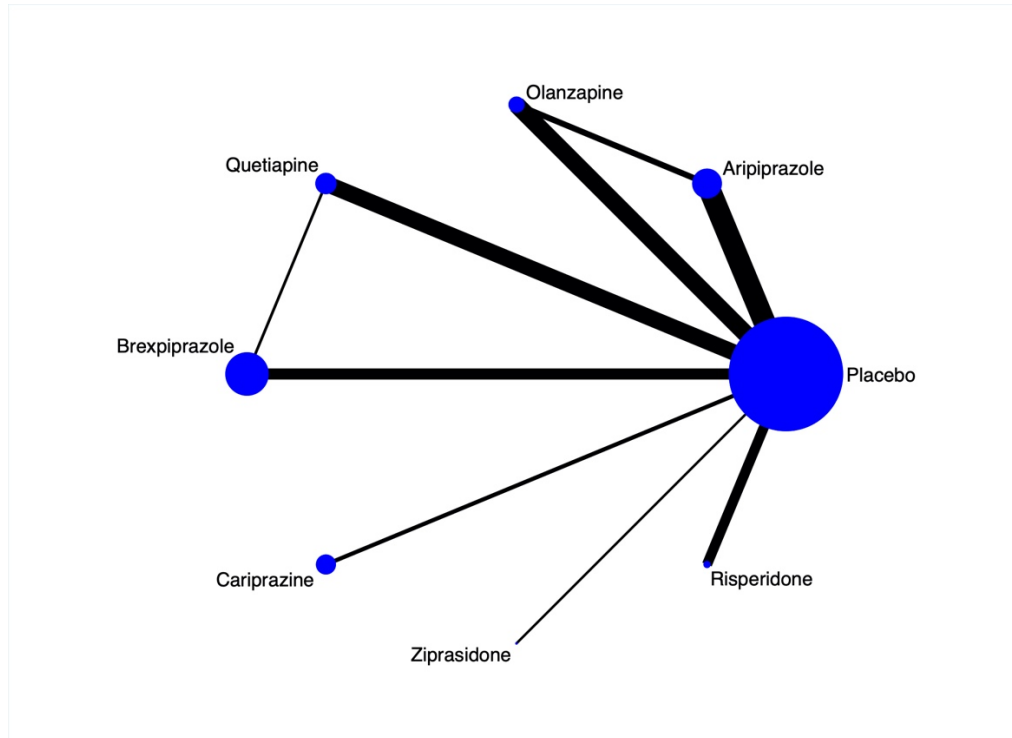


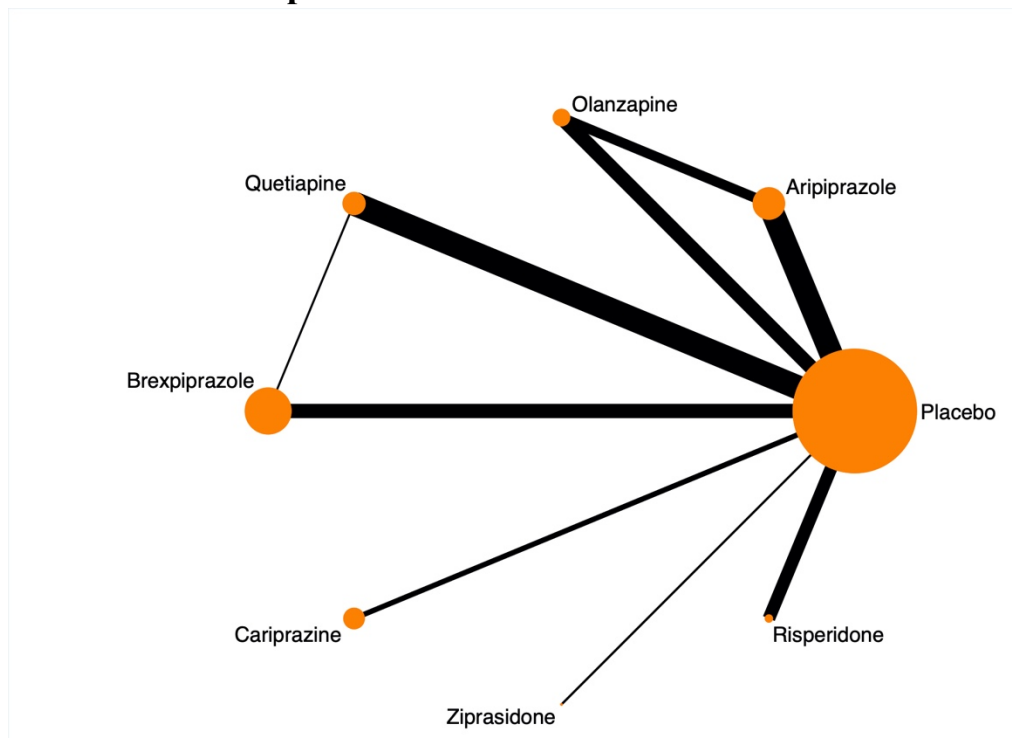
# Supplementary Material

## 1. Network plots

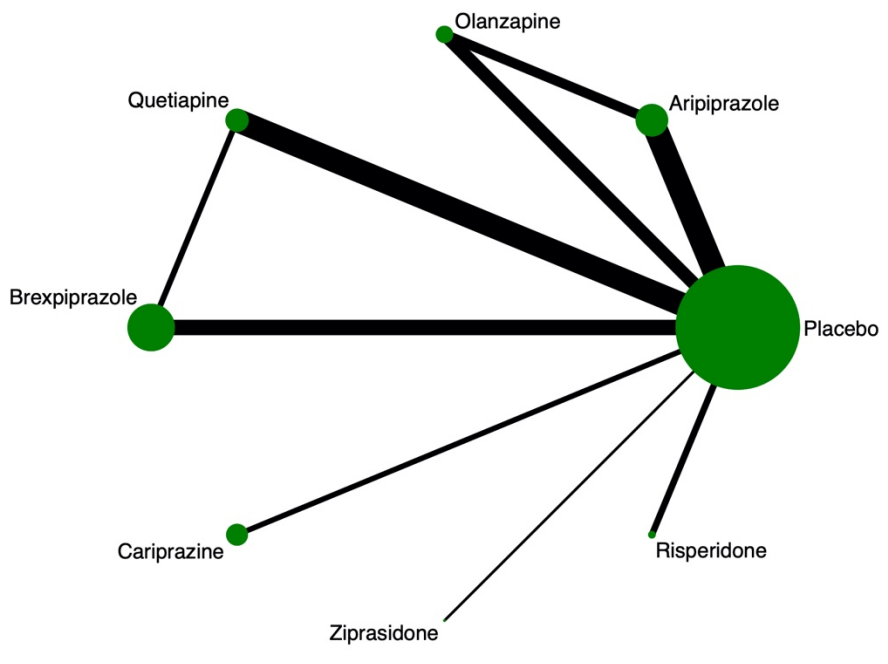
### 1.1 Response



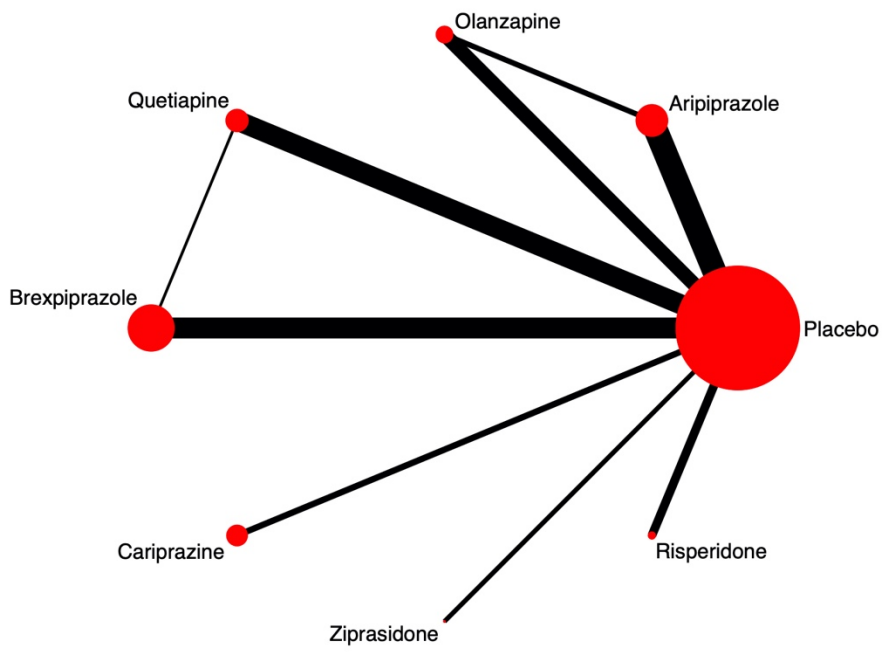
### 1.2 All-cause dropout



### 1.3 Remission



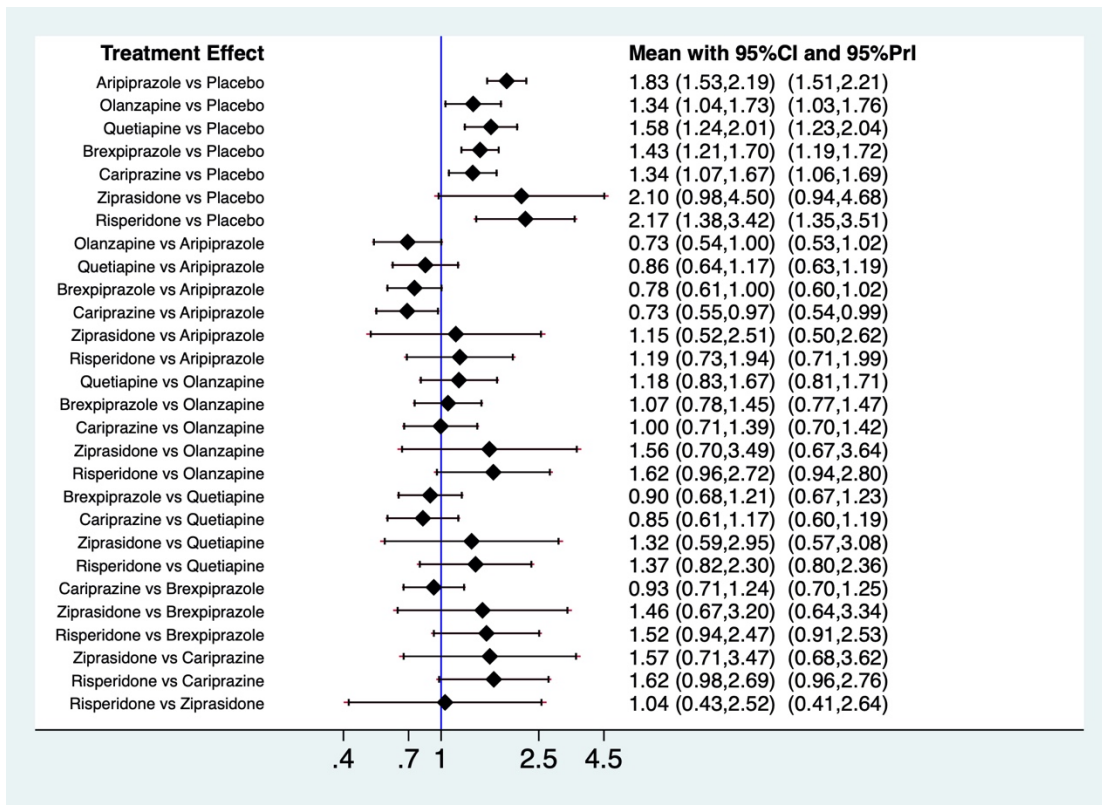
### 1.4 Dropout due to AE



## 2. Evaluation of heterogeneity

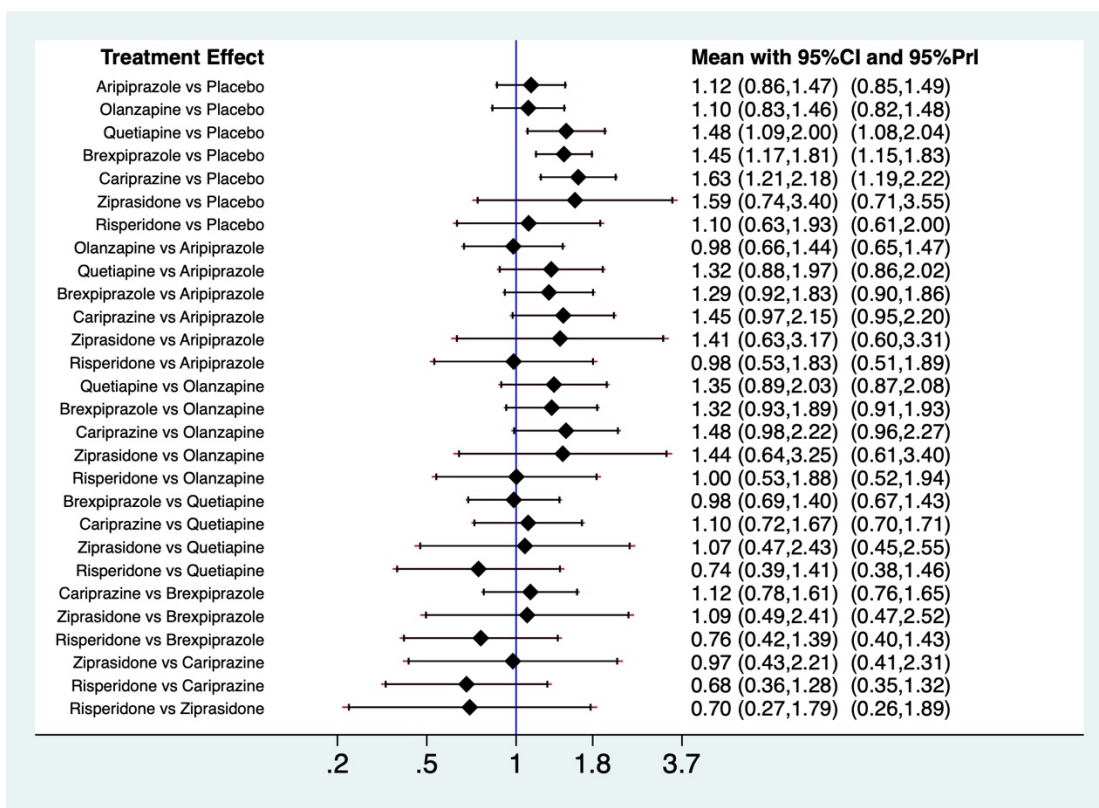
### 2.1 Response

Measure	Value	df	p-value	I <sup>2</sup>
aripiprazole vs placebo	2.59	7	0.920	0.0%
olanzapine vs placebo	3.70	5	0.594	0.0%
quetiapine vs placebo	1.76	5	0.882	0.0%
risperidone vs placebo	0.02	2	0.989	0.0%
brexpiprazole vs placebo	3.26	6	0.775	0.0%
