Data supplement to: Takeuchi et al. One-year symptom trajectories in patients with stable schizophrenia maintained on antipsychotics v. placebo: meta-analysis. Br J Psychiatry doi: 10.1192/bjp.bp.116.186007

Supplemental Table DS1. Stabilization criteria

Author	Criteria for symptom stabilization	Criteria for treatment stabilization	Stabilization phase duration (weeks)
Arato et al.	Patients who had been hospitalized for ≥2 months and had scores of ≤5 on the CGI-S, and did not have a recent acute exacerbation of schizophrenia, a score of ≥5 on items P7 or G8 of the PANSS, or displayed a significant risk of suicide, or had treatment resistance (defined as lack of therapeutic response to a conventional antipsychotic during an acute exacerbation on ≥2 occasions in the previous 2 years)	NA	NA
Beasley et al.	Patients who were in a remitted state as defined by the following criteria: minimal symptoms defined as a BPRS score of ≤36; outpatient status; GAF score of ≥40; lack of specific positive symptoms, as measured by a score of ≥4 on the BPRS positive items of conceptual disorganization, suspiciousness, hallucinatory behavior, and unusual thought content; and taking a fixed individual dosage of olanzapine (10, 15, or 20 mg/d), and did not meet the following relapse criteria during the stabilization phase: an increase in any BPRS positive item to >4, and either an absolute increase of 2 on that specific item or an absolute increase of 4 on the BPRS positive subscale (P2, P3, P6, G9); or hospitalization due to positive psychotic symptoms during the stabilization phase	NA	8
Clark et al.	Outpatient status for ≥3 months	Patients who were maintained on medication for ≥3 months	NA
Cooper et al.	Patients who had a score of ≥3 on the CGI-S and a history of recurrence within the past 18 months	Patients who were currently maintained on antipsychotic medication	NA
Fu et al.	Patients who met the following stabilization criteria: PANSS total scores ≤70; YMRS scores ≤12; and HDRS-21 scores ≤12, and maintained symptom stabilization throughout the stabilization period	Patients who did not need for dose adjustments of paliperidone-LAI	12
Hough et al.	Patients who were stabilized with PANSS total score ≤75 and selected PANSS item scores ≤4 (P1, P2, P3, P6, P7, G8 and G14)	Patients who continued established maintenance dose of paliperidone	24
Kane et al.	Patients who met the following stability criteria for 4 consecutive weeks (2 consecutive visits 2 weeks apart): outpatient status; PANSS total score ≤80; lack of specific psychotic symptoms on the PANSS, as measured by a score of ≤4 on each of the following items: P2, P3, P6, G9; CGI-S score ≤4; CGI-SS score ≤2 on part 1 and ≤5 on part 2	NA	4-12
Kramer et al.	Patients who were deemed stable (≥2 weeks)	Patients who remained on established dose of paliperidone	6
Pigott et al.	Patients who had a stable[a] condition (no significant improvement or worsening of symptoms within the past 3 months), and had a PANSS score of ≥60 and a score of ≤4 on the subscale for P7 or G8, and a score ≤4 on the CGI-S	Patients who received antipsychotic treatment and showed a response to this treatment	NA
Rui et al.	Patients who had no deliberate self-injury or violent behavior resulting in clinically significant injury to self or another person or property damage, no psychiatric hospitalization (involuntary or voluntary admission to a psychiatric hospital for decompensation of the patient's schizophrenic symptoms, PANSS score <70) and prespecified individual PANSS scores (P1, P2, P3, P6, P7 and G8) ≤4	Patients who received no changes in established dose of paliperidone	6
Tandon et al.	Patients who achieved and maintained the following clinical stability criteria for ≥12 weeks: a PANSS total score ≤70, with PANSS item scores ≤4 on all positive subscale items and item G8; and a CGI-S score <4[b]	Patients who remained on a stable dose of lurasidone for 4 weeks	12-24

Abbreviations: BPRS, Brief Psychiatric Rating Scale; CGI-S, Clinical Global Impression - Severity scale; CGI-SS, Clinical Global Impression - Severity of Suicidality scale; GAF, Global Assessment of Functioning; HDRS-21, Hamilton Depression Rating Scale 21-item version; LAI, long-acting injection; NA, not applicable; PANSS, Positive and Negative Syndrome Scale; YMRS, Young Mania Rating Scale

[a]The term “stable” refers to a consistency of residual symptomatology over the past 3 months and does not include those patients doing well or controlled on treatment with current medication.

