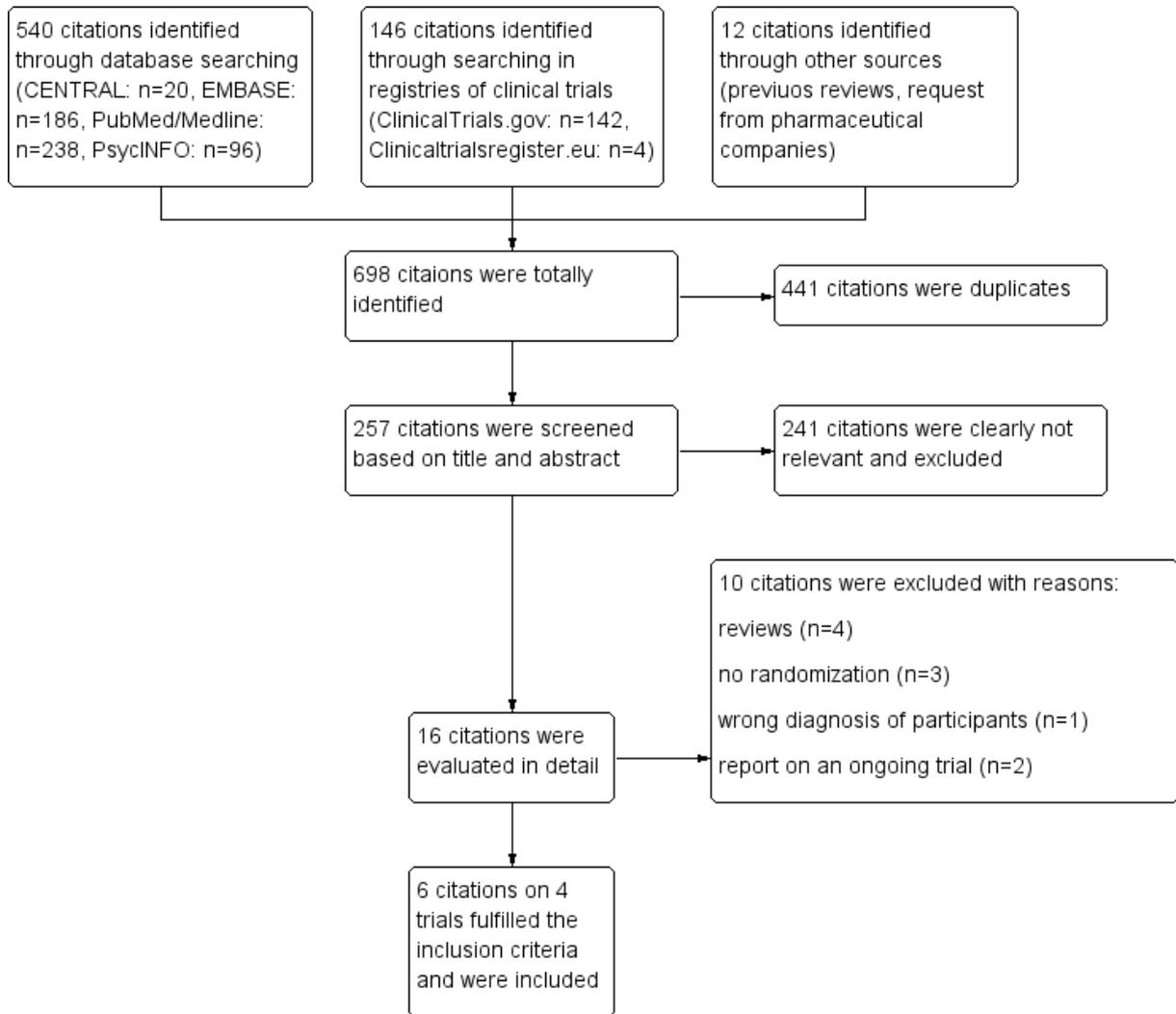


Study; country	Study groups with number of participants	Trial duration	Study design (setting)	Dose of the antipsychotic	Diagnosis	Mean BMI at baseline (in kg/m ²)	Mean age (in years)	Gender	Comments
Attia et al. [31]; USA, Canada	OLA: n=11 PLA: n=12	8 weeks	DB-RCT (outpatients)	OLA: mean final dose: 7.95 ± 2.7 mg/d	Anorexia nervosa (DSM-IV) (excluding amenorrhea)	OLA: 16.7 ± 1.5 PLA: 17.4 ± 1.0	27.7 ± 9.1	22 F, 1 M	No psychiatric medication for at least 4 weeks prior to study enrollment with the exception of stable doses of SSRI/SNRIs.
Bissada et al. [29]; Canada	EDP+OLA: n=16 EDP+PLA: n=18	10 weeks	DB-RCT (day hospital patients)	OLA: mean dose: 6.61 ± 2.32 mg/d	Anorexia nervosa (DSM-IV); 47% with AN-R and 53% with AN-BP	OLA: 16.39 ± 1.13 PLA: 15.93 ± 1.39	OLA: 23.61 ± 6.5 PLA: 29.67 ± 11.59	34 F	All participants attended a day hospital program for eating disorders including supervised meals and group therapy. Participants were required to remain free from psychotropic medication for a 2-week period prior to receiving study medication.
Brambilla et al. [28]; Italy	CBT+OLA: n=18 CBT+PLA: n=17	3 months	DB-RCT (outpatients)	OLA: 5 mg/d	Anorexia nervosa (DSM-IV); 60% with AN-R and 40% with AN-BP	OLA: 15.5 ± 1.9 PLA: 15.8 ± 1.1	OLA: 23.7 ± 4.8 PLA: 26.3 ± 8.5	35 F	All participants received a standardized course of CBT according to the same methodological protocol. No co-medication with other drugs.
Court et al. [30]; Australia	TAU+QUE: n=15 TAU: n=18	12 weeks	NB-RCT (in- and outpatients)	QUE: mean dose: 322.5 mg/d	Anorexia nervosa (DSM-IV); 71% AN-R and 29% AN-BP	QUE: 16.9 ± 1.7 TAU: 16.3 ± 1.8	QUE: 23.8 ± 9.4 TAU: 21.0 ± 3.3	32 F, 1 M	TAU contains a combination of CBT, supportive individual, group and family therapies, and other psychosocial interventions. 18 subjects received co-medication with SSRIs and/or benzodiazepines.

