Appendix D. Study Characteristics

Table D1. Study characteristics

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Alacqua et al., 2008 [96] **Country:** Italy **Condition category:** Mixed conditions (ADHD, ASD, schizophrenia-related, tics) **Funding:** NR **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Jan 2002 to Dec 2003 **Study design:** Retrospective cohort **Diagnostic criteria:** DSM-IV **Setting:** Outpatient/community **Inclusion criteria:** (1) ≤18 yr, (2) received an incident treatment with atypical antipsychotics or SSRIs during the study period **Exclusion criteria:** NR	**Enrolled:** 73 **Analyzed:** 73 **Completed:** 50 **GROUP 1** **N:** 2 **Age, mean±SD (range):** 15.5±0.7 **Males %:** 50 **Caucasian %:** NR **Diagnostic breakdown (n):** psychosis (1), schizophrenia (1) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 24 **Age, mean±SD (range):** 14.7±2.3 **Males %:** 42 **Caucasian %:** NR **Diagnostic breakdown (n):** affective disorder (2), anxiety disease (4), autism (1), CD (1), MR (3), personality disorder (2), psychosis (9), schizophrenia (2) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis**	**Treatment duration:** 3 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 150±70.1 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.1±4.4 **Concurrent treatments:** NR **GROUP 3** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 375±318.2 **Concurrent treatments:** NR **GROUP 4** **Drug name:** Risperidone **Dosing variability:** variable	**Benefits:** NR **Harms:** Behavioral issues, dyskinesia, dystonia, dermatologic AE, liver function, hepatic volume, prolactin, prolactin-related AE, sedation, sleepness, total AE, weight change	Adverse events occurred frequently during first 3 months of treatment with atypical antipsychotics.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		(n): NR **Comorbidities:** NR **GROUP 3** **N:** 2 **Age, mean±SD (range):** 16.5±1.5 **Males %:** 100 **Caucasian %:** NR **Diagnostic breakdown (n):** psychosis (2) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 4** **N:** 45 **Age, mean±SD (range):** 13±3.9 **Males %:** 80 **Caucasian %:** NR **Diagnostic breakdown (n):** ADHD (1), anxiety disease (2), autism (14), CD (7), conversion disorder (2), MR (8), psychosis (7), schizophrenia (2), tic disorder (2) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2±1.3 **Concurrent treatments:** NR		
Aman et al., 2014 [4] **Country:** USA **Condition category:** ADHD	**Recruitment dates:** August 2008 – November 2012 **Study design:** RCT (parallel)	**Enrolled:** 168 **Analyzed:** 168 **Completed:** 137 **GROUP 1** **N:** 84	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 2 wk most drugs, 4 wk antipsychotics and fluoxetine	**Benefits:** NCBRF, ABS, CGI-I, CGI-S, response **Harms:** metabolic effects, prolactin	Risperidone provided moderate but variable improvement in aggressive and other seriously

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Funding: Non-industry **Risk of bias:** Medium (subjective), Medium (objective)	**Setting:** NR **Diagnostic criteria:** DSM-IV **Inclusion criteria:** 6-12 yr, DSM-IV diagnosis of DBD (CD or ODD) or ADHD, serious physical aggression (Overt Aggression Scale – M ≥3), evidence of seriously disruptive behavior (parent rating NCBRF D-Total ≥ 27, CGI-S ≥ 4 by blinded clinician **Exclusion criteria:** IQ < 71, pregnancy, history of seizure disorder or neurological or medical disorder, abnormal liver function, PDD, schizophrenia or other psychotic disorders, ED, hypomanic/biphasic score ≥ 36 on GBI (mood disorder), current or previous major depressive disorder or diagnosis of bipolar disorder, current use of psychotropic medications where discontinuation would be a significant risk,	**Age, mean±SD (range):** 9.03±2.05 yr **Males %:** 77.4% **Caucasian %:** 57.1% **Diagnostic breakdown (n):** ADHD (84) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** CD (22), ODD (62) **GROUP 2** **N:** 84 **Age, mean±SD (range):** 8.75±1.98 yr **Males %:** 76.2% **Caucasian %:** 48.8% **Diagnostic breakdown (n):** ADHD (84) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** CD (22), ODD (62)	**Permitted drugs:** methylphenidate **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.7±0.75 mg/day **Concurrent treatments:** Methylphenidate, parent training (PT) **GROUP 2** **Drug name:** Placebo **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.9±0.72 mg/day **Concurrent treatments:** Methylphenidate, parent training (PT)	effects, sedation and sleep issues, GI, headache	disruptive child behaviors when added to PT and optimized stimulant treatment.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	active substance use disorder, current child abuse or neglect, history of suicide attempt (past year) or current suicidal ideation, family history type 2 diabetes in ≥ 2 first-degree relatives				
Aman et al., 2009 [3] **Country:** USA **Condition category:** ADHD **Funding:** NR **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (crossover) **Diagnostic criteria:** DSM-IV, IQ test (Stanford-Binet, Weschsler Intelligence, Kaufman Brief) **Setting:** Inpatient and outpatient **Inclusion criteria:** (1) 4–14 yr, (2) IQ ≤84, (3) ODD or CD, (4) dx of austistic or PDD NOS, (5) availability of a reliable informant, (6) good physical health **Exclusion criteria:** (1) presence of psychosis, (2) history of NMS, (3) history of severe drug allergy/hypersensitivity, (4) medical disease, (5) pregnancy	**Enrolled:** 16 **Analyzed:** 15 **Completed:** NR **GROUP 1** **N:** 16 (crossover) **Age, mean±SD (range):** 8.56±2.6 yr **Males %:** 87.5% **Caucasian %:** 81.2% **Diagnostic breakdown (n):** ADHD (1), ADHD + CD (2), ADHD + ODD (6), CD (1), ODD (3), ASD (3) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** Borderline intellectual disability (10), mild intellectual disability (4), moderate intellectual disability (1) **GROUP 2** **N:** 16 (crossover) **Age, mean±SD (range):** See group 1 **Males %:** See group 1 **Caucasian %:** See group 1 **Diagnostic breakdown**	**Treatment duration:** 4 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk **Permitted drugs: c**lonidine, lithium **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.65±1.3 (0.4–5) **Concurrent treatments:** psychostimulants (5) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** ABC, NCBRF Cognitive (MTS, STRM, CPT, GHT) **Harms:** Dyskinesia, SBP, DBP, pulse	Risperidone may have a beneficial effect on efficiency or responding, activity level, static tremor, and aspects of behavior.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		(n): See group 1 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** See group 1			
Aman et al., 2004 [97] (see Aman 2002, Snyder 2002) **Country:** Canada, South Africa, USA **Condition category:** ADHD **Funding:** NR **Newcastle-Ottawa Scale:** 7/8 stars	**Study design:** Observational (pooled analysis)	**Enrolled:** NA **Analyzed:** 155 **Completed:** NA **GROUP 1** **N:** 43 **Age, mean±SD (range):** 8.6±2.1 yr **Males %:** 81.4% **Caucasian %:** 55.8% **Diagnostic breakdown (n):** CD, ODD, or DBD-NOS with ADHD (43) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** All have ADHD **GROUP 2** **N:** 35 **Age, mean±SD (range):** 9.0±1.7 yr **Males %:** 85.7% **Caucasian %:** 65.7% **Diagnostic breakdown (n):** CD, ODD, or DBD-NOS with ADHD (35) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** All have ADHD	**GROUP 1** **Drug name:** Risperidone (only) **Dosing variability:** Variable **Target dose (mg/day):** 0.06 mg/kg/day **Daily dose (mg/day), mean±SD (range):** 1.11 mg/day **Concurrent treatments:** See Aman 2002 and Snyder 2002 **GROUP 2** **Drug name:** Risperidone + stimulant **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.07 mg/day **Concurrent treatments:** See Aman 2002 and Snyder 2002 - psychostimulants **GROUP 3** **Drug name:** Placebo (only) **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** See Aman 2002 and Snyder 2002 **GROUP 4** **Drug name:** Placebo + stimulant **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**	**Benefits:** NCBRF, ABC **Harms:** metabolic effects, somnolence, headache, infections	Risperidone was a safe and effective treatment with or without stimulant added, for DBD and comorbid ADHD in children.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
			(range): NR **Concurrent treatments:** See Aman 2002 and Snyder 2002 - psychostimulants		
		GROUP 3 **N:** 39 **Age, mean±SD (range):** 8.3±2.2 yr **Males %:** 74.4% **Caucasian %:** 56.4% **Diagnostic breakdown (n):** CD, ODD, or DBD-NOS with ADHD (39) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** All have ADHD **GROUP 4** **N:** 38 **Age, mean±SD (range):** 8.9±2.1 yr **Males %:** 92.1% **Caucasian %:** 73.7% **Diagnostic breakdown (n):** CD, ODD, or DBD-NOS with ADHD (38) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** All have ADHD			
Aman et al., 2002 [2] **Country:** USA **Condition category:** ADHD **Funding:** Industry	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:**	**Enrolled:** 119 **Analyzed:** 118 **Completed:** 118 **GROUP 1** **N:** NR **Age, mean±SD (range):** 8.7±2.1 yr **Males %:** 85	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk **Permitted drugs:** antihistamines, chloral hydrate, medication for EPS, melatonin, psychostimulants (dose stable for ≥30 day before study)	**Benefits:** ABC, BPI, CGI-I, NCBRF, VAS-MS Medication adherence, response (CGI) **Harms:** ECG changes, EPS,	Risperidone was well tolerated and effective in children with disturbed behaviors and subaverage intelligence.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Risk of bias: High (subjective), High (objective)	DSM-IV, NCBRF **Inclusion criteria:** (1) total rating of ≥24 on the conduct problem subscale of the NCBRF, (2) dx of CD, ODD, or DBD NOS, (3) dx of subaverage IQ (≥36 and ≤84) and a VABS score ≤84, (4) patients with ADHD eligible if meeting all other criteria, (5) healthy, (6) 5–12 yr, (7) symptoms sufficiently severe for antipsychotic treatment, (8) a responsible person to accompany patient to study visits, provide reliable assessments, dispense study medication **Exclusion criteria:** (1) dx of PDD, schizophrenia, other psychotic disorders, (2) head injury as a cause of intellectual disability, (3) seizure disorder/ neuroleptics, (4) known hypersensitivity to risperidone or neuroleptics, (5) history of tardive dyskinesia or NMS, (6) serious or progressive illnesses, (7) presence of HIV, (8) use of an	**Caucasian %:** 51 **Diagnostic breakdown (n):** CD (9), CD + ADHD (12), DBD (1) DBD + ADHD (4), ODD (12), ODD+ ADHD (17) **Treatment naïve (n):** 55 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (33), MR (borderline (32), mild (16), moderate (7)) **GROUP 2** **N:** NR **Age, mean±SD (range):** 8.1±2.3 yr **Males %:** 79 **Caucasian %:** 62 **Diagnostic breakdown (n):** CD (12), CD + ADHD (14), DBD (1) DBD + ADHD (2), ODD (13), ODD + ADHD (21) **Treatment naïve (n):** 63 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (37), MR (borderline (28), mild (22), moderate (13))	**Prohibited drugs:** anticonvulsants, antidepressants, antipsychotics, carbamazepine, cholinesterase inhibitors, lithium, medications for sleep/anxiety, valproic acid **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.2±0.6 **Concurrent treatments:** all groups: methylphenidate hydrochloride (35) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** see group 1	prolactin, prolactin-related AE, SAE, sedation, total AE, WAE, weight change	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	investigational drug within the previous 30 day, (9) previously received risperidone, (10) lab values outside of normal range unless not clinically relevant, (11) females of childbearing age, sexually active and not using birth control, (12) patients whose NCBRF conduct problem subscale score was reduced to <24 in response to a 1 wk placebo treatment before the study				
Aman et al., 1991 [1] **Country:** New Zealand **Condition category:** ADHD **Funding:** Non-industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (crossover) **Setting:** Outpatient **Diagnostic criteria:** DISC-P, DSM-III **Inclusion criteria:** Met criteria for ADD or CD, subnormal IQ (<76), attending special classes or special schools for mental retardation or adjustment classes for youngest children **Exclusion criteria:** NR	**Enrolled:** 30 **Analyzed:** 30 **Completed:** 30 **All participants** **N:** 30 **Age, mean±SD (range):** 10.1 (4.1-16.5) yr **Males %:** 83% **Caucasian %:** 70% **Diagnostic breakdown (n):** ADHD (24), ADD (4), ADD Residual type (1), CD (3) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities (n):** Significantly subnormal IQ (27), PDD (1) Subjects assigned to three	**Treatment duration:** 9 wk (3 wk per treatment) **Run-in phase:** Yes **Run-in phase duration:** NR **Permitted drugs:** epilepsy drugs (phenytoin, carbamazepine, phenobarbital, sodium valproate) **Prohibited drugs:** All psychotropics **GROUP 1** **Drug name:** Thioridazine **Dosing variability:** Fixed **Target dose (mg/day):** 1.75 mg/kg/day **Daily dose (mg/day), mean±SD (range):** 1.75 mg/kg/day in 2 daily doses **Concurrent treatments:** Phenytoin + carbamazepine (2), Phenobarbital +	**Benefits:** CTRS, RBPC, DCB, RLRS **Harms:** HR, BP, Weight, cognition	Clinical response to thioridazine was substantially less than the response to methylphenidate, with significant improvements confined to conduct and hyperactivity problems on teacher ratings.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		orders of drugs: Thioridazine, methylphenidate, placebo	**GROUP 2** **Drug name:** Placebo **Dosing variability:** Fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2 identical placebo capsules per day **Concurrent treatments:** See group 1		
Anderson et al., 1989 [5] **Country:** USA **Condition category:** ASD **Funding:** Non-Industry **Risk of bias:** High (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (crossover) **Setting:** NR **Diagnostic criteria:** DSM-III **Inclusion criteria:** (1) Dx of infantile autism using DSM III, made independently by three child psychiatrists **Exclusion criteria:** (1) Patients with history of seizure disorder, gross neurological deficit, endocrine or systematic disease, or those with an identifiable cause for autism, (2) patients rated as hypoactive and anergic on baseline	**Enrolled:** 45 **Analyzed:** 42 **Completed:** 42 **GROUP 1** **N:** 14 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** NR **Inpatients (n):** 14 **First episode psychosis (n):** NR **Comorbidities:** see below **GROUP 2** **N:** 14 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** NR **Inpatients (n):** 14 **First episode psychosis (n):** NR **Comorbidities:** see below	**Treatment duration:** 14 wk **Run–in phase:** Yes **Run–in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** RN **GROUP 1** **Drug name:** Haloperidol, Placebo, Placebo **Dosing variability:** variable **Target dose (mg/day):** 4.0 **Daily dose (mg/day), mean±SD (range):** 0.84±0.57 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo, Haloperidol, Placebo **Dosing variability:** variable **Target dose (mg/day):** 4.0 **Daily dose (mg/day), mean±SD (range):** 0.84±0.57 **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo, Placebo, Haloperidol **Dosing variability:** variable **Target dose (mg/day):** 4.0 **Daily dose (mg/day), mean±SD (range):** 0.84±0.57	**Benefits:** CPRS, CGI-I, CGI-S, CGI-Efficacy, Conners PTQ, medication adherence **Harms:** sedation, acute dystonic reaction	Haloperidol did not have generalized facilitating effects on discrimination learning. However, it is important that haloperidol administration did not have an adverse effect on learning during the 4-wk period, and this itself is important information regarding a population where the majority is of subnormal intellectual functioning, having severe learning difficulties.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
			Concurrent treatments: NR		
		GROUP 3 **N:** 14 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** NR **Inpatients (n):** 14 **First episode psychosis:**NR **Comorbidities:** NR **First episode psychosis (n):** NA **Comorbidities:** see below **Overall age, mean±SD (range):** 4.49±1.16 yr **Overall males %:** 77.8 **Overall comorbidities:** mild/low level retardation (42), of these, profoundly or severely retarded (29)			
Arango et al., 2014[98] **Country:** Spain **Condition category:** Mixed conditions **Funding:** Non-industry **Newcastle-Ottawa Scale:** 5/8 stars	**Recruitment dates:** May 2005 to Feb 2009 **Study design:** Prospective **Setting:** Inpatient/outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 4-7 yr, (2) ≤30 days of lifetime exposure to SGAs, (3) met DSM-IV	**Enrolled:** 303 **Analyzed:** 279 **Completed:** 165 (at 6mo) **GROUP 1** **N:** 157 **Age, mean±SD (range):** 14.0±3.3 yr **Males %:** 64.3 **Caucasian %:** 84.7 **Diagnostic breakdown (n):** Schizophrenia spectrum (48), mood spectrum disorders (34), behavioral disorders (42), other diagnosis (29)	**Treatment duration:** 6 mo **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Antidepressants (14),	**Benefits:** NA **Harms:** Weight (BMI, BMI-z), lipid values, fasting glucose, insulin, blood pressure (systolic/ diastolic)	Close screening and monitoring of cadio-metabolic side effects (CSE) is imperative, at least during the initial months of treatment, and suggest that there are differences in CSE risk and temporal pattern with olanzapine, risperidone, and quetiapine.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	psychiatric diagnosis other than a primary eating disorder **Exclusion criteria:** NR	**Treatment naïve (n):** 80 **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 44 **Age, mean±SD (range):** 15.4±1.8 yr **Males %:** 63.6 **Caucasian %:** 93.2 **Diagnostic breakdown (n):** Schizophrenia spectrum (15), mood spectrum disorders (17), behavioral disorders (5), other diagnosis (6) **Treatment naïve (n):** 14 **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 47 **Age, mean±SD (range):** 15.7±1.6 yr **Males %:** 53.2 **Caucasian %:** 89.4 **Diagnostic breakdown (n):** Schizophrenia spectrum (21), mood spectrum disorders (21), behavioral disorders (0), other diagnosis (3) **Treatment naïve (n):** 24 **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR	benzodiazepines (40), mood stabilizers (19), stimulants (1) **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Antidepressants (14), benzodiazepines (18), mood stabilizers (7), stimulants (0) **GROUP 3** **Drug name:** Quetiapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Antidepressants (11), benzodiazepines (12), mood stabilizers (7), stimulants (0)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Overall inpatients (n): 200			
Arango et al., 2009 [6] **Country:** Spain **Condition category:** Schizophrenia and related **Funding:** Industry, Academic **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) adolescents admitted to the hospital with psychosis (schizophrenia or any other psychotic disorder (DSM-IV)) **Exclusion criteria:** (1) psychotic symptoms appearing to result from acute intoxication or withdrawal (if psychotic symptoms did not persist after 14 day of a negative urine drug screening), (2) DSM-IV criteria for any substance abuse, MR, or PDD, (3) organic CNS disorder, (4) history of TBI with loss of consciousness, (5) IQ <70 and a clinical criterion of impaired functioning prior to the onset of the disorder, (6) pregnant or breast	**Enrolled:** 50 **Analyzed:** 49 **Completed:** 32 **GROUP 1** **N:** 26 **Age, mean±SD (range):** 15.7±1.4 **Males %:** 76 **Caucasian %:** 76 **Diagnostic breakdown (n):** bipolar disorder (5), other psychoses (12: major depressive episode with psychotic features (3), psychosis NOS (4), schizoaffective disorder (3), schizophreniform disorder (2)), schizophrenia (9) **Treatment naïve (n):** 10 **Inpatients (n):** all **First episode psychosis (n):** all **Comorbidities:** psychosis (all) **GROUP 2** **N:** 24 **Age, mean±SD (range):** 16.3±1.1 **Males %:** 79.2 **Caucasian %:** 87.5 **Diagnostic breakdown (n):** bipolar disorder (8), other psychoses (8; major depressive episode with psychotic features (2), psychosis NOS (2),	**Treatment duration:** 6 mo **Run-in phase:** Yes **Run-in phase duration:** 3–5 day **Permitted drugs:** adjunctive medications **Prohibited drugs:** antipsychotics **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 9.7±6.6 **Concurrent treatments:** anticholinergics (8), antidepressants (10), antiepileptics (7), benzodiazepines (17), β-blockers (1), lithium (2) **GROUP 2** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 532.8±459.6 **Concurrent treatments:** analgesics (2), anticholinergics (3), antidepressants (8), antiepileptics (7), benzodiazepines (14), β-blockers (2), cough medications (1), iron compouNRs (1), lithium (6), NSAIDs (1)	**Benefits:** CGAS, CGI-S, PANSS, SDQ, YMRS, Cognitive function, medication adherence **Harms:** UKU, BAS, SAS, Akathisia, behavioral issues, BMI, constipation, hypokinesia, orthostatic dizziness prolactin-related AE, SAE, sedation, tachycardia, total AE, weight change	Psychotic symptoms in adolescents were reduced with both olanzapine and quetiapine, but cognitive measures were not improved. Significantly more weight gain was observed in patients treated with olanzapine.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	feeding, (7) taking olanzapine or quetiapine before enrolment	schizoaffective disorder (2), schizophreniform disorder (2)), schizophrenia (8) **Treatment naïve (n):** 15 **Inpatients (n):** all **First episode psychosis (n):** all **Comorbidities:** psychosis (all)			
Armenteros et al., 2007 [7] **Country:** USA **Condition category:** ADHD **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, C-DISC 4 **Inclusion criteria:** (1) 7–12 yr, (2) constant dose of stimulant medication in the past 3 wk, (3) 3 acts of aggression in the past wk, 2 of which had to be acts of physical aggression against other people, objects, or self, (4) Aggression Questionnaire Predatory-Affective index score ≤0, (5) CGI-S ≥4, (6) Full Scale IQ ≥75, (7) normal results at screening from physical examination and laboratory tests	**Enrolled:** 25 **Analyzed:** 25 **Completed:** 23 **GROUP 1** **N:** 12 **Age, mean±SD (range):** 7.3±3.7 **Males %:** 83.3 **Caucasian %:** 50 **Diagnostic breakdown (n):** ADHD + aggressive behavior (12) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0), ODD (13), conduct disorder (6), GAD (1), separation anxiety disorder (3) **GROUP 2** **N:** 13 **Age, mean±SD (range):** 8.8±3.1 **Males %:** 92.3 **Caucasian %:** 46 **Diagnostic breakdown (n):** ADHD + aggressive behavior (13)	**Treatment duration:** 4 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** current psychostimulants **Prohibited drugs:** all medications other than current psychostimulants **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.1±0.6 mg/day **Concurrent treatments:** all groups: methylphenidate (15), mixed salts amphetamine (10) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1±0.5 mg/day **Concurrent treatments:** see group 1	**Benefits:** CGI-I, CGI-S Medication adherence, response (CAS-P, CAS-T, CGI-I) **Harms:** Behavioral issues, BMI, somnolence, total AE, WAE, weight change	Compared to placebo, risperidone was modestly effective in combination with psychostimulants for treatment-resistant agression in ADHD.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	Exclusion criteria: (1) substance use disorder, (2) unstable medical or neurological illness, (3) history of intolerance or failure to respond to an adequate trial of risperidone, (4) suicidal or homicidal	**Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group1			
Bastiaens et al., 2009 [99] **Country:** USA **Condition category:** Mixed conditions (BP, Schizophrenia, MDD, ASD) **Funding:** Internal funding **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Dec 2004 to Sep 2005 **Study design:** Retrospective cohort **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, Mini International Neuropsychiatric Interview for Children and Adolescents, Child/Adolescent Symptom Inventory **Inclusion criteria:** (1) 6–18 yr, (2) clinically significant aggressive behavior **Exclusion criteria:** NR	**Enrolled:** 46 **Analyzed:** 34 **Completed:** 34 **GROUP 1** **N:** 24 **Age, mean±SD (range):** 11.7±2.4 **Males %:** 83 **Caucasian %:** NR **Diagnostic breakdown (n):** bipolar disorder (6), CD (8), depressive disorder (0), mood disorder NOS (6), PDD (0), psychotic disorder (4) **Treatment naïve (n):** 18 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 22 **Age, mean±SD (range):** 12.1±2.9 **Males %:** 91 **Caucasian %:** NR **Diagnostic breakdown (n):** bipolar disorder (6), CD (6), depressive disorder (6), mood	**Treatment duration:** 8.7 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** stable doses of concomitant medications **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 4.5±2.3 **Concurrent treatments:** atomoxetine (8), stimulants (2) **GROUP 2** **Drug name:** Ziprasidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 42.9±18 **Concurrent treatments:** atomoxetine (6), stimulants (8)	**Benefits:** NA **Harms:** Behavioral issues, EPS, sedation, WAE, weight change	The two medications appeared to be tolerated well: the most common reported side effect was sedation. Excessive sedation was responsible for all documented disruptions in treatment. Ziprasidone resulted in three times more frequent discontinuations, compared to Aripiprazole.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		disorder NOS (2), PDD (2), psychotic disorder (0) **Treatment naïve (n):** 16 **Inpatients (n):** NR **First episode psychosis (n):** NR			
Berger et al., 2008[8] **Country:** Australia **Condition category:** Schizophrenia and related **Funding:** Industry, Academic **Risk of bias:** Low (subjective), Low (objective)	**Recruitment dates:** July 2003 to Jan 2006 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, SCID-I/P **Inclusion criteria:** (1) 15–25 yr, (2) first episode psychosis, (3) ≥1 of the following symptoms, present daily for ≥1 wk according to BPRS: somatic concerns, guilt, suspiciousness, hallucinations, unusual thought content, bizarre behavior, and/or conceptual disorganization **Exclusion criteria:** (1) previous treatment with antipsychotic medication (>1 wk), (2) presence of concurrent manic syndrome, MR (IQ<70), organic disorders presenting with a psychotic	**Enrolled:** 141 **Analyzed:** 126 **Completed:** 126 **GROUP 1** **N:** 69 **Age, mean±SD (range):** 19.7±2.6 (15–24) **Males %:** 71 **Caucasian %:** NR **Treatment naïve (n):** 22 **Inpatients (n):** NR **First episode psychosis (n):** all **Comorbidities:** MR (0), psychosis (all), SA (28) **GROUP 2** **N:** 72 **Age, mean±SD (range):** 19±2.9 (15–24) **Males %:** 64.1 **Caucasian %:** NR **Treatment naïve (n):** 25 **Inpatients (n):** NR **First episode psychosis (n):** all **Comorbidities:** MR (0), psychosis (all), SA (30)	**Treatment duration:** 4 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** anticholinergics, benzodiazepines, sertraline (50–200 mg/day), zopiclone, zolpidem **Prohibited drugs:** antipsychotics **GROUP 1** **Drug name:** Quetiapine (low) **Dosing variability:** fixed **Target dose (mg/day):** 200 **Daily dose (mg/day), mean±SD (range):** 200 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Quetiapine (high) **Dosing variability:** fixed **Target dose (mg/day):** 400 **Daily dose (mg/day), mean±SD (range):** 400 **Concurrent treatments:** NR	**Benefits:** BPRS, CGI-S, GAF, SANS, SOFAS, YMRS, health care system utilization, legal interaction, medication adherence, response, suicide **Harms:** UKU, Blood pressure, EPS, sedation, sexual dysfunction, somnolence, WAE, weight change	Quetiapine was safe and well-tolerated in acutely ill drug naïve first-episode psychosis patients.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	syndrome, epilepsy, (3) clinically significant physical illness, (4) history of brain surgery or brain infarct, (5) concomitant medications that prolong the QT interval, (6) 20% deviation from normal-range laboratory values at baseline, (7) participation in any other studies involving investigational or marketed products concomitantly or within 30 days (8) having donated blood or blood products within the past 4 wk, (9) pregnant or lactating women, or women of childbearing potential not using an acceptable method of contraception				
Biederman et al., 2005 [9] **Country:** USA **Condition category:** Bipolar (manic, hypomanic, mixed) **Funding:** Government, Academic **Risk of bias:** High (subjective), High	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, K-SADS **Inclusion criteria:** (1) 4–6 yr, (2) DSM-IV bipolar I or II disorder or bipolar disorder	**Enrolled:** 31 **Analyzed:** 31 **Completed:** 24 **GROUP 1** **N:** 15 **Age, mean±SD (range):** 5.0±0.8 **Males %:** 67 **Caucasian %:** 100 **Diagnostic breakdown (n):** major depression (11), mania (all) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis**	**Treatment duration:** 8 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** benztropine mesylate (max 2 mg/day), lorazepam (≤2 mg/day) **Prohibited drugs:** antidepressants, antimanic or mood-stabilizing medications **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR	**Benefits:** BPRS, CDRS, YMRS, Response **Harms:** Behavioral issues, blood pressure, cardiovascular AE, dermatologic AE, glucose, lipid profile, neurologic AE, prolactin, pulse, sedation, weight change	Rispiradone and olanzapine showed reduction of symptoms of mania in preschool children with bipolar disorder.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(objective)	NOS with current manic, hypomanic , or mixed symptoms (with or without psychotic features), (3) YMRS score >15 **Exclusion criteria:** (1) any serious, unstable medical illness, (2) history of treatment with both study medications	**(n):** NR **Comorbidities:** ADHD (15), DBD (8) **GROUP 2** **N:** 16 **Age, mean±SD (range):** 5.3±0.8 **Males %:** 75 **Caucasian %:** 94 **Diagnostic breakdown (n):** major Depression (11), mania (all) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (14), DBD (5)	**Daily dose (mg/day), mean±SD (range):** 6.3±2.3 (1.3–10) **Concurrent treatments:** all groups: benztropine (1), lorazepam (1) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.4±0.5 (0.3–2.0) **Concurrent treatments:** see group 1		
Bobo et al., 2013 [100] **Country:** USA **Condition category:** Mixed conditions **Funding:** Non-industry **Newcastle-Ottawa Scale:** 8/8 stars	**Recruitment dates:** Jan 1996 to Dec 2007 **Study design:** Retrospective **Setting:** NR **Diagnostic criteria:** NR **Inclusion criteria:** (1) adequate enrollment and health care utilization in the past year to ensure availability of data for study variables, (2) no evidence of life-threatening illness or institutional residence, (3) no evidence of	**Enrolled:** NA **Analyzed:** 43287 **Completed:** 43287 **GROUP 1** **N:** 28858 **Age, mean±SD (range):** 14.5 yr **Males %:** 56.0 **Caucasian %:** 72.8 **Diagnostic breakdown (n):** BP (5281), depression (5569), other mood disorder (9609), ADHD (11225), CD (7301), anxiety (5944), alcohol use (894), other substance use (2568) **Treatment naïve (n):** 0 **Inpatients (n):** 4184 **First episode psychosis (n):** NR	**Treatment duration:** ≥1 yr **Run-in phase:** Yes **Run-in phase duration:** 365 d **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Antipsychotic users **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** [starting dose, median(IQ range)] 67(33-100)mg of chlorpromazine equivalents **Concurrent treatments:** Li (1212), valproate (2741), lamotrigine, carbamazepine, oxcarbazepine (2539), other mood stabilizer (519), SSRI (13563), heterocyclic antidepressant (4299),	**Benefits:** NA **Harms:** Type 2 diabetes mellitus	In the study cohort (6 to24 yr), those recently initiating an antipsychotic medication had a 3-fold greater risk of newly diagnosed type 2 diabetes than did propensity score–matched controls. Risk was elevated during the first year of antipsychotic use, increased with increasing cumulative dose, and was present for children <18 yr.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	diabetes, (4) no evidence of pregnancy (gestational diabetes might be misdiagnosed) or polycystic ovarian syndrome (treated with oral hypoglycemics), (5) cohort members could not have been in the hospital in the past month because changes in the medication regimen cannot be identified until up to 30 days following hospital discharge, (6) could have non-qualifying use of antipsychotics in the 90 days preceding the qualifying prescription but had to have a prior period of 365 days free of antipsychotic use, (7) cohort was restricted to recent users to include cases of diabetes that occurred early in therapy and to ensure that baseline covariateswere unaffected by chronic antipsychotic effects **Exclusion criteria:** (1) patientswithdiagnosed conditions for which antipsychotics	**Comorbidities:** Menstruation absent or infrequent (1096), menstruation disorder (1414), diagnosed obesity (1096), metabolic disorder (606), blood chemistry panel with glucose (6608), hypertension (750), other diagnosed cardiovascular disease (1298) **GROUP 2** **N:** 14429 **Age, mean±SD (range):** 14.5 yr **Males %:** 55.9 **Caucasian %:** 73.5 **Diagnostic breakdown (n):** BP (2654), depression (2813), other mood disorder (4689), ADHD (5526), CD (3592), anxiety (2871), alcohol use (476), other substance use (1341) **Treatment naïve (n):** NR **Inpatients (n):** 1991 **First episode psychosis (n):** NR **Comorbidities:** Menstruation absent or infrequent (533), menstruation disorder (72), diagnosed obesity (562), metabolic disorder (303), blood chemistry panel with glucose (3246), hypertension (360), other diagnosed cardiovascular disease (606)	psychostimulant (9840), α-agonist (4213), benzodiazepine (3578) **GROUP 2** **Drug name:** Controls **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Li (591), valproate (1341), lamotrigine, carbamazepine, oxcarbazepine (1298), other mood stabilizer (259), SSRI (6723), heterocyclic antidepressant (2063), psychostimulant (4862), α-agonist (2048), benzodiazepine (1818)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	generally are the only recommended treatment (eg. schizophrenia or related psychoses, organic psychoses, autism, mental retardation, Tourette syndrome, or other tic disorders), (2) patients prescribed clozapine or long-acting injectable preparations, usually indicators of schizophrenia or related psychoses, as well as those with parenterally administered drugs, typically given for transient agitation.				
Bruggeman et al., 2001 [10] **Country:** Belgium, Netherlands, South Africa **Condition category:** Tic disorders **Funding:** Industry **Risk of bias:** NA (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-III-TR **Inclusion criteria:** (1) 10–65 yr, (2) primary dx of Tourette syndrome (DSM-III-R), (3) ≥3 on TSSS and CGI-S **Exclusion criteria:** NR	**Enrolled:** 50 **Analyzed:** 50 **Completed:** 41 **GROUP 1** **N:** 24 **Age, mean±SD (range):** NR (11–45) **Males %:** 87.5 **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (24) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (1), GAD (2), OCD (14) **GROUP 2**	**Treatment duration:** 2.8 mo **Run-in phase:** Yes **Run-in phase duration:** 2–5 wk **Permitted drugs:** antiparkinsonian medication and benzodiazepines (discontinued during washout period, limited during treatment) **Prohibited drugs:** antiparkinsonian medication and benzodiazepines (discontinued during washout period, limited during treatment), psychotropics (within 2 wk prior to and during study) **GROUP 1** **Drug name:** Pimozide **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**	**Benefits:** NR **Harms:** Weight	Risperidone and pimozide were efficacious and well tolerated in patients with Tourette syndrome, but risperidone had a more favorable efficacy and tolerability profile.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		N: 26 **Age, mean±SD (range):** NR (11–50) **Males %:** 88.5 **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (26) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (1), GAD (1), OCD (9)	**(range):** 2. 9 (1–6) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.8 (0.5–6) **Concurrent treatments:** NR		
Buchsbaum et al., 2007 [11] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** Industry, government **Risk of bias:** Medium (subjective), NA (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** DSM-IV using CASH (at least Psychosis NOS) **Inclusion criteria:** (1) 13-21 yr, (2) never previously medicated **Exclusion criteria:** NR	**Enrolled:** 30 **Analyzed:** 22 **Completed:** 22 **GROUP 1** **N:** 10 **Age, mean±SD (range):** both groups: 16.2±2.0 **Males %:** both groups: 52 **Caucasian %:** NR **Treatment naïve (n):** 10 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 12 **Age, mean±SD (range):** see group 1 **Males %:** see group 1 **Caucasian %:** NR **Treatment naïve (n):** 12 **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 8-9 wks **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** up to 20mg/day **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** up to 20mg/day **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** BPRS **Harms:** NR	Both patients treated with olanzapine and haloperidol improved significantly from baseline to week 8 on the BPRS (positive, negative, and total symptom scores).
Buitelaar et al., 2001 [12]	**Recruitment dates:** NR	**Enrolled:** 38 **Analyzed:** 38	**Treatment duration:** 6 wk **Run-in phase:** Yes	**Benefits:** ABC, CGI-S, OAS-M	Risperidone may be effective for severe

