APPENDIX 29: INTERVENTIONS FOR CHILDREN AND YOUNG PEOPLE – FOREST PLOTS

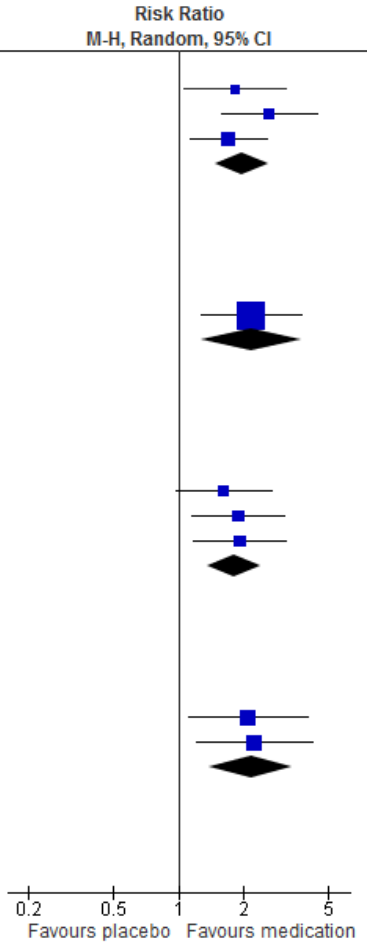
PHARMACOLOGICAL INTERVENTIONS FOR MANIA

Antipsychotics

Outcomes for antipsychotics compared with placebo

Response (50% reduction in manic symptoms) at post-treatment

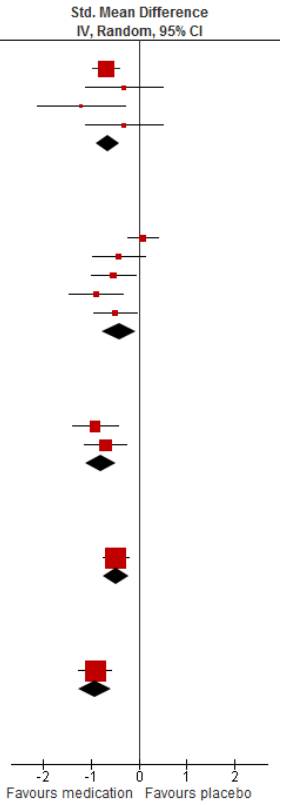
Study or Subgroup	Medication Events	Medication Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Aripiprazole						
FINDLING2009 (10mg Arip)	43	98	12	50	26.1%	1.83 [1.06, 3.14]
FINDLING2009 (30mg Arip)	63	99	12	50	28.8%	2.65 [1.58, 4.44]
TRAMONTINA2009	16	18	13	25	45.1%	1.71 [1.13, 2.58]
Subtotal (95% CI)		**215**		**125**	**100.0%**	**1.97 [1.50, 2.61]**
Total events	122		37			
Heterogeneity: Tau² = 0.00; Chi² = 2.02, df = 2 (P = 0.36); I² = 1%						
Test for overall effect: Z = 4.80 (P < 0.00001)						
1.1.2 Olanzapine						
TOHEN2007*	51	105	12	54	100.0%	2.19 [1.28, 3.74]
Subtotal (95% CI)		**105**		**54**	**100.0%**	**2.19 [1.28, 3.74]**
Total events	51		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.86 (P = 0.004)						
1.1.3 Quetiapine						
DELBELLO2002*	13	15	8	15	31.6%	1.63 [0.97, 2.72]
PATHAK2013 (400mg Quet)	51	93	13	45	34.1%	1.90 [1.16, 3.11]
PATHAK2013 (600mg Quet)	53	95	13	45	34.4%	1.93 [1.18, 3.16]
Subtotal (95% CI)		**203**		**105**	**100.0%**	**1.82 [1.36, 2.43]**
Total events	117		34			
Heterogeneity: Tau² = 0.00; Chi² = 0.30, df = 2 (P = 0.86); I² = 0%						
Test for overall effect: Z = 4.06 (P < 0.0001)						
1.1.4 Risperidone						
HAAS2009 (risp 0.5-2.5mg)	29	50	8	29	48.9%	2.10 [1.11, 3.97]
HAAS2009 (risp 3-6mg)	38	61	8	29	51.1%	2.26 [1.21, 4.20]
Subtotal (95% CI)		**111**		**58**	**100.0%**	**2.18 [1.40, 3.40]**
Total events	67		16			
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.87); I² = 0%						
Test for overall effect: Z = 3.44 (P = 0.0006)						