Hagman et al. [32]; USA	EDP+RIS: n=19 EDP+PLA: n=22	11 weeks	DB-RCT (inpatient, day hospital patients)	RIS: mean dose: 2.5 ± 1.2 mg/d	Anorexia nervosa (DSM-IV)	RIS: 15.9 ± 1.0 PLA: 16.1 ± 1.3	RIS: 16.2 ± 2.5 PLA: 15.8 ± 2.3	41 F	All participants attended an eating disorder program with family-centered care, individual, family, and group psychotherapies, nutritional consultation and meal plans. 16 subjects received stable co-medication with antidepressants.
Kafantaris et al. [33]; USA	EDP+OLA: n=10 EDP+PLA: n=10	10 weeks	DB-RCT (in- and outpatients, day-hospital patients)	OLA: mean dose: 8.5 mg/d	Anorexia nervosa with restricting subtype	OLA: 16.9 ± 0.6 PLA: 16.0 ± 1.5	OLA: 16.41 ± 2.2 PLA: 18.1 ± 2.04	20 F	All participants attended an eating disorder program with individualized medical care, nutritional management, and psychological treatment consisting of individual, group, family, and multifamily group therapy.
Powers et al. [34]; USA	QUE: n=6 PLA: n=9	8 weeks	DB-RCT	QUE: mean dose: 177.7 ± 90.8 mg/d	Anorexia nervosa (DSM-IV-TR); 53% with AN-R and 47% with AN-BP	15.9 ± 2.27	34.0 ± 13.48	14 F, 1 M	The majority of the participants had at least three additional Axis I diagnoses, most of them major depressive disorders.

Supplementary online Table 1: Characteristics of the included randomized, controlled trials investigating pharmacotherapy with second-generation antipsychotic drugs in anorexia nervosa (arranged alphabetically according to the last name of the first author of the original study).