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Completed: 35	**Run-in phase duration:** 2 wk	Medication adherence	aggression in adolescents with disruptive behavior disorders and subaverage intelligence.
Country: Netherlands **Condition category:** ADHD **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) overt aggressive behavior persisted during hospitalization (modified OAS score ≥1), (2) failure to respond to behavioral treatment approaches, (3) clinical indication for drug treatment, (4) 12–18 yr, (5) principal dx of CD, ODD, or ADHD according to DSM-IV, (6) full-scale IQ 60–90 (WISC-R) **Exclusion criteria:** (1) neurologic, cardiac, pulmonary, or hepatic diseases, (2) primary mood disorders, schizophrenia or other active psychosis, or suicidality, (3) comorbid substance abuse disorder (DSM-IV), (4) pregnant or use of inadequate contraception, (5) major change in treatment strategy expected, (6) not feasible to discontinue	**GROUP 1** **N:** 19 **Age, mean±SD (range):** 14.0±1.5 (11–18) **Males %:** 89.5 **Caucasian %:** NR **Diagnostic breakdown (n):** CD (14), DBD NOS (1), ODD (4) **Treatment naïve (n):** 13 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (14), MR (6) **GROUP 2** **N:** 19 **Age, mean±SD (range):** 13.7±2 (11–18) **Males %:** 84.2 **Caucasian %:** NR **Diagnostic breakdown (n):** CD (16), DBD NOS (1), ODD (2) **Treatment naïve (n):** 13 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (12), anxiety disorder (3), MR (8)	**Permitted drugs:** biperidine, medication for somatic illness, oxazepam **Prohibited drugs:** psychotropics **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.9 (1.5–4) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Harms:** Akathisia, dyskinesia, dystonia, ECG changes, fatigue, oculogyric crisis, parkinsonism, prolactin, prolactin-related AE, SAE, somnolence, total AE, weight change, ESRS	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	current psychotropic medication				
Calarge et al., 2014 [101] **Country:** USA **Condition category:** Mixed **Funding:** Non-industry **Newcastle-Ottawa Scale:** 5/8 stars	**Recruitment dates:** NR **Study design:** Prospective **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, DISC-IV **Inclusion criteria:** (1) 7-7 yr, (2) treated with risperidone ≥6 mo, irrespective of primary diagnosis **Exclusion criteria:** (1) Participants with neurological or medical conditions that could confound the cardiometabolic assessments (e.g., seizure disorder, hypothyroidism, dyslipidemia, diabetes), (2) pregnant females, (3) those receiving hormonal contraception	**Enrolled:** 108 **Analyzed:** 101 **Completed:** 101 **GROUP 1** **N:** 74 **Age, mean±SD (range):** 13.3±2.7 yr **Males %:** 95 **Caucasian %:** 80 **Diagnostic breakdown (n):** DBD (68), ADHD (65), anxiety disorder (23), depressive disorder (3), ASD (12), tic disorder (17) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 9 **Age, mean±SD (range):** 12.3±2.6 yr **Males %:** 89 **Caucasian %:** 67 **Diagnostic breakdown (n):** DBD (7), ADHD (7), anxiety disorder (3), depressive disorder (0), ASD (2), tic disorder (3) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 18	**Treatment duration:** 6 mo, followed-up after 1.5 yr **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone Continued **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** (mg/kg/d) 0.03±0.02 **Concurrent treatments:** Psychostimulants (59), α_2-agonists (25), antidepressants (43), mood stabilizers (6) **GROUP 2** **Drug name:** SGA Continued **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Psychostimulants (5), α_2-agonists (6), antidepressants (8), mood stabilizers (0) **GROUP 3** **Drug name:** SGA Discontinued **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Psychostimulants (11), α_2-agonists	**Benefits:** NA **Harms:** Weight (BMI-z), lipid values, glucose, insulin, blood pressure (systolic/ diastolic), prolactin	Discontinuation of risperidone is associated with largely spontaneous resolution of the excessive weight and a favorable change in cardiometabolic parameters.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Age, mean±SD (range): 13.1±2.3 yr **Males %:** 89 **Caucasian %:** 94 **Diagnostic breakdown (n):** DBD (14), ADHD (17), anxiety disorder (5), depressive disorder (2), ASD (5), tic disorder (5) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	(5), antidepressants (20), mood stabilizers (2)		
Castro-Fornieles et al., 2008 [102] **Country:** Spain **Condition category:** Schizophrenia and related **Funding:** Government **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** NR **Study design:** Prospective cohort **Setting:** Inpatient (84% at recruitment) and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 7 to 17 yr, (2) psychotic episode less than 6 mo duration **Exclusion criteria:** (1) ASD, PTSD, SUD and other Axis I associated with psychosis, (2) MR and PDD	**Enrolled:** 110 **Analyzed:** 60 (only those remaining on same medication) **Completed:** 60 **All patients:** 15.5±1.8; Males 67%; White: 86%; 49% drug naive **GROUP 1** **N:** 31 **Age, mean±SD (range):** 15.1±2.1 **Males %:** 68 **Caucasian %: NR** **Treatment naïve (n):** NR **Inpatients (n): NR** **First episode psychosis (n):** 31 **GROUP 2** **N:** 15 **Age, mean±SD (range):** 16.4±1.1 **Males %:** 67	**Treatment duration:** 24 mo **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability: variable** **Target dose (mg/day): NR** **Daily dose (mg/day), mean±SD (range):** 2.8±1.2mg/day **Concurrent treatments:** NR **GROUP 2** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 626.8±526 mg/day **Concurrent treatments:** NR **GROUP 3** **Drug name:** Olanzapine **Dosing variability:** variable	**Benefits:** PANSS, CGI, GAF **Harms:** Weight, BMI, UKU, neurological AEs	Using the baseline score as covariate, there were no statistically significant differences between the three antipsychotics in the improvement achieved on any scale. Clinicians seem to prefer quetiapine or olanzapine to risperidone when there are marked affective symptoms.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Caucasian %: NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** 15 **GROUP 3** **N:** 14 **Age, mean±SD (range):** 15.7±1.2 **Males %:** 71 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** 14	**Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 11.7±7.0 mg/day **Concurrent treatments:** NR		
Cianchetti et al., 2011 [103] **Country:** Italy **Condition category:** Schizophrenia and related **Funding:** NR **Newcastle-Ottawa Scale:** 5/8 stars	**Recruitment dates:** 1990 to 2005 **Study design:** Cohort study **Setting:** Inpatient (at recruitment) and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** schizophrenia or schizoaffective disorder **Exclusion criteria:** (1) concomitant axis I disorder, (2) IQ less than 70, (3) neurological disorders and previous commotive head trauma	**Enrolled:** 58 **Analyzed:** 47 **Completed:** 47 **Whole cohort:** **Age:** 15.5 (range 10-17) **Males:** 45% **Caucasian**: 100%	**Treatment duration:** see below: 3 to 11 yrs **Run-in phase:** **Run-in phase duration:** **Permitted drugs:** mood stabilizers, anti-EPS (for haloperidol and high dose risperidone) **Prohibited drugs:** NR All patients treated per protocol, with analysis based on drugs used (haloperidol, risperidone, olanzapine, clozapine, quetiapine, aripiprazole; latter two had too few patients to compare) Haloperidol: (29) mean months treatment 9.4±14.3 Risperidone: (33) mean months of treatment 19.6±17.9 Olanzapine: (12) mean months of treatment 11.7±9.2 Clozapine: (28) mean months of treatment 31.5±916.3	**Benefits:** PANSS, CGI-I, CGI-EI, C-GAS, response **Harms:** EPS, weight, ECG, glucose, liver function tests, discontinuations, neutropenia, suicide	In the long-term, clozapine is more effective than haloperidol, risperidone and olanzapine. Despite a relevant incidence of adverse effects, clozapine seems to have unique effectiveness in treating children and adolescents with early-onset schizophrenic disorders.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Connor et al., 2008 [13] **Country:** USA **Condition category:** ADHD **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Nov 2003 to May 2005 **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** K-SADS-E **Inclusion criteria:** (1) 12–17 yr, (2) primary psychiatric dx of CD, (3) moderate to severe aggression (OAS score ≥25), (4) at least moderate severity of symptoms (CGI-S score ≥4) **Exclusion criteria:** (1) comorbid schizophrenia, schizoaffective disorder, psychotic disorder NOS, bipolar disorder, psychotic depression, or bipolar disorder NOS, (2) alcohol or substance abuse or dependence within 3 mo, (3) significantly subaverage IQ, (4) current or past history of leticular abnormality or juvenile cataracts, (5) seizure disorder, (6) concurrent administration of any	**Enrolled:** 19 **Analyzed:** 19 **Completed:** 11 **GROUP 1** **N:** 9 **Age, mean±SD (range):** 13.1±1.2 yr **Males %:** 78% **Caucasian %:** 78% **Diagnostic breakdown:** CD with moderate to severe aggression (9) **Treatment naïve (n):** 2 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (8), DBD (8), depression (1), dysthymia (2), GAD (3), MR (0), OCD (2), panic disorder (1), psychosis (0), PTSD (2), SA (1), separation anxiety (2), social phobia (2) **GROUP 2** **N:** 10 **Age, mean±SD (range):** 15±1.4 yr **Males %:** 70% **Caucasian %:** 70% **Diagnostic breakdown:** CD with moderate to severe aggression (10) **Treatment naïve (n):** 1 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (7), DBD (10), depression (3), dysthymia (3), GAD	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 1–4 wk **Permitted drugs:** benztropine **Prohibited drugs:** psychotropics, rescue medications for aggression **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 200 **Daily dose (mg/day), mean±SD (range):** 294±78 (200–600) **Concurrent treatments:** benztropine (0) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** 200 **Daily dose (mg/day), mean±SD (range):** 530±245 **Concurrent treatments:** benztropine (0)	**Benefits:** CGI-I, CGI-S, Conner PRS, OAS Quality of life (Q-LES-Q), school attendance **Harms:** Akathisia, Behavioral issues, ECG changes, EPS, prolactin, pulse, SAE, sedation, severity of AE, WAE, weight change, AIMS	Quetiapine may be efficacious in the treatment of CD, but further research is required.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	psychoactive medication, (7) pregnant or lactating females, (8) women of childbearing potential not using a medically accepted means of birth control, (9) unstable medical disease	(0), MR (0), OCD (1), panic disorder (0), psychosis (0), PTSD (1) SA (5), separation anxiety (1), social phobia (1)			
Conus et al., 2015 [14] **Country:** Australia **Condition category:** Bipolar **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** October 2001 and February 2006 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) participants (males and females aged 15 to 28) met DSM-IV criteria for a first manic or mixed episode with psychotic features within bipolar 1 or schizoaffective disorder, and had baseline Yound Mania Rating Scale (YMRS) score ≥ 20. **Exclusion criteria:** immediate risk of committing harm to self or others; use of neuroleptic medication or mood-stabilizers	**Enrolled:** 98 **Analyzed:** 83 **Completed:** 74 **GROUP 1** **N:** 41 **Age, mean±SD (range):** 22.0±3.0 **Males %:** 63.9 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** 30 **First episode psychosis (n):** all **GROUP 2** **N:** 42 **Age, mean±SD (range):** 21.1±2.7 **Males %:** 71.1 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** 29 **First episode psychosis (n):** all	**Treatment duration:** 8 wks **Run-in phase:** Yes **Run-in phase duration:** 24 hours **Permitted drugs:** Benzodiazepines and anticholinergics **Prohibited drugs:** **GROUP 1** **Drug name:** Chlorpromazine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 185.9±126.7 **Concurrent treatments:** Lithium **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 12.2±7.8 **Concurrent treatments:** Lithium	**Benefits:** response, remission and symptomatic recovery **Harms:** weight, extrapyramidal side effects, neutropenia, sedation	Olanzapine and chlorpromazine have a similar safety profile in a uniquely representative cohort of patients with first episode psychotic mania.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	within two months of admission to the Early Psychosis Prevention and Intervention Centre (EPPIC); organic mental disease; mental retardation; clinically signficant illness; clinically relevant biochemical or hematological abnormalities; pregnancy or lactation; history of epilespsy; drug allergy or hypersensitivity; or non-fluency in English.				
Correll et al., 2009 [104] **Country:** USA **Condition category:** Mixed conditions (bipolar, ADHD, ASD, schizophrenia-related) **Funding:** Government, Academic **Newcastle-Ottawa Scale:** 8/8 stars	**Recruitment dates:** Dec 2001 to Sep 2007 **Study design:** Prospective cohort **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, chart review, discussion with treating clinician, clinical interview **Inclusion criteria:** (1) 4–19 yr, (2) <1 wk lifetime antipsychotic treatment, (3) psychiatric illness prompting antipsychotic medication initiation, (4) consent, (5)	**Enrolled:** 312 **Analyzed:** 257 **Completed:** 192 **GROUP 1** **N:** 47 **Age, mean±SD (range):** 13.4±3.1 (7–19.7) **Males %:** 56.1 **Caucasian %:** NR **Diagnostic breakdown (n):** disruptive or aggressive behavior spectrum disorder (9: ASD (4), ODD, CD, IED, ICD (5)), mood disorder spectrum (11: bipolar (3), MDD (10), NOS (5)), schizophrenia spectrum (14: psychosis NOS (11), schizophrenia/ schizoaffective disorder (3)) **Treatment naïve (n):** all	**Treatment duration:** 2.8 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** co-medications as necessary **Prohibited drugs:** co-medications as necessary **GROUP 1** **Drug name:** Aripriprazole **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergics (2), antidepressants (13), anxiolytics or hypnotics (1), mood stabilizers (6), none (16), psychostimulants (5), psychotropics (4) **GROUP 2**	**Benefits:** NR **Harms:** Fat mass, glucose, insulin resistance, lipid profile, metabolic syndrome, waist circumference, WAE, weight change	First-time SGA medication use was associated with significant weight gain and variable metabolic changes for each medication.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	baseline anthropometric and biochemical assessments obtained within 7 day of antipsychotic medication initiation **Exclusion criteria:** (1) treatment with >1 antipsychotic agent, (2) active or past eating disorder, (3) biochemical evidence of thyroid dysfunction, (4) acute medical disorders, (5) pregnancy or breastfeeding, (6) wards of the state, (7) leaving the catchment area within 4 wk	**Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 52 **Age, mean±SD (range):** 14.7±3.2 (6.6–18.6) **Males %:** 64.4 **Caucasian %:** NR **Diagnostic breakdown (n):** disruptive or aggressive behavior spectrum disorder (9: ASD (2), ODD, CD, IED, ICD (7)), mood disorder spectrum (16: bipolar (9), MDD (8), NOS (4)), schizophrenia spectrum (14: psychosis NOS (5), schizophrenia/ schizoaffective disorder (9)) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 45 **Age, mean±SD (range):** 14±3.1 (6.1–19.4) **Males %:** 36.1 **Caucasian %:** NR **Diagnostic breakdown (n):** disruptive or aggressive behavior spectrum disorder (6: ASD (2), ODD, CD, IED, ICD (4)), mood disorder	**Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergics (0), antidepressants (10), anxiolytics or hypnotics (3), mood stabilizers (18), none (14), psychostimulants (4), psychotropics (1) **GROUP 3** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergics (2), antidepressants (10), anxiolytics or hypnotics (1), mood stabilizers (15), none (8), psychostimulants (4), psychotropics (1) **GROUP 4** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergics (18), antidepressants (43), anxiolytics or hypnotics (13), mood stabilizers (32), none (32), psychostimulants (26), psychotropics (9)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		spectrum (9: bipolar (10), MDD (8), NOS (6)), schizophrenia spectrum (6: psychosis NOS (4), schizophrenia/ schizoaffective disorder (2)) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 4** **N:** 168 **Age, mean±SD (range):** 13.6±4 (4.3–19.9) **Males %:** 62.2 **Caucasian %:** NR **Diagnostic breakdown (n):** disruptive or aggressive behavior spectrum disorder (34: ASD (13), ODD, CD, IED, ICD (21)), mood disorder spectrum (55: bipolar (17), MDD (19), NOS (19)), schizophrenia spectrum (46: psychosis NOS (33), schizophrenia/ schizoaffective disorder (13)) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR			
Crocq et al., 2007 [15] **Country:** France	**Recruitment dates:** NR **Study design:** NRCT	**Enrolled:** NR **Analyzed:** 52 **Completed:** NR	**Treatment duration:** 2.8 mo **Run-in phase:** No **Run-in phase duration:** NR	**Benefits:** NR **Harms:** BMI, weight	Significantly greater increases in weight and BMI were found for olanzapine SOT

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	(parallel)	**GROUP 1** **N:** NR	**Permitted drugs:** NR		compared to olanzapine ODT, as well as for olanzapine ODT compared to risperidone.
Condition category: Schizophrenia and related **Funding:** NR **Risk of bias:** NA (subjective), High (objective)	**Setting:** Inpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) hospitalized adolescents with schizophreniform disorder **Exclusion criteria:** NR	**Age, mean±SD (range):** 16.5±1.7 **Males %:** 31.3 **Caucasian %:** all **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR **GROUP 2** **N:** NR **Age, mean±SD (range):** 17±1.3 **Males %:** 60 **Caucasian %:** all **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR **GROUP 3** **N:** NR **Age, mean±SD (range):** 15.2±1.4 **Males %:** 57.7 **Caucasian %:** all **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR	**Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine (oral disintegrating tablet) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 16.6±4.4 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine (standard oral tablet) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 18±4.2 **Concurrent treatments:** NR **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2. 8±1.2 **Concurrent treatments:** NR		
Cuerda et al., 2011 [105] **Country:** Spain **Condition category:** Mixed conditions **Funding:** Non-	**Recruitment dates:** Feb 2005-Sept 2007 **Study design:** Prospective **Setting:** NR **Diagnostic criteria:** DSM-IV	**Enrolled:** 61 **Analyzed:** 46 **Completed:** 16 **GROUP 1** **N:** 18 **Age, mean±SD (range):** 16.1±1.9 yr **Males %:** 83.3 **Caucasian %:** 72.2	**Treatment duration:** 1 yr **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone	**Benefits:** NR **Harms:** Weight, BMI, lipid values, glucose, insulin, prolactin	Hypometabolism may explain weight gain in patients taking SGAs. Lifestyle recommendations involving reduced calorie intake and increased physical activity should be

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
industry **Newcastle-Ottawa Scale:** 6/8 stars	**Inclusion criteria:** (1) 11-18 yr, (2) mental disorder requiring treatment with antipsychotics, (3) antipsychotic naïve patients or quasi-naïve (<72hr of exposure to antipsychotics), (4) written informed consent signed by parents or legal representatives and patients after the syudy was explained **Exclusion criteria:** (1) Concomitant use of medications that can influence body weight (corticosterioids, valproic acid or lithium), (2) presence of diabetes mellitus and severe dyslipidemia, (3) if a second antipsychotic was prescribed, (4) if treatment was changed or withdrawn during follow up, (5) if adherence was poor	**Diagnostic breakdown (n):** BP (1), brief psychosis/schizophria disorder (4), conduct disorder (3), depression with psychotic symptoms (2), OCD (0), psychosis NOS (6), schizophrenia (2), scholar phobia (0), depression (0), intellectual disability (0), personality disorder (0) **Treatment naïve (n):** 10 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 12 **Age, mean±SD (range):** 16.1±1.3 yr **Males %:** 66.7 **Caucasian %:** 91.7 **Diagnostic breakdown (n):** BP (4), brief psychosis/schizophria disorder (2), conduct disorder (1), depression with psychotic symptoms (0), OCD (1), psychosis NOS (2), schizophrenia (1), scholar phobia (1), depression (0), intellectual disability (0), personality disorder (0) **Treatment naïve (n):** 5 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 3** **Drug name:** Quetiapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		prescribed in all patients starting these treatments.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		GROUP 3 **N:** 16 **Age, mean±SD (range):** 16.6±0.7 yr **Males %:** 62.5 **Caucasian %:** 81.3 **Diagnostic breakdown (n):** BP (2), brief psychosis/schizophria disorder (4), conduct disorder (0), depression with psychotic symptoms (1), OCD (2), psychosis NOS (3), schizophrenia (1), scholar phobia (0), depression (1), intellectual disability (1), personality disorder (1) **Treatment naïve (n):** 5 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR			
de Haan et al., 2003 [16] **Country:** Netherlands **Condition category:** Schizophrenia and related **Funding:** Government **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 17–28 yr, (2) DSM-IV criteria for schizophrenia, (3) admitted to the Adolescent Clinic	**Enrolled:** 24 **Analyzed:** 19 **Completed:** 20 **GROUP 1** **N:** 12 **Age, mean±SD (range):** 21.0±2.8 (17–26) **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 9 **Comorbidities:** MR (0) **GROUP 2** **N:** 12	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk **Permitted drugs:** oxazepam **Prohibited drugs:** antidepressants, antipsychotics, mood stabilizers **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.5 **Concurrent treatments:** oxazepam (6)	**Benefits:** CGI-I, PANSS, health related quality of life (Subjective Well-Being Under Neuroleptics scale), medication adherence **Harms:** BAS, SAS, akathisia, parkinsonism	Olanzapine showed no superior subjective response over haloperidol in patients with recent-onset schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	Exclusion criteria: (1) neurological or endocrine disease, (2) MR, (3) use of adjunctive medications such as mood stabilizers or antidepressants, (4) history of treatment with clozapine, (5) history of unresponsiveness to haloperidol or olanzapine, (6) intramuscular antipsychotic treatment within the last yr	**Age, mean±SD (range):** 21±2.3 (17–25) **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 11 **Comorbidities:** MR (0)	**GROUP 2** **Drug name:** Olanzapine **Dosing variability: f**ixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.5 **Concurrent treatments:** oxazepam (5)		
DelBello et al., 2009 [19] **Country:** USA **Condition category:** Bipolar (depressive) **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Mar 2006 to June 2007 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV-TR, WASH-U-KSADS **Inclusion criteria:** (1) 12–18 yr, (2) dx of bipolar I disorder, depressive episode, (3) screening and baseline CDRS-R score ≥40 **Exclusion criteria:** (1) substance use disorder (other than nicotine)	**Enrolled:** 32 **Analyzed:** 32 **Completed:** 20 **GROUP 1** **N:** 17 **Age, mean±SD (range):** 16.0±2 **Males %:** 29 **Caucasian %:** 82 **Treatment naïve (n):** 12 **Inpatients (n):** 7 **First episode psychosis (n):** NR **Comorbidities:** ADHD (2), anxiety disorder (5), DBD (6), psychosis (2) **GROUP 2** **N:** 15 **Age, mean±SD (range):** 15±2 **Males %:** 33 **Caucasian %:** 80	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** NR **Permitted drugs:** lorazepam (max 4 mg/day days 1–7, 2 mg/day days 8–14) **Prohibited drugs:** antidepressants (<3 day), anticonvulsants (<3 day), antipsychotics or atomoxetine (<3 day), fluoxetine (<4 wk), psychostimulant (<48 hr) **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 600 **Daily dose (mg/day), mean±SD (range):** 403±133 (300–600) **Concurrent treatments:** lorazepam (0) **GROUP 2**	**Benefits:** CDRS, CGI-BP, HAM-A, YMRS, response (response, remission, suicide attempt) **Harms:** Blood pressure, BMI, diabetes, EPS, glucose, LFT, lipid profile, mania, prolactin, pulse, SAE, sedation, tachycardia, WAE, weight change, EPS	Quetiapine monotherapy was no more effective in treating depression in adolescents with bipolar disorder than treatment with placebo.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	within the previous 3 mo, (2) unstable medical or neurological illness, (3) history of intolerance or nonresponse to quetiapine monotherapy, (4) treatment with an antidepressant (other than fluoxetine), an anticonvulsant (other than valproate or carbamazepine), antipsychotic or atomoxetine within 3 day, fluoxetine within 4 wk, or a psychostimulant within 48 hr of baseline, (5) risk of suicide	**Treatment naïve (n):** 11 **Inpatients (n):** 8 **First episode psychosis (n):** NR **Comorbidities:** ADHD (2), anxiety disorder (3), DBD (2), psychosis (1)	**Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** 600 **Daily dose (mg/day), mean±SD (range):** 413±151 (300–600) **Concurrent treatments:** lorazepam (0)		
DelBello et al., 2008 [18] **Country:** USA **Condition category:** Bipolar & schizophrenia-related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV-TR **Inclusion criteria:** (1) 10–17 yr, (2) bipolar I disorder (YMRS score ≥17), (3) schizophrenia-related disorder (BPRS-A score ≥35, with a score of ≥4 on at least one of: unusual thought	**Enrolled:** 63 **Analyzed:** 63 **Completed:** 38 **GROUP 1** **N:** 23 **Age, mean±SD (range):** 13.2 (bipolar), 14.4 (schiz) **Males %:** 52 **Caucasian %:** NR **Diagnostic breakdown (n):** bipolar I (15), schizophrenia or schizoaffective disorder (8) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0), SA (0)	**Treatment duration:** 3 wk **Run-in phase:** Yes **Run-in phase duration:** 24 hr **Permitted drugs:** benztropine and/or propranolol, lorazepam or similar benzodiazepine **Prohibited drugs:** antidepressants, mood stabilizers, stimulants **GROUP 1** **Drug name:** Ziprasidone (low) **Dosing variability:** fixed **Target dose (mg/day):** 80 **Daily dose (mg/day), mean±SD (range):** (20–80) **Concurrent treatments:** benztropine (3) **GROUP 2**	**Benefits:** YMRS, BPRS, CGI-S **Harms:** Akathisia, behavioral issues, dystonia, ECG changes, EPS (AIMS, SAS, BAS), fatigue, glucose, lipid profile, prolactin, SAE, sedation, somnolence, WAE, weight change	Neither low- nor high- dose ziprasidone was associated with unexpected tolerability findings, and a starting dose of 20 mg/d, titrated to 80–160 mg/d over 1–2 wk was optimal.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	content, hallucinations, suspiciousness, or conceptual disorganization), (4) BMI between 5th and 95th percentile **Exclusion criteria:** (1) currently on stable well-tolerated treatment, (2) substance-induced psychotic disorder, (3) treatment with clozapine within 12 wk, (4) depot antipsychotic within 4 wk, (5) MAO-I within 2 wk, (6) imminent risk of suicide or homicide, (7) MR, (8) autism or other PDD, (8) pregnancy, breastfeeding, or unwillingness to use birth control, (9) serious unstable medical or neurologic illness, (10) any screening laboratory value that deviated significantly from reference range, (11) clinically significant hypokalemia or hypomagnesemia, (12) history of cardiac arryhthmias, conduction abnormalities, QTc prolongation, or genetic risk for prolonged QT	**GROUP 2** **N:** 40 **Age, mean±SD (range):** 13.8 (bipolar), 14.7 (schiz) **Males %:** 75 **Caucasian %:** NR **Diagnostic breakdown (n):** biploar I (31), schizophrenia or schizoaffective disorder (9) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0), SA (0)	**Drug name:** Ziprasidone (high) **Dosing variability:** fixed **Target dose (mg/day):** 160 **Daily dose (mg/day), mean±SD (range):** (40–160) **Concurrent treatments:** benztropine (4)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	syndrome, (13) psychoactive substance or alcohol abuse or dependence (other than nicotine or caffeine) within 1 mo (DSM-IV-TR)				
DelBello et al., 2002 [17] **Country:** USA **Condition category:** Bipolar (manic, mixed) **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** May 2000 to May 2001 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, WASH-U-KSADS **Inclusion criteria:** (1) 12–18 yr, (2) DSM-IV criteria for bipolar I disorder, currently mixed or manic, (3) YMRS score ≥20 **Exclusion criteria:** (1) pregnant, (2) manic symptoms secondary to substance intoxication or withdrawal, (3) substance use disorder within the past 3 mo, (4) MR, (5) unstable medical or neurological disorder, cataracts, or clinically significant baseline laboratory abnormalities, (6) history of	**Enrolled:** 30 **Analyzed:** 30 **Completed:** 22 **GROUP 1** **N:** 15 **Age, mean±SD (range):** 14.1±2 **Males %:** 53 **Caucasian %:** 80 **Diagnostic breakdown (n):** mixed episode (10) **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR **Comorbidities:** ADHD (10), psychosis (7) **GROUP 2** **N:** 15 **Age, mean±SD (range):** 14.5±2 **Males %:** 53 **Caucasian %:** 87 **Diagnostic breakdown (n):** mixed episode (13) **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR **Comorbidities:** ADHD (8), psychosis (7)	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** NR **Permitted drugs:** lorazepam (≤2 mg/day for first 14 day) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 450 **Daily dose (mg/day), mean±SD (range):** 432 **Concurrent treatments:** lorazepam (2) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** lorazepam (3)	**Benefits:** YMRS, Medication adherence, response **Harms:** Blood cells, blood pressure, ECG changes, prolactin, SAE, sedation, thyroid function, WAE, weight change, EPS (AIMS, BAS, SAS)	Quetiapine in combination with divalproate is more effective for the treatment of adolescent bipolar mania than divalproate with placebo.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	hypersensitivity, intolerance, or nonresponse to quetiapine or valproate, (7) treated with a depot neuroleptic within 3 mo, an antidepressant or antipsychotic within 1 wk (fluoxetine within 1 mo), a benzodiazepine or psychostimulant within 72 hr, or other antiepileptic agents within 72 hr				
Ebert et al., 2014 [106] **Country:** Israel **Condition category:** Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 5/8 stars	**Recruitment dates:** 2011-2012 **Study design:** Retrospective **Setting:** Inpatient **Diagnostic criteria:** NR **Inclusion criteria:** NR **Exclusion criteria:** NR	**Enrolled:** 72 **Analyzed:** 56 **Completed:** 56 **GROUP 1** **N:** 32 **Age, mean±SD (range):** 9.6±1.6 yr **Males %:** 91.7 **Caucasian %:** NR **Diagnostic breakdown (n):** See below **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** Anemia (1), ichthyosis (1) **GROUP 2** **N:** 24 **Age, mean±SD (range):** 9.3±1.8 yr **Males %:** 87.5 **Caucasian %:** NR **Diagnostic breakdown**	**Treatment duration:** mean 10-17 wk for groups **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Atypical antipsychotic treatment **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Control **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** NR **Harms:** Weight, BMI, lipid values, fasting glucose, transaminases (ALT, AST)	Weight and metabolic monitoring is essential as supposedly weight neutral antipsychotics (aripiprazole, ziprasidone, and amisulpride) may not be weight neutral in youth, especially in antipsychotic-naïve youth.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		(n): See below **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** Epilepsy (1), central precocious puberty (1) **Overall diagnostic breakdown (n):** Psychotic spectrum disorder (15), BP (4), DBD (29), ADHD (26), anxiety spectrum disorder (8), depression disorder (13), PDD (5), MR (3), OCD (1), adjustment disorder (2), ED (1), tic disorder (2)			
Findling et al., 2015b [30] **Country:** USA **Condition category:** Bipolar I (manic, mixed) **Funding:** Industry **Risk of bias:** Low (subjective), Low (objective)	**Recruitment dates:** Jul 2011 to Sept 2013 **Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) Dx of bipolar I disorder acute manic or mixed episode with DSM-IV-TR and K-SADS-PL, (2) YMRS score ≥20, (3) CGI-BP overall ≥4, (4) guardian living with the child who was able to ensure adherence	**Enrolled:** 404 **Analyzed:** 403 **Completed:** 350 **GROUP 1** **N:** 104 **Age, mean±SD (range):** 13.7±2.1 yr **Males %:** 50 **Caucasian %:** 72.1 **Diagnostic breakdown (n):** Manic (40), mixed (64) **Treatment naïve (n):** 38 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (62) **GROUP 2** **N:** 99	**Treatment duration:** 3 wk **Run-in phase:** Yes **Run-in phase duration:** 2-14 d **Permitted drugs:** Chronic use medication such as hormonal birth control, common over-the-counter medications (i.e., nutritional supplements, pain relievers, antacids); short-acting benzodiazepines (e.g., lorazepam and equivalents) as needed or diazepam; use of psychostimulants and other ADHD medications, medications to treat extrapyramidal symptoms (EPS; e.g., anticholinergics, short-acting benzodiazepines). . **Prohibited drugs:** Antipsychotics, depot neuroleptics, benzodiazepines [except for	**Benefits:** YMRS, CGI-BP-S, CGAS, CDRS-R, response, suicidal ideation, attempted suicide, psychiatric disorders, worsening of mania, medication adherence **Harms:** Mortality, somnolence, EPS (ESRS), akathisia, dystonia, weight gain, BMI, ECG, lipid values, fasting insulin, glucose, prolactin, nausea, orthostatic hypotension related adverse events	All asenapine doses versus placebo were superior based on change in YMRS at day 21. Asenapin was generally well tolerated in patients aged 10 to 17years with bipolar I disorder in manic or mixed states. Increases in weight and fasting insulin were associated with asenapine.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	with treatment, outpatient visits, and study protocol **Exclusion criteria:** (1) Pervasive development disorder, schizophrenia, schizoaffective disorder, posttraumatic stress disorder, obsessive-compulsive disorder, psychosis due to a medical condition, (2) prohibited concomitant medication, (3) uncontrolled, unstable, clinically significant medical condition	**Age, mean±SD (range):** 13.8±2.0 yr **Males %:** 43.4 **Caucasian %:** 67.7 **Diagnostic breakdown (n):** Manic (43), mixed (56) **Treatment naïve (n):** 24 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (45) **GROUP 3** **N:** 99 **Age, mean±SD (range):** 13.9±2.1 yr **Males %:** 58.6 **Caucasian %:** 65.7 **Diagnostic breakdown (n):** Manic (44), mixed (55) **Treatment naïve (n):** 32 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (61) **GROUP 4** **N:** 101 **Age, mean±SD (range):** 13.7±2.0 yr **Males %:** 37.6 **Caucasian %:** 67.3 **Diagnostic breakdown (n):** Manic (44), mixed (57) **Treatment naïve (n):** 43 **Inpatients (n):** 0 **First episode psychosis**	lorazepam, up to 4 mg daily, or otherwise the equivalent dose of short-acting benzodiazepines that were clinically indicated], antidepressants, mood stabilizers, miscellaneous psychotropics, and herbal drugs/dietary supplements for depression, anxiety, or insomnia) **GROUP 1** **Drug name:** Asenapine (2.5 mg) **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Stimulant (29) **GROUP 2** **Drug name:** Asenapine (5 mg) **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Stimulant (22) **GROUP 3** **Drug name:** Asenapine (10 mg) **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Stimulant (25) **GROUP 4** **Drug name:** Placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		(n): NR **Comorbidities:** ADHD (52)	**(range):** NR **Concurrent treatments:** Stimulant (20)		
Findling et al., 2015a [29] **Country:** USA (19 centers), international (60 centers) **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** Low (subjective), Low (objective)	**Recruitment dates:** April 2011 to April 2013 **Study design:** RCT (parallel) **Setting:** in and outpatient (mostly outpatient) **Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) 12-17 yrs, (2) schizophrenia, (3) PANSS total ≥80, CGI-S ≥4, and ≥4 on 2+ items on PANSS positive subscale **Exclusion criteria:** (1) treatment with clozapine, (2) comorbid Axis I condition responsible for current symptoms, (3) uncontrolled or unstable clinically significant general medical condition (eg, renal, endocrine, hepatic, respiratory, cardiovascular, hematologic,	**Enrolled:** 306 **Analyzed:** **Completed:** **GROUP 1** **N:** 106 **Age, mean±SD (range):** 15.4±1.5 **Males %: 63** **Caucasian %: 52** **Treatment naïve (n):** 33 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 98 **Age, mean±SD (range):** 15.2±1.5 **Males %:** 63 **Caucasian %: 55** **Treatment naïve (n):** 28 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 3** **N:** 102 **Age, mean±SD (range):** 15.4±1.4 **Males %:** 61 **Caucasian %:** 56 **Treatment naïve (n):** 36 **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 3-10 day **Permitted drugs:** short-acting benzodiazepines (lorazepam 4mg or equivalent; or diazepam £ 40 mg/day in countries with no approved short-acting benzodiazepines) for relief of transient symptoms of agitation, anxiety, insomnia, restlessness, or akathisia, and anticholinergics or short-acting benzodiazepines to treat EPS symptoms **Prohibited drugs:** antipsychotics; depot neuroleptics; antidepressants; benzodiazepines; mood stabilizers; stimulants and other ADHD medications; miscellaneous psychotropics; and herbal drugs/dietary supplements for depression, anxiety, and insomnia **GROUP 1** **Drug name:** Asenapine **Dosing variability:** fixed **Target dose (mg/day):** 5mg bid (2.5mg bid days 1-4; 5mg bid onwards) **Daily dose (mg/day), mean±SD (range):** **Concurrent treatments:** anti-EPS (12) **GROUP 2**	**Benefits:** PANSS, CGI-S, response **Harms:** EPS, somnolence, weight, BMI, lipids, glucose, insulin, prolactin, metabolic syndrome, mortality, suicide, any AE, serious AEs,	Although improvements in PANSS total score at day 56 of the acute phase were numerically greater for both asenapine 2.5 and 5mg b.i.d. than for placebo and were maintained in the OLE, the primary end-point did not achieve statistical significance in the acute phase.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	immunologic, or cerebrovascular disease, or malignancy) or an abnormal laboratory, vital sign, physical examination, or ECG findings), (4) uncontrolled diabetes or significant abnormal blood glucose, (5) suicide ideation over past 2 mo or behavior over past 6 mo, (6) beginning psychotherapy after trial initiation, (7) MR or SUD		**Drug name:** Asenapine **Dosing variability:** fixed **Target dose (mg/day):** 2.5mg bid **Daily dose (mg/day), mean±SD (range):** **Concurrent treatments:** anti-EPS (2) **GROUP 3** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NA **Daily dose (mg/day), mean±SD (range):** NA **Concurrent treatments:** anti-EPS (3)		
Findling et al., 2014b [28] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Mar 2011 to Jun 2012 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, ADI-R **Inclusion criteria:** (1) Male of female, (2) 6-17 yr, (3) meets DSM-IV-TR criteria for autistic disorder, confirmed by ADI-R and also had serious behavioural problems (ie, tantrums, aggression, self-injurious behaviour, or a combination of these), (4) ABC-I score	**Enrolled:** 85 **Analyzed:** 82 **Completed:** 41 **GROUP 1** **N:** 41 **Age, mean±SD (range):** 10.1±2.8 yr **Males %:** 73.2 **Caucasian %:** 75.6 **Diagnostic breakdown (n):** ASD (all) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 44 **Age, mean±SD (range):** 10.8±2.8 yr **Males %:** 86.4 **Caucasian %:** 63.6	**Treatment duration:** 16 wk **Run–in phase:** No **Run–in phase duration:** NA **Permitted drugs:** Diphenhydramine for sleep or serious behaviour problems, nonbenzodiazepine sleep aids (eg, zolpidem, zaleplon, zopiclone, eszopiclone) for insomnia, and melatonin for insomnia (not permitted to start or make changes to their sleep aid treatment durng phase 2) **Prohibited drugs:** Antipsychotics other than aripiprazole, antidepressants, benzodiazepines, stimulants, α-agonists, mood stabilizers, and atomoxetine **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** NR	**Benefits:** ABC-I, CGI-I, CGI-S, PedsQL, CGSQ, relapse, medication adherence **Harms:** Constipation, EPS (AIMS, BAS, SAS), akathisia, mortality, lipid profile, glucose, prolactin, sexual maturation	The safety and efficacy of aripiprazole and risperidone were comparable. The choice between these two medications should be on the basis of clinical equipoise considering the patient's preference and clinical profile.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	≥18, CGI-S score ≥4 at screening and baseline **Exclusion criteria:** (1) Treatment resistant to antipsychotic medication (lack of therapeutic response to 2 different antipsychotics with treatment of ≥3 wks each) or previously treated with an adequate dose of aripiprazole for ≥3 wks without a clinically meaningful response, (2) lifetime dx of bipolar disorder, psychosis, or shizophrenia or a current dx of major depressive disorder, pervasive developmental disorder-NOS, Asperger syndrome, Rett syndrome, childhood disintegrativedisorder, or fragile X syndrome, (3) hisory of neoroleptic malignant syndrome, history of seizures within the past year or of severe head trauma or stroke, a history or current unstable medical conditions, a history of low white blood cell count, or abnormal	**Diagnostic breakdown (n):** ASD (all) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**Daily dose (mg/day), mean±SD (range):** 9.0±4.5 [initial of phase 2], 9.7±4.9 [end dose at wk 16] **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 9.5±4.2 [initial of phase 2], 10.0±4.2 [end dose at wk 16] **Concurrent treatments:** NR		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	laboratory test results that were medically significant				
Findling et al., 2014a [27] **Country:** USA **Condition category:** Bipolar I,II (depressed) **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Jan 2009 to Nov 2010 **Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) Boys and girls, (2) 10–17 yr, (3) dx of bipolar I or bipolar II disorder, current or most recent episode depressed; duration ≥4 wk (DSM-IV-TR, confirmed by K-SADS-PL), (4) CDRS-R total score ≥45 (5) YMRS score ≤16 at screening and baseline, (6) Patients with rapid cycling, defined as ≥4 episodes/yr, and a secondary diagnosis of comorbid ADHD, were permitted **Exclusion criteria:** (1) current DSM-IV-TR Axis I disorder other than bipolar I or bipolar II depression or ADHD, (2) YMRS total score >16 at screening or	**Enrolled:** 193 **Analyzed:** 192 **Completed:** 144 **GROUP 1** **N:** 92 **Age, mean±SD (range):** 13.9±2.2 yr **Males %:** 48.9 **Caucasian %:** 70.7 **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (38) **GROUP 2** **N:** 100 **Age, mean±SD (range):** 14.0±2.1 yr **Males %:** 52.0 **Caucasian %:** 60.0 **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (46)	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 7-28 d **Permitted drugs:** Psychostimulants (centrally acting sympathomimetics, including amphetamine, dexamphetamine, methylphenidate) in patients with ADHD if prescribed dose stable ≥30 d prior to baseline. No dose adjustment allowed during study. Nonpsychoactive medications considered necessary for patient's well being **Prohibited drugs:** Adjunctive medications for EPS **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 300 **Daily dose (mg/day), mean±SD (range):** mean modal dose, 204.9mg/day **Concurrent treatments: Total** psychostimulants (20), other (35) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** psychostimulants (27), other (37)	**Benefits:** CDRS-R, CGI-BP-S, CGI-BP-C, response, remission, suicidal ideation, aggression, medication adherence, health care system utilization, exacerbation of bipolar I and depressive symptoms, mania (YMRS) **Harms:** somnolence, fatigue, nausea, agitation, EPS (AIMS, BAS, SAS), ECG, transaminase, fasting glucose, dyslipidemia, TSH, throxine, prolactin, weight gain, blood pressure, pulse	QuetiapineXR(150 to 300 mg/day) did not demonstrate efficacy relative to placebo in this large, 8 week, randomized study of youth with bipolar I or II depression. These observations contrast with the efficacy of quetiapine XR demonstrated in adults with bipolar de-pression or MDD. Consistent with studies in adults, quetiapine XR at the dose range investigated was generally safe and well tolerated in these pediatric patients.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	baseline, (3) criteria for bipolar disorder, most recent episode mania/ hypomania/ mixed, as determined by the K-SADS-PL, (4) history of nonresponse to adequate treatment with more than two antidepressants during the current episode or of treatment noncompliance, (5) use of valproate within 3 days, an antipsychotic, other mood stabilizer, antidepressant, an-xiolytic, hypnotic, or other psychoactive drug within 7 days, or fluoxetine within 28 days before baseline, (6) a requirement for psychotherapy during the study period, unless initiated at least 3 mo before, (7) being a current serious suicidal or homicidal risk, CDRS-R intem 13 score ≥3 at enrollment or randomization, (8) clinically significant deviations from normal reference ranges of clinical laboratory parameters				
Findling, 2013a [25] **Country:** Canada,	**Recruitment dates:** Apr 2006 to Mar 2009 (terminated	**Enrolled:** 284 **Analyzed:** 283 **Completed:** NR	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 14 days	**Benefits:** BPRS-A, PANSS, CGI-S, CGI-I, CGAS, health	Oral ziprasidone failed to demonstrate

