eAppendix

Table of Content

eAppendix 1

PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3-4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4 and eAppendix
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.	4-5
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.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	eAppendix
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).	6
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.	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.	5-6
Risk of bias in 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.	6 and eAppendix
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6-7

Section/topic	#	Checklist item	Reported on page #
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).	6-7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
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.	7 and PRISMA diagram in Fig 1 included and excluded studies table in eAppendix5
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.	Included studies table eAppendix5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8 and Risk of bias summary in eAppendix5
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 3,4 and eAppendix
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	figures 3, 4, eAppendix
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	eAppendix5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9 and eAppendix
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).	12-13

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).	15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15
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.	16

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

eAppendix 2

Protocol

Protocol as published in www.prospero.org (Registration number: CRD42014014919)

Review title and timescale

1 Review title

Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.

Informing clinicians, patients and guidelines: network meta-analysis on 24 antipsychotic drugs and a broad ragne of important outcomes for schizophrenia.

2 Original language title

For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3 Anticipated or actual start date

Give the date when the systematic review commenced, or is expected to commence.

01/12/2014

4 Anticipated completion date

Give the date by which the review is expected to be completed.

30/12/2017

5 Stage of review at time of this submission

Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.

The review has not yet started √

Review stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No

Data analysis	No	No

Provide any other relevant information about the stage of the review here.

Review team details

6 Named contact

The named contact acts as the guarantor for the accuracy of the information presented in the register record.

Mr Huhn

7 Named contact email

Enter the electronic mail address of the named contact.

maximilian.huhn@lrz.tum.de

8 Named contact address

Enter the full postal address for the named contact.

Klinik für Psychiatrie und Psychotherapie der TU-Mnchen Klinikum rechts der Isar Ismaningerstr. 22 81675 Mnchen Germany

9 Named contact phone number

Enter the telephone number for the named contact, including international dialing code.

+498941406466

10 Organisational affiliation of the review

Full title of the organisational affiliations for this review, and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Department of Psychiatry and Psychotherapy, Technische Universität München, Klinikum rechts der Isar

Website address:

http://www.cfdm.de/

11 Review team members and their organisational affiliations

Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.

Title	First name	Last name	Affiliation
Professor	Stefan	Leucht	Department of Psychiatry and Psychotherapy, Technische Universität München, Klinikum rechts der Isar
Dr	Maximilian	Huhn	Department of Psychiatry and Psychotherapy, Technische Universität München, Klinikum rechts der Isar
Dr	Johannes	Schneider	Department of Psychiatry and Psychotherapy, Technische Universität München, Klinikum rechts der Isar

Professor	John	Davis	Department of Psychiatry and Psychotherapy, University of Illinois at Chicagots der Isar
Mr	Mark	Krause	Department of Psychiatry and Psychotherapy, Technische Universität München, Klinikum rechts der Isar

12 Funding sources/sponsors

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.

Bundesministerium für Bildung und Forschung (BMBF) Grant: 01KG1406

13 Conflicts of interest

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

Are there any actual or potential conflicts of interest?

Yes

Stefan Leucht has received honoraria for lectures from Abbvie, Astra Zeneca, BristolMyersSquibb, ICON, EliLilly, Janssen, Johnson & Johnson, Roche, SanofiAventis, Lundbeck and Pfizer; for consulting/advisory boards from Roche, EliLilly, Medavante, BristolMyersSquibb, Alkermes, Janssen, Johnson & Johnson and Lundbeck. EliLilly has provided medication for a study with SL as primary investigator. Claudia Leucht is Stefan Leucht's spouse so that the same conflict of interest may also relate to her.

14 Collaborators

Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

Title	First name	Last name	Organisation details
Professor	Georgia	Salanti	Department of Hygiene and Epidemiology, University of Ioannina
Dr	Adriani	Nikolakopoulou	Department of Hygiene and Epidemiology, University of Ioannina

Review methods

15 Review question(s)

State the question(s) to be addressed / review objectives. Please complete a separate box for each question.

To examine the comparative efficacy, acceptability, and tolerability of twelve second- and twelve first-generation antipsychotic drugs in schizophrenia by applying a network meta-analysis approach.

16 Searches

Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.

1. We will search the Cochrane Schizophrenia Group Controlled Trials Register (compiled by regular systematic hand searches and searches of more than 15 databases, clinical trial registers, the Food and Drug Administration web site, and conference proceedings

without language restrictions; available to us until version August 2009), MEDLINE, EMBASE, PsycINFO, Cochrane Library, Pubmed, Biosis, ClinicalTrials.gov and WHO ICTRP. The search phrases will combine terms for schizophrenia (schizophrenia-like psychoses), randomization, and antipsychotic drugs. The exact search terms will be detailed with the an expert librarian (Samantha Roberts, previous trial search coordinator of the Cochrane Schizophrenia Group. Term for MEDLINE: 1 Benperidol/ or Chlorpromazine/ or Clopenthixol/ or Clozapine/ or Flupenthixol/ or Fluphenazine/ or Fluspirilene/ or Haloperidol/ or Methotrimeprazine/ or Loxapine/ or Molindone/ or Penfluridol/ or Perazine/ or Perphenazine/ or Pimozide/ or Risperidone/ or Sulpiride/ or Thioridazine/ or Thiothixene/ or Trifluoperazine/ or Clopenthixol/ (53027) 2 (Amisulpride or Aripiprazole or Asenapine or Benperidol or Brexpiprazole or Cariprazine or Chlorpromazine or Clopenthixol or Clozapine or Flupenthixol or Fluphenazine or Haloperidol or Iloperidone or Levomepromazine or Loxapine or Lurasidone or Molindone or Olanzapine or Paliperidone or Quetiapine or Penfluridol or Perazine or Perphenazine or Pimozide or Risperidone or Sertindole or Sulpiride or Thioridazine or Thiothixene or Trifluoperazine or Ziprasidone or Zotepine or Zuclopenthixol).tw. (57996) 3 or/1-2 (75450) 4 exp schizophrenia/ (90375) 5 exp Paranoid Disorders/ (3848) 6 schizo$.mp. (142254) 7 hebephreni$.mp. (269) 8 oligophreni$.mp. (1063) 9 psychotic$.mp. (52549) 10 psychosis.mp. (27356) 11 psychoses.mp. (19225) 12 or/4-11 (190571) 13 exp clinical trial/ (848995) 14 exp randomized controlled trials/ (104559) 15 exp cross-over studies/ (37337) 16 randomized controlled trial.pt. (413628) 17 clinical trial.pt. (506934) 18 controlled clinical trial.pt. (91880) 19 (clinic$ adj2 trial).mp. (626861) 20 (random$ adj5 control$ adj5 trial$).mp. (558179) 21 (crossover or cross-over).mp. (75106) 22 ((singl$ or double$ or trebl$ or tripl$) adj (blind$ or mask$)).mp. (194708) 23 randomi$.mp. (662230) 24 (random$ adj5 (assign$ or allocat$ or assort$ or reciev$)).mp. (188450) 25 or/13-24 (1227013) 26 3 and 12 and 25 (6235) 2. Previous reviews: We will search previous reviews investigating antipsychotics in general schizophrenia. 3. Personal contact: We will contact the first author of each included study published in the last 30 years for missing information. 4. Drug companies: We will contact the principal manufacturers of the antipsychotic drugs and ask them for further relevant trials and for missing information concerning the identified studies. 5. Hand search: There will be no extra hand search for this review, because a number of psychiatric journals (especially old issues which are important for this project) and the abstract books of major conferences are regularly hand searched anyways for the 'Cochrane Schizophrenia Group Trials Register'. There will be no language restriction applied concerning the literature. As an exception we will exclude Chinese studies which often do not use appropriate randomization procedures and do not report their methods so that it is impossible to check on these issues.

17 URL to search strategy

If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.

I give permission for this file to be made publicly available

Yes

18 Condition or domain being studied

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

Schizophrenia

19 Participants/population

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

We will include adult people (age >= 18, no upper age limit, no restriction in setting, gender, ethnicity) with schizophrenia or related disorders (such as schizophreniform, or schizoaffective disorders). There is no clear evidence that the latter schizophrenia-like psychoses are caused by fundamentally different disease processes or require different treatment approaches. However, as in our previous report we will exclude studies in treatment resistant patients, in patients with predominant negative symptoms, in patients with concomitant medical illness, and studies in stable patients (mainly relapse prevention studies), because these are different patient populations and it is an important requirement of network meta-analysis to have reasonably homogeneous samples. Studies in which less than 20% of the participants were suffering from other psychiatric disorders than schizophrenia (e.g. depression or mental retardation) will be acceptable. We will include the trials irrespective of the diagnostic criteria used. It is a general strategy of the Cochrane Schizophrenia Group (CSG) to include not only studies that used specific diagnostic criteria such as ICD-10 or DSM-IV, because these criteria are not meticulously used in clinical routine either. This decision should increase generalizability.

20 Intervention(s), exposure(s)

Give full and clear descriptions of the nature of the interventions or the exposures to be reviewed

We will include all second-generation ("atypical") antipsychotic drugs available in Europe or the US (amisulpride, aripiprazole, asenapine, brexpiprazole, cariprazine, clozapine, iloperidone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, sertindole, ziprasidone, zotepine), placebo and a selection of first-generation ("typical", "conventional") antipsychotics (benperidol, chlopromazine, clopenthixol, flupenthixol, fluphenazine, fluspirilene, haloperidol, levomepromazine, loxapine, methotrimeprazine, molindone, penfluridol, perazine, perphenazine, pimozide, sulpiride, thioridazine, thiothixene, trifluoperazine, zuclopenthixol). Second-generation antipsychotics are in some countries such as the US or Germany nowadays the most frequently prescribed compounds, they are overall more costly (especially the most recent ones which still have patent protection) and they are thus obvious choices. One novel aspect of the network meta-analysis is the inclusion of first-generation antipsychotics. In addition to the reasons already mentioned (the classification in SGAs and FGAs is no longer valid, even in industrialised countries FGAs are still frequently used and FGAs are the mainstay of treatment world-wide), some FGAs suggested excellent properties in recent influential studies (e.g. perphenazine in CATIE (Lieberman et al. 2005) or sulpiride in CUtLASS (Jones et al. 2006)) and some may have atypical properties (e.g. thioridazine, sulpiride, flupenthixol, perazine). To guide our choice of FGAs we conducted a survey of 60 international schizophrenia experts whom we asked to choose 10 of the 52 FGAs listed by the "WHO Collaborating Centre for Drug Statistics" which they find most important for such a meta-analysis (http://www.whocc.no/atc_ddd_methodology/who_collaborating_centre/, detailed results can be found on our website www.cfdm.de/media/doc/Antipsychotic Survey.doc). We added benperidol and perazine which are frequently used FGAs in Germany. The selection includes FGAs from various classes, there are high-potency (e.g. haloperidol), mid-potency (zuclopenthixol, perphenazine) and low-potency (e.g. thioridazine) drugs, butyrophenones (e.g. benperidol, haloperidol), phenothiazines (e.g. fluphenazine), thioxantenes (zuclopenthixol) and a substituted benzamide (sulpiride). We will include all these compounds in any oral forms of administration (for example tablets or liquid). In fixed-dose studies we will only included target to maximum doses according to the International Consensus Study on Antipsychotic dose. We will include all flexible-dose studies, because these allow the investigators to titrate to the adequate dose for the individual patient. We will exclude depot formulations which are mainly used for long-term relapse prevention which is not the focus of this review.

21 Comparator(s)/control

Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group).

In a network meta-analysis each treatment is compared with each other, therefore any treatment can be the comparator. But placebo is a natural reference that will be used in our occasion.

22 Types of study to be included

Give details of the study designs to be included in the review. If there are no restrictions on the types of study design eligible for inclusion, this should be stated.

We will included open and blinded randomized controlled trials (RCTs) comparing one antipsychotic drug with another antipsychotic agent or placebo. Results from non double-blinded trials will be considered only for objective outcomes. Trials in which antipsychotic drugs were used as an augmentation- or combination strategy will be excluded. In the case of cross-over studies we will use only the first cross-over phase to avoid the problem of carry-over effects which are very likely in schizophrenia. We will exclude cluster randomized trials due to the unit-of-analysis-problems associated with this design (it is anyhow unlikely that such studies on our question exist). We will also only include double-blinded studies for subjective outcomes because we recently showed that a lack of blinding can exaggerate differences between treatments in this area. For objective outcomes (e.g. weight gain) blinding is less of a problem. The minimum duration of follow-up will be 3 weeks as shorter trials are unlikely to find significant differences. In addition, short-term results (3 weeks-3 months weeks) and longer term results (>3 months) will be analysed in separate publications.

23 Context

Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

We will include adult people (age >= 18, no upper age limit, no restriction in setting, gender, ethnicity) with schizophrenia, schizophreniform or schizoaffective disorders with an acute exacerbation, primarily irrespective of the diagnostic criteria used. There is no clear evidence that the latter schizophrenia-like psychoses are caused by fundamentally different disease processes or require different treatment approaches. It is also a general strategy of the Cochrane Schizophrenia Group to include not only studies that used specific diagnostic criteria such as ICD-10 or DSM-IV, because these criteria are not meticulously used in clinical routine either. Studies in which less than 20% of the participants were suffering from other psychiatric disorders (e.g. depression or mental retardation) will be included. We will exclude studies in participants with no or only subclinical symptoms at baseline that are usually conducted to

address the relapse preventing effects of antipsychotics, studies in patients with predominant negative symptoms and studies including exclusively participants with major concomitant somatic illness or psychiatric disorders (e.g. substance abuse).

24 Primary outcome(s)

Give the most important outcomes.

Mean reduction in overall symptoms of schizophrenia

Give information on timing and effect measures, as appropriate.

The primary outcome will be overall symptoms of schizophrenia as measured by rating scales such as the Positive and Negative Syndrome Scale (PANSS), the Brief Psychiatric Rating Scale (BPRS) or of any other validated scale (e.g. the Manchester Scale) for the assessment of overall schizophrenic symptomatology. Overall symptoms of schizophrenia as measured by such scales was the primary outcome in numerous previous systematic reviews. As not all studies will have used the same scale, we will apply the following hierarchy: mean change of the PANSS total score from baseline to endpoint, if not available mean change of the BPRS, or if again not available the mean values at endpoint of the PANSS/ BPRS. The results of other rating scales will only be used if the instrument has been published in a peer-reviewed journal, because it has been shown that unvalidated schizophrenia scales exaggerate differences. The minimum duration of follow-up will be 3 weeks as shorter trials are unlikely to find significant differences. Outcomes will be classified into short-term results (3 weeks-3 months) where the primary time point will be six weeks, if available, and longer term results (>3 months).

25 Secondary outcomes

List any additional outcomes that will be addressed. If there are no secondary outcomes enter None.

1. Response to treatment (study defined) (s) 2. Change in positive symptoms of schizophrenia (s) 3. Change in negative symptoms of schizophrenia (s) 4. Change in depressive symptoms (s) 5. Dropout due to any reason (all-cause discontinuation) (s) 6. Dropout due to inefficacy of treatment (s) 7. Adverse events a) Use of antiparkinson medication (s) b) Akathisia (s) c) Weight gain d) Prolactin levels e) At least one sexual side-effect (s) f) Sedation/somnolence (s) g) Cardiac side-effects, in particular QTc prolongation h) At least one anticholinergic side-effect (s). i) 8. Patient subjective well-being, quality of life (s) +9. Overall functioning (s) + Subjective outcomes are marked with an (s).

Give information on timing and effect measures, as appropriate.

The minimum duration of follow-up will be 3 weeks as shorter trials are unlikely to find significant differences. Outcomes will be classified into short-term results (3 weeks-3 months) where the primary time point will be six weeks, if available, and longer term results (>3 months).

26 Data extraction (selection and coding)

Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.

1. Selection of trials: Two reviewers will independently inspect all abstracts identified in the searches. Disagreement will be resolved by discussion, and where doubt still remains, we will acquire the full article for further inspection. Once the full articles are obtained, at least two reviewers will independently decide whether the studies meet the review criteria. If disagreement can not be resolved by discussion, we will resolve it with a third reviewer or seek further information from the study authors. 2. Data extraction: Two reviewers will independently extract data from all selected trials on electronic forms. When disagreement arises we will resolve it by discussion with a third reviewer. Where this is not possible we will contact the study authors.

27 Risk of bias (quality) assessment

State whether and how risk of bias will be assessed, how the quality of individual studies will be assessed, and whether and how this will influence the planned synthesis.

Study quality in terms of sequence generation, allocation concealment, blinding, the completeness of outcome data, selective reporting and other biases will be assessed with the Cochrane Collaboration risk of bias tool.

28 Strategy for data synthesis

Give the planned general approach to be used, for example whether the data to be used will be aggregate or at the level of individual participants, and whether a quantitative or narrative (descriptive) synthesis is planned. Where appropriate a brief outline of analytic approach should be given.

1. Two-step procedure In a first step we will perform series of conventional pair-wise meta-analyses by combining studies that compared the same interventions. In a second step we will then perform a network meta-analysis within a Bayesian framework. 2. Continuous outcomes: The effect size measure for continuous outcomes will be the standardized mean difference (SMD) because we expect that the studies use different rating scales of overall schizophrenia symptomatology, especially the Positive and Negative Syndrome Scale (PANSS) or the Brief Psychiatric Rating Scale (BPRS) (see outcomes, above). Intention-to-treat (ITT) data will be used whenever available. Missing standard deviations: When standard errors instead of standard deviations (SD) are presented, the former will be converted to standard deviations (SDs). If both are missing we will estimate SDs from confidence intervals, t-values, or p-values as described in Section 7.7.3 of the Cochrane Handbook for Systematic Reviews. If none of these options is viable we will contact the original authors. When no information can be obtained we will derive SDs from those of the other studies using a validated imputation technique. 3. Dichotomous outcomes: The effect size for dichotomous outcomes will be the odds ratio (OR) and its 95% confidence intervals (CIs). The main reason to prefer odds ratios to relative risks is that this measure has mathematical properties that make it more appropriate for network meta-analysis (e.g. the odds ratio is symmetrical). Another reason justifying the calculation of the odds ratios is the expectation that different definitions of 'response to treatment' will be used in the original trials and in such a situation the odds ratio has been shown to yield the most consistent results which are largely independent from the response cut-off used. Therefore, although the relative risk is more intuitive for clinician, the odds ratio has clear advantages for the purpose of our review. Analyses will be carried out in accordance to the 'intention-to-treat' principal when possible ('once randomized always analyze'). Everyone allocated to the intervention will be counted whether they completed the follow up or not. If the authors applied such a strategy, we will use their results. If the original authors presented only the results of the per-protocol or completer population, we will assume that those participants lost to follow-up would not have changed in a given outcome. In terms of efficacy this means that they would be conservatively considered to have not responded to treatment. In terms of tolerability it would mean that participants would not have developed a side-effect which we feel is appropriate, because otherwise side-effects, many of which are rare, would be overestimated. Applying this approach led to meaningful results in our previous reports on which we build. 4. Assessment of heterogeneity The heterogeneity (variability in relative treatment effects within the same treatment comparison) will be measured with the tau-squared (the variance of the random effects distribution). The heterogeneity variance will be assumed common across the various treatment comparisons and the empirical distributions will be used to characterise the amount of heterogeneity as low, moderate or high using the first and third quantiles (https://www.ncbi.nlm.nih.gov/pubmed/26679486 and https://www.ncbi.nlm.nih.gov/pubmed /22461129). Potential reasons for heterogeneity will be explored by subgroup analysis and meta-regressions (see 8. below). 5. Assessment of the transitivity assumption Joint analysis of treatments can be misleading if the network is substantially intransitive. We will need to investigate the distribution of clinical and methodological variables that can act as effect modifiers across treatment comparisons. The main features, which have been demonstrated to date to moderate efficacy of antipsychotics, at least compared to placebo, are the degree of placebo response (which has increased over the years) and industry sponsorship. Less robust factors include severity of illness at baseline, gender, chronicity and publication year. We will investigate if these variables are similarly distributed across studies grouped by comparison, whereas it is clear a priori that publication year, a composite of various factors, will differ between older and more recent antipsychotics. We will consider that placebo response in schizophrenia has increased over the years and that there could be differences between placebo-controlled trials and head-to-head trials as it is known from antidepressant trials in major depressive disorder. 6. Network meta-analyses We assume that patients who fulfill the inclusion criteria outlined above are equally likely to be randomised to any of the antipsychotic that we plan to compare. If the collected studies appear to be sufficiently similar with respect to the distribution of effect modifiers (refer to "assessment of transitivity assumption" section), we will conduct a random effects NMA to synthesize all evidence for each outcome, and obtain a comprehensive ranking of all treatments. We will use arm-level data and the binomial likelihood for dichotomous outcomes. We will account for the correlations induced by multi-arm studies by employing multivariate distributions. We will assume a single heterogeneity parameter for each network. We will present the summary ORs or SMD for all pairwise comparisons in a league table. We will also estimate the prediction intervals to assess how much the common heterogeneity affects the relative effect with respect to the extra uncertainty anticipated in a future study. To rank the various treatments for each outcome, we will use the surface under the cumulative ranking curve (SUCRA) and the mean ranks. 7. Assessment of inconsistency The strategical and conceptual evaluation of transitivity will be supplemented with a statistical evaluation of consistency, the agreement between direct and indirect evidence. We will employ local as well as global methods to evaluate consistency. Local methods detect 'hot spots' of inconsistency, evidence loops that are inconsistent or comparisons for which direct and indirect evidence disagree. We will employ the loop-specific approach to evaluate inconsistency within each loop of evidence, and a method that separates direct evidence from indirect evidence provided by the entire network. We will also evaluate consistency in the entire network by calculating the I2 for network heterogeneity, inconsistency, and for both. Tests for inconsistency are known to have low power, and empirical evidence has suggested that 10% of evidence loops published in the medical literature are expected to be inconsistent. Therefore, interpretation of the statistical inference about inconsistency will be carried out with caution and possible sources of inconsistency will be explored even in the absence of evidence for inconsistency. 8. Exploring heterogeneity and inconsistency and sensitivity analyses We expect small amounts of heterogeneity and inconsistency to be present given the variety of study settings we plan to include. We will explore whether treatment effect for the primary outcome is robust in subgroup analyses and network meta-regression using the characteristics presented under 'analysis of subgroups or subsets'. 9. Publication bias We will explore the association between study size and effect size with a comparison-adjusted funnel plot that has been adapted to network meta-analysis. 10. Statistical software The analysis and

presentation of results will be performed using the Stata packages network and network_graphs, the R package netmeta and self-programmed codes in OpenBUGS.

29 Analysis of subgroups or subsets

Give any planned exploration of subgroups or subsets within the review. 'None planned' is a valid response if no subgroup analyses are planned.

The following potential effect moderators of the primary outcome will be explored by subgroup or meta-regression analysis: 1. Dose of the antipsychotics in olanzapine-equivalents according to Gardner et al. 2010 2. Publication date (to address the effect of possibly generally decreasing effect sizes over time) 3. Severity of illness at baseline 4. Industry sponsorship 5. Length of follow-up 6. Mean participant age 7. Percentage men 8. Degree of placebo response 9. Small versus large studies by regressing on the variance of the estimated effect size. Sensitivity analyses will be performed as follows 1. Excluding studies characterized as pertaining to high risk of bias (defined as in the protocol of "GRISELDA", a NMA on antidepressants) 2. Excluding studies that presented only completer analyses. 3. Excluding placebo-controlled studies 4. Excluding studies with imputed standard deviations.

Review general information

30 Type and method of review

Select the type of review and the review method from the drop down list.

Intervention, Systematic review

31 Language

Select the language(s) in which the review is being written and will be made available, from the drop down list. Use the control key to select more than one language.

English, German

Will a summary/abstract be made available in English?

Yes

32 Country

Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved. Use the control key to select more than one country.

Germany

33 Other registration details

Give the name of any organisation where the systematic review title or protocol is registered together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here.

34 Reference and/or URL for published protocol

Give the citation for the published protocol, if there is one.

Give the link to the published protocol, if there is one. This may be to an external site or to a protocol deposited with CRD in pdf format.

I give permission for this file to be made publicly available

Yes

35 Dissemination plans

Give brief details of plans for communicating essential messages from the review to the appropriate audiences.

The results will be published in major psychiatric journals and presented at major international and German psychiatric conferences. Our findings will be rapidly implemented in national and international treatment guidelines, for some of which Stefan Leucht is a co-author.

Do you intend to publish the review on completion?

Yes

36 Keywords

Give words or phrases that best describe the review. (One word per box, create a new box for each term)

schizophrenia

antipsychotics

meta-analysis

placebo

FGA

SGA

37 Details of any existing review of the same topic by the same authors

Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38 Current review status

Review status should be updated when the review is completed and when it is published.

Ongoing

39 Any additional information

Provide any further information the review team consider relevant to the registration of the review.

40 Details of final report/publication(s)

This field should be left empty until details of the completed review are available.

Give the full citation for the final report or publication of the systematic review.

Give the URL where available.

Differences between protocol and review:
It should be noted that the short-term studies of up to 13 weeks duration have been published in a different publication (Huhn et al. Lancet. 2019 Sep 14;394(10202):939-95). Compared to this previous publication on short-term studies we made the following changes:

- **The review team was adapted**
- **The drugs lumateperone and samidorphan which were licenced after the Huhn et al. 2019 publication (there were no eligible studies), and long-acting injectable formulations were eligible for this review on long-term outcomes (there were eligible studies)**

- We asked authors and companies only for important missing data
- To improve transitivity, we excluded studies which were restricted to *any* subgroup by their inclusion criteria, not only to treatment resistant patients, predominant negative symptoms and concomitant medical illness
- As only one placebo-controlled RCT had data for the primary outcome, olanzapine was used as the reference drug
- We included only double-blind trials and only trials lasting at least 24 weeks to have a more homogeneous dataset
- We did not analyse response to treatment because various response cutoffs have been used increasing variability, and we did not analyse a number of other secondary outcomes due to paucity of data.
- We applied a frequentist network meta-analysis with the R netmeta package and not a Bayesian approach. We ranked drugs according to their point estimates and not according to SUCRAs, but only for easons of presentation, no ranking is implied.
- Instead of preplanned meta-regression and subgroup analyses, we addressed sponsorship by excluding studies from olanzapine's manufacturer, baseline severity and dose by excluding the CATIE study (CATIE had a relatively low baseline severity with a mean PANSS of 75, and it had been criticized for using a high olanzapine dose of up to 30mg/day), and study duration including only studies of at least 1 year duration insensitivity analyses. Degree of placebo response and the related factor publication year were not examined because only one placebo-controlled study had data for the primary outcome, and mean age and gender because they did not differ very much between relevant studies. Sample size was only addressed in the context of the funnel-plot.
- We post-hoc added sensitivity analyses excluding long-term extensions of initially acute phase studies because it was sometimes unclear whether all patients were followed up. Moreover, we examined oral and long-acting injectable formulations separately.

Formula for transformation of OR to RR and results of single-arm meta-analyses

We performed the statistical analysis using odds ratios (OR) and not risk ratios (RR). The reason is that OR provide more stable estimates of treatment effects across study-conditions with different baseline risks. However, as OR are more difficult to interpret than RR, we transformed OR to RR to present RR in addition to ORs in the forest plots. The control even rates (CER) in the olanzapine groups derived from single-arm meta-analysis of proportions were used for this purpose (results see below).

Formula for the transformations:
RR= OR/[(1-CER)+(OR*CER)]

eAppendix 3

Search strategy

1. Previous projects

We used the included studies from the following recent meta-analyses of our group as a basis.

1.1 Systematic review and pairwise meta-analysis of the effects of antipsychotic drugs in subgroups of people with schizophrenia

In this project we compared the effects of antipsychotics in different subgroups of people with schizophrenia. Short- and long-term studies in acutely ill patients were included. We excluded studies with a duration shorter than 24 weeks and we excluded studies restricted to specific subgroups in the current project.

Reference

Leucht S, Chaimani A, Krause M, Schneider-Thoma J, Wang D, Dong S, Samara M, Peter N, Huhn M, Priller J, Davis JM. The response of schizophrenia subgroups to different antipsychotic drugs: systematic review and meta-analysis. The Lancet Psychiatry 2022; in press

1.2 Systematic review and network meta-analysis of long-term studies on the metabolic side-effects of antipsychotic drugs in schizophrenia

The inclusion criteria of this project overlapped with the one described under 1.1. In 1.1 we had, however, not included long-term extensions studies and we had not included long-acting injectable formulations (depots). We used this publication to add these studies to the current meta-analysis.

Reference

Kapfhammer A, Metabolic side effects in persons with schizophrenia during Schneider-Thoma J, Chioccia V, Schestag K, Wang D, Siafis S, Bighelli I, Wu H, Hansen W-P, Priller-J, Davis JM, Salanti G, Leucht S. mid- to long-term treatment with antipsychotics: a network meta-analysis of randomized controlled trials. World Psychiatry 2022; in press

2. Update searches of the Cochrane Schizophrenia Group Register of Controlled Trials from February 2020 until March 2022

We made update searches of the Cochrane Schizophrenia Group Register. There was no search term, we searched the whole register for randomised **schizophrenia controlled trials** which were added to the register from February 2020 until March 20222.

2.1 Description of the Cochrane Schizophrenia Group's Study-Based Register of Trials

The information specialist Farhad Shokraneh has regularly updated the Cochrane Schizophrenia Group's Register. In such a study-based register, searching the major concept retrieves all the synonyms and relevant studies. This is because the studies have already been organised, based on their interventions, and linked to the relevant topics. This allows rapid and accurate searches that

reduce waste in the next steps of systematic reviewing. The details of classification of pharmacological interventions and this register were reported elsewhere [1-4].

Following the methods from Cochrane [5], 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.

References to database details

1. Shokraneh F, Adams CE. Study-based registers of randomized controlled trials: Starting a systematic review with data extraction or meta-analysis. *BioImpacts* 2017;7(4):209-17. [DOI: 10.15171/bi.2017.25]
2. Shokraneh F, Adams CE. Study-based registers reduce waste in systematic reviewing: discussion and case report. *Systematic Reviews* 2019;8:129. [DOI: 10.1186/s13643-019-1035-3]
3. Shokraneh F, Adams CE. Classification of all pharmacological interventions tested in trials relevant to people with schizophrenia: A study-based analysis. *Health Information and Libraries Journal* [Accepted]
4. Shokraneh F, Adams CE. Cochrane Schizophrenia Group's Study-Based Register of Randomized Controlled Trials: Development and Content Analysis. *Schizophrenia Bulletin Open* 2020 [Revised]
5. Lefebvre C, Glanville J, Briscoe S, Littlewood A, Marshall C, Metzendorf M, et al. Searching for and selecting studies. In: Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editor(s). Cochrane Handbook for Systematic Reviews of Interventions. 2nd edition. John Wiley and Sons, 2019:67-107. [DOI: 10.1002/9781119536604.ch4]

We made three searches in the Cochrane Schizophrenia Group Register:

2.1 Search from 17.04.20 to 10.02.2021

1080 hits

2.2 Search from 01.02.2021 to 19.09.2021

482 hits

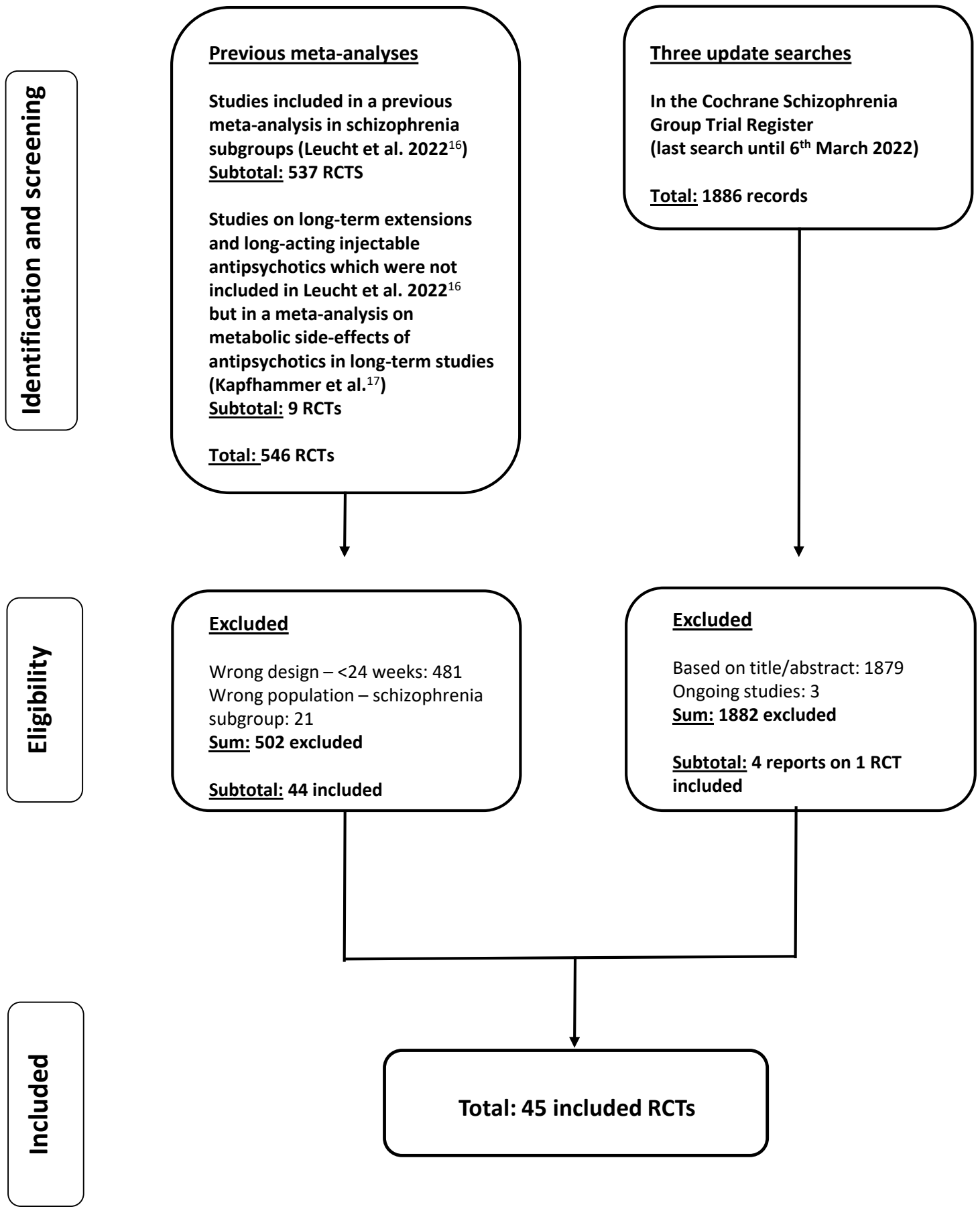
2.3 Search from 19.09.2021 to 06.03.2022

324 hits

eAppendix 4

PRISMA diagram of the search

PRISMA diagram of the search



References (the reference numbers are those in the main body of the manuscript)

16. Leucht S, Chaimani A, Krause M, Schneider-Thoma J, Wang D, Dong S, Samara M, Peter N, Huhn M, Priller J, Davis JM. The response of schizophrenia subgroups to different antipsychotic drugs: systematic review and meta-analysis. The Lancet Psychiatry 2022 epub

17. Kapfhammer A, Metabolic side effects in persons with schizophrenia during Schneider-Thoma J, Chioccia V, Schestag K, Wang D, Siafis S, Bighelli I, Wu H, Hansen W-P, Priller-J, Davis JM, Salanti G, Leucht S. mid- to long-term treatment with antipsychotics: a network meta-analysis of randomized controlled trials. World Psychiatry 2022; in press

eAppendix 5

Included studies

1. Table of study characteristics
2. Risk of bias single-studies
3. Risk of bias across studies

Characteristics of included studies

Study name	Inter-ventions	Oral /LAI	Dosing inter-val	Dose mean (range) in mg	Blin-ding	Duration in weeks	Diagnostic term (diagnostic criteria)	Number of participants randomized	Percent women	Mean age in years
Abuzzahab 1977[1]	Penfluridol	oral	daily	75 (61.82-90)	double blind	26	Chronic schizophrenia (clinical diagnosis)	23	39	44
	Trifluo-perazine	oral	daily	167.2 (145.9-183.47)				22	41	43.2
Abuzzahab 1977a[2]	Fluphe-nazine	oral	daily	12.7 (3-30)	double blind	156	Chronic schizophrenic (clinical diagnosis)	31	76	34.8
	Pimozide	oral	daily	5.5 (2-20)				31	58	30.8
Abuzzahab 1982[3]	Haloperidol	oral	daily	17.5 (5-40)	double blind	24	Schizophrenic (clinical diagnosis)	29	64	35
	Tiotixene	oral	daily	31.8 (10-80)				28	50	34
Alvarez 2012[4]	Olanzapine	oral	daily	15 (10-20)	double blind	26	Schizophrenia (DSM-IV-TR)	24	33	35.1
	Ziprasidone	oral	daily	107.4 (80-160)				28	25	40.8
Bankier 1968[5]	Fluphe-nazine	LAI	n.i.	n.i. (n.i.-n.i.)	double blind	26	Schizophrenic (clinical diagnosis)	35	n.i.	47.8
	Trifluo-perazine	oral	daily	n.i. (n.i.-n.i.)				35	n.i.	47.8
Breier 2005[6]	Olanzapine	oral	daily	15.3 (10-20)	double blind	28	Schizophrenia (DSM-IV)	277	35	40
	Ziprasidone	oral	daily	116 (80-160)				271	37	38.2
Burgoyne 1998[7]	Haloperidol	oral	daily	n.i. (n.i.-n.i.)	double blind	52	Schizophrenia (n.i.)	24	n.i.	n.i.
	Olanzapine	oral	daily	n.i. (n.i.-n.i.)				48	n.i.	n.i.
Clark 1970b[8]	Chlorpro-mazine	oral	daily	459 (300-600)	double blind	24	Chronic schizophrenia (clinical diagnosis)	32	100	43.8
	Placebo	oral	-	-				17	100	43.8
Cole 1967[9]	Chlorpro-mazine	oral	daily	n.i. (200-n.i.)	double blind	26	Schizophrenia (clinical diagnosis)	n.i.	n.i.	n.i.
	Fluphe-nazine	oral	daily	n.i. (2-n.i.)				n.i.	n.i.	n.i.

Daston 1959[10]	Chlorpro-mazine	oral	daily	400 (400-400)	double blind	90	Chronic schizophrenia (clinical diagnosis)	7	n.i.	n.i.
	Placebo	oral	-	-				6	n.i.	n.i.
Dutta 2014[11]	Asenapine	oral	daily	n.i. (n.i.-n.i.)	single blind	24	Schizophrenia (DSM-V)	41	n.i.	n.i.
	Clozapine	oral	daily	n.i. (n.i.-n.i.)				38	n.i.	n.i.
	Ziprasidone	oral	daily	n.i. (n.i.-n.i.)				40	n.i.	n.i.
Engelhardt 1978[12]	Haloperidol	oral	daily	5.7 (1.25-25)	double blind	24	Schizophrenic outpatients (clinical diagnosis)	38	n.i.	39.2
	Tiotixene	oral	daily	16 (5-60)				42	n.i.	31.8
Gardos 1970[13]	Tiotixene	oral	daily	24.2 (10-30)	double blind	52	Chronic schizophrenia (clinical diagnosis)	n.i.	n.i.	44.8
	Trifluo-perazine	oral	daily	22 (10-30)				n.i.	n.i.	48.5
Gureje 2003[14]	Olanzapine	oral	daily	17.2 (10-20)	double blind	30	Schizophrenia, schizoaffective-, or schizophreniform disorder (DSM-IV)	32	38	35.6
	Risperidone	oral	daily	6.6 (4-8)				33	45	34.8
Hera 041-021+Hera 041-022_1y[15]	Asenapine	oral	daily	n.i. (10-20)	double blind	52	n.i. (n.i.)	n.i.	n.i.	n.i.
	Olanzapine	oral	daily	n.i. (5-20)				n.i.	n.i.	n.i.
Ibrahim 2011[16]	Haloperidol	oral	daily	n.i. (5-10)	double blind	26	Schizophrenia (clinical diagnosis)	9	n.i.	n.i.
	Quetiapine	oral	daily	n.i. (600-1200)				11	n.i.	n.i.
Kane 2009_28 weeks[17]	Aripiprazole	oral	daily	18.9 (10-30)	double blind	28	Schizophrenia (DSM-IV-TR)	285	33	38.2
	Olanzapine	oral	daily	16.4 (10-20)				281	31	39.3
Kane 2010a_52w[18]	Asenapine	oral	daily	n.i. (10-20)	double blind	58	Schizophrenia (DSM-IV-TR)	93	40	35.3
	Haloperidol	oral	daily	n.i. (4-16)				43	58	39.9
Kasper 2003[19]	Aripiprazole	oral	daily	29 (29-29	double blind	52	Schizophrenia, acute relapse (DSM-IV)	861	41	37.3
	Haloperidol	oral	daily	8.9 (8.9-8.9)				433	43	36.8
Keefe 2006[20]	Haloperidol	oral	daily	8.2 (8.2-8.2)	double blind	52	Schizophrenia or schizoaffective disorder	97	29	39.8
	Olanzapine	oral	daily	12.3 (12.3-12.3)				159	28	38.4

	Risperidone	oral	daily	5.2 (5.2-5.2)			(DSM-IV)	158	30	39.5
Kissling 1985[21]	Flupheazine	LAI	every 2 weeks	11 (n.i.-n.i.)	double blind	24	Schizophrenia (ICD-9)	22	64	33.9
	Haloperidol	LAI	every 4 weeks	5 (n.i.-n.i.)				32	81	34.1
Kongsakon 2006[22]	Haloperidol	oral	daily	8.7 (5-20)	double blind	24	Schizophrenia (DSM-IV)	132	37	31.8
	Olanzapine	oral	daily	10.2 (5-20)				144	49	32.7
Laborde 2000[23]	Haloperidol	oral	daily	15 (n.i.-n.i.)	double blind	26	Chronic or subchronic schizophrenia (DSM-III-R)	66	25	34.8
	Zotepine	oral	daily	225 (n.i.-n.i.)				59	25	33.5
Lieberman 2005_18months[24]	Olanzapine	oral	daily	20.1 (7.5-30)	double blind	78	Schizophrenia (DSM-IV)	336	27	40.8
	Perphe-nazine	oral	daily	20.8 (8-32)				261	24	40
	Quetiapine	oral	daily	543.4 (200-800)				337	24	40.9
	Risperidone	oral	daily	3.9 (1.5-6)				341	26	40.6
	Ziprasidone	oral	daily	112.8 (40-160)				185	30	40.1
Loebel 2013_12m[25]	Lurasidone	oral	daily	n.i. (40-160)	double blind	52	Schizophrenia (DSM-IV-TR)	151	28	37.1
	Quetiapine	oral	daily	637.6 (200-800)				85	39	38.5
Malyarov 1999[26]	Haloperidol	oral	daily	12.5 (5-20)	single blind	26	Schizophrenia with acute psychotic state (ICD-10)	18	n.i.	24.5
	Olanzapine	oral	daily	10 (5-15)				15	n.i.	24.5
	Risperidone	oral	daily	4.5 (3-6)				10	n.i.	24.5
Mortimer 2004[27]	Amisulpride	oral	daily	504 (200-800)	double blind	26	Schizophrenia or schizophreniform disorder (DSM-IV)	189	34	38.2
	Olanzapine	oral	daily	13 (5-20)				188	36	37.4
Naukkarinen 2000[28]	Olanzapine	oral	daily	n.i. (5-20)	double blind	26	Schizophrenia (DSM-IV)	23	43	37.4
	Perphe-nazine	oral	daily	n.i. (8-32)				23	35	37.7

NCT00210717 2012[29]	Paliperidone	LAI	every 4 weeks	63.5 (39-234)	double blind	53	Schizophrenia (DSM-IV)	379	43	40.7
	Risperidone	LAI	every 2 weeks	32.4 (25-50)				370	38	40.6
NCT03345979 2020[30]	Aripiprazole	LAI	every 8 weeks	1064 (1064-1064)	double blind	25	Schizophrenia (DSM-V)	99	26	43.5
	Paliperidone	LAI	every 4 weeks	156 (156-156)				101	25	43.4
Paredes 1966[31]	Chlorpro-mazine	oral	daily	n.i. (n.i.-n.i.)	double blind	24	Schizophrenia (clinical diagnosis)	48	100	n.i.
	Placebo	oral	-	-				24	100	n.i.
Platz 1967[32]	Chlorpro-mazine	oral	daily	980 (600-1600)	double blind	24	Chronic schizophrenia (clinical diagnosis)	n.i.	n.i.	n.i.
	Trifluo-perazine	oral	daily	21 (12-32)				n.i.	n.i.	n.i.
Rappaport 1978[33]	Chlorpro-mazine	oral	daily	n.i. (300-900)	double blind	156	Acute schizophrenia (clinical diagnosis)	39	0	n.i.
	Placebo	oral	-	-				41	0	n.i.
Russell 1982[34]	Fluphe-nazine	LAI	every week	9.6 (n.i.-n.i.)	double blind	24	Schizophrenia (ICD-9)	13	40	34.1
	Fluspirilene	LAI	every week	9.6 (n.i.-n.i.)				20	67	37.7
Schoemaker 2010[35]	Asenapine	oral	daily	13.5 (10-20)	double blind	52	Schizophrenia, schizoaffective disorder (DSM-IV-TR)	913	48	36.8
	Olanzapine	oral	daily	13.6 (10-20)				312	41	36.2
Sechter 2002[36]	Amisulpride	oral	daily	683 (400-1000)	double blind	26	Chronic schizophrenia (DSM-IV)	152	45	38.4
	Risperidone	oral	daily	6.9 (4-10)				158	45	38.4
Singam 2011[37]	Chlorpro-mazine	oral	daily	n.i. (100-2000)	single blind	52	Schizophrenia (ICD-10)	50	42	35.7
	Risperidone	oral	daily	n.i. (3-16)				50	56	35
Spiegel 1967[38]	Chlorpro-mazine	oral	daily	976 (200-1600)	double blind	24	Chronic schizophrenia (clinical diagnosis)	n.i.	0	44.5
	Trifluo-perazine	oral	daily	23 (4-32)				n.i.	0	44.5

Study 3001_52wks[39]	Haloperidol	oral	daily	11.9 (5-20)	double blind	52	Schizophrenia or schizoaffective disorder (DSM-IV)	146	n.i.	37.3
	Iloperidone	oral	daily	11.4 (4-16)				454	n.i.	37.3
Study 3002_52wks[39]	Haloperidol	oral	daily	14 (5-20)	double blind	52	Schizophrenia or schizoaffective disorder (DSM-IV)	137	n.i.	33.7
	Iloperidone	oral	daily	12.9 (4-16)				420	n.i.	33.7
Study 3003_52wks[39]	Haloperidol	oral	daily	14.5 (5-20)	double blind	52	Schizophrenia or schizoaffective disorder (DSM-IV)	122	n.i.	36.1
	Iloperidone	oral	daily	13.3 (4-16)				365	n.i.	n.i.
Tran 1997[40]	Olanzapine	oral	daily	17.2 (10-20)	double blind	28	Schizophrenia, schizophreniform-, or schizoaffective disorder (DSM-IV)	172	34	36
	Risperidone	oral	daily	7.2 (4-12)				167	37	36.4
Voruganti 2007[41]	Olanzapine	oral	daily	17.2 (n.i.-n.i.)	single blind	52	Schizophrenia (DSM-IV)	42	17	41.3
	Quetiapine	oral	daily	612.8 (n.i.-n.i.)				43	35	38.7
Vyas 1980[42]	Chlorpro-mazine	oral	daily	453 (300-900)	double blind	26	Schizophrenia (clinical diagnosis)	15	40	31.9
	Loxapine	oral	daily	44 (30-90)				15	47	32.9
Wolpert 1968[43]	Placebo	oral	-	-	double blind	31	Chronic schizophrenia (clinical diagnosis)	28	0	55
	Thioridazine	oral	daily	200 (n.i.-1200)				29	0	53
	Tiotixene	oral	daily	10 (n.i.-60)				35	0	53