quetiapine vs brexpiprazole	0.00	0	.	.
cariprazine vs placebo	1.03	2	0.597	0.0%
ziprasidone vs placebo	0.00	0	.	.
aripiprazole vs olanzapine	0.00	0	.	.
Overall	18.19	35	0.991	0.0%
Between	5.83	8	0.666	



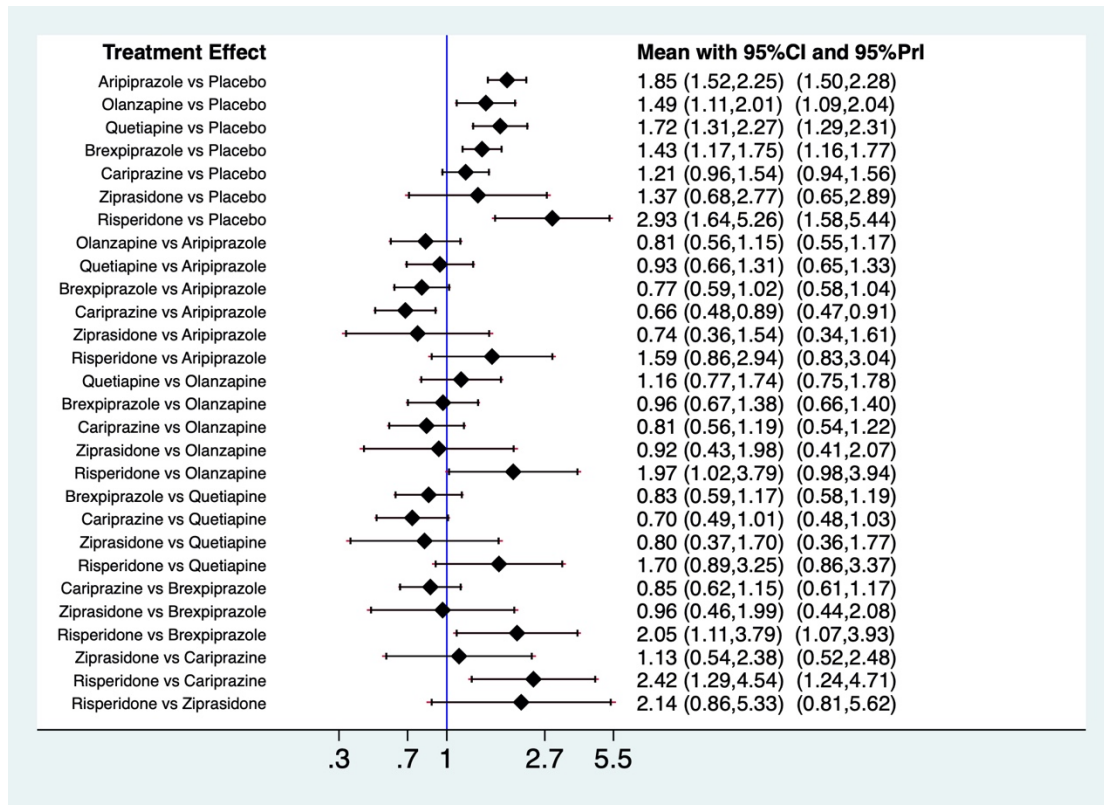
## 2.2 All-cause dropout

Measure	Value	df	p-value	I <sup>2</sup>
aripiprazole vs placebo	4.59	7	0.709	0.0%
olanzapine vs placebo	2.86	4	0.581	0.0%
quetiapine vs placebo	2.51	4	0.643	0.0%
risperidone vs placebo	4.00	2	0.135	50.0%
brexpiprazole vs placebo	3.08	6	0.799	0.0%
quetiapine vs brexpiprazole	0.00	0	.	.
cariprazine vs placebo	1.29	2	0.525	0.0%
ziprasidone vs placebo	0.00	0	.	.
aripiprazole vs olanzapine	0.00	0	.	.
Overall	24.59	33	0.854	0.0%
Between	6.65	8	0.575	