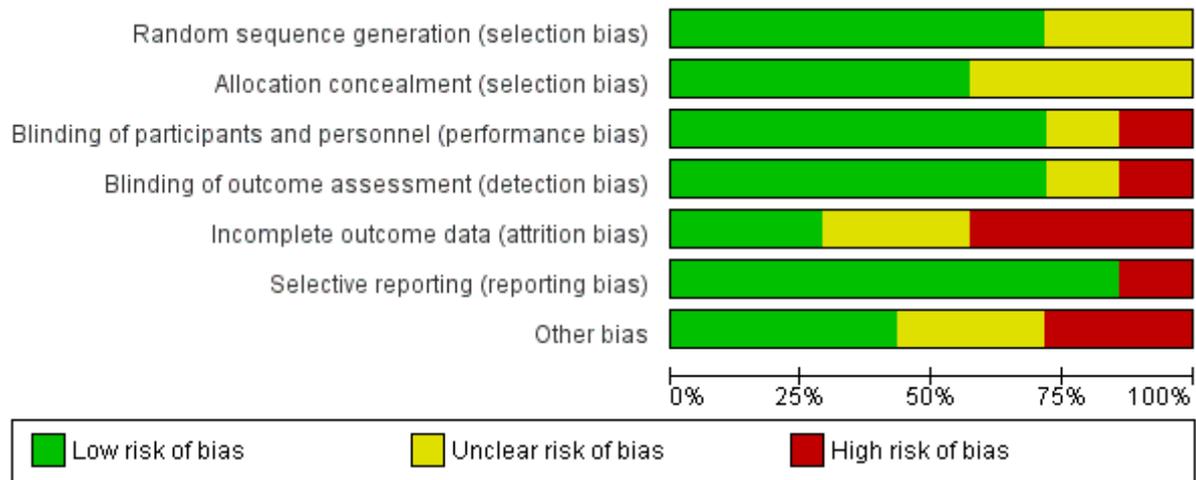
Abbreviations (alphabetical order): AN-BP = Anorexia nervosa binge-purging subtype; AN-R = Anorexia nervosa restricting subtype; BMI = body mass index; CBT = cognitive behavioral therapy; DB = double-blind; DSM-IV, DSM-IV-TR = various versions of the Diagnostic and Statistical Manual of Mental Disorders; EDP = eating disorder program; F = female; M = male; n = number of participants; NB = non-blinded; mg/d = mg/day; OLA = olanzapine; PLA = placebo; QUE = quetiapine; RCT = randomized controlled trial; RIS = risperidone; TAU = treatment as usual.



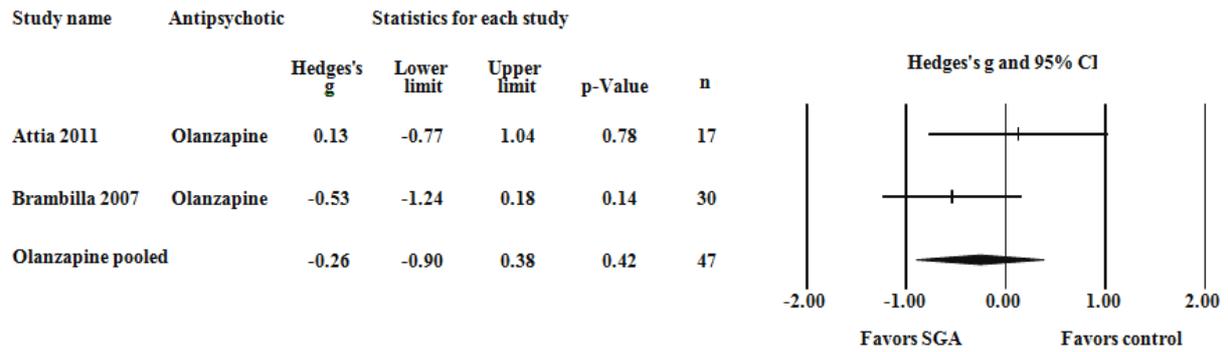
Supplementary online Figure 1: Flowchart of the systematic literature search

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Attia 2011	+	+	+	+	-	+	+
Bissada 2008	+	+	+	+	?	+	?
Brambilla 2007	?	?	+	+	?	+	+
Court 2007	+	?	-	-	-	+	-
Hagman 2011	+	+	+	+	+	-	-
Kafantaris 2011	+	+	+	+	+	+	+
Powers 2012	?	?	?	?	-	+	?

