

eTable 1. The characteristics and demographics of the included studies

Author Year, Country	Diagnosis, Structure Interview	Severity Threshold	Population, Age	Study Design, Setting	Duration	Intervention, Meain Daily dose of antipsychotics, Sample Size	Age (Female, %)	Measurement	Baseline Severity
¹ Bourin 2014, International	DSM-IV-TR, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, 18-65 y/o	Double-blind RCT, Inpatients and discharge with follow-up	6 weeks	Quetiapine, 666.9 mg, 183 Quetiapine + Lithium, 623.1 mg, 173	38.8 ± 12.1 (33.9) 37.9 ± 12.7 (41.6)	YMRS	29.9 30.0
² Bowden 2005, USA	DSM-IV; nil	YMRS ≥ 20	Bipolar I disorder, acute manic episode, ≥18 y/o	Double-blind RCT, Inpatients	3 weeks	Quetiapine, 586.0 mg, 107 Lithium, 98 Placebo, 97	38.0 (43.9) 41.3 (40.8) 38.8 (42.1)	YMRS	32.7 33.3 34.0
³ Calabrese 2015, International	DSM-IV-TR, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, 18-65 y/o	Double-blind RCT, Inpatients and discharge with follow-up	3 weeks	Cariprazine, 4.8 mg, 167 Cariprazine, 9.1 mg, 169 Placebo, 161	43.1 ± 12.2 (46.1) 41.2 ± 11.3 (49.7) 41.5 ± 11.4 (44.7)	YMRS	33.2 ± 5.6 32.9 ± 4.7 32.6 ± 5.8
⁴ Cutler 2011, USA	DSM-IV-TR, SCID	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, 18-65 y/o	Double-blind RCT, Inpatients	3 weeks	Quetiapine, (603.8 mg), 151 Placebo, 160	41.3 ± 10.3 (38.3) 40.8 ± 10.7 (41.5)	YMRS	28.8 ± 5.4 28.4 ± 5.1
⁵ Durgam 2015, USA, Russia, India	DSM-IV-TR, MINI	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, 18-65 y/o	Double-blind RCT, Inpatients and discharge with follow-up	3 weeks	Cariprazine, 8.8 mg, 118 Placebo, 117	38.0 ± 10.3 (32.2) 38.7 ± 11.0 (34.7)	YMRS	30.6 ± 5.4 30.2 ± 5.4
⁶ Feifel 2011, USA	DSM-IV, nil	YMRS ≥ 17	Bipolar I disorder, manic or mixed episode, 18-65 y/o	Single-blind RCT, Inpatients	3 weeks	Quetiapine, 800.0 mg, 15 Valproic acid, 13	36.9 (46.7) 42.4 (38.5)	YMRS	25.7 ± 4.3 29.3 ± 5.0
⁷ Garfinkel 1980, Canada	Criteria of Feighner for mania	nil	Bipolar I disorder, manic episode	Double-blind RCT, Inpatients	3 weeks	Haloperidol, 28.0 mg, 7 Lithium, 7 Haloperidol + Lithium, 24.2 mg, 7	37.0 ± 5.3 (42.9) 41.5 ± 5.8 (71.4) 37.0 ± 6.1 (57.1)	TRAM	40.0 ± 5.4 41.2 ± 5.0 40.6 ± 5.1
⁸ Gopal 2005, India	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, 18-65 y/o	Double-blind RCT, Inpatients and discharge with follow-up	3 weeks	Risperidone, 5.6 mg, 146 Placebo, 145	34.7 ± 12.0 (32.0) 35.5 ± 12.3 (44.0)	YMRS	36.9 ± 8.0 37.4 ± 7.9
⁹ Hirschfeld 2004, USA	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic episode, ≥ 18 y/o	Double-blind RCT, Inpatients	3 weeks	Risperidone, 4.1 mg, 127 Placebo, 119	38.1 ± 11.9 (47.0) 39.5 ± 12.2 (39.0)	YMRS	29.1 ± 5.1 29.2 ± 5.2
¹⁰ Kanba 2012, Asia	DSM-IV-TR, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, 18-64 y/o	Double-blind RCT, Inpatients and outpatients	3 weeks	Aripiprazole, 22.9 mg, 128 Placebo, 130	37.5 ± 12.5 (57.4) 37.8 ± 12.7 (60.0)	YMRS	28.3 ± 6.0 28.0 ± 6.0
¹¹ Katagiri 2012, Japan	DSM-IV-TR, MINI	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, ≥ 18 y/o	Double-blind RCT, Inpatients and outpatients	3 weeks	Olanzapine, 11.2 mg, 104 Haloperidol, 5.0 mg, 20 Placebo, 97	43.1 ± 12.0 (52.9) 49.3 ± 11.9 (45.0) 42.5 ± 10.9 (58.8)	YMRS)	27.7 ± 5.9 26.6 ± 4.5 26.9 ± 5.6
¹² Keck 2003 (Aripiprazole), USA	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, ≥18 y/o	Double-blind RCT , Inpatients and discharge with follow-up	3 weeks	Aripiprazole, (27.9mg), 130 Placebo, 132	40.5 ± 12.7 (55.0) 40.5 ± 11.8 (58.0)	YMRS	28.2 ± 6.1 29.7 ± 5.8
¹³ Keck 2003 (Ziprasidone), USA, Brazil	DSM-IV, SCID	SADS-MRS ≥ 14	Bipolar I disorder, manic or mixed episode, ≥18 y/o	Double-blind RCT, Inpatients	3 weeks	Ziprasidone, 130.1 mg, 140 Placebo, 70	39.0 ±10.6 (44.0) 37.0± 10.3 (49.0)	SADS-MRS	27.0 ± 3.8 26.7 ± 7.0
¹⁴ Keck 2009, USA	DSM-IV-TR MINI	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, ≥ 18 y/o	Double-blind RCT, Inpatients and discharge with follow-up	3 weeks	Lithium, 155 Aripiprazole, 23.2 mg, 154 Placebo, 163	39.6 ± 10.5 (49.0) 39.6 ± 10.6 (88.0) 39.8 ± 11.3 (48.0)	YMRS	29.2 ± 5.0 28.5 ± 5.0 28.9 ± 5.1
¹⁵ Khanna 2005, India	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, ≥18 y/o	Double-blind RCT, Inpatients	3 weeks	Risperidone, 5.6 mg, 146 Placebo, 144	35.7 ± 12.1 (32.0) 34.5 ± 12.0 (44.0)	YMRS	37.1 ± 8.5 37.5 ± 8.4
¹⁶ Li 2008, China	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic episode, 18-65 y/o	Double-blind RCT, Inpatients	4 weeks	Quetiapine, 648.2 mg, 77 Lithium, 77	32.7 ± 11.5 (57.1) 33.6 ± 11.4 (48.1)	YMRS	29.3 ± 5.8 29.8 ± 5.7
¹⁷ McIntyre 2005, South America	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic episode, ≥ 18 y/o	Double-blind RCT, Inpatients	3 weeks	Quetiapine 559 mg, 102 Haloperidol, 101 Placebo, 99	42.8 (18-79) (63.4) 45.1 (18-76) (63.3) 40.6 (18-72) (63.0)	YMRS	
¹⁸ McIntyre 2009, International	DSM-IV-TR, MINI	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, ≥ 18 y/o	Single-blind RCT, Inpatients	3 weeks	Olanzapine, 15.8 mg, 190 Asenapine, 18.2 mg, 194 Placebo, 104	40.1 ± 11.3 (40.0) 38.7 ± 11.9 (41.2) 39.4 ± 12.0 (50.0)	YMRS	29.7 ± 6.6 29.4 ± 6.7 28.3 ± 6.3
¹⁹ McIntyre 2010, International	DSM-IV-TR, MINI	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, ≥ 18 y/o	Double-blind RCT, Inpatients and outpatients	3 weeks	Olanzapine, 15.9 mg, 203 Asenapine, 18.4 mg, 183 Placebo, 94	38.4 ± 10.8 (42.9) 39.1 ± 12.3 (50.3) 38.1 ± 12.5 (51.0)	YMRS	27.7 ± 5.9 26.6 ± 4.5 26.9 ± 5.6
²⁰ Moreno 2007, Brazil	DSM-IV-SCID	YMRS ≥ 20	Bipolar I disorder, acute manic episode, adult	Double-blind RCT, Inpatients	6 weeks	Olanzapine, 13.6 mg, 7 Haloperidol, 5.8 mg, 5	38.6 ± 14.2 (57.0) 39.2 ± 11.2 (100.0)	YMRS	30.6 ± 5.0 30.6 ± 8.6
²¹ Niufan 2008, China	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode ,18-50 y/o	Double-blind RCT, Inpatients and outpatients	4 weeks	Olanzapine, 18.4 mg, 69 Lithium, 71	31.2 ± 12.6 (56.5) 34.0 ± 13.8 (49.3)	YMRS	34.0 ± 6.8 32.4 ± 7.2
²² Perlis 2006, USA	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode ,18-70 y/o	Inpatients	3 weeks	Olanzapine, 14.7 mg, 165 Risperidone, 3.9 mg, 164	38.1 ± 11.1 (57.0) 37.7 ± 10.9 (52.4)	YMRS	26.6 ± 5.0 26.7 ± 5.0

