

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Correll 2015	+	+	+	+	+	+	?
Ishigooka 2018	+	+	+	+	+	+	?
Kane 2015	+	+	+	+	+	+	+
NCT00905307	?	?	+	+	+	+	?

Supplementary Figure 1 Risk of bias. Light dark circle with “+” marker denotes ‘low risk’ of bias. Heavy dark circle denotes ‘high risk’ of bias. Gray circle with “?” marker denotes ‘unclear risk’ due to a lack of information for assessment.

Supplementary Table 1 Search Strategy *(from database inception to March 29, 2022)*

Data sources	Search strategy	Numbers
PubMed	((brexpiprazole[Title/Abstract]) OR (REXULTI[Title/Abstract])) AND (schizophre*[Title/Abstract])	144
Cochrane Library	((brexpiprazole):ti,ab,kw OR (REXULTI):ti,ab,kw) AND (schizophre*):ti,ab,kw	86
Embase	(brexpiprazole:ab,ti OR REXULTI:ab,ti) AND schizophre*:ab,ti	240
Web of Science	((TI=(brexpiprazole)) OR TI=(REXULTI)) AND TI=(schizophre*)	121
ClinicalTrials	(brexpiprazole or REXULTI) AND schizophre*	76
PsycINFO	(brexpiprazole.ti. OR REXULTI.ti.) AND (schizophre*).ti.	29

Supplementary Table 2 Secondary Outcomes

Outcome	Comparison	SMD	95%CI	Heterogeneity	P-value
PANSS positive subscale score change	low-dose brexpiprazole vs placebo	-0.02	-0.18,0.13	$P=0.20, I^2=36\%$	$P=0.76$
	low-dose brexpiprazole vs standard-dose brexpiprazole	0.12	0.00,0.23	$P=0.47, I^2=0\%$	$P=0.05$
PANSS negative subscale score change	low-dose brexpiprazole vs placebo	-0.14	-0.26,-0.01	$P=0.60, I^2=0\%$	$P=0.03$
	low-dose brexpiprazole vs standard-dose brexpiprazole	0.11	-0.00,0.23	$P=0.84, I^2=0\%$	$P=0.05$
Outcome		RR	95%CI	Heterogeneity	P-value
discontinuation due to AEs	low-dose brexpiprazole vs placebo	0.84	0.60,1.18	$P=0.95, I^2=0\%$	$P=0.31$
	low-dose brexpiprazole vs standard-dose brexpiprazole	1.33	0.95,1.85	$P=0.91, I^2=0\%$	$P=0.09$
total TEAEs	low-dose brexpiprazole vs placebo	0.94	0.83,1.07	$P=0.23, I^2=30\%$	$P=0.38$
	low-dose brexpiprazole vs standard-dose brexpiprazole	0.98	0.89,1.09	$P=0.34, I^2=10\%$	$P=0.77$
N-increase in body weight \geq 7%	low-dose brexpiprazole vs placebo	2.9	1.26,6.67	$P=0.58, I^2=0\%$	$P=0.01$
	low-dose brexpiprazole vs standard-dose brexpiprazole	0.9	0.53,1.52	$P=0.67, I^2=0\%$	$P=0.68$
Outcome	Comparison	SMD	95%CI	Heterogeneity	P-value
total cholesterol(mg/dl)	low-dose brexpiprazole vs placebo	-0.00	-0.15,0.15	$P=0.60, I^2=0\%$	$P=1.00$
	low-dose brexpiprazole vs standard-dose brexpiprazole	-0.12	-0.25,0.01	$P=0.42, I^2=0\%$	$P=0.07$
HDL cholesterol(mg/dl)	low-dose brexpiprazole vs placebo	0.10	-0.07,0.27	$P=0.26, I^2=25\%$	$P=0.24$
	low-dose brexpiprazole vs standard-dose brexpiprazole	-0.17	-0.31,-0.04	$P=0.44, I^2=0\%$	$P=0.01$
LDL cholesterol(mg/dl)	low-dose brexpiprazole vs placebo	0.00	-0.15,0.15	$P=0.51, I^2=0\%$	$P=0.98$
	low-dose brexpiprazole vs standard-dose brexpiprazole	-0.03	-0.16,0.10	$P=0.63, I^2=0\%$	$P=0.67$

Abbreviations: PANSS, Positive and Negative syndrome scale; AEs, adverse events; TEAEs, treatment-emergent adverse events; HDL, high density lipoprotein; LDL, low density lipoprotein