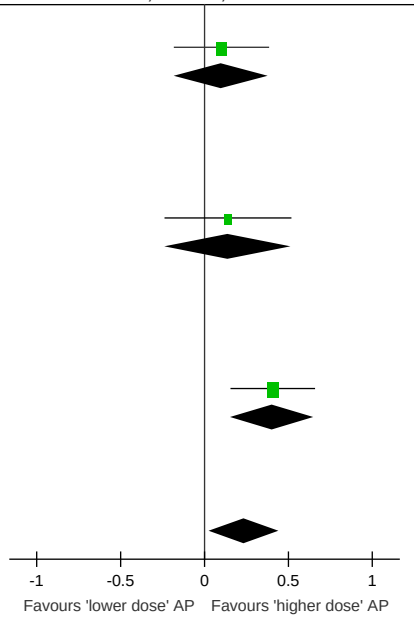
17.3 Mental state: mean change in negative symptoms (PANSS negative)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
17.4.1 Quetiapine 400mg/day versus 800mg/day								
AstraZenecaD1441C00112	-6.35	5.73	54	-6.21	4.58	55	23.2%	-0.03 [-0.40, 0.35]
Subtotal (95% CI)			**54**			**55**	**23.2%**	**-0.03 [-0.40, 0.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.14 (P = 0.89)								
17.4.2 Risperidone 1-3mg/day versus 4-6mg/day								
HAAS2009	-2.5	6.43	131	-5.5	7.88	124	32.0%	0.42 [0.17, 0.67]
Subtotal (95% CI)			**131**			**124**	**32.0%**	**0.42 [0.17, 0.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.29 (P = 0.0010)								
17.4.3 Risperidone 0.15-0.6mg/day versus 1.5-6.0mg/day								
HASS2009B	-5.4	6.1	54	-4.9	4.9	50	22.6%	-0.09 [-0.47, 0.30]
Subtotal (95% CI)			**54**			**50**	**22.6%**	**-0.09 [-0.47, 0.30]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.45 (P = 0.65)								
17.4.4 Paliperidone 1.5mg/day versus 3-6mg/day								
SINGH2011	-2.4	4.31	54	-3.7	3.85	48	22.2%	0.31 [-0.08, 0.71]
Subtotal (95% CI)			**54**			**48**	**22.2%**	**0.31 [-0.08, 0.71]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.58 (P = 0.11)								
Total (95% CI)			**293**			**277**	**100.0%**	**0.18 [-0.08, 0.44]**
Heterogeneity: Tau² = 0.04; Chi² = 6.79, df = 3 (P = 0.08); I² = 56%								
Test for overall effect: Z = 1.34 (P = 0.18)								
Test for subgroup differences: Chi² = 6.79, df = 3 (P = 0.08), I² = 55.8%								



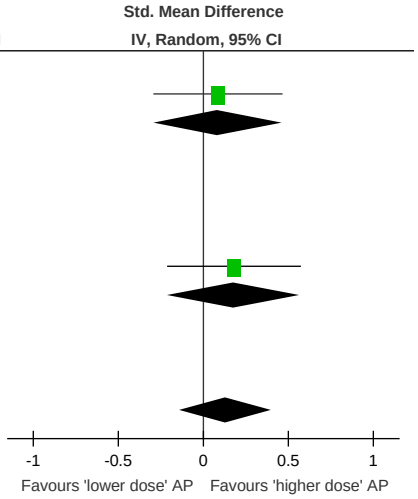
17.4 Global state (CGI-S)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
17.5.1 Aripriprazole 10mg/day versus 30mg/day								
FINDLING2008	-1.2	0.99	99	-1.3	0.98	97	35.4%	0.10 [-0.18, 0.38]
Subtotal (95% CI)			**99**			**97**	**35.4%**	**0.10 [-0.18, 0.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.71 (P = 0.48)								
17.5.2 Quetiapine 400mg/day versus 800mg/day								
AstraZenecaD1441C00112	-1.15	0.97	55	-1.28	0.87	55	23.4%	0.14 [-0.23, 0.51]
Subtotal (95% CI)			**55**			**55**	**23.4%**	**0.14 [-0.23, 0.51]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.73 (P = 0.46)								
17.5.3 Risperidone 1-4mg/day versus 4-6mg/day								
HAAS2009	-0.9	1.22	131	-1.4	1.23	124	41.2%	0.41 [0.16, 0.66]
Subtotal (95% CI)			**131**			**124**	**41.2%**	**0.41 [0.16, 0.66]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.21 (P = 0.001)								
Total (95% CI)			**285**			**276**	**100.0%**	**0.24 [0.03, 0.44]**
Heterogeneity: Tau² = 0.01; Chi² = 2.95, df = 2 (P = 0.23); I² = 32%								
Test for overall effect: Z = 2.25 (P = 0.02)								
Test for subgroup differences: Chi² = 2.95, df = 2 (P = 0.23), I² = 32.2%								



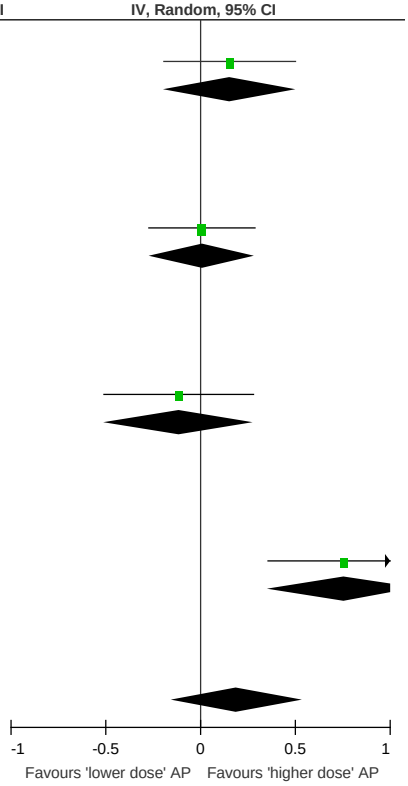
17.5 Depression (Positive and Negative Syndrome Scales: Depression; Anxiety and Depression)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
17.6.1 Quetiapine 400mg/day versus 800mg/day								
AstraZenecaD1441C00112	-2.96	2.31	54	-3.16	2.31	55	51.8%	0.09 [-0.29, 0.46]
Subtotal (95% CI)			**54**			**55**	**51.8%**	**0.09 [-0.29, 0.46]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.45 (P = 0.65)								
17.6.2 Paliperidone 1.5mg/day versus 3-6mg/day								
SINGH2011	-1.4	2.22	54	-1.9	3.25	48	48.2%	0.18 [-0.21, 0.57]
Subtotal (95% CI)			**54**			**48**	**48.2%**	**0.18 [-0.21, 0.57]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.91 (P = 0.36)								
Total (95% CI)			**108**			**103**	**100.0%**	**0.13 [-0.14, 0.40]**
Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 1 (P = 0.73); I² = 0%								
Test for overall effect: Z = 0.95 (P = 0.34)								
Test for subgroup differences: Chi² = 0.12, df = 1 (P = 0.73), I² = 0%								



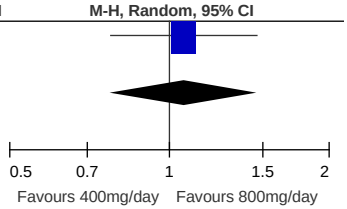
17.6 Psychosocial functioning (CGAS)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
17.7.1 Quetiapine 400mg/day versus 800mg/day								
AstraZenecaD1441C00112	-13.04	12.34	65	-14.94	12.22	63	25.3%	0.15 [-0.19, 0.50]
Subtotal (95% CI)			**65**			**63**	**25.3%**	**0.15 [-0.19, 0.50]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.87 (P = 0.39)								
17.7.2 Aripriprazole 10mg/day versus 30mg/day								
FINDLING2008	-14.7	14.92	99	-14.8	12.8	97	27.8%	0.01 [-0.27, 0.29]
Subtotal (95% CI)			**99**			**97**	**27.8%**	**0.01 [-0.27, 0.29]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.05 (P = 0.96)								
17.7.3 Risperidone 0.15-.06 mg/day versus 1.5-6.0 mg/day								
HASS2009B	16.9	16	51	18.9	18.4	48	23.6%	-0.12 [-0.51, 0.28]
Subtotal (95% CI)			**51**			**48**	**23.6%**	**-0.12 [-0.51, 0.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.57 (P = 0.57)								
17.7.4 Paliperidone 1.5mg/day versus 3-6mg/day								
SINGH2011	-4.4	10.72	54	-13.1	12.07	48	23.3%	0.76 [0.36, 1.16]
Subtotal (95% CI)			**54**			**48**	**23.3%**	**0.76 [0.36, 1.16]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.69 (P = 0.0002)								
Total (95% CI)			**269**			**256**	**100.0%**	**0.19 [-0.15, 0.54]**
Heterogeneity: Tau² = 0.09; Chi² = 11.50, df = 3 (P = 0.009); I² = 74%								
Test for overall effect: Z = 1.08 (P = 0.28)								
Test for subgroup differences: Chi² = 11.50, df = 3 (P = 0.009), I² = 73.9%								



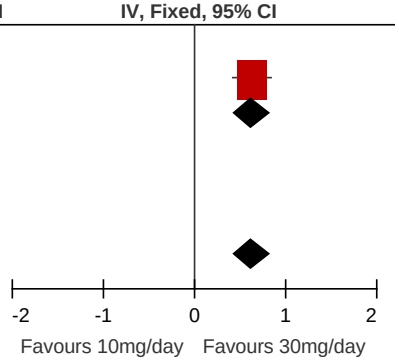
17.7 Response (CGI-I)

Study or Subgroup	Quetiapine 400mg/day Events	Total	Quetiapine 800mg/day Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
AstraZenecaD1441C00112	33	55	31	55	100.0%	1.06 [0.78, 1.46]
Total (95% CI)		**55**		**55**	**100.0%**	**1.06 [0.78, 1.46]**
Total events	33		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.39 (P = 0.70)						



17.8 Quality of life (Calculated using Total and Overall scores from the Paediatric Quality of Life Enjoyment and Satisfaction Questionnaire)

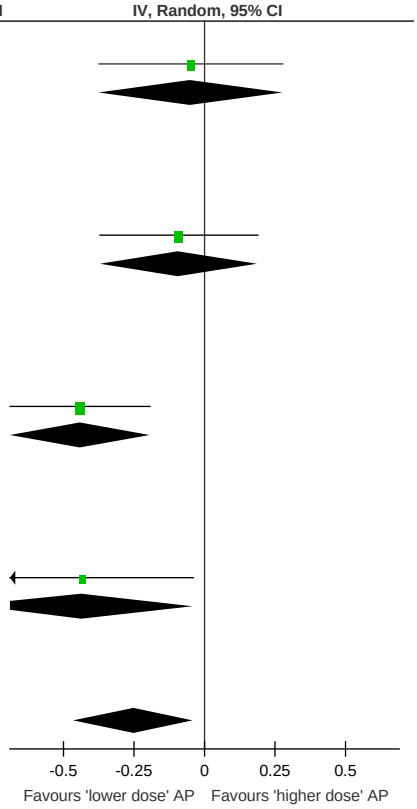
Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
17.17.1 Aripriprazole 10mg/day versus 30mg/day				
FINDLING2008	0.63	0.107143	100.0%	0.63 [0.42, 0.84]
Subtotal (95% CI)			**100.0%**	**0.63 [0.42, 0.84]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 5.88 (P < 0.00001)				
Total (95% CI)			**100.0%**	**0.63 [0.42, 0.84]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 5.88 (P < 0.00001)				
Test for subgroup differences: Not applicable				



18. 'Lower dose' antipsychotic medication versus 'higher dose' antipsychotic medication: post-treatment side effect outcomes

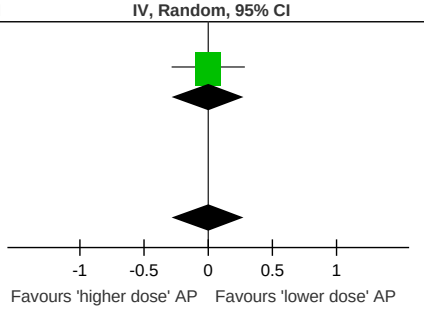
18.1 Mean change in weight (kg)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.1.1 Quetiapine 400mg vs 800mg								
AstraZenecaD1441C00112	1.4	1.2	72	1.5	2.63	73	23.4%	-0.05 [-0.37, 0.28]
Subtotal (95% CI)			**72**			**73**	**23.4%**	**-0.05 [-0.37, 0.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.29 (P = 0.77)								
18.1.2 Aripriprazole 10mg vs 30mg								
FINDLING2008A	0	2.1	99	0.2	2.3	97	27.3%	-0.09 [-0.37, 0.19]
Subtotal (95% CI)			**99**			**97**	**27.3%**	**-0.09 [-0.37, 0.19]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.63 (P = 0.53)								
18.1.3 Risperidone 1-3mg vs 4-6mg								
HAAS2009	1.7	3.29	132	3.2	3.49	125	30.5%	-0.44 [-0.69, -0.19]
Subtotal (95% CI)			**132**			**125**	**30.5%**	**-0.44 [-0.69, -0.19]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.49 (P = 0.0005)								
18.1.4 Paliperidone 1.5mg/day versus 3-6mg/day								
SINGH2011	0.3	1.52	54	1.1	2.13	48	18.7%	-0.43 [-0.83, -0.04]
Subtotal (95% CI)			**54**			**48**	**18.7%**	**-0.43 [-0.83, -0.04]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.16 (P = 0.03)								
Total (95% CI)			**357**			**343**	**100.0%**	**-0.25 [-0.46, -0.04]**
Heterogeneity: Tau² = 0.02; Chi² = 5.83, df = 3 (P = 0.12); I² = 49%								
Test for overall effect: Z = 2.32 (P = 0.02)								
Test for subgroup differences: Chi² = 5.83, df = 3 (P = 0.12), I² = 48.6%								



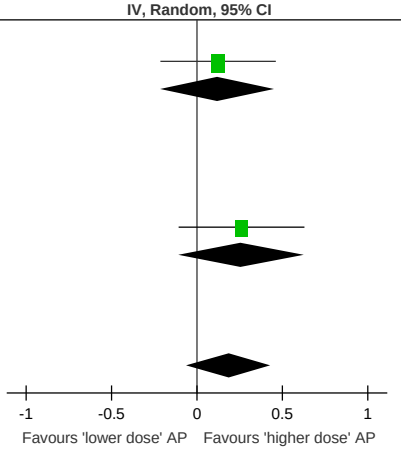
18.2 Mean change in BMI (kg/m2)