²³ Potkin 2005, USA, Brazil, Maxico	DSM-IV, SCID	SADS-MRS ≥ 14	Bipolar I disorder, manic or mixed episode, ≥18 y/o	Double-blind RCT, Inpatients	3 weeks	Ziprasidone, 112.0 mg, 139 Placebo, 66	38.9 ±11.6 (51.1) 39.0 ± 11.5 (45.5)	SADS-MRS	26.2 ± 7.2 26.4 ± 7.5
²⁴ Rezayat 2014, Iran	DSM-IV-TR	nil	Bipolar I disorder, acute manic episode	Double-blind RCT, Inpatients	4 weeks	Aripiprazole, 27.0 mg, 31 Risperidone, 6.0 mg, 31	34.0 ± 8.6 (50.0) 34.0 ± 9.1 (50.0)	YMRS	39.4 ± 6.8 39.7 ± 9.9
²⁵ Sachs 2006, USA	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, ≥ 18 y/o	Double-blind RCT, Inpatients and discharge with follow-up	3 weeks	Aripiprazole, 27.3 mg, 137 Placebo, 135	40.4 ± 10.5 (50.0) 37.3 ± 10.5 (53.0)	YMRS	28.8 ± 4.9 28.5 ± 4.9
²⁶ Sachs 2015, USA, India	DSM-IV-TR, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode ,18-65 y/o	Double-blind RCT, Inpatients and discharge with follow-up	3 weeks	Cariprazine, 9.0 mg, 158 Placebo,154	35.8 ± 11.4 (33.5) 36.7 ± 11.8 (38.3)	YMRS	32.3 ± 5.8 32.1 ± 5.6
²⁷ Shafti 2010, Iran	DSM-IV-TR, nil	nil	Bipolar I disorder, manic episode	Double-blind RCT, Inpatients	3 weeks	Olanzapine, 20.3 mg, 20 Lithium, 20	nil, (100.0) nil, (100.0)	MSRS	Frequency 78.5 ± 12.6 77.1 ± 10.7 Intensity 80.3 ± 8.7 79.2 ± 9.6
²⁸ Shafti 2018, Iran	DSM-IV-TR, nil	nil	Bipolar I disorder, manic episode	Double-blind RCT, Inpatients	3 weeks	Aripiprazole, 25.8 mg, 15 Lithium, 15	30.7±10.4(0.0) 29.8±2.1(0.0)	MSRS	Frequency 79.6±10.5 80.5±9.9 Intensity 79.3±9.8 82.2±10.3
²⁹ Smulevich 2005, Russia	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic episode ≥18 y/o	Double-blind RCT, Inpatients	3 weeks	Risperidone, 4.2 mg, 153 Placebo, 138 Haloperidol, 8.0 mg, 144	41.3 ± 13.1 (46.1) 39.4 ± 13.0 (49.3) 38.5 ± 12.2 (45.8)	YMRS	32.1 ± 6.9 31.5 ± 6.7 31.3 ± 6.5
³⁰ Tohen 1999, USA	DSM-IV, SCID	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, 18-65 y/o	Double-blind RCT, Inpatients	3 weeks	Olanzapine, 14.9 mg, 70 Placebo, 69	39.5 ± 11.0 (51.8) 39.5 ± 11.0 (51.8)	YMRS	28.7 ± 6.7 27.7 ± 6.5
³¹ Tohen 2000, USA	DSM-IV, SCID-P	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, 18-70 y/o	Double-blind RCT, Inpatients and outpatients	4 weeks	Olanzapine, 16.4 mg, 54 Placebo, 56	38.3 ± 10.7 (50.9) 39.0 ± 10.1 (50.0)	YMRS	28.8 ± 6.7 29.4 ± 6.8
³² Tohen 2002, USA	DSM-IV, SCID	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, 18-75 y/o	Double-blind RCT, Inpatients	3 weeks	Olanzapine, 17.4 mg, 125 Valproic acid, 126	40.0 ± 12.0 (57.6) 41.1 ± 12.3 (57.1)	YMRS	27.4 ± 5.2 27.9 ± 6.6
³³ Tohen 2003, International	DSM-IV, SCID	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, ≥ 18 y/o	Double-blind RCT, Inpatients and outpatients	6 weeks	Olanzapine, 15.0 mg, 219 Haloperidol, 7.1 mg, 234	41.0 ± 13.0 (63.2) 40.0 ± 13.0 (57.1)	YMRS	31.1±7.6 30.6±7.7
³⁴ Tohen 2008, USA	DSM-IV, SCID	30 ≥ SADS-MRS ≥ 20	Bipolar I disorder, manic or mixed episode without psychotic feature, 18-65 y/o	Double-blind RCT, Inpatients and outpatients	3 weeks	Valproic acid, 201 Olanzapine, 11.4 mg, 215 Placebo, 105	39.2 ± 11.7 (53.2) 39.5 ± 11.9 (54.2) 40.6 ± 12.8 (46.5)	YMRS	23.9 ± 2.8 23.8 ± 2.8 23.5 ± 2.5
³⁵ Vieta 2005, International	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, 18-65 y/o	Double-blind RCT, Inpatients and outpatients	3 weeks	Aripiprazole, 22.6 mg, 175 Haloperidol, 11.6 mg, 172	42.6 ± 11.9 (56.6) 41.0 ± 11.8 (66.9)	YMRS	31.1 ± 6.6 31.5 ± 7.9
³⁶ Vieta 2010 (Paliperidone), International	DSM-IV, nil	YMRS ≥ 20	Bipolar I disorder, manic or mixed episode, ≥ 18 y/o	Double-blind RCT, Inpatients and discharge with follow-up	3 weeks	Quetiapine, 600.0 mg, 192 Paliperidone, 9.0 mg, 190 Placebo, 104	39.0 ± 11.0 (40.0) 40.0 ± 11.3 (42.0) 38.0 ± 10.0 (47.0)	YMRS	28.0 ± 5.1 27.0 ± 5.0 27.0 ± 5.0
³⁷ Vieta 2010 (Ziprasidone) International	DSM-IV, SCID	SADS-MRS ≥ 14	Bipolar I disorder, manic or mixed episode, ≥ 18 y/o	Double-blind RCT, Inpatients and discharge with follow-up	3 weeks	Ziprasidone, 116.2 mg, 178 Haloperidol, 16.0 mg, 172 Placebo, 88	38.5 ± 11.6 (39.3) 38.9 ± 12.2 (42.1) 36.9 ± 13.8 (43.2)	SADS-MRS	
³⁸ Vieta 2021, International	DSM-5, MINI	YMRS ≥ 24	Bipolar I disorder, manic or mixed episode, 18-65 y/o	Double-blind RCT, Inpatients	3 weeks	Brexpiprazole 3.21mg, 158 placebo, 164	43.4 ± 11.7 (50.6) 44.5 ± 11.2 (50.6)	YMRS	30.4 ± 4.7 30.5 ± 4.2
³⁸ Vieta 2021, International	DSM-5, MINI	YMRS ≥ 24	Bipolar I disorder, manic or mixed episode, 18-65 y/o	Double-blind RCT, Inpatients	3 weeks	Brexpiprazole 3.22mg, 163 placebo, 170	44.6 ± 10.7 (52.1) 44.3 ± 12.0 (48.2)	YMRS	30.7 ± 4.3 30.7 ± 4.0
³⁹ Xu 2015, China	DSM-IV, nil	YMRS ≥ 17	Bipolar I disorder, acute manic episode, 19-60 y/o	Double-blind RCT, Inpatients	4 weeks	Valproic acid, 40 Olanzapine, 16.3 mg, 40 Valproic acid + Olanzapine, 13.1mg, 40	31.7 ± 8.2 (51.4) 30.9 ± 9.1 (51.3) 30.2 ± 7.8 (52.6)	YMRS	34.4 ± 9.1 34.6 ± 7.0 34.3 ± 6.1
⁴⁰ Young 2009, USA	DSM-IV-TR MINI	YMRS ≥ 20	Bipolar I, manic or mixed episode, ≥ 18 y/o	Double-blind RCT, Inpatients and discharge with follow-up	3 weeks	Aripiprazole, 23.6 mg, 167 Haloperidol, 8.5 mg, 165 Placebo, 153	40.5 (57.0) 41.6 (56.0) 40.2 (54.0)	YMRS	28.0 ± 5.8 27.6 ± 5.7 28.4 ± 5.9
⁴¹ Zajacka 2002, USA	DSM-IV-SADS	SADS-MRS ≥ 25	Bipolar I disorder, manic or mixed episode, ≥ 18 y/o	Double-blind RCT, Inpatients	3 weeks	Olanzapine, 14.7mg, 57 Valproic acid, 63	38.1 ± 12.2 (47.0) 38.9 ± 12.1 (44.0)	SADS-MRS	32.3 30.8