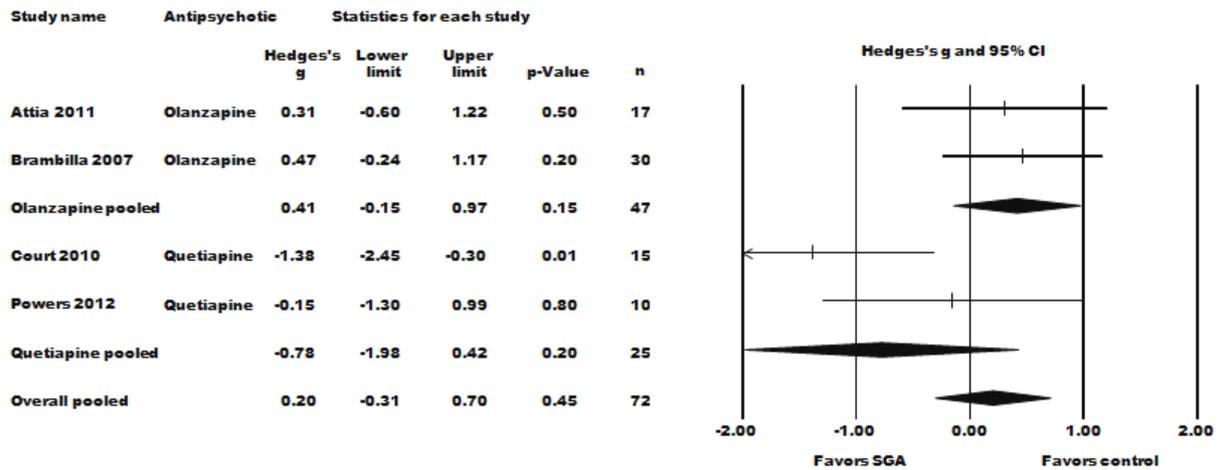
Supplementary online Figure 2: Overview regarding the single judgments for every item of the “risk of bias” tool of the Cochrane Collaboration [27]. A plus in a green circle illustrates “low risk of bias”, a question mark in a yellow circle displays “unclear risk of bias”, and a minus in a red circle indicates the rating of “high risk of bias”.



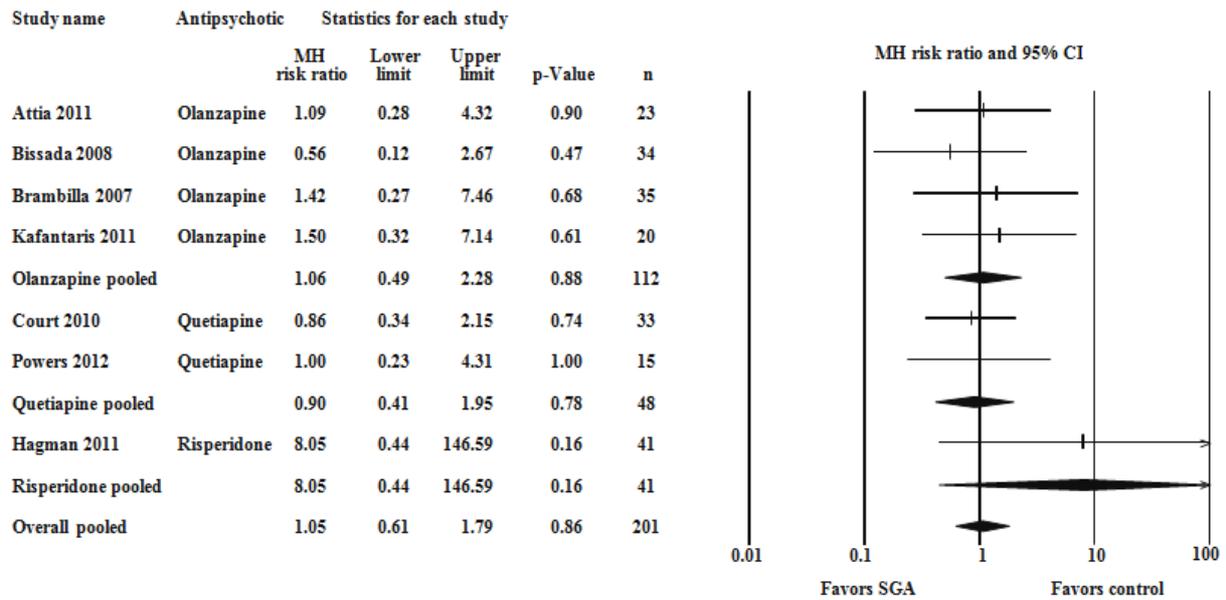
Supplementary online Figure 3: The graph illustrates the judgments for each “risk of bias” item presented as percentages across all included studies. The green part of the vertical-bar graph indicates the rating “low risk of bias” whereas the yellow part displays the judgment “unclear risk of bias” and the red one “high risk of bias”.



