METABOLIC SIDE EFFECTS IN PERSONS WITH SCHIZOPHRENIA DURING MID- TO LONG-TERM TREATMENT WITH ANTIPSYCHOTICS: A NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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1 PRISMA checklist

PRISMA NMA Checklist of Items to Include When Reporting A Systematic Review Involving a Network Meta-analysis

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).*	Title, abstract, page 5
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: **Background:** main objectives **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.* **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; *treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.* **Discussion/Conclusions:** limitations; conclusions and implications of findings. **Other:** primary source of funding; systematic review registration number with registry name.	Page 3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, *including mention of why a network meta-analysis has been conducted.*	Page 4
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page 4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	Page 5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. *Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).*	Page 5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Page 5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 2.1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Page 5 and appendix 5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Page 6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Page 5
Geometry of the network	**S1**	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	Page 5, network plots figure 1 and appendix 8

Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Page 6 and appendix 14
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.*	Page 6 and appendix 4
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • *Handling of multi-arm trials;* • *Selection of variance structure;* • *Selection of prior distributions in Bayesian analyses; and* • *Assessment of model fit.*	Page 6 and details of statistical analysis in appendix 4
Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	Page 6 and appendix 9
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Page 6 and appendix 13
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • *Alternative formulations of the treatment network; and* • *Use of alternative prior distributions for Bayesian analyses (if applicable).*	Page 6
RESULTS†			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Page 7 and appendix 5
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	Figure 1 and appendix 8
Summary of network geometry	**S4**	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	Page 7-10, network plots figure 1 and appendix 8; Characteristics of included studies and Risk-of-bias assessment in appendix 6 and 14
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Appendix 6.3
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	Page 7, appendix 14.3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.*	Forest plots of pairwise meta-analyses for each outcome in appendix 8
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. *In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons.* If additional summary measures were explored (such as treatment rankings), these should also be presented.	Page 7-8, league tables and forest plots (figure 2-5 and appendix8)
Exploration for inconsistency	**S5**	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	Page 7 and appendix 9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	Page 7,10, appendix 13
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, *alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses*, and so forth).	Page 7, appendix 11-12

DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	Page 9
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).*	Page 10 and specific issues in appendix15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page 9-10
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	Funding/Support in Declaration section

PICOS = population, intervention, comparators, outcomes, study design.

* Text in italics indicates wording specific to reporting of network meta-analyses that has been added to guidance from the PRISMA statement.

† Authors may wish to plan for use of appendices to present all relevant information in full detail for items in this section.

2 Search strategy

2.1 Search strings and dates of searches

We searched the register of the Cochrane Schizophrenia Group's Study-Based Register of trials.

Following the methods from Cochrane [1], the Information Specialist compiles this register from systematic searches of major resources and their monthly updates (unless otherwise specified):

1. MEDLINE;
2. Embase;
3. Allied and Complementary Medicine (AMED);
4. Cumulative Index to Nursing and Allied Health Literature (CINAHL);
5. PsycINFO;
6. PubMed;
7. US National Institute of Health Ongoing Trials Register ClinicalTrials.gov;
8. World Health Organization International Clinical Trials Registry Platform (www.who.int/ictrp);
9. ProQuest Dissertations and Theses A&I and its quarterly update;
10. Chinese databases (Chinese Biomedical Literature Database, China Knowledge Resource Integrated Database, and Wanfang) and their annual updates until the end of 2016.

The register also includes handsearches and conference proceedings (see Group's website: http://schizophrenia.cochrane.org/register-trials). It does not place any limitations on language, date, document type or publication status.

Further information about the register has been published by Shokraneh et al [2-5].

The search string of the first search in the Cochrane Schizophrenia Group's Study-Based Register of trials (27/04/2020) was:

(*Amisulpride* OR *Aripiprazole* OR *Asenapine* OR *Benperidol* OR *Brexpiprazole* OR *Cariprazine* OR *Chlorpromazine* OR *Clopenthixol* OR *Clozapine* OR *Flupentixol* OR *Fluphenazine* OR *Fluspirilene* OR *Haloperidol* OR *Iloperidone* OR *Levomepromazine* OR *Loxapine* OR *Lumateperone* OR *Lurasidone* OR *Molindone* OR *Olanzapine* OR *Paliperidone* OR *Penfluridol* OR *Perazine* OR *Perphenazine* OR *Pimozide* OR *Quetiapine* OR *Risperidone* OR *Sertindole* OR *Sulpiride* OR *Thioridazine* OR *Tiotixene* OR *Trifluoperazine* OR *Ziprasidone* OR *Zotepine* OR *Zuclopenthixol*) in Intervention Field of STUDY

The update search was conducted in PubMed (14/06/2021) with the following search string:

(amisulpride OR aripiprazole OR asenapine OR benperidol OR brexpiprazole OR cariprazine OR chlorpromazine OR clopenthixol OR clozapine OR flupenthixol OR fluphenazine OR fluspirilene OR haloperidol OR Iloperidone OR levomepromazine OR methotrimeprazine OR loxapine OR lumateperone OR lurasidone OR molindone OR olanzapine OR paliperidone OR penfluridol OR perazine OR perphenazine OR pimozide OR quetiapine OR sertindole OR sulpiride OR thioridazine OR thiothixene OR trifluoperazine OR ziprasidone OR zotepine OR zuclopenthixol OR risperidone) AND random*

Filter: Publication date: From 2020/4/1 onwards

2.2 Survey to inform the choice of the searched first-generation antipsychotic drugs

As the aim of our network meta-analysis is to provide a comprehensive overview on long-term metabolic side effects of antipsychotic drugs, we did not apply any restrictions in form of administration and included all newer antipsychotics developed in the last decades (formerly called second-generation antipsychotics (SGAs)) as well as a selection of the most important older antipsychotics.

The selection of the older antipsychotics, formerly called first-generation antipsychotics, was informed by a survey of international schizophrenia experts [6]. In a simple survey 56 international experts were asked to select 10 formerly called first-generation antipsychotics that they found most important (for whatever reason) out of an alphabetically ordered list of at that time 52 antipsychotics listed by the "WHO Collaborating Centre for Drug Statistics" (http://www.whocc.no/atc_ddd_methodology/who_collaborating_centre/). Although the survey has methodological limitations in the selection of experts and statistical evaluation, it provides some guidance on which older antipsychotics are still clinically relevant. The 15 drugs with the most votes were chosen (chlorpromazine, clopenthixol, flupenthixol, fluphenazine, haloperidol, levomepromazine, loxapine, molindone, perazine, perphenazine, pimozide, sulpiride, thioridazine, trifluoperazine and zuclopenthixol). Benperidol and fluspirilene are frequently used in Germany and were therefore added to the selection because the project was sponsored by the German Ministry of Education and Research. Penfluridol and tiotixene were also supplemented because we knew from Cochrane reviews that many studies have been conducted, unlike for other older antipsychotics.

Of note, our list of included antipsychotics contains all antipsychotics listed in the WHO list of essential medicines [7].

3 Protocol

The protocol of this systematic review with network meta-analysis was registered in Prospero (CRD42020175414) and published in BMC Systematic Reviews [8].

3.1 Changes with respect to the protocol

In our protocol we planned a meta-regression on antipsychotic dose. However, due to methodological concerns regarding an appropriate model for this meta-regression, we decided to perform instead a post-hoc sensitivity analysis excluding doses of antipsychotics at the lower and upper ends of the International Consensus Study on Antipsychotic Dosing [9] to investigate the robustness of our primary results.

Additionally, we conducted one post-hoc sensitivity analysis of the primary outcome in which we pooled oral and LAI applications of the same drug to increase statistical power and connectivity.

4 Details of the data analysis

4.1 Measures of treatment effect

The effect size for continuous outcomes was mean difference (MD) as weight, glucose and lipid parameters were always measured on the same scale. In some cases units were converted: for weight, pounds were converted to kg and, for lipid and glucose parameters, mmol/l was converted to mg/dl.

If both data from observed cases and imputation methods to account for participants lost to follow-up (last-observation-carried forward, mixed-model-of-repeated-measurements) were available, we preferred the latter. (Data of observed cases for the primary outcome were also evaluated in a sensitivity analysis.)

If the original study investigators presented only the observed number of participants with the event, we assumed that participants lost to follow-up i.e., without reporting an event while they were observed in the study, would not have had the event should they have stayed in the study for the total follow-up.

If information on standard deviations (SDs) was missing, we derived SDs from standard errors, confidence intervals, t statistics, or P values for differences in means as described in Section 6.5.2.3 of the Cochrane Handbook for Systematic Reviews [10]. When no such information was available in the individual study, we derived SDs from those of the other studies using a validated imputation technique [11].

The effect size for the dichotomous outcome weight gain was odds ratio (OR) and its 95% credible interval (CrI). OR are prefered to risk ratios (RR) for meta-analyses due to their mathematical properties [12,13].

4.2 Statistical details for network meta-analysis and meta-regression models

When the consistency assumption was deemed reasonable, Bayesian network meta-analyses (NMA) and network meta-regression-analyses (NMR) were fitted as hierarchical model.

Bayesian NMA and NMR were fitted in R using using the BUGSnet package [14] and network meta-regression analyses using self-programmed routines with the rjags package [15], respectively. We accounted for the correlations induced by multi-arm studies by employing multivariate distributions.

The heterogeneity (variability in relative treatment effects within the same treatment comparison) was measured with the tau-squared (the variance of the random effects distribution). The heterogeneity variance was assumed common across the various treatment comparisons.

Network meta-analysis:

For the model without covariates we fitted a random effects consistency model using Placebo as reference. All models were run using three chains and 10 000 iterations after an initial burn-in of 1 000.

Network meta-regressions:

In the network meta-regression models, we set

$\theta^*_{i,\kappa}=\theta_{i,\kappa} + \beta_\kappa \times x_i$ where x_i indicates the continuous covariate (e.g. study duration) in study i,

or

$\theta^*_{i,\kappa}=\theta_{i,\kappa} + \beta_{1,\kappa} \times x_{1,i} + \cdots + \beta_{j,k} \times x_{j,i}$, in case the covariate is categorical (e.g. gender) and x_i indicates the frequency of j category (e.g. proportion of women) in i study.

If the study includes placebo as a reference, then $\beta_\kappa = B$ (or $\beta_{j,\kappa} = B$) is the increase in the effect of treatment k versus placebo for one unit of increase in the covariate. If study i involves only active treatments, we assume $\beta_\kappa = 0$ (or $\beta_{j,\kappa} = 0$).

Priors:

We assume vague normal priors $N(0, 10^4)$ for the parameters u_i and d_B, d_C, d_D, ... and B.
For heterogeneity we employed a uniform distribution $\tau \sim U(0,5)$.

Convergence:

All models were run using two chains and 100 000 iterations after an initial burn-in of 1 000; a thinning of 2 was used. This was deemed appropriate based on autocorrelation plots and the visualization of the chain convergence.

5 Characteristics and references of included studies

5.1 Overview of characteristics of studies with usable data

Characteristic	Value
N studies with usable data	137
N participants	35007
N antipsychotic drugs used	31
N studies using double blind design (%)	96 (70%)
N studies using enriched design (%)	26 (19%)
N studies sponsored by pharmaceutical companies (%)	108 (79%)
Years when studies were published	1967 to 2020
Median average age of participants (IQR, range)	38.93 (35.25 to 41.36, 15.35 to 69.45) years
Median percentage of women (IQR, range)	37.06 (29.23 to 42.75, 0 to 100) %
Median duration of studies (IQR, range)	45 (26 to 52, 16 to 104) weeks
Median dose in olanzapine equivalents used (IQR, range)	14 (11.41 to 17.78, 2.61 to 33.01) mg/day
Median baseline weight (IQR, range)	76.55 (72.03 to 81.60, 53.51 to 103.66) kg

Table of summary characteristics of studies with usable data for any analysis. N = number, IQR = Interquartile Range.

5.2 Overview of characteristics of studies reporting the primary outcome "weight gain"

Characteristic	Value
N studies with usable data	110
N participants	29215
N antipsychotic drugs used	28
N studies using double blind design (%)	81 (74%)
N studies using enriched design (%)	22 (20%)
N studies sponsored by pharmaceutical companies (%)	95 (86%)
Years when studies were published	1970 to 2018
Median average age of participants (IQR, range)	38.93 (35.51 to 41.05, 15.35 to 69.45) years
Median percentage of women (IQR, range)	37.06 (30.06 to 42.21, 15 to 100) %
Median duration of studies (IQR, range)	48 (26 to 52, 16 to 104) weeks
Median dose in olanzapine equivalents used (IQR, range)	14 (11.3 to 17.35, 2.61 to 32.86) mg/day
Median baseline weight (IQR, range)	76.55 (71.76 to 81.46, 53.51 to 103.66) kg

Table of summary characteristics of studies with usable data for any analysis. N = number, IQR = Interquartile Range.

5.3 Characteristics and references of specific studies with usable data

Study	Year of publication	Blinding	Duration (wks)	Diagnostic term (diagnostic criteria)	Intervention	Application	Dosing interval	Dose mean and range (mg)	N (randomized)	% female	Age mean (y)	Baseline weight mean (kg)
Abuzzahab 1977a [16]	1980	double blind	156	Schizophrenia (Clinical Diagnosis)	Fluphenazine	oral	daily	12.7 (3-30)	31	76%	34.8	-
					Pimozide	oral	daily	5.5 (2-20)	31	58%	30.8	-
Abuzzahab 1982 [17]	1982	double blind	24	Schizophrenia (Clinical Diagnosis)	Haloperidol	oral	daily	17.5 (5-40)	29	64%	35.0	72.1
					Tiotixene	oral	daily	31.8 (10-80)	28	50%	34.0	74.4
Actrn12618001113246 [18]	2018	open-label	26	Schizophrenia (DSM-V)	Paliperidone	LAI	every 4 wks	- (50-150)	36	-	46.4	-
					Paliperidone	oral	daily	- (6-12)	36	-	46.4	-
Adrianzen 2008 [19]	2008	open-label	39	Schizophrenia or schizophreniform disorder (DSM-IV)	Haloperidol	oral	daily	- (5-20)	40	48%	31.8	-
					Olanzapine	oral	daily	- (5-20)	31	29%	28.9	-
Alvarez 2006 [20]	2006	open-label	52	Schizophrenia with prominent negative symptoms (DSM-IV)	Olanzapine	oral	daily	12.2 (10--)	124	31%	37.0	73.8
					Risperidone	oral	daily	4.9 (3--)	123	24%	35.5	80.5
Alvarez 2012 [21]	2012	double blind	26	Schizophrenia (DSM-IV-TR)	Olanzapine	oral	daily	15 (10-20)	24	33%	35.1	72.0
					Ziprasidone	oral	daily	107.4 (80-160)	28	25%	40.8	79.9
Amin 1977 [22]	1977	double blind	16	Schizophrenia (Clinical diagnosis)	Pimozide	oral	daily	4.6 (2-12)	10	70%	38.6	-
					Trifluoperazine	oral	daily	14 (5-30)	10	70%	38.6	-
Arato 2002 [23]	2002	double blind	52	Chronic stable Schizophrenia (DSM-III-R)	Placebo	oral	-	-	71	17%	48.7	73.5
					Ziprasidone	oral	daily	160 (160-160)	67	34%	49.6	71.3
Arvanitis 1993 [24]	1995	double blind	52	Schizophrenia (DSM-III-R)	Haloperidol	oral	daily	12 (12-12)	41	15%	37	84.3
					Quetiapine 600mg	oral	daily	600 (600-600)	87	21%	38	82.3
Bai 2006 [25]	2007	single blind	48	Schizophrenia (DSM-IV)	Risperidone	LAI	every 2 wks	- (25-50)	25	52%	44.7	-
					Risperidone	oral	daily	-	25	48%	48.1	-
Barak 2002 [26]	2002	open-label	-	Schizophrenia (DSM-IV (APA))	Haloperidol	oral	daily	7.2 (-)	10	-	69.2	-
					Olanzapine	oral	daily	13.1 (5-25)	10	-	69.2	-
Beasley 2003 [27]	2003	double blind	52	Schizophrenia or schizoaffective disorder (DSM-IV)	Olanzapine	oral	daily	13.4 (10-20)	224	47%	36.2	79.1
					Placebo	oral	-	-	102	47%	35.1	79.3
Berwaerts 2015 [28]	2015	double blind	-	Schizophrenia (DSM-IV-TR)	Paliperidone	LAI	every 12 wks	402 (175-525)	160	26%	37.1	79.4
					Placebo	LAI	-	-	145	24%	38.5	79
Bitter 2004 [29]	2004	double blind	18	Schizophrenia, treatment-resistant (DSM-IV)	Clozapine	oral	daily	216.2 (100-500)	72	40%	37.4	-
					Olanzapine	oral	daily	17.2 (5-25)	75	40%	37.6	-
Breier 2005 [30]	2005	double blind	28	Schizophrenia (DSM-IV)	Olanzapine	oral	daily	15.3 (10-20)	277	35%	40.0	77.7
					Ziprasidone	oral	daily	116.0 (80-160)	271	37%	38.2	77.1
Buchanan 2005 [31]	2005	double blind	16	Schizophrenia or schizoaffective disorder (DSM-IV)	Haloperidol	oral	daily	18.3 (10-30)	34	29%	46.4	87.2
					Olanzapine	oral	daily	20.3 (10-30)	29	24%	41.9	83.4
Buchanan 2012a_26 weeks [32]	2012	double blind	26	Schizophrenia (DSM-IV-TR)	Asenapine	oral	daily	14.5 (10-20)	244	28%	43.1	84.2
					Olanzapine	oral	daily	14 (5-20)	224	24%	42.8	84.7
Buchanan 2012b_26 weeks [33]	2012	double blind	26	Schizophrenia (DSM-IV-TR)	Asenapine	oral	daily	14.4 (10-20)	241	32%	40.7	79.3
					Olanzapine	oral	daily	12.5 (5-20)	240	32%	40.3	80.3
Carrière 2000 [34]	2000	double blind	16	Schizophrenia or schizophreniform disorder (DSM-IV)	Amisulpride	oral	daily	700 (400-1200)	94	32%	31.8	67.8
					Haloperidol	oral	daily	17.5 (10-30)	105	31%	30.0	67.2
Chan 2010a [35]	2010	single blind	24	Schizophrenia, schizophreniform	Olanzapine	oral	daily	12.6 (2.5-20)	30	63%	48.0	60.8
					Risperidone	oral	daily	4.1 (0.5-6)	30	67%	42.7	60.8

				or schizoaffective disorder (DSM-IV)								
Chen 2010 [36]	2010	double blind	52	Schizophrenia or related disorders (DSM-IV)	Placebo	oral	-	-	89	54%	24.9	66.3
					Quetiapine	oral	daily	400 (400-400)	89	56%	23.5	66
Chetvertnykh 2008 [37]	2008	-	52	Schizophrenia or schizophreniform disorder (ICD-10)	Haloperidol	oral	daily	4.8 (-)	15	-	-	-
					Olanzapine	oral	daily	12.4 (-)	15	-	-	-
					Quetiapine	oral	daily	24.6 (-)	15	-	-	-
					Risperidone	oral	daily	3.3 (-)	15	-	-	-
Chowdhury 1999 [38]	1999	-	16	Schizophrenia and subtypes (ICD-10)	Clozapine	oral	daily	342.9 (200-500)	30	27%	30.3	-
					Risperidone	oral	daily	5.8 (4-8)	30	23%	32.4	-
Chrzanowski 2006 [39]	2006	open-label	52	Schizophrenia (DSM-IV)	Aripiprazole	oral	daily	22 (15-30)	104	43%	41.7	73.6
					Olanzapine	oral	daily	14.2 (10-20)	110	48%	41.3	72.1
Citrome 2012 [40]	2012	double blind	52	Schizophrenia or schizoaffective disorder (DSM-IV)	Lurasidone	oral	daily	84.7 (40-120)	427	28%	41.7	83
					Risperidone	oral	daily	4.3 (2-6)	202	38%	41.6	80.9
Claghorn 1974 [41]	1974	double blind	24	Schizophrenia (Clinical diagnosis)	Pimozide	oral	daily	5.2 (2-12)	43	63%	40.1	-
					Trifluoperazine	oral	daily	12.5 (5-30)	44	84%	44.9	-
Clark 1968b [42]	1968	double blind	14	Chronic schizophrenic patients (clinical diagnosis)	Chlorpromazine	oral	daily	663 (258-835)	18	100%	41.6	-
					Placebo	oral	-	-	18	100%	41.3	-
Clark 1970 [43]	-	double blind	16	Chronic schizophrenic females (-)	Chlorpromazine	oral	daily	600 (--800)	39	100%	-	57.9
					Placebo	oral	-	-	19	100%	-	58.8
Clark 1970b [44]	1970	double blind	24	Chronic Schizophrenia (clinical diagnosis)	Chlorpromazine 300mg/d	oral	daily	300 (300-300)	15	100%	43	58.3
					Chlorpromazine 600mg/d	oral	daily	600 (600-600)	17	100%	44.6	56.9
					Placebo	oral	-	-	17	100%	43.8	58.3
Clark 1975a [45]	1975	double blind	24	Schizophrenia (Clinical diagnosis)	Pimozide	oral	daily	5.3 (2-16)	15	100%	42.5	-
					Placebo	oral	-	-	10	100%	42.1	-
					Thioridazine	oral	daily	188.8 (75-375)	15	100%	43.5	-
Colonna 2000 [46]	2000	open-label	52	Subchronic or chronic Schizophrenia with acute exazerbation (DSM-III-R)	Amisulpride	oral	daily	605 (200-800)	370	31%	36.8	72.1
					Haloperidol	oral	daily	14.6 (5-20)	119	38%	39.6	72.2
Cooper 2000b [47]	2000	double blind	26	Schizophrenia (DSM-III-R)	Placebo	oral	-	-	58	28%	41.6	75.8
					Zotepine	oral	daily	260.7 (150-300)	63	34%	43	76.2
Csernansky 2002 [48]	2002	double blind	104	Schizophrenia or schizoaffective disorder (DSM-IV)	Haloperidol	oral	daily	11.7 (5-20)	188	32%	40.1	82.8
					Risperidone	oral	daily	4.9 (2-8)	179	28%	40.3	82.8
Ctri-2014-10-005144 [49]	2016	open-label	52	Newly diagnosed cases of Schizophrenia, schizotypal and delusional disorders (ICD-10)	Iloperidone	oral	daily	- (8-12)	50	36%	28.8	55.1
					Olanzapine	oral	daily	- (10-20)	50	28%	30.5	55.3
Ctri-2016-02-006660 [50]	2017	open-label	14	Schizophrenia (ICD-10)	Clozapine	oral	daily	322.5 (150-450)	24	35%	39.4	-
					Quetiapine	oral	daily	790 (400-800)	29	30%	39.4	-
Cuomo 2017 [51]	2018	open-label	52	Schizophrenia spectrum and other psychotic disorders or bipolar disorder with psychotic features (DSM-V)	Aripiprazole	LAI	every 4 wks	- (300-400)	50	18%	32.9	78.4
					Paliperidone	LAI	every 4 wks	100 (-)	51	22%	36.9	77.3
Daniel 1998 [52]	1998	double blind	52	Schizophrenia (DSM-III-R or DSM-IV)	Haloperidol	oral	daily	10 (10-10)	141	25%	38.3	84.3
					Sertindole	oral	daily	24 (24-24)	141	24%	39.5	84.1
Deberdt 2008 [53]	2008		26		Olanzapine	oral	daily	16.9 (7.5-20)	68	35%	45.4	100.7

		double blind		Schizophrenia/schizo affective disorder (DSM-IV)	Quetiapine	oral	daily	439.7 (300-800)	65	43%	42.5	106.7
Del Giudice 1975 [54]	1975	single blind	104	Schizophrenia (Clinical diagnosis)	Fluphenazine	LAI	every 2 wks	25 (25-25)	27	0%	-	-
					Fluphenazine	oral	daily	21.7 (5-80)	31	0%	-	-
Detke 2014 [55]	2012	open-label	104	Schizophrenia (DSM-IV or DSM-IV-TR)	Olanzapine	LAI	every 4 wks	386.6 (150-405)	264	34%	41.7	81.6
					Olanzapine	oral	daily	- (5-20)	260	32%	40.1	79.8
Dossenbach 2004 [56]	2004	double blind	22	Schizophrenia or schizoaffective disorder (DSM-IV)	Fluphenazine	oral	daily	11.7 (6-21)	30	53%	35.4	75.6
					Olanzapine	oral	daily	14.8 (5-20)	30	53%	35.4	73
Durgam 2016b [57]	2015	double blind	72	Schizophrenia (DSM-IV-TR)	Cariprazine	oral	daily	7.07 (3-9)	101	39%	39.2	75.7
					Placebo	oral	-	-	99	29%	37.7	74.9
Emsley 2005 [58]	2005	single blind	52	Schizophrenia or schizoaffective disorder with tardive dyskinesia (DSM-IV)	Haloperidol	oral	daily	8.5 (--20)	23	35%	50.1	66.6
					Quetiapine	oral	daily	400 (400-800)	22	36%	49.2	71.9
EQUATOR [59]	2015	double blind	52	Schizophrenia (DSM-IV-TR)	Brexpiprazole	oral	daily	3.6 (1-4)	97	40%	38.8	-
					Placebo	oral	-	-	105	38%	41.6	-
Fleischhacker 2014 [60]	2014	double blind	38	Schizophrenia (DSM-IV-TR)	Aripiprazole	LAI	every 4 wks	392 (300-400)	265	40%	41.7	83.4
					Aripiprazole	oral	daily	20 (10-30)	266	37%	41.2	83.7
Fu 2015 [61]	2015	double blind	65	Schizoaffective disorder (DSM-IV)	Paliperidone	LAI	every 4 wks	114.3 (50-150)	164	48%	39.3	79.7
					Placebo	LAI	-	-	170	51%	38	82.3
Gaebel 2010 [62]	2010	open-label	104	Schizophrenia or schizoaffective disorder (DSM-IV)	Quetiapine	oral	daily	413.4 (300-750)	342	43%	42.6	79.2
					Risperidone	LAI	every 2 wks	33.6 (25-50)	343	41%	40.6	80.8
Gureje 2003 [63]	2003	double blind	30	Schizophrenia, schizoaffective disorder, or schizophreniform disorder (DSM-IV)	Olanzapine	oral	daily	17.2 (10-20)	32	38%	35.6	84.5
					Risperidone	oral	daily	6.6 (4-8)	33	45%	34.8	77.2
Hirsch 2002 [64]	2002	double blind	28	Schizophrenia (DSM-III-R)	Haloperidol	oral	daily	8.6 (5-15)	153	31%	39.4	75.9
					Ziprasidone	oral	daily	116.5 (80-160)	148	38%	39.2	76
Hough 2010 [65]	2010	double blind	-	Schizophrenia (DSM-IV)	Paliperidone	LAI	every 4 wks	82.8 (25-100)	206	47%	38.8	79.5
					Placebo	LAI	-	-	204	46%	39.4	79
Ishigooka 2015 [66]	2015	double blind	52	Schizophrenia (DSM-IV-TR)	Aripiprazole	LAI	every 4 wks	393.8 (300-400)	228	40%	40.2	65.2
					Aripiprazole	oral	daily	15.7 (6-24)	227	38%	38.2	64.9
Jarema 2003 [67]	2003	double blind	18	Schizophrenia (DSM-IV)	Olanzapine	oral	daily	13.8 (10-20)	47	-	35.2	76.3
					Perphenazine	oral	daily	29.7 (8-40)	48	-	35.2	74.5
Kahn 2008 [68]	2008	open-label	52	Schizophrenia, schizophreniform disorder, or schizoaffective disorder (DSM-IV)	Amisulpride	oral	daily	450.8 (200-800)	104	44%	25.2	-
					Haloperidol	oral	daily	3 (1-4)	103	38%	25.4	-
					Olanzapine	oral	daily	12.6 (5-20)	105	36%	26.3	-
					Quetiapine	oral	daily	498.6 (200-750)	104	35%	26.4	-
					Ziprasidone	oral	daily	107.2 (40-160)	82	50%	26.7	-
Kane 2009_28 weeks [69]	2009	double blind	28	Schizophrenia (DSM-IV-TR)	Aripiprazole	oral	daily	18.9 (10-30)	285	33%	38.2	80.2
					Olanzapine	oral	daily	16.4 (10-20)	281	31%	39.3	80.9
Kane 2010a_52w [70]	2010	double blind	58	Schizophrenia with an acute exacerbation (DSM-IV-TR)	Asenapine	oral	daily	- (10-20)	93	40%	35.3	-
					Haloperidol	oral	daily	- (4-16)	43	58%	39.9	-
Kane 2010c [71]	2010	double blind	24	Schizophrenia (DSM-IV or DSM-IV-TR)	Olanzapine	LAI	every 2 wks	150 (150-150)	140	40%	37.7	78.4
					Olanzapine	LAI	every 2 wks	300 (300-300)	141	33%	39.5	75.2
					Olanzapine	LAI	every 4 wks	405 (405-405)	318	33%	39.0	77.8
					Olanzapine	oral	daily	14.3 (10-20)	322	35%	39.0	77.0
Kane 2011 [72]	2011		26		Asenapine	oral	daily	17.6 (--20)	194	46%	39.2	76.7

		double blind		Schizophrenia (DSM-IV)	Placebo	oral	-	-	192	40%	38.7	76.4
Kane 2012 [73]	2012	double blind	52	Schizophrenia (DSM-IV-TR)	Aripiprazole	LAI	every 4 wks	396.3 (300-400)	269	40%	40.1	80.6
					Placebo	LAI	-	-	134	41%	41.7	84.8
Kasper 2003 [74]	2003	double blind	52	Schizophrenia, acute relapse (DSM-IV)	Aripiprazole	oral	daily	29.0 (29.0-29.0)	861	41%	37.3	74.5
					Haloperidol	oral	daily	8.9 (8.9-8.9)	433	43%	36.8	73.1
Kasthurip 2012 [75]	2012	-	26	Schizophrenia (Clinical Diagnosis)	Haloperidol	oral	daily	-	30	-	-	-
					Olanzapine	oral	daily	-	30	-	-	-
Keefe 2006 [76]	2006	double blind	52	Schizophrenia or schizoaffective disorder (DSM-IV)	Haloperidol	oral	daily	8.2 (8.2-8.2)	97	29%	39.8	88.8
					Olanzapine	oral	daily	12.3 (12.3-12.3)	159	28%	38.4	88.1
					Risperidone	oral	daily	5.2 (5.2-5.2)	158	30%	39.5	86.1
Keks 2007 [77]	2007	open-label	53	Schizophrenia or schizoaffective disorder (DSM-IV)	Olanzapine	oral	daily	14.6 (5-20)	300	42%	35.2	76.5
					Risperidone	LAI	every 2 wks	40.7 (25-50)	318	44%	35.1	75.9
Kern 2006 [78]	2006	open-label	26	Schizophrenia or schizoaffective disorder (DSM-IV)	Aripiprazole	oral	daily	30 (30-30)	128	37%	39.6	-
					Olanzapine	oral	daily	15 (15-15)	127	34%	40.4	-
Kinon 2006a [79]	2006	double blind	24	Schizophrenia or schizoaffective disorder (DSM-IV)	Olanzapine	oral	daily	15.6 (10-20)	171	33%	41.7	91.8
					Quetiapine	oral	daily	455.8 (300-700)	175	35%	40.5	89.5
Kinon 2006b [80]	2006	double blind	24	Schizophrenia or schizoaffective disorder with prominent depressive symptoms (DSM-IV)	Olanzapine	oral	daily	14.2 (10-20)	202	35%	41.1	89.5
					Ziprasidone	oral	daily	110.2 (80-160)	192	40%	42.1	87.9
Kline 1977 [81]	1977	double blind	16	Schizophrenia (Clinical diagnosis)	Pimozide	oral	daily	6.5 (4-12)	22	57%	-	-
					Trifluoperazine	oral	daily	15.7 (5-25)	22	67%	-	-
Kongsakon 2006 [82]	2006	double blind	24	Schizophrenia (DSM-IV)	Haloperidol	oral	daily	8.7 (5-20)	132	37%	31.8	56.2
					Olanzapine	oral	daily	10.2 (5-20)	144	49%	32.7	56.6
Koshikawa 2016 [83]	2016	open-label	24	Schizophrenia or schizoaffective disorder (DSM-IV-TR)	Paliperidone	LAI	every 4 wks	- (--150)	14	60%	43.5	65.6
					Risperidone	LAI	every 2 wks	- (25-50)	16	36%	46.4	74.8
Kramer 2007 [84]	2007	double blind	-	Schizophrenia (DSM-IV)	Paliperidone	oral	daily	10.8 (3-15)	105	45%	39	72.6
					Placebo	oral	-	-	102	38%	37.5	75.9
Laborde 2000 [85]	2000	double blind	26	Chronic or subchronic Schizophrenia (DSM-III-R)	Haloperidol	oral	daily	15 (20-20)	66	25%	34.8	75.1
					Zotepine	oral	daily	225 (300-300)	59	25%	33.5	73
Laties 2014 [86]	2014	open-label	104	Schizophrenia or schizoaffective disorder (DSM-IV)	Quetiapine	oral	daily	386.3 (200-800)	596	42%	40.2	91.7
					Risperidone	oral	daily	3.2 (2-8)	502	40%	40.6	91.2
Lecrubier 2006 [87]	2006	double blind	26	Schizophrenia, residual, disorganised or catatonic (DSM-IV)	Amisulpride	oral	daily	150 (150-150)	70	29%	37.8	71.7
					Olanzapine 20mg	oral	daily	20 (20-20)	70	26%	36.4	70.6
					Olanzapine 5mg	oral	daily	5 (5-5)	70	40%	38.1	70.2
					Placebo	oral	-	-	34	35%	38.2	75.4
Lieberman 2003a_2y [88]	2003	double blind	104	First-episode of Schizophrenia, schizophreniform disorder, and schizoaffective disorder (DSM-IV)	Haloperidol	oral	daily	4.8 (2-20)	132	16%	24	73.0
					Olanzapine	oral	daily	10.2 (5-20)	131	21%	23.5	71.7
Lieberman 2003b [89]	2003	double blind	52	First-episode of Schizophrenia, schizophreniform disorder, and schizoaffective disorder (DSM-IV)	Chlorpromazine	oral	daily	319 (-)	83	48%	28.7	60.3
					Clozapine	oral	daily	292 (-)	81	48%	28.7	61.6
Lieberman 2005_18months [90]	2005	double blind	78	Schizophrenia (DSM-IV)	Olanzapine	oral	daily	20.1 (7.5-30)	336	27%	40.8	87.2
					Perphenazine	oral	daily	20.8 (8-32)	261	24%	40	88.8

					Quetiapine	oral	daily	543.4 (200-800)	337	24%	40.9	88.8
					Risperidone	oral	daily	3.9 (1.5-6)	341	26%	40.6	89.4
					Ziprasidone	oral	daily	112.8 (40-160)	185	30%	40.1	88.8
Loo 1997 [91]	1997	double blind	26	Schizophrenia with predominant negative symptoms (DSM-III-R)	Amisulpride	oral	daily	100 (100-100)	69	33%	33	69.4
					Placebo	oral	-	-	72	25%	36	71.3
McEvoy 2006 [92]	2006	double blind	-	Chronic Schizophrenia, not responsive to prior atypical antipsychotics (DSM-IV)	Olanzapine	oral	daily	23.4 (7.5-30)	19	5%	44.3	-
					Quetiapine	oral	daily	642.9 (200-800)	15	20%	37.1	-
					Risperidone	oral	daily	4.8 (1.5-6)	16	38%	37.7	-
McEvoy 2007a [93]	2007	double blind	52	Schizophrenia, schizophreniform disorder or schizoaffective disorder (DSM-IV)	Olanzapine	oral	daily	11.7 (2.5-20)	133	24%	24.7	78
					Quetiapine	oral	daily	506 (100-800)	134	31%	25	77.2
					Risperidone	oral	daily	2.4 (0.5-4)	133	26%	23.9	78.5
McEvoy 2014 [94]	2014	double blind	104	Schizophrenia or schizoaffective disorder (DSM-IV-TR)	Haloperidol	LAI	every 4 wks	75 (25-200)	154	24%	45	90
					Paliperidone	LAI	every 4 wks	150 (39-234)	157	27%	43	90
McQuade 2004_26weeks [95]	2004	double blind	26	Schizophrenia, acute relapse (DSM-IV)	Aripiprazole	oral	daily	25.1 (15-30)	156	27%	38.6	80.8
					Olanzapine	oral	daily	16.5 (10-20)	161	29%	38.2	80.4
Mortimer 2004 [96]	2004	double blind	26	Schizophrenia or schizophreniform disorder (DSM-IV)	Amisulpride	oral	daily	504 (200-800)	189	34%	38.2	73.4
					Olanzapine	oral	daily	13 (5-20)	188	36%	37.4	72.8
Naber 2005 [97]	2005	double blind	26	Schizophrenia (DSM-IV)	Clozapine	oral	daily	209.4 (100-400)	57	39%	35.2	-
					Olanzapine	oral	daily	16.2 (5-25)	57	40%	32.9	-
Naber 2013 [98]	2013	open-label	52	Schizophrenia, schizoaffective disorder or schizophreniform disorder (DSM-IV-TR)	Quetiapine	oral	daily	566.5 (400-800)	395	41%	39.3	-
					Risperidone	oral	daily	3.9 (2-6)	403	43%	40	-
Naber 2015 [99]	2015	open-label	28	Schizophrenia (DSM-IV-TR)	Aripiprazole	LAI	every 4 wks	387 (300-400)	148	40%	42.6	-
					Paliperidone	LAI	every 4 wks	110 (50-150)	147	40%	41.2	-
Naukkarinen 2000 [100]	2000	double blind	26	Schizophrenia (DSM-IV)	Olanzapine	oral	daily	- (5-20)	23	43%	37.4	76.7
					Perphenazine	oral	daily	- (8-32)	23	35%	37.7	78.2
NCT00191555 [101]	2007	double blind	48	Schizophrenia (DSM-IV)	Haloperidol	oral	daily	8.7 (5-20)	134	26%	41.5	76.7
					Olanzapine	oral	daily	9.8 (5-20)	141	33%	40.7	79.0
NCT00210717 [102]	2012	double blind	53	Schizophrenia with acute symptomatic and diagnosed for at least 1 y (DSM-IV)	Paliperidone	LAI	every 4 wks	63.5 (39-234)	379	43%	40.7	80.7
					Risperidone	LAI	every 2 wks	32.4 (25-50)	370	38%	40.6	82.2
NCT00236379 [103]	2003	double blind	24	Schizophrenia, schizoaffective disorder or schizophreniform disorder (DSM-IV)	Olanzapine	oral	daily	17.9 (10-20)	31	42%	39.6	86.6
					Risperidone	oral	daily	5.5 (2-6)	28	21%	39.8	85.6
NCT01149655 [104]	2015	double blind	52	Schizophrenia (DSM-IV-TR)	Aripiprazole	oral	daily	19.2 (10-30)	98	37%	15.3	-
					Placebo	oral	-	-	48	29%	15.5	-
Nct01625897_60w [105]	2015	open-label	60	Schizophrenia (DSM-IV-TR)	Cariprazine	oral	daily	- (1.5-9)	83	53%	-	-
					Risperidone	oral	daily	- (2-12)	42	43%	-	-
NCT03345979 [106]	2020	double blind	25	Schizophrenia (DSM-V)	Aripiprazole	LAI	every 8 wks	1064 (1064-1064)	99	26%	43.5	84.8
					Paliperidone	LAI	every 4 wks	156 (156-156)	101	25%	43.4	85.0
Nemeth 2017 [107]	2017	double blind	26	Schizophrenia (DSM-IV-TR)	Cariprazine	oral	daily	4.2 (3-6)	230	46%	40.2	78.7
					Risperidone	oral	daily	3.8 (3-6)	231	39%	40.7	76.6
Newcomer 2008 [108]	2008	double blind	16	Schizophrenia or schizoaffective	Aripiprazole	oral	daily	16 (5-30)	88	43%	39.7	91.3
					Olanzapine	oral	daily	15.9 (10-40)	85	28%	38.7	92.7

				disorder (DSM-IV-TR)								
Newcomer 2009 [109]	2009	open-label	24	Schizophrenia (DSM-IV)	Olanzapine	oral	daily	15.2 (10-20)	169	34%	40.5	71.9
					Quetiapine	oral	daily	607 (338-785)	168	34%	39.4	73.6
					Risperidone	oral	daily	5.2 (3-8)	173	35%	38.3	72.1
Ohkuma 1987 [110]	1985	double blind	24	Schizophrenia (Clinical diagnosis)	Haloperidol	LAI	every 4 wks	195 (100-299)	144	39%	-	-
					Haloperidol	oral	daily	10.35 (6-13.5)	144	36%	-	-
Parabiaghi 2015 [111]	2015	single blind	52	Schizophrenia (DSM-IV)	Aripiprazole	oral	daily	19.7 (10-30)	100	45%	40.2	73.2
					Haloperidol	oral	daily	4 (1-10)	97	44%	43.9	76
					Olanzapine	oral	daily	13.7 (5-20)	103	36%	44.1	76.8
Peuskens 2007 [112]	2007	double blind	52	Schizophrenia (DSM-IV)	Placebo	oral	-	-	103	37%	33.0	73.9
					Quetiapine	oral	daily	669 (400-800)	94	39%	37.0	73.0
Pigott 2003 [113]	2003	double blind	26	Schizophrenia (DSM-IV)	Aripiprazole	oral	daily	15 (15-15)	155	46%	42.2	75
					Placebo	oral	-	-	155	42%	41.7	75
Potkin 2008a_104 weeks [114]	2008	double blind	104	Schizophrenia (DSM-IV)	Haloperidol	oral	daily	- (5-20)	37	-	-	80.8
					Iloperidone	oral	daily	- (4-16)	142	-	-	87.1
Potkin 2008b_52weeks [114]	2008	double blind	52	Schizophrenia (DSM-IV)	Iloperidone	oral	daily	- (4-16)	131	-	-	77.1
					Risperidone	oral	daily	- (2-8)	67	-	-	82.8
Potkin 2009 [115]	2009	double blind	40	Chronic or subchronic Schizophrenia or schizoaffective disorder (DSM-III-R)	Haloperidol	oral	daily	11.64 (5-20)	151	-	40.0	-
					Ziprasidone 80-160mg	oral	daily	111.74 (80-160)	227	-	39.9	-
Purdon 2000 [116]	2000	double blind	54	Schizophrenia (DSM-IV)	Haloperidol	oral	daily	9.7 (5-20)	23	35%	28.8	78.6
					Olanzapine	oral	daily	11 (5-20)	21	19%	26	78.1
					Risperidone	oral	daily	6 (4-10)	21	33%	31.8	72.8
Purdon 2001 [117]	2001	double blind	26	Schizophrenia (DSM-IV)	Haloperidol	oral	daily	15.5 (10-20)	12	17%	35.3	-
					Quetiapine	oral	daily	468.2 (300-600)	13	23%	32.7	-
REPRIEVE [118]	2015	double blind	26	Schizophrenia (DSM-IV)	Iloperidone	oral	daily	15 (8-24)	153	37%	38.4	75.5
					Placebo	oral	-	-	150	45%	38.2	72.9
RIS JPN S31 [119]	2006	open-label	24	Schizophrenia (DSM-IV)	Risperidone	LAI	every 2 wks	- (12.5-50)	153	-	-	-
					Risperidone	oral	daily	- (2-6)	52	-	-	-
RIS SCH 4178 [120]	2014	open-label	52	Schizophrenia or schizoaffective disorder (DSM-IV)	Risperidone	LAI	every 2 wks	33.82 (25-50)	20	47%	36.9	69.7
					Risperidone	oral	daily	3.75 (0.5-10)	25	33%	32.8	73.4
Ritchie 2003 6m [121]	2006	open-label	24	Schizophrenia (Clinical Diagnosis)	Olanzapine	oral	daily	12.4 (-)	34	71%	69.5	67.5
					Risperidone	oral	daily	1.97 (-)	32	72%	69.4	67.5
Robinson 2006 [122]	2006	single blind	16	Schizophrenia, schizophreniform disorder or schizoaffective disorder (DSM-IV)	Olanzapine	oral	daily	11.8 (2.5-20)	60	30%	23.3	70.1
					Risperidone	oral	daily	3.9 (1-6)	60	30%	23.3	70.1
Ruhrmann 2007 [123]	2007	double blind	24	Chronic Schizophrenia (ICD-10)	Flupentixol	oral	daily	6.68 (4-12)	76	38%	40.9	76.8
					Risperidone	oral	daily	3.51 (2-6)	77	38%	39.8	79.5
Rui 2014 [124]	2014	double blind	-	Schizophrenia (DSM-IV-TR)	Paliperidone	oral	daily	9.5 (3-12)	65	61%	31.1	65.2
					Placebo	oral	-	-	71	58%	32.3	66.1
Russell 1982 [125]	1982	double blind	24	Schizophrenia (ICD-9)	Fluphenazine	LAI	every week	9.6 (-)	13	40%	34.1	72.0
					Fluspirilene	LAI	every week	9.6 (-)	20	67%	37.7	67.1
Sacchetti 2009 [126]	2009	double blind	18	Schizophrenia, treatment resistant (DSM-IV)	Clozapine	oral	daily	345.7 (250-600)	74	33%	38.3	83
					Ziprasidone	oral	daily	130.4 (80-160)	73	29%	41.6	81.7
Sahni 2016 [127]	2016	open-label	26	First-episode Schizophrenia, treatmentnaive (ICD-10)	Clozapine	oral	daily	289.28 (200-600)	28	-	-	-
					Risperidone	oral	daily	6.85 (4-8)	27	-	-	-
San 2012 [128]	2012		52		Haloperidol	oral	daily	4 (1.5-8.5)	21	14%	26.5	61

		open-label		Schizophrenia, schizophreniform or schizoaffective disorder, psychotic disorder NOS, brief psychotic disorder, bipolar disorder, substance induced psychosis (DSM-IV-TR)	Olanzapine	oral	daily	12 (7.5-40)	25	32%	25.3	63
					Quetiapine	oral	daily	572 (100-1500)	23	35%	26.7	67
					Risperidone	oral	daily	3.7 (1.5-7)	25	24%	22.6	65
					Ziprasidone	oral	daily	81 (40-240)	20	20%	27.6	67
Savitz 2015_26weeks [129]	2015	double blind	26	Schizophrenia (DSM-IV)	Aripiprazole	oral	daily	11.56 (5-15)	115	34%	15.4	60.4
					Paliperidone	oral	daily	6.75 (3-9)	113	35%	15.3	59.4
Schoemaker 2010 [130]	2010	double blind	52	Schizophrenia or schizoaffective disorder (DSM-IV-TR)	Asenapine	oral	daily	13.5 (10-20)	913	48%	36.8	74.6
					Olanzapine	oral	daily	13.6 (10-20)	312	41%	36.2	73.6
Schooler 2005 [131]	2005	double blind	104	Schizophrenia, schizophreniform disorder or schizoaffective disorder (DSM-IV)	Haloperidol	oral	daily	2.9 (1-8)	278	28%	25.7	-
					Risperidone	oral	daily	3.3 (1-8)	281	29%	25.2	-
Schreiner 2012 [132]	2012	open-label	26	Schizophrenia (DSM-IV)	Olanzapine	oral	daily	11.6 (10-15)	220	40%	37.5	77.8
					Paliperidone	oral	daily	6.9 (6-9)	239	44%	38.8	75.8
Sechter 2002 [133]	2002	double blind	26	Chronic Schizophrenia (DSM-IV)	Amisulpride	oral	daily	683 (400-1000)	152	45%	38.4	71.4
					Risperidone	oral	daily	6.92 (4-10)	158	45%	38.4	71.3
Sharma 1991 [134]	1991	double blind	48	chronic Schizophrenia (DSM-III)	Fluphenazine	LAI	every 4 wks	-	30	50%	53	-
					Haloperidol	LAI	every 4 wks	-	29	34%	50	-
Simpson 1967 [135]	1967	double blind	14	Schizophrenia (Clinical Diagnosis)	Haloperidol low	oral	daily	6 (6-6)	8	0%	36.5	-
					Placebo	oral	-	-	8	0%	36.5	-
Smith 2009 [136]	2009	open-label	22	Schizophrenia or schizoaffective psychosis (DSM-IV)	Olanzapine	oral	daily	25.2 (5-40)	25	0%	41.2	-
					Risperidone	oral	daily	6.1 (2-12)	24	4%	42.5	-
Speller 1997 [137]	1997	double blind	52	Chronic Schizophrenia (DSM-III-R)	Amisulpride	oral	daily	- (100-800)	29	31%	64	69.2
					Haloperidol	oral	daily	- (3-20)	31	16%	63	69.8
Stroup 2006 [138]	2006	double blind	-	Chronic Schizophrenia (DSM-IV)	Olanzapine	oral	daily	20.5 (7.5-30)	68	32%	40	-
					Quetiapine	oral	daily	565.2 (200-800)	63	29%	40.1	-
					Risperidone	oral	daily	4.1 (1.5-6)	70	31%	41.8	-
					Ziprasidone	oral	daily	115.9 (40-160)	137	30%	41.3	-
Subotnik 2015 [139]	2015	open-label	52	Schizophrenia, schizoaffective disorder (depressed type) or schizophrenieform disorder (DSM-IV)	Risperidone	LAI	every 2 wks	26.3 (12.5-37.5)	43	22%	21.9	-
					Risperidone	oral	daily	3.6 (1-7.5)	43	21%	21.1	-
Suresh 2016 [140]	2016	double blind	48	Schizophrenia (DSM-IV)	Olanzapine	oral	daily	14.4 (5-20)	36	-	41.5	54.1
					Risperidone	oral	daily	5.8 (2-8)	35	-	39.8	52.9
Tandon 2016 [141]	2016	double blind	28	Schizophrenia (DSM-IV-TR)	Lurasidone	oral	daily	78.9 (40-80)	144	38%	43	89.1
					Placebo	oral	-	-	141	38%	42.4	89.3
Thomas 2010_MetabolicSubgroup [142]	2010	open-label	-	Schizophrenia (ICD-10)	Risperidone	oral	daily	4 (4-6)	130	54%	37	73.9
					Sertindole	oral	daily	12 (12-20)	131	51%	35	72.8
Tollefson 2001 [143]	2001	double blind	18	Schizophrenia, treatment resistant (DSM-IV)	Clozapine	oral	daily	303.6 (200-600)	90	40%	38.6	-
					Olanzapine	oral	daily	20.5 (15-25)	90	32%	38.6	-
Tran 1997 [144]	1997	double blind	28	Schizophrenia, schizophreniform disorder or schizoaffective disorder (DSM-IV)	Olanzapine	oral	daily	17.2 (10-20)	172	34%	36.0	76.7
					Risperidone	oral	daily	7.2 (4-12)	167	37%	36.4	76.4
Tunis 2006 [145]	2006	open-label	52	Schizophrenia, schizoaffective disorder or	Olanzapine	oral	daily	13.49 (2.5-20)	229	37%	42.7	85.8
					Risperidone	oral	daily	4.95 (4-16)	221	40%	42.1	87.1

				schizophreniform disorder (DSM-IV)								
Vangala 1998 [146]	1998	double blind	14	Schizophrenia, schizophreniform or schizoaffective disorder (DSM-IV)	Haloperidol	oral	daily	- (5-20)	14	-	31.1	59
					Olanzapine	oral	daily	- (5-20)	17	-	31.1	60.2
Volavka 2002 [147]	2002	double blind	14	Chronic Schizophrenia or schizoaffective disorder with suboptimal response to previous treatment (DSM-IV)	Clozapine	oral	daily	526.6 (200-800)	40	11%	42.6	82.3
					Haloperidol	oral	daily	25.7 (10-30)	37	22%	37.3	78.6
					Olanzapine	oral	daily	30.4 (10-40)	39	13%	41.0	82.6
					Risperidone	oral	daily	11.6 (4-16)	41	15%	42.9	87.9
Voruganti 2007[148]	2007	single blind	52	Schizophrenia (DSM-IV)	Olanzapine	oral	daily	17.2 (-)	42	17%	41.3	-
					Quetiapine	oral	daily	612.8 (-)	43	35%	38.7	-
Wang 2006 [149]	2006	double blind	21	Schizophrenia spectrum disorder (DSM-IV)	Olanzapine	oral	daily	13.8 (5-15)	17	47%	48.9	84.3
					Risperidone	oral	daily	5.3 (2-6)	19	58%	45.2	81.3
Wani 2015 [150]	2015	open-label	24	Schizophrenia (DSM-IV-TR)	Aripiprazole	oral	daily	- (10-30)	31	39%	29.7	-
					Olanzapine	oral	daily	- (10-20)	31	35%	29.8	-
Wistedt 1984 [151]	1984	double blind	20	Subchronic or chronic Schizophrenia (Spitzer Research Diagnostic Criteria)	Fluphenazine	LAI	every 4 wks	84 (12.5-200)	30	38%	35.6	-
					Haloperidol	LAI	every 4 wks	122 (50-300)	29	32%	39.1	-

5.4 Characteristics and references of specific studies without usable data

Study	Interventions	Application
Abrams 1958 [152]	Chlorpromazine	oral
	Placebo	oral
Adelson 1962 [153]	Chlorpromazine	oral
	Perphenazine	oral
	Placebo	oral
Ahlfors 1980 [154]	Clopenthixol	depot
	Perphenazine	depot
Altamura 2002 [155]	Haloperidol	oral
	Olanzapine	oral
Alvarez 2005 [156]	Haloperidol	oral
	Olanzapine	oral
	Risperidone	oral
Ananth 2001 [157]	Risperidone	oral
	Ziprasidone	oral
Andrews 1976 [158]	Chlorpromazine	oral
	Placebo	oral
Aquila 2000 [159]	Olanzapine	oral
	Risperidone	oral
Arango 2006 [160]	Zuclopenthixol	depot
	Zuclopenthixol	oral
Athanassenas 1983 [161]	Fluphenazine	oral
	Loxapine	oral
	Pimozide	oral
Bai 2005 [162]	Amisulpride	oral
	Olanzapine	oral
Baker 1958 [163]	Chlorpromazine	oral
	Levomepromazine	oral
Bankier 1968 [164]	Fluphenazine	depot
	Trifluoperazine	oral
Bankier 1973 [165]	Fluspirilene	depot
	Trifluoperazine	oral
Barnes 1983 [166]	Fluphenazine	depot
	Pimozide	oral
Barsa 1965 [167]	Fluphenazine	depot
	Placebo	depot
Brankovic 1998 [168]	Clozapine	oral
	Fluphenazine	oral
Browne 1988 [169]	Haloperidol	oral
	Placebo	oral
Brugmans 1968 [170]	Pimozide	oral
	Placebo	oral
Buchsbaum 2010 [171]	Aripiprazole	oral
	Risperidone	oral
Burgoyne 1998 [172]	Haloperidol	oral
	Olanzapine	oral
Castellani 1988 [173]	Fluphenazine	depot
	Haloperidol	depot
Charalampous 1977 [174]	Fluphenazine	oral
	Penfluridol	oral once weekly
ChiCTR-IPR-15007635 [175]	Haloperidol	-
	Paliperidone	-
Chouinard 1989 [176]	Fluphenazine	depot
	Haloperidol	depot
Claghorn 1974 PT [177]	Chlorpromazine	oral
	Tiotixene	oral
Claghorn 1979 [178]	Chlorpromazine	oral

	Penfluridol	oral once weekly
Clark 1961 [179]	Chlorpromazine	oral
	Placebo	oral
Clark 1968a [180]	Chlorpromazine	oral
	Placebo	oral
Cole 1967 [181]	Chlorpromazine	oral
	Fluphenazine	oral
COMBINE [182]	Amisulpride	oral
	Olanzapine	oral
Conley 2001-Extension [183]	Olanzapine	oral
	Risperidone	oral
Cookson 1991 [184]	Fluphenazine	depot
	Haloperidol	depot
Covington 2000 [185]	Clozapine	oral
	Haloperidol	oral
Crane 1970 [186]	Placebo	oral
	Trifluoperazine	oral
Crawford 1974 [187]	Fluphenazine	depot
	Trifluoperazine	oral
Ctri-2015-01-005438 [188]	Clozapine	oral
	Risperidone	oral
Ctri-2015-02-005575 [189]	Haloperidol	oral
	Olanzapine	oral
de Sena 2003 [190]	Haloperidol	oral
	Risperidone	oral
Dejanovic 2002 [191]	Clozapine	oral
	Haloperidol	oral
Dencker 1980 [192]	Clopenthixol	depot
	Flupentixol	depot
Dencker 1994 [193]	Haloperidol	depot
	Perphenazine	depot
Denijs 1973 [194]	Pimozide	oral
	Placebo	oral
Donlon 1977 [195]	Fluphenazine	oral
	Pimozide	oral
Donlon 1978 [196]	Penfluridol	oral once weekly
	Trifluoperazine	oral
Dotti 1979 [197]	Fluphenazine	depot
	Placebo	depot
Dutta 2014 [198]	Asenapine	oral
	Clozapine	oral
	Ziprasidone	oral
Eberhard 1986 [199]	Flupentixol	depot
	Haloperidol	depot
Ehrlich 2012_24w [200]	Olanzapine	oral
	Ziprasidone	oral
Eklund 1991[201]	Haloperidol	depot
	Placebo	depot
Engelhardt 1969_15m [202]	Chlorpromazine	oral
	Placebo	oral
Engelhardt 1978 [203]	Haloperidol	oral
	Tiotixene	oral
Estrella 1996 [204]	Clozapine	oral
	Risperidone	oral
Euctr2018-000178-31 [205]	Aripiprazole	oral
	Olanzapine	oral
Fawzi 2009 [206]	Aripiprazole	oral
	Olanzapine	oral
Frangos 1978 [207]	Fluphenazine	depot

	Fluspirilene	depot
Fransella 1960 [208]	Chlorpromazine	oral
	Placebo	oral
Freedman 1967 [209]	Chlorpromazine	oral
	Placebo	oral
Freeman 1962 [210]	Chlorpromazine	oral
	Placebo	oral
Fricchione 2010 [211]	Risperidone	depot
	Zuclopenthixol	depot
Gaebel 2007 [212]	Haloperidol	oral
	Risperidone	oral
Gafoor 2010_52w [213]	Quetiapine	oral
	Risperidone	oral
Gardos 1970 [214]	Tiotixene	oral
	Trifluoperazine	oral
Gardos 1974 [215]	Chlorpromazine	oral
	Tiotixene	oral
Glazer 1985 [216]	Haloperidol	oral
	Molindone	oral
Glick 2005 [217]	Haloperidol	depot
	Quetiapine	oral
Goldstein 1966 [218]	Haloperidol	oral
	Trifluoperazine	oral
Grecu 2006 [219]	Haloperidol	oral
	Olanzapine	oral
	Quetiapine	oral
	Risperidone	oral
Green 2015 [220]	Risperidone	depot
	Risperidone	oral
Grinspoon 1967 [221]	Placebo	oral
	Thioridazine	oral
Grootens 2009_52w [222]	Olanzapine	oral
	Ziprasidone	oral
Gross 1974 [223]	Pimozide	oral
	Placebo	oral
	Trifluoperazine	oral
Gwynne 1962 [224]	Chlorpromazine	oral
	Placebo	oral
	Trifluoperazine	oral
Hagger 1997 [225]	Risperidone	oral
	Ziprasidone	oral
Hamilton 1963 [226]	Placebo	both
	Trifluoperazine	both
Hamilton 1979 [227]	Flupenthixol	depot
	Fluphenazine	depot
Hera 041-021+Hera 041-022 _1y [228]	Asenapine	oral
	Olanzapine	oral
Hershon 1972 [229]	Placebo	oral
	Trifluoperazine	oral
Hine 1958 [230]	Chlorpromazine	oral
	Placebo	oral
Hirsch 1973 [231]	Fluphenazine	depot
	Placebo	depot
Hirsch 1989 [232]	Fluphenazine	depot
	Placebo	depot
Hirsch 1996 [233]	Fluphenazine	depot
	Placebo	depot
Hogarty 1973[234]	Chlorpromazine	oral
	Placebo	oral

Hogarty 1979 [235]	Fluphenazine	depot
	Fluphenazine	oral
Hollister 1960 [236]	Chlorpromazine	oral
	Trifluoperazine	oral
Hranov 1998 [237]	Fluphenazine	depot
	Haloperidol	depot
Ibrahim 2007 [238]	Haloperidol	oral
	Quetiapine low	oral
	Quetiapine high	oral
Ibrahim 2011 [239]	Haloperidol	oral
	Quetiapine	oral
Iqbal 1978 [240]	Fluphenazine	depot
	Penfluridol	oral once weekly
Jambur 1998 [241]	Risperidone	oral
	Ziprasidone	oral
James 1977 [242]	Fluphenazine	depot
	Penfluridol	oral
Jerrell 2002 [243]	Olanzapine	oral
	Risperidone	oral
Johnstone 1988 [244]	Pimozide	oral
	Placebo	oral
Jprn-umin000007942 [245]	Aripiprazole	oral
	Paliperidone	oral
Jprn-umin000021800 [246]	Asenapine	oral
	Olanzapine	oral
Kane 1979 [247]	Fluphenazine	depot
	Placebo	depot
Kane 1982 [248]	Fluphenazine	depot
	Fluphenazine	oral
	Placebo	oral
Kane 2001 [249]	Clozapine	oral
	Haloperidol	oral
Kelly 1977 [250]	Flupentixol	depot
	Fluphenazine	depot
Kim 2006 [251]	Aripiprazole	oral
	Haloperidol	oral
King 1958 [252]	Chlorpromazine	oral
	Placebo	oral
Kissling 1985 [253]	Fluphenazine	depot
	Haloperidol	depot
Kissling 1990 [254]	Flupentixol	depot
	Haloperidol	depot
Knights 1979 [255]	Flupentixol	depot
	Fluphenazine	depot
Kolivakis 1974 [256]	Chlorpromazine	oral
	Pimozide	oral
Kopelowicz 2006 [257]	Olanzapine	oral
	Risperidone	oral
Lapierre 1976 (Evaluation of drug arms) [258]	Fluphenazine	oral
	Pimozide	oral
Lapierre 1978 [259]	Fluphenazine	oral
	Penfluridol	oral once weekly
Lauriello 2005 [260]	Haloperidol	oral
	Quetiapine	oral
Lepola 1989 [261]	Perphenazine	oral
	Sulpiride	oral
Letemendia 1967 [262]	Chlorpromazine	oral
	Placebo	oral
Levine 1980 [263]	Fluphenazine	oral

	Fluphenazine	depot
	Placebo	oral
	Placebo	depot
Linden 1972 [264]	Fluspirilene	both
	Penfluridol	both
Littrell 1999 [265]	Olanzapine	oral
	Risperidone	oral
Lundin 1990 [266]	Flupenthixol	depot
	Fluphenazine	depot
Magnus 1979 [267]	Fluphenazine	depot
	Fluspirilene	depot
Malyarov 1999 [268]	Haloperidol	oral
	Olanzapine	oral
	Risperidone	oral
Marder 2003 [269]	Haloperidol	oral
	Risperidone	oral
Marder 2007 [270]	Olanzapine	oral
	Risperidone	oral
Marjerrison 1964 [271]	Placebo	oral
	Trifluoperazine	oral
Martyns 1993 [272]	Clopenthixol	depot
	Flupenthixol	depot
Mathur 1981 [273]	Chlorpromazine	oral
	Placebo	oral
May 1968 [274]	Trifluoperazine	oral
	Control	-
McCreadie 1980 [275]	Fluphenazine	depot
	Pimozide	oral on 4 subsequent days a week
McCreadie 1982 [276]	Fluphenazine	depot
	Pimozide	oral once weekly
McCreadie 1983 [277]	Fluphenazine	depot
	Pimozide	depot
McGurk 2005 [278]	Clozapine	oral
	Risperidone	oral
McKane 1987 [279]	Fluphenazine	depot
	Haloperidol	depot
Messier 1969 [280]	Placebo	oral
	Thioridazine	oral
NCT00169091 [281]	Clozapine	oral
	Haloperidol	oral
NCT00208143 [282]	Quetiapine	oral
	Risperidone	oral
NCT00288353 [283]	Aripiprazole	oral
	Ziprasidone	oral
NCT00288366 [284]	Aripiprazole	oral
	Ziprasidone	oral
NCT00480844_24w [285]	Risperidone	oral
	Sertindole	oral
NCT00645515 [286]	Risperidone	oral
	Ziprasidone	oral
NCT00956189 [287]	Amisulpride	oral
	Aripiprazole	oral
NCT01451736 [288]	Paliperidone	depot
	Risperidone	oral
NCT02146547 [289]	Aripiprazole	depot
	Aripiprazole	oral
	Paliperidone	depot
	Paliperidone	oral

NCT03345342 [290]	Paliperidone 1M	depot
	Paliperidone 3M low	depot
	Paliperidone 3M high	depot
	Paliperidone 6M	depot
	Placebo	depot
NCT03503318 [291]	Placebo	depot
	Risperidone A	depot
	Risperidone B	depot
NCT03593213 [292]	Cariprazine low	oral
	Cariprazine high	oral
	Placebo	oral
NCT03893825 [293]	Placebo	oral
	Risperidone A	oral
	Risperidone B	oral
Nishikawa 1982 [294]	Chlorpromazine	oral
	Haloperidol	oral
	Placebo	oral
Nishikawa 1984 [295]	Haloperidol	oral
	Placebo	oral
Nishikawa 1985 [296]	Pimozide	oral
	Thioridazine	oral
Noordsy 2010 [297]	Clozapine	oral
	Risperidone	oral
Odejide 1982 [298]	Fluphenazine	depot
	Placebo	depot
Paredes 1966 [299]	Chlorpromazine	oral
	Placebo	oral
Patel 1995 [300]	Chlorpromazine	oral
	Sulpiride	oral
Patel 1996 [301]	Chlorpromazine	oral
	Sulpiride	oral
Perro 1999 [302]	Olanzapine	oral
	Risperidone	oral
	Sertindole	oral
	Zotepin	oral
PERSIST [303]	Amisulpride	oral
	Olanzapine	oral
	Quetiapine	oral
	Risperidone	oral
	Zotepin	oral
Pinto 1979 [304]	Flupenthixol	depot
	Fluphenazine	depot
Pivac 2002 [305]	Fluphenazine	oral
	Olanzapine	oral
Platz 1967 [306]	Chlorpromazine	oral
	Trifluoperazine	oral
Potapov 2008 [307]	Olanzapine	depot
	Risperidone	depot
Povlsen 1987 [308]	Haloperidol	oral
	Perphenazine	oral
Prien 1968a [309]	Chlorpromazine	oral
	Placebo	oral
Prien 1969 [310]	Placebo	oral
	Trifluoperazine	oral
Quitkin 1978 [311]	Fluphenazine	depot
	Penfluridol	oral once weekly
Rapp 1986 [312]	Haloperidol	depot
	Perphenazine	depot
Rappaport 1978 [313]	Chlorpromazine	oral

	Placebo	oral
Rasmussen 1976 [314]	Chlorpromazine	oral
	Thioridazine	oral
Ravaris 1965 [315]	Fluphenazine	depot
	Fluphenazine	oral
Ravaris 1967 [316]	Fluphenazine	depot
	Placebo	depot
Rémillard 2005y1 [317]	Haloperidol	oral
	Risperidone	oral
Remillard 2008 [318]	Haloperidol	oral
	Risperidone	oral
Reynolds 2001 [319]	Quetiapine	oral
	Risperidone	oral
Rifkin 1977 [320]	Fluphenazine	depot
	Fluphenazine	oral
	Placebo	oral
Robinson 2015_1y [321]	Aripiprazole	oral
	Risperidone	oral
Robles 2011 [322]	Olanzapine	oral
	Quetiapine	oral
ROCKSAN [323]	Clozapine	oral
	Olanzapine	oral
Roelofs 1974 [324]	Penfluridol	oral once weekly
	Placebo	oral
Rosen 1972 [325]	Chlorpromazine	oral
	Placebo	oral
Ruskin 1991 [326]	Haloperidol	oral
	Placebo	oral
Sampath 1992 [327]	Fluphenazine	depot
	Placebo	depot
Saxena 1996 [328]	Fluphenazine	depot
	Zuclopenthixol	depot
Sayers 2005 [329]	Haloperidol	oral
	Olanzapine	oral
Schiele 1961, 06602 [330]	Chlorpromazine	oral
	Placebo	oral
	Thioridazine	oral
	Trifluoperazine	oral
Schlosberg 1978 [331]	Fluphenazine	depot
	Placebo	depot
Schnell 2014 [332]	Clozapine	oral
	Ziprasidone	oral
Schooler 1993 [333]	Fluphenazine low	depot
	Fluphenazine high	depot
	Placebo	depot
Schooler 2011 [334]	Risperidone	depot
	Risperidone	oral
Sharma 2002a [335]	Clozapine	oral
	Olanzapine	oral
Shawver 1959 [336]	Chlorpromazine	oral
	Placebo	oral
Shrivastava 2000 [337]	Haloperidol	oral
	Risperidone	oral
Singam 2011 [338]	Chlorpromazine	oral
	Risperidone	oral
Singh 1981 [339]	Chlorpromazine	oral
	Haloperidol	oral
Smith 2007 [340]	Olanzapine	oral
	Risperidone	oral

Spiegel 1967 [341]	Chlorpromazine	oral
	Trifluoperazine	oral
Steuber 1978 [342]	Fluphenazine	depot
	Placebo	depot
Talbot 1964 [343]	Chlorpromazine	oral
	Trifluoperazine	oral
Tamminga 1994 [344]	Clozapine	oral
	Haloperidol	oral
Tanghe 1972 [345]	Fluspirilene	depot
	Penfluridol	oral
Tegeler 1979 [346]	Fluspirilene	depot
	Perphenazine	depot
Tran 1999 [347]	Haloperidol	oral
	Olanzapine	oral
Vandecasteele 1974 [348]	Penfluridol	oral once weekly
	Placebo	oral once weekly
Vasile 2015 [349]	Aripiprazole	oral
	Olanzapine	oral
	Quetiapine	oral
	Risperidone	oral
Velligan 1999a [350]	Haloperidol	oral
	Quetiapine	oral
Vergara 1977 [351]	Pimozide	oral
	Trifluoperazine	oral
Vontour 2005 [352]	Aripiprazole	oral
	Olanzapine	oral
Vyas 1980 [353]	Chlorpromazine	oral
	Loxapine	oral
Walker 1983 [354]	Clopenthixol	depot
	Fluphenazine	depot
Wang 1982 [355]	Chlorpromazine	oral
	Penfluridol	oral once weekly
Weston 1961 [356]	Placebo	oral
	Trifluoperazine	oral
Wetzel 1998_12m [357]	Amisulpride	oral
	Flupenthixol	oral
Wilson 1982 [358]	Chlorpromazine	oral
	Pimozide	oral
Wistedt 1991 [359]	Haloperidol	depot
	Zuclopenthixol	depot
Wolpert 1968 [360]	Placebo	oral
	Thioridazine	oral
	Tiotixene	oral
Yazici 2002 [361]	Olanzapine	oral
	Risperidone	oral
Zissis 1981 [362]	Haloperidol	depot
	Placebo	depot
Zuardi 1983 [363]	Haloperidol	depot
	Haloperidol	oral

6 Transitivity assessment

We included only RCTs in participants with schizophrenia or related disorders (such as schizophreniform or schizoaffective disorders) with a study duration > 13 weeks (3 months) and with doses within the target to maximum doses of the International Consensus Study on Antipsychotic Dosing [9]. We did not apply restrictions in stage of the disease (acute episode; maintenance phase), participant age, gender or setting (inpatients or outpatients) because we deem the development of metabolic side effects rather independent of these factors. Based on these inclusion criteria, we assumed that participants in the selected studies were equally likely to be randomized to any of the antipsychotics investigated. To assess transitivity of the network as recommended by the Cochrane handbook [10], we visually compared the distribution of potential effect modifiers across comparisons including baseline weight, age, gender, ethnicity, life-time exposure to antipsychotics (if not available duration of illness was used as a proxy), study duration and antipsychotic dose. The box-plots used are presented below.