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Columbia, Costa Rica, Germany, India, Malaysia, Mexico, Peru, Russia, Singapore, Sweden, Ukraine, USA **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	prematurely) **Study design:** RCT (parallel) **Setting:** In- and outpatient **Diagnostic criteria:** DSM-IV, KID-SCID **Inclusion criteria:** (1) 13–17 yr, (2) schizophrenia (DSM-IV, confirmed by KID-SCID), (3) current symptoms present for ≥7 days prior to screening, (4) first episode psychosis allowed, (5) BPRS Anchored score ≥35 and a score ≥4 on ≥1 of the following items: unusual thought content, hallucinations, suspiciousness, or conceptual disorganization at screening and baseline visits, (6) BMI Z-score 1.65–2.00, inclusive **Exclusion criteria:** substance-induced psychotic disorder, a DSM-IV–defined psychoactive substance or alcohol abuse/ dependence in the preceding month, a rating of 7 on the	**GROUP 1** **N:** 193 **Age, mean±SD (range):** 15.3 **Males %:** 56 **Caucasian %:** 60 **Diagnostic breakdown (n):** paranoid type (127) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 90 **Age, mean±SD (range):** 15.4 **Males %:** 69 **Caucasian %:** 67 **Diagnostic breakdown (n):** paranoid type (57) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Permitted drugs:** lorazepam or diazepam, diphenhydramine, zolpidem, benzotropine, anticholinergics, propranolol **Prohibited drugs:** antipsychotic, mood stabilizers, stimulants, antidepressants, anti-emetics, several antihypertensives **GROUP 1** **Drug name:** Ziprasidone **Dosing variability:** variable **Target dose (mg/day):** 40–80 (<45 kg), 120–160 (≥45 kg) **Daily dose (mg/day), mean±SD (range):** 67.8 (<45kg), 129.3 (≥45kg) **Concurrent treatments:** 51% **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** 60–80 (<45 kg), 120–160 (≥45 kg) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** 39%	related quality of life (Child Health Questionnaire), suicide, depression **Harms:** Serious AE, SARS, BARS, AIMS, akathisia, behavioral issues, dermatologic AE, ECG changes, QTcF, fatigue, EPS, liver function, mortality, SAE, somnolence, total AE, WAE, weight change, blood pressure, pulse rate, lipids	superiority over placebo in adolescents with schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	single suicidal ideation item on the Child Depression Rating Scale-Revised (CDRS-R), significant MR, or ASD, or if they were judged by investigator to be at imminent risk of suicide or homicide. Other general criteria for exclusion included serious/ unstable medical conditions, history of significant cardiovascular disease, cardiac arrhythmias, conduction abnormalities, QT prolongation, clinically significant ECG abnormalities, and Fridericia's corrected QT (QTcF) interval ‡460ms at screening or baseline.				
Findling et al., 2013b [26] **Country:** USA **Condition category:** Bipolar I (manic, mixed) **Funding:** Industry, non-industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Jan 2006 to Jul 2007 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV, K-SADS **Inclusion criteria:** (1) 10–17 yr, (2) primary dx of bipolar I disorder (DSM-IV, confirmed by K-SADS), (3) current	**Enrolled:** 238 **Analyzed:** 229 **Completed:** 148 **GROUP 1** **N:** 149 **Age, mean±SD (range):** 13.2±2.4 yr (males), 14.1±2.0 yr (females) **Males %:** 56.4 **Caucasian %:** 81.2 **Diagnostic breakdown (n):** Single manic (14), manic (45), mixed (90) **Treatment naïve (n):** 149 **Inpatients (n):** NR	**Treatment duration:** 4 wk **Run-in phase:** Yes **Run-in phase duration:** 1–10 day **Permitted drugs:** Lorazepam or a comparable benzodiazepine as required ≤2mg/day. Not to be administered ≤6 hours prior to clinical assessments. **Prohibited drugs:** Other antipsychotics, lithium and anticonvulsants, stimulants, antidepressants, antiemetics (dopamine antagonists such as prochlorperazine and	**Benefits:** YMRS, CGI-S, CGI-I, CGAS, CDRS-R, suicidal ideation, aggression **Harms:** dystonia, akathisia, dyskinesia, EPS (AIMS, BAS, SARS), somnolence, weight change, nausea, prolonged QTc interval, increased hepatic enzymes, extrapyramidal disorder, self-	Ziprasidone at doses of 40–160 mg/day is an effective and generally well-tolerated treatment for children and adolescents 10–17 years of age with a manic or mixed episode associated with bipolar I disorder.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	symptoms present for ≥7 day prior to screening, (4) YMRS score >17 at screening and baseline visits, (5) BMI Z-score 1.65–2.00, inclusive **Exclusion criteria:** (1) current or prior treatment with ziprasidone, (2) known allergy to ziprasidone, (3) serious suicidal risk, (4) a Fridericia-corrected QT interval (QTcF) ≥460 ms, (5) DSM-IV substance abuse/dependence (except nicotine or caffeine) in the preceding month, and (5) numerous other standard medical and psychiatric exclusion criteria	**First episode psychosis (n):** NR **Comorbidities:** ADHD (66) **GROUP 2** **N:** 88 **Age, mean±SD (range):** 13.5±2.0 yr (males), 14.0±1.9 yr (females) **Males %:** 53.4 **Caucasian %:** 81.8 **Diagnostic breakdown (n):** Single manic (8), manic (23), mixed (57) **Treatment naïve (n):** 88 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (36)	metoclopramide), treatment with clozapine ≤12 weeks, treatment with a depot antipsychotic ≤4 weeks, treatment with a monoamine oxidase inhibitor ≤2 weeks, or treatment with an investigational agent ≤4 weeks of baseline. **GROUP 1** **Drug name:** Ziprasidone **Dosing variability:** variable **Target dose (mg/day):** 60–80 (<45 kg), 120–160 (≥45 kg) **Daily dose (mg/day), mean±SD (range):** 69.2(<45 kg), 118.8 (≥45 kg) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** 60–80 (<45 kg), 120–160 (>45 kg) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	injurious behavior, prolactin, lipid profile, fatigue	
Findling et al., 2012b [24] **Country:** USA **Condition category:** Bipolar I,II, NOS, cyclothymia **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** May 2004 to Nov 2008 **Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 4-9 yr, (2) met DSM-IV criteria for bipolar I, II, NOS or cyclothymia,	**Enrolled:** 60 **Analyzed:** 60 **Completed:** 6 **GROUP 1** **N:** 30 **Age, mean±SD (range):** 7.1±1.5 yr **Males %:** 63 **Caucasian %:** NR **Diagnostic breakdown (n):** bipolar disorder NOS (17), bipolar I disorder (10), cyclothymia (3) **Treatment naïve (n):** 0	**Treatment duration:** 72 wk (after 16 wk of open label study: phase I) **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** Continued coadministration of stable dose of psychostimulants from phase 1 **Prohibited drugs:** Other psychotropic medications **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** variable	**Benefits:** YMRS, CDRS-R, CGAS, CGI-S, time to discontinuation of medication **Harms:** weight, EPS (AIMS, BAS, SAS), lipid values, prolactin, fasting glucose, blood pressure, pulse, mortality	Even though aripiprazole maintenance was statistically superior to placebo maintenance, alone it was not sufficient to keep most youth stable for extended periods of time.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	(3) screened by highly trained raters completing K-SADS-PL, (4) patients must have adhered to study-related procedures during phase 1, (5) tolerated a minimum daily aripiprazole dose of 0.05 mg/kg/day for at least 6 wk, (6) met a priori response criteria **Exclusion criteria:** (1) evidence of pervasive developmental disorder, Rett's syndrome, mental retardation, (2) a general medical or neurologic condition for which treatment with aripiprazole would be contraindicated	**Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** DBD (6), ADHD (27), any anxiety disorder (0) **GROUP 2** **N:** 30 **Age, mean±SD (range):** 6.7±1.7 yr **Males %:** 77 **Caucasian %:** NR **Diagnostic breakdown (n):** bipolar disorder NOS (16), bipolar I disorder (11), cyclothymia (3) **Treatment naïve (n):** 0 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** DBD (5), ADHD (27), any anxiety disorder (2)	**Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0.23±0.07 [at randomization], 0.26±0.11 [end of study] **Concurrent treatments:** Stimulants (12) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0.22±0.07 [at randomization], 0.22±0.07 [end of study] **Concurrent treatments:** Stimulants (13)		
Findling et al., 2012a [23] **Country:** Asia, Central and Eastern Europe, South Africa, United States **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High	**Recruitment dates:** Oct 2004 to June 2007 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) inpatients and outpatients, (2) 13–17 yr, (3) schizophrenia (DSM-IV, confirmed by	**Enrolled:** 222 **Analyzed:** 220 **Completed:** 220 **GROUP 1** **N:** 73 **Age, mean±SD (range):** 15.5±1.3 (13–17) **Males %:** 58.9 **Caucasian %:** 61.6 **Diagnostic breakdown (n):** disorganized (6), paranoid (53), residual (0), undifferentiated (14) **Treatment naïve (n):** NR **Inpatients (n):** 31 **First episode psychosis**	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 1 day–4 wk **Permitted drugs:** antidepressants, lorazepam **Prohibited drugs:** antipsychotics, psychostimulants, CYP3A4 inhibitors/inducres, monoamine oxidase inhibitors, atomoxetine, prophylactic benztropine **GROUP 1** **Drug name:** Quetiapine (low) **Dosing variability:** fixed	**Benefits:** BSPSd, CGAS, CGI-I, CGI-S, PANSS, Caregiver Strain Questionnaire, response, agitation, aggression, medication adherence **Harms:** Withdrawals from AEs, serious AEs, SAS, BARS, AIMS-7, behavioral issues, ECG changes, EPS, fatigue, lipid profile, glucose	Quetiapine at a dose of 400 mg/day and 800 mg/day provided significant improvements in symptoms associated with schizophrenia in adolescent patients, including the primary efficacy measure of PANSS total score change. Quetiapine was generally well tolerated with a profile broadly similar to that

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(subjective), High (objective)	K-SADS-PL), (4) PANSS total score ≥60 and a score ≥4 on delusions, conceptual disorganization, or hallucinations **Exclusion criteria:** DSM-IV Axis I diagnosis of BD, schizophreniform disorder, schizoaffective disorder, psychotic disorder NOS, or acute PTSD, psychosis judged to be a direct consequence of a medical condition or its treatment, history of suicide attempts or homicidal risk or behavior within the past 3 months, DSM-IV-defined SUD, laboratory test results outside the normal reference range, hospital admission for diabetes or diabetes-related illness in the past 3 months, renal, cardiovascular, hepatic, hematologic, endocrinologic, ophthalmologic, or other medical conditions that were unstable or may have affected or been affected by the study medication, pregnancy	**(n):** NR **GROUP 2** **N:** 74 **Age, mean±SD (range):** 15.5±1.3 (13–17) **Males %:** 59.5 **Caucasian %:** 59.5 **Diagnostic breakdown (n):** disorganized (5), paranoid (50), residual (1), undifferentiated (18) **Treatment naïve (n):** NR **Inpatients (n):** 28 **First episode psychosis (n):** NR **GROUP 3** **N:** 73 **Age, mean±SD (range):** 15.3±1.4 (13–17) **Males %:** 57.5 **Caucasian %:** 63 **Diagnostic breakdown (n):** disorganized (5), paranoid (52), residual (0), undifferentiated (16) **Treatment naïve (n):** NR **Inpatients (n):** 36 **First episode psychosis (n):** NR	**Target dose (mg/day):** 400 **Daily dose (mg/day), mean±SD (range):** 400 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Quetiapine (high) **Dosing variability:** fixed **Target dose (mg/day):** 800 **Daily dose (mg/day), mean±SD (range):** 800 **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability: fixed** **Target dose (mg/day):** NA **Daily dose (mg/day), mean±SD (range):** NA **Concurrent treatments:** NR	concentration, mortality, prolactin, pulse, SAE, sedation, somnolence, tachycardia, thyroid, liver and renal function, total AE, WAE, weight change	reported previously in adult and adolescent populations.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	and lactation.				
Findling et al., 2009 [22] **Country:** USA **Condition category:** Bipolar (manic, mixed) **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** Mar 2005 to Feb 2007 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 10–17 yr, (2) bipolar I disorder with current manic or mixed episodes, with or without psychotic features (DSM-IV), (3) YMRS score ≥20 **Exclusion criteria:** (1) bipolar II disorder, bipolar disorder NOS, PDD, schizophrenia, schizoaffective disorder, psychosis due to other medical condition or concomitant medication, (2) MR, (3) DSM-IV substance or alcohol use disorder, (4) positive drug screen for cocaine or other substances of abuse during screening, (5) sexual activity without contraceptive use, pregnancy, lactation,	**Enrolled:** 296 **Analyzed:** 294 **Completed:** 237 **GROUP 1** **N:** 98 **Age, mean±SD (range):** 13.7±2.2 **Males %:** 53.1 **Caucasian %:** 66.3 **Diagnostic breakdown (n):** manic (41), mixed (43), unknown (14) **Treatment naïve (n):** 41 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (48), DBD (28) **GROUP 2** **N:** 99 **Age, mean±SD (range):** 13.3±2.3 **Males %:** 51.5 **Caucasian %:** 68.7 **Diagnostic breakdown (n):** manic (40), mixed (39), unknown (20) **Treatment naïve (n):** 49 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (50), DBD (34) **GROUP 3** **N:** 99 **Age, mean±SD (range):** 13.3±2.1 **Males %:** 56.6	**Treatment duration:** 4 wk **Run-in phase:** Yes **Run-in phase duration:** 3 day **Permitted drugs:** anticholinergics, benzodiazepines **Prohibited drugs:** Mood stabilizers, other psychotropics **GROUP 1** **Drug name:** Aripiprazole (low) **Dosing variability:** variable **Target dose (mg/day):** 10 **Daily dose (mg/day), mean±SD (range):** (2–10) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Aripiprazole (high) **Dosing variability:** variable **Target dose (mg/day):** 30 **Daily dose (mg/day), mean±SD (range):** (2–30) **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** CDRS, CGAS, CGI-BP, YMRS, health related quality of life (P-QLES-Q), response, suicide **Harms:** Akathisia, BMI, dyskinesia, dystonia, ECG changes, EPS (AIMS, BAS, SAS), fatigue, glucose, lipid profile, mortality, parkinsonism, prolactin, SAE, somnolence, total AE, WAE, weight change	Aripiprazole in daily doses of 10 mg or 30 mg was effective and generally well-tolerated for acute treatment of pediatric subjects with bipolar I mania or mixed episodes.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	(6) other medical reason determined by investigator, (7) noncompliance with medication washout, (8) inability to swallow tablets whole, (9) history of antipsychotic treatment resistance or NMS, (10) suicide attempt in the past 6 mo, score >3 on the Suicidal Ideation item of the CDRS-R, or determined by the investigator to be at risk of suicide, (11) clinically important laboratory test results, vital signs, or ECG, and unstable medical conditions, diabetes melitus, epilepsy, (12) prior participation in an aripiprazole study, allergy or hypersensitivity to aripiprazole, or participation in an investigational drug trial in the past month	**Caucasian %:** 60.6 **Diagnostic breakdown (n):** manic (38), mixed (43), unknown (18) **Treatment naïve (n):** 36 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (55), DBD (31)			
Findling et al., 2008a [21] **Country:** Asia, Caribbean, Europe, South Africa, South America, USA **Condition category:**	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL	**Enrolled:** 302 **Analyzed:** 294 **Completed:** 258 **GROUP 1** **N:** 100 **Age, mean±SD (range):** 15.6±1.3 **Males %:** 45 **Caucasian %:** 54 **Diagnostic breakdown**	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** ≥3 day **Permitted drugs:** anticholinergics, benzodiazepines **Prohibited drugs:** antidepressants, atomoxetine, mood stabilizers, other psychotropics, stimulants	**Benefits:** CGAS, CGI-I, CGI-S, PANSS Health related quality of life (P-QLES-Q), response, suicide **Harms:** Akathisia, behavioral issues, BMI, dyskinesia, dystonia, ECG changes, EPS, EPS	Aripiprazole (10 or 30 mg/d) was well tolerated and was more effective than placebo in improving symptoms of schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Schizophrenia and related **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Inclusion criteria:** (1) 13–17 yr, (2) primary dx of schizophrenia (DSM-IV Axis I, confirmation with K-SADS-PL), (3) baseline PANSS ≥ 70 **Exclusion criteria:** (1) current psychiatric comorbidity requiring pharmacology, (2) evidence of suicide risk, (3) history, or current dx of schizoaffective disorder, MR, major depressive episodes, NMS, any neurologic disorder other than Tourette syndrome, severe head trauma, unstable medical condition, (4) resistant to antipsychotics according to trials of two different antipsychotics of adequate dose and duration, (5) pregnancy, breast-feeding, sexually active patients who refused abstinence or birth control, (6) positive screens for illegal drugs within 3 mo of baseline or during study, (7) hospitalized for acute schizophrenia within 4 wk of baseline	**(n):** For all: schizophrenia (1), BP (12), Tourette syndrome (5), ADHD/CD (1), OCD (1), PDD (1) **Treatment naïve (n):** 25 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 102 **Age, mean±SD (range):** 15.4±1.4 **Males %:** 63.7 **Caucasian %:** 60.8 **Diagnostic breakdown (n):** See group 1 **Treatment naïve (n):** 27 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 100 **Age, mean±SD (range):** 15.4±1.4 **Males %:** 61 **Caucasian %:** 64 **Diagnostic breakdown (n):** See group 1 **Treatment naïve (n):** 27 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**GROUP 1** **Drug name:** Aripiprazole (low) **Dosing variability:** variable **Target dose (mg/day):** 10 **Daily dose (mg/day), mean±SD (range):** 9.8 (2–10) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Aripiprazole (high) **Dosing variability:** variable **Target dose (mg/day):** 30 **Daily dose (mg/day), mean±SD (range):** 28.9 (2–30) **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	(SAS), glucose, lipid profile, mortality, prolactin, parkinsonism, SAE, somnolence, WAE, weight change	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Findling et al., 2008b [107] **Country:** USA **Condition category:** Mixed conditions **Funding:** Industry **Newcastle-Ottawa Scale:** 5/8 stars	**Recruitment dates:** NR **Study design:** OLE **Setting:** NR **Diagnostic criteria:** **Inclusion criteria:** (1) 13-17 yr; (2) dx of schizophrenia or bipolar **Exclusion criteria:** (1) sexually active pt not practicing double-barrier birth control; (2) pregnancy/lactation; (3) current/hx of drug or alcohol abuse; (4) mental retardation; (5) neurologic disorders (except PDD, ADHD, or TS); (6) use of antipsychotic or psychotropic medication, CYP2D6 and CYP3A4 inhibitors, or CYP3A4 inducers <14 d; (7) participation in another clinical study <1 mo (or 6 mo if the study involved psychotropic medication); (8) major surgery or blood transfusion/donation <30 d; (9) abnormal physical, ECG, or clinical laboratory examinations; (10)	**Enrolled:** 24 **Analyzed:** 21 (safety); 20 (efficacy) **Completed:** 17 **All** **N:** 21 **Age, mean±SD (range):** 12.2±2.1 **Males %:** 66.7 **Caucasian %:** 76.1 **Diagnostic breakdown (n):** schizophrenia (1); bipolar disorder (12); TS (5); ADHD and CD (1); OCD (1); PDD (1) **Treatment naïve (n):** **Inpatients (n):** **First episode psychosis (n):** **Comorbidities:** GROUP **1** **N:** 8 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 7 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR	**Treatment duration:** 26 d **Run-in phase:** NR **Run-in phase duration:** NR **Concurrent treatments:** Analgesics (paracetamol; Vicks formula 44M) (5); anesthetics (lidocaine) (4); antiasthmatics (budesonide; salbutamol; other) (2); antiparkinsonism drugs (benztropine; benztropine mesylate) (2); anti-inflammatories or antirheumatics (naproxen sodium; ibuprofen) (2); antipruritics including antihistamines (diphenhydramine hydrochloride) (1); antacids (dihydroxyaluminum sodium carbonate) (1); antibacterials (minocycline) (1); sex hormones (progestogens and estrogens) (1); antidiabetics (insulin lispro; insulin and analog) (1); nasal preparations (Dimetapp) (1) **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** 2 mg/d (starting dose), then increased to target dose every 2 d for 8 d **Target dose (mg/day):** 20 mg/d **Daily dose (mg/day), mean±SD (range):** NR **GROUP 2** **Drug name:** Aripiprazole **Dosing variability:** 2 mg/d (starting dose), then increased to target dose every 2 d for 10 d **Target dose (mg/day):** 25 mg/d **Daily dose (mg/day), mean±SD (range):** NR	**Benefits:** CGI-I/S **Harms:** AEs, physical examination, vital signs, ECGs, clinical laboratory parameters, and EPS (SAS, AIMS, BARS)	Aripiprazole at doses of 20, 25, and 30 mg/d seemed generally safe and well tolerated in children and adolescents with psychiatric disorders. All 3 planned aripiprazole dose levels were judged to be tolerated.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	significant risk of suicide or homicide	**Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 6 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**GROUP 3** **Drug name:** Aripiprazole **Dosing variability:** 2 mg/d (starting dose), then increased to target dose every 2 d for 12 d **Target dose (mg/day):** 30 mg/d **Daily dose (mg/day), mean±SD (range):** NR		
Findling et al., 2000 [20] **Country:** USA **Condition category:** ADHD **Funding:** Industry, Foundation **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, K-SADS, clinical interview **Inclusion criteria:** (1) outpatients with primary dx of CD, (2) 5–15 yr, (3) at least moderate degree of overall symptom severity (CGI), (4) Aggression subscale	**Enrolled:** 20 **Analyzed:** 20 **Completed:** 9 **GROUP 1** **N:** 10 **Age, mean±SD (range):** 10.7±3.4 yr **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown:** CD with aggression (10) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 10 **Age, mean±SD (range):**	**Treatment duration:** 10 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** benztropine **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0±0.004 (0.8–1.5) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**	**Benefits:** CBCL, CGI-I, CGI-S, Conner PRS, RAAPP Medication adherence **Harms:** Dermatologic AE, EPS, liver function, sedation, total AE, WAE, AIMS, SAS	Low doses of risperidone may be effective in the treatment of youths with CD and are not associated with extrapyramidal symptoms.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	T-score ≥2 SD above the mean for age- and gender-matched peers (CBCL) **Exclusion criteria:** (1) moderate/severe ADHD, (2) significant psychiatric comorbidity (including mood disorder), (3) treatment with a psychotropic medication within 1 wk of initiating double-blind therapy, (4) positive toxicology screen, (5) suicide attempt within the past mo, (6) organic mental syndromes, (7) pregnant or nursing females and females of childbearing potential who were not using an acceptable method of birth control, (8) a standard score equivalent to <70 on the Peabody Picture Vocabulary Test-Revised	8.2±1.9 yr **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown:** CD with aggression (10) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR	**(range):** (0.3–3) **Concurrent treatments:** NR		
Findling et al., 2015 [31] **Country:** USA **Condition category:** Mixed conditions **Funding:** Industry	**Recruitment dates:** June 2012 to May 2013 **Study design:** Prospective cohort **Setting:** Outpatient **Diagnostic criteria:** NR	**Enrolled:** 105 **Analyzed:** 102 **Completed:** 90 **GROUP 1** **N:** 20 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** see below **Diagnostic breakdown**	**Treatment duration:** 3 wk **Run-in phase:** Yes **Run-in phase duration:** 2 days **Permitted drugs:** NR . **Prohibited drugs:** Inhibitors or inducers of CYP3A4 or any medication that could have significantly prolonged the QT/QTc interval	**Benefits:** NR **Harms:** AE, laboratory tests, weight	Adverse events were qualitiatively similar to those reported in adults. Discontinuation due to adverse events were dose related with lurasidone doses <120 mg/d being better tolerated than higher

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Risk of bias: NA (subjective), High (objective)	**Inclusion criteria:** male or female outpatients between the ages of 6 and 17 years with a diagnosis of schizophrenia spectrum disorder, bipolar spectrum disorder, autism spectrum disorder, attention deficit/hyperactivity disorder with aggressive behavior (ie comorbid conduct disorder or other disruptive behavior), or Tourette's syndrome. **Exclusion criteria:** clinically significant alcohol or drug abuse/dependence within the previous 6 months or a positive breath alcohol test or urine screen for drugs of abuse at screening; severe cognitive impairment; clinical instability or an imminent risk for suicide or injury to self, others, or property; a clinically significant major medical condition or abnormal laboratory value or vital sign measurement; and/or pregnant, breastfeeding, or	**(n):** see below **Treatment naïve (n):** NR **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 25 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** see below **Diagnostic breakdown (n):** see below **Treatment naïve (n):** NR **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 19 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** see below **Diagnostic breakdown (n):** see below **Treatment naïve (n):** NR **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 4** **N:** 25 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** see below **Diagnostic breakdown**	**GROUP 1** **Drug name:** Lurasidone **Dosing variability:** fixed **Target dose (mg/day):** 20 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Lurasidone **Dosing variability:** fixed **Target dose (mg/day):** 40 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 3** **Drug name:** Lurasidone **Dosing variability:** fixed **Target dose (mg/day):** 80 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 4** **Drug name:** Lurasidone **Dosing variability:** fixed **Target dose (mg/day):** 120 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 5** **Drug name:** Lurasidone **Dosing variability:** fixed **Target dose (mg/day):** 160 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		doses, especially in younger children. The PK and tolerability results suggest that the dose range of 20 to 80 mg/d provides adequate serum concentrations, but with improved tolerability compared with higher doses.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	sexual activity without the use of medically approved birth control.	**(n):** See below **Treatment naïve (n):** NR **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 5** **N:** 16 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** see below **Diagnostic breakdown (n):** see below **Treatment naïve (n):** NR **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **All Groups** **N:** 102 **Age, mean±SD (range):** 12.7 **Males %:** 65 **Caucasian %:** 78 **Diagnostic breakdown (n):** ADHD (78), BP (19), Schizophrenia (5), Tourette's (2), ASD (1). **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR			
Fleischhaker et al., 2006 [108] **Country:** Germany	**Recruitment dates:** NR **Study design:** Prospective cohort	**Enrolled:** 51 **Analyzed:** 51 **Completed:** 51 **GROUP 1**	**Treatment duration:** 7.4 wk (mean) **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR	**Benefits:** NR **Harms:** Akathisia, behavioral issues, bradycardia, blood	Olanzapine caused significant weight gain in children and adolescents, potentially

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Condition category: Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 3/8 stars	**Setting:** Inpatient **Diagnostic criteria:** ICD-10 **Inclusion criteria:** NR **Exclusion criteria:** NR	**N:** 16 **Age, mean±SD (range):** 17.2±1.8 (14.4–21.3) **Males %:** 68.9 **Caucasian %:** NR **Treatment naïve (n):** NR **Diagnostic breakdown (n):** Schizophrenia (31), PDD (5), AN (1), Cannabis-related disorders (4), AD (3), DBD (3), OCD (2), TD (1) for all groups **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR **GROUP 2** **N:** 16 **Age, mean±SD (range):** 15.8±1.4 (12.8–17.8) **Males %:** 56.3 **Caucasian %:** NR **Treatment naïve (n):** NR **Diagnostic breakdown (n):** See group 1 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR **GROUP 3** **N:** 19 **Age, mean±SD (range):** 15.6±2.6 (9.7–19) **Males %:** 68.4 **Caucasian %:** NR **Treatment naïve (n):** NR **Diagnostic breakdown (n):** See group 1 **Inpatients (n):** NR	**Prohibited drugs:** NR **GROUP 1** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 321.9±156.5 (125–600) **Concurrent treatments:** all groups: amisulpride, biperiden, chlorprotixene, fluboxamine, fluoxetine, haloperidol, imipramine, lactulose, levomepromazine, lorazepam, metixene, metoclopramid, metoprolol, paroxetine, perazine, pimozide, pipamperone, pirenzepine, promethazine **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 16.6±7.1 (7.5–30) **Concurrent treatments:** see group 1 **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.9±1.7 (1–6) **Concurrent treatments:** see group 1	cells, blood pressure, BMI, constipation, dystonia, dermatologic AE, ECG changes, liver function tachycardia, tardive dyskinesia, weight change	influencing medication compliance and health risk. Clozapine and risperidone were associated with less marked changes in weight, but gains were still more pronounced than those seen in adults.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		First episode psychosis (n): NR **Comorbidities (n):** NR			
Fraguas et al., 2008 [109] **Country:** Spain **Condition category:** Mixed conditions **Funding:** Government, Foundation, Other NR **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Mar 2005 to Oct 2006 **Study design:** Prospective cohort **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) new prescription of olanzapine, risperidone of quetiapine within 30 days, (2) no history of prior lifetime antipsychotic treatment **Exclusion criteria:** (1) receiving >1 antipsychotic or needed another antipychotic during followup	**Enrolled:** 92 **Analyzed:** 66 **Completed:** 66 **GROUP 1** **N:** 25 **Age, mean±SD (range):** 15.9±1.5 (12–17) **Males %:** 65 **Caucasian %:** 90 **Diagnostic breakdown (n):** bipolar (2), depression (1), eating disorders (3), PDD (1), psychosis NOS (5), schizophrenia (3), schizophreniform (5) **Treatment naïve (n):** 9 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** psychosis (14), SA (12) **GROUP 2** **N:** 29 **Age, mean±SD (range):** 16.3±1.3 (13–18) **Males %:** 58.3 **Caucasian %:** 95.8 **Diagnostic breakdown (n):** ADHD (0), bipolar (5), CD (1), depression (2), eating disorders (2), OCD (2), PDD (0), psychosis NOS (4), schizophrenia (4), schizophreniform (4) **Treatment naïve (n):** 8	**Treatment duration:** 6 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** anticholinergics, antidepressants, benzodiazepines **Prohibited drugs:** antipsychotics **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 9.8±5.6 **Concurrent treatments:** antidepressants (3), benzodiazepines (14), biperiden (4) **GROUP 2** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 390.8±321.2 **Concurrent treatments:** antidepressants (9), benzodiazepines (12), biperiden (4) **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.5±3.1 **Concurrent treatments:** antidepressants (9), benzodiazepines (11), biperiden (6)	**Benefits:** NR **Harms:** Blood pressure, BMI, glucose, lipid profile, thyroid function, weight change	Metabolic and hormonal adverse events should be carefully monitored when prescribing SGAs.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Inpatients (n): NR **First episode psychosis (n):** NR **Comorbidities:** psychosis (14), SA (18) **GROUP 3** **N:** 38 **Age, mean±SD (range):** 13.4±4 (4–17) **Males %:** 77.3 **Caucasian %:** 81.8 **Diagnostic breakdown (n):** ADHD (4), bipolar (1), CD (7), depression (1), eating disorders (1), OCD (2), PDD (1), psychosis NOS (3), schizophrenia (2), schizophreniform (0) **Treatment naïve (n):** 8 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** psychosis (6), SA (13)			
Friedlander et al., 2001 [110] **Country:** Canada **Condition category:** Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 4/8 stars	**Recruitment dates:** NR **Study design:** Retrospective cohort **Setting:** NR **Diagnostic criteria:** DSM-IV, author consensus on chart review **Inclusion criteria:** (1) 13–24 yr, (2) developmental disabilities and	**Enrolled:** 44 **Analyzed:** 44 **Completed:** NR **GROUP 1** **N:** 14 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Diagnostic breakdown (n):** Developmental disabilities (all), Schizophrenia/other psychotic (15), PDD (16), mood disorders (11),	**Treatment duration:** 6 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** all groups: anticholinergics (5), anticonvulsants (12), anxiolytics (9), clonidine (1),	**Benefits:** NR **Harms:** Akathisia, dyskinesia, dystonia, EPS, prolactin-related AE, sedation, total AE, WAE, weight change	Adolescents and young adults with developmental disabilities treated with SGAs for multiple conditions were particularly sensitive to neuroleptic induced movement disorders.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	complex psychiatric problems, (3) active files with the mental health sites in the Greater Vancouver area **Exclusion criteria:** NR	ADHD/DBD (6), Tic-related disorders (3), AD (2), Impulse control disorder (1) for all patients **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** Addison's disease (1), hypothyroidism (4), MR (borderline (1), mild (17), moderate (15), severe (9)), Neurodevelopmental syndrome (15), Seizure disorder (9) **GROUP 2** **N:** 40 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Diagnostic breakdown (n):** see group 1 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	mood stabilizers (21), non-SSRI antidepressants (8), SSRIs (9), stimulants (2), tetrabenazine (2) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** see group 1		
Germano et al., 2014 [111] **Country:** Italy **Condition category:** Mixed **Funding:** NR **Newcastle-Ottawa Scale:** 5/8 stars	**Recruitment dates:** Jan 2009-Dec 2012 **Study design:** Prospective **Setting:** NR **Diagnostic criteria:** NR **Inclusion criteria:** (1)	**Enrolled:** 65 **Analyzed:** 60 **Completed:** 60 **GROUP 1** **N:** 29 **Age, mean±SD (range):** See below **Males %:** See below **Caucasian %:** NR **Diagnostic breakdown (n):** See below	**Treatment duration:** 2 mo **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** NR **Target dose (mg/day):** NR	**Benefits:** NR **Harms:** ECG parameters	Treatment with risperidone and aripiprazole in children and adolescents with psychiatric disorders is not associated with clinically relevant modifications of the QT interval on ECG. Aripiprazole use can

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	child and adolescent pateints, (2) ≤17 yr **Exclusion criteria:** NR	**Treatment naïve (n):** See below **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 31 **Age, mean±SD (range):** See below **Males %:** See below **Caucasian %:** NR **Diagnostic breakdown (n):** See below **Treatment naïve (n):** See below **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **Overall age, mean±SD (range):** 10.2±2.6 yr **Overall Males %:** 91.6 **Overall diagnostic breakdown (n):** PDD (22), ODD (12), ADHD (21), MR with psychotic disorder (11), Tourette syndrome and other tic disorders (9) **Overall treatment naïve (n):** 22	**Daily dose (mg/day), mean±SD (range):** 7.4±3.1 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.5±1.0 **Concurrent treatments:** NR		be associated to a slight increase of QTd value only, along with risperidone use that can be associated to an increase of both QTc and QTd values. Therefore, monitoring of both QTc and QTd parameters during AP treatment in pediatric Population should be considered.
Ghanizadeh et al., 2014a [32] **Country:** Iran **Condition category:** ASD	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient	**Enrolled:** 59 **Analyzed:** 59 **Completed:** 50 **GROUP 1** **N:** 29 **Age, mean±SD (range):**	**Treatment duration:** 2 mo **Run–in phase:** NR **Run–in phase duration:** NR **Permitted drugs:** Any (with no marked change in dose allowed during the trial and during 2 wk	**Benefits:** ABC, CGI-S, CGI-I, discontinuation due to lack of efficacy **Harms:** Fatigue, constipation,	The safety and efficacy of aripiprazole and risperidone were comparable. The choice between these two

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		9.6±3.3 yr	before the trial onset)	dystonia, dyskinesia, nausea, seizure, agitation, weight	medications should be on the basis of clinical equipoise considering the patient's preference and clinical profile.
Funding: Industry/ non-industry **Risk of bias:** Medium (subjective), Medium (objective)	**Diagnostic criteria:** DSM-IV-TR, ADI-R **Inclusion criteria:** (1) Meets DSM-IV-TR and ADI-R criteria,(2) has a clinicain rating of at least moderate severity of autistic symptoms (CGI severity score of C4) **Exclusion criteria:** (1) Children with a history of medically significant or uncontrolled medical conditions such as hypothyroidism, diabetes or cancer, (2) history of drug or alcohol abuse, (3) could not have received risperidone or aripiprazole during at least 2 wk before entering this trial, (4) could not have received additional behavioural interventions above the regular educational programming during this trial	**Males %:** 86.2 **Caucasian %:** NR **Diagnostic breakdown (n):** see below **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 30 **Age, mean±SD (range):** 9.5±4.6 yr **Males %:** 76.7 **Caucasian %:** NR **Diagnostic breakdown (n):** see below **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR **Overall diagnostic breakdown (n):** Autism (38), Asperger disorder (8), PDD-NOS (9), childhood disruptive behavior disorder (1)	**Prohibited drugs:** Antipsychotics **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** 10 (<40 kg), 15 (>40kg) **Daily dose (mg/day), mean±SD (range):** 5.5 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** 2 (<40 kg), 3 (>40kg) **Daily dose (mg/day), mean±SD (range):** 1.12 **Concurrent treatments:** NR		
Ghanizadeh et al., 2014b [33] **Country:** Iran **Condition category:** Tic disorders	**Recruitment Dates:** NR **Study design:** RCT (parallel) **Diagnostic criteria:** DSM-IV-TR	**Enrolled:** 60 **Analyzed:** 60 **Completed:** 35 **GROUP 1:** **N:**31 **Age, mean±SD (range):**11.12±3.3 yr	**Treatment duration:** 8 weeks **Run-in phase:** Unclear **Run-in phase duration:** 2 weeks **Permitted drugs:** Nortriptyline, Biperiden, Citalopram, Clonidine, Fluvoxamine, Propanolol, Methylphenidate	**Benefits:** YGTSS, PedsQL, ADHD RS-IV **Harms:** Neuromotor effects, metabolic effects, somnolence, exercise intollerance	Aripiprazole decreased tic scores as much as risperidone in children and adolescents with tic disorder. However this should not be