Note: DSM-III-R, IV, IV-TR, and 5: The Diagnostic and Statistical Manual of Mental Disorders 3rd revision, 4th, 4th text revision, and 5th edition; SADS: Schedule for Affective Disorders and Schizophrenia; KSADS: Schedule for Affective Disorders and Schizophrenia for School-Age Children; SADS-MRS: Schedule for Affective Disorders and Schizophrenia-Mania Rating Score; SCID: Structured Clinical Interview for DSM-IV Disorders; SCID-P: Structured Clinical Interview for DSM-IV Disorders, Patient version; MINI: Mini-International Neuropsychiatric Interview; YMRS: Young Mania Rating Scale; CGI-BP: Clinical Global Impressions-Bipolar Scale; TRAM: Treatment Response Assessment Method; MSRS: Manic State Rating Scale

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eTable 2. Quantifying heterogeneity

Between study variance: τ^2	Assessment of heterogeneity by τ^2
0.02	Low to moderate heterogeneity

As we anticipated considerable between-study heterogeneity, a random-effects model was used to pool effect sizes. The restricted maximum likelihood estimator (Viechtbauer, 2005) was used to calculate the heterogeneity variance. We inferred the magnitude of heterogeneity by comparing the estimated τ^2 to empirical distributions of heterogeneity typically found in meta-analyses. The predictive τ^2 distribution for mental health outcomes has a median of 0.049 and an IQR of 0.01 to 0.242 (Rhodes et al., 2016). Low heterogeneity could be considered when the estimated τ^2 is less than the 25% quantile of the empirical distribution, moderate heterogeneity for τ^2 between 25% and 50% quantile, and high heterogeneity for τ^2 larger than the 50% quantile.