Summary of transitivity assessment:

The assessment of transitivity is performed by comparing the distribution of potential effect modifiers for each comparison and is limited when only one or very few studies per comparison are available. Overall, we judged that there are no clear violations of the transitivity assumption considering the following specific reflections:

In the boxplot for baseline weight it can be seen that for most of the comparisons the baseline weight was between 70 and 90 kg. Four studies showed a lower baseline weight. These studies were conducted in Asian and/or younger populations or in women in 1970. For these populations lower values of baseline weight can be expected. Nevertheless the frequency of overweight (i.e. the distribution of BMI) can be similar compared to the study population of other studies (BMI was not evaluated because it was not available for many studies).

The median mean age observed in the comparisons ranged between 15 to 52 years with most of the comparisons between 30 and 45 years. The distribution of proportion women ranged for most comparisons between 0.25 and 0.5 with four studies above and four studies below this range. As stated above we did not apply restrictions in these classical population characteristics age and gender because we assumed that these do not affect the development of metabolic side-effects to an important extent.

However, different ethnicities may have a different propensity to develop metabolic side effects. Therefore, we explored exemplary the distribution of proportion of white and black ethnicity within the included studies. The provided information in the original studies did not allow a more detailed evaluation of ethnicities. Since the influence of ethnicity has not yet been conclusively clarified we further examined the role of ethnicity in network meta-regression analyses.

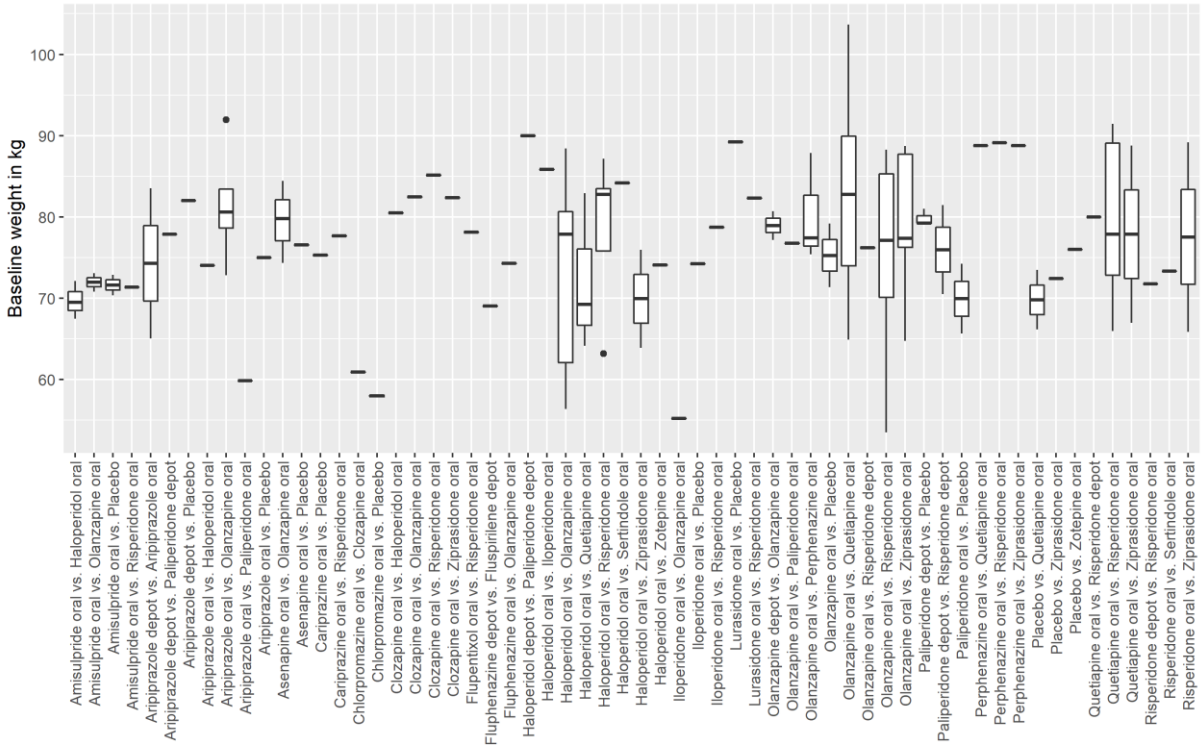
We expected metabolic side effects to occur rather independent of population characteristics with the exception of previous antipsychotic exposure that could have led to antipsychotic-induced weight gain before study participation. The average life-time exposure to antipsychotics was around 10 years for most comparisons. 7 of 137 studies were conducted in participants with minimal prior antipsychotic exposure. Those studies were excluded in a sensitivity analysis.

Regarding study duration, we only included trials with a duration > 13 weeks (3 months) because we were focussing on mid- to long-term side effects. The median study duration of most comparisons was between 6 and 12 months.

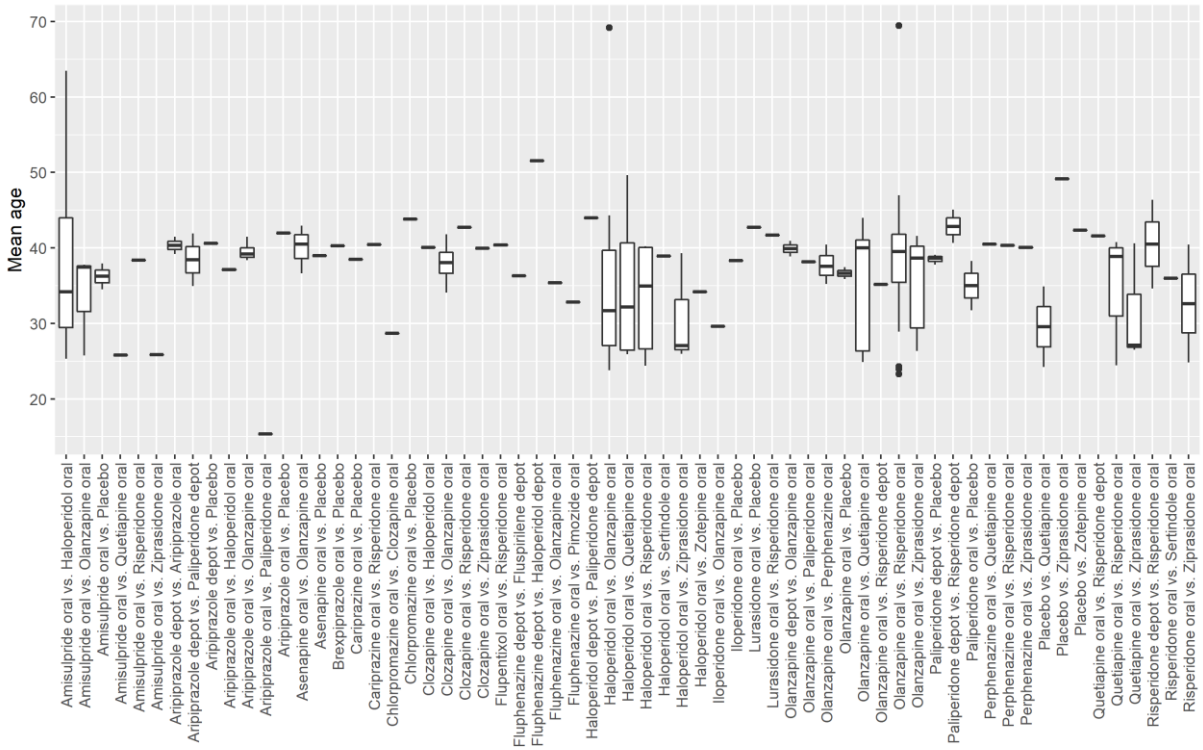
Concerning antipsychotic dosing, we included only study arms with doses within the target to maximum range according to the International Consensus Study on Antipsychotic Dosing [9]. Only for special populations such as patients with first episode or primarily negative symptoms for which clinically different dosing regiments are recommended, we included lower doses. These study arms were excluded in a sensitivity analysis, which did not change the results. Two comparisons (aripiprazole oral vs. haloperidol oral and clozapine oral vs. haloperidol oral, see box-plots) with one study each had a median mean dose above 30 mg/d olanzapine equivalent (maximum dose range for olanzapine according to the International Consensus Study on Antipsychotic Dosing [9]). However, the original doses used in the studies (30 mg/d aripiprazole oral in Kasper 2003 and 401 mg/d clozapine in Volavka 2002) were below the maximum dose of the International Consensus Study on Antipsychotic Dosing [9]. Therefore, the conversion in olanzapine equivalents leads to these increased doses in olanzapine equivalents.

Boxplots per study design and population characteristic:

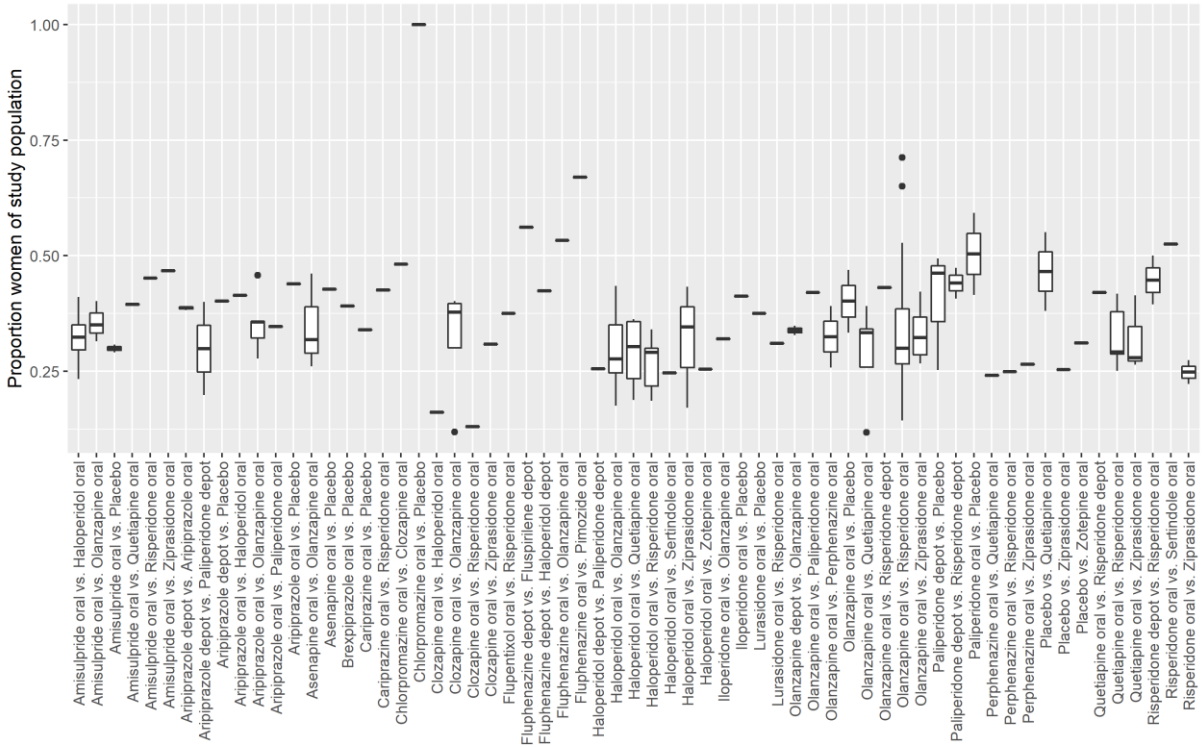
6.1 Baseline weight



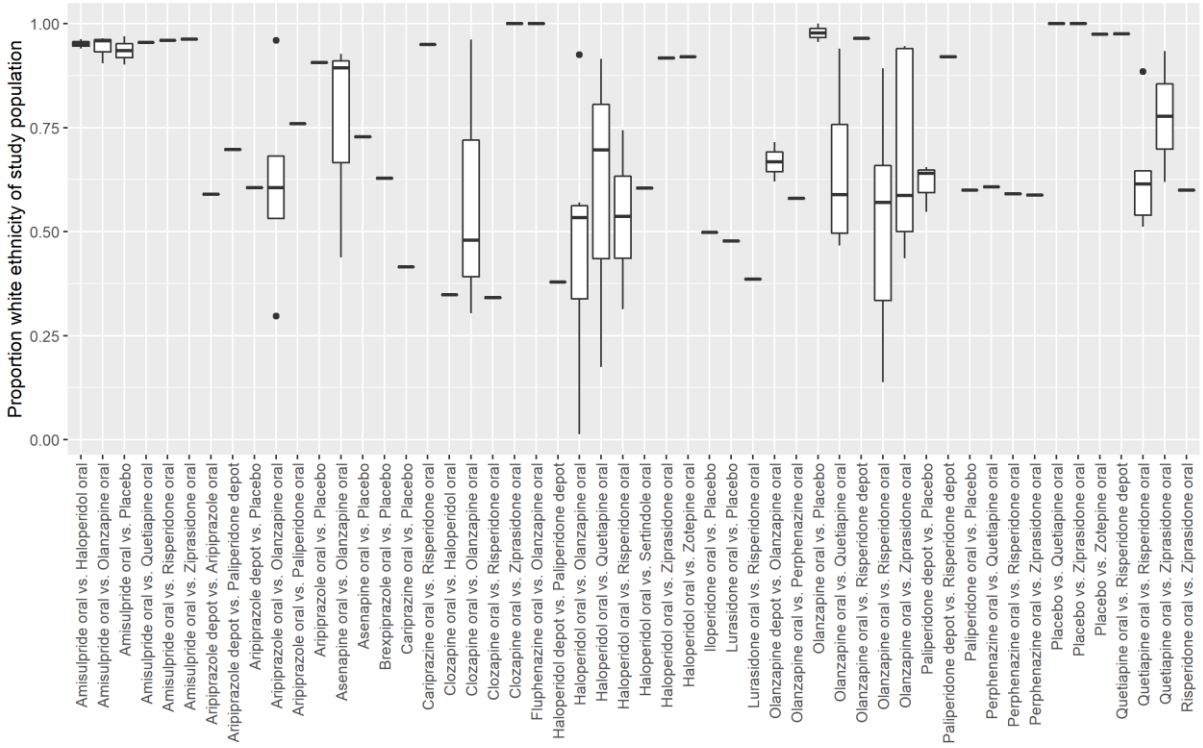
6.2 Mean age of participants

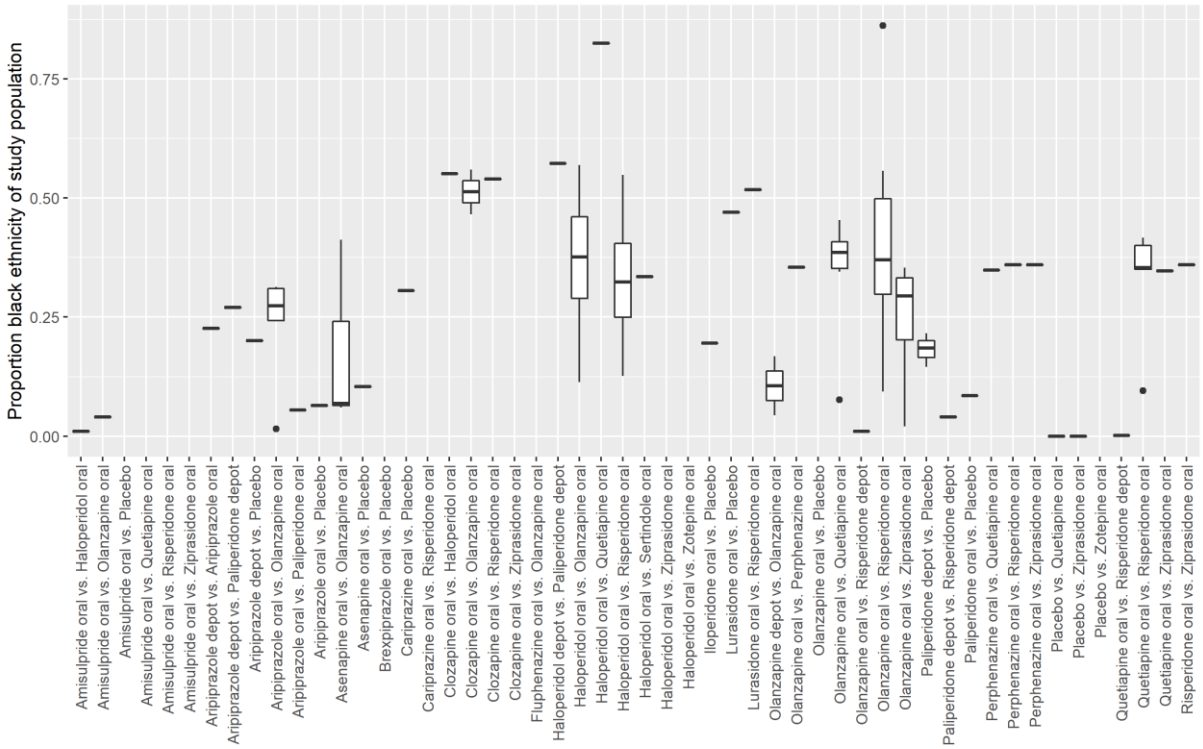


6.3 Proportion women of study participants

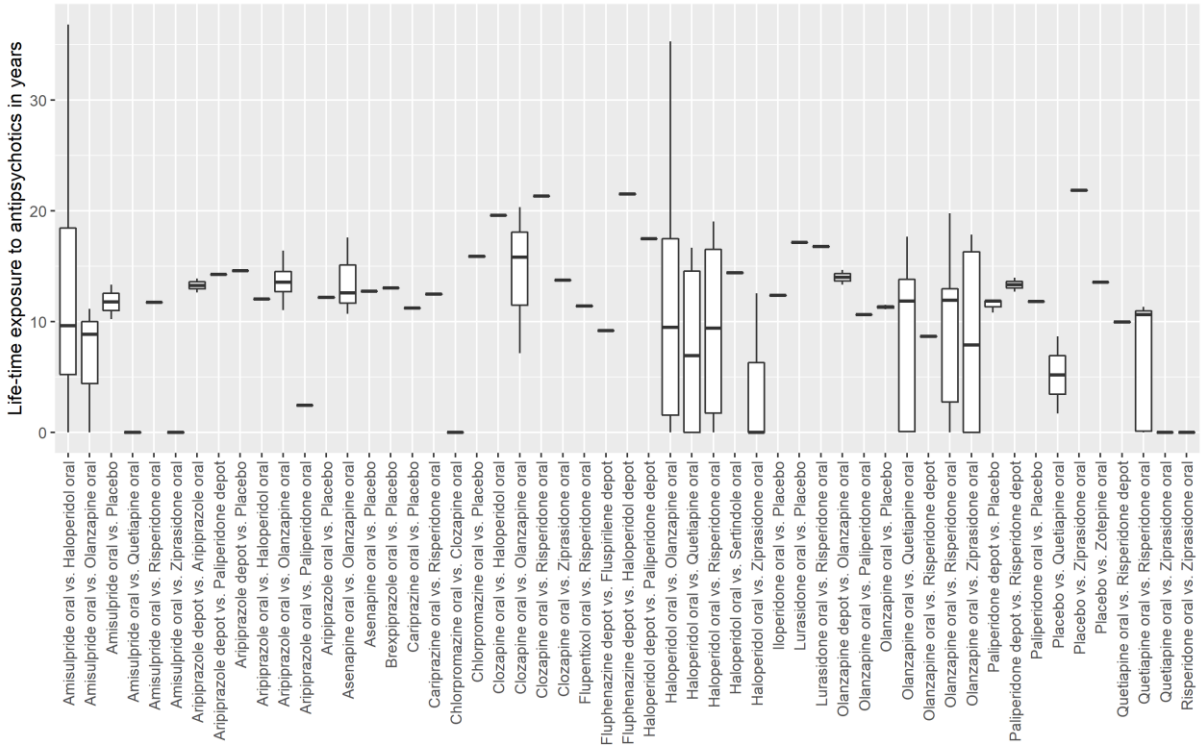


6.4 Proportion of white and black ethnicity in study population

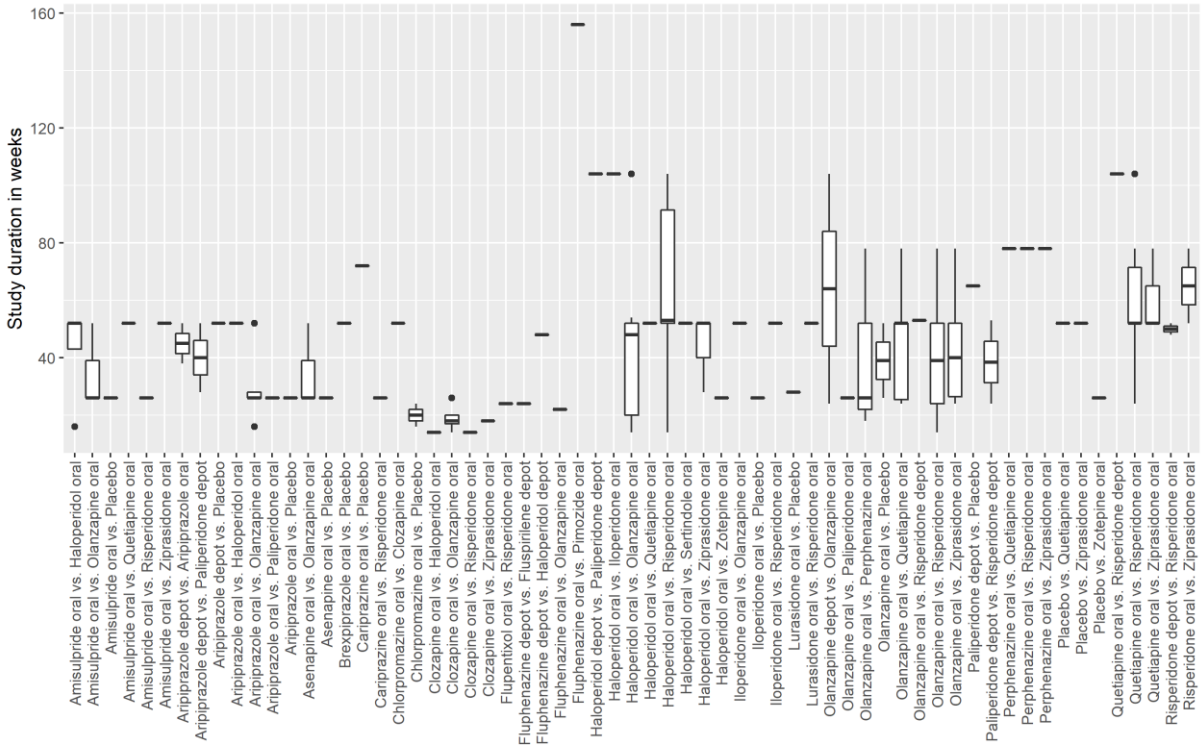




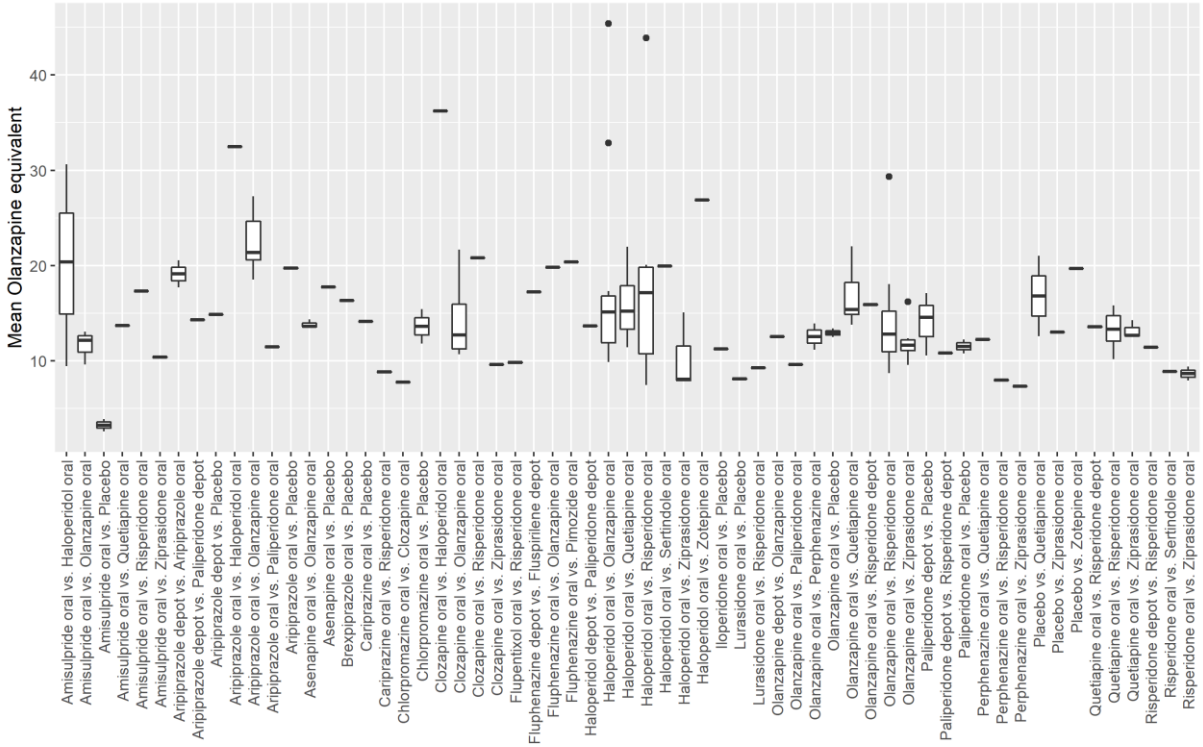
6.5 Life-time exposure to antipsychotics (if not available duration of illness used as a proxy)



6.6 Study duration



6.7 Antipsychotic dose in olanzapine equivalents based on scientific equivalents



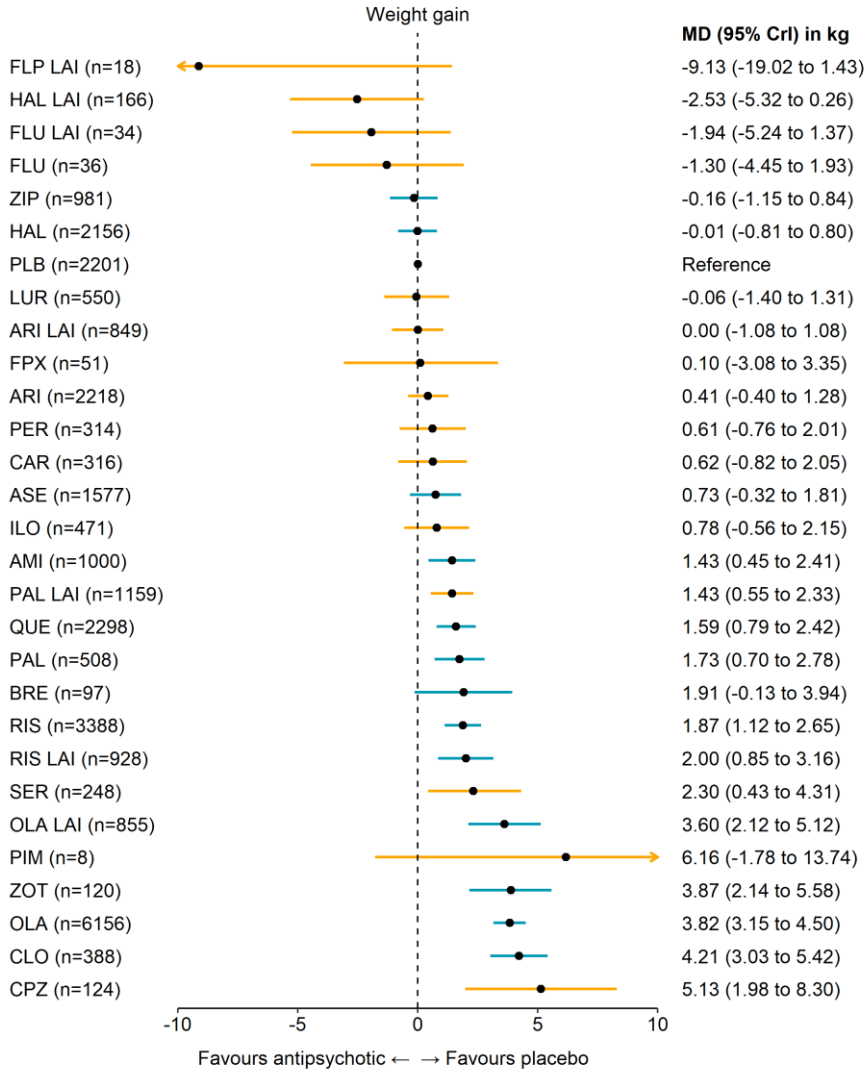
7 Additional results of the network meta-analysis of the primary outcome "weight gain" and secondary outcomes

For each outcome we present below (in this order, if not shown in the manuscript)

- Network plot
- Forest-plot of results of network meta-analysis (reference intervention placebo)
- League-table of results of network meta-analysis (presenting results for all comparisons)
- Forest-plot of results of pairwise meta-analyses (also indicating data of individual studies)

7.1 Primary outcome "weight gain"

Forest-plot of results of network meta-analysis for antipsychotic drugs versus placebo



Network meta-analysis estimates of treatment effect of each drug vs. placebo reported as mean differences (MDs) and 95% credible intervals (CrIs) with their confidence rating assessed with the Confidence in Network Meta-Analysis (CINeMA) tool with blue representing moderate confidence, and orange representing low confidence. The order of treatments is according to surface under the cumulative ranking curve (SUCRA) ranking. The direction of the effect is indicated below the x-axis.

Abbreviations: n=number of patients, MD=mean difference, 95%-CrI =95% credible interval, LAI=long-acting injectable, AMI – amisulpride, ARI – aripiprazole, ASE – asenapine, BRE – brexpiprazole, CAR – cariprazine, CLO – clozapine, CPZ – chlorpromazine, FLP – fluspirilene, FLU – fluphenazine, FPX – flupentixol, HAL – haloperidol, ILO – iloperidone, LUR – lurasidone, OLA – olanzapine, PAL – paliperidone, PER – perphenazine, PIM – pimozide, PLB – placebo, QUE – quetiapine, RIS – risperidone, SER – sertindole, ZIP – ziprasidone, ZOT – zotepine.

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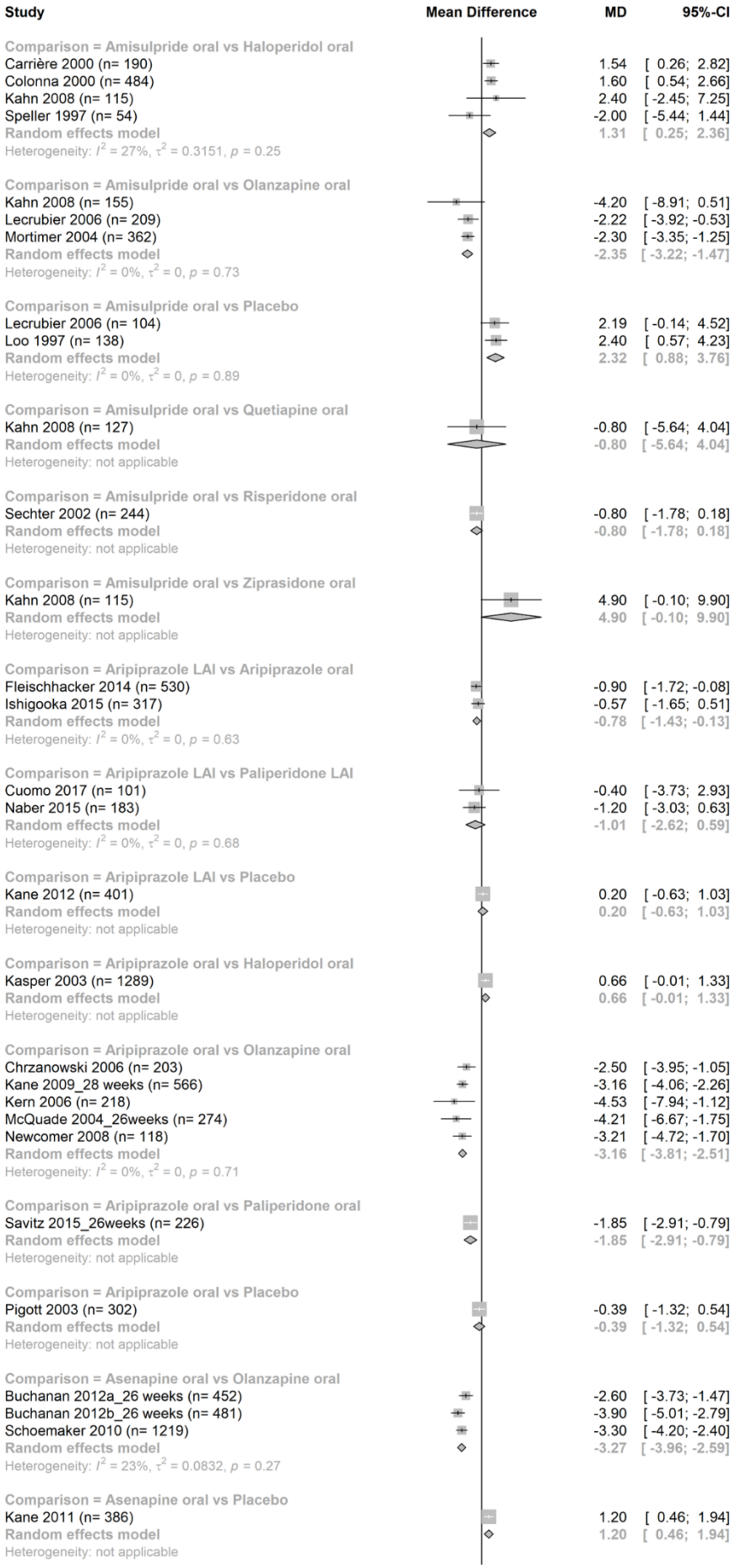
League-table

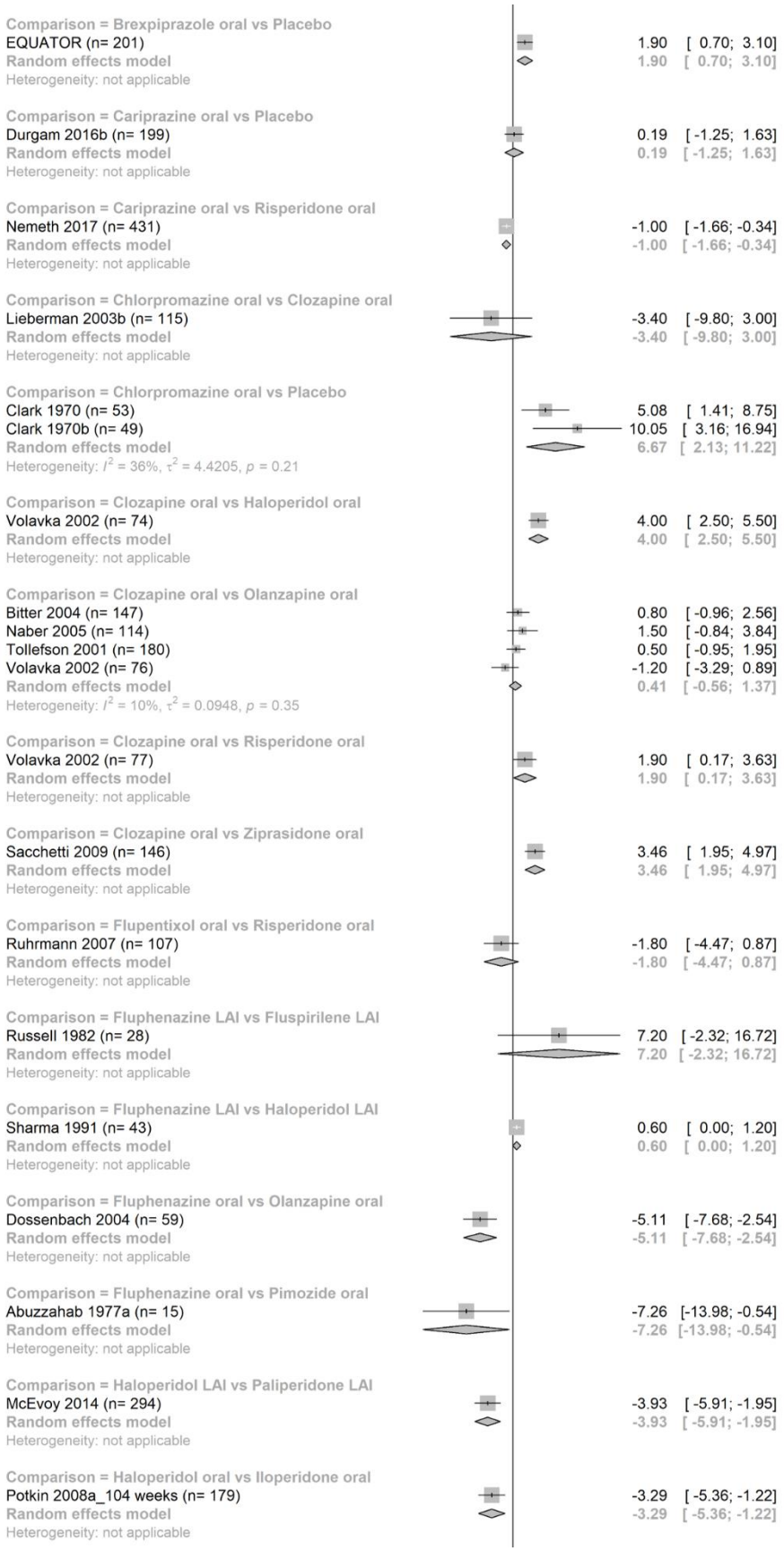
FLP LAI	NA	-7.20 (-16.85 to 2.45)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-6.57 (-16.28 to 3.34)	**HAL LAI**	-0.60 (-2.31 to 1.11)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	**-3.93 (-6.48 to -1.38)**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-7.16 (-16.75 to 2.63)	-0.59 (-2.32 to 1.17)	**FLU LAI**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-7.82 (-18.28 to 3.12)	-1.25 (-5.36 to 3.06)	-0.67 (-5.13 to 3.98)	**FLU oral**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	**-7.26 (-14.17 to -0.35)**	NA	**-5.11 (-8.14 to -2.08)**	NA	NA
-8.96 (-18.94 to 1.62)	-2.37 (-5.28 to 0.56)	-1.78 (-5.21 to 1.66)	-1.14 (-4.34 to 2.08)	**ZIP oral**	-0.23 (-2.22 to 1.76)	0.70 (-2.03 to 3.43)	NA	NA	NA	NA	0.18 (-1.94 to 2.30)	NA	NA	NA	-4.90 (-10.15 to 0.35)	NA	-1.83 (-3.71 to 0.05)	NA	NA	-1.12 (-3.13 to 0.88)	NA	NA	NA	NA	NA	**-4.69 (-5.70 to -3.68)**	**-3.46 (-5.66 to -1.26)**	NA
-9.11 (-19.05 to 1.45)	-2.52 (-5.34 to 0.34)	-1.91 (-5.26 to 1.46)	-1.29 (-4.45 to 1.90)	-0.15 (-1.06 to 0.77)	**HAL oral**	NA	NA	NA	NA	-0.66 (-2.40 to 1.08)	NA	NA	NA	**-3.29 (-5.91 to -0.67)**	-1.22 (-2.49 to 0.05)	NA	**-3.90 (-6.16 to -1.64)**	NA	NA	**-2.09 (-3.12 to -1.06)**	NA	-4.90 (-10.03 to 0.23)	NA	NA	**-3.00 (-5.52 to -0.48)**	**-3.49 (-4.30 to -2.67)**	**-4.00 (-6.19 to -1.81)**	NA
-9.13 (-19.02 to 1.43)	-2.53 (-5.32 to 0.26)	-1.94 (-5.24 to 1.37)	-1.30 (-4.45 to 1.93)	-0.16 (-1.15 to 0.84)	-0.01 (-0.81 to 0.80)	**PLB**	-0.44 (-2.23 to 1.35)	-0.20 (-2.00 to 1.60)	NA	0.39 (-1.46 to 2.24)	NA	-0.19 (-2.34 to 1.96)	-1.20 (-2.96 to 0.56)	-0.17 (-2.02 to 1.68)	**-2.31 (-4.15 to -0.47)**	**-1.50 (-2.55 to -0.45)**	-1.71 (-3.47 to 0.05)	**-1.76 (-3.19 to -0.33)**	-1.90 (-3.90 to 0.10)	NA	NA	NA	NA	NA	**-4.60 (-6.87 to -2.33)**	**-2.82 (-4.27 to -1.38)**	NA	**-6.28 (-9.77 to -2.80)**
-9.06 (-19.06 to 1.57)	-2.48 (-5.53 to 0.64)	-1.88 (-5.39 to 1.70)	-1.24 (-4.60 to 2.18)	-0.10 (-1.66 to 1.45)	0.04 (-1.41 to 1.48)	0.06 (-1.31 to 1.40)	**LUR oral**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	**-2.44 (-4.26 to -0.62)**	NA	NA	NA	NA	NA	NA	NA	NA
-9.10 (-19.07 to 1.43)	-2.53 (-5.40 to 0.38)	-1.94 (-5.30 to 1.46)	-1.29 (-4.57 to 2.05)	-0.15 (-1.52 to 1.21)	-0.01 (-1.23 to 1.21)	0.00 (-1.08 to 1.08)	-0.05 (-1.72 to 1.62)	**ARI LAI**	NA	-0.75 (-2.06 to 0.57)	NA	NA	NA	NA	NA	-0.96 (-2.99 to 1.07)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-9.22 (-19.59 to 1.71)	-2.64 (-6.88 to 1.58)	-2.05 (-6.69 to 2.56)	-1.40 (-5.89 to 3.04)	-0.26 (-3.53 to 2.98)	-0.12 (-3.32 to 3.06)	-0.10 (-3.35 to 3.08)	-0.16 (-3.56 to 3.21)	-0.12 (-3.51 to 3.22)	**FPX oral**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	-1.80 (-4.91 to 1.31)	NA	NA	NA	NA	NA	NA	NA	NA
-9.54 (-19.48 to 1.02)	**-2.95 (-5.79 to -0.07)**	-2.35 (-5.69 to 1.02)	-1.72 (-4.88 to 1.50)	-0.58 (-1.65 to 0.50)	-0.43 (-1.30 to 0.44)	-0.41 (-1.28 to 0.40)	-0.48 (-1.98 to 1.02)	-0.42 (-1.48 to 0.62)	-0.32 (-3.54 to 2.98)	**ARI oral**	NA	NA	NA	NA	NA	NA	NA	-1.85 (-3.77 to 0.07)	NA	NA	NA	NA	NA	NA	NA	**-3.26 (-4.31 to -2.20)**	NA	NA
-9.72 (-19.83 to 0.87)	**-3.14 (-6.17 to -0.09)**	-2.54 (-6.11 to 0.99)	-1.91 (-5.24 to 1.46)	-0.77 (-2.20 to 0.65)	-0.62 (-1.98 to 0.71)	-0.61 (-2.01 to 0.76)	-0.66 (-2.50 to 1.15)	-0.62 (-2.28 to 1.03)	-0.52 (-3.86 to 2.89)	-0.19 (-1.65 to 1.23)	**PER oral**	NA	NA	NA	NA	NA	-1.41 (-3.45 to 0.63)	NA	NA	-1.27 (-3.31 to 0.77)	NA	NA	NA	NA	NA	**-3.51 (-4.85 to -2.16)**	NA	NA
-9.75 (-19.78 to 0.88)	**-3.16 (-6.27 to -0.03)**	-2.58 (-6.14 to 1.04)	-1.91 (-5.31 to 1.51)	-0.78 (-2.36 to 0.86)	-0.64 (-2.12 to 0.88)	-0.62 (-2.05 to 0.82)	-0.67 (-2.54 to 1.25)	-0.62 (-2.37 to 1.12)	-0.50 (-3.90 to 2.92)	-0.20 (-1.77 to 1.37)	-0.01 (-1.84 to 1.91)	**CAR oral**	NA	NA	NA	NA	NA	NA	NA	-1.00 (-2.73 to 0.73)	NA	NA	NA	NA	NA	NA	NA	NA
-9.86 (-19.83 to 0.69)	**-3.27 (-6.19 to -0.30)**	-2.66 (-6.10 to 0.81)	-2.03 (-5.29 to 1.25)	-0.89 (-2.14 to 0.37)	-0.75 (-1.85 to 0.37)	-0.73 (-1.81 to 0.32)	-0.79 (-2.41 to 0.83)	-0.74 (-2.19 to 0.69)	-0.64 (-3.92 to 2.71)	-0.31 (-1.51 to 0.88)	-0.12 (-1.67 to 1.44)	-0.11 (-1.83 to 1.59)	**ASE oral**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	**-3.27 (-4.37 to -2.17)**	NA	NA
-9.89 (-19.97 to 0.75)	**-3.31 (-6.38 to -0.24)**	-2.72 (-6.26 to 0.83)	-2.09 (-5.46 to 1.35)	-0.94 (-2.48 to 0.62)	-0.79 (-2.19 to 0.60)	-0.78 (-2.15 to 0.56)	-0.84 (-2.70 to 1.01)	-0.79 (-2.47 to 0.89)	-0.68 (-4.06 to 2.75)	-0.36 (-1.87 to 1.13)	-0.17 (-1.99 to 1.67)	-0.16 (-2.09 to 1.73)	-0.05 (-1.69 to 1.60)	**ILO oral**	NA	NA	NA	NA	NA	-0.34 (-3.44 to 2.76)	NA	NA	NA	NA	NA	**-8.21 (-12.66 to -3.76)**	NA	NA
-10.53 (-20.50 to 0.07)	**-3.98 (-6.86 to -1.05)**	-3.37 (-6.76 to 0.08)	-2.73 (-5.90 to 0.53)	**-1.58 (-2.74 to -0.45)**	**-1.44 (-2.32 to -0.57)**	**-1.43 (-2.41 to -0.45)**	-1.49 (-3.04 to 0.08)	**-1.44 (-2.79 to -0.08)**	-1.32 (-4.57 to 1.94)	-1.01 (-2.11 to 0.08)	-0.82 (-2.30 to 0.68)	-0.81 (-2.40 to 0.80)	-0.70 (-1.98 to 0.59)	-0.65 (-2.18 to 0.91)	**AMI oral**	NA	-0.80 (-5.90 to 4.30)	NA	NA	-0.80 (-2.68 to 1.08)	NA	NA	NA	NA	NA	**-2.43 (-3.84 to -1.01)**	NA	NA
-10.55 (-20.42 to -0.10)	**-3.96 (-6.60 to -1.36)**	**-3.37 (-6.55 to -0.20)**	-2.73 (-6.00 to 0.57)	**-1.59 (-2.86 to -0.33)**	**-1.45 (-2.56 to -0.32)**	**-1.43 (-2.33 to -0.55)**	-1.49 (-3.06 to 0.09)	**-1.44 (-2.65 to -0.22)**	-1.33 (-4.55 to 2.03)	-1.02 (-2.14 to 0.11)	-0.83 (-2.39 to 0.79)	-0.82 (-2.49 to 0.84)	-0.70 (-2.04 to 0.64)	-0.65 (-2.24 to 0.96)	-0.01 (-1.25 to 1.26)	**PAL LAI**	NA	NA	NA	NA	-0.43 (-1.92 to 1.06)	NA	NA	NA	NA	NA	NA	NA
-10.71 (-20.66 to -0.19)	**-4.13 (-6.99 to -1.29)**	**-3.52 (-6.92 to -0.19)**	-2.90 (-6.04 to 0.28)	**-1.75 (-2.73 to -0.79)**	**-1.60 (-2.39 to -0.82)**	**-1.59 (-2.42 to -0.79)**	**-1.64 (-3.08 to -0.21)**	**-1.59 (-2.83 to -0.38)**	-1.49 (-4.68 to 1.76)	**-1.17 (-2.13 to -0.23)**	-0.98 (-2.30 to 0.36)	-0.97 (-2.49 to 0.51)	-0.86 (-1.99 to 0.28)	-0.81 (-2.26 to 0.65)	-0.16 (-1.17 to 0.84)	-0.16 (-1.26 to 0.94)	**QUE oral**	NA	NA	0.02 (-0.88 to 0.93)	-1.25 (-3.18 to 0.68)	NA	NA	NA	NA	**-2.87 (-3.75 to -2.00)**	NA	NA
-10.85 (-20.82 to -0.15)	**-4.26 (-7.21 to -1.29)**	**-3.67 (-7.14 to -0.25)**	-3.04 (-6.29 to 0.28)	**-1.90 (-3.20 to -0.57)**	**-1.75 (-2.92 to -0.55)**	**-1.73 (-2.78 to -0.70)**	**-1.79 (-3.48 to -0.14)**	**-1.74 (-3.12 to -0.35)**	-1.63 (-4.96 to 1.72)	**-1.32 (-2.44 to -0.20)**	-1.12 (-2.76 to 0.54)	-1.11 (-2.85 to 0.61)	-1.01 (-2.39 to 0.40)	-0.95 (-2.61 to 0.71)	-0.31 (-1.63 to 1.01)	-0.30 (-1.64 to 1.02)	-0.15 (-1.33 to 1.07)	**PAL oral**	NA	NA	NA	NA	NA	NA	**-2.65 (-4.53 to -0.77)**	NA	NA
-11.02 (-21.14 to -0.24)	**-4.42 (-7.86 to -0.99)**	-3.83 (-7.71 to -0.00)	-3.21 (-6.93 to 0.58)	-2.06 (-4.32 to 0.19)	-1.91 (-4.11 to 0.28)	-1.91 (-3.94 to 0.13)	-1.96 (-4.39 to 0.48)	-1.91 (-4.18 to 0.40)	-1.81 (-5.57 to 2.01)	-1.47 (-3.66 to 0.71)	-1.30 (-3.69 to 1.16)	-1.29 (-3.81 to 1.19)	-1.16 (-3.45 to 1.12)	-1.13 (-3.56 to 1.36)	-0.48 (-2.73 to 1.77)	-0.47 (-2.70 to 1.74)	-0.31 (-2.49 to 1.86)	-0.18 (-2.44 to 2.14)	**BRE oral**	NA	NA	NA	NA	NA	NA	NA	NA
-10.99 (-20.92 to -0.46)	**-4.41 (-7.26 to -1.54)**	**-3.81 (-7.15 to -0.43)**	-3.17 (-6.29 to 0.00)	**-2.03 (-2.94 to -1.13)**	**-1.89 (-2.55 to -1.23)**	**-1.87 (-2.65 to -1.12)**	**-1.92 (-3.27 to -0.58)**	**-1.87 (-3.08 to -0.70)**	-1.77 (-4.88 to 1.38)	**-1.45 (-2.32 to -0.58)**	-1.26 (-2.57 to 0.06)	-1.25 (-2.67 to 0.13)	**-1.14 (-2.23 to -0.06)**	-1.09 (-2.47 to 0.30)	-0.44 (-1.34 to 0.46)	-0.43 (-1.53 to 0.64)	-0.28 (-0.96 to 0.40)	-0.13 (-1.31 to 1.02)	0.04 (-2.15 to 2.19)	**RIS oral**	0.52 (-2.40 to 3.44)	-0.10 (-1.94 to 1.74)	NA	NA	NA	**-2.18 (-2.84 to -1.52)**	-1.90 (-4.26 to 0.46)	NA
-11.10 (-21.08 to -0.57)	**-4.52 (-7.40 to -1.66)**	**-3.93 (-7.35 to -0.60)**	-3.30 (-6.60 to 0.05)	**-2.16 (-3.49 to -0.80)**	**-2.02 (-3.22 to -0.77)**	**-2.00 (-3.16 to -0.85)**	**-2.06 (-3.72 to -0.36)**	**-2.00 (-3.44 to -0.56)**	-1.88 (-5.21 to 1.46)	**-1.58 (-2.86 to -0.30)**	-1.38 (-3.01 to 0.28)	-1.38 (-3.13 to 0.39)	-1.27 (-2.70 to 0.22)	-1.22 (-2.92 to 0.51)	-0.57 (-1.92 to 0.80)	-0.57 (-1.72 to 0.58)	-0.41 (-1.55 to 0.74)	-0.26 (-1.74 to 1.24)	-0.10 (-2.39 to 2.25)	-0.13 (-1.26 to 1.05)	**RIS LAI**	NA	NA	NA	NA	**-2.26 (-4.41 to -0.11)**	NA	NA
-11.46 (-21.54 to -0.72)	**-4.84 (-8.21 to -1.44)**	**-4.26 (-8.03 to -0.46)**	**-3.61 (-7.16 to -0.04)**	**-2.47 (-4.50 to -0.50)**	**-2.32 (-4.21 to -0.49)**	**-2.30 (-4.31 to -0.43)**	**-2.36 (-4.64 to -0.17)**	**-2.30 (-4.49 to -0.22)**	-2.21 (-5.76 to 1.35)	-1.89 (-3.89 to 0.06)	-1.70 (-3.91 to 0.48)	-1.69 (-4.03 to 0.55)	-1.57 (-3.70 to 0.44)	-1.52 (-3.80 to 0.69)	-0.87 (-2.91 to 1.06)	-0.87 (-3.03 to 1.14)	-0.71 (-2.66 to 1.15)	-0.57 (-2.72 to 1.50)	-0.40 (-3.25 to 2.36)	-0.43 (-2.26 to 1.31)	-0.31 (-2.46 to 1.76)	**SER oral**	NA	NA	NA	NA	NA	NA
-12.70 (-22.78 to -2.00)	**-6.13 (-9.27 to -3.01)**	**-5.55 (-9.12 to -1.94)**	**-4.90 (-8.26 to -1.51)**	**-3.76 (-5.32 to -2.21)**	**-3.62 (-5.07 to -2.16)**	**-3.60 (-5.12 to -2.12)**	**-3.65 (-5.56 to -1.75)**	**-3.60 (-5.37 to -1.86)**	**-3.49 (-6.91 to -0.05)**	**-3.18 (-4.71 to -1.65)**	**-2.99 (-4.80 to -1.15)**	**-2.98 (-4.97 to -1.03)**	**-2.88 (-4.53 to -1.20)**	**-2.82 (-4.73 to -0.91)**	**-2.18 (-3.75 to -0.57)**	**-2.16 (-3.87 to -0.52)**	**-2.02 (-3.48 to -0.54)**	**-1.87 (-3.60 to -0.16)**	-1.70 (-4.23 to 0.82)	**-1.73 (-3.16 to -0.30)**	-1.59 (-3.38 to 0.13)	-1.30 (-3.54 to 1.02)	**OLA LAI**	NA	NA	-0.22 (-1.52 to 1.08)	NA	NA
-15.02 (-27.80 to -2.11)	**-8.66 (-16.79 to -0.26)**	-8.07 (-16.38 to 0.48)	**-7.41 (-14.25 to -0.22)**	-6.30 (-13.95 to 1.58)	-6.14 (-13.79 to 1.77)	-6.16 (-13.74 to 1.78)	-6.19 (-13.87 to 1.82)	-6.15 (-13.79 to 1.78)	-5.99 (-14.34 to 2.44)	-5.72 (-13.32 to 2.19)	-5.53 (-13.17 to 2.51)	-5.54 (-13.28 to 2.40)	-5.40 (-13.03 to 2.52)	-5.35 (-13.04 to 2.60)	-4.72 (-12.37 to 3.27)	-4.73 (-12.37 to 3.33)	-4.53 (-12.14 to 3.37)	-4.41 (-12.03 to 3.54)	-4.26 (-11.97 to 3.88)	-4.26 (-11.89 to 3.63)	-4.16 (-11.81 to 3.84)	-3.83 (-11.55 to 4.20)	-2.53 (-10.20 to 5.48)	**PIM oral**	NA	NA	NA	NA
-12.97 (-23.12 to -2.33)	**-6.40 (-9.67 to -3.09)**	**-5.81 (-9.52 to -2.03)**	**-5.16 (-8.69 to -1.56)**	**-4.03 (-5.94 to -2.12)**	**-3.88 (-5.62 to -2.11)**	**-3.87 (-5.58 to -2.14)**	**-3.93 (-6.05 to -1.76)**	**-3.88 (-5.86 to -1.85)**	**-3.76 (-7.32 to -0.14)**	**-3.45 (-5.29 to -1.59)**	**-3.27 (-5.36 to -1.08)**	**-3.25 (-5.47 to -1.02)**	**-3.14 (-5.09 to -1.14)**	**-3.09 (-5.22 to -0.93)**	**-2.44 (-4.33 to -0.54)**	**-2.44 (-4.36 to -0.49)**	**-2.28 (-4.09 to -0.44)**	**-2.13 (-4.12 to -0.16)**	-1.97 (-4.61 to 0.71)	**-2.00 (-3.77 to -0.19)**	-1.88 (-3.87 to 0.16)	-1.56 (-4.03 to 1.00)	-0.27 (-2.47 to 1.94)	2.26 (-5.78 to 9.97)	**ZOT oral**	NA	NA	NA
-12.95 (-22.88 to -2.41)	**-6.35 (-9.15 to -3.49)**	**-5.76 (-9.09 to -2.42)**	**-5.13 (-8.21 to -2.00)**	**-3.98 (-4.80 to -3.17)**	**-3.83 (-4.41 to -3.25)**	**-3.82 (-4.50 to -3.15)**	**-3.87 (-5.24 to -2.51)**	**-3.83 (-4.95 to -2.70)**	**-3.73 (-6.85 to -0.52)**	**-3.40 (-4.16 to -2.65)**	**-3.21 (-4.46 to -1.97)**	**-3.20 (-4.65 to -1.78)**	**-3.09 (-4.06 to -2.13)**	**-3.04 (-4.41 to -1.67)**	**-2.39 (-3.26 to -1.53)**	**-2.39 (-3.42 to -1.36)**	**-2.23 (-2.87 to -1.58)**	**-2.08 (-3.17 to -1.01)**	-1.92 (-4.05 to 0.20)	**-1.95 (-2.48 to -1.42)**	**-1.82 (-2.97 to -0.72)**	-1.52 (-3.32 to 0.38)	-0.22 (-1.56 to 1.11)	2.32 (-5.56 to 9.87)	0.05 (-1.73 to 1.79)	**OLA oral**	-0.40 (-1.63 to 0.83)	NA
-13.33 (-23.27 to -2.64)	**-6.74 (-9.73 to -3.74)**	**-6.14 (-9.63 to -2.65)**	**-5.51 (-8.75 to -2.23)**	**-4.36 (-5.56 to -3.19)**	**-4.22 (-5.38 to -3.08)**	**-4.21 (-5.42 to -3.03)**	**-4.26 (-5.96 to -2.58)**	**-4.22 (-5.73 to -2.71)**	**-4.10 (-7.44 to -0.74)**	**-3.79 (-5.07 to -2.54)**	**-3.60 (-5.18 to -1.99)**	**-3.59 (-5.37 to -1.83)**	**-3.48 (-4.91 to -2.06)**	**-3.42 (-5.12 to -1.72)**	**-2.77 (-4.13 to -1.46)**	**-2.77 (-4.22 to -1.37)**	**-2.62 (-3.81 to -1.41)**	**-2.47 (-3.98 to -1.02)**	-2.31 (-4.66 to 0.04)	**-2.34 (-3.47 to -1.21)**	**-2.21 (-3.74 to -0.71)**	-1.91 (-3.98 to 0.25)	-0.60 (-2.30 to 1.06)	1.91 (-5.93 to 9.59)	-0.33 (-2.38 to 1.66)	-0.38 (-1.44 to 0.65)	**CLO oral**	3.40 (-3.20 to 10.00)
-14.25 (-24.45 to -3.30)	**-7.67 (-11.81 to -3.46)**	**-7.07 (-11.58 to -2.56)**	**-6.42 (-10.89 to -1.92)**	**-5.29 (-8.55 to -2.11)**	**-5.15 (-8.34 to -1.98)**	**-5.13 (-8.30 to -1.98)**	**-5.19 (-8.55 to -1.83)**	**-5.15 (-8.44 to -1.85)**	**-5.02 (-9.42 to -0.64)**	**-4.72 (-7.90 to -1.49)**	**-4.50 (-7.88 to -1.20)**	**-4.51 (-7.94 to -1.13)**	**-4.39 (-7.65 to -1.14)**	**-4.34 (-7.70 to -0.97)**	**-3.70 (-6.96 to -0.51)**	**-3.69 (-7.00 to -0.49)**	**-3.53 (-6.75 to -0.41)**	**-3.39 (-6.69 to -0.10)**	-3.22 (-6.96 to 0.50)	**-3.26 (-6.45 to -0.17)**	-3.14 (-6.48 to 0.13)	-2.80 (-6.50 to 0.78)	-1.53 (-4.93 to 1.86)	0.96 (-7.37 to 9.10)	-1.24 (-4.84 to 2.26)	-1.30 (-4.50 to 1.81)	-0.92 (-4.19 to 2.26)	**CPZ oral**

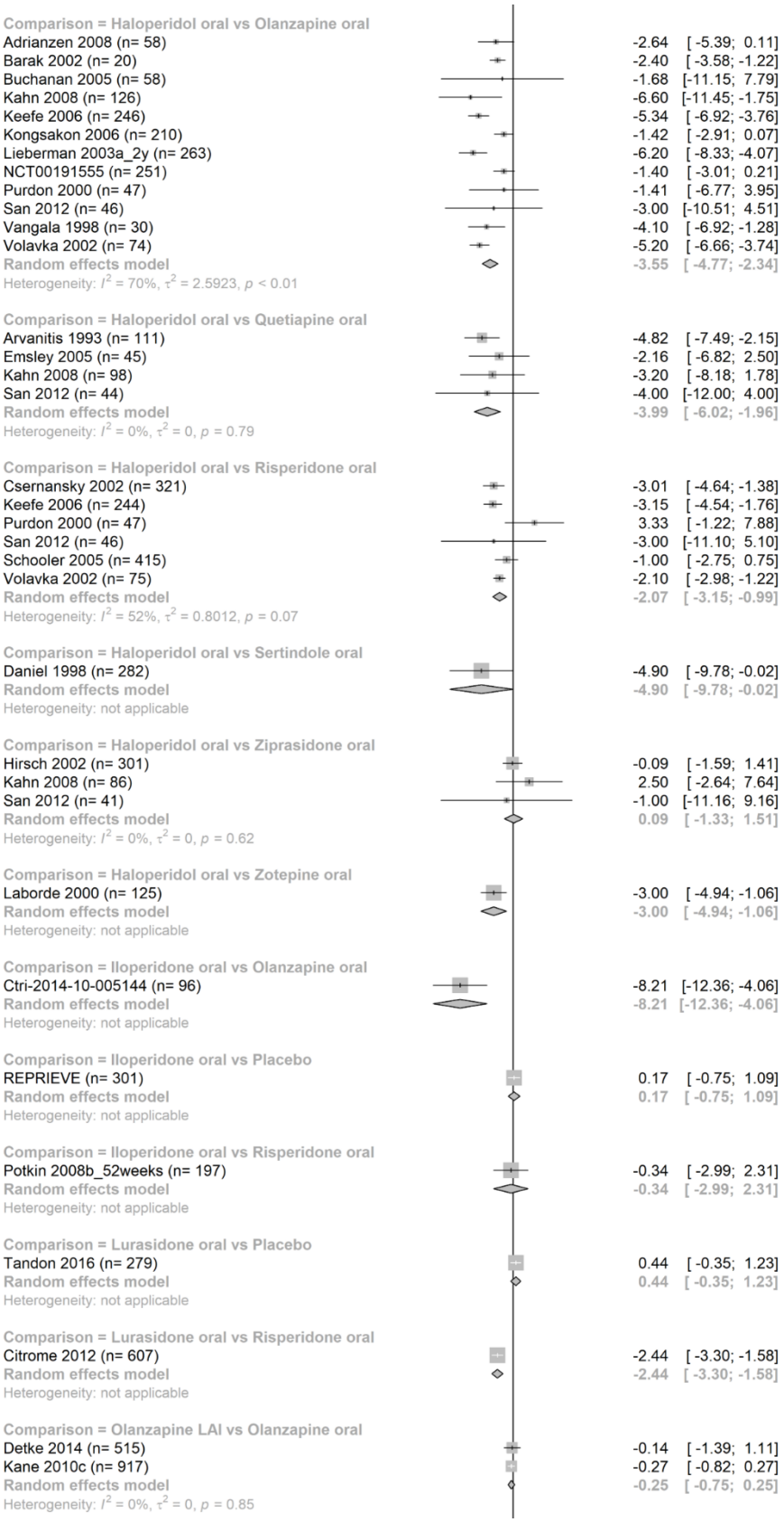
The order of treatments is according to SUCRA ranking. Results of the network-meta-analysis are presented in the left lower half and results of pairwise meta-analyses in the right upper half. Each cell provides the mean difference and the corresponding 95% CrI of a comparison (treatment in column vs treatment in row for the network meta-analysis; treatment in row vs treatment in column for the pairwise meta-analysis). Bold print indicates 95% CrIs excluding the point of no effect. For the results of the network meta-analysis, the background colours of the cells reflect confidence in the estimates, with blue representing moderate confidence, orange representing low confidence, and red representing very low confidence.

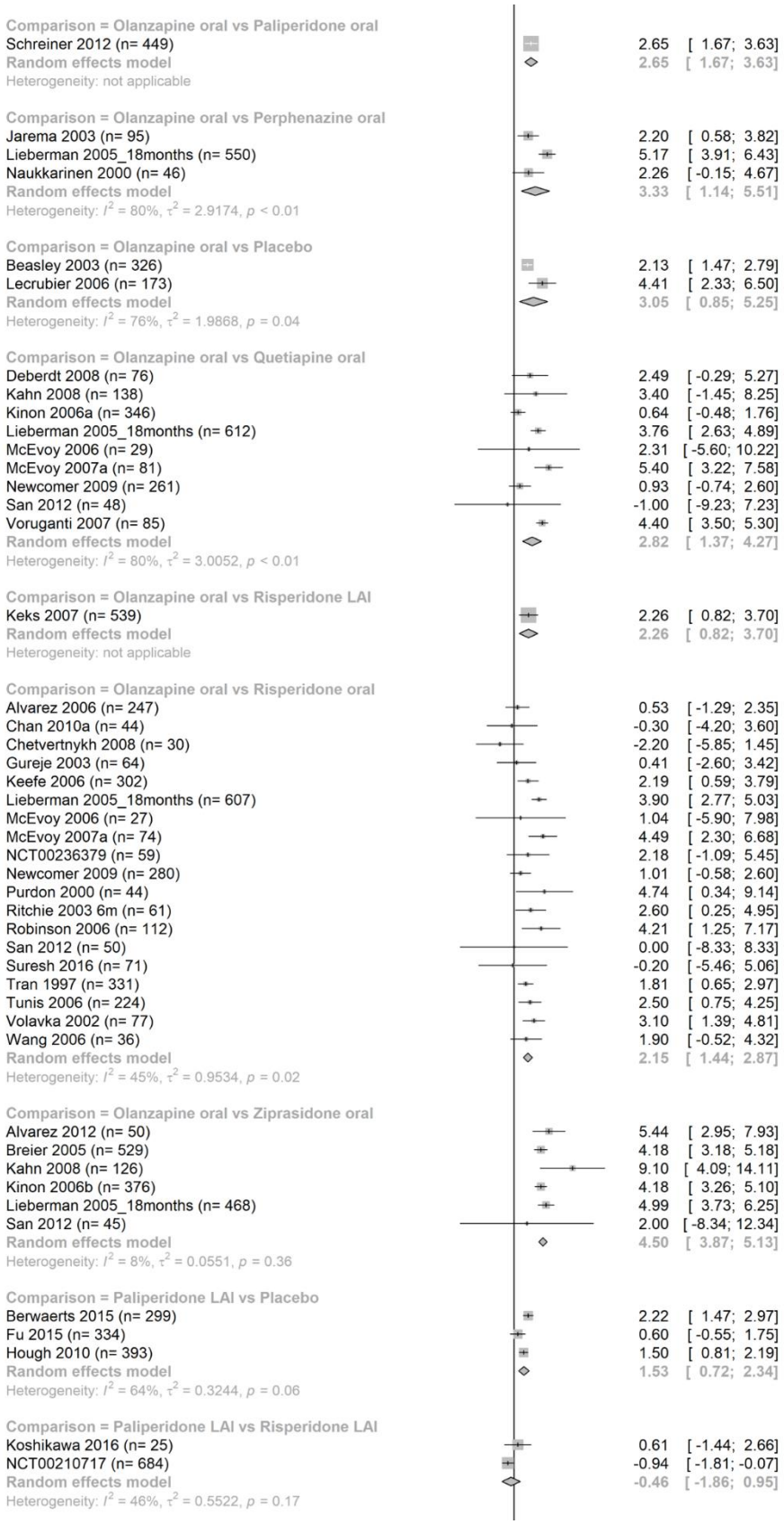
Abbreviations: CrI=credible interval. LAI=long-acting injectable, NA=not available, AMI=Amisulpride, ARI=Aripiprazole, ASE=Asenapine, BRE=Brexpiprazole, CAR=Cariprazine, CLO=Clozapine, CPZ=Chlorpromazine, FLP=Fluspirilene, FLU=Fluphenazine, FPX=Flupentixol, HAL=Haloperidol, ILO=Iloperidone, LUR=Lurasidone, OLA=Olanzapine, PAL=Paliperidone, PER=Perphenazine, PIM=Pimozide, PLB=Placebo, QUE=Quetiapine, RIS=Risperidone, SER=Sertindole, THIOR=Thioridazine, TIOT=Tiotixene, TRI=Trifluoperazine, ZIP=Ziprasidone, ZOT=Zotepine.