[b]Two excursions (defined as a PANSS total score ≤80 and/or a CGI-S score of ≤4 and/or PANSS positive subscale item score of ≤5) after initial attainment of these stability criteria were permitted, except during the last 4 weeks of the open-label stabilization phase.

Supplemental Table DS2. Sample size at each time point in antipsychotic treatment arm[a]

Study	0W	1W	2W	3W	4W	8W	12W	16W	20W	24W	28W	32W	36W	40W	44W	48W	52W
Arato et al. (arm 1)	71																71
Arato et al. (arm 2)	68																68
Arato et al. (arm 3)	67																67
Beasley et al.	224											224					
Clark et al. (arm 1)	15									15							
Clark et al. (arm 2)	15									15							
Cooper et al.	61		61		61	61		61	61		61						
Fu et al.	164				164	164	164	164	164	164	164	164	164	164	164	164	164
Hough et al.	205				205	205	205	205	205	205	205	205	205	205			
Kane et al.	269		269		269	269	269	269	269	269	269	269	269	269	269	269	269
Kramer et al.	104	104	104	104	104	104	104	104	104	104	104	104	104	104			
Pigott et al.	148					148					148						
Rui et al.	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64
Tandon et al.	143	143	143		143	143	143	143	143	143	143						
Total	**1618**	**311**	**641**	**168**	**1010**	**1158**	**949**	**1010**	**1010**	**979**	**1158**	**1030**	**806**	**806**	**497**	**497**	**703**

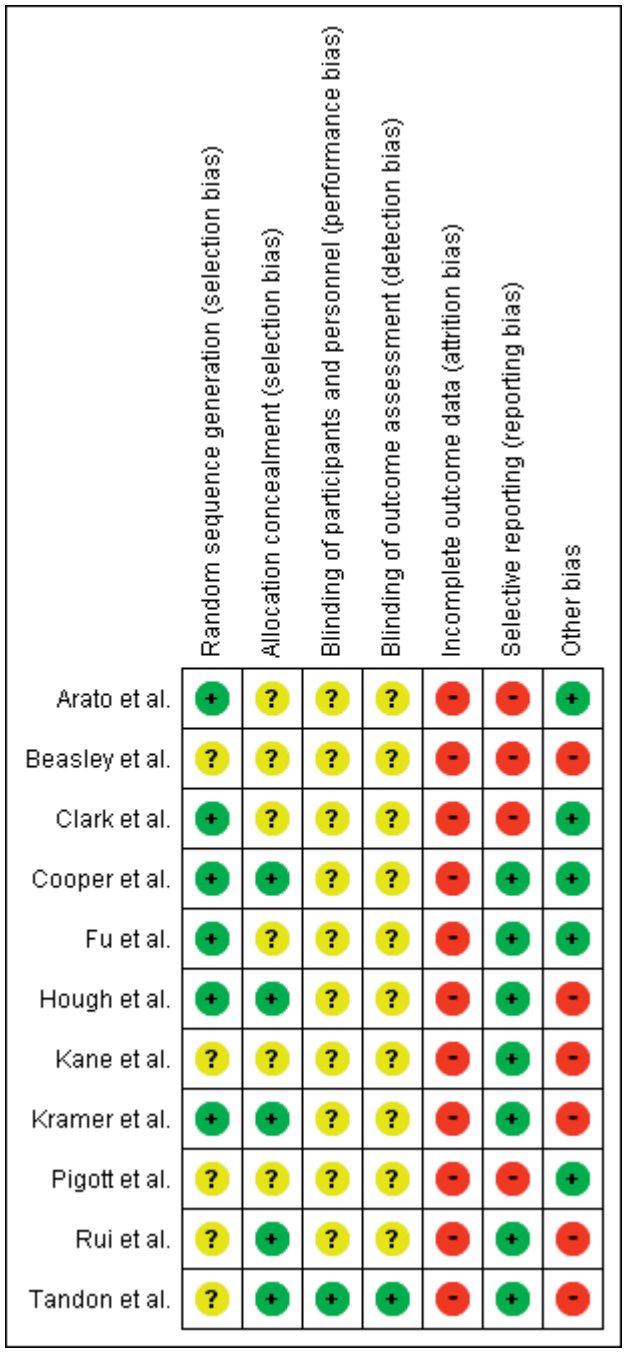
[a]PANSS or BPRS total scores were collected for each study for up to 52 weeks from randomization; weekly for the first 4 weeks and at 4-week intervals thereafter. Values at 4n weeks + 2 weeks were recorded as values at 4(n+1) weeks.