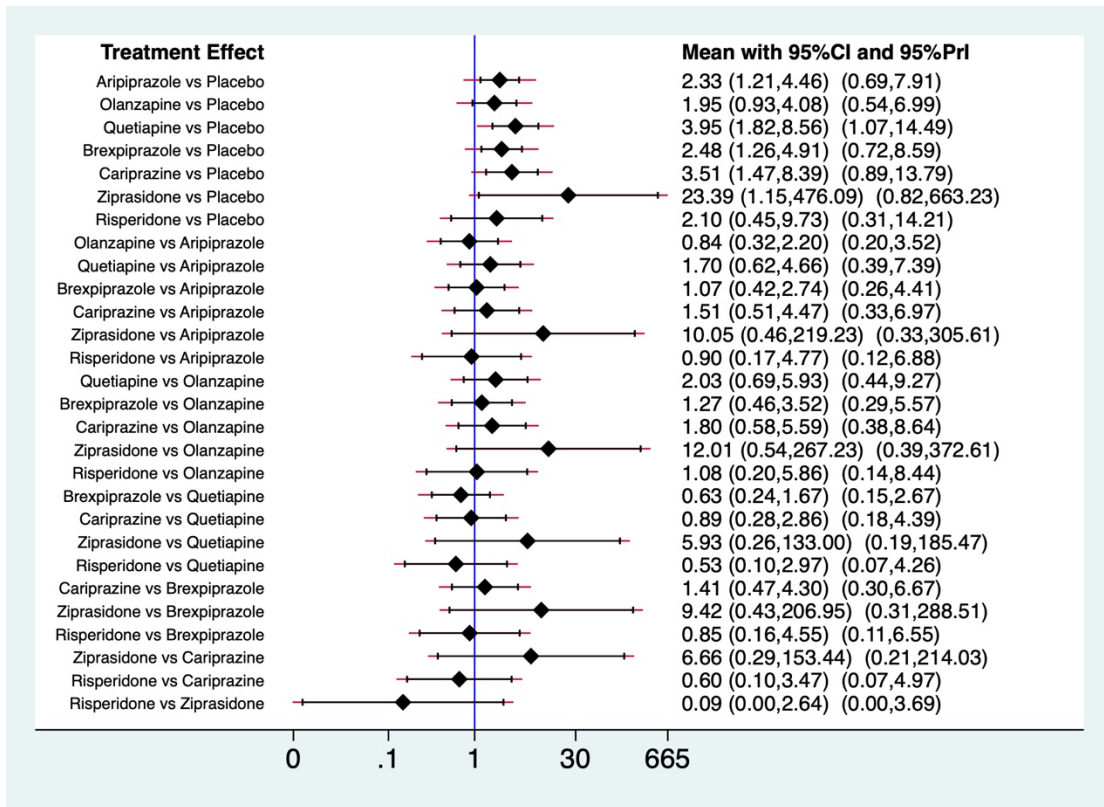
## 2.3 Remission

Measure	Value	df	p-value	I <sup>2</sup>
aripiprazole vs placebo	2.61	7	0.919	0.0%
olanzapine vs placebo	2.70	4	0.609	0.0%
quetiapine vs placebo	2.49	5	0.778	0.0%
risperidone vs placebo	0.02	1	0.901	0.0%
brexpiprazole vs placebo	3.11	6	0.795	0.0%
quetiapine vs brexpiprazole	0.00	0	.	.
cariprazine vs placebo	0.57	2	0.754	0.0%
ziprasidone vs placebo	0.00	0	.	.
aripiprazole vs olanzapine	0.00	0	.	.
Overall	20.74	33	0.952	0.0%
Between	9.25	8	0.321	



## 2.4 Dropout due to AE

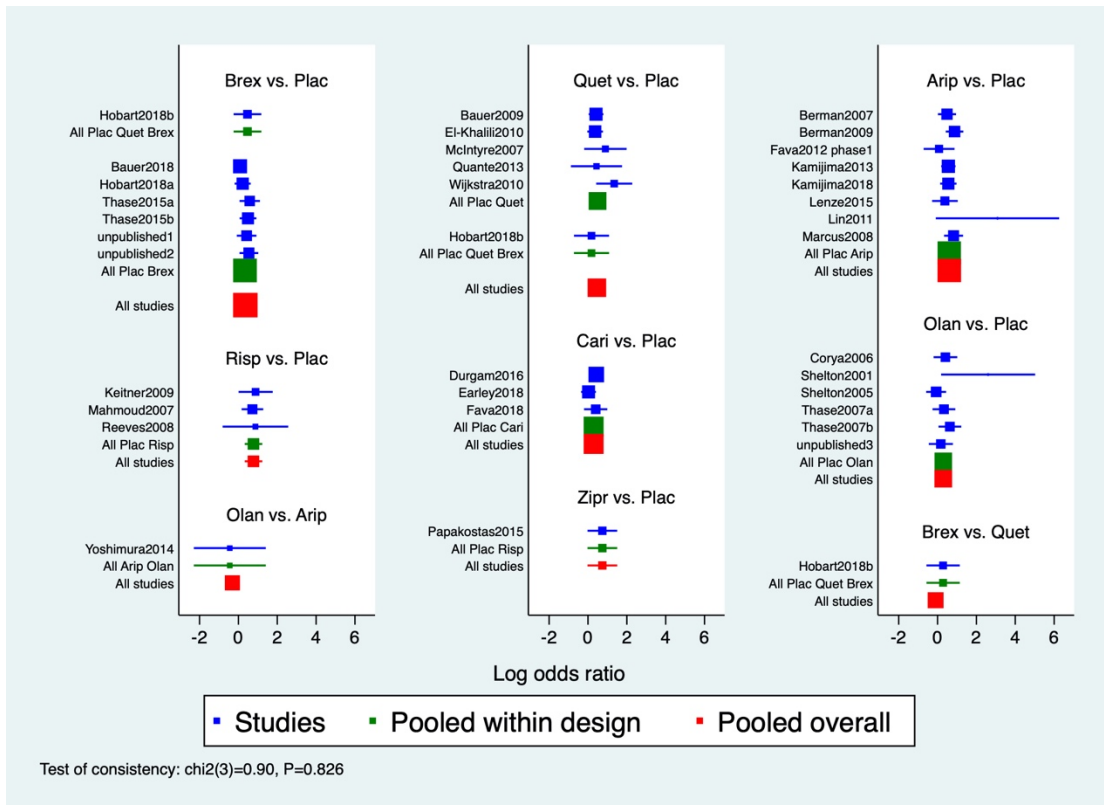
Measure	Value	df	p-value	I <sup>2</sup>
aripiprazole vs placebo	2.85	6	0.827	0.0%
olanzapine vs placebo	12.23	3	0.007	75.5%
quetiapine vs placebo	6.62	4	0.157	39.6%
risperidone vs placebo	0.00	0	.	.
brexpiprazole vs placebo	3.23	6	0.780	0.0%
quetiapine vs brexpiprazole	0.00	0	.	.
cariprazine vs placebo	3.94	2	0.139	49.3%
ziprasidone vs placebo	0.00	0	.	.
aripiprazole vs olanzapine	0.00	0	.	.
Overall	41.47	29	0.063	30.1%
Between	11.33	8	0.184	



### 3. Evaluation of inconsistency

#### 3.1 Response

##### 3.1.1 Global inconsistency



### 3.12 Local inconsistency (loop-specific)

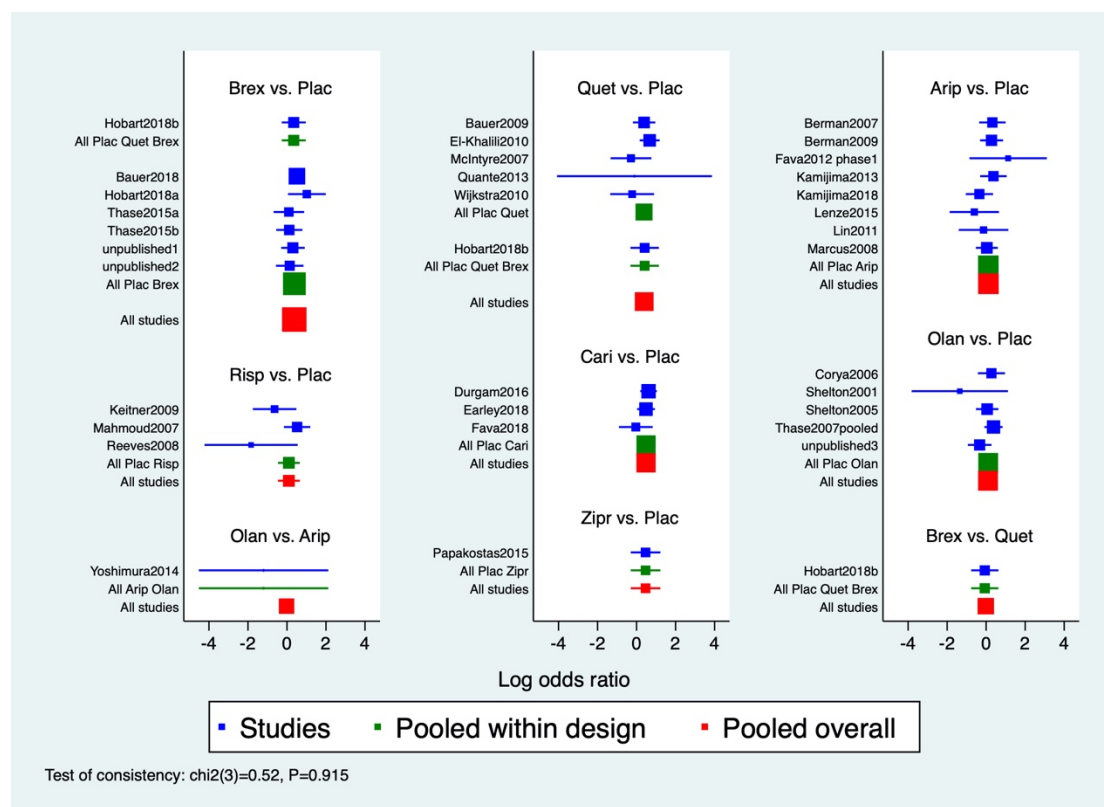
Loop	ROR	z_value	p_value	CI_95	Loop_Heterog_tau2
Pla-Que-Bre	1.512	0.891	0.373	(1.00, 3.76)	0.000
Pla-Ari-Ola	1.158	0.147	0.883	(1.00, 8.18)	0.014

### 3.13 Local inconsistency (node-splitting)

Side	Direct		Indirect		Difference			tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z	
A B	.6031691	.0924444	.7396602	.9539908	-.1364911	.9584594	0.887	3.10e-11
A C	.2978865	.1315209	.1612986	.9494018	.1365878	.9584684	0.887	1.09e-10
A D *	.470299	.1240977	.0121844	.6736426	.4581146	.6786767	0.500	3.86e-10
A E *	.3495859	.0882543	1.107824	.8601168	-.7582384	.8660467	0.381	1.35e-07
A F	.	.	.	.	.	.	.	.
A G	.	.	.	.	.	.	.	.
A H	.	.	.	.	.	.	.	.
B C	-.4418297	.9449111	-.3052831	.1607598	-.1365466	.9584887	0.887	3.13e-11
D E	.2570092	.4237516	-.1476285	.1573064	.4046376	.4491775	0.368	6.66e-10