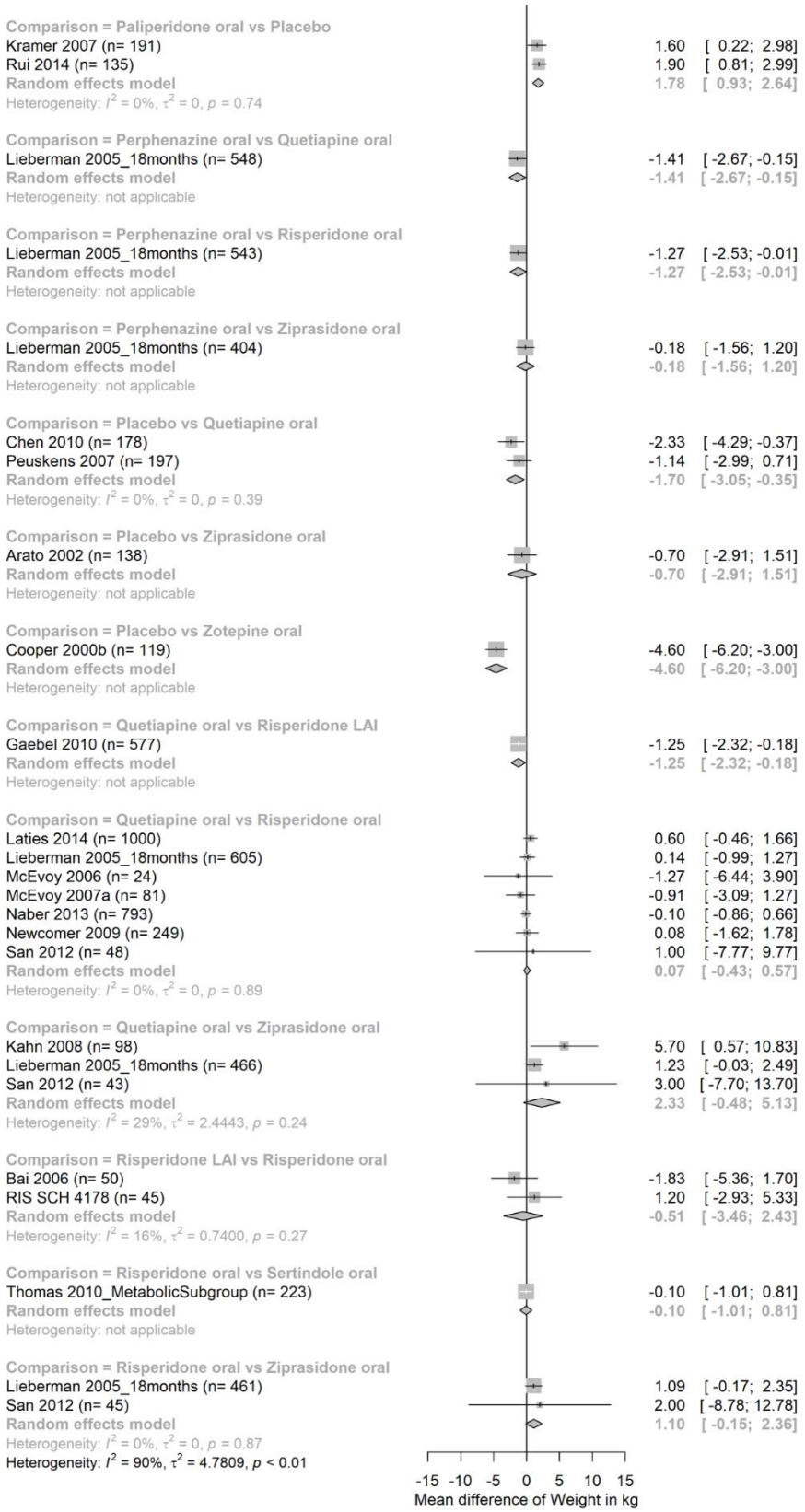
Forest-plot of results of pairwise meta-analyses (also indicating data of individual studies)




Comparison = Brexpiprazole oral vs Placebo
EQUATOR (n= 201) 1.90 [0.70; 3.10]
Random effects model 1.90 [0.70; 3.10]
Heterogeneity: not applicable
Comparison = Cariprazine oral vs Placebo
Durgam 2016b (n= 199) 0.19 [-1.25; 1.63]
Random effects model 0.19 [-1.25; 1.63]
Heterogeneity: not applicable
Comparison = Cariprazine oral vs Risperidone oral
Nemeth 2017 (n= 431) -1.00 [-1.66; -0.34]
Random effects model -1.00 [-1.66; -0.34]
Heterogeneity: not applicable
Comparison = Chlorpromazine oral vs Clozapine oral
Lieberman 2003b (n= 115) -3.40 [-9.80; 3.00]
Random effects model -3.40 [-9.80; 3.00]
Heterogeneity: not applicable
Comparison = Chlorpromazine oral vs Placebo
Clark 1970 (n= 53) 5.08 [1.41; 8.75]
Clark 1970b (n= 49) 10.05 [3.16; 16.94]
Random effects model 6.67 [2.13; 11.22]
Heterogeneity: I^2 = 36%, τ^2 = 4.4205, p = 0.21
Comparison = Clozapine oral vs Haloperidol oral
Volavka 2002 (n= 74) 4.00 [2.50; 5.50]
Random effects model 4.00 [2.50; 5.50]
Heterogeneity: not applicable
Comparison = Clozapine oral vs Olanzapine oral
Bitter 2004 (n= 147) 0.80 [-0.96; 2.56]
Naber 2005 (n= 114) 1.50 [-0.84; 3.84]
Tollefson 2001 (n= 180) 0.50 [-0.95; 1.95]
Volavka 2002 (n= 76) -1.20 [-3.29; 0.89]
Random effects model 0.41 [-0.56; 1.37]
Heterogeneity: I^2 = 10%, τ^2 = 0.0948, p = 0.35
Comparison = Clozapine oral vs Risperidone oral
Volavka 2002 (n= 77) 1.90 [0.17; 3.63]
Random effects model 1.90 [0.17; 3.63]
Heterogeneity: not applicable
Comparison = Clozapine oral vs Ziprasidone oral
Sacchetti 2009 (n= 146) 3.46 [1.95; 4.97]
Random effects model 3.46 [1.95; 4.97]
Heterogeneity: not applicable
Comparison = Flupentixol oral vs Risperidone oral
Ruhrmann 2007 (n= 107) -1.80 [-4.47; 0.87]
Random effects model -1.80 [-4.47; 0.87]
Heterogeneity: not applicable
Comparison = Fluphenazine LAI vs Fluspirilene LAI
Russell 1982 (n= 28) 7.20 [-2.32; 16.72]
Random effects model 7.20 [-2.32; 16.72]
Heterogeneity: not applicable
Comparison = Fluphenazine LAI vs Haloperidol LAI
Sharma 1991 (n= 43) 0.60 [0.00; 1.20]
Random effects model 0.60 [0.00; 1.20]
Heterogeneity: not applicable
Comparison = Fluphenazine oral vs Olanzapine oral
Dossenbach 2004 (n= 59) -5.11 [-7.68; -2.54]
Random effects model -5.11 [-7.68; -2.54]
Heterogeneity: not applicable
Comparison = Fluphenazine oral vs Pimozide oral
Abuzzahab 1977a (n= 15) -7.26 [-13.98; -0.54]
Random effects model -7.26 [-13.98; -0.54]
Heterogeneity: not applicable
Comparison = Haloperidol LAI vs Paliperidone LAI
McEvoy 2014 (n= 294) -3.93 [-5.91; -1.95]
Random effects model -3.93 [-5.91; -1.95]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Iloperidone oral
Potkin 2008a_104 weeks (n= 179) -3.29 [-5.36; -1.22]
Random effects model -3.29 [-5.36; -1.22]
Heterogeneity: not applicable


Comparison = Haloperidol oral vs Olanzapine oral
Adrianzen 2008 (n= 58) -2.64 [-5.39; 0.11]
Barak 2002 (n= 20) -2.40 [-3.58; -1.22]
Buchanan 2005 (n= 58) -1.68 [-11.15; 7.79]
Kahn 2008 (n= 126) -6.60 [-11.45; -1.75]
Keefe 2006 (n= 246) -5.34 [-6.92; -3.76]
Kongsakon 2006 (n= 210) -1.42 [-2.91; 0.07]
Lieberman 2003a_2y (n= 263) -6.20 [-8.33; -4.07]
NCT00191555 (n= 251) -1.40 [-3.01; 0.21]
Purdon 2000 (n= 47) -1.41 [-6.77; 3.95]
San 2012 (n= 46) -3.00 [-10.51; 4.51]
Vangala 1998 (n= 30) -4.10 [-6.92; -1.28]
Volavka 2002 (n= 74) -5.20 [-6.66; -3.74]
Random effects model -3.55 [-4.77; -2.34]
Heterogeneity: I^2 = 70%, τ^2 = 2.5923, p < 0.01
Comparison = Haloperidol oral vs Quetiapine oral
Arvanitis 1993 (n= 111) -4.82 [-7.49; -2.15]
Emsley 2005 (n= 45) -2.16 [-6.82; 2.50]
Kahn 2008 (n= 98) -3.20 [-8.18; 1.78]
San 2012 (n= 44) -4.00 [-12.00; 4.00]
Random effects model -3.99 [-6.02; -1.96]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.79
Comparison = Haloperidol oral vs Risperidone oral
Csernansky 2002 (n= 321) -3.01 [-4.64; -1.38]
Keefe 2006 (n= 244) -3.15 [-4.54; -1.76]
Purdon 2000 (n= 47) 3.33 [-1.22; 7.88]
San 2012 (n= 46) -3.00 [-11.10; 5.10]
Schooler 2005 (n= 415) -1.00 [-2.75; 0.75]
Volavka 2002 (n= 75) -2.10 [-2.98; -1.22]
Random effects model -2.07 [-3.15; -0.99]
Heterogeneity: I^2 = 52%, τ^2 = 0.8012, p = 0.07
Comparison = Haloperidol oral vs Sertindole oral
Daniel 1998 (n= 282) -4.90 [-9.78; -0.02]
Random effects model -4.90 [-9.78; -0.02]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Ziprasidone oral
Hirsch 2002 (n= 301) -0.09 [-1.59; 1.41]
Kahn 2008 (n= 86) 2.50 [-2.64; 7.64]
San 2012 (n= 41) -1.00 [-11.16; 9.16]
Random effects model 0.09 [-1.33; 1.51]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.62
Comparison = Haloperidol oral vs Zotepine oral
Laborde 2000 (n= 125) -3.00 [-4.94; -1.06]
Random effects model -3.00 [-4.94; -1.06]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Olanzapine oral
Ctri-2014-10-005144 (n= 96) -8.21 [-12.36; -4.06]
Random effects model -8.21 [-12.36; -4.06]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Placebo
REPRIEVE (n= 301) 0.17 [-0.75; 1.09]
Random effects model 0.17 [-0.75; 1.09]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Risperidone oral
Potkin 2008b_52weeks (n= 197) -0.34 [-2.99; 2.31]
Random effects model -0.34 [-2.99; 2.31]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Placebo
Tandon 2016 (n= 279) 0.44 [-0.35; 1.23]
Random effects model 0.44 [-0.35; 1.23]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Risperidone oral
Citrome 2012 (n= 607) -2.44 [-3.30; -1.58]
Random effects model -2.44 [-3.30; -1.58]
Heterogeneity: not applicable
Comparison = Olanzapine LAI vs Olanzapine oral
Detke 2014 (n= 515) -0.14 [-1.39; 1.11]
Kane 2010c (n= 917) -0.27 [-0.82; 0.27]
Random effects model -0.25 [-0.75; 0.25]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.85


Comparison = Olanzapine oral vs Paliperidone oral
Schreiner 2012 (n= 449) 2.65 [1.67; 3.63]
Random effects model 2.65 [1.67; 3.63]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Perphenazine oral
Jarema 2003 (n= 95) 2.20 [0.58; 3.82]
Lieberman 2005_18months (n= 550) 5.17 [3.91; 6.43]
Naukkarinen 2000 (n= 46) 2.26 [-0.15; 4.67]
Random effects model 3.33 [1.14; 5.51]
Heterogeneity: I^2 = 80%, τ^2 = 2.9174, p < 0.01
Comparison = Olanzapine oral vs Placebo
Beasley 2003 (n= 326) 2.13 [1.47; 2.79]
Lecrubier 2006 (n= 173) 4.41 [2.33; 6.50]
Random effects model 3.05 [0.85; 5.25]
Heterogeneity: I^2 = 76%, τ^2 = 1.9868, p = 0.04
Comparison = Olanzapine oral vs Quetiapine oral
Deberdt 2008 (n= 76) 2.49 [-0.29; 5.27]
Kahn 2008 (n= 138) 3.40 [-1.45; 8.25]
Kinon 2006a (n= 346) 0.64 [-0.48; 1.76]
Lieberman 2005_18months (n= 612) 3.76 [2.63; 4.89]
McEvoy 2006 (n= 29) 2.31 [-5.60; 10.22]
McEvoy 2007a (n= 81) 5.40 [3.22; 7.58]
Newcomer 2009 (n= 261) 0.93 [-0.74; 2.60]
San 2012 (n= 48) -1.00 [-9.23; 7.23]
Voruganti 2007 (n= 85) 4.40 [3.50; 5.30]
Random effects model 2.82 [1.37; 4.27]
Heterogeneity: I^2 = 80%, τ^2 = 3.0052, p < 0.01
Comparison = Olanzapine oral vs Risperidone LAI
Keks 2007 (n= 539) 2.26 [0.82; 3.70]
Random effects model 2.26 [0.82; 3.70]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Risperidone oral
Alvarez 2006 (n= 247) 0.53 [-1.29; 2.35]
Chan 2010a (n= 44) -0.30 [-4.20; 3.60]
Chetvertnykh 2008 (n= 30) -2.20 [-5.85; 1.45]
Gureje 2003 (n= 64) 0.41 [-2.60; 3.42]
Keefe 2006 (n= 302) 2.19 [0.59; 3.79]
Lieberman 2005_18months (n= 607) 3.90 [2.77; 5.03]
McEvoy 2006 (n= 27) 1.04 [-5.90; 7.98]
McEvoy 2007a (n= 74) 4.49 [2.30; 6.68]
NCT00236379 (n= 59) 2.18 [-1.09; 5.45]
Newcomer 2009 (n= 280) 1.01 [-0.58; 2.60]
Purdon 2000 (n= 44) 4.74 [0.34; 9.14]
Ritchie 2003 6m (n= 61) 2.60 [0.25; 4.95]
Robinson 2006 (n= 112) 4.21 [1.25; 7.17]
San 2012 (n= 50) 0.00 [-8.33; 8.33]
Suresh 2016 (n= 71) -0.20 [-5.46; 5.06]
Tran 1997 (n= 331) 1.81 [0.65; 2.97]
Tunis 2006 (n= 224) 2.50 [0.75; 4.25]
Volavka 2002 (n= 77) 3.10 [1.39; 4.81]
Wang 2006 (n= 36) 1.90 [-0.52; 4.32]
Random effects model 2.15 [1.44; 2.87]
Heterogeneity: I^2 = 45%, τ^2 = 0.9534, p = 0.02
Comparison = Olanzapine oral vs Ziprasidone oral
Alvarez 2012 (n= 50) 5.44 [2.95; 7.93]
Breier 2005 (n= 529) 4.18 [3.18; 5.18]
Kahn 2008 (n= 126) 9.10 [4.09; 14.11]
Kinon 2006b (n= 376) 4.18 [3.26; 5.10]
Lieberman 2005_18months (n= 468) 4.99 [3.73; 6.25]
San 2012 (n= 45) 2.00 [-8.34; 12.34]
Random effects model 4.50 [3.87; 5.13]
Heterogeneity: I^2 = 8%, τ^2 = 0.0551, p = 0.36
Comparison = Paliperidone LAI vs Placebo
Berwaerts 2015 (n= 299) 2.22 [1.47; 2.97]
Fu 2015 (n= 334) 0.60 [-0.55; 1.75]
Hough 2010 (n= 393) 1.50 [0.81; 2.19]
Random effects model 1.53 [0.72; 2.34]
Heterogeneity: I^2 = 64%, τ^2 = 0.3244, p = 0.06
Comparison = Paliperidone LAI vs Risperidone LAI
Koshikawa 2016 (n= 25) 0.61 [-1.44; 2.66]
NCT00210717 (n= 684) -0.94 [-1.81; -0.07]
Random effects model -0.46 [-1.86; 0.95]
Heterogeneity: I^2 = 46%, τ^2 = 0.5522, p = 0.17



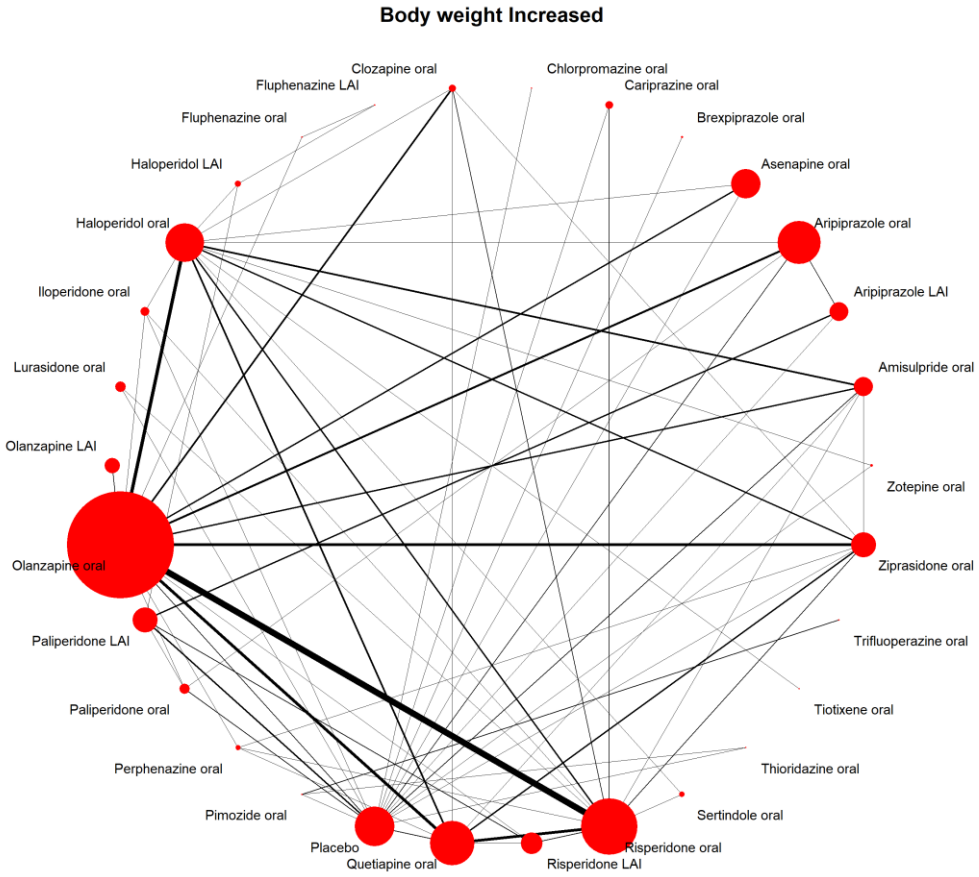
Pairwise meta-analyses are ordered by comparison investigated (in alphabetical order) and a summary effect size is calculated by pairwise meta-analyses of all studies of a specific comparison. The type of effect size measure is mean difference (MD).

Abbreviations: MD=mean difference, 95% CI=95% confidence interval, LAI=long-acting injectable.

7.2 Number of participants with weight gain

106 studies on 29 antipsychotics with 31519 participants included reported on dichotomous weight gain.

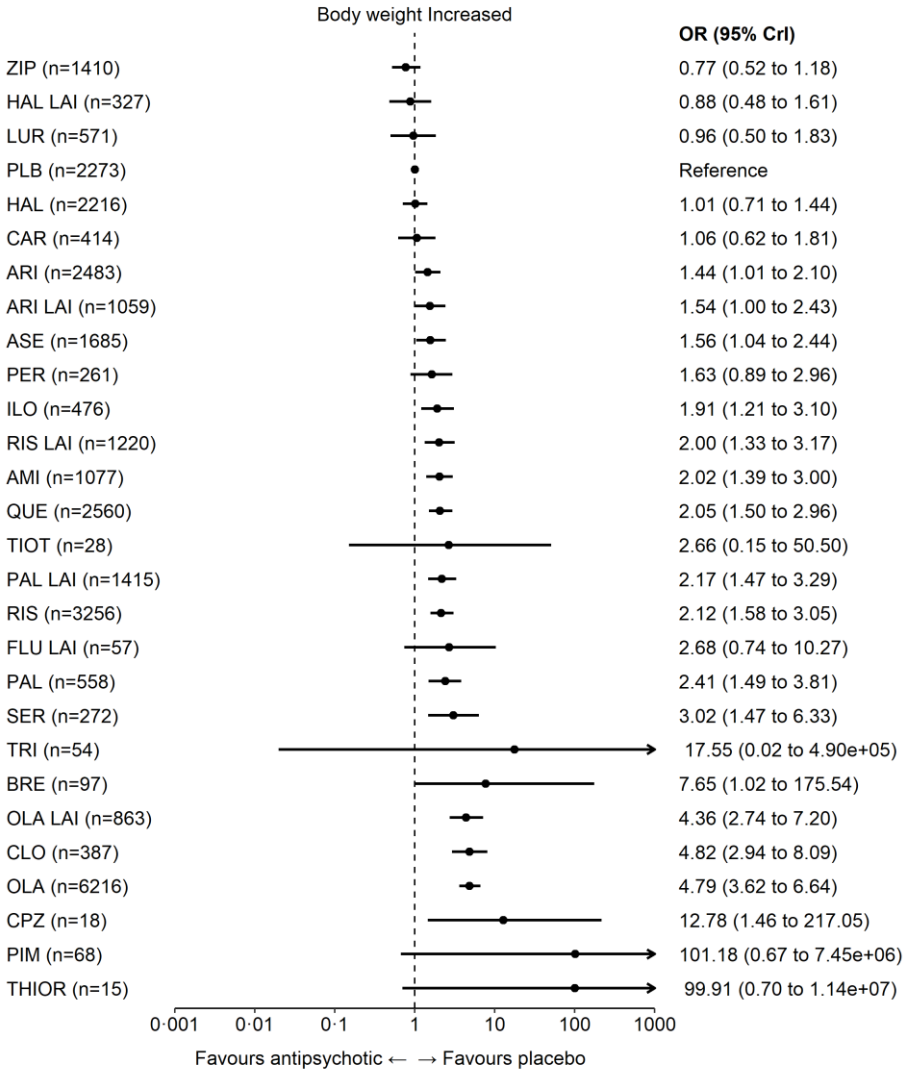
Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Abbreviations: LAI=long-acting injectable.

Forest-plot of results of network meta-analysis for antipsychotic drugs versus placebo



Network meta-analysis estimates of treatment effect of each drug versus placebo reported as odds ratio (OR) and 95% credible interval (CrI). Order of treatments is according to SUCRA ranking. The direction of the effect is indicated below the x-axis. For better presentability fluphenazine and zotepine are not presented in the graph (see comment below).

Abbreviations: n=number of patients, OR=odds ratio, 95%-CrI =95% credible interval, LAI=long-acting injectable, AMI=Amisulpride, ARI=Aripiprazole, ASE=Asenapine, BRE=Brexpiprazole, CAR=Cariprazine, CLO=Clozapine, CPZ=Chlorpromazine, FLP=Fluspirilene, FLU=Fluphenazine, FPX=Flupentixol, HAL=Haloperidol, ILO=Iloperidone, LUR=Lurasidone, OLA=Olanzapine, PAL=Paliperidone, PER=Perphenazine, PIM=Pimozide, PLB=Placebo, QUE=Quetiapine, RIS=Risperidone, SER=Sertindole, THIOR=Thioridazine, TIOT=Tiotixene, TRI=Trifluoperazine, ZIP=Ziprasidone, ZOT=Zotepine.

Comments to the secondary outcome number of participants with weight gain

The results of fluphenazine oral and zotepine oral are not shown in the graph above because the analyses yielded extreme but unreliable estimates. For fluphenazine oral the odds ratio was 0.00 (CrI 0.00 to 0.07) and for zotepine oral 2493.60 (CrI 26.34 to 616036.25). The reason was the presence of no events in at least one intervention in all studies of these drugs which prevents proper modeling. No events occurred in 61 patients treated with fluphenazine oral in two studies. 11 events occurred in 122 patients treated with zotepine oral in two studies however there were no events in the comparator interventions.

Overall, the ranking of the outcome number of participants with weight gain was very similar to the primary outcome. Notable exceptions were fluphenazine LAI which did, however, not significantly differ from placebo in both continuous weight gain and number of participants with weight gain (the change in the ranking and the uncertainty of the effect estimate is probably influenced by the 0 events in fluphenazine oral to which it was compared, see above and network plot). Additionally, the ranking of cariprazine and risperidone LAI differed slightly as compared to continuous data.

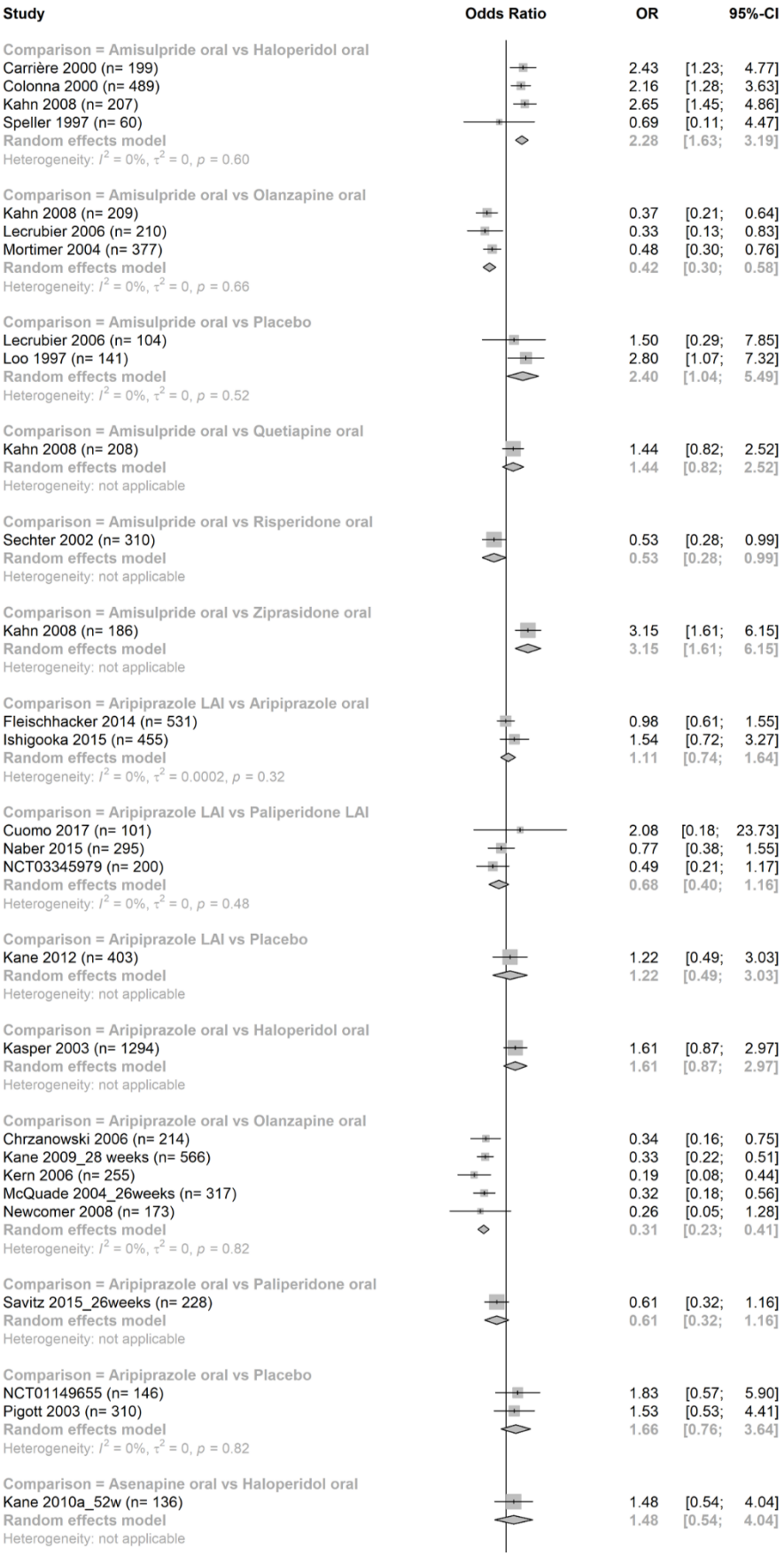
League-table

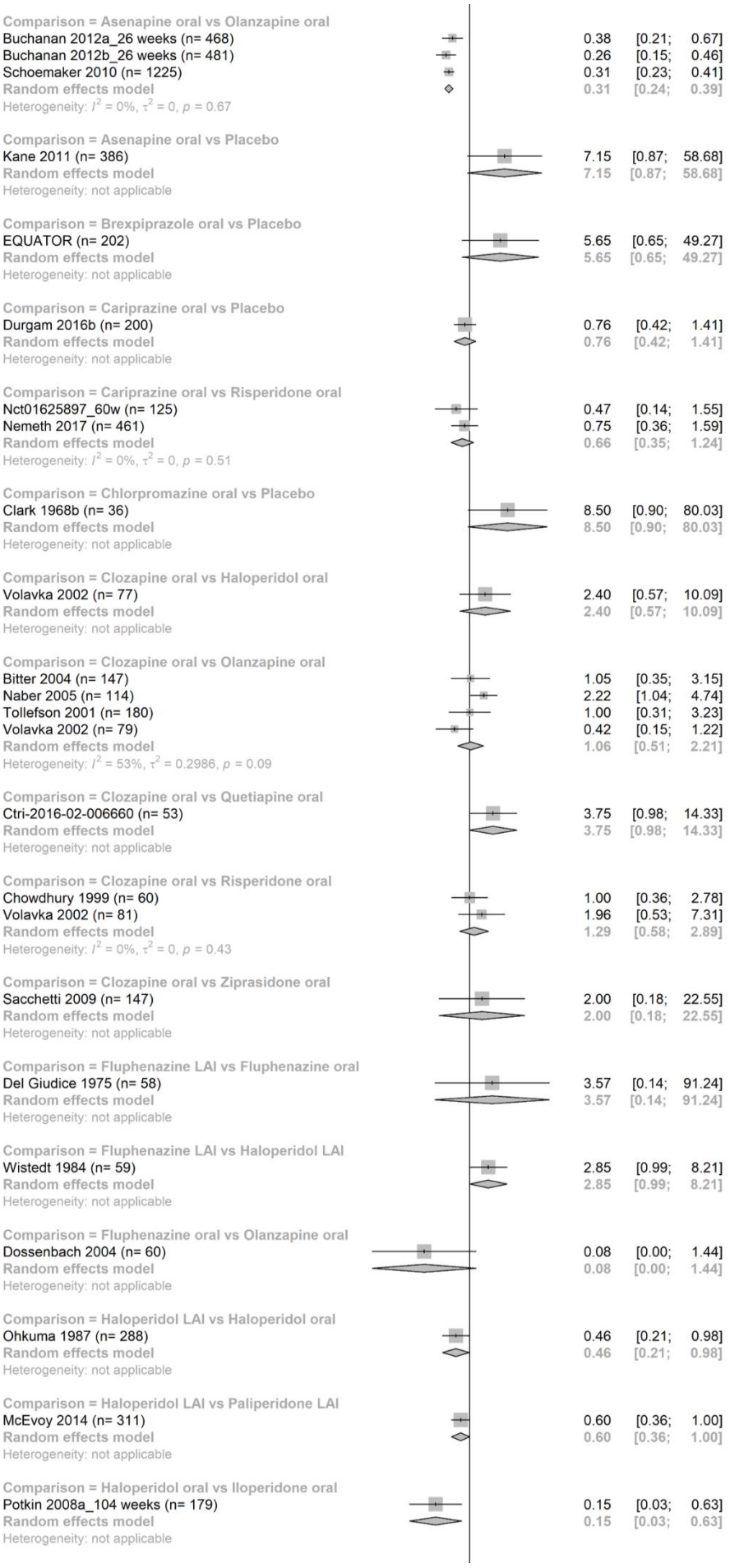
FLU	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.28 (0.01 to 7.25)	NA	NA	NA	NA	NA	NA	0.08 (0.00 to 1.46)	NA	NA	NA	NA
0.00 (0.00 to 0.08)	**ZIP**	NA	NA	2.23 (0.52 to 9.51)	0.76 (0.44 to 1.31)	NA	NA	NA	NA	0.55 (0.26 to 1.17)	NA	NA	**0.32 (0.16 to 0.65)**	**0.39 (0.25 to 0.61)**	NA	NA	**0.39 (0.22 to 0.68)**	NA	NA	NA	NA	NA	NA	0.50 (0.04 to 5.71)	**0.15 (0.11 to 0.20)**	NA	NA	NA	NA
0.00 (0.00 to 0.07)	0.87 (0.47 to 1.67)	**HAL LAI**	NA	NA	0.46 (0.20 to 1.03)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.60 (0.34 to 1.06)	NA	0.35 (0.12 to 1.04)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
0.00 (0.00 to 0.07)	0.81 (0.41 to 1.63)	0.92 (0.40 to 2.12)	**LUR**	0.69 (0.21 to 2.28)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	**0.49 (0.27 to 0.90)**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
0.00 (0.00 to 0.07)	0.77 (0.52 to 1.18)	0.88 (0.48 to 1.61)	0.96 (0.50 to 1.83)	**PLB**	NA	1.31 (0.68 to 2.53)	0.60 (0.27 to 1.35)	0.82 (0.32 to 2.09)	0.14 (0.02 to 1.17)	NA	0.82 (0.41 to 1.65)	NA	**0.42 (0.18 to 0.99)**	0.74 (0.29 to 1.84)	NA	**0.35 (0.19 to 0.66)**	NA	NA	0.57 (0.26 to 1.27)	NA	NA	0.18 (0.02 to 1.57)	NA	NA	**0.19 (0.06 to 0.65)**	0.12 (0.01 to 1.12)	0.26 (0.01 to 6.01)	0.26 (0.01 to 6.01)	0.06 (0.00 to 1.17)
0.00 (0.00 to 0.06)	0.76 (0.55 to 1.08)	0.86 (0.49 to 1.56)	0.93 (0.50 to 1.80)	0.99 (0.69 to 1.40)	**HAL**	NA	0.62 (0.32 to 1.20)	NA	0.68 (0.24 to 1.90)	NA	**0.15 (0.03 to 0.65)**	NA	**0.44 (0.31 to 0.63)**	**0.44 (0.26 to 0.75)**	0.46 (0.04 to 5.50)	NA	**0.40 (0.17 to 0.97)**	NA	NA	NA	**0.14 (0.04 to 0.50)**	NA	NA	NA	0.42 (0.10 to 1.79)	**0.26 (0.20 to 0.35)**	NA	NA	NA	0.09 (0.00 to 1.78)
0.00 (0.00 to 0.07)	0.73 (0.41 to 1.37)	0.83 (0.39 to 1.82)	0.91 (0.41 to 1.96)	0.94 (0.55 to 1.62)	0.96 (0.55 to 1.72)	**CAR**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.66 (0.34 to 1.27)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
0.00 (0.00 to 0.05)	**0.54 (0.35 to 0.80)**	0.61 (0.33 to 1.12)	0.66 (0.34 to 1.29)	**0.70 (0.48 to 0.99)**	**0.70 (0.49 to 0.98)**	0.74 (0.40 to 1.29)	**ARI**	0.89 (0.57 to 1.38)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.61 (0.31 to 1.21)	NA	NA	NA	NA	NA	**0.30 (0.22 to 0.42)**	NA	NA	NA	NA
0.00 (0.00 to 0.04)	**0.51 (0.30 to 0.84)**	0.57 (0.29 to 1.10)	0.62 (0.30 to 1.30)	0.65 (0.41 to 1.00)	0.66 (0.41 to 1.05)	0.69 (0.35 to 1.29)	0.94 (0.63 to 1.38)	**ARI LAI**	NA	NA	NA	NA	NA	NA	NA	0.68 (0.39 to 1.19)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
0.00 (0.00 to 0.04)	**0.49 (0.32 to 0.76)**	0.56 (0.29 to 1.08)	0.61 (0.30 to 1.21)	**0.64 (0.41 to 0.97)**	**0.65 (0.44 to 0.94)**	0.68 (0.35 to 1.23)	0.92 (0.60 to 1.39)	0.98 (0.58 to 1.65)	**ASE**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	**0.31 (0.23 to 0.41)**	NA	NA	NA	NA
0.00 (0.00 to 0.04)	**0.47 (0.26 to 0.87)**	0.53 (0.25 to 1.19)	0.58 (0.26 to 1.34)	0.61 (0.34 to 1.12)	0.62 (0.35 to 1.10)	0.66 (0.31 to 1.35)	0.88 (0.48 to 1.62)	0.95 (0.47 to 1.87)	0.96 (0.52 to 1.81)	**PER**	NA	NA	NA	0.73 (0.42 to 1.28)	NA	NA	0.89 (0.51 to 1.56)	NA	NA	NA	NA	NA	NA	NA	**0.33 (0.20 to 0.56)**	NA	NA	NA	NA
0.00 (0.00 to 0.03)	**0.41 (0.24 to 0.68)**	**0.47 (0.23 to 0.90)**	0.50 (0.24 to 1.04)	**0.52 (0.32 to 0.83)**	**0.53 (0.33 to 0.87)**	0.56 (0.28 to 1.06)	0.77 (0.45 to 1.23)	0.82 (0.45 to 1.43)	0.82 (0.48 to 1.44)	0.85 (0.43 to 1.73)	**ILO**	NA	NA	NA	NA	NA	1.07 (0.52 to 2.20)	NA	NA	NA	NA	NA	NA	NA	**0.29 (0.12 to 0.68)**	NA	NA	NA	NA
0.00 (0.00 to 0.03)	**0.39 (0.25 to 0.60)**	**0.44 (0.23 to 0.79)**	**0.48 (0.23 to 0.92)**	**0.50 (0.32 to 0.75)**	**0.51 (0.33 to 0.74)**	**0.53 (0.27 to 0.96)**	0.72 (0.46 to 1.11)	0.76 (0.46 to 1.27)	0.78 (0.48 to 1.23)	0.81 (0.42 to 1.53)	0.94 (0.55 to 1.61)	**RIS LAI**	NA	1.10 (0.57 to 2.13)	NA	1.04 (0.64 to 1.69)	1.23 (0.48 to 3.14)	NA	NA	NA	NA	NA	NA	NA	**0.33 (0.21 to 0.53)**	NA	NA	NA	NA
0.00 (0.00 to 0.03)	**0.38 (0.26 to 0.56)**	**0.43 (0.23 to 0.80)**	**0.47 (0.24 to 0.91)**	**0.49 (0.33 to 0.72)**	**0.50 (0.37 to 0.67)**	**0.52 (0.28 to 0.92)**	0.70 (0.48 to 1.07)	0.75 (0.46 to 1.25)	0.77 (0.50 to 1.19)	0.80 (0.44 to 1.45)	0.93 (0.56 to 1.57)	0.98 (0.64 to 1.56)	**AMI**	1.44 (0.78 to 2.66)	NA	NA	0.53 (0.27 to 1.04)	NA	NA	NA	NA	NA	NA	NA	**0.41 (0.28 to 0.60)**	NA	NA	NA	NA
0.00 (0.00 to 0.03)	**0.37 (0.27 to 0.53)**	**0.43 (0.23 to 0.77)**	**0.46 (0.24 to 0.86)**	**0.49 (0.34 to 0.67)**	**0.49 (0.36 to 0.64)**	**0.51 (0.29 to 0.87)**	0.69 (0.49 to 1.00)	0.74 (0.47 to 1.19)	0.76 (0.51 to 1.11)	0.79 (0.45 to 1.33)	0.92 (0.57 to 1.48)	0.97 (0.67 to 1.44)	0.98 (0.70 to 1.37)	**QUE**	NA	NA	0.99 (0.77 to 1.27)	NA	NA	NA	NA	NA	NA	0.27 (0.07 to 1.04)	**0.44 (0.33 to 0.57)**	NA	NA	NA	NA
0.00 (0.00 to 0.02)	0.29 (0.01 to 4.60)	0.33 (0.02 to 5.56)	0.35 (0.02 to 8.07)	0.38 (0.02 to 6.53)	0.37 (0.02 to 6.19)	0.39 (0.02 to 8.15)	0.53 (0.03 to 9.76)	0.57 (0.03 to 12.16)	0.60 (0.03 to 9.92)	0.61 (0.03 to 11.85)	0.71 (0.04 to 12.81)	0.75 (0.04 to 13.33)	0.77 (0.04 to 12.62)	0.77 (0.04 to 12.73)	**TIOT**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
0.00 (0.00 to 0.03)	**0.35 (0.22 to 0.57)**	**0.40 (0.23 to 0.68)**	**0.44 (0.21 to 0.89)**	**0.46 (0.30 to 0.68)**	**0.47 (0.30 to 0.71)**	**0.49 (0.26 to 0.88)**	0.67 (0.42 to 1.01)	0.71 (0.42 to 1.10)	0.72 (0.43 to 1.18)	0.74 (0.39 to 1.41)	0.87 (0.48 to 1.52)	0.93 (0.59 to 1.39)	0.94 (0.58 to 1.48)	0.95 (0.62 to 1.44)	1.23 (0.07 to 24.92)	**PAL LAI**	NA	NA	1.00 (0.02 to 52.19)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
0.00 (0.00 to 0.03)	**0.36 (0.26 to 0.50)**	**0.41 (0.23 to 0.73)**	**0.44 (0.24 to 0.80)**	**0.47 (0.33 to 0.63)**	**0.47 (0.36 to 0.60)**	**0.49 (0.28 to 0.81)**	**0.67 (0.48 to 0.95)**	0.71 (0.45 to 1.12)	0.73 (0.51 to 1.05)	0.76 (0.43 to 1.29)	0.88 (0.56 to 1.39)	0.93 (0.65 to 1.38)	0.94 (0.69 to 1.29)	0.96 (0.76 to 1.21)	1.24 (0.08 to 23.70)	1.01 (0.68 to 1.55)	**RIS**	NA	NA	1.07 (0.51 to 2.25)	NA	NA	NA	0.77 (0.34 to 1.77)	**0.42 (0.34 to 0.52)**	NA	NA	NA	NA
0.00 (0.00 to 0.02)	0.29 (0.08 to 1.07)	0.33 (0.10 to 1.04)	0.36 (0.08 to 1.41)	0.37 (0.10 to 1.36)	0.38 (0.10 to 1.33)	0.39 (0.09 to 1.57)	0.54 (0.14 to 1.92)	0.58 (0.15 to 2.11)	0.59 (0.15 to 2.14)	0.60 (0.15 to 2.33)	0.71 (0.19 to 2.71)	0.76 (0.20 to 2.80)	0.76 (0.20 to 2.77)	0.78 (0.21 to 2.74)	1.01 (0.04 to 26.50)	0.81 (0.22 to 2.88)	0.81 (0.22 to 2.83)	**FLU LAI**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
0.00 (0.00 to 0.03)	**0.32 (0.19 to 0.56)**	**0.37 (0.18 to 0.74)**	**0.40 (0.19 to 0.83)**	**0.42 (0.26 to 0.67)**	**0.42 (0.26 to 0.68)**	**0.44 (0.23 to 0.85)**	**0.59 (0.38 to 0.96)**	0.64 (0.37 to 1.15)	0.65 (0.39 to 1.14)	0.67 (0.34 to 1.36)	0.78 (0.44 to 1.50)	0.83 (0.48 to 1.49)	0.85 (0.51 to 1.43)	0.86 (0.54 to 1.43)	1.12 (0.05 to 22.36)	0.90 (0.53 to 1.62)	0.90 (0.57 to 1.46)	1.11 (0.31 to 4.46)	**PAL**	NA	NA	NA	NA	**0.57 (0.34 to 0.95)**	NA	NA	NA	NA
0.00 (0.00 to 0.02)	**0.26 (0.13 to 0.51)**	**0.29 (0.12 to 0.67)**	**0.32 (0.13 to 0.72)**	**0.33 (0.16 to 0.68)**	**0.34 (0.17 to 0.65)**	**0.36 (0.15 to 0.78)**	**0.48 (0.23 to 0.95)**	0.51 (0.23 to 1.07)	0.52 (0.25 to 1.05)	0.54 (0.23 to 1.28)	0.63 (0.29 to 1.35)	0.67 (0.32 to 1.37)	0.68 (0.33 to 1.33)	0.69 (0.35 to 1.39)	0.90 (0.04 to 17.48)	0.72 (0.34 to 1.49)	0.72 (0.37 to 1.38)	0.90 (0.21 to 3.75)	0.80 (0.35 to 1.80)	**SER**	NA	NA	NA	NA	NA	NA	NA	NA
0.00 (0.00 to 0.02)	0.04 (0.00 to 42.69)	0.05 (0.00 to 49.49)	0.05 (0.00 to 52.11)	0.06 (0.00 to 49.18)	0.06 (0.00 to 53.17)	0.06 (0.00 to 56.84)	0.08 (0.00 to 75.60)	0.09 (0.00 to 77.29)	0.09 (0.00 to 82.38)	0.09 (0.00 to 86.32)	0.11 (0.00 to 103.29)	0.12 (0.00 to 104.49)	0.12 (0.00 to 111.61)	0.12 (0.00 to 106.51)	0.06 (0.00 to 367.59)	0.13 (0.00 to 109.30)	0.13 (0.00 to 113.51)	0.15 (0.00 to 223.69)	0.14 (0.00 to 139.46)	0.18 (0.00 to 176.21)	**TRI**	NA	NA	NA	NA	NA	0.31 (0.05 to 2.06)	NA	NA
0.00 (0.00 to 0.01)	**0.10 (0.00 to 0.79)**	**0.11 (0.00 to 0.93)**	0.13 (0.01 to 1.21)	**0.13 (0.01 to 0.98)**	0.13 (0.01 to 1.03)	0.14 (0.01 to 1.18)	0.19 (0.01 to 1.61)	0.20 (0.01 to 1.75)	0.21 (0.01 to 1.62)	0.22 (0.01 to 1.74)	0.25 (0.01 to 2.08)	0.27 (0.01 to 2.10)	0.27 (0.01 to 2.10)	0.28 (0.01 to 2.09)	0.28 (0.01 to 15.51)	0.29 (0.01 to 2.23)	0.29 (0.01 to 2.21)	0.34 (0.01 to 4.05)	0.32 (0.01 to 2.79)	0.39 (0.02 to 3.64)	3.59 (0.00 to 39351.05)	**BRE**	NA	NA	NA	NA	NA	NA
0.00 (0.00 to 0.01)	**0.18 (0.11 to 0.29)**	**0.20 (0.10 to 0.40)**	**0.22 (0.11 to 0.45)**	**0.23 (0.14 to 0.36)**	**0.23 (0.15 to 0.35)**	**0.24 (0.12 to 0.46)**	**0.33 (0.20 to 0.52)**	**0.35 (0.20 to 0.62)**	**0.36 (0.22 to 0.59)**	**0.37 (0.19 to 0.71)**	**0.44 (0.24 to 0.78)**	**0.46 (0.28 to 0.78)**	**0.47 (0.29 to 0.74)**	**0.47 (0.31 to 0.73)**	0.61 (0.04 to 11.89)	**0.49 (0.29 to 0.87)**	**0.49 (0.33 to 0.75)**	0.61 (0.16 to 2.33)	**0.56 (0.30 to 0.96)**	0.69 (0.32 to 1.49)	3.92 (0.00 to 107085.96)	1.71 (0.21 to 39.71)	**OLA LAI**	NA	0.91 (0.67 to 1.23)	NA	NA	NA	NA
0.00 (0.00 to 0.01)	**0.16 (0.09 to 0.27)**	**0.18 (0.09 to 0.37)**	**0.20 (0.09 to 0.42)**	**0.21 (0.12 to 0.34)**	**0.21 (0.13 to 0.34)**	**0.22 (0.11 to 0.42)**	**0.30 (0.18 to 0.50)**	**0.32 (0.18 to 0.59)**	**0.32 (0.19 to 0.56)**	**0.34 (0.17 to 0.67)**	**0.39 (0.22 to 0.74)**	**0.41 (0.24 to 0.74)**	**0.42 (0.25 to 0.71)**	**0.43 (0.27 to 0.69)**	0.56 (0.03 to 10.79)	**0.45 (0.26 to 0.81)**	**0.45 (0.28 to 0.71)**	0.55 (0.15 to 2.13)	**0.50 (0.27 to 0.92)**	0.62 (0.28 to 1.39)	3.66 (0.00 to 100940.94)	1.59 (0.17 to 37.58)	0.90 (0.52 to 1.62)	**CLO**	1.15 (0.70 to 1.91)	NA	NA	NA	NA
0.00 (0.00 to 0.01)	**0.16 (0.12 to 0.22)**	**0.18 (0.10 to 0.32)**	**0.20 (0.11 to 0.37)**	**0.21 (0.15 to 0.28)**	**0.21 (0.17 to 0.27)**	**0.22 (0.13 to 0.37)**	**0.30 (0.23 to 0.40)**	**0.32 (0.21 to 0.49)**	**0.33 (0.24 to 0.45)**	**0.34 (0.20 to 0.57)**	**0.39 (0.25 to 0.62)**	**0.42 (0.30 to 0.60)**	**0.42 (0.32 to 0.57)**	**0.43 (0.35 to 0.54)**	0.56 (0.03 to 10.46)	**0.45 (0.31 to 0.68)**	**0.45 (0.37 to 0.54)**	0.55 (0.16 to 2.02)	**0.50 (0.32 to 0.76)**	0.63 (0.32 to 1.22)	3.58 (0.00 to 99615.34)	1.56 (0.20 to 35.93)	0.91 (0.63 to 1.32)	1.01 (0.64 to 1.55)	**OLA**	NA	NA	NA	NA
0.00 (0.00 to 0.01)	**0.06 (0.00 to 0.58)**	**0.07 (0.00 to 0.67)**	**0.07 (0.00 to 0.75)**	**0.08 (0.00 to 0.68)**	**0.08 (0.00 to 0.74)**	**0.08 (0.00 to 0.80)**	0.11 (0.01 to 1.05)	0.12 (0.01 to 1.16)	0.12 (0.01 to 1.15)	0.12 (0.01 to 1.26)	0.15 (0.01 to 1.40)	0.16 (0.01 to 1.50)	0.16 (0.01 to 1.48)	0.16 (0.01 to 1.51)	0.21 (0.00 to 9.19)	0.17 (0.01 to 1.61)	0.17 (0.01 to 1.58)	0.20 (0.01 to 2.50)	0.18 (0.01 to 1.86)	0.23 (0.01 to 2.38)	1.78 (0.00 to 30617.51)	0.60 (0.02 to 30.49)	0.34 (0.02 to 3.32)	0.37 (0.02 to 3.63)	0.38 (0.02 to 3.51)	**CPZ**	NA	NA	NA
0.00 (0.00 to 0.00)	0.01 (0.00 to 1.39)	0.01 (0.00 to 1.57)	0.01 (0.00 to 1.60)	0.01 (0.00 to 1.49)	0.01 (0.00 to 1.61)	0.01 (0.00 to 1.66)	0.01 (0.00 to 2.39)	0.02 (0.00 to 2.43)	0.02 (0.00 to 2.55)	0.02 (0.00 to 2.64)	0.02 (0.00 to 3.06)	0.02 (0.00 to 3.43)	0.02 (0.00 to 3.34)	0.02 (0.00 to 3.45)	0.01 (0.00 to 17.47)	0.02 (0.00 to 3.52)	0.02 (0.00 to 3.43)	0.02 (0.00 to 6.05)	0.02 (0.00 to 4.08)	0.03 (0.00 to 5.09)	0.17 (0.01 to 1.37)	0.05 (0.00 to 32.84)	0.04 (0.00 to 7.17)	0.05 (0.00 to 8.02)	0.05 (0.00 to 8.05)	0.11 (0.00 to 42.57)	**PIM**	1.00 (0.15 to 6.86)	NA
0.00 (0.00 to 0.00)	0.01 (0.00 to 1.18)	0.01 (0.00 to 1.31)	0.01 (0.00 to 1.33)	0.01 (0.00 to 1.42)	0.01 (0.00 to 1.42)	0.01 (0.00 to 1.48)	0.01 (0.00 to 2.08)	0.02 (0.00 to 2.17)	0.02 (0.00 to 2.21)	0.02 (0.00 to 2.41)	0.02 (0.00 to 2.78)	0.02 (0.00 to 2.98)	0.02 (0.00 to 2.89)	0.02 (0.00 to 2.95)	0.01 (0.00 to 18.27)	0.02 (0.00 to 3.13)	0.02 (0.00 to 3.06)	0.03 (0.00 to 4.61)	0.02 (0.00 to 3.43)	0.03 (0.00 to 4.36)	0.15 (0.00 to 3.10)	0.05 (0.00 to 32.50)	0.04 (0.00 to 6.21)	0.05 (0.00 to 6.94)	0.05 (0.00 to 6.83)	0.10 (0.00 to 35.50)	0.99 (0.08 to 10.62)	**THIOR**	NA
0.00 (0.00 to 0.00)	**0.00 (0.00 to 0.03)**	**0.00 (0.00 to 0.04)**	**0.00 (0.00 to 0.04)**	**0.00 (0.00 to 0.04)**	**0.00 (0.00 to 0.04)**	**0.00 (0.00 to 0.04)**	**0.00 (0.00 to 0.05)**	**0.00 (0.00 to 0.06)**	**0.00 (0.00 to 0.06)**	**0.00 (0.00 to 0.06)**	**0.00 (0.00 to 0.07)**	**0.00 (0.00 to 0.08)**	**0.00 (0.00 to 0.08)**	**0.00 (0.00 to 0.08)**	**0.00 (0.00 to 0.27)**	**0.00 (0.00 to 0.09)**	**0.00 (0.00 to 0.08)**	**0.00 (0.00 to 0.14)**	**0.00 (0.00 to 0.09)**	**0.00 (0.00 to 0.12)**	0.01 (0.00 to 5923.18)	0.00 (0.00 to 1.19)	**0.00 (0.00 to 0.17)**	**0.00 (0.00 to 0.19)**	**0.00 (0.00 to 0.18)**	0.00 (0.00 to 1.32)	0.07 (0.00 to 106990.10)	0.07 (0.00 to 126808.83)	**ZOT**

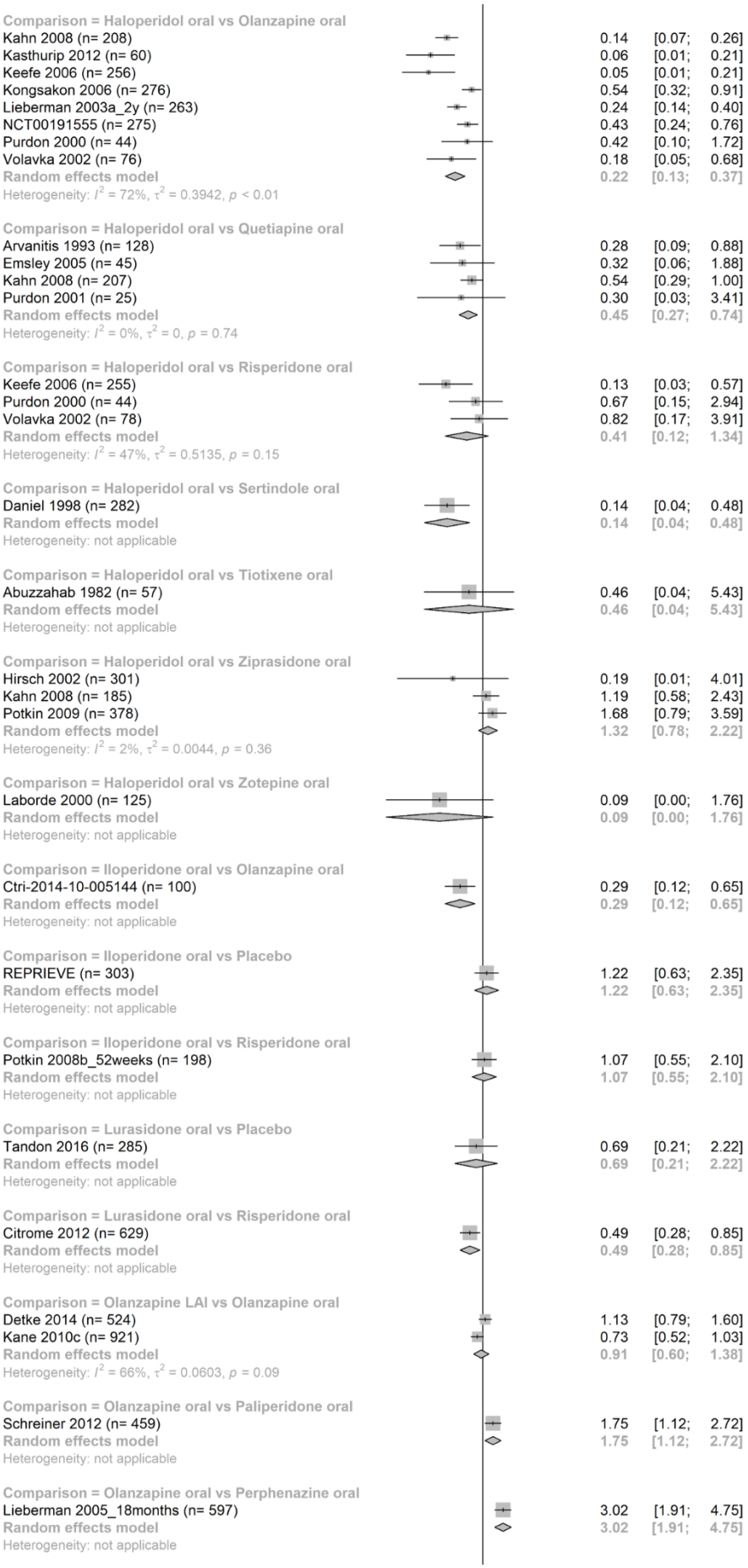
Order of treatments is according to SUCRA ranking. Results of the network meta-analysis are presented in the left lower half and results of pairwise meta-analyses in the right upper half. Each cell provides the effect estimate as odds ratio (OR) and the corresponding 95% credible interval (95% CrI) of a comparison (left lower half: treatment in column versus treatment in row; right upper half: treatment in row versus treatment in column). Bold print indicates 95% CrIs excluding the point of no effect.

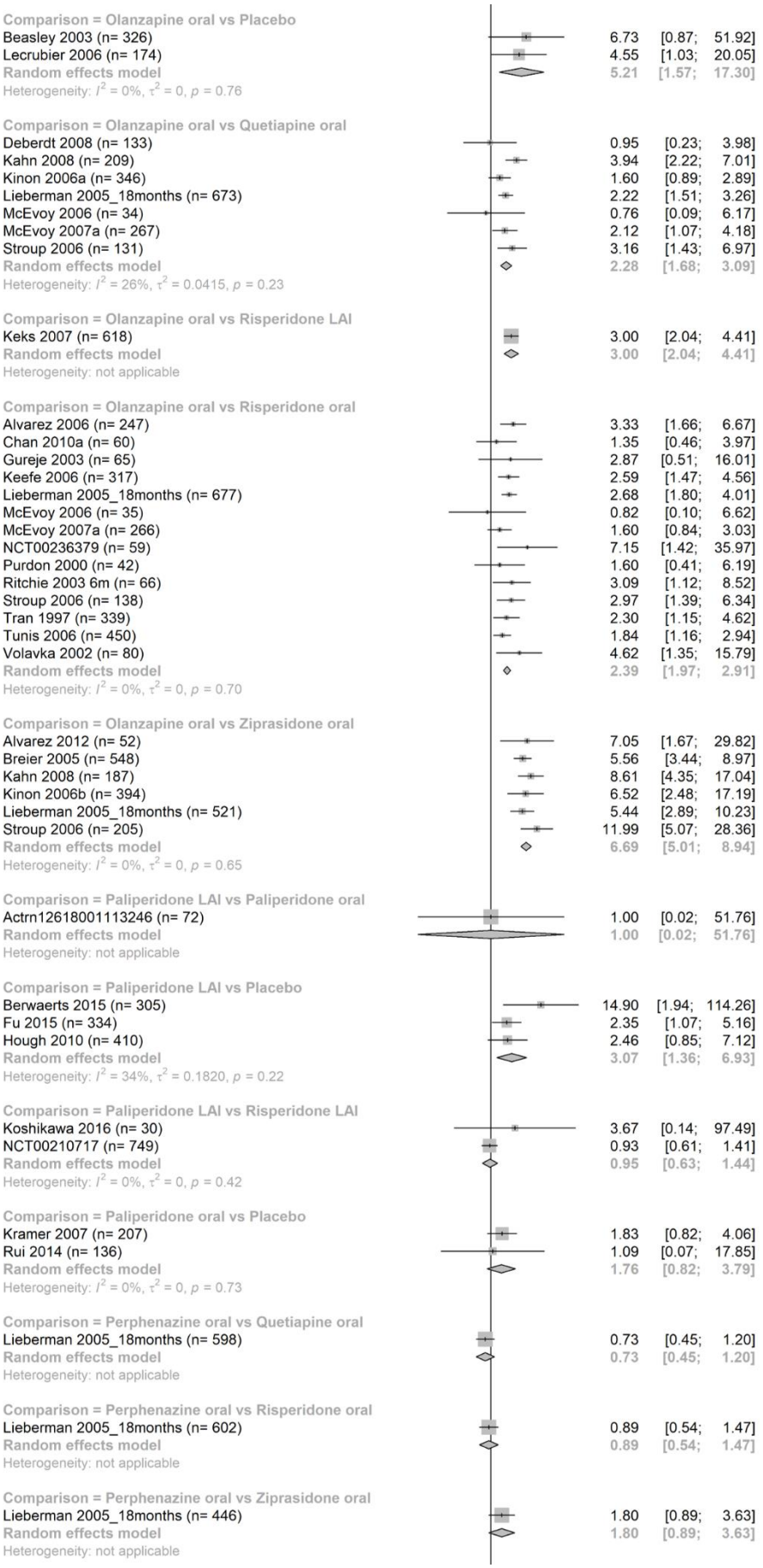
Abbreviations: NA=Not available, LAI=long-acting injectable, AMI=Amisulpride, ARI=Aripiprazole, ASE=Asenapine, BRE=Brexpiprazole, CAR=Cariprazine, CLO=Clozapine, CPZ=Chlorpromazine, FLP=Fluspirilene, FLU=Fluphenazine, FPX=Flupentixol, HAL=Haloperidol, ILO=Iloperidone, LUR=Lurasidone, OLA=Olanzapine, PAL=Paliperidone, PER=Perphenazine, PIM=Pimozide, PLB=Placebo, QUE=Quetiapine, RIS=Risperidone, SER=Sertindole, THIOR=Thioridazine, TIOT=Tiotixene, TRI=Trifluoperazine, ZIP=Ziprasidone, ZOT=Zotepine.