Reference

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eTable 3. Global inconsistency test (incoherence between direct and indirect estimates)

Random-effects design-by-treatment interaction model	
Q	P-value
49.923	0.002

We evaluated global consistency under the assumption of a full design-by-treatment interaction model, using the *decompose.design* function in R packagenetmeta.

eTable 4. Local inconsistency test (note-splitting method)

Arm 1	Arm 2	k	I2	Direct estimate	Indirect estimate	Network meta-analysis	Incoherence
Asenapine	Aripiprazole	0	.	.	0.11 (-0.16; 0.37)	0.11 (-0.16; 0.37)	.
Brexiprazole	Aripiprazole	0	.	.	0.38 (0.09; 0.67)	0.38 (0.09; 0.67)	.
Cariprazine	Aripiprazole	0	.	.	-0.03 (-0.28; 0.22)	-0.03 (-0.28; 0.22)	.
Haloperidol	Aripiprazole	2	50.0%	0.02 (-0.23; 0.27)	-0.25 (-0.48; -0.02)	-0.12 (-0.29; 0.05)	0.1171
Haloperidol+Lithium	Aripiprazole	0	.	.	0.00 (-1.10; 1.10)	0.00 (-1.10; 1.10)	.
Lithium	Aripiprazole	2	88.7%	-0.14 (-0.47; 0.19)	0.13 (-0.14; 0.41)	0.02 (-0.19; 0.23)	0.2112
Olanzapine	Aripiprazole	0	.	.	0.02 (-0.16; 0.20)	0.02 (-0.16; 0.20)	.
Olanzapine+Valproate	Aripiprazole	0	.	.	-1.08 (-1.60; -0.57)	-1.08 (-1.60; -0.57)	.
Paliperidone	Aripiprazole	0	.	.	-0.13 (-0.47; 0.22)	-0.13 (-0.47; 0.22)	.
Placebo	Aripiprazole	5	0.0%	0.39 (0.23; 0.55)	0.71 (0.42; 0.99)	0.47 (0.33; 0.61)	0.0574
Quetiapine	Aripiprazole	0	.	.	0.06 (-0.15; 0.27)	0.06 (-0.15; 0.27)	.
Quetiapine+Lithium	Aripiprazole	0	.	.	-0.24 (-0.64; 0.17)	-0.24 (-0.64; 0.17)	.
Risperidone	Aripiprazole	1	.	0.31 (-0.26; 0.89)	-0.28 (-0.50; -0.05)	-0.20 (-0.41; 0.01)	0.0613
Valproate	Aripiprazole	0	.	.	0.41 (0.16; 0.67)	0.41 (0.16; 0.67)	.
Ziprasidone	Aripiprazole	0	.	.	0.13 (-0.12; 0.38)	0.13 (-0.12; 0.38)	.
Asenapine	Brexiprazole	0	.	.	-0.28 (-0.61; 0.06)	-0.28 (-0.61; 0.06)	.
Asenapine	Cariprazine	0	.	.	0.14 (-0.17; 0.44)	0.14 (-0.17; 0.44)	.
Asenapine	Haloperidol	0	.	.	0.23 (-0.03; 0.49)	0.23 (-0.03; 0.49)	.
Asenapine	Haloperidol+Lithium	0	.	.	0.10 (-1.01; 1.22)	0.10 (-1.01; 1.22)	.
Asenapine	Lithium	0	.	.	0.09 (-0.20; 0.37)	0.09 (-0.20; 0.37)	.
Asenapine	Olanzapine	2	0.0%	0.12 (-0.13; 0.36)	-0.08 (-0.64; 0.47)	0.09 (-0.14; 0.31)	0.5221
Asenapine	Olanzapine+Valproate	0	.	.	1.19 (0.66; 1.72)	1.19 (0.66; 1.72)	.
Asenapine	Paliperidone	0	.	.	0.23 (-0.16; 0.62)	0.23 (-0.16; 0.62)	.
Asenapine	Placebo	2	37.3%	-0.40 (-0.67; -0.14)	-0.23 (-0.69; 0.23)	-0.36 (-0.59; -0.13)	0.5285