Test for subgroup differences: Chi² = 0.64, df = 3 (P = 0.89), I² = 0%

Symptoms of mania at post-treatment

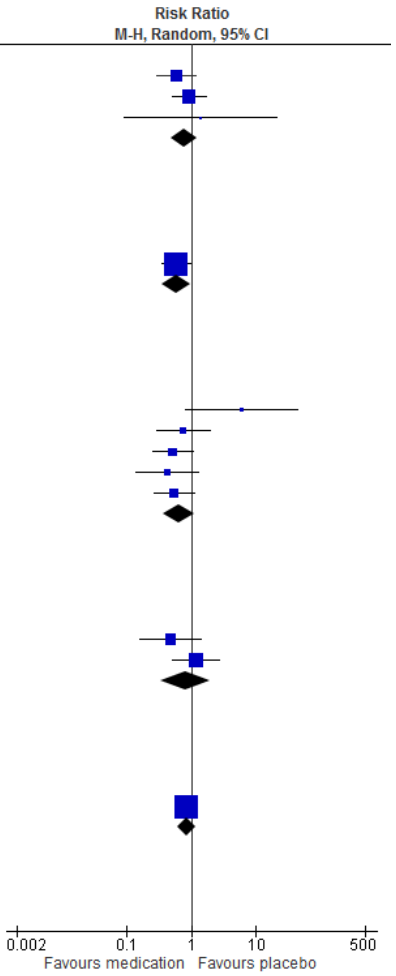
Study or Subgroup	Std. Mean Difference	SE	Medication Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.4.1 Aripiprazole						
FINDLING2009 (10mg Arip)	-0.68822692	0.14958078	96	46	73.5%	-0.69 [-0.98, -0.40]
FINDLING2009 (30mg Arip)	-0.31121187	0.41435252	99	46	9.6%	-0.31 [-1.12, 0.50]
TRAMONTINA2009 (12-17yrs)	-1.21186584	0.47119446	9	14	7.4%	-1.21 [-2.14, -0.29]
TRAMONTINA2009 (8-11yrs)	-0.31121187	0.41435252	9	11	9.6%	-0.31 [-1.12, 0.50]
Subtotal (95% CI)			**213**	**117**	**100.0%**	**-0.65 [-0.91, -0.40]**
Heterogeneity: Tau² = 0.00; Chi² = 2.82, df = 3 (P = 0.42); I² = 0%						
Test for overall effect: Z = 5.11 (P < 0.00001)						
1.4.3 Quetiapine						
DELBELLO2002*	0.08722867	0.16592846	15	15	24.7%	0.09 [-0.24, 0.41]
PATHAK2013a (10-12yrs)	-0.42115315	0.27976036	43	9	17.8%	-0.42 [-0.97, 0.13]
PATHAK2013a (13-17yrs)	-0.53675643	0.24035193	50	14	20.0%	-0.54 [-1.01, -0.07]
PATHAK2013b (10-12yrs)	-0.89455145	0.28980261	42	9	17.2%	-0.89 [-1.46, -0.33]
PATHAK2013b (13-17yrs)	-0.49014007	0.23734594	53	14	20.2%	-0.49 [-0.96, -0.02]
Subtotal (95% CI)			**203**	**61**	**100.0%**	**-0.41 [-0.76, -0.06]**
Heterogeneity: Tau² = 0.10; Chi² = 11.41, df = 4 (P = 0.02); I² = 65%						
Test for overall effect: Z = 2.31 (P = 0.02)						
1.4.4 Risperidone						
HAAS2009 (risp 0.5-2.5mg)	-0.91438034	0.24324661	49	15	47.3%	-0.91 [-1.39, -0.44]
HAAS2009 (risp 3-6mg)	-0.69820744	0.23023368	60	15	52.7%	-0.70 [-1.15, -0.25]
Subtotal (95% CI)			**109**	**30**	**100.0%**	**-0.80 [-1.13, -0.47]**
Heterogeneity: Tau² = 0.00; Chi² = 0.42, df = 1 (P = 0.52); I² = 0%						
Test for overall effect: Z = 4.79 (P < 0.00001)						
1.4.7 Ziprasidone						
PFIZER2011	-0.48528045	0.14032034	133	85	100.0%	-0.49 [-0.76, -0.21]
Subtotal (95% CI)			**133**	**85**	**100.0%**	**-0.49 [-0.76, -0.21]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.46 (P = 0.0005)						
1.4.8 Olanzapine						
TOHEN2007*	-0.91277921	0.17434059	105	54	100.0%	-0.91 [-1.25, -0.57]
Subtotal (95% CI)			**105**	**54**	**100.0%**	**-0.91 [-1.25, -0.57]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 5.24 (P < 0.00001)						



Test for subgroup differences: Chi² = 6.19, df = 4 (P = 0.19), I² = 35.4%

Number of participants withdrawing (for any reason)