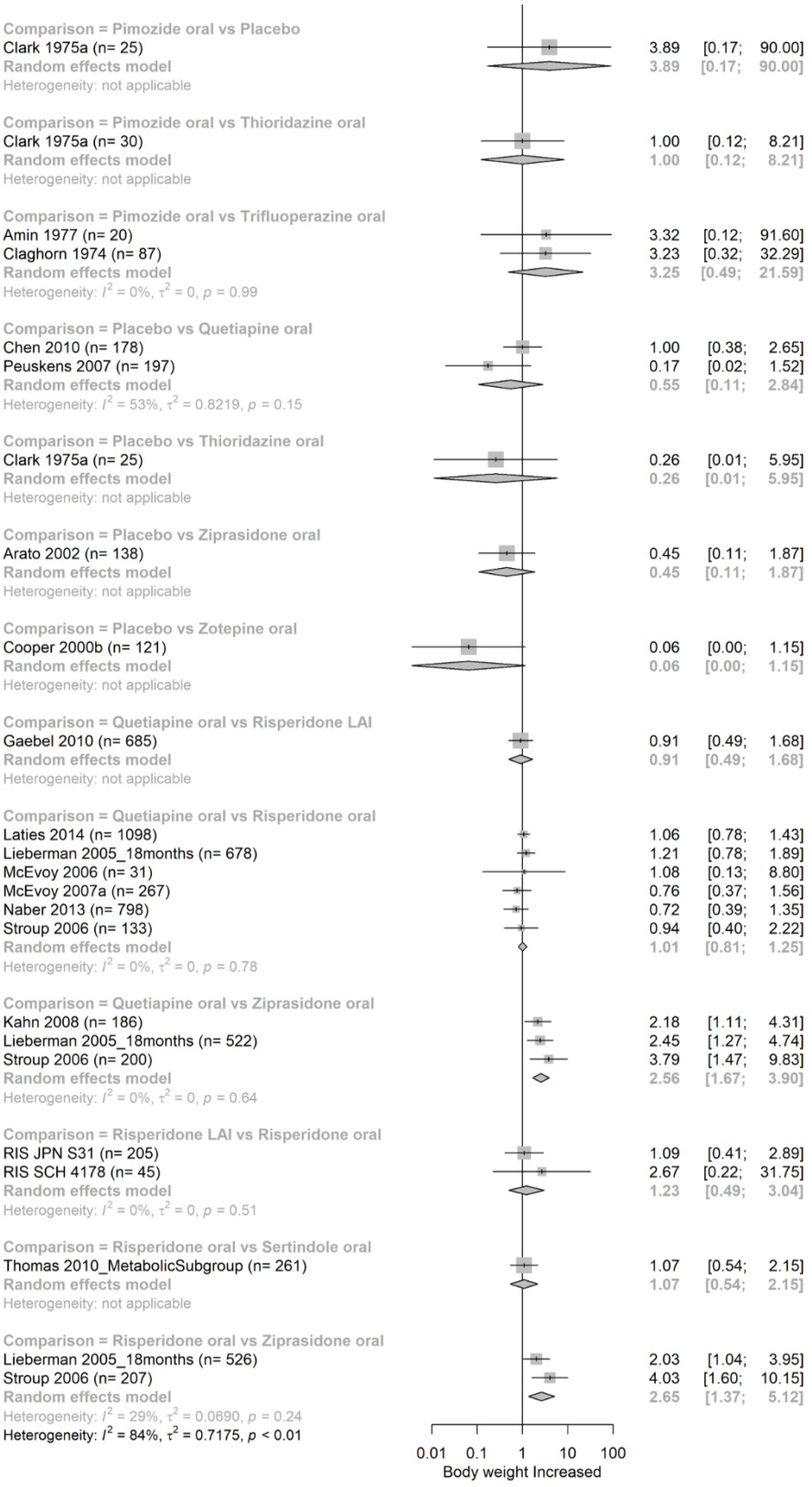
Forest-plot of results of pairwise meta-analyses (also indicating data of individual studies)




Comparison = Asenapine oral vs Olanzapine oral
Buchanan 2012a_26 weeks (n= 468) 0.38 [0.21; 0.67]
Buchanan 2012b_26 weeks (n= 481) 0.26 [0.15; 0.46]
Schoemaker 2010 (n= 1225) 0.31 [0.23; 0.41]
Random effects model 0.31 [0.24; 0.39]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.67
Comparison = Asenapine oral vs Placebo
Kane 2011 (n= 386) 7.15 [0.87; 58.68]
Random effects model 7.15 [0.87; 58.68]
Heterogeneity: not applicable
Comparison = Brexpiprazole oral vs Placebo
EQUATOR (n= 202) 5.65 [0.65; 49.27]
Random effects model 5.65 [0.65; 49.27]
Heterogeneity: not applicable
Comparison = Cariprazine oral vs Placebo
Durgam 2016b (n= 200) 0.76 [0.42; 1.41]
Random effects model 0.76 [0.42; 1.41]
Heterogeneity: not applicable
Comparison = Cariprazine oral vs Risperidone oral
Nct01625897_60w (n= 125) 0.47 [0.14; 1.55]
Nemeth 2017 (n= 461) 0.75 [0.36; 1.59]
Random effects model 0.66 [0.35; 1.24]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.51
Comparison = Chlorpromazine oral vs Placebo
Clark 1968b (n= 36) 8.50 [0.90; 80.03]
Random effects model 8.50 [0.90; 80.03]
Heterogeneity: not applicable
Comparison = Clozapine oral vs Haloperidol oral
Volavka 2002 (n= 77) 2.40 [0.57; 10.09]
Random effects model 2.40 [0.57; 10.09]
Heterogeneity: not applicable
Comparison = Clozapine oral vs Olanzapine oral
Bitter 2004 (n= 147) 1.05 [0.35; 3.15]
Naber 2005 (n= 114) 2.22 [1.04; 4.74]
Tollefson 2001 (n= 180) 1.00 [0.31; 3.23]
Volavka 2002 (n= 79) 0.42 [0.15; 1.22]
Random effects model 1.06 [0.51; 2.21]
Heterogeneity: I^2 = 53%, τ^2 = 0.2986, p = 0.09
Comparison = Clozapine oral vs Quetiapine oral
Ctri-2016-02-006660 (n= 53) 3.75 [0.98; 14.33]
Random effects model 3.75 [0.98; 14.33]
Heterogeneity: not applicable
Comparison = Clozapine oral vs Risperidone oral
Chowdhury 1999 (n= 60) 1.00 [0.36; 2.78]
Volavka 2002 (n= 81) 1.96 [0.53; 7.31]
Random effects model 1.29 [0.58; 2.89]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.43
Comparison = Clozapine oral vs Ziprasidone oral
Sacchetti 2009 (n= 147) 2.00 [0.18; 22.55]
Random effects model 2.00 [0.18; 22.55]
Heterogeneity: not applicable
Comparison = Fluphenazine LAI vs Fluphenazine oral
Del Giudice 1975 (n= 58) 3.57 [0.14; 91.24]
Random effects model 3.57 [0.14; 91.24]
Heterogeneity: not applicable
Comparison = Fluphenazine LAI vs Haloperidol LAI
Wistedt 1984 (n= 59) 2.85 [0.99; 8.21]
Random effects model 2.85 [0.99; 8.21]
Heterogeneity: not applicable
Comparison = Fluphenazine oral vs Olanzapine oral
Dossenbach 2004 (n= 60) 0.08 [0.00; 1.44]
Random effects model 0.08 [0.00; 1.44]
Heterogeneity: not applicable
Comparison = Haloperidol LAI vs Haloperidol oral
Ohkuma 1987 (n= 288) 0.46 [0.21; 0.98]
Random effects model 0.46 [0.21; 0.98]
Heterogeneity: not applicable
Comparison = Haloperidol LAI vs Paliperidone LAI
McEvoy 2014 (n= 311) 0.60 [0.36; 1.00]
Random effects model 0.60 [0.36; 1.00]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Iloperidone oral
Potkin 2008a_104 weeks (n= 179) 0.15 [0.03; 0.63]
Random effects model 0.15 [0.03; 0.63]
Heterogeneity: not applicable


Comparison = Haloperidol oral vs Olanzapine oral
Kahn 2008 (n= 208) 0.14 [0.07; 0.26]
Kasthurip 2012 (n= 60) 0.06 [0.01; 0.21]
Keefe 2006 (n= 256) 0.05 [0.01; 0.21]
Kongsakon 2006 (n= 276) 0.54 [0.32; 0.91]
Lieberman 2003a_2y (n= 263) 0.24 [0.14; 0.40]
NCT00191555 (n= 275) 0.43 [0.24; 0.76]
Purdon 2000 (n= 44) 0.42 [0.10; 1.72]
Volavka 2002 (n= 76) 0.18 [0.05; 0.68]
Random effects model 0.22 [0.13; 0.37]
Heterogeneity: I^2 = 72%, τ^2 = 0.3942, p < 0.01
Comparison = Haloperidol oral vs Quetiapine oral
Arvanitis 1993 (n= 128) 0.28 [0.09; 0.88]
Emsley 2005 (n= 45) 0.32 [0.06; 1.88]
Kahn 2008 (n= 207) 0.54 [0.29; 1.00]
Purdon 2001 (n= 25) 0.30 [0.03; 3.41]
Random effects model 0.45 [0.27; 0.74]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.74
Comparison = Haloperidol oral vs Risperidone oral
Keefe 2006 (n= 255) 0.13 [0.03; 0.57]
Purdon 2000 (n= 44) 0.67 [0.15; 2.94]
Volavka 2002 (n= 78) 0.82 [0.17; 3.91]
Random effects model 0.41 [0.12; 1.34]
Heterogeneity: I^2 = 47%, τ^2 = 0.5135, p = 0.15
Comparison = Haloperidol oral vs Sertindole oral
Daniel 1998 (n= 282) 0.14 [0.04; 0.48]
Random effects model 0.14 [0.04; 0.48]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Tiotixene oral
Abuzzahab 1982 (n= 57) 0.46 [0.04; 5.43]
Random effects model 0.46 [0.04; 5.43]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Ziprasidone oral
Hirsch 2002 (n= 301) 0.19 [0.01; 4.01]
Kahn 2008 (n= 185) 1.19 [0.58; 2.43]
Potkin 2009 (n= 378) 1.68 [0.79; 3.59]
Random effects model 1.32 [0.78; 2.22]
Heterogeneity: I^2 = 2%, τ^2 = 0.0044, p = 0.36
Comparison = Haloperidol oral vs Zotepine oral
Laborde 2000 (n= 125) 0.09 [0.00; 1.76]
Random effects model 0.09 [0.00; 1.76]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Olanzapine oral
Ctri-2014-10-005144 (n= 100) 0.29 [0.12; 0.65]
Random effects model 0.29 [0.12; 0.65]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Placebo
REPRIEVE (n= 303) 1.22 [0.63; 2.35]
Random effects model 1.22 [0.63; 2.35]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Risperidone oral
Potkin 2008b_52weeks (n= 198) 1.07 [0.55; 2.10]
Random effects model 1.07 [0.55; 2.10]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Placebo
Tandon 2016 (n= 285) 0.69 [0.21; 2.22]
Random effects model 0.69 [0.21; 2.22]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Risperidone oral
Citrome 2012 (n= 629) 0.49 [0.28; 0.85]
Random effects model 0.49 [0.28; 0.85]
Heterogeneity: not applicable
Comparison = Olanzapine LAI vs Olanzapine oral
Detke 2014 (n= 524) 1.13 [0.79; 1.60]
Kane 2010c (n= 921) 0.73 [0.52; 1.03]
Random effects model 0.91 [0.60; 1.38]
Heterogeneity: I^2 = 66%, τ^2 = 0.0603, p = 0.09
Comparison = Olanzapine oral vs Paliperidone oral
Schreiner 2012 (n= 459) 1.75 [1.12; 2.72]
Random effects model 1.75 [1.12; 2.72]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Perphenazine oral
Lieberman 2005_18months (n= 597) 3.02 [1.91; 4.75]
Random effects model 3.02 [1.91; 4.75]
Heterogeneity: not applicable


Comparison = Olanzapine oral vs Placebo
Beasley 2003 (n= 326) 6.73 [0.87; 51.92]
Lecrubier 2006 (n= 174) 4.55 [1.03; 20.05]
Random effects model 5.21 [1.57; 17.30]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.76
Comparison = Olanzapine oral vs Quetiapine oral
Deberdt 2008 (n= 133) 0.95 [0.23; 3.98]
Kahn 2008 (n= 209) 3.94 [2.22; 7.01]
Kinon 2006a (n= 346) 1.60 [0.89; 2.89]
Lieberman 2005_18months (n= 673) 2.22 [1.51; 3.26]
McEvoy 2006 (n= 34) 0.76 [0.09; 6.17]
McEvoy 2007a (n= 267) 2.12 [1.07; 4.18]
Stroup 2006 (n= 131) 3.16 [1.43; 6.97]
Random effects model 2.28 [1.68; 3.09]
Heterogeneity: I^2 = 26%, τ^2 = 0.0415, p = 0.23
Comparison = Olanzapine oral vs Risperidone LAI
Keks 2007 (n= 618) 3.00 [2.04; 4.41]
Random effects model 3.00 [2.04; 4.41]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Risperidone oral
Alvarez 2006 (n= 247) 3.33 [1.66; 6.67]
Chan 2010a (n= 60) 1.35 [0.46; 3.97]
Gureje 2003 (n= 65) 2.87 [0.51; 16.01]
Keefe 2006 (n= 317) 2.59 [1.47; 4.56]
Lieberman 2005_18months (n= 677) 2.68 [1.80; 4.01]
McEvoy 2006 (n= 35) 0.82 [0.10; 6.62]
McEvoy 2007a (n= 266) 1.60 [0.84; 3.03]
NCT00236379 (n= 59) 7.15 [1.42; 35.97]
Purdon 2000 (n= 42) 1.60 [0.41; 6.19]
Ritchie 2003 6m (n= 66) 3.09 [1.12; 8.52]
Stroup 2006 (n= 138) 2.97 [1.39; 6.34]
Tran 1997 (n= 339) 2.30 [1.15; 4.62]
Tunis 2006 (n= 450) 1.84 [1.16; 2.94]
Volavka 2002 (n= 80) 4.62 [1.35; 15.79]
Random effects model 2.39 [1.97; 2.91]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.70
Comparison = Olanzapine oral vs Ziprasidone oral
Alvarez 2012 (n= 52) 7.05 [1.67; 29.82]
Breier 2005 (n= 548) 5.56 [3.44; 8.97]
Kahn 2008 (n= 187) 8.61 [4.35; 17.04]
Kinon 2006b (n= 394) 6.52 [2.48; 17.19]
Lieberman 2005_18months (n= 521) 5.44 [2.89; 10.23]
Stroup 2006 (n= 205) 11.99 [5.07; 28.36]
Random effects model 6.69 [5.01; 8.94]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.65
Comparison = Paliperidone LAI vs Paliperidone oral
Actrn12618001113246 (n= 72) 1.00 [0.02; 51.76]
Random effects model 1.00 [0.02; 51.76]
Heterogeneity: not applicable
Comparison = Paliperidone LAI vs Placebo
Berwaerts 2015 (n= 305) 14.90 [1.94; 114.26]
Fu 2015 (n= 334) 2.35 [1.07; 5.16]
Hough 2010 (n= 410) 2.46 [0.85; 7.12]
Random effects model 3.07 [1.36; 6.93]
Heterogeneity: I^2 = 34%, τ^2 = 0.1820, p = 0.22
Comparison = Paliperidone LAI vs Risperidone LAI
Koshikawa 2016 (n= 30) 3.67 [0.14; 97.49]
NCT00210717 (n= 749) 0.93 [0.61; 1.41]
Random effects model 0.95 [0.63; 1.44]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.42
Comparison = Paliperidone oral vs Placebo
Kramer 2007 (n= 207) 1.83 [0.82; 4.06]
Rui 2014 (n= 136) 1.09 [0.07; 17.85]
Random effects model 1.76 [0.82; 3.79]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.73
Comparison = Perphenazine oral vs Quetiapine oral
Lieberman 2005_18months (n= 598) 0.73 [0.45; 1.20]
Random effects model 0.73 [0.45; 1.20]
Heterogeneity: not applicable
Comparison = Perphenazine oral vs Risperidone oral
Lieberman 2005_18months (n= 602) 0.89 [0.54; 1.47]
Random effects model 0.89 [0.54; 1.47]
Heterogeneity: not applicable
Comparison = Perphenazine oral vs Ziprasidone oral
Lieberman 2005_18months (n= 446) 1.80 [0.89; 3.63]
Random effects model 1.80 [0.89; 3.63]
Heterogeneity: not applicable



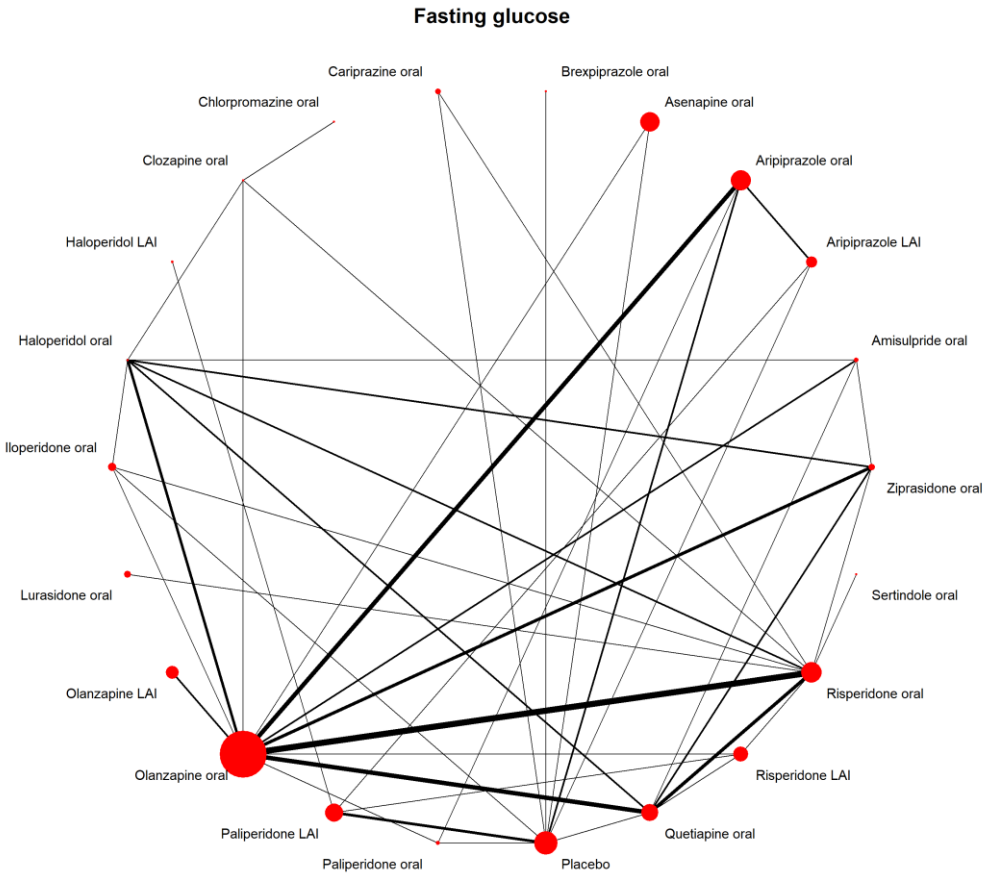
Pairwise meta-analyses are ordered by comparison investigated (in alphabetical order) and a summary effect size is calculated by pairwise meta-analyses of all studies of a specific comparison. The type of effect size measure is odds ratio (OR).

Abbreviations: OR=odds ratio, 95% CI=95% confidence interval, LAI=long-acting injectable.

7.3 Fasting glucose

50 studies on 21 antipsychotics with 17992 participants included reported on fasting glucose.

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Abbreviations: LAI=long-acting injectable

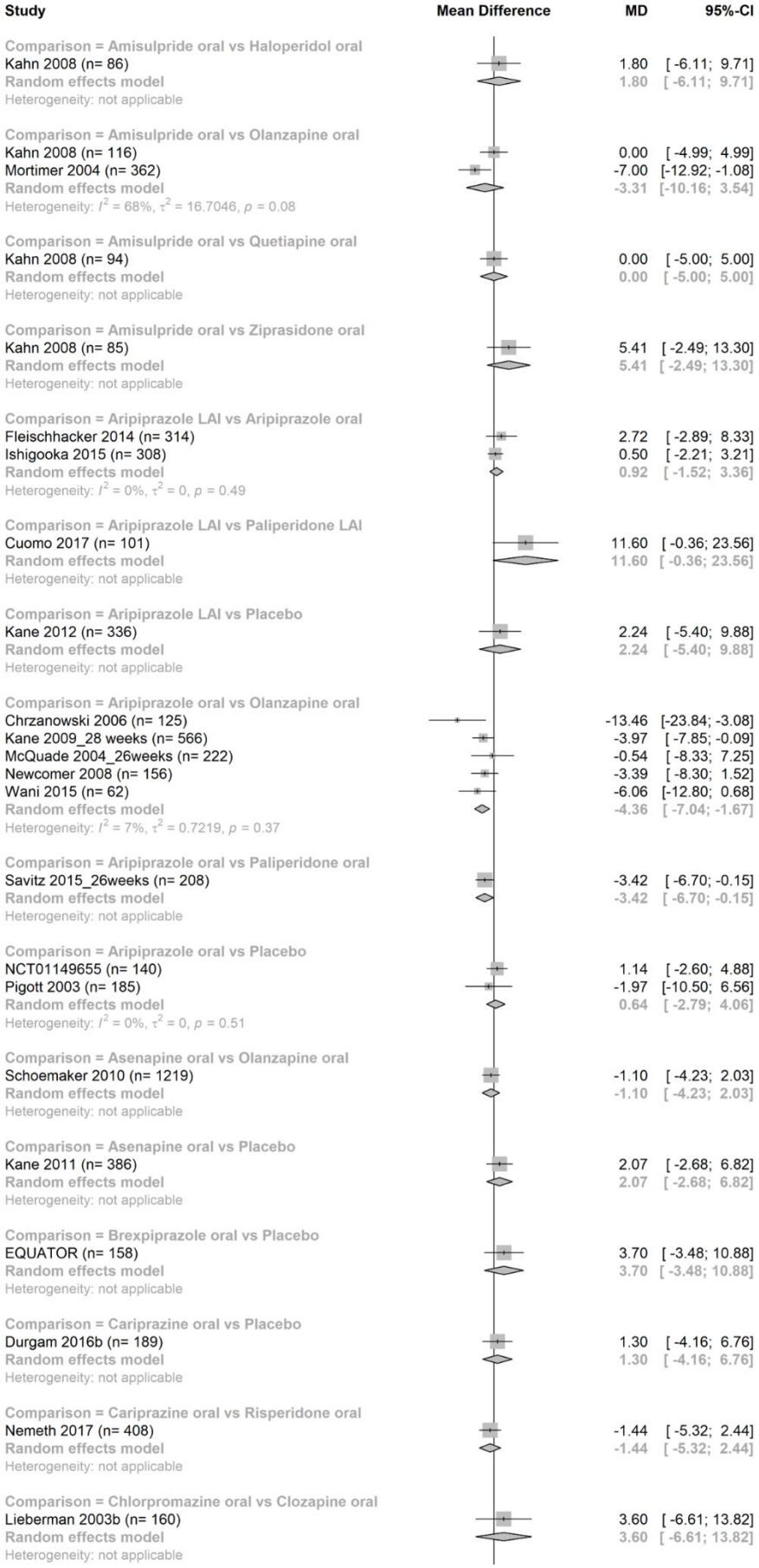
League-table

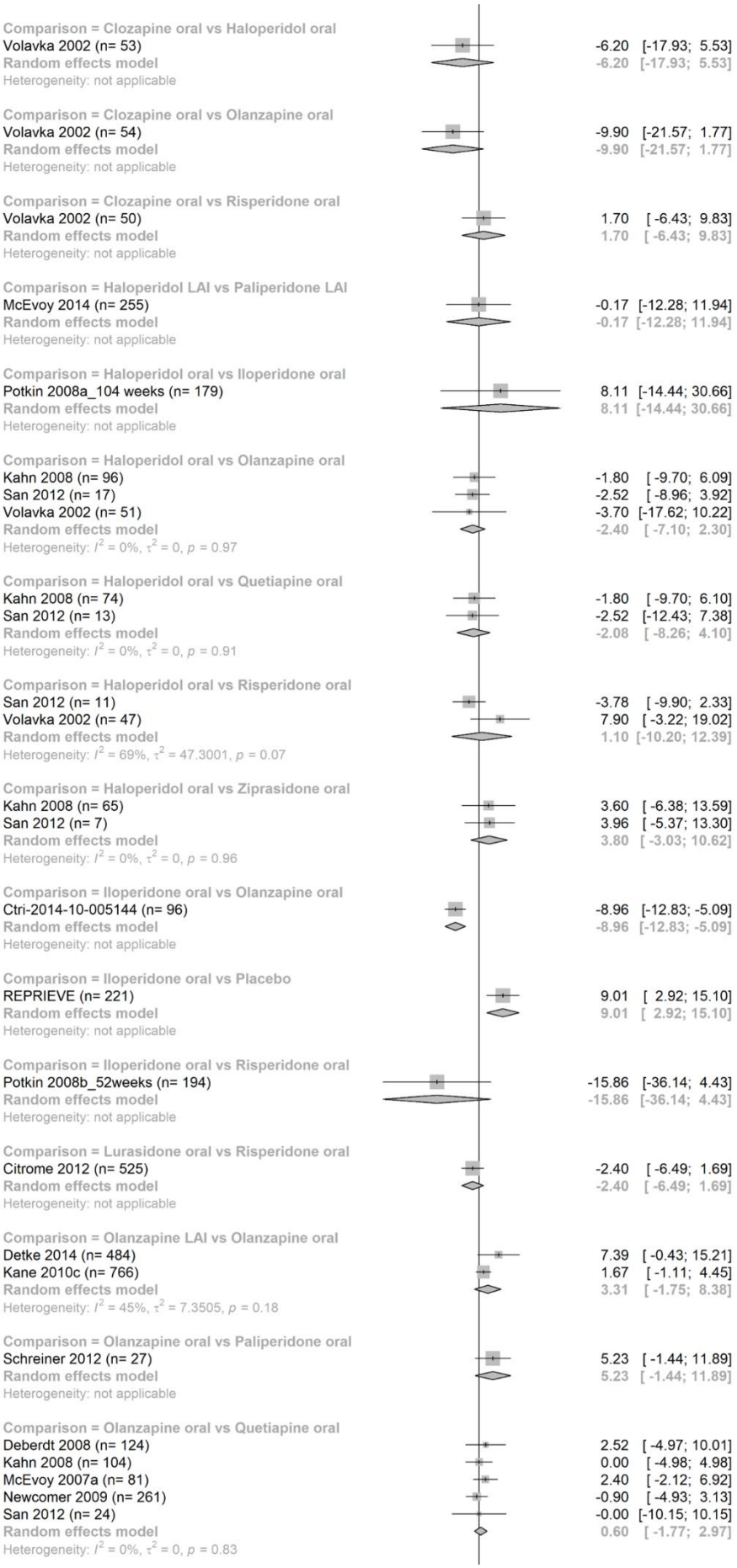
ZIP	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	-5.41 (-14.04 to 3.23)	NA	-3.79 (-11.05 to 3.46)	NA	-5.75 (-12.88 to 1.39)	NA	NA	-7.75 (-17.76 to 2.26)	NA	**-5.10 (-9.20 to -1.01)**	NA	NA
-0.67 (-5.40 to 4.24)	**PLB**	**-9.01 (-16.03 to -1.98)**	-0.41 (-4.88 to 4.07)	0.06 (-3.47 to 3.59)	NA	NA	NA	-1.30 (-7.78 to 5.18)	-0.36 (-5.96 to 5.24)	NA	-2.24 (-10.64 to 6.16)	NA	-3.70 (-11.69 to 4.29)	-2.70 (-9.35 to 3.95)	-2.07 (-7.97 to 3.83)	NA	NA	NA	NA	NA	NA
-0.47 (-6.33 to 5.11)	0.24 (-4.57 to 4.40)	**ILO**	NA	NA	NA	NA	NA	NA	NA	NA	NA	-8.11 (-30.93 to 14.71)	NA	NA	NA	NA	-15.86 (-36.44 to 4.73)	NA	**-8.96 (-14.18 to -3.74)**	NA	NA
-0.98 (-5.71 to 3.72)	-0.35 (-3.28 to 2.40)	-0.64 (-5.07 to 4.34)	**ARI**	NA	NA	NA	NA	NA	-3.42 (-8.22 to 1.37)	NA	-1.19 (-4.86 to 2.49)	NA	NA	NA	NA	NA	NA	NA	**-4.48 (-7.58 to -1.37)**	NA	NA
-1.49 (-6.73 to 4.07)	-0.83 (-4.00 to 2.49)	-1.02 (-5.87 to 4.55)	-0.47 (-4.14 to 3.62)	**PAL LAI**	NA	0.17 (-12.43 to 12.77)	NA	NA	NA	NA	-11.60 (-24.06 to 0.86)	NA	NA	NA	NA	0.36 (-4.49 to 5.21)	NA	NA	NA	NA	NA
-1.57 (-8.75 to 5.37)	-0.96 (-7.43 to 5.33)	-1.23 (-8.21 to 6.29)	-0.64 (-7.03 to 5.74)	-0.09 (-7.28 to 6.45)	**LUR**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	-2.40 (-7.79 to 2.99)	NA	NA	NA	NA
-1.49 (-14.73 to 11.91)	-0.84 (-13.36 to 11.92)	-0.99 (-13.88 to 12.53)	-0.50 (-13.00 to 12.46)	0.03 (-12.25 to 12.14)	0.01 (-13.48 to 14.27)	**HAL LAI**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-2.28 (-11.16 to 6.95)	-1.64 (-10.26 to 7.08)	-1.72 (-10.77 to 7.68)	-1.32 (-9.88 to 7.77)	-0.67 (-9.90 to 9.28)	-0.65 (-10.42 to 9.51)	-0.37 (-16.32 to 14.28)	**CLO**	NA	NA	NA	NA	-6.20 (-18.45 to 6.05)	NA	NA	NA	NA	1.70 (-7.15 to 10.55)	-3.60 (-14.41 to 7.20)	-9.90 (-22.08 to 2.28)	NA	NA
-2.45 (-8.29 to 3.65)	-1.76 (-6.42 to 2.82)	-2.06 (-7.69 to 4.31)	-1.42 (-6.24 to 3.53)	-0.89 (-6.48 to 4.23)	-0.77 (-7.60 to 6.25)	-0.97 (-14.57 to 12.15)	-0.00 (-10.43 to 8.90)	**CAR**	NA	NA	NA	NA	NA	NA	NA	NA	-1.44 (-6.67 to 3.79)	NA	NA	NA	NA
-2.54 (-8.04 to 3.06)	-1.85 (-5.64 to 1.89)	-2.17 (-7.33 to 3.59)	-1.53 (-5.07 to 2.11)	-1.05 (-5.94 to 3.54)	-0.89 (-7.80 to 6.17)	-1.01 (-14.36 to 11.69)	-0.29 (-9.50 to 8.74)	-0.10 (-5.71 to 5.54)	**PAL**	NA	NA	NA	NA	NA	NA	NA	NA	NA	-5.23 (-12.75 to 2.30)	NA	NA
-2.89 (-8.27 to 2.69)	-2.13 (-7.04 to 2.72)	-2.38 (-7.91 to 3.72)	-1.79 (-6.61 to 3.21)	-1.24 (-6.85 to 4.02)	-1.17 (-8.46 to 6.02)	-1.25 (-14.76 to 12.05)	-0.57 (-9.63 to 8.78)	-0.34 (-6.52 to 5.59)	-0.30 (-5.88 to 5.39)	**AMI**	NA	1.80 (-6.85 to 10.45)	NA	0.00 (-6.10 to 6.10)	NA	NA	NA	NA	-3.08 (-7.64 to 1.48)	NA	NA
-3.04 (-8.69 to 2.55)	-2.35 (-6.53 to 1.51)	-2.57 (-7.88 to 3.11)	-1.99 (-5.54 to 1.27)	-1.42 (-6.63 to 2.87)	-1.37 (-8.56 to 5.63)	-1.43 (-14.89 to 11.36)	-0.71 (-10.18 to 8.38)	-0.50 (-6.49 to 5.08)	-0.44 (-5.42 to 4.21)	-0.18 (-6.26 to 5.47)	**ARI LAI**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-3.44 (-9.05 to 2.16)	-2.72 (-7.96 to 2.32)	-3.02 (-8.80 to 3.18)	-2.44 (-7.63 to 2.70)	-1.84 (-8.03 to 3.48)	-1.81 (-8.93 to 5.29)	-1.87 (-15.74 to 11.53)	-1.05 (-10.15 to 7.68)	-0.95 (-7.21 to 4.86)	-0.89 (-6.83 to 4.97)	-0.57 (-6.59 to 5.01)	-0.37 (-6.29 to 5.62)	**HAL**	NA	-2.09 (-8.77 to 4.58)	NA	NA	-0.65 (-6.69 to 5.38)	NA	-2.42 (-7.62 to 2.79)	NA	NA
-4.16 (-13.58 to 4.95)	-3.62 (-11.71 to 4.37)	-3.74 (-12.79 to 5.36)	-3.23 (-11.75 to 5.09)	-2.90 (-11.65 to 5.61)	-2.53 (-12.74 to 7.30)	-2.81 (-18.08 to 11.66)	-2.21 (-13.73 to 9.51)	-1.80 (-11.13 to 7.23)	-1.66 (-10.75 to 7.01)	-1.54 (-10.82 to 7.86)	-1.28 (-10.15 to 7.62)	-0.79 (-10.30 to 8.54)	**BRE**	NA	NA	NA	NA	NA	NA	NA	NA
-3.82 (-8.29 to 0.67)	**-3.14 (-6.33 to -0.09)**	-3.37 (-7.85 to 1.51)	-2.80 (-6.13 to 0.48)	-2.24 (-6.61 to 1.38)	-2.21 (-8.32 to 3.96)	-2.22 (-15.21 to 10.31)	-1.44 (-10.45 to 6.83)	-1.34 (-6.18 to 3.35)	-1.28 (-5.63 to 3.01)	-1.05 (-5.57 to 3.52)	-0.75 (-5.12 to 3.71)	-0.44 (-5.00 to 4.39)	0.46 (-8.01 to 9.03)	**QUE**	NA	-3.06 (-8.85 to 2.72)	-0.27 (-3.40 to 2.86)	NA	-0.68 (-3.62 to 2.26)	NA	NA
-4.04 (-9.38 to 1.71)	-3.37 (-7.36 to 0.80)	-3.57 (-8.70 to 2.33)	-3.03 (-7.19 to 1.45)	-2.51 (-7.56 to 2.25)	-2.42 (-9.31 to 4.71)	-2.40 (-15.64 to 10.52)	-1.90 (-11.13 to 7.41)	-1.57 (-7.31 to 4.29)	-1.48 (-6.49 to 3.72)	-1.32 (-6.67 to 4.62)	-1.12 (-6.04 to 4.59)	-0.70 (-6.14 to 5.55)	0.28 (-8.41 to 9.28)	-0.27 (-4.41 to 4.35)	**ASE**	NA	NA	NA	-1.10 (-5.80 to 3.60)	NA	NA
-4.02 (-9.13 to 1.18)	-3.34 (-7.21 to 0.38)	-3.54 (-8.54 to 1.90)	-2.99 (-6.90 to 1.00)	-2.49 (-6.62 to 1.08)	-2.43 (-9.04 to 4.50)	-2.44 (-15.41 to 10.12)	-1.86 (-11.49 to 7.02)	-1.54 (-7.08 to 3.86)	-1.44 (-6.43 to 3.35)	-1.26 (-6.50 to 4.11)	-1.09 (-5.77 to 3.98)	-0.68 (-6.04 to 5.10)	0.30 (-8.49 to 9.14)	-0.22 (-3.71 to 3.39)	-0.02 (-5.06 to 4.86)	**RIS LAI**	12.28 (-8.98 to 33.54)	NA	-1.44 (-6.45 to 3.57)	NA	NA
-4.21 (-8.61 to 0.40)	**-3.51 (-6.80 to -0.21)**	-3.72 (-8.10 to 1.26)	-3.13 (-6.47 to 0.20)	-2.62 (-7.00 to 1.35)	-2.58 (-7.94 to 3.05)	-2.62 (-15.63 to 10.01)	-1.84 (-10.42 to 6.21)	-1.74 (-6.08 to 2.56)	-1.63 (-5.99 to 2.71)	-1.34 (-6.05 to 3.46)	-1.18 (-5.54 to 3.50)	-0.77 (-5.18 to 3.99)	0.09 (-8.32 to 8.68)	-0.37 (-3.00 to 2.38)	-0.08 (-4.77 to 4.25)	-0.13 (-4.08 to 3.75)	**RIS**	NA	-1.09 (-3.97 to 1.79)	-2.88 (-8.57 to 2.80)	NA
-5.61 (-19.40 to 7.65)	-4.94 (-18.90 to 7.93)	-5.25 (-18.88 to 8.41)	-4.67 (-18.20 to 8.43)	-4.09 (-18.36 to 8.78)	-4.03 (-18.48 to 10.01)	-4.04 (-23.51 to 14.04)	-3.47 (-14.14 to 7.08)	-3.28 (-17.24 to 10.36)	-3.12 (-17.26 to 10.30)	-2.70 (-16.95 to 10.45)	-2.69 (-16.44 to 10.84)	-2.23 (-15.79 to 11.04)	-1.48 (-17.14 to 13.81)	-1.82 (-15.35 to 11.08)	-1.48 (-15.72 to 11.64)	-1.53 (-15.51 to 11.51)	-1.44 (-14.88 to 11.38)	**CPZ**	NA	NA	NA
-5.75 (-9.76 to -1.63)	**-5.07 (-7.98 to -2.44)**	**-5.27 (-9.23 to -0.96)**	**-4.70 (-7.23 to -2.16)**	**-4.17 (-8.22 to -0.75)**	-4.14 (-10.13 to 1.95)	-4.20 (-17.11 to 8.30)	-3.45 (-11.99 to 4.65)	-3.29 (-7.98 to 1.33)	-3.19 (-7.10 to 0.59)	-2.97 (-7.17 to 1.29)	-2.71 (-6.60 to 1.35)	-2.34 (-6.66 to 2.30)	-1.48 (-9.77 to 6.93)	-1.91 (-4.37 to 0.48)	-1.65 (-5.76 to 1.94)	-1.70 (-5.20 to 1.61)	-1.57 (-4.17 to 0.90)	-0.12 (-13.02 to 13.26)	**OLA**	NA	-2.90 (-6.86 to 1.07)
-7.17 (-14.32 to 0.31)	-6.44 (-13.06 to 0.21)	-6.60 (-13.97 to 1.00)	-6.04 (-12.86 to 0.70)	-5.65 (-12.91 to 1.28)	-5.54 (-13.29 to 2.69)	-5.70 (-19.59 to 8.15)	-4.90 (-15.38 to 5.15)	-4.65 (-11.81 to 2.50)	-4.56 (-11.75 to 2.75)	-4.33 (-11.76 to 3.31)	-4.21 (-11.16 to 3.53)	-3.70 (-10.94 to 3.78)	-2.76 (-13.10 to 7.66)	-3.27 (-9.58 to 3.11)	-3.16 (-10.31 to 4.25)	-3.17 (-10.03 to 3.88)	-2.92 (-8.77 to 2.88)	-1.47 (-15.40 to 13.21)	-1.39 (-7.55 to 5.05)	**SER**	NA
-8.34 (-14.34 to -2.84)	**-7.64 (-13.20 to -3.17)**	**-7.91 (-14.08 to -2.39)**	**-7.35 (-12.58 to -2.85)**	**-6.88 (-13.19 to -1.80)**	-6.72 (-14.50 to 0.23)	-6.94 (-20.98 to 6.30)	-6.19 (-15.62 to 2.75)	**-5.95 (-12.68 to -0.05)**	**-5.87 (-11.92 to -0.48)**	**-5.57 (-11.97 to -0.11)**	-5.37 (-11.25 to 0.08)	-4.92 (-11.24 to 0.89)	-4.22 (-13.74 to 4.87)	**-4.53 (-9.70 to -0.21)**	-4.36 (-10.62 to 0.78)	-4.39 (-10.10 to 0.59)	-4.18 (-9.55 to 0.24)	-2.65 (-16.70 to 11.02)	-2.65 (-7.18 to 1.06)	-1.27 (-9.30 to 5.91)	**OLA LAI**

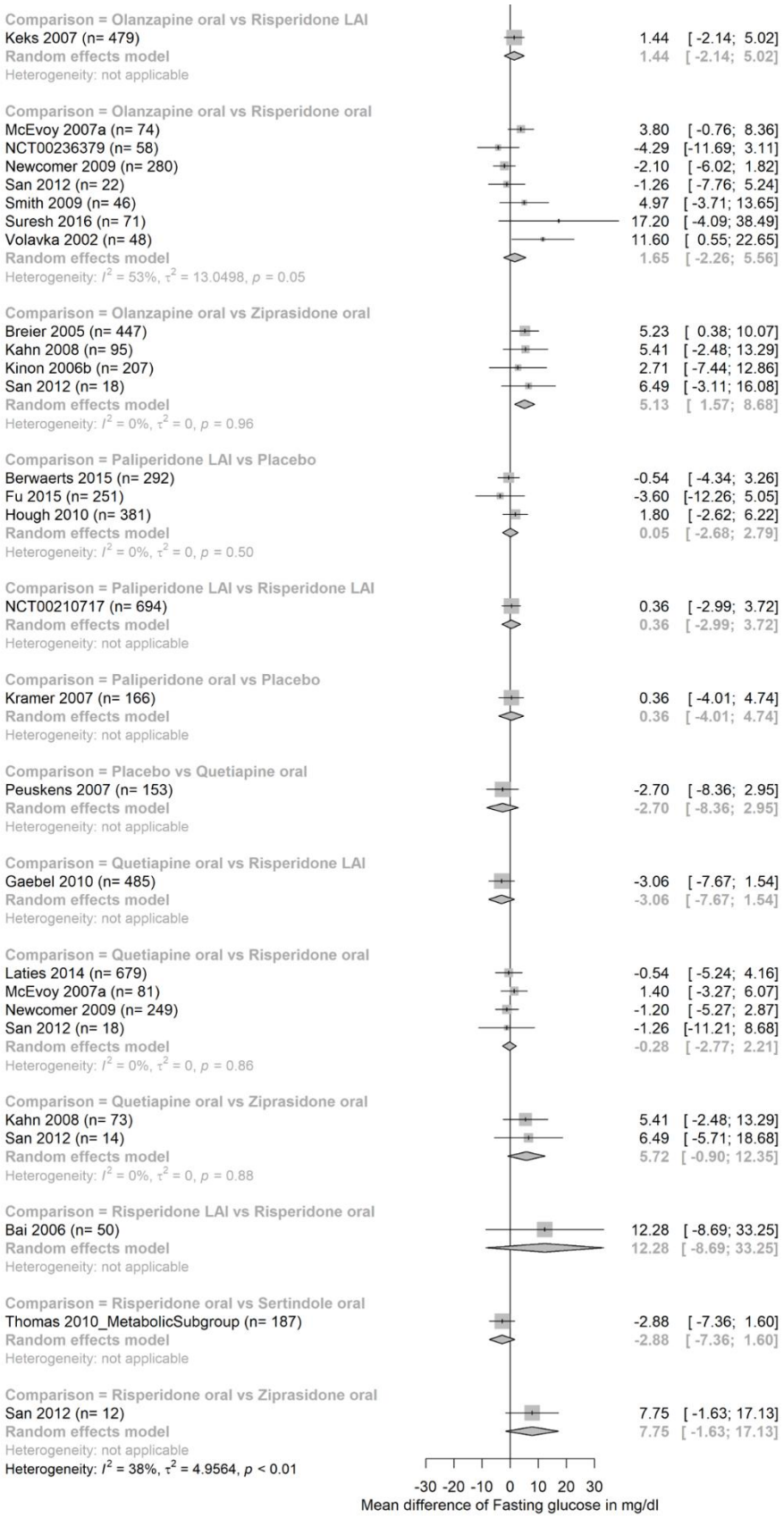
Order of treatments is according to SUCRA ranking. Results of the network meta-analysis are presented in the left lower half and results of pairwise meta-analyses in the right upper half. Each cell provides the effect estimate as mean difference (MD) and the corresponding 95% credible interval (95%CrI) of a comparison (left lower half: treatment in column versus treatment in row; right upper half: treatment in row versus treatment in column). Bold print indicates 95% CrI excluding the point of no effect.

Abbreviations: NA=Not available, LAI=long-acting injectable, AMI=Amisulpride, ARI=Aripiprazole, ASE=Asenapine, BRE=Brexpiprazole, CAR=Cariprazine, CLO=Clozapine, CPZ=Chlorpromazine, FLP=Fluspirilene, FLU=Fluphenazine, FPX=Flupentixol, HAL=Haloperidol, ILO=Iloperidone, LUR=Lurasidone, OLA=Olanzapine, PAL=Paliperidone, PER=Perphenazine, PIM=Pimozide, PLB=Placebo, QUE=Quetiapine, RIS=Risperidone, SER=Sertindole, THIOR=Thioridazine, TIOT=Tiotixene, TRI=Trifluoperazine, ZIP=Ziprasidone, ZOT=Zotepine.

Forest-plot of results of pairwise meta-analyses (also indicating data of individual studies)




Comparison = Clozapine oral vs Haloperidol oral
Volavka 2002 (n= 53) -6.20 [-17.93; 5.53]
Random effects model -6.20 [-17.93; 5.53]
Heterogeneity: not applicable
Comparison = Clozapine oral vs Olanzapine oral
Volavka 2002 (n= 54) -9.90 [-21.57; 1.77]
Random effects model -9.90 [-21.57; 1.77]
Heterogeneity: not applicable
Comparison = Clozapine oral vs Risperidone oral
Volavka 2002 (n= 50) 1.70 [-6.43; 9.83]
Random effects model 1.70 [-6.43; 9.83]
Heterogeneity: not applicable
Comparison = Haloperidol LAI vs Paliperidone LAI
McEvoy 2014 (n= 255) -0.17 [-12.28; 11.94]
Random effects model -0.17 [-12.28; 11.94]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Iloperidone oral
Potkin 2008a_104 weeks (n= 179) 8.11 [-14.44; 30.66]
Random effects model 8.11 [-14.44; 30.66]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Olanzapine oral
Kahn 2008 (n= 96) -1.80 [-9.70; 6.09]
San 2012 (n= 17) -2.52 [-8.96; 3.92]
Volavka 2002 (n= 51) -3.70 [-17.62; 10.22]
Random effects model -2.40 [-7.10; 2.30]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.97
Comparison = Haloperidol oral vs Quetiapine oral
Kahn 2008 (n= 74) -1.80 [-9.70; 6.10]
San 2012 (n= 13) -2.52 [-12.43; 7.38]
Random effects model -2.08 [-8.26; 4.10]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.91
Comparison = Haloperidol oral vs Risperidone oral
San 2012 (n= 11) -3.78 [-9.90; 2.33]
Volavka 2002 (n= 47) 7.90 [-3.22; 19.02]
Random effects model 1.10 [-10.20; 12.39]
Heterogeneity: I^2 = 69%, τ^2 = 47.3001, p = 0.07
Comparison = Haloperidol oral vs Ziprasidone oral
Kahn 2008 (n= 65) 3.60 [-6.38; 13.59]
San 2012 (n= 7) 3.96 [-5.37; 13.30]
Random effects model 3.80 [-3.03; 10.62]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.96
Comparison = Iloperidone oral vs Olanzapine oral
Ctri-2014-10-005144 (n= 96) -8.96 [-12.83; -5.09]
Random effects model -8.96 [-12.83; -5.09]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Placebo
REPRIEVE (n= 221) 9.01 [2.92; 15.10]
Random effects model 9.01 [2.92; 15.10]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Risperidone oral
Potkin 2008b_52weeks (n= 194) -15.86 [-36.14; 4.43]
Random effects model -15.86 [-36.14; 4.43]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Risperidone oral
Citrome 2012 (n= 525) -2.40 [-6.49; 1.69]
Random effects model -2.40 [-6.49; 1.69]
Heterogeneity: not applicable
Comparison = Olanzapine LAI vs Olanzapine oral
Detke 2014 (n= 484) 7.39 [-0.43; 15.21]
Kane 2010c (n= 766) 1.67 [-1.11; 4.45]
Random effects model 3.31 [-1.75; 8.38]
Heterogeneity: I^2 = 45%, τ^2 = 7.3505, p = 0.18
Comparison = Olanzapine oral vs Paliperidone oral
Schreiner 2012 (n= 27) 5.23 [-1.44; 11.89]
Random effects model 5.23 [-1.44; 11.89]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Quetiapine oral
Deberdt 2008 (n= 124) 2.52 [-4.97; 10.01]
Kahn 2008 (n= 104) 0.00 [-4.98; 4.98]
McEvoy 2007a (n= 81) 2.40 [-2.12; 6.92]
Newcomer 2009 (n= 261) -0.90 [-4.93; 3.13]
San 2012 (n= 24) -0.00 [-10.15; 10.15]
Random effects model 0.60 [-1.77; 2.97]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.83



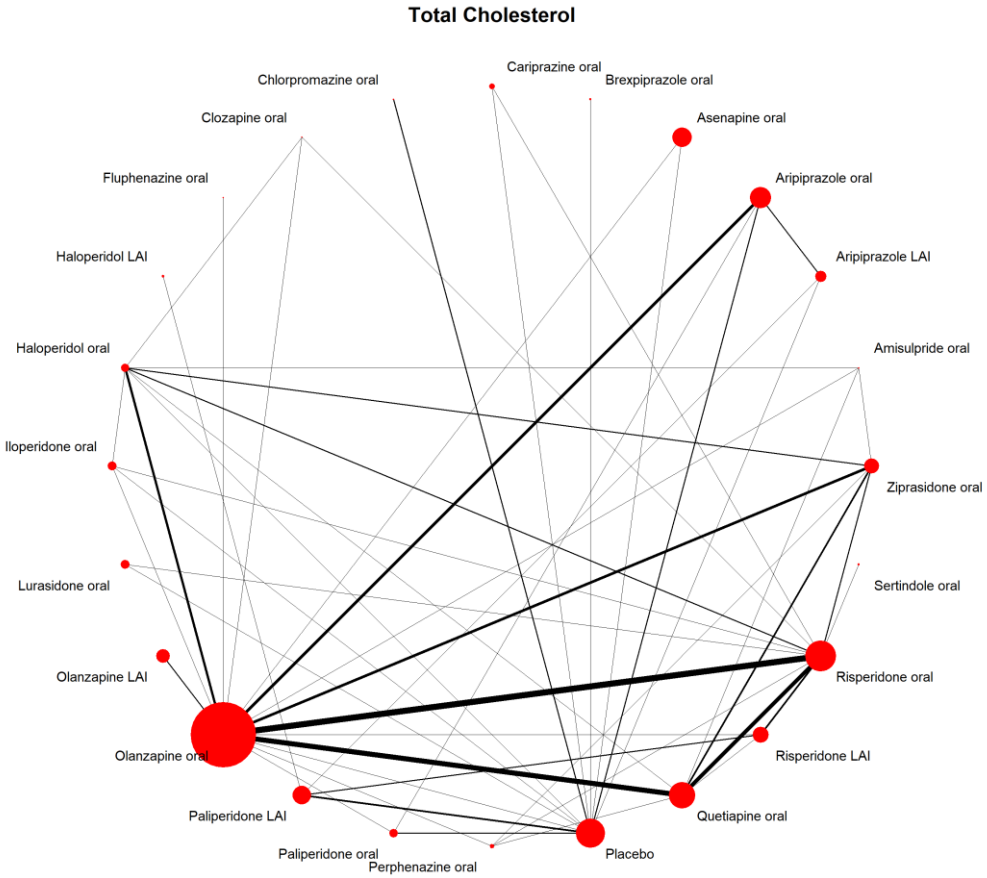
Pairwise meta-analyses are ordered by comparison investigated (in alphabetical order) and a summary effect size is calculated by pairwise meta-analyses of all studies of a specific comparison. The type of effect size measure is mean difference (MD).

Abbreviations: MD=mean difference, 95% CI=95% confidence interval, LAI=long-acting injectable.

7.4 Total cholesterol

63 studies on 23 antipsychotics with 18012 participants included reported on total cholesterol.

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Abbreviations: LAI=long-acting injectable.

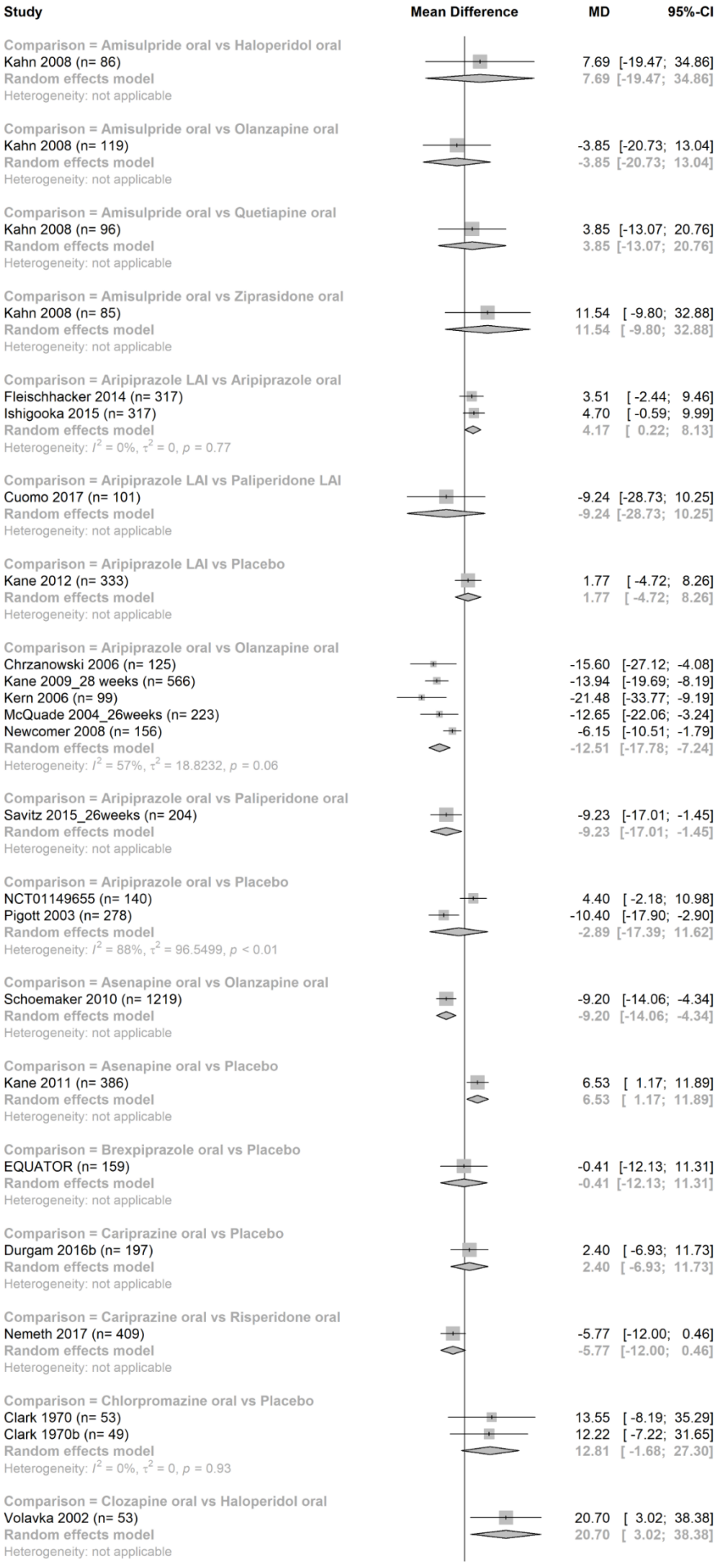
League-table

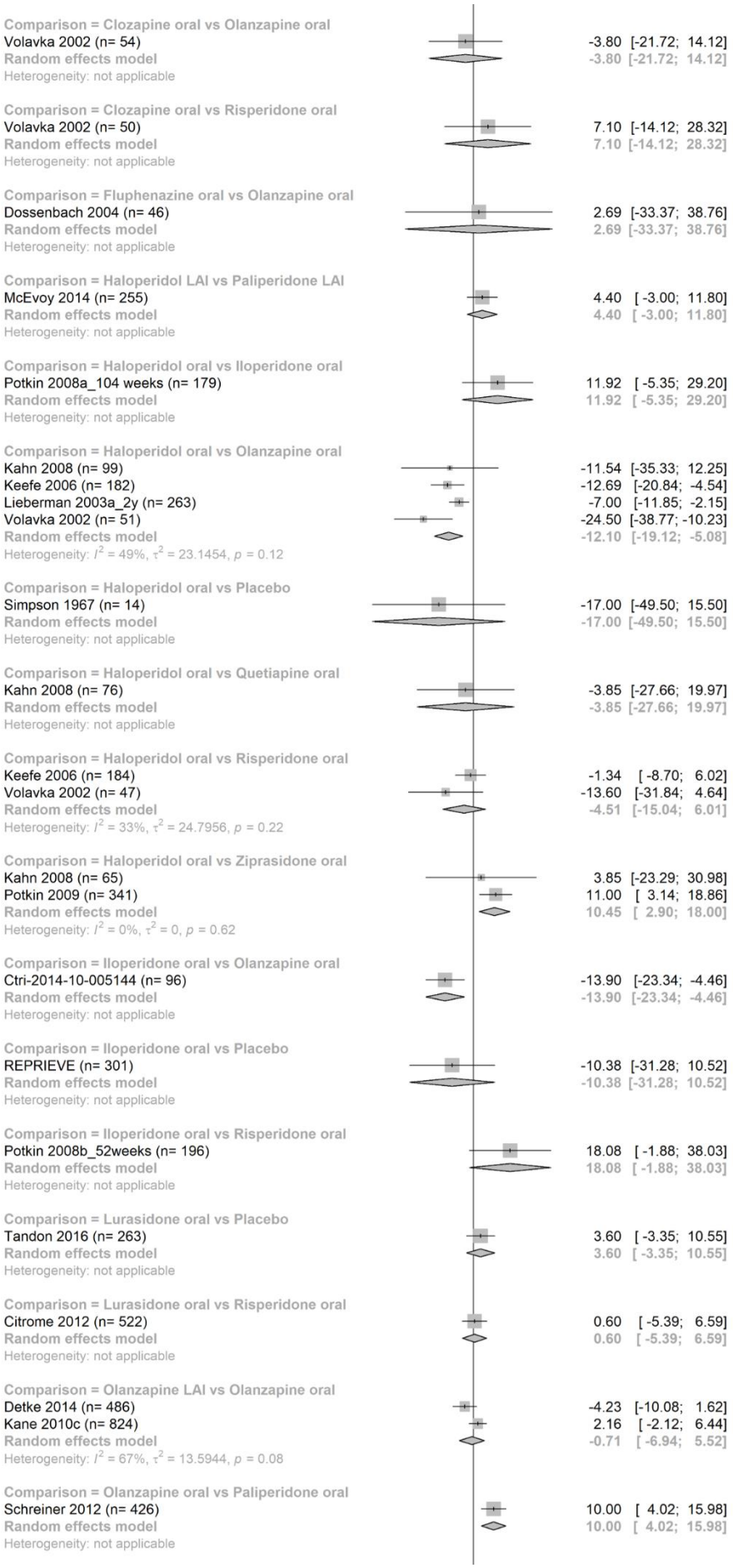
ZIP	NA	NA	NA	NA	NA	NA	**-10.15 (-19.78 to -0.51)**	NA	-8.56 (-17.36 to 0.25)	NA	-9.70 (-22.65 to 3.25)	NA	NA	NA	NA	NA	-11.54 (-33.87 to 10.80)	**-14.40 (-22.31 to -6.49)**	NA	NA	NA	NA	**-17.43 (-22.52 to -12.33)**
-3.93 (-9.65 to 2.02)	**ARI**	-2.49 (-9.30 to 4.33)	NA	NA	NA	-4.13 (-10.26 to 1.99)	NA	NA	NA	NA	NA	NA	NA	-9.23 (-19.43 to 0.97)	NA	NA	NA	NA	NA	NA	NA	NA	**-12.12 (-16.71 to -7.53)**
-4.69 (-10.39 to 1.23)	-0.75 (-4.90 to 3.21)	**PLB**	-2.40 (-13.83 to 9.03)	10.38 (-11.53 to 32.30)	0.41 (-13.04 to 13.86)	-1.77 (-11.03 to 7.49)	17.00 (-16.17 to 50.17)	-2.35 (-7.79 to 3.09)	NA	-3.60 (-13.19 to 5.99)	NA	-6.53 (-15.03 to 1.97)	NA	**-11.16 (-18.99 to -3.32)**	NA	NA	NA	NA	NA	-12.82 (-28.05 to 2.41)	NA	NA	**-15.00 (-24.67 to -5.33)**
-4.12 (-13.05 to 4.42)	-0.24 (-8.80 to 7.78)	0.55 (-7.52 to 8.18)	**CAR**	NA	NA	NA	NA	NA	-5.77 (-14.84 to 3.30)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-4.01 (-13.21 to 5.21)	-0.12 (-8.93 to 8.73)	0.59 (-8.02 to 9.37)	0.15 (-10.63 to 11.32)	**ILO**	NA	NA	-11.92 (-30.42 to 6.57)	NA	18.08 (-2.94 to 39.10)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	**-13.90 (-25.42 to -2.38)**
-4.34 (-19.40 to 10.58)	-0.42 (-15.07 to 13.84)	0.28 (-13.51 to 14.06)	-0.16 (-15.73 to 15.74)	-0.34 (-16.74 to 15.93)	**BRE**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-7.16 (-14.57 to 0.41)	-3.25 (-8.34 to 1.94)	-2.51 (-8.05 to 3.35)	-2.99 (-12.14 to 6.64)	-3.16 (-13.10 to 6.77)	-2.83 (-17.47 to 12.52)	**ARI LAI**	NA	-9.24 (-29.82 to 11.34)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-7.47 (-13.07 to -1.58)	-3.52 (-9.47 to 2.45)	-2.77 (-8.69 to 3.21)	-3.34 (-11.84 to 5.82)	-3.40 (-12.36 to 5.68)	-3.11 (-18.04 to 12.27)	-0.25 (-7.86 to 7.26)	**HAL**	NA	-3.87 (-12.67 to 4.94)	NA	NA	NA	NA	NA	NA	NA	-7.69 (-35.65 to 20.26)	-3.85 (-28.56 to 20.86)	NA	NA	NA	**-20.70 (-39.58 to -1.82)**	**-11.38 (-17.18 to -5.57)**
-8.02 (-15.07 to -1.19)	-4.06 (-10.19 to 1.38)	-3.31 (-8.13 to 1.18)	-3.84 (-12.59 to 5.02)	-3.96 (-13.92 to 5.30)	-3.71 (-18.10 to 10.59)	-0.83 (-8.10 to 5.85)	-0.57 (-7.88 to 6.15)	**PAL LAI**	NA	NA	NA	NA	-4.40 (-14.32 to 5.52)	NA	-3.15 (-10.93 to 4.64)	NA	NA	NA	NA	NA	NA	NA	NA	NA
-8.31 (-13.57 to -3.18)	-4.33 (-9.39 to 0.31)	-3.62 (-8.28 to 0.93)	-4.11 (-11.42 to 3.23)	-4.27 (-12.97 to 4.07)	-3.93 (-18.48 to 10.61)	-1.15 (-8.01 to 5.46)	-0.85 (-6.34 to 4.29)	-0.25 (-5.98 to 5.39)	**RIS**	-0.60 (-9.51 to 8.31)	-2.60 (-11.42 to 6.22)	NA	NA	NA	-4.00 (-10.42 to 2.43)	-5.38 (-20.05 to 9.28)	NA	**-6.02 (-10.61 to -1.42)**	NA	NA	NA	-7.10 (-29.32 to 15.12)	**-9.60 (-13.91 to -5.29)**
-8.58 (-16.82 to -0.18)	-4.58 (-12.59 to 2.81)	-3.88 (-11.07 to 3.11)	-4.38 (-13.92 to 5.53)	-4.49 (-15.34 to 5.99)	-4.11 (-19.72 to 11.41)	-1.33 (-10.33 to 7.18)	-1.12 (-9.59 to 7.11)	-0.52 (-8.51 to 7.72)	-0.28 (-7.03 to 6.75)	**LUR**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-9.17 (-17.60 to -0.76)	-5.23 (-13.67 to 2.97)	-4.46 (-12.73 to 3.72)	-5.02 (-15.22 to 5.49)	-5.14 (-16.11 to 5.80)	-4.82 (-21.15 to 11.52)	-2.01 (-11.59 to 7.39)	-1.67 (-10.49 to 6.90)	-1.12 (-10.19 to 8.07)	-0.86 (-8.41 to 6.88)	-0.57 (-10.54 to 9.43)	**PER**	NA	NA	NA	NA	NA	NA	-4.80 (-13.79 to 4.19)	NA	NA	NA	NA	**-9.20 (-18.19 to -0.21)**
-9.61 (-17.16 to -2.00)	-5.66 (-12.75 to 1.03)	-4.86 (-11.32 to 1.25)	-5.48 (-14.75 to 4.39)	-5.60 (-15.70 to 4.38)	-5.29 (-20.37 to 10.07)	-2.43 (-10.76 to 5.57)	-2.17 (-10.03 to 5.39)	-1.58 (-8.99 to 6.07)	-1.33 (-8.09 to 5.72)	-1.08 (-10.11 to 8.12)	-0.47 (-10.14 to 9.36)	**ASE**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	**-9.20 (-17.40 to -1.00)**
-12.40 (-24.63 to -0.43)	-8.43 (-20.26 to 2.72)	-7.68 (-18.90 to 3.09)	-8.18 (-21.46 to 5.06)	-8.27 (-22.75 to 5.22)	-8.08 (-25.49 to 9.17)	-5.21 (-17.63 to 6.63)	-4.95 (-17.48 to 7.02)	-4.36 (-14.44 to 5.49)	-4.10 (-15.59 to 7.29)	-3.86 (-16.75 to 8.92)	-3.26 (-16.92 to 10.15)	-2.79 (-15.52 to 9.58)	**HAL LAI**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-12.28 (-19.47 to -5.27)	**-8.36 (-14.32 to -2.83)**	**-7.58 (-13.17 to -2.21)**	-8.17 (-17.14 to 1.21)	-8.25 (-17.90 to 1.31)	-7.98 (-22.71 to 7.04)	-5.09 (-12.66 to 1.86)	-4.84 (-12.20 to 2.13)	-4.28 (-11.14 to 2.78)	-4.02 (-10.25 to 2.33)	-3.78 (-12.34 to 4.84)	-3.18 (-12.49 to 6.15)	-2.69 (-10.65 to 5.11)	0.07 (-12.01 to 12.32)	**PAL**	NA	NA	NA	NA	NA	NA	NA	NA	**-10.00 (-18.90 to -1.10)**
-12.29 (-18.39 to -5.94)	**-8.35 (-13.99 to -2.94)**	**-7.58 (-12.90 to -2.33)**	-8.12 (-16.23 to 0.53)	-8.22 (-17.46 to 0.77)	-7.88 (-22.58 to 7.05)	-5.10 (-12.27 to 1.84)	-4.84 (-11.25 to 1.51)	-4.26 (-9.74 to 1.54)	-4.03 (-8.30 to 0.76)	-3.71 (-11.54 to 4.25)	-3.12 (-11.55 to 5.44)	-2.67 (-10.11 to 4.89)	0.11 (-11.07 to 11.71)	-0.01 (-6.83 to 7.04)	**RIS LAI**	NA	NA	1.54 (-8.32 to 11.40)	NA	NA	NA	-5.96 (-14.79 to 2.87)
-13.73 (-29.26 to 1.31)	-9.77 (-25.26 to 5.03)	-9.07 (-24.54 to 6.01)	-9.64 (-25.82 to 6.59)	-9.68 (-26.64 to 6.51)	-9.36 (-30.00 to 10.36)	-6.51 (-22.88 to 9.08)	-6.26 (-22.11 to 8.73)	-5.76 (-21.47 to 9.63)	-5.41 (-20.15 to 8.75)	-5.22 (-21.18 to 10.51)	-4.62 (-21.22 to 11.61)	-4.13 (-20.22 to 11.54)	-1.38 (-20.07 to 17.04)	-1.43 (-17.43 to 14.04)	-1.48 (-16.92 to 13.45)	**SER**	NA	NA	NA	NA	NA	NA
-14.62 (-31.23 to 2.73)	-10.53 (-27.57 to 6.29)	-9.77 (-26.68 to 6.96)	-10.35 (-28.19 to 8.41)	-10.41 (-28.82 to 7.96)	-10.07 (-32.28 to 12.21)	-7.21 (-24.87 to 10.02)	-7.09 (-24.03 to 9.95)	-6.42 (-23.74 to 11.13)	-6.23 (-22.76 to 10.82)	-5.87 (-23.63 to 12.18)	-5.34 (-23.24 to 13.01)	-4.88 (-22.51 to 12.87)	-1.92 (-22.17 to 17.95)	-2.11 (-19.56 to 15.32)	-2.26 (-19.32 to 15.12)	-0.52 (-22.85 to 21.54)	**AMI**	3.85 (-14.31 to 22.00)	NA	NA	NA	NA	-3.85 (-21.97 to 14.28)
-12.89 (-18.26 to -7.61)	**-8.93 (-14.33 to -3.94)**	**-8.20 (-13.30 to -3.33)**	**-8.71 (-16.68 to -0.60)**	**-8.86 (-17.64 to -0.23)**	-8.54 (-23.40 to 6.22)	-5.69 (-12.86 to 1.02)	-5.42 (-11.27 to 0.08)	-4.87 (-10.97 to 1.36)	**-4.59 (-8.25 to -0.76)**	-4.31 (-12.01 to 3.08)	-3.75 (-11.38 to 3.93)	-3.21 (-10.46 to 3.66)	-0.51 (-12.18 to 11.53)	-0.55 (-7.12 to 5.92)	-0.58 (-5.76 to 4.32)	0.87 (-13.83 to 15.99)	1.61 (-15.16 to 17.95)	**QUE**	NA	NA	NA	**-4.96 (-9.16 to -0.77)**
-20.04 (-55.87 to 15.38)	-16.15 (-52.09 to 18.48)	-15.45 (-51.29 to 19.43)	-15.94 (-52.52 to 19.47)	-16.19 (-53.40 to 19.70)	-16.26 (-53.97 to 22.20)	-12.99 (-49.14 to 21.82)	-12.59 (-48.66 to 22.42)	-12.15 (-48.13 to 23.29)	-11.70 (-47.28 to 22.92)	-11.61 (-47.99 to 24.00)	-11.06 (-46.93 to 24.65)	-10.59 (-46.56 to 24.41)	-8.04 (-45.13 to 29.25)	-7.78 (-43.94 to 27.10)	-7.73 (-43.78 to 26.85)	-6.46 (-45.66 to 32.08)	-5.86 (-45.15 to 31.82)	-7.20 (-42.79 to 27.89)	**FLU**	NA	NA	NA	2.69 (-33.97 to 39.36)
-17.51 (-34.57 to -1.61)	-13.73 (-30.27 to 2.03)	-13.00 (-29.08 to 2.21)	-13.39 (-31.32 to 3.75)	-13.67 (-31.90 to 3.88)	-13.46 (-33.89 to 6.75)	-10.60 (-27.62 to 5.50)	-10.19 (-27.12 to 6.18)	-9.68 (-26.14 to 6.28)	-9.27 (-25.88 to 6.52)	-9.14 (-26.54 to 7.58)	-8.39 (-26.63 to 8.73)	-8.07 (-25.24 to 8.26)	-5.35 (-24.42 to 13.65)	-5.36 (-22.31 to 10.83)	-5.34 (-22.16 to 10.50)	-3.98 (-25.83 to 18.20)	-3.28 (-26.86 to 19.77)	-4.69 (-21.52 to 11.27)	2.69 (-35.87 to 42.42)	**CPZ**	NA	NA	NA
-16.72 (-23.99 to -9.25)	**-12.74 (-19.88 to -5.91)**	**-12.02 (-19.01 to -5.07)**	**-12.53 (-22.18 to -2.48)**	**-12.66 (-22.64 to -2.68)**	-12.32 (-27.82 to 3.12)	**-9.48 (-17.97 to -1.31)**	**-9.28 (-16.80 to -1.79)**	**-8.70 (-16.53 to -0.58)**	**-8.40 (-15.08 to -1.57)**	-8.16 (-17.46 to 1.03)	-7.55 (-17.11 to 2.10)	-7.11 (-15.52 to 1.57)	-4.26 (-16.96 to 8.44)	-4.44 (-12.37 to 3.81)	-4.42 (-11.88 to 3.02)	-3.02 (-18.61 to 13.19)	-2.19 (-20.02 to 15.34)	-3.83 (-10.65 to 3.18)	3.32 (-31.73 to 39.46)	0.95 (-15.67 to 18.30)	**OLA LAI**	NA	-0.67 (-6.54 to 5.20)
-20.39 (-37.45 to -2.05)	-16.58 (-33.39 to 1.70)	-15.83 (-32.73 to 2.44)	-16.35 (-34.28 to 3.27)	-16.35 (-34.82 to 2.86)	-15.99 (-38.53 to 6.96)	-13.29 (-30.92 to 5.55)	-13.15 (-29.43 to 4.95)	-12.59 (-29.57 to 6.13)	-12.28 (-28.63 to 5.82)	-11.99 (-29.55 to 7.18)	-11.29 (-29.24 to 7.94)	-10.92 (-28.26 to 7.92)	-8.03 (-28.11 to 13.51)	-8.23 (-25.48 to 10.58)	-8.32 (-25.03 to 10.35)	-6.57 (-28.76 to 16.19)	-6.39 (-28.18 to 19.09)	-7.68 (-24.18 to 10.67)	1.11 (-39.88 to 39.08)	-2.63 (-25.72 to 22.10)	-3.84 (-21.35 to 15.17)	**CLO**	-3.80 (-22.90 to 15.30)
-17.33 (-21.86 to -12.83)	**-13.38 (-17.30 to -9.65)**	**-12.65 (-16.51 to -8.73)**	**-13.18 (-20.73 to -5.32)**	**-13.28 (-21.48 to -5.28)**	-12.97 (-27.30 to 1.50)	**-10.18 (-16.24 to -4.27)**	**-9.88 (-14.75 to -5.21)**	**-9.30 (-14.57 to -3.83)**	**-9.04 (-12.24 to -5.61)**	**-8.74 (-15.97 to -1.68)**	**-8.20 (-15.66 to -0.70)**	**-7.71 (-13.92 to -1.54)**	-4.94 (-16.14 to 6.52)	-5.02 (-10.55 to 0.56)	**-5.04 (-9.69 to -0.52)**	-3.59 (-18.18 to 11.47)	-2.77 (-19.51 to 13.51)	**-4.45 (-7.94 to -0.83)**	2.71 (-32.00 to 38.42)	0.22 (-15.22 to 16.63)	-0.61 (-6.55 to 5.16)	3.25 (-14.86 to 19.52)	**OLA**

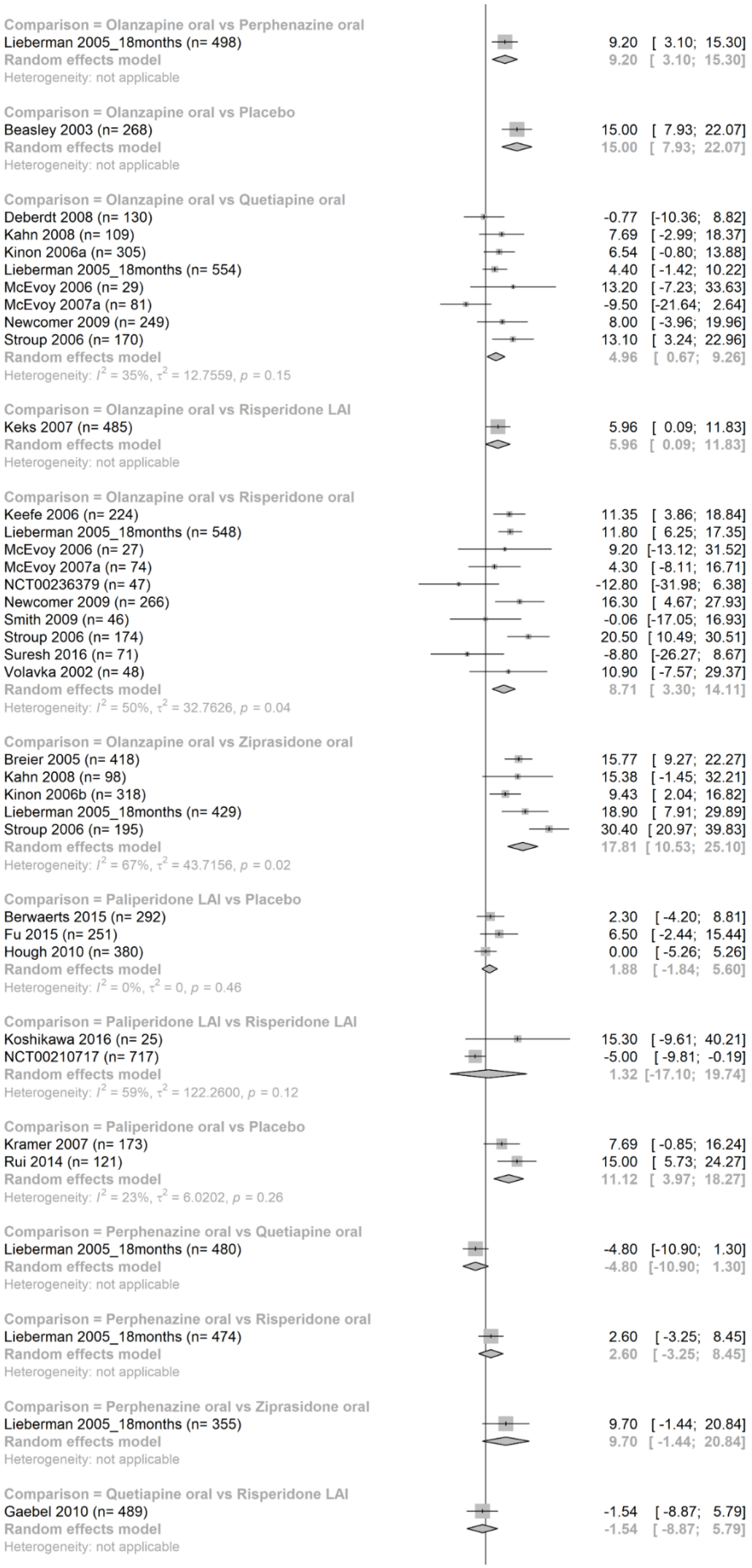
Order of treatments is according to SUCRA ranking. Results of the network meta-analysis are presented in the left lower half and results of pairwise meta-analyses in the right upper half. Each cell provides the effect estimate as mean difference (MD)and the corresponding 95% credible interval (95%CrI) of a comparison (left lower half: treatment in column versus treatment in row; right upper half: treatment in row versus treatment in column). Bold print indicates 95% CrI excluding the point of no effect.