Study or Subgroup	'Higher dose' AP Mean	SD	Total	'Lower dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.2.1 Aripriprazole 10mg vs 30mg								
FINDLING2008A	0	0.8	99	0	0.8	97	100.0%	0.00 [-0.28, 0.28]
Subtotal (95% CI)			**99**			**97**	**100.0%**	**0.00 [-0.28, 0.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Total (95% CI)			**99**			**97**	**100.0%**	**0.00 [-0.28, 0.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (P = 1.00)								
Test for subgroup differences: Not applicable								



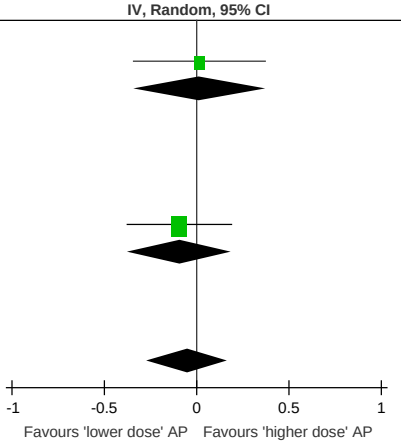
18.3 Side effects: mean change in fasting serum glucose level (mg/dl)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.4.1 Quetiapine 400mg vs 800mg								
AstraZenecaD1441C00112	-0.0735	12.07602	68	-1.4	9.08	70	54.4%	0.12 [-0.21, 0.46]
Subtotal (95% CI)			**68**			**70**	**54.4%**	**0.12 [-0.21, 0.46]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.73 (P = 0.47)								
18.4.2 Ariprirprazole 10mg vs 30mg								
FINDLING2008A	2.1	12.65	62	-0.98	10.57	55	45.6%	0.26 [-0.10, 0.63]
Subtotal (95% CI)			**62**			**55**	**45.6%**	**0.26 [-0.10, 0.63]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.40 (P = 0.16)								
Total (95% CI)			**130**			**125**	**100.0%**	**0.19 [-0.06, 0.43]**
Heterogeneity: Tau² = 0.00; Chi² = 0.30, df = 1 (P = 0.59); I² = 0%								
Test for overall effect: Z = 1.48 (P = 0.14)								
Test for subgroup differences: Chi² = 0.30, df = 1 (P = 0.59), I² = 0%								



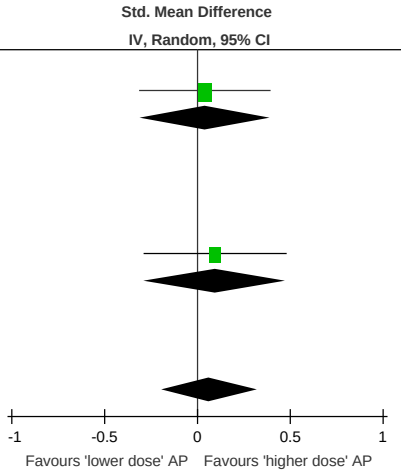
18.4 Side effects: mean change in fasting total cholesterol (mg/dl)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.5.1 Quetiapine 400mg vs 800mg								
AstraZenecaD1441C00112	7.8226	28.8231	62	7.4237	24.6571	59	38.6%	0.01 [-0.34, 0.37]
Subtotal (95% CI)			**62**			**59**	**38.6%**	**0.01 [-0.34, 0.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.08 (P = 0.94)								
18.5.2 Aripriprazole 10mg vs 30mg								
FINDLING2008A	-7.43	27.99	98	-5.01	23.28	95	61.4%	-0.09 [-0.38, 0.19]
Subtotal (95% CI)			**98**			**95**	**61.4%**	**-0.09 [-0.38, 0.19]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.65 (P = 0.52)								
Total (95% CI)			**160**			**154**	**100.0%**	**-0.05 [-0.27, 0.17]**
Heterogeneity: Tau² = 0.00; Chi² = 0.22, df = 1 (P = 0.64); I² = 0%								
Test for overall effect: Z = 0.46 (P = 0.65)								
Test for subgroup differences: Chi² = 0.22, df = 1 (P = 0.64), I² = 0%								



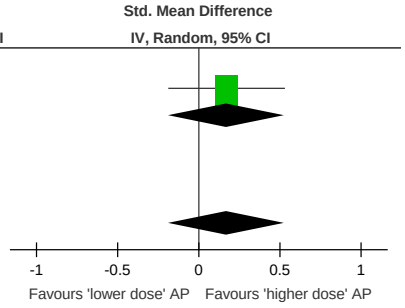
18.5 Side effects: mean change in fasting high-density lipoprotein cholesterol level (mg/dl)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.6.1 Quetiapine 400mg vs 800mg								
AstraZenecaD1441C00112	2.8226	9.24267	62	2.4603	8.95297	63	54.3%	0.04 [-0.31, 0.39]
Subtotal (95% CI)			**62**			**63**	**54.3%**	**0.04 [-0.31, 0.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.22 (P = 0.82)								
18.6.2 Aripriprazole 10mg vs 30mg								
FINDLING2008A	-0.13	6.99	47	-0.9667	9.90115	60	45.7%	0.09 [-0.29, 0.48]
Subtotal (95% CI)			**47**			**60**	**45.7%**	**0.09 [-0.29, 0.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.49 (P = 0.63)								
Total (95% CI)			**109**			**123**	**100.0%**	**0.06 [-0.19, 0.32]**
Heterogeneity: Tau² = 0.00; Chi² = 0.04, df = 1 (P = 0.83); I² = 0%								
Test for overall effect: Z = 0.49 (P = 0.62)								
Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.83), I² = 0%								



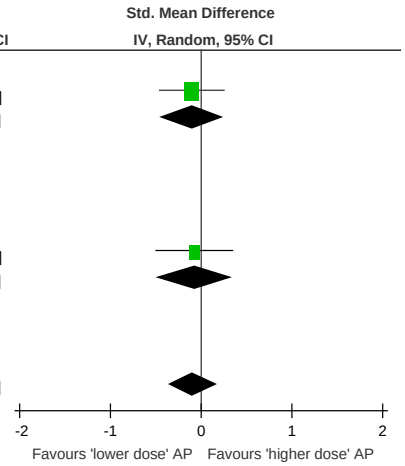
18.6 Side effects: mean change in low- density lipoprotein cholesterol level (mg/dl)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.7.1 Quetiapine 400mg vs 800mg								
AstraZenecaD1441C00112	8.6613	22.73579	62	4.8167	21.78515	60	100.0%	0.17 [-0.18, 0.53]
Subtotal (95% CI)			**62**			**60**	**100.0%**	**0.17 [-0.18, 0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.95 (P = 0.34)								
Total (95% CI)			**62**			**60**	**100.0%**	**0.17 [-0.18, 0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.95 (P = 0.34)								
Test for subgroup differences: Not applicable								



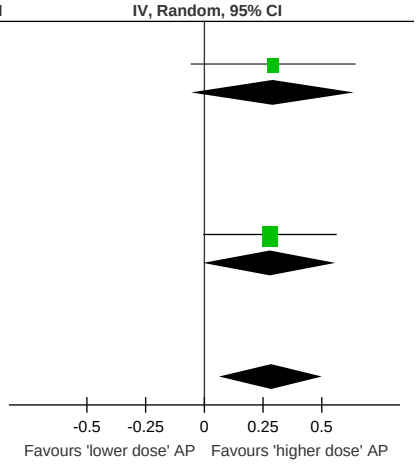
18.7 Side effects: mean change in fasting triglycerides (mg/dl)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.8.1 Quetiapine 400mg vs 800mg								
AstraZenecaD1441C00112	9.6613	64.77172	62	15.5833	47.94357	60	58.5%	-0.10 [-0.46, 0.25]
Subtotal (95% CI)			**62**			**60**	**58.5%**	**-0.10 [-0.46, 0.25]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.57 (P = 0.57)								
18.8.2 Aripriprazole 10mg vs 30mg								
FINDLING2008A	-4.53	48.72	47	-0.73	51.85	40	41.5%	-0.08 [-0.50, 0.35]
Subtotal (95% CI)			**47**			**40**	**41.5%**	**-0.08 [-0.50, 0.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.35 (P = 0.73)								
Total (95% CI)			**109**			**100**	**100.0%**	**-0.09 [-0.36, 0.18]**
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.92); I² = 0%								
Test for overall effect: Z = 0.66 (P = 0.51)								
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.92), I² = 0%								



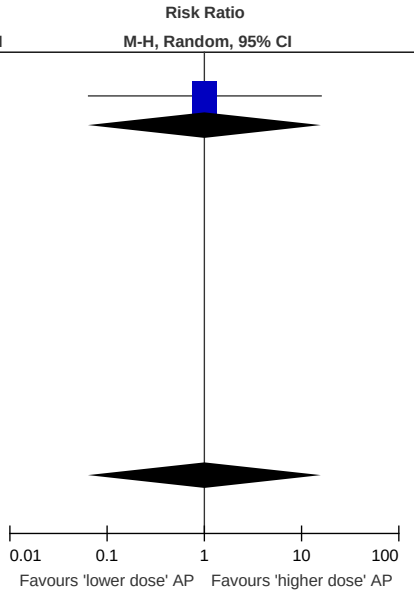
18.8 Side effects: mean change in QT interval (msec)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.9.1 Quetiapine 400mg vs 800mg								
AstraZenecaD1441C00112	-4.88	26.39	64	-12.97	28.46	64	39.5%	0.29 [-0.06, 0.64]
Subtotal (95% CI)			**64**			**64**	**39.5%**	**0.29 [-0.06, 0.64]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.65 (P = 0.10)								
18.9.2 Aripriprazole 10mg vs 30mg								
FINDLING2008A	0	14	99	-5.4	23.4	97	60.5%	0.28 [-0.00, 0.56]
Subtotal (95% CI)			**99**			**97**	**60.5%**	**0.28 [-0.00, 0.56]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.95 (P = 0.05)								
Total (95% CI)			**163**			**161**	**100.0%**	**0.28 [0.07, 0.50]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.95); I² = 0%								
Test for overall effect: Z = 2.55 (P = 0.01)								
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.95), I² = 0%								



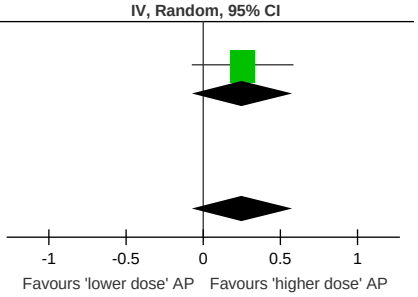
18.9 Side effects: mean change in prolonged QT interval (msec)

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.10.1 Quetiapine 400mg vs 800mg						
AstraZenecaD1441C00112	1	73	1	74	100.0%	1.01 [0.06, 15.90]
Subtotal (95% CI)		**73**		**74**	**100.0%**	**1.01 [0.06, 15.90]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						
18.10.2 Paliperidone 1.5mg/day versus 3-6mg/day						
SINGH2011	0	54	0	48		Not estimable
Subtotal (95% CI)		**54**		**48**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**127**		**122**	**100.0%**	**1.01 [0.06, 15.90]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.01 (P = 0.99)						
Test for subgroup differences: Not applicable						



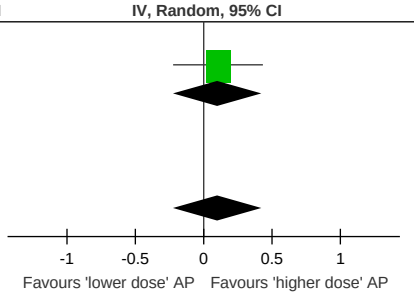
18.10 Side effects: mean change in systolic BP (mm Hg)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.11.1 Quetiapine 400mg vs 800mg								
AstraZenecaD1441C00112	2.3	10.78	73	-0.4	10.26	74	100.0%	0.26 [-0.07, 0.58]
Subtotal (95% CI)			**73**			**74**	**100.0%**	**0.26 [-0.07, 0.58]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.54 (P = 0.12)								
Total (95% CI)			**73**			**74**	**100.0%**	**0.26 [-0.07, 0.58]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.54 (P = 0.12)								
Test for subgroup differences: Not applicable								



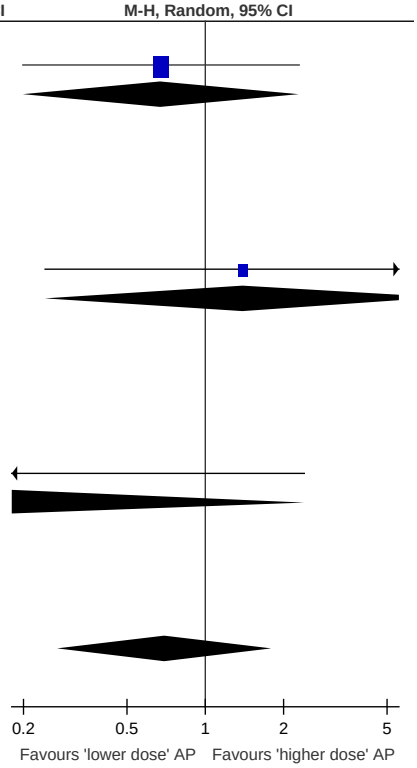
18.11 Side effects: mean change in diastolic blood pressure (mm Hg)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.12.1 Quetiapine 400mg vs 800mg								
AstraZenecaD1441C00112	2.1	8.65	73	1.1	10.24	74	100.0%	0.10 [-0.22, 0.43]
Subtotal (95% CI)			**73**			**74**	**100.0%**	**0.10 [-0.22, 0.43]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.64 (P = 0.53)								
Total (95% CI)			**73**			**74**	**100.0%**	**0.10 [-0.22, 0.43]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.64 (P = 0.53)								
Test for subgroup differences: Not applicable								



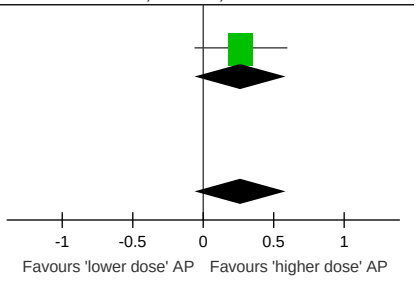
18.12 Side effects: tachycardia

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.13.1 Quetiapine 400mg vs 800mg						
AstraZenecaD1441C00112	4	73	6	74	60.1%	0.68 [0.20, 2.30]
Subtotal (95% CI)		**73**		**74**	**60.1%**	**0.68 [0.20, 2.30]**
Total events	4		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.63 (P = 0.53)						
18.13.2 Risperidone 1-3mg vs 4-6mg						
HAAS2009B	3	55	2	51	29.4%	1.39 [0.24, 7.99]
Subtotal (95% CI)		**55**		**51**	**29.4%**	**1.39 [0.24, 7.99]**
Total events	3		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.37 (P = 0.71)						
18.13.3 Paliperidone 1.5mg/day versus 3-6mg/day						
SINGH2011	0	54	3	48	10.4%	0.13 [0.01, 2.40]
Subtotal (95% CI)		**54**		**48**	**10.4%**	**0.13 [0.01, 2.40]**
Total events	0		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.38 (P = 0.17)						
Total (95% CI)		**182**		**173**	**100.0%**	**0.70 [0.27, 1.81]**
Total events	7		11			
Heterogeneity: Tau² = 0.00; Chi² = 1.94, df = 2 (P = 0.38); I² = 0%						
Test for overall effect: Z = 0.73 (P = 0.47)						
Test for subgroup differences: Chi² = 1.89, df = 2 (P = 0.39), I² = 0%						