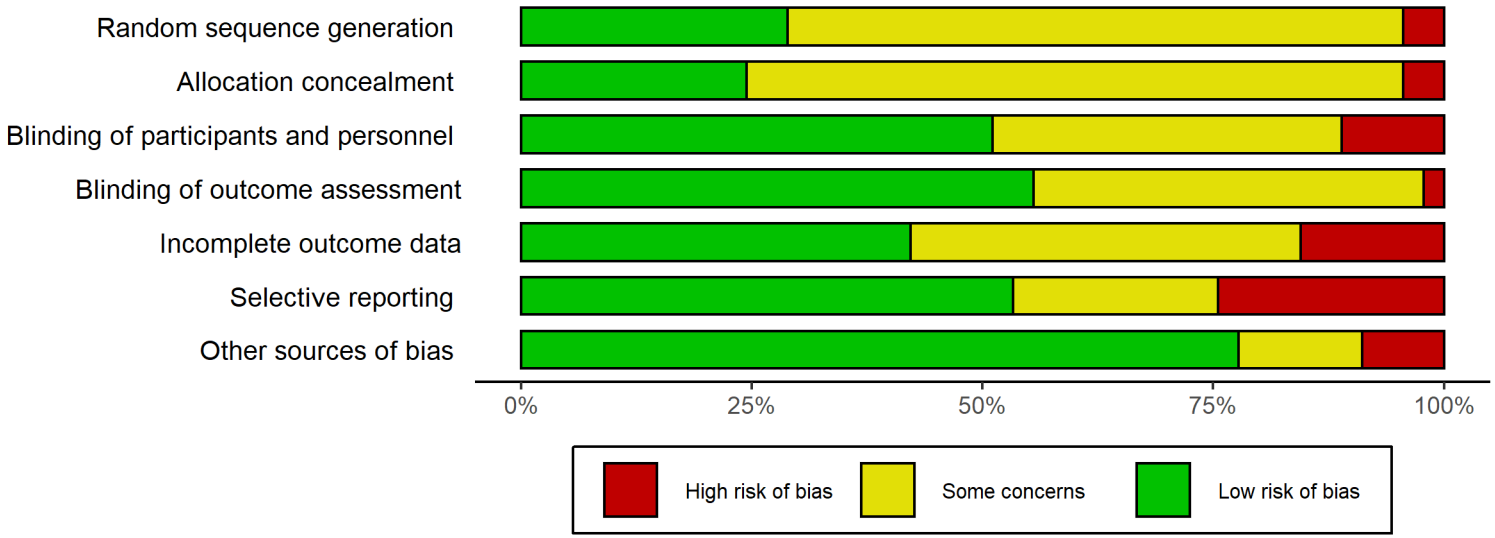
LAI = long-acting injectable formulation, n.i. = not indicated, DSM = Diagnostic and Statistical Manual, various versions, ICD-9 = International Classification of Disorders, 9th edition

Risk of bias of included studies (Risk of bias tool version 1)

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias	Overall
Abuzahab 1977	Unclear	Unclear	Unclear	Unclear	Low	High	Low	Moderate
Abuzzahab 1977a	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	Moderate
Abuzzahab 1982	Unclear	Unclear	Low	Low	High	Low	Low	Moderate
Alvarez 2012	Unclear	Unclear	Low	Low	Low	Low	Low	Low
Bankier 1968	Unclear	Unclear	Low	Low	High	Unclear	Low	Moderate
Breier 2005	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Moderate
Burgoyne 1998	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Moderate
Clark 1970b	Unclear	Unclear	Low	Unclear	Unclear	High	Low	Moderate
Cole 1967	Unclear	Unclear	Unclear	Unclear	Unclear	High	Low	Moderate
Daston 1959	Unclear	Unclear	Low	Low	Unclear	Low	Low	Low
Dutta 2014	Unclear	Unclear	High	Unclear	Unclear	Unclear	Unclear	Moderate
Engelhardt 1978	Low	Unclear	Low	Low	High	Low	Low	Moderate
Gardos 1970	Unclear	Unclear	Low	Low	Unclear	High	Low	Moderate
Gureje 2003	Low	Low	Low	Low	Low	Low	Low	Low
Hera 041-021+Hera 041-022_1y	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Moderate
Ibrahim 2011	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Moderate
Kane 2009_28 weeks	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Moderate
Kane 2010a_52w	High	High	Unclear	Unclear	Low	Low	Low	High
Kasper 2003	Unclear	Unclear	Unclear	Unclear	Low	High	Low	Moderate
Keefe 2006	Low	Low	Low	Low	Low	Low	High	Moderate
Kissling 1985	Low	Unclear	Unclear	Unclear	Unclear	Low	High	Moderate

Kongsakon 2006	Low	Low	Low	Low	Low	Low	High	Moderate
Laborde 2000	Low	Low	Low	Low	Unclear	Low	Low	Low
Lieberman 2005_18months	Unclear	Unclear	Low	Low	Low	Low	Low	Low
Loebel 2013_12m	High	High	Low	Low	Low	Low	Low	High
Malyarov 1999	Unclear	Unclear	High	Low	Unclear	Unclear	Unclear	Moderate
Mortimer 2004	Low	Low	Low	Low	Low	Low	Low	Low
Naukkarinen 2000	Low	Low	Low	Low	Low	Unclear	Unclear	Low
NCT00210717	Low	Low	Low	Low	Low	Low	Low	Low
NCT03345979	Low	Low	Low	Low	Low	Low	Low	Low
Paredes 1966	Unclear	Unclear	Unclear	Unclear	Unclear	High	Low	Moderate
Platz 1967	Unclear	Unclear	Low	Low	Unclear	High	Low	Moderate
Rappaport 1978	Unclear	Unclear	Unclear	Low	Unclear	High	Low	Moderate
Russell 1982	Unclear	Unclear	Low	Low	High	Low	Low	Moderate
Schoemaker 2010	Low	Low	Low	Low	Low	Low	Low	Low
Sechter 2002	Low	Low	Unclear	Unclear	Low	Low	Low	Low
Singam 2011	Unclear	Unclear	High	Low	High	High	Low	High
Spiegel 1967	Unclear	Unclear	Low	Low	High	High	Low	High
Study 3001_52wks	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Moderate
Study 3002_52wks	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Moderate
Study 3003_52wks	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Moderate
Tran 1997	Low	Low	Low	Low	Low	Low	Low	Low
Voruganti 2007	Unclear	Unclear	High	Unclear	High	Low	Low	High
Vyas 1980	Unclear	Unclear	Low	Low	Low	Low	Low	Low
Wolpert 1968	Unclear	Unclear	High	High	Unclear	High	High	High

Risk of bias across studies



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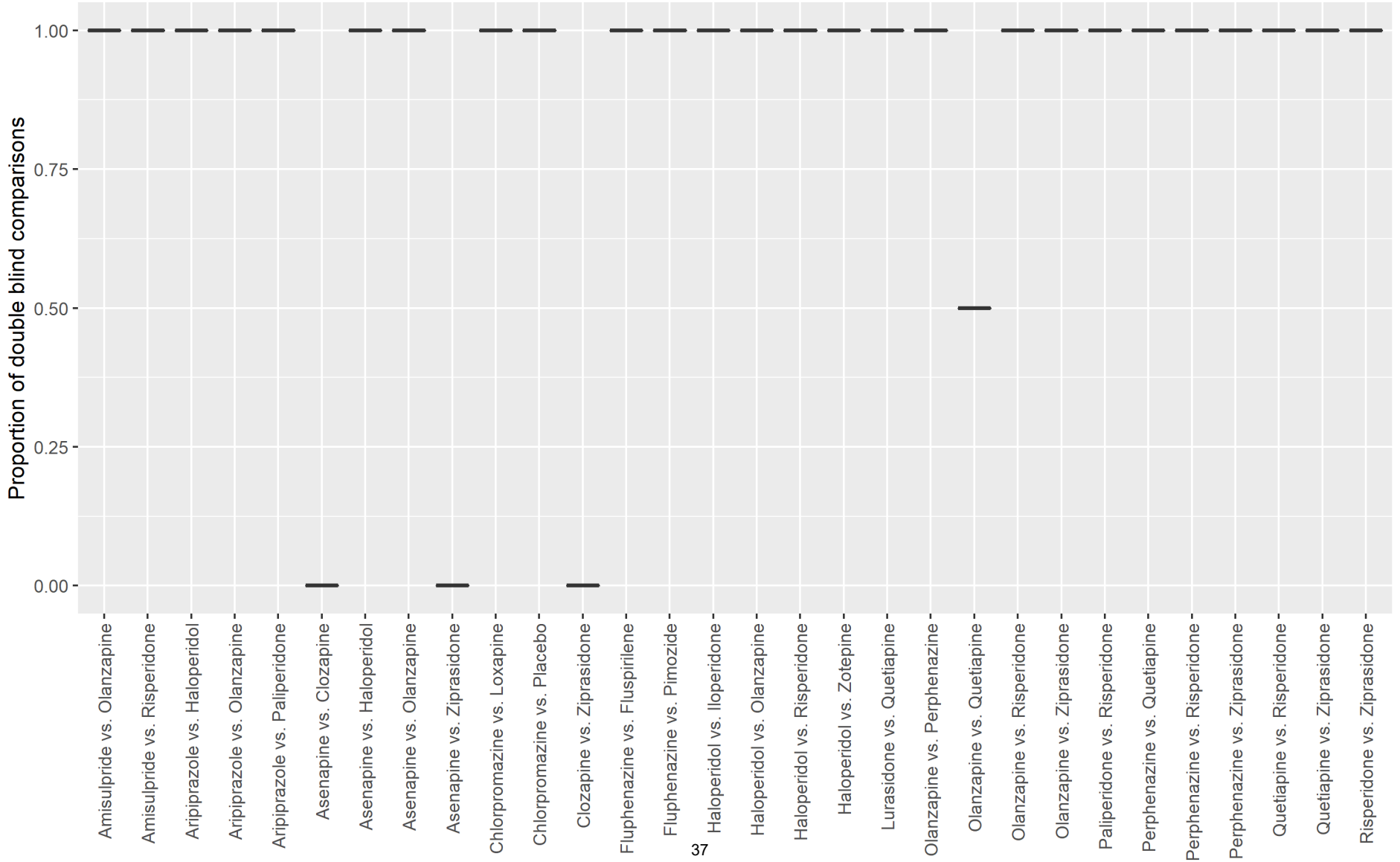
eAppendix 6

Primary outcome additional results

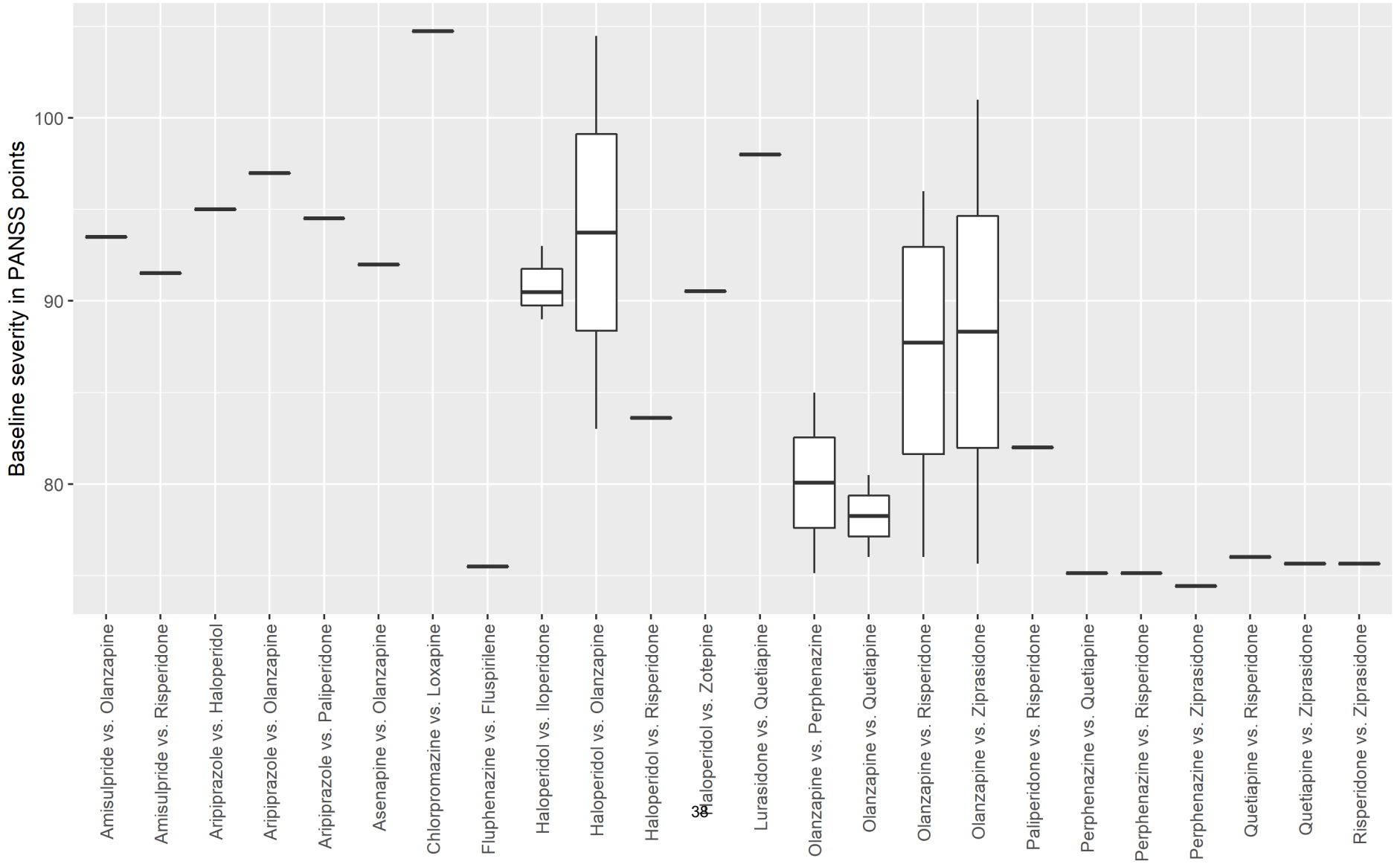
1. Assessment of the transitivity assumption
2. Results of pairwise meta-analyses
3. Sensitivity analysis oral and long-acting injectable drugs separately
4. Sensitivity analysis only double-blind studies
5. Sensitivity analysis without continuation studies
6. Sensitivity analysis without the CATIE study which also covered potentially unfair doses (olanzapine up to 30mg/day)
7. Sensitivity analysis excluding olanzapine sponsored studies
8. Sensitivity analysis only studies of at least 1 year duration
9. Sensitivity analysis without studies judged at high risk of bias)
10. Sensitivity analysis without placebo-controlled studies
11. Sensitivity analysis without completer analysis
12. Sensitivity analysis without imputed SDs
13. Confidence in the evidence according to CINeMA
14. Small trial/publication bias

Transitivity analysis – blinding: Most comparisons included only double-blind studies. We checked in a sensitivity analysis whether excluding single-blind studies changed the results to an important extent but it did not.

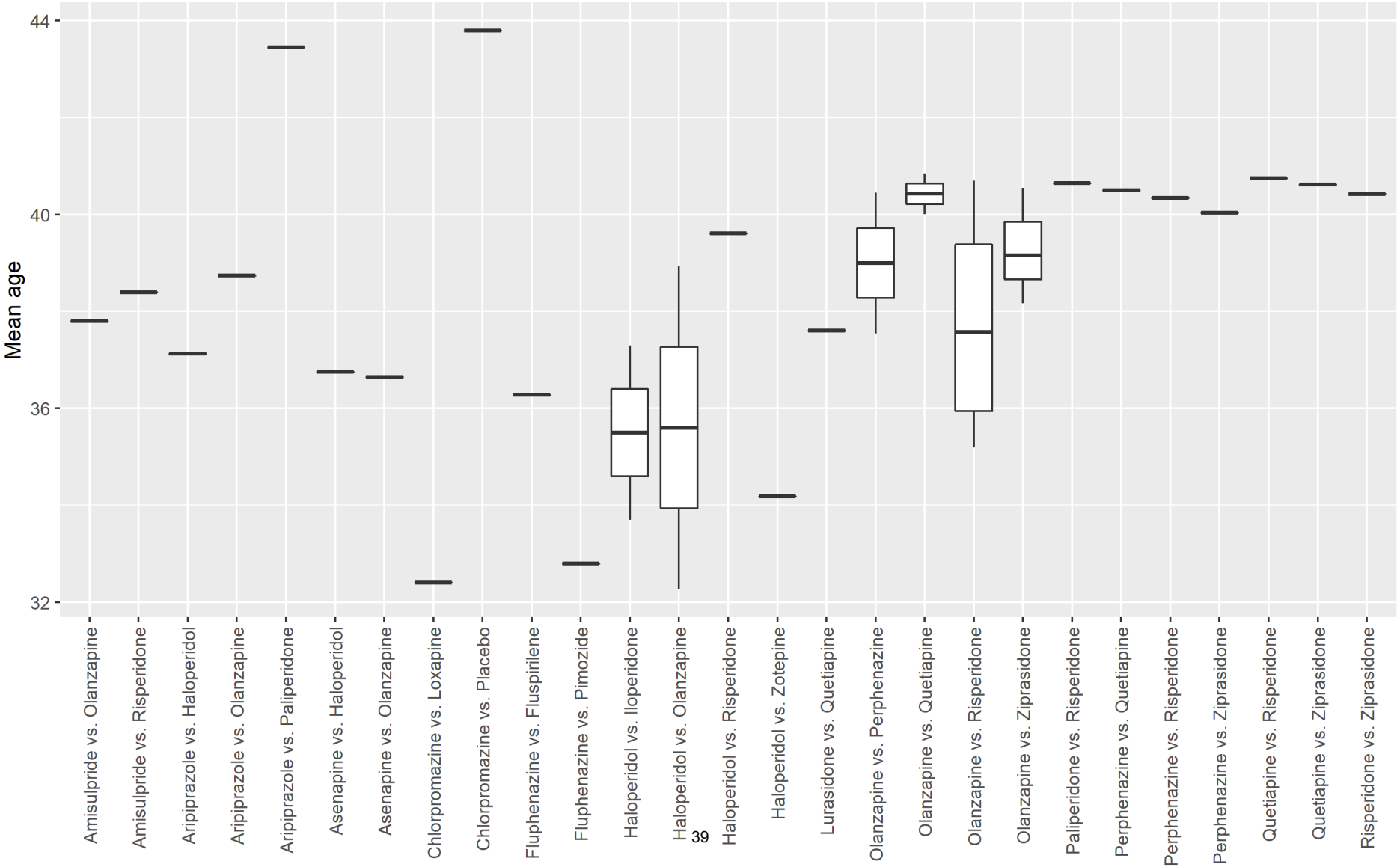


Transitivity analysis – baseline severity: Most included studies had a mean PANSS total score between 90 and 100 at baseline. The figure shows that there were a few outliers with higher and lower mean PANSS at baseline. Some of these were in studies of first-generation antipsychotics. These studies were few and small in size and, therefore, had not much weight in the network meta-analysis or did not contribute at all.

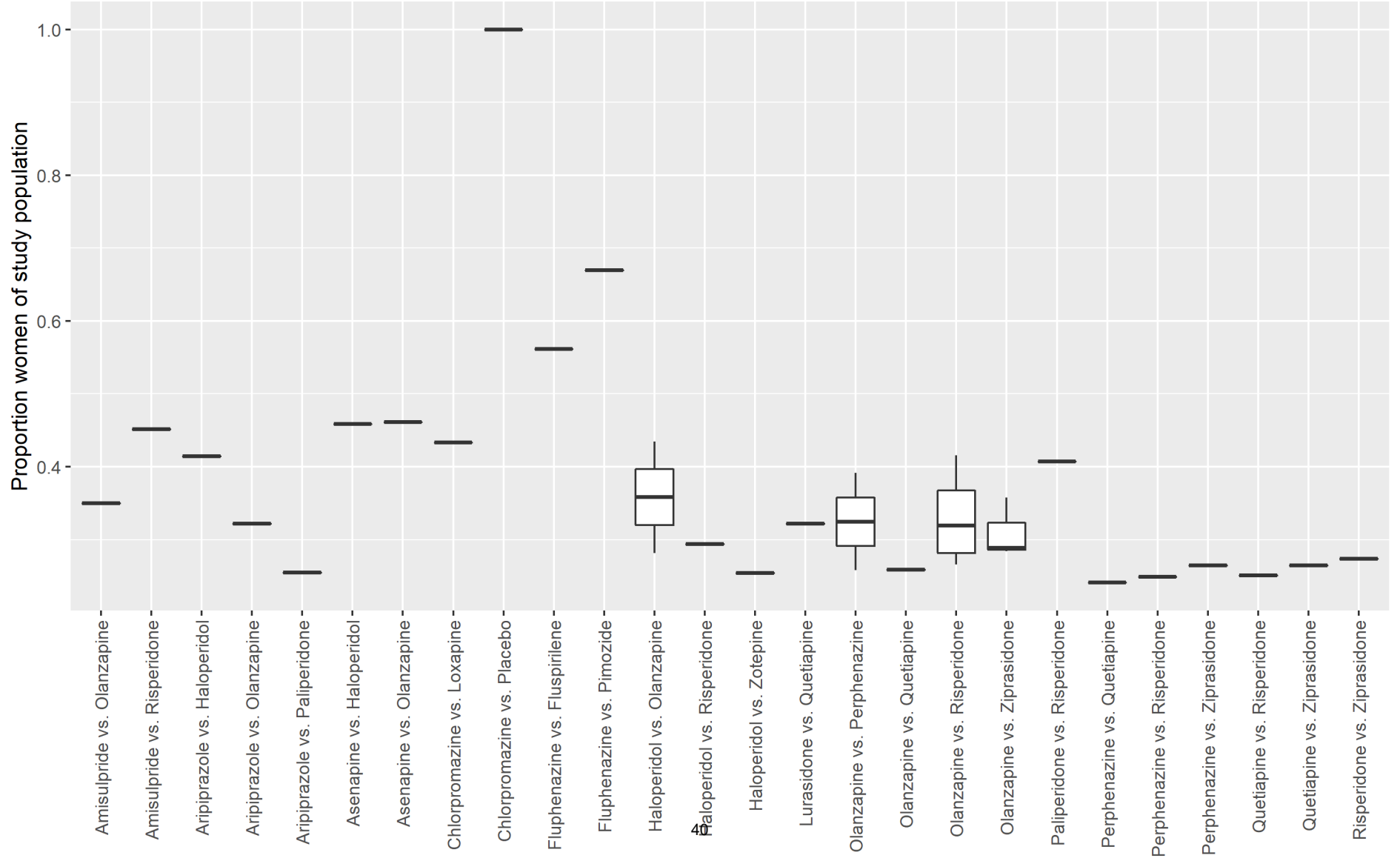
More important are comparisons at the right side with a relatively low PANSS of 75. These are from the CATIE study[1] into which in essence any chronic patient with schizophrenia could be included. The study contributed results to olanzapine, quetiapine, perphenazine, risperidone and ziprasidone. We, therefore, excluded this study in a post-hoc sensitivity analysis but it did not lead to marked changes of the evidence.



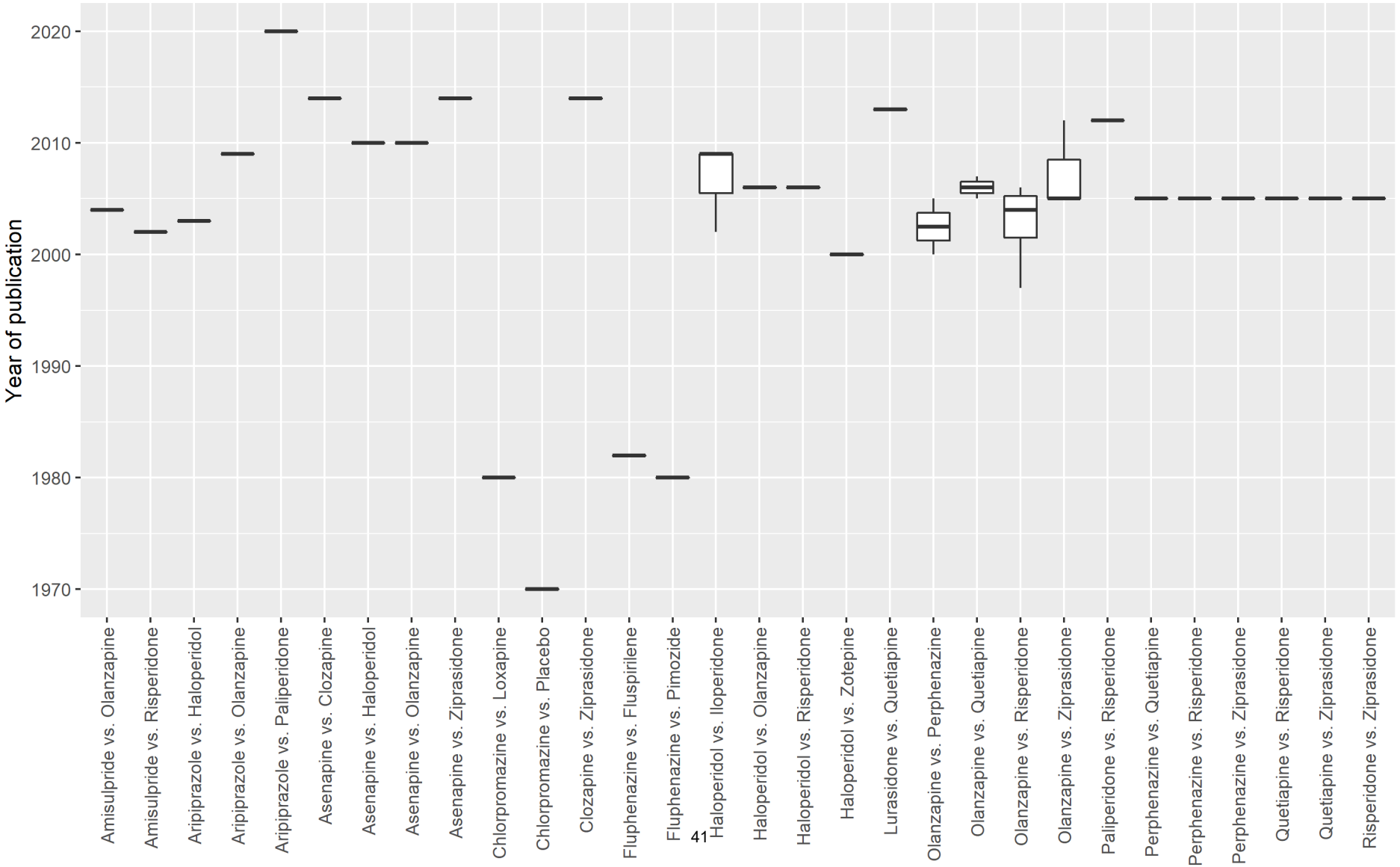
Transitivity analysis – age: Patients' chronicity had been identified as an effect moderator in an individual-patient-data meta-analysis, at least compared to placebo[2]. In the current meta-analysis mean age at baseline scattered around 40, except for a few comparisons which mainly involved first-generation antipsychotics. As the latter were small in numbers of participants or did not contribute at all and therefore did not have a lot of weight in the analysis, it is unlikely that age had an important impact on the results.



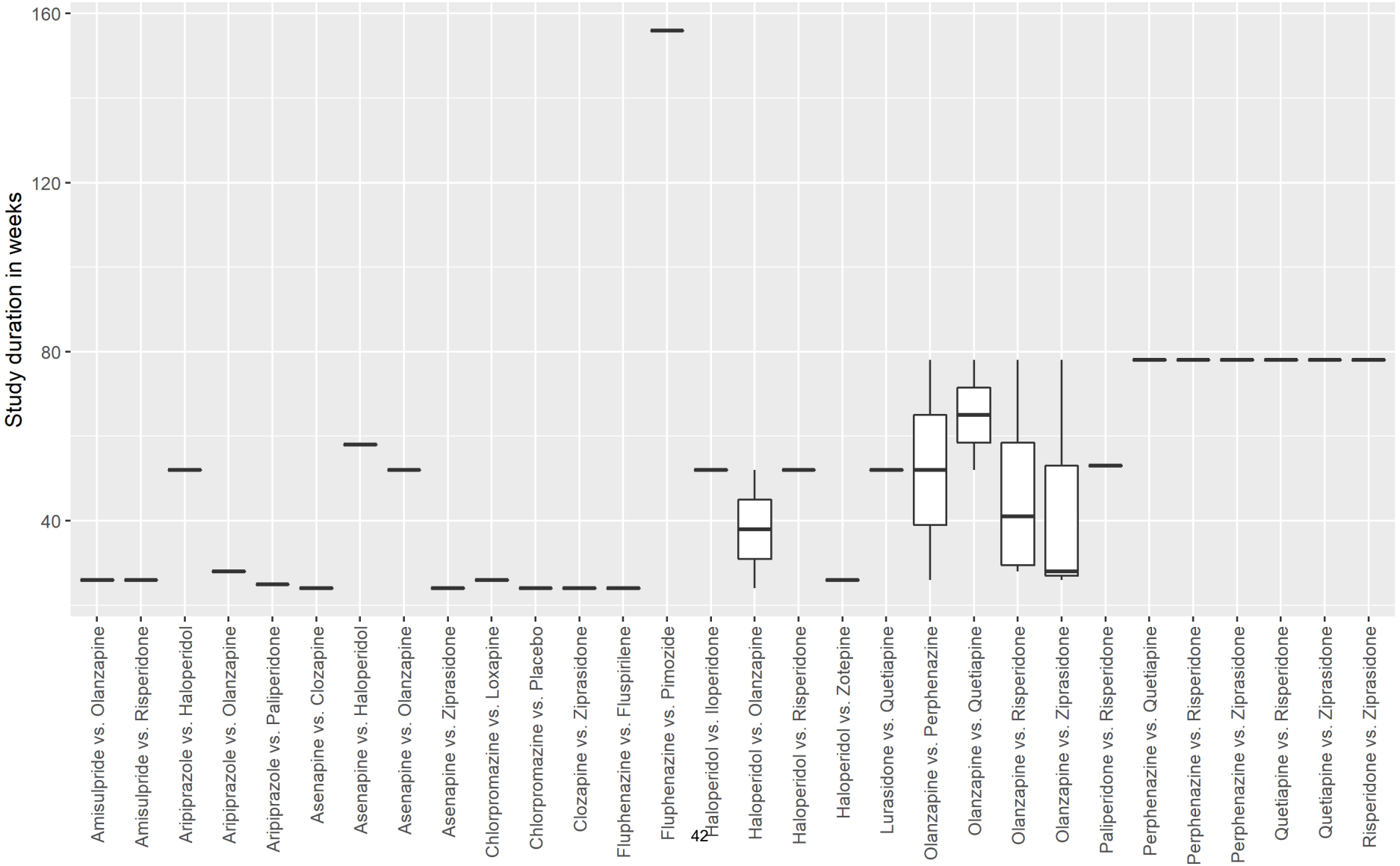
Transitivity analysis – sex: Sex had been identified as an effect moderator in an individual-patient-data meta-analysis with women responding better to antipsychotics compared to placebo than men[2]. The figure below mainly shows the preponderance of men in antipsychotic drug trials. It could be said that this preponderance limits generalisability because according to epidemiological data schizophrenia approximately affects women and men to the same extent. The few outliers with more women again come mainly from comparisons with first-generation antipsychotics which were small in numbers.



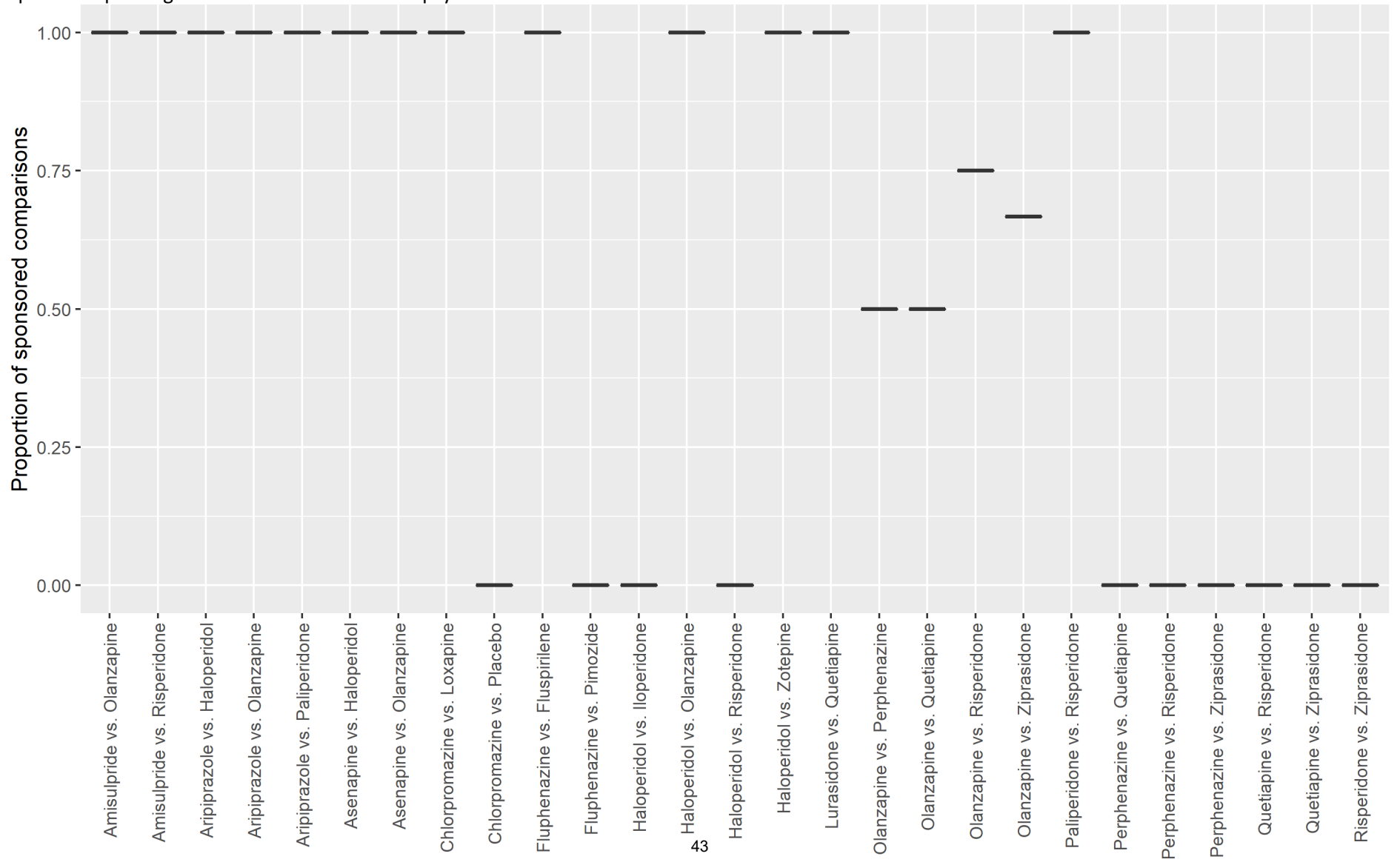
Transitivity analysis – publication year: The figure shows the obvious - studies on antipsychotics which were lincensed earlier were also published earlier. It had been shown that earlier studies had lower placebo-response than more recent studies[3]. But as there were very few placebo-controlled studies, the meaning for the current analysis is unclear.



Transitivity analysis – study duration: The figure shows that with few exceptions study duration ranged between 6 months and 1 year. The major exception was a single study comparing fluphenazine and pimozide and the CATIE study (78 weeks)[1] which was excluded in a post-hoc sensitivity analysis without much effect on the results. As it has shown that most antipsychotic drug effects occur in the first 4 weeks[4,5] we do not believe that study duration had an important impact on the results.



Transitivity analysis – pharmaceutical sponsor: The figure shows that most studies on second-generation antipsychotics were industry sponsored, the CATIE study[1] which contributed data on olanzapine, perphenazine, quetiapine, risperidone and ziprasidone again being a major exception. Excluding the CATIE study did not change the results to an important content. Moreover, we excluded studies from olanzapine's manufacturer and again the results did not notably change. Too few studies were available for a more detailed analysis of industry sponsorhip, but previous analyses of this type did not find that sponsorship changed differences between antipsychotics much[5,6].



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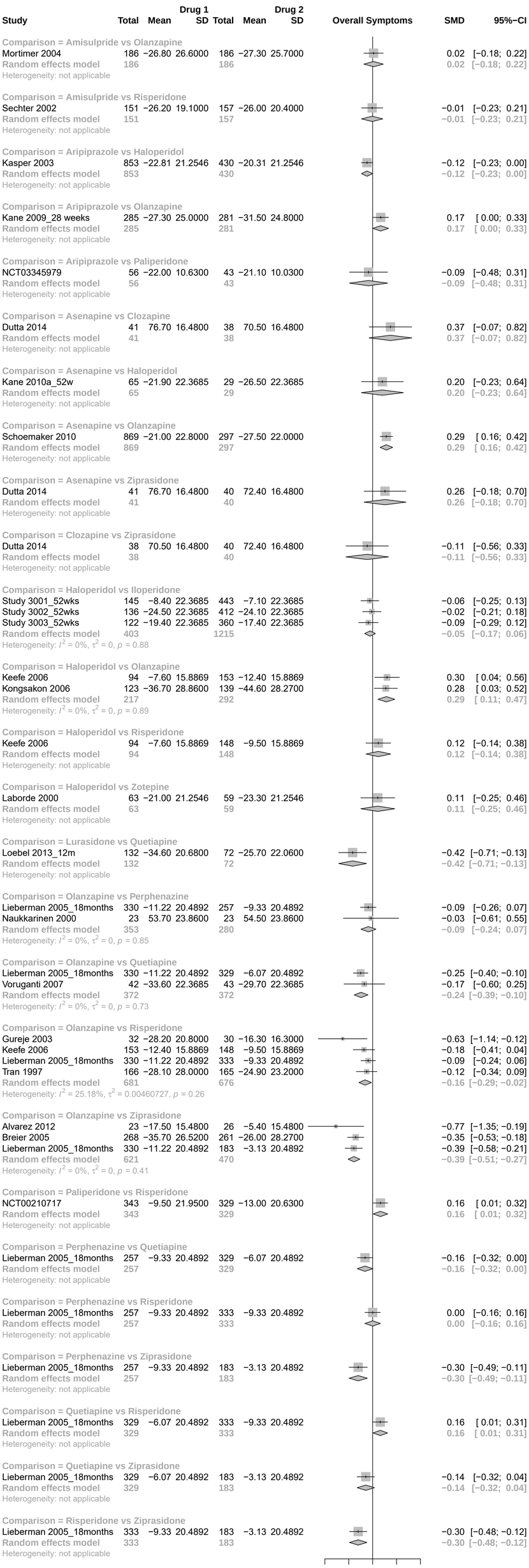
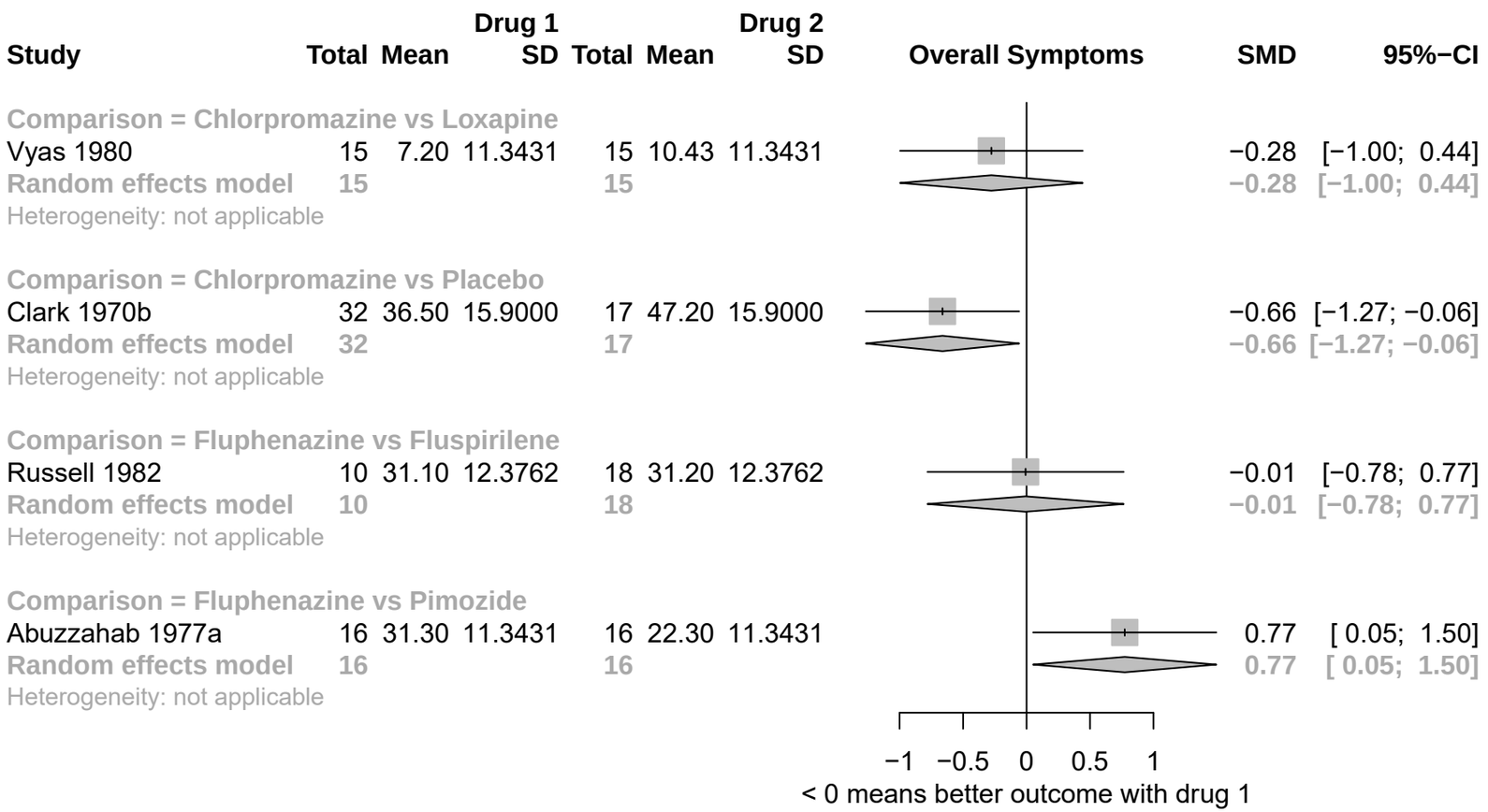
Pairwise meta-analyses of drugs included in the network: Overall Symptoms (primary outcome)

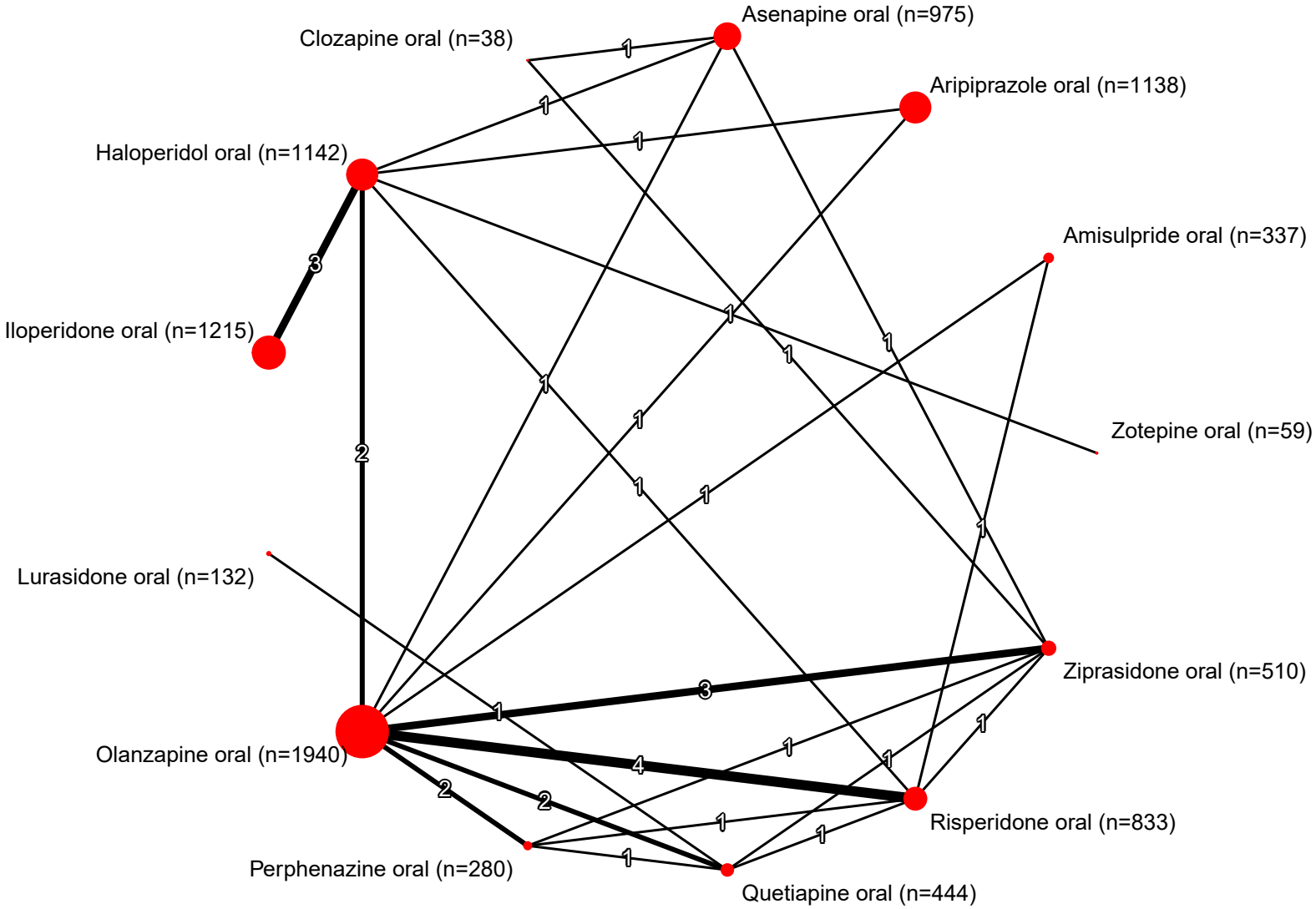


Pairwise meta-analyses of drugs outside the network: Overall Symptoms (primary outcome)



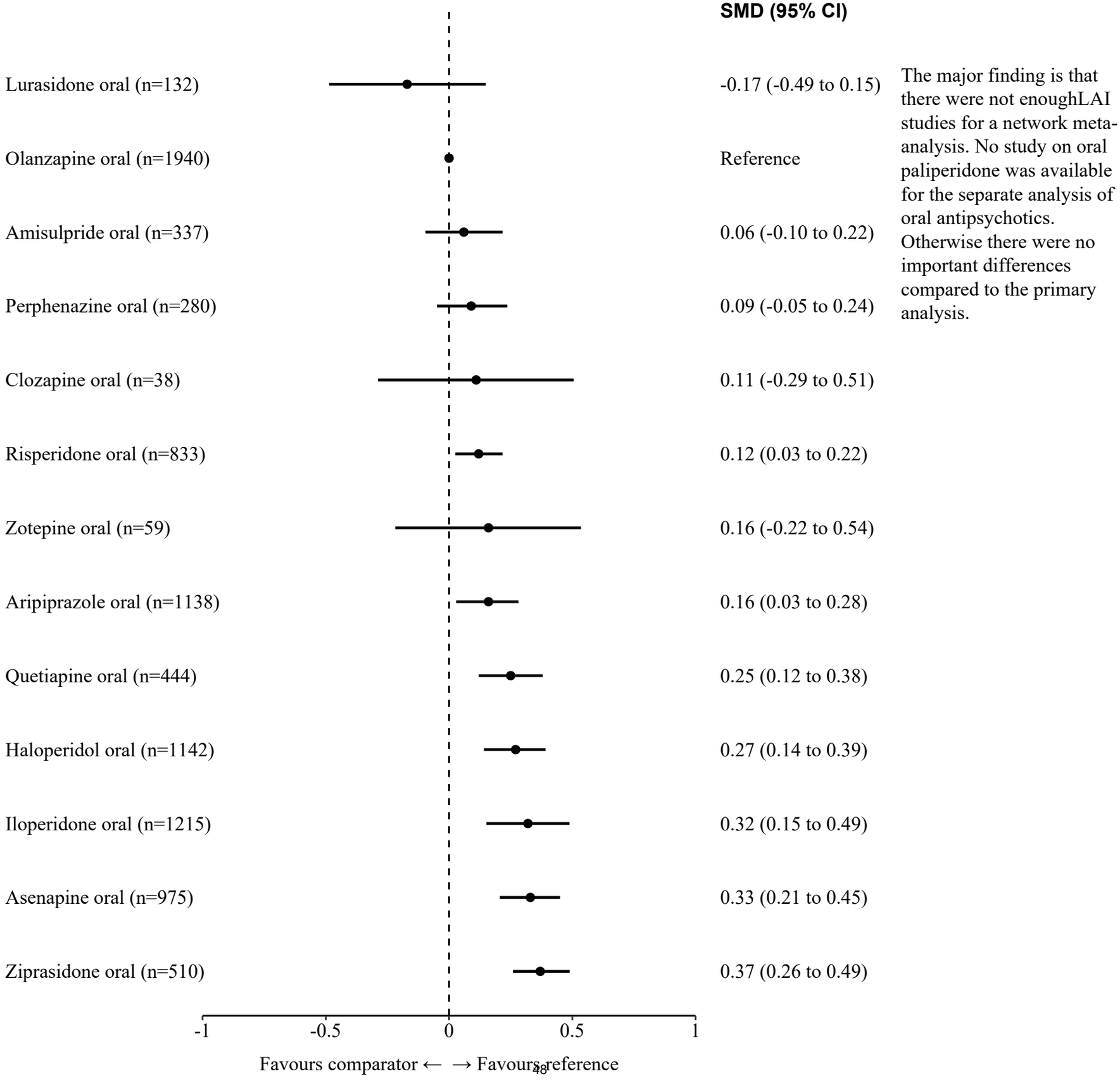
Sensitivity analysis: Overall Symptoms (oral and LAI separate)

Please note that there were too few LAI studies to form a separate network



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials

Sensitivity analysis: network meta-analysis overall Symptoms (oral and LAI separate)



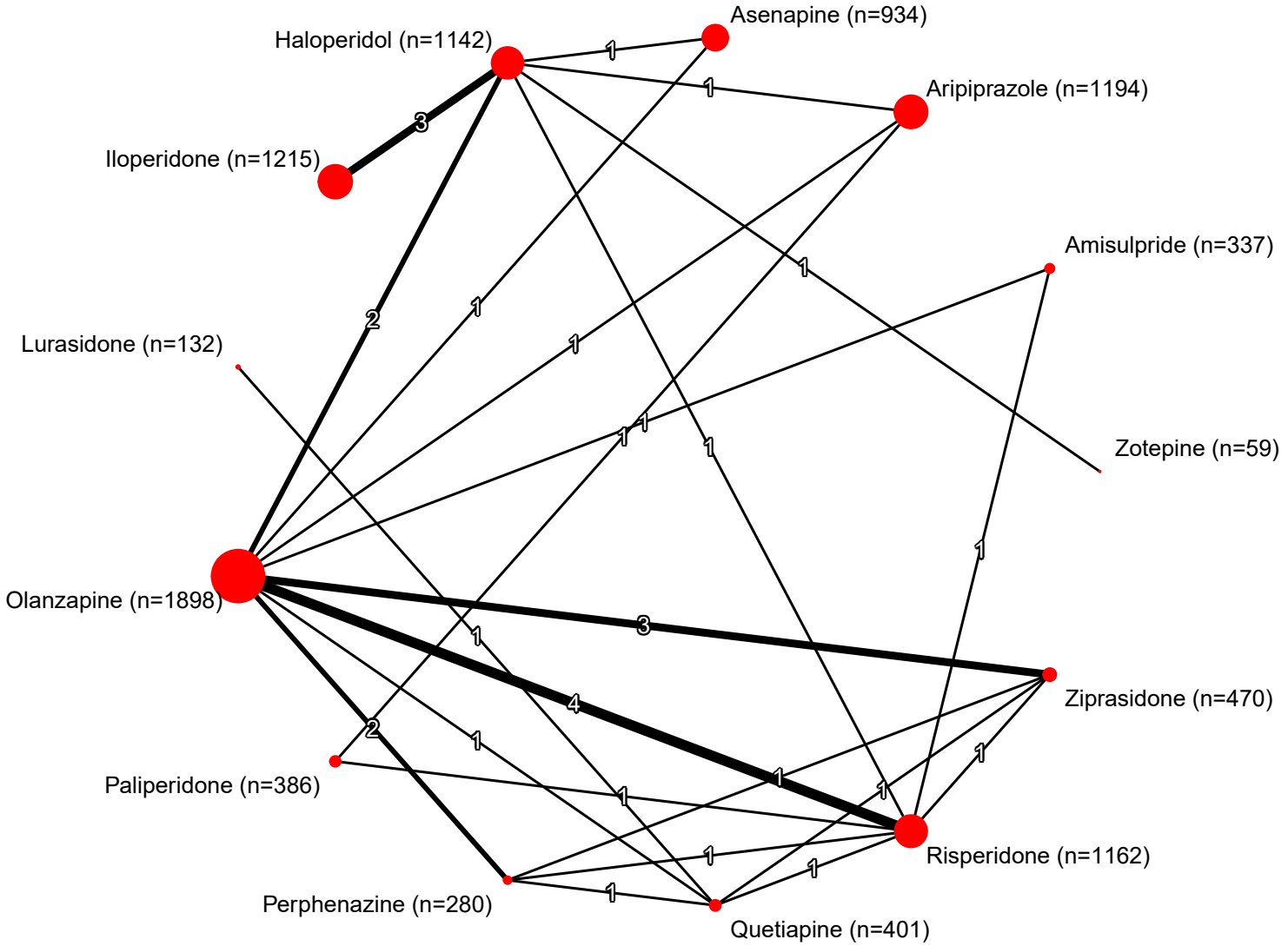
The major finding is that there were not enoughLAI studies for a network meta-analysis. No study on oral paliperidone was available for the separate analysis of oral antipsychotics. Otherwise there were no important differences compared to the primary analysis.