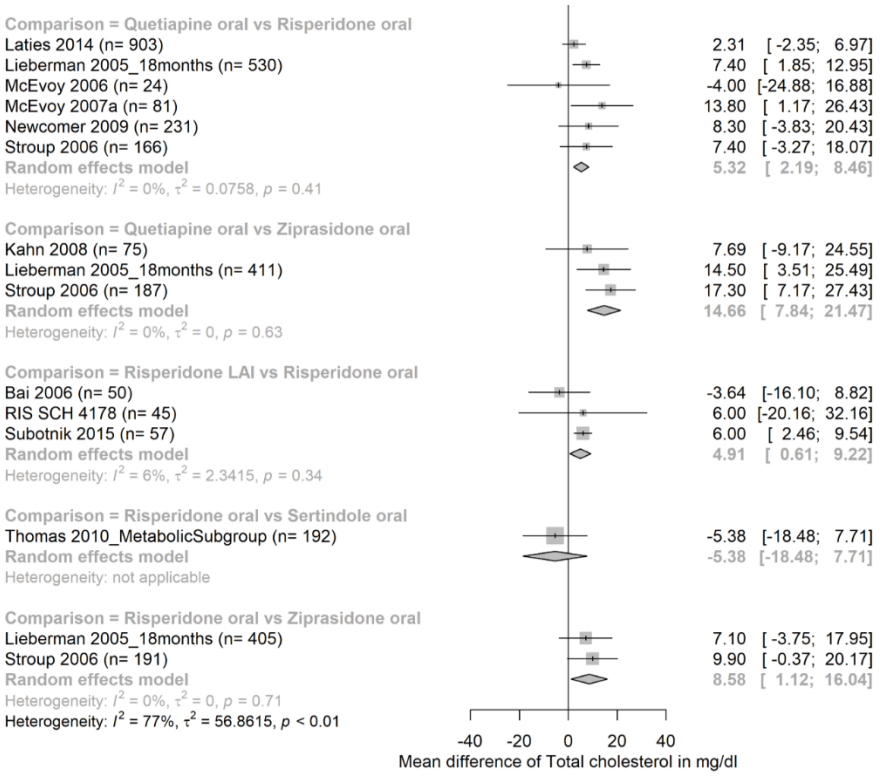
Abbreviations: NA=Not available, LAI=long-acting injectable, AMI=Amisulpride, ARI=Aripiprazole, ASE=Asenapine, BRE=Brexpiprazole, CAR=Cariprazine, CLO=Clozapine, CPZ=Chlorpromazine, FLP=Fluspirilene, FLU=Fluphenazine, FPX=Flupentixol, HAL=Haloperidol, ILO=Iloperidone, LUR=Lurasidone, OLA=Olanzapine, PAL=Paliperidone, PER=Perphenazine, PIM=Pimozide, PLB=Placebo, QUE=Quetiapine, RIS=Risperidone, SER=Sertindole, THIOR=Thioridazine, TIOT=Tiotixene, TRI=Trifluoperazine, ZIP=Ziprasidone, ZOT=Zotepine.

Forest-plot of results of pairwise meta-analyses (also indicating data of individual studies)




Comparison = Clozapine oral vs Olanzapine oral
Volavka 2002 (n= 54) -3.80 [-21.72; 14.12]
Random effects model -3.80 [-21.72; 14.12]
Heterogeneity: not applicable
Comparison = Clozapine oral vs Risperidone oral
Volavka 2002 (n= 50) 7.10 [-14.12; 28.32]
Random effects model 7.10 [-14.12; 28.32]
Heterogeneity: not applicable
Comparison = Fluphenazine oral vs Olanzapine oral
Dossenbach 2004 (n= 46) 2.69 [-33.37; 38.76]
Random effects model 2.69 [-33.37; 38.76]
Heterogeneity: not applicable
Comparison = Haloperidol LAI vs Paliperidone LAI
McEvoy 2014 (n= 255) 4.40 [-3.00; 11.80]
Random effects model 4.40 [-3.00; 11.80]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Iloperidone oral
Potkin 2008a_104 weeks (n= 179) 11.92 [-5.35; 29.20]
Random effects model 11.92 [-5.35; 29.20]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Olanzapine oral
Kahn 2008 (n= 99) -11.54 [-35.33; 12.25]
Keefe 2006 (n= 182) -12.69 [-20.84; -4.54]
Lieberman 2003a_2y (n= 263) -7.00 [-11.85; -2.15]
Volavka 2002 (n= 51) -24.50 [-38.77; -10.23]
Random effects model -12.10 [-19.12; -5.08]
Heterogeneity: I^2 = 49%, τ^2 = 23.1454, p = 0.12
Comparison = Haloperidol oral vs Placebo
Simpson 1967 (n= 14) -17.00 [-49.50; 15.50]
Random effects model -17.00 [-49.50; 15.50]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Quetiapine oral
Kahn 2008 (n= 76) -3.85 [-27.66; 19.97]
Random effects model -3.85 [-27.66; 19.97]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Risperidone oral
Keefe 2006 (n= 184) -1.34 [-8.70; 6.02]
Volavka 2002 (n= 47) -13.60 [-31.84; 4.64]
Random effects model -4.51 [-15.04; 6.01]
Heterogeneity: I^2 = 33%, τ^2 = 24.7956, p = 0.22
Comparison = Haloperidol oral vs Ziprasidone oral
Kahn 2008 (n= 65) 3.85 [-23.29; 30.98]
Potkin 2009 (n= 341) 11.00 [3.14; 18.86]
Random effects model 10.45 [2.90; 18.00]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.62
Comparison = Iloperidone oral vs Olanzapine oral
Ctri-2014-10-005144 (n= 96) -13.90 [-23.34; -4.46]
Random effects model -13.90 [-23.34; -4.46]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Placebo
REPRIEVE (n= 301) -10.38 [-31.28; 10.52]
Random effects model -10.38 [-31.28; 10.52]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Risperidone oral
Potkin 2008b_52weeks (n= 196) 18.08 [-1.88; 38.03]
Random effects model 18.08 [-1.88; 38.03]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Placebo
Tandon 2016 (n= 263) 3.60 [-3.35; 10.55]
Random effects model 3.60 [-3.35; 10.55]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Risperidone oral
Citrome 2012 (n= 522) 0.60 [-5.39; 6.59]
Random effects model 0.60 [-5.39; 6.59]
Heterogeneity: not applicable
Comparison = Olanzapine LAI vs Olanzapine oral
Detke 2014 (n= 486) -4.23 [-10.08; 1.62]
Kane 2010c (n= 824) 2.16 [-2.12; 6.44]
Random effects model -0.71 [-6.94; 5.52]
Heterogeneity: I^2 = 67%, τ^2 = 13.5944, p = 0.08
Comparison = Olanzapine oral vs Paliperidone oral
Schreiner 2012 (n= 426) 10.00 [4.02; 15.98]
Random effects model 10.00 [4.02; 15.98]
Heterogeneity: not applicable


Comparison = Olanzapine oral vs Perphenazine oral
Lieberman 2005_18months (n= 498) 9.20 [3.10; 15.30]
Random effects model 9.20 [3.10; 15.30]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Placebo
Beasley 2003 (n= 268) 15.00 [7.93; 22.07]
Random effects model 15.00 [7.93; 22.07]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Quetiapine oral
Deberdt 2008 (n= 130) -0.77 [-10.36; 8.82]
Kahn 2008 (n= 109) 7.69 [-2.99; 18.37]
Kinon 2006a (n= 305) 6.54 [-0.80; 13.88]
Lieberman 2005_18months (n= 554) 4.40 [-1.42; 10.22]
McEvoy 2006 (n= 29) 13.20 [-7.23; 33.63]
McEvoy 2007a (n= 81) -9.50 [-21.64; 2.64]
Newcomer 2009 (n= 249) 8.00 [-3.96; 19.96]
Stroup 2006 (n= 170) 13.10 [3.24; 22.96]
Random effects model 4.96 [0.67; 9.26]
Heterogeneity: I^2 = 35%, τ^2 = 12.7559, p = 0.15
Comparison = Olanzapine oral vs Risperidone LAI
Keks 2007 (n= 485) 5.96 [0.09; 11.83]
Random effects model 5.96 [0.09; 11.83]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Risperidone oral
Keefe 2006 (n= 224) 11.35 [3.86; 18.84]
Lieberman 2005_18months (n= 548) 11.80 [6.25; 17.35]
McEvoy 2006 (n= 27) 9.20 [-13.12; 31.52]
McEvoy 2007a (n= 74) 4.30 [-8.11; 16.71]
NCT00236379 (n= 47) -12.80 [-31.98; 6.38]
Newcomer 2009 (n= 266) 16.30 [4.67; 27.93]
Smith 2009 (n= 46) -0.06 [-17.05; 16.93]
Stroup 2006 (n= 174) 20.50 [10.49; 30.51]
Suresh 2016 (n= 71) -8.80 [-26.27; 8.67]
Volavka 2002 (n= 48) 10.90 [-7.57; 29.37]
Random effects model 8.71 [3.30; 14.11]
Heterogeneity: I^2 = 50%, τ^2 = 32.7626, p = 0.04
Comparison = Olanzapine oral vs Ziprasidone oral
Breier 2005 (n= 418) 15.77 [9.27; 22.27]
Kahn 2008 (n= 98) 15.38 [-1.45; 32.21]
Kinon 2006b (n= 318) 9.43 [2.04; 16.82]
Lieberman 2005_18months (n= 429) 18.90 [7.91; 29.89]
Stroup 2006 (n= 195) 30.40 [20.97; 39.83]
Random effects model 17.81 [10.53; 25.10]
Heterogeneity: I^2 = 67%, τ^2 = 43.7156, p = 0.02
Comparison = Paliperidone LAI vs Placebo
Berwaerts 2015 (n= 292) 2.30 [-4.20; 8.81]
Fu 2015 (n= 251) 6.50 [-2.44; 15.44]
Hough 2010 (n= 380) 0.00 [-5.26; 5.26]
Random effects model 1.88 [-1.84; 5.60]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.46
Comparison = Paliperidone LAI vs Risperidone LAI
Koshikawa 2016 (n= 25) 15.30 [-9.61; 40.21]
NCT00210717 (n= 717) -5.00 [-9.81; -0.19]
Random effects model 1.32 [-17.10; 19.74]
Heterogeneity: I^2 = 59%, τ^2 = 122.2600, p = 0.12
Comparison = Paliperidone oral vs Placebo
Kramer 2007 (n= 173) 7.69 [-0.85; 16.24]
Rui 2014 (n= 121) 15.00 [5.73; 24.27]
Random effects model 11.12 [3.97; 18.27]
Heterogeneity: I^2 = 23%, τ^2 = 6.0202, p = 0.26
Comparison = Perphenazine oral vs Quetiapine oral
Lieberman 2005_18months (n= 480) -4.80 [-10.90; 1.30]
Random effects model -4.80 [-10.90; 1.30]
Heterogeneity: not applicable
Comparison = Perphenazine oral vs Risperidone oral
Lieberman 2005_18months (n= 474) 2.60 [-3.25; 8.45]
Random effects model 2.60 [-3.25; 8.45]
Heterogeneity: not applicable
Comparison = Perphenazine oral vs Ziprasidone oral
Lieberman 2005_18months (n= 355) 9.70 [-1.44; 20.84]
Random effects model 9.70 [-1.44; 20.84]
Heterogeneity: not applicable
Comparison = Quetiapine oral vs Risperidone LAI
Gaebel 2010 (n= 489) -1.54 [-8.87; 5.79]
Random effects model -1.54 [-8.87; 5.79]
Heterogeneity: not applicable



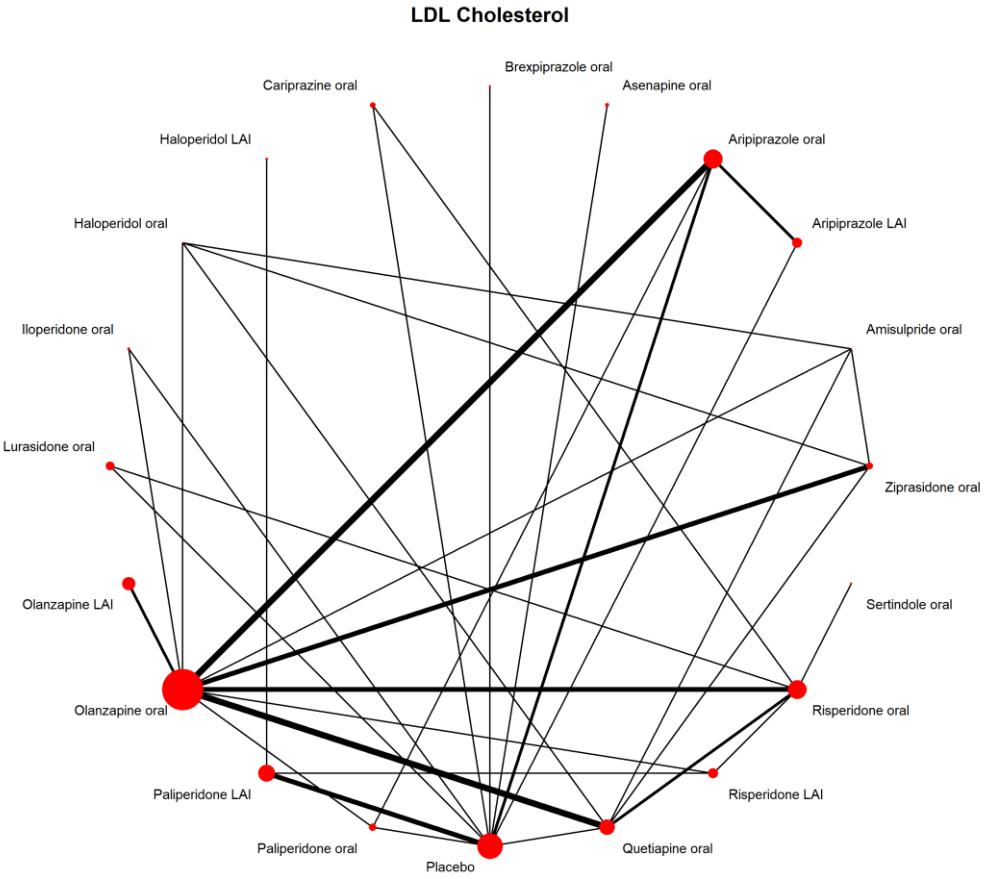
Pairwise meta-analyses are ordered by comparison investigated (in alphabetical order) and a summary effect size is calculated by pairwise meta-analyses of all studies of a specific comparison. The type of effect size measure is mean difference (MD).

Abbreviations: MD=mean difference, 95% CI=95% confidence interval, LAI=long-acting injectable.

7.5 LDL cholesterol

40 studies on 19 antipsychotics with 11954 participants included reported on LDL cholesterol.

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Abbreviations: LAI=long-acting injectable.

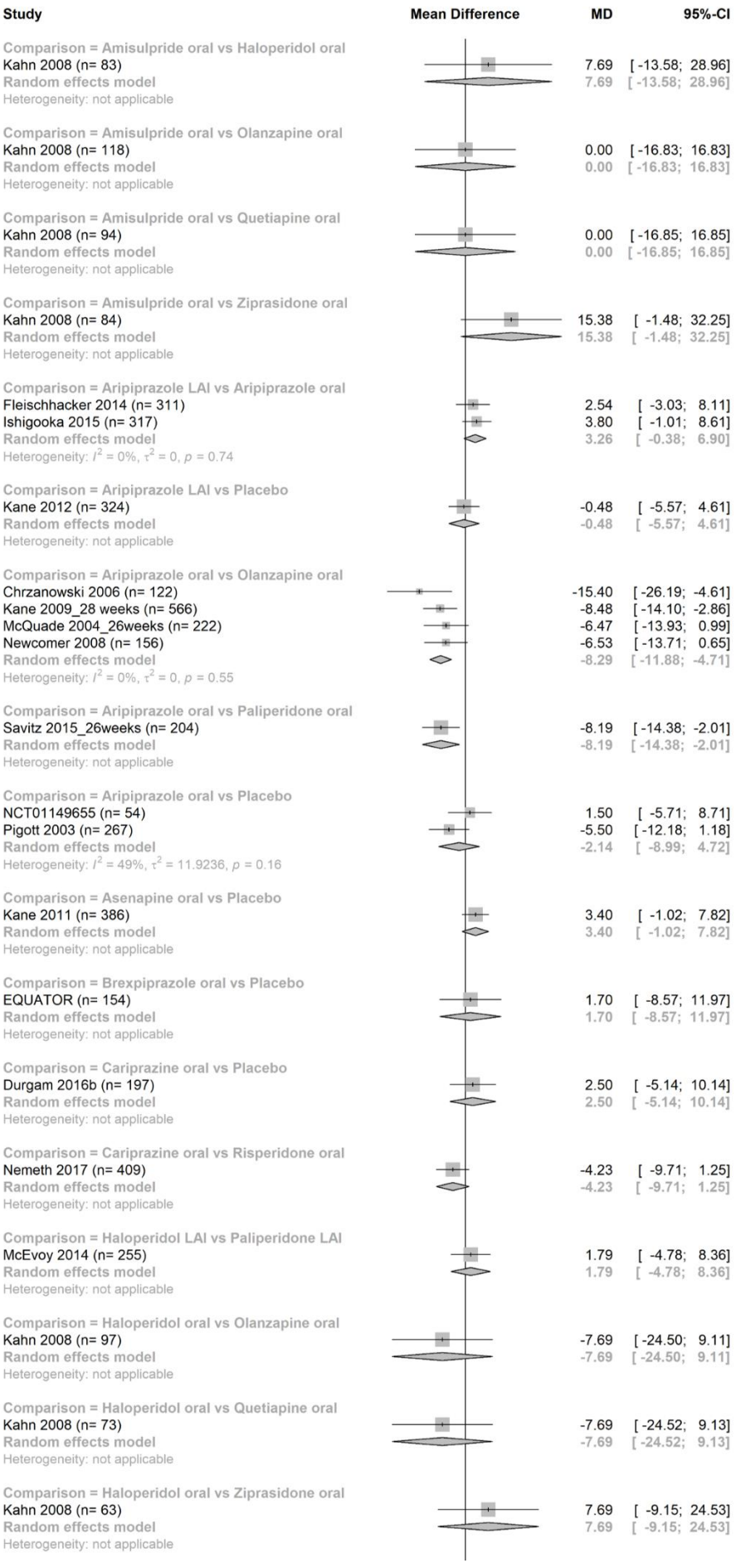
League-table

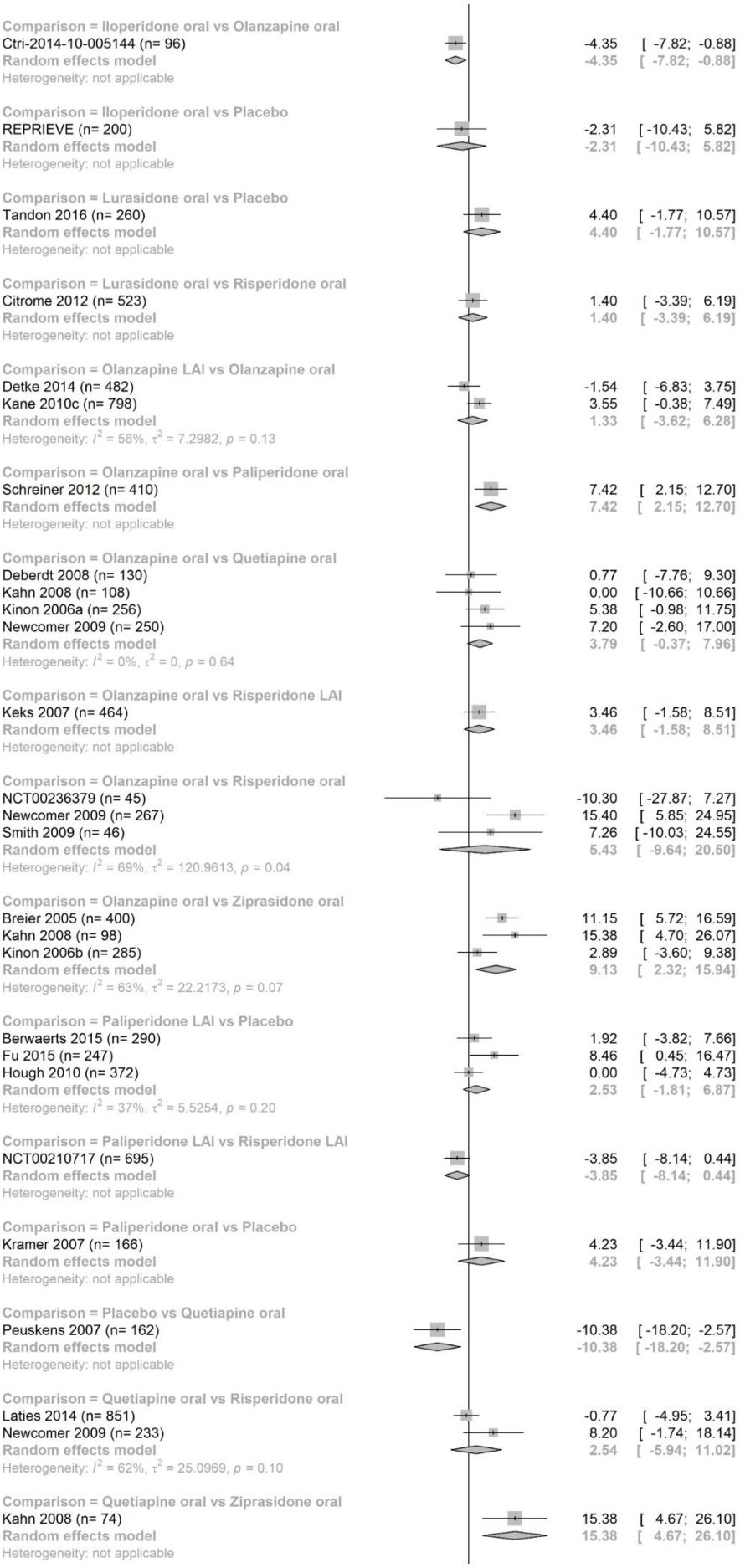
ARI	NA	-2.20 (-7.92 to 3.53)	-3.23 (-7.93 to 1.47)	NA	NA	NA	NA	NA	NA	**-8.19 (-15.65 to -0.73)**	NA	NA	NA	NA	NA	NA	NA	**-8.41 (-12.63 to -4.18)**	NA
-0.60 (-6.10 to 5.26)	**ZIP**	NA	NA	NA	NA	-7.69 (-25.04 to 9.66)	NA	NA	NA	NA	NA	NA	NA	NA	NA	**-15.38 (-26.89 to -3.88)**	-15.38 (-32.76 to 1.99)	**-8.82 (-13.50 to -4.14)**	NA
-1.92 (-5.64 to 1.96)	-1.32 (-7.32 to 4.38)	**PLB**	0.48 (-6.11 to 7.07)	-2.50 (-11.21 to 6.21)	-2.48 (-6.66 to 1.70)	NA	2.31 (-6.83 to 11.44)	-1.70 (-12.78 to 9.38)	-3.40 (-9.48 to 2.68)	-4.23 (-12.96 to 4.50)	NA	NA	-4.40 (-11.85 to 3.05)	NA	NA	**-10.38 (-19.25 to -1.52)**	NA	NA	NA
-2.50 (-6.76 to 1.58)	-1.91 (-8.89 to 4.73)	-0.60 (-5.49 to 4.06)	**ARI LAI**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-2.67 (-9.29 to 4.26)	-2.09 (-9.84 to 5.91)	-0.73 (-6.97 to 5.51)	-0.14 (-7.62 to 7.42)	**CAR**	NA	NA	NA	NA	NA	NA	-4.23 (-11.12 to 2.66)	NA	NA	NA	NA	NA	NA	NA	NA
-4.19 (-9.31 to 0.93)	-3.56 (-10.45 to 2.95)	-2.29 (-6.35 to 1.62)	-1.65 (-7.68 to 4.23)	-1.51 (-8.88 to 5.51)	**PAL LAI**	NA	NA	NA	NA	NA	NA	-1.79 (-9.57 to 5.99)	NA	NA	-3.85 (-9.83 to 2.14)	NA	NA	NA	NA
-3.28 (-21.72 to 12.99)	-2.89 (-21.22 to 12.81)	-1.49 (-20.28 to 14.95)	-0.80 (-19.46 to 15.97)	-0.70 (-19.73 to 16.77)	0.73 (-17.87 to 17.38)	**HAL**	NA	NA	NA	NA	NA	NA	NA	NA	NA	-7.69 (-25.03 to 9.64)	-7.69 (-29.37 to 13.98)	-7.69 (-25.01 to 9.62)	NA
-4.26 (-9.78 to 1.96)	-3.66 (-10.27 to 3.27)	-2.36 (-7.67 to 3.70)	-1.71 (-8.22 to 5.40)	-1.60 (-9.24 to 6.50)	-0.14 (-6.19 to 7.01)	-0.69 (-17.90 to 17.08)	**ILO**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	-4.35 (-9.78 to 1.08)	NA
-4.05 (-16.99 to 8.20)	-3.46 (-16.28 to 9.71)	-2.18 (-14.08 to 9.70)	-1.50 (-14.64 to 11.09)	-1.43 (-15.15 to 11.95)	0.15 (-12.52 to 12.67)	-0.50 (-21.62 to 21.14)	0.16 (-12.27 to 13.07)	**BRE**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-5.29 (-12.50 to 2.13)	-4.71 (-13.35 to 3.82)	-3.25 (-9.67 to 2.93)	-2.75 (-10.59 to 5.32)	-2.70 (-11.47 to 6.40)	-1.12 (-8.26 to 6.55)	-1.99 (-19.13 to 18.13)	-0.98 (-9.79 to 7.20)	-1.23 (-14.71 to 12.66)	**ASE**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-5.36 (-10.08 to -0.57)	-4.74 (-11.47 to 1.74)	-3.35 (-8.56 to 1.44)	-2.87 (-8.93 to 3.31)	-2.70 (-10.54 to 4.87)	-1.15 (-7.18 to 4.89)	-2.05 (-18.28 to 16.95)	-1.04 (-8.12 to 5.12)	-1.37 (-14.21 to 12.12)	-0.10 (-8.35 to 7.82)	**PAL**	NA	NA	NA	NA	NA	NA	NA	**-7.42 (-14.15 to -0.69)**	NA
-5.90 (-11.04 to -0.46)	-5.35 (-11.68 to 1.11)	-4.02 (-9.04 to 0.91)	-3.35 (-9.55 to 3.08)	-3.31 (-8.95 to 2.75)	-1.82 (-7.66 to 4.56)	-2.43 (-19.24 to 16.28)	-1.68 (-8.25 to 4.81)	-1.84 (-14.62 to 10.35)	-0.63 (-8.79 to 7.50)	-0.65 (-6.84 to 5.93)	**RIS**	NA	-1.40 (-7.75 to 4.95)	-2.69 (-14.44 to 9.06)	-12.30 (-34.08 to 9.48)	-1.30 (-6.48 to 3.88)	NA	**-8.63 (-16.68 to -0.58)**	NA
-5.99 (-15.75 to 3.39)	-5.52 (-15.96 to 5.06)	-4.00 (-13.15 to 4.67)	-3.47 (-14.11 to 6.46)	-3.26 (-14.13 to 7.27)	-1.81 (-9.70 to 6.02)	-2.61 (-20.61 to 16.92)	-1.79 (-12.43 to 8.29)	-2.02 (-16.88 to 12.19)	-0.77 (-11.92 to 9.98)	-0.72 (-10.47 to 9.17)	-0.05 (-10.34 to 9.49)	**HAL LAI**	NA	NA	NA	NA	NA	NA	NA
-6.96 (-13.11 to -0.31)	-6.39 (-13.86 to 1.29)	-5.08 (-10.65 to 0.94)	-4.47 (-11.33 to 3.05)	-4.30 (-11.52 to 3.37)	-2.82 (-9.38 to 4.39)	-3.55 (-20.51 to 15.89)	-2.71 (-10.50 to 4.80)	-2.85 (-16.01 to 9.69)	-1.74 (-10.07 to 7.13)	-1.69 (-8.74 to 5.99)	-0.97 (-6.55 to 4.29)	-0.96 (-11.10 to 9.77)	**LUR**	NA	NA	NA	NA	NA	NA
-8.72 (-21.59 to 4.02)	-8.28 (-21.80 to 5.03)	-6.91 (-19.49 to 5.68)	-6.27 (-19.45 to 7.08)	-6.00 (-19.41 to 6.99)	-4.64 (-17.55 to 8.64)	-5.59 (-26.57 to 17.24)	-4.63 (-17.91 to 8.63)	-4.64 (-21.71 to 11.57)	-3.53 (-17.50 to 10.48)	-3.44 (-16.74 to 9.76)	-2.80 (-15.05 to 8.61)	-2.74 (-18.05 to 12.81)	-1.83 (-14.88 to 10.94)	**SER**	NA	NA	NA	NA	NA
-7.75 (-13.81 to -2.01)	**-7.14 (-14.45 to -0.43)**	**-5.84 (-11.38 to -0.49)**	-5.18 (-12.12 to 1.38)	-5.13 (-13.14 to 2.57)	-3.58 (-8.69 to 1.57)	-4.27 (-21.45 to 14.28)	-3.40 (-11.01 to 2.94)	-3.77 (-16.83 to 9.37)	-2.51 (-11.00 to 5.57)	-2.49 (-9.18 to 4.10)	-1.80 (-8.54 to 4.41)	-1.80 (-11.14 to 7.54)	-0.76 (-8.72 to 6.34)	0.96 (-12.69 to 14.15)	**RIS LAI**	NA	NA	-3.46 (-10.01 to 3.09)	NA
-7.77 (-12.41 to -3.02)	**-7.19 (-12.97 to -1.61)**	**-5.87 (-10.51 to -1.33)**	-5.27 (-11.08 to 0.71)	-5.13 (-11.74 to 1.44)	-3.66 (-9.11 to 2.16)	-4.28 (-20.69 to 13.93)	-3.48 (-10.04 to 2.27)	-3.70 (-16.31 to 8.42)	-2.48 (-10.42 to 5.12)	-2.48 (-8.16 to 3.31)	-1.87 (-6.47 to 2.48)	-1.78 (-11.41 to 8.14)	-0.82 (-7.39 to 5.34)	0.99 (-11.68 to 13.42)	-0.07 (-6.06 to 6.22)	**QUE**	-0.00 (-17.36 to 17.36)	-3.68 (-8.41 to 1.04)	NA
-11.65 (-28.82 to 5.21)	-11.17 (-28.00 to 5.71)	-9.72 (-26.88 to 6.90)	-9.02 (-26.67 to 8.23)	-9.24 (-27.16 to 9.42)	-7.52 (-25.06 to 9.68)	-7.57 (-30.92 to 12.78)	-7.58 (-24.73 to 10.00)	-7.57 (-29.46 to 15.12)	-6.38 (-24.49 to 11.50)	-6.41 (-23.45 to 10.73)	-5.88 (-22.94 to 12.11)	-5.64 (-25.38 to 13.56)	-4.81 (-22.52 to 13.28)	-3.02 (-23.35 to 18.23)	-4.00 (-21.47 to 13.21)	-4.03 (-20.83 to 12.75)	**AMI**	0.00 (-17.34 to 17.34)	NA
-10.00 (-13.46 to -6.59)	**-9.38 (-14.20 to -4.86)**	**-8.09 (-11.89 to -4.32)**	**-7.46 (-12.53 to -2.44)**	**-7.37 (-13.90 to -0.87)**	**-5.89 (-10.56 to -0.77)**	-6.57 (-22.66 to 11.14)	**-5.73 (-11.09 to -1.11)**	-5.89 (-18.35 to 6.23)	-4.77 (-12.18 to 2.61)	-4.72 (-9.24 to 0.04)	-4.08 (-8.91 to 0.42)	-4.00 (-13.27 to 5.35)	-3.03 (-9.39 to 2.95)	-1.23 (-13.74 to 11.38)	-2.30 (-7.34 to 3.14)	-2.26 (-6.04 to 1.64)	1.83 (-14.77 to 18.27)	**OLA**	-1.41 (-5.78 to 2.96)
-11.47 (-17.14 to -5.61)	**-10.95 (-17.38 to -4.41)**	**-9.59 (-15.49 to -3.61)**	**-8.89 (-15.84 to -2.01)**	**-8.80 (-16.85 to -0.87)**	**-7.36 (-13.67 to -0.41)**	-7.93 (-24.88 to 9.62)	**-7.27 (-14.10 to -0.75)**	-7.38 (-20.68 to 4.98)	-6.22 (-14.99 to 2.55)	-6.16 (-12.50 to 0.57)	-5.56 (-12.15 to 0.82)	-5.47 (-15.82 to 4.97)	-4.54 (-12.26 to 2.92)	-2.82 (-15.83 to 10.74)	-3.77 (-10.51 to 3.41)	-3.79 (-9.45 to 2.41)	0.37 (-16.78 to 17.20)	-1.52 (-5.90 to 3.22)	**OLA LAI**

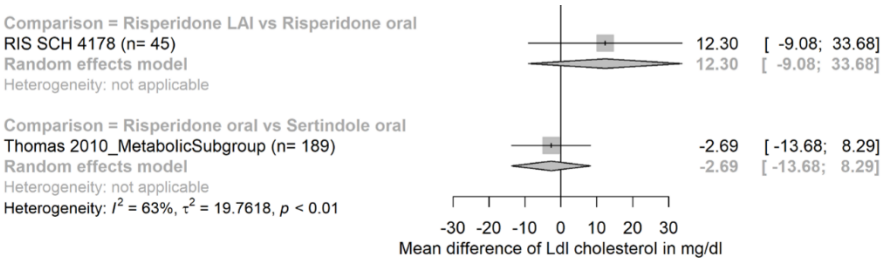
Order of treatments is according to SUCRA ranking. Results of the network meta-analysis are presented in the left lower half and results of pairwise meta-analyses in the right upper half. Each cell provides the effect estimate as mean difference (MD) and the corresponding 95% credible interval (95%CrI) of a comparison (left lower half: treatment in column versus treatment in row; right upper half: treatment in row versus treatment in column). Bold print indicates 95% CrI excluding the point of no effect.

Abbreviations: NA=Not available, LAI=long-acting injectable, AMI=Amisulpride, ARI=Aripiprazole, ASE=Asenapine, BRE=Brexpiprazole, CAR=Cariprazine, CLO=Clozapine, CPZ=Chlorpromazine, FLP=Fluspirilene, FLU=Fluphenazine, FPX=Flupentixol, HAL=Haloperidol, ILO=Iloperidone, LUR=Lurasidone, OLA=Olanzapine, PAL=Paliperidone, PER=Perphenazine, PIM=Pimozide, PLB=Placebo, QUE=Quetiapine, RIS=Risperidone, SER=Sertindole, THIOR=Thioridazine, TIOT=Tiotixene, TRI=Trifluoperazine, ZIP=Ziprasidone, ZOT=Zotepine.

Forest-plot of results of pairwise meta-analyses (also indicating data of individual studies)




Comparison = Iloperidone oral vs Olanzapine oral
Ctri-2014-10-005144 (n= 96) -4.35 [-7.82; -0.88]
Random effects model -4.35 [-7.82; -0.88]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Placebo
REPRIEVE (n= 200) -2.31 [-10.43; 5.82]
Random effects model -2.31 [-10.43; 5.82]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Placebo
Tandon 2016 (n= 260) 4.40 [-1.77; 10.57]
Random effects model 4.40 [-1.77; 10.57]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Risperidone oral
Citrome 2012 (n= 523) 1.40 [-3.39; 6.19]
Random effects model 1.40 [-3.39; 6.19]
Heterogeneity: not applicable
Comparison = Olanzapine LAI vs Olanzapine oral
Detke 2014 (n= 482) -1.54 [-6.83; 3.75]
Kane 2010c (n= 798) 3.55 [-0.38; 7.49]
Random effects model 1.33 [-3.62; 6.28]
Heterogeneity: I^2 = 56%, τ^2 = 7.2982, p = 0.13
Comparison = Olanzapine oral vs Paliperidone oral
Schreiner 2012 (n= 410) 7.42 [2.15; 12.70]
Random effects model 7.42 [2.15; 12.70]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Quetiapine oral
Deberdt 2008 (n= 130) 0.77 [-7.76; 9.30]
Kahn 2008 (n= 108) 0.00 [-10.66; 10.66]
Kinon 2006a (n= 256) 5.38 [-0.98; 11.75]
Newcomer 2009 (n= 250) 7.20 [-2.60; 17.00]
Random effects model 3.79 [-0.37; 7.96]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.64
Comparison = Olanzapine oral vs Risperidone LAI
Keks 2007 (n= 464) 3.46 [-1.58; 8.51]
Random effects model 3.46 [-1.58; 8.51]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Risperidone oral
NCT00236379 (n= 45) -10.30 [-27.87; 7.27]
Newcomer 2009 (n= 267) 15.40 [5.85; 24.95]
Smith 2009 (n= 46) 7.26 [-10.03; 24.55]
Random effects model 5.43 [-9.64; 20.50]
Heterogeneity: I^2 = 69%, τ^2 = 120.9613, p = 0.04
Comparison = Olanzapine oral vs Ziprasidone oral
Breier 2005 (n= 400) 11.15 [5.72; 16.59]
Kahn 2008 (n= 98) 15.38 [4.70; 26.07]
Kinon 2006b (n= 285) 2.89 [-3.60; 9.38]
Random effects model 9.13 [2.32; 15.94]
Heterogeneity: I^2 = 63%, τ^2 = 22.2173, p = 0.07
Comparison = Paliperidone LAI vs Placebo
Berwaerts 2015 (n= 290) 1.92 [-3.82; 7.66]
Fu 2015 (n= 247) 8.46 [0.45; 16.47]
Hough 2010 (n= 372) 0.00 [-4.73; 4.73]
Random effects model 2.53 [-1.81; 6.87]
Heterogeneity: I^2 = 37%, τ^2 = 5.5254, p = 0.20
Comparison = Paliperidone LAI vs Risperidone LAI
NCT00210717 (n= 695) -3.85 [-8.14; 0.44]
Random effects model -3.85 [-8.14; 0.44]
Heterogeneity: not applicable
Comparison = Paliperidone oral vs Placebo
Kramer 2007 (n= 166) 4.23 [-3.44; 11.90]
Random effects model 4.23 [-3.44; 11.90]
Heterogeneity: not applicable
Comparison = Placebo vs Quetiapine oral
Peuskens 2007 (n= 162) -10.38 [-18.20; -2.57]
Random effects model -10.38 [-18.20; -2.57]
Heterogeneity: not applicable
Comparison = Quetiapine oral vs Risperidone oral
Laties 2014 (n= 851) -0.77 [-4.95; 3.41]
Newcomer 2009 (n= 233) 8.20 [-1.74; 18.14]
Random effects model 2.54 [-5.94; 11.02]
Heterogeneity: I^2 = 62%, τ^2 = 25.0969, p = 0.10
Comparison = Quetiapine oral vs Ziprasidone oral
Kahn 2008 (n= 74) 15.38 [4.67; 26.10]
Random effects model 15.38 [4.67; 26.10]
Heterogeneity: not applicable



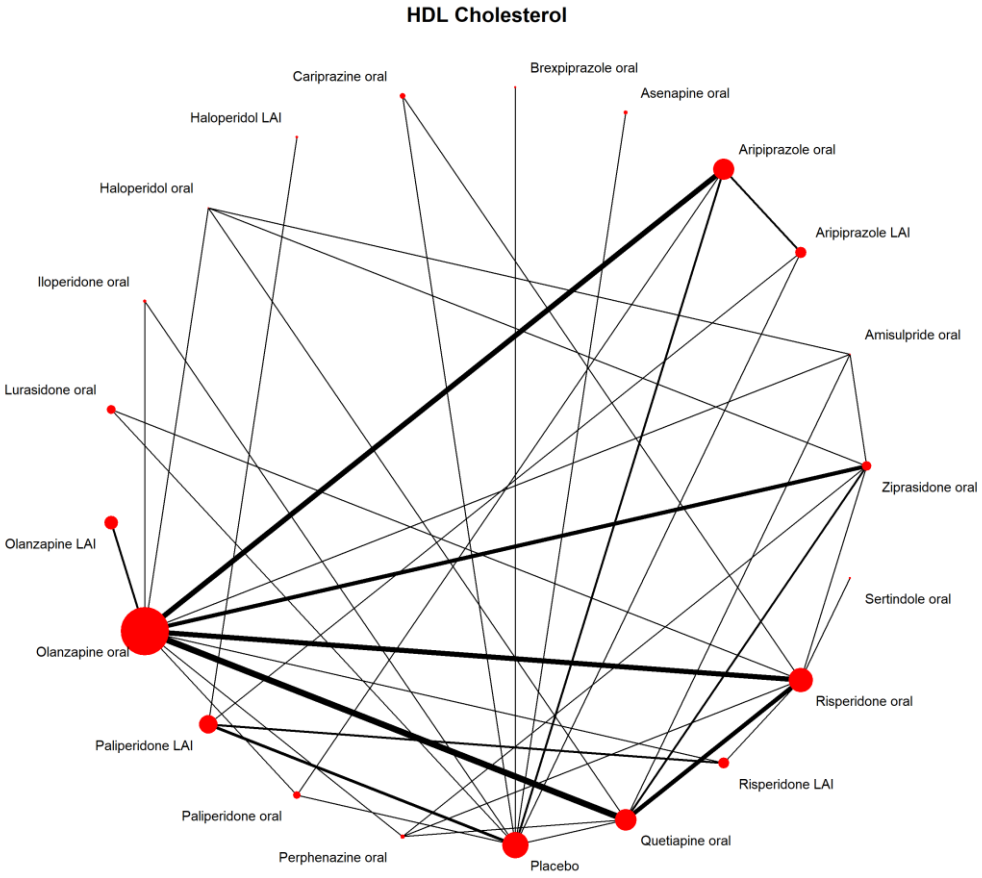
Pairwise meta-analyses are ordered by comparison investigated (in alphabetical order) and a summary effect size is calculated by pairwise meta-analyses of all studies of a specific comparison. The type of effect size measure is mean difference (MD).

Abbreviations: MD=mean difference, 95% CI=95% confidence interval, LAI=long-acting injectable.

7.6 HDL cholesterol

45 studies on 20 antipsychotics with 13736 participants included reported on HDL cholesterol.

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Abbreviations: LAI=long-acting injectable.

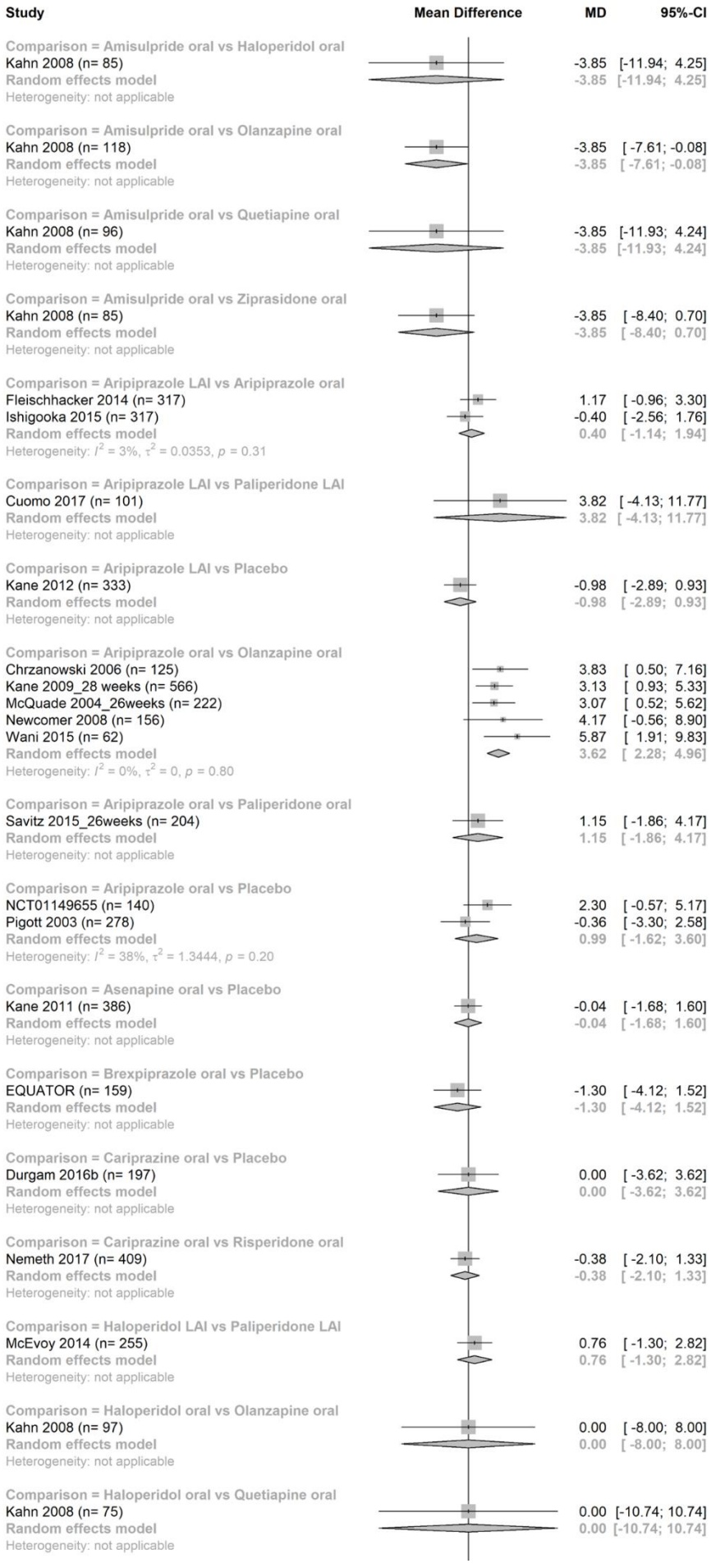
League-table

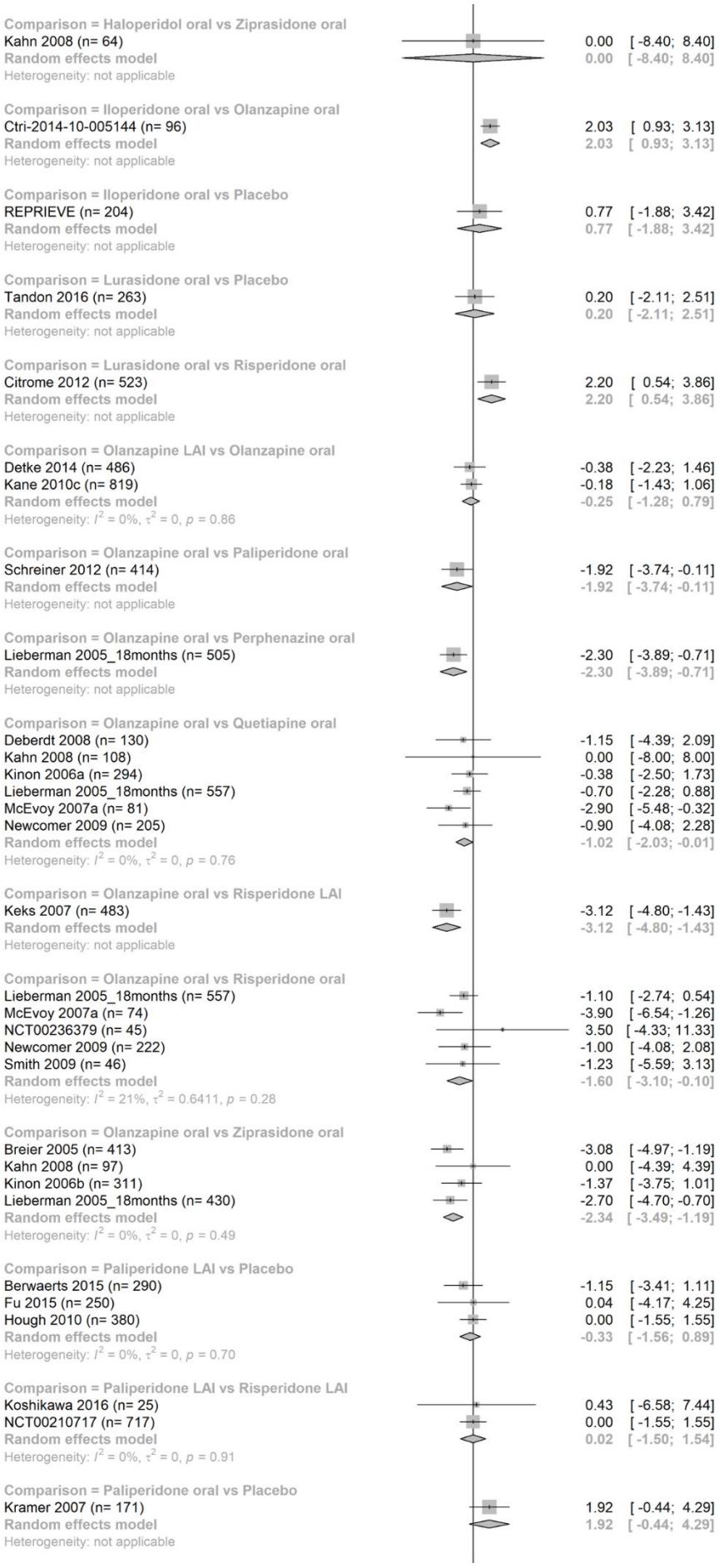
AMI	NA	**-3.85 (-7.61 to -0.08)**	-3.85 (-11.93 to 4.24)	NA	NA	NA	-3.85 (-11.94 to 4.25)	NA	NA	NA	NA	-3.85 (-8.40 to 0.70)	NA	NA	NA	NA	NA	NA	NA	NA
-2.33 (-6.32 to 0.96)	**OLA LAI**	-0.25 (-1.28 to 0.79)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-2.58 (-6.32 to 0.38)	-0.30 (-1.45 to 0.91)	**OLA**	**-1.02 (-2.03 to -0.01)**	**-1.57 (-2.77 to -0.37)**	NA	NA	-0.00 (-8.00 to 8.00)	NA	**-2.03 (-3.13 to -0.93)**	**-2.30 (-3.89 to -0.71)**	**-3.12 (-4.80 to -1.43)**	**-2.34 (-3.49 to -1.19)**	NA	NA	NA	**-1.92 (-3.74 to -0.11)**	NA	NA	NA	**-3.62 (-4.96 to -2.28)**
-3.71 (-7.36 to -0.44)	-1.28 (-2.74 to 0.24)	**-1.00 (-1.92 to -0.05)**	**QUE**	-0.26 (-1.21 to 0.69)	NA	NA	-0.00 (-10.74 to 10.74)	NA	NA	-1.60 (-3.22 to 0.02)	NA	-1.89 (-3.87 to 0.09)	NA	-1.92 (-4.87 to 1.03)	NA	NA	NA	NA	NA	NA
-4.01 (-7.81 to -0.82)	**-1.67 (-3.22 to -0.11)**	**-1.39 (-2.38 to -0.33)**	-0.37 (-1.39 to 0.59)	**RIS**	0.38 (-1.33 to 2.10)	NA	NA	NA	NA	-1.20 (-2.88 to 0.48)	3.20 (-3.54 to 9.94)	-1.60 (-3.68 to 0.48)	NA	NA	-1.54 (-5.43 to 2.36)	NA	NA	NA	**-2.20 (-3.86 to -0.54)**	NA
-4.02 (-8.40 to -0.39)	-1.62 (-3.88 to 0.62)	-1.32 (-3.30 to 0.62)	-0.31 (-2.31 to 1.52)	0.06 (-1.66 to 1.74)	**CAR**	NA	NA	NA	NA	NA	NA	NA	NA	0.00 (-3.62 to 3.62)	NA	NA	NA	NA	NA	NA
-3.86 (-9.21 to 0.40)	-1.58 (-4.87 to 1.90)	-1.25 (-4.43 to 1.98)	-0.29 (-3.54 to 2.95)	0.09 (-3.10 to 3.34)	0.01 (-3.60 to 3.73)	**BRE**	NA	NA	NA	NA	NA	NA	NA	-1.30 (-4.12 to 1.52)	NA	NA	NA	NA	NA	NA
-3.79 (-11.12 to 4.24)	-1.32 (-8.69 to 7.18)	-1.04 (-8.37 to 7.37)	0.01 (-7.38 to 8.42)	0.34 (-7.03 to 8.88)	0.32 (-7.20 to 9.13)	0.26 (-7.94 to 9.20)	**HAL**	NA	NA	NA	NA	0.00 (-8.40 to 8.40)	NA	NA	NA	NA	NA	NA	NA	NA
-4.93 (-8.79 to -1.54)	**-2.57 (-4.40 to -0.68)**	**-2.29 (-3.73 to -0.75)**	-1.26 (-3.01 to 0.32)	-0.87 (-2.60 to 0.69)	-0.93 (-3.31 to 1.27)	-0.97 (-4.21 to 2.15)	-1.09 (-9.79 to 6.34)	**PAL LAI**	NA	NA	0.02 (-1.50 to 1.54)	NA	NA	-0.33 (-1.56 to 0.89)	NA	NA	-3.82 (-11.77 to 4.13)	-0.76 (-2.82 to 1.30)	NA	NA
-4.96 (-8.98 to -1.55)	**-2.56 (-4.29 to -0.89)**	**-2.26 (-3.60 to -1.06)**	-1.25 (-2.86 to 0.21)	-0.88 (-2.49 to 0.63)	-0.96 (-3.18 to 1.35)	-0.97 (-4.34 to 2.38)	-1.23 (-9.70 to 6.21)	-0.01 (-1.84 to 1.77)	**ILO**	NA	NA	NA	NA	0.77 (-1.88 to 3.42)	NA	NA	NA	NA	NA	NA
-5.11 (-9.08 to -1.68)	**-2.71 (-4.94 to -0.68)**	**-2.41 (-4.17 to -0.86)**	-1.42 (-2.96 to 0.13)	-1.03 (-2.68 to 0.59)	-1.11 (-3.45 to 1.26)	-1.08 (-4.75 to 2.32)	-1.44 (-9.82 to 6.06)	-0.13 (-2.30 to 1.96)	-0.16 (-2.07 to 1.88)	**PER**	NA	-0.40 (-2.44 to 1.64)	NA	NA	NA	NA	NA	NA	NA	NA
-5.04 (-8.98 to -1.75)	**-2.75 (-4.53 to -0.89)**	**-2.43 (-3.91 to -1.02)**	-1.45 (-3.25 to 0.20)	-1.06 (-2.77 to 0.56)	-1.12 (-3.53 to 1.21)	-1.12 (-4.54 to 2.16)	-1.24 (-9.97 to 6.10)	-0.17 (-1.53 to 1.26)	-0.17 (-2.03 to 1.77)	-0.04 (-2.18 to 2.17)	**RIS LAI**	NA	NA	NA	NA	NA	NA	NA	NA	NA
-5.11 (-8.80 to -1.82)	**-2.75 (-4.30 to -1.01)**	**-2.46 (-3.59 to -1.20)**	**-1.44 (-2.77 to -0.03)**	-1.07 (-2.49 to 0.42)	-1.09 (-3.27 to 1.14)	-1.19 (-4.64 to 2.29)	-1.40 (-9.86 to 5.98)	-0.14 (-2.03 to 1.68)	-0.18 (-1.85 to 1.66)	-0.02 (-1.82 to 1.78)	-0.00 (-1.75 to 1.84)	**ZIP**	NA	NA	NA	NA	NA	NA	NA	NA
-5.11 (-9.47 to -1.43)	**-2.80 (-5.25 to -0.25)**	**-2.47 (-4.70 to -0.35)**	-1.47 (-3.81 to 0.74)	-1.09 (-3.35 to 1.11)	-1.13 (-3.92 to 1.50)	-1.20 (-4.76 to 2.29)	-1.52 (-10.26 to 6.27)	-0.20 (-2.41 to 2.03)	-0.19 (-2.61 to 2.19)	-0.07 (-2.71 to 2.52)	-0.04 (-2.43 to 2.33)	0.00 (-2.52 to 2.27)	**ASE**	-0.04 (-1.68 to 1.60)	NA	NA	NA	NA	NA	NA
-5.24 (-8.94 to -2.05)	**-2.91 (-4.45 to -1.18)**	**-2.59 (-3.71 to -1.44)**	**-1.59 (-2.91 to -0.27)**	-1.20 (-2.45 to 0.15)	-1.22 (-3.25 to 0.73)	-1.31 (-4.31 to 1.70)	-1.58 (-9.94 to 5.91)	-0.30 (-1.48 to 0.93)	-0.33 (-1.80 to 1.27)	-0.18 (-1.98 to 1.66)	-0.17 (-1.61 to 1.40)	-0.14 (-1.74 to 1.38)	-0.12 (-1.90 to 1.77)	**PLB**	NA	-1.92 (-4.29 to 0.44)	0.98 (-0.93 to 2.89)	NA	-0.20 (-2.51 to 2.11)	-1.00 (-3.06 to 1.05)
-5.54 (-11.66 to -0.76)	-3.08 (-7.56 to 0.83)	-2.80 (-7.20 to 0.91)	-1.82 (-6.20 to 1.89)	-1.45 (-5.59 to 2.16)	-1.58 (-5.80 to 2.56)	-1.51 (-6.82 to 3.10)	-1.76 (-11.61 to 6.61)	-0.61 (-5.06 to 3.23)	-0.56 (-5.02 to 3.44)	-0.36 (-4.92 to 3.45)	-0.40 (-4.83 to 3.53)	-0.39 (-4.85 to 3.47)	-0.42 (-5.09 to 3.81)	-0.24 (-4.61 to 3.42)	**SER**	NA	NA	NA	NA	NA
-5.35 (-9.43 to -1.97)	**-3.05 (-4.90 to -1.16)**	**-2.73 (-4.19 to -1.29)**	**-1.73 (-3.41 to -0.11)**	-1.33 (-3.12 to 0.34)	-1.42 (-3.77 to 0.92)	-1.46 (-4.84 to 1.80)	-1.65 (-10.07 to 5.65)	-0.44 (-2.36 to 1.34)	-0.46 (-2.30 to 1.42)	-0.34 (-2.47 to 1.82)	-0.30 (-2.24 to 1.55)	-0.25 (-2.20 to 1.49)	-0.32 (-2.63 to 2.21)	-0.15 (-1.75 to 1.42)	0.06 (-3.63 to 4.61)	**PAL**	NA	NA	NA	-1.15 (-4.17 to 1.86)
-5.56 (-9.71 to -2.22)	**-3.18 (-5.14 to -1.17)**	**-2.90 (-4.43 to -1.38)**	**-1.88 (-3.66 to -0.17)**	-1.51 (-3.31 to 0.21)	-1.56 (-3.91 to 0.71)	-1.59 (-5.17 to 1.75)	-1.90 (-10.27 to 5.62)	-0.66 (-2.41 to 1.21)	-0.65 (-2.54 to 1.30)	-0.44 (-2.71 to 1.69)	-0.44 (-2.42 to 1.46)	-0.44 (-2.50 to 1.26)	-0.42 (-2.74 to 1.94)	-0.32 (-1.81 to 1.26)	-0.05 (-4.08 to 4.42)	-0.13 (-2.23 to 1.69)	**ARI LAI**	NA	NA	0.40 (-1.12 to 1.91)
-5.84 (-10.23 to -1.54)	**-3.40 (-6.31 to -0.39)**	**-3.12 (-5.81 to -0.31)**	-2.06 (-5.00 to 0.75)	-1.70 (-4.58 to 1.10)	-1.74 (-5.09 to 1.40)	-1.85 (-5.59 to 2.19)	-2.03 (-10.90 to 5.91)	-0.85 (-2.97 to 1.52)	-0.79 (-3.76 to 2.19)	-0.70 (-3.76 to 2.48)	-0.66 (-3.19 to 2.01)	-0.67 (-3.54 to 2.28)	-0.58 (-3.74 to 2.52)	-0.49 (-3.04 to 2.08)	-0.19 (-4.66 to 4.80)	-0.36 (-3.26 to 2.57)	-0.15 (-3.08 to 2.72)	**HAL LAI**	NA	NA
-5.93 (-9.98 to -2.39)	**-3.57 (-5.63 to -1.50)**	**-3.30 (-5.09 to -1.61)**	**-2.29 (-4.22 to -0.58)**	**-1.90 (-3.54 to -0.41)**	-1.95 (-4.28 to 0.25)	-2.00 (-5.54 to 1.39)	-2.25 (-10.90 to 5.31)	-1.00 (-3.03 to 0.97)	-1.04 (-3.05 to 1.08)	-0.88 (-3.10 to 1.45)	-0.85 (-2.96 to 1.18)	-0.85 (-2.95 to 1.14)	-0.81 (-3.38 to 1.78)	-0.70 (-2.54 to 0.97)	-0.47 (-4.50 to 3.94)	-0.57 (-2.76 to 1.57)	-0.38 (-2.69 to 1.75)	-0.17 (-3.21 to 2.75)	**LUR**	NA
-5.89 (-9.88 to -2.73)	**-3.55 (-5.13 to -1.86)**	**-3.25 (-4.38 to -2.24)**	**-2.30 (-3.65 to -0.84)**	**-1.90 (-3.31 to -0.49)**	-1.94 (-4.04 to 0.22)	-2.00 (-5.22 to 1.26)	-2.28 (-10.68 to 5.24)	-1.02 (-2.53 to 0.76)	-1.03 (-2.58 to 0.68)	-0.87 (-2.73 to 1.08)	-0.87 (-2.54 to 0.96)	-0.81 (-2.52 to 0.71)	-0.82 (-3.01 to 1.57)	-0.71 (-1.98 to 0.76)	-0.44 (-4.33 to 3.88)	-0.52 (-2.24 to 1.05)	-0.38 (-1.69 to 1.01)	-0.21 (-3.02 to 2.62)	0.02 (-1.85 to 2.01)	**ARI**

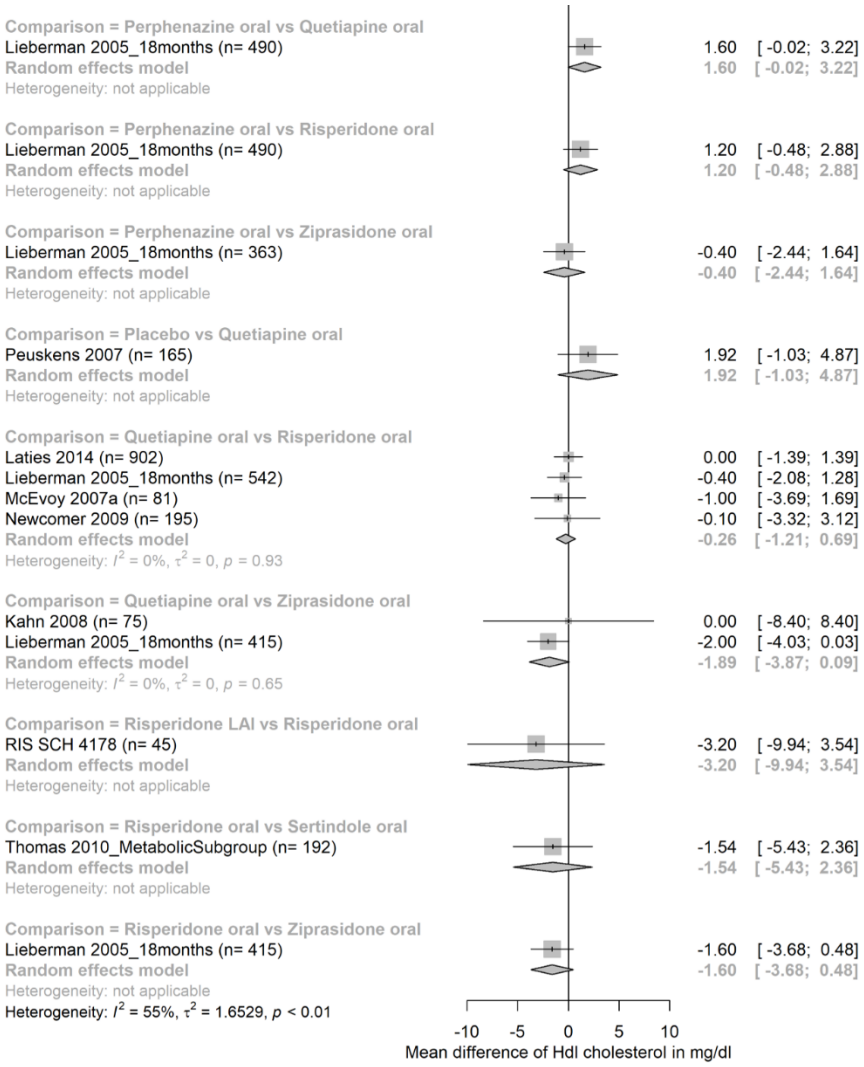
Order of treatments is according to SUCRA ranking. Results of the network meta-analysis are presented in the left lower half and results of pairwise meta-analyses in the right upper half. Each cell provides the effect estimate as mean difference (MD) and the corresponding 95% credible interval (95%CrI) of a comparison (left lower half: treatment in column versus treatment in row; right upper half: treatment in row versus treatment in column). Bold print indicates 95% CrI excluding the point of no effect.

Abbreviations: NA=Not available, LAI=long-acting injectable, AMI=Amisulpride, ARI=Aripiprazole, ASE=Asenapine, BRE=Brexpiprazole, CAR=Cariprazine, CLO=Clozapine, CPZ=Chlorpromazine, FLP=Fluspirilene, FLU=Fluphenazine, FPX=Flupentixol, HAL=Haloperidol, ILO=Iloperidone, LUR=Lurasidone, OLA=Olanzapine, PAL=Paliperidone, PER=Perphenazine, PIM=Pimozide, PLB=Placebo, QUE=Quetiapine, RIS=Risperidone, SER=Sertindole, THIOR=Thioridazine, TIOT=Tiotixene, TRI=Trifluoperazine, ZIP=Ziprasidone, ZOT=Zotepine.