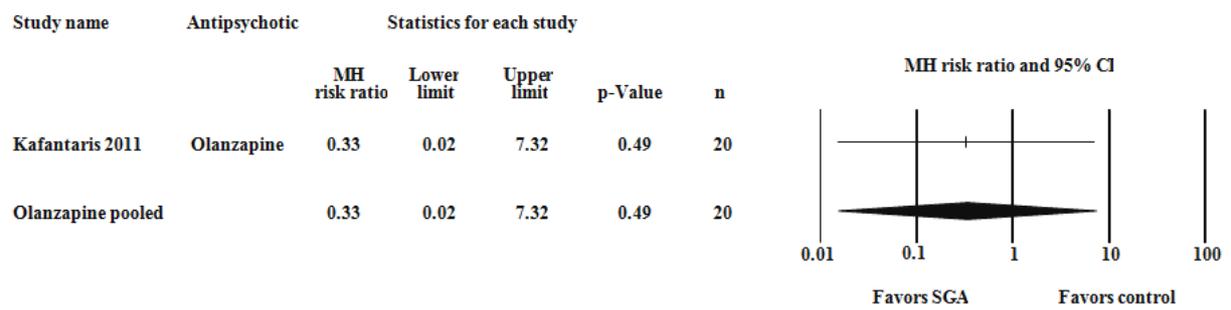
Supplementary online Figure 4: Effect sizes for mean changes in Yale–Brown–Cornell Eating Disorders Scale (YBC-EDS). Forest plot: comparison: second-generation antipsychotic drug (SGA) vs. placebo/no treatment. The forest plot illustrates the standardized mean differences based on Hedges's g with the corresponding 95% confidence intervals (CI). Numerical values <0 indicate a larger decrease in YBC-EDS total score in the SGA group than in the control group. Abbreviations: CI = confidence interval; n = number of participants; SGA = second generation antipsychotic drug.



Supplementary online Figure 5: Effect sizes for mean change in Eating Disorders Inventory (EDI). Forest plot: comparison: second-generation antipsychotic drug (SGA) vs. placebo/no treatment. The forest plot illustrates the standardized mean differences based on Hedges's g with the corresponding 95% confidence intervals (CI). Numerical values <0 indicate a larger decrease in EDI total score in the SGA group than in the control group. Abbreviations: CI = confidence interval; n = number of participants; SGA = second generation antipsychotic drug.

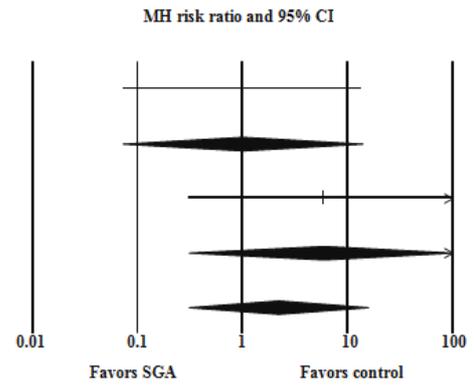


Supplementary online Figure 6: Effect sizes for all-cause discontinuation. Forest plot: comparison: second-generation antipsychotic drug (SGA) vs. placebo/no treatment; outcome: dropouts due to any reason. The forest plot illustrates the relative risks (RRs) with the associated 95% confidence intervals (CIs). The RR refers to the ratio between dropouts in the SGA group and in the control group. Numerical values greater than 1 indicate a higher rate of dropouts in the SGA group than in the control group. Abbreviations: CI = confidence interval; MH = Mantel-Haenszel; n = number of participants; SGA = second generation antipsychotic drug.