## 3.2 All-cause dropout

### 3.21 Global inconsistency



### 3.22 Local inconsistency (loop-specific)

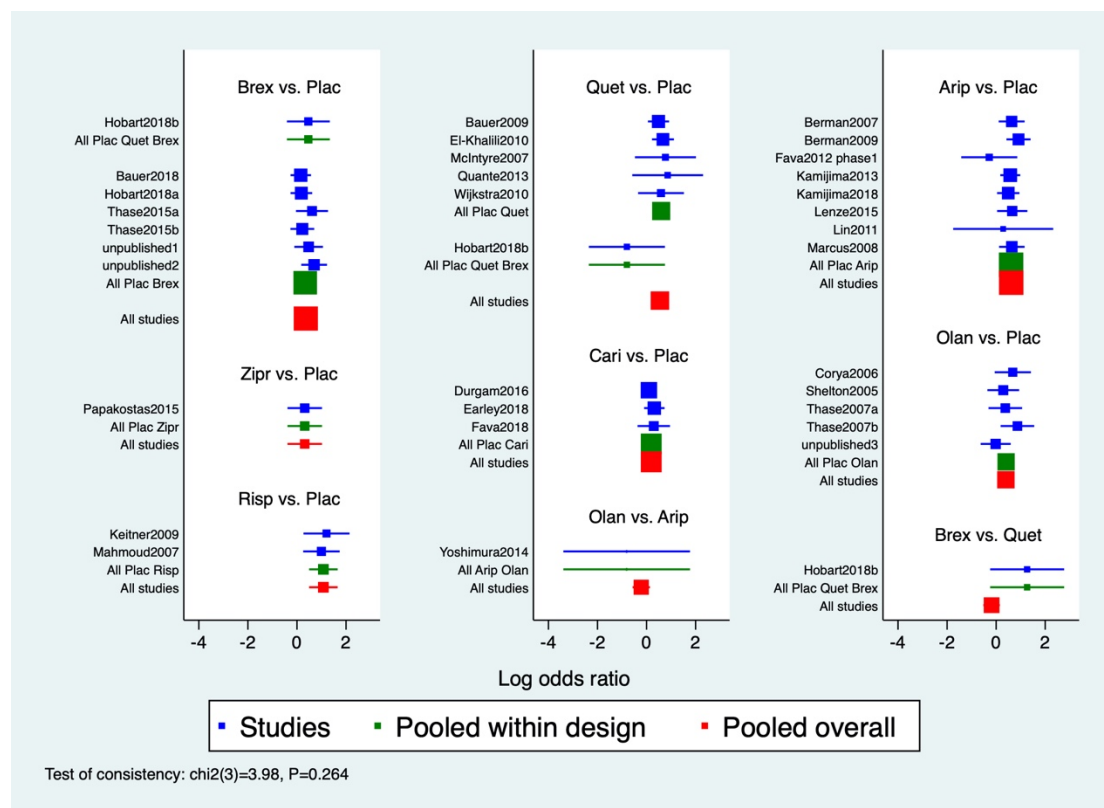
Loop	ROR	z_value	p_value	CI_95	Loop_Heterog_tau2
Pla-Ari-Ola	3.298	0.700	0.484	(1.00, 93.21)	0.000
Pla-Que-Bre	1.064	0.152	0.879	(1.00, 2.37)	0.000

### 3.23 Local inconsistency (node-splitting)

Side	Direct		Indirect		Difference		P> z	tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.		
A B	.1097111	.1369004	1.302903	1.699285	-1.193192	1.704791	0.484	2.01e-09
A C	.1043549	.144089	-1.088962	1.698782	1.193317	1.704882	0.484	8.39e-10
A D *	.3878753	.1576586	.4798952	.608137	-.0920199	.6202795	0.882	7.51e-07
A E *	.377191	.1131018	.277584	.742984	.0996071	.7534305	0.895	1.12e-07
A F	.	.	.	.	.	.	.	.
A G	.	.	.	.	.	.	.	.
A H	.	.	.	.	.	.	.	.
B C	-1.198682	1.693261	-.0053562	.1987545	-1.193326	1.704886	0.484	1.07e-09
D E	-.0685274	.3515024	-.0001814	.2105983	-.068346	.4059951	0.866	1.09e-07

## 3.3 Remission

### 3.31 Global inconsistency



### 3.32 Local inconsistency (loop-specific)

Loop	ROR	z_value	p_value	CI_95	Loop_Heterog_tau2
Pla-Que-Bre	4.388	1.872	0.061	(1.00, 20.63)	0.000
Pla-Ari-Ola	1.833	0.456	0.649	(1.00, 24.86)	0.000

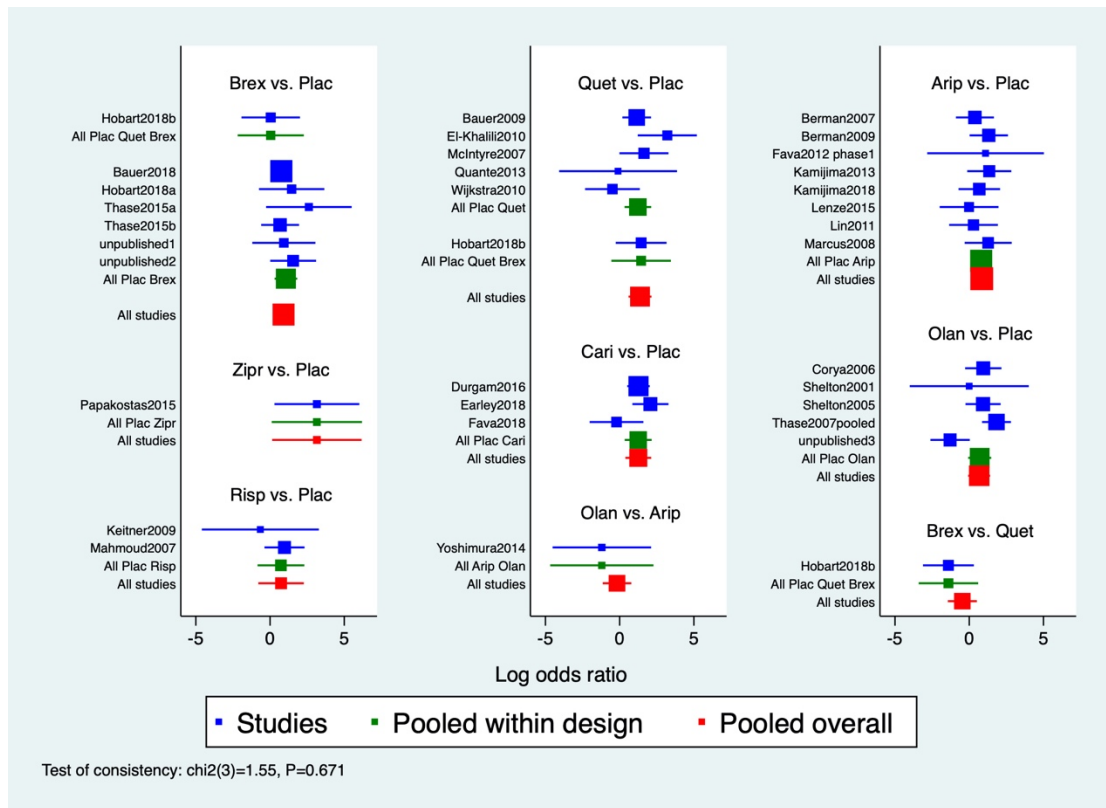


### 3.33 Local inconsistency (node-splitting)

Side	Direct		Indirect		Difference		P> z	tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.		
A B	.6115608	.1002938	1.217442	1.326406	-.6058807	1.330192	0.649	7.85e-11
A C	.406637	.1529472	-.1993907	1.321408	.6060277	1.33023	0.649	5.84e-13
A D *	.5520469	.1412144	-.2019022	.8719237	.7539491	.8689679	0.386	5.94e-11
A E *	.3445458	.1016182	3.278686	1.522158	-2.93414	1.526693	0.055	4.63e-11
A F	.	.	.	.	.	.	.	.
A G	.	.	.	.	.	.	.	.
A H	.	.	.	.	.	.	.	.
B C	-.8109127	1.317613	-.2049243	.1828981	-.6059884	1.330246	0.649	2.75e-14
D E	.7655064	.6518045	-.2471954	.1772082	1.012702	.6697976	0.131	5.98e-11

## 3.4 Dropout due to AE

### 3.41 Global inconsistency






### 3.42 Local inconsistency (loop-specific)

Loop	ROR	z_value	p_value	CI_95	Loop_Heterog_tau2
Pla-Que-Bre	3.033	1.112	0.266	(1.00, 21.46)	0.027
Pla-Ari-Ola	2.975	0.586	0.558	(1.00, 114.29)	0.313

### 3.43 Local inconsistency (node-splitting)

Side	Direct		Indirect		Difference		P> z	tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.		
A B	.8073222	.3383725	1.911536	1.804172	-1.104214	1.835409	0.547	.4906239
A C	.7131244	.3842038	-.3914027	1.795073	1.104527	1.83551	0.547	.4906224
A D *	1.264173	.4094828	3.516073	2.01308	-2.251901	2.0736	0.277	.4971708
A E *	.9580837	.3599637	-.3924651	1.907464	1.350549	1.940988	0.487	.5072992
A F	.	.	.	.	.	.	.	.
A G	.	.	.	.	.	.	.	.
A H	.	.	.	.	.	.	.	.
B C	-1.198646	1.762908	-.0941992	.5111798	-1.104447	1.835523	0.547	.4906237
D E	-1.351678	1.000333	-.1568262	.5878623	-1.194852	1.163957	0.305	.5005186

## 4. Risk of bias

Study ID	D1	D2	D3	D4	D5	Overall	
kamijima2013	!	+	+	+	+	!	 Low risk  Some concerns  High risk
corya2006	+	+	+	+	+	+	
fava2012	!	+	+	+	+	!	
el-khalili2010	+	+	+	+	+	+	
keitner2009	!	+	+	+	!	!	D1 Randomisation process
mahmoud2007	+	+	+	+	+	+	D2 Deviations from the intended interventions
marcus2008	!	+	+	+	+	!	D3 Missing outcome data
mcintyre2007	!	+	-	+	+	-	D4 Measurement of the outcome
shelton2001	!	+	-	+	+	-	D5 Selection of the reported result
bauer2009	!	+	+	+	+	!	
berman2007	+	+	+	+	+	+	
wijkstra2010	!	+	+	+	+	!	
berman2009	!	+	+	+	+	!	
kamijima2018	+	+	+	+	+	+	
thase2015a	+	+	+	+	+	+	
thase2015b	+	+	+	+	+	+	
bauer2018	+	+	+	+	+	+	
hobart2018a	+	+	+	+	+	+	
hobart2018b	+	+	+	+	+	+	
fava2018	+	+	+	+	+	+	
papakostas2015	+	+	+	+	+	+	
durgam2016	+	+	-	+	+	-	
lenze2015	+	+	+	+	+	+	
earley2018	+	+	+	+	+	+	
reeves2008	-	!	-	+	+	-	
unpublished1	!	+	+	+	!	!	
unpublished2	!	+	+	+	!	!	
yoshimura2014	!	+	+	+	!	!	
lin2011	!	+	-	+	+	-	
quante2013	!	+	+	+	+	!	
unpublished3	!	+	-	+	!	-	
shelton2005	!	+	+	+	+	!	
thase2007	+	+	+	+	+	+	