Forest-plot of results of pairwise meta-analyses (also indicating data of individual studies)




Comparison = Haloperidol oral vs Ziprasidone oral
Kahn 2008 (n= 64) 0.00 [-8.40; 8.40]
Random effects model 0.00 [-8.40; 8.40]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Olanzapine oral
Ctri-2014-10-005144 (n= 96) 2.03 [0.93; 3.13]
Random effects model 2.03 [0.93; 3.13]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Placebo
REPRIEVE (n= 204) 0.77 [-1.88; 3.42]
Random effects model 0.77 [-1.88; 3.42]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Placebo
Tandon 2016 (n= 263) 0.20 [-2.11; 2.51]
Random effects model 0.20 [-2.11; 2.51]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Risperidone oral
Citrome 2012 (n= 523) 2.20 [0.54; 3.86]
Random effects model 2.20 [0.54; 3.86]
Heterogeneity: not applicable
Comparison = Olanzapine LAI vs Olanzapine oral
Detke 2014 (n= 486) -0.38 [-2.23; 1.46]
Kane 2010c (n= 819) -0.18 [-1.43; 1.06]
Random effects model -0.25 [-1.28; 0.79]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.86
Comparison = Olanzapine oral vs Paliperidone oral
Schreiner 2012 (n= 414) -1.92 [-3.74; -0.11]
Random effects model -1.92 [-3.74; -0.11]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Perphenazine oral
Lieberman 2005_18months (n= 505) -2.30 [-3.89; -0.71]
Random effects model -2.30 [-3.89; -0.71]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Quetiapine oral
Deberdt 2008 (n= 130) -1.15 [-4.39; 2.09]
Kahn 2008 (n= 108) 0.00 [-8.00; 8.00]
Kinon 2006a (n= 294) -0.38 [-2.50; 1.73]
Lieberman 2005_18months (n= 557) -0.70 [-2.28; 0.88]
McEvoy 2007a (n= 81) -2.90 [-5.48; -0.32]
Newcomer 2009 (n= 205) -0.90 [-4.08; 2.28]
Random effects model -1.02 [-2.03; -0.01]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.76
Comparison = Olanzapine oral vs Risperidone LAI
Keks 2007 (n= 483) -3.12 [-4.80; -1.43]
Random effects model -3.12 [-4.80; -1.43]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Risperidone oral
Lieberman 2005_18months (n= 557) -1.10 [-2.74; 0.54]
McEvoy 2007a (n= 74) -3.90 [-6.54; -1.26]
NCT00236379 (n= 45) 3.50 [-4.33; 11.33]
Newcomer 2009 (n= 222) -1.00 [-4.08; 2.08]
Smith 2009 (n= 46) -1.23 [-5.59; 3.13]
Random effects model -1.60 [-3.10; -0.10]
Heterogeneity: I^2 = 21%, τ^2 = 0.6411, p = 0.28
Comparison = Olanzapine oral vs Ziprasidone oral
Breier 2005 (n= 413) -3.08 [-4.97; -1.19]
Kahn 2008 (n= 97) 0.00 [-4.39; 4.39]
Kinon 2006b (n= 311) -1.37 [-3.75; 1.01]
Lieberman 2005_18months (n= 430) -2.70 [-4.70; -0.70]
Random effects model -2.34 [-3.49; -1.19]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.49
Comparison = Paliperidone LAI vs Placebo
Berwaerts 2015 (n= 290) -1.15 [-3.41; 1.11]
Fu 2015 (n= 250) 0.04 [-4.17; 4.25]
Hough 2010 (n= 380) 0.00 [-1.55; 1.55]
Random effects model -0.33 [-1.56; 0.89]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.70
Comparison = Paliperidone LAI vs Risperidone LAI
Koshikawa 2016 (n= 25) 0.43 [-6.58; 7.44]
NCT00210717 (n= 717) 0.00 [-1.55; 1.55]
Random effects model 0.02 [-1.50; 1.54]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.91
Comparison = Paliperidone oral vs Placebo
Kramer 2007 (n= 171) 1.92 [-0.44; 4.29]
Random effects model 1.92 [-0.44; 4.29]
Heterogeneity: not applicable



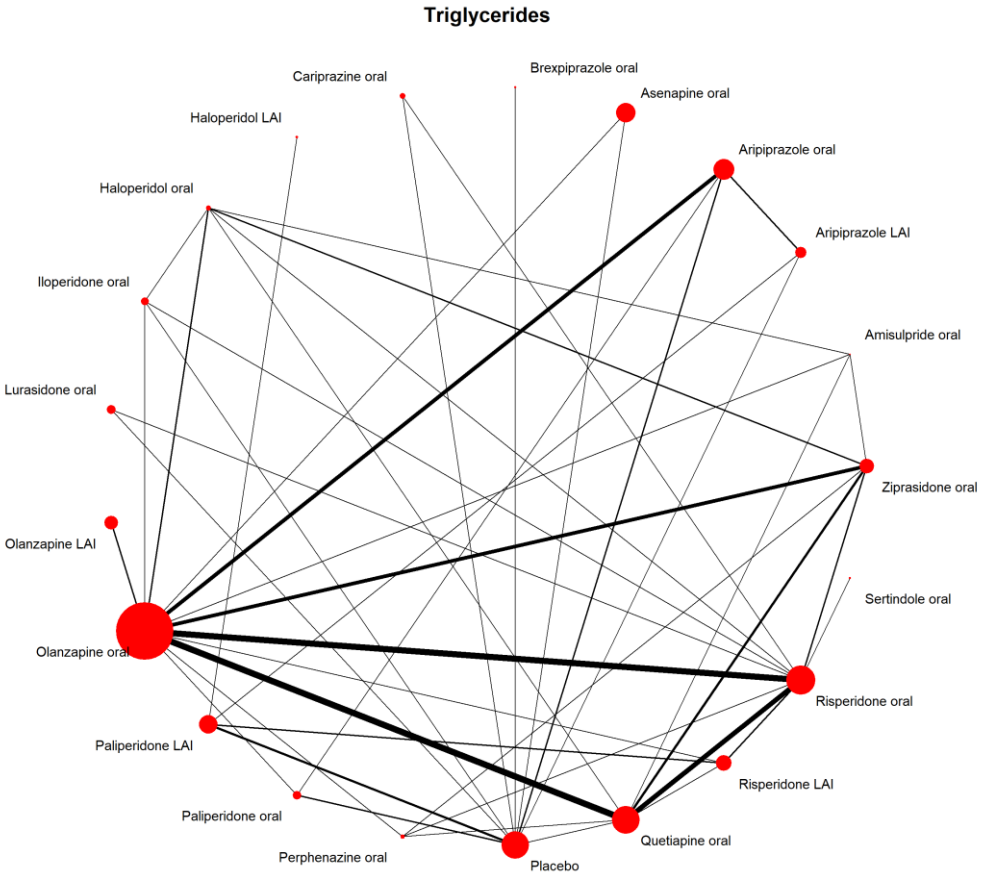
Pairwise meta-analyses are ordered by comparison investigated (in alphabetical order) and a summary effect size is calculated by pairwise meta-analyses of all studies of a specific comparison. The type of effect size measure is mean difference (MD).

Abbreviations: MD=mean difference, 95% CI=95% confidence interval, LAI=long-acting injectable.

7.7 Trigylcerides

55 studies on 20 antipsychotics with 17010 participants included reported on triglycerides.

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Abbreviations: LAI=long-acting injectable.

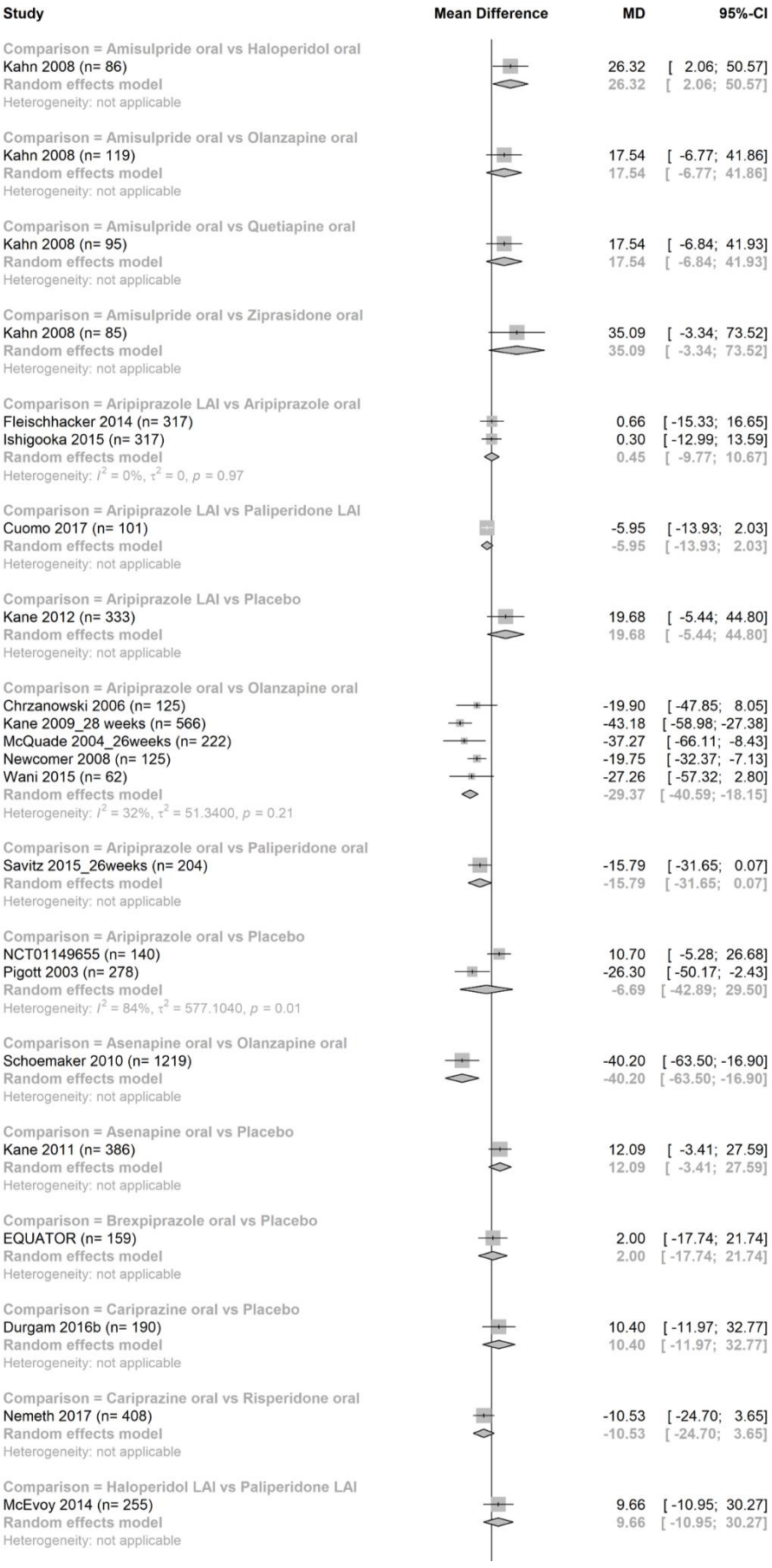
League-table

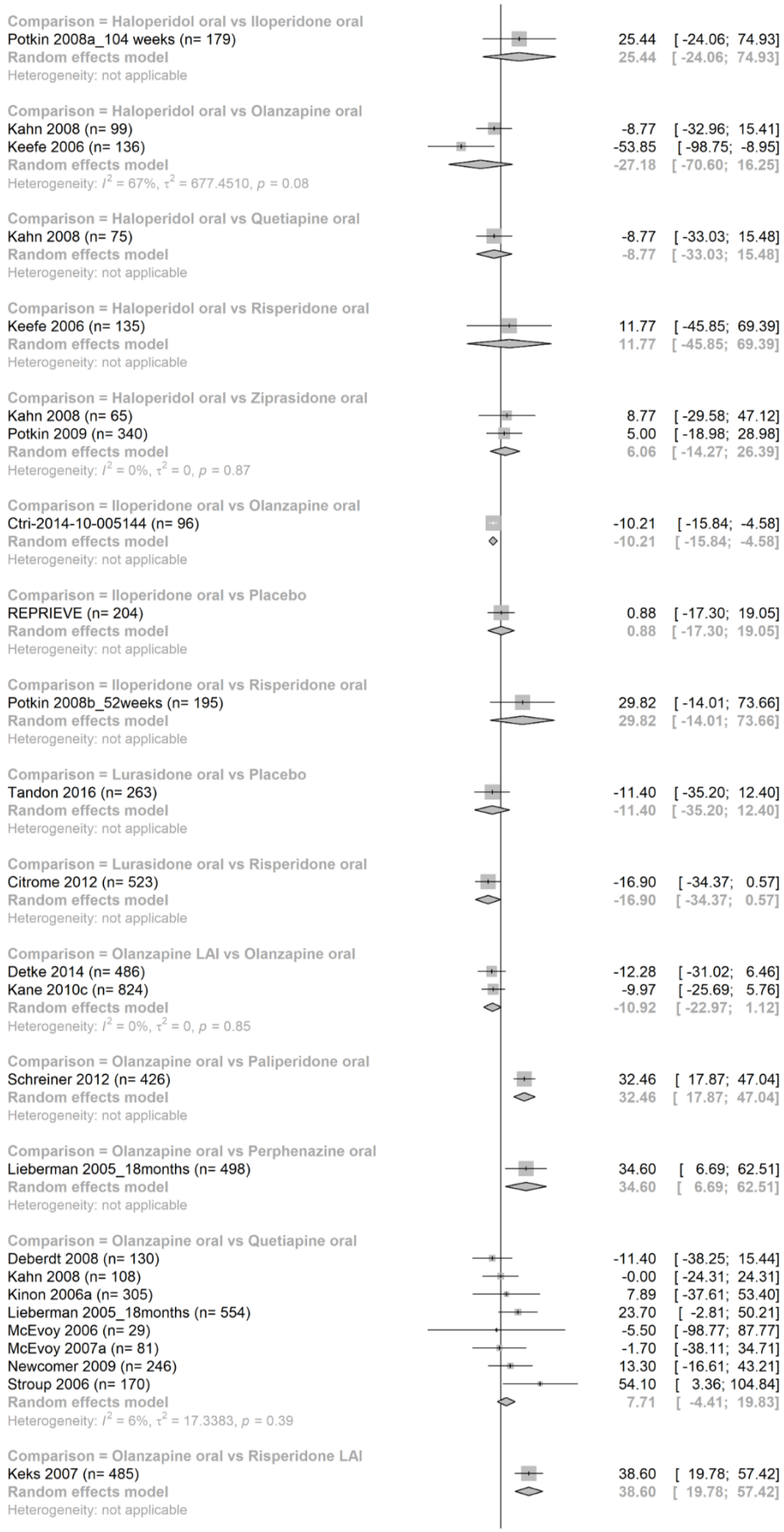
ZIP	NA	NA	NA	NA	NA	NA	NA	-10.46 (-33.27 to 12.34)	NA	NA	-6.26 (-30.65 to 18.14)	-26.40 (-60.53 to 7.73)	NA	NA	NA	NA	NA	**-33.86 (-56.06 to -11.66)**	**-51.55 (-67.02 to -36.08)**	-35.09 (-77.44 to 7.27)
1.25 (-22.88 to 25.07)	**LUR**	NA	NA	-11.40 (-41.12 to 18.32)	NA	NA	NA	-16.90 (-41.85 to 8.05)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-10.84 (-27.10 to 5.80)	-12.07 (-33.65 to 10.02)	**ARI**	NA	-3.81 (-22.46 to 14.84)	NA	-0.47 (-16.75 to 15.82)	NA	NA	NA	-15.79 (-39.64 to 8.06)	NA	NA	NA	NA	NA	NA	NA	NA	**-29.48 (-41.92 to -17.04)**	NA
-10.72 (-34.06 to 12.14)	-12.09 (-38.04 to 13.64)	-0.05 (-21.32 to 20.97)	**CAR**	10.40 (-18.19 to 38.99)	NA	NA	NA	-10.53 (-33.29 to 12.23)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-11.85 (-28.44 to 4.95)	-13.09 (-33.06 to 7.51)	-1.07 (-12.26 to 9.87)	-1.08 (-20.58 to 18.71)	**PLB**	3.37 (-11.24 to 17.98)	-19.68 (-50.47 to 11.11)	-2.00 (-28.58 to 24.58)	NA	-12.09 (-35.70 to 11.52)	-2.10 (-20.92 to 16.72)	NA	NA	NA	NA	NA	-0.88 (-26.32 to 24.57)	NA	-17.54 (-56.38 to 21.29)	NA	NA
-11.70 (-30.03 to 7.26)	-13.01 (-35.26 to 10.07)	-1.01 (-14.74 to 13.54)	-1.02 (-22.83 to 21.78)	0.09 (-11.33 to 12.14)	**PAL LAI**	5.95 (-13.56 to 25.46)	NA	NA	NA	NA	NA	NA	NA	-9.66 (-36.90 to 17.58)	-9.68 (-30.74 to 11.37)	NA	NA	NA	NA	NA
-11.63 (-31.84 to 7.31)	-12.89 (-37.22 to 10.43)	-0.94 (-14.48 to 11.66)	-0.94 (-24.48 to 22.06)	0.14 (-14.37 to 13.47)	0.21 (-15.29 to 13.40)	**ARI LAI**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-14.11 (-45.97 to 17.46)	-15.46 (-48.70 to 18.67)	-3.35 (-32.39 to 25.24)	-3.15 (-36.45 to 30.47)	-2.18 (-28.63 to 24.34)	-2.21 (-31.99 to 26.46)	-2.36 (-31.94 to 28.01)	**BRE**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-14.72 (-29.84 to 1.01)	-15.96 (-35.49 to 3.99)	-3.90 (-17.89 to 10.16)	-3.95 (-22.14 to 14.99)	-2.88 (-16.07 to 10.54)	-3.00 (-19.00 to 12.98)	-3.08 (-19.45 to 15.19)	-0.69 (-30.42 to 29.48)	**RIS**	NA	NA	-11.77 (-72.08 to 48.54)	-10.90 (-42.17 to 20.37)	-6.14 (-30.17 to 17.89)	NA	-3.75 (-32.39 to 24.88)	-29.82 (-77.14 to 17.49)	NA	**-22.50 (-36.75 to -8.24)**	**-33.99 (-48.98 to -19.00)**	NA
-15.89 (-39.53 to 8.04)	-17.48 (-43.57 to 10.27)	-5.29 (-25.28 to 15.32)	-5.19 (-31.32 to 21.96)	-4.22 (-22.67 to 14.87)	-4.27 (-25.71 to 17.16)	-4.30 (-26.00 to 19.29)	-1.99 (-34.09 to 31.10)	-1.28 (-22.58 to 20.10)	**ASE**	NA	NA	NA	NA	NA	NA	NA	NA	NA	**-40.20 (-69.53 to -10.87)**	NA
-16.51 (-35.49 to 2.93)	-17.75 (-40.93 to 5.94)	-5.74 (-19.87 to 8.33)	-5.71 (-28.37 to 17.36)	-4.61 (-18.29 to 8.80)	-4.78 (-21.96 to 11.86)	-4.95 (-21.70 to 13.40)	-2.37 (-32.11 to 27.63)	-1.84 (-18.82 to 14.82)	-0.51 (-22.78 to 21.34)	**PAL**	NA	NA	NA	NA	NA	NA	NA	NA	**-32.46 (-55.47 to -9.44)**	NA
-18.75 (-37.22 to 0.55)	-19.94 (-46.17 to 7.21)	-7.99 (-28.28 to 12.95)	-7.92 (-33.78 to 18.88)	-6.90 (-27.06 to 13.58)	-7.03 (-29.18 to 15.56)	-7.04 (-29.01 to 16.51)	-4.77 (-38.35 to 29.22)	-4.07 (-23.81 to 16.16)	-2.69 (-28.99 to 23.46)	-2.35 (-24.85 to 20.90)	**HAL**	NA	NA	NA	NA	25.44 (-27.16 to 78.04)	NA	-8.77 (-38.86 to 21.32)	-21.34 (-46.84 to 4.17)	-26.32 (-56.40 to 3.77)
-20.76 (-50.19 to 9.52)	-21.92 (-56.50 to 11.99)	-9.84 (-40.71 to 19.96)	-9.89 (-43.05 to 23.52)	-8.79 (-39.49 to 20.83)	-8.85 (-40.70 to 21.87)	-8.96 (-40.73 to 22.82)	-6.65 (-46.53 to 33.07)	-5.89 (-34.72 to 22.02)	-4.47 (-39.18 to 29.33)	-4.18 (-36.46 to 26.83)	-1.91 (-35.22 to 30.95)	**PER**	NA	NA	NA	NA	NA	-10.90 (-46.35 to 24.55)	**-34.60 (-67.71 to -1.49)**	NA
-20.84 (-48.46 to 7.64)	-21.89 (-52.69 to 9.01)	-9.93 (-36.98 to 17.25)	-10.03 (-39.67 to 20.96)	-8.79 (-35.51 to 18.02)	-8.92 (-37.14 to 19.09)	-9.10 (-37.18 to 20.85)	-6.73 (-44.88 to 31.47)	-5.98 (-29.74 to 17.64)	-4.63 (-37.26 to 26.43)	-4.13 (-33.03 to 24.32)	-1.87 (-32.94 to 28.73)	-0.18 (-36.76 to 37.30)	**SER**	NA	NA	NA	NA	NA	NA	NA
-21.15 (-53.69 to 11.31)	-22.49 (-57.78 to 12.61)	-10.45 (-40.62 to 19.93)	-10.39 (-44.74 to 24.31)	-9.22 (-38.70 to 19.68)	-9.37 (-36.72 to 17.24)	-9.32 (-39.60 to 21.77)	-7.18 (-46.60 to 32.42)	-6.35 (-37.81 to 24.19)	-5.20 (-39.89 to 29.15)	-4.67 (-36.80 to 26.99)	-2.36 (-37.58 to 31.91)	-0.45 (-41.51 to 40.06)	-0.21 (-39.83 to 38.24)	**HAL LAI**	NA	NA	NA	NA	NA	NA
-20.24 (-38.86 to -1.46)	-21.51 (-45.18 to 2.33)	-9.47 (-25.92 to 6.65)	-9.41 (-31.71 to 13.58)	-8.40 (-23.83 to 6.63)	-8.45 (-24.12 to 6.32)	-8.56 (-26.48 to 10.11)	-6.31 (-36.96 to 25.22)	-5.52 (-21.11 to 9.62)	-4.17 (-27.66 to 18.17)	-3.72 (-22.65 to 14.70)	-1.60 (-24.62 to 20.57)	0.69 (-30.91 to 30.86)	0.60 (-27.94 to 28.23)	0.83 (-30.16 to 31.79)	**RIS LAI**	NA	NA	5.26 (-22.82 to 33.34)	**-38.60 (-64.51 to -12.69)**	NA
-26.54 (-44.42 to -5.99)	**-27.72 (-50.62 to -2.01)**	-15.73 (-31.02 to 2.24)	-15.60 (-38.00 to 9.52)	-14.66 (-29.36 to 3.01)	-14.79 (-32.30 to 5.18)	-14.77 (-32.95 to 7.19)	-12.41 (-42.23 to 19.99)	-11.80 (-27.64 to 6.36)	-10.44 (-32.96 to 13.46)	-10.04 (-28.07 to 10.66)	-7.73 (-29.02 to 15.15)	-5.67 (-36.48 to 27.53)	-5.58 (-33.43 to 24.19)	-5.29 (-36.47 to 28.54)	-6.18 (-24.57 to 14.92)	**ILO**	NA	NA	-10.21 (-28.89 to 8.47)	NA
-32.27 (-54.37 to -10.13)	**-33.63 (-60.83 to -6.07)**	**-21.50 (-41.88 to -1.38)**	-21.37 (-48.20 to 4.91)	-20.46 (-41.68 to 0.40)	-20.58 (-43.42 to 1.85)	-20.69 (-43.43 to 3.08)	-18.23 (-52.49 to 15.86)	-17.62 (-38.57 to 3.08)	-16.36 (-43.35 to 9.31)	-15.72 (-38.57 to 6.94)	-13.75 (-39.25 to 11.89)	-11.79 (-45.09 to 22.31)	-11.56 (-43.10 to 19.86)	-11.26 (-45.89 to 24.17)	-12.11 (-34.76 to 10.83)	-5.86 (-29.93 to 15.55)	**OLA LAI**	NA	-11.03 (-28.52 to 6.47)	NA
-33.62 (-49.00 to -18.30)	**-35.00 (-56.79 to -12.67)**	**-22.93 (-37.52 to -8.87)**	**-22.88 (-43.55 to -1.99)**	**-21.87 (-35.81 to -7.79)**	**-21.98 (-38.49 to -5.75)**	**-21.92 (-39.07 to -3.80)**	-19.58 (-49.84 to 10.97)	**-19.03 (-30.74 to -7.37)**	-17.79 (-39.42 to 3.72)	**-17.25 (-34.53 to -0.24)**	-14.96 (-34.95 to 4.14)	-13.02 (-42.07 to 15.75)	-12.96 (-39.64 to 13.39)	-12.56 (-43.53 to 19.18)	-13.44 (-28.79 to 2.05)	-7.24 (-26.19 to 8.89)	-1.25 (-22.31 to 19.07)	**QUE**	-8.14 (-21.81 to 5.52)	-17.54 (-47.74 to 12.65)
-43.32 (-57.03 to -29.92)	**-44.66 (-65.54 to -23.39)**	**-32.56 (-42.85 to -22.65)**	**-32.59 (-52.70 to -12.25)**	**-31.66 (-42.84 to -20.32)**	**-31.61 (-46.24 to -17.69)**	**-31.72 (-46.21 to -16.25)**	-29.34 (-58.19 to 0.20)	**-28.70 (-40.01 to -17.67)**	**-27.29 (-47.20 to -8.36)**	**-26.92 (-41.17 to -12.79)**	**-24.64 (-43.22 to -6.76)**	-22.76 (-51.28 to 6.24)	-22.67 (-49.03 to 3.10)	-22.22 (-52.43 to 7.90)	**-23.09 (-37.83 to -8.64)**	**-16.80 (-33.01 to -4.06)**	-11.16 (-28.62 to 6.39)	-9.70 (-20.73 to 1.89)	**OLA**	-17.54 (-47.68 to 12.59)
-50.95 (-78.09 to -24.51)	**-52.28 (-84.01 to -20.69)**	**-40.13 (-67.24 to -13.94)**	**-40.34 (-71.69 to -8.88)**	**-38.98 (-66.49 to -12.66)**	**-39.26 (-67.66 to -11.40)**	**-39.18 (-67.97 to -10.76)**	-36.73 (-75.02 to 0.21)	**-36.36 (-63.01 to -10.81)**	**-34.96 (-67.02 to -3.87)**	**-34.40 (-62.98 to -6.93)**	**-31.95 (-59.46 to -5.96)**	-30.30 (-67.31 to 6.40)	-30.08 (-66.43 to 4.72)	-29.87 (-68.54 to 8.95)	**-30.93 (-58.97 to -3.05)**	-24.46 (-54.27 to 2.76)	-18.57 (-49.59 to 11.66)	-17.21 (-43.05 to 7.52)	-7.50 (-32.72 to 17.10)	**AMI**

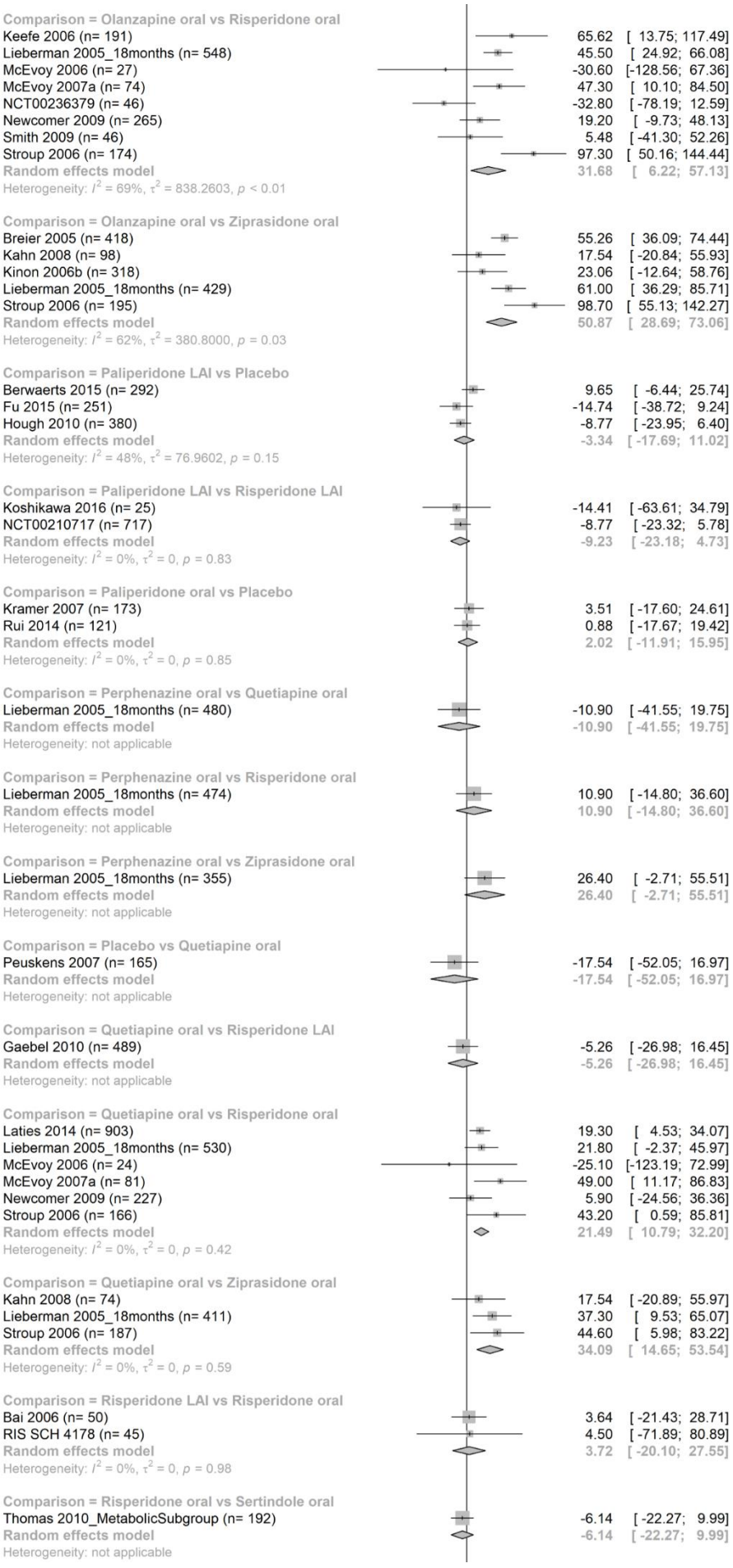
Order of treatments is according to SUCRA ranking. Results of the network meta-analysis are presented in the left lower half and results of pairwise meta-analyses in the right upper half. Each cell provides the effect estimate as mean difference (MD)and the corresponding 95% credible interval (95%CrI) of a comparison (left lower half: treatment in column versus treatment in row; right upper half: treatment in row versus treatment in column). Bold print indicates 95% CrI excluding the point of no effect.

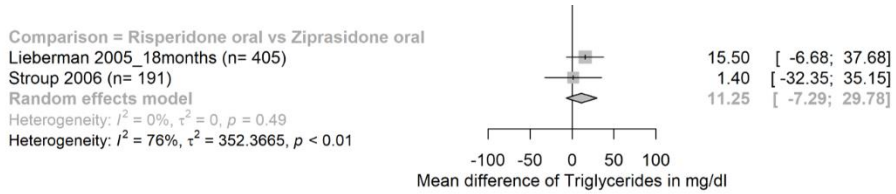
Abbreviations: NA=Not available, LAI=long-acting injectable, AMI=Amisulpride, ARI=Aripiprazole, ASE=Asenapine, BRE=Brexpiprazole, CAR=Cariprazine, CLO=Clozapine, CPZ=Chlorpromazine, FLP=Fluspirilene, FLU=Fluphenazine, FPX=Flupentixol, HAL=Haloperidol, ILO=Iloperidone, LUR=Lurasidone, OLA=Olanzapine, PAL=Paliperidone, PER=Perphenazine, PIM=Pimozide, PLB=Placebo, QUE=Quetiapine, RIS=Risperidone, SER=Sertindole, THIOR=Thioridazine, TIOT=Tiotixene, TRI=Trifluoperazine, ZIP=Ziprasidone, ZOT=Zotepine.

Forest-plot of results of pairwise meta-analyses (also indicating data of individual studies)




Comparison = Haloperidol oral vs Iloperidone oral
Potkin 2008a_104 weeks (n= 179) 25.44 [-24.06; 74.93]
Random effects model 25.44 [-24.06; 74.93]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Olanzapine oral
Kahn 2008 (n= 99) -8.77 [-32.96; 15.41]
Keefe 2006 (n= 136) -53.85 [-98.75; -8.95]
Random effects model -27.18 [-70.60; 16.25]
Heterogeneity: I^2 = 67%, τ^2 = 677.4510, p = 0.08
Comparison = Haloperidol oral vs Quetiapine oral
Kahn 2008 (n= 75) -8.77 [-33.03; 15.48]
Random effects model -8.77 [-33.03; 15.48]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Risperidone oral
Keefe 2006 (n= 135) 11.77 [-45.85; 69.39]
Random effects model 11.77 [-45.85; 69.39]
Heterogeneity: not applicable
Comparison = Haloperidol oral vs Ziprasidone oral
Kahn 2008 (n= 65) 8.77 [-29.58; 47.12]
Potkin 2009 (n= 340) 5.00 [-18.98; 28.98]
Random effects model 6.06 [-14.27; 26.39]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.87
Comparison = Iloperidone oral vs Olanzapine oral
Ctri-2014-10-005144 (n= 96) -10.21 [-15.84; -4.58]
Random effects model -10.21 [-15.84; -4.58]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Placebo
REPRIEVE (n= 204) 0.88 [-17.30; 19.05]
Random effects model 0.88 [-17.30; 19.05]
Heterogeneity: not applicable
Comparison = Iloperidone oral vs Risperidone oral
Potkin 2008b_52weeks (n= 195) 29.82 [-14.01; 73.66]
Random effects model 29.82 [-14.01; 73.66]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Placebo
Tandon 2016 (n= 263) -11.40 [-35.20; 12.40]
Random effects model -11.40 [-35.20; 12.40]
Heterogeneity: not applicable
Comparison = Lurasidone oral vs Risperidone oral
Citrome 2012 (n= 523) -16.90 [-34.37; 0.57]
Random effects model -16.90 [-34.37; 0.57]
Heterogeneity: not applicable
Comparison = Olanzapine LAI vs Olanzapine oral
Detke 2014 (n= 486) -12.28 [-31.02; 6.46]
Kane 2010c (n= 824) -9.97 [-25.69; 5.76]
Random effects model -10.92 [-22.97; 1.12]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.85
Comparison = Olanzapine oral vs Paliperidone oral
Schreiner 2012 (n= 426) 32.46 [17.87; 47.04]
Random effects model 32.46 [17.87; 47.04]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Perphenazine oral
Lieberman 2005_18months (n= 498) 34.60 [6.69; 62.51]
Random effects model 34.60 [6.69; 62.51]
Heterogeneity: not applicable
Comparison = Olanzapine oral vs Quetiapine oral
Deberdt 2008 (n= 130) -11.40 [-38.25; 15.44]
Kahn 2008 (n= 108) -0.00 [-24.31; 24.31]
Kinon 2006a (n= 305) 7.89 [-37.61; 53.40]
Lieberman 2005_18months (n= 554) 23.70 [-2.81; 50.21]
McEvoy 2006 (n= 29) -5.50 [-98.77; 87.77]
McEvoy 2007a (n= 81) -1.70 [-38.11; 34.71]
Newcomer 2009 (n= 246) 13.30 [-16.61; 43.21]
Stroup 2006 (n= 170) 54.10 [3.36; 104.84]
Random effects model 7.71 [-4.41; 19.83]
Heterogeneity: I^2 = 6%, τ^2 = 17.3383, p = 0.39
Comparison = Olanzapine oral vs Risperidone LAI
Keks 2007 (n= 485) 38.60 [19.78; 57.42]
Random effects model 38.60 [19.78; 57.42]
Heterogeneity: not applicable


Comparison = Olanzapine oral vs Risperidone oral
Keefe 2006 (n= 191) 65.62 [13.75; 117.49]
Lieberman 2005_18months (n= 548) 45.50 [24.92; 66.08]
McEvoy 2006 (n= 27) -30.60 [-128.56; 67.36]
McEvoy 2007a (n= 74) 47.30 [10.10; 84.50]
NCT00236379 (n= 46) -32.80 [-78.19; 12.59]
Newcomer 2009 (n= 265) 19.20 [-9.73; 48.13]
Smith 2009 (n= 46) 5.48 [-41.30; 52.26]
Stroup 2006 (n= 174) 97.30 [50.16; 144.44]
Random effects model 31.68 [6.22; 57.13]
Heterogeneity: I^2 = 69%, τ^2 = 838.2603, p < 0.01
Comparison = Olanzapine oral vs Ziprasidone oral
Breier 2005 (n= 418) 55.26 [36.09; 74.44]
Kahn 2008 (n= 98) 17.54 [-20.84; 55.93]
Kinon 2006b (n= 318) 23.06 [-12.64; 58.76]
Lieberman 2005_18months (n= 429) 61.00 [36.29; 85.71]
Stroup 2006 (n= 195) 98.70 [55.13; 142.27]
Random effects model 50.87 [28.69; 73.06]
Heterogeneity: I^2 = 62%, τ^2 = 380.8000, p = 0.03
Comparison = Paliperidone LAI vs Placebo
Berwaerts 2015 (n= 292) 9.65 [-6.44; 25.74]
Fu 2015 (n= 251) -14.74 [-38.72; 9.24]
Hough 2010 (n= 380) -8.77 [-23.95; 6.40]
Random effects model -3.34 [-17.69; 11.02]
Heterogeneity: I^2 = 48%, τ^2 = 76.9602, p = 0.15
Comparison = Paliperidone LAI vs Risperidone LAI
Koshikawa 2016 (n= 25) -14.41 [-63.61; 34.79]
NCT00210717 (n= 717) -8.77 [-23.32; 5.78]
Random effects model -9.23 [-23.18; 4.73]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.83
Comparison = Paliperidone oral vs Placebo
Kramer 2007 (n= 173) 3.51 [-17.60; 24.61]
Rui 2014 (n= 121) 0.88 [-17.67; 19.42]
Random effects model 2.02 [-11.91; 15.95]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.85
Comparison = Perphenazine oral vs Quetiapine oral
Lieberman 2005_18months (n= 480) -10.90 [-41.55; 19.75]
Random effects model -10.90 [-41.55; 19.75]
Heterogeneity: not applicable
Comparison = Perphenazine oral vs Risperidone oral
Lieberman 2005_18months (n= 474) 10.90 [-14.80; 36.60]
Random effects model 10.90 [-14.80; 36.60]
Heterogeneity: not applicable
Comparison = Perphenazine oral vs Ziprasidone oral
Lieberman 2005_18months (n= 355) 26.40 [-2.71; 55.51]
Random effects model 26.40 [-2.71; 55.51]
Heterogeneity: not applicable
Comparison = Placebo vs Quetiapine oral
Peuskens 2007 (n= 165) -17.54 [-52.05; 16.97]
Random effects model -17.54 [-52.05; 16.97]
Heterogeneity: not applicable
Comparison = Quetiapine oral vs Risperidone LAI
Gaebel 2010 (n= 489) -5.26 [-26.98; 16.45]
Random effects model -5.26 [-26.98; 16.45]
Heterogeneity: not applicable
Comparison = Quetiapine oral vs Risperidone oral
Laties 2014 (n= 903) 19.30 [4.53; 34.07]
Lieberman 2005_18months (n= 530) 21.80 [-2.37; 45.97]
McEvoy 2006 (n= 24) -25.10 [-123.19; 72.99]
McEvoy 2007a (n= 81) 49.00 [11.17; 86.83]
Newcomer 2009 (n= 227) 5.90 [-24.56; 36.36]
Stroup 2006 (n= 166) 43.20 [0.59; 85.81]
Random effects model 21.49 [10.79; 32.20]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.42
Comparison = Quetiapine oral vs Ziprasidone oral
Kahn 2008 (n= 74) 17.54 [-20.89; 55.97]
Lieberman 2005_18months (n= 411) 37.30 [9.53; 65.07]
Stroup 2006 (n= 187) 44.60 [5.98; 83.22]
Random effects model 34.09 [14.65; 53.54]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.59
Comparison = Risperidone LAI vs Risperidone oral
Bai 2006 (n= 50) 3.64 [-21.43; 28.71]
RIS SCH 4178 (n= 45) 4.50 [-71.89; 80.89]
Random effects model 3.72 [-20.10; 27.55]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.98
Comparison = Risperidone oral vs Sertindole oral
Thomas 2010_MetabolicSubgroup (n= 192) -6.14 [-22.27; 9.99]
Random effects model -6.14 [-22.27; 9.99]
Heterogeneity: not applicable



Pairwise meta-analyses are ordered by comparison investigated (in alphabetical order) and a summary effect size is calculated by pairwise meta-analyses of all studies of a specific comparison. The type of effect size measure is mean difference (MD).

Abbreviations: MD=mean difference, 95% CI=95% confidence interval, LAI=long-acting injectable.

7.8 Map of antipsychotics ranked according to associated alteration in "weight gain" and metabolic parameters – in colour

	Weight gain	Fasting glucose	Total cholesterol	Ldl cholesterol	Hdl cholesterol	Triglycerides
Fluspirilene LAI	-9.13 (-19.02 to 1.43)					
Haloperidol LAI	-2.53 (-5.32 to 0.26)	0.84 (-11.92 to 13.36)	7.68 (-3.09 to 18.90)	4.00 (-4.67 to 13.15)	0.49 (-2.08 to 3.04)	9.22 (-19.68 to 38.70)
Fluphenazine LAI	-1.94 (-5.24 to 1.37)					
Fluphenazine	-1.30 (-4.45 to 1.93)		15.45 (-19.43 to 51.29)			
Ziprasidone	-0.16 (-1.15 to 0.84)	-0.67 (-5.40 to 4.24)	-4.69 (-10.39 to 1.23)	-1.32 (-7.32 to 4.38)	-0.14 (-1.74 to 1.38)	-11.85 (-28.44 to 4.95)
Haloperidol	-0.01 (-0.81 to 0.80)	2.72 (-2.32 to 7.96)	2.77 (-3.21 to 8.69)	1.49 (-14.95 to 20.28)	-1.58 (-9.94 to 5.91)	6.90 (-13.58 to 27.06)
Placebo	0	0	0	0	0	0
Lurasidone	-0.06 (-1.40 to 1.31)	0.96 (-5.33 to 7.43)	3.88 (-3.11 to 11.07)	5.08 (-0.94 to 10.65)	0.70 (-0.97 to 2.54)	-13.09 (-33.06 to 7.51)
Aripiprazole LAI	-0.00 (-1.08 to 1.08)	2.35 (-1.51 to 6.53)	2.51 (-3.35 to 8.05)	0.60 (-4.06 to 5.49)	0.32 (-1.26 to 1.81)	-0.14 (-13.47 to 14.37)
Flupentixol	0.10 (-3.08 to 3.35)					
Aripiprazole	0.41 (-0.40 to 1.28)	0.35 (-2.40 to 3.28)	-0.75 (-4.90 to 3.21)	-1.92 (-5.64 to 1.96)	0.71 (-0.76 to 1.98)	-1.07 (-12.26 to 9.87)
Perphenazine	0.61 (-0.76 to 2.01)		4.46 (-3.72 to 12.73)		-0.18 (-1.98 to 1.66)	8.79 (-20.83 to 39.49)
Cariprazine	0.62 (-0.82 to 2.05)	1.76 (-2.82 to 6.42)	-0.55 (-8.18 to 7.52)	0.73 (-5.51 to 6.97)	-1.22 (-3.25 to 0.73)	-1.08 (-20.58 to 18.71)
Asenapine	0.73 (-0.32 to 1.81)	3.37 (-0.80 to 7.36)	4.86 (-1.25 to 11.32)	3.25 (-2.93 to 9.67)	-0.12 (-1.90 to 1.77)	4.22 (-14.87 to 22.67)
Iloperidone	0.78 (-0.56 to 2.15)	-0.24 (-4.40 to 4.57)	-0.59 (-9.37 to 8.02)	2.36 (-3.70 to 7.67)	-0.33 (-1.80 to 1.27)	14.66 (-3.01 to 29.36)
Amisulpride	1.43 (0.45 to 2.41)	2.13 (-2.72 to 7.04)	9.77 (-6.96 to 26.68)	9.72 (-6.90 to 26.88)	-5.24 (-8.94 to -2.05)	38.98 (12.66 to 66.49)
Paliperidone LAI	1.43 (0.55 to 2.33)	0.83 (-2.49 to 4.00)	3.31 (-1.18 to 8.13)	2.29 (-1.62 to 6.35)	-0.30 (-1.48 to 0.93)	-0.09 (-12.14 to 11.33)
Quetiapine	1.59 (0.79 to 2.42)	3.14 (0.09 to 6.33)	8.20 (3.33 to 13.30)	5.87 (1.33 to 10.51)	-1.59 (-2.91 to -0.27)	21.87 (7.79 to 35.81)
Paliperidone	1.73 (0.70 to 2.78)	1.85 (-1.89 to 5.64)	7.58 (2.21 to 13.17)	3.35 (-1.44 to 8.56)	0.15 (-1.42 to 1.75)	4.61 (-8.80 to 18.29)
Brexpiprazole	1.91 (-0.13 to 3.94)	3.62 (-4.37 to 11.71)	-0.28 (-14.06 to 13.51)	2.18 (-9.70 to 14.08)	-1.31 (-4.31 to 1.70)	2.18 (-24.34 to 28.63)
Risperidone	1.87 (1.12 to 2.65)	3.51 (0.21 to 6.80)	3.62 (-0.93 to 8.28)	4.02 (-0.91 to 9.04)	-1.20 (-2.45 to 0.15)	2.88 (-10.54 to 16.07)
Risperidone LAI	2.00 (0.85 to 3.16)	3.34 (-0.38 to 7.21)	7.58 (2.33 to 12.90)	5.84 (0.49 to 11.38)	-0.17 (-1.61 to 1.40)	8.40 (-6.63 to 23.83)
Sertindole	2.30 (0.43 to 4.31)	6.44 (-0.21 to 13.06)	9.07 (-6.01 to 24.54)	6.91 (-5.68 to 19.49)	0.24 (-3.42 to 4.61)	8.79 (-18.02 to 35.51)
Olanzapine LAI	3.60 (2.12 to 5.12)	7.64 (3.17 to 13.20)	12.02 (5.07 to 19.01)	9.59 (3.61 to 15.49)	-2.91 (-4.45 to -1.18)	20.46 (-0.40 to 41.68)
Pimozide	6.16 (-1.78 to 13.74)					
Zotepine	3.87 (2.14 to 5.58)					
Olanzapine	3.82 (3.15 to 4.50)	5.07 (2.44 to 7.98)	12.65 (8.73 to 16.51)	8.09 (4.32 to 11.89)	-2.59 (-3.71 to -1.44)	31.66 (20.32 to 42.84)
Clozapine	4.21 (3.03 to 5.42)	1.64 (-7.08 to 10.26)	15.83 (-2.44 to 32.73)			
Chlorpromazine	5.13 (1.98 to 8.30)	4.94 (-7.93 to 18.90)	13.00 (-2.21 to 29.08)			

Numbers present the MDs with their 95% CrIs from the network-meta-analysis compared to placebo. The order of treatments is according to SUCRA value of the primary outcome weight gain. Colours represent the SUCRA value with more red indicating a higher probability of being the worst drug. Grey cells indicate that no data were available.

Abbreviations: CrI=credible interval, MD=mean difference.

8 Inconsistency in the network meta-analyses of the primary and secondary outcomes

Summary of results:

There was no evidence of inconsistency in direct and indirect estimates for the primary outcome "weight gain", total cholesterol, LDL cholesterol and HDL cholesterol. Little evidence of inconsistency was observed for number of participants with weight gain, fasting glucose and triglycerides.

Details:

In network meta-analysis, consistency is the agreement between direct and indirect evidence.

We employed global as well as local methods to evaluate consistency.

We investigated consistency locally, i.e. for each comparison that is part of a closed loop, by a SIDE-(Separating Indirect from Direct Evidence)-test [364].

We investigated consistency globally, i.e. of the network as a whole, by a Design-by-treatment interaction test [365].

Outcome	**Type of outcome**	**Model**	**Number of studies (comparisons) [interventions]**	**Inconsistent comparisons of detachable comparisons (%) (SIDE-test p <0.10)**	**p-value of Design-by-treatment test**	**Judgement**
Weight gain	Continuous	Frequentist	110 (57) [29]	5 of 57 (8.8%)	0.471	No evidence of inconsistency
Weight gain	Dichotomous	Frequentist	106 (62) [30]	7 of 62 (11.3%)	0.189	Little evidence of inconsistency
Fasting glucose	Continuous	Frequentist	50 (39) [22]	5 of 39 (12.8%)	0.263	Little evidence of inconsistency
Total cholesterol	Continuous	Frequentist	63 (46) [24]	2 of 46 (4.3%)	0.453	No evidence of inconsistency
LDL cholesterol	Continuous	Frequentist	40 (29) [20]	0 of 29 (0%)	0.443	No evidence of inconsistency
HDL cholesterol	Continuous	Frequentist	45 (35) [21]	3 of 35 (8.6%)	0.654	No evidence of inconsistency
Triglycerides	Continuous	Frequentist	55 (42) [21]	1 of 42 (2.4%)	0.082	Little evidence of inconsistency

It needs to be considered that the statistical power of tests for inconsistency are low when a network is not well connected and/or when there are few/small studies per comparison which is the case for some secondary networks (see network plots).

9 Heterogeneity in the network meta-analysis of the primary outcome "weight gain"

Summary of results:

Estimated across the various treatment comparisons in the NMA, the heterogeneity standard deviation (common-τ) of the Bayesian random effects model was 0.82 kg. No empirical comparators are available to judge heterogeneity for our primary outcome "weight gain" measured as mean difference (MD). Therefore, we additionally calculated effect sizes in standardized mean difference (SMD) in a frequentist setting for which an emipirical comparator exist and found low to moderate heterogeneity in comparison with the empirical comparator.

Moreover, we estimated prediction intervals for antipsychotics vs. placebo to assess how much the common heterogeneity affects the relative effect with respect to the extra uncertainty anticipated in a future study. We judged heterogeneity as moderate because the prediction intervals of 15/28 comparisons were different compared to credible intervals in regard to clinically important thresholds followin the CINeMA approach.

Details:

In the table the estimator of between-study-heterogeneity common-τ of the primary outcome is presented. Unfortunately, no empirical comparator is available to judge heterogeneity. As Rhodes et al. [366] provided empirical distributions for continuous outcomes only measured as standardized mean difference, we additionally calculated effect sizes in SMD in a frequentist setting and found low to moderate heterogeneity for our primary outcome weight gain.

Outcome	**Common-τ of the Bayesian model estimated in NMA**	**Outcome type used as comparator ***	**Empirical predictive distribution of τ**	**Location of the estimated common-τ compared to the quartiles of the empirical predictive distribution**	**Judgement of heterogeneity**
Continuous	**Mean**	**From Rhodes et al. [366]**	**Median (IQR)**		
Body weight (MD [kg])	0.82	Outcome estimated as mean difference (MD). No comparator available			
Body weight (SMD)	0.15	Biological marker	0.16 (IQR 0.06, 0.44)	Between 25%- and 50%-quantile	low-moderate

**Intervention comparison type pharmacological vs pharmacological*

We present in the following table the results for the primary outcome “weight gain” antipsychotics vs. placebo with prediction intervals. Prediction intervals, which capture heterogeneity, inform about the range of possible effects which could be expected in future studies in different settings. This can be also interpreted as the range of possible effects which could be expected for different patients and is therefore valuable for clinical interpretation [367]. Additionally, following the CINeMA approach [368], we assessed whether the prediction intervals were different compared to credible intervals in regard to the clincally important thresholds (-2/ +2 kg) and the line of no effect (0 kg). We observed that for 14 comparisons prediction intervals in contrast to the credible intervals crossed one threshold (= some concerns) and for one comparison the prediction interval crossed of these clinically important thresholds two (= major concerns). Therefore, overall, we judge the impact of heterogeneity on the interpretation of the primary results as moderate. Please note that the impact of heterogeneity for each possible comparison in the network is included in the CINeMA assessment (see appendix 15).

Drug	**Mean difference**	**Lower limit of 95%-CrI**	**Higher limit of 95%-CrI**	**Lower limit of prediction interval**	**Higher limit of prediction interval**	**Judgement following CINeMA**
Fluspirilene LAI	-9,13	-19,02	1,43	-19,503	1,565	no concerns
Haloperidol LAI	-2,53	-5,32	0,26	-5,679	0,624	no concerns
Fluphenazine LAI	-1,94	-5,24	1,37	-5,478	1,67	no concerns
Fluphenazine oral	-1,3	-4,45	1,93	-4,831	2,229	some concerns
Ziprasidone oral	-0,16	-1,15	0,84	-2,074	1,742	some concerns
Haloperidol oral	-0,01	-0,81	0,8	-1,811	1,843	no concerns
Placebo	0					
Lurasidone oral	-0,06	-1,4	1,31	-2,135	2,08	major concerns
Aripiprazole LAI	0	-1,08	1,08	-1,958	2,003	some concerns
Flupentixol oral	0,1	-3,08	3,35	-3,515	3,674	no concerns
Aripiprazole oral	0,41	-0,4	1,28	-1,429	2,278	some concerns
Perphenazine oral	0,61	-0,76	2,01	-1,498	2,748	no concerns
Cariprazine oral	0,62	-0,82	2,05	-1,568	2,813	no concerns
Asenapine oral	0,73	-0,32	1,81	-1,228	2,683	some concerns
Iloperidone oral	0,78	-0,56	2,15	-1,357	2,923	no concerns
Amisulpride oral	1,43	0,45	2,41	-0,461	3,348	some concerns
Paliperidone LAI	1,43	0,55	2,33	-0,432	3,294	some concerns
Quetiapine oral	1,59	0,79	2,42	-0,191	3,439	some concerns
Paliperidone oral	1,73	0,7	2,78	-0,206	3,684	some concerns
Brexpiprazole oral	1,91	-0,13	3,94	-0,735	4,492	no concerns
Risperidone oral	1,87	1,12	2,65	0,1	3,728	no concerns
Risperidone LAI	2	0,85	3,16	-0,006	4,007	some concerns
Sertindole oral	2,3	0,43	4,31	-0,151	4,877	some concerns
Olanzapine LAI	3,6	2,12	5,12	1,422	5,815	some concerns
Pimozide oral	6,16	-1,78	13,74	-2,001	13,705	some concerns
Zotepine oral	3,87	2,14	5,58	1,492	6,293	some concerns
Olanzapine oral	3,82	3,15	4,5	2,084	5,618	no concerns

Clozapine oral	4,21	3,03	5,42	2,195	6,289	no concerns
Chlorpromazine oral	5,13	1,98	8,3	1,53	8,559	no concerns

10 Results of the network meta-regression analyses of the primary outcome "weight gain"

First we present a summary of the results of the different network meta-regression analyses conducted.

Then we present for each network meta-regression analysis (in this order)

- Network plot (because the network can be different from the primary network because not all studies reported the explored moderator)
- Forest-plot of results of adjusted network meta-analysis (reference intervention placebo)

Summary of results:

In network meta-regression analyses, we investigated the role of several potential effect modifiers (baseline weight, age, gender (percentage women), ethnicity, lifetime exposure to antipsychotics, pharmaceutical sponsorship and study duration). Meta-regression analyses on study level basis could not identify clear moderators of weight gain, because the credibility intervals for the effect (B) were imprecise and/or included the point of no effect except for sponsorship. The MD of any antipsychotic versus placebo was on average 0.45 kg (95%CrI: 0.01 to 0.89 kg) higher in sponsored arms than in non-sponsored study arms. After adjusting for pharmaceutical sponsoring common-τ was reduced from 0.82 to 0.65.

The following table presents the estimated average increase in MD of weight gain (=B) due to the potential moderator in the network meta-regression model and the effects of adjusting for the moderator on the common estimate of heterogeneity (=common-τ).

Analysis	Moderator	B	Credible interval of B	Common-τ (MD)	Credible interval of common tau
NMA	-	-	-	0.82	
NMR	Baseline age (years)	0.02	-0.10, 0.14	0.81	0.58, 1.08
NMR	Gender (proportion women)	-2.05	-7.13, 3.22	0.78	0.54, 1.05
NMR	Ethnicity (black percentage)	0.03	-0.02, 0.08	0.51	0.14, 0.86
NMR	Ethnicity (white percentage)	-0.02	-0.05, 0.01	0.61	0.33, 0.92
NMR	Lifetime exposure to antipsychotics (years)	0.06	-0.11, 0.23	0.78	0.53, 1.09
NMR	Sponsored study arm (yes/no)	0.45	0.01, 0.89	0.65	0.17, 0.99
NMR	Study duration (weeks)	-0.03	-0.07, 0.02	0.84	0.59, 1.12
NMR	Baseline weight (kg)	-0.04	-0.14, 0.06	0.78	0.52, 1.07

Abbreviations: NMA: Network meta-analysis of the primary outcome; NMR: network meta-regression analysis of the primary outcome.

B is the increase in MD that could happen due to the moderator on average according to the network meta-regression model.

The point estimates of B indicate the following moderating effect:

MD of body weight increases on average by 0.02 kg per year of baseline age.

The body weight is on average 2.05 kg more in a study including only women compared to a study including only men.

The body weight is on average 0.03 kg less in a study including only black ethnicity compared to a study including no black ethnicity.

The body weight is on average 0.02 kg more in a study including only white ethnicity compared to a study including no white ethnicity.

MD of body weight increases on average by 0.06 kg per year life time exposure to antipsychotics.

MD of body weight increases on average by 0.45 kg when the study drug is sponsored.

MD of body weight decreases on average by 0.03 kg per week study duration.

MD of body weight decreases on average by 0.04 kg for every kg baseline weight.

Please note that the credible intervals of B for all moderators (except sponsorship) contain the value of no effect (MD=0).

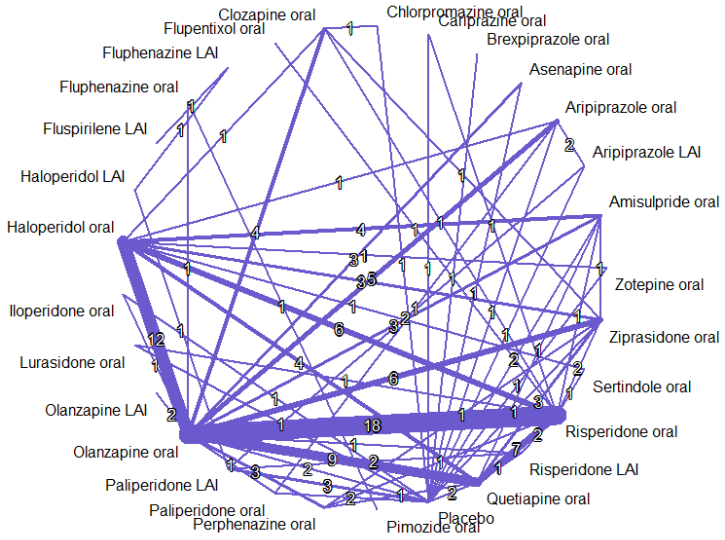
* The common-τ in this NMR is reduced compared to the primary analysis. However, it needs to be noted that information for the specific moderator was only available for a subset of all studies included in the primary analysis. Thus, the common-τ of the adjusted model (NMR) could be compared with the common-τ of the unadjusted models (NMA) in studies with the moderator available. For sponsorship almost no information was missing (only 2 small studies out of 110: Chetvertnykh 2008 and Sharma 1991). Therfore, we assumed that common-τ of the unadjusted model NMA after exclusion of these two studies with missing information would not change significantly.

Interpretation:

We identified no clear effect moderator in the network meta-regressions except of potentially sponsorship. Sponsored studies showed 0.45 kg more weight gain compared to non-sponsored studies, but the 95% CrI is rather wide ranging from 0.01 to 0.89 kg. After adjusting for sponsorship common-τ was reduced from 0.82 to 0.65.

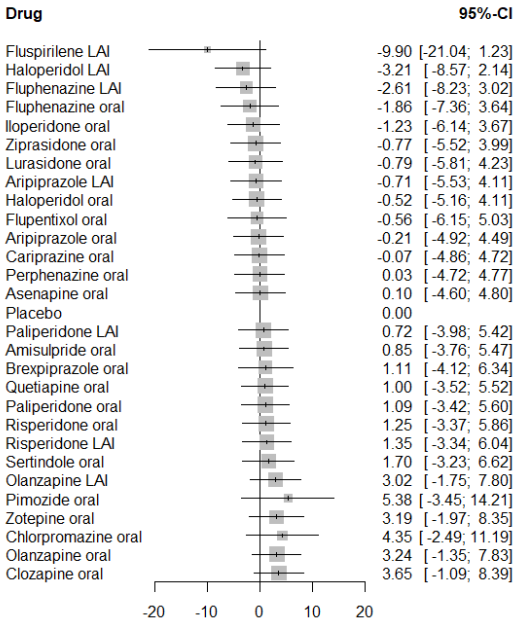
10.1 Baseline age

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison.

Forest-plot of results of adjusted network meta-analysis for antipsychotic drugs versus placebo

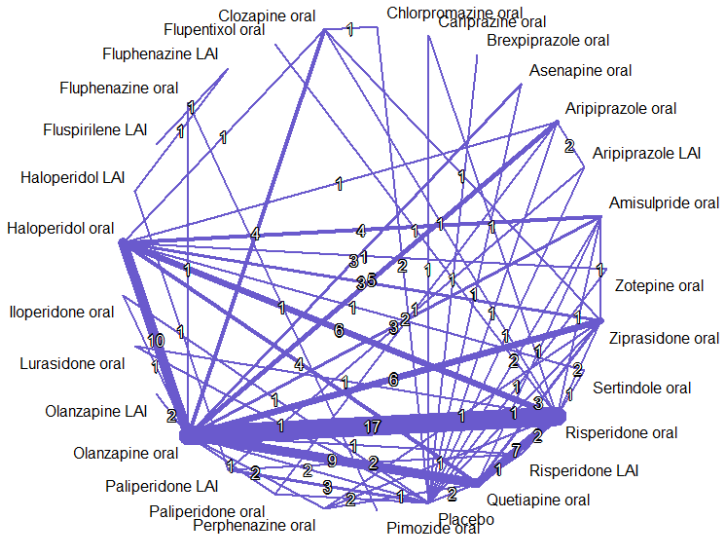


Network meta-regression estimates of treatment effect of each drug versus placebo at the mean value of the predictor reported as mean difference (MD) in kg and 95% CI. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95%CI=95% credible interval, LAI=long-acting injectable.

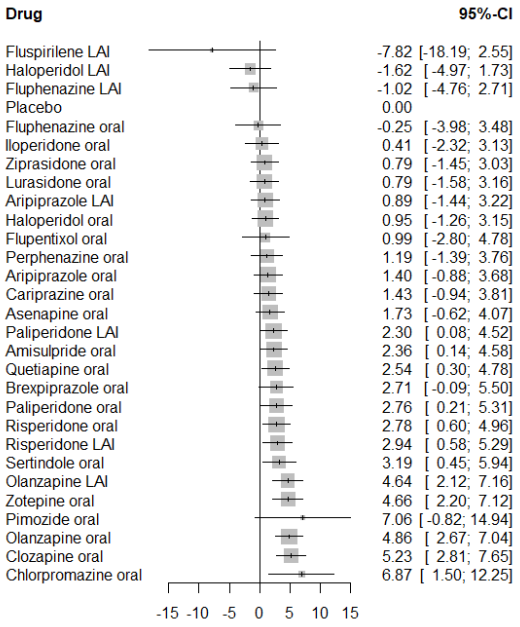
10.2 Gender (proportion women)

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison.

Forest-plot of results of adjusted network meta-analysis for antipsychotic drugs versus placebo

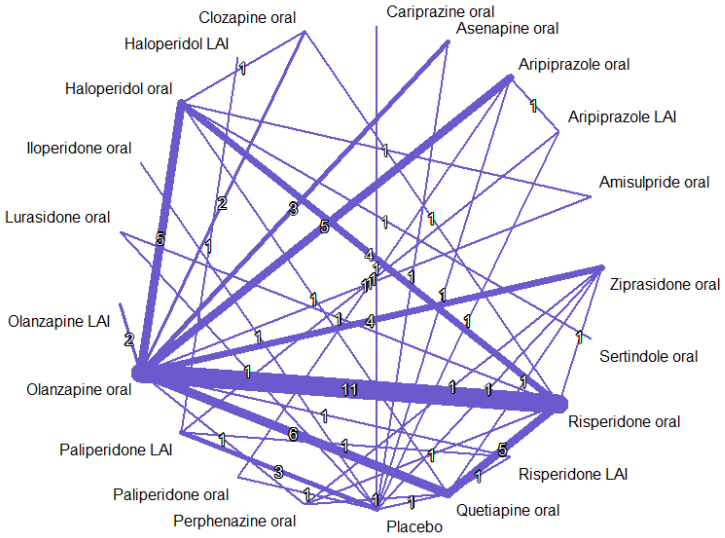


Network meta-regression estimates of treatment effect of each drug versus placebo at the mean value of the predictor reported as mean difference (MD) in kg and 95% CI. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95%CI=95% credible interval, LAI=long-acting injectable.

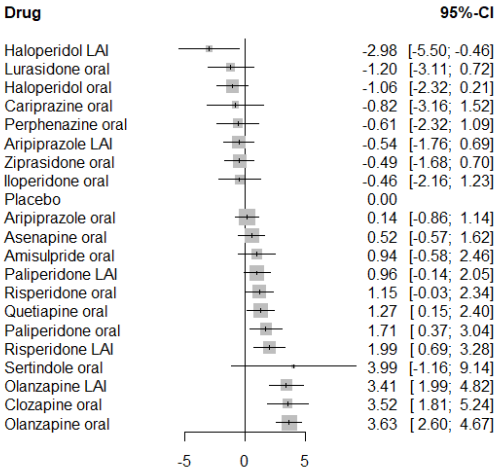
10.3 Ethnicity (black percentage)

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison.

Forest-plot of results of adjusted network meta-analysis for antipsychotic drugs versus placebo

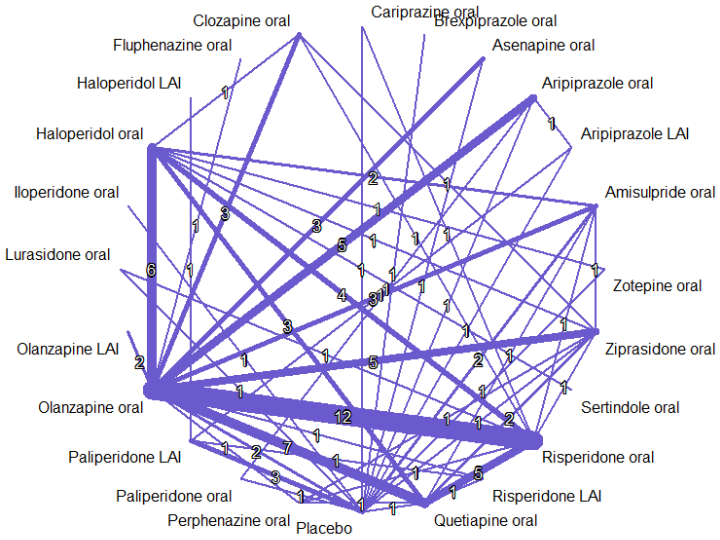


Network meta-regression estimates of treatment effect of each drug versus placebo at the mean value of the predictor reported as mean difference (MD) in kg and 95% CI. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95%CI=95% credible interval, LAI=long-acting injectable.

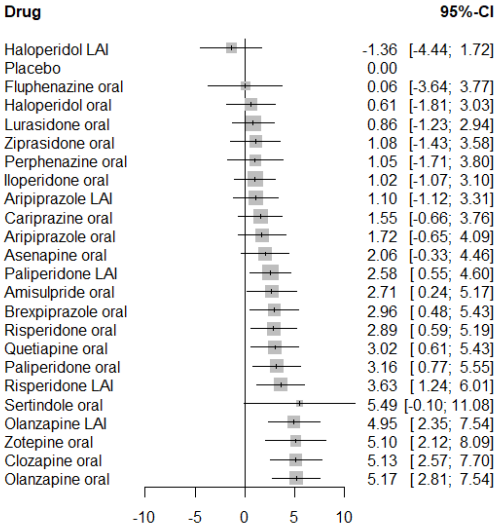
10.4 Ethnicity (white percentage)

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison.

Forest-plot of results of adjusted network meta-analysis for antipsychotic drugs versus placebo

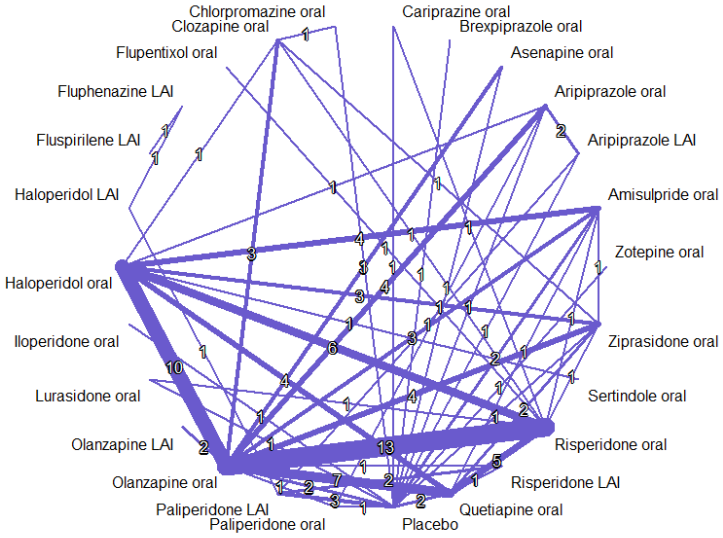


Network meta-regression estimates of treatment effect of each drug versus placebo at the mean value of the predictor reported as mean difference (MD) in kg and 95% CI. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95%CI=95% credible interval, LAI=long-acting injectable.

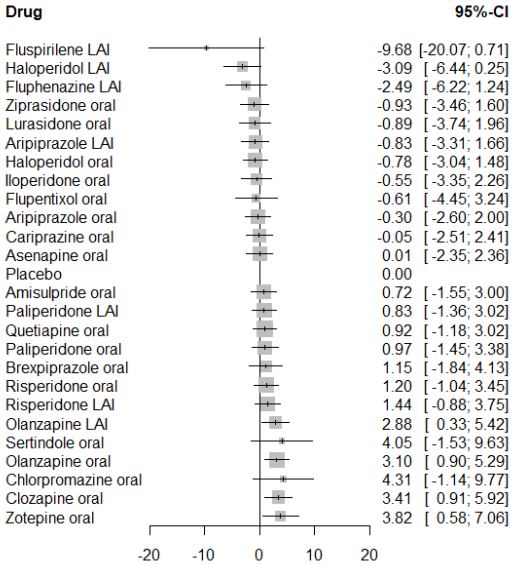
10.5 Lifetime exposure to antipsychotics in years

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison.

Forest-plot of results of adjusted network meta-analysis for antipsychotic drugs versus placebo

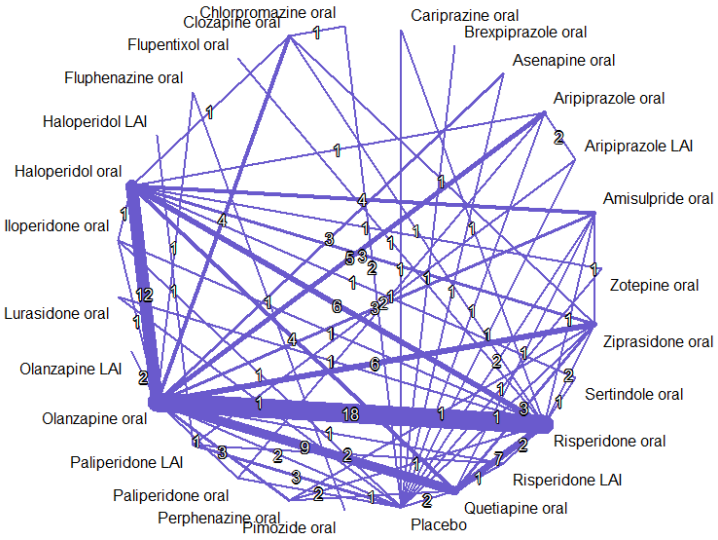


Network meta-regression estimates of treatment effect of each drug versus placebo at the mean value of the predictor reported as mean difference (MD) in kg and 95% CI. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95%CI=95% credible interval, LAI=long-acting injectable.