Sensitivity analysis league table: Overall Symptoms (oral and LAI separate)

Lurasidoneoral	NA	NA	NA	NA	NA	NA	NA	**-0.42 (-0.71 to -0.13)**	NA	NA	NA	NA
-0.17 (-0.49 to 0.15)	**Olanzapineoral**	-0.02 (-0.22 to 0.18)	-0.09 (-0.24 to 0.07)	NA	**-0.14 (-0.25 to -0.04)**	-0.17 (-0.33 to 0.00)	NA	**-0.24 (-0.39 to -0.10)**	**-0.29 (-0.47 to -0.11)**	NA	**-0.29 (-0.42 to -0.16)**	**-0.39 (-0.51 to -0.27)**
-0.23 (-0.58 to 0.12)	-0.06 (-0.22 to 0.10)	**Amisulprideoral**	NA	NA	-0.01 (-0.23 to 0.21)	NA	NA	NA	NA	NA	NA	NA
-0.26 (-0.59 to 0.07)	-0.09 (-0.24 to 0.05)	-0.03 (-0.24 to 0.17)	**Perphenazineoral**	NA	0.00 (-0.16 to 0.16)	NA	NA	-0.16 (-0.32 to 0.00)	NA	NA	NA	**-0.30 (-0.49 to -0.11)**
-0.28 (-0.78 to 0.23)	-0.11 (-0.51 to 0.29)	-0.05 (-0.47 to 0.38)	-0.01 (-0.43 to 0.40)	**Clozapineoral**	NA	NA	NA	NA	NA	NA	-0.37 (-0.82 to 0.07)	-0.11 (-0.56 to 0.33)
-0.29 (-0.61 to 0.03)	**-0.12 (-0.22 to -0.03)**	-0.06 (-0.22 to 0.10)	-0.03 (-0.18 to 0.12)	-0.01 (-0.42 to 0.39)	**Risperidoneoral**	NA	NA	**-0.16 (-0.31 to -0.01)**	-0.12 (-0.38 to 0.14)	NA	NA	**-0.30 (-0.48 to -0.12)**
-0.32 (-0.66 to 0.02)	**-0.16 (-0.28 to -0.03)**	-0.09 (-0.29 to 0.10)	-0.06 (-0.25 to 0.13)	-0.05 (-0.46 to 0.37)	-0.03 (-0.19 to 0.12)	**Aripiprazoleoral**	NA	NA	-0.12 (-0.23 to 0.00)	NA	NA	NA
-0.33 (-0.82 to 0.16)	-0.16 (-0.54 to 0.22)	-0.10 (-0.50 to 0.31)	-0.06 (-0.47 to 0.34)	-0.05 (-0.60 to 0.50)	-0.04 (-0.42 to 0.35)	-0.00 (-0.37 to 0.37)	**Zotepineoral**	NA	-0.11 (-0.46 to 0.25)	NA	NA	NA
-0.42 (-0.71 to -0.13)	**-0.25 (-0.38 to -0.12)**	-0.19 (-0.38 to 0.01)	-0.16 (-0.32 to 0.00)	-0.14 (-0.55 to 0.27)	-0.13 (-0.27 to 0.01)	-0.10 (-0.27 to 0.08)	-0.09 (-0.49 to 0.31)	**Quetiapineoral**	NA	NA	NA	-0.14 (-0.32 to 0.04)
-0.43 (-0.77 to -0.09)	**-0.27 (-0.39 to -0.14)**	**-0.21 (-0.40 to -0.01)**	-0.17 (-0.36 to 0.01)	-0.16 (-0.57 to 0.26)	-0.15 (-0.29 to 0.00)	**-0.11 (-0.21 to -0.01)**	-0.11 (-0.46 to 0.25)	-0.02 (-0.19 to 0.16)	**Haloperidoloral**	-0.05 (-0.17 to 0.06)	-0.20 (-0.64 to 0.23)	NA
-0.49 (-0.85 to -0.13)	**-0.32 (-0.49 to -0.15)**	**-0.26 (-0.49 to -0.03)**	**-0.23 (-0.44 to -0.01)**	-0.21 (-0.64 to 0.22)	**-0.20 (-0.39 to -0.01)**	**-0.16 (-0.32 to -0.01)**	-0.16 (-0.53 to 0.21)	-0.07 (-0.28 to 0.14)	-0.05 (-0.17 to 0.06)	**Iloperidoneoral**	NA	NA
-0.50 (-0.84 to -0.16)	**-0.33 (-0.45 to -0.21)**	**-0.27 (-0.47 to -0.07)**	**-0.23 (-0.42 to -0.05)**	-0.22 (-0.62 to 0.18)	**-0.21 (-0.36 to -0.05)**	-0.17 (-0.34 to 0.00)	-0.17 (-0.56 to 0.22)	-0.08 (-0.25 to 0.10)	-0.06 (-0.23 to 0.11)	-0.01 (-0.21 to 0.19)	**Asenapineoral**	0.26 (-0.18 to 0.70)
-0.54 (-0.87 to -0.22)	**-0.37 (-0.49 to -0.26)**	**-0.31 (-0.50 to -0.12)**	**-0.28 (-0.44 to -0.12)**	-0.27 (-0.66 to 0.13)	**-0.25 (-0.39 to -0.12)**	**-0.22 (-0.39 to -0.05)**	-0.22 (-0.61 to 0.18)	-0.12 (-0.28 to 0.03)	-0.11 (-0.28 to 0.06)	-0.05 (-0.26 to 0.15)	-0.05 (-0.21 to 0.12)	**Ziprasidoneoral**

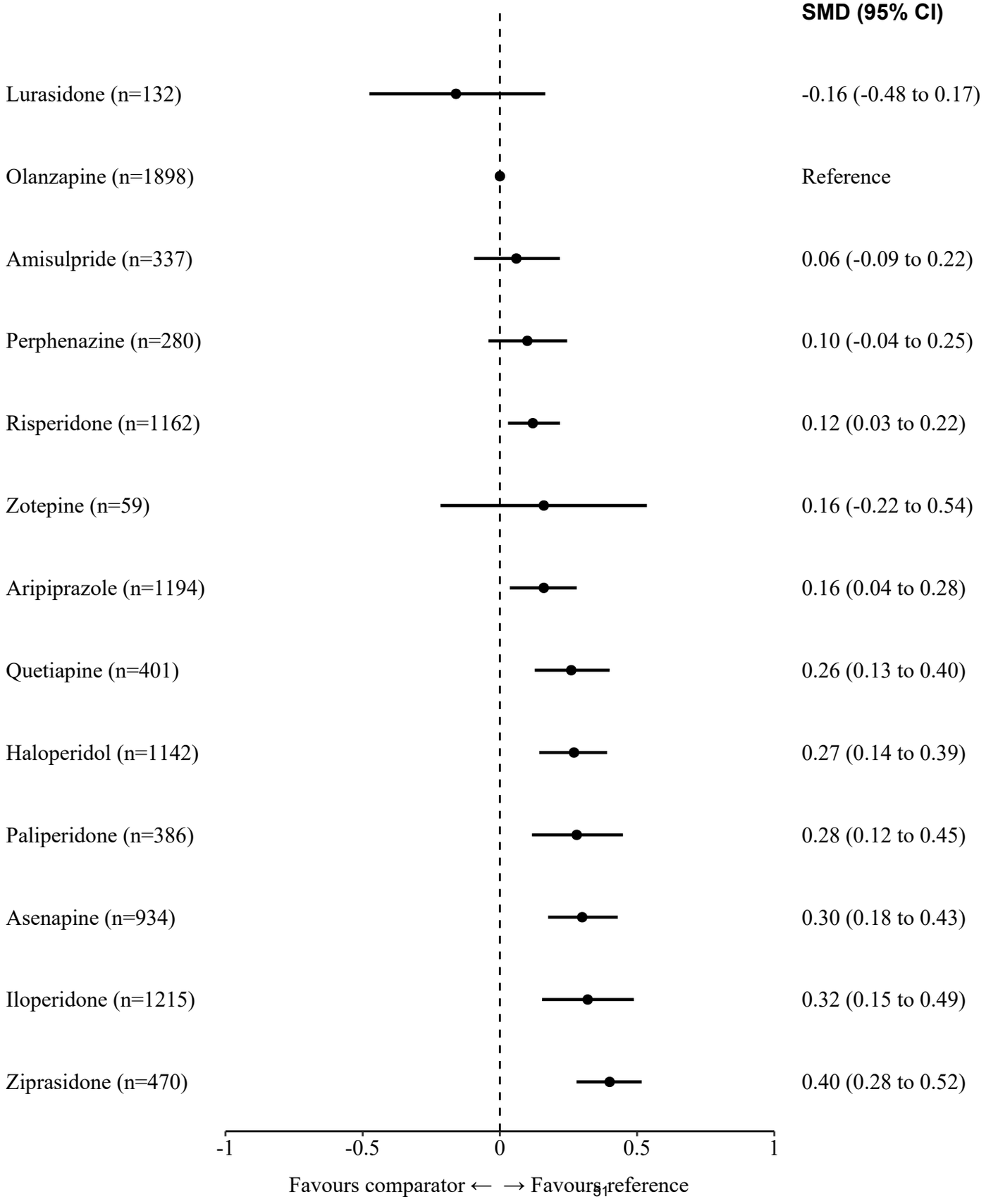
The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval of 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always + except for lurasidone, but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Sensitivity analysis: Overall Symptoms (only double blind studies)



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials

Sensitivity analysis: Network meta-analysis overall Symptoms (only double blind studies)



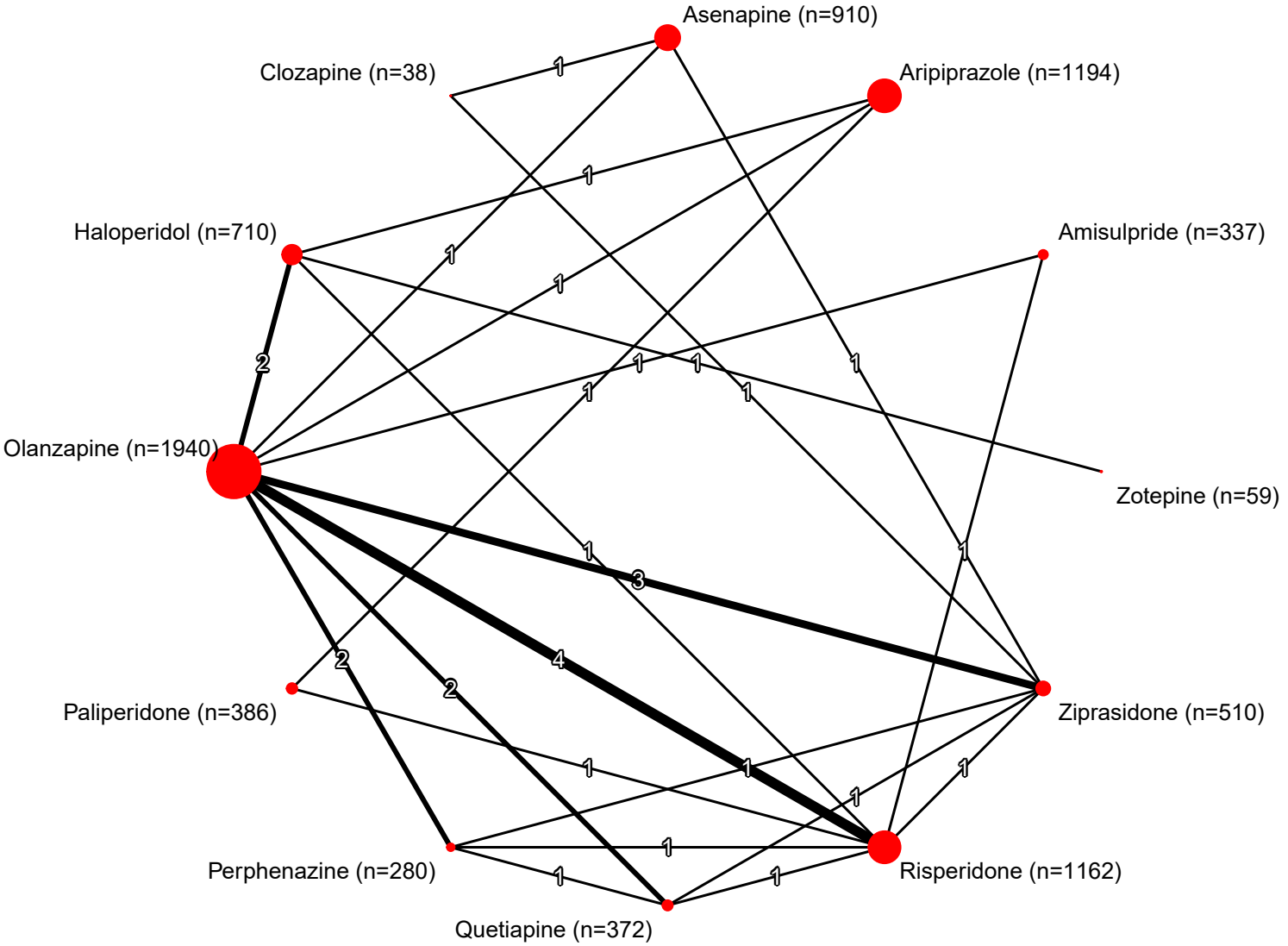
When single-blind studies were excluded, no data on clozapine remained. Asenapine and iloperidone changed their ranks. Otherwise the results are in essence the same as those of the primary analysis.

Sensitivity analysis league table for the outcome: Overall Symptoms (only double blind studies)

Lurasidone	NA	NA	NA	NA	NA	NA	**-0.42 (-0.71 to -0.13)**	NA	NA	NA	NA	NA
-0.16 (-0.48 to 0.17)	**Olanzapine**	-0.02 (-0.22 to 0.18)	-0.09 (-0.24 to 0.07)	**-0.14 (-0.25 to -0.04)**	-0.17 (-0.33 to 0.00)	NA	**-0.25 (-0.40 to -0.10)**	**-0.29 (-0.47 to -0.11)**	NA	**-0.29 (-0.42 to -0.16)**	NA	**-0.39 (-0.51 to -0.27)**
-0.22 (-0.57 to 0.13)	-0.06 (-0.22 to 0.09)	**Amisulpride**	NA	-0.01 (-0.23 to 0.21)	NA	NA	NA	NA	NA	NA	NA	NA
-0.26 (-0.59 to 0.08)	-0.10 (-0.25 to 0.04)	-0.04 (-0.24 to 0.16)	**Perphenazine**	0.00 (-0.16 to 0.16)	NA	NA	-0.16 (-0.32 to 0.00)	NA	NA	NA	NA	**-0.30 (-0.49 to -0.11)**
-0.28 (-0.60 to 0.04)	**-0.12 (-0.22 to -0.03)**	-0.06 (-0.22 to 0.10)	-0.02 (-0.17 to 0.13)	**Risperidone**	NA	NA	**-0.16 (-0.31 to -0.01)**	-0.12 (-0.38 to 0.14)	**-0.16 (-0.32 to -0.01)**	NA	NA	**-0.30 (-0.48 to -0.12)**
-0.31 (-0.65 to 0.03)	**-0.16 (-0.28 to -0.04)**	-0.10 (-0.29 to 0.10)	-0.06 (-0.24 to 0.13)	-0.03 (-0.18 to 0.11)	**Aripiprazole**	NA	NA	-0.12 (-0.23 to 0.00)	-0.09 (-0.48 to 0.31)	NA	NA	NA
-0.31 (-0.81 to 0.18)	-0.16 (-0.54 to 0.22)	-0.10 (-0.50 to 0.31)	-0.06 (-0.46 to 0.34)	-0.04 (-0.42 to 0.35)	-0.00 (-0.37 to 0.37)	**Zotepine**	NA	-0.11 (-0.46 to 0.25)	NA	NA	NA	NA
-0.42 (-0.71 to -0.13)	**-0.26 (-0.40 to -0.13)**	-0.20 (-0.40 to 0.00)	-0.16 (-0.32 to 0.00)	-0.14 (-0.28 to 0.00)	-0.11 (-0.28 to 0.07)	-0.10 (-0.50 to 0.29)	**Quetiapine**	NA	NA	NA	NA	-0.14 (-0.32 to 0.04)
-0.42 (-0.76 to -0.08)	**-0.27 (-0.39 to -0.14)**	**-0.20 (-0.40 to -0.01)**	-0.17 (-0.35 to 0.02)	-0.14 (-0.29 to 0.00)	**-0.11 (-0.21 to -0.01)**	-0.11 (-0.46 to 0.25)	-0.00 (-0.18 to 0.18)	**Haloperidol**	NA	-0.20 (-0.64 to 0.23)	-0.05 (-0.17 to 0.06)	NA
-0.44 (-0.79 to -0.09)	**-0.28 (-0.45 to -0.12)**	**-0.22 (-0.43 to -0.01)**	-0.18 (-0.38 to 0.02)	**-0.16 (-0.30 to -0.02)**	-0.12 (-0.31 to 0.06)	-0.12 (-0.53 to 0.28)	-0.02 (-0.22 to 0.18)	-0.02 (-0.21 to 0.18)	**Paliperidone**	NA	NA	NA
-0.46 (-0.80 to -0.11)	**-0.30 (-0.43 to -0.18)**	**-0.24 (-0.44 to -0.04)**	**-0.20 (-0.39 to -0.01)**	**-0.18 (-0.34 to -0.02)**	-0.14 (-0.32 to 0.03)	-0.14 (-0.54 to 0.25)	-0.04 (-0.23 to 0.15)	-0.04 (-0.21 to 0.13)	-0.02 (-0.23 to 0.19)	**Asenapine**	NA	NA
-0.48 (-0.84 to -0.12)	**-0.32 (-0.49 to -0.15)**	**-0.26 (-0.48 to -0.03)**	-0.22 (-0.44 to 0.00)	**-0.20 (-0.38 to -0.01)**	**-0.16 (-0.32 to -0.01)**	-0.16 (-0.53 to 0.21)	-0.06 (-0.27 to 0.15)	-0.05 (-0.17 to 0.06)	-0.04 (-0.26 to 0.19)	-0.02 (-0.22 to 0.19)	**Iloperidone**	NA
-0.55 (-0.88 to -0.22)	**-0.40 (-0.52 to -0.28)**	**-0.34 (-0.53 to -0.14)**	**-0.30 (-0.46 to -0.13)**	**-0.27 (-0.41 to -0.14)**	**-0.24 (-0.41 to -0.07)**	-0.24 (-0.63 to 0.15)	-0.13 (-0.29 to 0.02)	-0.13 (-0.30 to 0.04)	-0.12 (-0.31 to 0.08)	-0.10 (-0.27 to 0.08)	-0.08 (-0.28 to 0.13)	**Ziprasidone**

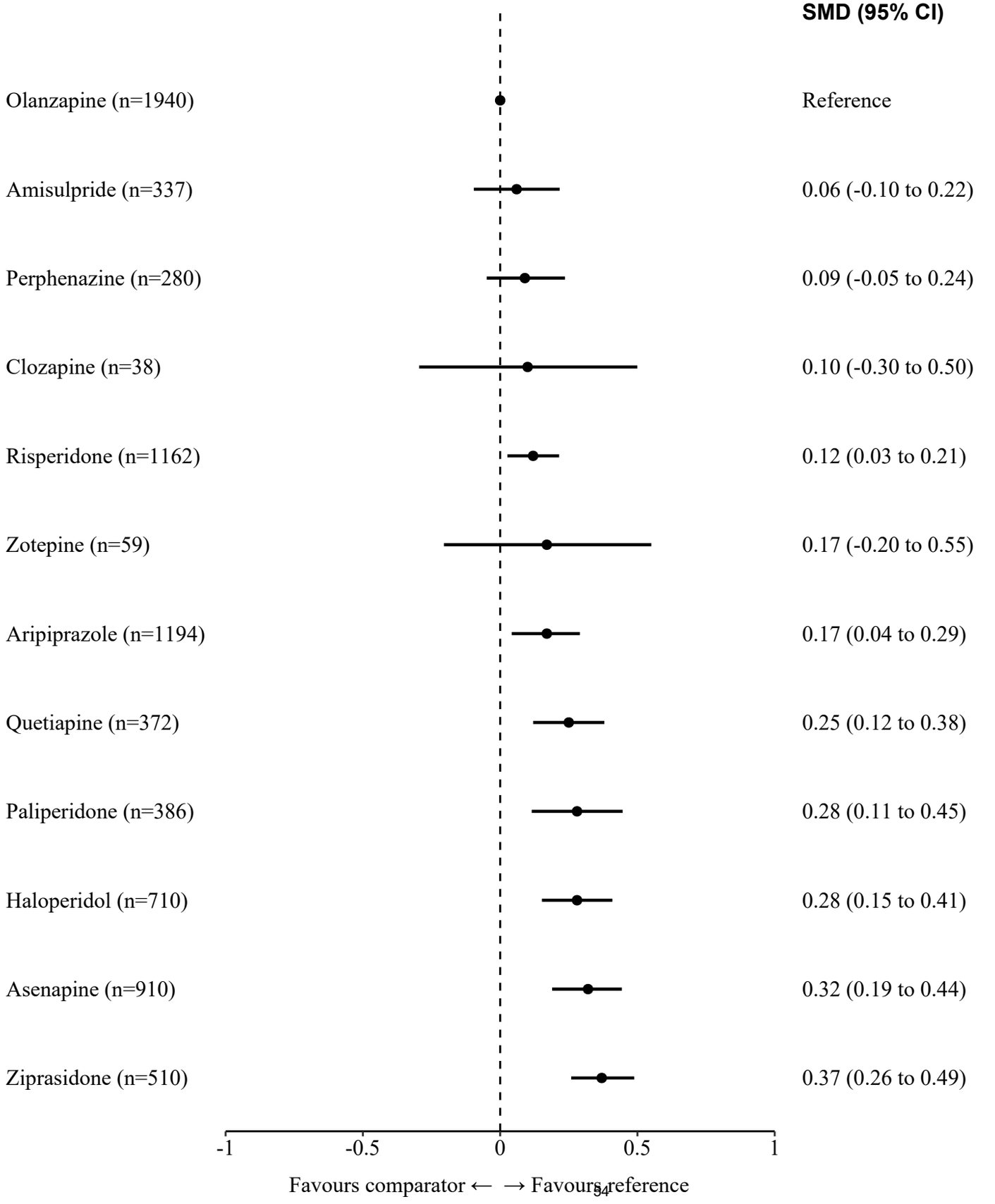
The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval of 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always + except for lurasidone, but the results are the same.Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Sensitivity analysis: Overall Symptoms (without continuation studies)



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials

Sensitivity analysis: network meta-analysis overall Symptoms (without continuation studies)



Lurasidone and iloperidone which had only "continuation" studies are no longer present. Apart from this a few drugs changed their places in the hierarchy. But the same drugs which were less efficacious than olanzapine with 95% CIs excluding opposite effects are also less efficacious here.

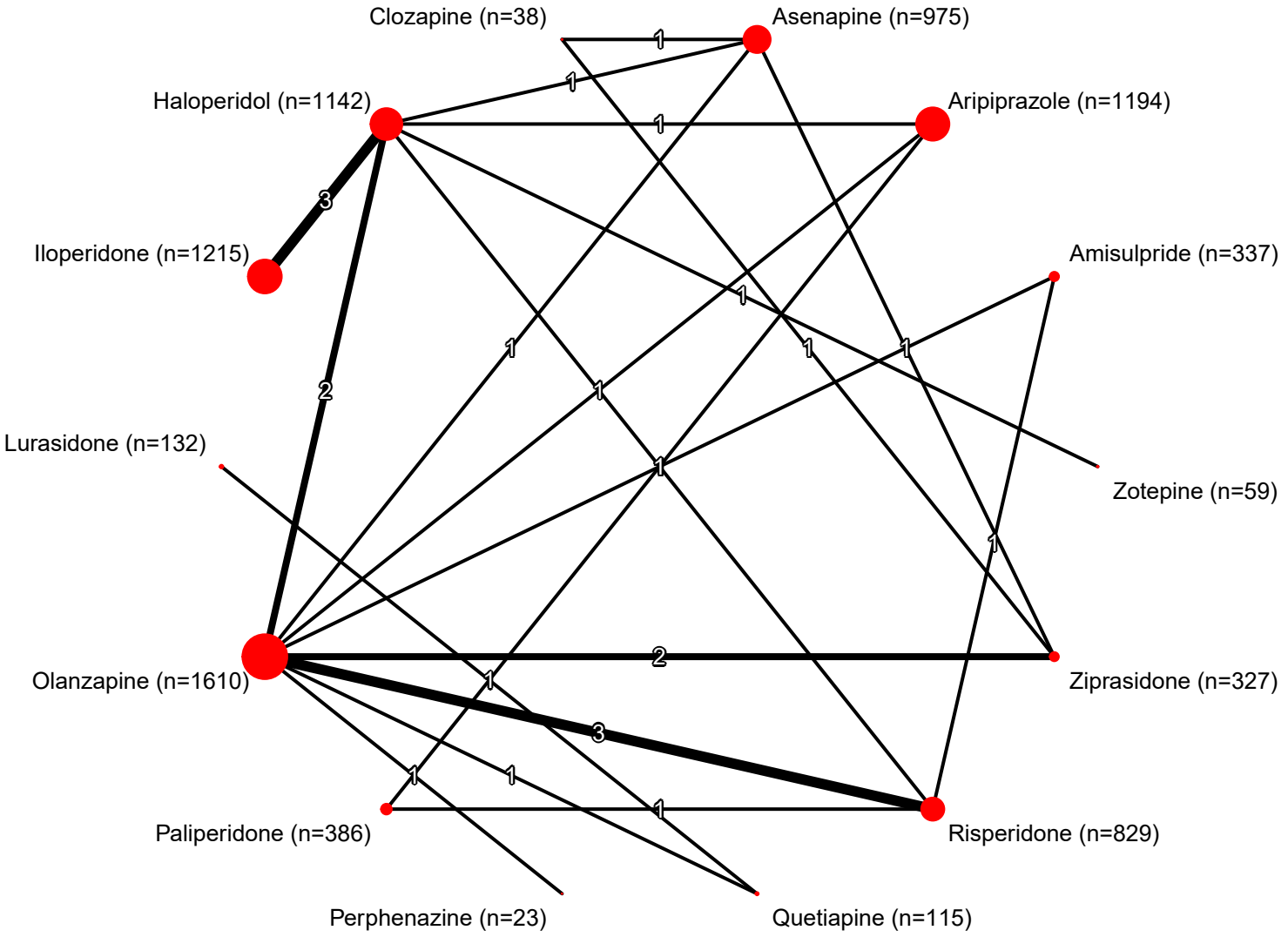
Sensitivity analysis league table for the outcome: Overall Symptoms (without continuation studies)

Olanzapine	-0.02 (-0.22 to 0.18)	-0.09 (-0.24 to 0.07)	NA	**-0.14 (-0.25 to -0.04)**	-0.17 (-0.33 to 0.00)	NA	**-0.24 (-0.39 to -0.10)**	**-0.29 (-0.47 to -0.11)**	NA	**-0.29 (-0.42 to -0.16)**	**-0.39 (-0.51 to -0.27)**
-0.06 (-0.22 to 0.10)	**Amisulpride**	NA	NA	-0.01 (-0.23 to 0.21)	NA	NA	NA	NA	NA	NA	NA
-0.09 (-0.24 to 0.05)	-0.03 (-0.24 to 0.17)	**Perphenazine**	NA	0.00 (-0.16 to 0.16)	NA	NA	-0.16 (-0.32 to 0.00)	NA	NA	NA	**-0.30 (-0.49 to -0.11)**
-0.10 (-0.50 to 0.30)	-0.04 (-0.47 to 0.38)	-0.01 (-0.43 to 0.41)	**Clozapine**	NA	NA	NA	NA	NA	NA	-0.37 (-0.82 to 0.07)	-0.11 (-0.56 to 0.33)
-0.12 (-0.21 to -0.03)	-0.06 (-0.22 to 0.10)	-0.03 (-0.18 to 0.12)	-0.02 (-0.42 to 0.39)	**Risperidone**	NA	NA	**-0.16 (-0.31 to -0.01)**	-0.12 (-0.38 to 0.14)	**-0.16 (-0.32 to -0.01)**	NA	**-0.30 (-0.48 to -0.12)**
-0.17 (-0.29 to -0.04)	-0.11 (-0.30 to 0.09)	-0.07 (-0.26 to 0.11)	-0.06 (-0.48 to 0.35)	-0.05 (-0.19 to 0.10)	**Aripiprazole**	NA	NA	-0.12 (-0.23 to 0.00)	-0.09 (-0.48 to 0.31)	NA	NA
-0.17 (-0.55 to 0.20)	-0.11 (-0.52 to 0.29)	-0.08 (-0.48 to 0.32)	-0.07 (-0.62 to 0.48)	-0.05 (-0.44 to 0.33)	-0.01 (-0.38 to 0.36)	**Zotepine**	NA	-0.11 (-0.46 to 0.25)	NA	NA	NA
-0.25 (-0.38 to -0.12)	-0.19 (-0.38 to 0.01)	-0.16 (-0.32 to 0.00)	-0.15 (-0.56 to 0.27)	-0.13 (-0.27 to 0.01)	-0.08 (-0.26 to 0.09)	-0.08 (-0.47 to 0.32)	**Quetiapine**	NA	NA	NA	-0.14 (-0.32 to 0.04)
-0.28 (-0.41 to -0.15)	**-0.22 (-0.42 to -0.02)**	-0.19 (-0.37 to 0.00)	-0.18 (-0.60 to 0.24)	**-0.16 (-0.31 to -0.01)**	**-0.11 (-0.22 to -0.01)**	-0.11 (-0.46 to 0.25)	-0.03 (-0.21 to 0.15)	**Haloperidol**	NA	NA	NA
-0.28 (-0.45 to -0.11)	**-0.22 (-0.43 to -0.01)**	-0.19 (-0.39 to 0.02)	-0.18 (-0.61 to 0.25)	**-0.16 (-0.30 to -0.02)**	-0.11 (-0.30 to 0.08)	-0.11 (-0.51 to 0.30)	-0.03 (-0.23 to 0.16)	-0.00 (-0.20 to 0.19)	**Paliperidone**	NA	NA
-0.32 (-0.44 to -0.19)	**-0.26 (-0.46 to -0.05)**	**-0.22 (-0.41 to -0.03)**	-0.21 (-0.61 to 0.18)	**-0.20 (-0.35 to -0.04)**	-0.15 (-0.33 to 0.03)	-0.14 (-0.54 to 0.26)	-0.07 (-0.25 to 0.11)	-0.04 (-0.22 to 0.14)	-0.04 (-0.24 to 0.17)	**Asenapine**	0.26 (-0.18 to 0.70)
-0.37 (-0.49 to -0.26)	**-0.31 (-0.50 to -0.12)**	**-0.28 (-0.44 to -0.12)**	-0.27 (-0.67 to 0.12)	**-0.25 (-0.39 to -0.12)**	**-0.21 (-0.37 to -0.04)**	-0.20 (-0.59 to 0.19)	-0.12 (-0.28 to 0.03)	-0.09 (-0.26 to 0.08)	-0.09 (-0.29 to 0.10)	-0.06 (-0.22 to 0.11)	**Ziprasidone**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was the reference which explains why in the figure the sign of all comparisons with olanzapine was always +, but the results are the same.Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

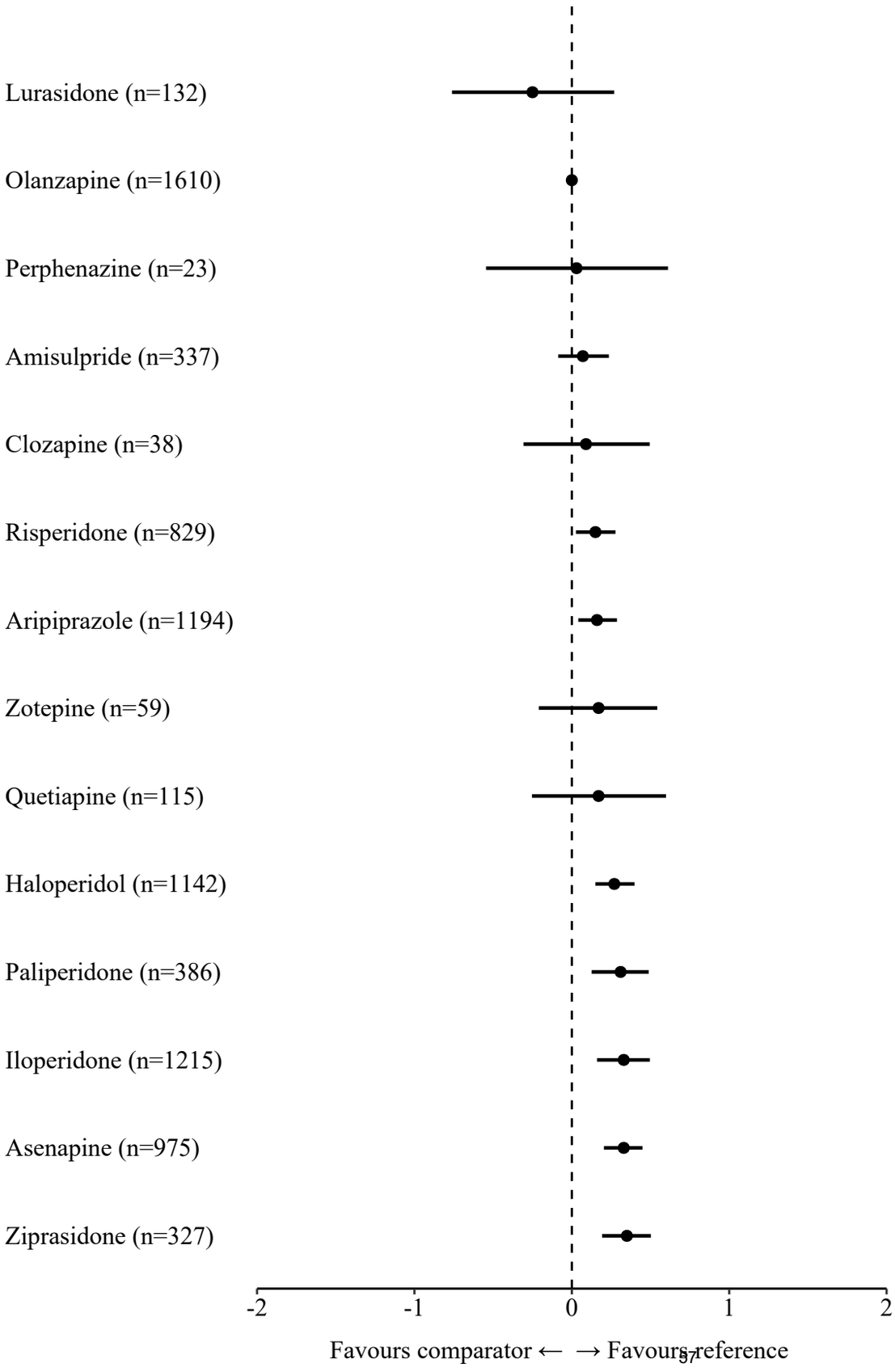
Sensitivity analysis: Overall Symptoms without CATIE study (also covering potentially unfair doses)

The CATIE study had a comparably low baseline severity (PANSS total ~ 75). Moreover, it has been criticized for potentially unfair doses, because olanzapine, which was superior to several other drugs in this NMA, could be given in doses as high as 30mg/day. In our opinion this was the clearest potential problem in terms of doses. The sensitivity analysis excluding studies with unfair doses was thus restricted to removing CATIE.



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials

Sensitivity analysis: network meta-analsyis overall Symptoms without the CATIE study



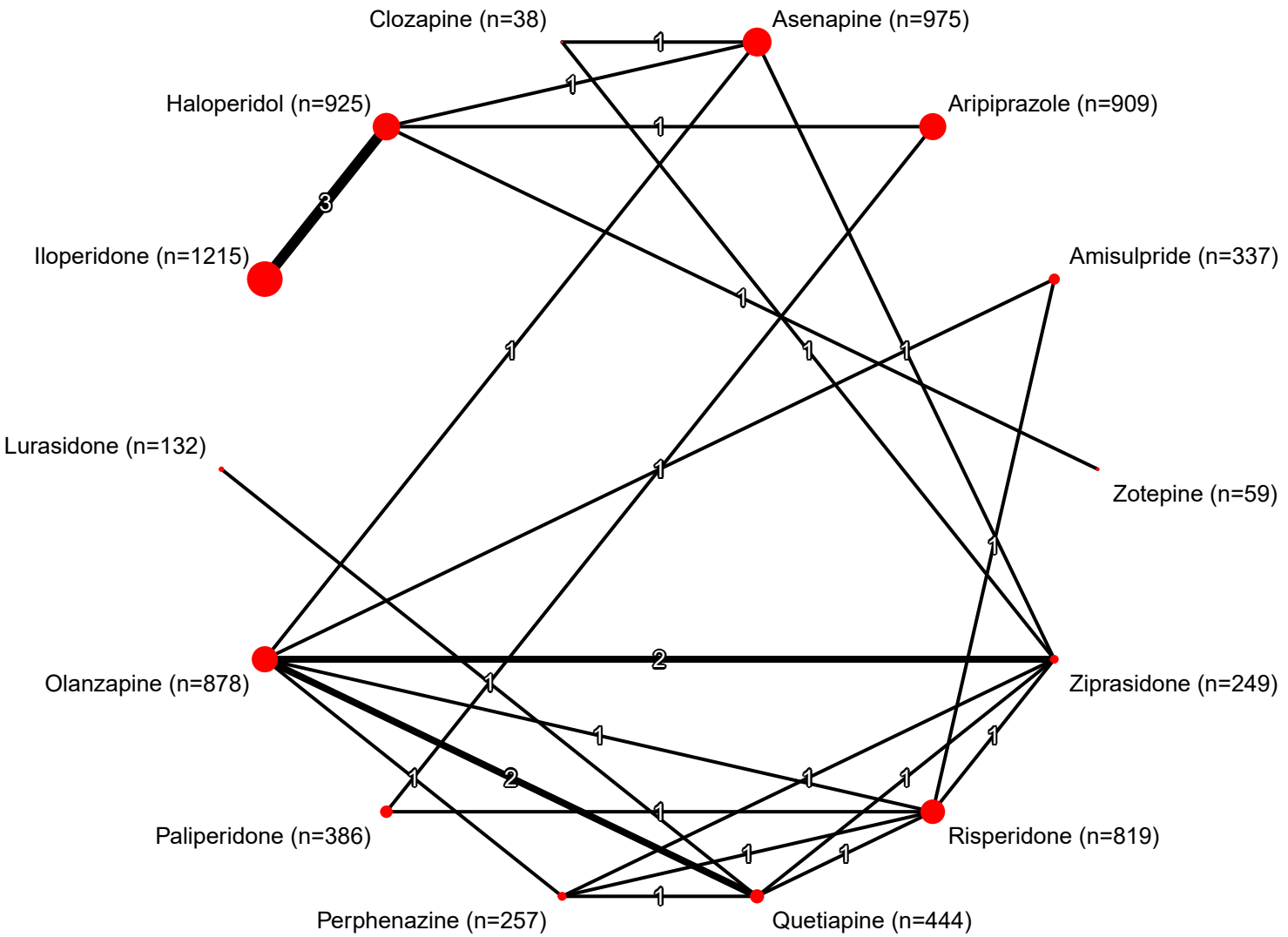
Lurasidone and olanzapine remained on the top. Other than perphenazine and amisulpride, and zotepine and aripiprazole changing their places in the hierarchy, there were no major differences compared to the primary analysis.