## 5. Characteristics of the included studies

Study_ID	Register_number	Recruitment	Multi/Single centre	Diagnostic criteria	History of inadequate antidepressants response	Screening phase (day)	Antidepressant run in					Randomised phase						
							Drugs	Length (week)	Masking	Scale	Length (week)	Antidepressants	Antipsychotics augmented	No. randomised	Mean age (SD)	Female%	Duration of the current episode (month)	Mean baseline severity
Kamijima2013	NCT00876343	Japan	multicentre	DSM-IV-TR	1-3 antidepressant for at least 6 weeks	1-28	based on the investigator's judgment	8	single-blind (patient)	MADRS	6	maintained ongoing ADT treatment	aripiprazole (3-15 mg/day)	194	38.1 (9.6)	41.90%	17.5	25.3
													aripiprazole (3 mg/day)	197	39.2 (9.1)	31.10%	15.7	25.2
													placebo	195	38.7 (9.2)	41.00%	15.6	25.5
Corya2006	*	16 countries	multicentre	DSM-IV	SSRIs for at least 6 weeks	2-7	venlafaxine 75-375 mg/day	7	open-label	MADRS	12	fluoxetine 25 or 50 mg/day	olanzapine (6 or 12 mg/day)	243	*	*	*	*
													placebo	60	*	*	*	*
Fava2012 phase1	NCT00683852	USA	multicentre	DSM	SSRIs/SNRIs for at least 8 weeks	14-28	*	*	*	MADRS	30 days	In accordance to screen phase	aripiprazole (2 mg/day)	56	45.36 (10.35)	66.07%	*	30.69
													placebo	169	45.06 (11.34)	63.91%	*	31.2
El-Khalili2010	NCT00326105	USA	multicentre	DSM-IV	amitriptyline, bupropion, citalopram, duloxetine, escitalopram, fluoxetine, paroxetine, sertraline, or venlafaxine for >=6 weeks	<=14	*	*	*	MADRS	6	maintained ongoing ADT treatment	quetiapine (150 mg/day)	148	45.9 (11.0)	76.20%	*	27.2
													quetiapine (300 mg/day)	150	44.3 (11.3)	72.60%	*	27.6
													placebo	148	46.2 (10.9)	68.50%	*	27.6
Keitner2009	*	*	multicentre	DSM-IV	was not treated with ADT; ADT dose or duration was not adequate; ADT was not well documented	NA	based on clinician choice	5	open-label	MADRS	4	maintained ongoing ADT treatment	risperidone	64	45.5 (11.6)	57.80%	15	25.8
													placebo	33	44.6 (11.1)	54.50%	13	25.5
Marcus2008	NCT00095758	USA	multicentre	DSM-IV	inadequate response to previous ADT	7-28	based on investigator assessment	8	single-blind (patient)	MADRS	6	maintained ongoing ADT treatment	aripiprazole	191	44.6 (11.0)	66.00%	43.7	25.2
													placebo	190	44.4 (10.7)	67.40%	48.5	27
McIntyre2007	*	Canada	single centre	DSM-IV	SSRI/venlafaxine for at least 6 weeks	NA	*	*	*	HAMD	8	maintained ongoing ADT treatment	quetiapine	29	44 (10)	65%	*	23.4
													placebo	29	45 (12)	59%	*	23.2
Shelton2001	*	*	*	DSM-IV	two different classes (one of which was not an SSRI) for at least 4 weeks	NA	fluoxetine 20-60 mg/day	6	open-label	MADRS	8	fluoxetine	olanzapine	10	*	*	*	*
													placebo	10	*	*	*	*

<b>Bauer2009</b>	NCT00351910	4 countries	multicentre	DSM-IV-TR	amitriptyline, bupropion, citalopram, duloxetine, escitalopram, fluoxetine, paroxetine, sertraline, or venlafaxine for >=6 weeks	14	*	*	*	MADRS	6	maintained ongoing ADT treatment	quetiapine (150 mg/day)	167	46.0	69.30%	*	28.6				
													(10.1)									
													quetiapine (300 mg/day)	163	45.5	68.30%	*	28.4				
													placebo	163	44.8	65%	*	28.2				
													(10.4)									
<b>Berman2007</b>	NCT00095823	USA	multicentre	DSM-IV-TR	at least 1 and no more than 3 ADTs for >6 weeks	7-28	based on investigator assessment of clinical factors	8	single-blind (patient)	MADRS	6	maintained ongoing ADT treatment	aripiprazole	182	46.5	61.50%	38.6	26				
													(10.6)									
													placebo	176	44.2	64.20%	43.6	25.9				
													(10.9)									
<b>Wijkstra2010</b>	*	Netherlands	multicentre	DSM-IV-TR	*	>=4	*	*	*	HAMD	7	venlafaxine 75-375mg/day	quetiapine	41	50.6	53.70%	10.1	31.6				
													(11.2)									
													placebo	39	49.5	43.60%	10.675	31.6				
													(12.0)									
<b>Berman2009</b>	NCT00105196	USA	multicentre	DSM-IV-TR	1-3 antidepressant for at least 6 weeks	7-28	in accordance with current product labeling guidelines	8	single-blind	MADRS	6	maintained ongoing ADT treatment	aripiprazole	177	45.1	78%	18.8	26.6				
													(10.6)									
													placebo	172	45.6	68%	17.2	27.1				
													(11.3)									
<b>Kamijima2018</b>	NCT02046564	Japan, Korea, Malaysia, Taiwan, Austria	multicentre	DSM-V	1-3 courses of ADT	1-28	sertraline 25-100mg/day	8	single-blind	MADRS	6	sertraline 100mg/day	aripiprazole (3-12 mg/day)	209	38.3	38.00%	11.3	24.9				
													(11.8)									
													placebo	203	39.5	35.50%	15.8	25.2				
													(11.8)									
<b>Thase2015a</b>	NCT01360645	USA, Poland, France, Canada, Slovakia	multicentre	DSM-IV-TR	1-3 courses of ADT	7-28	standard ADT	8	single-blind	MADRS	6	maintained ongoing ADT treatment	brexpiprazole	188	44.1	69.10%	13.5	26.6				
													(11.6)									
													placebo	191	45.2	71.70%	13.7	27.1				
													(11.3)									
<b>Thase2015b</b>	NCT01360632	USA, Germany, Ukraine, Russia, Hungary, Canada, Romania	multicentre	DSM-IV-TR	1-3 courses of ADT	7-28	physician determined ADT	8	single-blind	MADRS	6	maintained ongoing ADT treatment	brexpiprazole (1 mg/day)	226	45.7	69.90%	18.7	26.7				
													(11.6)									
													brexpiprazole (3 mg/day)	230	44.5	67.80%	17.4	26.4				
													placebo	221	46.6	66.10%	16.9	26.3				
													(11.0)									
<b>Bauer2018</b>	NCT01838681	16 countries	multicentre	DSM-IV-TR	at least 1 and no more than 3 ADTs	NA	one of six ADTs	8	open-label	MADRS	24	maintained ongoing ADT treatment	brexpiprazole (1-3 mg/day)	444	47.1	69.10%	8.6	25.9				
													(12.1)									
													placebo	441	46.4	68.50%	8.9	25.8				
													(12.1)									
<b>Hobart2018a</b>	NCT02196506	USA, Germany, Poland, Slovakia, Hungary	multicentre	DSM-IV-TR	1-3 antidepressant for at least 6 weeks	7-28	investigator determined	8	open-label	MADRS	6	maintained ongoing ADT treatment	brexpiprazole (2 mg/day)	202	43.0	76.60%	13.3	27.1				
													(12.7)									
													placebo	192	42.7	71.30%	19.4	26.2				
													(12.5)									

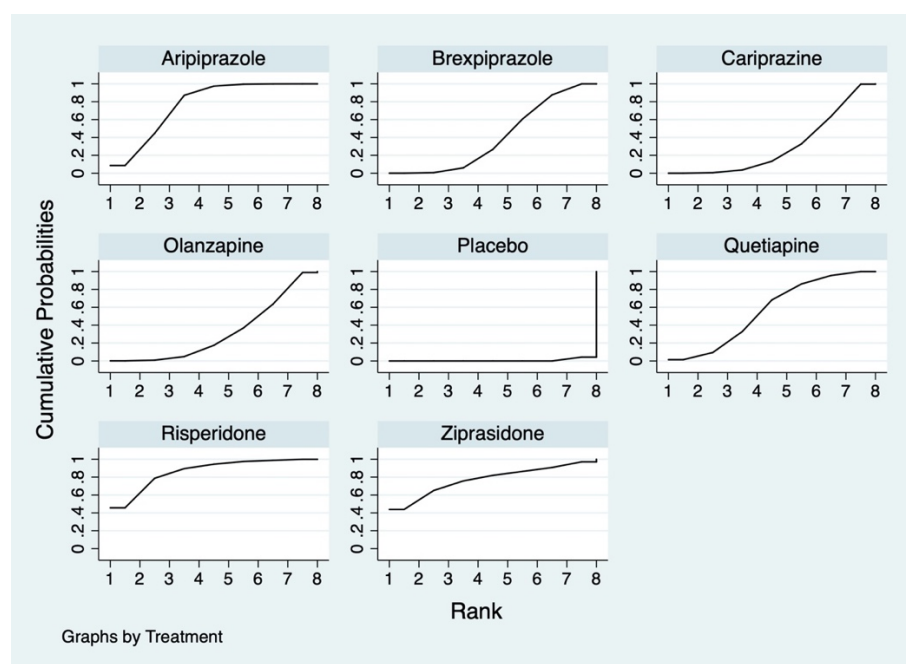
<b>Hobart2018b</b>	NCT01727726	USA, Russia, Poland, France, Serbia, Germany, Canada	multicentre	DSM-IV-TR	1-3 antidepressant for at least 6 weeks	7-28	investigator determined	8 or 10	open-label	MADRS	6	maintained ongoing ADT treatment	brexpiprazole (2-3 mg/day)	197	43.6 (11.5)	65.00%	12.3	25.4
													quetiapine (150-300 mg/day)	100	44.6 (11.6)	66.00%	14.3	25.6
													placebo	206	41.8 (11.7)	72.30%	11.7	25.4
<b>Fava2018</b>	NCT00854100	USA	multicentre	DSM-IV-TR	1 or 2 ADTs	7	citalopram, duloxetine, escitalopram, sertraline, or venlafaxine ER	8	open-label	MADRS	8	maintained ongoing ADT treatment	cariprazine (0.1-0.3 mg/day)	76	44.2 (12.1)	69.90%	26.5	26.3
													cariprazine (1-2 mg/day)	73	46.6 (11.7)	68.40%	25	26.6
													placebo	81	45.2 (10.2)	75.30%	31.9	26.4
<b>Papakostas2015</b>	NCT00633399	USA	multicentre	DSM-IV	*	NA	escitalopram 10-30 mg/day	8	open-label	HAMD	8	escitalopram	ziprasidone	71	44.7 (13.8)	69%	*	17.6
													placebo	68	44.2 (11.9)	72%	*	17.3
<b>Durgam2016</b>	NCT01469377	USA, Europe	multicentre	DSM-IV-TR	ADT >=6 weeks	7-14	*	*	*	MADRS	8	maintained ongoing ADT treatment	cariprazine (1-2 mg/dy)	274	45.5 (11.9)	68.50%	7.3	29
													cariprazine (2-4.5 mg/day)	276	45.1 (11.4)	73.60%	7.4	29.3
													placebo	269	46.4 (11.6)	71.40%	7.7	28.9
<b>Lenze2015</b>	NCT00892047	USA, Canada	multicentre	DSM	*	NA	venlafaxine 150-300 mg/day	*	open-label	MADRS	12	maintained ongoing venlafaxine treatment	aripiprazole	91	66.4	57%	29.5	24
													placebo	90	65.7	57%	26	23
<b>Earley2018</b>	NCT01715805	USA	multicentre	DSM-IV-TR	1 or 2 ADTs	7-14	investigator determined	8	open-label	MADRS	8	maintained ongoing ADT treatment	cariprazine (1.5-4.5 mg/day)	269	44.2 (11.6)	64.70%	7.36	25.4
													placebo	258	43.8 (11.8)	65.90%	6.94	25.2
<b>Reeves2008</b>	NCT00167154	USA	single	DSM-IV	up to 2 ADT for >=3 weeks	NA	*	*	*	MADRS	8	maintained ongoing ADT treatment	risperidone	12	46.5 (12.1)	91.70%	*	36.42
													placebo	11	41.3 (12.6)	45.50%	*	35
<b>unpublished1</b>	NCT00797966	USA	multicentre	DSM-IV-TR	at least 1 and no more than 3 ADTs	28	physician assigned ADTs	8	single-blind	MADRS	6	maintained ongoing ADT treatment	brexpiprazole (0.15 mg/day)	62	43.9 (10.8)	66.10%	*	*
													brexpiprazole (0.25- 0.75 mg/day)	120	44.0 (11.8)	71.70%	*	*
													brexpiprazole (1-2 mg/day)	121	43.7 (11.6)	66.10%	*	*
													placebo	126	43.3 (11.5)	65.10%	*	*