Asenapine	Quetiapine	0	.	.	0.05 (-0.23; 0.33)	0.05 (-0.23; 0.33)	.
Asenapine	Quetiapine+Lithium	0	.	.	0.34 (-0.10; 0.79)	0.34 (-0.10; 0.79)	.
Asenapine	Risperidone	0	.	.	0.30 (0.03; 0.58)	0.30 (0.03; 0.58)	.
Asenapine	Valproate	0	.	.	-0.31 (-0.60; -0.02)	-0.31 (-0.60; -0.02)	.
Asenapine	Ziprasidone	0	.	.	-0.02 (-0.33; 0.29)	-0.02 (-0.33; 0.29)	.
Brexipiprazole	Cariprazine	0	.	.	0.41 (0.09; 0.74)	0.41 (0.09; 0.74)	.
Brexipiprazole	Haloperidol	0	.	.	0.50 (0.22; 0.79)	0.50 (0.22; 0.79)	.
Brexipiprazole	Haloperidol+Lithium	0	.	.	0.38 (-0.74; 1.50)	0.38 (-0.74; 1.50)	.
Brexipiprazole	Lithium	0	.	.	0.36 (0.05; 0.67)	0.36 (0.05; 0.67)	.
Brexipiprazole	Olanzapine	0	.	.	0.36 (0.08; 0.64)	0.36 (0.08; 0.64)	.
Brexipiprazole	Olanzapine+Valproate	0	.	.	1.46 (0.91; 2.02)	1.46 (0.91; 2.02)	.
Brexipiprazole	Paliperidone	0	.	.	0.51 (0.11; 0.92)	0.51 (0.11; 0.92)	.
Brexipiprazole	Placebo	2	49.1%	-0.09 (-0.34; 0.16)	.	-0.09 (-0.34; 0.16)	.
Brexipiprazole	Quetiapine	0	.	.	0.32 (0.02; 0.62)	0.32 (0.02; 0.62)	.
Brexipiprazole	Quetiapine+Lithium	0	.	.	0.62 (0.16; 1.08)	0.62 (0.16; 1.08)	.
Brexipiprazole	Risperidone	0	.	.	0.58 (0.27; 0.88)	0.58 (0.27; 0.88)	.
Brexipiprazole	Valproate	0	.	.	-0.03 (-0.36; 0.30)	-0.03 (-0.36; 0.30)	.
Brexipiprazole	Ziprasidone	0	.	.	0.25 (-0.08; 0.58)	0.25 (-0.08; 0.58)	.
Cariprazine	Haloperidol	0	.	.	0.09 (-0.16; 0.34)	0.09 (-0.16; 0.34)	.
Cariprazine	Haloperidol+Lithium	0	.	.	-0.03 (-1.14; 1.08)	-0.03 (-1.14; 1.08)	.
Cariprazine	Lithium	0	.	.	-0.05 (-0.33; 0.23)	-0.05 (-0.33; 0.23)	.
Cariprazine	Olanzapine	0	.	.	-0.05 (-0.29; 0.19)	-0.05 (-0.29; 0.19)	.
Cariprazine	Olanzapine+Valproate	0	.	.	1.05 (0.51; 1.59)	1.05 (0.51; 1.59)	.
Cariprazine	Paliperidone	0	.	.	0.10 (-0.28; 0.48)	0.10 (-0.28; 0.48)	.
Cariprazine	Placebo	3	0.0%	-0.50 (-0.70; -0.29)	.	-0.50 (-0.70; -0.29)	.
Cariprazine	Quetiapine	0	.	.	-0.09 (-0.35; 0.18)	-0.09 (-0.35; 0.18)	.

Cariprazine	Quetiapine+Lithium	0	.	.	0.21 (-0.23; 0.64)	0.21 (-0.23; 0.64)	.
Cariprazine	Risperidone	0	.	.	0.17 (-0.10; 0.44)	0.17 (-0.10; 0.44)	.
Cariprazine	Valproate	0	.	.	-0.44 (-0.74; -0.15)	-0.44 (-0.74; -0.15)	.
Cariprazine	Ziprasidone	0	.	.	-0.16 (-0.46; 0.14)	-0.16 (-0.46; 0.14)	.
Haloperidol	Haloperidol+Lithium	1	.	-0.12 (-1.21; 0.96)	.	-0.12 (-1.21; 0.96)	.
Haloperidol	Lithium	0	.	.	-0.14 (-0.36; 0.08)	-0.14 (-0.36; 0.08)	.
Haloperidol	Olanzapine	3	0.0%	-0.20 (-0.48; 0.08)	-0.11 (-0.32; 0.10)	-0.14 (-0.31; 0.02)	0.6036
Haloperidol	Olanzapine+Valproate	0	.	.	0.96 (0.45; 1.47)	0.96 (0.45; 1.47)	.
Haloperidol	Paliperidone	0	.	.	0.01 (-0.34; 0.35)	0.01 (-0.34; 0.35)	.
Haloperidol	Placebo	5	57.2%	-0.59 (-0.77; -0.41)	-0.59 (-0.81; -0.36)	-0.59 (-0.73; -0.45)	0.9985
Haloperidol	Quetiapine	1	.	-0.25 (-0.65; 0.14)	-0.15 (-0.39; 0.08)	-0.18 (-0.38; 0.02)	0.6661
Haloperidol	Quetiapine+Lithium	0	.	.	0.11 (-0.29; 0.52)	0.11 (-0.29; 0.52)	.
Haloperidol	Risperidone	1	.	0.13 (-0.23; 0.49)	0.05 (-0.20; 0.29)	0.07 (-0.13; 0.28)	0.6929
Haloperidol	Valproate	0	.	.	-0.54 (-0.78; -0.29)	-0.54 (-0.78; -0.29)	.
Haloperidol	Ziprasidone	1	.	-0.52 (-0.87; -0.17)	-0.04 (-0.35; 0.27)	-0.25 (-0.49; -0.02)	0.0467*
Haloperidol+Lithium	Lithium	0	.	.	-0.02 (-1.12; 1.09)	-0.02 (-1.12; 1.09)	.
Haloperidol+Lithium	Olanzapine	0	.	.	-0.02 (-1.12; 1.08)	-0.02 (-1.12; 1.08)	.
Haloperidol+Lithium	Olanzapine+Valproate	0	.	.	1.08 (-0.12; 2.28)	1.08 (-0.12; 2.28)	.
Haloperidol+Lithium	Paliperidone	0	.	.	0.13 (-1.01; 1.27)	0.13 (-1.01; 1.27)	.
Haloperidol+Lithium	Placebo	0	.	.	-0.47 (-1.56; 0.63)	-0.47 (-1.56; 0.63)	.
Haloperidol+Lithium	Quetiapine	0	.	.	-0.06 (-1.16; 1.05)	-0.06 (-1.16; 1.05)	.
Haloperidol+Lithium	Quetiapine+Lithium	0	.	.	0.24 (-0.92; 1.40)	0.24 (-0.92; 1.40)	.
Haloperidol+Lithium	Risperidone	0	.	.	0.20 (-0.91; 1.30)	0.20 (-0.91; 1.30)	.
Haloperidol+Lithium	Valproate	0	.	.	-0.41 (-1.52; 0.70)	-0.41 (-1.52; 0.70)	.
Haloperidol+Lithium	Ziprasidone	0	.	.	-0.13 (-1.24; 0.98)	-0.13 (-1.24; 0.98)	.
Lithium	Olanzapine	2	93.5%	-0.00 (-0.37; 0.37)	-0.00 (-0.25; 0.25)	-0.00 (-0.21; 0.20)	0.9961