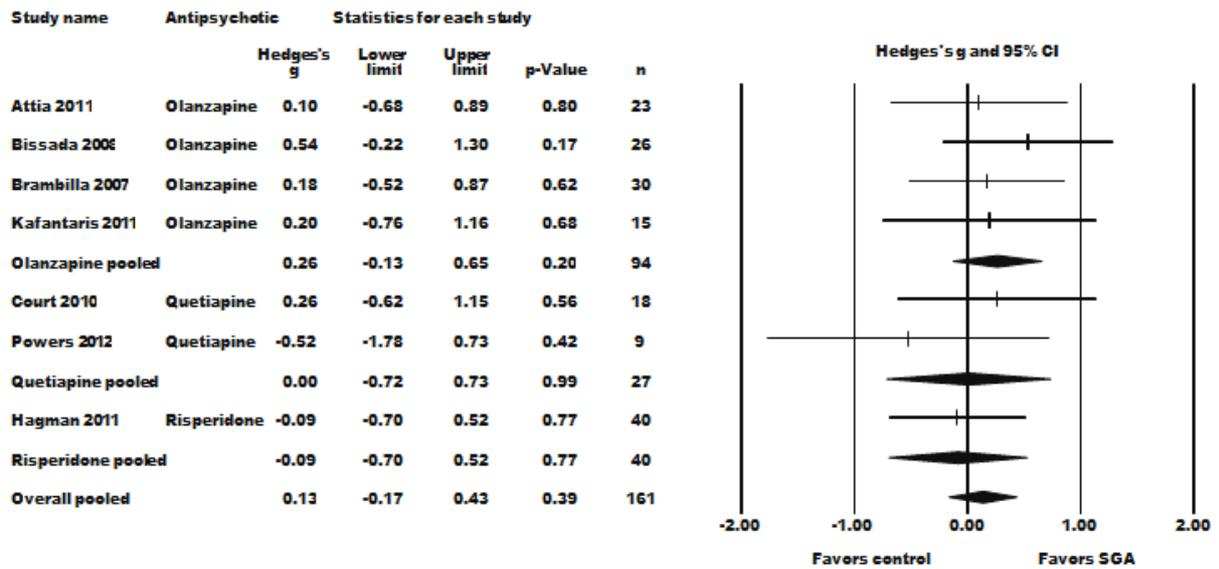


Supplementary online Figure 7: Effect sizes for the number of dropouts due to inefficacy of treatment; comparison: second-generation antipsychotic drug (SGA) vs. placebo/no treatment. The forest plot illustrates the relative risks (RRs) with the associated 95% confidence intervals (CIs). The RR refers to the ratio between dropouts in the SGA group and in the control group. Abbreviations: CI = confidence interval; MH = Mantel-Haenszel; n = number of participants; SGA = second generation antipsychotic drug.

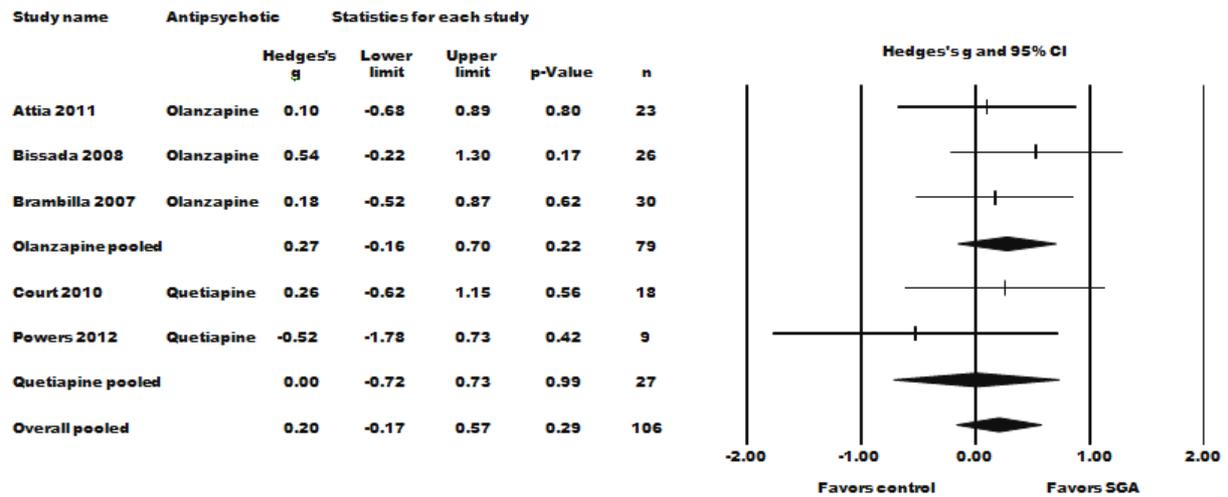
Study name	Antipsychotic	Statistics for each study				
		MH risk ratio	Lower limit	Upper limit	p-Value	n
Kafantaris 2011	Olanzapine	1.00	0.07	13.87	1.00	20
Olanzapine pooled		1.00	0.07	13.87	1.00	20
Court 2010	Quetiapine	5.94	0.31	114.88	0.24	33
Quetiapine pooled		5.94	0.31	114.88	0.24	33
Overall pooled		2.19	0.31	15.67	0.43	53