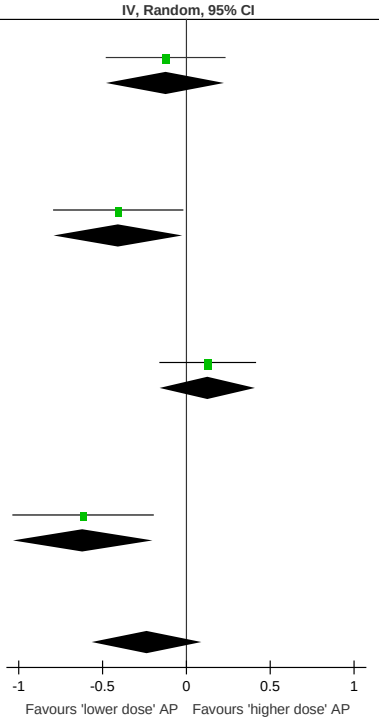
18.13 Side effects: mean change in standing pulse (beats/min)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.14.1 Quetiapine 400mg vs 800mg								
AstraZenecaD1441C00112	6.3	13.12	73	2.2	17.08	74	100.0%	0.27 [-0.06, 0.59]
Subtotal (95% CI)			**73**			**74**	**100.0%**	**0.27 [-0.06, 0.59]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.61 (P = 0.11)								
Total (95% CI)			**73**			**74**	**100.0%**	**0.27 [-0.06, 0.59]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.61 (P = 0.11)								
Test for subgroup differences: Not applicable								



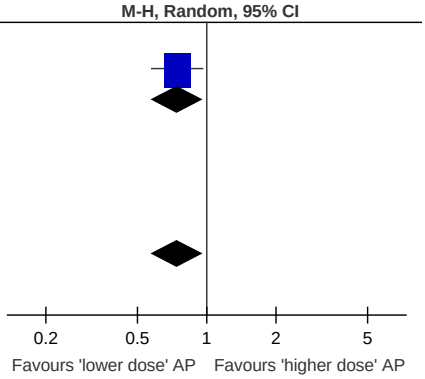
18.14 Side effects: mean change in prolactin level (mg/dl)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.15.1 Quetiapine 400mg vs 800mg								
AstraZenecaD1441C00112	-10.5476	16.12225	63	-7.8333	26.47357	60	25.3%	-0.12 [-0.48, 0.23]
Subtotal (95% CI)			**63**			**60**	**25.3%**	**-0.12 [-0.48, 0.23]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.69 (P = 0.49)								
18.15.2 Risperidone 1-3mg vs 4-6mg								
HAAS2009B	25.5	32.859	55	40.37255	39.717708	51	23.9%	-0.41 [-0.79, -0.02]
Subtotal (95% CI)			**55**			**51**	**23.9%**	**-0.41 [-0.79, -0.02]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.07 (P = 0.04)								
18.15.3 Aripriprazole 10mg vs 30mg								
FINDLING2008A	-11.93	23.29	98	-15.14	26.87	92	28.2%	0.13 [-0.16, 0.41]
Subtotal (95% CI)			**98**			**92**	**28.2%**	**0.13 [-0.16, 0.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.88 (P = 0.38)								
18.15.4 Paliperidone 1.5mg/day versus 3-6mg/day								
SINGH2011	29.173922	22.606218	51	43.778571	24.565112	42	22.6%	-0.62 [-1.03, -0.20]
Subtotal (95% CI)			**51**			**42**	**22.6%**	**-0.62 [-1.03, -0.20]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.89 (P = 0.004)								
Total (95% CI)			**267**			**245**	**100.0%**	**-0.23 [-0.56, 0.09]**
Heterogeneity: Tau² = 0.08; Chi² = 10.07, df = 3 (P = 0.02); I² = 70%								
Test for overall effect: Z = 1.39 (P = 0.16)								
Test for subgroup differences: Chi² = 10.07, df = 3 (P = 0.02), I² = 70.2%								



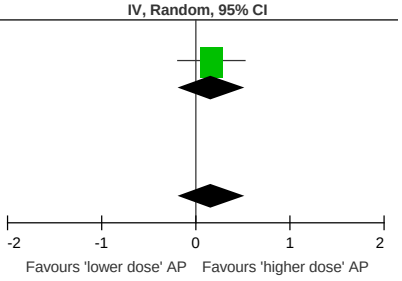
18.15 Side effects: elevated prolactin level (mg/dl)

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.16.1 Risperidone 1-3mg vs 4-6mg						
HAAS2009	55	132	70	125	100.0%	0.74 [0.58, 0.96]
Subtotal (95% CI)		**132**		**125**	**100.0%**	**0.74 [0.58, 0.96]**
Total events	55		70			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.27 (P = 0.02)						
Total (95% CI)		**132**		**125**	**100.0%**	**0.74 [0.58, 0.96]**
Total events	55		70			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.27 (P = 0.02)						
Test for subgroup differences: Not applicable						



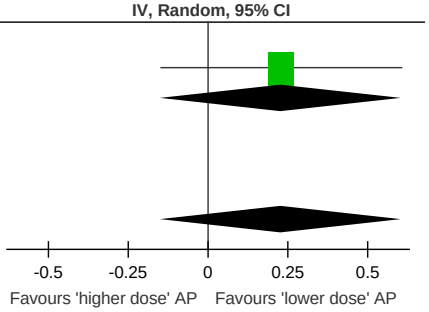
18.16 Side effects: mean change in insulin level (mg/dl)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.17.1 Quetiapine 400mg vs 80mg								
AstraZenecaD1441C00112	4.2742	19.25938	62	1.2203	17.29567	59	100.0%	0.17 [-0.19, 0.52]
Subtotal (95% CI)			**62**			**59**	**100.0%**	**0.17 [-0.19, 0.52]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.91 (P = 0.36)								
Total (95% CI)			**62**			**59**	**100.0%**	**0.17 [-0.19, 0.52]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.91 (P = 0.36)								
Test for subgroup differences: Not applicable								



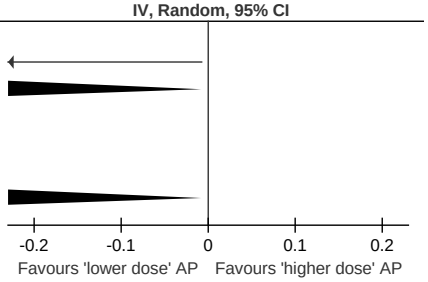
18.17 Side effects: extra pyramidal (mean change in AIMS scores)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.18.1 Risperidone 1-3mg vs 4-6mg								
HAAS2009B	0.1	2	55	-0.3	1.4	54	100.0%	0.23 [-0.15, 0.61]
Subtotal (95% CI)			**55**			**54**	**100.0%**	**0.23 [-0.15, 0.61]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.20 (P = 0.23)								
Total (95% CI)			**55**			**54**	**100.0%**	**0.23 [-0.15, 0.61]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.20 (P = 0.23)								
Test for subgroup differences: Not applicable								



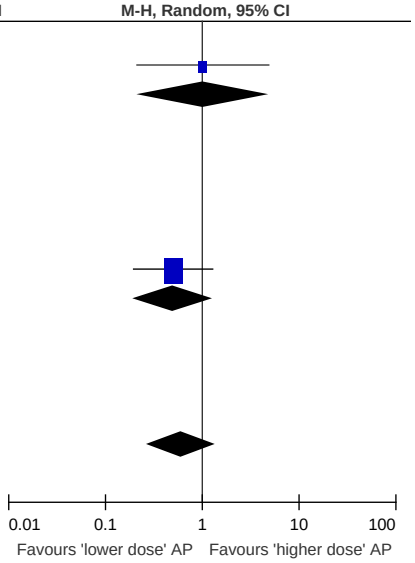
18.18 Side effects: extra pyramidal (mean change in SAS scores)

Study or Subgroup	'Lower dose' AP Mean	SD	Total	'Higher dose' AP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
18.19.1 Risperidone 1-3mg vs 4-6mg								
HAAS2009B	0	0.2	55	0.1	0.3	51	100.0%	-0.39 [-0.78, -0.01]
Subtotal (95% CI)			**55**			**51**	**100.0%**	**-0.39 [-0.78, -0.01]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.00 (P = 0.05)								
Total (95% CI)			**55**			**51**	**100.0%**	**-0.39 [-0.78, -0.01]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.00 (P = 0.05)								
Test for subgroup differences: Not applicable								



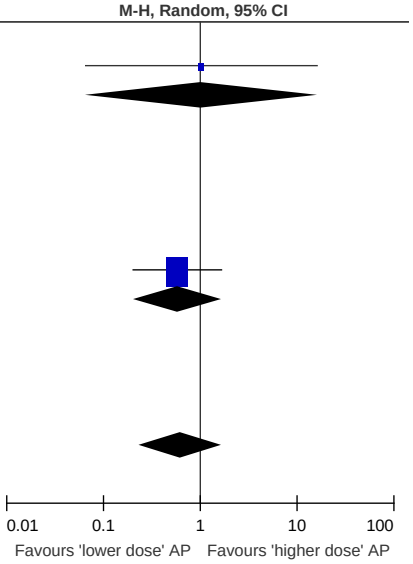
18.19 Side effects: akathesia

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.21.1 Quetiapine 400mg vs 800mg						
AstraZenecaD1441C00112	3	73	3	74	26.5%	1.01 [0.21, 4.86]
Subtotal (95% CI)		**73**		**74**	**26.5%**	**1.01 [0.21, 4.86]**
Total events	3		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.99)						
18.21.2 Aripriprazole 10mg vs 30mg						
FINDLING2008A	6	100	12	100	73.5%	0.50 [0.20, 1.28]
Subtotal (95% CI)		**100**		**100**	**73.5%**	**0.50 [0.20, 1.28]**
Total events	6		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.45 (P = 0.15)						
Total (95% CI)		**173**		**174**	**100.0%**	**0.60 [0.27, 1.35]**
Total events	9		15			
Heterogeneity: Tau² = 0.00; Chi² = 0.57, df = 1 (P = 0.45); I² = 0%						
Test for overall effect: Z = 1.23 (P = 0.22)						
Test for subgroup differences: Chi² = 0.57, df = 1 (P = 0.45), I² = 0%						



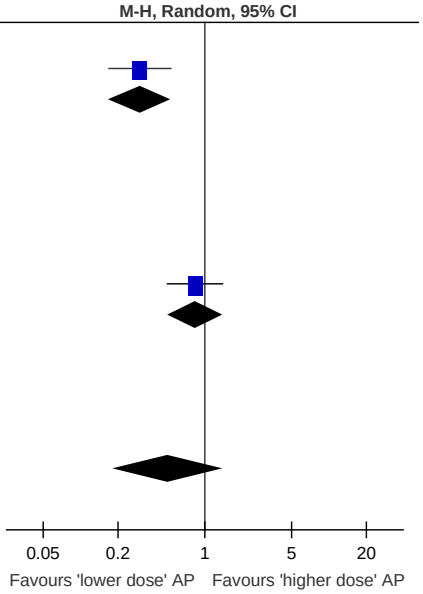
18.20 Side effects: extra pyramidal disorder

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.22.1 Quetiapine 400mg vs 800mg						
AstraZenecaD1441C00112	1	73	1	75	12.7%	1.03 [0.07, 16.12]
Subtotal (95% CI)		**73**		**75**	**12.7%**	**1.03 [0.07, 16.12]**
Total events	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (P = 0.98)						
18.22.2 Risperidone 1-3mg/day versus 4-6mg/day						
HAAS2009B	5	55	8	51	87.3%	0.58 [0.20, 1.66]
Subtotal (95% CI)		**55**		**51**	**87.3%**	**0.58 [0.20, 1.66]**
Total events	5		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						
Total (95% CI)		**128**		**126**	**100.0%**	**0.62 [0.23, 1.66]**
Total events	6		9			
Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%						
Test for overall effect: Z = 0.94 (P = 0.35)						
Test for subgroup differences: Chi² = 0.15, df = 1 (P = 0.70), I² = 0%						



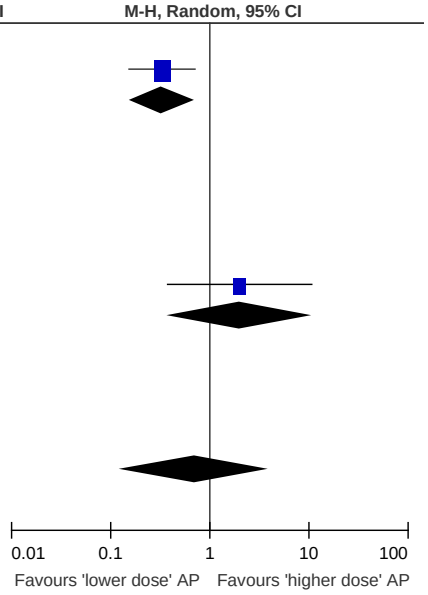
18.21 Side effects: extra pyramidal symptoms

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.23.1 0.15-0.6mg vs 1.5-6mg						
HAAS2009	13	132	41	125	49.2%	0.30 [0.17, 0.53]
Subtotal (95% CI)		**132**		**125**	**49.2%**	**0.30 [0.17, 0.53]**
Total events	13		41			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.11 (P < 0.0001)						
18.23.2 1-3mg vs 4-6mg						
HAAS2009B	18	55	20	51	50.8%	0.83 [0.50, 1.39]
Subtotal (95% CI)		**55**		**51**	**50.8%**	**0.83 [0.50, 1.39]**
Total events	18		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
Total (95% CI)		**187**		**176**	**100.0%**	**0.50 [0.18, 1.41]**
Total events	31		61			
Heterogeneity: Tau² = 0.47; Chi² = 7.12, df = 1 (P = 0.008); I² = 86%						
Test for overall effect: Z = 1.31 (P = 0.19)						
Test for subgroup differences: Chi² = 6.81, df = 1 (P = 0.009), I² = 85.3%						