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Males %: 82.8			interpreted as arapiprazole and risperidone being equivalent. Efficacsy and safety of other doses of these medications are recommended. Long term use of the medications needs further studies.
Funding: Non-industry **Risk of Bias:** High (subjective), High (objective)	**Setting:** outpatient **Inclusion criteria:** 6-18 yr, primary diagnosis of tic disorder **Exclusion criteria:** Current mood disorders, psychotic symptoms, PDD, substance-related disorder, severe uncontrolled medical conditions such as neurological problems, diabetes, epilepsy, Huntington's chorea, reported cardiac problems, or clinically estimated mental retardation	**Caucasian %:**NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR **GROUP 2:** **N:** 29 **Age, mean±SD (range):** 10.22±2.3 yr **Males %:** 86.2 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR	**Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** Variable **Target dose (mg/day):** 15mg/day **Daily dose (mg/day), mean±SD (range):** 4.0±2.4 mg/day **Concurrent treatments:** Nortripyline (1), Citalopram (1), Clonidine + fluvoxamine + propranolol (1), Methylphenidate (2) **GROUP 2:** **Drug name:** Risperidone **Dosing variability:** Variable **Target dose (mg/day):** 3mg/day **Daily dose (mg/day), mean±SD (range):** 0.6±0.2 mg/day **Concurrent treatments:** Nortriptyline (1), Biperiden (1), Clonidine (1), Methylphenidate (2)		
Gilbert et al., 2004 [34] **Country:** USA **Condition category:** Tic disorders **Funding:** Industry, Government **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (crossover) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, clinical assessment **Inclusion criteria:** (1) 7–17 yr, (2) Tourette syndrome or chronic motor tic disorder, (3) CGI tic severity score >4 after 2 wk with no	**Enrolled:** 19 **Analyzed:** NR **Completed:** 13 **GROUP 1** **N:** 19 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (16), Chronic tic disorder (3) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Pimozide **Dosing variability:** variable **Target dose (mg/day):** 4 **Daily dose (mg/day), mean±SD (range):** 2.4 (1–4) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone	**Benefits:** CGI-I, TSSR, YGTSS **Harms:** EPS (ESRS), ECG changes, weight changes	Risperidone was superior to pimozide for tic suppression but it induced weight gain.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	medication **Exclusion criteria:** (1) transient tic disorder, anorexia nervosa, PDD, substance/alcohol abuse or dependence within the past yr, or any psychotic disorder, (2) serious or unstable medical illness or abnormal ECG or laboratory findings, (3) sexually active females of childbearing potential not using contraceptives	**Comorbidities:** ADHD (7), **c**onduct disorder (1), learning disorder (3), OCD (2), oppositional defiant disorder (2) **GROUP 2** **N:** 19 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** See group 1 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	**Dosing variability:** variable **Target dose (mg/day):** 4 **Daily dose (mg/day), mean±SD (range):** 2.5 (1–4) **Concurrent treatments:** NR		
Gothelf et al., 2002 [112] **Country:** Israel **Condition category:** Schizophrenia and related **Funding:** Government **Newcastle-Ottawa Scale:** 3/8 stars	**Recruitment dates:** NR **Study design:** Prospective cohort (NR) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV, K-SADS **Inclusion criteria:** NR **Exclusion criteria:** (1) taking medications that affect weight	**Enrolled:** 20 **Analyzed:** NR **Completed:** NR **GROUP 1** **N:** 10 **Age, mean±SD (range):** 17.0±1.6 **Males %:** 100 **Caucasian %:** NR **Treatment naïve (n):** ND **Inpatients (n):** all **First episode psychosis (n):** NR **GROUP 2** **N:** 10 **Age, mean±SD (range):** 17±1.6 **Males %:** 100 **Caucasian %:** NR **Treatment naïve (n):** 1	**Treatment duration:** 4 wk **Run-in phase:** Yes **Run-in phase duration:** 17.6 day (mean) **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 6.5±3.4 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**	**Benefits:** NR **Harms:** Abdominal circumference, BMI, weight	Body mass index significantly increased in adolescent male inpatients treated with olanzapine but not in those given haloperidol.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Inpatients (n): all **First episode psychosis (n):** NR	**(range):** 14±4.1 **Concurrent treatments:** NR		
Gulisano et al., 2011 [35] **Country:** Italy **Condition category:** Tic disorders **Funding:** Non-industry **Risk of Bias:** NA (subjective), Medium (objective)	**Recruitment Dates:** NR **Study design:** NRCT (parallel) **Diagnostic criteria:** DSM-IV-TR **Setting:** NR **Inclusion criteria:** With TS, 6-18 yr, normal IQ **Exclusion criteria:** Patient or family history of cardiovascular symptoms	**Enrolled:** 50 **Analyzed:** 50 **Completed:** 50 **GROUP 1:** **N:**25 **Age, mean±SD (range):** 13.1±2.3 yr **Males %:** 84 **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (25) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (15), OCD (11) **GROUP 2:** **N:**25 **Age, mean±SD (range):** 9.1±2.9 yr **Males %:** 88 **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (25) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (13), OCD (13)	**Treatment duration:** 24 mo **Run-in phase:** Yes **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Arapiprazole **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 5.3±2.4 **Concurrent treatments:** NR **GROUP 2:** **Drug name:** Pimozide **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 4.4±1.5 **Concurrent treatments:** NR	**Benefits:** NR **Harms:** HR, BP, QTc	At equivalent doses, arapiprazole is characterized by a safer cardiovascular profile than pimozide, being associated with a lower frequency of QTc prolongation.
Haas et al., 2009b [37]	**Recruitment dates:** Aug 2004 to Dec 2005	**Enrolled:** 160 **Analyzed:** 158 **Completed:** 125	**Treatment duration:** 6 wk **Run–in phase:** Yes **Run–in phase duration:** ≤5 day	**Benefits:** CGAS, CGI-I, CGI-S, PANSS, response,	Risperidone treatment for 6-weeks was safe and

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Country: India, Russia, Ukraine, USA **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Study design:** RCT (parallel) **Setting:** Inpatient/outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) male and females, (2) aged 13 to 17 years, (3) DSM-IV diagnosis of schizophrenia, (4) inpatients or outpatients, experiencing an acute episode with a total PANSS score of 60 to 120 (inclusive), (5) no serious illnesses or neurological conditions, (6) females were required to a have negative pregnancy test and to be using an acceptable form of contraception. **Exclusion criteria:** (1) DSM-IV criteria for dissociative disorder, bipolar disorder, MDD, schizoaffective disorder, schizophreniform disorder, autistic disorder, or primary substance-induced psychotic disorder at screening, (2) MR (IQ<70), (3) substance	**GROUP 1** **N:** 55 **Age, mean±SD (range):** 15.7±1.3 **Males %:** 55 **Caucasian %:** 60 **Diagnostic breakdown (n):** Paranoid (38), Undifferentiated (8), Disorganized (8), Catatonic (1), Residual (0) **Treatment naïve (n):** NR **Inpatients (n):** 30 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 51 **Age, mean±SD (range):** 15.7±1.3 **Males %:** 73 **Caucasian %:** 47 **Diagnostic breakdown (n):** Paranoid (34), Undifferentiated (13), Disorganized (4), Catatonic (0), Residual (0) **Treatment naïve (n):** NR **Inpatients (n):** 25 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 54 **Age, mean±SD (range):** 15.5±1.4 **Males %:** 65 **Caucasian %: 50** **Diagnostic breakdown**	**Permitted drugs:** Propanolol was allowed for treatment-emergent akathisia. Antiparkinsonian medications could be initiated for treatment-emergent EPS. Use of all rescue medications was kept to a minimum, and the permitted doses of certain medications progressively decreased over the course of the study. Subjects could receive limited supportive psychotherapy or psychoeducation. **Prohibited drugs:** antidepressants, mood stabilizers, anticonvulsants, psychostimulants, direct dopamine agonists, cholinesterase inhibitors, herbal or over-the-counter medications with psychotripic properties, or antipsychotic other than the study medication. Drugs with sedative, hypnotic, or anxiolytic properties were not allowed, with some exceptions. Subjects were not permitted to receive insight-oriented or cognitive-behavioral psychotherapy. **GROUP 1** **Drug name:** Risperidone (low) **Dosing variability:** fixed **Target dose (mg/day):** 1–3 **Daily dose (mg/day), mean±SD (range):** NR (1–3) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone (high) **Dosing variability:** fixed **Target dose (mg/day):** 4–6 **Daily dose (mg/day), mean±SD**	suicide **Harms:** SAS, BAS, AIMS, Behavioral issues, BMI, EPS, glucose-related AE, mortality, prolactin, prolactin-related AE, SAE, somnolence, tachycardia, tardive dyskinesia, total AE, WAE, weight change	effective at daily doses of 1–3 and 4–6 mg in adolescents experiencing acute exacerbations of schizophrenia

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	dependence diagnosed by DSM-IV criteria in 3 months preceding screening, (4) significant risk of suicide or violent behavior, (5) failed to respond to adequate treatment with >2 antipsychotic drugs during the current psychotic episode, (6) hypersensitivity or intolerance to risperidone, (7) history of neuroleptic malignant syndrome or any severe drug allergy,	**(n):** Paranoid (38), Undifferentiated (12), Disorganized (3), Catatonic (0), Residual (1) **Treatment naïve (n):** NR **Inpatients (n):** 23 **First episode psychosis (n):** NR **Comorbidities:** NR	**(range):** NR (4–6) **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Haas et al., 2009c[38] **Country:** USA **Condition category:** Bipolar (manic, mixed) **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Dec 2003 to Dec 2005 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 10–17 yr, (2) medically stable, (3) acute manic/mixed episode (K-SADS-PL), (4) total score ≥20 at screening and baseline on YMRS, (5) responsible caregiver **Exclusion criteria:** (1)	**Enrolled:** 170 **Analyzed:** 169 **Completed:** 137 **GROUP 1** **N:** 50 **Age, mean±SD (range):** NR (10–17) **Males %:** 56 **Caucasian %:** 70 **Diagnostic breakdown (n):** manic episode (20), mixed episode (30) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (25), DBD (27) **GROUP 2** **N:** 61 **Age, mean±SD (range):**	**Treatment duration:** 3 wk **Run-in phase:** Yes **Run-in phase duration:** ≤5 day **Permitted drugs:** medication for EPS; sedatives/hypnotics (run-in and wk 1 only) **Prohibited drugs:** anticonvulsants, antidepressants, antimanic medications, other antipsychotics (including herbal substances); methylphenidate/other medication for ADHD **GROUP 1** **Drug name:** Risperidone (low) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** (0.5–2.5) **Concurrent treatments:** NR	**Benefits:** BPRS, CGI-BP, YMRS, Medication adherence, response, suicide **Harms:** Behavioral issues, BMI, dermatologic AE, EPS (AIMS, BAS, SAS), fatigue, glucose, lipid profile, mortality, prolactin, prolactin-related AE, SAE, sedation, somnolence, tardive dyskinesia, total AE, WAE, weight change	A significant reduction in manic symptoms was seen in youth when treated with risperidone (0.5–2.5 mg/d or 3–6 mg/d) compared to placebo.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	known intellectual impairment	NR (10–17) **Males %:** 43 **Caucasian %:** 82 **Diagnostic breakdown (n):** manic episode (21), mixed episode (40) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (33), DBD (40) **GROUP 3** **N:** 58 **Age, mean±SD (range):** NR (10–17) **Males %:** 48 **Caucasian %:** 78 **Diagnostic breakdown (n):** manic episode (19), mixed episode (39) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (27), DBD (34)	**GROUP 2** **Drug name:** Risperidone (high) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3 (26%), 4 (19%), 5 (15%), 6 (41%) (3–6) **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Haas et al., 2009a[36] **Country:** Belgium, Bulgaria, Czech Republic, Estonia, Germany, Poland, Romania, USA **Condition category:** Schizophrenia and related	**Recruitment dates:** Apr 2001 to Mar 2006 **Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 13–17 yr, (2) schizophrenia, (3)	**Enrolled:** 257 **Analyzed:** 255 **Completed:** 172 **GROUP 1** **N:** 132 **Age, mean±SD (range):** 15.6±1.32 (13–17) **Males %:** 61 **Caucasian %:** 85 **Diagnostic breakdown (n):** catatonic (3), disorganized (6), paranoid (92), residual (7),	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** ≥7 day **Permitted drugs:** antiparkinsonian medications (first 3 wk), propranolol, rescue medications (diazepam, hydroxyzine, lorazepam, zolpidem, zopiclone) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone (low)	**Benefits:** CGI-I, CGI-S, PANSS, medication adherence, response, suicide **Harms:** SAS, BAS, AIMS, Akathisia, behavioral issues, dyskinesia, dystonia, ECG changes, EPS, glucose, mortality, prolactin, prolactin-related AE, SAE,	A greater improvement in total PANSS score was found with high dose risperidone than with low dose risperidone.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Funding: Industry **Risk of bias:** High (subjective), High (objective)	currently hospitalized for an acute episode (PANSS total score 60–120) **Exclusion criteria:** (1) significant risk for suicidal or violent behavior, (2) history of NMS, tardative dyskinesia, or a known or suspected seizure disorder, (3) BMI <5th percentile or >95th percentile, (4) schizophreniform disorder	undifferentiated (24) **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR **GROUP 2** **N:** 125 **Age, mean±SD (range):** 15.6±1.25 (13–17) **Males %:** 52 **Caucasian %:** 85 **Diagnostic breakdown (n):** catatonic (4), disorganized (13), paranoid (83), residual (0), undifferentiated (25) **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR	**Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0.4 (0.2–0.6) **Concurrent treatments:** all groups: rescue medication (133) **GROUP 2** **Drug name:** Risperidone (high) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 4 (1.5–6) **Concurrent treatments:** see group 1	somnolence, tachycardia, total AE, WAE, weight change	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Hagman et al., 2011 [39] **Country:** USA **Condition category:** Eating disorders **Funding:** Non-industry **ROB:** Medium (subjective), Medium (objective)	**Recruitment dates:** Aug 2004 to Sept 2008 **Study design:** RCT (parallel) **Setting:** Inpatient/outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) primary diagnosis of AN, (2) female gender, (3) 12-21 yr, (4) active in a level of care in the eating disorders program **Exclusion criteria:** (1) previous enrollment in study, (2) allergic reaction to risperidone or another atypical neuroleptic drug, (3) a positive pregnancy test result, (4) taking a psychotropic medication other than an antidepressant, (5) active hepatic or renal disease, (6) male gender, (7) wards of court	**Enrolled:** 41 **Analyzed:** 40 **Completed:** 40 **GROUP 1** **N:** 18 **Age, mean±SD (range):** 16.2±(2.5) yr **Males %:** 0 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** depression (NR), obsessive-compulsive disorder (NR), anxiety disorder (NR), bulimia nervosa (NR) **GROUP 2** **N:** 22 **Age, mean±SD (range):** 15.8±(2.3) yr **Males %:** 0 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	**Treatment duration:** 9 wk **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** antidepressants (if on stable dose for >1 wk before entering the study, no dose adjustments during study), multivitamin, zinc, medications for other medical conditions (constipation, asthma, gastritis) **Prohibited drugs:** new psychotropic medications **GROUP 1** **Drug name:** Risperidone **Dosing variability:** flexible **Target dose (mg/day):** 4.0 **Daily dose (mg/day), mean±SD (range):** 2.5±1.2 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** flexible **Target dose (mg/day):** 4.0 **Daily dose (mg/day), mean±SD (range):** 3.0±1.0 **Concurrent treatments:** NR	**Benefits:** EDI-2 DT, EDI-2 BD, ADJ-current, ADJ-desired, CAPT, MASC, suicidal ideation, anxiety, depression **Harms:** EPS (AIMS, SAS), glucose, lipid profile, prolactin, fatigue, blood pressure	This exploratory pilot study does not demonstrate a clear benefit from the addition of risperidone in the course of active treatment and weight restoration in adolescents with AN.
Hellings et al., 2006 [40] **Country:** USA	**Recruitment dates:** NR **Study design:** RCT	**Enrolled:** 26 **Analyzed:** 26 **Completed:** NR	**Treatment duration:** 5.1 mo (6 wk at each dose) **Run-in phase:** Yes	**Benefits:** ABC, CGI-I, PAC, VAS **Harms:** NMS, tardive	Compared to placebo, risperidone was more effective in treating

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	(crossover)	**GROUP 1** **N:** 26 (crossover)	**Run-in phase duration:** 5–7 wk	dyskinesia, weight change	problematic behaviors in children and adolescents with MR. Low doses were better tolerated and were equally effective compared to high doses.
Condition category: ASD **Funding:** Industry, Government **Risk of bias:** High (subjective), High (objective)	**Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 6–65 yr, (2) MR (IQ <70), (3) at least 6 mo history of aggression, property destruction, or self-injury, (4) above normal baseline Irritability score for age, gender and setting (ABC-C) **Exclusion criteria:** (1) previous risperidone hypersensitivity, (2) history of NMS, (3) seizures within the past yr, (4) degenerative brain disease, (5) problematic living situation	**Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** Autistic Disorder (ND), MR (Mild (8), moderate (6), severe (8), profound (4)), PDD-NOS (ND) **GROUP 2** **N:** 26 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1 **GROUP 3** **N:** 26 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	**Permitted drugs:** divalproex, gabapentin (if epilepsy was in remission ≥1 yr) **Prohibited drugs:** psychotropics, including stimulants **GROUP 1** **Drug name:** Risperidone (low) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** all groups: divalproex (5), gabapentin (1) **GROUP 2** **Drug name:** Risperidone (high) **Dosing variability:** variable **Target dose (mg/day):** 0.05 mg/kg/day **Daily dose (mg/day), mean±SD (range):** 2 (1.2–2.9) **Concurrent treatments:** see group 1 **GROUP 3** **Drug name:** Placebo II **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** see group 1		
Hollander et al.,	**Recruitment dates:**	**Enrolled:** 11	**Treatment duration:** 8 wk	**Benefits:** CGI-I,	Olazapine improved

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
2006 [41] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	NR **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV, ADI-R, ADOS **Inclusion criteria:** (1) 6–17 yr, (2) meets DSM-IV and ADI-R criteria with a rating of at least moderate (≥4) on the CGI **Exclusion criteria:** (1) response to prior pharmacological treatment, (2) psychotic disorders and a history of any clinically significant medical illness (with the exception of a stable seizure disorder)	**Analyzed:** 11 **Completed:** 8 **GROUP 1** **N:** 6 **Age, mean±SD (range):** 9.3±2.9 (6–14.8) **Males %:** 100 **Caucasian %:** 50 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (normal (2), mild (2), severe (2)) **GROUP 2** **N:** 5 **Age, mean±SD (range):** 8.9±2.1 (6.1–11) **Males %:** 60 **Caucasian %:** 80 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (normal (2), mild (3))	**Run-in phase:** Yes **Run-in phase duration:** 4 wk **Permitted drugs:** anticonvulsants (stable dose ≥3 mo), clonidine, chloral hydrate **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 10±2 (7.5–12.5) **Concurrent treatments:** none **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 10±2 (7.5–12.5) **Concurrent treatments:** none	response (CGI-I, CPRS) **Harms:** Constipation, EPS (AIMS, BAS, SAS), sedation, weight change	global functioning in children and adolescents with PDD, but was associated with a significant risk of weight gain.
Hrdlicka et al., 2009 [113] **Country:** Czech Republic **Condition category:** Schizophrenia and related **Funding:** Government,	**Recruitment dates:** 1997 to 2007 **Study design:** Retrospective cohort **Setting:** Inpatient **Diagnostic criteria:** ICD-10 **Inclusion criteria:** (1) schizophrenia dx (F20-	**Enrolled:** 109 **Analyzed:** NR **Completed:** 52 **GROUP 1** **N:** 24 **Age, mean±SD (range):** 15.8±1.6yr (all) **Males %:** 48% (all) **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis**	**Treatment duration:** 6 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Typical (Haloperidol, Perphenazine, Sulpiride) **Dosing variability:** variable **Target dose (mg/day):** NR	**Benefits:** NR **Harms:** Weight changes	Weight gain did not differ between the groups on typical and atypical antipsychotics.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Academic **Newcastle-Ottawa Scale:** 5/8 stars	29), (2) medical record quality sufficient to evaluate the patient, (3) the first treatment used following admission was considered (with the exception of clozapine), (4) only antipsychotic treatments initiated after admission to the Department of Child Psychiatry were analyzed **Exclusion criteria:** NR	**(n):** NR **GROUP 2** **N:** 85 **Age, mean±SD (range):** see above **Males %:** see above **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Daily dose (mg/day), mean±SD (range):** Haloperidol 6.8±1.1, Perphenazine 12±6.9, Sulpiride 450±409.3 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Atypical (Clozapine, Olanzapine, Risperidone, Ziprasidone) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** Clozapine 247.5±118, Olanzapine 15±6.1, Risperidone 2.7±1.3, Ziprasidone 80±0 **Concurrent treatments:** NR		
Jensen et al., 2008 [42] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** NR **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** May 2003 to June 2006 **Study design:** RCT (parallel) **Setting:** Inpatient (most) **Diagnostic criteria:** DSM-IV, K-SADS **Inclusion criteria:** (1) 10–18 yr, (2) schizophrenia/ schizoaffective disorder, schizophreniform, or psychotic disorder NOS, (3) ≥1 positive or negative symptom associated with schizophrenia present	**Enrolled:** 30 **Analyzed:** 29 **Completed:** 21 **GROUP 1** **N:** 10 **Age, mean±SD (range):** 15.3±1.5 **Males %:** 50 **Caucasian %:** 50 **Diagnostic breakdown (n):** psychotic disorder NOS (6), schizophrenia, schizoaffective, schizophreniform disorder (4) **Treatment naïve (n):** NR **Inpatients (n):** 9 **First episode psychosis (n):** NR **Comorbidities:** MR (0), psychosis (all) **GROUP 2**	**Treatment duration:** 2.8 mo **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** diphenhydramine (≤100 mg/day), lorazepam (0.5–2 mg/day) **Prohibited drugs:** antidepressants, mood stabilizers, and stimulants (discontinued prior to or within first 2 wk of trial) **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** 20 **Daily dose (mg/day), mean±SD (range):** 14±4.6 (5–20) **Concurrent treatments:** anticholinergics (0), dietary counselling, psychoeducation **GROUP 2**	**Benefits:** PANSS, CGAS, CGI-S, medication adherence, response **Harms:** AIMS, SAS, akathisia, behavioral issues, dyskinesia, EPS, mastitis, sedation, WAE, weight change	There was no statistically significant difference between groups in the reduction of PANSS scores; however a larger RCT may be warranted to test the clinical significance of differences between treatment with quetiapine and risperidone.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	throughout the past 2 wk (PANSS) **Exclusion criteria:** (1) MR or affective disorder with psychotic features, (2) current alcohol or drug dependence or abuse, (3) history of serious adverse reactions or nonresponse to an adequate trial of any of the proposed treatments, (4) pregnant or refusal to practice contraception, (5) serious and unstable medical condition	**N:** 10 **Age, mean±SD (range):** 14.8±2.3 **Males %:** 70 **Caucasian %:** 60 **Diagnostic breakdown (n):** psychotic disorder NOS (3), schizophrenia, schizoaffective, schizophreniform disorder (7) **Treatment naïve (n):** NR **Inpatients (n):** 9 **First episode psychosis (n):** NR **Comorbidities:** MR (0), psychosis (all) **GROUP 3** **N:** 10 **Age, mean±SD (range):** 15.6±2.5 **Males %:** 80 **Caucasian %:** 70 **Diagnostic breakdown (n):** psychotic disorder NOS (0), schizophrenia, schizoaffective, schizophreniform disorder (10) **Treatment naïve (n):** NR **Inpatients (n):** 9 **First episode psychosis (n):** NR **Comorbidities:** MR (0), psychosis (all)	**Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 800 **Daily dose (mg/day), mean±SD (range):** 611±253.4 (100–800) **Concurrent treatments:** anticholinergics (0), dietary counselling, psychoeducation **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** 6 **Daily dose (mg/day), mean±SD (range):** 3.4±1.5 (1–6) **Concurrent treatments:** anticholinergics (0), dietary counselling, psychoeducation,		
Jerrell et al., 2008 [114] **Country:** USA **Condition**	**Recruitment dates:** Jan 1996 to Dec 2005 **Study design:** Retrospective	**Enrolled:** NA **Analyzed:** 4140 **Completed:** 4140 **GROUP 1** **N:** 4140	**Treatment duration:** ≥9 mo **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR	**Benefits:** NR **Harms:** Weight gain, type 2 diabetes mellitus, dyslipidemia, hypertension,	When evaluating the overall benefit-risk ratio of all psychotropics prescribed in

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
category: Mixed **Questions:** KQ2, KQ3 **Funding:** Non-industry **Newcastle-Ottawa Scale:** 6/8 stars	**Setting:** Inpatient/ outpatient **Diagnostic criteria:** ICD-9-CM **Inclusion criteria:** (1) Child and adolescent pateints, (2) ≤17 yr, (3) enrolled in and eligible for Medicaid for ≥ 9 mo in each calendar year, (4) who had a service encounter, (5) who were prescribed 1 of 5 atypical (aripiprazole, ziprasidone, quetiapine, risperidone, olanzapine) or 2 conventional antipsychotics (haloperidol or fluphenazine) **Exclusion criteria:** NR	**Age, mean±SD (range):** NR **Males %:** 68 **Caucasian %:** 42 **Diagnostic breakdown (n):** Schizophrenia or other psychotic disorders (1507), major affective disorders (2261), ADHD (3258) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** Epilepsy (954), CNS disorders (919), organic brain syndrome or severe MR (704), congenital heart defects (146), endocrine disorder (168), preexisting obesity (680), preexisting type II diabetes mellitus or dyslipidemia (404), preexisting cardiovascular disorder (246)	**Prohibited drugs:** NR **GROUP 1** **Drug name:** Antipsychotics cohort **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.4±3.1 **Concurrent treatments:** SSRI (2367), , weight-inducing antidepressants (3292), psychostimulants (3170), multiple antipsychotics (1756), mood stabilizers (1898)	cardiovascular/ cerebrovascular events, orthostatic hypotension/ syncope, EPS, seizures, sedation/ somnolence, sexual/ reproductive	children and adolescents, the practitioner needs to give careful consideration to possible toxicities that have been previously demonstrated in this and other studies, especially in individuals receiving concomitant psychotropic medications, and to children with preexisting/comorbid medical conditions or diet/family risk factors that might increase their potential for experiencing adverse reactions.
Johnson & Johnson, 2011 [43] **Country:** NR **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High	**Recruitment dates:** Mar to Aug 2006 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR **Inclusion criteria:** (1) male or female, (2) aged 10 to 17 years,	**Enrolled:** 25 **Analyzed:** 25 **Completed:** 24 **GROUP 1** **N:** 8 **Age, mean±SD (range):** all groups: 14.6±2.2 (10–17) **Males %:** all groups: 72 **Caucasian %:** all groups: 56 **Diagnostic breakdown (n):** all groups:	**Treatment duration:** 7 days **Run–in phase:** Yes **Run–in phase duration:** 21 days maximum **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Paliperidone ER **Dosing variability:** fixed **Target dose (mg/day):** 0.086 mg/kg/day	**Benefits:** NR **Harms:** total AE, serious AEs, mortality, prolactin, prolactin-related AE, orthostatic hypotension, ECG changes, EPS scales	Pediatric subjects tolerated doses from 4 to 12 mg paliperidone ER (corresponding to weight-adjusted doses ranging from 0.086 and 0.171 mg/kg).

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(objective)	(3) height and weight within the 5th to 95th percentile for age and sex, (4) DSM-IV-TR diagnosis of schizophrenia of any subtype, schizoaffective or schizophreniform (3) otherwise healthy, (4) CGI-S score of =< 3 **Exclusion criteria:** NR	schizophreniform disorder (8), schizoaffective disorder (7), paranoid (6), undifferentiated (3), disorganized (1) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 9 **Age, mean±SD (range):** see group 1 **Males %:** see group 1 **Caucasian %:** see group 1 **Diagnostic breakdown (n):** see group 1 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 3** **N:** 8 **Age, mean±SD (range):** see group 1 **Males %:** see group 1 **Caucasian %:** see group 1 **Diagnostic breakdown (n):** see group 1 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Paliperidone ER **Dosing variability:** fixed **Target dose (mg/day):** 0.129 mg/kg/day **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 3** **Drug name:** Paliperidone ER **Dosing variability:** fixed **Target dose (mg/day):** 0.171 mg/kg/day **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Kafantaris et al., 2011 [44] **Country:** USA	**Recruitment dates:** NR **Study design:** RCT (parallel)	**Enrolled:** 20 **Analyzed:** 20 **Completed:** 15 **GROUP 1**	**Treatment duration:** 10 wk **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR	**Benefits:** HDRS, Brief Psychiatric Rating Scale, EDE, YBC-EDS, medication	The lack of support for olanzapine's efficacy relative to placebo in the context of our

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Condition category: Eating disorders **Funding:** Industry **ROB:** Medium (subjective), Medium (objective)	**Setting:** Inpatient/outpatient **Diagnostic criteria:** EDE (Eating Disorder Examination) **Inclusion criteria:** (1) females who received treatment for AN at the Eating Disorder Treatment Program over a 4 yr period, (2) between 12-21 yr, (3) primary diagnosis of ANR **Exclusion criteria:** (1) past or current binge/purge type, (2) serious suicidal risk, (3) prior treatment with olanzapine, (4) not on a sable medication regimen for 8 wk prior to study entry	**N:** 10 **Age, mean±SD (range):** 16.4±2.2 yr **Males %:** 0 **Caucasian %:** see below **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 10 **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 10 **Age, mean±SD (range):** 18.1±2.0 yr **Males %:** 0 **Caucasian %:** see below **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 10 **Inpatients (n):** see below **First episode psychosis (n):** NR **Comorbidities:** NR **Overall Caucasian %:** 80 **Overall inpatients (n):** 9	**Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** flexible **Target dose (mg/day):** 10 **Daily dose (mg/day), mean±SD (range):** NR (started with 2.5mg single oral dose; increased by 2.5mg each wk to reach target dose) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** flexible **Target dose (mg/day):** 10 **Daily dose (mg/day), mean±SD (range):** NR (started with 2.5mg single oral dose; increased by 2.5mg each wk to reach target dose) **Concurrent treatments:** NR	adherence **Harms:** dystonia, akathisia, dyskinesia, weight gain (BMI), glucose, insulin, cardiac function	comprehensive treatment setting, coupled with concerns regarding increases in insulin and glucose, dissuaded us from pursuing a larger placebo-controlled study of adjunctive olanzapine for adolescents with AN-R at our setting.
Kent et al., 2013 [45] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** Medium (subjective),	**Recruitment dates:** Dec 2007 to Mar 2010 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, ADI-R **Inclusion criteria:** (1)	**Enrolled:** 96 **Analyzed:** 96 **Completed:** 77 **GROUP 1** **N:** 30 **Age, mean±SD (range):** NR **Males %:** 83 **Caucasian %:** 70 **Diagnostic breakdown (n):** autistic disorder (all)	**Treatment duration:** 6 wk **Run–in phase:** Yes **Run–in phase duration:** 3 wk **Permitted drugs:** Anticholinergics, antihistamine, hypnotic, sedative (lorazepam, diphenhydramine) **Prohibited drugs:** Psychotropic medications for atleast 1 week (4 weeks for fluoxetine, 8 weeks for depot medications)	**Benefits:** ABC-I, ABC (other sub scales), CGI-S, CYBOCS, CGI-I, response, aggression **Harms:** EPS (AIMS, BAS, SAS) Somnolence, weight increase (BMI), mortality, akathisia, tardive dyskinesia,	Data from this study demonstrate that risperidone at higher doses of 1.25 and 1.75 mg/day were efficacious; however, risperidone at doses <0.25 mg did not demonstrate significant efficacy in the treatment of

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Medium (objective)	Male or female 5–17 years old, (2) Body weight of ≥20 kg (3) DSM-IV diagnosis of Autistic Disorder (299.00), corroborated by standard cut-off scores on the ADI-R, ABC-I Subscale score of 18 or more, CGI-S of ≥4, (4) mental age >18 months, (5) patients with history of seizures required to be seixure free for at least 6 consecutive months or on stable dosage of antiepileptic frugs ≥ 4 weeks before screening, (6) normal fasting glucose and creatinine, and liver funcion tests levels <1.5 times normal upper limit **Exclusion criteria:** (1) Previous or current DSM-IV diagnosis of psychotic disorder or PDD other than autism, (2) neurologic disorders, (3) moderate/severe extrapyramidal symptoms or tardive dyskinesia, (4) lack of response to risperidone treatment in the past, (5) pregnant/breast feeding girls	**Treatment naïve (n):** 26 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 31 **Age, mean±SD (range):** NR **Males %:** 90 **Caucasian %:** 81 **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** 29 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 35 **Age, mean±SD (range):** NR **Males %:** 89 **Caucasian %:** 60 **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** 32 **Inpatients (n):** NR **First episode psychosis:**NR **Comorbidities:** NR	**GROUP 1** **Drug name:** Risperidone **Dosing variability:** fixed **Target dose (mg/day):** 0.125 (20<45 kg), 0.175 (≥45kg) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** methylphenidate (1) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** fixed **Target dose (mg/day):** 1.25 (20<45 kg), 1.75 (≥45kg) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** methylphenidate (1) **GROUP 3** **Drug name:** Placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** methylphen-idate (1), alprazolam (1), melatonin (2)	prolactin, prolactin-related AE (oligomenorrhea), glucose metabolism related AE, elevated insulin levels, lipid profile, nausea, ECG, constipation, agitation	irritability and related behaviors associated with autistic disorder in children and adolescents, consistent with current labeling.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Khan et al., 2009 [115] **Country:** USA **Condition category:** Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Sept 2003 to Aug 2005 **Study design:** Retrospective **Setting:** Inpatient **Diagnostic criteria:** Medical record **Inclusion criteria:** (1) <18 yr, (2) treated with olanzapine or risperidone between Sept 2003 to Aug 2005 at the child and adolescent psychiatric unit of the Austin State Hospital **Exclusion criteria:** (1) ≥18 yr, (2) who received antipsychotic polypharmacy or >2 wk of cross titration between antipsychotics, (3) who received one of the study medications within 4 wk prior to their inpatient admission or who received the study medication <2 wk during inpatient hospital stay, (4) subjects who did not have either a lipid profile or a glucose level drawn during admission	**Enrolled:** NA **Analyzed:** 49 **Completed:** 49 **GROUP 1** **N:** 25 **Age, mean±SD (range):** 13.0±3.5 yr **Males %:** 64 **Caucasian %:** 72 **Diagnostic breakdown (n):** See below **Treatment naïve (n):** NR **Inpatients (n):** 25 **First episode psychosis (n):** NR **Comorbidities:** See below **GROUP 2** **N:** 24 **Age, mean±SD (range):** 13.0±3.5 yr **Males %:** 83 **Caucasian %:** 58 **Diagnostic breakdown (n):** See below **Treatment naïve (n):** NR **Inpatients (n):** 24 **First episode psychosis (n):** NR **Comorbidities:** See below **Overall diagnostic breakdown (n):** BP (NR), mood disorder NOS (NR), major depressive disorder (NR), schizoaffective disorder, schizophrenia, and schizophreniform disorder (7)	**Treatment duration:** Olanzapine 27±12 d, risperidone 26±13 d **Run-in phase:** Yes **Run-in phase duration:** 2-4 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 12.5 (range 5-25 mg) **Concurrent treatments:** Stimulants (5) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.6 (range 1-7 mg) **Concurrent treatments:** Stimulants (6)	**Benefits:** NA **Harms:** BMI, systolic/ diastolic blood pressure, lipid profile, fasting glucose	Treatment with both olanzapine and risperidone results in a significant increase in BMI. Also, olanzapine significantly increases risk factors for diabetes mellitus and overall risk factors for metabolic syndrome. Clinicians should consider potential metabolic effects while selecting antipsychotics and educate patients on these effects.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Overall comorbidities: SUD (14), ADHD (8)			
Khan et al., 2006 [116] **Country:** USA **Condition category:** Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 4/8 stars	**Recruitment dates:** Jan 2003 to Jan 2005 **Study design:** Retrospective cohort **Setting:** Inpatient **Diagnostic criteria:** NR **Inclusion criteria:** (1) <18 yr, (2) hospitalized with any mental illness, (3) treatment with IM ziprasidone or olanzapine for acute agitation/agression, (4) hospitalized during study period **Exclusion criteria:** (1) >18 yr, (2) moderate, severe or profound MR, (3) patients who did not receive IM ziprasidone/ olanzapine for agitation or agression during their inpatient stay, (4) patients receiving both IM ziprasidone and olanzapine	**Enrolled:** NA **Analyzed:** 100 **Completed:** 100 **GROUP 1** **N:** 50 **Age, mean±SD (range):** 13.7±2.4 **Males %:** 68 **Caucasian %:** 60 **Diagnostic breakdown (n):** any Axis I dx with psychosis (18) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** PTSD (18), SA (27) **GROUP 2** **N:** 50 **Age, mean±SD (range):** 14.6±2.1 **Males %:** 32 **Caucasian %:** 68 **Diagnostic breakdown (n):** any Axis I dx with psychosis (16) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	**Treatment duration:** Olanzapine 3.7 (2.4) wk, Ziprasidone 4.9 (3.4) wk (mean(SD)) **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** total 8.2±2.4, children 6±2.2, adolescents 9.20±1.8 **Concurrent treatments:** antipsychotic other than ziprasidone (41); aripiprazole, quetiapine most commonly prescribed **GROUP 2** **Drug name:** Ziprasidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** total 19.1±2.7, children 15.7±4.4, adolescents 19.5±2.1 **Concurrent treatments:** antipsychotics (48) (olanzapine (13), clozapine (4)); aripiprazole, quetiapine the most commonly prescribed	**Benefits:** NA **Harms:** Dermatologic AE, pseudoparkinsonism, sedation	IM ziprasidone and IM olanzapine may be equally effective for the treatment of children and adolescents with agitation and aggression.
Kowatch et al., 2015 [46]	**Recruitment dates:** Sept 2005 to Sept 2010	**Enrolled:** 25 **Analyzed:** 25 **Completed:** 23	**Treatment duration:** 6 wk **Run–in phase:** Yes **Run–in phase duration:** 4 wk	**Benefits:** YMRS, CGI-I, CDRS, response, irritability	In this small sample of preschool children with BD, risperidone