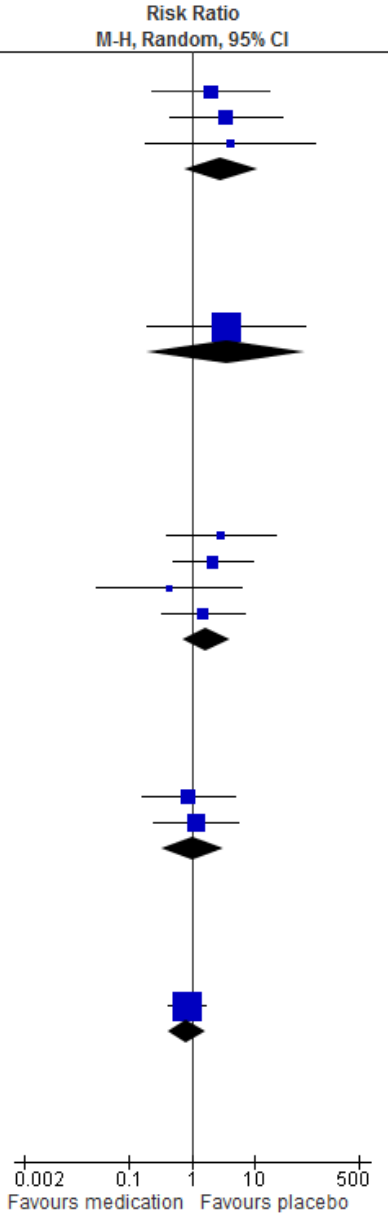
Study or Subgroup	Medication Events	Medication Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 Aripiprazole						
FINDLING2009 (10mg Arip)	14	98	12	50	43.0%	0.60 [0.30, 1.19]
FINDLING2009 (30mg Arip)	22	99	12	50	54.2%	0.93 [0.50, 1.71]
TRAMONTINA2009	1	18	1	25	2.8%	1.39 [0.09, 20.77]
Subtotal (95% CI)		**215**		**125**	**100.0%**	**0.77 [0.49, 1.22]**
Total events	37		25			
Heterogeneity: Tau² = 0.00; Chi² = 1.06, df = 2 (P = 0.59); I² = 0%						
Test for overall effect: Z = 1.10 (P = 0.27)						
1.2.2 Olanzapine						
TOHEN2007*	22	107	19	54	100.0%	0.58 [0.35, 0.98]
Subtotal (95% CI)		**107**		**54**	**100.0%**	**0.58 [0.35, 0.98]**
Total events	22		19			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.03 (P = 0.04)						
1.2.3 Quetiapine						
DELBELLO2002*	6	15	1	15	6.5%	6.00 [0.82, 44.00]
PATHAK2013a (10-12yrs)	9	43	5	18	20.7%	0.75 [0.29, 1.94]
PATHAK2013a (13-17yrs)	10	50	10	26	27.7%	0.52 [0.25, 1.09]
PATHAK2013b (10-12yrs)	5	42	5	18	16.7%	0.43 [0.14, 1.30]
PATHAK2013b (13-17yrs)	11	53	10	26	28.5%	0.54 [0.26, 1.10]
Subtotal (95% CI)		**203**		**103**	**100.0%**	**0.64 [0.38, 1.10]**
Total events	41		31			
Heterogeneity: Tau² = 0.13; Chi² = 6.22, df = 4 (P = 0.18); I² = 36%						
Test for overall effect: Z = 1.61 (P = 0.11)						
1.2.4 Risperidone						
HAAS2009 (risp 0.5-2.5mg)	5	50	6	29	42.0%	0.48 [0.16, 1.44]
HAAS2009 (risp 3-6mg)	15	61	6	29	58.0%	1.19 [0.51, 2.75]
Subtotal (95% CI)		**111**		**58**	**100.0%**	**0.81 [0.34, 1.95]**
Total events	20		12			
Heterogeneity: Tau² = 0.16; Chi² = 1.64, df = 1 (P = 0.20); I² = 39%						
Test for overall effect: Z = 0.46 (P = 0.64)						
1.2.7 Ziprasidone						
PFIZER2011	53	150	37	88	100.0%	0.84 [0.61, 1.17]
Subtotal (95% CI)		**150**		**88**	**100.0%**	**0.84 [0.61, 1.17]**
Total events	53		37			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.04 (P = 0.30)						