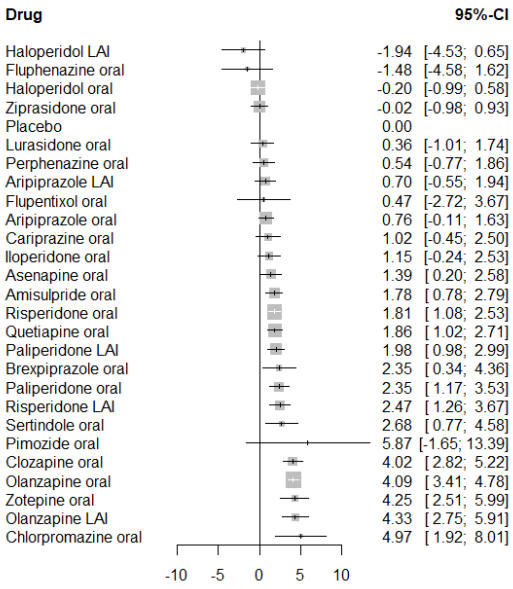
10.6 Sponsorship

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison.

Forest-plot of results of adjusted network meta-analysis for antipsychotic drugs versus placebo

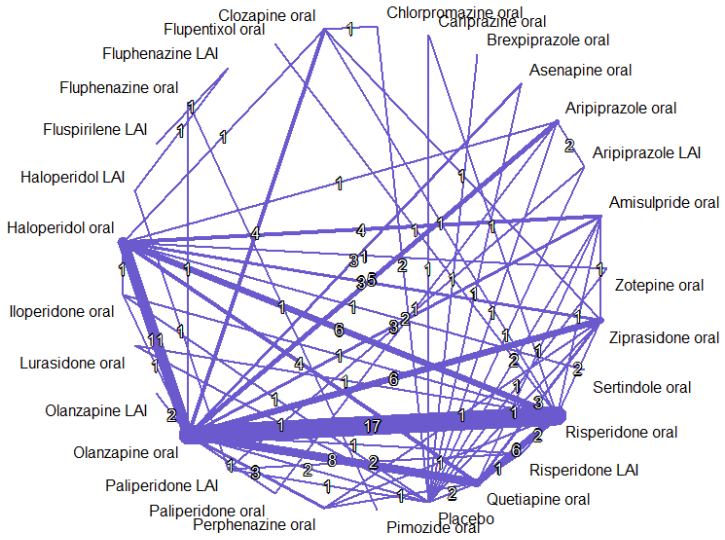


Network meta-regression estimates of treatment effect of each drug versus placebo at the mean value of the predictor reported as mean difference (MD) in kg and 95% CI. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95%CI=95% credible interval, LAI=long-acting injectable.

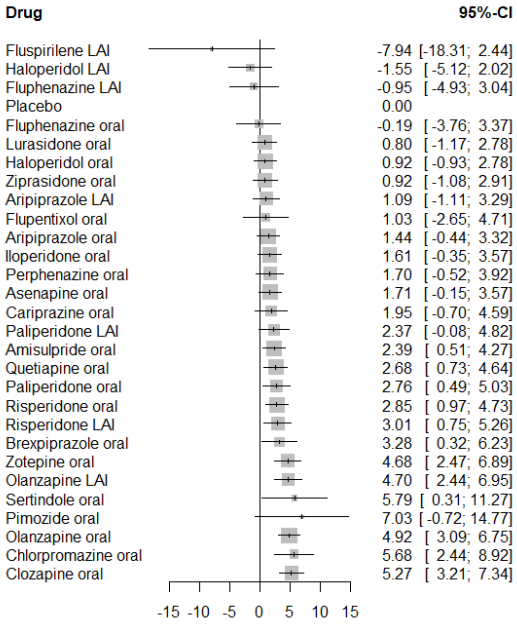
10.7 Study duration

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison.

Forest-plot of results of adjusted network meta-analysis for antipsychotic drugs versus placebo

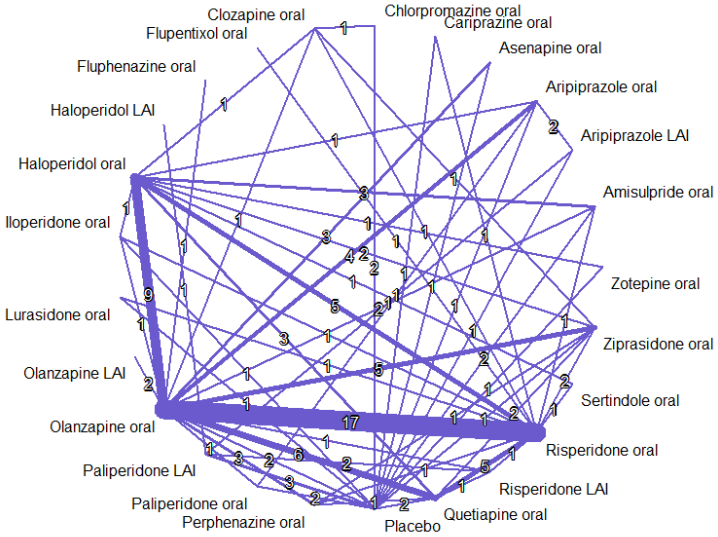


Network meta-regression estimates of treatment effect of each drug versus placebo at the mean value of the predictor reported as mean difference (MD) in kg and 95% CI. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95%CI=95% credible interval, LAI=long-acting injectable.

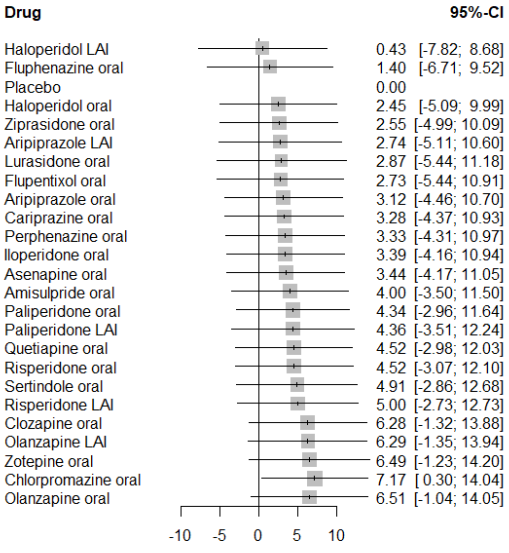
10.8 Baseline weight

Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison.

Forest-plot of results of adjusted network meta-analysis for antipsychotic drugs versus placebo



Network meta-regression estimates of treatment effect of each drug versus placebo at the mean value of the predictor reported as mean difference (MD) in kg and 95% CI. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95%CI=95% credible interval, LAI=long-acting injectable.

11 Results of the sensitivity analyses of the primary outcome "weight gain"

For each sensitivity analysis we present below (in this order)

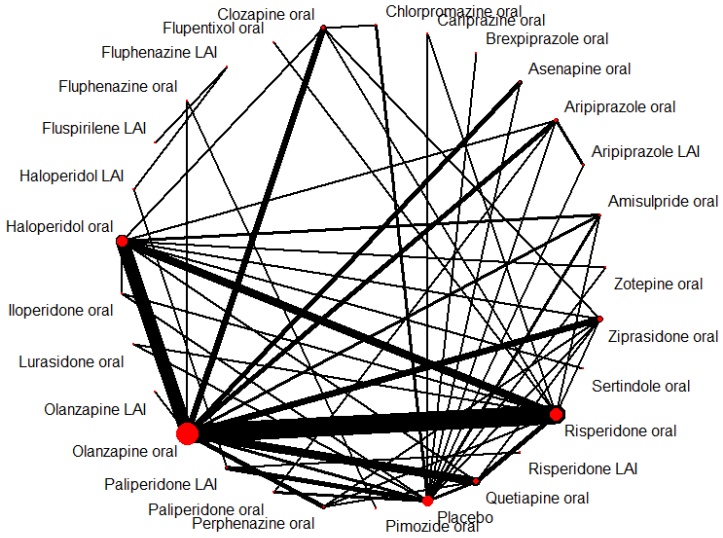
- Network plot
- Results of statistical test for inconsistency of the network and common estimate for heterogeneity
- Forest-plot of results of the network meta-analysis (reference placebo)

Summary of results: In all eight sensitivity analyses, the effect estimates for the primary outcome weight gain and the ranking of antipsychotics remained similar. The observed heterogeneity did not change much. Thus, sensitivity analyses confirmed the primary analysis.

Interestingly, when enriched design studies were excluded, all antipsychotics showed larger MDs (on average +0.63 kg). When only observed cases were considered, more pronounced differences between the antipsychotics were observed.

11.1 Double blind studies only

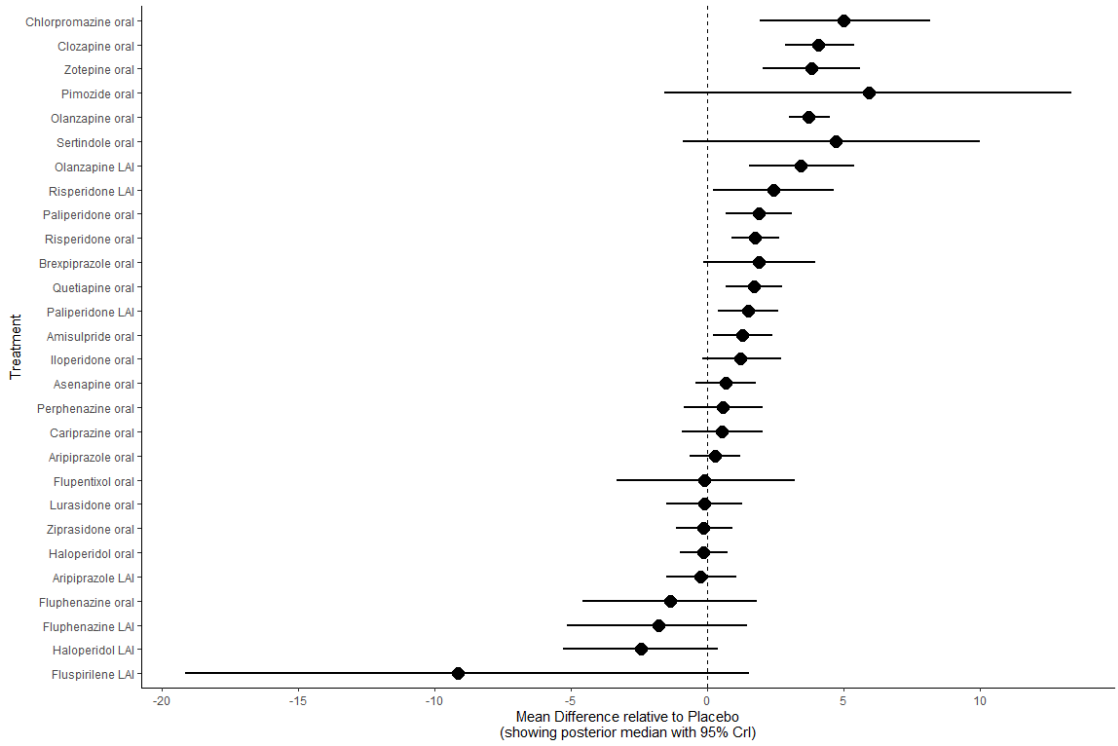
Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Inconsistent comparisons of detachable comparisons (%) (SIDE-test)	**P-value of Design-by-treatment test**	**Common-Tau (standard deviation of differences in effect size between studies of the same comparison)**
6 of 45 (13.3%)	0.02	0.804

Forest-plot of results of network meta-analysis for antipsychotic drugs versus placebo

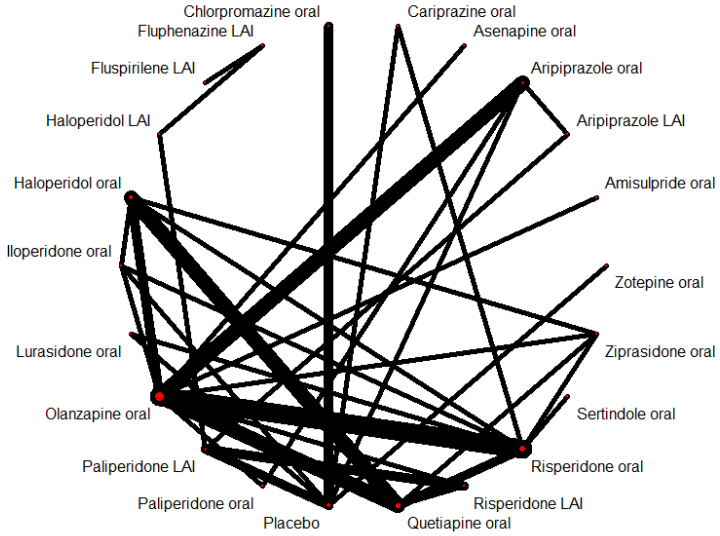


Network meta-analysis estimates of treatment effect of each drug versus placebo reported as mean difference (MD) in kg. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95% CrI=95% credible interval, LAI=long-acting injectable.

11.2 Analysis of only data of observed cases

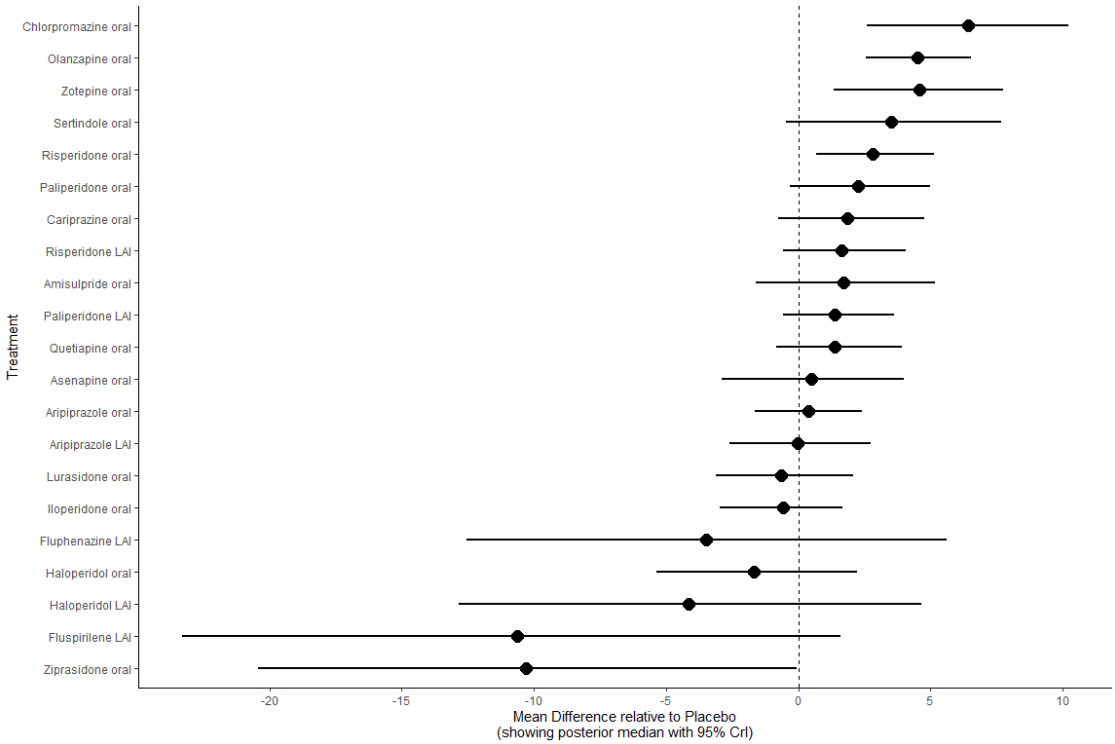
Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Inconsistent comparisons of detachable comparisons (%) (SIDE-test)	P-value of Design-by-treatment test	Common-Tau (standard deviation of differences in effect size between studies of the same comparison) with 95% CrI
1 of 28 (3.6%)	0.656	0.78

Forest-plot of results of network meta-analysis for antipsychotic drugs versus placebo

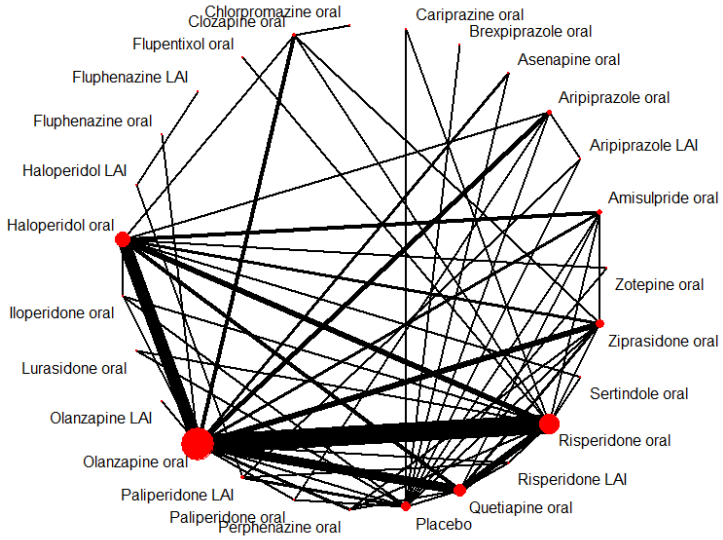


Network meta-analysis estimates of treatment effect of each drug versus placebo reported as mean difference (MD) in kg. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95% CrI=95% credible interval, LAI=long-acting injectable.

11.3 Exclusion of studies that did not use operationalized criteria to diagnose schizophrenia

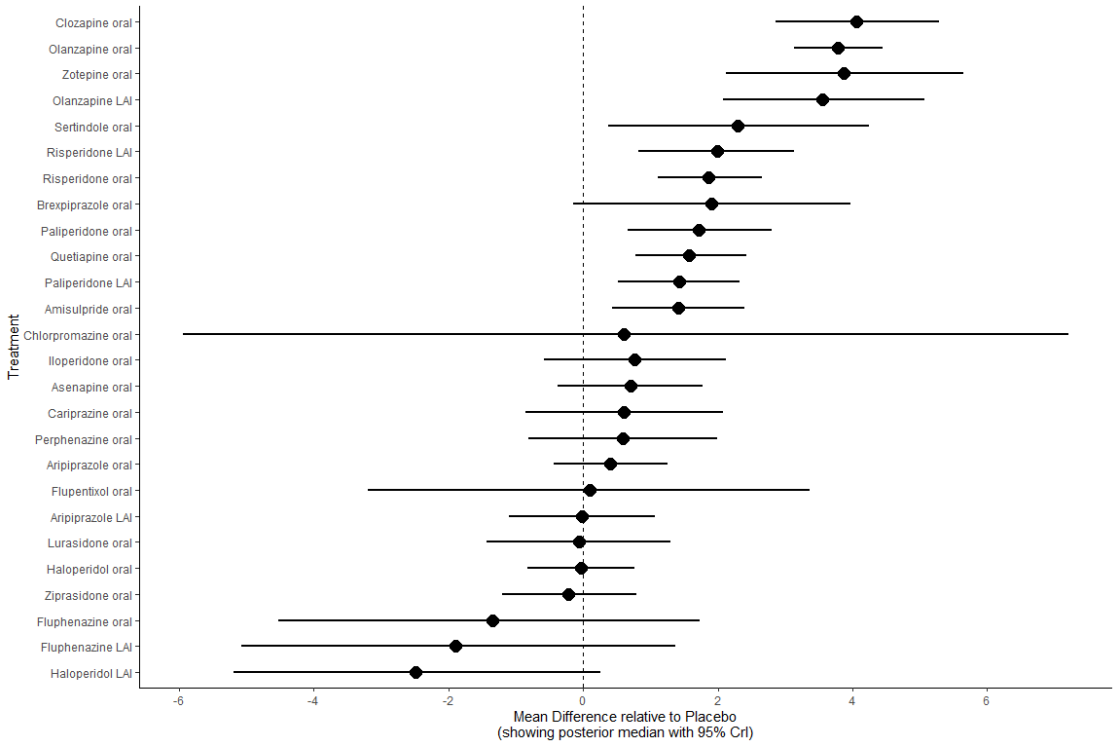
Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Inconsistent comparisons of detachable comparisons (%) (SIDE-test)	P-value of Design-by-treatment test	Common-Tau (standard deviation of differences in effect size between studies of the same comparison) with 95% CrI
5 of 55 (9.1%)	0.508	0.815

Forest-plot of results of network meta-analysis for antipsychotic drugs versus placebo

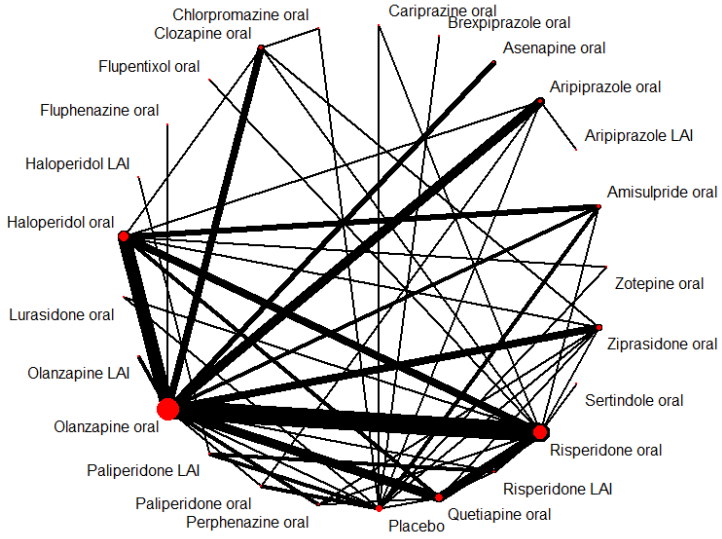


Network meta-analysis estimates of treatment effect of each drug versus placebo reported as mean difference (MD) in kg. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95% CrI=95% credible interval, LAI=long-acting injectable.

11.4 Exclusion of studies with an overall assessment of high risk of bias

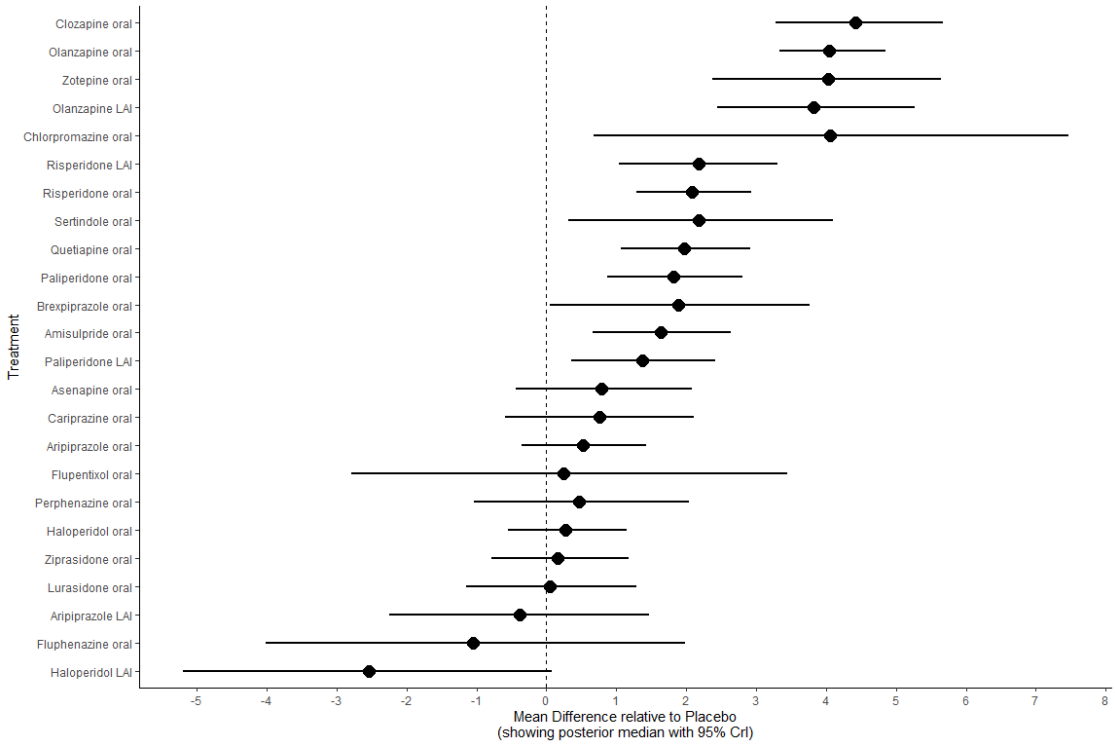
Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Inconsistent comparisons of detachable comparisons (%) (SIDE-test)	P-value of Design-by-treatment test	Common-Tau (standard deviation of differences in effect size between studies of the same comparison) with 95% CrI
5 of 44 (11.4%)	0.005	0.656

Forest-plot of results of network meta-analysis for antipsychotic drugs versus placebo

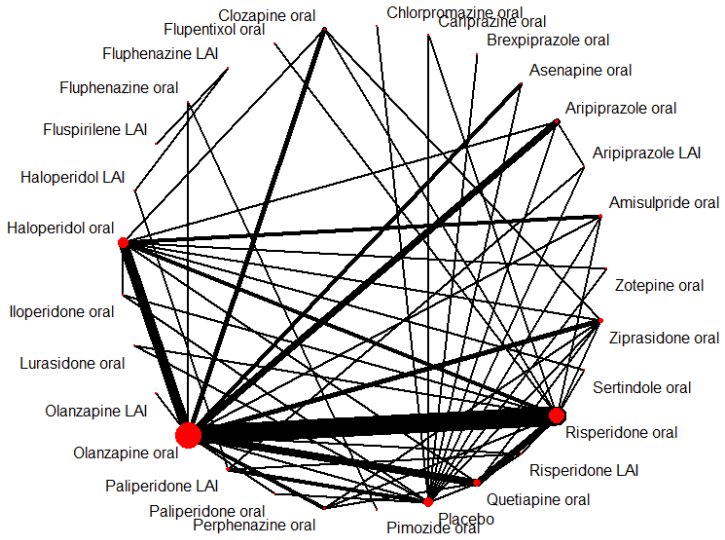


Network meta-analysis estimates of treatment effect of each drug versus placebo reported as mean difference (MD) in kg. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95% CrI=95% credible interval, LAI=long-acting injectable.

11.5 Exclusion of studies in patients with minimal prior exposure to antipsychotics

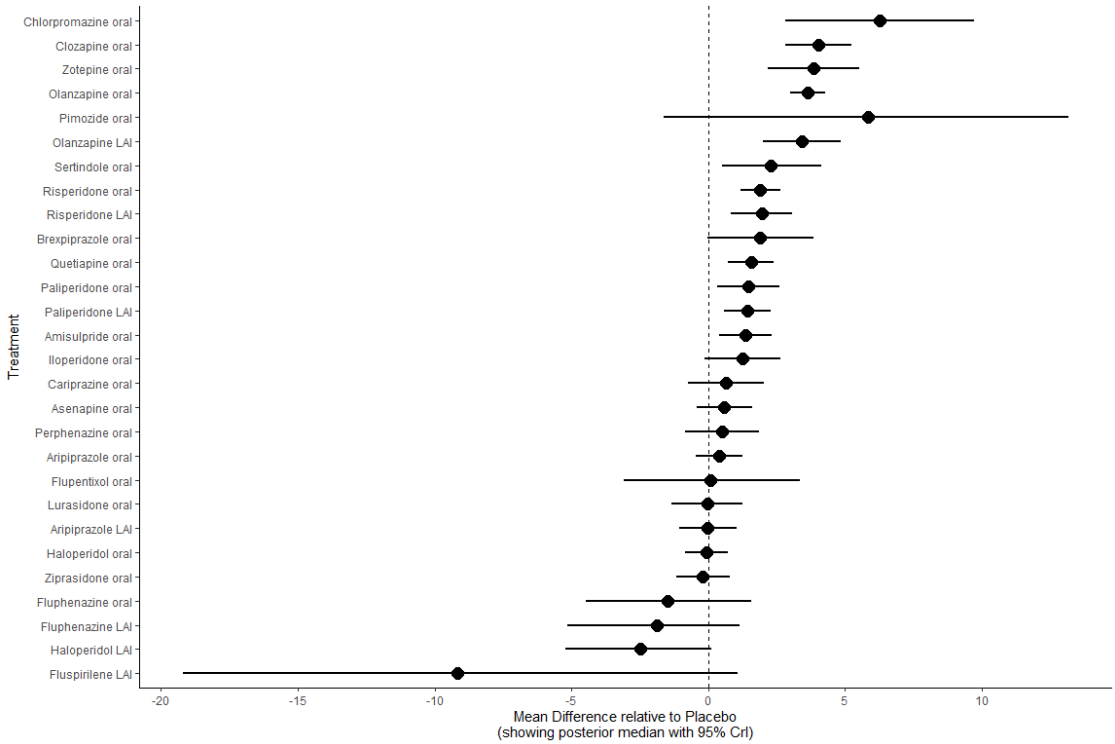
Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Inconsistent comparisons of detachable comparisons (%) (SIDE-test)	**P-value of Design-by-treatment test**	**Common-Tau (standard deviation of differences in effect size between studies of the same comparison) with 95% CrI**
6 of 51 (11.8%)	0.003	0.752

Forest-plot of results of network meta-analysis for antipsychotic drugs versus placebo

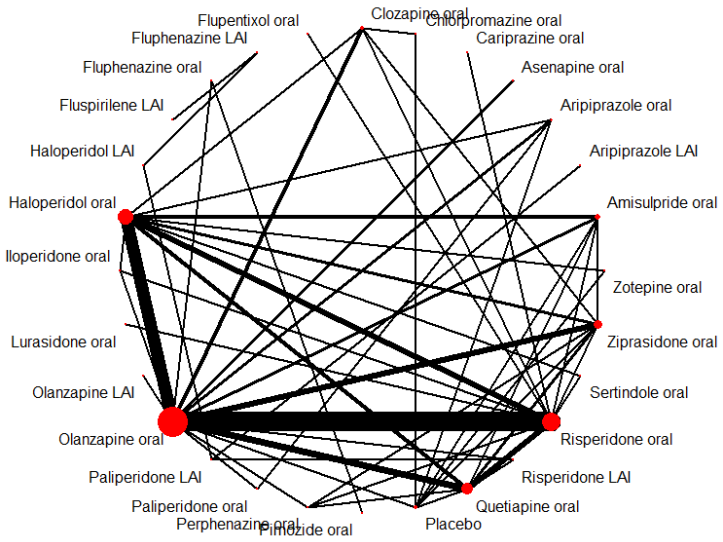


Network meta-analysis estimates of treatment effect of each drug versus placebo reported as mean difference (MD) in kg. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95% CrI=95% credible interval, LAI=long-acting injectable.

11.6 Exclusion of enriched design studies

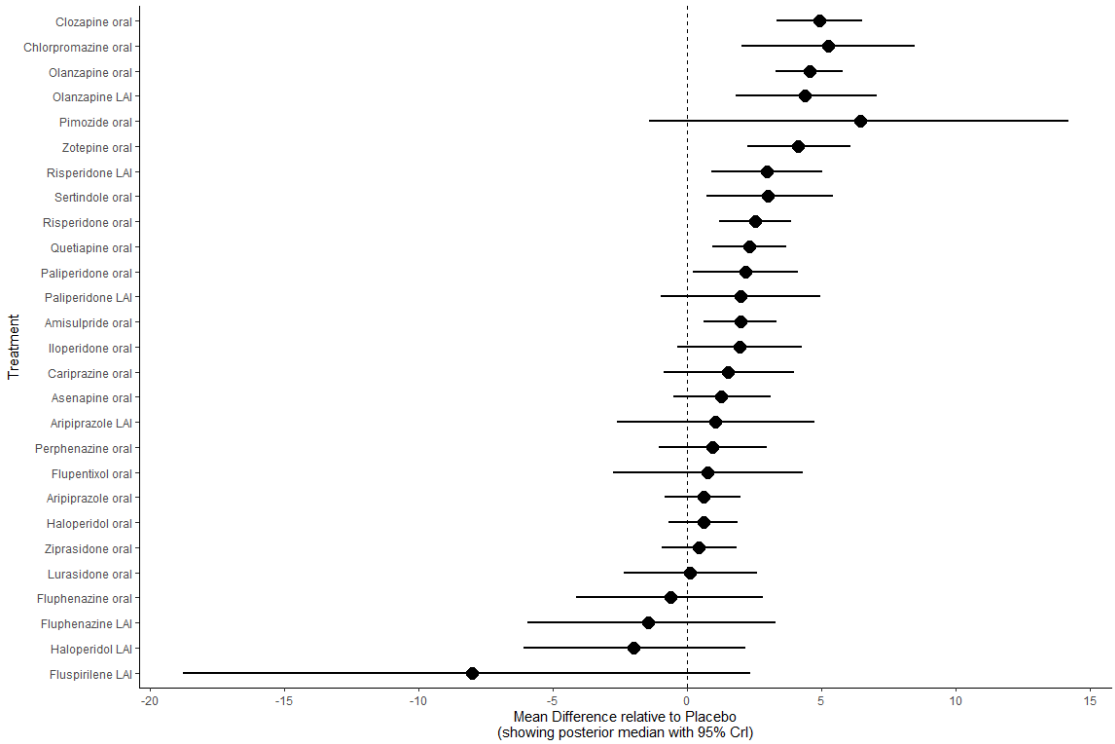
Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Inconsistent comparisons of detachable comparisons (%) (SIDE-test)	**P-value of Design-by-treatment test**	**Common-Tau (standard deviation of differences in effect size between studies of the same comparison) with 95% CrI**
5 of 43 (11.6%)	0.807	0.926

Forest-plot of results of network meta-analysis for antipsychotic drugs versus placebo



Network meta-analysis estimates of treatment effect of each drug versus placebo reported as mean difference (MD) in kg. Order of treatments is according to the SUCRA ranking.

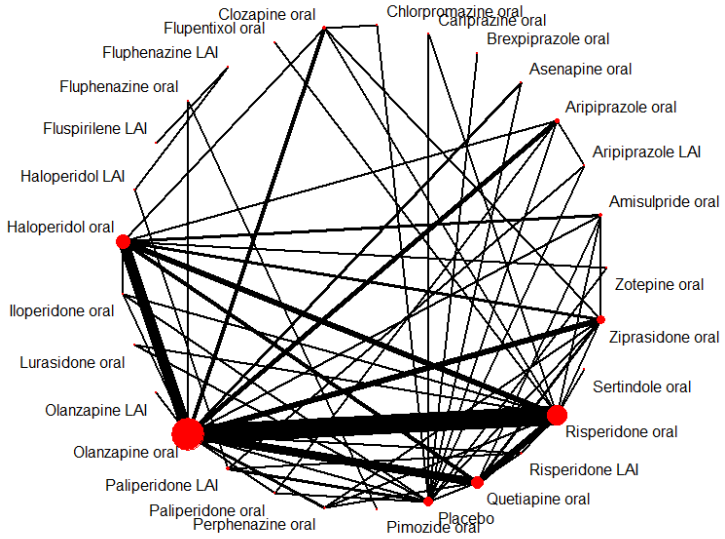
Abbreviations: 95% CrI=95% credible interval, LAI=long-acting injectable.

11.7 Exclusion of arms at the lower and upper ends of the range recommended by the International Consensus Study on Antipsychotic Dosing (post-hoc)

In the primary analysis, we included only study arms with doses within the target to maximum range according to the International Consensus Study on Antipsychotic Dosing [9]. Only for special populations such as patients with first episode or primarily negative symptoms for which clinically different dosing regiments are recommended, we included lower doses.

In the following sensitivity analysis, we excluded these studies in special populations using lower doses, specifically, we excluded one study in first episode patients (Kahn 2008), three studies focussing primarily on negative symptoms (Speller 1997, Loo 1997 and Lecrubier 2006). Moreover, we excluded Daniel 1998 which used a dose of Sertindole minimally above the upper end of the International Consensus Study on Antipsychotic Dosing [9].

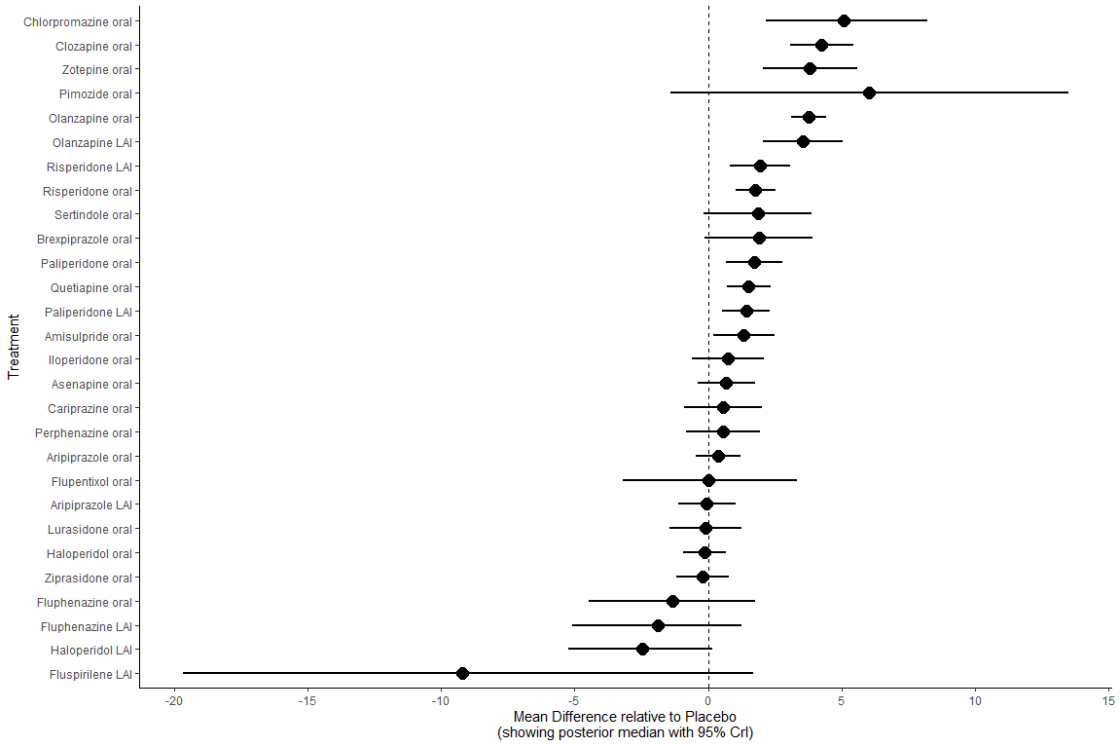
Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Inconsistent comparisons of detachable comparisons (%) (SIDE-test)	P-value of Design-by-treatment test	Common-Tau (standard deviation of differences in effect size between studies of the same comparison) with 95% CrI
5 of 54 (9.3%)	0.442	0.813

Forest-plot of results of network meta-analysis for antipsychotic drugs versus placebo

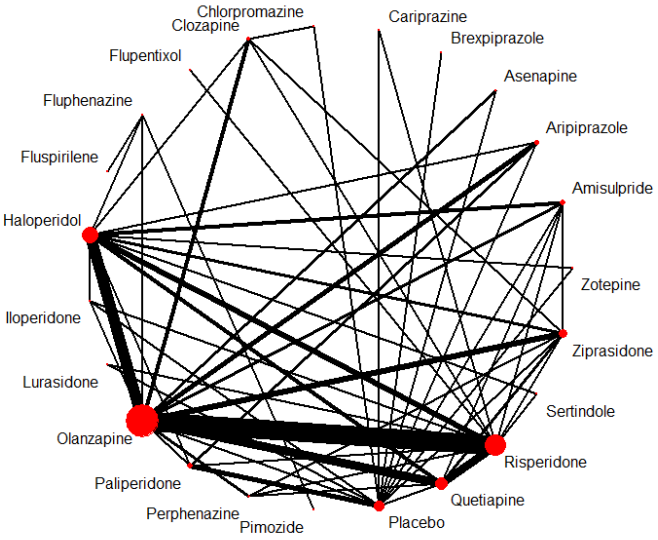


Network meta-analysis estimates of treatment effect of each drug versus placebo reported as mean difference (MD) in kg. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95% CrI=95% credible interval, LAI=long-acting injectable.

11.8 Pooling LAI and oral formulations of the same antipsychotic (post-hoc)

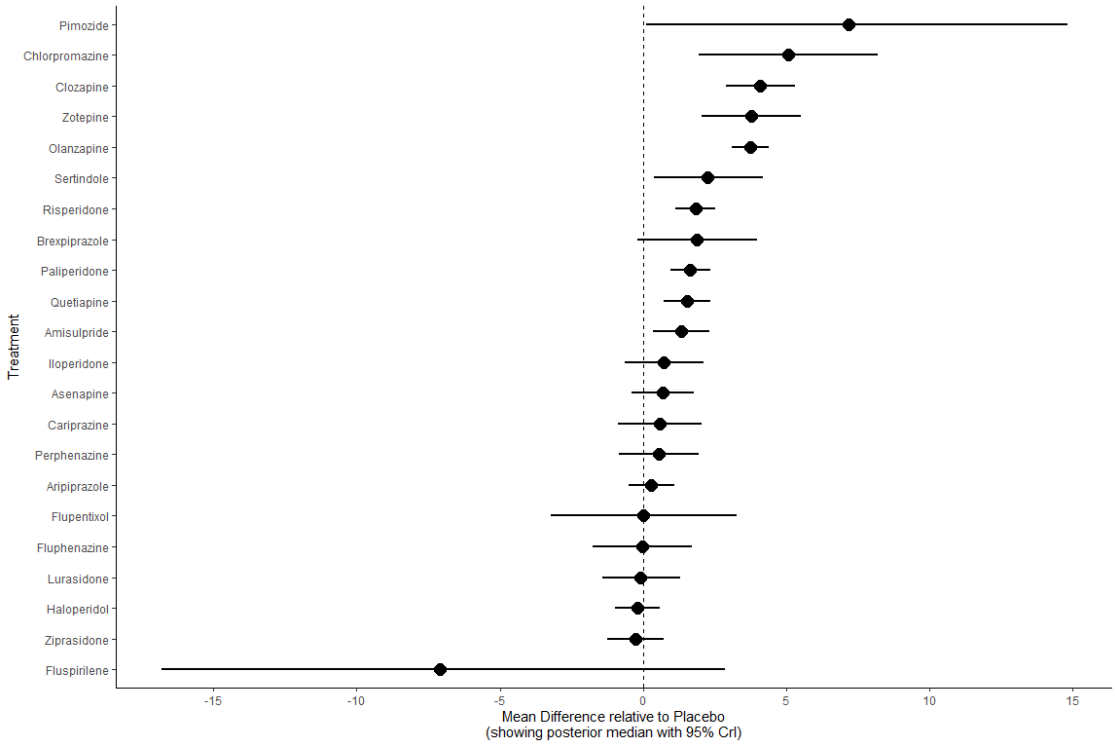
Network plot



Lines link treatments with direct comparisons in trials; thickness of lines corresponds to the number of trials evaluating the comparison; size of the nodes corresponds to the number of participants assigned to the treatment.

Inconsistent comparisons of detachable comparisons (%) (SIDE-test)	P-value of Design-by-treatment test	Common-Tau (standard deviation of differences in effect size between studies of the same comparison) with 95% CrI
6 of 53 (11.3%)	0.339	0.829

Forest-plot of results of network meta-analysis for antipsychotic drugs versus placebo



Network meta-analysis estimates of treatment effect of each drug versus placebo reported as mean difference (MD) in kg. Order of treatments is according to the SUCRA ranking.

Abbreviations: 95% CrI=95% credible interval, LAI=long-acting injectable.

12 Assessment of small-study effect

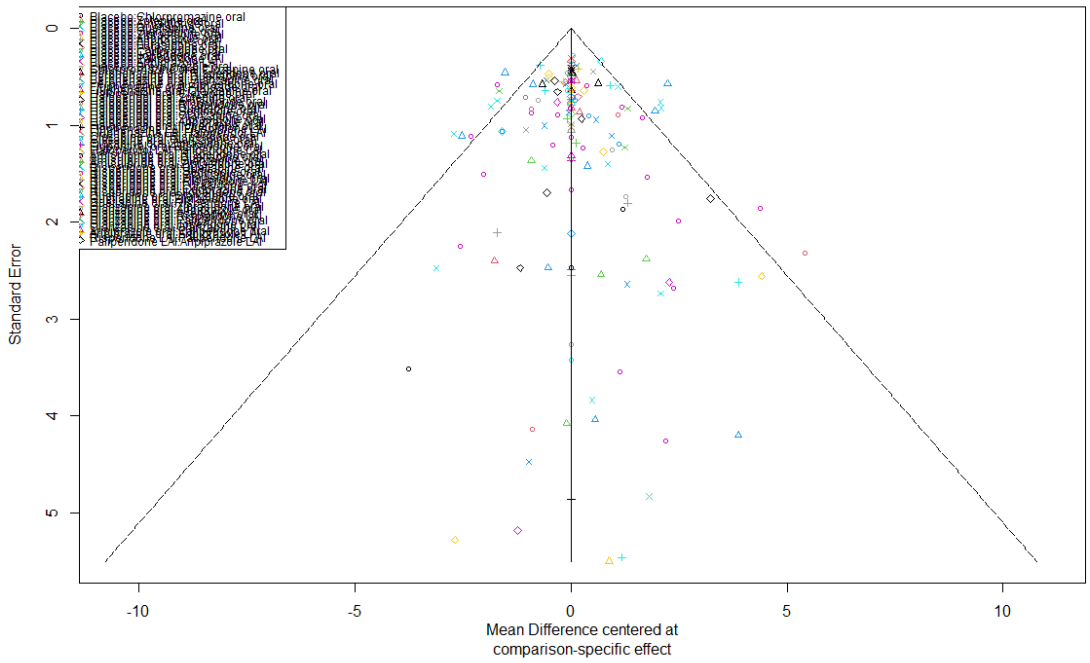
12.1 General notes and findings

We assessed small-study effect (a proxy for publication bias) for the primary outcome "weight gain". In general, we deem it unlikely that a study was not published because of unfavourable results in secondary outcomes of the original studies. Because the majority of studies assessed weight gain as a secondary safety outcome and only few studies were designed to examine weight gain as primary outcome, the presence of a publication bias is unlikely on a theoretical basis.

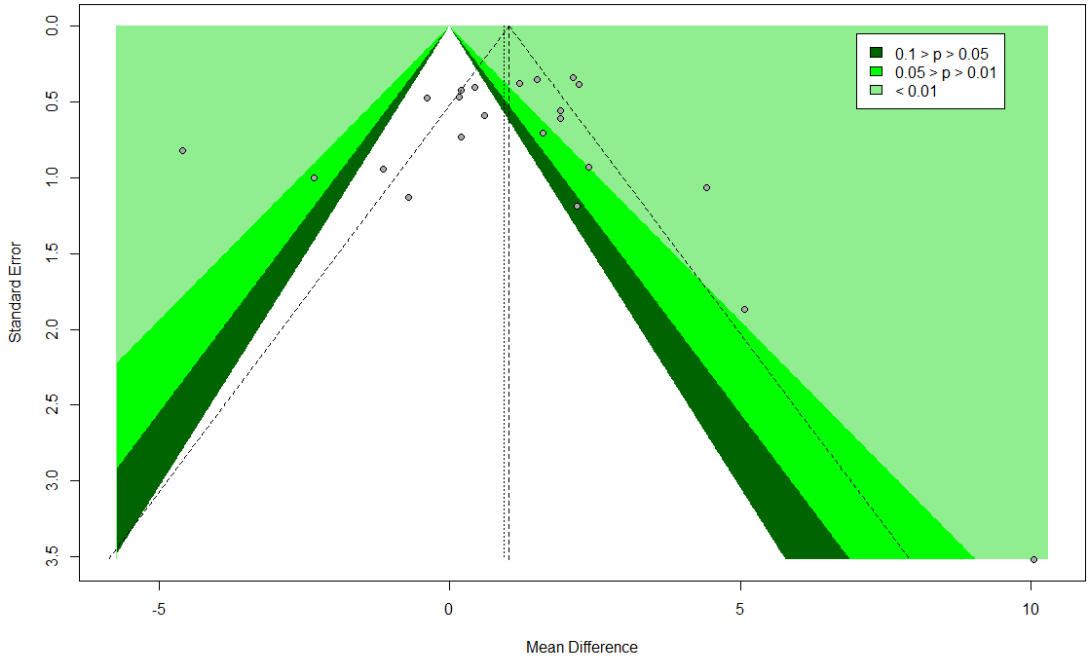
Nevertheless, for our primary outcome "weight gain", we assessed small-study effects by performing a comparison-adjusted funnel plot, a contour-enhanced funnel plot of all antipsychotics versus placebo and additionally contour-enhanced funnel plots comparing active antipsychotics versus placebo for comparisons with more than 10 studies available.

For our secondary outcomes, we did not assess risk of small-study effect because we deemed the risk for non-publication even lower for fasting glucose and the other lipid parameters compared to our primary outcome "weight gain".

Comparison-adjusted funnel plot



Contour-enhanced funnel plot of antipsychotics versus placebo



Egger's test for small-study effect

Linear regression test of funnel plot asymmetry
Test result: t = -0.31, df = 20, **p-value = 0.7588**

Sample estimates:

bias	se.bias	intercept	se.intercept
-0.4085	1.3125	1.2278	0.2

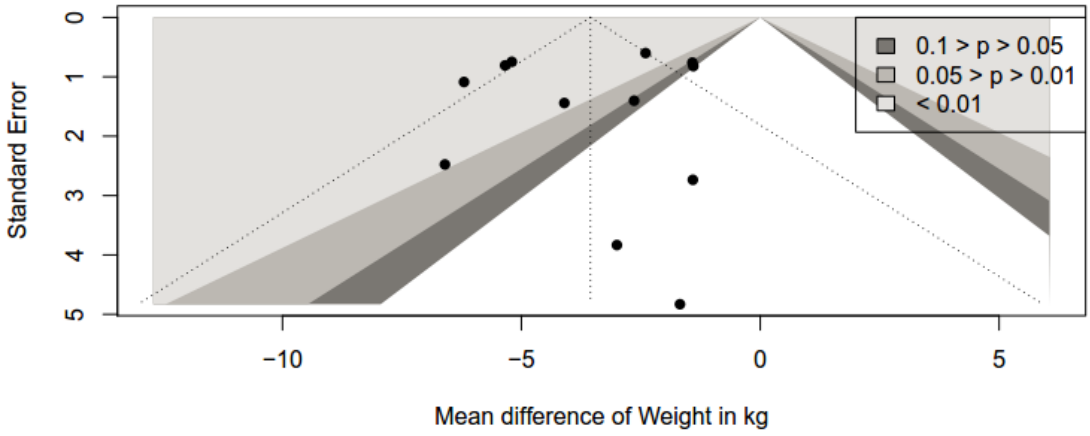
Details:
- multiplicative residual heterogeneity variance (tau^2 = 6.8836)
- predictor: standard error
- weight: inverse variance
- reference: Egger et al. (1997), BMJ

Interpretation:

The comparison-adjusted funnel plot showed a symmetrical distribution of studies. In the contour-enhanced funnel plot of all antipsychotics versus placebo there is one small study with a large significant effect but small studies around the pooled effect, small studies with large effects in the opposite direction as well as small studies which found no significant difference between antipsychotics and placebo are missing. This may indicate some small-study effect as a proxy for publication bias. However, as there is only one small-study it is unlikely that small-study bias has an impact on the overall results. Accordingly, the Egger's test indicates no evidence of small-study effect.

12.2 Additional funnel plots for comparisons with more than 10 studies

Contour-enhanced funnel plot for the comparison haloperidol oral vs. olanzapine oral



Egger's test for small-study effect

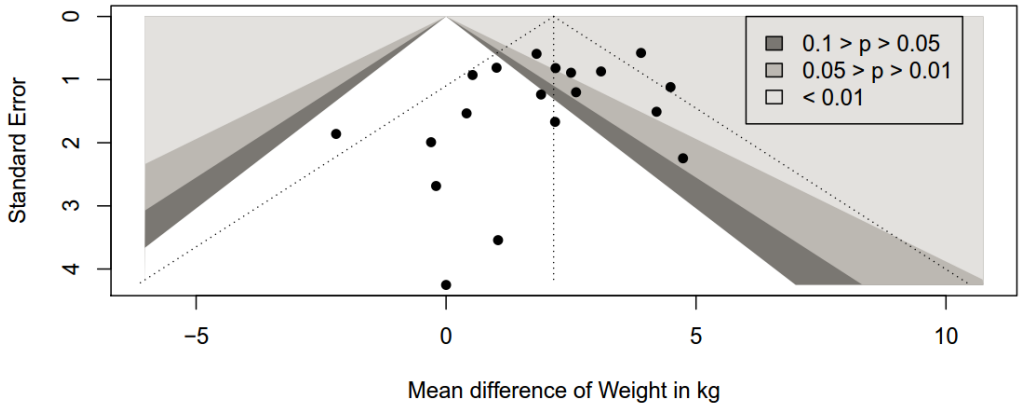
Linear regression test of funnel plot asymmetry
Test result: t = -0.37, df = 10, **p-value = 0.7177**

Sample estimates:

	bias	se.bias	intercept	se.intercept
	-0.4259	1.1449	-2.9762	1.1666

Details:
- multiplicative residual heterogeneity variance (tau^2 = 3.6039)
- predictor: standard error
- weight: inverse variance
- reference: Egger et al. (1997), BMJ

Contour-enhanced funnel plot for the comparison olanzapine oral vs. risperidone oral



Egger test: p-value = 0.22

Egger's test for small-study effect

Linear regression test of funnel plot asymmetry

Test result: t = -1.28, df = 17, **p-value = 0.2165**

Sample estimates:

bias	se.bias	intercept	se.intercept
-0.8658	0.6745	3.1277	0.7130

Details:
- multiplicative residual heterogeneity variance (tau^2 = 1.6716)
- predictor: standard error
- weight: inverse variance
- reference: Egger et al. (1997), BMJ

Interpretation:

The available small studies are in the white area of no significant difference between the two drugs compared, which are typically those studies which are expected to be unpublished. However, in the specific case of an assessment of a side effect, it may be possible that preferentially non-significant (and not signficant results showing a worse outcome with one drug) are published. Thus, the presence of publication bias can not be excluded beforehand. In fact, there was some assymetry in the funnel plots with small studies missing at one side of the pooled effect. However, there are only few small studies with respect to the overall number of studies so that the pooled effect is not much driven by them.

13 Assessment of risk of bias

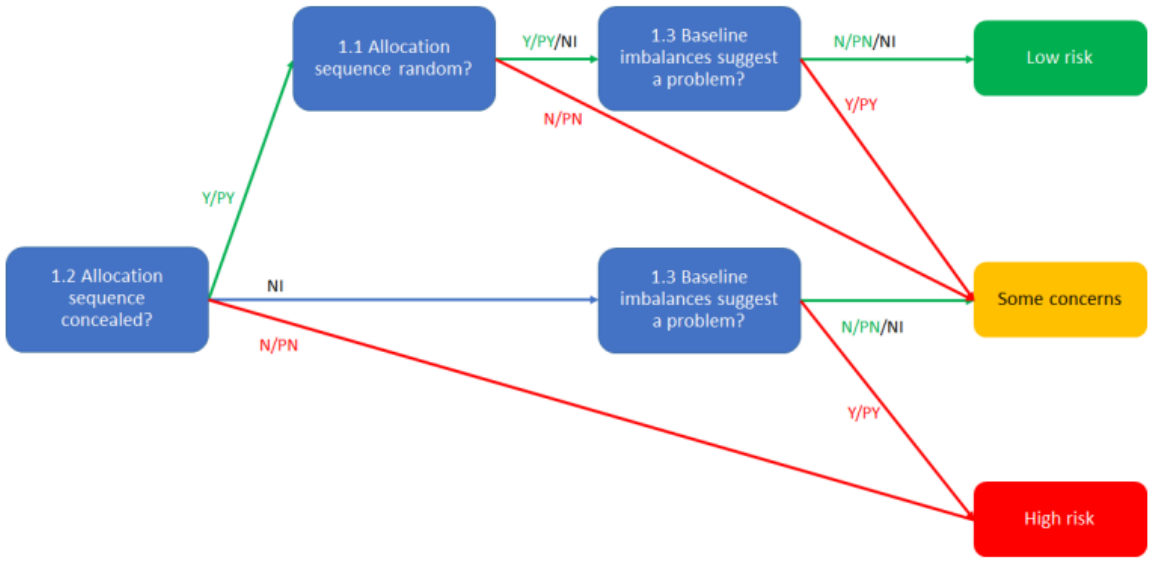
13.1 General notes

For judgement of risk of bias, we followed the concept of the Cochrane Risk of Bias tool 2 [369]. This tool provides a framework for evaluating potential risks of bias in five different domains and provides guidance by signaling questions.

However, it must be noted, that there are not always clear rules and specific situations found in the analysed trials may deviate from the ideal case. Thus, judgement is needed to make decisions and these specific judgements and decisions made by the authors of the review are described below.

13.2 Details of the assessment

Domain 1: RANDOMISATION PROCESS



Algorithm for suggested judgement of risk of bias arising from the randomization process

1.1 Was the allocation sequence random?

In principle, if there was no information about the exact methods (e.g. only stated "randomized"), we stated "not indicated". For trials investigating second-generation-antipsychotic drugs that were sponsored by pharmaceutical companies, we assume that the sequence generation for randomisation was appropriate, even when it is only stated "randomized", and we stated "probably yes". The reason is that we contacted many pharmaceutical companies in the past and all reported use of appropriate methods in these modern studies, even when it was not clearly stated in the primary publications.

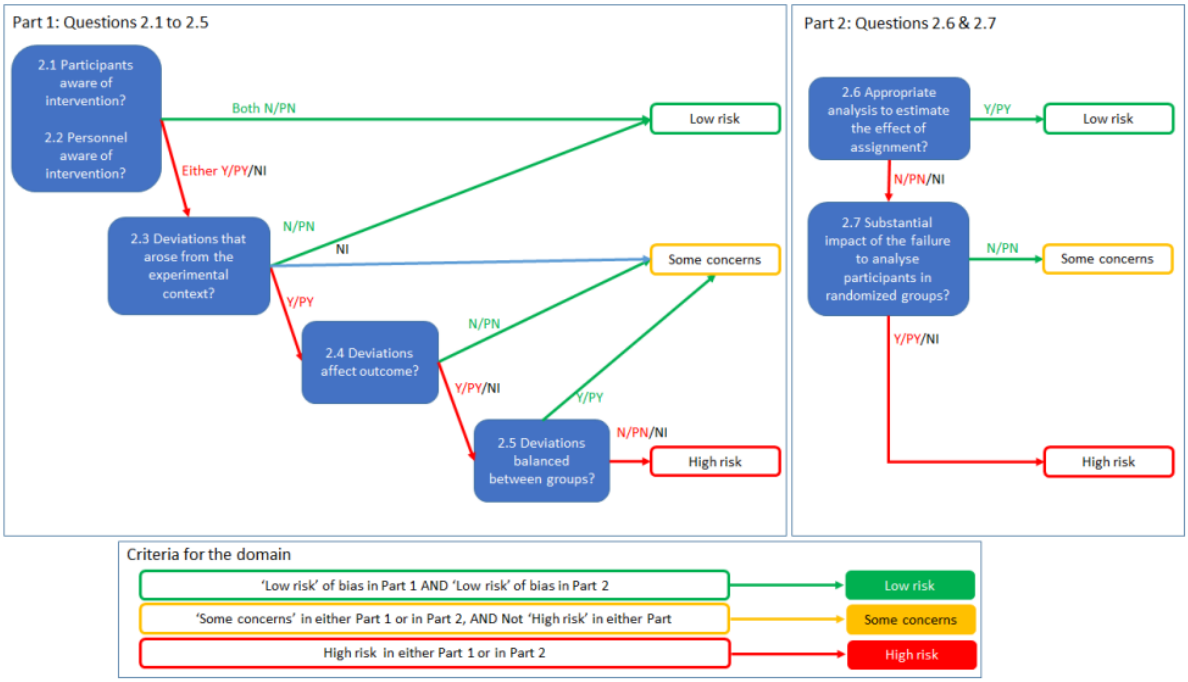
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?

Similar to 1.1.

1.3 Did baseline differences between intervention groups suggest a problem with the randomisation process?

No specific comments.

Domain 2: DEVIATIONS FROM INTENDED INTERVENTIONS



Algorithm for suggested judgement of risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Part 1:

2.1 Were participants aware of their assigned intervention during the trial?

If only stated "double-blind" without further information about the methods, a judgement is needed. We decided to assume that the method of blinding was appropriate and to state "probably no", as in studies of antipsychotic drugs blinding can be rather easily achieved by encapsulating drugs with identical capsules.

In placebo-controlled trials, following the suggestion of the RoB2-guidance document [369], we assumed unblinding due to side effects. In head-to-head trials of antipsychotics, we did not make this assumption, because the different antipsychotics still have some similarities (overlapping receptor-binding-profiles). Consequently, differences in side-effects are more difficult to evaluate for patients and personal which makes it more difficult to guess the assigned intervention.

2.2 Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?

Similar to 2.1.

2.3 If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?

This question is only relevant for unblinded studies (open, single-blind or placebo-controlled (unblinded due to side effects) trials).

Typically protocol deviations are not reported in detail, which leads to a judgement of "some concerns". Although protocol deviations due to the experimental context cannot be excluded, we do not deem that substantial protocol deviations (that potentially affect the outcome, see questions below), happen frequently. Thus, we do not expect important bias from deviations of the outcome and a judgement of "some concerns" seems fair or even too punitive.

2.4. Were these deviations likely to have affected the outcome?

No specific comments.

2.5. Were these deviations from intended intervention balanced between groups?

No specific comments.

Part 2:

2.6. Was an appropriate analysis used to estimate the effect of assignment to intervention?

We considered completer analyses as inappropriate because from such analyses patients are excluded post-randomisation due to toxicity or lack of efficacy.

2.7. Was there potential for a substantial impact (on the results) of the failure to analyse participants in the group to which they were randomized?

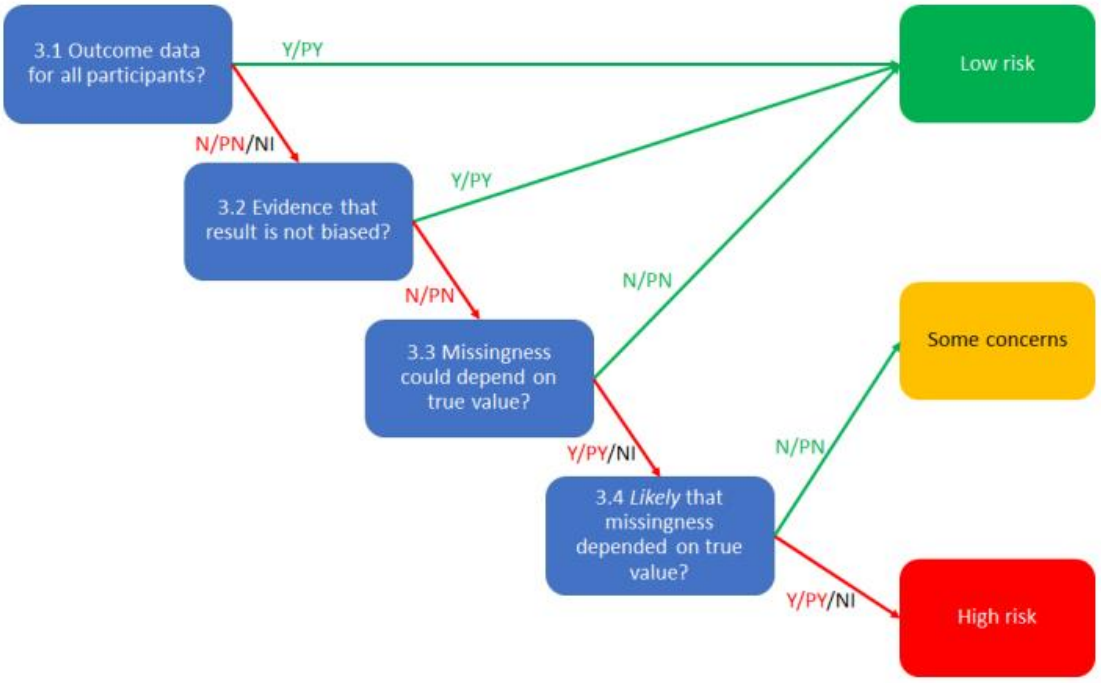
According to the guidance, authors need to make a decision about when exclusion of patients post-randomisation could have a substantial impact on the results.

We considered completer analyses at "some concerns" when the total number of patients with premature study discontinuation was at maximum 20% of the number randomized.

We considered completer analyses at "high risk" when more than 20% of the patients randomized discontinued prematurely.

The decision for this threshold was informed by the work of Xia et al. [370].

Domain 3: MISSING OUTCOME DATA



Algorithm for suggested judgement of risk of bias due to missing outcome data

3.1 Were data for this outcome available for all, or nearly all, participants randomized?

For our continuous outcome we used the threshold of 5% (study discontinuation rate at maximum 5% of number of patients randomized) mentioned in the RoB2-guidance-document.

Also, for dichotomous outcomes, we decided for the same threshold of 5%, to rate continuous and dichotomous outcomes similarly.

It must be noted that from the available aggregate data for dichotomous outcomes, it is not possible to know whether a patient who discontinued the study prematurely, already had an event (no missing data) or not (missing data). Thus, there is unevitable uncertainty and the judgement is possibly too punative because data of patients that discontinued prematurely, but had an event before, are infact included in the results.

Moreover, it must be noted that the available aggregate data for continuous outcomes is usually Last-observation-carried-forward (LOCF). Thus some information of patients that discontinued prematurely is included in the results.

3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?

For all outcomes, the available aggregate data is not sufficient to conduct sensitivity analyses: For continuous outcomes, time-point of study discontinuation and characteristics of patients that discontinued are typically not reported. Moreover, the aggregate data typically already include some data of the patients who discontinued prematurely (by LOCF or MMRM) and cannot be used as a basis for a sensitivity analysis (which would mean adding assumed outcomes of patients with premature study discontinuation to the reported result).

Rarely, results were presented by the original investigators using sophisticated methods such as “multiple imputation (MI)” or “mixed-model-of-repeated-measurement (MMRM)” to account for missing outcome data. However, the RoB2-guidance-document recommends to critically consider the underlying assumptions in these analyses. Based on the reported data, this critical assessment of methods is however not possible. Thus we did not consider them appropriate and continued in the decision tree.

3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?

If no reasons for study discontinuation are reported, then "probably yes", because in studies of antipsychotics in schizophrenia, discontinuation due to side effects are likely.

Also for many reported reasons, doubts remain whether the reason is related to side effects.

Moreover, it needs to be noted that in our aggregate data (where events are usually reported from all patients randomized and continuous data is usually reported using LOCF/MMRM) also patients that discontinued due to reasons unrelated to the outcome can affect the result: This is because patients who discontinued prematurely are not at risk for the event anymore and, for continuous data, results of early time points are included in the results.

Thus, all studies with rates of premature study discontinuation above the threshold mentionend in 3.1 need further evaluation.

3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?

As recommended in the RoB2-guidance-document, we investigated whether there were differences in the total number of participants with premature study discontinuation (dropouts) and in the number of participants with premature study discontinuation for reasons related to the outcome. Thereby, we judged whether it is likely that missingness depended on the outcome and that missingness influenced the outcome substantially (high risk) or to some extend (some concerns).

For the outcomes, we judged the mechanism of missingness and its potential impact on the result according to the following algorithm:

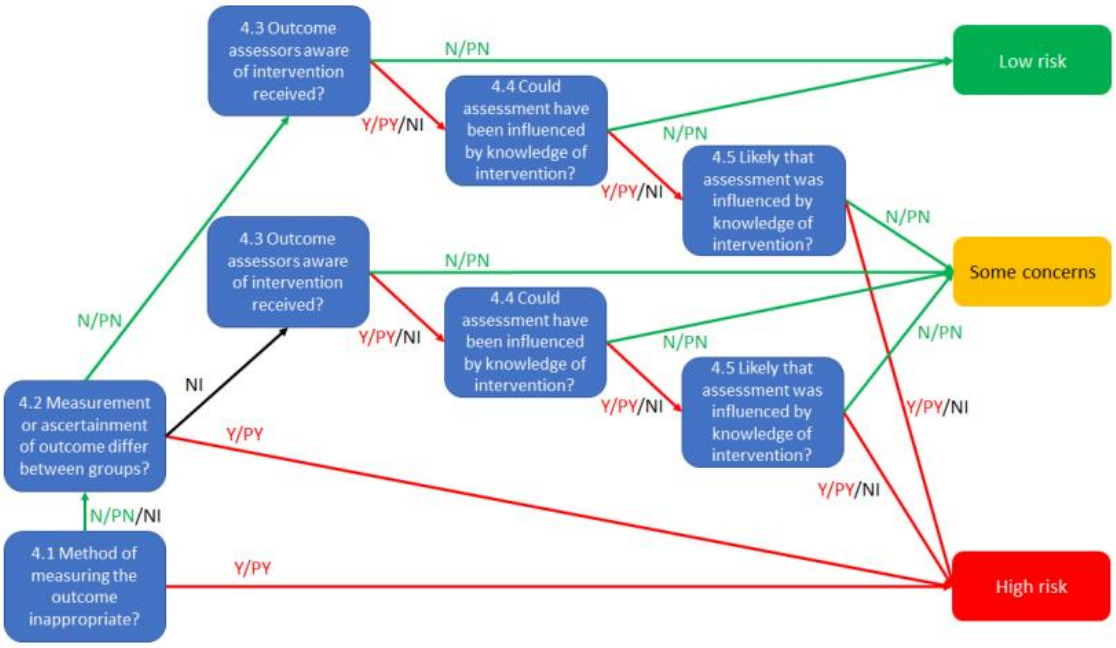
When the rate of study discontinuation for any reason was ≤ 20%, we judged at some concerns. This threshold was informed by the work of Sackett et al. [371] and Xia et al. [370]. Otherwise proceed.

When the rate ratio of study discontinuation for any reason (between two groups compared in a trial) is <0.5/ >2 (half/double), we judged at high risk. Otherwise proceed.

When the rate of study discontinuation due to related reasons (i.e. due to metabolic side effects) was ≤ 20%, we judged at some concerns. Otherwise proceed.

When the rate of study discontinuation due to related reasons (between two groups compared in a trial) is <0.5/ >2 (half/double), we judged at high risk of bias, when ≥0.5/ ≤2, we judge at some concerns.

Domain 4: MEASUREMENT OF THE OUTCOME



Algorithm for suggested judgement of risk of bias in measurement of the outcome

4.1. Was the method of measuring the outcome inappropriate?

No specific comments.