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Country: USA **Condition category:** Bipolar disorder **Funding:** Non-industry **Risk of bias:** Medium (subjective), Medium (objective)	**Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** DSM-IV-TR, K-SADS, PAPA **Inclusion criteria:** (1) Male and female, (2) aged 3-7yr 11 mo, (3) bipolar I disorder , mixed or manic, psychotic or nonpsychotic (according to DSM-IV-TR, K-SADS [for 6-7 yr] and PAPA [for3-5 yr]), (4)) permitted to have comorbid ADHD **Exclusion criteria:** (1) Clinically significant or unstable hepatic, renal, gastroenterological, respiratory, cardiovascular, endocrine, immunological, hematological, or other systemic medical conditions, (2) neurological disorders including epilepsy, stroke, or severe head trauma, (3) clinically significant laboratory abnormalities on complete blood count (CBC) with differential, electrolytes, blood urea	**GROUP 1** **N:** 18 **Age, mean±SD (range):** 5.31±1.3 yr **Males %:** 61 **Caucasian %:** 61 **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (37%), ODD (4.3%), GAD (8.7%) **GROUP 2** **N:** 7 **Age, mean±SD (range):** 5.19±1.0 yr **Males %:** 71 **Caucasian %:** 71 **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (15.2%), ODD (0%), GAD (6.5%)	(aripiprazole/fluoxetine), 2 wk (other psychotropic) **Permitted drugs:** Oral chlorpromazine in low doses for sleep disturbance and agitation during the first 2 wk of trial **Prohibited drugs:** Antipsychotic, antidepressant, mood stabilizer/ anticonvulsant other than study drug **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0.5(0.5-0.75)mg/day **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Harms:** EPS (AIMS, BAS, SAS), ECG, lipid profile, liver function tests, prolactin, insulin, weight (BMI), hematologic values	demonstrated clear efficacy versus placebo. Treatment with risperidone over 6 weeks led to increased prolactin levels, liver functions, metabolic measures, and weight/BMI.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	nitrogen (BUN), creatinine, hepatic transaminases, urinalysis, thyroid indices (T3, total T4, tree T4, thyroid-stimulating hormone [TSH]) and electrocardiogram (ECG), (4) mania caused by a general medical condition or substance-induced mania, (5) mental retardation (intelligence quotient [IQ] < 70); evidence of fetal alcohol syndrome or an alcohol-related neurodevelopmental disorder, (6) or schizophrenia or other psychotic disorders (including schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder caused by a general medical condition, substance-induced psychotic disorder, psychotic disorder not otherwise specified) as defined in the DSM-IV				
Kryzhanovskaya et al., 2009 [47]	**Recruitment dates:** Nov 2002 to Apr 2005	**Enrolled:** 107 **Analyzed:** 107	**Treatment duration:** 6 wk **Run-in phase:** Yes	**Benefits:** BPRS-C, PANSS, CGI-I, CGI-	Adolescents with schizophrenia

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Completed: 64	**Run-in phase duration:** 2–14 day	S, OAS, medication adherence, response, suicide	experienced significant symptom improvement when treated with olanzapine compared to placebo.
Country: Russia, USA	**Study design:** RCT (parallel)	**GROUP 1** **N:** 72	**Permitted drugs:** anticholinergics (2–6mg/day), benzodiazepines (2 mg/day lorazepam equivalents for ≤3 consecutive days)	**Harm:** AIMS, BAS, SAS, BMI, ECG changes, glucose, hepatic enzyme, lipid profile, mortality, prolactin, sedation, schizophrenia, somnolence, WAE, weight change	
Condition category: Schizophrenia and related	**Setting:** Inpatient and outpatient	**Age, mean±SD (range):** 16.1±1.3 (13–18) **Males %:** 70.8 **Caucasian %:** 72.2 **Treatment naïve (n):** 21 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0), SA (0)	**Prohibited drugs:** NR		
Funding: Industry	**Diagnostic criteria:** DSM-IV-TR, K-SADS		**GROUP 1** **Drug name:** Olanzapine **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 11.1 (2.5–20) **Concurrent treatments:** anticholinergics (3), benzodiazepines (21)		
Risk of bias: High (subjective), High (objective)	**Inclusion criteria:** (1) 13–17 yr, (2) schizophrenia (paranoid, disorganized, catatonic, undifferentiated, and residual types), (3) able to perform all protocol–required examinations, (4) total score ≥35 on the anchored version of the BPRS-C16 and a score ≥3 on at least one of the following BPRS-C items at enrolment and randomization: hallucinations, delusions, or peculiar fantasies, (5) previously treated with clozapine and other atypical antipsychotics	**GROUP 2** **N:** 35 **Age, mean±SD (range):** 16.3±1.6 (13.1–18) **Males %:** 68.6 **Caucasian %:** 71.4 **Treatment naïve (n):** 5 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0), SA (0)	**GROUP 2** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergics (2), benzodiazepines (18)		
	Exclusion criteria: (1) previous participation in a clinical trial of oral olanzapine, (2) treatment within 30 day of the trial with a drug				

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	without regulatory approval for any indication, (3) documented olanzapine allergic reaction, (4) previous nonresponse to an adequate dose/duration of olanzapine treatment, (5) potential safety concerns, (6) pregnancy, nursing, or refusal to practice acceptable contraception, (7) acute/ unstable medical conditions, (8) current/expected use of any concomitant psychotropic medications (except for permitted drugs), (9) baseline prolactin ≥200 ng/mL, (10) clinically significant laboratory abnormalities, (11) DSM-IV-TR substance dependence within 30 day (except nicotine and caffeine) (12) current DSM-IV-TR dx of a comorbid psychiatric or developmental disorder				
Kumra et al., 2008[49] **Country:** USA **Condition**	**Recruitment dates:** Sep 2001 to Mar 2006 **Study design:** RCT (parallel)	**Enrolled:** 40 **Analyzed:** 39 **Completed:** 28 **GROUP 1** **N:** 19	**Treatment duration:** 2.8 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** current medications tapered as tolerated	**Benefits:** BPRS, CGAS, CGI-I, CGI-S, SANS, response **Harms:** Blood cells, BMI, constipation,	A greater number of children diagnosed with schizophrenia/ schizoaffective disorder and treated with clozapine met

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
category: Schizophrenia and related **Funding:** NR **Risk of bias:** High (subjective), High (objective)	**Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL, structured interview **Inclusion criteria:** (1) 10–18 yr, (2) schizophrenia or schizoaffective disorder, (3) treatment refractoriness (documented treatment failure of ≥2 prior adequate antipsychotic trials and a baseline BRPS total score ≥35 and at least moderate on one or more psychotic items on the BRPS) **Exclusion criteria:** (1) premorbid dx of MR, (2) history of serious adverse reactions to the proposed treatments, (3) pregnant, (4) serious and unstable medical condition, (5) failed an adequate trial of clozapine (≥12 wk) at adequate doses (≥300mg/day) and/or failed an adequate trial of olanzapine (≥8wk) at high doses (≥20mg/day)	**Age, mean±SD (range):** 15.8±2.2 **Males %:** 44.4 **Caucasian %:** 11.1 **Diagnostic breakdown (n):** schizoaffective disorder (7), schizophrenia (11) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 0 **Comorbidities:** MR (0) **GROUP 2** **N:** 21 **Age, mean±SD (range):** 15.5±2.1 **Males %:** 61.9 **Caucasian %:** 28.6 **Diagnostic breakdown (n):** schizoaffective disorder (7), schizophrenia (14) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 0 **Comorbidities:** MR (0)	(first 4 wk of trial) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 403.1±201.8 (50–700) **Concurrent treatments:** all groups: antidepressants (4), depakoate (3), lithium (7), mood stabilizer (6), naltrexone (1), stimulant (1); group 1: n=6 **GROUP 2** **Drug name:** Olanzapine (high dose) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 26.2±6.5 (10–30) **Concurrent treatments:** see group 1; group 2: n=11	diabetes, EPS, glucose, lipid profile, prolactin, SAE, WAE, weight change	drug response criteria than children treated with olanzapine. Clinicians should be aware of potential metabolic adverse events of long-term clozapine treatment.
Kumra et al., 1998 [117]	**Recruitment dates:** NR	**Enrolled:** 23 **Analyzed:** 23	**Treatment duration:** Clozapine 6 wk, Olanzapine 8 wk	**Benefits:** BPRS, SANS, SAPS,	Preliminary data suggested clozapine

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Completed: 21	**Run-in phase:** Yes	response	and olanzapine
Country: USA	**Study design:** Prospective cohort	**GROUP 1**	**Run-in phase duration:** 17.5 day (mean)	**Harms:** Behavioral issues, blood cells, constipation, EPS, liver function, seizure, somnolence, tachycardia, weight change	were efficacious in children and adolescents with treatment-refractory schizophrenia.
Condition category: Schizophrenia and related	**Setting:** Inpatient	**N:** 15	**Permitted drugs:** benzodiazepines (<8 mg/day)		
Funding: Industry	**Diagnostic criteria:** DSM-III-TR, K-SADS-E	**Age, mean±SD (range):** 13.6±1.5	**Prohibited drugs:** NR		
Newcastle-Ottawa Scale: 5/8 stars	**Inclusion criteria:** (1) schizophrenia with psychotic symptoms documented by 12 yr (DSM-III-R), (2) failure of two prior neuroleptic treatments, (3) communication capability, (4) premorbid Full Scale IQ >70	**Males %:** 53.3	**GROUP 1**		
		Caucasian %: NR	**Drug name:** Clozapine		
		Diagnostic breakdown (n): disorganized (8), paranoid (2), undifferentiated (5)	**Dosing variability:** variable		
		Treatment naïve (n): 0	**Target dose (mg/day):** NR		
		Inpatients (n): all	**Daily dose (mg/day), mean±SD (range):** 317±147 (100–600)		
		First episode psychosis (n): 0	**Concurrent treatments:** NR		
	Exclusion criteria: (1) any significant unstable neurological or medical disorder, (2) current serious suicidal risk, (3) active alcohol or drug abuse	**GROUP 2**	**GROUP 2**		
		N: 8	**Drug name:** Olanzapine		
		Age, mean±SD (range): 15.3±2.3	**Dosing variability:** variable		
		Males %: 50	**Target dose (mg/day):** NR		
		Caucasian %: NR	**Daily dose (mg/day), mean±SD (range):** 17.5±2.3 (12.5–20)		
		Diagnostic breakdown (n): disorganized (3), paranoid (1), undifferentiated (4)	**Concurrent treatments:** benzodiazepines (7), lithium (1)		
		Treatment naïve (n): 0			
		Inpatients (n): all			
		First episode psychosis (n): 0			
Kumra et al., 1996 [48]	**Recruitment dates:** NR	**Enrolled:** 21	**Treatment duration:** 6 wk	**Benefits:** BPRS-C, CGAS, CGI-I, SANS, SAPS,	Clozapine was more effective in controlling positive and negative symptoms in treatment-refractory childhood onset schizophrenia than haloperidol.
		Analyzed: 21	**Run-in phase:** Yes		
		Completed: 17	**Run-in phase duration:** 6 wk		
Country: USA	**Study design:** RCT (parallel)	**GROUP 1**	**Permitted drugs:** group 1: benztropine mesylate (≤6 mg/day); group 2: identical placebo; all: atenolol, antibiotics, anticonvulsants	**Harms:** Blood cells, blood pressure, EPS (SAS, AIMS), drowsiness, hepatic enzyme, NMS, seizure, tachycardia, weight	
Condition category: Schizophrenia and related	**Setting:** Inpatient	**N:** 11			
	Diagnostic criteria: DSM-III-TR, K-SADS, DICA-R	**Age, mean±SD (range):** 13.7±1.6			
		Males %: 54.6			
Funding: NR		**Caucasian %:** NR	**Prohibited drugs:** NR		
		Diagnostic breakdown			

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Risk of bias: High (subjective), High (objective)	**Inclusion criteria:** (1) schizophrenia with documented psychotic symptoms by 12 yr (DSM-III-TR), (2) intolerance, nonresponse, or both to ≥2 different neuroleptic drugs, (3) full-scale IQ ≥70 **Exclusion criteria:** (1) neurologic or medical disease	**(n):** disorganized (5), paranoid (1), undifferentiated (5) **Treatment naïve (n):** NR **Inpatients (n):** 11 **First episode psychosis (n):** 0 **GROUP 2** **N:** 10 **Age, mean±SD (range):** 14.4±2.9 **Males %:** 50 **Caucasian %:** NR **Diagnostic breakdown (n):** disorganized (5), undifferentiated (5) **Treatment naïve (n):** NR **Inpatients (n):** 10 **First episode psychosis (n):** 0	**GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 16±8 (7–27) **Concurrent treatments:** benzotropine **GROUP 2** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 176±149 (25–525) **Concurrent treatments:** amoxicillin (1), penicillin (1)		
Loebel et al., 2016 [50] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of Bias:** Medium (subjective, Medium (objective)	**Recruitment dates:** Sept 2013 to Nov 2014 **Study design:** RCT **Setting:** Outpatient **Diagnostic criteria:** DSM-IV-TR **Inclusion criteria:** (1) ≥18 on the Irritability subscale of the Aberrant behavior checklist, (2) ≥4 on the Clinical Global Impression severity **Exclusion criteria:** current diagnosis of	**Enrolled:** 150 **Analyzed:** 149 **Completed:** 128 **GROUP 1** **N:** 48 **Age, mean±SD (range):** 10.5±3 **Males %:** 79.2 **Caucasian %:** 71 **Treatment naïve (n):** 64.6 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 51 **Age, mean±SD (range):** 10.5±3 **Males %:** 84.3	**Treatment duration:** 6 weeks **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** diphenhydramine, melatonin, benztropine, diphenhydramine or propranolol **Prohibited drugs:** psychotropic medications **GROUP 1** **Drug name:** Lurasidone **Dosing variability:** fixed **Target dose (mg/day):** 20 mg/d **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2**	**Benefits:** ABC irritability, hyperactivity, stereotypic behavior, inappropriate speech, lethargy/withdrawal, CGI-I, CGI-S, CY-BOCS, CGSQ global strain **Harms:** TEAE, weight, BMI, fasting laboratory parameters	Modest changes were observed in weight and selected metabolic parameters. Doses of 20 and 60mg/day of lurasidone were not demonstrated to be efficacious compared to placebo for the short-term treatment of children and adolescents with moderate-to-severe irritability associated with autistic disorder.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	bipolar disorder, schizophrenia, major depressive disorder, Fragile-X syndrome, or childhood disintegrative disorder or a confirmed genetic disorder associated with cognitive and/or behavioral disturbance or profound intellectual disability. History of seizures, unless they were seizure-free and off antiepileptic drugs for at least 6 months.	**Caucasian %:** 74.5 **Treatment naïve (n):** 67.6 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 3** **N:** 49 **Age, mean±SD (range):** 11±3 **Males %:** 81.6 **Caucasian %:** 86 **Diagnostic breakdown (n): Treatment naïve (n):** 61.2 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR	**Drug name:** Lurasidone **Dosing variability:** fixed **Target dose (mg/day):** 60 mg/d **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 3** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Luby et al., 2006 [51] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** Medium (subjective), Low (objective)	**Recruitment dates:** Nov 1999 to Nov 2002 **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 2.5–6 yr, (2) autism or PDD-NOS (DSM-IV), (3) absence of other known significant CNS disorders, (4) absence of significant medical problems or other	**Enrolled:** 24 **Analyzed:** 23 **Completed:** NR **GROUP 1** **N:** 12 **Age, mean±SD (range):** 4.1±0.9 **Males %:** 75 **Caucasian %:** 91 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 12 **Age, mean±SD (range):** 4±1.1 **Males %:** 66.7	**Treatment duration:** 6 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.1±0.3 (0.5–1.5) **Concurrent treatments:** applied behavior analysis (mean 21.2 hr/wk) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable	**Benefits:** CARS **Harms:** Constipation, EPS, mortality, prolactin, SAE, sedation, WAE, weight change	Risperidone was well tolerated in preschoolers, but only minimal improvement in target symptoms was evident.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	psychiatric disorders requiring pharmacotherapy **Exclusion criteria:** NR	**Caucasian %:** 92 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.4±0.6 (0.5–1.5) **Concurrent treatments:** applied behavior analysis (mean 11.3 hr/wk)		
Malone et al., 2001[52] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** High (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) primary dx of PDD, (2) 5–17 yr, (3) at least moderate impairment on ≥2 of the first 28 items on the CPRS **Exclusion criteria:** (1) major medical problems, (2) seizure disorder or gross neurological deficit, (3) treatment with concomitant psychotropic medication, (4) history of previous treatment with haloperidol or olanzapine	**Enrolled:** 12 **Analyzed:** 12 **Completed:** 12 **GROUP 1** **N:** 6 **Age, mean±SD (range):** 7.3±1.9 (5–10.1) **Males %:** 66.7 **Caucasian %:** 66.7 **Diagnostic breakdown (n):** autistic disorder (5), PDD NOS (1) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (mild (1), moderate (2), severe (3)) **GROUP 2** **N:** 6 **Age, mean±SD (range):** 8.5±2.4 (4.9–11.8) **Males %:** 66.7 **Caucasian %:** 50 **Diagnostic breakdown (n):** autistic disorder (all) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (mild (0), moderate (3), severe (2))	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.4±0.7 (0.5–2.5) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.9±2.5 (5–10) **Concurrent treatments:** NR	**Benefits:** CGI-S, CPRS, response (CGI-I) **Harms:** Dermatologic AE, EPS (AIMS, SAS), EPS, fatigue, tachycardia, weight changes	The use of olanzapine is promising in children with autistic disorder, although placebo-controlled and long-term studies are needed.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Mankoski et al., 2013 [118] (see Marcus 2009 & Owen 2009) **Country:** USA **Condition category:** ASD **Funding:** Industry **Newcastle-Ottawa Scale:** 6/8 stars	**Study design:** Retrospective (pooled analysis), evaluate impact of prior antipsychotic exposure (PAE) on safety and tolerability outcomes in pediatric subjects receiving aripiprazole treatment	**Enrolled:** NA **Analyzed:** 313 **Completed:** NA **GROUP 1** **N:** 176 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 176 **Inpatients (n):** NR **First episode psychosis (n):** NA **Comorbidities:** NR **GROUP 2** **N:** 80 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 80 **Inpatients (n):** NR **First episode psychosis (n):** NA **Comorbidities:** NR **GROUP 3** **N:** 36 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR	**GROUP 1** **Drug name:** Aripiprazole (antipsychotic naïve) **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo (antipsychotic naïve) **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 3** **Drug name:** Aripiprazole (PAE) **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 4** **Drug name:** Placebo (PAE) **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** ABC-I, CGI-S **Harms:** NA	Antipsychotic naïve subjects receiving aripiprazole for the treatment of irritability associated with ASD showed greater risk for weight gain and somnolence-related AEs than subjects receiving placebo. Changes in metabolic parameters in antipsychotic naïve subjects receiving aripiprazole treatment were small and similar to those in subjects receiving placebo.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		First episode psychosis (n): NA **Comorbidities:** NR **GROUP 4** **N:** 21 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NA **Comorbidities:** NR **Overall Age, mean±SD (range):** mean(9.4-10) yr **Overall Males %:** 87.3-96.5%			
Marcus et al., 2009 [53] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** June 2006 to Jun 2008 **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV-TR, ADI-R, CGI-S, ABC-I **Inclusion criteria:** (1) 6–17 yr, (2) DSM-IV-TR criteria for autistic disorder and behaviors such as tantrums, aggression, self–injury, or a combination, with	**Enrolled:** 218 **Analyzed:** 213 **Completed:** 178 **GROUP 1** **N:** 53 **Age, mean±SD (range):** 9.0±2.8 **Males %:** 88.7 **Caucasian %:** 69.8 **Treatment naïve (n):** 43 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 59 **Age, mean±SD (range):** 10±3.2 **Males %:** 84.7	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** ≤6 wk **Permitted drugs:** anxiolytics, benztropine or propranolol, diphenhydramine (≤50 mg/day), psychotropic medication, sleep aids **Prohibited drugs:** antidepressants, antipsychotics, anxiolytics, mood stabilizers, neuroleptics, psychostimulants (washout ≥4 day) **GROUP 1** **Drug name:** Aripiprazole (low) **Dosing variability:** fixed **Target dose (mg/day):** 5 **Daily dose (mg/day), mean±SD (range):** NR	**Benefits:** ABC, CYBOCS, CGI-I, CGI-S, PedsQL, CGSQ, medication adherence, response (ABC-I, CGI-I), suicide **Harms:** Akathisia, BMI, dermatologic AE, ECG changes, EPS, EPS (AIMS, BAS, SAS), fatigue, glucose, lipid profile, mortality, prolactin, SAE, sedation, seizure/convulsion, somnolence, total AE, WAE, weight change, constipation	Aripiprazole was efficacious, safe, and well tolerated in children and adolescents with irritability assocated with autistic disorder.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	a dx corroborated by ADI-R certified trainer, (3) CGI-S score ≥4 and ABC Irritability subscale score ≥18 at screening and baseline, (4) ≥15 kg, (5) stable nonpharmacologic therapy **Exclusion criteria:** (1) bipolar disorder, psychosis, schizophrenia, major depression, fragile X syndrome, or another ASD, (2) history of NMS, (3) significant risk of committing suicide, (4) seizure in the past yr, (5) history of severe head trauma or stroke, (6) history or current evidence of any unstable medical condition or or an abnormal laboratory test result considered clinically significant, (7) antipsychotic treatment resistant, (8) known allergy or hypersensitivity to aripiprazole	**Caucasian %:** 69.5 **Treatment naïve (n):** 45 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 3** **N:** 54 **Age, mean±SD (range):** 9.5±3.1 **Males %:** 92.6 **Caucasian %:** 77.8 **Treatment naïve (n):** 44 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 4** **N:** 52 **Age, mean±SD (range):** 10.2±3.1 **Males %:** 92.3 **Caucasian %:** 67.3 **Treatment naïve (n):** 40 **Inpatients (n):** NR **First episode psychosis (n):** NR	**Concurrent treatments:** analgesics and antipyretics (12), anxiolytics (2), benztropine (2), hypnotics and sedatives (2), propranolol (2) **GROUP 2** **Drug name:** Aripiprazole (medium) **Dosing variability:** fixed **Target dose (mg/day):** 10 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics and antipyretics (12), anxiolytics (1), benztropine (1), hypnotics and sedatives (1) **GROUP 3** **Drug name:** Aripiprazole (high) **Dosing variability:** fixed **Target dose (mg/day):** 15 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics and antipyretics (12), anxiolytics (1), benzotropine (5), hypnotics and sedatives (1) **GROUP 4** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics and antipyretics (9), anxiolytics (3), hypnotics and sedatives (2), propranolol (1)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Martin et al., 2000 [119] **Country:** USA **Condition category:** Mixed conditions **Funding:** Non--industry **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** 1998 **Study design:** Retrospective **Setting:** Inpatient **Diagnostic criteria:** NR **Inclusion criteria:** All children and adolescents admitted to Riverview Hospital in 1998, (2) started on risperidone during their hospital stay, (3) no previous neuroleptic exposure, (4) no change in other psychotropic drugs used for 4 wk prior to risperidone introduction, (5) maintained on risperidone for ≥6 consecutive mo **Exclusion criteria:** NR	**Enrolled:** NA **Analyzed:** 70 **Completed:** 70 **GROUP 1** **N:** 37 **Age, mean±SD (range):** 12.5±2.4 yr **Males %:** 76 **Caucasian %:** 64 **Diagnostic breakdown (n):** Psychotic (9), affective (11), anxiety (12), disruptive (30), PDD/MR (10), polysubstance (0), ED (0) **Treatment naïve (n):** NR **Inpatients (n):** 37 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 33 **Age, mean±SD (range):** 13.5±2.9 yr **Males %:** 49 **Caucasian %:** 61 **Diagnostic breakdown (n):** Psychotic (2), affective (19), anxiety (11), disruptive (27), PDD/MR (8), polysubstance (2), ED (2) **Treatment naïve (n):** NR **Inpatients (n):** 33 **First episode psychosis (n):** NR **Comorbidities:** NR	**Treatment duration:** ≥6 mo **Run-in phase:** Yes **Run-in phase duration:** 4 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.8±1.9 **Concurrent treatments:** Valproate (12), SSRI (8), stimulant (8), α_2 agonist (8), traditional neuroleptic (0) **GROUP 2** **Drug name:** Control **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Valproate (10), SSRI (9), stimulant (6), α_2 agonist (6), traditional neuroleptic (9)	**Benefits:** NR **Harms:** Weight (BMI, BMI z-score)	Studies of children and adolescents are needed to prospectively monitor weight change (as well as serum glucose, liver enzyme, and triglyceride levels) during chronic exposure to risperidone and other atypical neuroleptics. Long-term effects, as well as changes following drug discontinuation are likewise needed. Until those empirical data become available, it seems prudent to recommend careful monitoring of height, weight, and BMI of all children treated with atypical antipsychotics, as well as to consider glucose, liver enzyme, and lipid levels as part of their routine safety monitoring.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Masi et al., 2015 [55] **Country:** Italy **Condition category:** Bipolar II (hypomanic) **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Jan 2013 to Jan 2014 **Study design:** RCT (parallel) **Setting:** Inpatient/outpatient **Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) diagnosis of Bipolar II hypomanic episode as confirmed by DSM-IV-TR, K-SADS-PL and YMRS total score of ≥17 at baseline, (2) CGI-S≥4, (3) CGAS≤50 **Exclusion criteria:** NR	**Enrolled:** 24 **Analyzed:** 22 **Completed:** 22 **GROUP 1** **N:** 12 **Age, mean±SD (range):** 14.9±1.1 **Males %:** 41.7 **Caucasian %:** 100 **Diagnostic breakdown (n):** hypomanic (all) **Treatment naïve (n):** 12 **Inpatients (n):** 3 **First episode psychosis (n):** NR **Comorbidities:** CD (all) ADHD (2), anxiety disorders (3), substance use disorder (1), eating disorder NOS (1) **GROUP 2** **N:** 10 **Age, mean±SD (range):** 15.1±1.8 **Males %:** 70 **Caucasian %:** 100 **Diagnostic breakdown (n):** hypomanic (all) **Treatment naïve (n):** 12 **Inpatients (n):** 3 **First episode psychosis (n):** NR **Comorbidities:** CD (all), ADHD (3), anxiety disorders (2), substance use disorder (2), eating disorder NOS (1)	**Treatment duration:** 12 wk **Run–in phase:** NR **Run–in phase duration:** NR (all treatment naïve) **Permitted drugs:** Methyphenidate at stable dose in 1 patient in risperidone group **Prohibited drugs:** Psychotropics≤6mo **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 163.30±55.20 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.90±0.60 **Concurrent treatments:** NR	**Benefits:** YMRS, CGI-S, CGAS, HDRS, HAM-A, MOAS, response **Harms:** BMI, prolactin, somnolence, fatigue, EPS, ECG	Risperidone and quetiapine did not differ in BMI increase according to the main analysis, although the post hoc analysis suggests a possible BMI increase with risperidone but not with quetiapine. Data on higher prolactin increase during risperidone treatment, compared with quetiapine, are in line with previous studies. However, our findings about safety, namely, the modest BMI increase and the absence ofQTc prolongation, should be cautiously considered in the context of the limited time of the study.
Masi et al., 2013 [54] **Country:** Italy	**Recruitment Dates:** NR	**Enrolled:** 69 **Analyzed:** 69 **Completed:** 69	**Treatment duration:** ≥ 12 wk **Run-in phase:** NR **Run-in phase duration:** NR	**Benefits:** C-GAS, CGI-S, CGI-I, response	In tic-related pediatric OCD, augmentation of

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Condition category: OCD **Funding:** No funding provided **Risk of Bias:** High (subjective), Medium (objective)	**Study design:** NRCT (parallel) **Diagnostic criteria:** DSM-IV, K-SADS-PL (OCD), DSM-IV-TR (Tic) **Setting:** Outpatient **Inclusion criteria:** Diagnosis of OCD, CGI score ≥ 4 and C-GAS score ≤ 60. Comorbid tic disorder, ≥ 40 on YGTSS, non-responder to SSRI **Exclusion criteria:** Diagnosis of mental retardation, PDD, schizophrenia	**GROUP 1:** **N:** 35 **Age, mean±SD (range):** 13.3±2.2 yr **Males %:** 94.3% **Caucasian %:** NR **Diagnostic breakdown (n):** OCD with comorbid tic disorder (35) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** GAD (7), separation AD (4), panic disorder (2), social phobia (13), simple phobia (4), depression (8), BP (6), ADHD (6), ODD (9) **GROUP 2:** **N:** 34 **Age, mean±SD (range):** 13.9±2.5 yr **Males %:** 85.3% **Caucasian %:** NR **Diagnostic breakdown (n):** OCD with comorbid tic disorder (34) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** GAD (1), separation AD (1), panic disorder (1), social phobia (6), depression (4), BP (2), ADHD (14), ODD (7)	**Permitted drugs:** SSRI **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** Variable **Target dose (mg/day):** 3 mg/day **Daily dose (mg/day), mean±SD (range):** 1.7±0.8 (0.5-3) mg/day **Concurrent treatments:** SSRI (35), mood stabilizers (3), stimulants (1), psychotherapy (20) **GROUP 2:** **Drug name:** Aripiprazole **Dosing variability:** Variable **Target dose (mg/day):** 12.5 mg/day **Daily dose (mg/day), mean±SD (range):** 8.9±3.1 (2.5-12.5) mg/day **Concurrent treatments:** SSRI (34), mood stabilizers (1), stimulants (1), psychotherapy (14)	**Harms:** Weight, sedation, tremors	SSRIs with risperidone or aripiprazole was tolerated and effective in about half of the patients who did not respond to SSRIs alone.
McCracken et al., 2002 [56]	**Recruitment dates:** Jun 1999 to Apr 2001	**Enrolled:** 101 **Analyzed:** 101	**Treatment duration:** 8 wk **Run-in phase:** Yes	**Benefits:** ABC, CYBOCS, CGI-I,	Risperidone was effective and well

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Completed: 80	**Run-in phase duration:** 1–4 wk	CGI-S, RFRLRS, VAS, AIMS, Cognitive, medication adherence, patient, parent/care provider reported outcomes (diet/intake, sleep), response **Harms:** Behavioral issues, blood cells, BMI, constipation, dyskinesia, dermatologic AE, ECG changes, EPS (AIMS, SAS), fatigue, liver function, prolactin, prolactin-related AE, SAE, seizure, tachycardia, WAE, weight change	tolerated for the treatment of tantrums, aggression, or self-injurious behavior in children with autistic disorder. Discontinuation, after 6 month of treatment, was associated with rapid return of disruptive and aggressive behavior in most subjects.
Country: USA **Condition category:** ASD **Funding:** Industry, Government, Foundation **Risk of bias:** Medium (subjective), Medium (objective)	**Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, ADI-R **Inclusion criteria:** (1) ASD (DSM-IV), (2) 5–17 yr, (3) weight ≥15 kg, (4) score ≥18 on the Irritability subscale of the ABC at baseline, (5) free of serious medical disorders and of other psychiatric disorders requiring medication, (6) medication free for at least 2 wk for all psychotropic medications (4 wk for fluoxetine or depot neuroleptics), (7) anticonvulsants used for the treatment of a seizure disorder were permitted if the dosage had been stable for 4 wk and the patient had been seizure free for ≥6 mo, (8) CGI-S score ≥ 4 at baseline, (9) mental age ≥18 mo as measured by the age-appropriate form of the IQ test, (10) inpatients or outpatients	**GROUP 1** **N:** 49 **Age, mean±SD (range):** NR **Males %:** 80 **Caucasian %:** NR **Treatment naïve (n):** 45 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (average/above average IQ (3), borderline IQ (8), mild/ moderate retardation (20), severe retardation (15)) **GROUP 2** **N:** 52 **Age, mean±SD (range):** NR **Males %:** 83 **Caucasian %:** NR **Treatment naïve (n):** 51 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (average/above average IQ (2), borderline IQ (4), mild/ moderate retardation (23), severe retardation (16))	**Permitted drugs:** anticonvulsants (constant dose ≥4 wk and seizure-free for ≥6 mo), benztropine **Prohibited drugs:** antihistamines, ceterazine, erythromycin, metoclopromide, pseudoephedrine, and any drug that may impact risperidone concentrations or lead to drug interactions; psychotropics **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.8±0.7 (0.5–3.5) **Concurrent treatments:** anticonvulsants (2) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.4±0.6 (0.5–3.5) **Concurrent treatments:** anticonvulsants (2)		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	Exclusion criteria: (1) receiving a psychotropic drug that was deemed effective for the treatment of aggression, tantrums, or self-injurious behavior, (2) positive β-HCG pregnancy test, (3) evidence of a prior adequate trial with risperidone, (4) evidence of hypersensitivity to risperidone, (5) past history of NMS, (6) DSM-IV dx of schizophrenia, another psychotic disorder, or substance abuse, (7) significant medical condition, (8) weight <15 kg				
McGorry et al., 2013 [57] **Country:** Australia **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** August 2000 to May 2006 **Study design:** RCT (parallel) **Setting:** Outpatient **Diagnostic criteria:** Ultra-high risk: (1) the presence of attenuated (subthreshold) psychotic symptoms within the previous 12 months; (2) a history of brief self-limited psychotic symptoms, which spontaneously	**Enrolled:** 87 **Analyzed:** NR **Completed:** 56 **GROUP 1** **N:** 43 **Age, mean±SD (range):** 17.6±3.0 **Males %:** 35 **Caucasian %:** NR **Treatment naïve (n):** 100 **Inpatients (n):** 0 **First episode psychosis (n):** UHR **GROUP 2** **N:** 44 **Age, mean±SD (range):** 18.0±2.7	**Treatment duration:** 52 wk **Run-in phase:** NA **Run-in phase duration:** NA **Permitted drugs:** NR **Prohibited drugs:** mood-stabilizing medications **GROUP 1** **Drug name:** Cognitive therapy + risperidone **Dosing variability:** variable **Target dose (mg/day):** up to 2mg/day **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** BPRS, SANS, GAF, HDRS, quality of life, transition rates **Harms:** UKU	The equivalent transition rates fail to provide support for the first-line use of antipsychotic medications in patients at ultra-high risk of psychosis, and an initial approach with supportive therapy is likely to be effective and carries fewer risks.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	resolve, within the previous 12 months; and (3) a presumed genetic vulnerability to psychotic disorder plus persistent low functioning for at least 1 month within the previous 12 months **Inclusion criteria:** 14-30 yrs; see above criteria **Exclusion criteria:** (1) known history of a previous psychotic or manic episode, (2) history of a medical condition that may account for symptoms leading to initial referral (eg, epilepsy), (3) clinically relevant neurologic, biochemical, or hematologic abnormalities, (4) serious coexisting illnesses, (5) lifetime antipsychotic dose of 15mg of haloperidol (or equivalent) or greater, (6) any previous or current use of mood-stabilizing medication, (7) history of severe drug allergy, (8) intellectual disability (IQ < 70), (9) pregnancy or lactation,	**Males %:** 39 **Caucasian %:** NR **Treatment naïve (n):** 100 **Inpatients (n): 0** **First episode psychosis (n):** UHR	**GROUP 2** **Drug name:** Cogntive therapy + placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0 **Concurrent treatments:** NR		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	(10) insufficient English language				
Migliardi et al., 2009 [120] **Country:** Italy **Condition category:** Mixed conditiopns **Funding:** NR **Risk of bias:** 7/8 stars	**Recruitment dates:** NR **Study design:** Retrospective cohort **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) children and adolescents seen at the Division of Child and Neurology at the University of Messina, Italy, (2) not previously treated with antipsychotics for various psychiatric disorders, (3) completed at least 12 months of treatment on only one antipsychotic and no co-medication **Exclusion criteria:** NR	**Enrolled:** 42 **Analyzed:** 41 **Completed:** 42 **GROUP 1** **N:** 13 **Age, mean±SD (range):** 14.1 **Males %:** 53.8 **Caucasian %:** NR **Treatment naïve (n):** all **Diagnostic breakdown (n):** DBD (4), early-onset schizophrenia (3), BD (2), autism/PDD (2), OCD (1) **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 29 **Age, mean±SD (range):** 10.7 **Males %:** 78.6 **Caucasian %:** NR **Treatment naïve (n):** all **Diagnostic breakdown (n):** Autism/PDD (13), DBD (9), early-onset schizophrenia (2), OCD (2), Tic disorder (2) **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** NR	**Treatment duration:** 12 mo **Run–in phase:** No **Run–in phase duration:** NA **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 8.1 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.8 **Concurrent treatments:** NR	**Benefits:** NA **Harms:** prolactin-related AE, prolactin	After adjusting for dose and greater potency of risperidone, the increase in prolactin levels during risperidone treatment was 10.3 times higher than during olanzapine treatment.
Miral et al., 2008 [58] **Country:** Turkey **Condition**	**Recruitment dates:** NR **Study design:** RCT (parallel)	**Enrolled:** 30 **Analyzed:** 28 **Completed:** 28 **GROUP 1**	**Treatment duration:** 24 wk **Run-in phase:** Yes **Run-in phase duration:** 1–2 wk **Permitted drugs:** antianalgesics,	**Benefits:** ABC, CGI, RFRLRS **Harms:** Blood pressure,	Risperidone was more effective than haloperidol, showing improvements in behavioral