Supplemental Table DS3. Sample size at each time point in placebo treatment arm[a]

Study	0W	1W	2W	3W	4W	8W	12W	16W	20W	24W	28W	32W	36W	40W	44W	48W	52W
Arato et al.	71																71
Beasley et al.	100											100					
Clark et al.	10									10							
Cooper et al.	58		58		58	58		58	58		58						
Fu et al.	170				170	170	170	170	170	170	170	170	170	170	170	170	170
Hough et al.	203				203	203	203	203	203	203	203	203	203	203			
Kane et al.	134		134		134	134	134	134	134	134	134	134	134	134	134	134	134
Kramer et al.	101	101	101	101	101	101	101	101	101	101	101	101	101	101			
Pigott et al.	149					149					149						
Rui et al.	71	71	71	71	71	71	71	71	71	71	71	71	71	71	71	71	71
Tandon et al.	141	141	141		141	141	141	141	141	141	141						
Total	**1208**	**313**	**505**	**172**	**878**	**1027**	**820**	**878**	**878**	**830**	**1027**	**779**	**679**	**679**	**375**	**375**	**446**

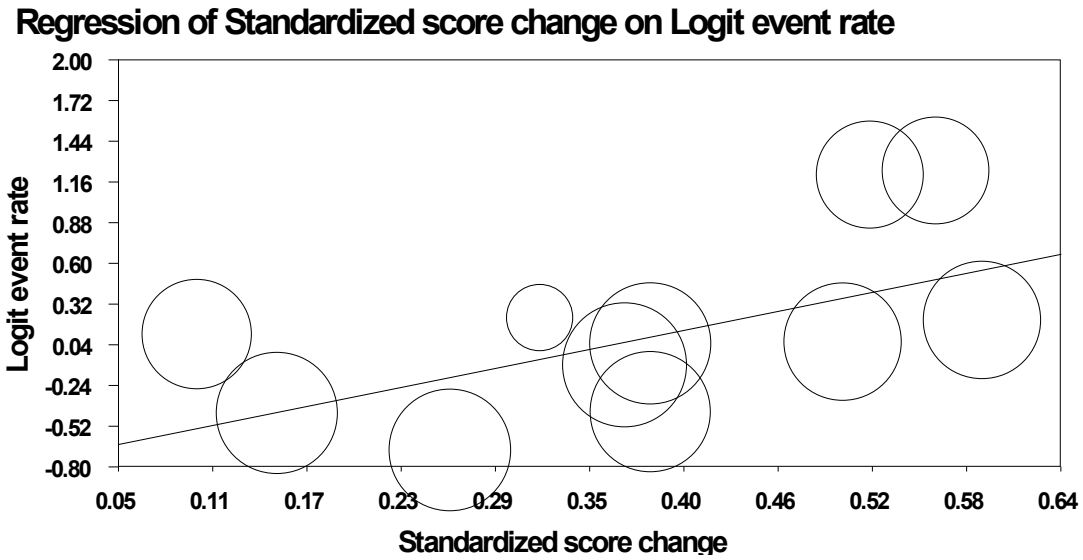
[a]PANSS or BPRS total scores were collected for each study for up to 52 weeks from randomization; weekly for the first 4 weeks and at 4-week intervals thereafter. Values at 4n weeks + 2 weeks were recorded as values at 4(n+1) weeks.

Supplemental Figure DS1. Risk of bias summary



Note: +, low risk of bias; -, high risk of bias; ?, questionable risk of bias

Supplemental Figure DS2. Meta-regression analysis (mixed effects unrestricted maximum likelihood) examining the moderator effect of standardized score changes on relapse rates in patients switching to placebo



Mixed effects regression (unrestricted maximum likelihood)

	Point estimate	Standard error	Lower limit	Upper limit	Z-value	p-Value
Slope	2.22518	0.89117	0.47852	3.97185	2.49692	0.01253
Intercept	-0.75981	0.36164	-1.46861	-0.05100	-2.10100	0.03564
Tau-squared	0.15425					

	Q	df	p-value
Model	6.23460	1.00000	0.01253
Residual	11.25674	9.00000	0.25852
Total	17.49133	10.00000	0.06417