Test for subgroup differences: Chi² = 1.71, df = 4 (P = 0.79), I² = 0%

Number of participants withdrawing because of side effects

Study or Subgroup	Medication Events	Medication Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 Aripiprazole						
FINDLING2009 (10mg Arip)	4	98	1	50	38.9%	2.04 [0.23, 17.78]
FINDLING2009 (30mg Arip)	7	99	1	50	42.7%	3.54 [0.45, 27.95]
TRAMONTINA2009	1	18	0	25	18.4%	4.11 [0.18, 95.37]
Subtotal (95% CI)		**215**		**125**	**100.0%**	**2.93 [0.76, 11.32]**
Total events	12		2			
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 2 (P = 0.91); I² = 0%						
Test for overall effect: Z = 1.56 (P = 0.12)						
1.5.2 Olanzapine						
TOHEN2007*	3	107	0	54	100.0%	3.56 [0.19, 67.79]
Subtotal (95% CI)		**107**		**54**	**100.0%**	**3.56 [0.19, 67.79]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.85 (P = 0.40)						
1.5.3 Quetiapine						
DELBELLO2002*	0	15	0	15		Not estimable
PATHAK2013a (10-12yrs)	7	43	1	18	19.3%	2.93 [0.39, 22.13]
PATHAK2013a (13-17yrs)	8	50	2	27	36.2%	2.16 [0.49, 9.46]
PATHAK2013b (10-12yrs)	1	42	1	18	10.7%	0.43 [0.03, 6.48]
PATHAK2013b (13-17yrs)	6	53	2	27	33.7%	1.53 [0.33, 7.07]
Subtotal (95% CI)		**203**		**105**	**100.0%**	**1.71 [0.70, 4.17]**
Total events	22		6			
Heterogeneity: Tau² = 0.00; Chi² = 1.39, df = 3 (P = 0.71); I² = 0%						
Test for overall effect: Z = 1.19 (P = 0.23)						
1.5.5 Risperidone						
HAAS2009 (risp 0.5-2.5mg)	3	50	2	29	45.5%	0.87 [0.15, 4.91]
HAAS2009 (risp 3-6mg)	5	61	2	29	54.5%	1.19 [0.25, 5.77]
Subtotal (95% CI)		**111**		**58**	**100.0%**	**1.03 [0.32, 3.31]**
Total events	8		4			
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 1 (P = 0.79); I² = 0%						
Test for overall effect: Z = 0.05 (P = 0.96)						
1.5.7 Ziprasidone						
PFIZER2011	17	150	12	88	100.0%	0.83 [0.42, 1.66]
Subtotal (95% CI)		**150**		**88**	**100.0%**	**0.83 [0.42, 1.66]**
Total events	17		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.53 (P = 0.60)						

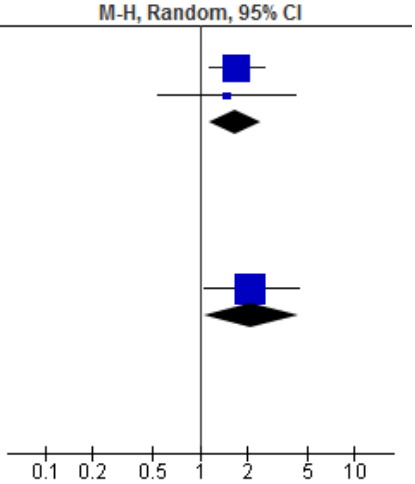


Test for subgroup differences: Chi² = 3.95, df = 4 (P = 0.41), I² = 0%

Outcomes for antipsychotics compared with valproate

Response (50% reduction of manic symptoms) at post-treatment

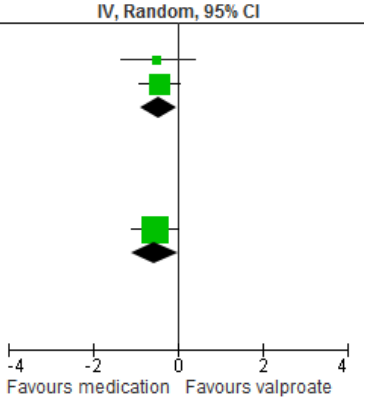
Study or Subgroup	Medication Events	Medication Total	Valproate Events	Valproate Total	Weight	Risk Ratio M-H, Random, 95% CI
11.1.1 Risperidone						
PAVULURI2010	26	33	15	33	86.0%	1.73 [1.15, 2.62]
PAVULURI2012*	6	14	4	14	14.0%	1.50 [0.54, 4.18]
Subtotal (95% CI)		**47**		**47**	**100.0%**	**1.70 [1.16, 2.49]**
Total events	32		19			
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 1 (P = 0.79); I² = 0%						
Test for overall effect: Z = 2.71 (P = 0.007)						
11.1.4 Quetiapine						
DELBELLO2006*	15	25	7	25	100.0%	2.14 [1.06, 4.34]
Subtotal (95% CI)		**25**		**25**	**100.0%**	**2.14 [1.06, 4.34]**
Total events	15		7			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.12 (P = 0.03)						



Test for subgroup differences: Chi² = 0.32, df = 1 (P = 0.57), I² = 0%

Symptoms of mania at post-treatment

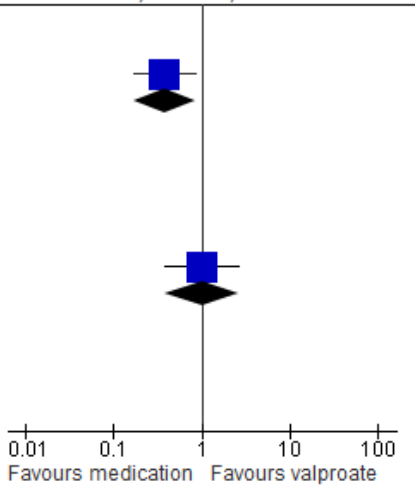
Study or Subgroup	Medication Mean	Medication SD	Medication Total	Valproate Mean	Valproate SD	Valproate Total	Weight	Std. Mean Difference IV, Random, 95% CI
11.2.1 Risperidone								
PAVULURI2012*	10	6.4	10	14	9.3	11	24.2%	-0.48 [-1.35, 0.39]
PAVULURI2010	10.22	10.5	32	15.24	12.49	33	75.8%	-0.43 [-0.92, 0.06]
Subtotal (95% CI)			**42**			**44**	**100.0%**	**-0.44 [-0.87, -0.01]**
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.93); I² = 0%								
Test for overall effect: Z = 2.02 (P = 0.04)								
11.2.4 Quetiapine								
DELBELLO2006*	-23	7.28011	25	-19	7.382412	25	100.0%	-0.54 [-1.10, 0.03]
Subtotal (95% CI)			**25**			**25**	**100.0%**	**-0.54 [-1.10, 0.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.86 (P = 0.06)								