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
category: ASD **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Setting:** NR **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 8–18 yr, (2) parental informed consent, (3) agree to followup **Exclusion criteria:** (1) epilepsy, (2) concomitant neuropsychiatric illness, (3) psychotic disorder or symptoms, (4) other PDDs	**N:** 15 **Age, mean±SD (range):** 10.9±2.9 (7–17) **Males %:** 86.7 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (0), psychosis (0) **GROUP 2** **N:** 15 **Age, mean±SD (range):** 10±2.7 (7–17) **Males %:** 73.3 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (0), psychosis (0)	antibiotics, anticholinergics, antipyretics, decongestants **Prohibited drugs:** benzodiazepines/other sedatives **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** 0.08 mg/kg/day **Daily dose (mg/day), mean±SD (range):** 2.6±1.3 (1–5.7) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** 0.08 mg/kg/day **Daily dose (mg/day), mean±SD (range):** 2.6±0.8 (1.2–4.0) **Concurrent treatments:** NR	constipation, EPS (ESRS, UKU), height, parkinsonism/ dystonia/ dyskinesia (ESRS), prolactin-related AE, SAE, weight	symptoms and social skills.
Mozes et al., 2006 [59] **Country:** Israel **Condition category:** Schizophrenia and related **Funding:** No funding **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV, K-SADS **Inclusion criteria:** (1) hospitalized childhood-onset schizophrenic children **Exclusion criteria:** (1) MR	**Enrolled:** 25 **Analyzed:** 25 **Completed:** 20 **GROUP 1** **N:** 12 **Age, mean±SD (range):** 11.5±1.6 (8.5–14) **Males %:** 41.7 **Caucasian %:** NR **Diagnostic breakdown (n):** disorganized schizophrenia (3), paranoid schizophrenia (2), schizophreniform disorder (6), unspecified schizoprehenia (1) **Treatment naïve (n):** NR	**Treatment duration:** 2.8 mo **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** biperiden, prior nonantipsychotics (continued for 2–12 wk) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 8.2±4.4 (2.5–20) **Concurrent treatments:** biperiden (2), carbamazepine (2), citalopram	**Benefits:** BPRS, CGAS, PANSS, response **Harms:** BAS, SAS akathisia, prolactin, WAE, weight change	Risperidone and olanzapine were efficacious and well tolerated in pediatric inpatients with child-onset schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Inpatients (n): all **First episode psychosis (n):** NR **Comorbidities:** ADHD (2), familial mediterranean fever (1), MR (0), tic disorder (1) **GROUP 2** **N:** 13 **Age, mean±SD (range):** 10.7±1.4 (8.8–13.3) **Males %:** 38.5 **Caucasian %:** NR **Diagnostic breakdown (n):** disorganized schizophrenia (4), paranoid schizophrenia (4), schizophreniform disorder (4), unspecified schizoprehenia (1) **Treatment naïve (n):** NR **Inpatients (n):** all **First episode psychosis (n):** NR **Comorbidities:** ADHD (1), epilepsy (2), MR (0), neurofibromatosis (1), OCD (3)	(1), colchicine (1), methylphenidate (2), promethizine (2), valproic acid (1) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.6±1 (0.3–4.5) **Concurrent treatments:** biperiden (4), citalopram (2), fluoxetine (1), phenytoin (1), promethizine (1), valproic acid (1)		
Nagaraj et al., 2006 [60] **Country:** India **Condition category:** ASD **Funding:** Industry, Academic **Risk of bias:** Low (subjective), Low	**Recruitment dates:** Jan 2002 to Dec 2003 **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1)	**Enrolled:** 40 **Analyzed:** 39 **Completed:** 39 **GROUP 1** **N:** 19 **Age, mean±SD (range):** 4.8±1.7 **Males %:** 84.2 **Caucasian %:** NR **Treatment naïve (n):** 15 **Inpatients (n):** 0 **First episode psychosis**	**Treatment duration:** 6 mo **Run-in phase:** Yes **Run-in phase duration:** ≥1 mo **Permitted drugs:** antiepileptics **Prohibited drugs:** no other drugs permitted **GROUP 1** **Drug name:** Risperidone **Dosing variability:** fixed **Target dose (mg/day):** NR	**Benefits:** CARS, CGAS, response (CARS, CGAS, Global Impression of Parents) **Harms:** Dyskinesia, sedation, weight change	Risperidone improved global functioning and social responsiveness, reduced hyperactivity and aggression, and was well tolerated in children with autism.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(objective)	≤12 yr, (2) autism (DSM-IV) **Exclusion criteria:** (1) severe MR, (2) any significant coexisting disease or illness, (3) severe malnutrition	**(n):** NR **Comorbidities:** aggression (9), irritability (17), seizures (5), self-injurious behavior (7) **GROUP 2** **N:** 21 **Age, mean±SD (range):** 5.3±1.7 **Males %:** 90 **Caucasian %:** NR **Treatment naïve (n):** 16 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** aggression (11), irritability (19), seizures (3), self-injurious behavior (5)	**Daily dose (mg/day), mean±SD (range):** 1 (0.5–1) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1 (0.5–1) **Concurrent treatments:** NR		
NCT00194012, 2013 [61] **Country:** USA **Condition category:** Bipolar **Funding:** Industry, Institution (hospital) **Risk of bias:** High (subjective). High (objective)	**Recruitment dates:** August 2004-May 2012 **Study design:** RCT **Setting:** Outpatient **Diagnostic criteria:** (1) DSM-IV criteria for either cyclothymia, or BP NOS based on K-SADS-PL and WASH-U K-SADS, (2) a clinical interview with a child and adolescent psychiatrist **Inclusion criteria:** (1) outpatient, (2) 5-17	**Enrolled:** 59 **Analyzed:** NR **Completed:** 21 (15 Group 1; 6 Group 2) **GROUP 1** **N:** 30 **Age, mean±SD (range):** <18 yr (all) **Males %:** 66.7 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** None **First episode psychosis (n):** NR **GROUP 2** **N:** 29 **Age, mean±SD (range):** <18 yr (all) **Males %:** 51.7 **Caucasian %:** NR	**Treatment duration:** 12 wk, plus 6 wk open label extension **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** psychotropic agents taken <1 wk of baseline (2 wk for fluoxetine; 3 days for psychostimulants) **GROUP 1** **Drug name:** Abilify (aripiprazole) **Dosing variability:** 2-15 mg **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo	**Benefits:** YMRS **Harms:** AEs (major and minor)	NR

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	yr, (3) symptoms of mania, depression, or both <2 wk, (4) offspring of a parent with BP spectrum disorder, (5) another 1st or 2nd degree relative with a mood disorder, (6) participated in ≥4 sessions of psychotherapy and continues to have clinically significant symptomatology **Exclusion criteria:** intolerance to APZ at doses of 0.1mg/kg/day, (2) manic episode with APZ monotherapy at a dose of 0.2 mg/kg/day, (3) contraindications for which tx with APZ, (4) ASD, Asperger's disorder, Rett's syndrome or other PDD, (5) mental retardation, (6) allergic or hypersensitive to APZ, (7) unable to swallow pills/capsules, (8) hospitalization during the study, (9) started a new psychotherapeutic intervention <4 wk prior to randomization, (10) general medical or	**Treatment naïve (n):** NR **Inpatients (n):** None **First episode psychosis (n):** None	**Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	neurological condition that: i) may be the etiology of the pts mood disorder, ii) contraindicate tx with an AAP, iii) may interfere with the interpretation of clinical response to APZ; (11) other psychotropic agents <1 wk of baseline (2 wk for fluoxetine; 3 days for psychostimulants); (12) <6 mo prior to randomization: i) a suicide attempt requiring medical/ psychiatric, ii) met DSM-IV criteria for SA, (13) pt who are pregnant or lactating, (14) sexually active females, not using an adequate birth control				
NCT00619190, 2013 [121] **Country:** USA **Condition category:** ASD **Funding:** Institution (University)	**Recruitment dates:** NR **Study design:** Controlled before-after study **Setting:** NR **Diagnostic criteria:** NR	**Enrolled:** 30 **Analyzed:** **Completed:** 29 **GROUP 1** **N:** 21 **Age, mean±SD (range):** 8.3±3.75 **Males %:** 90.5 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR	**Treatment duration:** 12 wk **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Apriprazole **Dosing variability:** 1-30 mg **Target dose (mg/day):** NR	**Benefits:** ABC-I, CGI-S, ABC-Lethargy/Social Withdrawal **Harms:** AEs (major and minor)	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Newcastle-Ottawa Scale: 4/8	**Inclusion criteria:** NR **Exclusion criteria:** NR	**First episode psychosis (n):** NR **GROUP 2** **N:** 9 **Age, mean±SD (range):** 11.1±4.5 **Males %:** 88.9 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** No medication **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
NCT01149655, 2014 [62] **Country:** Multiple countries **Condition category:** Schizophrenia and related **Funding:** Industry (pharmaceutical) **Risk of bias:** High (subjective). High (objective)	**Recruitment dates:** July 2011-Dec 2013 **Study design:** RCT **Setting:** Outpatient **Diagnostic criteria:** DSM-IV-TR diagnosis of schizophrenia **Inclusion Criteria:** (1) schizophrenia, (2) hx of illness ≥6 mo prior to screening, (3) shown previous response to antipsychotic tx (other than clozapine), (4) currently being treated with oral or depot antipsychotics other than clozapine, (5) hx of relapse and/or exacerbation of symptoms when off antipsychotic tx.	**Enrolled:** 146 **Analyzed:** **Completed:** 21 (15 (group 1), 6 (groupd 2)) **GROUP 1** **N:** 98 **Age, mean±SD (range):** 15.3±1.3 (male); 15.4±1.1 (female) **Males %:** 63.3 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 48 **Age, mean±SD (range):** 15.6±1.1 (males), 15.3±1.0 (females) **Males %:** 70.8 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 52 wk **Run-in phase:** Yes (stabilized on 10-30 mg/day of aripiprazole prior to randomization) **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Apriprazole **Dosing variability:** 10-30 mg/day **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** Relapse Rate (CGI-I/S, PANSS, hospitalization, suicide ideation, violent/aggressive behavior), % exacerbation or relapse/impending relapse, % responders, % achieved remission, % discontinued, CGAS **Harms:** AEs (minor and serious)	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	Exclusion criteria: (1) dx other than schizophrenia, (2) delirium, dementia, amnesia or other cognitive disorders, (3) psychotic symptoms better accounted for by another medical condition(s) or direct effect of a substance, (4)comorbid dx of ADD or ADHD, (5) tx with stimulants at any time over the last 1 yr prior to screening, (6) any neurodevelopmental disorder, except Tourette's syndrome, (7) acute depressive symptoms ≤30 days prior to screening, (8) DSM-IV-TR criteria for substance dependence ≤180 days prior to screening, (9) Hx of: epilepsy, seizures, severe head trauma, stroke, or other unstable medical conditions, subclinical hypothyroidism (TSH ≥ 4.0 mIU/L), known hypothyroidism or hyperthyroidism (unless stabilized with medication for ≥ 90 days prior to entry into Phase 1 or Phase 2), uncontrolled diabetes, labile or unstable diabetes (brittle				

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	diabetes), newly diagnosed diabetes, or clinically significant abnormal blood glucose levels				
Norris et al., 2011 [122] **Country:** Canada **Condition category:** Eating disorders (Anorexia nervosa) **Funding:** Non-industry **Newcastle-Ottawa Scale:** 7/8 stars	**Recruitment dates:** Jan 2000 to Dec 2006 **Study design:** Retrospective **Setting:** inpatient and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 10-17 yr, (2) female, (3) diagnosed with AN or EDNOS according to DSM-IV **Exclusion criteria:** (1) males, (2) concurrent diagnosis of psychosis, or a concurrent illness with psychotic features, or whose primary treatment was not under the direction of the eating disorder team	**Enrolled:** 86 **Analyzed:** 86 **Completed:** 86 **GROUP 1** **N:** 43 **Age, mean±SD (range):** 14.4±1.9 yr **Males %:** 0 **Caucasian %:** NR **Diagnostic breakdown (n):** ANR (29), ANBP (2), EDNOS-R (12) **Treatment naïve (n):** NR **Inpatients (n):** 35 **First episode psychosis (n):** NR **Comorbidities:** Anxiety (29), depression (26), obsessive compulsive disorder (3) **GROUP 2** **N:** 43 **Age, mean±SD (range):** 14.8±1.6 yr **Males %:** 0 **Caucasian %:** NR **Diagnostic breakdown (n):** ANR (29), ANBP (2), EDNOS-R (12) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities: :** Anxiety (13), depression (15),	**Treatment duration:** 2 wk for weight outcomes **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** SSRI/SNRI (17), benzodiazepine (3) (at the time of olanzapine initiation) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** flexible **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** [median (IQR)] 5.0 (3.75-7.5) **Concurrent treatments:** SSRI/SNRI (17), benzodiazepine (3) **GROUP 2** **Drug name:** Not olanzapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** CDI, MASC, EDI-2DT, EDI-2BD **Harms:** change in body composition (weight, BMI), dyslipidemia, liver function test, sedation, rebound weight loss and increased psychological stress after initial discontinuation of olanzapine	Patients treated with olanzapine presented with greater acuity and more complex psychopathology than those patients not treated with olanzapine, which made comparisons regarding efficacy of the drug impossible. The observed side-effect profile noted in patients treated with olanzapine indicates the need for close monitoring during the entire course of treatment, regardless of the patient's absolute weight.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		obsessive compulsive disorder (1)			
Novaes et al., 2008 [123] **Country:** Brazil **Condition category:** ASD **Funding:** Foundation **Newcastle-Ottawa Scale:** 8/8 stars	**Recruitment dates:** Jan 2001 to June 2006 **Study design:** Retrospective cohort **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) ASD, (2) behavioral disturbances (psychomotor agression or agitation) **Exclusion criteria:** NR	**Enrolled:** NA **Analyzed:** 26 **Completed:** 26 **GROUP 1** **N:** 1 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** Aggression/Agitation (26), MR (20) **GROUP 2** **N:** 13 and 5 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** see group 1 **GROUP 3** **N:** 4 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR	**Treatment duration:** 17 mo (mean) **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Typical antipsychotic **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone/Risperidone + Typical antipsychotic **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 3** **Drug name:** Atypical antipsychotic (not risperidone) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 4** **Drug name:** Typical + atypical antipsychotic	**Benefits:** Response (CGI-I) **Harms:** NR	SGAs appeared to reduce agitation and aggression in patients with ASD.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Inpatients (n): NR **First episode psychosis (n):** NR **Comorbidities:** see group 1 **GROUP 4** **N:** 3 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	**Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** one treatment (12), ≥2 treatments (7)		
O'Donoghue et al., 2014 [124] **Country:** Austria **Condition category:** Schizophrenia and related **Funding:** NR **Newcastle-Ottawa Scale:** 3/8 stars	**Recruitment dates:** January 2001 to August 2005 **Study design:** Prospective cohort **Setting:** NR **Diagnostic criteria:** DSM-III **Inclusion criteria:** (1) 13-17 yr, (2) schizophrenia spectrum disorder, (3) no previous antipsychotic medications **Exclusion criteria:** (1) IQ <70	**Enrolled:** 44 **Analyzed:** 36 **Completed:** 36 **GROUP 1** **N:** 16 **Age, mean±SD (range):** 15.9±1.2 (all groups) **Males %:** 58 **Caucasian %:** NR **Treatment naïve (n):** 16 **Inpatients (n):** NR **First episode psychosis (n):** 16 **GROUP 2** **N:** 20 **Age, mean±SD (range):** 15.9±1.2 (all groups) **Males %:** 58 **Caucasian %:** NR **Treatment naïve (n):** 20 **Inpatients (n):** NR **First episode psychosis**	**Treatment duration:** mean 31 wk **Run-in phase:** No **Run-in phase duration:** NA **Permitted drugs:** SSRI **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine & quetiapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** SSRI (31% all groups) **GROUP 2** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR	**Benefits:** NR **Harms:** triglycerides, BMI, cholesterol	One-third of children and adolescents had abnormal serum triglycerides and cholesterol; however, a dose–response was not demonstrated. Olanzapine and quetiapine had a greater increase in serum triglycerides.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		(n): 20	**Concurrent treatments:** SSRI (31% all groups)		
Oh et al., 2013 [125] **Country:** South Korea **Condition category:** Bipolar I, II, NOS **Funding:** NR **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Jan 2010 to Oct 2011 **Study design:** Retrospective **Setting:** Outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) Male and female outpatients, (2) aged 4 to 18 years, (3) DSM-IV diagnosis of bipolar I disorder, bipolar II disorder, bipolar disorder, and bipolar affective disorder **Exclusion criteria:** (1) Another diagnosis as main reason for treatment (eg: tic disorder, ADHD), (2) who visited the clinic only once or did not take medication	**Enrolled:** 183 **Analyzed:** 127 **Completed:** 32 **GROUP 1** **N:** 62 **Age, mean±SD (range):** 13.16±2.80 yr **Males %:** 66.1 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** See below **GROUP 2** **N:** 65 **Age, mean±SD (range):** 11.46±3.95 yr **Males %:** 76.9 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** See below **Overall comorbidities:** ADHD (50), tic related disorders (17), conduct disorders and ODD (5), autism spectrum disorder	**Treatment duration:** 7-8 mo **Run–in phase:** NR **Run–in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 9.58±5.38 **Concurrent treatments:** See below **GROUP 2** **Drug name:** Others **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** Risperidone (1.46±1.08), quetiapine (207.46±200.53), paliperidone (4.50±2.12) **Concurrent treatments:** See below **Overall concurrent treatments:** mood stabilizers (20), methyphenidate (34), atomoxetine (12), antidepressants (27)	**Benefits:** ADHD RS-IV, CGI-S, CGI-I **Harms:** Akathisia, sedation, nausea	The early treatment effects and long-term tolerability of aripiprazole were found to be excellent compared with those of other atypical antipsychotics. The superior treatment effects of aripiprazole, which was also associated with comparatively mild side effects, may enhance the treatment compliance of pediatric patients and their guardians. However, these results must be confirmed in the future through multi-center, double-blind, placebo-control studies.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		(12)			
Olfson et al., 2012 [126] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** Government **Newcastle-Ottawa Scale:** 7/8 stars	**Recruitment dates:** Medicaid claims file 2001-2005 **Study design:** Retrospective cohort **Setting:** Inpatients (<10%) and outpatients **Diagnostic criteria:** ICD-9-CM **Inclusion criteria:** (1) 6-17 yr, (2) eligible for Medicaid (fee-for-service plans) for ≥180 days after antipsychotic Initiation, (3) schizophrenia and related disorders **Exclusion criteria:** (1) not enrolled in Medicare, (2) free of any antipsychotic prescriptions for at least 180 continuous days before filling a risperidone, olanza-pine, aripiprazole, quetiapine, or ziprasidone prescrip-tion of ≤30 days supply	**Enrolled:** 1745 **Analyzed:** 1745 **Completed:** NA **GROUP 1** **N:** 805 **Age, mean±SD (range):** NR **Males %:** 62 **Caucasian %: 38** **Treatment naïve (n):** 805 **Inpatients (n):** **First episode psychosis (n):** NR **GROUP 2** **N:** 382 **Age, mean±SD (range):** NR **Males %:** 69 **Caucasian %:** 38 **Treatment naïve (n):** 382 **Inpatients (n):** **First episode psychosis (n):** NR **GROUP 3** **N:** 260 **Age, mean±SD (range):** NR **Males %:** 52 **Caucasian %: 48** **Treatment naïve (n):** 260 **Inpatients (n):** **First episode psychosis (n):** NR **GROUP 4** **N:** 173	**Treatment duration:** **Run-in phase:** **Run-in phase duration:** **Permitted drugs:** None **Prohibited drugs:** None **GROUP 1** **Drug name:** Risperidone **Dosing variability:** **Target dose (mg/day):** **Daily dose (mg/day), mean±SD (range):** **Concurrent treatments:** **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** **Target dose (mg/day):** **Daily dose (mg/day), mean±SD (range):** **Concurrent treatments:** **GROUP 3** **Drug name:** Quetiapine **Dosing variability:** **Target dose (mg/day):** **Daily dose (mg/day), mean±SD (range): Concurrent treatments:** **GROUP 4** **Drug name:** Aripiprazole **Dosing variability:** **Target dose (mg/day):** **Daily dose (mg/day), mean±SD (range): Concurrent treatments:** **GROUP 5**	**Benefits:** Medication adherence (all-cause discontinuation), psychiatric hospital admission **Harms:** NR	The results suggest that rapid antipsychotic medication discontinuation and psychiatric hospital admission are common in the community treatment of early-onset schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Age, mean±SD (range): NR **Males %:** 55 **Caucasian %: 42** **Treatment naïve (n):** 173 **Inpatients (n):** **First episode psychosis (n):** NR **GROUP 5** **N:** 125 **Age, mean±SD (range):** NR **Males %:** 57 **Caucasian %:** 44 **Treatment naïve (n):** 125 **Inpatients (n):** **First episode psychosis (n):** NR	**Drug name:** Ziprasidone **Dosing variability:** **Target dose (mg/day): Daily dose (mg/day), mean±SD (range):** **Concurrent treatments:**		
Omranifard et al, 2013 [63] **Country:** Iran **Condition category:** Behavioral issues **Funding:** Institution (University) **Risk of bias:** High (subjective), NA (objective)	**Recruitment dates:** 2009 **Study design:** RCT **Setting:** Outpatient **Diagnostic criteria:** NR **Inclusion criteria:** (1) informed consent; (2) boys and girls 3-7 yr; (3) dx masturbation problem by a psychiatrist; (4) masturbates as a daily habit **Exclusion criteria:** (1) any condition that would interfere with the safe study	**Enrolled:** 90 **Analyzed:** 87 **Completed:** 87 **GROUP 1** **N:** 42 **Age, mean±SD (range):** 5.3±1.1 **Males %:** 52.3 **Caucasian %:** NR **Diagnostic breakdown (n):** **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 45 **Age, mean±SD (range):** 49.9±1.1 **Males %:** 57.7 **Caucasian %:** NR	**GROUP 1** **Drug name:** risperidone **Dosing variability:** 0.25-1 mg/d **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** Efficacy (frequency of masturbation) **Harms:** None	In contrast to the behavioral treatment which was only effective in younger ages in the control group, the addition of risperidone to the behavioral treatment was effective in all ages.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	participation; (2) any current neurological or axis I psychiatric disorders that needs chronic drug treatment; (3) treated for masturbation in the last month; (4) infection of genitalia.	**Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR			
Owen et al., 2009 [64] **Country:** USA **Condition category:** ASD **Funding:** Industry **Risk of bias:** Medium (subjective), Low (objective)	**Recruitment dates:** June 2006 to April 2008 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, ADI-R, CGI-S, ABC-I **Inclusion criteria:** (1) 6–17 yr, (2) DSM-IV-TR criteria for autistic disorder and behaviors such as tantrums, aggression, self–injury, or a combination, with a dx corroborated by ADI-R certified trainer, (3) CGI-S score ≥4 and ABC Irritability subscale score ≥18 at screening and baseline, (4) ≥15 kg, (5) stable nonpharmacologic therapy **Exclusion criteria:** (1) bipolar disorder,	**Enrolled:** 164 **Analyzed:** 98 **Completed:** 75 **GROUP 1** **N:** 47 **Age, mean±SD (range):** 9.7±3.2 **Males %:** 89.4 **Caucasian %:** 68.1 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NA **GROUP 2** **N:** 51 **Age, mean±SD (range):** 8.8±2.6 **Males %:** 86.3 **Caucasian %:** 80.4 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NA	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** ≤6 wk **Permitted drugs:** anxiolytics, benztropine or propranolol, diphenhydramine (≤50 mg/day), psychotropic medication, sleep aids **Prohibited drugs:** antidepressants, antipsychotics, anxiolytics, mood stabilizers, neuroleptics, psychostimulants (washout ≥4 day), fluoxetine, olanzapine/fluoxetine (washout ≥4 wk before screen visit) **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** flexible **Target dose (mg/day):** 5, 10, 15 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics and antipyretics hypnotics and sedatives **GROUP 2** **Drug name:** Placebo **Dosing variability:** flexible **Target dose (mg/day):** 5, 10, 15 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:**	**Benefits:** ABC, CYBOCS, CGI-I, CGI-S, PedsQL, CGSQ, response (ABC-I, CGI-I), suicide **Harms:** EPS (AIMS, BAS, SAS), fatigue, glucose, lipid profile, prolactin, LDL, total cholesterol, HDL, somnolence, aggression, total AE, weight change	During an 8-week period, aripiprazole was efficacious and generally well tolerated in the treatment of irritability associated with autistic disorder in children and adolescents who may be experiencing tantrums, aggression, self-injurious behavious, or a combination ofthese symptoms.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	psychosis, schizophrenia, major depression, fragile X syndrome, or another ASD, (2) history of NMS, (3) significant risk of committing suicide, (4) seizure in the past yr, (5) history of severe head trauma or stroke, (6) history or current evidence of any unstable medical condition or or an abnormal laboratory test result considered clinically significant, (7) antipsychotic treatment resistant, (8) known allergy or hypersensitivity to aripiprazole		analgesics and antipyretics, hypnotics and sedatives		
Pandina et al., 2007 [127] (see Aman 2002, Snyder 2002) **Country:** Canada, South Africa, USA **Condition category:** ADHD **Funding:** NR **Newcastle-Ottawa Scale:** 6/8 stars	**Study design:** Observational (pooled analysis)	**Enrolled:** NA **Analyzed:** 228 **Completed:** NA **GROUP 1** **N:** 108 **Age, mean±SD (range):** 8.6 yr **Males %:** 81 **Caucasian %:** 64 **Diagnostic breakdown (n):** CD (40), ODD (29), Axis 1 (34), BD NOS (5) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (78)	**GROUP 1** **Drug name:** Risperidone **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.3±0.7 mg/day **Concurrent treatments:** See Aman 2002 and Snyder 2002 **GROUP 2** **Drug name:** Placebo **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** See Aman 2002 and Snyder 2002	**Benefits:** continuous performance task (CPT), VLT-C **Harms:** NA	Cognitive function was not altered by risperidone in short term studies.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		GROUP 2 **N:** 88 **Age, mean±SD (range):** 8.4 yr **Males %:** 77 **Caucasian %:** 68 **Diagnostic breakdown (n):** CD (48), ODD (30), Axis 1 (37), BD NOS (5) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (77)			
Pathak et al., 2013 [65] **Country:** USA **Condition category:** Bipolar I (manic) **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Aug 2004 to Jul 2006 **Study design:** RCT (parallel) **Setting:** Inpatient/outpatient **Diagnostic criteria:** DSM-IV, KID-SCAD-PL **Inclusion criteria:** (1) Male and female inpatients and outpatients, (2) aged 10 to 17 years, (3) DSM-IV diagnosis of Bipolar I mania as confirmed by K-SADS-PL, (4) YMRS total score of ≥20 at both screening and randomization, (5) permitted to have secondary diagnosis of	**Enrolled:** 284 **Analyzed:** 277 **Completed:** 222 **GROUP 1** **N:** 93 **Age, mean±SD (range):** 13.1±2.2 **Males %:** 50.5 **Caucasian %:** 78.5 **Diagnostic breakdown (n):** manic (92), mixed (1) **Treatment naïve (n):** 68 **Inpatients (n):** NR **First episode psychosis (n):** 6 **Comorbidities:** ADHD (49) **GROUP 2** **N:** 95 **Age, mean±SD (range):** 13.2±2.2 **Males %:** 57.9 **Caucasian %:** 76.8 **Diagnostic breakdown (n):** manic (91), mixed (4)	**Treatment duration:** 3 wk **Run–in phase:** Yes **Run–in phase duration:** 1–28 day **Permitted drugs:** Psychostimulants, diphenhydramine, hydroxyzine, lorazepam, benztropine **Prohibited drugs:** Prophylactic use of benztropine **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 400 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** 600 **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** CGAS, CGI-BP-S, CGI-BP-I, YMRS,CDRS-R, OAS-M, CGSQ, response, remission, suicidal ideation, aggression, bipolar disorder exacerbation **Harms:** EPS (AIMS, BAS, SAS), akathisia, mortality, weight gain, somnolence, fatigue, glucose measures, lipid values, liver function, thyroid function, prolactin, tachycardia, pulse, heart rate, ECG changes, hematology values,	Quetiapine at 400 mg/d and 600 mg/d was significantly more effective than placebo for treating acute manic symptoms in youth with bipolar I disorder. Quetiapine at these doses was generally well tolerated and AE were consistent with the profile of quetiapine in adults with bipolar disorder.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	ADHD **Exclusion criteria:** (1) Current DSM-IV-diagnosed Axis I disorder other than bipolar I disorder or ADHD, (2) history of serious suicide attempts, (3) current risk for suicide or homicide in the judgment of investigators	**Treatment naïve (n):** 79 **Inpatients (n):** NR **First episode psychosis (n):** 6 **Comorbidities:** ADHD (40) **GROUP 3** **N:** 89 **Age, mean±SD (range):** 13.3±2.1 **Males %:** 60.7 **Caucasian %:** 74.2 **Diagnostic breakdown (n):** manic (all) **Treatment naïve (n):** 74 **Inpatients (n):** NR **First episode psychosis (n):** 7 **Comorbidities:** ADHD (35)	**GROUP 3** **Drug name:** Placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Perry et al., 1989 [66] **Country:** USA **Condition category:** ASD **Funding:** Industry, Government, Foundation **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-III-TR **Inclusion criteria:** (1) dx of infantile autism, full syndrome present, (2) only children with good response to haloperidol and requiring further drug treatment were accepted into the study	**Enrolled:** 70 **Analyzed:** 60 **Completed:** 52 **GROUP 1** **N:** 34 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 36 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR	**Treatment duration:** 6 mo **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol (continuous) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.2 (0.5–4) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Haloperidol (discontinuous) **Dosing variability:** variable	**Benefits:** CGI-I, Response (CGI-I, CGI-S) **Harms:** Dyskinesia, parkinsonism, sedation	Haloperidol, administered on a long-term basis, effectively reduced maladaptive symptoms in austic children. Drug efficacy was not deminished by discontinuous drug administration.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Treatment naïve (n): NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1 (0.5–4.0) **Concurrent treatments:** NR		
	Exclusion criteria: (1) identifiable cause for autism, (2) seizure disorder, (3) preexisting movement disorder				
Pogge et al., 2005 [128] **Country:** USA **Condition category:** Mixed conditions **Funding:** NR **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** NR **Study design:** Prospective **Setting:** Inpatient **Diagnostic criteria:** NR **Inclusion criteria:** All adolescent inpatients discharged from a private psychiatric hospital during a 2 yr period who received 1 of the medications (olanzapine, risperidone) as an inpatient and a follow up prescription **Exclusion criteria:** NR	**Enrolled:** 86 **Analyzed:** 86 **Completed:** 86 **GROUP 1** **N:** 43 **Age, mean±SD (range):** See below **Males %:** See below **Caucasian %:** See below **Diagnostic breakdown (n):** Depressive disorder (11), mood disorder NOS (10), SUD (8), DBD (7), psychotic disorder (9), anxiety disorder (7), BP (8), ADHD (4), ED (1) **Treatment naïve (n):** 0 **Inpatients (n):** 43 **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 43 **Age, mean±SD (range):** See below **Males %:** See below **Caucasian %:** See below **Diagnostic breakdown (n):** Depressive disorder (26), mood disorder NOS (7), SUD (7), DBD (8), psychotic disorder (3), anxiety disorder (5), BP	**Treatment duration:** 12 wk -18 mo follow up **Run-in phase:** NA **Run-in phase duration:** NA **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** NA **Harms:** Weight	The general lack of significant relationships between symptoms or diagnosis, other than substance abuse, and non adherence is not surprising, given heterogeneity of the sample and the general tendencies toward non adherence on the part of adolescents with both medical and psychiatric conditions.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		(2), ADHD (3), ED (1) **Treatment naïve (n):** 0 **Inpatients (n):** 43 **First episode psychosis (n):** NR **Comorbidities:** NR **Overall age, mean±SD (range):** 14.9±1.3 yr **Overall males %:** 41.9 **Overall Caucasian %:** 65.1			
Ratzoni et al., 2002 [129] **Country:** Israel **Condition category:** Schizophrenia and related **Funding:** Government, Foundation **Newcastle-Ottawa Scale:** 3/8 stars	**Recruitment dates:** Jan 2000 to Aug 2000 **Study design:** Prospective cohort **Setting:** Inpatient **Diagnostic criteria:** DSM-IV, K-SADS-PL (Hebrew version), consensus of 2 child psychiatrists **Inclusion criteria:** (1) adolescent patients who started treatment with olanzapine, risperidone, or haloperidol from Jan to Aug 2000 **Exclusion criteria:** (1) receiving other medications that cause weight gain/loss, (2) alcohol/substance abuse, (3) medical illnesses affecting body	**Enrolled:** 50 **Analyzed:** 50 **Completed:** 36 **GROUP 1** **N:** 8 **Age, mean±SD (range):** 17.3±1.3 (15–19) **Males %:** 62.5 **Caucasian %:** NR **Treatment naïve (n):** 1 **Inpatients (n):** all **First episode psychosis (n):** NR **GROUP 2** **N:** 21 **Age, mean±SD (range):** 17±1.6 (14–19) **Males %:** 66.7 **Caucasian %:** NR **Treatment naïve (n):** 2 **Inpatients (n):** all **First episode psychosis (n):** NR **GROUP 3** **N:** 21 **Age, mean±SD (range):**	**Treatment duration:** 2.8 mo **Run-in phase:** Yes **Run-in phase duration:** 5.2 day (mean) **Permitted drugs:** anticholinergics, lorazepam **Prohibited drugs:** antipsychotics, heterocyclic antidepressants, lithium, medications that can cause weight gain/loss, SSRIs, valproic acid **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.6±4 (3–15) **Concurrent treatments:** biperiden (6), lorazepam (5), trihexyphenidyl (2) **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD	**Benefits:** PANSS, medication adherence **Harms:** Akathisia, behavioral issues, BMI, constipation, dermatologic AE, dystonia, any EPS, fatigue, hypokinesia-akinesia, sedation, seizure, sexual desire, tachycardia, WAE, weight	Adolsecents experienced greater weight gain when taking olanzapine or risperidone compared to effects reported in adults.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	weight	17.1±2.1 (13–20.5) **Males %:** 57.1 **Caucasian %:** NR **Treatment naïve (n):** 3 **Inpatients (n):** all **First episode psychosis (n):** NR	**(range):** 12.7±3.1 (7.5–20) **Concurrent treatments:** biperiden (6), lorazepam (5), trihexyphenidyl (2) **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.2±1.1 (1–5) **Concurrent treatments:** biperiden (6), lorazepam (5), trihexyphenidyl (2)		
Remington et al., 2001 [67] **Country:** Canada **Condition category:** ASD **Funding:** Non-industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (crossover) **Setting:** NR **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) DSM-IV diagnosis of autism confirmed independently bt two investigators, (2) evidence that haloperidol or clomipramine had not been used previously, or, if so, that an adequate therapeutic trial was not completed **Exclusion criteria:** NR	**Enrolled:** 37 **Analyzed:** 33 **Completed:** 23/33 (H), 12/32 C, 21/32 (P) **GROUP 1** **N:** 33 **Age, mean±SD (range):** 16.3 (10–36) yr **Males %:** 83.3 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**Treatment duration:** 7 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk before and between each arm of the treatment regimen **Permitted drugs:** benztropine **Prohibited drugs:** no other antipsychotic medications **GROUP 1** **Drug name:** Chlomipramine-Placebo-Haloperidol (CPH), PHC, HCP **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1-1.5 **Concurrent treatments:** NR	**Benefits:** ABC, CARS **Harms:** fatigue, ESRS, dystonia, depression, ECG, arrythmias	Results favor haloperidol over clomipramine in the treatment of autistic disorder. The two agents demonstrated comparable improvement when compared with baseline if there was a full therapeutic trial; however, significantly fewer individuals treated with clomipramine were able to do this, for reasons related both to side effects and efficacy.
Reyes et al., 2006 [68]	**Recruitment dates:** Aug 2001 to Sep 2003	**Enrolled:** 335 **Analyzed:** 335	**Treatment duration:** 7.4 mo **Run-in phase:** Yes	**Benefits:** CGAS, CGI-I, CGI-S,	Patients who responded to initial