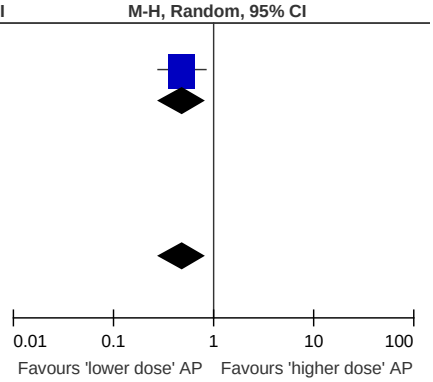
18.22 Side effects: dystonia

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.24.1 Risperidone 1-3mg vs 4-6mg						
HAAS2009	8	132	23	125	58.9%	0.33 [0.15, 0.71]
Subtotal (95% CI)		**132**		**125**	**58.9%**	**0.33 [0.15, 0.71]**
Total events	8		23			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.84 (P = 0.005)						
18.24.2 Aripriprazole 10mg vs 30mg						
FINDLING2008A	4	100	2	100	41.1%	2.00 [0.37, 10.67]
Subtotal (95% CI)		**100**		**100**	**41.1%**	**2.00 [0.37, 10.67]**
Total events	4		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.81 (P = 0.42)						
Total (95% CI)		**232**		**225**	**100.0%**	**0.69 [0.12, 3.94]**
Total events	12		25			
Heterogeneity: Tau² = 1.19; Chi² = 3.69, df = 1 (P = 0.05); I² = 73%						
Test for overall effect: Z = 0.42 (P = 0.68)						
Test for subgroup differences: Chi² = 3.68, df = 1 (P = 0.05), I² = 72.9%						



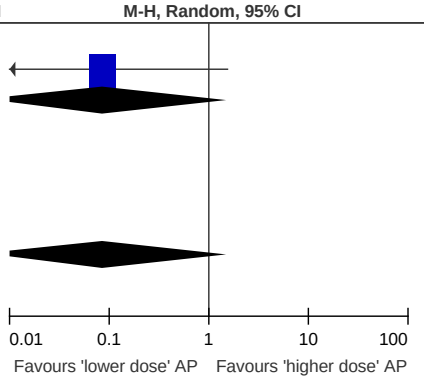
18.23 Side effects: parkinsonism

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.25.1 Aripriprazole 10mg vs 30mg						
FINDLING2008A	15	100	31	100	100.0%	0.48 [0.28, 0.84]
Subtotal (95% CI)		**100**		**100**	**100.0%**	**0.48 [0.28, 0.84]**
Total events	15		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.58 (P = 0.010)						
Total (95% CI)		**100**		**100**	**100.0%**	**0.48 [0.28, 0.84]**
Total events	15		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.58 (P = 0.010)						
Test for subgroup differences: Not applicable						



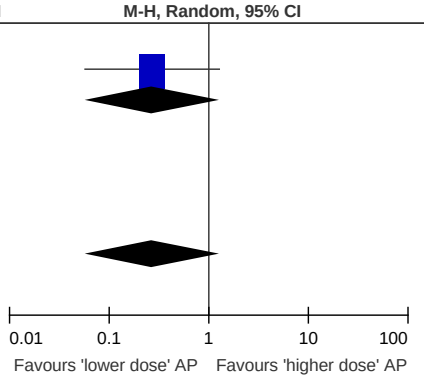
18.24 Side effects: parkinsonism symptoms

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.26.1 Risperidone 0.15-0.6mg vs 1.5-6.0mg						
HAAS2009	0	132	5	125	100.0%	0.09 [0.00, 1.54]
Subtotal (95% CI)		**132**		**125**	**100.0%**	**0.09 [0.00, 1.54]**
Total events	0		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.67 (P = 0.10)						
Total (95% CI)		**132**		**125**	**100.0%**	**0.09 [0.00, 1.54]**
Total events	0		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.67 (P = 0.10)						
Test for subgroup differences: Not applicable						



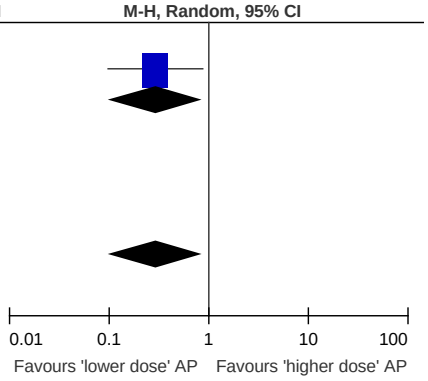
18.25 Side effects: dyskinesia

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.28.1 Risperidone 0.15-0.6mg vs 1.5-6.0mg						
HAAS2009	2	132	7	125	100.0%	0.27 [0.06, 1.28]
Subtotal (95% CI)		**132**		**125**	**100.0%**	**0.27 [0.06, 1.28]**
Total events	2		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.65 (P = 0.10)						
Total (95% CI)		**132**		**125**	**100.0%**	**0.27 [0.06, 1.28]**
Total events	2		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.65 (P = 0.10)						
Test for subgroup differences: Not applicable						



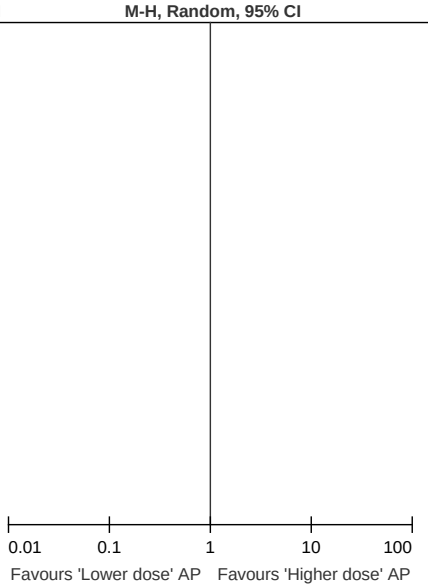
18.26 Side effects: tremor

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.29.1 Risperidone 0.15-0.6mg vs 1.5-6.0mg						
HAAS2009	4	132	13	125	100.0%	0.29 [0.10, 0.87]
Subtotal (95% CI)		**132**		**125**	**100.0%**	**0.29 [0.10, 0.87]**
Total events	4		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.21 (P = 0.03)						
Total (95% CI)		**132**		**125**	**100.0%**	**0.29 [0.10, 0.87]**
Total events	4		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.21 (P = 0.03)						
Test for subgroup differences: Not applicable						



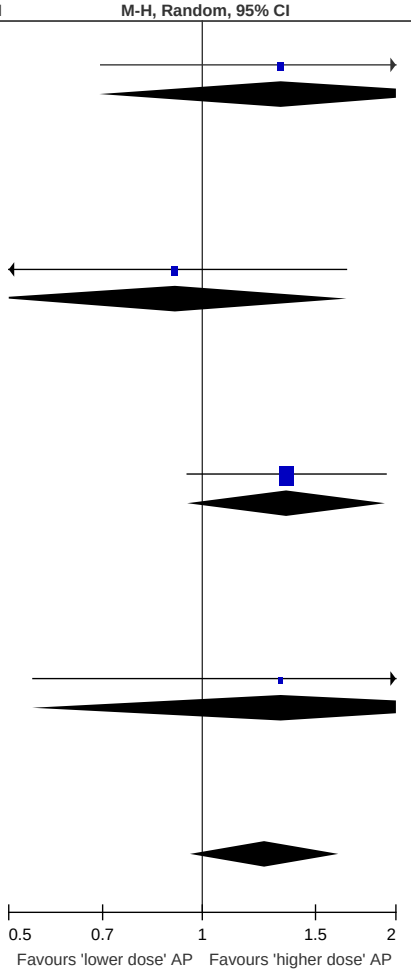
18.27 Side effects: mortality (including suicide)

Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.30.1 Risperidone 1-3mg vs 4-6mg						
HAAS2009B	0	55	0	51		Not estimable
Subtotal (95% CI)		**55**		**51**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
18.30.2 Aripriprazole 10mg vs 30mg						
FINDLING2008A	0	100	0	100		Not estimable
Subtotal (95% CI)		**100**		**100**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**155**		**151**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



18.28 Leaving the study early for any reason

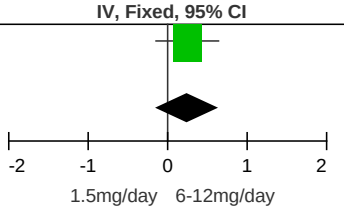
Study or Subgroup	'Lower dose' AP Events	Total	'Higher dose' AP Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
18.49.1 Quetiapine 400mg vs 800 mg						
AstraZenecaD1441C00112	17	73	13	74	16.9%	1.33 [0.70, 2.53]
Subtotal (95% CI)		**73**		**74**	**16.9%**	**1.33 [0.70, 2.53]**
Total events	17		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.86 (P = 0.39)						
18.49.2 Aripriprazole 10mg vs 30mg						
FINDLING2008A	16	100	18	102	18.6%	0.91 [0.49, 1.68]
Subtotal (95% CI)		**100**		**102**	**18.6%**	**0.91 [0.49, 1.68]**
Total events	16		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.31 (P = 0.75)						
18.49.3 Risperidone 0.15-0.6mg vs 1.5-6.0mg						
HAAS2009	50	132	35	125	55.5%	1.35 [0.95, 1.93]
Subtotal (95% CI)		**132**		**125**	**55.5%**	**1.35 [0.95, 1.93]**
Total events	50		35			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.66 (P = 0.10)						
18.49.4 Risperidone 1-3mg vs 4-6mg						
HAAS2009B	10	55	7	51	8.9%	1.32 [0.55, 3.22]
Subtotal (95% CI)		**55**		**51**	**8.9%**	**1.32 [0.55, 3.22]**
Total events	10		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.62 (P = 0.53)						
Total (95% CI)		**360**		**352**	**100.0%**	**1.25 [0.96, 1.63]**
Total events	93		73			
Heterogeneity: Tau² = 0.00; Chi² = 1.29, df = 3 (P = 0.73); I² = 0%						
Test for overall effect: Z = 1.64 (P = 0.10)						
Test for subgroup differences: Chi² = 1.29, df = 3 (P = 0.73), I² = 0%						



19. 'Lower dose' paliperidone (1.5mg/day) versus additional (high dose) paliperidone (6-12mg/day): post-treatment efficacy outcomes

19.1 Mental state: mean change in total symptoms (PANSS)

Study or Subgroup	1.5mg/day Mean	SD	Total	6-12mg/day Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
SINGH2011	-9.8	16.31	54	-13.8	15.74	47	100.0%	0.25 [-0.15, 0.64]
Total (95% CI)			**54**			**47**	**100.0%**	**0.25 [-0.15, 0.64]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.24 (P = 0.22)								

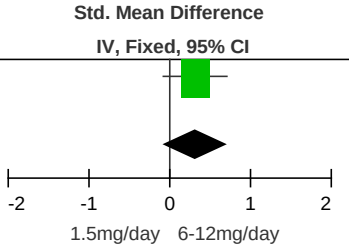


19.2 Mental state: mean change in positive symptoms (PANSS positive)

	1.5mg/day			6-12mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
SINGH2011	-3.1	6.53	54	-5	5.3	47	100.0%	0.31 [-0.08, 0.71]
Total (95% CI)			**54**			**47**	**100.0%**	**0.31 [-0.08, 0.71]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.57 (P = 0.12)

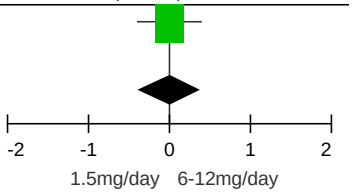


19.3 Mental state: mean change in negative symptoms (PANSS negative)

	1.5mg/day			6-12mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
SINGH2011	-2.4	4.31	54	-2.4	5.56	47	100.0%	0.00 [-0.39, 0.39]
Total (95% CI)			**54**			**47**	**100.0%**	**0.00 [-0.39, 0.39]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)

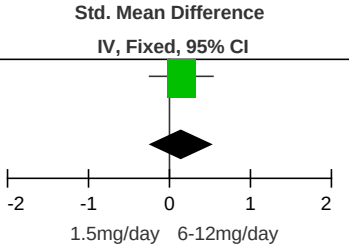


19.4 Mean change in depression (Positive and Negative Syndrome Scale - Anxiety and Depression)

	1.5mg/day			6-12mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
SINGH2011	-1.4	2.22	54	-1.8	3.19	47	100.0%	0.15 [-0.25, 0.54]
Total (95% CI)			**54**			**47**	**100.0%**	**0.15 [-0.25, 0.54]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.73 (P = 0.46)

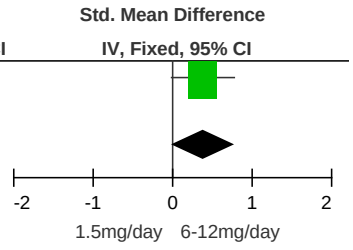


19.5 Mean change in psychosocial functioning (CGAS)

	1.5mg/day			6-12mg/day				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
SINGH2011	-4.4	10.72	54	-8.6	11.18	47	100.0%	0.38 [-0.01, 0.78]
Total (95% CI)			**54**			**47**	**100.0%**	**0.38 [-0.01, 0.78]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.89 (P = 0.06)



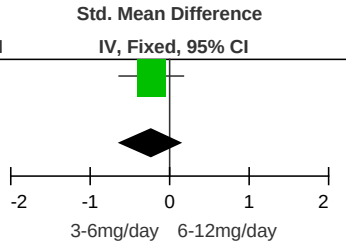
20. 'Higher dose' paliperidone (3-6mg/day) versus additional (high dose) paliperidone (6-12mg/day): post-treatment efficacy outcomes

20.1 Mental state: mean change in total symptoms (PANSS)

Study or Subgroup	3-6mg/day Mean	SD	Total	6-12mg/day Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
SINGH2011	-17.3	14.33	48	-13.8	15.74	47	100.0%	-0.23 [-0.63, 0.17]
Total (95% CI)			**48**			**47**	**100.0%**	**-0.23 [-0.63, 0.17]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.12 (P = 0.26)

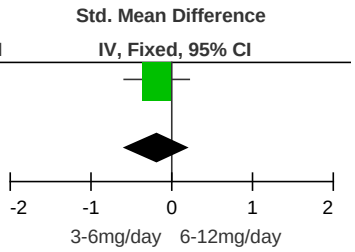


20.2 Mental state: mean change in positive symptoms (PANSS positive)

Study or Subgroup	3-6mg/day Mean	SD	Total	6-12mg/day Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
SINGH2011	-6	5.39	48	-5	5.3	47	100.0%	-0.19 [-0.59, 0.22]
Total (95% CI)			**48**			**47**	**100.0%**	**-0.19 [-0.59, 0.22]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.90 (P = 0.37)