Test for subgroup differences: Chi² = 0.07, df = 1 (P = 0.79), I² = 0%

Number of participants withdrawing (for any reason)

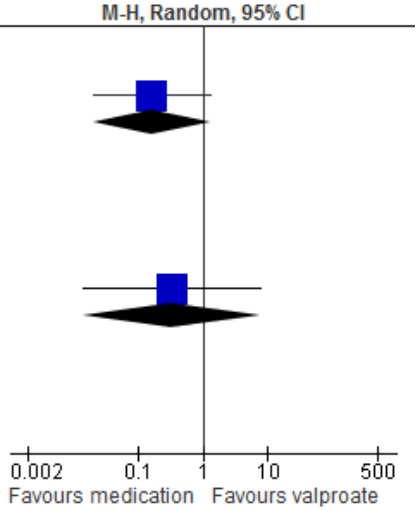
Study or Subgroup	Medication Events	Medication Total	Valproate Events	Valproate Total	Weight	Risk Ratio M-H, Random, 95% CI
11.3.1 Risperidone						
PAVULURI2012*	0	14	0	14		Not estimable
PAVULURI2010	6	33	16	33	100.0%	0.38 [0.17, 0.84]
Subtotal (95% CI)		**47**		**47**	**100.0%**	**0.38 [0.17, 0.84]**
Total events	6		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.39 (P = 0.02)						
11.3.4 Quetiapine						
DELBELLO2006*	6	25	6	25	100.0%	1.00 [0.37, 2.68]
Subtotal (95% CI)		**25**		**25**	**100.0%**	**1.00 [0.37, 2.68]**
Total events	6		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						



Test for subgroup differences: Chi² = 2.28, df = 1 (P = 0.13), I² = 56.1%

Number of participants withdrawing because of side effects

Study or Subgroup	Medication Events	Medication Total	Valproate Events	Valproate Total	Weight	Risk Ratio M-H, Random, 95% CI
11.4.1 Risperidone						
PAVULURI2012*	0	14	0	14		Not estimable
PAVULURI2010	1	33	6	33	100.0%	0.17 [0.02, 1.31]
Subtotal (95% CI)		**47**		**47**	**100.0%**	**0.17 [0.02, 1.31]**
Total events	1		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.70 (P = 0.09)						
11.4.4 Quetiapine						
DELBELLO2006*	0	25	1	25	100.0%	0.33 [0.01, 7.81]
Subtotal (95% CI)		**25**		**25**	**100.0%**	**0.33 [0.01, 7.81]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						



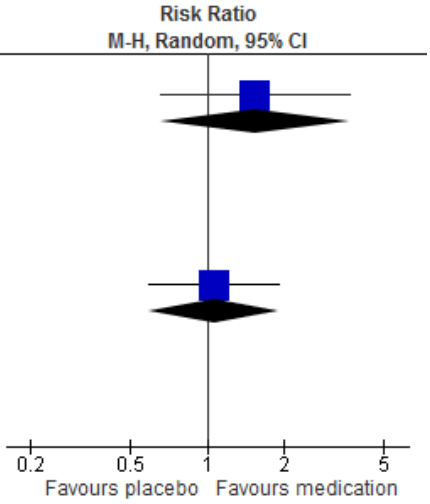
Test for subgroup differences: Chi² = 0.13, df = 1 (P = 0.72), I² = 0%

Anticonvulsants

Outcomes for anticonvulsants compared with placebo

Response (50% reduction in manic symptoms) at post-treatment

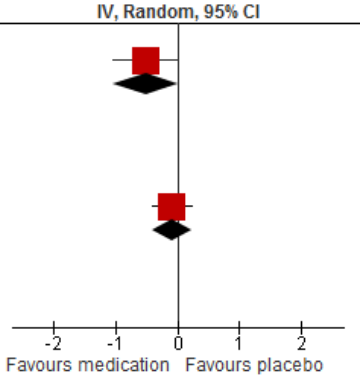
Study or Subgroup	Medication Events	Medication Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
2.1.5 Topiramate						
DELBELLO2005	10	29	6	27	100.0%	1.55 [0.65, 3.69]
Subtotal (95% CI)		**29**		**27**	**100.0%**	**1.55 [0.65, 3.69]**
Total events	10		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.99 (P = 0.32)						
2.1.6 Valproate						
WAGNER2009	18	74	16	70	100.0%	1.06 [0.59, 1.92]
Subtotal (95% CI)		**74**		**70**	**100.0%**	**1.06 [0.59, 1.92]**
Total events	18		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.84)						