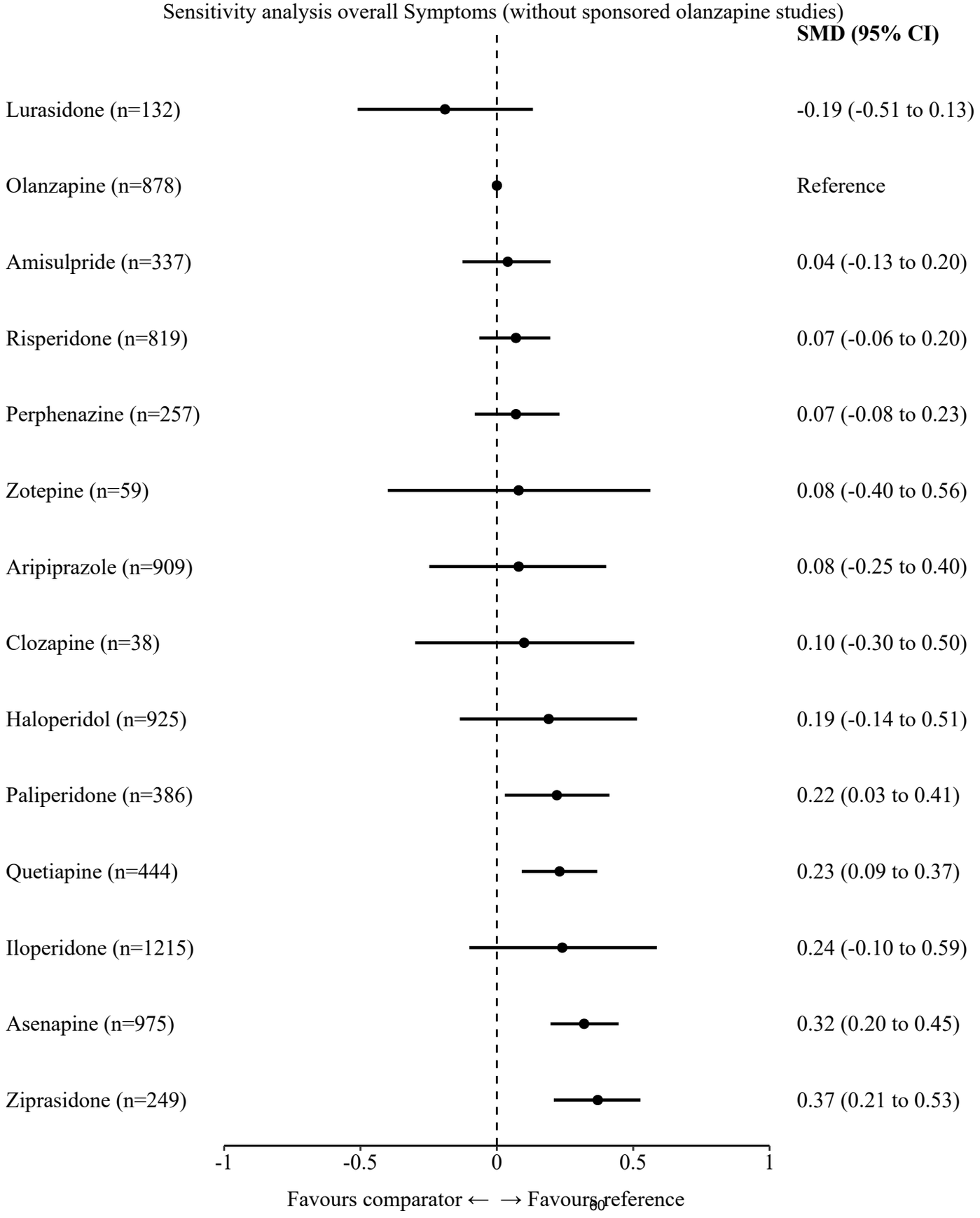
Sensitivity analysis league table for the outcome: Overall Symptoms without the CATIE study

Lurasidone	NA	NA	NA	NA	NA	NA	NA	**-0.42 (-0.71 to -0.13)**	NA	NA	NA	NA	NA
-0.25 (-0.76 to 0.27)	**Olanzapine**	-0.03 (-0.61 to 0.55)	-0.02 (-0.22 to 0.18)	NA	**-0.19 (-0.34 to -0.04)**	-0.17 (-0.33 to 0.00)	NA	-0.17 (-0.60 to 0.25)	**-0.29 (-0.47 to -0.11)**	NA	**-0.29 (-0.42 to -0.16)**	NA	**-0.39 (-0.55 to -0.22)**
-0.28 (-1.05 to 0.50)	-0.03 (-0.61 to 0.55)	**Perphenazine**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-0.32 (-0.86 to 0.22)	-0.07 (-0.24 to 0.09)	-0.04 (-0.64 to 0.56)	**Amisulpride**	NA	-0.01 (-0.23 to 0.21)	NA	NA	NA	NA	NA	NA	NA	NA
-0.34 (-0.99 to 0.31)	-0.09 (-0.50 to 0.31)	-0.06 (-0.76 to 0.64)	-0.02 (-0.45 to 0.41)	**Clozapine**	NA	NA	NA	NA	NA	NA	-0.37 (-0.82 to 0.07)	NA	-0.11 (-0.56 to 0.33)
-0.40 (-0.93 to 0.13)	**-0.15 (-0.28 to -0.03)**	-0.12 (-0.71 to 0.47)	-0.08 (-0.24 to 0.09)	-0.06 (-0.48 to 0.36)	**Risperidone**	NA	NA	NA	-0.12 (-0.38 to 0.14)	**-0.16 (-0.32 to -0.01)**	NA	NA	NA
-0.41 (-0.94 to 0.12)	**-0.16 (-0.29 to -0.04)**	-0.13 (-0.72 to 0.46)	-0.09 (-0.29 to 0.11)	-0.07 (-0.49 to 0.35)	-0.01 (-0.17 to 0.15)	**Aripiprazole**	NA	NA	-0.12 (-0.23 to 0.00)	-0.09 (-0.48 to 0.31)	NA	NA	NA
-0.41 (-1.05 to 0.23)	-0.17 (-0.54 to 0.21)	-0.13 (-0.82 to 0.56)	-0.09 (-0.50 to 0.31)	-0.07 (-0.62 to 0.48)	-0.01 (-0.40 to 0.37)	-0.00 (-0.37 to 0.37)	**Zotepine**	NA	-0.11 (-0.46 to 0.25)	NA	NA	NA	NA
-0.42 (-0.71 to -0.13)	-0.17 (-0.60 to 0.25)	-0.14 (-0.86 to 0.58)	-0.10 (-0.55 to 0.36)	-0.08 (-0.66 to 0.51)	-0.02 (-0.47 to 0.42)	-0.01 (-0.45 to 0.43)	-0.01 (-0.57 to 0.56)	**Quetiapine**	NA	NA	NA	NA	NA
-0.52 (-1.05 to 0.01)	**-0.27 (-0.40 to -0.15)**	-0.24 (-0.83 to 0.35)	-0.20 (-0.40 to 0.00)	-0.18 (-0.60 to 0.24)	-0.12 (-0.28 to 0.04)	**-0.11 (-0.21 to -0.01)**	-0.11 (-0.46 to 0.25)	-0.10 (-0.55 to 0.34)	**Haloperidol**	NA	-0.20 (-0.64 to 0.23)	-0.05 (-0.17 to 0.06)	NA
-0.55 (-1.10 to -0.01)	**-0.31 (-0.49 to -0.13)**	-0.27 (-0.88 to 0.33)	**-0.23 (-0.45 to -0.02)**	-0.21 (-0.65 to 0.23)	**-0.16 (-0.30 to -0.01)**	-0.14 (-0.34 to 0.06)	-0.14 (-0.55 to 0.27)	-0.13 (-0.60 to 0.33)	-0.03 (-0.23 to 0.17)	**Paliperidone**	NA	NA	NA
-0.57 (-1.10 to -0.04)	**-0.33 (-0.45 to -0.20)**	-0.29 (-0.88 to 0.30)	**-0.25 (-0.45 to -0.05)**	-0.23 (-0.63 to 0.17)	-0.17 (-0.35 to 0.00)	-0.16 (-0.33 to 0.01)	-0.16 (-0.55 to 0.23)	-0.15 (-0.60 to 0.29)	-0.05 (-0.22 to 0.12)	-0.02 (-0.24 to 0.20)	**Asenapine**	NA	0.26 (-0.18 to 0.70)
-0.57 (-1.12 to -0.03)	**-0.33 (-0.50 to -0.16)**	-0.30 (-0.90 to 0.31)	**-0.25 (-0.48 to -0.03)**	-0.23 (-0.67 to 0.20)	-0.18 (-0.37 to 0.02)	**-0.16 (-0.32 to -0.01)**	-0.16 (-0.53 to 0.21)	-0.16 (-0.61 to 0.30)	-0.05 (-0.17 to 0.06)	-0.02 (-0.25 to 0.21)	-0.00 (-0.20 to 0.20)	**Iloperidone**	NA
-0.59 (-1.13 to -0.05)	**-0.35 (-0.50 to -0.19)**	-0.31 (-0.91 to 0.28)	**-0.27 (-0.50 to -0.05)**	-0.25 (-0.65 to 0.15)	-0.20 (-0.39 to 0.00)	-0.18 (-0.38 to 0.01)	-0.18 (-0.59 to 0.23)	-0.17 (-0.63 to 0.28)	-0.07 (-0.27 to 0.12)	-0.04 (-0.28 to 0.20)	-0.02 (-0.21 to 0.17)	-0.02 (-0.25 to 0.21)	**Ziprasidone**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always + except for lurasidone, but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Sensitivity analysis overall Symptoms (without sponsored olanzapine studies)





When studies conducted by the manufacturer of olanzapine were excluded, lurasidone and olanzapine remained on top of the hierarchy. Below these two antipsychotics, drugs sometimes changed their places. The differences of olanzapine compared to risperidone, aripiprazole, haloperidol, iloperidone were no longer clear in that 95% CIs included a possibility of opposite effects, but the direction of the point estimates was the same.

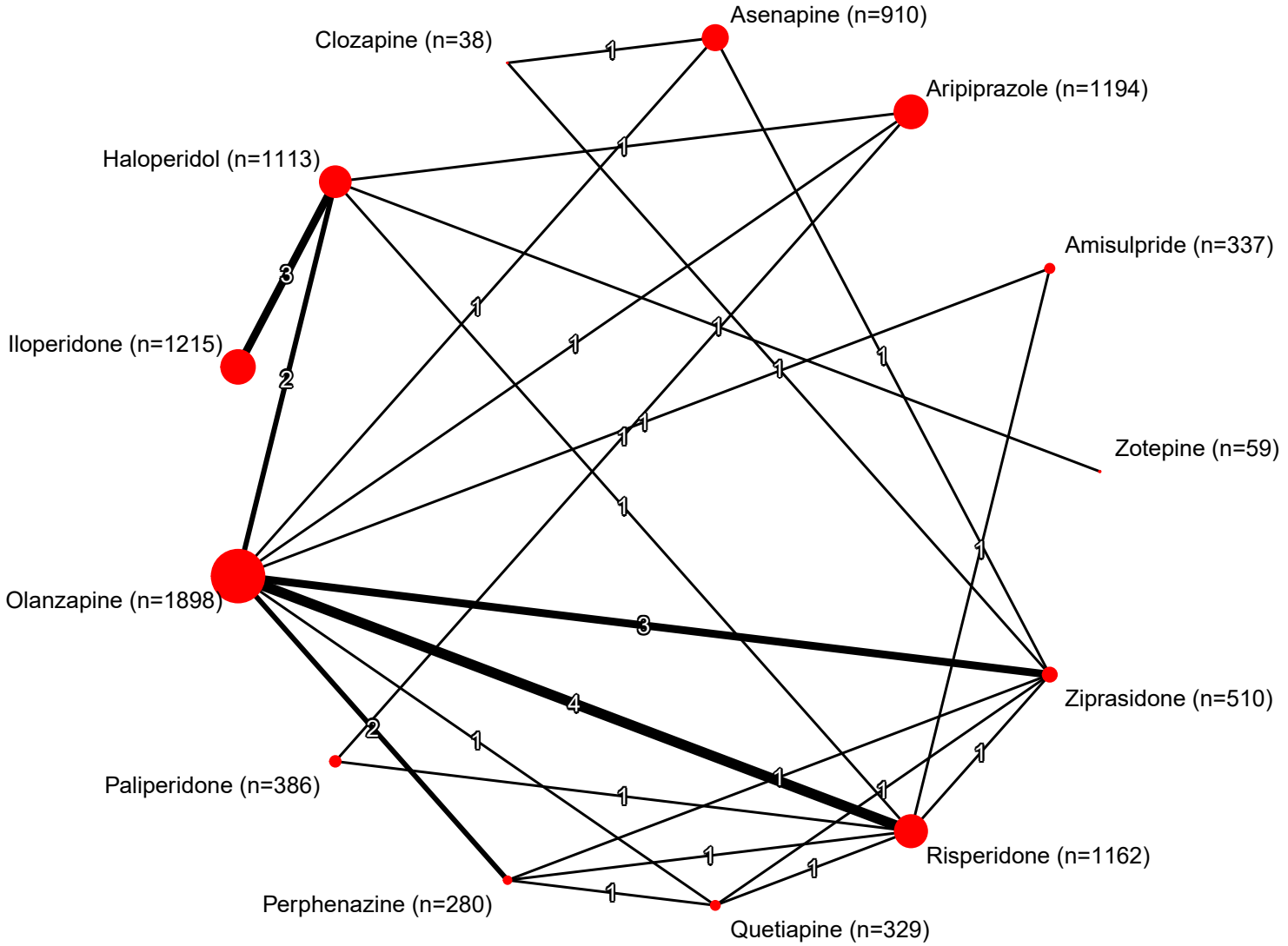
As many studies were done by olanzapine's original manufacturer, the evidence base is smaller.

Sensitiviy analysis league table for the outcome: Overall Symptoms (without sponsored olanzapine studies)

Lurasidone	NA	NA	NA	NA	NA	NA	NA	NA	NA	**-0.42 (-0.71 to -0.13)**	NA	NA	NA
-0.19 (-0.51 to 0.13)	**Olanzapine**	-0.02 (-0.22 to 0.18)	-0.09 (-0.24 to 0.06)	-0.09 (-0.26 to 0.07)	NA	NA	NA	NA	NA	**-0.24 (-0.39 to -0.10)**	NA	**-0.29 (-0.42 to -0.16)**	**-0.43 (-0.60 to -0.25)**
-0.22 (-0.57 to 0.13)	-0.04 (-0.20 to 0.13)	**Amisulpride**	-0.01 (-0.23 to 0.21)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
-0.25 (-0.58 to 0.07)	-0.07 (-0.20 to 0.06)	-0.03 (-0.20 to 0.14)	**Risperidone**	-0.00 (-0.16 to 0.16)	NA	NA	NA	NA	**-0.16 (-0.32 to -0.01)**	**-0.16 (-0.31 to -0.01)**	NA	NA	**-0.30 (-0.48 to -0.12)**
-0.26 (-0.60 to 0.07)	-0.07 (-0.23 to 0.08)	-0.04 (-0.25 to 0.17)	-0.01 (-0.17 to 0.15)	**Perphenazine**	NA	NA	NA	NA	NA	-0.16 (-0.32 to 0.00)	NA	NA	**-0.30 (-0.49 to -0.11)**
-0.27 (-0.71 to 0.18)	-0.08 (-0.40 to 0.25)	-0.04 (-0.39 to 0.31)	-0.01 (-0.33 to 0.31)	-0.00 (-0.35 to 0.34)	**Aripiprazole**	NA	NA	-0.12 (-0.23 to 0.00)	-0.09 (-0.48 to 0.31)	NA	NA	NA	NA
-0.27 (-0.84 to 0.30)	-0.08 (-0.56 to 0.40)	-0.05 (-0.55 to 0.45)	-0.02 (-0.50 to 0.46)	-0.01 (-0.50 to 0.49)	-0.01 (-0.38 to 0.37)	**Zotepine**	NA	-0.11 (-0.46 to 0.25)	NA	NA	NA	NA	NA
-0.29 (-0.80 to 0.21)	-0.10 (-0.50 to 0.30)	-0.07 (-0.50 to 0.36)	-0.04 (-0.45 to 0.38)	-0.03 (-0.45 to 0.39)	-0.03 (-0.53 to 0.48)	-0.02 (-0.64 to 0.60)	**Clozapine**	NA	NA	NA	NA	-0.37 (-0.82 to 0.07)	-0.11 (-0.56 to 0.33)
-0.38 (-0.83 to 0.07)	-0.19 (-0.51 to 0.14)	-0.15 (-0.50 to 0.20)	-0.12 (-0.45 to 0.20)	-0.11 (-0.46 to 0.23)	-0.11 (-0.23 to 0.00)	-0.11 (-0.46 to 0.25)	-0.09 (-0.59 to 0.42)	**Haloperidol**	NA	NA	-0.05 (-0.17 to 0.06)	-0.20 (-0.64 to 0.23)	NA
-0.41 (-0.76 to -0.06)	**-0.22 (-0.41 to -0.03)**	-0.19 (-0.41 to 0.03)	**-0.16 (-0.30 to -0.01)**	-0.15 (-0.36 to 0.07)	-0.14 (-0.46 to 0.17)	-0.14 (-0.62 to 0.34)	-0.12 (-0.55 to 0.32)	-0.03 (-0.35 to 0.29)	**Paliperidone**	NA	NA	NA	NA
-0.42 (-0.71 to -0.13)	**-0.23 (-0.37 to -0.09)**	-0.19 (-0.39 to 0.00)	**-0.16 (-0.31 to -0.02)**	-0.16 (-0.32 to 0.01)	-0.15 (-0.49 to 0.19)	-0.15 (-0.64 to 0.34)	-0.13 (-0.54 to 0.29)	-0.04 (-0.38 to 0.30)	-0.01 (-0.21 to 0.20)	**Quetiapine**	NA	NA	-0.14 (-0.32 to 0.04)
-0.43 (-0.89 to 0.03)	-0.24 (-0.59 to 0.10)	-0.21 (-0.58 to 0.16)	-0.18 (-0.52 to 0.16)	-0.17 (-0.53 to 0.20)	**-0.17 (-0.33 to -0.01)**	-0.16 (-0.53 to 0.21)	-0.14 (-0.66 to 0.38)	-0.05 (-0.17 to 0.06)	-0.02 (-0.36 to 0.32)	-0.01 (-0.37 to 0.35)	**Iloperidone**	NA	NA
-0.51 (-0.85 to -0.17)	**-0.32 (-0.45 to -0.20)**	**-0.29 (-0.49 to -0.08)**	**-0.26 (-0.43 to -0.08)**	**-0.25 (-0.44 to -0.05)**	-0.25 (-0.57 to 0.08)	-0.24 (-0.72 to 0.24)	-0.22 (-0.62 to 0.18)	-0.13 (-0.46 to 0.19)	-0.10 (-0.32 to 0.12)	-0.09 (-0.27 to 0.09)	-0.08 (-0.42 to 0.26)	**Asenapine**	0.26 (-0.18 to 0.70)
-0.56 (-0.89 to -0.22)	**-0.37 (-0.53 to -0.21)**	**-0.33 (-0.54 to -0.12)**	**-0.30 (-0.47 to -0.13)**	**-0.29 (-0.48 to -0.11)**	-0.29 (-0.64 to 0.06)	-0.29 (-0.78 to 0.21)	-0.27 (-0.66 to 0.13)	-0.18 (-0.53 to 0.17)	-0.15 (-0.37 to 0.07)	-0.14 (-0.31 to 0.03)	-0.12 (-0.49 to 0.24)	-0.05 (-0.24 to 0.14)	**Ziprasidone**

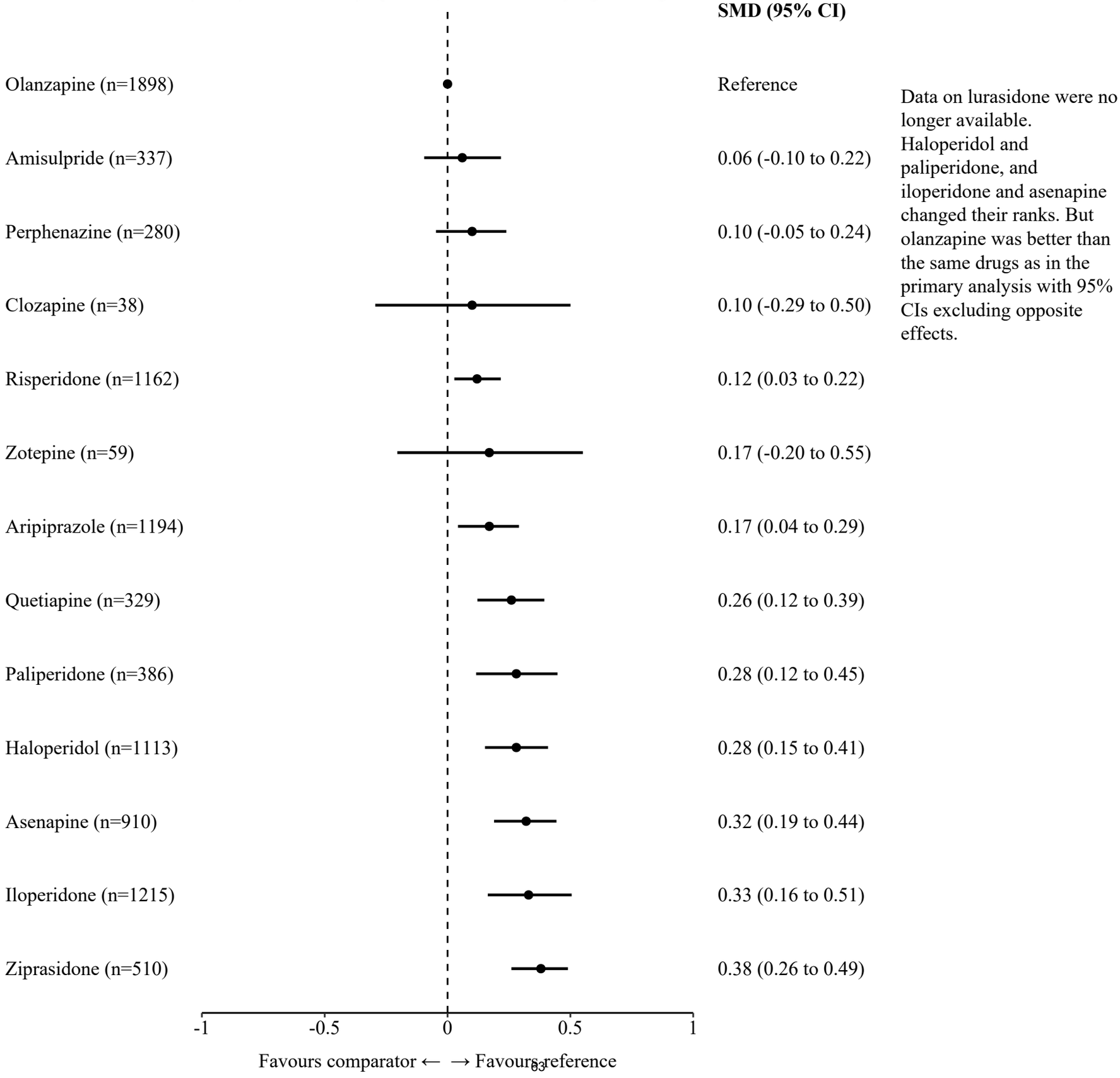
The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval of 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always + except for lurasidone, but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Sensitivity analysis - overall Symptoms (without studies judged at high risk of bias)



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials

Sensitivity analysis - overall Symptoms (without studies judged at high risk of bias)



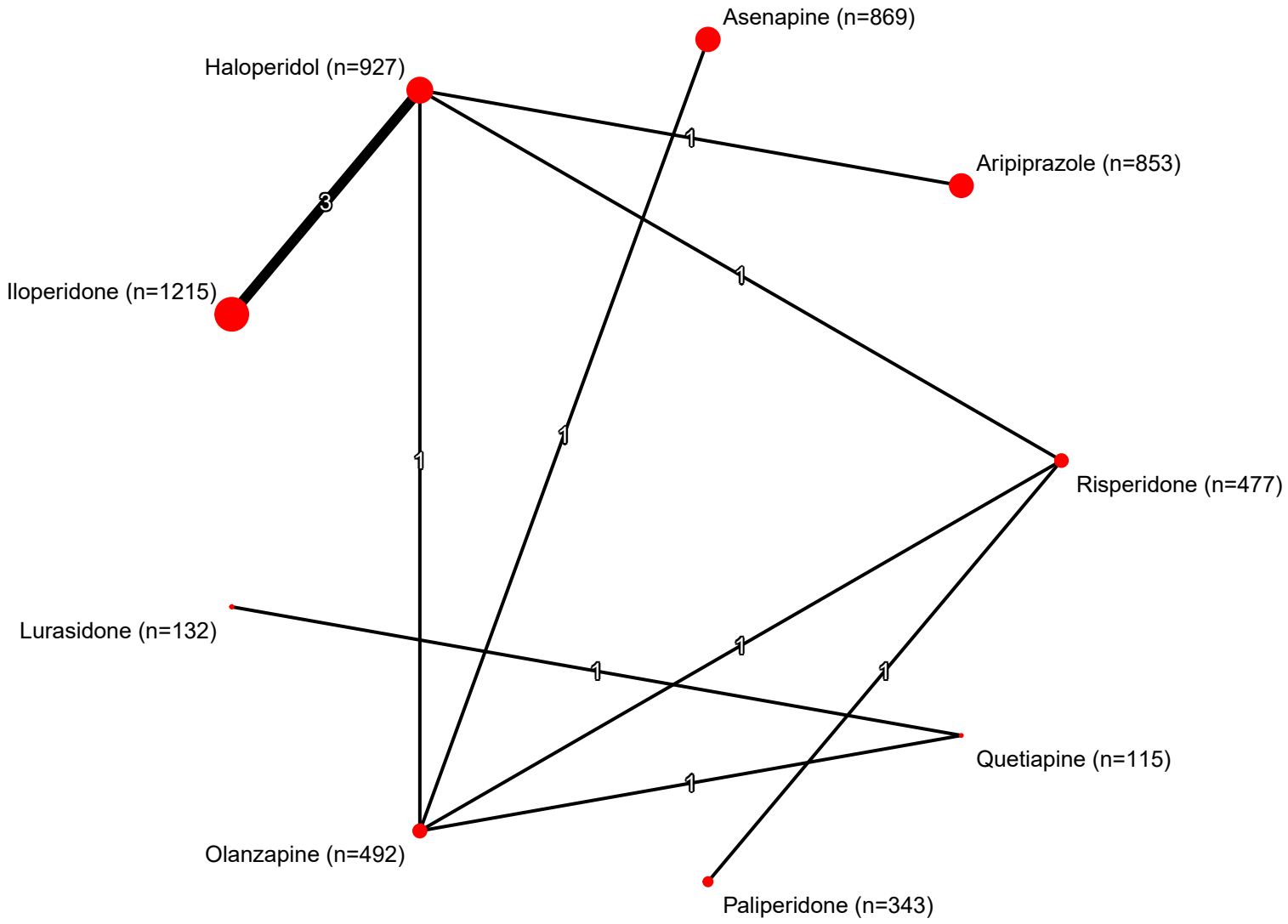
Data on lurasidone were no longer available. Haloperidol and paliperidone, and iloperidone and asenapine changed their ranks. But olanzapine was better than the same drugs as in the primary analysis with 95% CIs excluding opposite effects.

Sensitivity analysis - league table for the outcome: Overall Symptoms (without studies judged at high risk of bias)

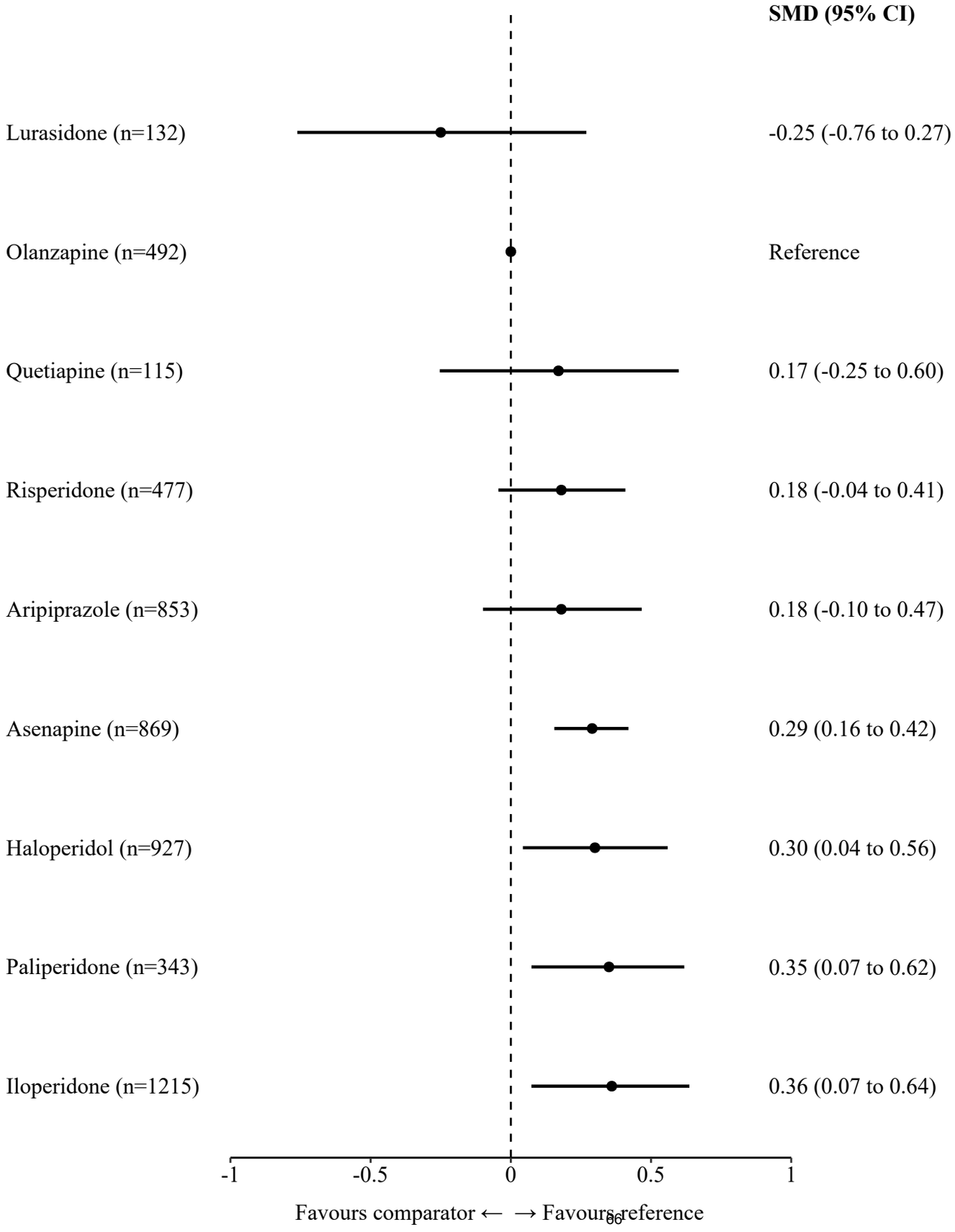
Olanzapine	-0.02 (-0.22 to 0.18)	-0.09 (-0.24 to 0.07)	NA	**-0.14 (-0.25 to -0.04)**	-0.17 (-0.33 to 0.00)	NA	**-0.25 (-0.40 to -0.10)**	**-0.29 (-0.47 to -0.11)**	NA	**-0.29 (-0.42 to -0.16)**	NA	**-0.39 (-0.51 to -0.27)**
-0.06 (-0.22 to 0.10)	**Amisulpride**	NA	NA	-0.01 (-0.23 to 0.21)	NA	NA	NA	NA	NA	NA	NA	NA
-0.10 (-0.24 to 0.05)	-0.03 (-0.24 to 0.17)	**Perphenazine**	NA	0.00 (-0.16 to 0.16)	NA	NA	-0.16 (-0.32 to 0.00)	NA	NA	NA	NA	**-0.30 (-0.49 to -0.11)**
-0.10 (-0.50 to 0.29)	-0.04 (-0.47 to 0.38)	-0.01 (-0.42 to 0.41)	**Clozapine**	NA	NA	NA	NA	NA	NA	-0.37 (-0.82 to 0.07)	NA	-0.11 (-0.56 to 0.33)
-0.12 (-0.22 to -0.03)	-0.06 (-0.22 to 0.10)	-0.03 (-0.17 to 0.12)	-0.02 (-0.42 to 0.39)	**Risperidone**	NA	NA	**-0.16 (-0.31 to -0.01)**	-0.12 (-0.38 to 0.14)	**-0.16 (-0.32 to -0.01)**	NA	NA	**-0.30 (-0.48 to -0.12)**
-0.17 (-0.29 to -0.04)	-0.11 (-0.30 to 0.09)	-0.07 (-0.26 to 0.12)	-0.06 (-0.48 to 0.35)	-0.04 (-0.19 to 0.10)	**Aripiprazole**	NA	NA	-0.12 (-0.23 to 0.00)	-0.09 (-0.48 to 0.31)	NA	NA	NA
-0.17 (-0.55 to 0.20)	-0.11 (-0.52 to 0.29)	-0.08 (-0.48 to 0.33)	-0.07 (-0.62 to 0.48)	-0.05 (-0.44 to 0.33)	-0.01 (-0.38 to 0.36)	**Zotepine**	NA	-0.11 (-0.46 to 0.25)	NA	NA	NA	NA
-0.26 (-0.39 to -0.12)	-0.20 (-0.40 to 0.00)	-0.16 (-0.32 to 0.00)	-0.15 (-0.57 to 0.26)	-0.14 (-0.28 to 0.00)	-0.09 (-0.27 to 0.09)	-0.08 (-0.48 to 0.32)	**Quetiapine**	NA	NA	NA	NA	-0.14 (-0.32 to 0.04)
-0.28 (-0.41 to -0.15)	**-0.22 (-0.42 to -0.02)**	-0.18 (-0.37 to 0.00)	-0.18 (-0.59 to 0.24)	**-0.16 (-0.31 to -0.01)**	**-0.11 (-0.22 to -0.01)**	-0.11 (-0.46 to 0.25)	-0.02 (-0.21 to 0.16)	**Haloperidol**	NA	NA	-0.05 (-0.17 to 0.06)	NA
-0.28 (-0.45 to -0.12)	**-0.22 (-0.43 to -0.01)**	-0.19 (-0.39 to 0.02)	-0.18 (-0.61 to 0.25)	**-0.16 (-0.30 to -0.02)**	-0.12 (-0.31 to 0.07)	-0.11 (-0.51 to 0.30)	-0.02 (-0.22 to 0.17)	-0.00 (-0.20 to 0.19)	**Paliperidone**	NA	NA	NA
-0.32 (-0.44 to -0.19)	**-0.26 (-0.46 to -0.05)**	**-0.22 (-0.41 to -0.03)**	-0.21 (-0.61 to 0.18)	**-0.19 (-0.35 to -0.04)**	-0.15 (-0.33 to 0.03)	-0.14 (-0.54 to 0.26)	-0.06 (-0.24 to 0.13)	-0.04 (-0.22 to 0.14)	-0.03 (-0.24 to 0.17)	**Asenapine**	NA	0.26 (-0.18 to 0.70)
-0.33 (-0.51 to -0.16)	**-0.27 (-0.50 to -0.05)**	**-0.24 (-0.46 to -0.02)**	-0.23 (-0.66 to 0.20)	**-0.21 (-0.40 to -0.03)**	**-0.17 (-0.32 to -0.02)**	-0.16 (-0.53 to 0.21)	-0.08 (-0.29 to 0.14)	-0.05 (-0.17 to 0.06)	-0.05 (-0.28 to 0.17)	-0.02 (-0.23 to 0.19)	**Iloperidone**	NA
-0.38 (-0.49 to -0.26)	**-0.31 (-0.50 to -0.12)**	**-0.28 (-0.44 to -0.11)**	-0.27 (-0.67 to 0.12)	**-0.25 (-0.39 to -0.12)**	**-0.21 (-0.38 to -0.04)**	-0.20 (-0.60 to 0.19)	-0.12 (-0.27 to 0.04)	-0.09 (-0.26 to 0.08)	-0.09 (-0.29 to 0.10)	-0.06 (-0.22 to 0.11)	-0.04 (-0.24 to 0.16)	**Ziprasidone**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always + but the results are the same.Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Sensitivity analysis Overall Symptoms (studies with a duration of 1 year only)



Sensitivity analysis Overall Symptoms (studies with a duration of 1 year only)

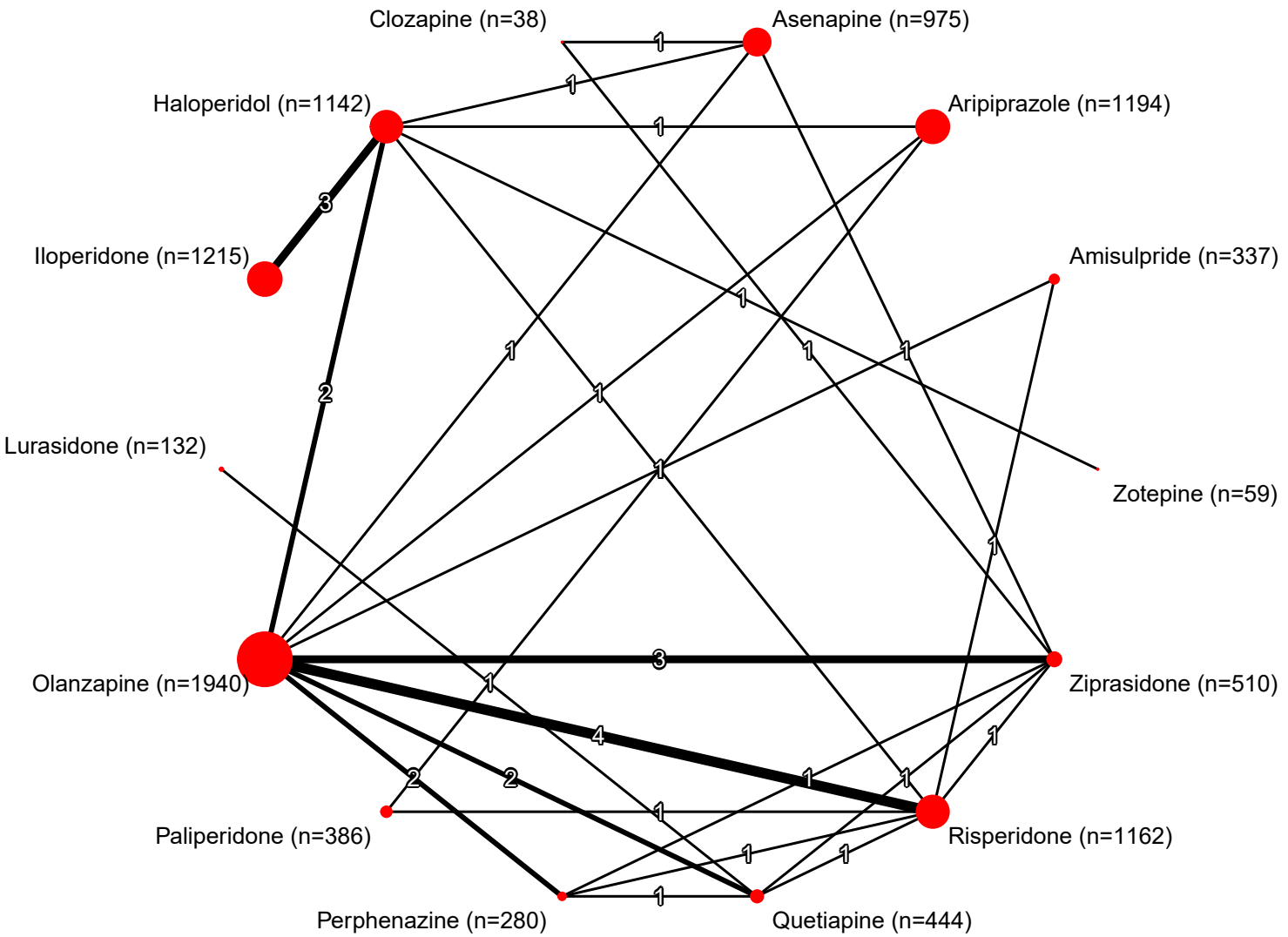


Much fewer data, and in consequence also drugs, were available when only studies of at least one year were included. Nevertheless, lurasidone and olanzapine remained on top of the hierarchy. Below olanzapine the hierarchy changed somewhat and the difference to quetiapine and risperidone did no longer exclude a possibility of no effect. However, the direction of the effects remained always the same.

Sensitivity analysis league table for the outcome: Overall Symptoms (studies with a duration of 1 year only)

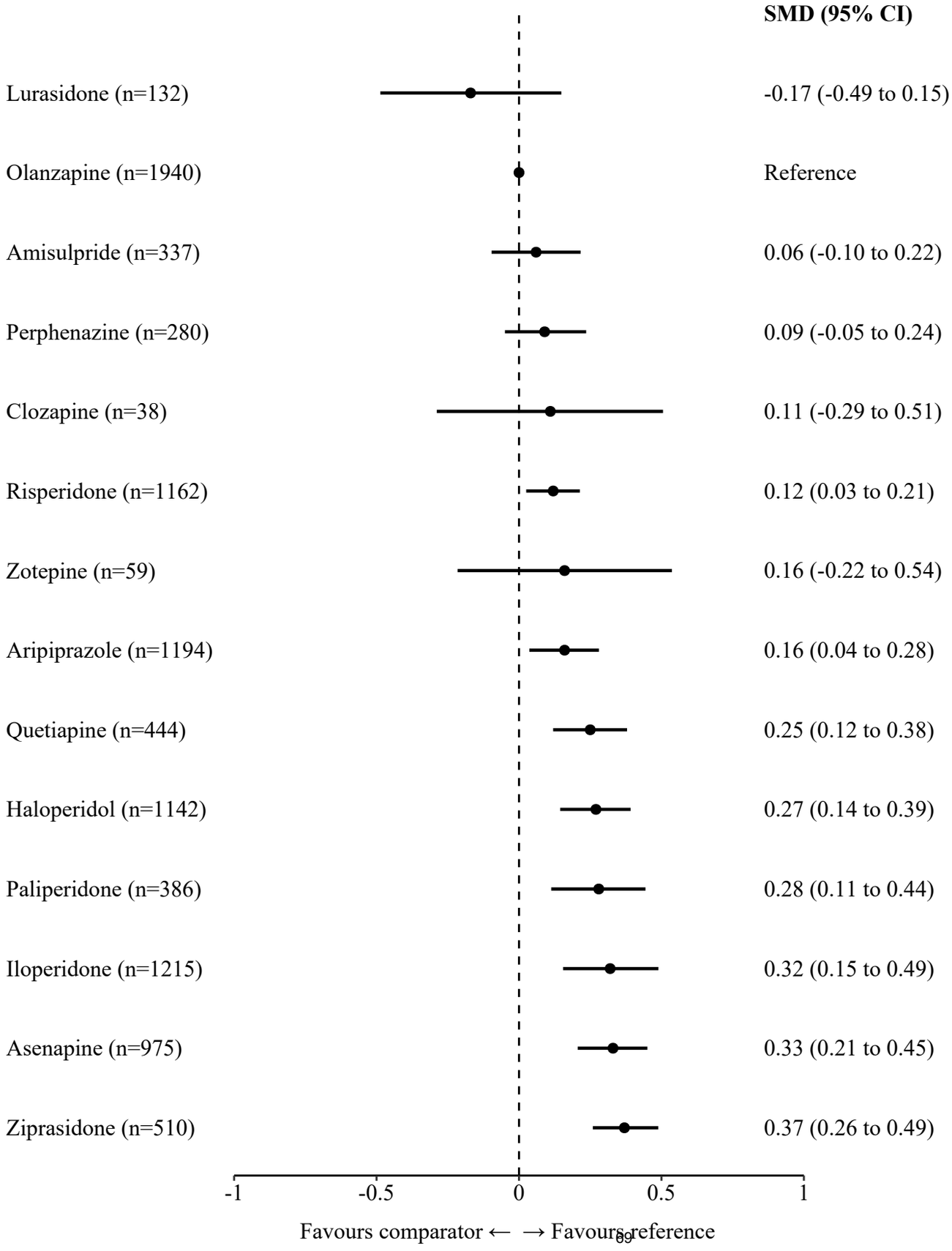
Lurasidone	NA	**-0.42 (-0.71 to -0.13)**	NA	NA	NA	NA	NA	NA
-0.25 (-0.76 to 0.27)	**Olanzapine**	-0.17 (-0.60 to 0.25)	-0.18 (-0.41 to 0.04)	NA	**-0.29 (-0.42 to -0.16)**	**-0.30 (-0.56 to -0.04)**	NA	NA
-0.42 (-0.71 to -0.13)	-0.17 (-0.60 to 0.25)	**Quetiapine**	NA	NA	NA	NA	NA	NA
-0.43 (-0.99 to 0.13)	-0.18 (-0.41 to 0.04)	-0.01 (-0.49 to 0.47)	**Risperidone**	NA	NA	-0.12 (-0.38 to 0.14)	**-0.16 (-0.32 to -0.01)**	NA
-0.43 (-1.02 to 0.16)	-0.18 (-0.47 to 0.10)	-0.01 (-0.52 to 0.50)	-0.00 (-0.29 to 0.28)	**Aripiprazole**	NA	-0.12 (-0.23 to 0.00)	NA	NA
-0.53 (-1.07 to 0.00)	**-0.29 (-0.42 to -0.16)**	-0.11 (-0.56 to 0.33)	-0.11 (-0.37 to 0.16)	-0.10 (-0.42 to 0.21)	**Asenapine**	NA	NA	NA
-0.55 (-1.12 to 0.03)	**-0.30 (-0.56 to -0.04)**	-0.13 (-0.63 to 0.37)	-0.12 (-0.38 to 0.14)	-0.12 (-0.23 to 0.00)	-0.01 (-0.30 to 0.28)	**Haloperidol**	NA	-0.05 (-0.17 to 0.06)
-0.59 (-1.18 to -0.01)	**-0.35 (-0.62 to -0.07)**	-0.17 (-0.68 to 0.33)	**-0.16 (-0.32 to -0.01)**	-0.16 (-0.48 to 0.16)	-0.06 (-0.36 to 0.24)	-0.04 (-0.34 to 0.25)	**Paliperidone**	NA
-0.60 (-1.19 to -0.01)	**-0.36 (-0.64 to -0.07)**	-0.18 (-0.69 to 0.33)	-0.17 (-0.46 to 0.11)	**-0.17 (-0.33 to -0.01)**	-0.07 (-0.38 to 0.24)	-0.05 (-0.17 to 0.06)	-0.01 (-0.33 to 0.31)	**Iloperidone**

Sensitivity analysis Overall Symptoms (without placebo−controlled studies)



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials

Sensitivity analysis Overall Symptoms (without placebo-controlled studies)



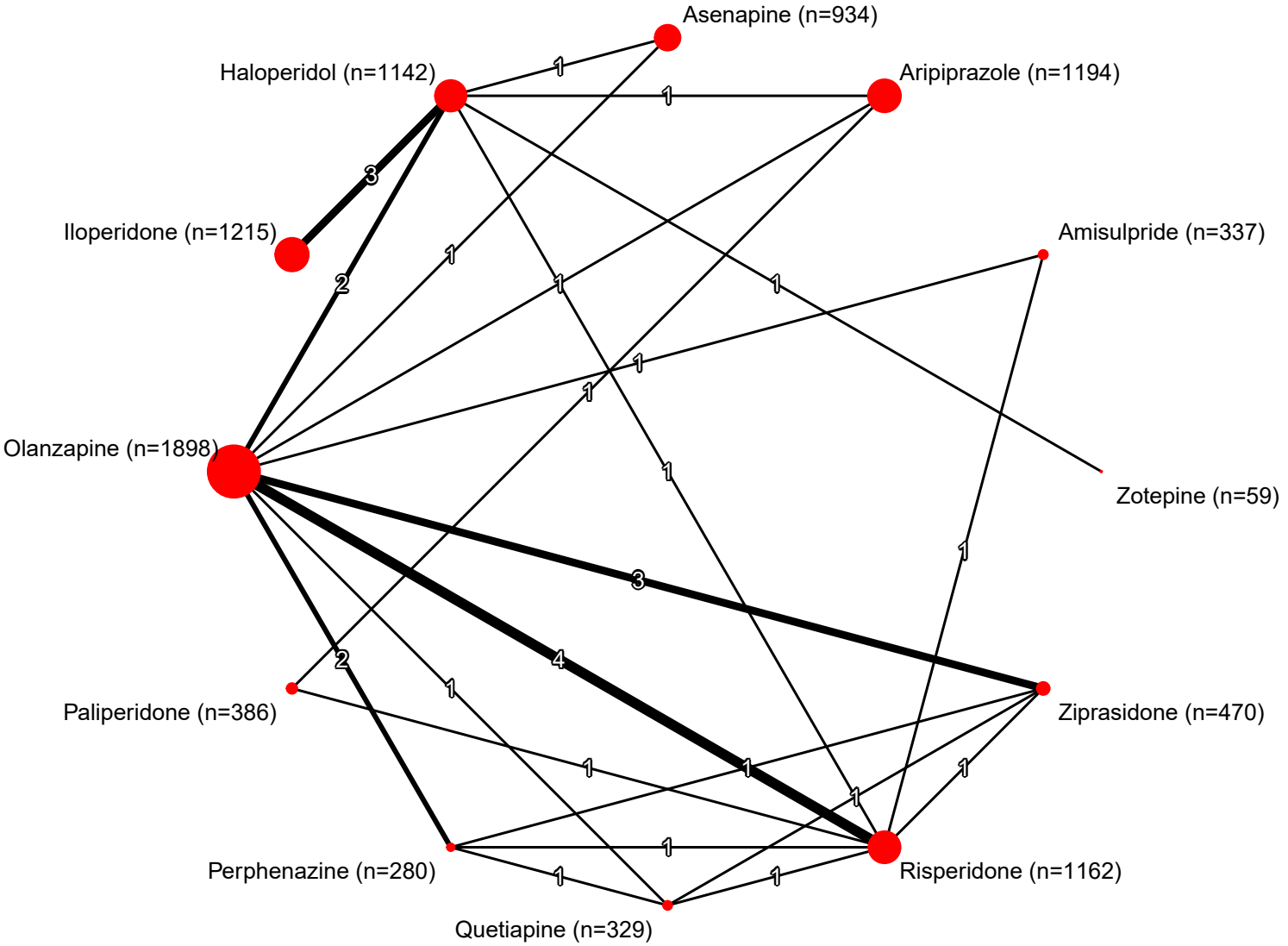
Placebo was not connected with the network in the primary analysis. Therefore, excluding placebo controlled studies had no impact on the results. They are the same as in the primary analysis.