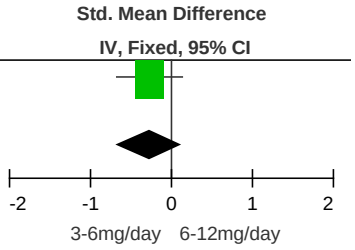


20.3 Mental state: mean change in negative symptoms (PANSS negative)

Study or Subgroup	3-6mg/day Mean	SD	Total	6-12mg/day Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
SINGH2011	-3.7	3.85	48	-2.4	5.56	47	100.0%	-0.27 [-0.67, 0.13]
Total (95% CI)			**48**			**47**	**100.0%**	**-0.27 [-0.67, 0.13]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.31 (P = 0.19)

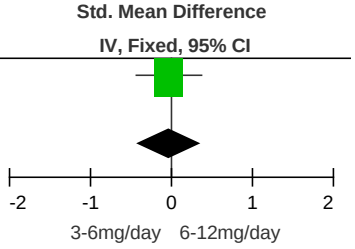


20.4 Mean change in depression (Positive and Negative Syndrome Scale - Anxiety and Depression)

Study or Subgroup	3-6mg/day Mean	SD	Total	6-12mg/day Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
SINGH2011	-1.9	3.25	48	-1.8	3.19	47	100.0%	-0.03 [-0.43, 0.37]
Total (95% CI)			**48**			**47**	**100.0%**	**-0.03 [-0.43, 0.37]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.15 (P = 0.88)

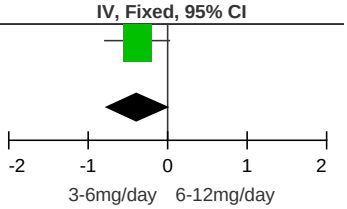


20.5 Mean change in psychosocial functioning (CGAS)

Study or Subgroup	3-6mg/day Mean	SD	Total	6-12mg/day Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
SINGH2011	-13.1	12.07	48	-8.6	11.18	47	100.0%	-0.38 [-0.79, 0.02]
Total (95% CI)			**48**			**47**	**100.0%**	**-0.38 [-0.79, 0.02]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.85 (P = 0.06)



21. 'Lower dose' paliperidone (1.5mg/day) versus additional (high dose) paliperidone (6-12mg/day): post-treatment side effect outcomes

21.1 Side effects: mean change in weight (kg)

Study or Subgroup	1.5mg/day Mean	SD	Total	6-12mg/day Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
22.2.4 Paliperidone 1.5mg/day versus 6-12mg/day								
SINGH2011	0.3	1.52	54	1.4	2.16	47	100.0%	-0.59 [-0.99, -0.19]
Subtotal (95% CI)			**54**			**47**	**100.0%**	**-0.59 [-0.99, -0.19]**

Heterogeneity: Not applicable

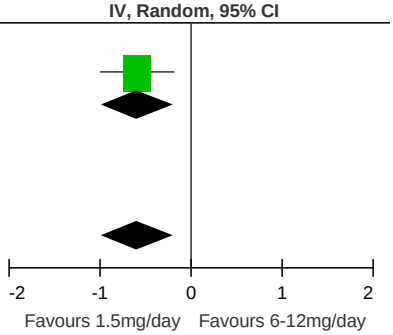
Test for overall effect: Z = 2.90 (P = 0.004)

Total (95% CI)			**54**			**47**	**100.0%**	**-0.59 [-0.99, -0.19]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.90 (P = 0.004)

Test for subgroup differences: Not applicable



21.2 Side effects: prolonged QT interval (msec)

Study or Subgroup	1.5mg/day Events	Total	6-12mg/day Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
22.11.2 Paliperidone 1.5mg/day versus 6-12mg/day						
SINGH2011	0	54	0	47		Not estimable
Subtotal (95% CI)		**54**		**47**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable

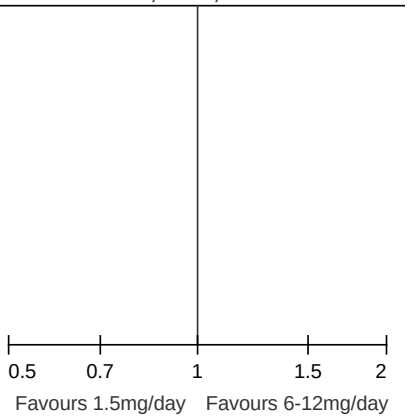
Test for overall effect: Not applicable

Total (95% CI)		**54**		**47**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable

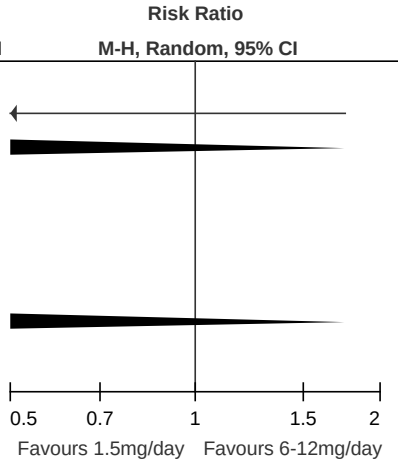
Test for overall effect: Not applicable

Test for subgroup differences: Not applicable



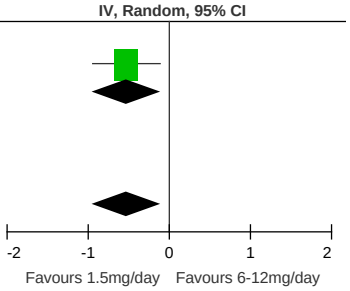
21.3 Side effects: tachycardia

Study or Subgroup	1.5mg/day Events	1.5mg/day Total	6-12mg/day Events	6-12mg/day Total	Weight	Risk Ratio M-H, Random, 95% CI
22.15.3 Paliperidone 1.5mg/day versus 6-12mg/day						
SINGH2011	0	54	4	47	100.0%	0.10 [0.01, 1.76]
Subtotal (95% CI)		**54**		**47**	**100.0%**	**0.10 [0.01, 1.76]**
Total events	0		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.58 (P = 0.11)						
Total (95% CI)		**54**		**47**	**100.0%**	**0.10 [0.01, 1.76]**
Total events	0		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.58 (P = 0.11)						
Test for subgroup differences: Not applicable						



21.4 Side effects: mean change in prolactin level (mg/dl)

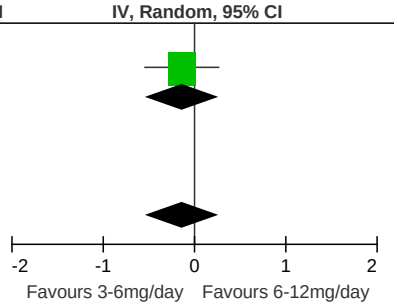
Study or Subgroup	1.5mg/day Mean	1.5mg/day SD	1.5mg/day Total	6-12mg/day Mean	6-12mg/day SD	6-12mg/day Total	Weight	Std. Mean Difference IV, Random, 95% CI
22.16.4 Paliperidone 1.5mg/day versus 6-12mg/day								
SINGH2011	29.173922	22.606218	51	44.864286	36.022343	42	100.0%	-0.53 [-0.94, -0.11]
Subtotal (95% CI)			**51**			**42**	**100.0%**	**-0.53 [-0.94, -0.11]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.49 (P = 0.01)								
Total (95% CI)			**51**			**42**	**100.0%**	**-0.53 [-0.94, -0.11]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.49 (P = 0.01)								
Test for subgroup differences: Not applicable								



22. 'Higher dose' paliperidone (3-6mg/day) versus additional (high dose) paliperidone (6-12mg/day): post-treatment side effect outcomes

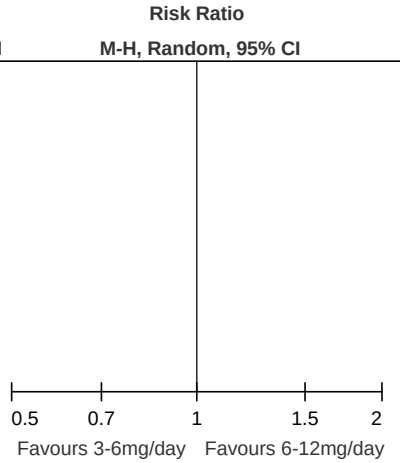
22.1 Side effects: mean change in weight (kg)

Study or Subgroup	3-6mg/day Mean	3-6mg/day SD	3-6mg/day Total	6-12mg/day Mean	6-12mg/day SD	6-12mg/day Total	Weight	Std. Mean Difference IV, Random, 95% CI
23.2.4 Paliperidone 3-6mg/day versus 6-12mg/day								
SINGH2011	1.1	2.13	48	1.4	2.16	47	100.0%	-0.14 [-0.54, 0.26]
Subtotal (95% CI)			**48**			**47**	**100.0%**	**-0.14 [-0.54, 0.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.68 (P = 0.50)								
Total (95% CI)			**48**			**47**	**100.0%**	**-0.14 [-0.54, 0.26]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.68 (P = 0.50)								
Test for subgroup differences: Not applicable								



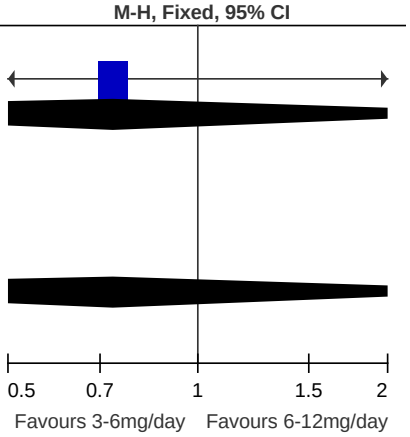
22.2 Side effects: prolonged QT interval (msec)

Study or Subgroup	3-6mg/day Events	3-6mg/day Total	6-12mg/day Events	6-12mg/day Total	Weight	Risk Ratio M-H, Random, 95% CI
23.11.2 Paliperidone 3-6mg/day versus 6-12mg/day						
SINGH2011	0	48	0	47		Not estimable
Subtotal (95% CI)		**48**		**47**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**48**		**47**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Test for subgroup differences: Not applicable						



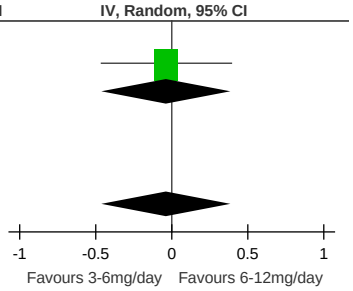
22.3 Side effects: tachycardia

Study or Subgroup	3-6mg/day Events	3-6mg/day Total	6-12mg/day Events	6-12mg/day Total	Weight	Risk Ratio M-H, Fixed, 95% CI
23.15.3 Paliperidone 3-6mg/day versus 6-12mg/day						
SINGH2011	3	48	4	47	100.0%	0.73 [0.17, 3.11]
Subtotal (95% CI)		**48**		**47**	**100.0%**	**0.73 [0.17, 3.11]**
Total events	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.42 (P = 0.67)						
Total (95% CI)		**48**		**47**	**100.0%**	**0.73 [0.17, 3.11]**
Total events	3		4			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.42 (P = 0.67)						
Test for subgroup differences: Not applicable						



22.4 Side effects: mean change in prolactin level (mg/dl)

Study or Subgroup	3-6mg/day Mean	3-6mg/day SD	3-6mg/day Total	6-12mg/day Mean	6-12mg/day SD	6-12mg/day Total	Weight	Std. Mean Difference IV, Random, 95% CI
23.16.4 Paliperidone 3-6mg/day versus 6-12mg/day								
SINGH2011	43.778571	24.565112	42	44.864286	36.022343	42	100.0%	-0.03 [-0.46, 0.39]
Subtotal (95% CI)			**42**			**42**	**100.0%**	**-0.03 [-0.46, 0.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.16 (P = 0.87)								
Total (95% CI)			**42**			**42**	**100.0%**	**-0.03 [-0.46, 0.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.16 (P = 0.87)								
Test for subgroup differences: Not applicable								

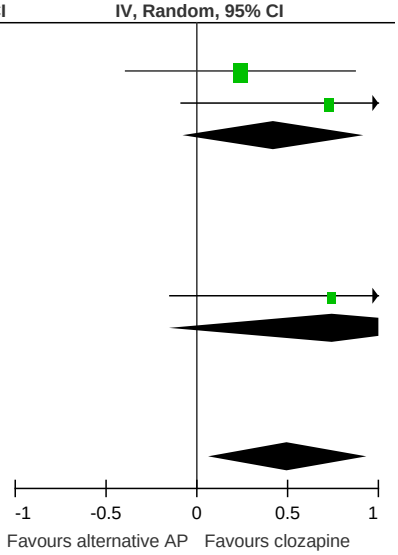


14ciii Treatment Resistant (TR)

1. Treatment resistant hildren and young people 18 years and younger: clozapine versus an alternative antipsychotic: post-treatment efficacy outcomes

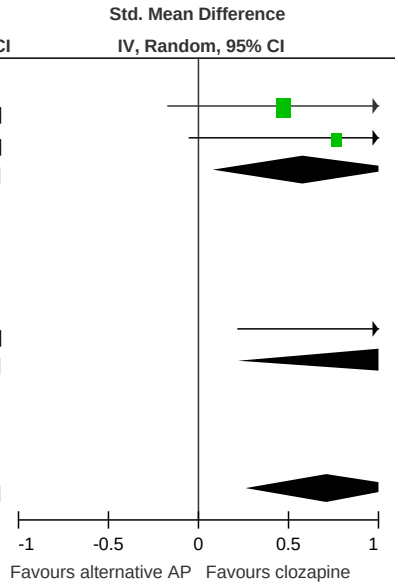
1.1 Mental state: total symptoms (BPRS)

Study or Subgroup	Alternative AP Mean	Alternative AP SD	Alternative AP Total	Clozapine Mean	Clozapine SD	Clozapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
8.1.1 Olanzapine								
KUMRA2008A	34.3	13.6	21	31.4	9.3	18	47.5%	0.24 [-0.39, 0.87]
SHAW2006	-1	11.584	13	-9	9.44	12	28.6%	0.73 [-0.09, 1.54]
Subtotal (95% CI)			**34**			**30**	**76.1%**	**0.42 [-0.08, 0.92]**
Heterogeneity: Tau² = 0.00; Chi² = 0.86, df = 1 (P = 0.35); I² = 0%								
Test for overall effect: Z = 1.66 (P = 0.10)								
8.1.2 Haloperidol								
KUMRA1996	64.7	18.1	11	52.5	12.6	10	23.9%	0.74 [-0.15, 1.64]
Subtotal (95% CI)			**11**			**10**	**23.9%**	**0.74 [-0.15, 1.64]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.64 (P = 0.10)								
Total (95% CI)			**45**			**40**	**100.0%**	**0.50 [0.06, 0.94]**
Heterogeneity: Tau² = 0.00; Chi² = 1.24, df = 2 (P = 0.54); I² = 0%								
Test for overall effect: Z = 2.25 (P = 0.02)								
Test for subgroup differences: Chi² = 0.38, df = 1 (P = 0.54), I² = 0%								