<b>unpublished2</b>	NCT01052077	USA	multicentre	DSM-IV-TR	at least 1 and no more than 3 ADTs	7-28	ADTs	8	single-blind	HAMD	6	maintained ongoing ADT treatment	brexpiprazole (1-3 mg/day)	185	44.7 (11.7)	66.50%	*	*
													placebo	187	42.4 (11.7)	69.50%	*	*
<b>Yoshimura2014</b>	*	Japan	*	DSM-IV-TR	*	NA	paroxetine	8	*	HAMD	4	paroxetine	aripiprazole	10	40 (10)	70%	*	22
													olanzapine	10	42 (7)	50%	*	24
<b>Lin2011</b>	*	Taiwan	single	DSM-IV	no	NA	*	*	*	HAMD	4	sertraline 50 mg/day	aripiprazole	21	35.86 (11.61)	80.95%	*	20.62
													placebo	20	35.15 (10.03)	80.00%	*	19.1
<b>Mahmoud2007</b>	NCT00095134	USA	multicentre	DSM-IV	*	NA	current antidepressant monotherapy	4	open-label	HAMD	6	maintained ongoing ADT treatment	risperidone	137	45.9 (10.1)	70.80%	*	24.3
													placebo	131	46.4 (10.7)	76.30%	*	24.9
<b>Quante2013</b>	*	Germany	multicentre	DSM-IV	*	NA	*	*	*	MADRS	6	citalopram 40 mg/day	quetiapine	19	45.1 (11.6)	61.90%	5.8	26.6
													placebo	17	48.4 (12.3)	60.00%	4.7	23.8
<b>unpublished3</b>	NCT01687478	China	multicentre	DSM-IV-TR	at least 2 ADT other than fluoxetine for >=6 weeks	NA	*	*	*	MADRS	8	fluoxetine 20-50 mg/day	olanzapine	88	38.63 (12.18)	46.60%	*	32.1
													placebo	88	41.45 (12.44)	40.90%	*	31.8
<b>Shelton2005</b>	*	USA, Canada	multicentre	DSM-IV	>=1 SSRI for >=4 weeks	2-7	nortriptyline	7	*	MADRS	8	fluoxetine	olanzapine	146	42.5 (10.7)	67.10%	12.47	28.5
													placebo	142	41.7 (11.0)	72.50%	11.27	28.4
<b>Thase2007pooled</b>	NCT00035321	USA, Canada	multicentre	DSM-IV	1 ADT except for fluoxetine for >=6 weeks	3-14	fluoxetine 20-50 mg/day	8	open-label	MADRS	8	fluoxetine 50mg/day	olanzapine	200	44.3 (12.1)	66%	103.85	30.1
													placebo	206	44.6 (10.0)	62.10%	107.15	29.9

## 6. SURCA

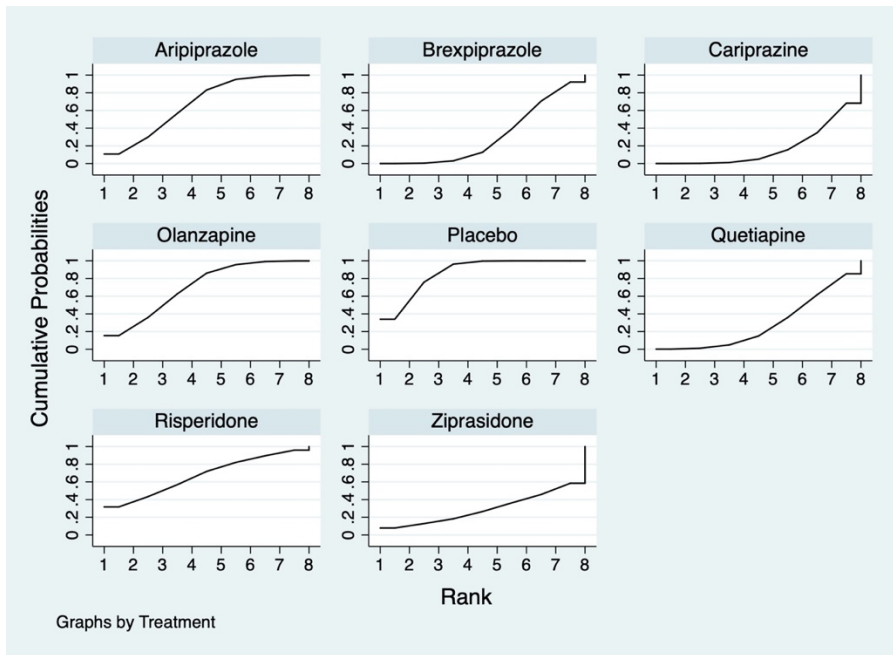
### 6.1 Response

Treatment	SUCRA	PrBest	MeanRank
Placebo	0.6	0.0	8.0
Aripiprazole	76.8	9.7	2.6
Olanzapine	31.7	0.1	5.8
Quetiapine	56.3	1.9	4.1
Brexipiprazole	40.5	0.0	5.2
Cariprazine	30.6	0.1	5.9
Ziprasidone	76.7	42.4	2.6
Risperidone	86.7	45.7	1.9



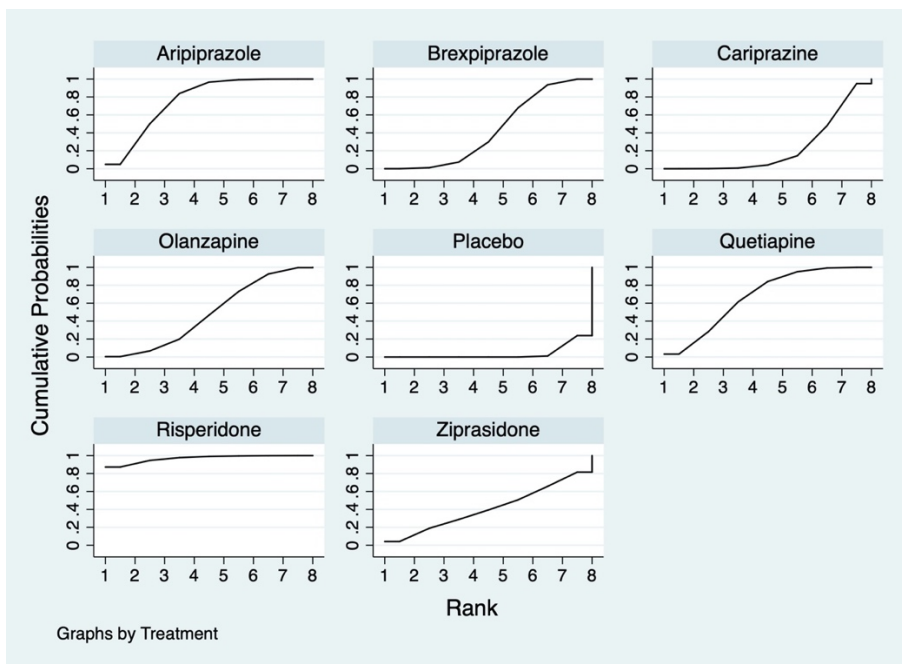
### 6.2 All-cause dropout

Treatment	SUCRA	PrBest	MeanRank
Placebo	86.8	33.9	1.9
Aripiprazole	68.0	11.6	3.2
Olanzapine	70.6	15.2	3.1
Quetiapine	29.5	0.3	5.9
Brexipiprazole	30.8	0.0	5.8
Cariprazine	18.1	0.0	6.7
Ziprasidone	29.5	8.8	5.9
Risperidone	66.6	30.3	3.3