Sensitivity analysis league table for the outcome: Overall Symptoms (without placebo-controlled studies)

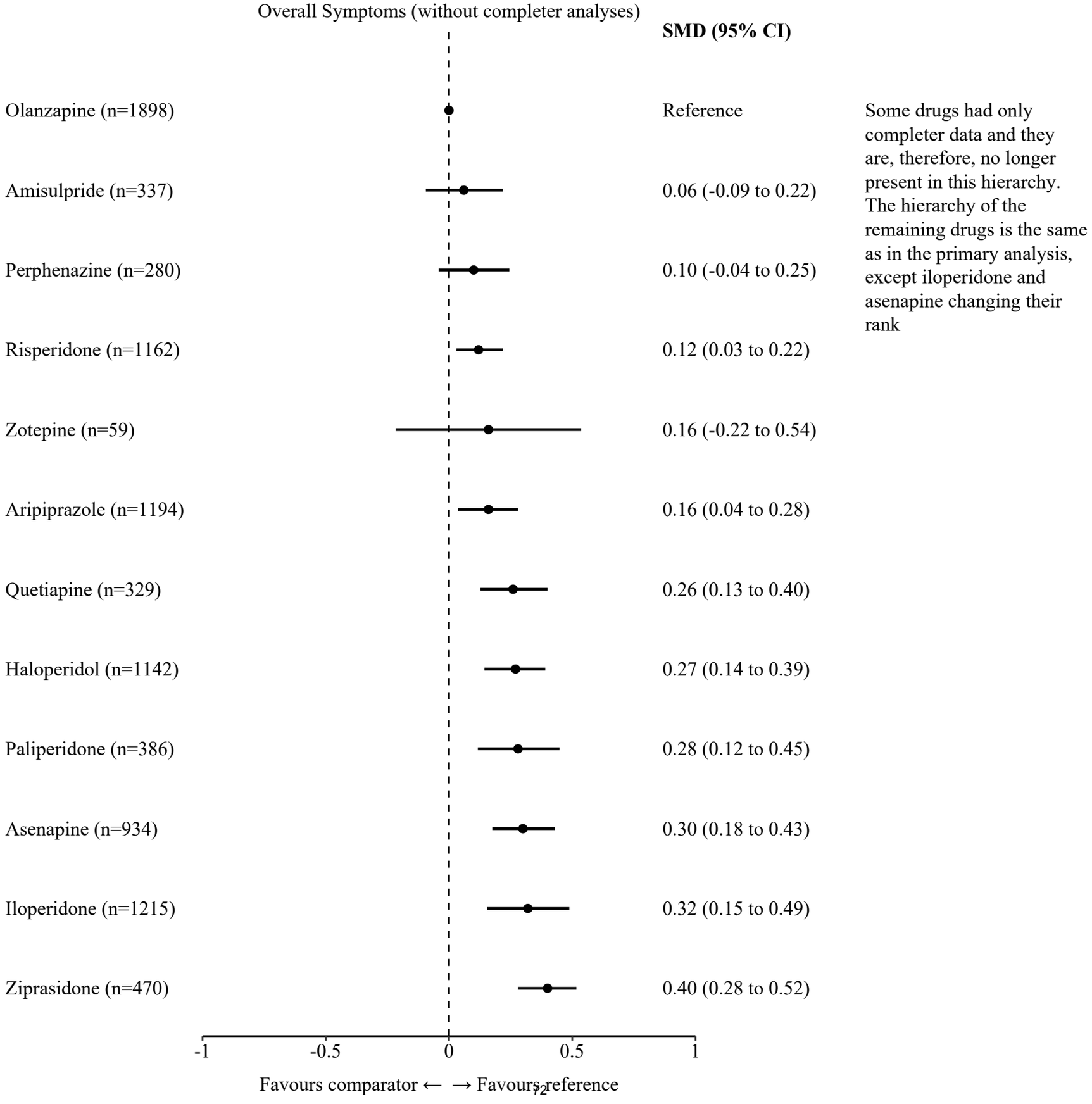
Lurasidone	NA	NA	NA	NA	NA	NA	NA	**-0.42 (-0.71 to -0.13)**	NA	NA	NA	NA	NA
-0.17 (-0.49 to 0.15)	**Olanzapine**	-0.02 (-0.22 to 0.18)	-0.09 (-0.24 to 0.07)	NA	**-0.14 (-0.25 to -0.04)**	-0.17 (-0.33 to 0.00)	NA	**-0.24 (-0.39 to -0.10)**	**-0.29 (-0.47 to -0.11)**	NA	NA	**-0.29 (-0.42 to -0.16)**	**-0.39 (-0.51 to -0.27)**
-0.23 (-0.58 to 0.12)	-0.06 (-0.22 to 0.10)	**Amisulpride**	NA	NA	-0.01 (-0.23 to 0.21)	NA	NA	NA	NA	NA	NA	NA	NA
-0.26 (-0.59 to 0.07)	-0.09 (-0.24 to 0.05)	-0.03 (-0.24 to 0.17)	**Perphenazine**	NA	0.00 (-0.16 to 0.16)	NA	NA	-0.16 (-0.32 to 0.00)	NA	NA	NA	NA	**-0.30 (-0.49 to -0.11)**
-0.28 (-0.78 to 0.23)	-0.11 (-0.51 to 0.29)	-0.05 (-0.47 to 0.38)	-0.02 (-0.43 to 0.40)	**Clozapine**	NA	NA	NA	NA	NA	NA	NA	-0.37 (-0.82 to 0.07)	-0.11 (-0.56 to 0.33)
-0.29 (-0.61 to 0.03)	**-0.12 (-0.21 to -0.03)**	-0.06 (-0.22 to 0.10)	-0.03 (-0.17 to 0.12)	-0.01 (-0.42 to 0.39)	**Risperidone**	NA	NA	**-0.16 (-0.31 to -0.01)**	-0.12 (-0.38 to 0.14)	**-0.16 (-0.32 to -0.01)**	NA	NA	**-0.30 (-0.48 to -0.12)**
-0.33 (-0.67 to 0.01)	**-0.16 (-0.28 to -0.04)**	-0.10 (-0.29 to 0.10)	-0.07 (-0.25 to 0.12)	-0.05 (-0.46 to 0.36)	-0.04 (-0.18 to 0.11)	**Aripiprazole**	NA	NA	-0.12 (-0.23 to 0.00)	-0.09 (-0.48 to 0.31)	NA	NA	NA
-0.33 (-0.82 to 0.16)	-0.16 (-0.54 to 0.22)	-0.10 (-0.51 to 0.30)	-0.07 (-0.47 to 0.33)	-0.05 (-0.60 to 0.49)	-0.04 (-0.42 to 0.34)	-0.00 (-0.37 to 0.37)	**Zotepine**	NA	-0.11 (-0.46 to 0.25)	NA	NA	NA	NA
-0.42 (-0.71 to -0.13)	**-0.25 (-0.38 to -0.12)**	-0.19 (-0.38 to 0.01)	-0.16 (-0.32 to 0.00)	-0.14 (-0.55 to 0.27)	-0.13 (-0.27 to 0.01)	-0.09 (-0.27 to 0.08)	-0.09 (-0.49 to 0.31)	**Quetiapine**	NA	NA	NA	NA	-0.14 (-0.32 to 0.04)
-0.44 (-0.78 to -0.10)	**-0.27 (-0.39 to -0.14)**	**-0.21 (-0.40 to -0.01)**	-0.18 (-0.36 to 0.01)	-0.16 (-0.57 to 0.25)	-0.15 (-0.29 to 0.00)	**-0.11 (-0.21 to -0.01)**	-0.11 (-0.46 to 0.25)	-0.02 (-0.19 to 0.16)	**Haloperidol**	NA	-0.05 (-0.17 to 0.06)	-0.20 (-0.64 to 0.23)	NA
-0.45 (-0.80 to -0.10)	**-0.28 (-0.44 to -0.11)**	**-0.22 (-0.43 to -0.01)**	-0.19 (-0.39 to 0.02)	-0.17 (-0.60 to 0.26)	**-0.16 (-0.30 to -0.02)**	-0.12 (-0.31 to 0.07)	-0.12 (-0.52 to 0.29)	-0.03 (-0.22 to 0.17)	-0.01 (-0.20 to 0.18)	**Paliperidone**	NA	NA	NA
-0.49 (-0.85 to -0.13)	**-0.32 (-0.49 to -0.15)**	**-0.26 (-0.49 to -0.04)**	**-0.23 (-0.45 to -0.01)**	-0.21 (-0.64 to 0.22)	**-0.20 (-0.39 to -0.02)**	**-0.16 (-0.32 to -0.01)**	-0.16 (-0.53 to 0.21)	-0.07 (-0.28 to 0.14)	-0.05 (-0.17 to 0.06)	-0.04 (-0.27 to 0.18)	**Iloperidone**	NA	NA
-0.50 (-0.84 to -0.16)	**-0.33 (-0.45 to -0.21)**	**-0.27 (-0.47 to -0.07)**	**-0.24 (-0.42 to -0.05)**	-0.22 (-0.62 to 0.18)	**-0.21 (-0.36 to -0.06)**	-0.17 (-0.34 to 0.00)	-0.17 (-0.56 to 0.22)	-0.08 (-0.26 to 0.10)	-0.06 (-0.23 to 0.11)	-0.05 (-0.25 to 0.15)	-0.01 (-0.21 to 0.19)	**Asenapine**	0.26 (-0.18 to 0.70)
-0.54 (-0.87 to -0.22)	**-0.37 (-0.49 to -0.26)**	**-0.31 (-0.50 to -0.12)**	**-0.28 (-0.44 to -0.12)**	-0.27 (-0.66 to 0.13)	**-0.25 (-0.39 to -0.12)**	**-0.22 (-0.38 to -0.05)**	-0.21 (-0.61 to 0.18)	-0.12 (-0.28 to 0.03)	-0.11 (-0.27 to 0.06)	-0.10 (-0.29 to 0.10)	-0.05 (-0.25 to 0.15)	-0.05 (-0.21 to 0.12)	**Ziprasidone**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always + except for lurasidone, but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Sensitivity analysis Overall Symptoms (without completer analyses)



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials



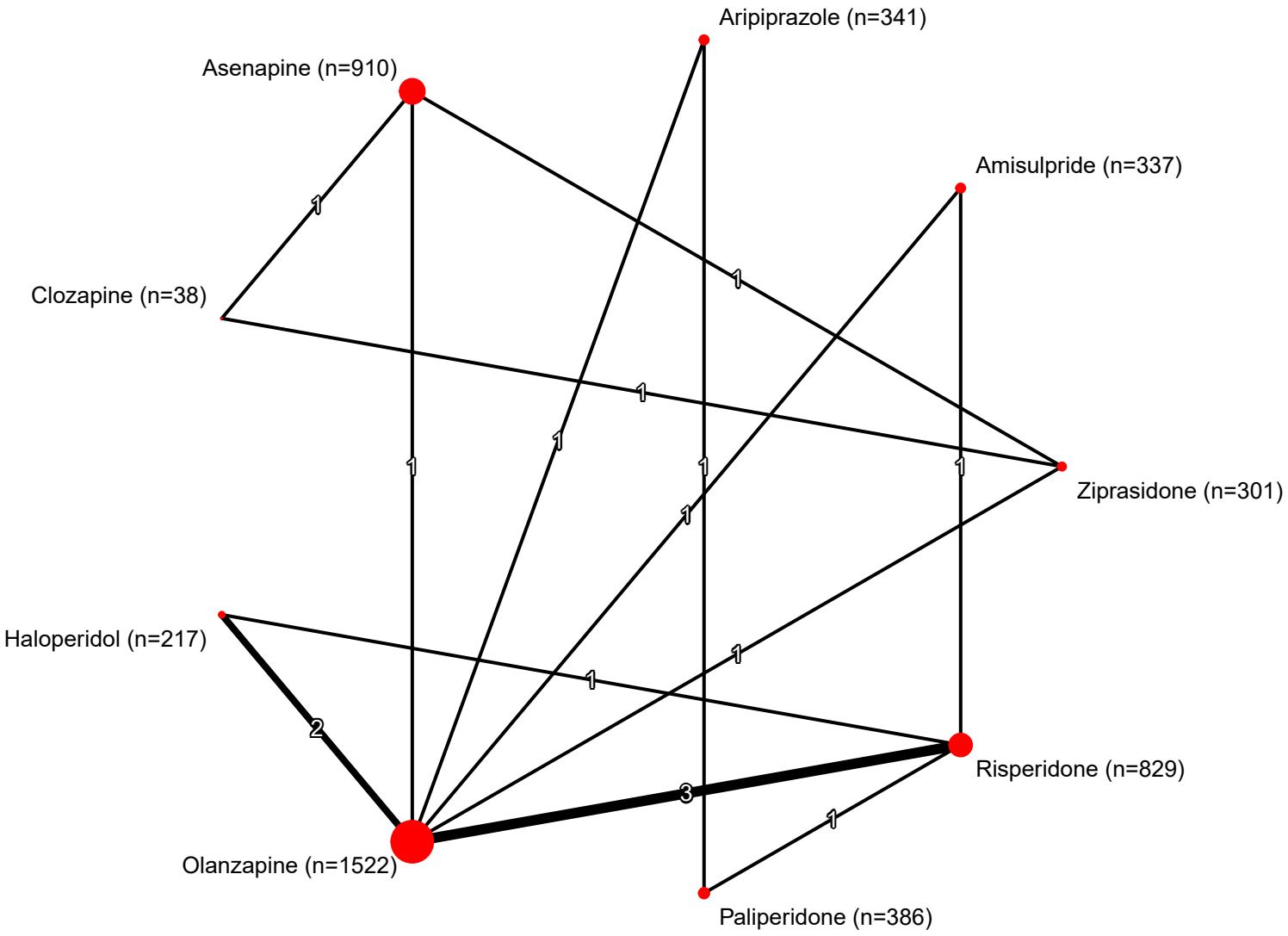
Some drugs had only completer data and they are, therefore, no longer present in this hierarchy. The hierarchy of the remaining drugs is the same as in the primary analysis, except iloperidone and asenapine changing their rank

League table for the outcome: Overall Symptoms (without completer analyses)

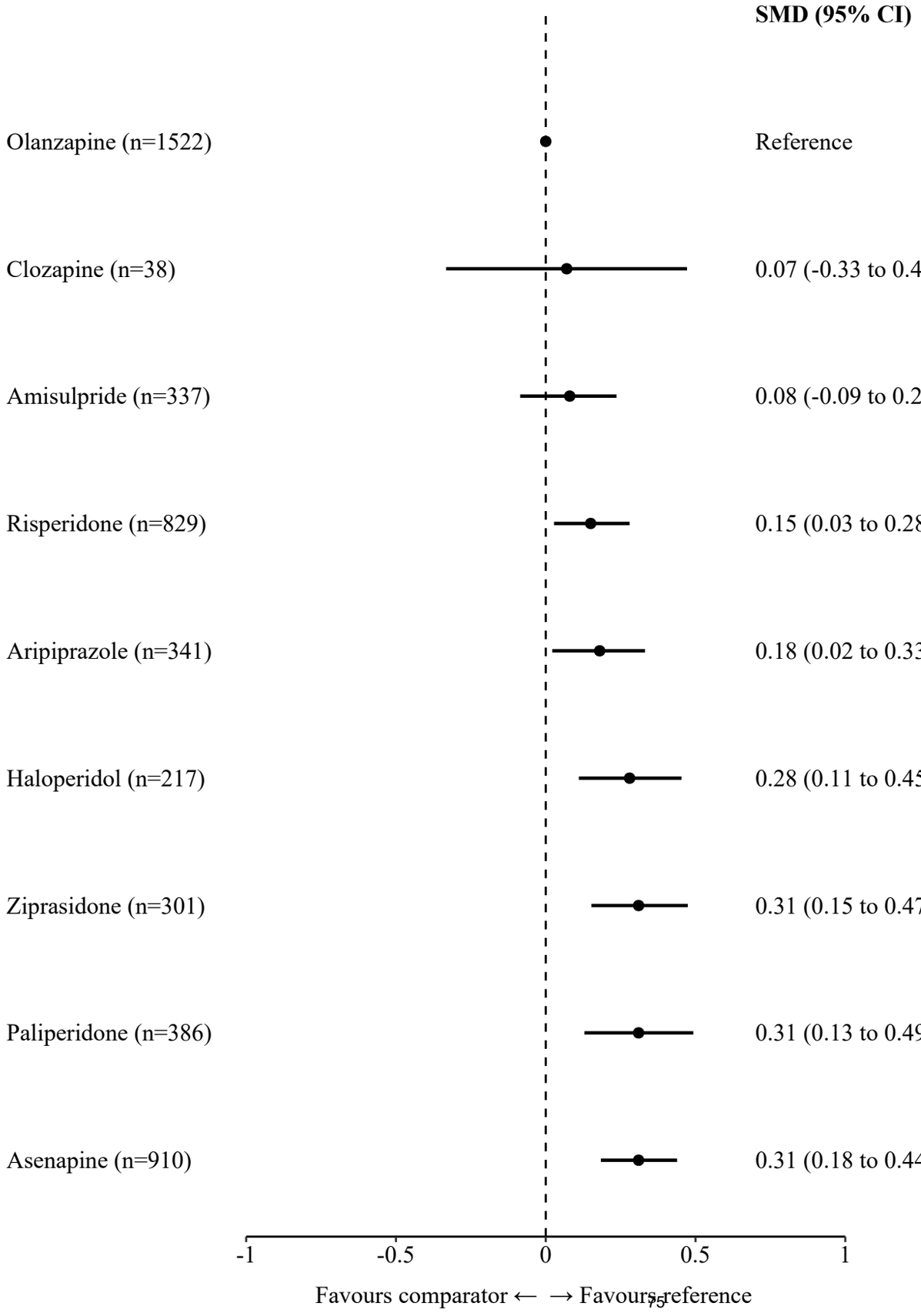
Olanzapine	-0.02 (-0.22 to 0.18)	-0.09 (-0.24 to 0.07)	**-0.14 (-0.25 to -0.04)**	-0.17 (-0.33 to 0.00)	NA	**-0.25 (-0.40 to -0.10)**	**-0.29 (-0.47 to -0.11)**	NA	**-0.29 (-0.42 to -0.16)**	NA	**-0.39 (-0.51 to -0.27)**
-0.06 (-0.22 to 0.09)	**Amisulpride**	NA	-0.01 (-0.23 to 0.21)	NA	NA	NA	NA	NA	NA	NA	NA
-0.10 (-0.25 to 0.04)	-0.04 (-0.24 to 0.16)	**Perphenazine**	0.00 (-0.16 to 0.16)	NA	NA	-0.16 (-0.32 to 0.00)	NA	NA	NA	NA	**-0.30 (-0.49 to -0.11)**
-0.12 (-0.22 to -0.03)	-0.06 (-0.22 to 0.10)	-0.02 (-0.17 to 0.13)	**Risperidone**	NA	NA	**-0.16 (-0.31 to -0.01)**	-0.12 (-0.38 to 0.14)	**-0.16 (-0.32 to -0.01)**	NA	NA	**-0.30 (-0.48 to -0.12)**
-0.16 (-0.28 to -0.04)	-0.10 (-0.29 to 0.10)	-0.06 (-0.24 to 0.13)	-0.03 (-0.18 to 0.11)	**Aripiprazole**	NA	NA	-0.12 (-0.23 to 0.00)	-0.09 (-0.48 to 0.31)	NA	NA	NA
-0.16 (-0.54 to 0.22)	-0.10 (-0.50 to 0.31)	-0.06 (-0.46 to 0.34)	-0.04 (-0.42 to 0.35)	-0.00 (-0.37 to 0.37)	**Zotepine**	NA	-0.11 (-0.46 to 0.25)	NA	NA	NA	NA
-0.26 (-0.40 to -0.13)	-0.20 (-0.40 to 0.00)	-0.16 (-0.32 to 0.00)	-0.14 (-0.28 to 0.00)	-0.11 (-0.28 to 0.07)	-0.10 (-0.50 to 0.29)	**Quetiapine**	NA	NA	NA	NA	-0.14 (-0.32 to 0.04)
-0.27 (-0.39 to -0.14)	**-0.20 (-0.40 to -0.01)**	-0.17 (-0.35 to 0.02)	-0.14 (-0.29 to 0.00)	**-0.11 (-0.21 to -0.01)**	-0.11 (-0.46 to 0.25)	-0.00 (-0.18 to 0.18)	**Haloperidol**	NA	-0.20 (-0.64 to 0.23)	-0.05 (-0.17 to 0.06)	NA
-0.28 (-0.45 to -0.12)	**-0.22 (-0.43 to -0.01)**	-0.18 (-0.38 to 0.02)	**-0.16 (-0.30 to -0.02)**	-0.12 (-0.31 to 0.06)	-0.12 (-0.53 to 0.28)	-0.02 (-0.22 to 0.18)	-0.02 (-0.21 to 0.18)	**Paliperidone**	NA	NA	NA
-0.30 (-0.43 to -0.18)	**-0.24 (-0.44 to -0.04)**	**-0.20 (-0.39 to -0.01)**	**-0.18 (-0.34 to -0.02)**	-0.14 (-0.32 to 0.03)	-0.14 (-0.54 to 0.25)	-0.04 (-0.23 to 0.15)	-0.04 (-0.21 to 0.13)	-0.02 (-0.23 to 0.19)	**Asenapine**	NA	NA
-0.32 (-0.49 to -0.15)	**-0.26 (-0.48 to -0.03)**	-0.22 (-0.44 to 0.00)	**-0.20 (-0.38 to -0.01)**	**-0.16 (-0.32 to -0.01)**	-0.16 (-0.53 to 0.21)	-0.06 (-0.27 to 0.15)	-0.05 (-0.17 to 0.06)	-0.04 (-0.26 to 0.19)	-0.02 (-0.22 to 0.19)	**Iloperidone**	NA
-0.40 (-0.52 to -0.28)	**-0.34 (-0.53 to -0.14)**	**-0.30 (-0.46 to -0.13)**	**-0.27 (-0.41 to -0.14)**	**-0.24 (-0.41 to -0.07)**	-0.24 (-0.63 to 0.15)	-0.13 (-0.29 to 0.02)	-0.13 (-0.30 to 0.04)	-0.12 (-0.31 to 0.08)	-0.10 (-0.27 to 0.08)	-0.08 (-0.28 to 0.13)	**Ziprasidone**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always + but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Sensitivity analysis Overall Symptoms (without studies with imputed SDs)



Sensitivity analysis Overall Symptoms (without studies with imputed SDs)



Some drugs which had only studies analysed based on completer data are no longer present. Olanzapine remained on the top. The hierarchy changed here and there, but the same drugs which were less efficacious than olanzapine with 95% CIs excluding opposite effects are also less efficacious here.

Sensitivity analysis league table for the outcome: Overall Symptoms (without studies with imputed SDs)

Olanzapine	NA	-0.02 (-0.22 to 0.18)	**-0.19 (-0.34 to -0.04)**	-0.17 (-0.33 to 0.00)	**-0.29 (-0.47 to -0.11)**	NA	**-0.29 (-0.42 to -0.16)**	**-0.35 (-0.53 to -0.18)**
-0.07 (-0.47 to 0.33)	**Clozapine**	NA	NA	NA	NA	NA	-0.37 (-0.82 to 0.07)	-0.11 (-0.56 to 0.33)
-0.08 (-0.24 to 0.09)	-0.01 (-0.44 to 0.43)	**Amisulpride**	-0.01 (-0.23 to 0.21)	NA	NA	NA	NA	NA
-0.15 (-0.28 to -0.03)	-0.08 (-0.51 to 0.34)	-0.08 (-0.24 to 0.09)	**Risperidone**	NA	-0.12 (-0.38 to 0.14)	**-0.16 (-0.32 to -0.01)**	NA	NA
-0.18 (-0.33 to -0.02)	-0.11 (-0.54 to 0.32)	-0.10 (-0.32 to 0.12)	-0.02 (-0.21 to 0.17)	**Aripiprazole**	NA	-0.09 (-0.48 to 0.31)	NA	NA
-0.28 (-0.45 to -0.11)	-0.21 (-0.65 to 0.22)	-0.21 (-0.43 to 0.02)	-0.13 (-0.32 to 0.06)	-0.11 (-0.33 to 0.12)	**Haloperidol**	NA	NA	NA
-0.31 (-0.49 to -0.13)	-0.24 (-0.68 to 0.20)	**-0.24 (-0.45 to -0.02)**	**-0.16 (-0.30 to -0.01)**	-0.13 (-0.35 to 0.08)	-0.03 (-0.26 to 0.21)	**Paliperidone**	NA	NA
-0.31 (-0.44 to -0.18)	-0.24 (-0.64 to 0.16)	**-0.24 (-0.44 to -0.03)**	-0.16 (-0.34 to 0.02)	-0.13 (-0.33 to 0.07)	-0.03 (-0.24 to 0.18)	-0.00 (-0.22 to 0.22)	**Asenapine**	0.26 (-0.18 to 0.70)
-0.31 (-0.47 to -0.15)	-0.24 (-0.64 to 0.16)	**-0.24 (-0.47 to -0.01)**	-0.16 (-0.36 to 0.04)	-0.14 (-0.36 to 0.09)	-0.03 (-0.27 to 0.20)	-0.00 (-0.25 to 0.24)	-0.00 (-0.20 to 0.19)	**Ziprasidone**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always + but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Confidence in the estimates using CINeMA

Comparison	Number of studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Amisulpride:Aripiprazole	0	Some concerns	Some concerns	No concerns	Some concerns	Some concerns	Some concerns	**Very low**
Amisulpride:Asenapine	0	No concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Amisulpride:Clozapine	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Amisulpride:Haloperidol	0	Some concerns	Some concerns	No concerns	No concerns	Some concerns	Some concerns	**Low**
Amisulpride:Iloperidone	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Amisulpride:Lurasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Amisulpride:Olanzapine	1	No concerns	Some concerns	No concerns	Some concerns	Some concerns	No concerns	**Low**
Amisulpride:Paliperidone	0	No concerns	Some concerns	No concerns	No concerns	Some concerns	Some concerns	**Low**
Amisulpride:Perphenazine	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Amisulpride:Quetiapine	0	No concerns	Some concerns	No concerns	Some concerns	No concerns	Some concerns	**Low**
Amisulpride:Risperidone	1	No concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	**Low**
Amisulpride:Ziprasidone	0	No concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Moderate**
Amisulpride:Zotepine	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Aripiprazole:Asenapine	0	Some concerns	Some concerns	No concerns	No concerns	Some concerns	Some concerns	**Low**
Aripiprazole:Clozapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Aripiprazole:Haloperidol	1	Some concerns	Some concerns	No concerns	No concerns	Some concerns	No concerns	**Low**
Aripiprazole:Iloperidone	0	Some concerns	Some concerns	No concerns	No concerns	Some concerns	Some concerns	**Low**
Aripiprazole:Lurasidone	0	Some concerns	Some concerns	No concerns	Some concerns	No concerns	Some concerns	**Low**
Aripiprazole:Olanzapine	1	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	**Moderate**
Aripiprazole:Paliperidone	1	No concerns	Some concerns	No concerns	Some concerns	No concerns	No concerns	**Moderate**
Aripiprazole:Perphenazine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Aripiprazole:Quetiapine	0	Some concerns	Some concerns	No concerns	Some concerns	Some concerns	Some concerns	**Very low**
Aripiprazole:Risperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Aripiprazole:Ziprasidone	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Aripiprazole:Zotepine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**

Asenapine:Clozapine	1	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	**Low**
Asenapine:Haloperidol	1	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	**Low**
Asenapine:Iloperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Asenapine:Lurasidone	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Asenapine:Olanzapine	1	No concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	**Moderate**
Asenapine:Paliperidone	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Asenapine:Perphenazine	0	No concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Asenapine:Quetiapine	0	No concerns	Some concerns	No concerns	Some concerns	Some concerns	Some concerns	**Low**
Asenapine:Risperidone	0	No concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Asenapine:Ziprasidone	1	No concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	**Low**
Asenapine:Zotepine	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Clozapine:Haloperidol	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Clozapine:Iloperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Clozapine:Lurasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Clozapine:Olanzapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Clozapine:Paliperidone	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Clozapine:Perphenazine	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Clozapine:Quetiapine	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Clozapine:Risperidone	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Clozapine:Ziprasidone	1	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	**Low**
Clozapine:Zotepine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Haloperidol:Iloperidone	3	Some concerns	Some concerns	No concerns	Some concerns	No concerns	Some concerns	**Low**
Haloperidol:Lurasidone	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Haloperidol:Olanzapine	2	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	**Moderate**
Haloperidol:Paliperidone	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Haloperidol:Perphenazine	0	Some concerns	Some concerns	No concerns	Some concerns	No concerns	Some concerns	**Low**
Haloperidol:Quetiapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Haloperidol:Risperidone	1	Some concerns	Some concerns	No concerns	No concerns	Some concerns	No concerns	**Low**
Haloperidol:Ziprasidone	0	Some concerns	Some concerns	No concerns	Some concerns	No concerns	Some concerns	**Low**
Haloperidol:Zotepine	1	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**

Iloperidone:Lurasidone	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Iloperidone:Olanzapine	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Iloperidone:Paliperidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Iloperidone:Perphenazine	0	Some concerns	Some concerns	No concerns	No concerns	Some concerns	Some concerns	**Low**
Iloperidone:Quetiapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Iloperidone:Risperidone	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Iloperidone:Ziprasidone	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Iloperidone:Zotepine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Lurasidone:Olanzapine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Lurasidone:Paliperidone	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Lurasidone:Perphenazine	0	Some concerns	Some concerns	No concerns	Some concerns	Some concerns	Some concerns	**Very low**
Lurasidone:Quetiapine	1	Major concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Lurasidone:Risperidone	0	Some concerns	Some concerns	No concerns	Some concerns	No concerns	Some concerns	**Low**
Lurasidone:Ziprasidone	0	Some concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Low**
Lurasidone:Zotepine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Olanzapine:Paliperidone	0	No concerns	Some concerns	No concerns	No concerns	No concerns	Some concerns	**Moderate**
Olanzapine:Perphenazine	2	No concerns	Some concerns	No concerns	Some concerns	No concerns	No concerns	**Moderate**
Olanzapine:Quetiapine	2	No concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	**Moderate**
Olanzapine:Risperidone	4	No concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	**Moderate**
Olanzapine:Ziprasidone	3	No concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	**Moderate**
Olanzapine:Zotepine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**
Paliperidone:Perphenazine	0	No concerns	Some concerns	No concerns	Some concerns	No concerns	Some concerns	**Low**
Paliperidone:Quetiapine	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Paliperidone:Risperidone	1	No concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	**Moderate**
Paliperidone:Ziprasidone	0	No concerns	Some concerns	No concerns	Some concerns	Some concerns	Some concerns	**Low**
Paliperidone:Zotepine	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Perphenazine:Quetiapine	1	No concerns	Some concerns	No concerns	Some concerns	No concerns	No concerns	**Moderate**
Perphenazine:Risperidone	1	No concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	**Low**
Perphenazine:Ziprasidone	1	No concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	**Moderate**
Perphenazine:Zotepine	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**

Quetiapine:Risperidone	1	No concerns	Some concerns	No concerns	Some concerns	No concerns	No concerns	**Moderate**
Quetiapine:Ziprasidone	1	No concerns	Some concerns	No concerns	Some concerns	No concerns	No concerns	**Moderate**
Quetiapine:Zotepine	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Risperidone:Ziprasidone	1	No concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	**Moderate**
Risperidone:Zotepine	0	No concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Low**
Ziprasidone:Zotepine	0	Some concerns	Some concerns	No concerns	Major concerns	No concerns	Some concerns	**Very low**

Explanations for CINeMA judgement

Due to a small number of studies per comparison we could not formally assess small trial / publication bias. We, therefore, generally coded the item 'reporting bias' as 'some concerns'. Moreover, the following general rules of the CINeMA framework were followed to judge the overall levels of confidence in the estimates. The overall confidence in the estimates is rated as 1. high, 2. moderate, 3. low, 4. very low. The CINeMA-guidance-document1 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 ncoherence. 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.) Nevertheless, it needs to be considered that this is a scarce network meaning that heterogeneity and inconsistency cannot be assessed well. We, therefore, downgraded the evidence for all comparisons which were entirely based on indirect evidence by one additional step. We did not do this for comparison for which direct evidence was available, because in these occasions the direct evidence matched well with the indirect and was usually based on a large sample size (approximately 1000 participants). If we had done only pairwise meta-analyses, we would not have judged the confidence to be low. The exception were comparisons with asenapine. Here, the indirect evidence was substantially different from the direct, probably driven by a single, small, single-blind study from India, available only as an abstract, comparing asenapine with clozapine and ziprasidone.2 Thus, we downgraded the confidence in the asenapine results one further step. Finally, for the CINeMA judgement it is necessary to set a minimum important SMD. We set it at SMD +/- 0.1.

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.

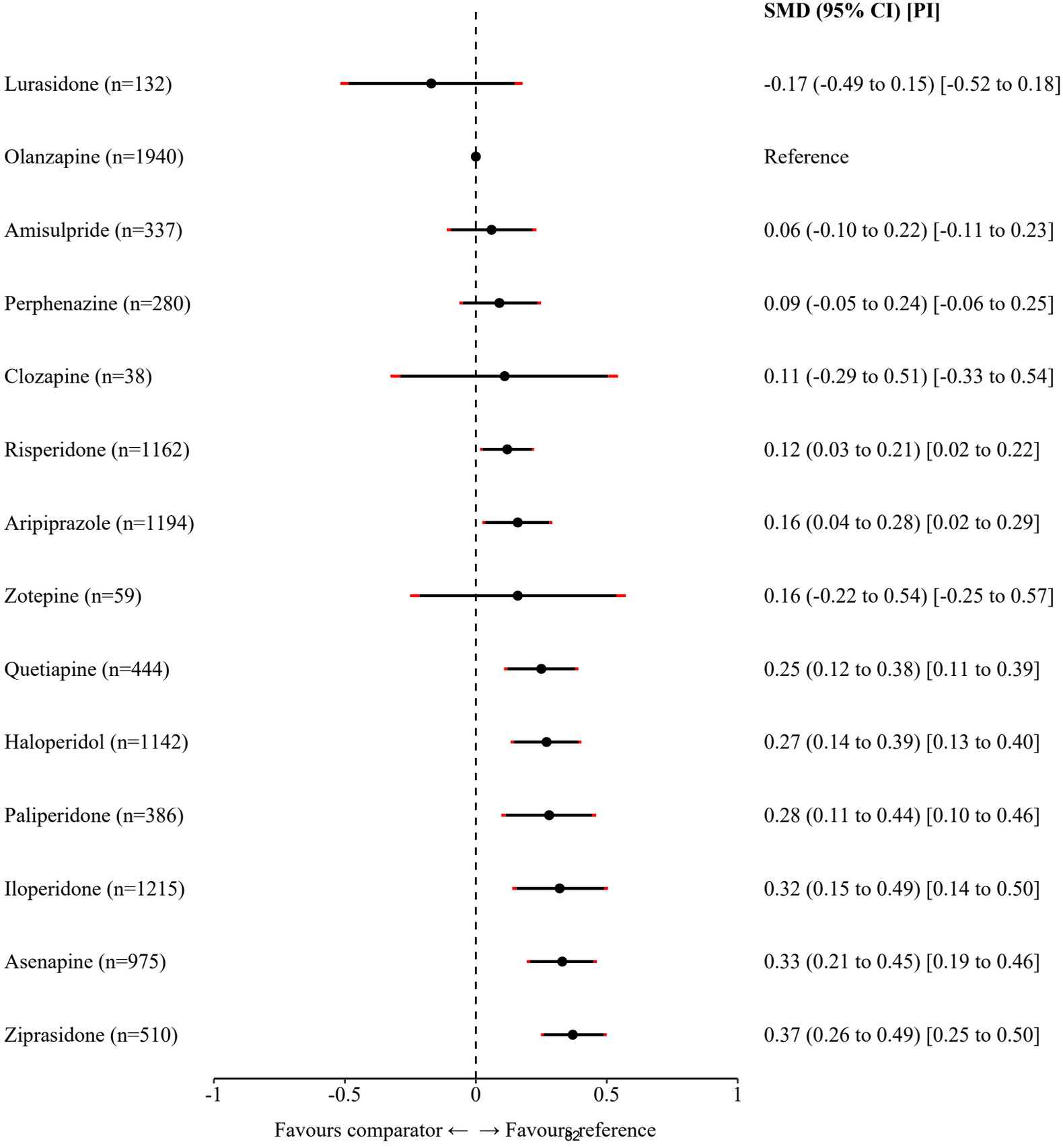
1 judgement of "major concerns" and up to 2 judgements of "some concerns" or 1 additional judgement of "major concerns" could be interconnected and do not justify downgrading by more than 2 levels.

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).

1. Nikolakopoulou A, Higgins JPT, Papakonstantinou T, Chaimani A, Del Giovane C, Egger M, Salanti G. CINeMA: An approach for assessing confidence in the results of a network meta-analysis. PLoS medicine 2020; 17(4): e1003082.

2. Dutta T, Bhowmick S, Mitra M, Nath S, Chatterjee RN, Bhattacharjee S. A comparative study of efficacy and safety of three atypical antipsychotic agents: asenapine, ziprasidone and clozapine in Indian schizophrenic patients: a randomized controlled trial. Indian J Pharmacol 2014; 46(7): S9.

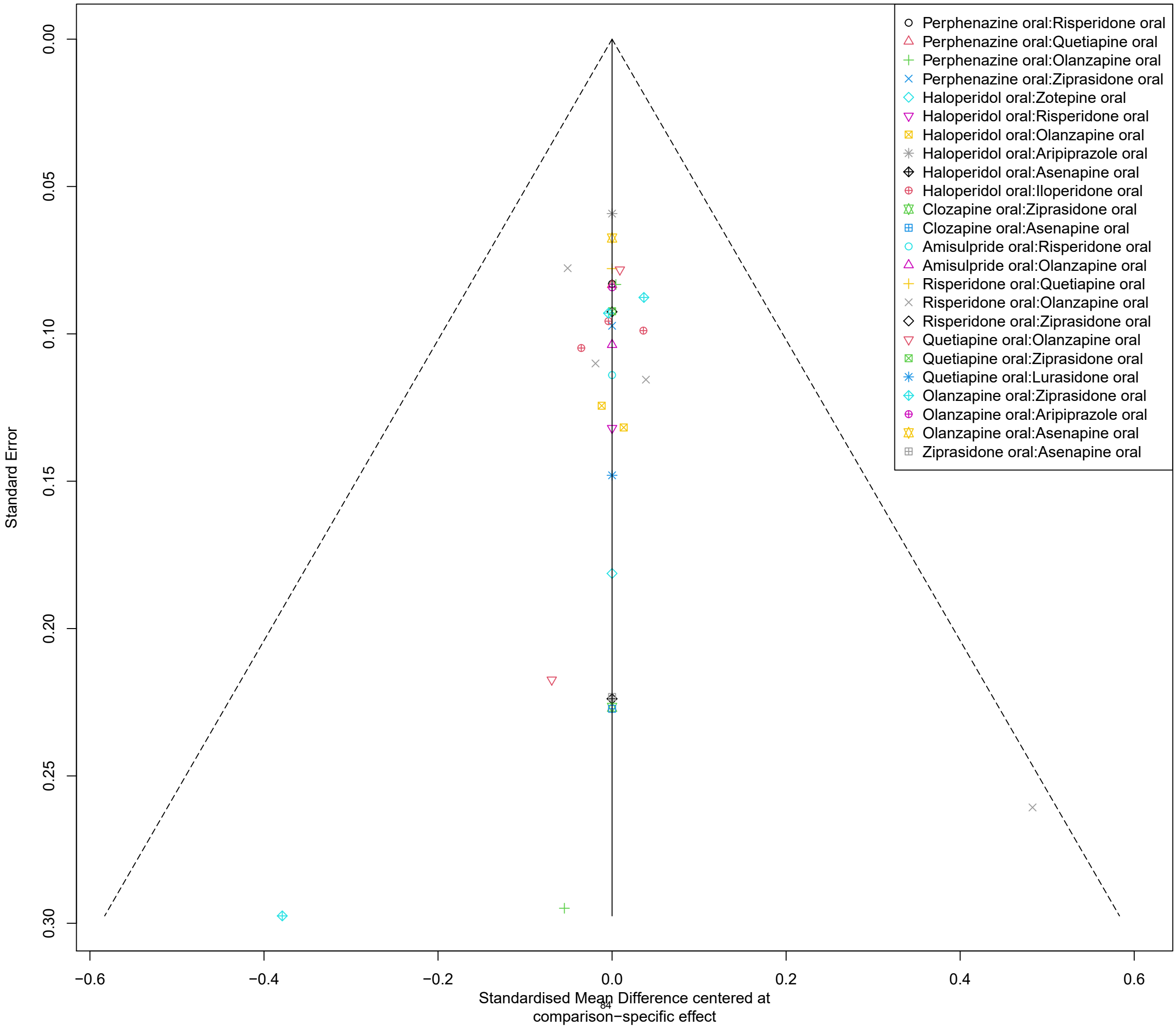
Forest plot primary outcome overall symptoms with prediction intervals



League table with prediction interval for the outcome: Overall Symptoms

Lurasidone													
-0.17 (-0.52 to 0.18)	**Olanzapine**												
-0.23 (-0.61 to 0.15)	-0.06 (-0.23 to 0.11)	**Amisulpride**											
-0.26 (-0.62 to 0.1)	-0.09 (-0.25 to 0.06)	-0.03 (-0.26 to 0.19)	**Perphenazine**										
-0.28 (-0.83 to 0.27)	-0.11 (-0.54 to 0.33)	-0.05 (-0.51 to 0.42)	-0.02 (-0.47 to 0.44)	**Clozapine**									
-0.29 (-0.64 to 0.06)	**-0.12 (-0.22 to -0.02)**	-0.06 (-0.23 to 0.11)	-0.03 (-0.19 to 0.14)	-0.01 (-0.45 to 0.43)	**Risperidone**								
-0.33 (-0.7 to 0.04)	**-0.16 (-0.29 to -0.02)**	-0.10 (-0.31 to 0.11)	-0.07 (-0.27 to 0.14)	-0.05 (-0.5 to 0.4)	-0.04 (-0.2 to 0.12)	**Aripiprazole**							
-0.33 (-0.87 to 0.21)	-0.16 (-0.57 to 0.25)	-0.10 (-0.54 to 0.34)	-0.07 (-0.51 to 0.37)	-0.05 (-0.65 to 0.54)	-0.04 (-0.46 to 0.38)	-0.00 (-0.41 to 0.4)	**Zotepine**						
-0.42 (-0.74 to -0.1)	**-0.25 (-0.39 to -0.11)**	-0.19 (-0.4 to 0.02)	-0.16 (-0.33 to 0.02)	-0.14 (-0.59 to 0.31)	-0.13 (-0.28 to 0.02)	-0.09 (-0.28 to 0.1)	-0.09 (-0.52 to 0.34)	**Quetiapine**					
-0.44 (-0.81 to -0.07)	**-0.27 (-0.4 to -0.13)**	-0.21 (-0.42 to 0.01)	-0.18 (-0.38 to 0.03)	-0.16 (-0.61 to 0.29)	-0.15 (-0.31 to 0.01)	-0.11 (-0.22 to 0)	-0.11 (-0.5 to 0.28)	-0.02 (-0.21 to 0.17)	**Haloperidol**				
-0.45 (-0.83 to -0.07)	**-0.28 (-0.46 to -0.1)**	-0.22 (-0.45 to 0.01)	-0.19 (-0.41 to 0.04)	-0.17 (-0.64 to 0.3)	-0.16 (-0.32 to 0)	-0.12 (-0.33 to 0.09)	-0.12 (-0.56 to 0.32)	-0.03 (-0.24 to 0.18)	-0.01 (-0.22 to 0.2)	**Paliperidone**			
-0.49 (-0.88 to -0.1)	**-0.32 (-0.5 to -0.14)**	**-0.26 (-0.51 to -0.02)**	-0.23 (-0.47 to 0.01)	-0.21 (-0.68 to 0.26)	-0.20 (-0.4 to 0)	-0.16 (-0.33 to 0)	-0.16 (-0.57 to 0.25)	-0.07 (-0.3 to 0.16)	-0.05 (-0.18 to 0.07)	-0.04 (-0.29 to 0.2)	**Iloperidone**		
-0.50 (-0.87 to -0.13)	**-0.33 (-0.46 to -0.19)**	**-0.27 (-0.48 to -0.05)**	**-0.24 (-0.44 to -0.03)**	-0.22 (-0.65 to 0.21)	**-0.21 (-0.38 to -0.04)**	-0.17 (-0.35 to 0.01)	-0.17 (-0.6 to 0.26)	-0.08 (-0.27 to 0.11)	-0.06 (-0.24 to 0.12)	-0.05 (-0.27 to 0.17)	-0.01 (-0.23 to 0.21)	**Asenapine**	
-0.54 (-0.9 to -0.18)	**-0.37 (-0.5 to -0.25)**	**-0.31 (-0.52 to -0.11)**	**-0.28 (-0.46 to -0.1)**	-0.27 (-0.7 to 0.17)	**-0.25 (-0.4 to -0.11)**	**-0.22 (-0.4 to -0.03)**	-0.21 (-0.64 to 0.22)	-0.12 (-0.29 to 0.04)	-0.11 (-0.29 to 0.08)	-0.10 (-0.31 to 0.11)	-0.05 (-0.27 to 0.17)	-0.05 (-0.22 to 0.13)	**Ziprasidone**

Comparison adjusted funnel-plot by year when antipsychotic was first licensed: Overall Symptoms (primary outcome)



Egger's test for small trial bias, primary outcome overall symptoms

Linear regression test of funnel plot asymmetry

data: metagen(TE.adj, seTE, data = comp_funnel)

t = 0.11854, df = 32, p-value = 0.9064

alternative hypothesis: asymmetry in funnel plot

sample estimates:

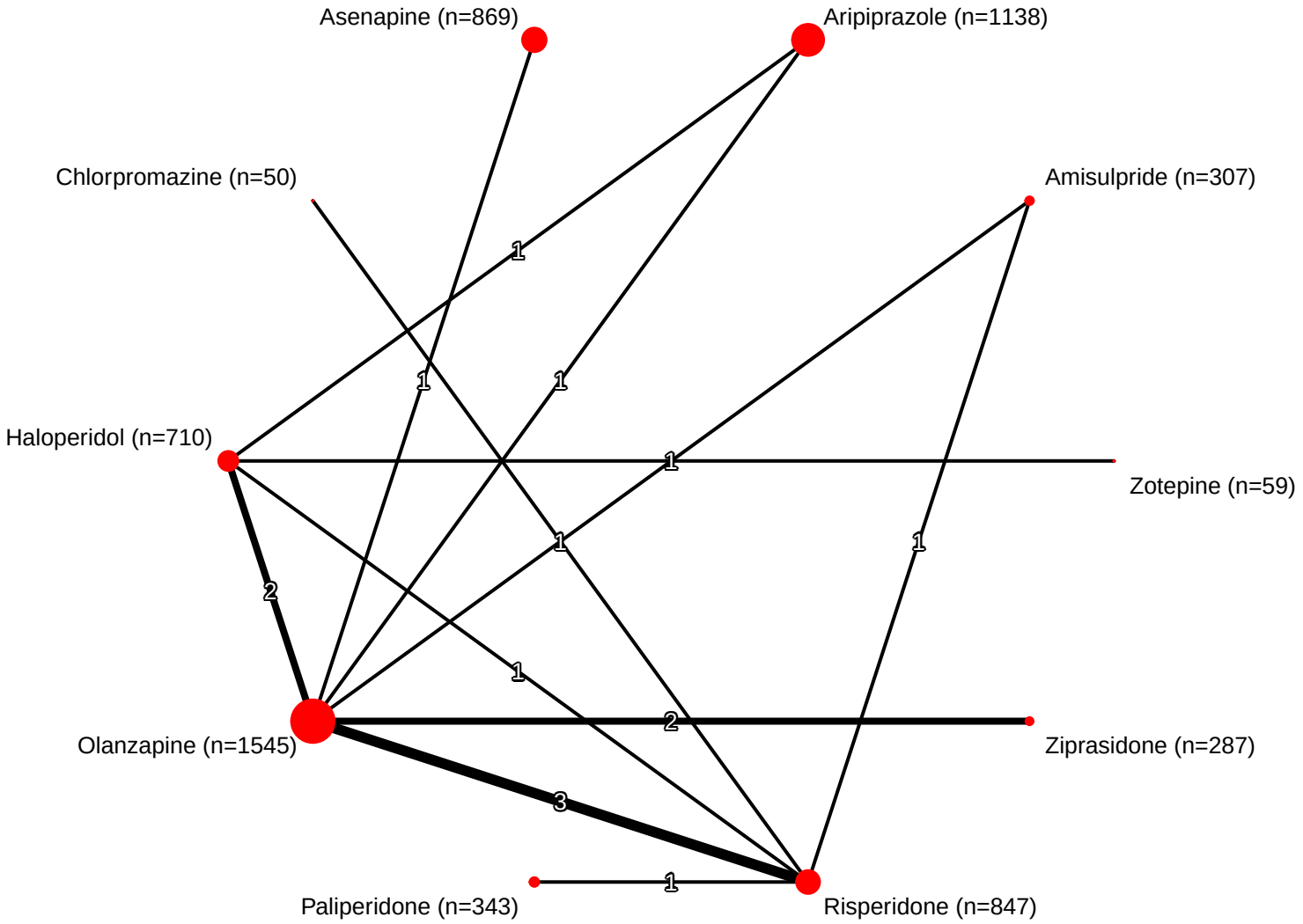
bias	se.bias	intercept
0.024928576	0.210303134	-0.002404281

eAppendix 7

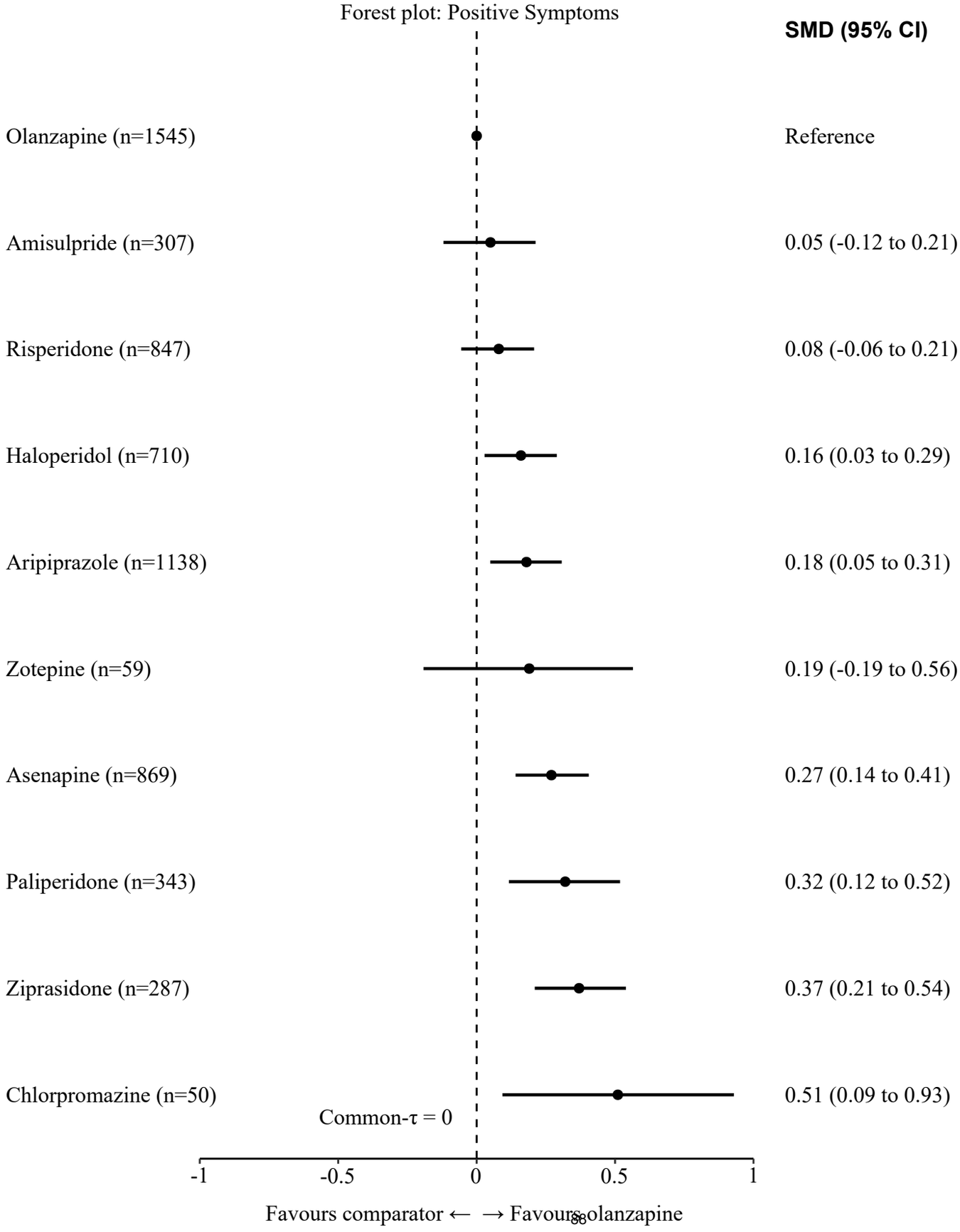
Positive symptoms

1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

Positive Symptoms



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials

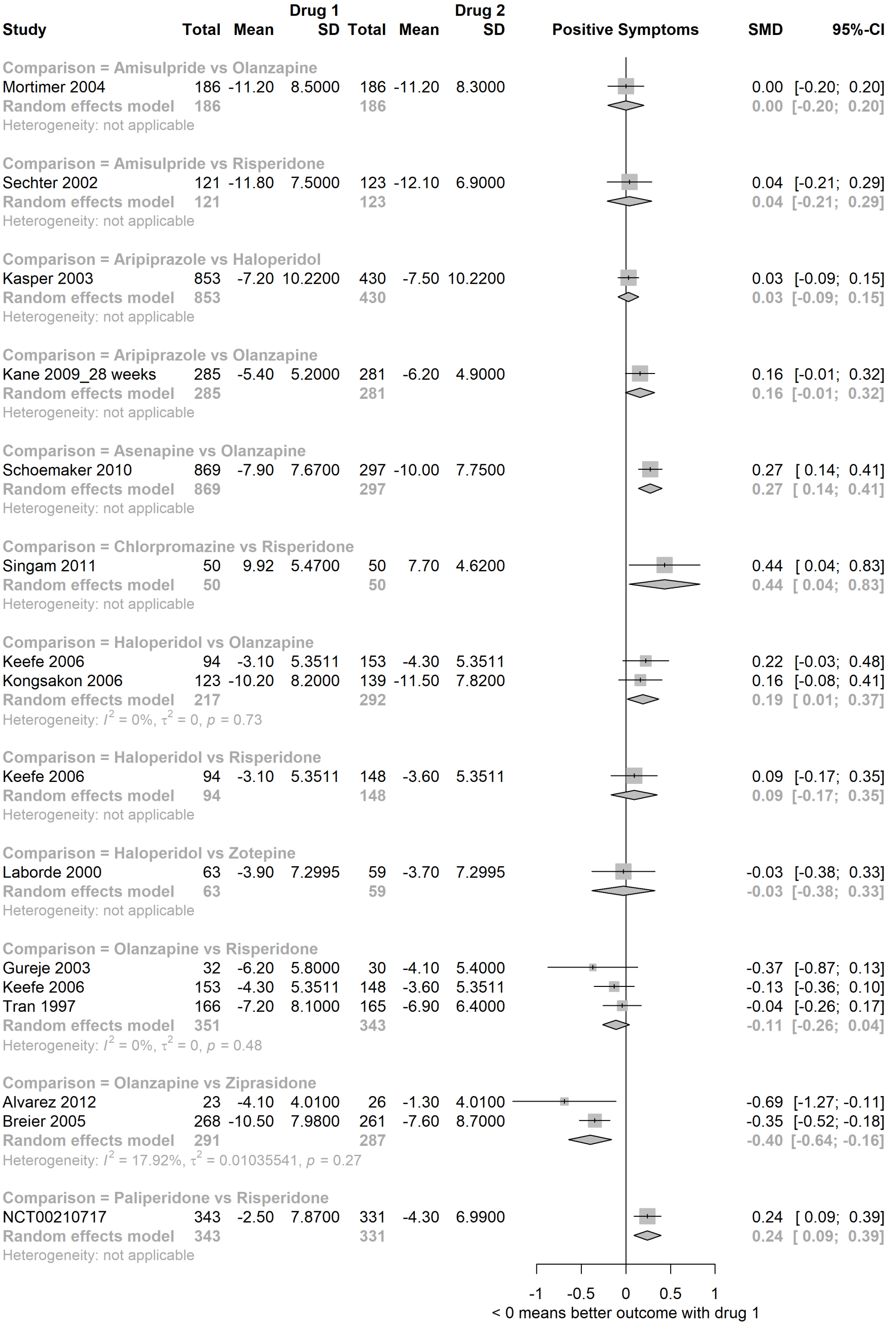

Forest plot: Positive Symptoms
SMD (95% CI)
Olanzapine (n=1545)
Reference
Amisulpride (n=307)
0.05 (-0.12 to 0.21)
Risperidone (n=847)
0.08 (-0.06 to 0.21)
Haloperidol (n=710)
0.16 (0.03 to 0.29)
Aripiprazole (n=1138)
0.18 (0.05 to 0.31)
Zotepine (n=59)
0.19 (-0.19 to 0.56)
Asenapine (n=869)
0.27 (0.14 to 0.41)
Paliperidone (n=343)
0.32 (0.12 to 0.52)
Ziprasidone (n=287)
0.37 (0.21 to 0.54)
Chlorpromazine (n=50)
0.51 (0.09 to 0.93)
Common-τ = 0
-1
-0.5
0
0.5
1
Favours comparator ← → Favours olanzapine

League table for the outcome: Positive Symptoms

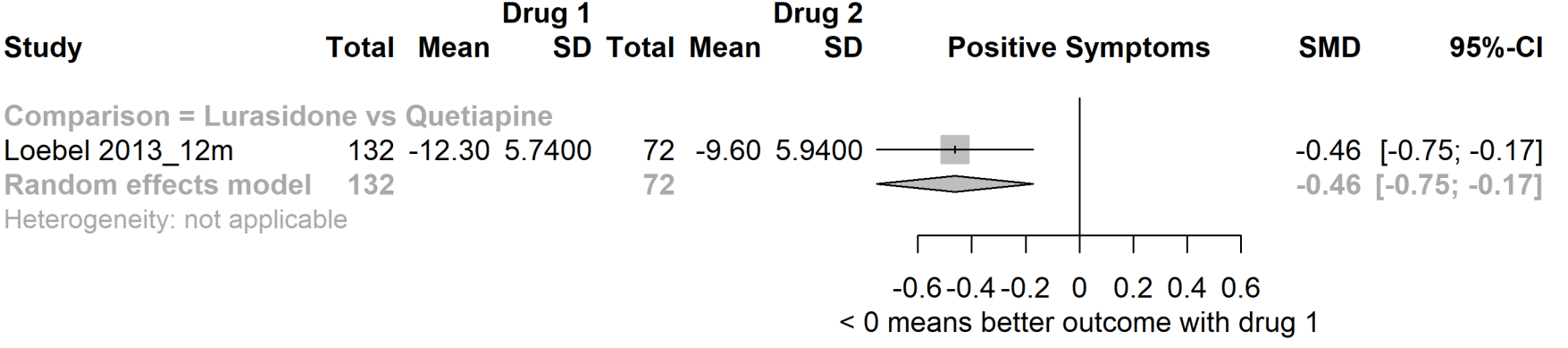
Olanzapine	-0.00 (-0.20 to 0.20)	-0.11 (-0.26 to 0.04)	**-0.19 (-0.37 to -0.01)**	-0.16 (-0.32 to 0.01)	NA	**-0.27 (-0.41 to -0.14)**	NA	**-0.37 (-0.54 to -0.21)**	NA
-0.05 (-0.21 to 0.12)	**Amisulpride**	0.04 (-0.21 to 0.29)	NA	NA	NA	NA	NA	NA	NA
-0.08 (-0.21 to 0.06)	-0.03 (-0.21 to 0.15)	**Risperidone**	-0.09 (-0.35 to 0.17)	NA	NA	NA	**-0.24 (-0.39 to -0.09)**	NA	**-0.44 (-0.83 to -0.04)**
-0.16 (-0.29 to -0.03)	-0.11 (-0.32 to 0.09)	-0.08 (-0.25 to 0.09)	**Haloperidol**	-0.03 (-0.15 to 0.09)	-0.03 (-0.38 to 0.33)	NA	NA	NA	NA
-0.18 (-0.31 to -0.05)	-0.13 (-0.34 to 0.08)	-0.10 (-0.28 to 0.07)	-0.02 (-0.12 to 0.08)	**Aripiprazole**	NA	NA	NA	NA	NA
-0.19 (-0.56 to 0.19)	-0.14 (-0.55 to 0.27)	-0.11 (-0.50 to 0.28)	-0.03 (-0.38 to 0.33)	-0.01 (-0.38 to 0.36)	**Zotepine**	NA	NA	NA	NA
-0.27 (-0.41 to -0.14)	**-0.23 (-0.44 to -0.01)**	**-0.20 (-0.38 to -0.01)**	-0.11 (-0.30 to 0.07)	-0.09 (-0.28 to 0.09)	-0.09 (-0.49 to 0.31)	**Asenapine**	NA	NA	NA
-0.32 (-0.52 to -0.12)	**-0.27 (-0.50 to -0.04)**	**-0.24 (-0.39 to -0.09)**	-0.16 (-0.39 to 0.07)	-0.14 (-0.37 to 0.09)	-0.13 (-0.55 to 0.29)	-0.04 (-0.28 to 0.20)	**Paliperidone**	NA	NA
-0.37 (-0.54 to -0.21)	**-0.33 (-0.56 to -0.09)**	**-0.30 (-0.51 to -0.09)**	**-0.22 (-0.43 to -0.01)**	-0.20 (-0.41 to 0.01)	-0.19 (-0.60 to 0.22)	-0.10 (-0.31 to 0.11)	-0.06 (-0.32 to 0.20)	**Ziprasidone**	NA
-0.51 (-0.93 to -0.09)	**-0.46 (-0.90 to -0.03)**	**-0.44 (-0.83 to -0.04)**	-0.35 (-0.78 to 0.08)	-0.33 (-0.77 to 0.10)	-0.32 (-0.88 to 0.23)	-0.24 (-0.68 to 0.20)	-0.19 (-0.62 to 0.23)	-0.14 (-0.59 to 0.31)	**Chlorpromazine**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always +, but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Forest plot of drugs in the network. Results on the left side of the y-axis are in favour of the first mentioned drug



Forest plot of pairwise meta-analyses - drugs outside the network. Results on the left side of the y-axis are in favour of the first mentioned drug

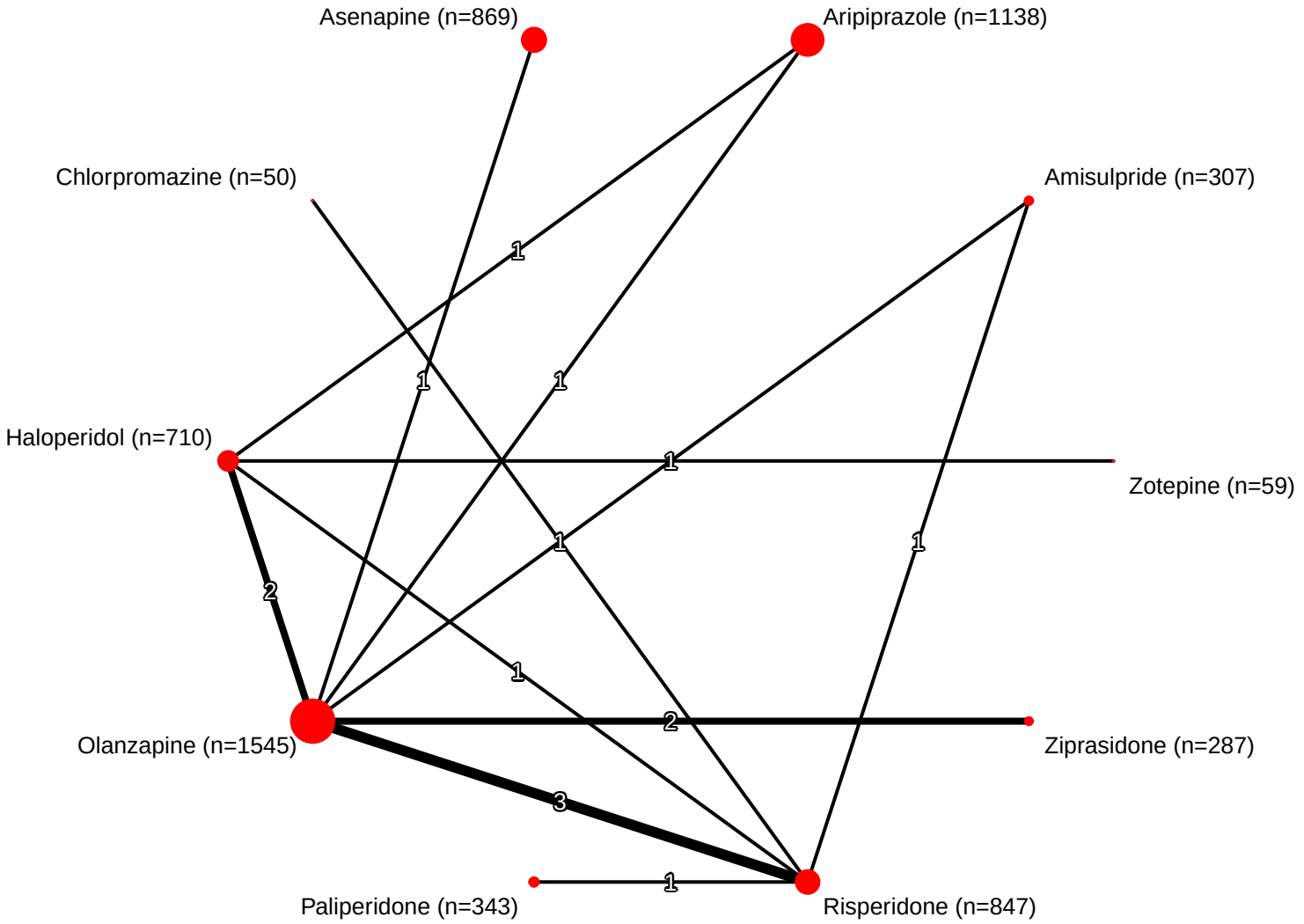


eAppendix 8

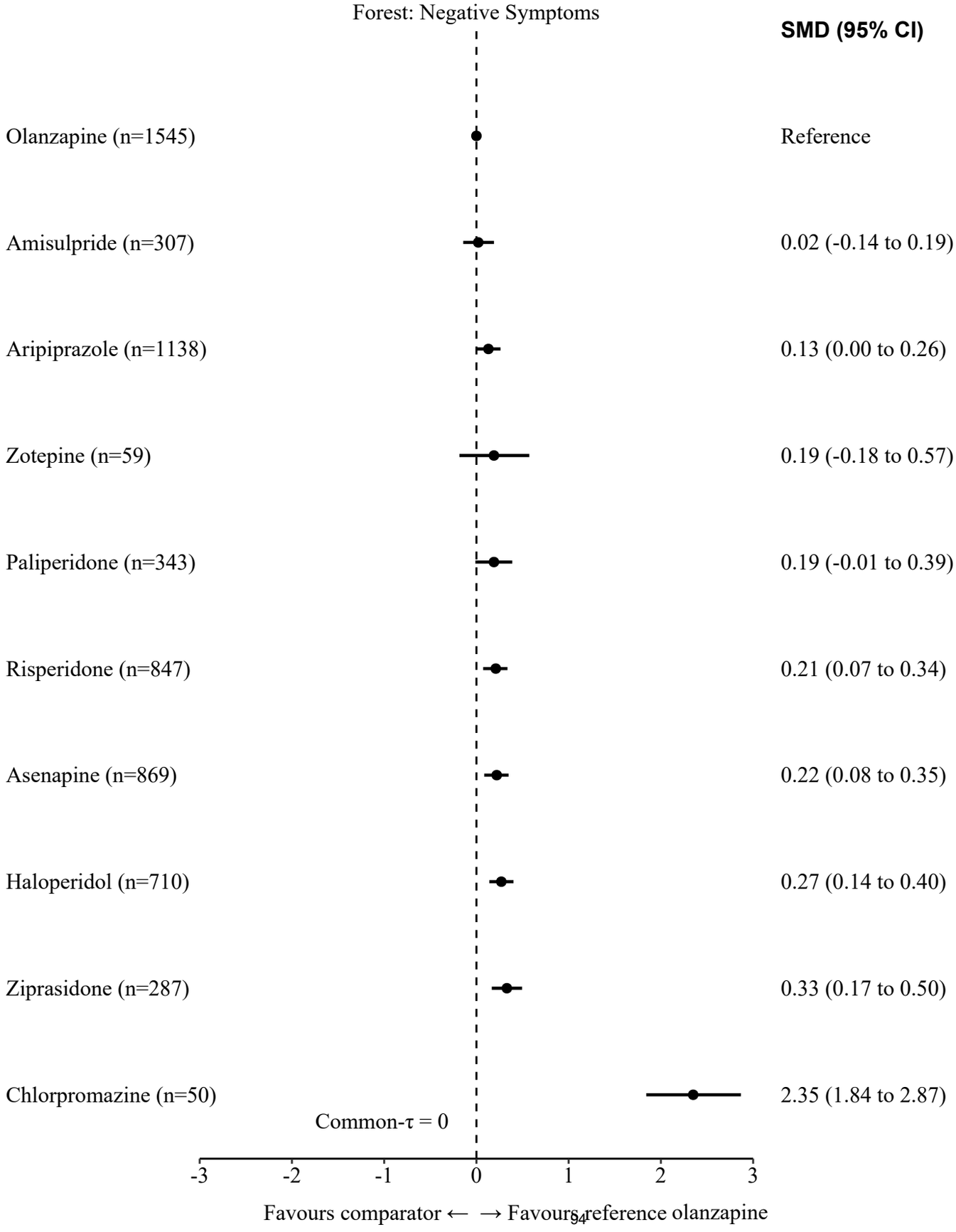
Negative symptoms

1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

Negative Symptoms



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials

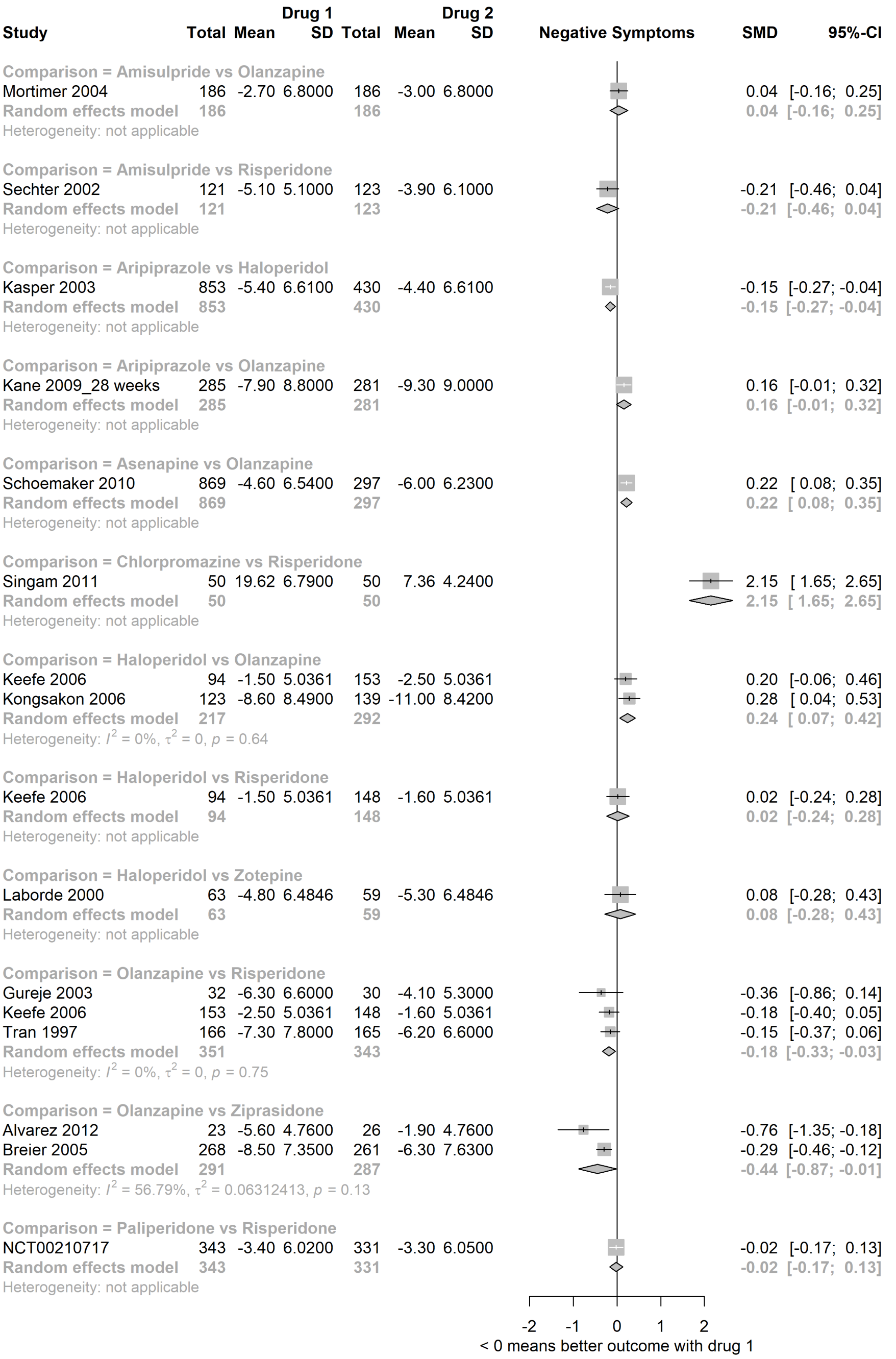

Forest: Negative Symptoms
SMD (95% CI)
Olanzapine (n=1545)
Reference
Amisulpride (n=307)
0.02 (-0.14 to 0.19)
Aripiprazole (n=1138)
0.13 (0.00 to 0.26)
Zotepine (n=59)
0.19 (-0.18 to 0.57)
Paliperidone (n=343)
0.19 (-0.01 to 0.39)
Risperidone (n=847)
0.21 (0.07 to 0.34)
Asenapine (n=869)
0.22 (0.08 to 0.35)
Haloperidol (n=710)
0.27 (0.14 to 0.40)
Ziprasidone (n=287)
0.33 (0.17 to 0.50)
Chlorpromazine (n=50)
2.35 (1.84 to 2.87)
Common-τ = 0
-3
-2
-1
0
1
2
3
Favours comparator ← → Favours reference olanzapine

League table for the outcome: Negative Symptoms

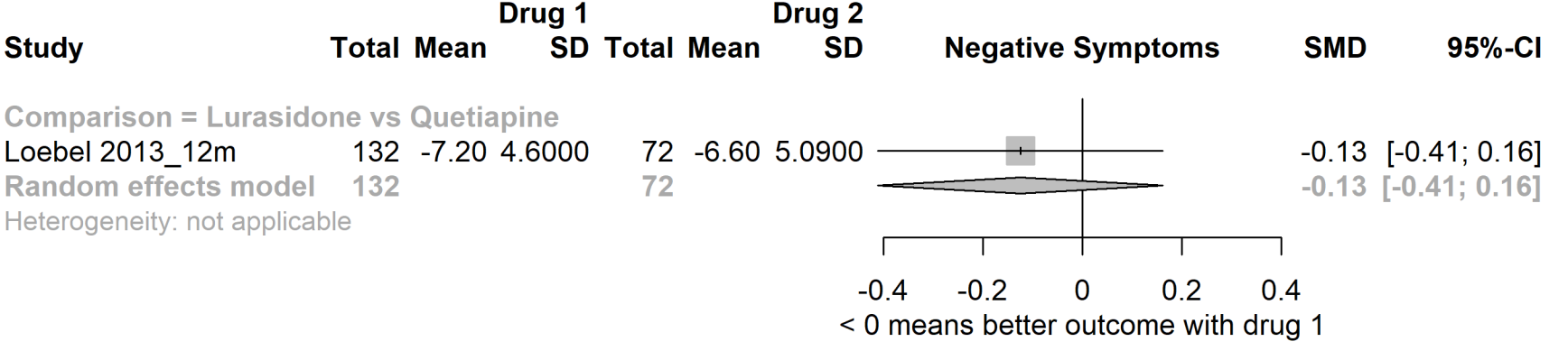
Olanzapine	-0.04 (-0.25 to 0.16)	-0.16 (-0.32 to 0.01)	NA	NA	**-0.18 (-0.33 to -0.03)**	**-0.22 (-0.35 to -0.08)**	**-0.24 (-0.42 to -0.07)**	**-0.33 (-0.50 to -0.17)**	NA
-0.02 (-0.19 to 0.14)	**Amisulpride**	NA	NA	NA	-0.21 (-0.46 to 0.04)	NA	NA	NA	NA
-0.13 (-0.26 to 0.00)	-0.11 (-0.32 to 0.10)	**Aripiprazole**	NA	NA	NA	NA	**-0.15 (-0.27 to -0.04)**	NA	NA
-0.19 (-0.39 to 0.01)	-0.16 (-0.40 to 0.07)	-0.06 (-0.29 to 0.17)	**Paliperidone**	NA	-0.02 (-0.17 to 0.13)	NA	NA	NA	NA
-0.19 (-0.57 to 0.18)	-0.17 (-0.58 to 0.24)	-0.06 (-0.43 to 0.31)	-0.01 (-0.43 to 0.42)	**Zotepine**	NA	NA	-0.08 (-0.43 to 0.28)	NA	NA
-0.21 (-0.34 to -0.07)	-0.18 (-0.36 to 0.00)	-0.07 (-0.25 to 0.10)	-0.02 (-0.17 to 0.13)	-0.01 (-0.40 to 0.38)	**Risperidone**	NA	-0.02 (-0.28 to 0.24)	NA	**-2.15 (-2.65 to -1.65)**
-0.22 (-0.35 to -0.08)	-0.19 (-0.41 to 0.02)	-0.08 (-0.27 to 0.10)	-0.03 (-0.27 to 0.21)	-0.02 (-0.42 to 0.38)	-0.01 (-0.20 to 0.18)	**Asenapine**	NA	NA	NA
-0.27 (-0.40 to -0.14)	**-0.25 (-0.45 to -0.04)**	**-0.14 (-0.24 to -0.03)**	-0.08 (-0.31 to 0.15)	-0.08 (-0.43 to 0.28)	-0.07 (-0.24 to 0.10)	-0.05 (-0.24 to 0.13)	**Haloperidol**	NA	NA
-0.33 (-0.50 to -0.17)	**-0.31 (-0.54 to -0.07)**	-0.20 (-0.41 to 0.01)	-0.14 (-0.40 to 0.12)	-0.14 (-0.55 to 0.28)	-0.13 (-0.34 to 0.08)	-0.11 (-0.33 to 0.10)	-0.06 (-0.27 to 0.15)	**Ziprasidone**	NA
-2.35 (-2.87 to -1.84)	**-2.33 (-2.86 to -1.80)**	**-2.22 (-2.75 to -1.70)**	**-2.17 (-2.68 to -1.65)**	**-2.16 (-2.79 to -1.53)**	**-2.15 (-2.65 to -1.65)**	**-2.14 (-2.67 to -1.61)**	**-2.08 (-2.61 to -1.56)**	**-2.02 (-2.56 to -1.48)**	**Chlorpromazine**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always +, but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Forest plot of drugs in the network. Results on the left side of the y-axis are in favour of the first mentioned drug



Forest plot of pairwise meta-analyses - drugs outside the network. Results on the left side of the y-axis are in favour of the first mentioned drug

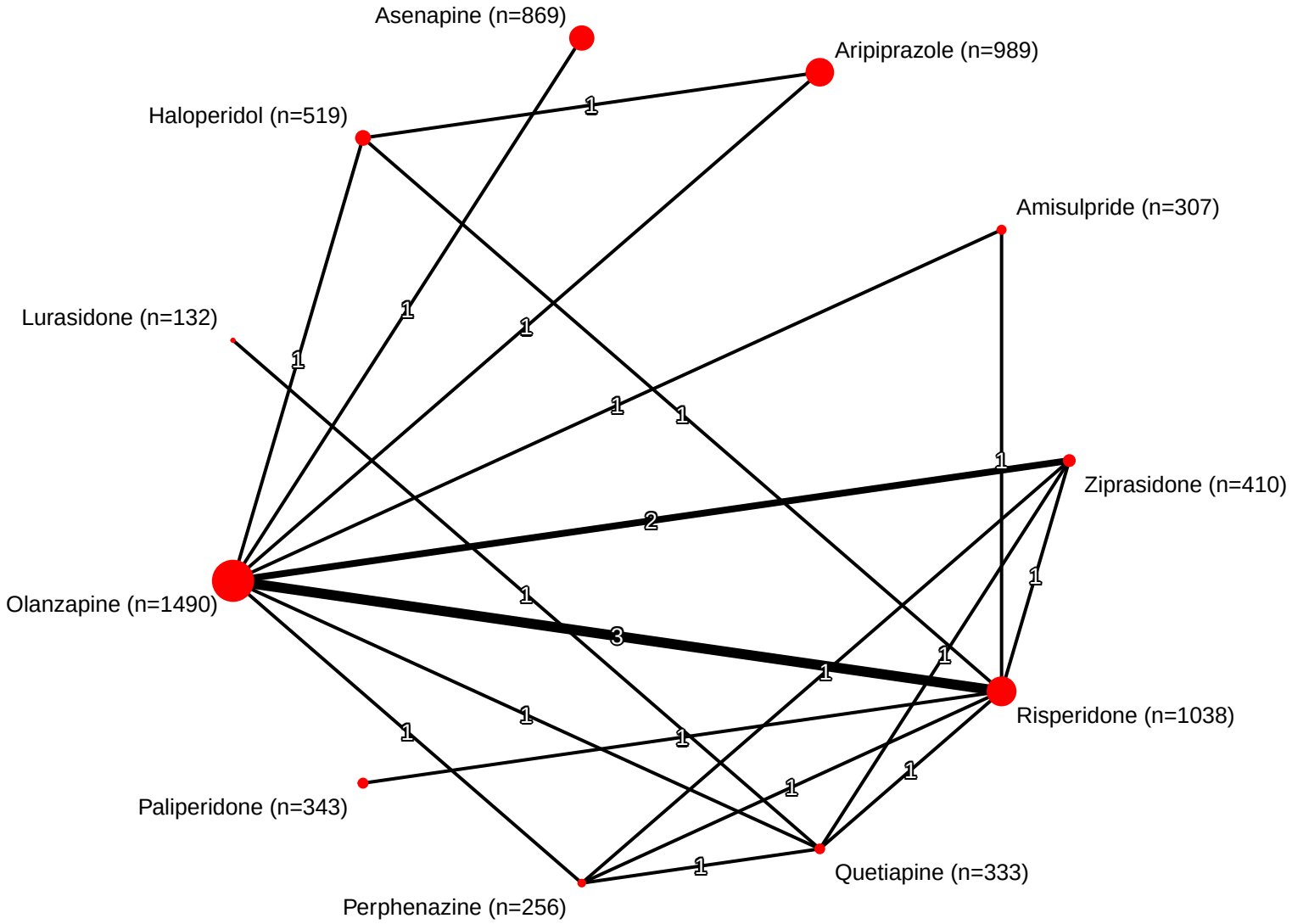


eAppendix 9

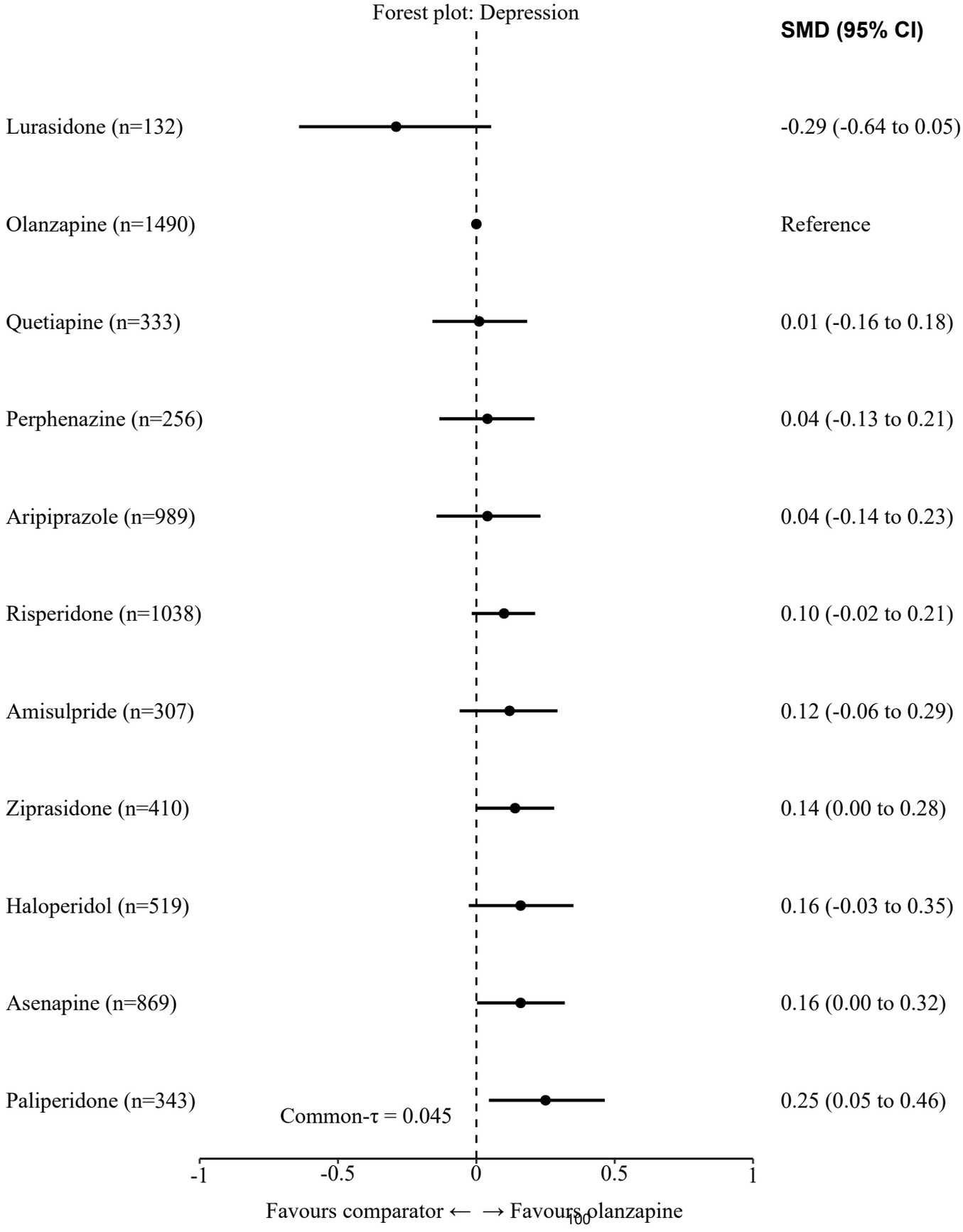
Depressive symptoms

1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

Depression



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials


Forest plot: Depression
SMD (95% CI)
Lurasidone (n=132)
-0.29 (-0.64 to 0.05)
Olanzapine (n=1490)
Reference
Quetiapine (n=333)
0.01 (-0.16 to 0.18)
Perphenazine (n=256)
0.04 (-0.13 to 0.21)
Aripiprazole (n=989)
0.04 (-0.14 to 0.23)
Risperidone (n=1038)
0.10 (-0.02 to 0.21)
Amisulpride (n=307)
0.12 (-0.06 to 0.29)
Ziprasidone (n=410)
0.14 (0.00 to 0.28)
Haloperidol (n=519)
0.16 (-0.03 to 0.35)
Asenapine (n=869)
0.16 (0.00 to 0.32)
Paliperidone (n=343)
0.25 (0.05 to 0.46)
Common-τ = 0.045
-1
-0.5
0
0.5
1
Favours comparator ← → Favours olanzapine

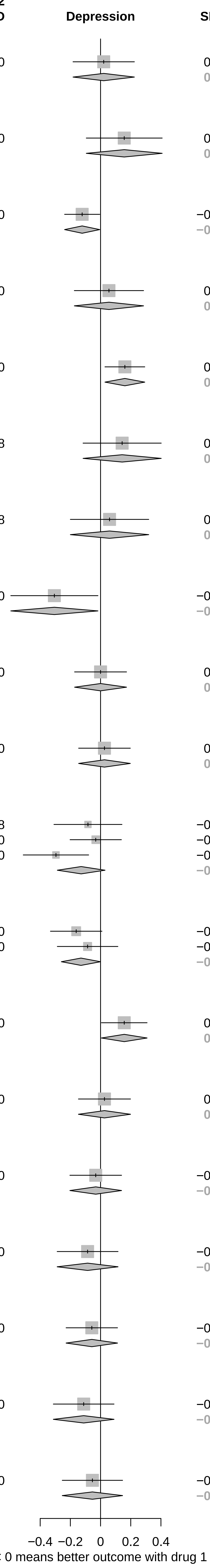
League table for the outcome: Depression

Lurasidone	NA	-0.31 (-0.61 to 0.00)	NA	NA	NA	NA	NA	NA	NA	NA
-0.29 (-0.64 to 0.05)	**Olanzapine**	0.03 (-0.17 to 0.22)	0.00 (-0.19 to 0.19)	-0.06 (-0.30 to 0.19)	-0.12 (-0.25 to 0.00)	-0.02 (-0.24 to 0.20)	-0.13 (-0.27 to 0.02)	-0.16 (-0.32 to 0.00)	-0.14 (-0.42 to 0.13)	NA
-0.31 (-0.61 to 0.00)	-0.01 (-0.18 to 0.16)	**Quetiapine**	-0.03 (-0.22 to 0.17)	NA	-0.06 (-0.25 to 0.13)	NA	-0.11 (-0.33 to 0.11)	NA	NA	NA
-0.33 (-0.69 to 0.03)	-0.04 (-0.21 to 0.13)	-0.03 (-0.22 to 0.17)	**Perphenazine**	NA	-0.03 (-0.22 to 0.16)	NA	-0.09 (-0.31 to 0.13)	NA	NA	NA
-0.34 (-0.73 to 0.05)	-0.04 (-0.23 to 0.14)	-0.03 (-0.28 to 0.22)	-0.01 (-0.26 to 0.24)	**Aripiprazole**	NA	NA	NA	NA	-0.12 (-0.27 to 0.02)	NA
-0.39 (-0.74 to -0.04)	-0.10 (-0.21 to 0.02)	-0.09 (-0.26 to 0.09)	-0.06 (-0.24 to 0.12)	-0.05 (-0.26 to 0.15)	**Risperidone**	-0.16 (-0.42 to 0.11)	-0.05 (-0.27 to 0.16)	NA	-0.06 (-0.33 to 0.21)	-0.16 (-0.33 to 0.02)
-0.41 (-0.79 to -0.03)	-0.12 (-0.29 to 0.06)	-0.10 (-0.34 to 0.13)	-0.08 (-0.31 to 0.16)	-0.07 (-0.33 to 0.18)	-0.02 (-0.20 to 0.16)	**Amisulpride**	NA	NA	NA	NA
-0.43 (-0.79 to -0.08)	-0.14 (-0.28 to 0.00)	-0.13 (-0.32 to 0.06)	-0.10 (-0.30 to 0.09)	-0.10 (-0.33 to 0.13)	-0.04 (-0.21 to 0.12)	-0.02 (-0.24 to 0.20)	**Ziprasidone**	NA	NA	NA
-0.45 (-0.84 to -0.07)	-0.16 (-0.32 to 0.00)	-0.15 (-0.38 to 0.08)	-0.12 (-0.36 to 0.11)	-0.12 (-0.36 to 0.13)	-0.06 (-0.26 to 0.13)	-0.04 (-0.28 to 0.19)	-0.02 (-0.23 to 0.19)	**Asenapine**	NA	NA
-0.46 (-0.85 to -0.06)	-0.16 (-0.35 to 0.03)	-0.15 (-0.40 to 0.10)	-0.12 (-0.37 to 0.13)	-0.12 (-0.25 to 0.02)	-0.06 (-0.27 to 0.14)	-0.05 (-0.30 to 0.21)	-0.02 (-0.25 to 0.21)	-0.00 (-0.25 to 0.25)	**Haloperidol**	NA
-0.55 (-0.94 to -0.16)	**-0.25 (-0.46 to -0.05)**	-0.24 (-0.49 to 0.01)	-0.22 (-0.46 to 0.03)	-0.21 (-0.48 to 0.06)	-0.16 (-0.33 to 0.02)	-0.14 (-0.39 to 0.12)	-0.11 (-0.35 to 0.12)	-0.09 (-0.36 to 0.17)	-0.09 (-0.36 to 0.18)	**Paliperidone**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always + except for lurasidone, but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Forest plot of pairwise meta-analyses. Results on the left side of the y-axis are in favour of the first mentioned drug

Study	Drug 1 Total	Drug 1 Mean	Drug 1 SD	Drug 2 Total	Drug 2 Mean	Drug 2 SD	SMD	95%−CI
Comparison = Amisulpride vs Olanzapine								
Mortimer 2004	186	−6.10	10.4000	186	−6.30	8.7000	0.02	[−0.18; 0.22]
Random effects model	**186**			**186**			**0.02**	**[−0.18; 0.22]**
Heterogeneity: not applicable								
Comparison = Amisulpride vs Risperidone								
Sechter 2002	121	4.90	6.6000	123	3.90	6.1000	0.16	[−0.09; 0.41]
Random effects model	**121**			**123**			**0.16**	**[−0.09; 0.41]**
Heterogeneity: not applicable								
Comparison = Aripiprazole vs Haloperidol								
Kasper 2003	851	−2.60	7.3800	427	−1.70	7.3800	−0.12	[−0.24; −0.01]
Random effects model	**851**			**427**			**−0.12**	**[−0.24; −0.01]**
Heterogeneity: not applicable								
Comparison = Aripiprazole vs Olanzapine								
Kane 2009_28 weeks	138	−5.70	5.3800	155	−6.00	5.3800	0.06	[−0.17; 0.29]
Random effects model	**138**			**155**			**0.06**	**[−0.17; 0.29]**
Heterogeneity: not applicable								
Comparison = Asenapine vs Olanzapine								
Schoemaker 2010	869	−2.70	3.7000	297	−3.30	3.7900	0.16	[0.03; 0.29]
Random effects model	**869**			**297**			**0.16**	**[0.03; 0.29]**
Heterogeneity: not applicable								
Comparison = Haloperidol vs Olanzapine								
Keefe 2006	92	−1.70	8.3648	153	−2.90	8.3648	0.14	[−0.12; 0.40]
Random effects model	**92**			**153**			**0.14**	**[−0.12; 0.40]**
Heterogeneity: not applicable								
Comparison = Haloperidol vs Risperidone								
Keefe 2006	92	−1.70	8.3648	150	−2.20	8.3648	0.06	[−0.20; 0.32]
Random effects model	**92**			**150**			**0.06**	**[−0.20; 0.32]**
Heterogeneity: not applicable								
Comparison = Lurasidone vs Quetiapine								
Loebel 2013_12m	132	−6.00	6.8900	72	−3.80	7.6400	−0.31	[−0.59; −0.02]
Random effects model	**132**			**72**			**−0.31**	**[−0.59; −0.02]**
Heterogeneity: not applicable								
Comparison = Olanzapine vs Perphenazine								
Lieberman 2005_18months	263	3.80	5.0000	256	3.80	5.0000	0.00	[−0.17; 0.17]
Random effects model	**263**			**256**			**0.00**	**[−0.17; 0.17]**
Heterogeneity: not applicable								
Comparison = Olanzapine vs Quetiapine								
Lieberman 2005_18months	263	3.80	5.0000	261	3.67	5.0000	0.03	[−0.15; 0.20]
Random effects model	**263**			**261**			**0.03**	**[−0.15; 0.20]**
Heterogeneity: not applicable								
Comparison = Olanzapine vs Risperidone								
Keefe 2006	153	−2.90	8.3648	150	−2.20	8.3648	−0.08	[−0.31; 0.14]
Lieberman 2005_18months	263	3.80	5.0000	269	3.96	5.0000	−0.03	[−0.20; 0.14]
Tran 1997	166	−1.10	1.3000	165	−0.70	1.4000	−0.30	[−0.51; −0.08]
Random effects model	**582**			**584**			**−0.13**	**[−0.29; 0.03]**
Heterogeneity: $I^2 = 45.22\%$, $\tau^2 = 0.00883662$, $p = 0.16$								
Comparison = Olanzapine vs Ziprasidone								
Breier 2005	270	−7.10	9.9900	260	−5.50	9.8000	−0.16	[−0.33; 0.01]
Lieberman 2005_18months	263	3.80	5.0000	150	4.23	5.0000	−0.09	[−0.29; 0.11]
Random effects model	**533**			**410**			**−0.13**	**[−0.26; 0.00]**
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.57$								
Comparison = Paliperidone vs Risperidone								
NCT00210717	343	−1.60	4.0100	331	−2.20	3.6100	0.16	[0.01; 0.31]
Random effects model	**343**			**331**			**0.16**	**[0.01; 0.31]**
Heterogeneity: not applicable								
Comparison = Perphenazine vs Quetiapine								
Lieberman 2005_18months	256	3.80	5.0000	261	3.67	5.0000	0.03	[−0.15; 0.20]
Random effects model	**256**			**261**			**0.03**	**[−0.15; 0.20]**
Heterogeneity: not applicable								
Comparison = Perphenazine vs Risperidone								
Lieberman 2005_18months	256	3.80	5.0000	269	3.96	5.0000	−0.03	[−0.20; 0.14]
Random effects model	**256**			**269**			**−0.03**	**[−0.20; 0.14]**
Heterogeneity: not applicable								
Comparison = Perphenazine vs Ziprasidone								
Lieberman 2005_18months	256	3.80	5.0000	150	4.23	5.0000	−0.09	[−0.29; 0.12]
Random effects model	**256**			**150**			**−0.09**	**[−0.29; 0.12]**
Heterogeneity: not applicable								
Comparison = Quetiapine vs Risperidone								
Lieberman 2005_18months	261	3.67	5.0000	269	3.96	5.0000	−0.06	[−0.23; 0.11]
Random effects model	**261**			**269**			**−0.06**	**[−0.23; 0.11]**
Heterogeneity: not applicable								
Comparison = Quetiapine vs Ziprasidone								
Lieberman 2005_18months	261	3.67	5.0000	150	4.23	5.0000	−0.11	[−0.31; 0.09]
Random effects model	**261**			**150**			**−0.11**	**[−0.31; 0.09]**
Heterogeneity: not applicable								
Comparison = Risperidone vs Ziprasidone								
Lieberman 2005_18months	269	3.96	5.0000	150	4.23	5.0000	−0.05	[−0.25; 0.15]
Random effects model	**269**			**150**			**−0.05**	**[−0.25; 0.15]**
Heterogeneity: not applicable								