Lithium	Olanzapine+Valproate	0	.	.	1.10 (0.58; 1.63)	1.10 (0.58; 1.63)	.
Lithium	Paliperidone	0	.	.	0.15 (-0.21; 0.50)	0.15 (-0.21; 0.50)	.
Lithium	Placebo	2	57.2%	-0.42 (-0.68; -0.15)	-0.48 (-0.74; -0.22)	-0.45 (-0.63; -0.26)	0.7467
Lithium	Quetiapine	2	33.2%	0.06 (-0.22; 0.35)	-0.16 (-0.47; 0.15)	-0.04 (-0.25; 0.17)	0.3083
Lithium	Quetiapine+Lithium	0	.	.	0.26 (-0.15; 0.66)	0.26 (-0.15; 0.66)	.
Lithium	Risperidone	0	.	.	0.22 (-0.03; 0.46)	0.22 (-0.03; 0.46)	.
Lithium	Valproate	0	.	.	-0.40 (-0.66; -0.13)	-0.40 (-0.66; -0.13)	.
Lithium	Ziprasidone	0	.	.	-0.11 (-0.39; 0.17)	-0.11 (-0.39; 0.17)	.
Olanzapine	Olanzapine+Valproate	1	.	0.65 (0.12; 1.17)	3.80 (2.52; 5.08)	1.10 (0.62; 1.59)	< 0.0001*
Olanzapine	Paliperidone	0	.	.	0.15 (-0.19; 0.49)	0.15 (-0.19; 0.49)	.
Olanzapine	Placebo	6	0.0%	-0.44 (-0.61; -0.28)	-0.45 (-0.67; -0.23)	-0.45 (-0.58; -0.32)	0.9666
Olanzapine	Quetiapine	0	.	.	-0.04 (-0.24; 0.16)	-0.04 (-0.24; 0.16)	.
Olanzapine	Quetiapine+Lithium	0	.	.	0.26 (-0.14; 0.66)	0.26 (-0.14; 0.66)	.
Olanzapine	Risperidone	1	.	0.32 (-0.04; 0.67)	0.17 (-0.06; 0.41)	0.22 (0.02; 0.41)	0.5035
Olanzapine	Valproate	4	90.0%	-0.41 (-0.62; -0.21)	-0.25 (-0.80; 0.31)	-0.39 (-0.59; -0.20)	0.5790
Olanzapine	Ziprasidone	0	.	.	-0.11 (-0.35; 0.14)	-0.11 (-0.35; 0.14)	.
Olanzapine+Valproate	Paliperidone	0	.	.	-0.95 (-1.55; -0.36)	-0.95 (-1.55; -0.36)	.
Olanzapine+Valproate	Placebo	0	.	.	-1.55 (-2.05; -1.05)	-1.55 (-2.05; -1.05)	.
Olanzapine+Valproate	Quetiapine	0	.	.	-1.14 (-1.66; -0.62)	-1.14 (-1.66; -0.62)	.
Olanzapine+Valproate	Quetiapine+Lithium	0	.	.	-0.85 (-1.47; -0.22)	-0.85 (-1.47; -0.22)	.
Olanzapine+Valproate	Risperidone	0	.	.	-0.89 (-1.41; -0.37)	-0.89 (-1.41; -0.37)	.
Olanzapine+Valproate	Valproate	1	.	-2.23 (-2.82; -1.64)	0.23 (-0.68; 1.14)	-1.50 (-1.99; -1.00)	< 0.0001*
Olanzapine+Valproate	Ziprasidone	0	.	.	-1.21 (-1.76; -0.67)	-1.21 (-1.76; -0.67)	.
Paliperidone	Placebo	1	.	-0.63 (-1.00; -0.26)	-0.49 (-1.12; 0.14)	-0.60 (-0.91; -0.28)	0.7116
Paliperidone	Quetiapine	1	.	-0.16 (-0.50; 0.18)	-0.32 (-1.08; 0.44)	-0.19 (-0.50; 0.13)	0.7116
Paliperidone	Quetiapine+Lithium	0	.	.	0.11 (-0.36; 0.58)	0.11 (-0.36; 0.58)	.

Paliperidone	Risperidone	0	.	.	0.07 (-0.29; 0.43)	0.07 (-0.29; 0.43)	.
Paliperidone	Valproate	0	.	.	-0.54 (-0.92; -0.16)	-0.54 (-0.92; -0.16)	.
Paliperidone	Ziprasidone	0	.	.	-0.26 (-0.64; 0.12)	-0.26 (-0.64; 0.12)	.
Placebo	Quetiapine	4	0.0%	0.41 (0.22; 0.59)	0.42 (0.06; 0.78)	0.41 (0.24; 0.58)	0.9641
Placebo	Quetiapine+Lithium	0	.	.	0.70 (0.32; 1.09)	0.70 (0.32; 1.09)	.
Placebo	Risperidone	3	0.0%	0.68 (0.47; 0.89)	0.63 (0.34; 0.93)	0.66 (0.49; 0.84)	0.7984
Placebo	Valproate	1	.	0.09 (-0.27; 0.46)	0.03 (-0.23; 0.30)	0.05 (-0.16; 0.27)	0.7920
Placebo	Ziprasidone	3	0.0%	0.43 (0.20; 0.66)	-0.28 (-0.88; 0.31)	0.34 (0.12; 0.55)	0.0291*
Quetiapine	Quetiapine+Lithium	1	.	0.30 (-0.05; 0.64)	.	0.30 (-0.05; 0.64)	.
Quetiapine	Risperidone	0	.	.	0.25 (0.02; 0.49)	0.25 (0.02; 0.49)	.
Quetiapine	Valproate	1	.	0.22 (-0.58; 1.01)	-0.42 (-0.70; -0.15)	-0.36 (-0.62; -0.10)	0.1363
Quetiapine	Ziprasidone	0	.	.	-0.07 (-0.34; 0.20)	-0.07 (-0.34; 0.20)	.
Quetiapine+Lithium	Risperidone	0	.	.	-0.04 (-0.46; 0.38)	-0.04 (-0.46; 0.38)	.
Quetiapine+Lithium	Valproate	0	.	.	-0.65 (-1.09; -0.22)	-0.65 (-1.09; -0.22)	.
Quetiapine+Lithium	Ziprasidone	0	.	.	-0.37 (-0.81; 0.07)	-0.37 (-0.81; 0.07)	.
Risperidone	Valproate	0	.	.	-0.61 (-0.87; -0.35)	-0.61 (-0.87; -0.35)	.
Risperidone	Ziprasidone	0	.	.	-0.33 (-0.60; -0.06)	-0.33 (-0.60; -0.06)	.
Valproate	Ziprasidone	0	.	.	0.28 (-0.02; 0.58)	0.28 (-0.02; 0.58)	.