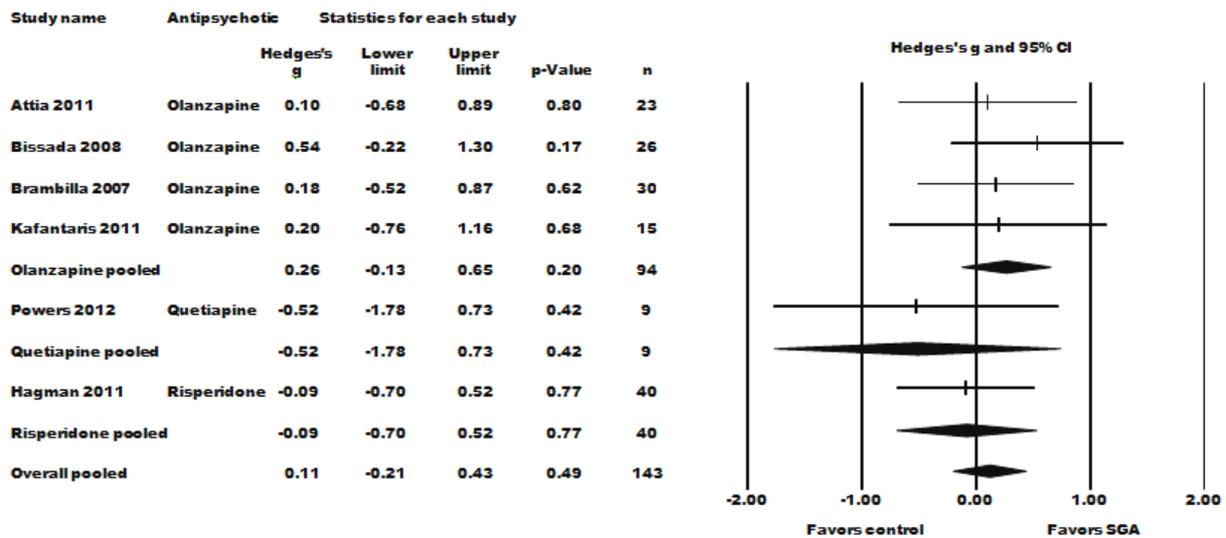
Supplementary online Figure 8: Effect sizes for the number of dropouts due to adverse effects; comparison: second-generation antipsychotic drug (SGA) vs. placebo/no treatment. The forest plot illustrates the relative risks (RRs) with the associated 95% confidence intervals (CIs). The RR refers to the ratio between dropouts in the SGA group and in the control group. Abbreviations: CI = confidence interval; MH = Mantel-Haenszel; n = number of participants; SGA = second generation antipsychotic drug.



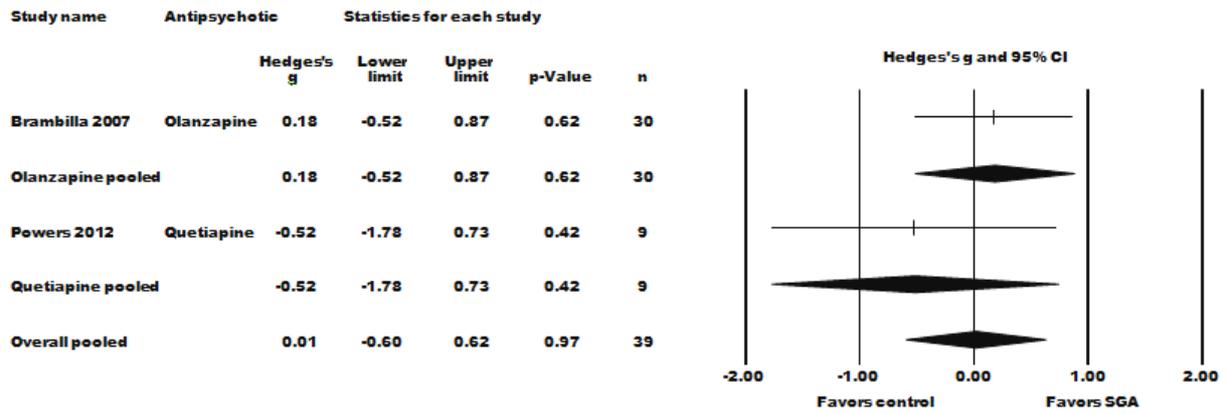
Supplementary online Figure 9: Sensitivity analysis: application of a fixed effects model instead of the random effects model; comparison: second-generation antipsychotic drug (SGA) vs. placebo/no treatment; outcome: mean change in body mass index (BMI). The forest plot illustrates the standardized mean differences based on Hedges's g with the corresponding 95% confidence intervals (CI). Abbreviations: CI = confidence interval; n = number of participants; SGA = second generation antipsychotic drug.