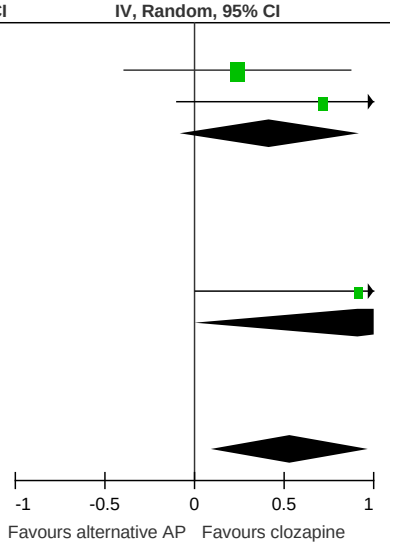
1.2 Mental state: positive symptoms (SAPS, BPRS-positive)

Study or Subgroup	Alternative AP Mean	Alternative AP SD	Alternative AP Total	Clozapine Mean	Clozapine SD	Clozapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
8.3.1 Olanzapine								
KUMRA2008A	8.1	4.5	21	6.3	2.6	18	48.3%	0.47 [-0.17, 1.11]
SHAW2006	3	22.34	13	-12	14.165	12	29.5%	0.77 [-0.05, 1.59]
Subtotal (95% CI)			**34**			**30**	**77.7%**	**0.58 [0.08, 1.09]**
Heterogeneity: Tau² = 0.00; Chi² = 0.32, df = 1 (P = 0.57); I² = 0%								
Test for overall effect: Z = 2.27 (P = 0.02)								
8.3.2 Haloperidol								
KUMRA1996	35.9	15.6	11	19.1	11.7	10	22.3%	1.16 [0.22, 2.10]
Subtotal (95% CI)			**11**			**10**	**22.3%**	**1.16 [0.22, 2.10]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.42 (P = 0.02)								
Total (95% CI)			**45**			**40**	**100.0%**	**0.71 [0.27, 1.16]**
Heterogeneity: Tau² = 0.00; Chi² = 1.44, df = 2 (P = 0.49); I² = 0%								
Test for overall effect: Z = 3.14 (P = 0.002)								
Test for subgroup differences: Chi² = 1.13, df = 1 (P = 0.29), I² = 11.2%								



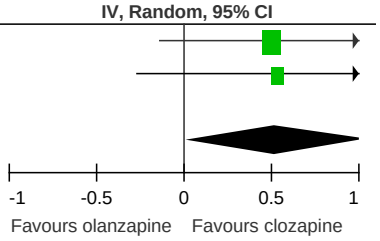
1.3 Mental state: negative symptoms (SANS)

Study or Subgroup	Alternative AP Mean	SD	Total	Clozapine Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
8.5.1 Olanzapine								
KUMRA2008A	7.6	3.8	21	6.6	4.4	18	47.9%	0.24 [-0.39, 0.87]
SHAW2006	-8	18.203	13	-22	19.674	12	28.9%	0.72 [-0.10, 1.53]
Subtotal (95% CI)			**34**			**30**	**76.9%**	**0.42 [-0.08, 0.92]**
Heterogeneity: Tau² = 0.00; Chi² = 0.82, df = 1 (P = 0.37); I² = 0%								
Test for overall effect: Z = 1.64 (P = 0.10)								
8.5.2 Haloperidol								
KUMRA1996	72.2	24.7	11	46	30.3	10	23.1%	0.91 [0.01, 1.82]
Subtotal (95% CI)			**11**			**10**	**23.1%**	**0.91 [0.01, 1.82]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.97 (P = 0.05)								
Total (95% CI)			**45**			**40**	**100.0%**	**0.53 [0.10, 0.97]**
Heterogeneity: Tau² = 0.00; Chi² = 1.70, df = 2 (P = 0.43); I² = 0%								
Test for overall effect: Z = 2.39 (P = 0.02)								
Test for subgroup differences: Chi² = 0.88, df = 1 (P = 0.35), I² = 0%								



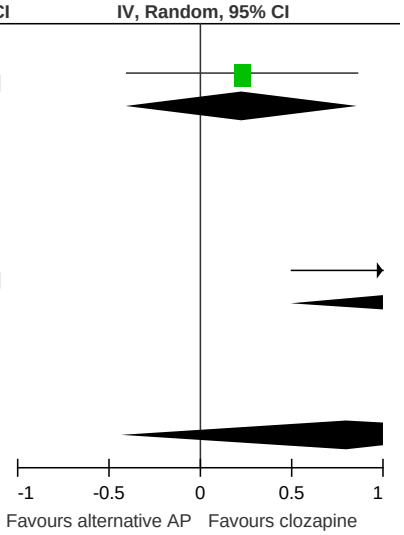
1.4 Global state: severity (CGI-S)

Study or Subgroup	Olazapine Mean	SD	Total	Clozapine Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
KUMRA2008A	3.9	1.3	21	3.3	1	18	61.0%	0.50 [-0.14, 1.14]
SHAW2006	-0.5	0.91	13	-1.1	1.259	12	39.0%	0.53 [-0.27, 1.33]
Total (95% CI)			**34**			**30**	**100.0%**	**0.51 [0.01, 1.01]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.95); I² = 0%								
Test for overall effect: Z = 2.01 (P = 0.04)								



1.5 Functioning: psychosocial (CGAS)

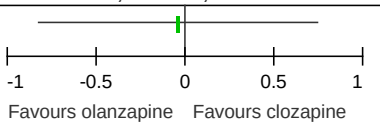
Study or Subgroup	Alternative AP Mean	SD	Total	Clozapine Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
8.11.1 Olanzapine								
KUMRA2008A	-46.4	19.4	21	-50.5	15	18	54.8%	0.23 [-0.40, 0.86]
Subtotal (95% CI)			**21**			**18**	**54.8%**	**0.23 [-0.40, 0.86]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.71 (P = 0.48)								
8.11.2 Haloperidol								
KUMRA1996	-27.9	12.1	11	-44.9	9.5	10	45.2%	1.49 [0.50, 2.48]
Subtotal (95% CI)			**11**			**10**	**45.2%**	**1.49 [0.50, 2.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.95 (P = 0.003)								
Total (95% CI)			**32**			**28**	**100.0%**	**0.80 [-0.43, 2.03]**
Heterogeneity: Tau² = 0.62; Chi² = 4.42, df = 1 (P = 0.04); I² = 77%								
Test for overall effect: Z = 1.27 (P = 0.20)								
Test for subgroup differences: Chi² = 4.42, df = 1 (P = 0.04), I² = 77.4%								



2. Treatment resistant children and young people 18 years and younger: clozapine versus an alternative antipsychotic: post-treatment side effect outcome

2.1 Side effects: weight (lbs)

	Olanzapine			Clozapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
SHAW2006	3.6	4	13	3.8	6	12		-0.04 [-0.82, 0.75]

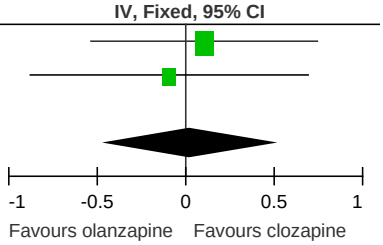


2.2 Side effects: BMI (kg/m²)

	Olanzapine			Clozapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
KUMRA2008A	29.2	5.5	21	28.7	3.4	17	60.1%	0.10 [-0.54, 0.74]
SHAW2006	1.4	1.6	13	1.6	2.5	12	39.9%	-0.09 [-0.88, 0.69]
Total (95% CI)			**34**			**29**	**100.0%**	**0.03 [-0.47, 0.52]**

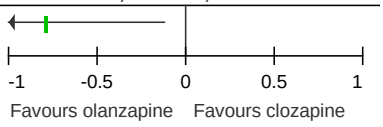
Heterogeneity: Chi² = 0.15, df = 1 (P = 0.70); I² = 0%

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



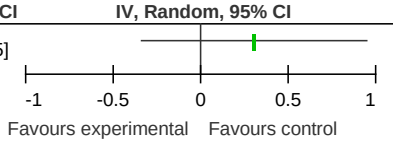
2.3 Side effects: fasting serum glucose level mg/dl

	Olanzapine			Clozapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
KUMRA2008A	84	7.7	21	94.1	16.8	17		-0.79 [-1.45, -0.12]



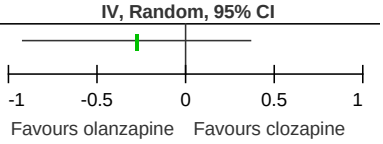
2.4 Side effects: fasting total cholesterol mg/dl

	Olanzapine			Clozapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
KUMRA2008A	178.2	33.8	21	167.8	32.6	17		0.31 [-0.34, 0.95]



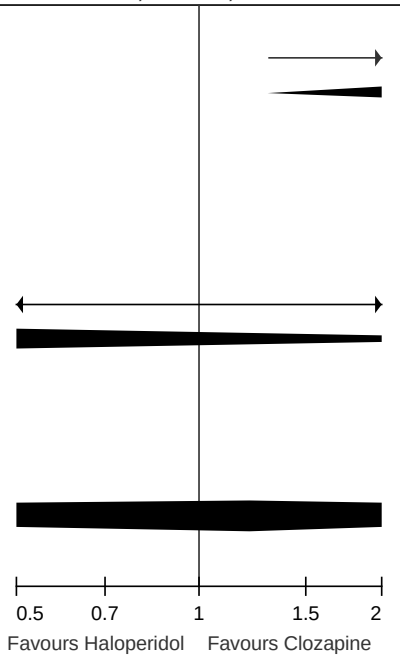
2.5 Side effects: fasting triglycerides mg/dl

	Olanzapine			Clozapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
KUMRA2008A	133.4	67.2	21	153.6	76.6	17		-0.28 [-0.92, 0.37]



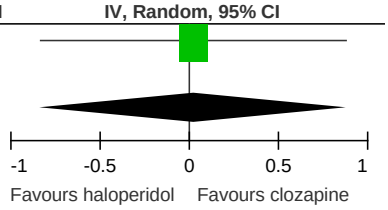
2.6 Side effects: tachycardia (number of participants)

Study or Subgroup	Haloperidol Events	Haloperidol Total	Clozapine Events	Clozapine Total	Weight	Risk Ratio M-H, Random, 95% CI
15.6.1 Olanzapine						
SHAW2006	8	10	2	12	57.9%	4.80 [1.30, 17.66]
Subtotal (95% CI)		**10**		**12**	**57.9%**	**4.80 [1.30, 17.66]**
Total events	8		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.36 (P = 0.02)						
15.6.2 Haloperidol						
KUMRA1996	0	11	2	10	42.1%	0.18 [0.01, 3.41]
Subtotal (95% CI)		**11**		**10**	**42.1%**	**0.18 [0.01, 3.41]**
Total events	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.14 (P = 0.26)						
Total (95% CI)		**21**		**22**	**100.0%**	**1.21 [0.05, 31.38]**
Total events	8		4			
Heterogeneity: Tau² = 4.31; Chi² = 4.23, df = 1 (P = 0.04); I² = 76%						
Test for overall effect: Z = 0.12 (P = 0.91)						
Test for subgroup differences: Chi² = 4.00, df = 1 (P = 0.05), I² = 75.0%						



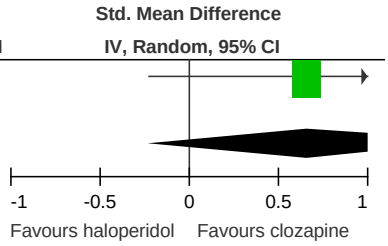
2.7 Side effects: extrapyramidal (AIMS)

Study or Subgroup	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Clozapine Mean	Clozapine SD	Clozapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
KUMRA1996	12.2	3.5	11	12.1	4.8	10	100.0%	0.02 [-0.83, 0.88]
Total (95% CI)			**11**			**10**	**100.0%**	**0.02 [-0.83, 0.88]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.05 (P = 0.96)								



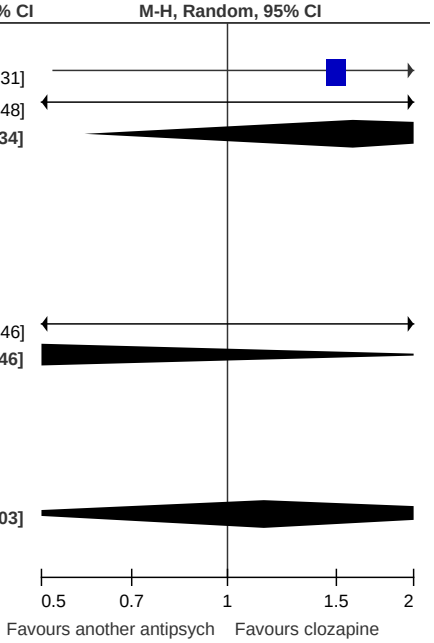
2.8 Side effects: extra pyramidal (SAS)

Study or Subgroup	Haloperidol Mean	Haloperidol SD	Haloperidol Total	Clozapine Mean	Clozapine SD	Clozapine Total	Weight	Std. Mean Difference IV, Random, 95% CI
KUMRA1996	13.9	3.5	11	12	1.6	10	100.0%	0.66 [-0.23, 1.54]
Total (95% CI)			**11**			**10**	**100.0%**	**0.66 [-0.23, 1.54]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.46 (P = 0.14)								



2.9 Leaving the study early for any reason

Study or Subgroup	Another antipsychotic Events	Total	Clozapine Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
15.20.1 Olanzapine						
KUMRA2008A	7	21	4	18	70.0%	1.50 [0.52, 4.31]
SHAW2006	1	13	0	12	9.5%	2.79 [0.12, 62.48]
Subtotal (95% CI)		**34**		**30**	**79.6%**	**1.60 [0.59, 4.34]**
Total events	8		4			
Heterogeneity: Tau² = 0.00; Chi² = 0.14, df = 1 (P = 0.71); I² = 0%						
Test for overall effect: Z = 0.92 (P = 0.36)						
15.20.2 Haloperidol						
KUMRA1996	1	11	3	10	20.4%	0.30 [0.04, 2.46]
Subtotal (95% CI)		**11**		**10**	**20.4%**	**0.30 [0.04, 2.46]**
Total events	1		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.12 (P = 0.26)						
Total (95% CI)		**45**		**40**	**100.0%**	**1.15 [0.43, 3.03]**
Total events	9		7			
Heterogeneity: Tau² = 0.06; Chi² = 2.12, df = 2 (P = 0.35); I² = 6%						
Test for overall effect: Z = 0.28 (P = 0.78)						
Test for subgroup differences: Chi² = 1.97, df = 1 (P = 0.16), I² = 49.3%						