eTable 5. CINeMA appraisal

Comparison	Number of studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Aripiprazole:Haloperidol	2	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	Very low
Aripiprazole:Lithium	2	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	Very low
Aripiprazole:Placebo	5	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	Moderate
Aripiprazole:Risperidone	1	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Asenapine:Olanzapine	2	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	Very low
Asenapine:Placebo	2	Some concerns	Some concerns	No concerns	No concerns	Major concerns	No concerns	Low
Brexipiprazole:Placebo	2	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Cariprazine:Placebo	3	Some concerns	Some concerns	No concerns	No concerns	No concerns	Major concerns	Very low
Haloperidol:Olanzapine	3	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	Very low
Haloperidol:Placebo	5	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	Moderate
Haloperidol:Quetiapine	1	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	Very low
Haloperidol:Risperidone	1	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	Very low
Haloperidol:Ziprasidone	1	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Lithium:Olanzapine	2	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	Very low
Lithium:Placebo	2	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	Moderate
Lithium:Quetiapine	2	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	Very low
Olanzapine:Placebo	6	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	Moderate
Olanzapine:Risperidone	1	Some concerns	Some concerns	No concerns	No concerns	Major concerns	No concerns	Very low
Olanzapine:Valproate	4	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	Moderate
Paliperidone:Placebo	1	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	Moderate
Paliperidone:Quetiapine	1	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	Very low

Placebo:Quetiapine	4	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	Moderate
Placebo:Risperidone	3	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	Moderate
Placebo:Valproate	1	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	Very low
Placebo:Ziprasidone	3	Some concerns	Some concerns	No concerns	No concerns	Major concerns	Major concerns	Very low
Quetiapine:Valproate	1	Some concerns	Some concerns	No concerns	No concerns	Major concerns	No concerns	Very low
Aripiprazole:Asenapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Aripiprazole:Brexiprazole	0	Some concerns	Some concerns	No concerns	No concerns	Major concerns	Major concerns	Very low
Aripiprazole:Cariprazine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Aripiprazole:Olanzapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Aripiprazole:Paliperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Aripiprazole:Quetiapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Aripiprazole:Valproate	0	Some concerns	Some concerns	No concerns	No concerns	Major concerns	Major concerns	Very low
Aripiprazole:Ziprasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Asenapine:Brexiprazole	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Asenapine:Cariprazine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Asenapine:Haloperidol	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Asenapine:Lithium	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Asenapine:Paliperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Asenapine:Quetiapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Asenapine:Risperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Asenapine:Valproate	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Asenapine:Ziprasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Brexiprazole:Cariprazine	0	Some concerns	Some concerns	No concerns	No concerns	Major concerns	Major concerns	Very low

Brexpiprazole:Haloperidol	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Major concerns	Very low
Brexpiprazole:Lithium	0	Some concerns	Some concerns	No concerns	No concerns	Major concerns	Major concerns	Very low
Brexpiprazole:Olanzapine	0	Some concerns	Some concerns	No concerns	No concerns	Major concerns	Major concerns	Very low
Brexpiprazole:Paliperidone	0	Some concerns	Some concerns	No concerns	No concerns	Major concerns	Major concerns	Very low
Brexpiprazole:Quetiapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Brexpiprazole:Risperidone	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Major concerns	Very low
Brexpiprazole:Valproate	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Brexpiprazole:Ziprasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Cariprazine:Haloperidol	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Cariprazine:Lithium	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Cariprazine:Olanzapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Cariprazine:Paliperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Cariprazine:Quetiapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Cariprazine:Risperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Cariprazine:Valproate	0	Some concerns	Some concerns	No concerns	No concerns	Major concerns	Major concerns	Very low
Cariprazine:Ziprasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Haloperidol:Lithium	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Haloperidol:Paliperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Haloperidol:Valproate	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Major concerns	Very low
Lithium:Paliperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Lithium:Risperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Lithium:Valproate	0	Some concerns	Some concerns	No concerns	No concerns	Major concerns	Major concerns	Very low
Lithium:Ziprasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low

Olanzapine:Paliperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Olanzapine:Quetiapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Olanzapine:Ziprasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Paliperidone:Risperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Paliperidone:Valproate	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Major concerns	Very low
Paliperidone:Ziprasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Quetiapine:Risperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Quetiapine:Ziprasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low
Risperidone:Valproate	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Major concerns	Very low
Risperidone:Ziprasidone	0	Some concerns	Some concerns	No concerns	No concerns	Major concerns	Major concerns	Very low
Valproate:Ziprasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Major concerns	Very low

eTable 6. Direct ratio analyses for dose equivalents to olanzapine 1 mg

Drug	Group	n	Dose	Upper	Lower	t	P-value	Change(%)	Certainty ^a
Haloperidol*	Mania	590	0.47	0.49	0.45	70.73	<0.001	-47.2%	Moderate
	Schizophrenia	1953	0.89	0.89	0.89				
Risperidone*	Mania	668	0.27	0.28	0.26	0	>0.999	0.0%	Moderate
	Schizophrenia	1623	0.27	0.27	0.27				
Asenapine	Mania	770	1.15	1.16	1.14			16.2%	High
	Schizophrenia	913	0.99	na					

^aThe certainty of evidence was according to the results of GRADE appraisal (eTable 7, eTable 8, and eTable 13).

eTable 7. GRADE for haloperidol dose equivalent to olanzapine 1 mg

Initial level of certainty	Downgrading or upgrading		Final level of certainty
High level of certainty All the included studies of haloperidol and olanzapine were blinded randomized controlled trials.	Risk of bias	All studies including haloperidol and olanzapine did not have high risk of bias, except for the study by Garfinkel et al (1980; haloperidol) had high risk of bias.	Weight mean dose: Low Direct ratio analyses: Low Direct and indirect ratio analyses: Very low
	Inconsistency	In meta-analysis of mean dose, the I ² was 99.9% for haloperidol, and 98.5% for olanzapine.	
	Indirectness	No serious indirectness for weight mean dose method and direct ratio analysis. Indirectness should be considered in direct and indirect ratio analysis.	
	Imprecision	Not serious. Narrow 95% confidence intervals with the point estimate for both haloperidol and olanzapine.	
	Publications	Not serious. Egger’s test (P value) was 0.26 for all included studies.	