Supplementary online Figure 10: Sensitivity analysis: exclusion of trials which mean age <18 years [32, 33]; comparison: second-generation antipsychotic drug (SGA) versus placebo/no treatment; outcome: mean change in body mass index (BMI). The forest plot illustrates the standardized mean differences based on Hedges's g with the corresponding 95% confidence intervals (CI). Abbreviations: CI = confidence interval; n = number of participants; SGA = second generation antipsychotic drug.

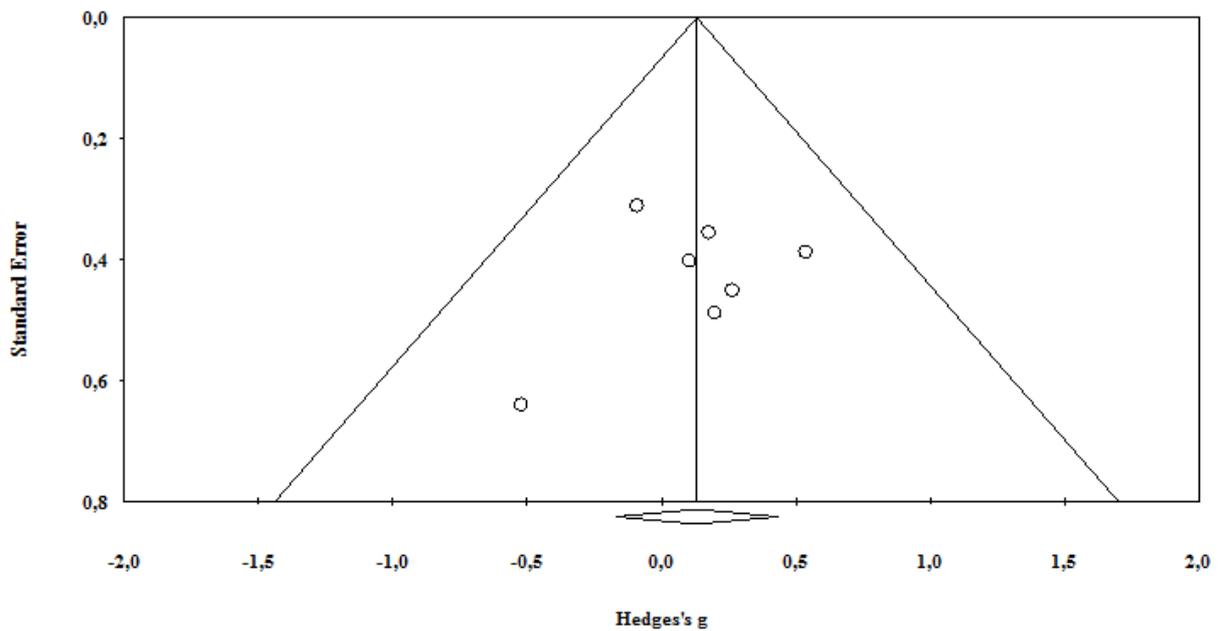


Supplementary online Figure 11: Sensitivity analysis: Exclusion of non-blinded trials [30]; comparison: second-generation antipsychotic drug (SGA) versus placebo/no treatment; outcome: mean change in body mass index (BMI). The forest plot illustrates the standardized mean differences based on Hedges's g with the corresponding 95% confidence intervals (CI). Abbreviations: CI = confidence interval; n = number of participants; SGA = second generation antipsychotic drug.



Supplementary online Figure 12: Sensitivity analysis: exclusion of trials that were sponsored by manufactures of antipsychotic drugs [29-33]; comparison: second-generation antipsychotic drug (SGA) vs. placebo/no treatment; outcome: mean change in body mass index (BMI). The forest plot illustrates the standardized mean differences based on Hedges's g with the corresponding 95% confidence intervals (CI). Abbreviations: CI = confidence interval; n = number of participants; SGA = second generation antipsychotic drug.

Funnel Plot of Standard Error by Hedges's g



Supplementary online Figure 13: In the funnel plot the standardized mean differences based on Hedges's g of all included studies are plotted against the standard errors (SEs) (referring to the primary outcome of mean BMI change). Based on the largely symmetrical arrangement of the single trials around the pooled effect size as equivalence line, there is no evidence for the presence of publication bias. Additionally, non-significant Egger's regression intercept test ($p=0.34$) suggests symmetry.