14civ: Side effect observational studies

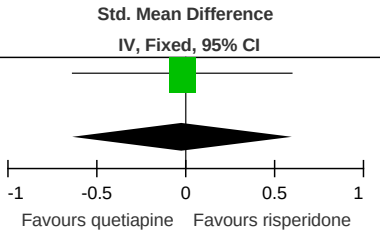
1. Side effects: weight change (kg)

1.1 Children and young people ≤18 Quetiapine vs Risperidone: Post-treatment

Study or Subgroup	quetiapine Mean	quetiapine SD	quetiapine Total	risperidone Mean	risperidone SD	risperidone Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
CASTROFORNILES2008	6	5.5	15	6.1	4.8	31	100.0%	-0.02 [-0.64, 0.60]
Total (95% CI)			**15**			**31**	**100.0%**	**-0.02 [-0.64, 0.60]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.06 (P = 0.95)

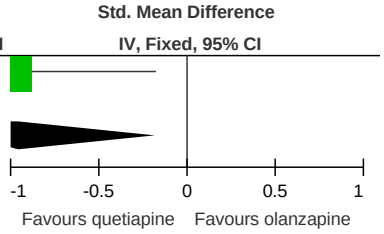


1.2 Children and young people ≤18 quetiapine vs olanzapine : post-treatment

Study or Subgroup	quetiapine Mean	quetiapine SD	quetiapine Total	olanzapine Mean	olanzapine SD	olanzapine Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
CASTROFORNILES2008	6	5.5	15	11.7	6.1	14	100.0%	-0.96 [-1.73, -0.18]
Total (95% CI)			**15**			**14**	**100.0%**	**-0.96 [-1.73, -0.18]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.42 (P = 0.02)

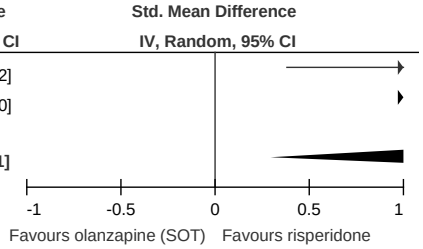


1.3 Children and young people ≤18 olanzapine (SOT) vs risperidone: post-treatment

Study or Subgroup	Olanzapine (SOT) Mean	Olanzapine (SOT) SD	Olanzapine (SOT) Total	Risperidone Mean	Risperidone SD	Risperidone Total	Weight	Std. Mean Difference IV, Random, 95% CI
CASTROFORNILES2008	11.7	6.1	14	6.1	4.8	31	52.8%	1.05 [0.38, 1.72]
CROCQ2007	8.9	5.1	10	1	1.8	26	47.2%	2.54 [1.58, 3.50]
Total (95% CI)			**24**			**57**	**100.0%**	**1.75 [0.30, 3.21]**

Heterogeneity: Tau² = 0.92; Chi² = 6.19, df = 1 (P = 0.01); I² = 84%

Test for overall effect: Z = 2.37 (P = 0.02)

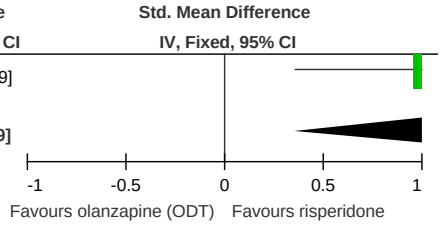


1.4 Children and young people ≤18 olanzapine (ODT) vs risperidone: post-treatment

Study or Subgroup	olanzapine (ODT) Mean	olanzapine (ODT) SD	olanzapine (ODT) Total	risperidone Mean	risperidone SD	risperidone Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
CROCQ2007	3	2.1	16	1	1.8	26	100.0%	1.02 [0.36, 1.69]
Total (95% CI)			**16**			**26**	**100.0%**	**1.02 [0.36, 1.69]**

Heterogeneity: Not applicable

Test for overall effect: Z = 3.02 (P = 0.003)

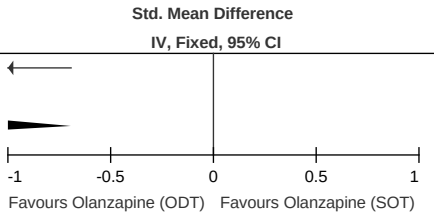


1.5 Children and young people ≤18 olanzapine (SOT) vs olanzapine (ODT): post-treatment

	Olanzapine (ODT)			Olanzapine (SOT)				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
CROCQ2007	3	2.1	16	8.9	5.1	10	100.0%	-1.62 [-2.54, -0.69]
Total (95% CI)			**16**			**10**	**100.0%**	**-1.62 [-2.54, -0.69]**

Heterogeneity: Not applicable

Test for overall effect: Z = 3.43 (P = 0.0006)



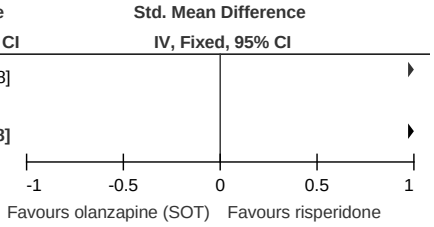
2. Side effects: BMI change

2.1 Children and young people ≤18 olanzapine (SOT) vs risperidone: post-treatment

	Olanzapine (SOT)			Risperidone				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
CROCQ2007	1.9	0.6	10	0.4	0.7	26	100.0%	2.17 [1.27, 3.08]
Total (95% CI)			**10**			**26**	**100.0%**	**2.17 [1.27, 3.08]**

Heterogeneity: Not applicable

Test for overall effect: Z = 4.72 (P < 0.00001)

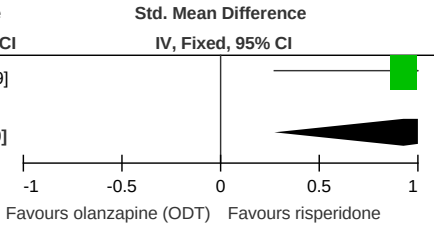


2.2 Children and young people ≤18 olanzapine (ODT) vs risperidone: post-treatment

	olanzapine (ODT)			risperidone				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
CROCQ2007	1.1	0.8	16	0.4	0.7	26	100.0%	0.93 [0.27, 1.59]
Total (95% CI)			**16**			**26**	**100.0%**	**0.93 [0.27, 1.59]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.77 (P = 0.006)

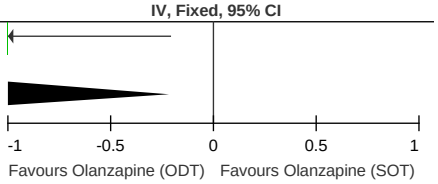


2.3 Children and young people ≤18 olanzapine (SOT) vs olanzapine (ODT): post-treatment

	Olanzapine (ODT)			Olanzapine (SOT)				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
CROCQ2007	1.1	0.8	16	1.9	0.6	10	100.0%	-1.06 [-1.91, -0.21]
Total (95% CI)			**16**			**10**	**100.0%**	**-1.06 [-1.91, -0.21]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.44 (P = 0.01)



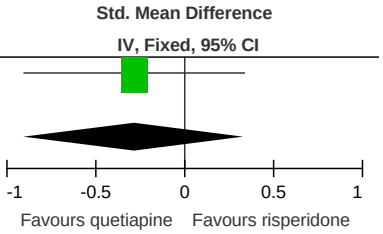
3. Side effects: neurological: UKU

3.1 Children and young people 18 years and younger: quetiapine vs risperidone: post-treatment

	quetiapine			risperidone				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
CASTROFORNILES2008	7.9	5.4	15	9.6	6.1	31	100.0%	-0.28 [-0.90, 0.34]
Total (95% CI)			**15**			**31**	**100.0%**	**-0.28 [-0.90, 0.34]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.90 (P = 0.37)

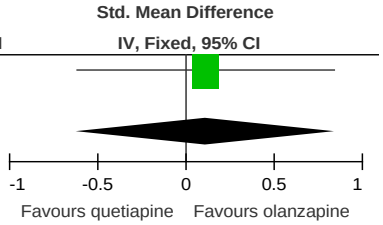


3.2 Children and young people 18 years and younger: quetiapine vs olanzapine: post-treatment

	quetiapine			olanzapine				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
CASTROFORNILES2008	7.9	5.4	15	7.3	5	14	100.0%	0.11 [-0.62, 0.84]
Total (95% CI)			**15**			**14**	**100.0%**	**0.11 [-0.62, 0.84]**

Heterogeneity: Not applicable

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

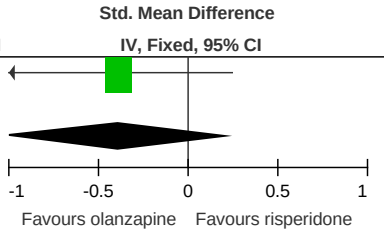


3.3 Children and young people 18 years and younger: olanzapine (SOT) vs risperidone: post-treatment

	olanzapine			risperidone				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
CASTROFORNILES2008	7.3	5	14	9.6	6.1	31	100.0%	-0.39 [-1.03, 0.25]
Total (95% CI)			**14**			**31**	**100.0%**	**-0.39 [-1.03, 0.25]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.20 (P = 0.23)



14d: COGNITION, EMPLOYMENT AND EDUCATION IN CHILDREN AND YOUNG PEOPLE WITH PSYCHOSIS AND SCHIZOPHRENIA

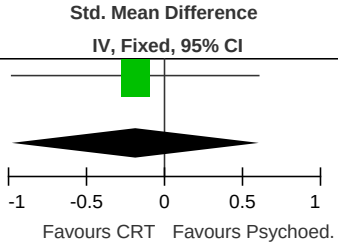
1. Cognitive remediation therapy (CRT) versus psychoeducation: 26 weeks post-treatment

1.1 Mental state: total symptoms (BPRS)

	CRT			Psychoeducation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
UELAND2004	45.1	11.7	14	47.5	13.2	11	100.0%	-0.19 [-0.98, 0.60]
Total (95% CI)			**14**			**11**	**100.0%**	**-0.19 [-0.98, 0.60]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.46 (P = 0.64)

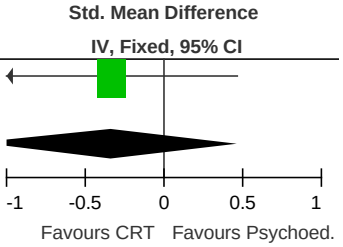


1.2 Mental state: positive symptoms (BPRS-positive)

	CRT			Psychoeducation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
UELAND2004	12.7	5.5	14	14.4	4.2	11	100.0%	-0.33 [-1.13, 0.47]
Total (95% CI)			**14**			**11**	**100.0%**	**-0.33 [-1.13, 0.47]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.81 (P = 0.42)

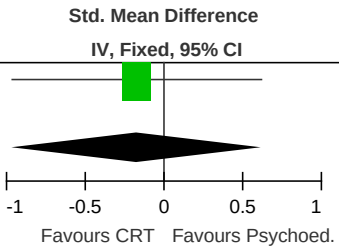


1.3 Mental state: negative symptoms (BPRS-negative)

	CRT			Psychoeducation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
UELAND2004	5.6	2.9	14	6.2	3.9	11	100.0%	-0.17 [-0.96, 0.62]
Total (95% CI)			**14**			**11**	**100.0%**	**-0.17 [-0.96, 0.62]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.43 (P = 0.67)

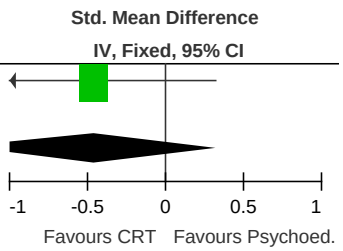


1.4 Functioning: psychosocial (GAS)

	CRT			Psychoeducation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
UELAND2004	-40	13.7	14	-33.3	14.5	12	100.0%	-0.46 [-1.24, 0.32]
Total (95% CI)			**14**			**12**	**100.0%**	**-0.46 [-1.24, 0.32]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.15 (P = 0.25)



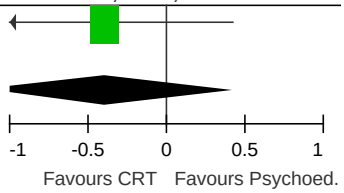
2. Cognitive remediation therapy (CRT) versus psychoeducation: 52 week's follow-up

2.1 Mental state: total symptoms (BPRS)

	CRT			Psychoeducation				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
UELAND2004	37.9	12	14	43.3	14.6	10	100.0%	-0.40 [-1.22, 0.42]	
Total (95% CI)			**14**			**10**	**100.0%**	**-0.40 [-1.22, 0.42]**	

Heterogeneity: Not applicable

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

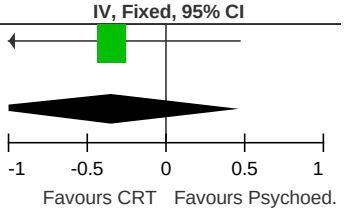


2.2 Mental state: positive symptoms (BPRS-positive)

	CRT			Psychoeducation				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
UELAND2004	11.6	4.7	14	13.9	8.2	10	100.0%	-0.35 [-1.17, 0.47]	
Total (95% CI)			**14**			**10**	**100.0%**	**-0.35 [-1.17, 0.47]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.83 (P = 0.40)

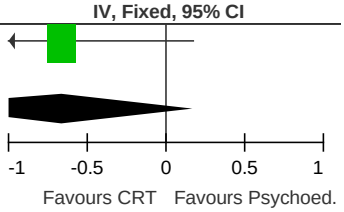


2.3 Mental state: negative symptoms (BPRS-negative)

	CRT			Psychoeducation				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
UELAND2004	4.1	1.9	14	6.8	5.7	10	100.0%	-0.66 [-1.50, 0.17]	
Total (95% CI)			**14**			**10**	**100.0%**	**-0.66 [-1.50, 0.17]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 1.55 (P = 0.12)

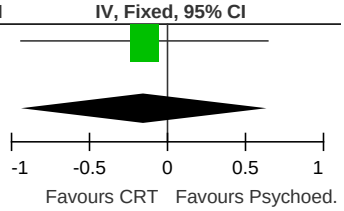


2.4 Functioning: psychosocial (GAS)

	CRT			Psychoeducation				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
UELAND2004	-48.9	11.3	14	-47.3	9.3	11	100.0%	-0.15 [-0.94, 0.64]	
Total (95% CI)			**14**			**11**	**100.0%**	**-0.15 [-0.94, 0.64]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.37 (P = 0.71)