eTable 8. GRADE for risperidone dose equivalent to olanzapine 1 mg

Initial level of certainty	Downgrading or upgrading		Final level of certainty
High level of certainty All the included studies of risperidone and olanzapine were blinded randomized controlled trials.	Risk of bias	All studies including risperidone and olanzapine did not have high risk of bias.	Weight mean dose: Moderate Direct ratio analyses: Moderate Direct and indirect ratio analyses: Low
	Inconsistency	In meta-analysis of mean dose, the I ² was 98.8% for risperidone, and 98.5% for olanzapine.	
	Indirectness	No serious indirectness for weight mean dose method and direct ratio analysis. Indirectness should be considered in direct and indirect ratio analysis.	
	Imprecision	Not serious. Narrow 95% confidence intervals with the point estimate for both risperidone and olanzapine.	
	Publications	Not serious. Egger’s test (P value) was 0.26 for all included studies.	

eTable 9. GRADE for paliperidone dose equivalent to olanzapine 1 mg

Initial level of certainty	Downgrading or upgrading		Final level of certainty
High level of certainty All the included studies of paliperidone and olanzapine were blinded randomized controlled trials.	Risk of bias	All studies including paliperidone and olanzapine did not have high risk of bias.	Weight mean dose: Moderate
	Inconsistency	In meta-analysis of mean dose, the I^2 was 98.5% for olanzapine, and there was only one study on paliperidone.	
	Indirectness	No serious indirectness for weight mean dose method.	
	Imprecision	Not serious. Narrow 95% confidence intervals with the point estimate for both paliperidone and olanzapine.	
	Publications	Not serious. Egger's test (P value) was 0.26 for all included studies.	

eTable 10. GRADE for ziprasidone dose equivalent to olanzapine 1 mg

Initial level of certainty	Downgrading or upgrading		Final level of certainty
High level of certainty All the included studies of ziprasidone and olanzapine were blinded randomized controlled trials.	Risk of bias	All studies including ziprasidone and olanzapine did not have high risk of bias.	Weight mean dose: Moderate Direct and indirect ratio analyses: Low
	Inconsistency	In meta-analysis of mean dose, the I^2 was 93.9% for ziprasidone, and 98.5% for olanzapine.	
	Indirectness	No serious indirectness for weight mean dose method. Indirectness should be considered in direct and indirect ratio analysis.	
	Imprecision	Not serious. Narrow 95% confidence intervals with the point estimate for both ziprasidone and olanzapine.	
	Publications	Not serious. Egger's test (P value) was 0.26 for all included studies.	

eTable 11. GRADE for quetiapine dose equivalent to olanzapine 1 mg

Initial level of certainty	Downgrading or upgrading		Final level of certainty
High level of certainty All the included studies of quetiapine and olanzapine were blinded randomized controlled trials.	Risk of bias	All studies including quetiapine and olanzapine did not have high risk of bias.	Weight mean dose: Moderate
	Inconsistency	In meta-analysis of mean dose, the I^2 was 95.0% for quetiapine, and 98.5% for olanzapine.	
	Indirectness	No serious indirectness for weight mean dose method.	
	Imprecision	Not serious. Narrow 95% confidence intervals with the point estimate for both quetiapine and olanzapine.	
	Publications	Not serious. Egger's test (P value) was 0.26 for all included studies.	

eTable 12. GRADE for aripiprazole dose equivalent to olanzapine 1 mg

Initial level of certainty	Downgrading or upgrading		Final level of certainty
High level of certainty All the included studies of aripiprazole and olanzapine were blinded randomized controlled trials.	Risk of bias	All studies including aripiprazole and olanzapine did not have high risk of bias.	Weight mean dose: Moderate Direct and indirect ratio analyses: Low
	Inconsistency	In meta-analysis of mean dose, the I ² was 96.5% for aripiprazole, and 98.5% for olanzapine.	
	Indirectness	No serious indirectness for weight mean dose method. Indirectness should be considered in direct and indirect ratio analysis.	
	Imprecision	Not serious. Narrow 95% confidence intervals with the point estimate for both aripiprazole and olanzapine.	
	Publications	Not serious. Egger’s test (P value) was 0.26 for all included studies.	

eTable 13. GRADE for asenapine dose equivalent to olanzapine 1 mg

Initial level of certainty	Downgrading or upgrading		Final level of certainty
High level of certainty All the included studies of asenapine and olanzapine were blinded randomized controlled trials.	Risk of bias	All studies including asenapine and olanzapine did not have high risk of bias.	Weight mean dose: Moderate Direct ratio analyses: Moderate Direct and indirect ratio analyses: Low
	Inconsistency	In meta-analysis of mean dose, the I ² was 0.0% for asenapine, and 98.5% for olanzapine.	
	Indirectness	No serious indirectness for weight mean dose method and direct ratio analysis. Indirectness should be considered in direct and indirect ratio analysis.	
	Imprecision	Not serious. Narrow 95% confidence intervals with the point estimate for both asenapine and olanzapine.	
	Publications	Not serious. Egger’s test (P value) was 0.26 for all included studies.	

eTable 14. GRADE for cariprazine dose equivalent to olanzapine 1 mg

Initial level of certainty	Downgrading or upgrading		Final level of certainty
High level of certainty All the included studies of cariprazine and olanzapine were blinded randomized controlled trials.	Risk of bias	All studies including cariprazine and olanzapine did not have high risk of bias.	Weight mean dose: Moderate
	Inconsistency	In meta-analysis of mean dose, the I ² was 98.1% for cariprazine, and 98.5% for olanzapine.	
	Indirectness	No serious indirectness for weight mean doe.	
	Imprecision	Not serious. Narrow 95% confidence intervals with the point estimate for both cariprazine and olanzapine.	
	Publications	Not serious. Egger’s test (P value) was 0.26 for all included studies.	

eTable 15. GRADE for brexpiprazole dose equivalent to olanzapine 1 mg

Initial level of certainty	Downgrading or upgrading		Final level of certainty
High level of certainty All the included studies of brexpiprazole and olanzapine were blinded randomized controlled trials.	Risk of bias	All studies including brexpiprazole and olanzapine did not have high risk of bias.	Weight mean dose: Low
	Inconsistency	In meta-analysis of mean dose, the I ² was 0.0% for brexpiprazole, and 98.5% for olanzapine.	
	Indirectness	No serious indirectness for weight mean dose method.	
	Imprecision	Not serious. Narrow 95% confidence intervals with the point estimate for both brexpiprazole and olanzapine. However, we downgraded the level of certainty, because brexpiprazole did not statistically differ from placebo in the efficacy of antimanic outcome assessed by network meta-analysis.	
	Publications	Not serious. Egger’s test (P value) was 0.26 for all included studies.	