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Completed: 162	**Run-in phase duration:** 6 wk	NCBRF, VAS-MS Cognitive (MVLT, CPT), growth (tannar stages), response (relapse, symptom recurrence) **Harms:** Akathisia, BMI, dystonia, EPS, fatigue, parkinsonism, prolactin, prolactin-related AE, SAE, somnolence, tardive dyskinesia, total AE, WAE, weight change	treatment with risperidone benefited from continued, long-term treatment. Risperidone was safe and well tolerated during a 1-year extension.
Country: Belgium, Germany, Great Britain, Israel, Netherlands, Poland, South Africa, Spain **Condition category:** ADHD **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV, K-SADS-PL **Inclusion criteria:** (1) 5–17 yr, (2) no moderate or severe intellectual impairment (IQ ≥55), (3) CD serious enough to warrant clinical treatment, (4) score ≥24 on the conduct problem subscale of the NCBRF, (5) responsible caregiver **Exclusion criteria:** (1) schizophrenia and bipolar disorder	**GROUP 1** **N:** 172 **Age, mean±SD (range):** 10.9±2.9 **Males %:** 82 **Caucasian %:** NR **Diagnostic breakdown (n):** CD (62), DBD NOS (3), ODD (107) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (117) **GROUP 2** **N:** 163 **Age, mean±SD (range):** 10.8±2.9 **Males %:** 91 **Caucasian %:** NR **Diagnostic breakdown (n):** CD (61), DBD NOS (5), ODD (97) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (110)	**Permitted drugs:** medication for EPS (only after dose reduction attempted), psychostimulants **Prohibited drugs:** anticonvulsants, antidepressants, antipsychotics, lithium **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 0.8±0.3 (<50 kg), 1.2±0.4 (≥50 kg) **Concurrent treatments:** analgesics (26), psychostimulants (36) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics (20), psychostimulants (36)		
Rizzo et al., 2012 [69] **Country:** Italy **Condition category:** Tic disorders	**Recruitment Dates:** NR **Study design:** NRCT (parallel) **Diagnostic criteria:** DSM-IV-TR	**Enrolled:** 75 **Analyzed:** 75 **Completed:** 75 **GROUP 1:** **N:** 25 **Age, mean±SD (range):** 11.6 ±2.2 yr **Males %:** 88%	**Treatment duration:** 24 mo **Run-in phase:** Yes **Run-in phase duration:** 4 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1**	**Benefits:** NR **Harms:** BMI, glycemia, triglyceridemia, cholesterolemia	Pimozide and aripiprazole have slightly different contraindications for use in children with Tourette syndrome. Pimozide may be less well-suited to diabetic patients.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Funding: Non-industry **Risk of Bias:** High (subjective), High (objective)	**Setting:** Outpatients **Inclusion criteria:** TS according to DSM-IV-TR, from Neurology Unit of Catania University **Exclusion criteria:** NR	**Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (25) **Treatment naïve (n):** (1) **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** OCD (11), ADHD (3) **GROUP 2:** **N:** 25 **Age, mean±SD (range):** 11.2±3.1 yr **Males %:** 92% **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (25) **Treatment naïve (n):** (22) **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** OCD (9), ADHD (5) **GROUP 3:** **N:** 25 **Age, mean±SD (range):** 10.2±2.8 yr **Males %:** 88% **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (25) **Treatment naïve (n):** (25) **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** OCD (0), ADHD (2)	**Drug name:** Aripiprazole **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.25-15 mg/day **Concurrent treatments:** Fluoxetine (10), Biperiden cloridrate (7) **GROUP 2:** **Drug name:** Pimozide **Dosing variability:** Variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1-4 mg/day **Concurrent treatments:** Fluoxetine (7), Biperiden cloridrate (12) **GROUP 3:** **Drug name:** No medication **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		Patients with predisposition to cholesterol problems may require closer monitoring when taking aripiprazole.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Ronsley et al., 2015 [130] **Country:** Canada **Condition category:** Mixed conditions **Funding:** Industry **Newcastle-Ottawa Scale:** 4/8 stars	**Recruitment dates:** Feb 2009 to Mar 2012 **Study design:** Prospective Cohort **Setting:** Outpatient **Diagnostic criteria:** DSM-IV-TR **Inclusion criteria:** (1) 2-18 years of age (2) having a mental health condition diagnosed based on the DSM-IV-TR, (3) SGA treatment with either risperidone or quetiapine independently initiated by a psychiatrist less than 7 days before study consent; and never previously exposed to an SGA. **Exclusion criteria:** pre-existing DM (types 1 or 2), diagnosis of an eating disorder, treatment with more than 1 antipsychotic, ortreatment with other medications known to affect meatbolism.	**Enrolled:** 130 **Analyzed:** 37 **Completed:** 37 **GROUP 1** **N:** 20 **Age, mean±SD (range):** 14 **Males %:** 50 **Caucasian %:** 40 **Diagnostic breakdown (n):** Psychotic disorders (5), mood disorder (1), depressive disorder (3), bipolar disorder(3), ADHD(4), ODD(4), Anxiety disorder(6), adjustment disorder(1), mental retardation or personality disorder(2) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 17 **Age, mean±SD (range):** 14.1 **Males %:** 47.1 **Caucasian %:** 52.9 **Diagnostic breakdown (n):** Psychotic disorders (4), mood disorder (3), depressive disorder (5), bipolar disorder(3), ADHD(4), PDD(1), Anxiety disorder(7), reactive attachment disorder(2), mental retardation or personality disorder(5)	**Treatment duration:** 12 months **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR **GROUP 2** **Drug name:** Quetiapine **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** NR **Harms:** weight, BMI, waist circumference, blood pressure, laboratory parameters	Children treated with risperidone or quetiapine are at a significant risk for developing obesity, elevated waist circumference, and dyslipidemia during 12 months of treatment. These data emphasize the importance for early idenification and treatment of metabolic side effects.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Treatment naïve (n): all **Inpatients (n):** NR **First episode psychosis (n):** NR			
RUPP et al., 2005 [70] **Country:** USA **Condition category:** ASD **Funding:** Industry/ Non-industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) responders at the end of 4 mo extension study. For initial inclusion criteria refer to McCracken 2002 **Exclusion criteria:** NR. For initial exclusion criteria refer to McCracken 2002	**Enrolled:** 38 **Analyzed:** NR **Completed:** 32 **GROUP 1** **N:** 16 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** see below **Diagnostic breakdown (n):** NR **Treatment naïve (n):** see below **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see below **GROUP 2** **N:** 16 **Age, mean±SD (range):** see below **Males %:** see below **Caucasian %:** see below **Diagnostic breakdown (n):** NR **Treatment naïve (n):** see below **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see below **Overall age, mean±SD**	**Treatment duration:** 8 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** anticonvulsant treatment if child had been taking stable dose for 4 wk and had been free of seizures for 6 mo **Prohibited drugs:** other psychotropic medication **GROUP 1** **Drug name:** Risperidone **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.5 (15-45 kg), 4.5 (>45 kg) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 25% dosage reduction/wk **Concurrent treatments:** NR	**Benefits:** Relapse, ABC **Harms:** NR	Risperidone showed persistent efficacy and good tolerability for intermediate-length treatment of children with autism characterized by tantrums, aggression, and/or self-injurious behavior. Discontinuation after 6 months was associated with a rapid return of disruptive and aggressive behavior in most subjects.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		(range): 9.0±2.5 yr **Overall males %:** 86.8 **Caucasian %:** 60.5 **Overall treatment naïve (n):** 7 **Overall comorbidities:** IQ average (2), IQ borderline (5), MR (27)			
Saito et al., 2004 [131] **Country:** USA **Condition category:** Mixed conditions **Funding:** Government **Newcastle-Ottawa Scale:** 6/8 stars	**Recruitment dates:** Sept 2001 to Mar 2003 **Study design:** Prospective cohort **Setting:** Inpatient/outpatient **Diagnostic criteria:** NR **Inclusion criteria:** (1) male and females, (2) aged 5 to 18 years, (3) treatment naïve or at least a 1-month interval since their last treatment with antipsychotic agents, (4) inpatients or outpatients at a suburban children's hospital **Exclusion criteria:** (1) females receiving hormonal contraception	**Enrolled:** 40 **Analyzed:** 40 **Completed:** 40 **GROUP 1** **N:** 13 **Age, mean±SD (range):** all groups: 13.4±3.4 (5–18) **Males %:** all groups: 55 **Caucasian %:** NR **Diagnostic breakdown (n):** all groups: schizophrenia or other psychosis (14), mood disorders (14), DBD (9), intermittent explosive disorder (1), PDD NOS (1), eating disorder NOS (1) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR **GROUP 2** **N:** 6 **Age, mean±SD (range):** see group 1 **Males %:** see group 1 **Caucasian %:** NR **Diagnostic breakdown (n):** see group 1	**Treatment duration:** 11.2 wk **Run–in phase:** Yes **Run–in phase duration:** 1 mo. **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 7.8±4.2 **Concurrent treatments:** all groups: divalproex sodium (7), lithium (5), SSRI (11), stimulants (9), benzodiazepines (3), alpha-adrenergic agonists (3) **GROUP 2** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 283.3±222.9 **Concurrent treatments:** see group 1 **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**	**Benefits:** NA **Harms:** prolactin, prolactin-related AEs	Prolactin levels were significantly increased in children and adolescents treated with risperidone, compared to those treated with olanzapine or quetiapine.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Treatment naïve (n): NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR **GROUP 3** **N:** 21 **Age, mean±SD (range):** see group 1 **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** see group 1 **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR	**(range):** 2.2±2 **Concurrent treatments:** see group 1		
Sallee et al., 2000 [73] **Country:** USA **Condition category:** Tic disorders **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 7–17 yr, (2) DSM-IV dx of Tourette syndrome or chronic tic disorder, with symptoms severe enough to warrant medication, (3) not pregnant or breast feeding	**Enrolled:** 28 **Analyzed:** 27 **Completed:** 24 **GROUP 1** **N:** 16 **Age, mean±SD (range):** 11.3 (7–14) **Males %:** 87.5 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (9), DBD (4), OCD (10; all groups), learning disability (2; all groups) **GROUP 2**	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 4–8 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Ziprasidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 28.2±9.6 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR	**Benefits:** CGI-TS, CYBOCS, YGTSS **Harms:** Akathisia, prolactin, prolactin-related AESAE, sedation, somnolence, total AE, WAE, weight change	Ziprasidone was well tolerated in children and adolscents with Tourette syndrome, and may also be an effective anti-tic medication.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	Exclusion criteria: (1) secondary tic disorder, (2) DSM-IV criteria for major depression, PDD, autism, MR, anorexia nervosa/bulimia, substance abuse, or any psychotic disorder	**N:** 12 **Age, mean±SD (range):** 11.8 (8–16) **Males %:** 66.7 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (6), DBD (1), OCD (10; all groups), learning disability (2; all groups)	**Concurrent treatments:** NR		
Sallee et al., 1997 [72] **Country:** USA **Condition category:** Tic disorders **Funding:** Industry, Government **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (crossover) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-III-TR, K-SADS-P **Inclusion criteria:** (1) principal DSM-III-R dx of Tourette syndrome; may have multiple Axis I and II dx, (2) 7–16 yr, 11 mo, (3) TSGS score >20, (4) previous exposure to neuroleptics permitted, but treatment must have been withdrawn ≥2 wk before baseline **Exclusion criteria:** (1) chronic motor tic	**Enrolled:** 22 **Analyzed:** 22 **Completed:** 22 **GROUP 1** **N:** 22 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (13), OCD (5) **GROUP 2** **N:** 22 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** >2 wk **Permitted drugs:** diphenhydramine hydrochloride **Prohibited drugs:** adjunctive treatment, anticholinergics, concomitant medications **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.5±2.2 (1–8) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Pimozide **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.4±1.6 (1–6) **Concurrent treatments:** NR	**Benefits:** CGAS, CGI-S Medication adherence, response **Harms:** Akathisia, akinesia, behavioral issues, electrocardiovascular, EPS (AIMS, ESRS), prolactin, treatment limiting AE, WAE, weight change	Pimozide is superior to haloperidol for controlling symptoms of Tourette syndrome in children and adolescents.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	disorder or transient tic disorder, (2) serious medical illness, (3) abnormal ECG, (4) inability to perform required measurements, (5) use of concurrent medication that may alter or interact with haloperidol or pimozide, (6) history of drug or alcohol abuse, (7) autism or childhood schizophrenia	**Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see G1 **GROUP 3** **N:** 22 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see G1	**GROUP 3** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		
Sallee et al., 1994 [71] **Country:** USA **Condition category:** Tic disorders **Funding:** Foundation **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-III-TR, TSGS **Inclusion criteria:** (1) consecutive outpatient children who met DSM-III-R criteria for Tourette syndrome and severity criteria using the TSGS **Exclusion criteria:** NR	**Enrolled:** 41 **Analyzed:** 41 **Completed:** NR **GROUP 1** **N:** 17 **Age, mean±SD (range):** 10.4 **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (6) **GROUP 2** **N:** 24 **Age, mean±SD (range):** 10.8 **Males %:** NR	**Treatment duration:** 6 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.5±0.6 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Pimozide **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.7±1.4 **Concurrent treatments:** NR	**Benefits:** CBCL-TRF, cognitive (CPT, MST) **Harms:** NR	The effect of pimozide treatment on cognition was superior to haloperidol in children with Tourette syndrome with comorbid ADHD.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Caucasian %: NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (7)			
Savitz et al., 2015 [74] **Country:** India, Romania, Russia, Slovakia, Spain, Ukraine, and the United States **Condition category:** Schizophrenia and related **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** November 2009 to June 2012 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 12-17 yr, (2) body weight ≥ 29kg, (3) diagnosis of schizophrenia ≥1yr, (4) Positive and Negative Symptom Score (PANSS) total score of 60 to 120 (inclusive) at screening, (5) ≥1 prior adequate treatment with antipsychotic medication, (6) clinician belief that suboptimnal current treatment **Exclusion criteria:** (1) diagnosis of BD, MDD, schizoaffective	**Enrolled:** 228 **Analyzed:** 226 **Completed:** 174 **GROUP 1** **N:** 112 **Age, mean±SD (range):** 15.2±1.5 **Males %:** 65 **Caucasian %:** 75 **Treatment naïve (n):** 13 **Inpatients (n):** 70 (at screening) **First episode psychosis (n):** 0 **GROUP 2** **N:** 114 **Age, mean±SD (range):** 15.4±1.5 **Males %:** 67 **Caucasian %:** 77 **Treatment naïve (n):** 11 **Inpatients (n):** 68 (at screening) **First episode psychosis (n):** 0	**Treatment duration:** 8wk acute, 18 wk maintenance **Run-in phase:** Yes **Run-in phase duration:** ≤3 wks **Permitted drugs:** antidepressants, certain benzodiazepines, and non-benzodiazepine hypnotics; anticholinergics, topical antifungal agents, antihistamines, anti-inflammatory drugs except systemic corticosteroids, histamine-2 (H2) blockers, and rescue medications for the treatment of restlessness, agitation, insomnia, or extrapyra-midal symptoms **Prohibited drugs:** antipsychotics, psychostimulants or other dopamine agonists, certain sedatives (including barbiturates), hypnotics, or anxiolytics, mood stabilizers or anticonvulsants, electroconvulsive therapy, inhibitors or inducers of CYP3A4 or CYP2D6 **GROUP 1** **Drug name:** Paliperidone ER **Dosing variability:** variable **Target dose (mg/day):** 6 mg per day [days 1–7], flexibly dosed 3, 6, or 9mg per day from day 8 to end of study [EOS] **Daily dose (mg/day), mean±SD**	**Benefits:** PANSS, maintenance of stability, CGI-S, response **Harms:** AIMS, BAS, SAS, any AE, C-SSRS, prolactin, weight, ECG, glucose, insulin, lipids	Palirperidone ER did not demonstrate superiority to aripiprazole in treating adolescent schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	disorder, schizophreniform disorder, ASD, MR, primary substance-induced psychotic disorder, dissociative disorder or SUD in 3 months before screening, (2) history of seizure disorder, neuroleptic malignant syndrome, encephalopathic syndrome, tardive dyskinesia, or insulin-dependent diabetes mellitus, (3) receiving clozapine (2 months before screening), (4) depot antipsychotic therapy within 2 treatment cycles before screening, or electroconvulsive therapy (3 months before baseline visit), (5) sexually nonabstinent girls who were pregnant, nursing, or of childbearing capacity.		**(range):** 6.75±1.8 **Concurrent treatments:** anti-EPS medications or antihistamines (26%) **GROUP 2** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** 2 mg per day ([days 1 and 2], 5 mg per day [days 3 and 4], 10 mg per day [days 5–7], flexibly dosed 5, 10, or 15 mg per day from day 8 to EOS **Daily dose (mg/day), mean±SD (range):** 11.6±3.0 **Concurrent treatments:** anti-EPS medications or antihistamines (25%)		
Scahill et al., 2003 [75] **Country:** USA **Condition category:** Tic disorders **Funding:** Industry, Government	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, joint parent	**Enrolled:** 26 **Analyzed:** 26 **Completed:** NR **GROUP 1** **N:** 12 **Age, mean±SD (range):** 11.1 (2.20) yrs (whole pediatric sample) **Males %:** 96% (whole pediatric sample)	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 1–2 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable	**Benefits:** CGI-I, YGTSS Response **Harms:** Weight, EPS, social phobia	For short-term treatment of tics in children, risperidone appeared to be safe and effective.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	and child interview	**Caucasian %:** NR	**Target dose (mg/day):** 3		
Risk of bias: Medium (subjective), Medium (objective)	**Inclusion criteria:** (1) 7–65 yr, (2) Tourette syndrome (DSM-IV), (3) Total Tic score ≥22 on the YGTSS **Exclusion criteria:** (1) evidence of current major depression, GAD, separation anxiety disorder, or psychotic symptoms (clinical evaluation or DSM-IV), (2) WISC age-appropriate IQ <70, (3) prior adequate trial of risperidone (dose ≥1.0 mg/day for ≥2 wk), (4) psychotropic medication within 2 wk, (5) significant medical problem, (6) moderate or greater obsessive-compulsive symptoms (YBOCS>15)	**Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (11), MR (0), OCD (4) **GROUP 2** **N:** 14 **Age, mean±SD (range):** See group 1 **Males %:** see group 1 **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** see group 1	**Daily dose (mg/day), mean±SD (range):** 2.5±0.9 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** 3 **Daily dose (mg/day), mean±SD (range):** 3.3±0.9 **Concurrent treatments:** NR		
Schneider et al., 2012 [76] **Country:** USA **Condition category:** Bipolar I (manic, mixed) **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) 10-17 yr, (2) DSM-IV-	**Enrolled:** 23 **Analyzed:** 17 **Completed:** 11 **GROUP 1** **N:** 14 **Age, mean±SD (range):** 14.7±2.3 yr **Males %:** 64 **Caucasian %:** 86 **Diagnostic breakdown (n):** mixed (9) **Treatment naïve (n):** see below	**Treatment duration:** 4 wk **Run-in phase:** Yes **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Ziprasidone **Dosing variability:** variable **Target dose (mg/day):** ≥45kg: 120-160, <45kg: 60-80 **Daily dose (mg/day), mean±SD**	**Benefits:** YMRS, response, medication adherence **Harms:** NR	Further research is needed to determine whether treatment related increases in ventral prefrontal activation are associated with improvements in sustained attention and other executive function domains, if there are differences in patterns of change patients

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	TR bipolar I disorder confirmed with K-SADS-PL, (3) YMRS score ≥16 at both screening and baseline **Exclusion criteria:** (1) dx of substance abuse or dependence in the previous month for any substance other than nicotine or caffeine, (2) being clinically stable on a well-tolerated treatment regimen, (3) prior treatment with ziprasidone, a known allergy to ziprasidone, or a serious suicidal risk, (4) any history of head injury resulting in loss of consciousness for > 10 minutes, or any unstable medical or neurological disorder.	**Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (3) **GROUP 2** **N:** 9 **Age, mean±SD (range):** 14.5±2.2 yr **Males %:** 22 **Caucasian %:** 89 **Diagnostic breakdown (n):** mixed (9) **Treatment naïve (n):** see below **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (7) **Overall Treatment naïve (n):** 7	**(range):** 20 [initial dose] **Concurrent treatments:** all groups: benztropine (1), lorazepam (1) **GROUP 2** **Drug name:** Placebo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR		experiencing manic versus mixed episodes, as well as to investigate whether functional alterations in specific regions of ventral prefrontal cortex may be useful as specific biomarkers of ziprasidone response in patients with mania.
Sehgal et al., 1999 [77] **Country:** USA **Condition category:** Tic disorders **Funding:** Industry, Government, Foundation **Risk of bias:** Medium (subjective), NA	**Recruitment dates:** Oct 1993 to Nov 1995 **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-III-TR **Inclusion criteria:** (1) DSM-III-R diagnostic criteria for Tourette syndrome at participating medical	**Enrolled:** 10 **Analyzed:** 10 **Completed:** 8 **GROUP 1** **N:** 4 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 8 mo **Run-in phase:** Yes **Run-in phase duration:** 4 mo **Permitted drugs:** NR **Prohibited drugs:** antidepressants, benzodiazepines, clonidine, stimulants (washout ≥2 wk prior to enrolment) **GROUP 1** **Drug name:** Pimozide (short-term) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD**	**Benefits:** Response **Harms:** Tardive dyskinesia, sedation	In children with Tourette syndrome, longer term treatment with pimozide appears to be more effective on the course of tics than a short-term course of the drug used to suppress an acute exacerbation of tics.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
(objective)	centers **Exclusion criteria:** NR	**Comorbidities (n):** NR **GROUP 2** **N:** 6 **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** NR	**(range):** 3. 8 (2–6) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Pimozide (long-term) **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 3.5 (1–7) **Concurrent treatments:** NR		
Shaw et al., 2006 [78] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** NR **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** Jan 1998 to June 2005 **Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV, K-SADS, medical and school record review, interview with child and parents **Inclusion criteria:** (1) schizophrenia with definite onset of symptoms ≤13 yr , (2) IQ >70, (3) no history of progressive neurological or medical disorders, (4) failure to respond to 2 antipsychotic medications (typical or atypical) used at	**Enrolled:** 25 **Analyzed:** 25 **Completed:** 24 **GROUP 1** **N:** 12 **Age, mean±SD (range):** 11.7±2.3 **Males %:** 66.7 **Caucasian %:** 58.3 **Treatment naïve (n):** 0 **Inpatients (n):** all **First episode psychosis (n):** 0 **Comorbidities:** ADHD (4), anxiety disorders (6), MR (0) **GROUP 2** **N:** 13 **Age, mean±SD (range):** 12.8±2.4 **Males %:** 53.8 **Caucasian %:** 53.8 **Treatment naïve (n):** 0 **Inpatients (n):** all **First episode psychosis**	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 3 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 327±113 (150–500) **Concurrent treatments:** diphenhydramine hydrochloride (4), guanfacine hydrochloride (1), lorazepam (2), sedatives (4), ≤4 hr specialized education, recreational and occupational therapy **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 18.1±4.3	**Benefits:** BPRS-24, CGI-S, SANS, SAPS, response **Harms:** Behavioral issues, blood cells, blood pressure, constipation, dermatologic AE, ECG changes, STESS, AIMS, SAS, lipid profile, seizure, sleepiness, somnolence, tachycardia, weight change, BMI change	Clozapine had a more favorable profile of clinical response and adverse events than olanzapine.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	adequate doses (>100 mg chlorpromazine equivalents) and for adequate duration (>4 wk unless terminated owing to intolerable adverse effects) **Exclusion criteria:** (1) nonresponse to an adequate trial of olanzapine or clozapine (8 wk of olanzapine at 20 mg/d or of clozapine at 200 mg/d)	**(n):** 0 **Comorbidities:** ADHD (3), anxiety disorders (1), MR (0)	**Concurrent treatments:** clomipramine hydrochloride (1), diphenhydramine hydrochloride (6), lorazepam (3), sedatives (3), valproate sodium (2), ≤4 hr specialized education, recreational and occupational therapy		
Shea et al., 2004 [79] **Country:** Canada **Condition category:** ASD **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) physically healthy outpatients, (2) 5–12 yr, (3) DSM-IV Axis I dx of PDD, (4) a total score >30 on the CARS with or without MR **Exclusion criteria:** (1) patients with schizophrenia, other psychotic disorders, clinically relevant	**Enrolled:** 80 **Analyzed:** 79 **Completed:** 72 **GROUP 1** **N:** 41 **Age, mean±SD (range):** 7.6±0 (5–12) **Males %:** 72.5 **Caucasian %:** NR **Diagnostic breakdown (n):** Asperger's disorder (5), autistic disorder (27), childhood disintegrative disorder (1), PDD NOS (7), Rett disorder (0) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (15) **GROUP 2** **N:** 39 **Age, mean±SD (range):** 7.3±0 (5–12)	**Treatment duration:** 8 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** anticholinergics, anticonvulsants and/or medications for sleep or anxiety (constant dose ≥30 days before enrolment), medications for preexisting organic disorders **Prohibited drugs:** α-2 antagonists, antidepressants, antipsychotics, cholinesterase inhibitors, clonidine, guanfacine, lithium, naltrexone, psychostimulants **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.2 **Concurrent treatments:** analgesics (15), anti-asthmatics (6), antibiotics (5), anticholinergics (3), cough and	**Benefits:** ABC, NCBRF, VAS-MS Response (ABC-I, CGI-C) **Harms:** Anorexia, behavioral issues, blood pressure, constipation, EPS (ESRS), fatigue, hyperkinesias, pulse, SAE, somnolence, tachycardia, tardive dyskinesia, total AE, WAE, weight change	In children with ASD, risperidone was well tolerated and efficacious in the treatment of autism associated behavioral symptoms.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	nonneurologic disease, clinically significant laboratory abnormalities, or a seizure disorder for which they were receiving >1 anticonvulsant or if they had had a seizure in the last 3 mo, (2) history of hypersensitivity to neuroleptics, tardive dyskinesia, NMS, drug or alcohol abuse, or HIV infection, (3) used risperidone in the last 3 mo or previously unresponsive or intolerant to risperidone, (4) using a prohibited medication	**Males %:** 82.1 **Caucasian %:** NR **Diagnostic breakdown (n):** Asperger's disorder (7), autistic disorder (28), childhood disintegrative disorder (0), PDD NOS (4), Rett disorder (0) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (12)	cold preparations (10), sedatives/hypnotics (11) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** analgesics (7), anti-asthmatics (4), antibiotics (5), anticholinergics (1), cough and cold preparations (4), sedatives/hypnotics (9)		
Sikich et al., 2008 [81] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** Government **Risk of bias:** Low (subjective), Low (objective)	**Recruitment dates:** Feb 2002 to May 2006 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, KID-SCID **Inclusion criteria:** (1) 8–19 yr (30% or fewer 16 or older), (2) DSM-IV dx of schizophrenia, schizoaffective disorder, or schizophreniform disorder with current	**Enrolled:**116 **Analyzed:** NR **Completed:** 70 **GROUP 1** **N:** 41 **Age, mean±SD (range):** NR **Males %:** 57.5 **Caucasian %:** 70 **Diagnostic breakdown (n):** schizoaffective disorder (14), schizophrenia (26) **Treatment naïve (n):** 16 **Inpatients (n):** 4 **First episode psychosis (n):** 35 **Comorbidities:** ADHD (12), affective disorder (9),	**Treatment duration:** 8 wk (10.1 mo extension) **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** antidepressants or non-antipsychotic mood stabilizers (≥4 wk prior to study entry); anticholinergics, benzodiazepines, propranolol (concomitant); thymoleptics (maintenance phase) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Molindone **Dosing variability:** variable **Target dose (mg/day):** 140 **Daily dose (mg/day), mean±SD**	**Benefits:** BPRS-C, CGI-I, CGI-S, CAFAS, PANSS, medication adherence, response, suicide **Harms:** Akathisia, behavioral issues, blood pressure, BMI, constipation, dystonia, ECG changes, SAS, BAS, AIMS, EPS, glucose, homeostasis, insulin, lipid profile, liver function, prolactin, prolactin-related AE, pulse, SAE, sedation, tardive dyskinesia,	Rispiridone and olanzapine failed to show superior efficacy over molindone in the treatment of early-onset schizophrenia and schizoaffective disorder.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	positive psychotic symptoms of at least moderate intensity, (PANSS or BRRS-C), (3) good physical health, (4) able to provide informed consent and guardian's written informed consent **Exclusion criteria:** (1) premorbid dx of MR, (2) current major depressive episode, active substance abuse, (3) history of intolerance or nonresponse to any of the study treatments during a prior episode, (4) history of successful use of the study treatments during the current episode (≥8 wk of treatment, including ≥2 wk at the maximal dose allowed in the current study), (5) imminent risk of harming themselves or others, (6) bipolar disorder, primary PTSD, primary personality disorder, or psychosis NOS (dx by clinician, confirmed by KID-SCID), (7) endocrinological or neurological conditions that confound the dx or	anxiety disorder (6), ASD (2), DBD (4), learning disability (7), MR (0), none (14), psychosis (7), SA (4) **GROUP 2** **N:** 36 **Age, mean±SD (range):** NR **Males %:** 71.4 **Caucasian %:** 60 **Diagnostic breakdown (n):** schizoaffective disorder (13), schizophrenia (22) **Treatment naïve (n):** 13 **Inpatients (n):** 2 **First episode psychosis (n):** 33 **Comorbidities:** ADHD (13), affective disorder (7), anxiety disorder (9), ASD (2), DBD (6), learning disability (1), MR (0), none (17), psychosis (4), SA (2) **GROUP 3** **N:** 42 **Age, mean±SD (range):** NR **Males %:** 65.9 **Caucasian %:** 61 **Diagnostic breakdown (n):** schizoaffective disorder (13), schizophrenia (28) **Treatment naïve (n):** 9 **Inpatients (n):** 6 **First episode psychosis (n):** 40 **Comorbidities:** ADHD (9), affective disorder (12),	**(range):** 59.9±33.5 (10–140) **Concurrent treatments:** antidepressants (4), benzodiazepines (39%), mood stabilizers (3), propranolol (13%), benzotropine (45%) **GROUP 2** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** 20 **Daily dose (mg/day), mean±SD (range):** 11.4±5 (2.5–20) **Concurrent treatments:** antidepressants (4), benzodiazepines (20%), benztropine (14%), mood stabilizers (2), propranolol (11%) **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** 6 **Daily dose (mg/day), mean±SD (range):** 2.8±1.4 (0.5–6) **Concurrent treatments:** antidepressants (5), benzodiazepines (41%), benztropine (34%), mood stabilizers (4), propranolol (7%)	total AE, WAE, weight change	

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	are a contraindication to treatment, (8) pregnancy or refusal to practice contraception during the study, (9) use of a depot antipsychotic within the past 6 mo	anxiety disorder (12), ASD (3), DBD (10), learning disability (2), MR (0), none (15), psychosis (6), SA (2)			
Sikich et al., 2004 [80] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** Industry, Government, Foundation **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Nov 1997 to May 2001 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, K-SADS-P **Inclusion criteria:** (1) ≥1 positive psychotic symptom of moderate or greater severity on the BPRS-C, present throughout the past 2 wk, (2) full scale IQ >69, (3) patients with current or recent dx of ADHD, Tourette syndrome, OCD, or a history of substance abuse or dependence were allowed to participate only if their psychotic symptoms were not better accounted for by the comorbid disorder **Exclusion criteria:** (1) psychotic symptoms resulting from acute	**Enrolled:** 50 **Analyzed:** 50 **Completed:** 32 **GROUP 1** **N:** 15 **Age, mean±SD (range):** 15.4±2.2 **Males %:** 53 **Caucasian %:** 73 **Diagnostic breakdown (n):** affective disorders (7), schizophrenia spectrum (8) **Treatment naïve (n):** 3 **Inpatients (n):** 10 **First episode psychosis (n):** 12 **GROUP 2** **N:** 16 **Age, mean±SD (range):** 14.6±3.1 **Males %:** 56 **Caucasian %:** 63 **Diagnostic breakdown (n):** affective disorders (11), schizophrenia spectrum (5) **Treatment naïve (n):** 8 **Inpatients (n):** 12 **First episode psychosis (n):** 12	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 1–2 wk **Permitted drugs:** amantadine (200 mg/day), antidepressants and mood stabilizers (if taken ≥4 wk preceding study entry or if clinically significant affective symptoms persisted after 4 wk of study treatment), benztropine (1–3 mg/day), lorazepam (0.5–3 mg/day), propranolol (20–60 mg/day), trihexyphenidyl (4–6 mg/day) **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** 1–5 **Daily dose (mg/day), mean±SD (range):** 5±2 (1–5) **Concurrent treatments:** amantadine (1), benztropine/trihexyphenidyl (7), buproprion (4), citalopram (1), gabapentin (1), lithium (1), lorazepam (3), paroxetine (1), sertraline (3), valproate (2), venlaflaxine (1), inpatient or residential treatment (9) **GROUP 2**	**Benefits:** BPRS-C, CPRS, CGI-I, CGI-S, response, medication adherence **Harms:** Withdrawal due to AEs, akathisia, BMI, constipation, dermatolodic AE, dystonia, ECG changes, EPS, SAS, AIMS, tardive dyskinesias, glucose, lipid profile, prolactin, prolactin-related AE, sedation, WAE, weight changes, white blood cells	Risperidone and olanzapine were effective in acutely reducing symptoms in psychotic youth.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	substance intoxication or withdrawal, (2) history of serious adverse reactions or nonresponse to an adequate trial of any of the study medications during this psychotic episode, (3) prior dx of PDD or a serious medical or neurological disorder, (4) pregnancy or refusal to practice contraception, (5) imminent risk in current setting to harm self or others	**GROUP 3** **N:** 19 **Age, mean±SD (range):** 14.6±2.9 **Males %:** 68 **Caucasian %:** 47 **Diagnostic breakdown (n):** affective disorders (6), schizophrenia spectrum (13) **Treatment naïve (n):** 2 **Inpatients (n):** 15 **First episode psychosis (n):** 15	**Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** 2.5–12.5 **Daily dose (mg/day), mean±SD (range):** 12.3±3.5 (2.5–12.5) **Concurrent treatments:** benztropine/trihexyphenidyl (5), buproprion (2), carbamazepine (1), fluoxetine (2), fluvoxamine (1), lithium (1), lorazepam (1), paroxetine (1), propranolol (2), sertraline (1), valproate (1), inpatient or residential treatment (10) **GROUP 3** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** 0.5–3 **Daily dose (mg/day), mean±SD (range):** 4±1.2 (0.5–3) **Concurrent treatments:** amantadine(2), benztropine/ trihexyphenidyl (4), citalopram (1), clomipramine (1), gabapentin with lamotrigine (1), lorazepam(2), propranolol (1), sertraline (2), trazadone (1), valproate (3), inpatient or residential treatment (11)		
Singh, 2011 [82] **Country:** Russia, India, Ukraine, United States, Romania **Condition category:** Schizophrenia and related **Funding:** Industry	**Recruitment dates:** Jul 2007 to Mar 2009 **Study design:** RCT (parallel) **Setting:** Hospitalization permitted for first 3 wks **Diagnostic criteria:** DSM-IV, K-SADS-PL	**Enrolled:** 201 **Analyzed:** 200 **Completed:** 139 **GROUP 1** **N:** 54 **Age, mean±SD (range):** 15.1±1.5 **Males %:** 56 **Caucasian %:** 65 **Treatment naïve (n):** 7 **Inpatients (n):** NR **First episode psychosis**	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** ≤3 wk **Permitted drugs:** propranolol (for akathisia), antiparkinsonians (benzotropine, biperiden), lorazepam (rescue) **Prohibited drugs:** alcohol, antipsychotics, antidepressants, drugs of abuse, lithium, psychostimulants, anticonvulsants,	**Benefits:** CGAS, CGI-S, PANSS, VAS-sleep, response rate, suicide, medication adherence **Harms:** Blood pressure, ECG changes, QTcLD, orthostatic hypotension, NMS, tachycardia, glucose, insulin resistance,	The medium dose paliperidone ER group was statistically superior to the placebo group according to the primary efficacy analysis by weight-based, fixed-dose treatment group. When analyzed by actual dose group, all three doses of