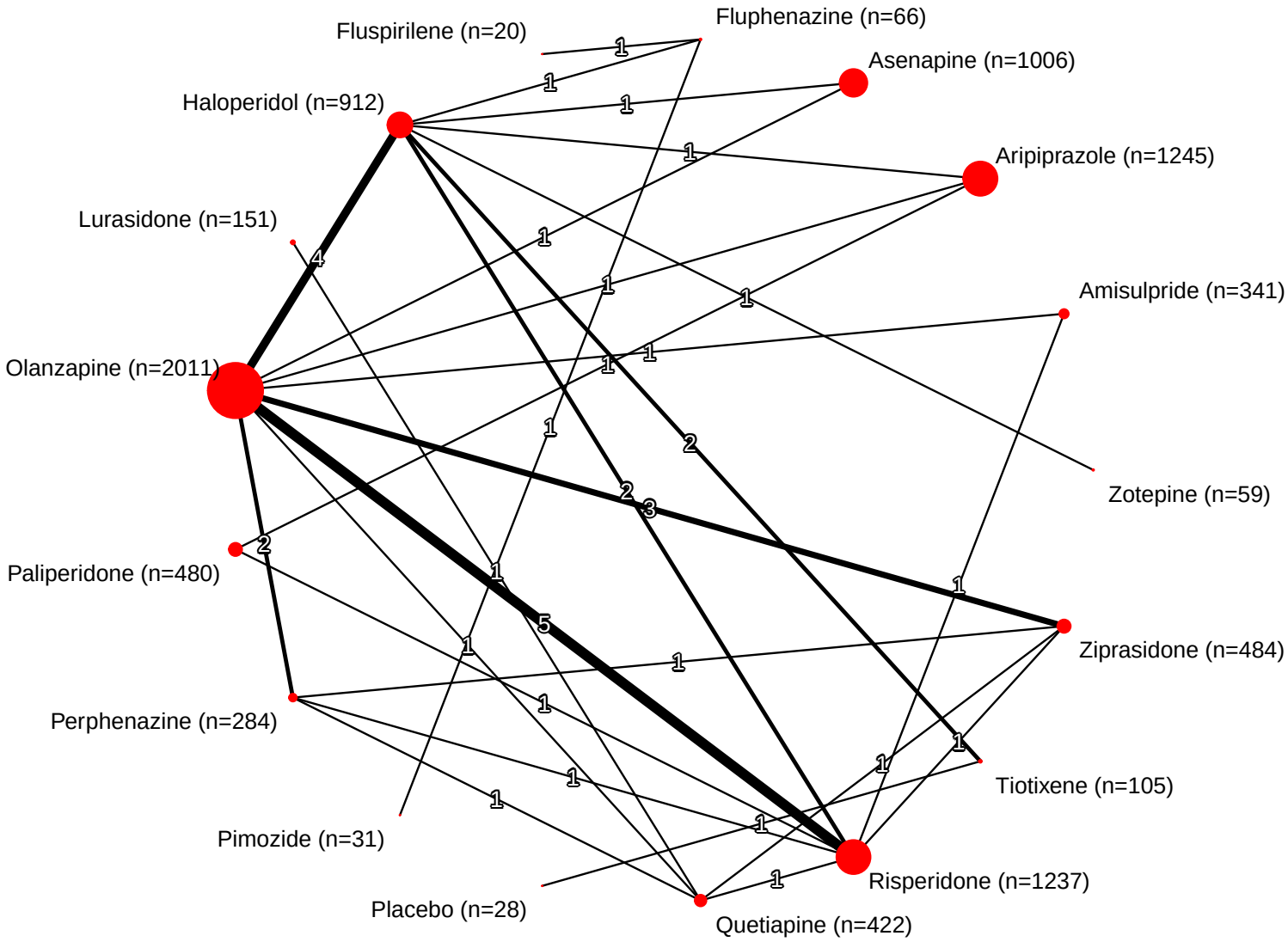


eAppendix 10

All-cause discontinuation

1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

Study discontinuation



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials

Forest plot: All-cause study discontinuation

	OR (95% CI)	RR (95% CI)
Olanzapine (n=2011)	Reference	
Amisulpride (n=341)	1.15 (0.83 to 1.59)	1.08 (0.89 to 1.28)
Aripiprazole (n=1245)	1.23 (0.97 to 1.57)	1.12 (0.98 to 1.27)
Lurasidone (n=151)	1.48 (0.79 to 2.78)	1.24 (0.86 to 1.61)
Risperidone (n=1237)	1.54 (1.27 to 1.87)	1.26 (1.14 to 1.38)
Perphenazine (n=284)	1.57 (1.14 to 2.15)	1.27 (1.08 to 1.46)
Zotepine (n=59)	1.97 (0.92 to 4.23)	1.41 (0.95 to 1.82)
Haloperidol (n=912)	2.07 (1.61 to 2.65)	1.44 (1.29 to 1.58)
Ziprasidone (n=484)	2.07 (1.61 to 2.67)	1.44 (1.29 to 1.58)
Asenapine (n=1006)	2.13 (1.67 to 2.74)	1.46 (1.31 to 1.60)
Paliperidone (n=480)	2.20 (1.61 to 2.99)	1.47 (1.29 to 1.65)
Tiotixene (n=105)	2.35 (1.13 to 4.89)	1.51 (1.07 to 1.88)
Fluspirilene (n=20)	2.43 (0.25 to 23.50)	1.53 (0.36 to 2.30)
Quetiapine (n=422)	2.49 (1.79 to 3.46)	1.55 (1.35 to 1.72)
Pimozide (n=31)	5.51 (1.07 to 28.48)	1.93 (1.04 to 2.32)
Fluphenazine (n=66)	6.57 (2.06 to 20.93)	2.00 (1.44 to 2.28)
Placebo (n=28)	10.21 (2.56 to 40.71)	2.14 (1.56 to 2.36)

Common-τ = 0

0·01 0·1 1 10 100

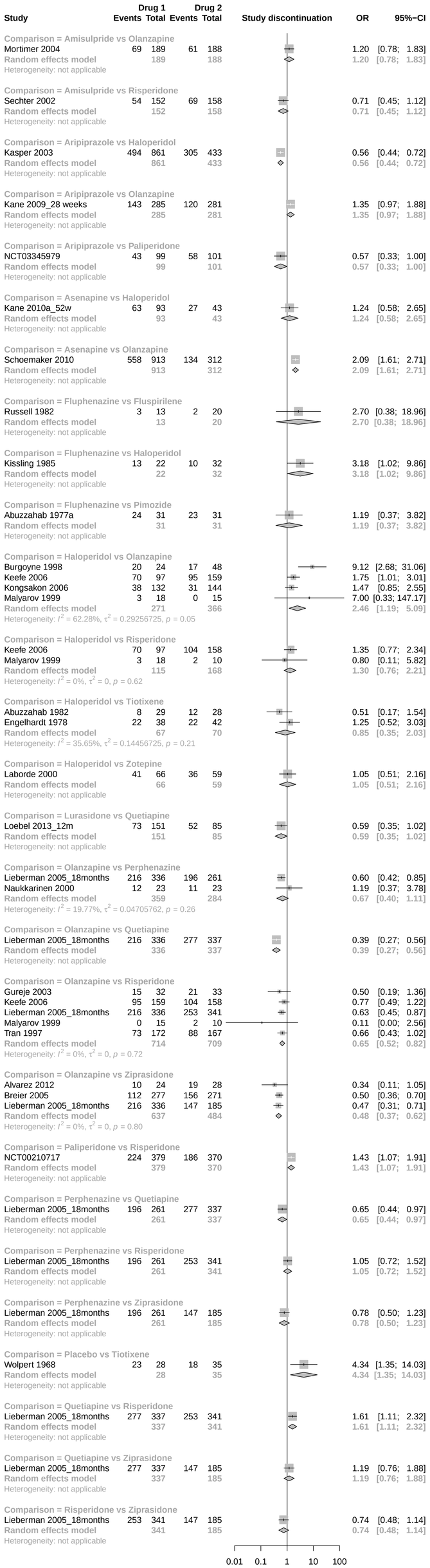
Favours comparator ← → Favours reference olanzapine

League table for the outcome: all-cause discontinuation - relative risk (in the figure above both relative risks and odds ratios are shown)

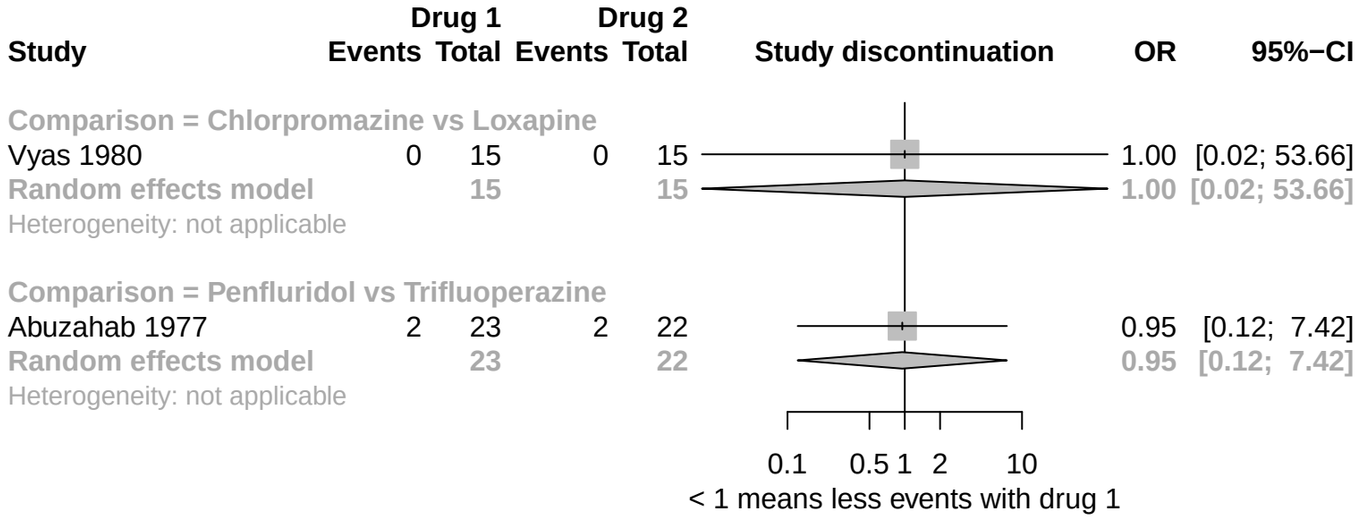
Amisulpride	NA	NA	0.84 (0.63 to 1.05)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1.11 (0.86 to 1.37)
0.96 (0.76 to 1.17)	**Aripiprazole**	NA	NA	NA	NA	**0.76 (0.66 to 0.86)**	NA	NA	0.77 (0.55 to 1)	NA	NA	NA	NA	NA	NA	1.18 (0.98 to 1.38)
0.88 (0.56 to 1.22)	0.91 (0.6 to 1.24)	**Lurasidone**	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.8 (0.6 to 1.01)	NA	NA	NA	NA
0.86 (0.71 to 1.02)	0.89 (0.76 to 1.03)	0.98 (0.68 to 1.28)	**Risperidone**	0.98 (0.8 to 1.15)	NA	0.9 (0.68 to 1.11)	0.87 (0.69 to 1.05)	NA	**0.86 (0.73 to 0.97)**	NA	NA	**0.82 (0.67 to 0.96)**	NA	NA	NA	**1.26 (1.12 to 1.39)**
0.85 (0.65 to 1.06)	0.89 (0.7 to 1.07)	0.97 (0.66 to 1.28)	0.99 (0.84 to 1.15)	**Perphenazine**	NA	NA	0.9 (0.71 to 1.08)	NA	NA	NA	NA	**0.84 (0.68 to 0.99)**	NA	NA	NA	**1.28 (1.07 to 1.48)**
0.77 (0.45 to 1.12)	0.79 (0.49 to 1.12)	0.88 (0.48 to 1.27)	0.89 (0.57 to 1.21)	0.9 (0.56 to 1.23)	**Zotepine**	0.98 (0.68 to 1.25)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
0.76 (0.59 to 0.92)	**0.79 (0.69 to 0.87)**	0.86 (0.58 to 1.13)	**0.88 (0.76 to 1)**	0.89 (0.72 to 1.05)	0.98 (0.68 to 1.25)	**Haloperidol**	NA	0.91 (0.6 to 1.2)	NA	0.95 (0.67 to 1.2)	NA	NA	NA	**0.71 (0.38 to 1)**	NA	**1.39 (1.17 to 1.6)**
0.75 (0.59 to 0.92)	**0.78 (0.64 to 0.93)**	0.86 (0.59 to 1.13)	0.87 (0.75 to 1)	0.89 (0.73 to 1.04)	0.98 (0.65 to 1.28)	1 (0.85 to 1.14)	**Ziprasidone**	NA	NA	NA	NA	0.93 (0.75 to 1.1)	NA	NA	NA	**1.45 (1.29 to 1.59)**
0.74 (0.58 to 0.91)	**0.77 (0.63 to 0.91)**	0.85 (0.57 to 1.12)	**0.86 (0.74 to 1)**	0.87 (0.7 to 1.04)	0.97 (0.64 to 1.26)	0.99 (0.85 to 1.12)	0.99 (0.84 to 1.12)	**Asenapine**	NA	NA	NA	NA	NA	NA	NA	**1.44 (1.29 to 1.59)**
0.73 (0.58 to 0.9)	**0.76 (0.63 to 0.9)**	0.84 (0.57 to 1.11)	**0.86 (0.75 to 0.96)**	0.86 (0.69 to 1.03)	0.96 (0.63 to 1.25)	0.98 (0.83 to 1.11)	0.98 (0.82 to 1.12)	0.99 (0.83 to 1.14)	**Paliperidone**	NA	NA	NA	NA	NA	NA	NA
0.72 (0.43 to 1.03)	0.74 (0.47 to 1.03)	0.82 (0.45 to 1.18)	0.84 (0.54 to 1.12)	0.84 (0.53 to 1.14)	0.93 (0.54 to 1.27)	0.95 (0.67 to 1.2)	0.95 (0.65 to 1.22)	0.96 (0.66 to 1.23)	0.97 (0.67 to 1.24)	**Tiotixene**	NA	NA	NA	NA	**0.71 (0.38 to 0.96)**	NA
0.7 (0.12 to 1.41)	0.74 (0.12 to 1.42)	0.81 (0.15 to 1.46)	0.82 (0.17 to 1.45)	0.83 (0.17 to 1.46)	0.92 (0.19 to 1.49)	0.94 (0.21 to 1.48)	0.94 (0.21 to 1.49)	0.95 (0.21 to 1.49)	0.96 (0.21 to 1.49)	0.99 (0.21 to 1.5)	**Fluspirilene**	NA	NA	0.77 (0.23 to 1.12)	NA	NA
0.7 (0.54 to 0.88)	**0.73 (0.57 to 0.89)**	0.8 (0.6 to 1.01)	**0.82 (0.68 to 0.95)**	**0.82 (0.67 to 0.97)**	0.91 (0.6 to 1.2)	0.93 (0.78 to 1.08)	0.93 (0.78 to 1.07)	0.94 (0.78 to 1.09)	0.95 (0.79 to 1.1)	0.98 (0.66 to 1.24)	0.99 (0.23 to 1.49)	**Quetiapine**	NA	NA	NA	**1.56 (1.35 to 1.75)**
0.56 (0.17 to 1.02)	0.58 (0.17 to 1.03)	0.64 (0.2 to 1.08)	0.65 (0.2 to 1.07)	0.65 (0.2 to 1.08)	0.73 (0.24 to 1.12)	0.75 (0.27 to 1.11)	0.75 (0.27 to 1.11)	0.76 (0.27 to 1.12)	0.76 (0.3 to 1.12)	0.78 (0.27 to 1.14)	0.79 (0.2 to 1.19)	0.8 (0.3 to 1.14)	**Pimozide**	0.97 (0.66 to 1.13)	NA	NA
0.53 (0.23 to 0.88)	**0.57 (0.26 to 0.89)**	**0.61 (0.26 to 0.97)**	**0.62 (0.3 to 0.94)**	**0.64 (0.3 to 0.95)**	0.7 (0.33 to 1.02)	**0.71 (0.38 to 1)**	0.72 (0.38 to 1.01)	0.72 (0.38 to 1.01)	0.73 (0.38 to 1.02)	0.76 (0.36 to 1.05)	0.77 (0.23 to 1.12)	0.77 (0.41 to 1.04)	0.97 (0.66 to 1.13)	**Fluphenazine**	NA	NA
0.5 (0.2 to 0.87)	**0.52 (0.2 to 0.88)**	**0.57 (0.2 to 0.94)**	**0.59 (0.25 to 0.93)**	**0.59 (0.25 to 0.93)**	**0.66 (0.25 to 0.99)**	**0.67 (0.3 to 0.97)**	**0.67 (0.3 to 0.98)**	**0.68 (0.3 to 0.98)**	**0.7 (0.3 to 0.98)**	**0.71 (0.38 to 0.96)**	0.72 (0.14 to 1.09)	0.72 (0.34 to 1)	0.9 (0.34 to 1.11)	0.94 (0.5 to 1.1)	**Placebo**	NA
1.08 (0.89 to 1.28)	1.12 (0.98 to 1.27)	1.24 (0.86 to 1.61)	**1.26 (1.14 to 1.38)**	**1.27 (1.08 to 1.46)**	1.41 (0.95 to 1.82)	**1.44 (1.29 to 1.58)**	**1.44 (1.29 to 1.58)**	**1.46 (1.31 to 1.6)**	**1.47 (1.29 to 1.65)**	**1.51 (1.07 to 1.88)**	1.53 (0.36 to 2.3)	**1.55 (1.35 to 1.72)**	**1.93 (1.04 to 2.32)**	**2 (1.44 to 2.28)**	**2.14 (1.56 to 2.36)**	**Olanzapine**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. We originally calculated odds ratios but then transformed them to relative risks which can be interpreted more easily. Thus, each cell provides the relative risk and the corresponding 95% confidence interval 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% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Forest plot of pairwise meta-analyses - drugs in the network. Results on the left side of the y-axis are in favour of the first mentioned drug



Forest plot of pairwise meta-analses - drugs outside the network. Results on the left side of the y-axis are in favour of the first mentioned drug

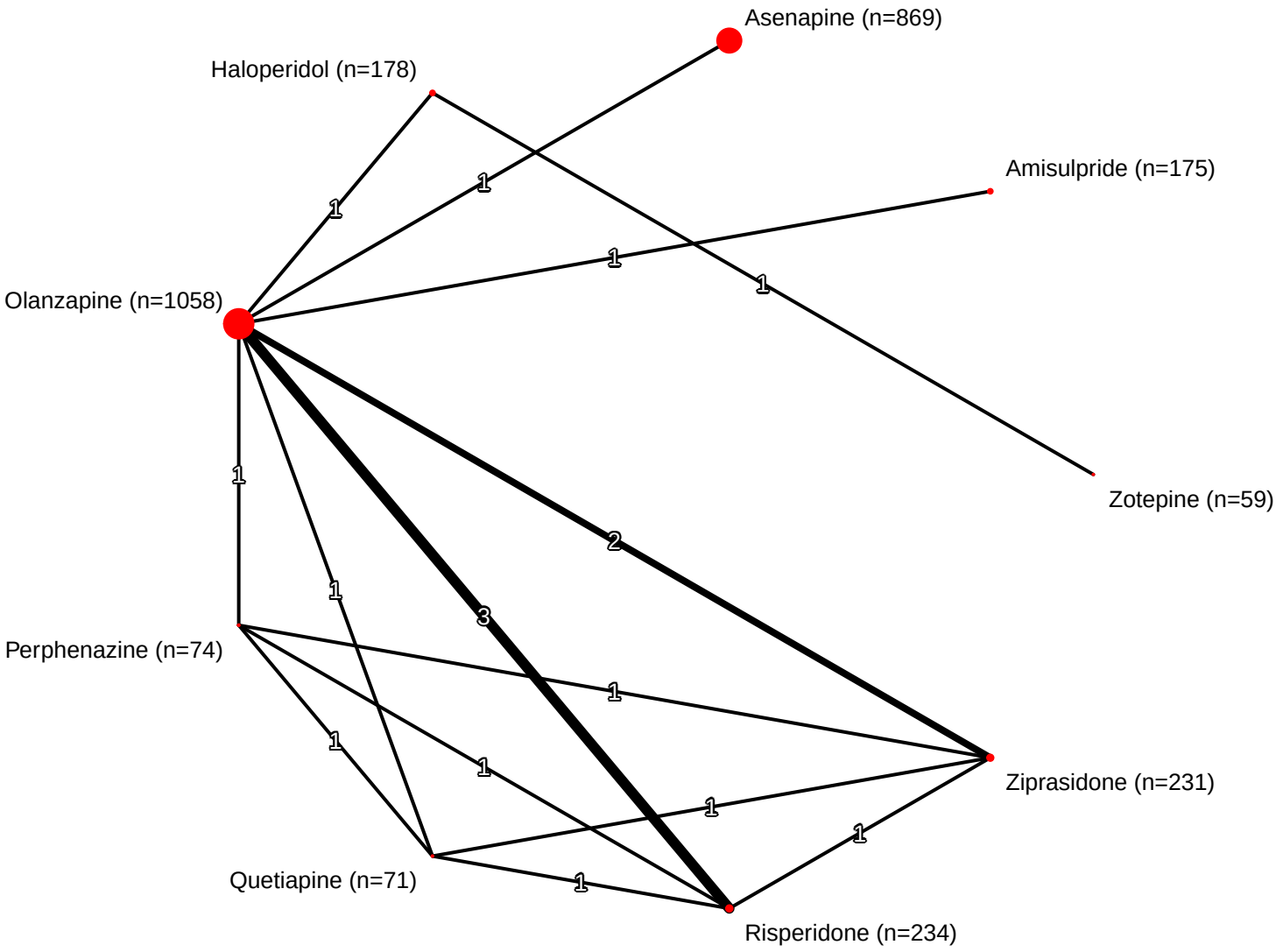


eAppendix 11

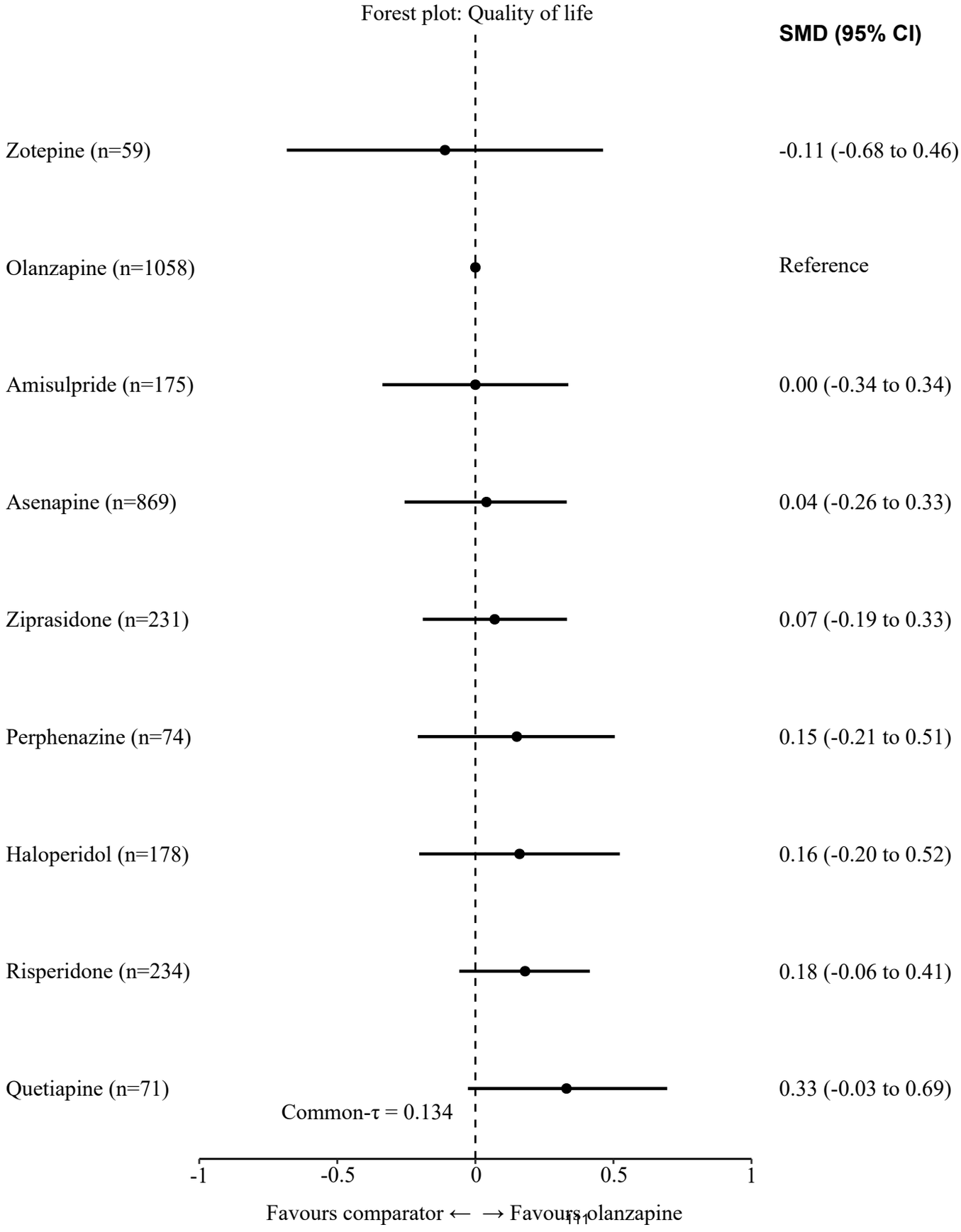
Quality of life

1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

Quality of life



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials


Forest plot: Quality of life
SMD (95% CI)
Zotepine (n=59)
-0.11 (-0.68 to 0.46)
Olanzapine (n=1058)
Reference
Amisulpride (n=175)
0.00 (-0.34 to 0.34)
Asenapine (n=869)
0.04 (-0.26 to 0.33)
Ziprasidone (n=231)
0.07 (-0.19 to 0.33)
Perphenazine (n=74)
0.15 (-0.21 to 0.51)
Haloperidol (n=178)
0.16 (-0.20 to 0.52)
Risperidone (n=234)
0.18 (-0.06 to 0.41)
Quetiapine (n=71)
0.33 (-0.03 to 0.69)
Common-τ = 0.134
-1
-0.5
0
0.5
1
Favours comparator ← → Favours olanzapine

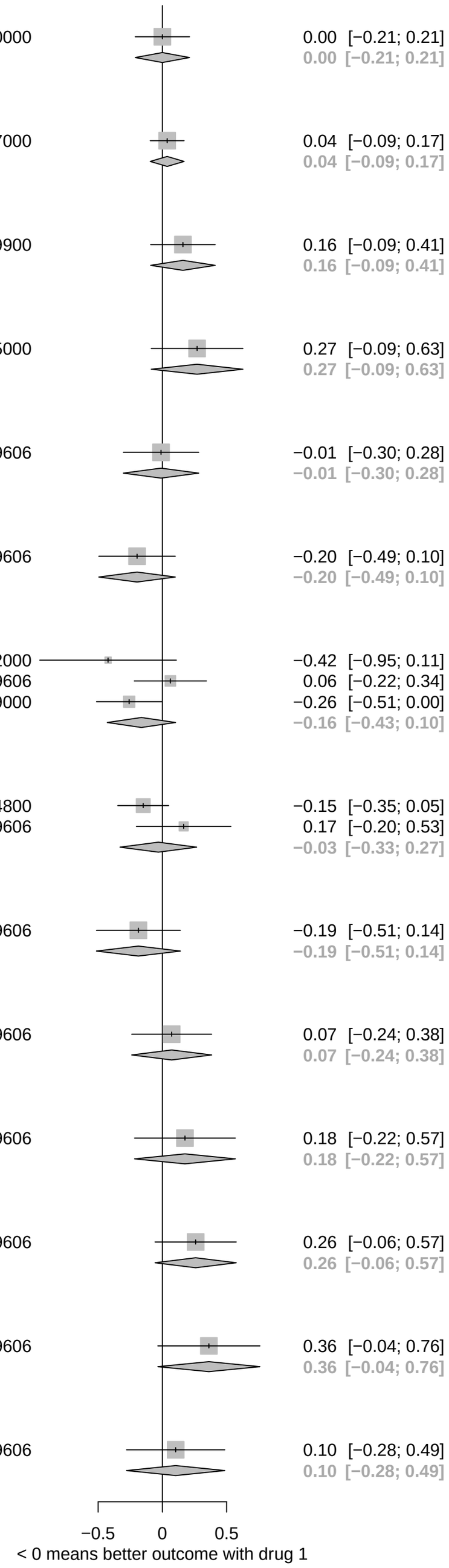
League table for the outcome: Quality of life

Zotepine	NA	NA	NA	NA	NA	-0.27 (-0.71 to 0.17)	NA	NA
-0.11 (-0.77 to 0.55)	**Amisulpride**	0.00 (-0.34 to 0.34)	NA	NA	NA	NA	NA	NA
-0.11 (-0.68 to 0.46)	-0.00 (-0.34 to 0.34)	**Olanzapine**	-0.04 (-0.33 to 0.26)	-0.04 (-0.31 to 0.23)	-0.01 (-0.40 to 0.38)	-0.16 (-0.52 to 0.20)	-0.16 (-0.40 to 0.08)	-0.20 (-0.59 to 0.20)
-0.15 (-0.79 to 0.50)	-0.04 (-0.48 to 0.41)	-0.04 (-0.33 to 0.26)	**Asenapine**	NA	NA	NA	NA	NA
-0.18 (-0.81 to 0.45)	-0.07 (-0.50 to 0.36)	-0.07 (-0.33 to 0.19)	-0.03 (-0.43 to 0.36)	**Ziprasidone**	-0.18 (-0.65 to 0.30)	NA	-0.10 (-0.57 to 0.36)	-0.36 (-0.84 to 0.11)
-0.26 (-0.93 to 0.42)	-0.15 (-0.64 to 0.34)	-0.15 (-0.51 to 0.21)	-0.11 (-0.57 to 0.35)	-0.08 (-0.48 to 0.32)	**Perphenazine**	NA	0.07 (-0.33 to 0.48)	-0.19 (-0.61 to 0.23)
-0.27 (-0.71 to 0.17)	-0.16 (-0.66 to 0.34)	-0.16 (-0.52 to 0.20)	-0.12 (-0.59 to 0.34)	-0.09 (-0.54 to 0.36)	-0.01 (-0.52 to 0.50)	**Haloperidol**	NA	NA
-0.29 (-0.91 to 0.33)	-0.18 (-0.59 to 0.23)	-0.18 (-0.41 to 0.06)	-0.14 (-0.52 to 0.24)	-0.11 (-0.43 to 0.22)	-0.03 (-0.40 to 0.34)	-0.02 (-0.45 to 0.42)	**Risperidone**	-0.26 (-0.67 to 0.15)
-0.44 (-1.12 to 0.23)	-0.33 (-0.83 to 0.16)	-0.33 (-0.69 to 0.03)	-0.30 (-0.76 to 0.17)	-0.26 (-0.67 to 0.14)	-0.19 (-0.60 to 0.23)	-0.17 (-0.69 to 0.34)	-0.16 (-0.53 to 0.22)	**Quetiapine**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always + except for zotepine, but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Forest plot of pairwise meta-analyses - drugs in the network. Results on the left side of the y-axis are in favour of the first mentioned drug

Study	Drug 1 Total	Drug 1 Mean	Drug 1 SD	Drug 2 Total	Drug 2 Mean	Drug 2 SD	SMD	95%−CI
Comparison = Amisulpride vs Olanzapine								
Mortimer 2004	175	−0.60	1.1000	170	−0.60	1.0000	0.00	[−0.21; 0.21]
Random effects model	**175**			**170**			**0.00**	**[−0.21; 0.21]**
Heterogeneity: not applicable								
Comparison = Asenapine vs Olanzapine								
Schoemaker 2010	869	−84.40	19.1000	297	−85.10	17.7000	0.04	[−0.09; 0.17]
Random effects model	**869**			**297**			**0.04**	**[−0.09; 0.17]**
Heterogeneity: not applicable								
Comparison = Haloperidol vs Olanzapine								
Kongsakon 2006	115	−62.52	22.0900	130	−66.14	22.9900	0.16	[−0.09; 0.41]
Random effects model	**115**			**130**			**0.16**	**[−0.09; 0.41]**
Heterogeneity: not applicable								
Comparison = Haloperidol vs Zotepine								
Laborde 2000	63	−1.90	19.0000	59	−7.00	18.5000	0.27	[−0.09; 0.63]
Random effects model	**63**			**59**			**0.27**	**[−0.09; 0.63]**
Heterogeneity: not applicable								
Comparison = Olanzapine vs Perphenazine								
Lieberman 2005_18months	113	−0.20	0.9606	74	−0.19	0.9606	−0.01	[−0.30; 0.28]
Random effects model	**113**			**74**			**−0.01**	**[−0.30; 0.28]**
Heterogeneity: not applicable								
Comparison = Olanzapine vs Quetiapine								
Lieberman 2005_18months	113	−0.20	0.9606	71	−0.01	0.9606	−0.20	[−0.49; 0.10]
Random effects model	**113**			**71**			**−0.20**	**[−0.49; 0.10]**
Heterogeneity: not applicable								
Comparison = Olanzapine vs Risperidone								
Gureje 2003	30	−11.90	13.4000	26	−4.90	19.2000	−0.42	[−0.95; 0.11]
Lieberman 2005_18months	113	−0.20	0.9606	86	−0.26	0.9606	0.06	[−0.22; 0.34]
Tran 1997	118	−13.40	18.6000	122	−8.80	16.9000	−0.26	[−0.51; 0.00]
Random effects model	**261**			**234**			**−0.16**	**[−0.43; 0.10]**
Heterogeneity: I^2 = 48.77%, τ^2 = 0.02651490, p = 0.14								
Comparison = Olanzapine vs Ziprasidone								
Breier 2005	200	−14.60	24.1600	193	−10.90	25.4800	−0.15	[−0.35; 0.05]
Lieberman 2005_18months	113	−0.20	0.9606	38	−0.36	0.9606	0.17	[−0.20; 0.53]
Random effects model	**313**			**231**			**−0.03**	**[−0.33; 0.27]**
Heterogeneity: I^2 = 54.04%, τ^2 = 0.02673030, p = 0.14								
Comparison = Perphenazine vs Quetiapine								
Lieberman 2005_18months	74	−0.19	0.9606	71	−0.01	0.9606	−0.19	[−0.51; 0.14]
Random effects model	**74**			**71**			**−0.19**	**[−0.51; 0.14]**
Heterogeneity: not applicable								
Comparison = Perphenazine vs Risperidone								
Lieberman 2005_18months	74	−0.19	0.9606	86	−0.26	0.9606	0.07	[−0.24; 0.38]
Random effects model	**74**			**86**			**0.07**	**[−0.24; 0.38]**
Heterogeneity: not applicable								
Comparison = Perphenazine vs Ziprasidone								
Lieberman 2005_18months	74	−0.19	0.9606	38	−0.36	0.9606	0.18	[−0.22; 0.57]
Random effects model	**74**			**38**			**0.18**	**[−0.22; 0.57]**
Heterogeneity: not applicable								
Comparison = Quetiapine vs Risperidone								
Lieberman 2005_18months	71	−0.01	0.9606	86	−0.26	0.9606	0.26	[−0.06; 0.57]
Random effects model	**71**			**86**			**0.26**	**[−0.06; 0.57]**
Heterogeneity: not applicable								
Comparison = Quetiapine vs Ziprasidone								
Lieberman 2005_18months	71	−0.01	0.9606	38	−0.36	0.9606	0.36	[−0.04; 0.76]
Random effects model	**71**			**38**			**0.36**	**[−0.04; 0.76]**
Heterogeneity: not applicable								
Comparison = Risperidone vs Ziprasidone								
Lieberman 2005_18months	86	−0.26	0.9606	38	−0.36	0.9606	0.10	[−0.28; 0.49]
Random effects model	**86**			**38**			**0.10**	**[−0.28; 0.49]**
Heterogeneity: not applicable								

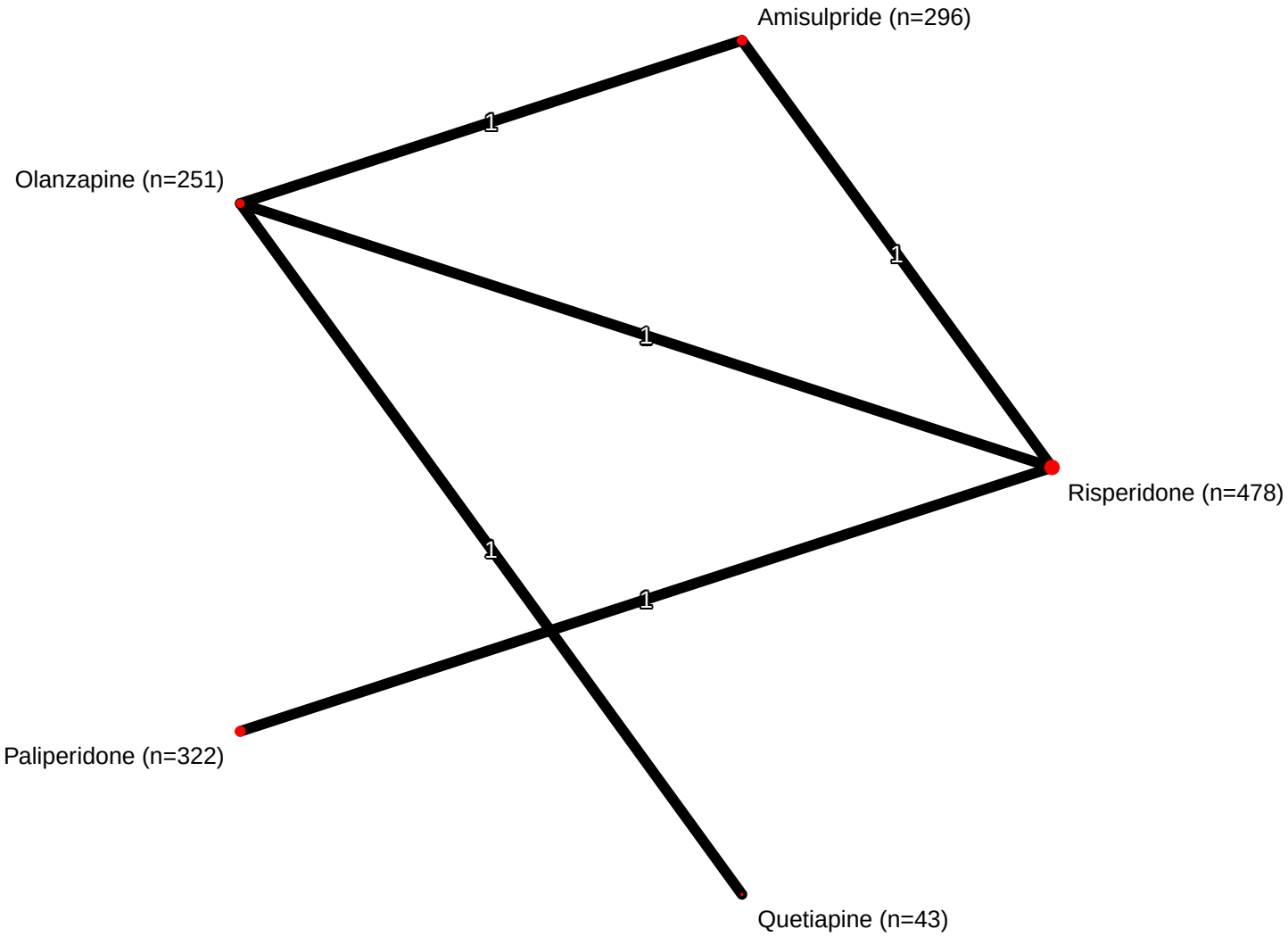


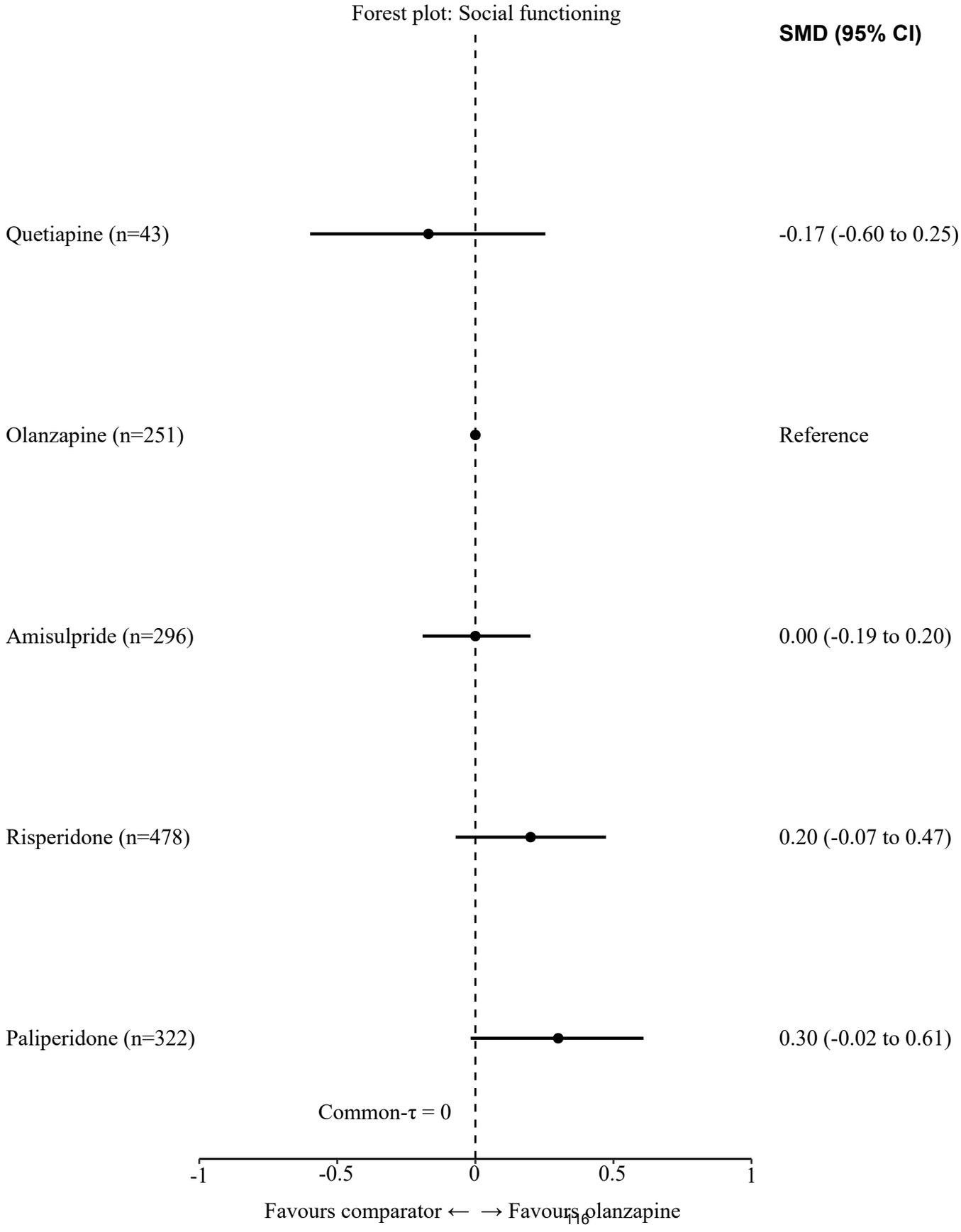
eAppendix 12

Functioning

1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

Social functioning



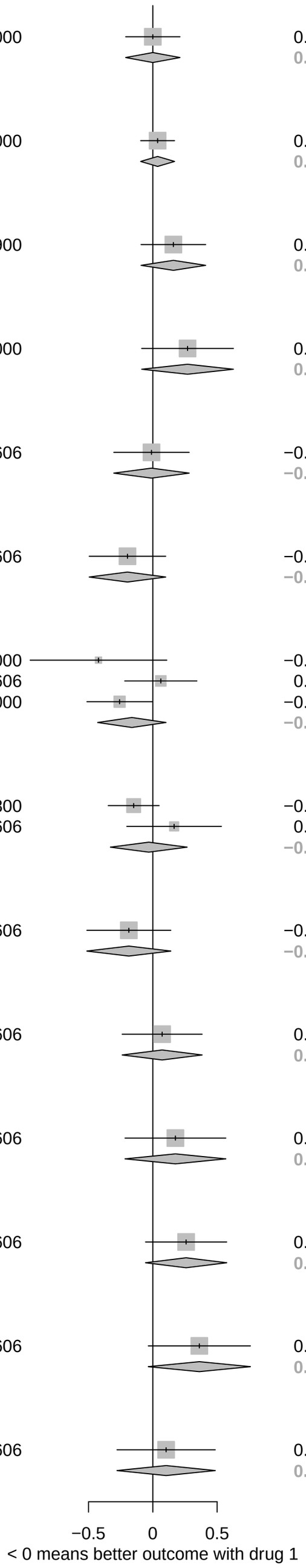

Forest plot: Social functioning
SMD (95% CI)
Quetiapine (n=43)
-0.17 (-0.60 to 0.25)
Olanzapine (n=251)
Reference
Amisulpride (n=296)
0.00 (-0.19 to 0.20)
Risperidone (n=478)
0.20 (-0.07 to 0.47)
Paliperidone (n=322)
0.30 (-0.02 to 0.61)
Common-τ = 0
-1
-0.5
0
0.5
1
Favours comparator ← → Favours olanzapine

League table for the outcome: Social functioning

Quetiapine	-0.17 (-0.60 to 0.25)	NA	NA	NA
-0.17 (-0.60 to 0.25)	**Olanzapine**	-0.00 (-0.21 to 0.21)	-0.20 (-0.69 to 0.29)	NA
-0.18 (-0.65 to 0.29)	-0.00 (-0.20 to 0.19)	**Amisulpride**	-0.20 (-0.45 to 0.06)	NA
-0.37 (-0.88 to 0.13)	-0.20 (-0.47 to 0.07)	-0.20 (-0.42 to 0.03)	**Risperidone**	-0.09 (-0.25 to 0.06)
-0.47 (-1.00 to 0.06)	-0.30 (-0.61 to 0.02)	**-0.29 (-0.57 to -0.02)**	-0.09 (-0.25 to 0.06)	**Paliperidone**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why in the figure the sign of all comparisons with olanzapine was always + except for quetiapine, but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available. It should be noted that teh 95% CI of amisulpride compared to paliperidone excluded 1 and thus made opposite effects unlikely. Nevertheless, the upper limit of the 95% CI was close to 1 (-0.02) and this evidence was entirely indirect.