Test for subgroup differences: Chi² = 0.50, df = 1 (P = 0.48), I² = 0%

Symptoms of mania at post-treatment

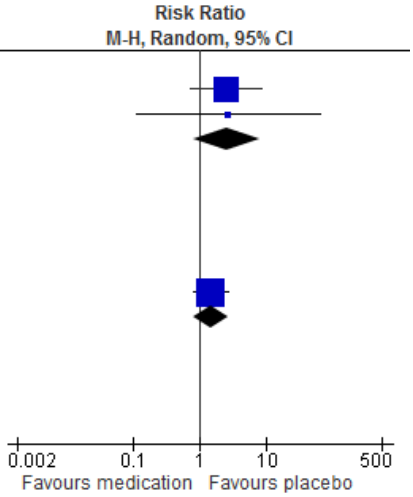
Study or Subgroup	Std. Mean Difference	SE	Medication Total	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.4.5 Topiramate						
DELBELLO2005	-0.5073478	0.26802248	29	27	100.0%	-0.51 [-1.03, 0.02]
Subtotal (95% CI)			**29**	**27**	**100.0%**	**-0.51 [-1.03, 0.02]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.89 (P = 0.06)						
2.4.6 Valproate						
WAGNER2009	-0.08722867	0.16592846	74	70	100.0%	-0.09 [-0.41, 0.24]
Subtotal (95% CI)			**74**	**70**	**100.0%**	**-0.09 [-0.41, 0.24]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.53 (P = 0.60)						



Test for subgroup differences: Chi² = 1.78, df = 1 (P = 0.18), I² = 43.7%

Number of participants withdrawing (for any reason)

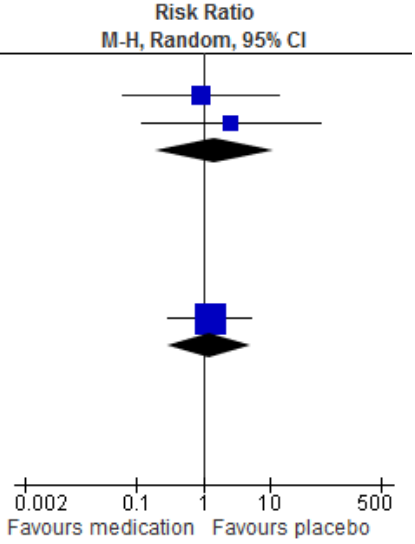
Study or Subgroup	Medication Events	Medication Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
2.2.5 Topiramate						
DELBELLO2005	8	29	3	27	86.8%	2.48 [0.73, 8.40]
ELILILLY2011	1	16	0	14	13.2%	2.65 [0.12, 60.21]
Subtotal (95% CI)		**45**		**41**	**100.0%**	**2.50 [0.80, 7.79]**
Total events	9		3			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%						
Test for overall effect: Z = 1.58 (P = 0.11)						
2.2.6 Valproate						
WAGNER2009	20	74	13	70	100.0%	1.46 [0.79, 2.70]
Subtotal (95% CI)		**74**		**70**	**100.0%**	**1.46 [0.79, 2.70]**
Total events	20		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.19 (P = 0.23)						



Test for subgroup differences: Chi² = 0.68, df = 1 (P = 0.41), I² = 0%

Number of participants withdrawing because of side effects

Study or Subgroup	Medication Events	Medication Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
2.5.5 Topiramate						
DELBELLO2005	1	29	1	27	56.9%	0.93 [0.06, 14.16]
ELILILLY2011	1	16	0	14	43.1%	2.65 [0.12, 60.21]
Subtotal (95% CI)		**45**		**41**	**100.0%**	**1.46 [0.19, 11.38]**
Total events	2		1			
Heterogeneity: Tau² = 0.00; Chi² = 0.25, df = 1 (P = 0.62); I² = 0%						
Test for overall effect: Z = 0.36 (P = 0.72)						
2.5.6 Valproate						
WAGNER2009	4	74	3	70	100.0%	1.26 [0.29, 5.44]
Subtotal (95% CI)		**74**		**70**	**100.0%**	**1.26 [0.29, 5.44]**
Total events	4		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.31 (P = 0.76)						

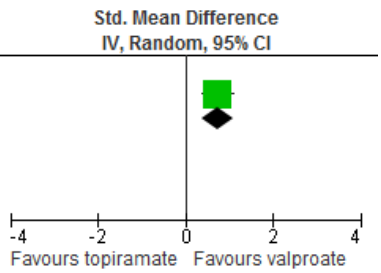


Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.91), I² = 0%

Outcomes for anticonvulsants compared with valproate

Symptoms of mania at post-treatment

Study or Subgroup	Topiramate Mean	Topiramate SD	Topiramate Total	Valproate Mean	Valproate SD	Valproate Total	Weight	Std. Mean Difference IV, Random, 95% CI
17.2.5 >12 years								
HEBRANI2009*	-18.59	23.29	59	-35	21.24	61	100.0%	0.73 [0.36, 1.10]
Subtotal (95% CI)			**59**			**61**	**100.0%**	**0.73 [0.36, 1.10]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.88 (P = 0.0001)								