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Risk of bias: High (subjective), Medium (objective)	**Inclusion criteria:** (1) 12–17 yr, (2) body weight ≥29 kg, (3) DSM-IV criteria for schizophrenia ≥1 yr before screening and history of at least 1 antipsychotic, (4) PANSS total score 60–120 (acute symptomatic), (5) physically healthy based on medical history, physical examination, ECG, and laboratory test results **Exclusion criteria:** (1) dissociative disorder, BD, MDD, schizoaffective disorder, schizophreniform disorder, ASD, or primary substance induced psychotic disorder (DSM-IV), (2) mild, moderate, or severe MR, (3) pregnant, (4) known or suspected history of seizure disorder, NMS, encephalopathic syndrome, tardive dyskinesia, or insulin dependent diabetes mellitus, (5) presence of any significant or unstable systemic disease, (6) clozapine in 2 months before treatment	**(n):** 0 **GROUP 2** **N:** 48 **Age, mean±SD (range):** 15.3±1.6 **Males %:** 65 **Caucasian %:** 71 **Treatment naïve (n):** 4 **Inpatients (n):** NR **First episode psychosis (n):** 0 **GROUP 3** **N:** 48 **Age, mean±SD (range):** 15.5±1.6 **Males %:** 70 **Caucasian %:** 68 **Treatment naïve (n):** 7 **Inpatients (n):** NR **First episode psychosis (n):** 0 **GROUP 4** **N:** 51 **Age, mean±SD (range):** 15.7±1.4 **Males %:** 55 **Caucasian %:** 69 **Treatment naïve (n):** 3 **Inpatients (n):** NR **First episode psychosis (n):** 0	sedatives, cholinesterase inhiitors **GROUP 1** **Drug name:** Paliperidone ER (low) **Dosing variability:** fixed **Target dose (mg/day):** 1.5 (all weights) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anti-EPS (2), benzodiazepines (13), propranolol (1) **GROUP 2** **Drug name:** Paliperidone ER (medium) **Dosing variability:** fixed **Target dose (mg/day):** 3 (<51 kg), 6 (≥51 kg) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anti-EPS (7), benzodiazepines (16), propranolol (1) **GROUP 3** **Drug name:** Paliperidone ER (high) **Dosing variability:** fixed **Target dose (mg/day):** 6 (<51 kg), 12 (≥51 kg **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anti-EPS (14), benzodiazepines (15), propranolol (1) **GROUP 4** **Drug name:** Placebo **Dosing variability:** fixed **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR	prolactin levels, mortality, NMS, serious AEs, seizure, total AE, WAE, weight change, glucose homeostasis, AIMS, SAS	paliperidone showed improvement relative to placebo.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
			Concurrent treatments: anti-EPS (0), benzodiazepines (19), propranolol (0)		
Snyder et al., 2002[83] **Country:** Canada, South Africa, USA **Condition category:** ADHD **Funding:** Foundation **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV, VABS **Inclusion criteria:** (1) CD, ODD, or DBD-NOS (DSM-IV), (2) parent/ caregiver rating ≥24 on the Conduct Problem subscale of the NCBRF, (3) IQ 36–84 inclusive, (4) VABS score ≤84, (5) healthy on the basis of a pretrial physical examination, medical history, and ECG, (6) consent by parent/ caregiver, (7) 5–12 yr **Exclusion criteria:** (1) PDD, schizophrenia, or other psychotic disorders, (2) head injury as a cause of impaired IQ, (3) seizure condition requiring medication, (4) females who were sexually active without a reliable form of birth	**Enrolled:** 110 **Analyzed:** 110 **Completed:** 85 **GROUP 1** **N:** 53 **Age, mean±SD (range):** 8.6±0.3 (5–12) **Males %:** 77.4% **Caucasian %:** 78.8% **Diagnostic breakdown (n):** CD (3), CD/ADHD (16), Combined/No ADHD (9), ODD/ DBD (6), ODD/DBD/ADHD (28) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (44) **GROUP 2** **N:** 57 **Age, mean±SD (range):** 8.8±0.3 (5–12) **Males %:** 73.7% **Caucasian %:** 73.7% **Diagnostic breakdown (n):** CD (7), CD/ADHD (15), Combined/No ADHD (17), ODD/ DBD (10), ODD/DBD/ADHD (25) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (40)	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 1 wk **Permitted drugs:** stable doses (≥30 days prior to study) of anticholinergics, antihistamines, chloral hydrate, medication for preexisting medical conditions, melatonin, psychostimulants (comorbid ADHD) **Prohibited drugs:** no other medication permitted **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1±0.1 SE (0.4–3.8) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** ABC, BPI, CGI-I, CGI-S, NCBRF, VAS Medication adherence **Harms:** Anorexia, behavioral issues, Bucco-linguo-masticatory score, BMI, ECG changes, EPS, fatigue, parkinsonism, prolactin, prolactin-related AE, pulse, SAE, somnolence, tardive dyskinesia, total AE, WAE, weight change	Risperidone was adequately tolerated and was effective in treating children with subaverage IQs and severe disruptive behaviors.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	control, (5) serious or progressive illness or clinically abnormal laboratory values, (6) history of tardive dyskinesia, NMS, or hypersensitivity to any antipsychotic drug, (7) known presence of HIV, (8) previous treatment with risperidone				
Spencer et al., 1994 [84] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** Industry, Government **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** Sep 1989 to May 1991 **Study design:** RCT (crossover) **Setting:** Inpatient **Diagnostic criteria:** DSM-III-TR, DICA-R **Inclusion criteria:** (1) actively psychotic prepubertal patients, (2) 5–11 yr, (3) admitted to the Bellevue Hospital Children's Inpatient Psychiatric Unit, (4) schizophrenia **Exclusion criteria:** (1) intercurrent systemic illness, (2) seizure disorder, (3) MR below borderline, (4) tardive dyskinesia, (5) infantile autism, (6) receipt of psychoactive medication within 4 wk	**Enrolled:** 16 **Analyzed:** 16 **Completed:** 16 **GROUP 1** **N:** 16 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 16 (crossover) **Age, mean±SD (range):** NR **Males %:** NR **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2 (0.5–3.5) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.5±0.5 (0.5–3.5) **Concurrent treatments:** NR	**Benefits:** BPRS-C, CGI-I, CGI-S, CPRS **Harms:** Drowsiness, dystonia	Haloperidol improved the target psychotic symptoms in children with schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	of double-blind treatment				
Stocks et al., 2012[85] **Country:** USA **Condition category:** ADHD **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** October 2008 – September 2009 **Study design:** RCT (parallel) **Setting:** outpatient **Diagnostic criteria:** K-SADS-PL, DSM-IV-TR **Inclusion criteria:** 6-12 yr, ADHD with persistent serious conduct problems (≥27 on DBD, ≥2 on Conduct problem subscale of NCBRF-TIQ for: knowingly destroys property, gets in physical fights, physically attacks people. Weigh ≥ 16kg, IQ ≥ 71, free of antipsychotics for at least 2 weeks pre-baseline, receiving stable dose of an FDA approved psychostimulant for at least 30 days pre-baseline, otherwise in good physical health **Exclusion criteria:** Current or lifetime diagnosis of BP, PTSD, personality	**Enrolled:** 78 **Analyzed:** 78 **Completed:** 55 **GROUP 1** **N:** 20 **Age, mean±SD (range):** 8.5±1.88 yr **Males %:** 95% **Caucasian %:** 55% **Diagnostic breakdown (n):** ADHD (20) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** 0 **Comorbidities (n):** Asthma (5), CD (2), Enuresis (4), Insomnia (1), ODD (6), Seasonal allergies (2) **GROUP 2** **N:** 19 **Age, mean±SD (range):** 9.4±1.98 yr **Males %:** 84.2% **Caucasian %:** 57.9% **Diagnostic breakdown (n):** ADHD (19) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** 0 **Comorbidities (n):** Asthma (3), CD (2), Eczema (3), Enuresis (3), Environmental allergies (1), Insomnia (2), ODD (7), Seasonal allergies (1)	**Treatment duration:** 8-11 wk (2-5 wk titration, 6 wk maintenance) **Run-in phase:** Yes **Run-in phase duration:** 2 wk **Permitted drugs:** methylphenidate, amphetamine, benzotropine **Prohibited drugs:** other antipsychotics, antidepressants, hypnotics, anticonvulsants, antihypertensives, antihistamines **GROUP 1** **Drug name:** Molindone hydrochloride **Dosing variability:** Fixed **Target dose (mg/day):** <30 kg: 5 mg/day; ≥ 30 kg: 10 mg/day **Daily dose (mg/day), mean±SD (range):** <30 kg: 5 mg/day; ≥ 30 kg: 10 mg/day **Concurrent treatments:** Stable dose of FDA approved psychostimulant (methylphenidate or amphetamine) **GROUP 2** **Drug name:** Molindone hydrochloride **Dosing variability:** Fixed **Target dose (mg/day):** <30 kg: 10 mg/day; ≥ 30 kg: 20 mg/day **Daily dose (mg/day), mean±SD (range):** <30 kg: 10 mg/day; ≥ 30 kg: 20 mg/day **Concurrent treatments:** Stable dose of FDA approved psychostimulant (methylphenidate or amphetamine)	**Benefits:** NCBRF-TIQ, CGI-I, CGI-S, SNAP-IV **Harms:** Somnolence, metabolic effects, neuromotor effects, infection, prolactin related events	Molindone showed clinical benefit with an acceptable side-effect profile in this study. Preliminary efficacy results suggest that molindone produces dose-related behavioral improvements over 9-12 weeks.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	disorder, psychotic disorder, currently meeting diagnostic criteria for major depressive disorder, OCD, PDD or other AD as primary disorder	**GROUP 3** **N:** 19 **Age, mean±SD (range):** 8.8±2.12 yr **Males %:** 68.4% **Caucasian %:** 42.1% **Diagnostic breakdown (n):** ADHD (19) **Treatment naïve (n):** **Inpatients (n):** **First episode psychosis (n):** 0 **Comorbidities (n):** Asthma (4), CD (3), Eczema (2), Enuresis (2), Environmental allergies (1), ODD (6) **GROUP 4** **N:** 20 **Age, mean±SD (range):** 8.8±2.00 yr **Males %:** 95% **Caucasian %:** 65% **Diagnostic breakdown (n):** ADHD (20) **Treatment naïve (n):** NR **Inpatients (n):** 0 **First episode psychosis (n):** 0 **Comorbidities (n):** Asthma (1), CD (1), Eczema (1), Enuresis (3), Environmental allergies (2), Insomnia (2), ODD (7), Seasonal allergies (2)	**GROUP 3** **Drug name:** Molindone hydrochloride **Dosing variability:** Fixed **Target dose (mg/day):** <30 kg: 15 mg/day; ≥ 30 kg: 30 mg/day **Daily dose (mg/day), mean±SD (range):** <30 kg: 15 mg/day; ≥ 30 kg: 30 mg/day **Concurrent treatments:** Stable dose of FDA approved psychostimulant (methylphenidate or amphetamine) **GROUP 4** **Drug name:** Molindone hydrochloride **Dosing variability:** Fixed **Target dose (mg/day):** <30 kg: 20 mg/day; ≥ 30 kg: 40 mg/day **Daily dose (mg/day), mean±SD (range):** <30 kg: 20 mg/day; ≥ 30 kg: 40 mg/day **Concurrent treatments:** Stable dose of FDA approved psychostimulant (methylphenidate or amphetamine)		
Swadi et al., 2010[86] **Country:** New Zealand	**Recruitment dates:** NR **Study design:** RCT (parallel)	**Enrolled:** 22 **Analyzed:** 22 **Completed:** 22 **GROUP 1**	**Treatment duration:** 6 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR	**Benefits:** BPRS, PANSS, response (BPRS, CGI-S, HAM-D, PANSS, YMRS)	Risperidone may be more beneficial than quetiapine for adolescent patients with bipolar disorder.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		N: 11		**Harms:** Blood pressure, SAS, BAS, AIMS, glucose, lipid profile, liver function, prolactin, sedation, weight change	
Condition category: Schizophrenia and related **Funding:** Industry **Risk of bias:** High (subjective), High (objective)	**Setting:** Inpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) <19 yr, (2) first obset psychotic disorder or a mood disorder with psychotic features **Exclusion criteria:** (1) alcohol or substance dependence not in full remission, (2) prior treatment with atypical antipsychotic drugs	**Age, mean±SD (range):** NR **Males %:** 54.5 **Caucasian %:** NR **Treatment naïve (n):** 11 **Inpatients (n):** all **First episode psychosis (n):** 11 **Comorbidties**: SUD (0) **GROUP 2** **N:** 11 **Age, mean±SD (range):** NR **Males %:** 63.6 **Caucasian %:** NR **Treatment naïve (n):** 11 **Inpatients (n):** all **First episode psychosis (n):** 11 **Comorbidties**: SUD (0)	**Prohibited drugs:** NR **GROUP 1** **Drug name:** Quetiapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 607 (100–800) **Concurrent treatments:** anticholinergics (1), cognitive behavioral therapy, family work, activity-based interventions allowed **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.9 (1.5–5) **Concurrent treatments:** anticholinergics (5), cognitive behavioral therapy, family work, activity-based interventions allowed		
Tohen et al., 2007 [87] **Country:** Puerto Rico, USA **Condition category:** Bipolar disorder **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** Nov 2002 to May 2005 **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV-TR, K-SADS-PL **Inclusion criteria:** (1) 12–17 yr, (2) manic or mixed bipolar episodes (with or without psychotic features), (3)	**Enrolled:** 161 **Analyzed:** 161 **Completed:** 120 **GROUP 1** **N:** 107 **Age, mean±SD (range):** 15.1±1.3 **Males %:** 57 **Caucasian %:** 66.4 **Diagnostic breakdown (n):** mixed (61), psychotic features (22), rapid cycling (25) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 3 wk **Run-in phase:** Yes **Run-in phase duration:** 2–14 day **Permitted drugs:** anticholinergics (2–6mg/day), benzodiazepines/hypnotics (≤2 mg/day lorazepam equivalents for ≤3 consecutive days), psychostimulants (constant dose ≥30 day prior to randomization and through study) **Prohibited drugs:** anticholinergics **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable	**Benefits:** CDRS, CGI-BP (overall, mania, depression subscales), ADHS IV, OAS, YMRS (total+item analysis), HRQoL(subscales); Olsen 2012, response, suicide **Harms:** Bipolar exacerbation, blood cells, blood pressure, BMI, ECG changes, EPS (AIMS, BAS, SAS), glucose, hepatic enzyme, lipid profile, mortality,	Olanzapine was more effective in treating adolescents with bipolar mania and placebo; however, it resulted in significantly greater weight gain.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	inpatient or outpatient, (4) total score ≥20 on the Adolescent Structured YMRS **Exclusion criteria:** (1) prior nonreponse to olanzapine, (2) treatment within the previous 30 day with an experimental medication not available for clinical use, (3) suicide risk, (4) clinically significant abnormal laboratory values at baseline, (5) DSM-IV-TR substance dependence (excluding nicotine and caffeine) within the last 30 days, (6) treatment with long-lasting neuroleptic within 14 day prior to randomization	**Comorbidities:** ADHD (45), DBD (37) **GROUP 2** **N:** 54 **Age, mean±SD (range):** 15.4±1.2 **Males %:** 44.4 **Caucasian %:** 75.9 **Diagnostic breakdown (n):** mixed (25), psychotic features (7), rapid cycling (5) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** ADHD (13), DBD (12)	**Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 8.9 (2.5–20) **Concurrent treatments:** anticholinergics (4.7%), benzodiazepines (12.1%) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** anticholinergic medication (0), benzodiazepines (7.4%)	prolactin, prolactin-related AE, pulse, SAE, weight change	
Tramontina et al., 2009 [88] **Country:** Brazil **Condition category:** Bipolar disorder **Funding:** Industry, Government, Hospital **Risk of bias:** Low (subjective), Low (objective)	**Recruitment dates:** Jan 2005 to Nov 2007 **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, K-SADS-E **Inclusion criteria:** (1) 8–17 yr, (2) DSM IV bipolar I or II disorder comorbid with ADHD, (3) clear reports of	**Enrolled:** 43 **Analyzed:** 43 **Completed:** 41 **GROUP 1** **N:** 18 **Age, mean±SD (range):** 11.7±2.7 **Males %:** 33 **Caucasian %:** 83 **Treatment naïve (n):** ND **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (all), anxiety disorders (8), DBD (15), psychosis (8),	**Treatment duration:** 6 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 13.6±5.4 (5–20) **Concurrent treatments:** none **GROUP 2**	**Benefits:** CDRS, CGI-S, CMRS-P, YMRS, medication adherence, response, suicide **Harms:** Akathisia, behavioral issues, dermatologic AE, dyskinesia, EPS, fatigue, seizure, somnolence, weight change	Aripiprazole was effective in decreasing mania symptoms and improving global functioning without resulting in severe advserse events or weight gain.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	ADHD symptom onset preceding any mood symptomology, (4) acutely manic or mixed states (YMRS score ≥20 at baseline visit) **Exclusion criteria:** (1) estimated IQ < 70 (WISC-III), (2) use of any medication 4 wk prior to entering the study, (3) dx of PDD, schizophrenia, or substance abuse or dependence, (4) severe suicide/homicide risk, (5) previous use of aripiprazole, (6) other acute or chronic diseases, (7) pregnancy	SA (0) **GROUP 2** **N:** 25 **Age, mean±SD (range):** 12.2±2.8 **Males %:** 56 **Caucasian %:** 96 **Treatment naïve (n):** ND **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities:** ADHD (all), anxiety disorders (13), DBD (20), psychosis (8), SA (0)	**Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 15±3.2 (10–20) **Concurrent treatments:** none		
Troost et al., 2005 [89] **Country:** Netherlands **Condition category:** ASD **Funding:** Industry, Foundation **Risk of bias:** Low (subjective), Low (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient and outpatient **Diagnostic criteria:** DSM-IV-TR, ADI-R **Inclusion criteria:** (1) DSM-IV-TR criteria for PDD, (2) demonstrated clinically significant tantrums, aggression, self-injurious behavior, or a combination of	**Enrolled:** 24 **Analyzed:** 24 **Completed:** NR **GROUP 1** **N:** 12 **Age, mean±SD (range):** 9.4±3.4 **Males %:** 91.6 **Caucasian %:** 100 **Diagnostic breakdown (n):** Asperger's disorder (1), autistic disorder (3), PDD NOS (8) **Treatment naïve (n):** 11 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (2)	**Treatment duration:** 6 mo **Run-in phase:** Yes **Run-in phase duration:** 1–4 wk **Permitted drugs:** anticonvulsants (stable dose for ≥4 wk and patient seizure-free for ≥6 mo), stimulants (comorbid ADHD) **Prohibited drugs:** psychotropics **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.9±0.7 **Concurrent treatments:** stimulants (1), stimulant and anticonvulsant (1)	**Benefits:** ABC (sub scores), CGI, VAB, cognitive (focused and divided attention task), response (relapse) **Harms:** Dyskinesia (SAS, AIMS)	Risperidone was effective in reducing disruptive behavior in about half of children with ASD.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	these, (3) 5–17 yr, (4) weight ≥15 kg, (5) mental age ≥18 mo **Exclusion criteria:** (1) children on effective psychotropic drug treatment for disruptive behavior	**GROUP 2** **N:** 12 **Age, mean±SD (range):** 8.7±1.2 **Males %:** 91.6 **Caucasian %:** 83 **Diagnostic breakdown (n):** Asperger's disorder (1), autistic disorder (3), PDD NOS (8) **Treatment naïve (n):** all **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** MR (0)	**GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.7±0.5 **Concurrent treatments:** stimulants (2)		
Van Bellinghen et al., 2001 [90] **Country:** Belgium **Condition category:** Behavioral issues **Funding:** Industry **Risk of bias:** Medium (subjective), Medium (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** clinical assessment and parent interview **Inclusion criteria:** (1) 6–18 yr, (2) IQ 45–85, (3) demonstrating persistent behavioral disturbances **Exclusion criteria:** (1) presence of a clinically relevant non-neurologic disease, (2) abnormal laboratory tests, (3) epileptic crisis in the previous 3 mo, (4) participation in	**Enrolled:** 13 **Analyzed:** 13 **Completed:** 13 **GROUP 1** **N:** 6 **Age, mean±SD (range):** NR (6–14) **Males %:** 33.3 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** anxiety (0), depression (0), mania (0), MR (all) **GROUP 2** **N:** 7 **Age, mean±SD (range):** NR (7–14) **Males %:** 42.9 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR	**Treatment duration:** 4 wk **Run-in phase:** No **Run-in phase duration:** NR **Permitted drugs:** antiepileptics **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 1.2 **Concurrent treatments:** valproate (1) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** NR	**Benefits:** ABC, CGI-I, PAC, VAS **Harms:** Parkinsonism, pulse, somnolence, total AE, weight change, EP disorder (ESRS)	Risperidone was well tolerated, and there was no difference between risperidone- and placebo-treated groups with respect to the occurrence of extrapyramidal side effects.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	a drug trial in the previous 4 wk, (5) remoxipride treatment in the previous 4 wk, (6) oral neuroleptics and other psychotropics in the previous wk, (6) previous treatment with remoxipride combined with abnormal hematologic values, (7) a depot neuroleptic injection within one treatment cycle of the time of selection, (8) female patients of reproductive age if their contraceptive use was considered inadequate, (9) pregnant or lactating	**First episode psychosis (n):** NR **Comorbidities:** anxiety (0), depression (0), mania (0), MR (all)			
Van Bruggen et al., 2003 [91] **Country:** Netherlands **Condition category:** Schizophrenia and related **Funding:** Industry, Government **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** Inpatient **Diagnostic criteria:** DSM-IV **Inclusion criteria:** (1) 16–28 yr, (2) first or second psychotic episode according to DSM-IV criteria of schizophrenia, schizofreniform or schizoaffective disorder, (3) actively	**Enrolled:** 44 **Analyzed:** 42 **Completed:** NR **GROUP 1** **N:** 18 **Age, mean±SD (range):** 21.0±2.8 **Males %:** 72 **Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** 16 **GROUP 2** **N:** 26 **Age, mean±SD (range):** 20.6±3.0 **Males %:** 85	**Treatment duration:** Olanzapine 9.8 wk, Risperidone 6.7 wk **Run-in phase:** No **Run-in phase duration:** NA **Permitted drugs:** NR **Prohibited drugs:** antipsychotics **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 15.6±4 (5–30) **Concurrent treatments:** anticholinergics (2), antidepressants (0), benzodiazepines (7), mood stabilizers (0)	**Benefits:** PANSS, medication adherence, response **Harms:** BAS, SAS, AIMS, akathisia, parkinsonism, prolactin, prolactin-related AE, sedation, seizure, sexual dysfunction, somnolence, tachycardia, tardive dyskinesia, weight change	Symptom response was similar in the olanzapine and risperidone groups.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	symptomatic at study entry (PANSS score of moderate or higher on items for delusions, conceptual disorganization, or hallucinations) **Exclusion criteria:** (1) epilepsy, (2) toxic psychosis or infectious disorder, (3) a primary dx of substance abuse (drugs or alcohol), (4) MR, (5) pregnant or lactating female patients, (6) concomitant use of other antipsychotic agents, (7) treatment with an injectable depot neuroleptic less than one dosing interval before study entry, (8) narrow-angle glaucoma and known hypersensitivity to olanzapine or risperidone, (9) insufficient knowledge of the Dutch language	**Caucasian %:** NR **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** 22	**GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 4.4±1.5 (1–8) **Concurrent treatments:** anticholinergics (7), antidepressants (4), benzodiazepines (8), mood stabilizers (0)		
Weisler et al., 2011 [132] **Country:** USA **Condition category:** Depression **Funding:** Industry	**Recruitment Dates:** NR **Study design:** Observational (pooled analysis of 2 trials) **Diagnostic criteria:** DSM-IV-TR **Setting:** outpatients	**Enrolled:** 35 **Analyzed:** 35 **Completed:** 35 **GROUP 1:** **N:** 16 **Age, mean±SD (range):** ≤ 25 yr **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown**	**Treatment duration:** 6 wk **Run-in phase:** No **Run-in phase duration:** NA **Permitted drugs:** Escitalopram, fluoxetine, paroxetine CR, sertraline, venlafaxine XR **Prohibited drugs:** NR **GROUP 1**	**Benefits:** suicide-related events and ideation **Harms:** NR	Adjunctive aripiprazole treatment represents a generally safe and relatively well-tolerated and efficacious treatment option for patients with MDD who had had an inadequate response to

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
Newcastle-Ottawa Scale: 6/8 stars	**Inclusion criteria:** Outpatients 18-65 yr (only looking at subgroup ≤ 25 yr here), major depressive episode ≥ 8 wk, inadequate response to ≥ 1 historical antidepressant **Exclusion criteria:** Significant risk of committing suicide during course of trial	**(n):** NR **Treatment naïve (n):** 0 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities (n):** NR **GROUP 2:** **N:** 19 **Age, mean±SD (range):** ≤ 25 yr **Males %:** NR **Caucasian %:** NR **Diagnostic breakdown (n):** NR **Treatment naïve (n):** 0 **Inpatients (n):** 0 **First episode psychosis (n):** NR **Comorbidities (n):** NR	**Drug name:** Aripiprazole **Dosing variability:** Variable **Target dose (mg/day):** 15 mg/day (paroxetine or fluoxetine) or 20 mg/day (all other patients) **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Escitalopram, fluoxetine, paroxetine CR, sertraline, venlafaxine XR **GROUP 2:** **Drug name:** Placebo **Dosing variability:** Variable **Target dose (mg/day):** NA **Daily dose (mg/day), mean±SD (range):** NA **Concurrent treatments:** Escitalopram, fluoxetine, paroxetine CR, sertraline, venlafaxine XR		standard antidepressant medication.
Wink et al., 2014 [133] **Country:** USA **Condition category:** ASD **Funding:** Industry/ non-industry **Newcastle-Ottawa Scale:** 7/8 stars	**Recruitment dates:** July 2004 to Apr 2012 **Study design:** Retrospective **Setting:** NR **Diagnostic criteria:** DSM-IV-TR **Inclusion criteria:** (1) 2-20 yr,(2) meets DSM-IV-TR criteria for ASD diagnosis, (3) subjects treated at the Christian Sarkine Autism Treatment Center (CSATC) **Exclusion criteria:** (1)	**Enrolled:** 142 **Analyzed:** 142 **Completed:** NR **GROUP 1** **N:** 72 **Age, mean±SD (range):** 8.41±3.59yr **Males %:** 83.3 **Caucasian %:** 77.8 **Diagnostic breakdown (n):** Autistic disorder (40), PDD-NOS (29), Asperger's disorder (3) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** intellectual disability (34)	**Treatment duration:** Risperidone (2.37±2.55 yr), Aripiprazole (1.47±1.21 yr) **Run–in phase:** NR **Run–in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 2.23±1.30 **Concurrent treatments:** SSRI (20), antiepileptic (5), stimulant (15), metformin (4), α 2-agonist (27), other (26)	**Benefits:** CGI-I **Harms:** Weight change (BMI, BMI-z)	Our results warrant further investigation using a prospective random assignment study design. Greater control of baseline characteristics, tracking detailed historical and lifestyle factors, use of methodical dosing guidelines, and limiting treatment duration may impact the results of such a study.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	Risperidone or aripiprazole use initiated prior to evaluation at CSATC, (2) individual received multiple antipsychotics at any time during treatment, (3) if <2 BMI data points were available	**GROUP 2** **N:** 70 **Age, mean±SD (range):** 9.74±3.46yr **Males %:** 80 **Caucasian %:** 75.7 **Diagnostic breakdown (n):** Autistic disorder (44), PDD-NOS (19), Asperger's disorder (7) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** intellectual disability (30)	**GROUP 2** **Drug name:** Aripiprazole **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 11.85±7.23 **Concurrent treatments:** SSRI (21), antiepileptic (4), stimulant (10), metformin (2), α 2-agonist (22), benzodiazepine (2), other (24)		
Wonodi et al., 2007 [134] **Country:** USA **Condition category:** Mixed conditions **Funding:** Non-industry **Newcastle-Ottawa Scale:** 8/8 stars	**Recruitment dates:** NR **Study design:** Retrospective **Setting:** Inpatient/ outpatient **Diagnostic criteria:** NR **Inclusion criteria:** All children (5-18 yr) already receiving or likely to be prescribed antipsychotic medications at the referring facilities **Exclusion criteria:** NR	**Enrolled:** 424 **Analyzed:** 198 **Completed:** 198 **GROUP 1** **N:** 118 **Age, mean±SD (range):** 11.9±2.8 yr **Males %:** 77.1 **Caucasian %:** 44.1 **Diagnostic breakdown (n):** Mood disorder NOS (103), ADHD (75) **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR **GROUP 2** **N:** 80 **Age, mean±SD (range):** 10.7±3.9 yr **Males %:** 72.5 **Caucasian %:** 28.8	**Treatment duration:** ≥6mo **Run-in phase:** NR **Run-in phase duration:** NR **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Antipsychotic treatment ≥ 6mo **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR **Concurrent treatments:** Anti-depressants (88), mood stabilizers (88), psychostimulants (80) **GROUP 2** **Drug name:** Antipsychotic naïve **Dosing variability:** NR **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** NR	**Benefits:** NR **Harms:** Tardive dyskinesia	Identifying the risk profiles of antipsychotic treatment in children would improve treatment outcomes in this vulnerable clinical population. Side-effect profile of the atypical antipsychotic drugs in children may be much different than in adults, underscoring the importance of risk-benefit discussions with patient families before treatment initiation, and ongoing monitoring for motor and other (e.g., metabolic) adverse events.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		Diagnostic breakdown (n): Mood disorder NOS (67), ADHD (48) **Treatment naïve (n):** 80 **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities:** NR	**Concurrent treatments:** Anti-depressants (38), mood stabilizers (22), psychostimulants (37)		
Woods et al., 2003 [92] **Country:** Canada, USA **Condition category:** Schizophrenia and related **Funding:** Industry, Government **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** Jan 1998 to July 2001 **Study design:** RCT (parallel) **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, COPS, Presence of Psychosis Scale **Inclusion criteria:** (1) help-seeking persons responding to advertisements or refered by clinicians, (2) 12–45 yr, (3) prodromal syndromes criteria using the Structured Interview for Prodromal Syndromes, (4) ability to understand and communicate with investigator, (5) informed consent/assent **Exclusion criteria:** (1) past or current DSM-IV psychotic disorder, (2)	**Enrolled:** 60 **Analyzed:** 59 **Completed:** 41 **GROUP 1** **N:** 31 **Age, mean±SD (range):** 18.2±5.5 **Males %:** 67.7 **Caucasian %:** 74.2 **Treatment naïve (n):** 28 **Inpatients (n):** NR **First episode psychosis (n):** all **Comorbidities:** SA (18) **GROUP 2** **N:** 29 **Age, mean±SD (range):** 17.2±4 **Males %:** 62.1 **Caucasian %:** 58.6 **Treatment naïve (n):** 26 **Inpatients (n):** NR **First episode psychosis (n):** all **Comorbidities:** SA (9)	**Treatment duration:** 1 yr **Run-in phase:** Yes **Run-in phase duration:** 3–14 day **Permitted drugs:** antidepressants, benztropine mesylate or biperiden (≤6 mg/day), chloral hydrate (max 1000 mg/day), diazepam (max 40 mg/day), lorazepam (max 8 mg/day), nizatidine (300–600 mg/day), propranalol hydrochloride **Prohibited drugs:** psychoactive medications **GROUP 1** **Drug name:** Olanzapine **Dosing variability:** variable fixed at 5-15 mg/d **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 8±3.1 (5–15) **Concurrent treatments:** anticholinergics (1), benzodiazepines (7), nizatidine (1) **GROUP 2** **Drug name:** Placebo **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 9.3±2.8 (5–15) **Concurrent treatments:** anticholinergics (2),	**Benefits:** SOPS, CGI-S, GAF, PANSS, MARDS, YMRS, cognitive (neurocognitive measures), medication adherence, response/conversion to psychosis **Harms:** Behavioral issues, blood pressure, EPS (AIMS, Barnes, ASA), glucose, fatigue, lipid profile, pulse, somnolence, WAE, weight change	The conversion-to-psychosis rate was not significantly different between treatment groups; however, olanzapine might reduce the conversion rate and delay onset of psychosis. Compared to placebo, olanzapine was efficacious for positive prodromal symptoms but induced weight gain.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	treatable psychiatric disorder that could account for prodromal symptoms, (3) suicidal or homicidal, (4) prodromal symptoms primarily sequelae of alcohol or drug use, (5) IQ <80, (6) seizure disorder without a clear or resolved etiology, (7) pregant or lactating, (8) took nonprotocol psychotropic medications		benzodiazepines (2)		
Wudarsky et al., 1999 [135] **Country:** USA **Condition category:** Schizophrenia and related **Funding:** NR **Newcastle-Ottawa Scale:** 7/8 stars	**Recruitment dates:** NR **Study design:** Prospective cohort **Setting:** Outpatient/community **Diagnostic criteria:** DSM-IV, DSM-III-TR, structured interviews **Inclusion criteria:** (1) DSM dx of schizophrenia, (2) resistant to treatment with two different FGAs **Exclusion criteria:** (1) onset of symptoms at ≥13 yr, (2) neurological or medical disease, (3) premorbid IQ <70	**Enrolled:** 47 **Analyzed:** 47 **Completed:** NR **GROUP 1** **N:** 15 **Age, mean±SD (range):** 13.7±1.5 **Males %:** 60 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 0 **GROUP 2** **N:** 22 **Age, mean±SD (range):** 14.7±2.3 **Males %:** 72.7 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 0 **GROUP 3**	**Treatment duration:** 6 wk **Run-in phase:** Yes **Run-in phase duration:** 3 wk **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 15.3±8.2 **Concurrent treatments:** NR **GROUP 2** **Drug name:** Clozapine **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 325.4±211 **Concurrent treatments:** NR **GROUP 3** **Drug name:** Olanzapine **Dosing variability:** variable	**Benefits:** NR **Harms:** Prolactin	Mean prolactin levels were significantly elevated after 6 weeks of treatment with haloperidol, clozapine, and olanzapine in patients with childhood-onset schizophrenia.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
		N: 10 **Age, mean±SD (range):** 14.2±2.9 **Males %:** 70 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** 0	**Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 17±3.5 **Concurrent treatments:** NR		
Yen et al., 2004 [93] **Country:** Taiwan **Condition category:** Schizophrenia and related **Funding:** Hospital **Risk of bias:** High (subjective), High (objective)	**Recruitment dates:** NR **Study design:** RCT (parallel) **Setting:** NR **Diagnostic criteria:** DSM-III-TR **Inclusion criteria:** (1) 18–65 yr, (2) total score >60 on PANSS **Exclusion criteria:** (1) psychoses other than schizophrenia, (2) early childhood brain damage, (3) unable to comply with the medication, (4) severe illness, (5) pregnant or lactating women	**Enrolled:** 8 **Analyzed:** 8 **Completed:** 8 **GROUP 1** **N:** 2 (≤24 yr) **Age, mean±SD (range):** 24.0 (24) **Males %:** 0 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR **GROUP 2** **N:** 6 (≤24 yr) **Age, mean±SD (range):** 20.7 (20–22) **Males %:** 66.7 **Caucasian %:** NR **Treatment naïve (n):** 0 **Inpatients (n):** NR **First episode psychosis (n):** NR	**Treatment duration:** 2.8 mo **Run-in phase:** Yes **Run-in phase duration:** 1–4 wk **Permitted drugs:** biperiden or trihexylphenidyl; lorazepam, oxazepam or temazepam **Prohibited drugs:** NR **GROUP 1** **Drug name:** Haloperidol **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 11.2±6.9 (2–25) **Concurrent treatments:** NR **GROUP 2** **Drug name:** Risperidone **Dosing variability:** variable **Target dose (mg/day):** NR **Daily dose (mg/day), mean±SD (range):** 4.4±2.6 (1–8) **Concurrent treatments:** NR	**Benefits:** PANSS **Harms:** NR	Risperidone was superior to haloperidol in improving negative symptoms and better tolerated during the treatment of schizophrenia.
Yoo et al., 2013 [95] **Country:** South Korea **Condition category:** Tic disorders	**Recruitment Dates:** August 2008 – April 2010 **Study design:** RCT (parallel) **Diagnostic criteria:**	**Enrolled:** 61 **Analyzed:** 61 **Completed:** 54 **GROUP 1:** **N:** 32 **Age, mean±SD (range):** 11±2.5 yr	**Treatment duration:** 10 wk **Run-in phase:** Yes **Run-in phase duration:** Free of antipsychotic or antiparkinson drugs 1 wk before randomization, free of fluoxetine 4 wk before **Permitted drugs:** Aripiprazole (for	**Benefits:** YGTSS, CGI-TS, response **Harms:** Neuromotor effects, GI disorders, metabolic effects, QT	Aripiprazole is efficacious and tolerated in children and adolescents with Tourette syndrome.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	DSM-IV	**Males %:** 93.8% **Caucasian %:** NR	group 1)		
Funding: Industry	**Setting:** Outpatient clinics	**Diagnostic breakdown (n):** Tourette syndrome (32)	**Prohibited drugs:** All other drugs		
Risk of Bias: High (subjective), High (objective)	**Inclusion criteria:** 6-18 yr, DSM-IV diagnosis of Tourette syndrome or chronic motor or vocal tic disorder. Baseline total tic score ≥22 on YGTSS	**Treatment naïve (n):** NR **Inpatients (n):** (0) **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (5), ODD (3), AD (0)	**GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** Fixed **Target dose (mg/day):** 20 mg/day **Daily dose (mg/day), mean±SD (range):** 11.0±6.1 mg/day **Concurrent treatments:** NR		
	Exclusion criteria: Current mood disorders, schizophrenia and other psychotic disorders, or other psychiatric comorbidity requiring medication during study period, history of psychotropic substance or alcohol use disorders during 3 months pre-screening. IQ ≤ 70, seizure disorders, history of neuroleptic malignant syndrome, serious brain injury, stroke, or other neurologic disorders. Secondary tic symptoms accompanied by tardive tics, Huntington disease, neuroacanthocytosis, autism. Significant medical problems. History of allergy or	**GROUP 2:** **N:** 29 **Age, mean±SD (range):** 10.9±3.0 yr **Males %:** 79.3% **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (29) **Treatment naïve (n):** NR **Inpatients (n):** (0) **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (1), ODD (0), AD (1)	**GROUP 2:** **Drug name:** Placebo **Dosing variability:** Fixed **Target dose (mg/day):** NA **Daily dose (mg/day), mean±SD (range):** NA **Concurrent treatments:** NR		

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	hypersensitivity reactions to aripiprazole, nonresponsive to antipsychotic treatment, participating in another clinical study within 1 month before screening, pregnant or lactating, female adolescents who did not consent to contraception during study and up to 8 weeks after. Requiring cognitive behavioral therapy during study period.				
Yoo et al., 2011 [94] **Country:** South Korea **Condition category:** Tic disorders **Funding:** NR **Risk of Bias:** High (subjective), High (objective)	**Recruitment Dates:** August 2005 – March 2007 **Study design:** NRCT (parallel) **Diagnostic criteria:** DSM-IV, Total tic scores ≥22 on Korean version of YGTSS **Setting:** outpatient **Inclusion criteria:** Tic disorders, drug free ≥ 2 weeks before study entry, no significant medical problems **Exclusion criteria:** Current mood disorders, psychotic symptoms, AD (OCD	**Enrolled:** 48 **Analyzed:** 48 **Completed:** 37 **GROUP 1:** **N:** 31 **Age, mean±SD (range):** 11.2±3.5 (6-18) yr **Males %:** 71% **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (19), Chronic motor and vocal tic disorder (7), Transient tic disorder (5) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (9), ODD (2), OCD (3) **GROUP 2:** **N:** 17	**Treatment duration:** 8 wk **Run-in phase:** Yes **Run-in phase duration:** Drug free for 2 wk before study entry **Permitted drugs:** NR **Prohibited drugs:** NR **GROUP 1** **Drug name:** Aripiprazole **Dosing variability:** Variable **Target dose (mg/day):** 20 mg/day **Daily dose (mg/day), mean±SD (range):** 10.6±5.2 (2.5-20) mg/day **Concurrent treatments:** NR **GROUP 2:** **Drug name:** Haloperidol **Dosing variability:** Variable **Target dose (mg/day):** 4.5 mg/day **Daily dose (mg/day), mean±SD (range):** 1.9±1.1 (0.75-4.5) mg/day **Concurrent treatments:** NR	**Benefits:** YGTSS, CGI-I, CGI-S **Harms:** ESRS, AE checklist	Aripiprazole may be effective and tolerable in the treatment of children and adolescents with tic disorders. Additional controlled studies are needed to determine efficacy and tolerability of aripiprazole in patients with tic disorders.

Study	Study Characteristics	Participant Characteristics	Treatment Characteristics	Outcomes Reported	Author Conclusions
	allowed), IQ ≤ 70, previous or current seizure episodes, EEG abnormalities, previously used aripiprazole	**Age, mean±SD (range):** 8.6±2.9 (6-16) yr **Males %:** 64.7% **Caucasian %:** NR **Diagnostic breakdown (n):** Tourette syndrome (7), Chronic motor and vocal tic disorder (4), Transient tic disorder (6) **Treatment naïve (n):** NR **Inpatients (n):** NR **First episode psychosis (n):** NR **Comorbidities (n):** ADHD (6)			

ABC = Aberrant Behavior Checklist; ABC-C = Aberrant Behavior Checklist-Community; ADI-R = Autism Diagnostic Interview-Revised; ADOS = Autism Diagnostic Observation Schedule; AE = Adverse Event; ASD = autism spectrum disorder; β-HCG = beta human chorionic gonadotropin; BMI = body mass index; BPRS = Brief Psychiatric Rating Scale; BPRS-A = Brief Psychiatric Rating Scale-Anchored; C-DISC 4 = Computerized Diagnostic Interview Schedule for Children, version four; CARS = Childhood Autism Rating Scale; CAS-P = Children's Aggression Scale-Parent; CAS-T = Children's Aggression Scale-Teacher; CBCL = Child Behavior Checklist; CD = conduct disorder; CDRS-R = Children's Depression Rating Scale, Revised; CGI-C = Clinical Global Impression-Change; CGI-I = Clinical Global Impressions-Improvement; CGI-S = Clinical Global Impressions-Severity; CNS = central nervous system; COPS = Criteria of Prodromal Syndromes; CPRS = Children's Psychiatric Rating Scale; day = day(s); CPT = Continuous performance task ; DBD = disruptive behavior disorder; DICA-R = Diagnostic Interview for Children and Adolescents-Revised; DSM = Diagnostic and Statistical Manual of Mental Disorders; ECG = electrocardiogram; FGA = first-generation antipsychotics; GAD = generalized anxiety disorder; HALFS = Health And Life Functioning Scale ; HIV = human immunodeficiency virus; hr = hour(s); IED = intermittent explosive disorder; IM = intramuscular; IQ = intelligence quotient; KID-SCID = childhood disorders form of the Structured Clinical Interview for DSM-IV Disorders; K-SADS = Kiddie-Schedule for Affective Disorders and Schizophrenia; K-SADS-E = Kiddie-Schedule for Affective Disorders and Schizophrenia (Epidemiological Version); K-SADS-P = Kiddie-Schedule for Affective Disorders and Schizophrenia (Present Episode Version); K-SADS-PL = Kiddie-Schedule for Affective Disorders and Schizophrenia (Present and Lifetime Version); KQ = key question; LT = long term; MAO-I = monoamine oxidase inhibitor; MDD = major depressive disorder; mo = month(s); MVLT = Modified Version of the California Verbal Learning Test; N = number; NCBRF = Nisonger Child Behavior Rating Form; NMS = neuroleptic malignant syndrome; NOS = not otherwise specified; NR = not reported; NRCT = non-randomized controlled trial; NSAID = non-steroidal anti-inflammatory drug; OAS = Overt Aggression Scale; ODD = oppositional defiant disorder; P-LES-Q = Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; PANSS = Positive and Negative Syndrome Scale; PDD = pervasive developmental disorder; PTSD = post-traumatic stress disorder; Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire; RCT = randomized controlled trial; SA = substance abuse; SCID-I/P = Clinical Interview for DSM-IV-TR Axis I Disorders-Patient Edition; SGA = second-generation antipsychotic; SSRI = selective serotonin reuptake inhibitor; ST = short term; TBI = traumatic brain injury; TSGS = Tourette Syndrome Global Scale; TSSS = Tourette Symptom Severity Scale; VABS = Vineland Adaptive Behavior Scale; WASH-U-KSADS = Washington University in St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia; WISC = Wechsler Intelligence Scale for Children; YBOCS = Yale-Brown Obsessive Compulsive Scale; YGTSS = Yale Global Tic Severity Scale; YMRS = Young Mania Rating Scale; yr = year(s)

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