4.2. Could measurement or ascertainment of the outcome have differed between intervention groups?

No specific comments.

4.3. Were outcome assessors aware of the intervention received by study participants?

In head-to-head studies of antipsychotic drugs, when only reported that the study was double-blind, we assumed that blinding was appropriate and stated "probably no" (similar to 2.1.).

In open trials or double-blind placebo-controlled trials (with potential unblinding of study personal, see 2.1.) we checked if there were particular methods to blind the outcome assessors. If such particular methods were not explicitly described, we assumed that the outcomes were assessed by study personal and answered "probably yes".

For all outcomes, we considered the personal/external raters (and not the patient him- or herself) to be most important for the outcome assessment (observer-reported outcome; modern single-blind studies in the field of schizophrenia have particularly blinded raters, e.g. with remote-ratings, which emphasizes the role of the rater as outcome assessor).

4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?

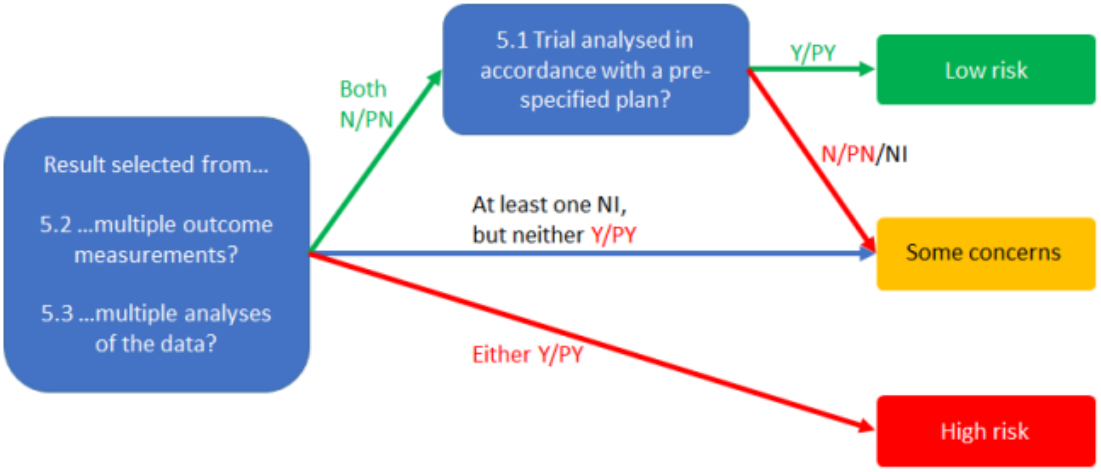
We judged the continuous tolerability outcomes (change in weight gain, parameters of the lipid and glucose metabolism) as not influenced by the knowledge of the intervention, because these are measured by independent objective measuring devices. If the dichotomous outcome number of participants with weight gain was assessed by using objective thresholds like 7% weight gain, we assumed that the assessment was not influenced by knowledge of the intervention and answered "no". If it was only stated that dichotomous weight gain was "significant" without further details, we assumed that objective criteria were underlying and stated "probably no".

Was dichotomous weight gain reported only as adverse event without further details we assumed that knowledge of the intervention could possibly have had an influence on the judgement and answered “not indicated”.

4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?

In general we considered the influence of knowledge of intervention received as minor, resulting in a judgement of some concerns.

Domain 5: SELECTION OF THE REPORTED RESULTS



Algorithm for suggested judgement of risk of bias in selection of the reported result

5.1. Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?

Typically the analysis plan was not available. In this case, we followed the recommendations of the Cochrane handbook [10] and compared the reported results with the reported methods section and with the outcomes that are expected for such trials as informed by other trials.

Is the numerical result being assessed likely to have been selected, on the basis of the results, from...

5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?

No specific comments.

5.3 ... multiple eligible analyses of the data?

No specific comments.

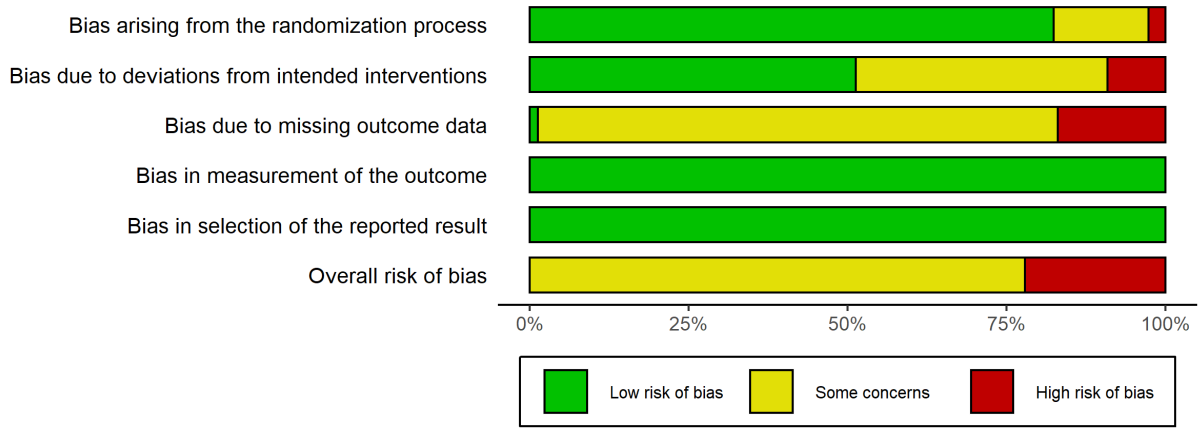
Overall risk of bias:

Overall risk-of-bias judgement	Criteria
Low risk of bias	The study is judged to be at **low risk of bias for all domains** for this result.
Some concerns	The study is judged to raise **some concerns** in at least one domain for this result, but not to be at high risk of bias for any domain.
High risk of bias	The study is judged to be at **high risk of bias** in at least one domain for this result. Or The study is judged to have **some concerns** for **multiple domains** in a way that substantially lowers confidence in the result.

We judged a study at overall high risk of bias when 4 or more domains were rated as “some concerns”.

13.3 Judgement per outcome (overall and per study)

13.3.1 Primary outcome “weight gain”



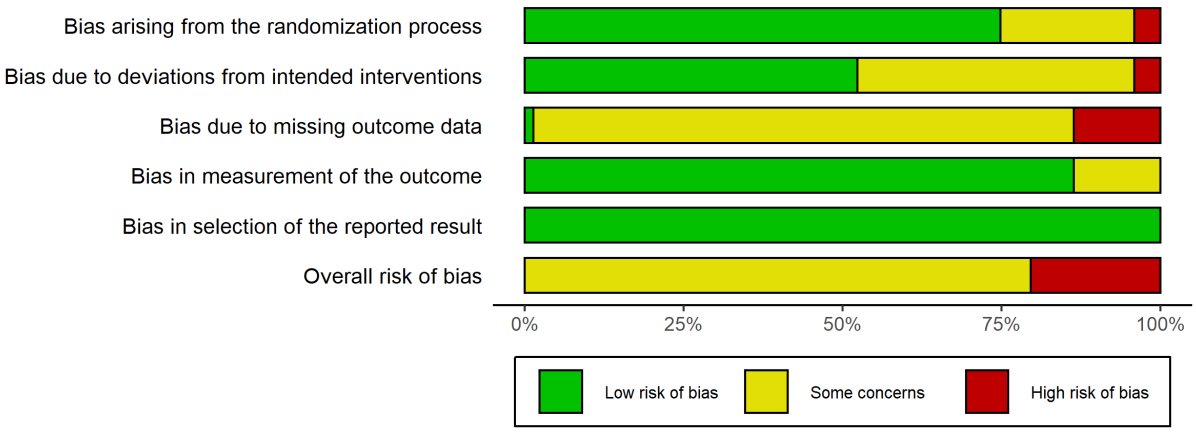
Study	Comparison	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall risk of bias
Abuzzahab 1977a	Fluphenazine oral vs Pimozide oral	Unclear	High	High	Low	Low	High
Adrianzen 2008	Haloperidol oral vs Olanzapine oral	Unclear	High	Unclear	Low	Low	High
Alvarez 2006	Olanzapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Alvarez 2012	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Arato 2002	Placebo vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Arvanitis 1993	Haloperidol oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Bai 2006	Risperidone depot vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Barak 2002	Haloperidol oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Beasley 2003	Olanzapine oral vs Placebo	Low	Unclear	High	Low	Low	High
Berwaerts 2015	Paliperidone depot vs Placebo	Low	Unclear	High	Low	Low	High
Bitter 2004	Clozapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Breier 2005	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Buchanan 2005	Haloperidol oral vs Olanzapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Buchanan 2012a_26 weeks	Asenapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Buchanan 2012b_26 weeks	Asenapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Carrière 2000	Amisulpride oral vs Haloperidol oral	Low	Low	Unclear	Low	Low	Unclear
Chan 2010a	Olanzapine oral vs Risperidone oral	Unclear	High	High	Low	Low	High
Chen 2010	Placebo vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Chetvertnykh 2008	Olanzapine oral vs Risperidone oral	Unclear	High	High	Low	Low	High
Chrzanowski 2006	Aripiprazole oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Citrome 2012	Lurasidone oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Clark 1970	Chlorpromazine oral vs Placebo	Unclear	Unclear	Unclear	Low	Low	Unclear
Clark 1970b	Chlorpromazine oral vs Placebo	Unclear	High	High	Low	Low	High
Colonna 2000	Amisulpride oral vs Haloperidol oral	Low	Unclear	Unclear	Low	Low	Unclear
Cooper 2000b	Placebo vs Zotepine oral	Low	Unclear	Unclear	Low	Low	Unclear
Csernansky 2002	Haloperidol oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Ctri-2014-10-005144	Iloperidone oral vs Olanzapine oral	High	Unclear	Low	Low	Low	High
Cuomo 2017	Aripiprazole depot vs Paliperidone depot	High	Unclear	Low	Low	Low	High
Daniel 1998	Haloperidol oral vs Sertindole oral	Low	Low	High	Low	Low	High
Deberdt 2008	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Detke 2014	Olanzapine depot vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Dossenbach 2004	Fluphenazine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear

Durgam 2016b	Cariprazine oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Emsley 2005	Haloperidol oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
EQUATOR	Brexpiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Fleischhacker 2014	Aripiprazole depot vs Aripiprazole oral	Low	Low	Unclear	Low	Low	Unclear
Fu 2015	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Gaebel 2010	Quetiapine oral vs Risperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
Gureje 2003	Olanzapine oral vs Risperidone oral	Low	Low	High	Low	Low	High
Hirsch 2002	Haloperidol oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Hough 2010	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Ishigooka 2015	Aripiprazole depot vs Aripiprazole oral	Low	High	Unclear	Low	Low	High
Jarema 2003	Olanzapine oral vs Perphenazine oral	Low	Low	High	Low	Low	High
Kahn 2008	Amisulpride oral vs Haloperidol oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Olanzapine oral	Low	Unclear	High	Low	Low	High
Kahn 2008	Haloperidol oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Quetiapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kane 2009_28 weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2010c	Olanzapine depot vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2011	Asenapine oral vs Placebo	Low	Unclear	High	Low	Low	High
Kane 2012	Aripiprazole depot vs Placebo	Low	Unclear	High	Low	Low	High
Kasper 2003	Aripiprazole oral vs Haloperidol oral	Low	Low	Unclear	Low	Low	Unclear
Keefe 2006	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Keefe 2006	Haloperidol oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Keefe 2006	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Keks 2007	Olanzapine oral vs Risperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
Kern 2006	Aripiprazole oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kinon 2006a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Kinon 2006b	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Kongsakon 2006	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Koshikawa 2016	Paliperidone depot vs Risperidone depot	Unclear	Unclear	Unclear	Low	Low	Unclear
Kramer 2007	Paliperidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Laborde 2000	Haloperidol oral vs Zotepine oral	Low	Low	Unclear	Low	Low	Unclear
Laties 2014	Quetiapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Lecrubier 2006	Amisulpride oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Lecrubier 2006	Amisulpride oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Lecrubier 2006	Olanzapine oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Lieberman 2003a_2y	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Lieberman 2003b	Chlorpromazine oral vs Clozapine oral	Low	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Perphenazine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Quetiapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Quetiapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Risperidone oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Loo 1997	Amisulpride oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
McEvoy 2006	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2006	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2006	Quetiapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear

McEvoy 2007a	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Quetiapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2014	Haloperidol depot vs Paliperidone depot	Unclear	Low	Unclear	Low	Low	Unclear
McQuade 2004_26weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Mortimer 2004	Amisulpride oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Naber 2005	Clozapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Naber 2013	Quetiapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Naber 2015	Aripiprazole depot vs Paliperidone depot	Low	High	Unclear	Low	Low	High
Naukkarinen 2000	Olanzapine oral vs Perphenazine oral	Low	Low	Unclear	Low	Low	Unclear
NCT00191555	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
NCT00210717	Paliperidone depot vs Risperidone depot	Low	Low	Unclear	Low	Low	Unclear
NCT00236379	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Nemeth 2017	Cariprazine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2008	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2009	Olanzapine oral vs Quetiapine oral	Low	High	High	Low	Low	High
Newcomer 2009	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Newcomer 2009	Quetiapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Peuskens 2007	Placebo vs Quetiapine oral	Low	Unclear	High	Low	Low	High
Pigott 2003	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Potkin 2008a_104 weeks	Haloperidol oral vs Iloperidone oral	High	Low	High	Low	Low	High
Potkin 2008b_52weeks	Iloperidone oral vs Risperidone oral	High	Low	High	Low	Low	High
Purdon 2000	Haloperidol oral vs Olanzapine oral	Low	Low	High	Low	Low	High
Purdon 2000	Haloperidol oral vs Risperidone oral	Low	Low	High	Low	Low	High
Purdon 2000	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
REPRIEVE	Iloperidone oral vs Placebo	Low	Unclear	High	Low	Low	High
RIS SCH 4178	Risperidone depot vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Ritchie 2003 6m	Olanzapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Robinson 2006	Olanzapine oral vs Risperidone oral	Unclear	Unclear	High	Low	Low	High
Ruhrmann 2007	Flupentixol oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Rui 2014	Paliperidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Russell 1982	Fluphenazine depot vs Fluspirilene depot	Unclear	High	High	Low	Low	High
Sacchetti 2009	Clozapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
San 2012	Haloperidol oral vs Olanzapine oral	Low	Unclear	High	Low	Low	High
San 2012	Haloperidol oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
San 2012	Haloperidol oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
San 2012	Haloperidol oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
San 2012	Olanzapine oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
San 2012	Olanzapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
San 2012	Olanzapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
San 2012	Quetiapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
San 2012	Quetiapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
San 2012	Risperidone oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Savitz 2015_26weeks	Aripiprazole oral vs Paliperidone oral	Low	Low	Unclear	Low	Low	Unclear
Schoemaker 2010	Asenapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Schooler 2005	Haloperidol oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Schreiner 2012	Olanzapine oral vs Paliperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Sechter 2002	Amisulpride oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Sharma 1991	Fluphenazine depot vs Haloperidol depot	Unclear	High	Unclear	Low	Low	High
Speller 1997	Amisulpride oral vs Haloperidol oral	Low	Low	Unclear	Low	Low	Unclear
Suresh 2016	Olanzapine oral vs Risperidone oral	Unclear	Low	High	Low	Low	High
Tandon 2016	Lurasidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Thomas 2010_MetabolicSubgroup	Risperidone oral vs Sertindole oral	Low	Unclear	Unclear	Low	Low	Unclear
Tollefson 2001	Clozapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Tran 1997	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Tunis 2006	Olanzapine oral vs Risperidone oral	Low	High	High	Low	Low	High

Vangala 1998	Haloperidol oral vs Olanzapine oral	Low	Low	High	Low	Low	High
Volavka 2002	Clozapine oral vs Haloperidol oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Clozapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Clozapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Haloperidol oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Voruganti 2007	Olanzapine oral vs Quetiapine oral	Low	High	High	Low	Low	High
Wang 2006	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear

13.3.2 Number of participants with weight gain



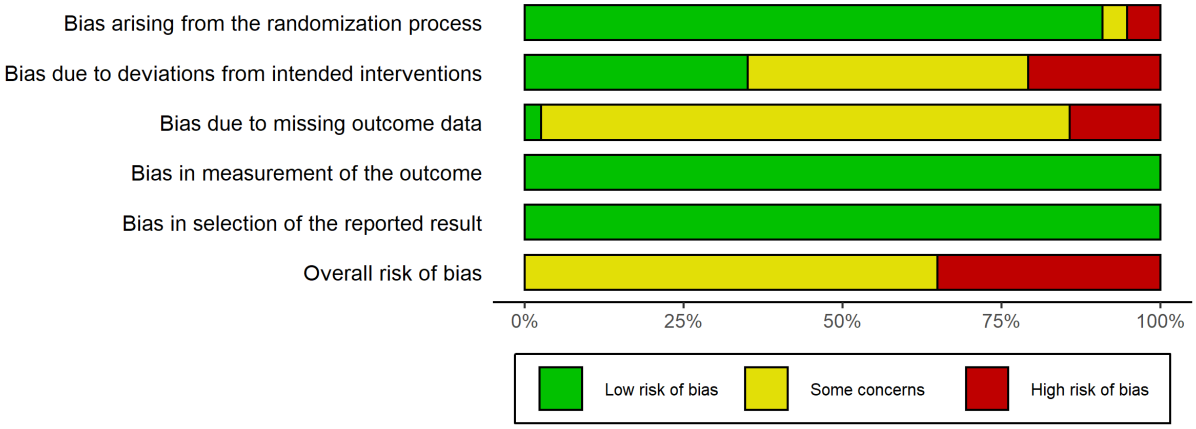
Study (Weight Increased)	Comparison	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall risk of bias
Abuzzahab 1982	Haloperidol oral vs Tiotixene oral	Unclear	High	Unclear	Low	Low	High
Actrn12618001113246	Paliperidone depot vs Paliperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Alvarez 2006	Olanzapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Alvarez 2012	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Amin 1977	Pimozide oral vs Trifluoperazine oral	Unclear	High	Unclear	Low	Low	High
Arato 2002	Placebo vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Arvanitis 1993	Haloperidol oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Beasley 2003	Olanzapine oral vs Placebo	Low	Unclear	High	Unclear	Low	High
Berwaerts 2015	Paliperidone depot vs Placebo	Low	Unclear	High	Low	Low	High
Bitter 2004	Clozapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Breier 2005	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Buchanan 2012a_26 weeks	Asenapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Buchanan 2012b_26 weeks	Asenapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Carrière 2000	Amisulpride oral vs Haloperidol oral	Low	Low	Unclear	Low	Low	Unclear
Chan 2010a	Olanzapine oral vs Risperidone oral	Unclear	Unclear	High	Low	Low	High
Chen 2010	Placebo vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Chowdhury 1999	Clozapine oral vs Risperidone oral	Unclear	Unclear	Unclear	Unclear	Low	High
Chrzanowski 2006	Aripiprazole oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Citrome 2012	Lurasidone oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Claghorn 1974	Pimozide oral vs Trifluoperazine oral	Unclear	Unclear	High	Low	Low	High
Clark 1968b	Chlorpromazine oral vs Placebo	Unclear	Unclear	Unclear	Unclear	Low	High
Clark 1975a	Pimozide oral vs Placebo	Unclear	Unclear	High	Unclear	Low	High
Clark 1975a	Pimozide oral vs Thioridazine oral	Unclear	Low	Unclear	Unclear	Low	Unclear

Clark 1975a	Placebo vs Thioridazine oral	Unclear	Unclear	High	Unclear	Low	High
Colonna 2000	Amisulpride oral vs Haloperidol oral	Low	Unclear	Unclear	Low	Low	Unclear
Cooper 2000b	Placebo vs Zotepine oral	Low	Unclear	Unclear	Unclear	Low	Unclear
Ctri-2014-10-005144	Iloperidone oral vs Olanzapine oral	High	Unclear	Low	Unclear	Low	High
Ctri-2016-02-006660	Clozapine oral vs Quetiapine oral	High	High	Unclear	Unclear	Low	High
Cuomo 2017	Aripiprazole depot vs Paliperidone depot	High	Unclear	Low	Low	Low	High
Daniel 1998	Haloperidol oral vs Sertindole oral	Low	High	High	Low	Low	High
Deberdt 2008	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Del Giudice 1975	Fluphenazine depot vs Fluphenazine oral	Unclear	Unclear	Unclear	Low	Low	Unclear
Detke 2014	Olanzapine depot vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Dossenbach 2004	Fluphenazine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Durgam 2016b	Cariprazine oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Emsley 2005	Haloperidol oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
EQUATOR	Brexpiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Fleischhacker 2014	Aripiprazole depot vs Aripiprazole oral	Low	Low	Unclear	Low	Low	Unclear
Fu 2015	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Gaebel 2010	Quetiapine oral vs Risperidone depot	Low	Unclear	Unclear	Unclear	Low	Unclear
Gureje 2003	Olanzapine oral vs Risperidone oral	Low	Low	High	Low	Low	High
Hirsch 2002	Haloperidol oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Hough 2010	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Ishigooka 2015	Aripiprazole depot vs Aripiprazole oral	Low	Low	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Haloperidol oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Olanzapine oral	Low	Unclear	High	Low	Low	High
Kahn 2008	Haloperidol oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Quetiapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kane 2009_28 weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2010a_52w	Asenapine oral vs Haloperidol oral	High	Unclear	Unclear	Low	Low	High
Kane 2010c	Olanzapine depot vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2011	Asenapine oral vs Placebo	Low	Unclear	High	Low	Low	High
Kane 2012	Aripiprazole depot vs Placebo	Low	Unclear	High	Low	Low	High
Kasper 2003	Aripiprazole oral vs Haloperidol oral	Low	Low	Unclear	Low	Low	Unclear
Kasthurip 2012	Haloperidol oral vs Olanzapine oral	Unclear	Unclear	High	Unclear	Low	High
Keefe 2006	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Keefe 2006	Haloperidol oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Keefe 2006	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Keks 2007	Olanzapine oral vs Risperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
Kern 2006	Aripiprazole oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kinon 2006a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Kinon 2006b	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Kongsakon 2006	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Koshikawa 2016	Paliperidone depot vs Risperidone depot	Unclear	High	Unclear	Low	Low	High
Kramer 2007	Paliperidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Laborde 2000	Haloperidol oral vs Zotepine oral	Low	Low	Unclear	Low	Low	Unclear
Laties 2014	Quetiapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Lecrubier 2006	Amisulpride oral vs Olanzapine oral	Low	Low	Unclear	Unclear	Low	Unclear
Lecrubier 2006	Amisulpride oral vs Placebo	Low	Unclear	Unclear	Unclear	Low	Unclear
Lecrubier 2006	Olanzapine oral vs Placebo	Low	Unclear	Unclear	Unclear	Low	Unclear
Lieberman 2003a_2y	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Perphenazine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear

Lieberman 2005_18months	Olanzapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Quetiapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Quetiapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Risperidone oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Loo 1997	Amisulpride oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
McEvoy 2006	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2006	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2006	Quetiapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Quetiapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2014	Haloperidol depot vs Paliperidone depot	Unclear	Low	Unclear	Low	Low	Unclear
McQuade 2004_26weeks	Aripiprazole oral vs Olanzapine oral	Low	High	Unclear	Low	Low	High
Mortimer 2004	Amisulpride oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Naber 2005	Clozapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Naber 2013	Quetiapine oral vs Risperidone oral	Low	Unclear	Unclear	Unclear	Low	Unclear
Naber 2015	Aripiprazole depot vs Paliperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
NCT00191555	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
NCT00210717	Paliperidone depot vs Risperidone depot	Low	Low	Unclear	Low	Low	Unclear
NCT00236379	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
NCT01149655	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Nct01625897_60w	Cariprazine oral vs Risperidone oral	Low	Unclear	Unclear	Unclear	Low	Unclear
NCT03345979	Aripiprazole depot vs Paliperidone depot	Low	Low	Unclear	Low	Low	Unclear
Nemeth 2017	Cariprazine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2008	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Ohkuma 1987	Haloperidol depot vs Haloperidol oral	Unclear	Low	Unclear	Low	Low	Unclear
Peuskens 2007	Placebo vs Quetiapine oral	Low	Unclear	High	Low	Low	High
Pigott 2003	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Potkin 2008a_104 weeks	Haloperidol oral vs Iloperidone oral	High	Unclear	High	Low	Low	High
Potkin 2008b_52weeks	Iloperidone oral vs Risperidone oral	High	Unclear	High	Low	Low	High
Potkin 2009	Haloperidol oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Purdon 2000	Haloperidol oral vs Olanzapine oral	Low	Low	High	Low	Low	High
Purdon 2000	Haloperidol oral vs Risperidone oral	Low	Low	High	Low	Low	High
Purdon 2000	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Purdon 2001	Haloperidol oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
REPRIEVE	Iloperidone oral vs Placebo	Low	Unclear	High	Low	Low	High
RIS JPN S31	Risperidone depot vs Risperidone oral	Low	Unclear	High	Unclear	Low	High
RIS SCH 4178	Risperidone depot vs Risperidone oral	Low	Unclear	Unclear	Unclear	Low	Unclear
Ritchie 2003 6m	Olanzapine oral vs Risperidone oral	Low	Unclear	Unclear	Unclear	Low	Unclear
Rui 2014	Paliperidone oral vs Placebo	Low	Unclear	Unclear	Unclear	Low	Unclear
Sacchetti 2009	Clozapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Savitz 2015_26weeks	Aripiprazole oral vs Paliperidone oral	Low	Low	Unclear	Low	Low	Unclear
Schoemaker 2010	Asenapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Schreiner 2012	Olanzapine oral vs Paliperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Sechter 2002	Amisulpride oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Speller 1997	Amisulpride oral vs Haloperidol oral	Low	Low	Unclear	Low	Low	Unclear
Stroup 2006	Olanzapine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Olanzapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Olanzapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Quetiapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Quetiapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Risperidone oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Tandon 2016	Lurasidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear

Thomas 2010_MetabolicSubgroup	Risperidone oral vs Sertindole oral	Low	Unclear	Unclear	Low	Low	Unclear
Tollefson 2001	Clozapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Tran 1997	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Tunis 2006	Olanzapine oral vs Risperidone oral	Low	Unclear	High	Low	Low	High
Volavka 2002	Clozapine oral vs Haloperidol oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Clozapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Clozapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Haloperidol oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Wistedt 1984	Fluphenazine depot vs Haloperidol depot	Unclear	Unclear	Unclear	Low	Low	Unclear

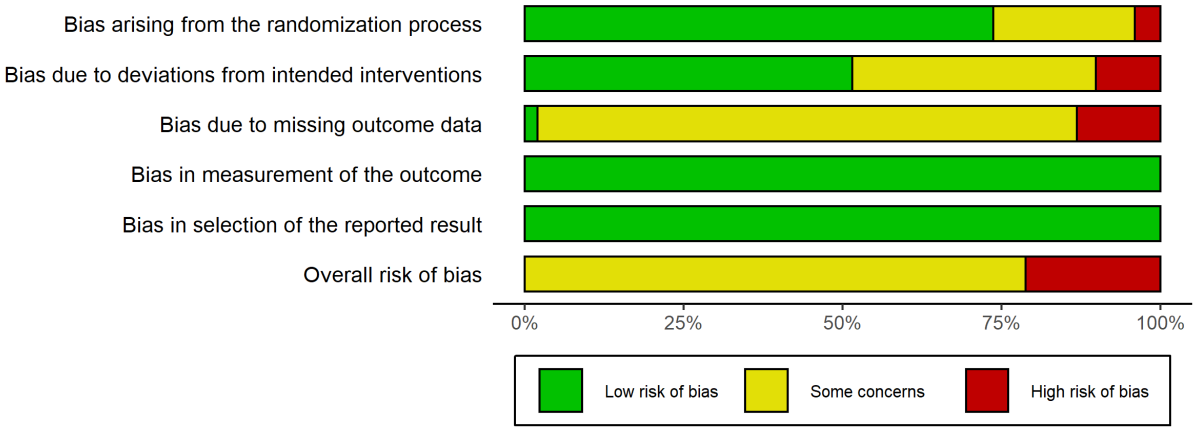
13.3.3 Fasting glucose



Study (Fasting glucose)	Comparison	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall risk of bias
Bai 2006	Risperidone depot vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Berwaerts 2015	Paliperidone depot vs Placebo	Low	Unclear	High	Low	Low	High
Breier 2005	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Chrzanowski 2006	Aripiprazole oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Citrome 2012	Lurasidone oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Ctri-2014-10-005144	Iloperidone oral vs Olanzapine oral	High	Unclear	Low	Low	Low	High
Cuomo 2017	Aripiprazole depot vs Paliperidone depot	High	Unclear	Low	Low	Low	High
Deberdt 2008	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Detke 2014	Olanzapine depot vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Durgam 2016b	Cariprazine oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
EQUATOR	Brexpiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Fleischhacker 2014	Aripiprazole depot vs Aripiprazole oral	Low	High	Unclear	Low	Low	High
Fu 2015	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Gaebel 2010	Quetiapine oral vs Risperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
Hough 2010	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Ishigooka 2015	Aripiprazole depot vs Aripiprazole oral	Low	High	Unclear	Low	Low	High
Kahn 2008	Amisulpride oral vs Haloperidol oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Olanzapine oral	Low	Unclear	High	Low	Low	High

Kahn 2008	Haloperidol oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Quetiapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kane 2009_28 weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2010c	Olanzapine depot vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2011	Asenapine oral vs Placebo	Low	Unclear	High	Low	Low	High
Kane 2012	Aripiprazole depot vs Placebo	Low	Unclear	High	Low	Low	High
Keks 2007	Olanzapine oral vs Risperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
Kinon 2006b	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Kramer 2007	Paliperidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Laties 2014	Quetiapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Lieberman 2003b	Chlorpromazine oral vs Clozapine oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Quetiapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2014	Haloperidol depot vs Paliperidone depot	Unclear	Low	Unclear	Low	Low	Unclear
McQuade 2004_26weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Mortimer 2004	Amisulpride oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
NCT00210717	Paliperidone depot vs Risperidone depot	Low	Low	Unclear	Low	Low	Unclear
NCT00236379	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
NCT01149655	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Nemeth 2017	Cariprazine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2008	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2009	Olanzapine oral vs Quetiapine oral	Low	High	High	Low	Low	High
Newcomer 2009	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Newcomer 2009	Quetiapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Peuskens 2007	Placebo vs Quetiapine oral	Low	Unclear	High	Low	Low	High
Pigott 2003	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Potkin 2008a_104 weeks	Haloperidol oral vs Iloperidone oral	High	Low	High	Low	Low	High
Potkin 2008b_52weeks	Iloperidone oral vs Risperidone oral	High	Low	High	Low	Low	High
REPRIEVE	Iloperidone oral vs Placebo	Low	Unclear	High	Low	Low	High
San 2012	Haloperidol oral vs Olanzapine oral	Low	High	High	Low	Low	High
San 2012	Haloperidol oral vs Quetiapine oral	Low	High	Unclear	Low	Low	High
San 2012	Haloperidol oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
San 2012	Haloperidol oral vs Ziprasidone oral	Low	High	Unclear	Low	Low	High
San 2012	Olanzapine oral vs Quetiapine oral	Low	High	Unclear	Low	Low	High
San 2012	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
San 2012	Olanzapine oral vs Ziprasidone oral	Low	High	Unclear	Low	Low	High
San 2012	Quetiapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
San 2012	Quetiapine oral vs Ziprasidone oral	Low	High	Unclear	Low	Low	High
San 2012	Risperidone oral vs Ziprasidone oral	Low	High	Unclear	Low	Low	High
Savitz 2015_26weeks	Aripiprazole oral vs Paliperidone oral	Low	Low	Unclear	Low	Low	Unclear
Schoemaker 2010	Asenapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Schreiner 2012	Olanzapine oral vs Paliperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Smith 2009	Olanzapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Suresh 2016	Olanzapine oral vs Risperidone oral	Unclear	Low	High	Low	Low	High
Thomas 2010_MetabolicSubgroup	Risperidone oral vs Sertindole oral	Low	Unclear	Unclear	Low	Low	Unclear
Volavka 2002	Clozapine oral vs Haloperidol oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Clozapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Clozapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Haloperidol oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Wani 2015	Aripiprazole oral vs Olanzapine oral	Unclear	Unclear	Unclear	Low	Low	Unclear

13.3.4 Total cholesterol

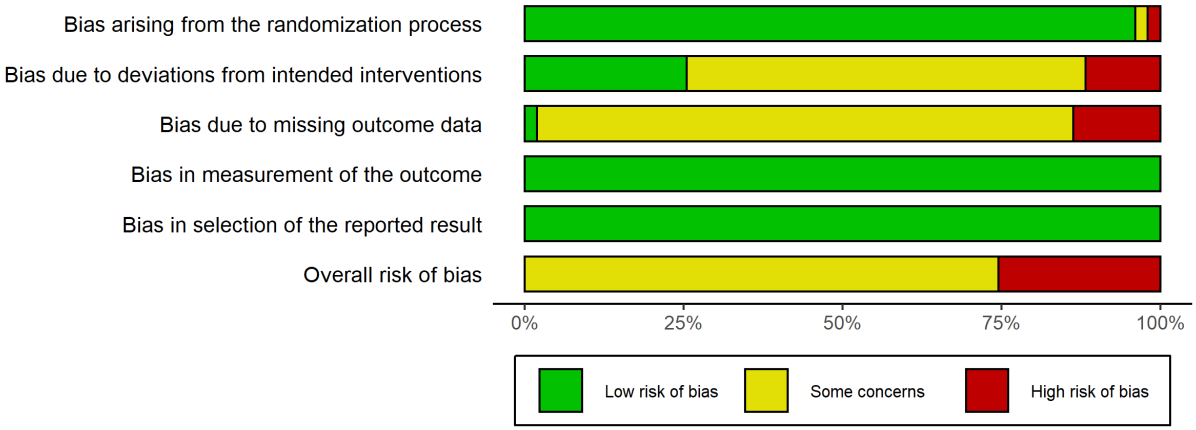


Study (Total Cholesterol)	Comparison	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall risk of bias
Bai 2006	Risperidone depot vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Beasley 2003	Olanzapine oral vs Placebo	Low	Unclear	High	Low	Low	High
Berwaerts 2015	Paliperidone depot vs Placebo	Low	Unclear	High	Low	Low	High
Breier 2005	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Chrzanowski 2006	Aripiprazole oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Citrome 2012	Lurasidone oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Clark 1970	Chlorpromazine oral vs Placebo	Unclear	Unclear	Unclear	Low	Low	Unclear
Clark 1970b	Chlorpromazine oral vs Placebo	Unclear	High	High	Low	Low	High
Ctri-2014-10-005144	Iloperidone oral vs Olanzapine oral	High	Unclear	Low	Low	Low	High
Cuomo 2017	Aripiprazole depot vs Paliperidone depot	High	Unclear	Low	Low	Low	High
Deberdt 2008	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Detke 2014	Olanzapine depot vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Dossenbach 2004	Fluphenazine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Durgam 2016b	Cariprazine oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
EQUATOR	Brexpiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Fleischhacker 2014	Aripiprazole depot vs Aripiprazole oral	Low	High	Unclear	Low	Low	High
Fu 2015	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Gaebel 2010	Quetiapine oral vs Risperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
Hough 2010	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Ishigooka 2015	Aripiprazole depot vs Aripiprazole oral	Low	High	Unclear	Low	Low	High
Kahn 2008	Amisulpride oral vs Haloperidol oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Olanzapine oral	Low	Unclear	High	Low	Low	High
Kahn 2008	Haloperidol oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Quetiapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kane 2009_28 weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2010c	Olanzapine depot vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2011	Asenapine oral vs Placebo	Low	Unclear	High	Low	Low	High
Kane 2012	Aripiprazole depot vs Placebo	Low	Unclear	High	Low	Low	High
Keefe 2006	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear

Keefe 2006	Haloperidol oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Keefe 2006	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Keks 2007	Olanzapine oral vs Risperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
Kern 2006	Aripiprazole oral vs Olanzapine oral	Low	High	Unclear	Low	Low	High
Kinon 2006a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Kinon 2006b	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Koshikawa 2016	Paliperidone depot vs Risperidone depot	Unclear	Unclear	Unclear	Low	Low	Unclear
Kramer 2007	Paliperidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Laties 2014	Quetiapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Lieberman 2003a_2y	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Perphenazine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Quetiapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Quetiapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Risperidone oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
McEvoy 2006	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2006	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2006	Quetiapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Quetiapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2014	Haloperidol depot vs Paliperidone depot	Unclear	Low	Unclear	Low	Low	Unclear
McQuade 2004_26weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
NCT00210717	Paliperidone depot vs Risperidone depot	Low	Low	Unclear	Low	Low	Unclear
NCT00236379	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
NCT01149655	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Nemeth 2017	Cariprazine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2008	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2009	Olanzapine oral vs Quetiapine oral	Low	High	High	Low	Low	High
Newcomer 2009	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Newcomer 2009	Quetiapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Pigott 2003	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Potkin 2008a_104 weeks	Haloperidol oral vs Iloperidone oral	High	Low	High	Low	Low	High
Potkin 2008b_52weeks	Iloperidone oral vs Risperidone oral	High	Low	High	Low	Low	High
Potkin 2009	Haloperidol oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
REPRIEVE	Iloperidone oral vs Placebo	Low	Unclear	High	Low	Low	High
RIS SCH 4178	Risperidone depot vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Rui 2014	Paliperidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Savitz 2015_26weeks	Aripiprazole oral vs Paliperidone oral	Low	Low	Unclear	Low	Low	Unclear
Schoemaker 2010	Asenapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Schreiner 2012	Olanzapine oral vs Paliperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Simpson 1967	Haloperidol oral vs Placebo	Unclear	High	High	Low	Low	High
Smith 2009	Olanzapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Stroup 2006	Olanzapine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Olanzapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Olanzapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Quetiapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Quetiapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Risperidone oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Subotnik 2015	Risperidone depot vs Risperidone oral	Low	High	High	Low	Low	High
Suresh 2016	Olanzapine oral vs Risperidone oral	Unclear	Low	High	Low	Low	High
Tandon 2016	Lurasidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear

Thomas 2010_MetabolicSubgroup	Risperidone oral vs Sertindole oral	Low	Unclear	Unclear	Low	Low	Unclear
Volavka 2002	Clozapine oral vs Haloperidol oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Clozapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Clozapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Haloperidol oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Volavka 2002	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear

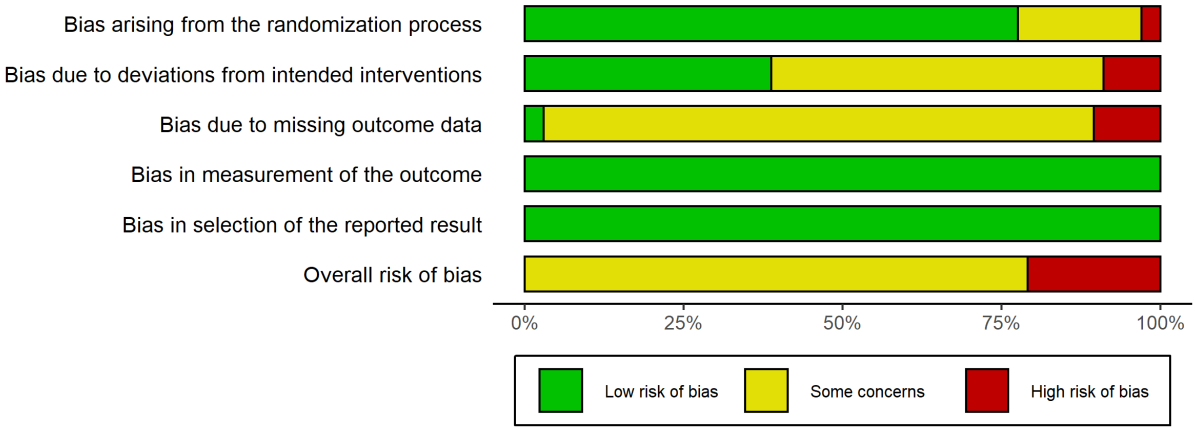
13.3.5 LDL cholesterol



Study (Ldl Cholesterol)	Comparison	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall risk of bias
Berwaerts 2015	Paliperidone depot vs Placebo	Low	Unclear	High	Low	Low	High
Breier 2005	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Chrzanowski 2006	Aripiprazole oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Citrome 2012	Lurasidone oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Ctri-2014-10-005144	Iloperidone oral vs Olanzapine oral	High	Unclear	Low	Low	Low	High
Deberdt 2008	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Detke 2014	Olanzapine depot vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Durgam 2016b	Cariprazine oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
EQUATOR	Brexpiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Fleischhacker 2014	Aripiprazole depot vs Aripiprazole oral	Low	High	Unclear	Low	Low	High
Fu 2015	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Hough 2010	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Ishigooka 2015	Aripiprazole depot vs Aripiprazole oral	Low	High	Unclear	Low	Low	High
Kahn 2008	Amisulpride oral vs Haloperidol oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Olanzapine oral	Low	Unclear	High	Low	Low	High
Kahn 2008	Haloperidol oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear

Kahn 2008	Haloperidol oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Quetiapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kane 2009_28 weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2010c	Olanzapine depot vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2011	Asenapine oral vs Placebo	Low	Unclear	High	Low	Low	High
Kane 2012	Aripiprazole depot vs Placebo	Low	Unclear	High	Low	Low	High
Keks 2007	Olanzapine oral vs Risperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
Kinon 2006a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Kinon 2006b	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Kramer 2007	Paliperidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Laties 2014	Quetiapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
McEvoy 2014	Haloperidol depot vs Paliperidone depot	Unclear	Low	Unclear	Low	Low	Unclear
McQuade 2004_26weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
NCT00210717	Paliperidone depot vs Risperidone depot	Low	Low	Unclear	Low	Low	Unclear
NCT00236379	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
NCT01149655	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Nemeth 2017	Cariprazine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2008	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2009	Olanzapine oral vs Quetiapine oral	Low	High	High	Low	Low	High
Newcomer 2009	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Newcomer 2009	Quetiapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Peuskens 2007	Placebo vs Quetiapine oral	Low	Unclear	High	Low	Low	High
Pigott 2003	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
REPRIEVE	Iloperidone oral vs Placebo	Low	Unclear	High	Low	Low	High
RIS SCH 4178	Risperidone depot vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Savitz 2015_26weeks	Aripiprazole oral vs Paliperidone oral	Low	Low	Unclear	Low	Low	Unclear
Schreiner 2012	Olanzapine oral vs Paliperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Smith 2009	Olanzapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Tandon 2016	Lurasidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Thomas 2010_MetabolicSubgroup	Risperidone oral vs Sertindole oral	Low	Unclear	Unclear	Low	Low	Unclear

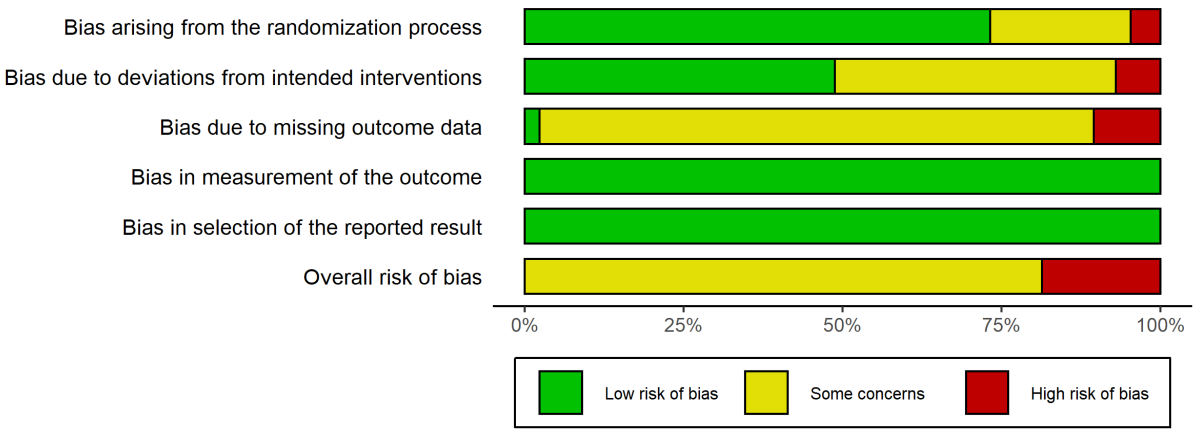
13.3.6 HDL cholesterol



Study (Hdl Cholesterol)	Comparison	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall risk of bias
Berwaerts 2015	Paliperidone depot vs Placebo	Low	Unclear	High	Low	Low	High
Breier 2005	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Chrzanowski 2006	Aripiprazole oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Citrome 2012	Lurasidone oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Ctri-2014-10-005144	Iloperidone oral vs Olanzapine oral	High	Unclear	Low	Low	Low	High
Cuomo 2017	Aripiprazole depot vs Paliperidone depot	High	Unclear	Low	Low	Low	High
Deberdt 2008	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Detke 2014	Olanzapine depot vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Durgam 2016b	Cariprazine oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
EQUATOR	Brexpiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Fleischhacker 2014	Aripiprazole depot vs Aripiprazole oral	Low	High	Unclear	Low	Low	High
Fu 2015	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Hough 2010	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Ishigooka 2015	Aripiprazole depot vs Aripiprazole oral	Low	High	Unclear	Low	Low	High
Kahn 2008	Amisulpride oral vs Haloperidol oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Olanzapine oral	Low	Unclear	High	Low	Low	High
Kahn 2008	Haloperidol oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Quetiapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kane 2009_28 weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2010c	Olanzapine depot vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2011	Asenapine oral vs Placebo	Low	Unclear	High	Low	Low	High
Kane 2012	Aripiprazole depot vs Placebo	Low	Unclear	High	Low	Low	High
Keks 2007	Olanzapine oral vs Risperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
Kinon 2006a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Kinon 2006b	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Koshikawa 2016	Paliperidone depot vs Risperidone depot	Unclear	Unclear	Unclear	Low	Low	Unclear
Kramer 2007	Paliperidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear

Laties 2014	Quetiapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Perphenazine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Quetiapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Quetiapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Risperidone oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Quetiapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2014	Haloperidol depot vs Paliperidone depot	Unclear	Low	Unclear	Low	Low	Unclear
McQuade 2004_26weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
NCT00210717	Paliperidone depot vs Risperidone depot	Low	Low	Unclear	Low	Low	Unclear
NCT00236379	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
NCT01149655	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Nemeth 2017	Cariprazine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2008	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2009	Olanzapine oral vs Quetiapine oral	Low	High	High	Low	Low	High
Newcomer 2009	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Newcomer 2009	Quetiapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Peuskens 2007	Placebo vs Quetiapine oral	Low	Unclear	High	Low	Low	High
Pigott 2003	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
REPRIEVE	Iloperidone oral vs Placebo	Low	Unclear	High	Low	Low	High
RIS SCH 4178	Risperidone depot vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Savitz 2015_26weeks	Aripiprazole oral vs Paliperidone oral	Low	Low	Unclear	Low	Low	Unclear
Schreiner 2012	Olanzapine oral vs Paliperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Smith 2009	Olanzapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Tandon 2016	Lurasidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Thomas 2010_MetabolicSubgroup	Risperidone oral vs Sertindole oral	Low	Unclear	Unclear	Low	Low	Unclear
Wani 2015	Aripiprazole oral vs Olanzapine oral	Unclear	Unclear	Unclear	Low	Low	Unclear

13.3.7 Triglycerides



Study (Triglycerides)	Comparison	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall risk of bias
Bai 2006	Risperidone depot vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Berwaerts 2015	Paliperidone depot vs Placebo	Low	Unclear	High	Low	Low	High
Breier 2005	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Chrzanowski 2006	Aripiprazole oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Citrome 2012	Lurasidone oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Ctri-2014-10-005144	Iloperidone oral vs Olanzapine oral	High	Unclear	Low	Low	Low	High
Cuomo 2017	Aripiprazole depot vs Paliperidone depot	High	Unclear	Low	Low	Low	High
Deberdt 2008	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Detke 2014	Olanzapine depot vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Durgam 2016b	Cariprazine oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
EQUATOR	Brexpiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Fleischhacker 2014	Aripiprazole depot vs Aripiprazole oral	Low	High	Unclear	Low	Low	High
Fu 2015	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Gaebel 2010	Quetiapine oral vs Risperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
Hough 2010	Paliperidone depot vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Ishigooka 2015	Aripiprazole depot vs Aripiprazole oral	Low	High	Unclear	Low	Low	High
Kahn 2008	Amisulpride oral vs Haloperidol oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Olanzapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Amisulpride oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Olanzapine oral	Low	Unclear	High	Low	Low	High
Kahn 2008	Haloperidol oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Haloperidol oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Quetiapine oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Olanzapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kahn 2008	Quetiapine oral vs Ziprasidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Kane 2009_28 weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2010c	Olanzapine depot vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Kane 2011	Asenapine oral vs Placebo	Low	Unclear	High	Low	Low	High
Kane 2012	Aripiprazole depot vs Placebo	Low	Unclear	High	Low	Low	High
Keefe 2006	Haloperidol oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Keefe 2006	Haloperidol oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Keefe 2006	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Keks 2007	Olanzapine oral vs Risperidone depot	Low	Unclear	Unclear	Low	Low	Unclear
Kinon 2006a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
Kinon 2006b	Olanzapine oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
Koshikawa 2016	Paliperidone depot vs Risperidone depot	Unclear	Unclear	Unclear	Low	Low	Unclear
Kramer 2007	Paliperidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Laties 2014	Quetiapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Perphenazine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Olanzapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Perphenazine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Quetiapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Quetiapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Lieberman 2005_18months	Risperidone oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
McEvoy 2006	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2006	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear

McEvoy 2006	Quetiapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Olanzapine oral vs Quetiapine oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Olanzapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2007a	Quetiapine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
McEvoy 2014	Haloperidol depot vs Paliperidone depot	Unclear	Low	Unclear	Low	Low	Unclear
McQuade 2004_26weeks	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
NCT00210717	Paliperidone depot vs Risperidone depot	Low	Low	Unclear	Low	Low	Unclear
NCT00236379	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
NCT01149655	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Nemeth 2017	Cariprazine oral vs Risperidone oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2008	Aripiprazole oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Newcomer 2009	Olanzapine oral vs Quetiapine oral	Low	High	High	Low	Low	High
Newcomer 2009	Olanzapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Newcomer 2009	Quetiapine oral vs Risperidone oral	Low	High	Unclear	Low	Low	High
Peuskens 2007	Placebo vs Quetiapine oral	Low	Unclear	High	Low	Low	High
Pigott 2003	Aripiprazole oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Potkin 2008a_104 weeks	Haloperidol oral vs Iloperidone oral	High	Low	High	Low	Low	High
Potkin 2008b_52weeks	Iloperidone oral vs Risperidone oral	High	Low	High	Low	Low	High
Potkin 2009	Haloperidol oral vs Ziprasidone oral	Low	Low	Unclear	Low	Low	Unclear
REPRIEVE	Iloperidone oral vs Placebo	Low	Unclear	High	Low	Low	High
RIS SCH 4178	Risperidone depot vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Rui 2014	Paliperidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Savitz 2015_26weeks	Aripiprazole oral vs Paliperidone oral	Low	Low	Unclear	Low	Low	Unclear
Schoemaker 2010	Asenapine oral vs Olanzapine oral	Low	Low	Unclear	Low	Low	Unclear
Schreiner 2012	Olanzapine oral vs Paliperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Smith 2009	Olanzapine oral vs Risperidone oral	Low	Unclear	Unclear	Low	Low	Unclear
Stroup 2006	Olanzapine oral vs Quetiapine oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Olanzapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Olanzapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Quetiapine oral vs Risperidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Quetiapine oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Stroup 2006	Risperidone oral vs Ziprasidone oral	Unclear	Low	Unclear	Low	Low	Unclear
Tandon 2016	Lurasidone oral vs Placebo	Low	Unclear	Unclear	Low	Low	Unclear
Thomas 2010_MetabolicSubgroup	Risperidone oral vs Sertindole oral	Low	Unclear	Unclear	Low	Low	Unclear
Wani 2015	Aripiprazole oral vs Olanzapine oral	Unclear	Unclear	Unclear	Low	Low	Unclear

14 Assessment of confidence in estimates

14.1 General notes

We used the official webtool at https://cinema.ispm.unibe.ch/ and followed the CINeMA-guidance-document [368].

The CINeMA-tool provides a framework for evaluating the confidence in the estimates of a network meta-analysis in six different domains. It uses the original data to run a network meta-analysis in order to evaluate the results for each comparison and to calculate a contribution matrix. Therefore, some settings and judgements need to be given, which we report in the following:

We evaluated confidence in estimates of network meta-analysis for the primary outcome "weight gain".

We chose random-effects models for network meta-analysis similar to the models used in our analyses. The default method is an inverse-variance meta-analysis.

The results of the CINeMA assessment for each comparison are given as a colour code in the league table for the primary outcome.

14.2 Details of the assessment for the primary outcome "weight gain"

Domain 1: WITHIN-STUDY-BIAS

We used the overall risk of bias rating from the Cochrane risk of bias tool 2 (see above).

For studies with multiple comparisons, we used the worst overall risk of bias rating of all comparisons as the overall risk of bias rating of the study (i.e. when one comparison was judged at high risk, then the whole study was considered as at high risk).

Domain 2: REPORTING BIAS

For this domain, suppression of negative findings (publication bias) and omission of unfavourable results from study reports (outcome reporting bias) needs to be considered (time-lag-bias is improbable as antipsychotic drugs are not very recently developed drugs).

For the judgment concerning a potential publication bias of the primary outcome "weight gain", we considered the funnel plots and the Egger-test reported above which did not yield strong indication for the presence of small-study effect (a proxy for publication bias). Moreover, in general, we deemed it unlikely that studies are not pubslished at all for unfavourable secondary outcomes and weight is mostly reported as such in studies of schizophrenia. Only few modern studies are designed to examine weight gain and metabolic parameters. Therefore we deemed the risk for publication bias low.

For the judgement of a potential outcome reporting bias, we considered the recommendations of the Cochrane handbook [10] and the ORBIT-framework [372]. We included in the assessment also studies that reported no usable data for any of the outcomes. We expected every study to report data on continuous weight gain as it is one of the most important side effects. The measurement of weight can be easily performed, is available everywhere and not associated with substantial costs. Even if not systematically recorded and analyzed, as it could be the case especially in older trials, probably in most of the studies weight was monitored. Therefore, we assumed all studies which did not report continuous weight gain as potentially suspicious for outcome reporting bias irrespective of their primary outcome.

We judged all comparisons for which direct evidence was available (i.e. the comparison was examined in at least one original trial) as potentially affected (high risk) by outcome reporting bias when the number of participants for which continuous weight data was not reported was above 20% of all participants across all studies for the specific comparison. Conversely, we judged all comparisons at low risk for outcome reporting bias when for at least 80% of the participants weight gain was reported across studies. For comparisons for which only indirect evidence was available it is difficult to assess the risk of outcome reporting bias (because the estimate is derived from multiple

other comparisons in the network which can be at high or low risk) and we assumed some concerns in the domain of reporting bias.

Domain 3: INDIRECTNESS

Population: We included all studies with participants diagnosed with schizophrenia or related disorders (such as schizophreniform or schizoaffective disorders) without further restrictions, because we assumed the occurrence of metabolic side effects not affected by the stage of the disease and comparable in special populations (e.g. participants with predominant negative symptoms).

Interventions: All investigated interventions were licenced antipsychotic drugs (or placebo) and thus directly relevant for the research question.

Outcomes: The selection of outcomes compromises the most important metabolic parameters and is thus directly relevant for the research question.

Setting: We included studies conducted with out-patients, in-patients or both.

Domain 4: IMPRECISION/ Domain 5: HETEROGENEITY/ Domain 6: INCOHERENCE

These three domains require to set thresholds for clinically important differences between interventions.

For our primary outcome "weight gain" we considered a difference outside the interval -2 kg to +2 kg clinically important.

Summarizing judgements across the six domains: OVERALL CINeMA LEVEL

In the CINeMA framework, the overall levels of confidence in the estimates are:

1. high

2. moderate

3. low

4. very low

The CINeMA-guidance-document [368] suggests for each comparison to start at the first level (i.e. high) and to downgrade for one level for a rating of "some concerns", and by two levels for a rating of "major concerns". In case, several domains are rated at some concerns or major concerns, it is recommended to consider judgements on different domains jointly rather than in isolation. The reason is that domains are interconnected and downgrading more than once for related concerns should be avoided. (The following examples are given in the guidance document: Heterogeneity will increase imprecision in treatment effects and may be related to variability in within-study bias or the presence of reporting bias. Indirectness includes considerations on intransitivity, which manifests itself in the data as statistical incoherence. In the worked example there is 'some concerns' for imprecision and heterogeneity and 'major concerns' for incoherence. Downgrading by two levels is considered to be sufficient in this situation, because imprecision, heterogeneity, and incoherence are interconnected.)

Based on these recommendations, we used the following approach to reach an overall level of confidence for each comparison and outcome:

1 judgement of "some concerns" leads to downgrading by 1 level.

1 judgement of "major concerns" leads to downgrading by 2 levels.

2 judgements of "some concerns" could be interconnected and do not justify downgrading more than by 1 level.

1 judgement of "major concerns" and up to 2 judgements of "some concerns" or 1 additional judgement of "major concerns" could be interconnected and do not justify downgrading by more than 2 levels.

2 judgements of “major concerns” and any additional judgements of “some concerns” or “major concerns” (or more than 4 judgements of some concerns) lead to downgrading by three levels (the maximum).

To rate the 65 direct and 341 indirect comparisons we used the generic approach described above.

15 Heterogeneity in the network meta-analyses of the secondary outcomes

Summary of results:

Heterogeneity was low for the dichotomous outcome number of participants with weight gain. When calculated in standardized mean difference (SMD) and compared to the empirical comparator of Rhodes et al. [366] we found low heterogeneity for LDL cholesterol and HDL cholesterol. For fasting glucose, total cholesterol and trigylcerides heterogeneity ranged from low to moderate.

Details:

For the dichotomous outcome number of participants with weight gain we compared the estimator of between-study-heterogeneity τ with empirical distributions for τ provided by Turner et al. [373].

For the other continuous outcomes measured as mean differences we added calculations in SMD to can compare them to Rhodes et al. [366].

We judged heterogeneity as low when common-τ was below the 25% quantile, as low-moderate when between 25% and 50% quantile, as moderate-high when between 50% and 75% and as high when above the 75% quantile.

Below, we present the heterogeneity observed in the network meta-analyses of all secondary outcomes.

Outcome	**Common-τ of the Bayesian model estimated in NMA**	**Outcome type used as comparator***	**Empirical predictive distribution of τ**	**Location of the estimated common tau compared to the quartiles of the empirical predictive distribution**	**Judgement of heterogeneity**
Dichotomous	**Mean (95%CrI)**	**From Turner et al. [373]**	**Median (IQR)**		
Weight gain (OR)	0.175	Adverse event	0.35 (IQR 0.21, 0.60)	Below 25%-quantile	low
Continuous	**Mean (95%CrI)**	**From Rhodes et al. [366]**	**Median (IQR)**		
Fasting Glucose (MD)	1.629	Outcome estimated as mean difference (MD). No comparator available	-	-	-
Fasting glucose (SMD)	0.092	Biological marker	0.16 (IQR 0.06, 0.44)	Between 25%- and 50%-quantile	low-moderate
Total cholesterol (MD)	3.138	Outcome estimated as mean difference (MD). No comparator available	-	-	-
Total Cholesterol (SMD)	0.094	Biological marker	0.16 (IQR 0.06, 0.44)	Between 25%- and 50%-quantile	low-moderate
LDL Cholesterol (MD)	1.947	Outcome estimated as mean difference (MD). No comparator available	-	-	-
LDL Cholesterol (SMD)	0.055	Biological marker	0.16 (IQR 0.06, 0.44)	Below the 25%-quantile	low
HDL Cholesterol (MD)	0.357	Outcome estimated as mean difference	-	-	-

		(MD). No comparator available			
HDL Cholesterol (SMD)	0	Biological marker	0.16 (IQR 0.06, 0.44)	Below the 25%-quantile	low
Triglycerides	8.219	Outcome estimated as mean difference (MD). No comparator available	-	-	-
Triglycerides (SMD)	0.077	Biological marker	0.16 (IQR 0.06, 0.44)	Between 25%- and 50%-quantile	low-moderate

** Intervention comparison type always pharmacological vs pharmacological*

16 Discussion of previous reviews

16.1 Pillinger 2020

Pillinger et al. [374] conducted a network meta-analysis to compare antipsychotics regarding metabolic side effects occuring in adults with **acute exacerbation** of schizophrenia or related disorders during **acute short-term treatment**. Only randomized double-blind controlled trials were included.

Continuous data of body weight, body-mass index (BMI), and metabolic measures (fasting glucose, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) were analysed.

100 studies (25952 participants) met the inclusion criteria with a treatment duration of 2–13 weeks (median 6 weeks [IQR 6–8]).

In 83 studies with 22960 participants evidence of weight gain was seen for 10 of the 18 antipsychotics with data (antipsychotics with evidence of weight gain compared with placebo: brexpiprazole, asenapine, risperidone and paliperidone, quetiapine, iloperidone, sertindole, olanzapine, zotepine, and clozapine; antipsychotics with no evidence of weight gain compared with placebo: ziprasidone, haloperidol, fluphenazine, aripiprazole, lurasidone, cariprazine, amisulpride, or flupenthixol).

Across all parameters clozapine and olanzapine were associated with the largest degree of metabolic dysregulation.

Additionally, predictors of metabolic dysregulation were examined: Higher baseline weight and male sex were found to predict greater increase in glucose. Non-white ethnicity was associated with greater increases in total cholesterol compared with white ethnicity.

Improvements in symptom severity were associated with increases in weight, BMI, total-cholesterol, and LDL cholesterol, and decreases in HDL cholesterol.

The most important difference to this work is that our network meta-analysis examines mid- to long-term treatment including studies with a duration > 13 weeks weeks. Additional minor differences are that we included studies irrespective of the blinding, examined oral and LAI formulations separately and did not pool risperidone and paliperidone.

16.2 Barton 2020

Barton et al. [375] conducted a meta-analysis covering RCTs reporting on antipsychotic induced weight gain with a sample size ≥ 100, published between 2014 and 2019, irrespective of the diagnosis. They included 27 RCTs (15 of them in individuals with schizophrenia). The included studies focused on **short-term effects** with durations ranging between 3 and 12 weeks. The included antipsychotics were aripiprazole, asenapine, brexpiprazole, cariprazine, lurasidone, quetiapine, olanzapine and risperidone. All compounds led to significant weight gain compared to placebo. Most weight-gain was found for olanzapine followed by asenapine, risperidone, aripiprazole, quetiapine XR, brexpiprazole, cariprazine and lurasidone.

16.3 Spertus 2018

Spertus et al. [376] examined 7% weight gain from randomisation in a hierarchical model network meta-analysis with individual patient level data of 3 antipsychotics (olanzapine, paliperidone and risperidone) and placebo. 14 randomized clinical trials (CATIE studies and studies available on YODA) contributing 5923 subjects were examined.

The adjusted odds for weight gain relative to no drug was highest for olanzapine followed by paliperidone and risperidone. An additional analysis of the intensity of exposure revealed a dose-dependent weight increase.

16.4 Zhang 2017

Zhang et al. [377] conducted a network meta-analysis evaluating the effect on glucose levels of 12 antipsychotics used for the treatment of schizophrenia and related disorders; 47 RCTs on 9846 individuals (aged from 15 to 65 years) reported the outcome of fasting glucose. The search was limited to January 1995 to June 2016 and only studies reported in English were included. A methodological limitation was that there was no registered protocol for this study.

They found that compared to a placebo only olanzapine was associated with significantly increased glucose levels and olanzapine also showed a significantly greater change in the glucose levels when compared to other antipsychotics (ziprasidone, lurasidone and risperidone).

16.5 Misawa 2016

Misawa et al. [378] conducted a meta-analysis of 16 randomized controlled trials including 4902 individuals with schizophrenia or schizoaffective disorder comparing long-acting injectable (LAI) verus oral antipsychotics and found no difference regarding weight change and other metabolic parameters. The only exception was low-density lipoprotein (LDL) cholesterol for which second generation LAIs were associated with significantly greater increases than oral antipsychotics.

16.6 Bak 2014

Bak et al. [379] conducted a meta-analysis examining clinical trials of antipsychotics that reported weight change in adults not restricted to the diagnosis of schizophrenia. Body weight change, BMI change, proportion of clinically relevant weight gain and proportion of clinically relevant weight loss were examined. Randomized controlled studies and long-term follow-ups after the end of the study were included. The search included the years 1999 to 2011; 307 articles were included. The evaluation was stratified by the duration of antipsychotic use in four groups (≤ 6 weeks, 6–16 weeks, 16–38 weeks and >38 weeks).

Most antipsychotics showed a statistically significant change in weight postbaseline. Only for amisulpride, aripiprazole and ziprasidone negligible weight change after prolonged exposure was observed. For antipsychotic-naïve patients, a more pronounced weight gain was detected. A significant increase in weight was seen for first-generation antipsychotics and olanzapine when exposure period 4 (>38 weeks) was compared to exposure period 1 (0-6 weeks).

16.7 Zhang 2013

Zhang et al. [380] conducted a meta-analysis covering first-episode schizophrenia-spectrum disorders (FES) and compared individual second-generation antipsychotics (SGA) with first-generation antipsychotics (FGA) as a group to evaluate efficacy and safety. The systematic literature search was until December 2010. Acute treatment studies and long-term data from acute RCTs excluding maintenance studies were included, in total 13 studies on 6 second-generation antipsychotics (olanzapine, risperidone, clozapine, amisulpride, quetiapine and ziprasidone). Among others continuous and dichotomous weight gain and changes of glucose, total cholesterol and triglycerides were examined.

Olanzapine and risperidone increased weight significantly more than the comparator first-generation antipsychotics. Clozapine was associated with more weight gain than sulpiride in one study. Pooled SGAs were associated with more weight gain than pooled FGAs. The difference at long-term follow-up between pooled SGAs and FGAs was halved compared to the short-term results. Likewise, weight gain ≥ 7 % was significantly more likely with olanzapine and risperidone than haloperidol and with SGAs than FGAs.

Olanzapine, risperidone, amisulpride and quetiapine showed similar glucose changes compared to haloperidol, only ziprasidone was significantly better than haloperidol in one study. Pooled SGAs were similar as FGAs.

Regarding short-term total cholesterol change, olanzapine was significantly worse than molindone and sulpiride and marginally worse than haloperidol. Pooled SGAs were associated with marginally larger total cholesterol increase than FGAs.

Only few studies reported on triglyceride changes and pooled SGAs showed marginally greater short-term trigylceride increase than FGAs.

16.8 De Hert 2012

De Hert et al. [381] conducted an exploratory meta-analysis limited to four antipsychotics (asenapine, iloperidone, lurasidone and paliperidone) in the treatment of schizophrenia or bipolar disorder and examined mean weight change, 7% weight change compared with pretreatment weight, and change in total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides and glucose.

They found that compared to placebo continuous weight gain was statistically significantly greater for all examined antipsychotics in the short-term. Sufficient long-term data was only available for asenapine and paliperidone showing statistically significant weight gain compared to placebo.

16.9 Rummel-Kluge 2010

Rummel-Kluge et al. [382] conducted pairwise meta-analyses on 9 second-generation antipsychotics and 48 studies in total (with an update search in January 2009). For olanzapine and clozapine the highest increase in weight gain was detected with no difference between the substances. Clozapine produced more weight gain than risperidone, risperidone more than amisulpride, and sertindole more than risperidone. A meta-regression of study duration could explain some of the observed heterogeneity with longer studies producing more weight gain than shorter studies; e.g. in short-term studies (≤12 weeks) olanzapine produced 2.5 kg more weight gain than ziprasidone, whereas in long-term studies the difference was about 4 kg.

16.10 Meta-analyses on metabolic side effects covering children

Pagsberg et al. [383] conducted 2017 a network meta-analysis of randomized controlled trials of acute antipsychotic treatment in children and adolescents with schizophrenia-spectrum disorders. 12 trials were included with a duration between 6 and 12 weeks covering 8 antipsychotics (aripiprazole, asenapine, paliperidone, risperidone, quetiapine, olanzapine, molindone, and ziprasidone). All tested antipsychotics showed more weight gain than placebo, except for molindone and ziprasidone. Weight gain was found to be primarily associated with olanzapine.

Kumar et al. [384] conducted 2013 a Cochrane review with meta-analysis of 13 RCTs examining atypical antipsychotics for psychosis in adolescents. Treatment with olanzapine, risperidone and clozapine was often associated with weight gain.

Almandil et al. [385] performed 2013 a meta-analysis including double-blind, randomized controlled trials investigating metabolic adverse effects (weight gain, lipid, glucose, and prolactin level abnormalities) associated with atypical antipsychotic use in children and adolescents aged ≤18 years irrespective of the diagnosis. They included 14 studies for risperidone (1331 patients), three for olanzapine (276 patients), and four for aripiprazole (848 patients). The majority of trials lasted less than 10 weeks. Compared with placebo, the mean weight increases for each drug were olanzapine 3.45 kg (95 % CI 2.93–3.98), risperidone 1.77 kg (95 % CI 1.35–2.20), and aripiprazole 0.94 kg (95 % CI 0.65–1.24).

Cohen et al. [386] conducted 2012 a meta-analysis of short-term (up to 12 weeks) controlled trials on adverse effects associated with second-generation antipsychotics in children and adolescents irrespective of the diagnosis. Dichotomous weight gain was reported by 25 studies (62 arms, 3401 participants). Odds ratios for risk of weight gain ranged from 3.77 (CI 0.37 to 16.27) for ziprasidone to 15.1 (CI 6.56 to 31.1) for olanzapine. Mean weight gain ranged from 0.89 to 3.99kg (30 studies, 66 arms, 3221 participants) and was highest for olanzapine (mean gain 2.99kg). Ziprasidone was associated with a mean weight loss of -0.1kg, which was not statistically significant.

Pringsheim et al. [387] conducted 2011 a meta-analysis of 35 double-blind, randomized controlled trials (RCTs) of SGA conducted in children with mental health disorders. They found that mean weight gain compared with placebo was highest for olanzapine at 3.47 kg (95% CI 2.94, 3.99) followed by risperidone at 1.72 kg (95% CI 1.17, 2.26), quetiapine at 1.41 kg (95% CI 1.10, 1.81) and aripiprazole at 0.85 kg (95% CI 0.58, 1.13). The majority of trials lasted 10 weeks or less.

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