### 6.3 Remission

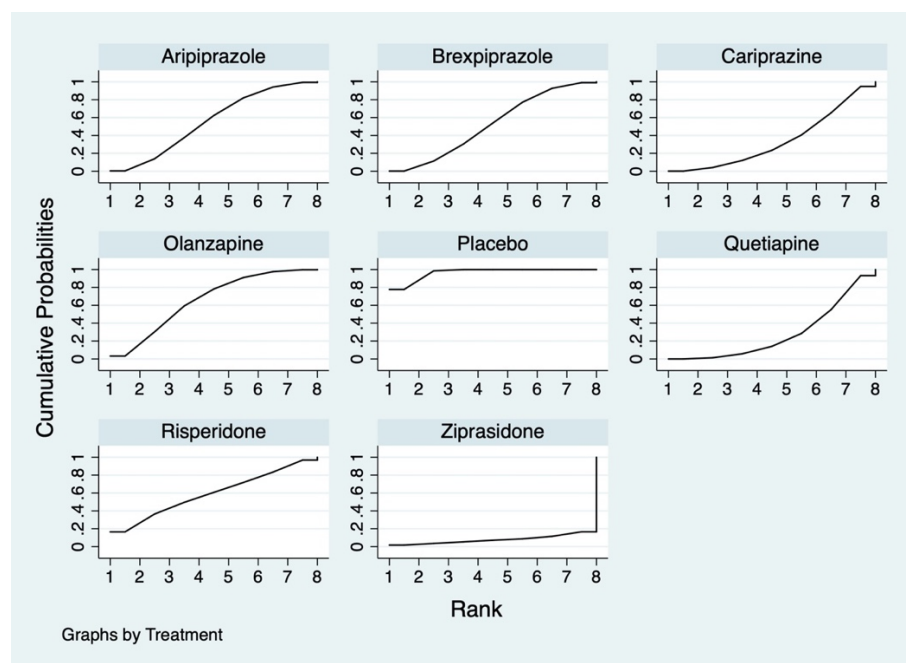
Treatment	SUCRA	PrBest	MeanRank
Placebo	3.5	0.0	7.8
Aripiprazole	76.6	4.5	2.6
Olanzapine	48.5	0.5	4.6
Quetiapine	67.3	2.7	3.3
Brexpiprazole	43.0	0.0	5.0
Cariprazine	23.5	0.0	6.4
Ziprasidone	40.8	4.4	5.1
Risperidone	96.8	87.9	1.2





## 6.4 Dropout due to AE

Treatment	SUCRA	PrBest	MeanRank
Placebo	96.4	76.1	1.3
Aripiprazole	55.8	0.5	4.1
Olanzapine	64.9	3.0	3.5
Quetiapine	28.2	0.0	6.0
Brexpiprazole	52.9	0.5	4.3
Cariprazine	33.8	0.2	5.6
Ziprasidone	8.0	1.8	7.4
Risperidone	60.0	17.9	3.8



## 7. Sensitivity analysis

### 7.1 Excluding small sample

Efficacy (Response)	Lower CrI	OR	Upper CrI	SUCRA	PrBest	MeanRank
Placebo	*	*	*	0.8	0	7.9
Aripiprazole	1.51	1.82	2.18	76.8	9.2	2.6
Olanzapine	1.01	1.31	1.7	29.7	0.1	5.9
Quetiapine	1.2	1.55	1.99	54.1	1.7	4.2
Brexpiprazole	1.2	1.43	1.7	42.3	0.1	5
Cariprazine	1.07	1.34	1.67	32.1	0.1	5.8
Ziprasidone	0.98	2.1	4.5	77.9	44	2.5
Risperidone	1.35	2.16	3.46	86.3	44.8	2

Acceptability (All-cause dropout)	Lower CrI	OR	Upper CrI	SUCRA	PrBest	MeanRank
Placebo	*	*	*	89.1	43	1.8
Aripiprazole	0.86	1.13	1.49	70.5	13.2	3.1

Olanzapine	0.85	1.13	1.5	69.8	13.3	3.1
Quetiapine	1.15	1.58	2.17	24.6	0.2	6.3
Brexpiprazole	1.17	1.46	1.82	34.5	0.1	5.6
Cariprazine	1.21	1.63	2.18	21.6	0	6.5
Ziprasidone	0.74	1.59	3.4	32.1	9.5	5.7
Risperidone	0.69	1.24	2.2	57.7	20.7	4

Response	All-cause dropout					
<b>Aripiprazole</b>	1.00 (0.68,1.49)	1.40 (0.92,2.13)	1.29 (0.91,1.84)	1.44 (0.96,2.15)	1.41 (0.62,3.16)	1.09 (0.58,2.08)
<b>1.38</b> <b>(1.01,1.90)</b>	<b>Olanzapine</b>	1.40 (0.91,2.14)	1.29 (0.90,1.85)	1.44 (0.96,2.16)	1.40 (0.62,3.16)	1.09 (0.57,2.08)
1.17 (0.86,1.60)	0.85 (0.59,1.22)	<b>Quetiapine</b>	0.92 (0.64,1.34)	1.03 (0.67,1.59)	1.00 (0.44,2.29)	0.78 (0.40,1.51)
1.27 (0.99,1.63)	0.92 (0.67,1.25)	1.08 (0.80,1.46)	<b>Brexpiprazole</b>	1.11 (0.77,1.61)	1.09 (0.49,2.40)	0.85 (0.46,1.57)
<b>1.36</b> <b>(1.02,1.80)</b>	0.98 (0.70,1.38)	1.16 (0.83,1.62)	1.07 (0.81,1.41)	<b>Cariprazine</b>	0.97 (0.43,2.21)	0.76 (0.40,1.45)
0.87 (0.40,1.90)	0.63 (0.28,1.40)	0.74 (0.33,1.65)	0.68 (0.31,1.49)	0.64 (0.29,1.41)	<b>Ziprasidone</b>	0.78 (0.30,2.03)
0.84 (0.51,1.39)	0.61 (0.36,1.04)	0.72 (0.42,1.22)	0.66 (0.40,1.09)	0.62 (0.37,1.04)	0.97 (0.40,2.38)	<b>Risperidone</b>

## 7.2 Excluding high-risk

Efficacy (Response)	Lower CrI	OR	Upper CrI	SUCRA	PrBest	MeanRank
Placebo	*	*	*	3.9	0	7.7
Aripiprazole	1.52	1.82	2.17	76.9	8.8	2.6
Olanzapine	1.01	1.34	1.77	36.1	0.3	5.5
Quetiapine	1.21	1.55	1.98	56.4	1.6	4.1
Brexpiprazole	1.2	1.43	1.7	44	0.1	4.9
Cariprazine	0.83	1.14	1.58	18.3	0	6.7
Ziprasidone	0.98	2.1	4.5	78	43.6	2.5
Risperidone	1.35	2.16	3.46	86.4	45.7	2

Acceptability (All-cause dropout)	Lower CrI	OR	Upper CrI	SUCRA	PrBest	MeanRank
Placebo	*	*	*	90.6	48.7	1.7
Aripiprazole	0.87	1.14	1.5	71	12.6	3
Olanzapine	0.92	1.27	1.75	54.2	4.9	4.2
Quetiapine	1.15	1.57	2.16	24.1	0	6.3
Brexpiprazole	1.17	1.46	1.82	33.7	0	5.6
Cariprazine	0.96	1.45	2.17	36.8	2.4	5.4
Ziprasidone	0.74	1.59	3.4	31.6	9.4	5.8
Risperidone	0.69	1.24	2.2	57.9	21.9	3.9

Response	All-cause dropout					
<b>Aripiprazole</b>	1.12 (0.73,1.70)	1.38 (0.91,2.10)	1.28 (0.90,1.82)	1.27 (0.78,2.07)	1.39 (0.62,3.13)	1.08 (0.57,2.06)
1.36 (0.97,1.89)	<b>Olanzapine</b>	1.24 (0.79,1.94)	1.15 (0.78,1.69)	1.14 (0.68,1.91)	1.25 (0.55,2.85)	0.97 (0.50,1.88)
1.17 (0.86,1.59)	0.86 (0.59,1.26)	<b>Quetiapine</b>	0.93 (0.64,1.34)	0.92 (0.55,1.54)	1.01 (0.44,2.30)	0.78 (0.41,1.52)
1.27 (0.99,1.63)	0.93 (0.67,1.30)	1.08 (0.81,1.45)	<b>Brexpiprazole</b>	0.99 (0.62,1.57)	1.09 (0.49,2.40)	0.85 (0.46,1.57)
<b>1.59</b> <b>(1.10,2.30)</b>	1.17 (0.76,1.79)	1.35 (0.90,2.03)	1.25 (0.87,1.80)	<b>Cariprazine</b>	1.10 (0.46,2.60)	0.85 (0.42,1.73)
0.87 (0.40,1.90)	0.64 (0.28,1.44)	0.74 (0.33,1.65)	0.68 (0.31,1.49)	0.55 (0.24,1.25)	<b>Ziprasidone</b>	0.78 (0.30,2.03)
0.84 (0.51,1.39)	0.62 (0.36,1.07)	0.72 (0.42,1.22)	0.66 (0.40,1.09)	<b>0.53</b> <b>(0.30,0.94)</b>	0.97 (0.40,2.38)	<b>Risperidone</b>

## 8. Network meta-regression

### 8.1 Adjusted for baseline depression severity

#### 8.1.1 Response

	Log Odds Ratio compared with PLA			beta		
	2.5%	Median	97.5%	2.5%	Median	97.5%
<b>Aripiprazole</b>	0.38	0.59	0.81	-1.19	-0.33	0.48
<b>Olanzapine</b>	-0.52	0.14	0.79	-1.02	0.22	1.48
<b>Quetiapine</b>	0.06	0.38	0.71	-0.48	0.53	1.56
<b>Brexpiprazole</b>	0.12	0.35	0.59	-1.68	1.20	4.21
<b>Cariprazine</b>	-0.10	0.20	0.52	-0.47	0.68	1.83
<b>Ziprasidone</b>	-11.25	0.24	8.74	-9.87	-0.42	6.63
<b>Risperidone</b>	0.32	0.81	1.32	-1.16	0.13	1.49

#### 8.1.2 All-cause dropout

	Log Odds Ratio compared with PLA			beta		
	2.5%	Median	97.5%	2.5%	Median	97.5%
<b>Aripiprazole</b>	-0.16	0.16	0.48	-0.54	0.49	1.57
<b>Olanzapine</b>	-0.81	0.10	0.93	-1.57	-0.06	1.53
<b>Quetiapine</b>	-0.01	0.38	0.74	-1.07	0.06	1.20
<b>Brexpiprazole</b>	0.05	0.38	0.72	-3.73	-0.47	2.15
<b>Cariprazine</b>	0.04	0.45	0.84	-1.07	0.29	1.70
<b>Ziprasidone</b>	-6.44	0.52	6.30	-5.64	0.03	4.75
<b>Risperidone</b>	-0.74	-0.07	0.55	-3.62	-1.36	0.18