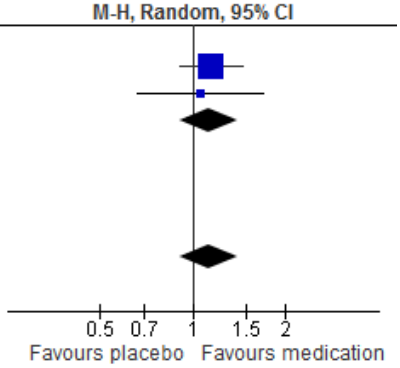
Test for subgroup differences: Not applicable

Acute depression

Outcomes for quetiapine compared with placebo

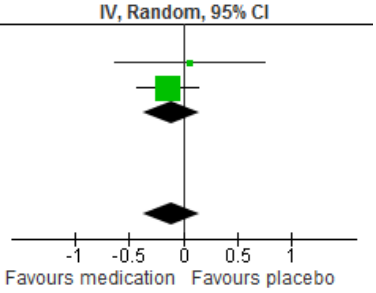
Number of participants responding to treatment (50% reduction in depressive symptoms)

Study or Subgroup	Medication Events	Medication Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
18.1.1 Quetiapine						
ASTRAZENECA2011B	58	92	55	100	79.9%	1.15 [0.90, 1.45]
DELBELLO2009*	12	17	10	15	20.1%	1.06 [0.66, 1.70]
Subtotal (95% CI)		**109**		**115**	**100.0%**	**1.13 [0.91, 1.39]**
Total events	70		65			
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.77); I² = 0%						
Test for overall effect: Z = 1.12 (P = 0.26)						
Total (95% CI)		**109**		**115**	**100.0%**	**1.13 [0.91, 1.39]**
Total events	70		65			
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.77); I² = 0%						
Test for overall effect: Z = 1.12 (P = 0.26)						
Test for subgroup differences: Not applicable						



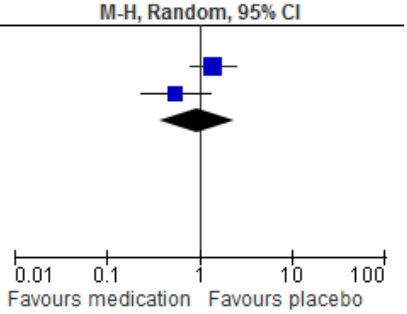
Symptoms of depression at post-treatment

Study or Subgroup	Medication Mean	Medication SD	Medication Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
19.2.1 Quetiapine								
DELBELLO2009*	-19	14	17	-20	17	15	14.3%	0.06 [-0.63, 0.76]
ASTRAZENECA2011B	-29.6	15.826	92	-27.3	16	100	85.7%	-0.14 [-0.43, 0.14]
Subtotal (95% CI)			**109**			**115**	**100.0%**	**-0.11 [-0.38, 0.15]**
Heterogeneity: Tau² = 0.00; Chi² = 0.29, df = 1 (P = 0.59); I² = 0%								
Test for overall effect: Z = 0.85 (P = 0.39)								
Total (95% CI)			**109**			**115**	**100.0%**	**-0.11 [-0.38, 0.15]**
Heterogeneity: Tau² = 0.00; Chi² = 0.29, df = 1 (P = 0.59); I² = 0%								
Test for overall effect: Z = 0.85 (P = 0.39)								
Test for subgroup differences: Not applicable								



Number of participants withdrawing (for any reason)

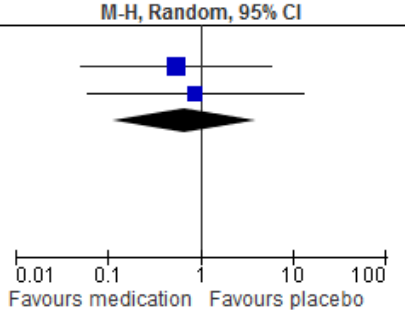
Study or Subgroup	Medication Events	Medication Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
19.3.1 Quetiapine						
ASTRAZENECA2011B	21	93	16	100	56.2%	1.41 [0.79, 2.54]
DELBELLO2009*	5	17	8	15	43.8%	0.55 [0.23, 1.32]
Subtotal (95% CI)		**110**		**115**	**100.0%**	**0.93 [0.37, 2.34]**
Total events	26		24			
Heterogeneity: Tau² = 0.30; Chi² = 3.09, df = 1 (P = 0.08); I² = 68%						
Test for overall effect: Z = 0.14 (P = 0.89)						
Test for subgroup differences: Not applicable						