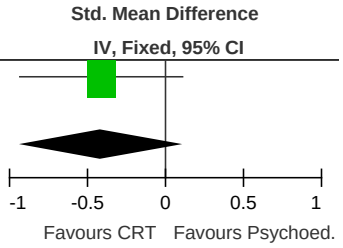
3. Cognitive enhancement therapy (CRT plus and group-based social cognition therapy) versus psychoeducation: 104 weeks post-treatment

3.1 Mental state: anxiety/ depression symptoms (BPRS)

	CRT			Psychoeducation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
EACK2009	1.97	0.82	31	2.28	0.64	27	100.0%	-0.41 [-0.93, 0.11]
Total (95% CI)			**31**			**27**	**100.0%**	**-0.41 [-0.93, 0.11]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.55 (P = 0.12)

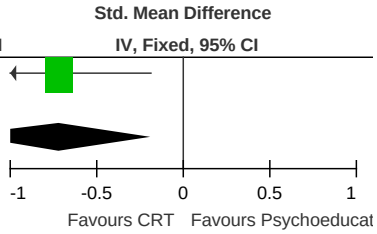


3.2 Mental state: total symptoms (composite score)

	CRT			Psychoeducation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
EACK2009	30.75	10.68	31	37.84	8.46	27	100.0%	-0.72 [-1.25, -0.19]
Total (95% CI)			**31**			**27**	**100.0%**	**-0.72 [-1.25, -0.19]**

Heterogeneity: Not applicable

Test for overall effect: Z = 2.65 (P = 0.008)

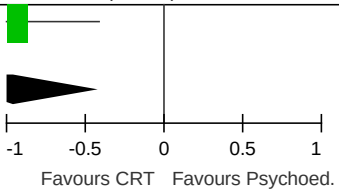


3.3 Mental state: negative symptoms (BPRS withdrawal-retardation)

	CRT			Psychoeducation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
EACK2009	1.63	0.6	31	2.3	0.78	27	100.0%	-0.96 [-1.51, -0.41]
Total (95% CI)			**31**			**27**	**100.0%**	**-0.96 [-1.51, -0.41]**

Heterogeneity: Not applicable

Test for overall effect: Z = 3.44 (P = 0.0006)

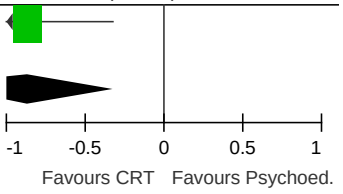


3.4 Functioning: psychosocial (GAS)

	CRT			Psychoeducation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
EACK2009	-69.18	8.2	31	-61.39	9.62	27	100.0%	-0.86 [-1.41, -0.32]
Total (95% CI)			**31**			**27**	**100.0%**	**-0.86 [-1.41, -0.32]**

Heterogeneity: Not applicable

Test for overall effect: Z = 3.13 (P = 0.002)

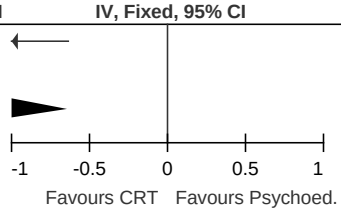


3.5 Cognition: social cognition (composite score)

	CRT			Psychoeducation				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
EACK2009	17.87	13.5	31	33.28	11.66	27	100.0%	-1.20 [-1.76, -0.64]
Total (95% CI)			**31**			**27**	**100.0%**	**-1.20 [-1.76, -0.64]**

Heterogeneity: Not applicable

Test for overall effect: Z = 4.17 (P < 0.0001)

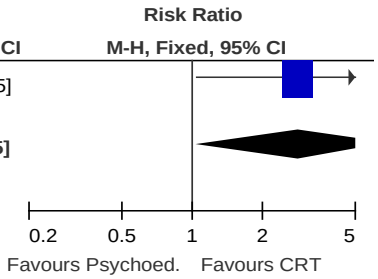


3.6 Number of participants in competitive employment (assuming drop outs did not gain employment; MRAI)

	CRT		Psychoeducation			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
EACK2009	13	31	4	27	100.0%	2.83 [1.05, 7.65]
Total (95% CI)		**31**		**27**	**100.0%**	**2.83 [1.05, 7.65]**
Total events	13		4			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.05 (P = 0.04)

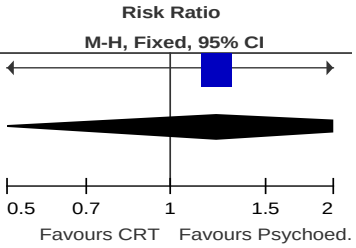


3.7 Leaving the study early for any reason

	CRT		Psychoeducation			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
EACK2009	7	31	5	27	100.0%	1.22 [0.44, 3.40]
Total (95% CI)		**31**		**27**	**100.0%**	**1.22 [0.44, 3.40]**
Total events	7		5			

Heterogeneity: Not applicable

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



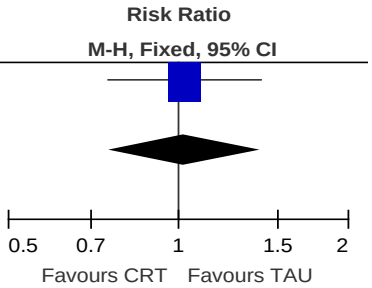
4. Cognitive remediation therapy (CRT) versus treatment as usual: 14 weeks post-treatment

4.1 Leaving the study early for any reason

	CRT		TAU			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
WYKES2007	17	21	15	19	100.0%	1.03 [0.75, 1.40]
Total (95% CI)		**21**		**19**	**100.0%**	**1.03 [0.75, 1.40]**
Total events	17		15			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.16 (P = 0.87)



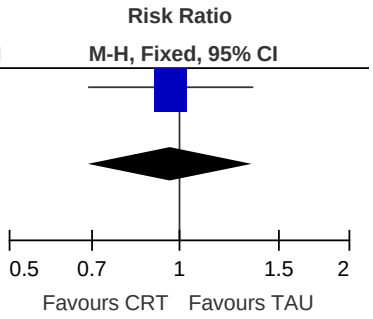
5. Cognitive remediation therapy (CRT) versus treatment as usual: 26 week's follow-up

5.1 Leaving the study early for any reason

Study or Subgroup	CRT Events	CRT Total	TAU Events	TAU Total	Weight	Risk Ratio M-H, Fixed, 95% CI
WYKES2007	16	21	15	19	100.0%	0.97 [0.69, 1.35]
Total (95% CI)		**21**		**19**	**100.0%**	**0.97 [0.69, 1.35]**
Total events	16		15			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.21 (P = 0.83)



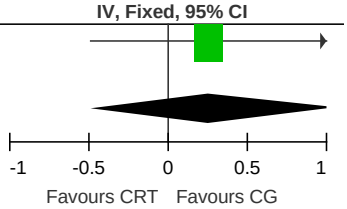
6. Cognitive remediation therapy (CRT) versus computer games (CG): 8 weeks post-treatment

6.1 Mental state: total symptoms (PANSS total)

Study or Subgroup	CRT Mean	CRT SD	CRT Total	Computer games Mean	Computer games SD	Computer games Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
URBEN2012	66.3	17.9	15	60.8	23.6	13	100.0%	0.26 [-0.49, 1.00]
Total (95% CI)			**15**			**13**	**100.0%**	**0.26 [-0.49, 1.00]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.68 (P = 0.50)

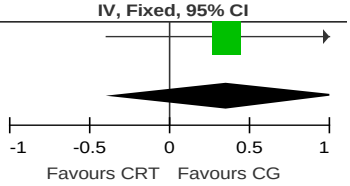


6.2 Mental state: positive symptoms (PANSS positive)

Study or Subgroup	CRT Mean	CRT SD	CRT Total	Computer games Mean	Computer games SD	Computer games Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
URBEN2012	14.3	5.2	15	12.4	5.2	13	100.0%	0.35 [-0.39, 1.10]
Total (95% CI)			**15**			**13**	**100.0%**	**0.35 [-0.39, 1.10]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.93 (P = 0.35)

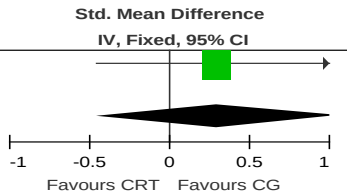


6.3 Mental state: negative symptoms (PANSS negative)

Study or Subgroup	CRT Mean	CRT SD	CRT Total	Computer games Mean	Computer games SD	Computer games Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
URBEN2012	18.3	8.3	15	15.8	8.4	13	100.0%	0.29 [-0.46, 1.04]
Total (95% CI)			**15**			**13**	**100.0%**	**0.29 [-0.46, 1.04]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.76 (P = 0.45)

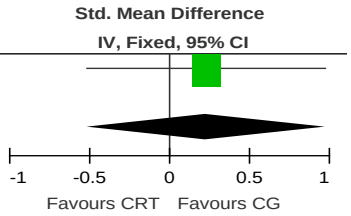


6.4 Mental state: general symptoms (PANSS general)

	CRT			Computer games				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
URBEN2012	33.6	8.6	15	31.1	12.5	13	100.0%	0.23 [-0.52, 0.97]
Total (95% CI)			**15**			**13**	**100.0%**	**0.23 [-0.52, 0.97]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.60 (P = 0.55)

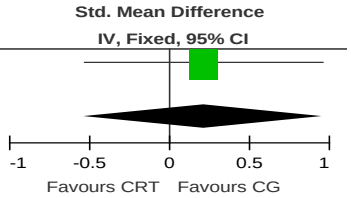


6.5 Global state (CGI-Severity)

	CRT			Computer games				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
URBEN2012	4.7	0.7	15	4.5	1.1	13	100.0%	0.21 [-0.53, 0.96]
Total (95% CI)			**15**			**13**	**100.0%**	**0.21 [-0.53, 0.96]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.56 (P = 0.57)

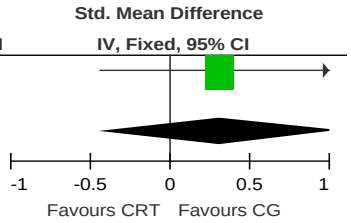


6.6 Social functioning (SOFAS)

	CRT			Computer games				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
URBEN2012	-50.5	8	15	-53.5	10.8	13	100.0%	0.31 [-0.44, 1.06]
Total (95% CI)			**15**			**13**	**100.0%**	**0.31 [-0.44, 1.06]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.81 (P = 0.42)



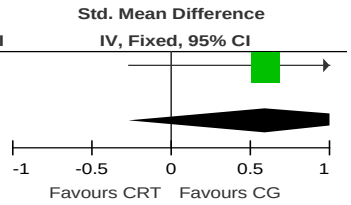
7. Cognitive remediation therapy (CRT) versus computer games (CG): 26 week's follow-up

7.1 Global state (CGI-severity)

	CRT			Computer games				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
URBEN2012	4.42	1.24	12	3.6	1.42	10	100.0%	0.60 [-0.27, 1.46]
Total (95% CI)			**12**			**10**	**100.0%**	**0.60 [-0.27, 1.46]**

Heterogeneity: Not applicable

Test for overall effect: Z = 1.36 (P = 0.18)

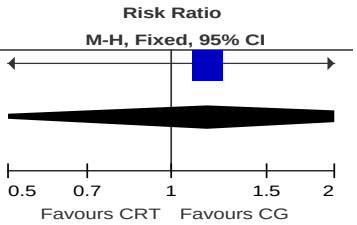


7.2 Leaving the study early for any reason

	CRT		Computer games			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
URBEN2012	6	18	4	14	100.0%	1.17 [0.41, 3.35]
Total (95% CI)		**18**		**14**	**100.0%**	**1.17 [0.41, 3.35]**
Total events	6		4			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.29 (P = 0.77)



Vocational Evidence

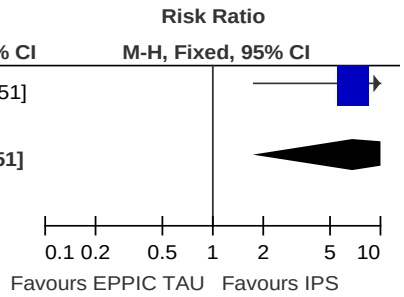
8. Individual placement and support (IPS) versus EPPIC treatment as usual: 26 weeks post-treatment

8.1 Number of participants in employment/enrolled on a course (assuming drop outs did not gain employment)

	IPS		EPPIC TAU			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
KILLACKEY2008	13	20	2	21	100.0%	6.83 [1.76, 26.51]
Total (95% CI)		**20**		**21**	**100.0%**	**6.83 [1.76, 26.51]**
Total events	13		2			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.77 (P = 0.006)

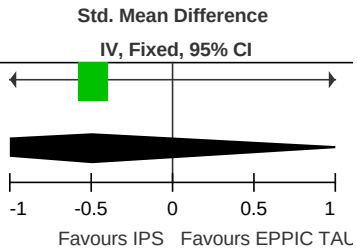


8.2 Number of weeks worked

	IPS			EPPIC TAU				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
KILLACKEY2008	-8.63	9.22	13	-3.8	10.7	2	100.0%	-0.49 [-1.99, 1.02]
Total (95% CI)			**13**			**2**	**100.0%**	**-0.49 [-1.99, 1.02]**

Heterogeneity: Not applicable

Test for overall effect: Z = 0.63 (P = 0.53)

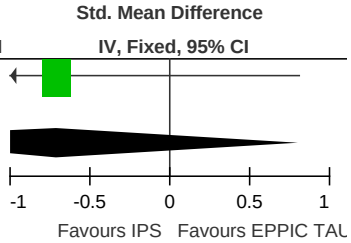


8.3 Number of hours worked per week

	IPS			EPPIC TAU				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
KILLACKEY2008	-33.9	15.51	13	-22.5	10.61	2	100.0%	-0.71 [-2.22, 0.81]
Total (95% CI)			**13**			**2**	**100.0%**	**-0.71 [-2.22, 0.81]**

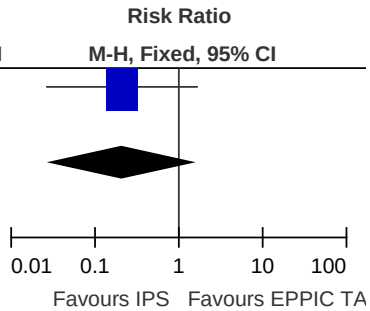
Heterogeneity: Not applicable

Test for overall effect: Z = 0.91 (P = 0.36)



8.4 Leaving the study early for any reason

	IPS		EPPIC TAU			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
KILLACKEY2008	1	20	5	21	100.0%	0.21 [0.03, 1.64]
Total (95% CI)		**20**		**21**	**100.0%**	**0.21 [0.03, 1.64]**
Total events	1		5			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.49 (P = 0.14)