## 8.2 Adjusted for study years

#### 8.2.1 Response

	Log Odds Ratio compared with PLA			beta		
	2.5%	Mean	97.5%	2.5%	Mean	97.5%
<b>Aripiprazole</b>	0.41	0.61	0.81	-0.67	-0.18	0.30
<b>Olanzapine</b>	-0.21	0.22	0.64	-0.92	-0.21	0.48

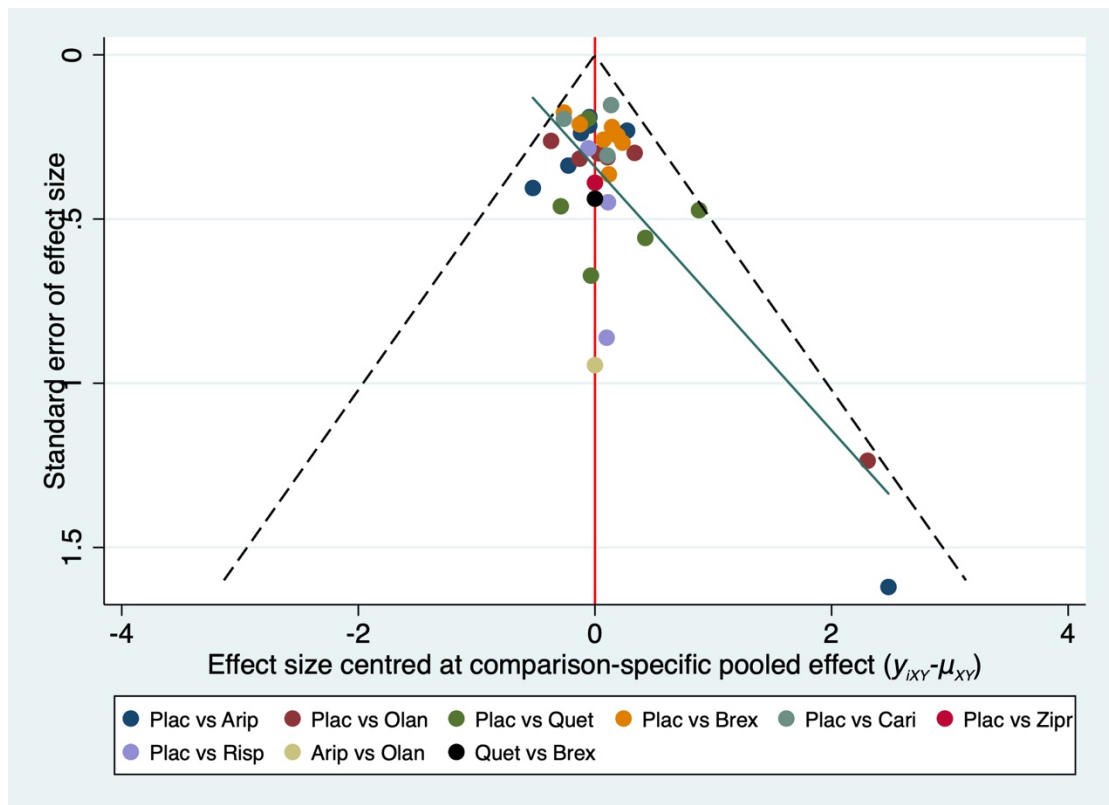
Quetiapine	0.10	0.41	0.71	-1.37	-0.47	0.38
Brexpiprazole	0.19	0.51	0.81	-0.95	-0.36	0.26
Cariprazine	-0.41	0.95	2.39	-3.51	-1.12	1.14
Ziprasidone	-6.61	0.66	5.13	-11.90	0.27	19.99
Risperidone	-0.91	1.03	2.89	-3.59	0.49	4.53

## 8.2.2 All-cause dropout

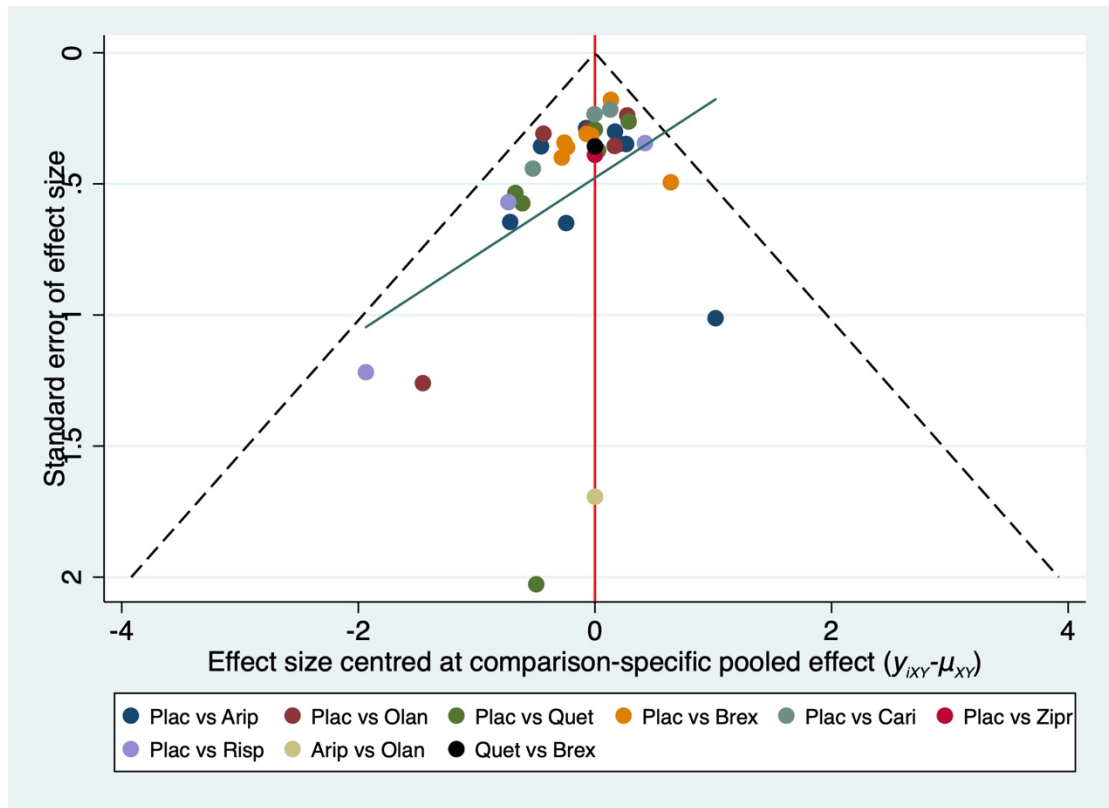
	Log Odds Ratio compared with PLA			beta		
	2.5%	Mean	97.5%	2.5%	Mean	97.5%
Aripiprazole	-0.21	0.08	0.39	-1.07	-0.38	0.30
Olanzapine	-0.50	-0.07	0.37	-1.09	-0.37	0.35
Quetiapine	0.06	0.40	0.74	-0.60	0.19	0.96
Brexpiprazole	-0.14	0.24	0.63	-0.36	0.34	1.04
Cariprazine	-0.56	0.82	2.39	-3.16	-0.57	1.67
Ziprasidone	-2.74	0.82	28.06	-75.81	-0.71	8.67
Risperidone	-4.35	-0.94	0.82	-9.47	-2.17	1.38

## 9. Published bias

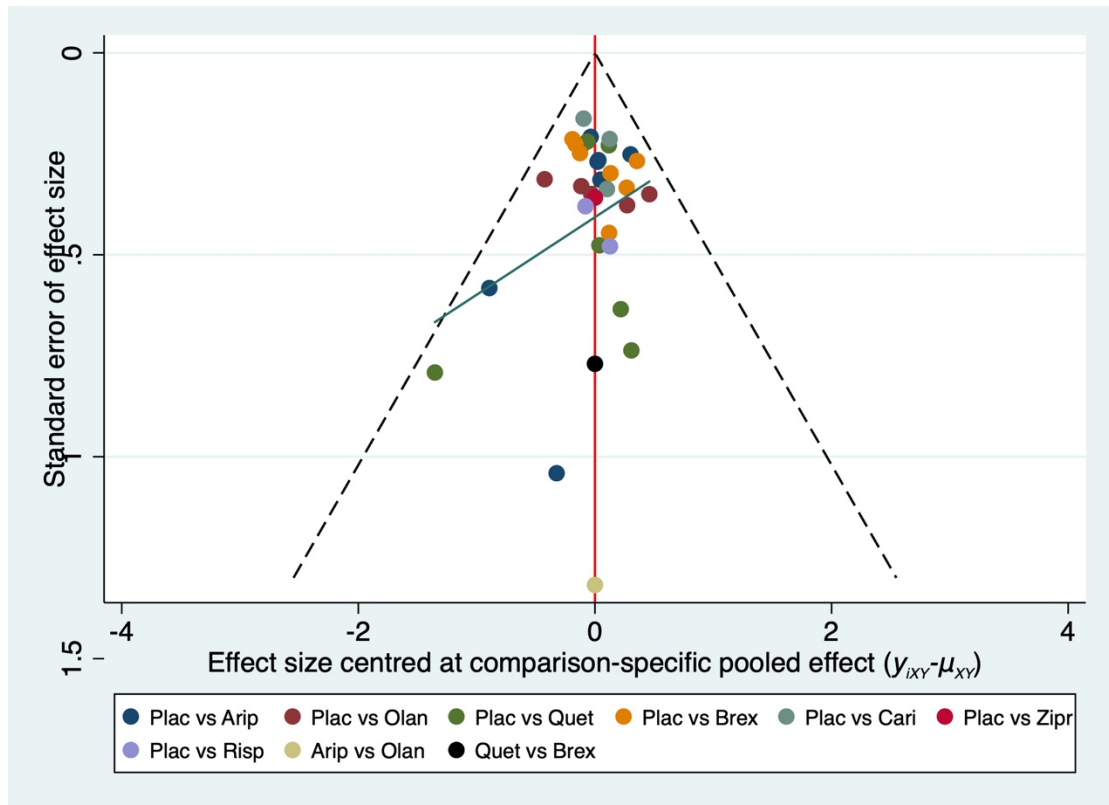
### 9.1 Response



## 9.2 All-cause dropout



## 9.3 Remission



## 9.4 Dropout due to AE