Number of participants withdrawing because of side effects

Study or Subgroup	Medication Events	Medication Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
19.4.1 Quetiapine						
ASTRAZENECA2011B	1	93	2	100	55.9%	0.54 [0.05, 5.83]
DELBELLO2009*	1	17	1	15	44.1%	0.88 [0.06, 12.91]
Subtotal (95% CI)		**110**		**115**	**100.0%**	**0.67 [0.11, 3.98]**
Total events	2		3			

Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 1 (P = 0.79); I² = 0%
Test for overall effect: Z = 0.44 (P = 0.66)

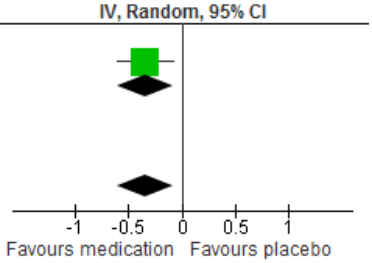


Test for subgroup differences: Not applicable

Outcomes for olanzapine and fluoxetine combination compared with placebo

Symptoms of depression at post-treatment

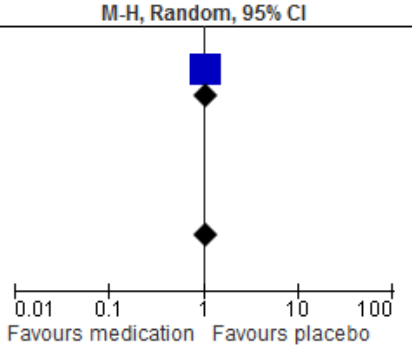
Study or Subgroup	Medication Mean	Medication SD	Medication Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
20.2.2 Fluoxetine + Olanzapine								
ELILILLY2013	-28.43	14.733	170	-23.4	13.656	84	100.0%	-0.35 [-0.61, -0.09]
Subtotal (95% CI)			**170**			**84**	**100.0%**	**-0.35 [-0.61, -0.09]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.60 (P = 0.009)								
Total (95% CI)			**170**			**84**	**100.0%**	**-0.35 [-0.61, -0.09]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.60 (P = 0.009)								



Test for subgroup differences: Not applicable

Number of participants withdrawing (for any reason)

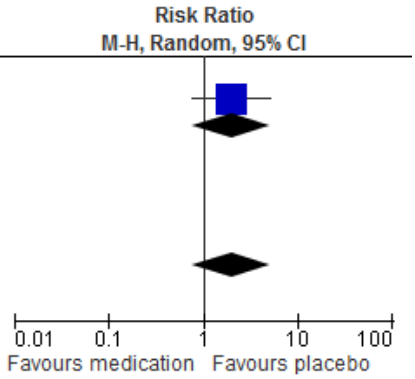
Study or Subgroup	Medication Events	Medication Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
20.3.2 Fluoxetine + Olanzapine						
ELILILLY2013	78	194	37	97	100.0%	1.05 [0.78, 1.43]
Subtotal (95% CI)		**194**		**97**	**100.0%**	**1.05 [0.78, 1.43]**
Total events	78		37			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.34 (P = 0.74)						
Total (95% CI)		**194**		**97**	**100.0%**	**1.05 [0.78, 1.43]**
Total events	78		37			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.34 (P = 0.74)						



Test for subgroup differences: Not applicable

Number of participants withdrawing because of side effects

Study or Subgroup	Medication Events	Medication Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
20.4.2 Fluoxetine + Olanzapine						
ELILILLY2013	20	194	5	97	100.0%	2.00 [0.77, 5.17]
Subtotal (95% CI)		**194**		**97**	**100.0%**	**2.00 [0.77, 5.17]**
Total events	20		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.43 (P = 0.15)						
Total (95% CI)		**194**		**97**	**100.0%**	**2.00 [0.77, 5.17]**
Total events	20		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.43 (P = 0.15)						

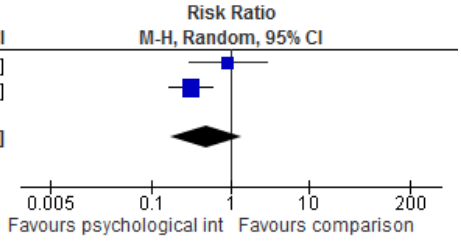


Test for subgroup differences: Not applicable

Psychological interventions

Outcomes for family focused therapy compared with TAU

Number of participants withdrawing (for any reason)

Study or Subgroup	Psychological int Events	Psychological int Total	Comparison Events	Comparison Total	Weight	Risk Ratio M-H, Random, 95% CI
MIKLOWITZ2008*	5	30	5	28	40.4%	0.93 [0.30, 2.88]
CUMMINGS2007	10	79	35	87	59.6%	0.31 [0.17, 0.59]
Total (95% CI)		**109**		**115**	**100.0%**	**0.49 [0.17, 1.39]**
Total events	15		40			

Heterogeneity: Tau² = 0.38; Chi² = 2.72, df = 1 (P = 0.10); I² = 63%
Test for overall effect: Z = 1.34 (P = 0.18)