Study	Drug 1 Total	Drug 1 Mean	Drug 1 SD	Drug 2 Total	Drug 2 Mean	Drug 2 SD	Quality of life	SMD	95%−CI
Comparison = Amisulpride vs Olanzapine									
Mortimer 2004	175	−0.60	1.1000	170	−0.60	1.0000		0.00	[−0.21; 0.21]
Random effects model	**175**			**170**				**0.00**	**[−0.21; 0.21]**
Heterogeneity: not applicable									
Comparison = Asenapine vs Olanzapine									
Schoemaker 2010	869	−84.40	19.1000	297	−85.10	17.7000		0.04	[−0.09; 0.17]
Random effects model	**869**			**297**				**0.04**	**[−0.09; 0.17]**
Heterogeneity: not applicable									
Comparison = Haloperidol vs Olanzapine									
Kongsakon 2006	115	−62.52	22.0900	130	−66.14	22.9900		0.16	[−0.09; 0.41]
Random effects model	**115**			**130**				**0.16**	**[−0.09; 0.41]**
Heterogeneity: not applicable									
Comparison = Haloperidol vs Zotepine									
Laborde 2000	63	−1.90	19.0000	59	−7.00	18.5000		0.27	[−0.09; 0.63]
Random effects model	**63**			**59**				**0.27**	**[−0.09; 0.63]**
Heterogeneity: not applicable									
Comparison = Olanzapine vs Perphenazine									
Lieberman 2005_18months	113	−0.20	0.9606	74	−0.19	0.9606		−0.01	[−0.30; 0.28]
Random effects model	**113**			**74**				**−0.01**	**[−0.30; 0.28]**
Heterogeneity: not applicable									
Comparison = Olanzapine vs Quetiapine									
Lieberman 2005_18months	113	−0.20	0.9606	71	−0.01	0.9606		−0.20	[−0.49; 0.10]
Random effects model	**113**			**71**				**−0.20**	**[−0.49; 0.10]**
Heterogeneity: not applicable									
Comparison = Olanzapine vs Risperidone									
Gureje 2003	30	−11.90	13.4000	26	−4.90	19.2000		−0.42	[−0.95; 0.11]
Lieberman 2005_18months	113	−0.20	0.9606	86	−0.26	0.9606		0.06	[−0.22; 0.34]
Tran 1997	118	−13.40	18.6000	122	−8.80	16.9000		−0.26	[−0.51; 0.00]
Random effects model	**261**			**234**				**−0.16**	**[−0.43; 0.10]**
Heterogeneity: I^2 = 48.77%, τ^2 = 0.02651490, p = 0.14									
Comparison = Olanzapine vs Ziprasidone									
Breier 2005	200	−14.60	24.1600	193	−10.90	25.4800		−0.15	[−0.35; 0.05]
Lieberman 2005_18months	113	−0.20	0.9606	38	−0.36	0.9606		0.17	[−0.20; 0.53]
Random effects model	**313**			**231**				**−0.03**	**[−0.33; 0.27]**
Heterogeneity: I^2 = 54.04%, τ^2 = 0.02673030, p = 0.14									
Comparison = Perphenazine vs Quetiapine									
Lieberman 2005_18months	74	−0.19	0.9606	71	−0.01	0.9606		−0.19	[−0.51; 0.14]
Random effects model	**74**			**71**				**−0.19**	**[−0.51; 0.14]**
Heterogeneity: not applicable									
Comparison = Perphenazine vs Risperidone									
Lieberman 2005_18months	74	−0.19	0.9606	86	−0.26	0.9606		0.07	[−0.24; 0.38]
Random effects model	**74**			**86**				**0.07**	**[−0.24; 0.38]**
Heterogeneity: not applicable									
Comparison = Perphenazine vs Ziprasidone									
Lieberman 2005_18months	74	−0.19	0.9606	38	−0.36	0.9606		0.18	[−0.22; 0.57]
Random effects model	**74**			**38**				**0.18**	**[−0.22; 0.57]**
Heterogeneity: not applicable									
Comparison = Quetiapine vs Risperidone									
Lieberman 2005_18months	71	−0.01	0.9606	86	−0.26	0.9606		0.26	[−0.06; 0.57]
Random effects model	**71**			**86**				**0.26**	**[−0.06; 0.57]**
Heterogeneity: not applicable									
Comparison = Quetiapine vs Ziprasidone									
Lieberman 2005_18months	71	−0.01	0.9606	38	−0.36	0.9606		0.36	[−0.04; 0.76]
Random effects model	**71**			**38**				**0.36**	**[−0.04; 0.76]**
Heterogeneity: not applicable									
Comparison = Risperidone vs Ziprasidone									
Lieberman 2005_18months	86	−0.26	0.9606	38	−0.36	0.9606		0.10	[−0.28; 0.49]
Random effects model	**86**			**38**				**0.10**	**[−0.28; 0.49]**
Heterogeneity: not applicable									

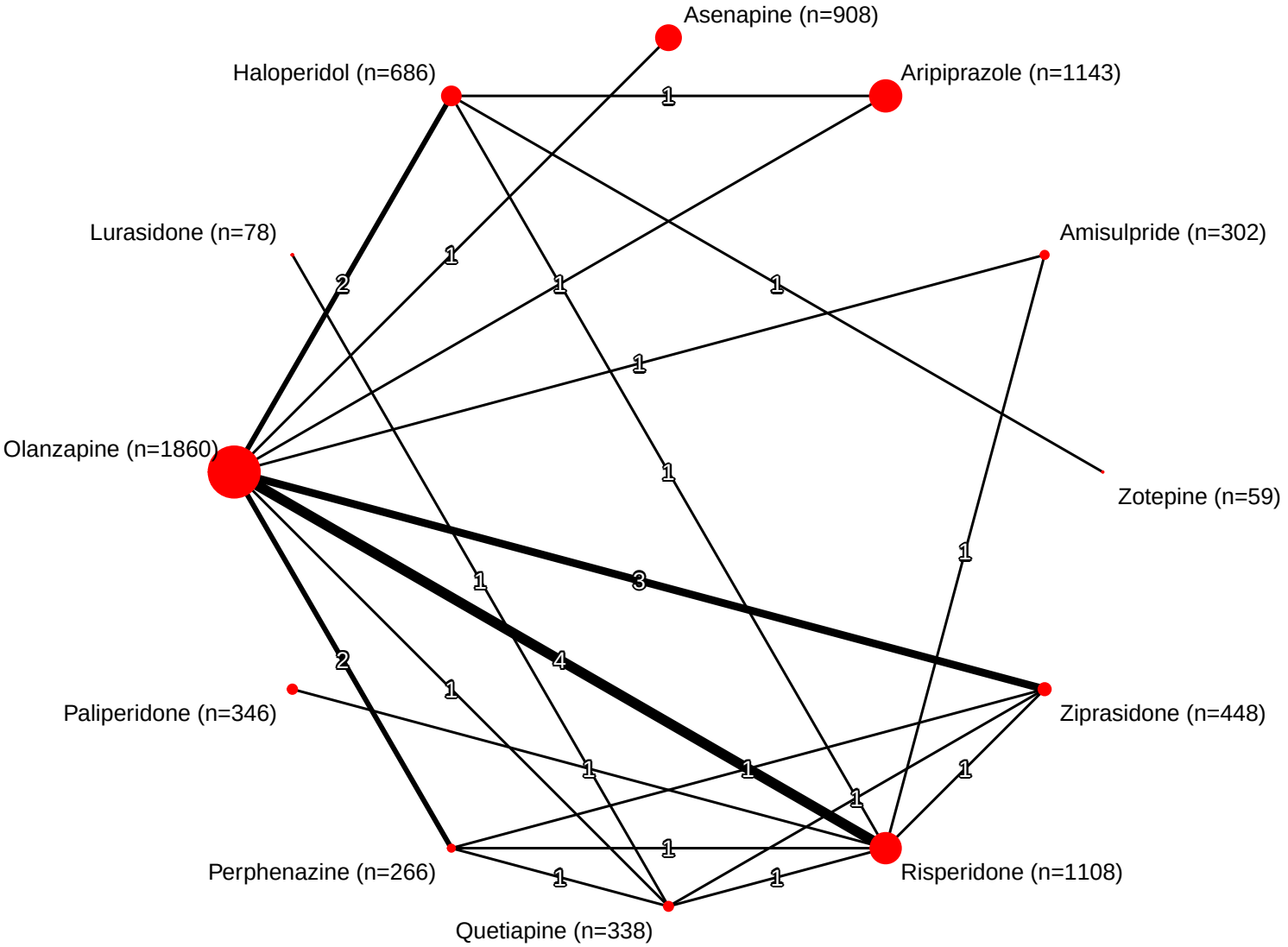


eAppendix 13

Weight gain

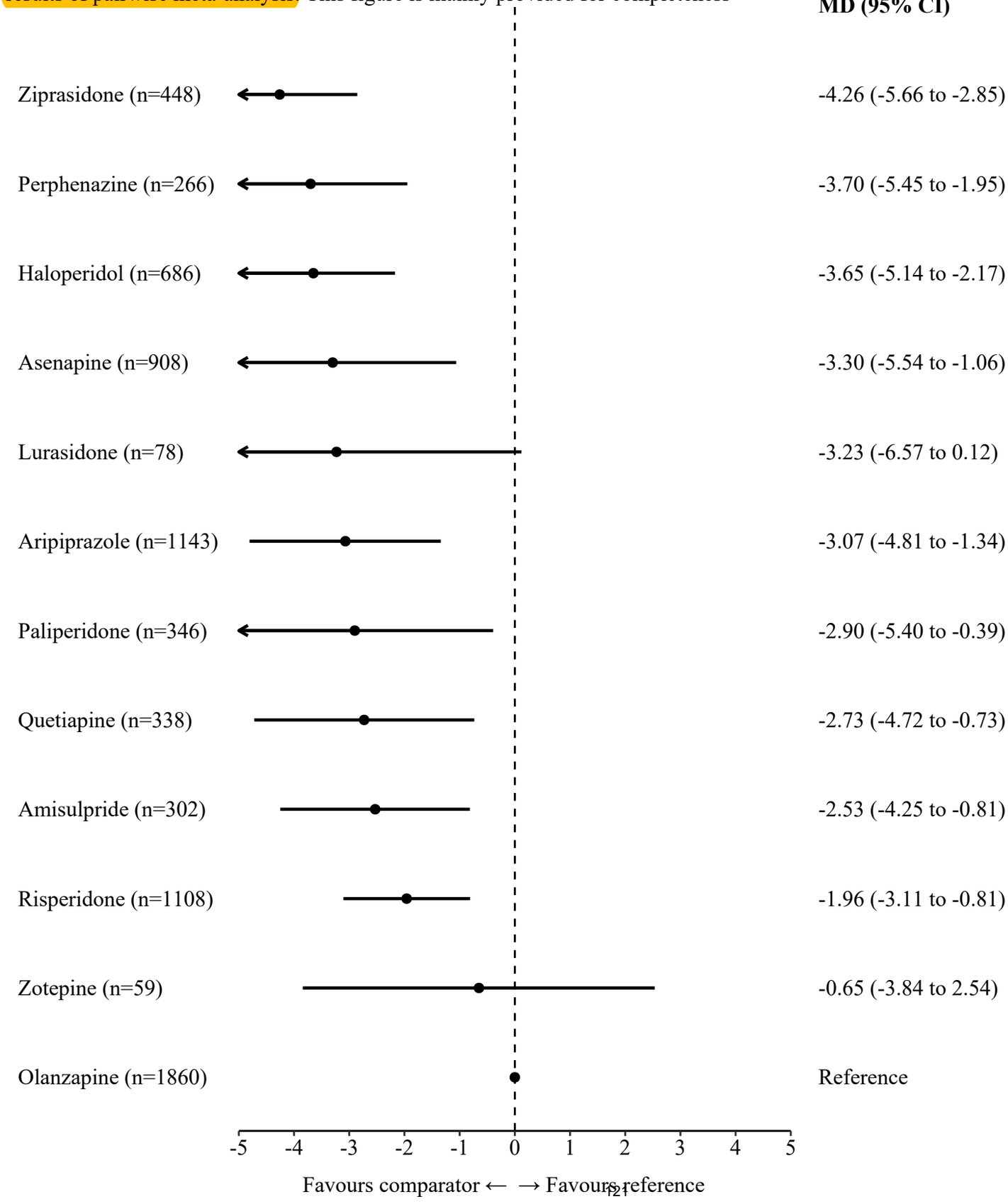
1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

Change in weight



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials

Change in weight It should be noted that the data were inconsistent. Readers should therefore focus on the results of pairwise meta-analysis. This figure is mainly provided for completeness



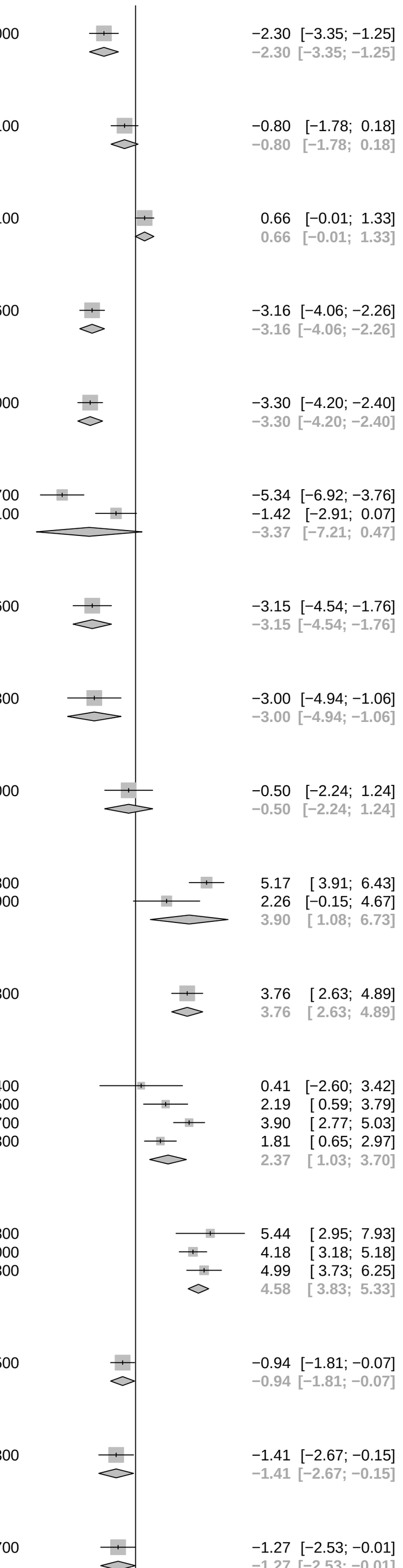
League table for the outcome: Change in weight It should be noted that the data were inconsistent. Readers should therefore focus on the results of pairwise meta-analysis. This table is mainly provided for completeness

Ziprasidone	0.18 (-2.29 to 2.65)	NA	NA	NA	NA	NA	-1.23 (-3.64 to 1.18)	NA	-1.09 (-3.50 to 1.32)	NA	**-4.75 (-6.22 to -3.27)**
-0.56 (-2.57 to 1.45)	**Perphenazine**	NA	NA	NA	NA	NA	-1.41 (-3.82 to 1.00)	NA	-1.27 (-3.68 to 1.14)	NA	**-4.10 (-6.02 to -2.19)**
-0.60 (-2.62 to 1.41)	-0.05 (-2.30 to 2.21)	**Haloperidol**	NA	NA	-0.66 (-2.82 to 1.50)	NA	NA	NA	**-3.15 (-5.63 to -0.67)**	**-3.00 (-5.82 to -0.18)**	**-3.34 (-5.15 to -1.53)**
-0.96 (-3.60 to 1.68)	-0.40 (-3.24 to 2.44)	-0.35 (-3.04 to 2.33)	**Asenapine**	NA	NA	NA	NA	NA	NA	NA	**-3.30 (-5.54 to -1.06)**
-1.03 (-4.48 to 2.41)	-0.47 (-3.99 to 3.05)	-0.43 (-4.05 to 3.20)	-0.07 (-4.10 to 3.95)	**Lurasidone**	NA	NA	-0.50 (-3.19 to 2.19)	NA	NA	NA	NA
-1.18 (-3.40 to 1.03)	-0.62 (-3.07 to 1.82)	-0.58 (-2.29 to 1.13)	-0.23 (-3.06 to 2.60)	-0.15 (-3.91 to 3.60)	**Aripiprazole**	NA	NA	NA	NA	NA	**-3.16 (-5.40 to -0.92)**
-1.36 (-4.14 to 1.42)	-0.80 (-3.73 to 2.13)	-0.76 (-3.56 to 2.04)	-0.40 (-3.76 to 2.96)	-0.33 (-4.39 to 3.73)	-0.18 (-3.17 to 2.82)	**Paliperidone**	NA	NA	-0.94 (-3.17 to 1.29)	NA	NA
-1.53 (-3.68 to 0.62)	-0.97 (-3.24 to 1.30)	-0.93 (-3.36 to 1.51)	-0.57 (-3.57 to 2.42)	-0.50 (-3.19 to 2.19)	-0.35 (-2.96 to 2.27)	-0.17 (-3.21 to 2.87)	**Quetiapine**	NA	0.14 (-2.20 to 2.48)	NA	**-3.76 (-6.10 to -1.42)**
-1.73 (-3.88 to 0.43)	-1.17 (-3.54 to 1.21)	-1.12 (-3.32 to 1.08)	-0.77 (-3.59 to 2.05)	-0.70 (-4.39 to 3.00)	-0.54 (-2.95 to 1.86)	-0.37 (-3.18 to 2.44)	-0.20 (-2.73 to 2.34)	**Amisulpride**	-0.80 (-3.07 to 1.47)	NA	-2.30 (-4.60 to 0.00)
-2.30 (-3.96 to -0.64)	-1.74 (-3.64 to 0.16)	-1.70 (-3.39 to 0.00)	-1.34 (-3.86 to 1.17)	-1.27 (-4.66 to 2.12)	-1.12 (-3.11 to 0.88)	-0.94 (-3.17 to 1.29)	-0.77 (-2.84 to 1.30)	-0.57 (-2.29 to 1.14)	**Risperidone**	NA	**-2.38 (-3.68 to -1.07)**
-3.60 (-7.07 to -0.14)	-3.05 (-6.66 to 0.57)	**-3.00 (-5.82 to -0.18)**	-2.65 (-6.54 to 1.25)	-2.57 (-7.17 to 2.02)	-2.42 (-5.72 to 0.88)	-2.24 (-6.22 to 1.73)	-2.07 (-5.80 to 1.65)	-1.88 (-5.46 to 1.70)	-1.30 (-4.60 to 1.99)	**Zotepine**	NA
-4.26 (-5.66 to -2.85)	**-3.70 (-5.45 to -1.95)**	**-3.65 (-5.14 to -2.17)**	**-3.30 (-5.54 to -1.06)**	-3.23 (-6.57 to 0.12)	**-3.07 (-4.81 to -1.34)**	**-2.90 (-5.40 to -0.39)**	**-2.73 (-4.72 to -0.73)**	**-2.53 (-4.25 to -0.81)**	**-1.96 (-3.11 to -0.81)**	-0.65 (-3.84 to 2.54)	**Olanzapine**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Forest plot of pairwise meta-analyses drugs in the network. Results on the left side of the y-axis are in favour of the first mentioned drug

Study	Drug 1 Total	Drug 1 Mean	Drug 1 SD	Drug 2 Total	Drug 2 Mean	Drug 2 SD	Change in weight	MD	95%−CI
Comparison = Amisulpride vs Olanzapine									
Mortimer 2004	181	1.60	4.9000	181	3.90	5.3000		−2.30	[−3.35; −1.25]
Random effects model	**181**			**181**				**−2.30**	**[−3.35; −1.25]**
Heterogeneity: not applicable									
Comparison = Amisulpride vs Risperidone									
Sechter 2002	121	1.30	3.9100	123	2.10	3.9100		−0.80	[−1.78; 0.18]
Random effects model	**121**			**123**				**−0.80**	**[−1.78; 0.18]**
Heterogeneity: not applicable									
Comparison = Aripiprazole vs Haloperidol									
Kasper 2003	858	1.05	5.8600	431	0.39	5.8100		0.66	[−0.01; 1.33]
Random effects model	**858**			**431**				**0.66**	**[−0.01; 1.33]**
Heterogeneity: not applicable									
Comparison = Aripiprazole vs Olanzapine									
Kane 2009_28 weeks	285	0.26	5.4600	281	3.42	5.4600		−3.16	[−4.06; −2.26]
Random effects model	**285**			**281**				**−3.16**	**[−4.06; −2.26]**
Heterogeneity: not applicable									
Comparison = Asenapine vs Olanzapine									
Schoemaker 2010	908	0.90	4.8000	311	4.20	7.6000		−3.30	[−4.20; −2.40]
Random effects model	**908**			**311**				**−3.30**	**[−4.20; −2.40]**
Heterogeneity: not applicable									
Comparison = Haloperidol vs Olanzapine									
Keefe 2006	94	−2.34	4.8000	152	3.00	7.8700		−5.34	[−6.92; −3.76]
Kongsakon 2006	95	2.58	5.5500	115	4.00	5.4100		−1.42	[−2.91; 0.07]
Random effects model	**189**			**267**				**−3.37**	**[−7.21; 0.47]**
Heterogeneity: I^2 = 91.99%, τ^2 = 7.06753598, p < 0.01									
Comparison = Haloperidol vs Risperidone									
Keefe 2006	94	−2.34	4.8000	150	0.81	6.2600		−3.15	[−4.54; −1.76]
Random effects model	**94**			**150**				**−3.15**	**[−4.54; −1.76]**
Heterogeneity: not applicable									
Comparison = Haloperidol vs Zotepine									
Laborde 2000	66	−0.50	5.5300	59	2.50	5.5300		−3.00	[−4.94; −1.06]
Random effects model	**66**			**59**				**−3.00**	**[−4.94; −1.06]**
Heterogeneity: not applicable									
Comparison = Lurasidone vs Quetiapine									
Loebel 2013_12m	78	0.70	3.4000	33	1.20	4.6000		−0.50	[−2.24; 1.24]
Random effects model	**78**			**33**				**−0.50**	**[−2.24; 1.24]**
Heterogeneity: not applicable									
Comparison = Olanzapine vs Perphenazine									
Lieberman 2005_18months	307	4.26	7.1500	243	−0.91	7.7800		5.17	[3.91; 6.43]
Naukkarinen 2000	23	2.63	4.9700	23	0.37	3.1900		2.26	[−0.15; 4.67]
Random effects model	**330**			**266**				**3.90**	**[1.08; 6.73]**
Heterogeneity: I^2 = 77.18%, τ^2 = 3.26804891, p = 0.04									
Comparison = Olanzapine vs Quetiapine									
Lieberman 2005_18months	307	4.26	7.1500	305	0.50	7.1300		3.76	[2.63; 4.89]
Random effects model	**307**			**305**				**3.76**	**[2.63; 4.89]**
Heterogeneity: not applicable									
Comparison = Olanzapine vs Risperidone									
Gureje 2003	32	4.88	7.4000	32	4.47	4.5400		0.41	[−2.60; 3.42]
Keefe 2006	152	3.00	7.8700	150	0.81	6.2600		2.19	[0.59; 3.79]
Lieberman 2005_18months	307	4.26	7.1500	300	0.36	7.0700		3.90	[2.77; 5.03]
Tran 1997	166	4.13	5.8800	165	2.32	4.8300		1.81	[0.65; 2.97]
Random effects model	**657**			**647**				**2.37**	**[1.03; 3.70]**
Heterogeneity: I^2 = 67.19%, τ^2 = 1.16763361, p = 0.03									
Comparison = Olanzapine vs Ziprasidone									
Alvarez 2012	23	5.36	4.4800	27	−0.08	4.4800		5.44	[2.95; 7.93]
Breier 2005	269	3.06	6.8700	260	−1.12	4.7000		4.18	[3.18; 5.18]
Lieberman 2005_18months	307	4.26	7.1500	161	−0.73	6.3300		4.99	[3.73; 6.25]
Random effects model	**599**			**448**				**4.58**	**[3.83; 5.33]**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.48									
Comparison = Paliperidone vs Risperidone									
NCT00210717	346	−0.17	6.0100	338	0.77	5.6500		−0.94	[−1.81; −0.07]
Random effects model	**346**			**338**				**−0.94**	**[−1.81; −0.07]**
Heterogeneity: not applicable									
Comparison = Perphenazine vs Quetiapine									
Lieberman 2005_18months	243	−0.91	7.7800	305	0.50	7.1300		−1.41	[−2.67; −0.15]
Random effects model	**243**			**305**				**−1.41**	**[−2.67; −0.15]**
Heterogeneity: not applicable									
Comparison = Perphenazine vs Risperidone									
Lieberman 2005_18months	243	−0.91	7.7800	300	0.36	7.0700		−1.27	[−2.53; −0.01]
Random effects model	**243**			**300**				**−1.27**	**[−2.53; −0.01]**
Heterogeneity: not applicable									
Comparison = Perphenazine vs Ziprasidone									
Lieberman 2005_18months	243	−0.91	7.7800	161	−0.73	6.3300		−0.18	[−1.56; 1.20]
Random effects model	**243**			**161**				**−0.18**	**[−1.56; 1.20]**
Heterogeneity: not applicable									
Comparison = Quetiapine vs Risperidone									
Lieberman 2005_18months	305	0.50	7.1300	300	0.36	7.0700		0.14	[−0.99; 1.27]
Random effects model	**305**			**300**				**0.14**	**[−0.99; 1.27]**
Heterogeneity: not applicable									
Comparison = Quetiapine vs Ziprasidone									
Lieberman 2005_18months	305	0.50	7.1300	161	−0.73	6.3300		1.23	[−0.03; 2.49]
Random effects model	**305**			**161**				**1.23**	**[−0.03; 2.49]**
Heterogeneity: not applicable									
Comparison = Risperidone vs Ziprasidone									
Lieberman 2005_18months	300	0.36	7.0700	161	−0.73	6.3300		1.09	[−0.17; 2.35]
Random effects model	**300**			**161**				**1.09**	**[−0.17; 2.35]**
Heterogeneity: not applicable									

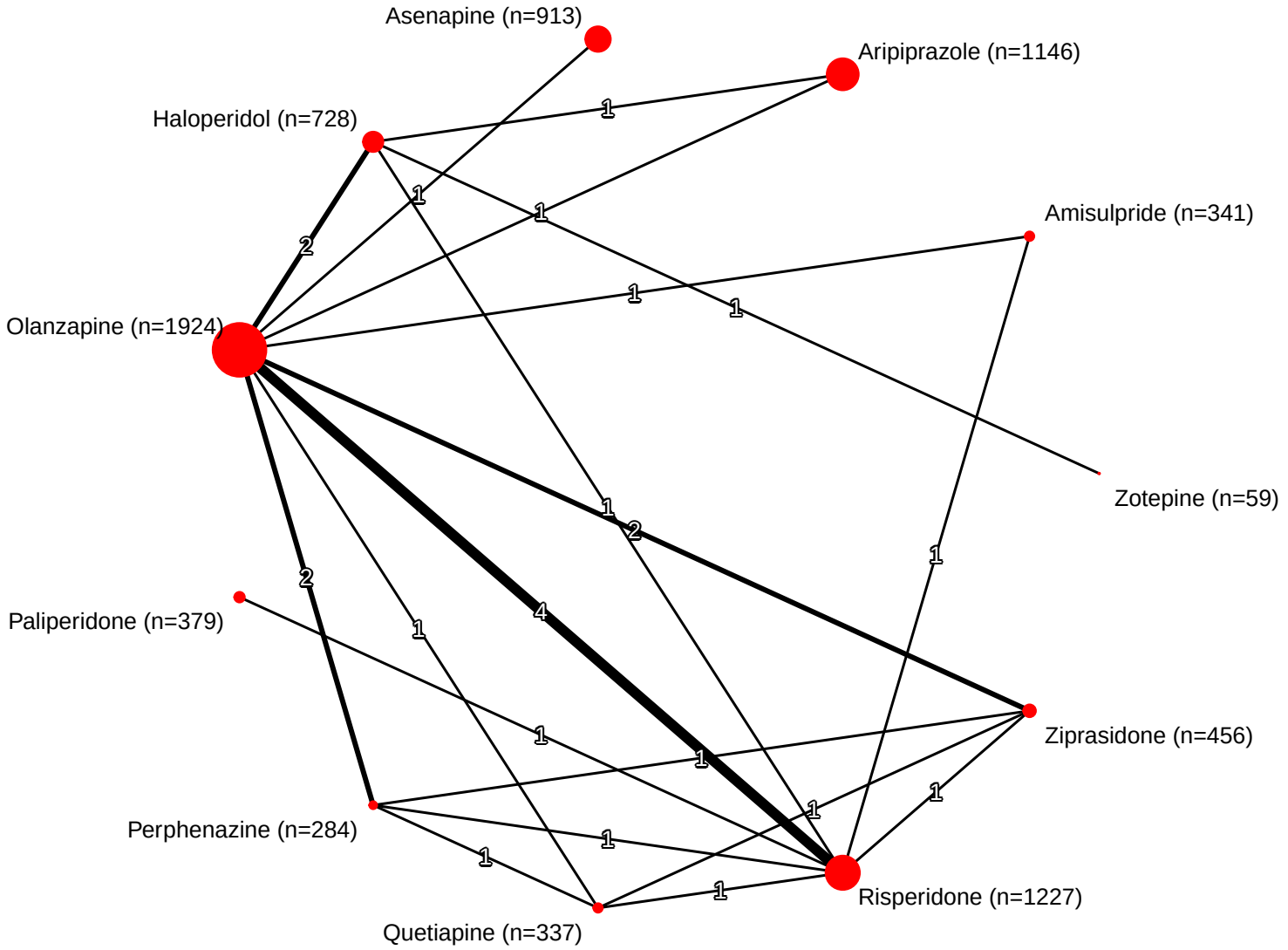


eAppendix 14

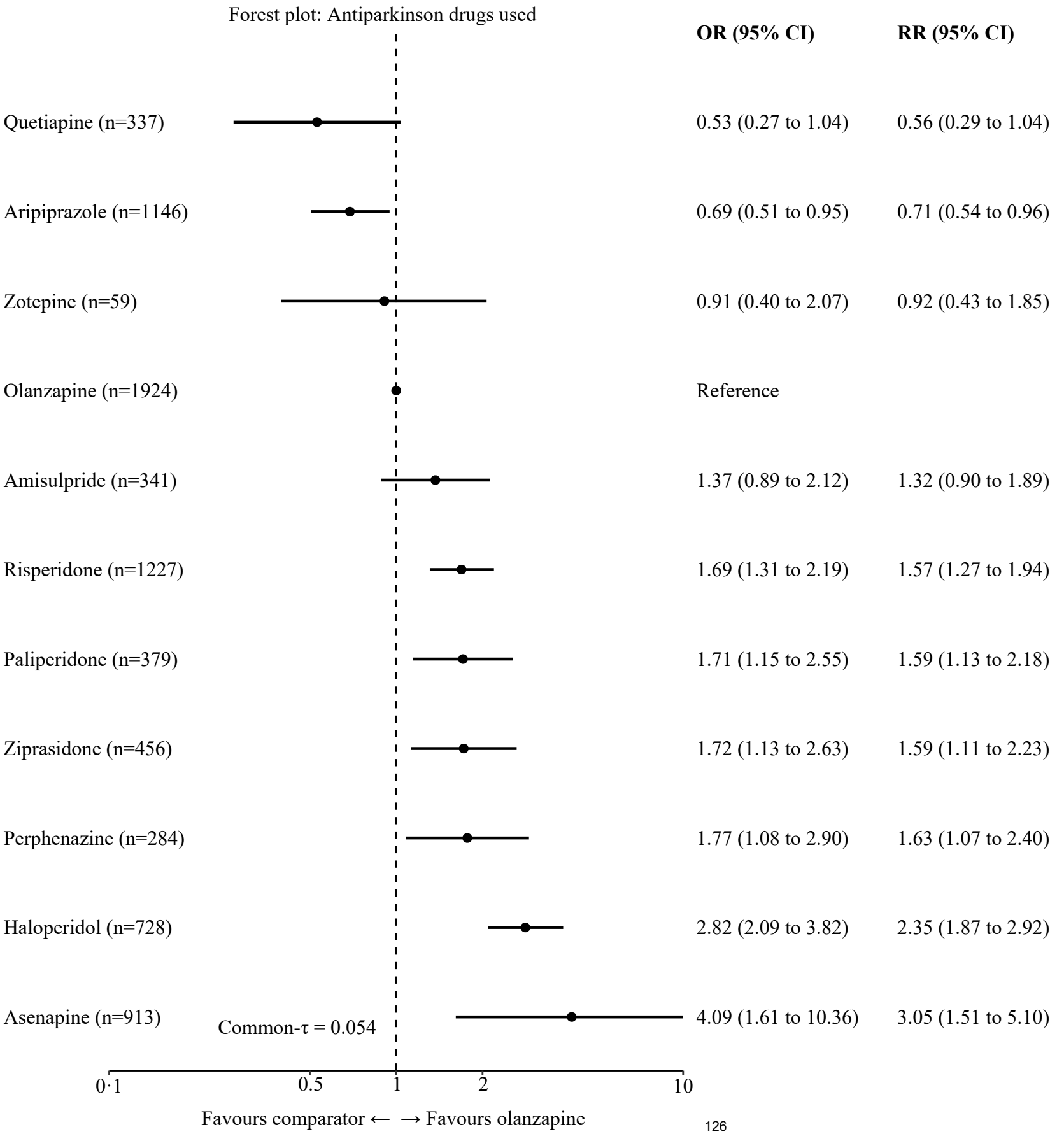
Antiparkinson medication

1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

Antiparkinson drugs used



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials



1.The poor result of asenapine was unexpected and needs a comment. Asenapine is only connected with the rest of the network via olanzapine (see network plot above). Thus, its estimate was driven by a single large trial (1) in which three times more asenapine treateted patients used antiparkinson medication medication than olanzapine treated patients, but this happened at a very low level (6% vs 2%, Schoemaker et al. 2010 (1)). The very wide confidence interval must also be considered.

2. Moreover, unlike in short-term (2) and relapse prevention network meta-analyses (3,4) aripiprazole was better than olanzapine concerning antiparkinson medication use. This result was based on indirect evidence from a trial in which aripiprazole was markedly better than haloperidol (5). In a large direct comparison with olanzapine (6) there was no difference (see pairwise meta-analyses two pages after this one).

References

1.Schoemaker J et al. Long-term assessment of Asenapine vs. Olanzapine in patients with schizophrenia or schizoaffective disorder. Pharmacopsychiatry. 2010;43(4):138-146

2. Huhn et al. Comparative efficacy and tolerability of 32 oral antipsychotics for the acute treatment of adults with multi-episode schizophrenia: a systematic review and network meta-analysis. Lancet 2019; 394(10202): 939-51.

3. Schneider-Thoma et al. Comparative efficacy and tolerability of 32 oral and long-acting injectable antipsychotics for the maintenance treatment of adults with schizophrenia: a systematic review and network meta-analysis. Lancet 2022; 399(10327): 824-36.

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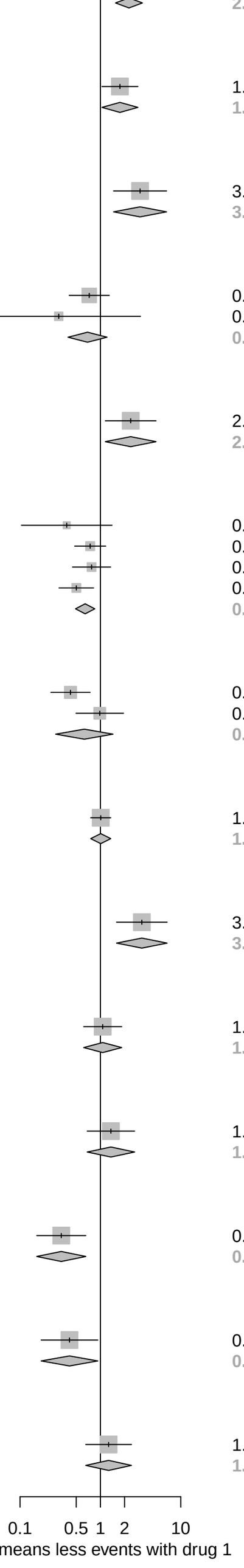
League table for the outcome: Antiparkinson medication used at least once - relative risk (in the figure above both relative risks and odds ratios are shown)

Quetiapine	NA	NA	NA	**0.37 (0.19 to 0.7)**	NA	**0.46 (0.21 to 0.94)**	**0.34 (0.18 to 0.67)**	NA	NA	**0.45 (0.22 to 0.88)**
0.78 (0.39 to 1.53)	**Aripiprazole**	NA	NA	NA	NA	NA	NA	**0.29 (0.22 to 0.37)**	NA	0.86 (0.58 to 1.25)
0.62 (0.22 to 1.57)	0.78 (0.36 to 1.6)	**Zotepine**	NA	NA	NA	NA	NA	**0.39 (0.19 to 0.75)**	NA	NA
0.43 (0.2 to 0.86)	**0.55 (0.33 to 0.88)**	0.69 (0.29 to 1.52)	**Amisulpride**	0.77 (0.49 to 1.18)	NA	NA	NA	NA	NA	1.5 (0.85 to 2.51)
0.35 (0.19 to 0.65)	**0.46 (0.32 to 0.64)**	0.59 (0.27 to 1.2)	0.84 (0.58 to 1.18)	**Risperidone**	0.99 (0.77 to 1.27)	1.21 (0.69 to 1.96)	0.95 (0.59 to 1.46)	**0.64 (0.41 to 0.98)**	NA	**1.46 (1.15 to 1.84)**
0.35 (0.18 to 0.69)	**0.46 (0.29 to 0.7)**	0.58 (0.25 to 1.24)	0.83 (0.53 to 1.27)	0.99 (0.77 to 1.27)	**Paliperidone**	NA	NA	NA	NA	NA
0.35 (0.18 to 0.68)	**0.45 (0.28 to 0.72)**	0.58 (0.24 to 1.26)	0.83 (0.49 to 1.34)	0.98 (0.66 to 1.42)	0.99 (0.62 to 1.53)	**Ziprasidone**	0.78 (0.42 to 1.36)	NA	NA	**1.56 (1.07 to 2.21)**
0.34 (0.17 to 0.67)	**0.44 (0.26 to 0.74)**	0.56 (0.23 to 1.26)	0.8 (0.46 to 1.34)	0.97 (0.63 to 1.42)	0.97 (0.59 to 1.53)	0.98 (0.59 to 1.54)	**Perphenazine**	NA	NA	1.38 (0.84 to 2.18)
0.24 (0.12 to 0.46)	**0.31 (0.24 to 0.38)**	**0.39 (0.19 to 0.75)**	**0.55 (0.36 to 0.85)**	**0.67 (0.49 to 0.89)**	**0.68 (0.45 to 0.98)**	0.68 (0.43 to 1.01)	0.7 (0.43 to 1.08)	**Haloperidol**	NA	**1.99 (1.45 to 2.66)**
0.18 (0.06 to 0.51)	**0.24 (0.09 to 0.55)**	**0.3 (0.09 to 0.83)**	**0.44 (0.17 to 0.96)**	0.51 (0.22 to 1.06)	0.52 (0.21 to 1.09)	0.52 (0.21 to 1.11)	0.53 (0.21 to 1.15)	0.77 (0.35 to 1.44)	**Asenapine**	**3.05 (1.51 to 5.1)**
0.56 (0.29 to 1.04)	**0.71 (0.54 to 0.96)**	0.92 (0.43 to 1.85)	1.32 (0.9 to 1.89)	**1.57 (1.27 to 1.94)**	**1.59 (1.13 to 2.18)**	**1.59 (1.11 to 2.23)**	**1.63 (1.07 to 2.4)**	**2.35 (1.87 to 2.92)**	**3.05 (1.51 to 5.1)**	**Olanzapine**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. We originally calculated odds ratios but then transformed them to relative risks which can be interpreted more easily. Thus, each cell provides the relative risk and the corresponding 95% confidence interval 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% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Forest plot of pairwise meta-analses - drugs in the network. Results on the left side of the y-axis are in favour of the first mentioned drug

Study	Drug 1 Events	Drug 1 Total	Drug 2 Events	Drug 2 Total	Antiparkinson drugs used	OR	95%−CI
Comparison = Amisulpride vs Olanzapine							
Mortimer 2004	26	189	17	188		1.60	[0.84; 3.07]
Random effects model		**189**		**188**		**1.60**	**[0.84; 3.07]**
Heterogeneity: not applicable							
Comparison = Amisulpride vs Risperidone							
Sechter 2002	36	152	47	158		0.73	[0.44; 1.22]
Random effects model		**152**		**158**		**0.73**	**[0.44; 1.22]**
Heterogeneity: not applicable							
Comparison = Aripiprazole vs Haloperidol							
Kasper 2003	198	861	246	433		0.23	[0.18; 0.29]
Random effects model		**861**		**433**		**0.23**	**[0.18; 0.29]**
Heterogeneity: not applicable							
Comparison = Aripiprazole vs Olanzapine							
Kane 2009_28 weeks	53	285	60	281		0.84	[0.56; 1.27]
Random effects model		**285**		**281**		**0.84**	**[0.56; 1.27]**
Heterogeneity: not applicable							
Comparison = Asenapine vs Olanzapine							
Schoemaker 2010	57	913	5	312		4.09	[1.62; 10.29]
Random effects model		**913**		**312**		**4.09**	**[1.62; 10.29]**
Heterogeneity: not applicable							
Comparison = Haloperidol vs Olanzapine							
Keefe 2006	60	97	65	159		2.35	[1.40; 3.93]
Kongsakon 2006	40	132	24	144		2.17	[1.22; 3.86]
Random effects model		**229**		**303**		**2.27**	**[1.54; 3.33]**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.85							
Comparison = Haloperidol vs Risperidone							
Keefe 2006	60	97	76	158		1.75	[1.05; 2.93]
Random effects model		**97**		**158**		**1.75**	**[1.05; 2.93]**
Heterogeneity: not applicable							
Comparison = Haloperidol vs Zotepine							
Laborde 2000	34	66	15	59		3.12	[1.46; 6.66]
Random effects model		**66**		**59**		**3.12**	**[1.46; 6.66]**
Heterogeneity: not applicable							
Comparison = Olanzapine vs Perphenazine							
Lieberman 2005_18months	25	336	26	261		0.73	[0.41; 1.29]
Naukkarinen 2000	1	23	3	23		0.30	[0.03; 3.15]
Random effects model		**359**		**284**		**0.69**	**[0.40; 1.21]**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.48							
Comparison = Olanzapine vs Quetiapine							
Lieberman 2005_18months	25	336	11	337		2.38	[1.15; 4.92]
Random effects model		**336**		**337**		**2.38**	**[1.15; 4.92]**
Heterogeneity: not applicable							
Comparison = Olanzapine vs Risperidone							
Gureje 2003	4	32	9	33		0.38	[0.10; 1.39]
Keefe 2006	65	159	76	158		0.75	[0.48; 1.16]
Lieberman 2005_18months	25	336	32	341		0.78	[0.45; 1.34]
Tran 1997	34	172	55	167		0.50	[0.31; 0.82]
Random effects model		**699**		**699**		**0.65**	**[0.49; 0.85]**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.48							
Comparison = Olanzapine vs Ziprasidone							
Breier 2005	20	277	42	271		0.42	[0.24; 0.74]
Lieberman 2005_18months	25	336	14	185		0.98	[0.50; 1.94]
Random effects model		**613**		**456**		**0.63**	**[0.28; 1.43]**
Heterogeneity: I^2 = 71.24%, τ^2 = 0.25085509, p = 0.06							
Comparison = Paliperidone vs Risperidone							
NCT00210717	174	379	169	370		1.01	[0.76; 1.35]
Random effects model		**379**		**370**		**1.01**	**[0.76; 1.35]**
Heterogeneity: not applicable							
Comparison = Perphenazine vs Quetiapine							
Lieberman 2005_18months	26	261	11	337		3.28	[1.59; 6.77]
Random effects model		**261**		**337**		**3.28**	**[1.59; 6.77]**
Heterogeneity: not applicable							
Comparison = Perphenazine vs Risperidone							
Lieberman 2005_18months	26	261	32	341		1.07	[0.62; 1.84]
Random effects model		**261**		**341**		**1.07**	**[0.62; 1.84]**
Heterogeneity: not applicable							
Comparison = Perphenazine vs Ziprasidone							
Lieberman 2005_18months	26	261	14	185		1.35	[0.69; 2.66]
Random effects model		**261**		**185**		**1.35**	**[0.69; 2.66]**
Heterogeneity: not applicable							
Comparison = Quetiapine vs Risperidone							
Lieberman 2005_18months	11	337	32	341		0.33	[0.16; 0.66]
Random effects model		**337**		**341**		**0.33**	**[0.16; 0.66]**
Heterogeneity: not applicable							
Comparison = Quetiapine vs Ziprasidone							
Lieberman 2005_18months	11	337	14	185		0.41	[0.18; 0.93]
Random effects model		**337**		**185**		**0.41**	**[0.18; 0.93]**
Heterogeneity: not applicable							
Comparison = Risperidone vs Ziprasidone							
Lieberman 2005_18months	32	341	14	185		1.26	[0.66; 2.44]
Random effects model		**341**		**185**		**1.26**	**[0.66; 2.44]**
Heterogeneity: not applicable							

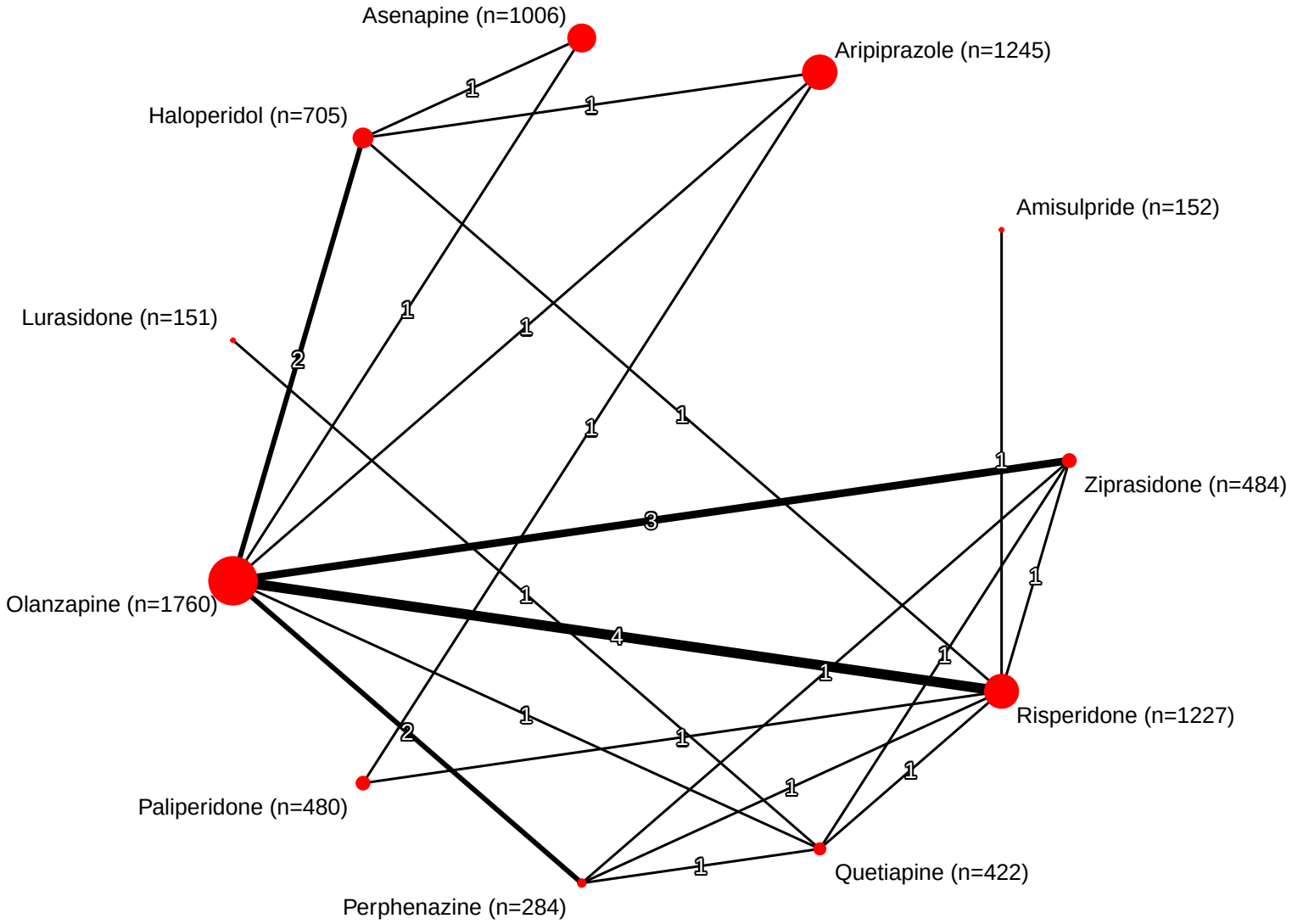


eAppendix 15

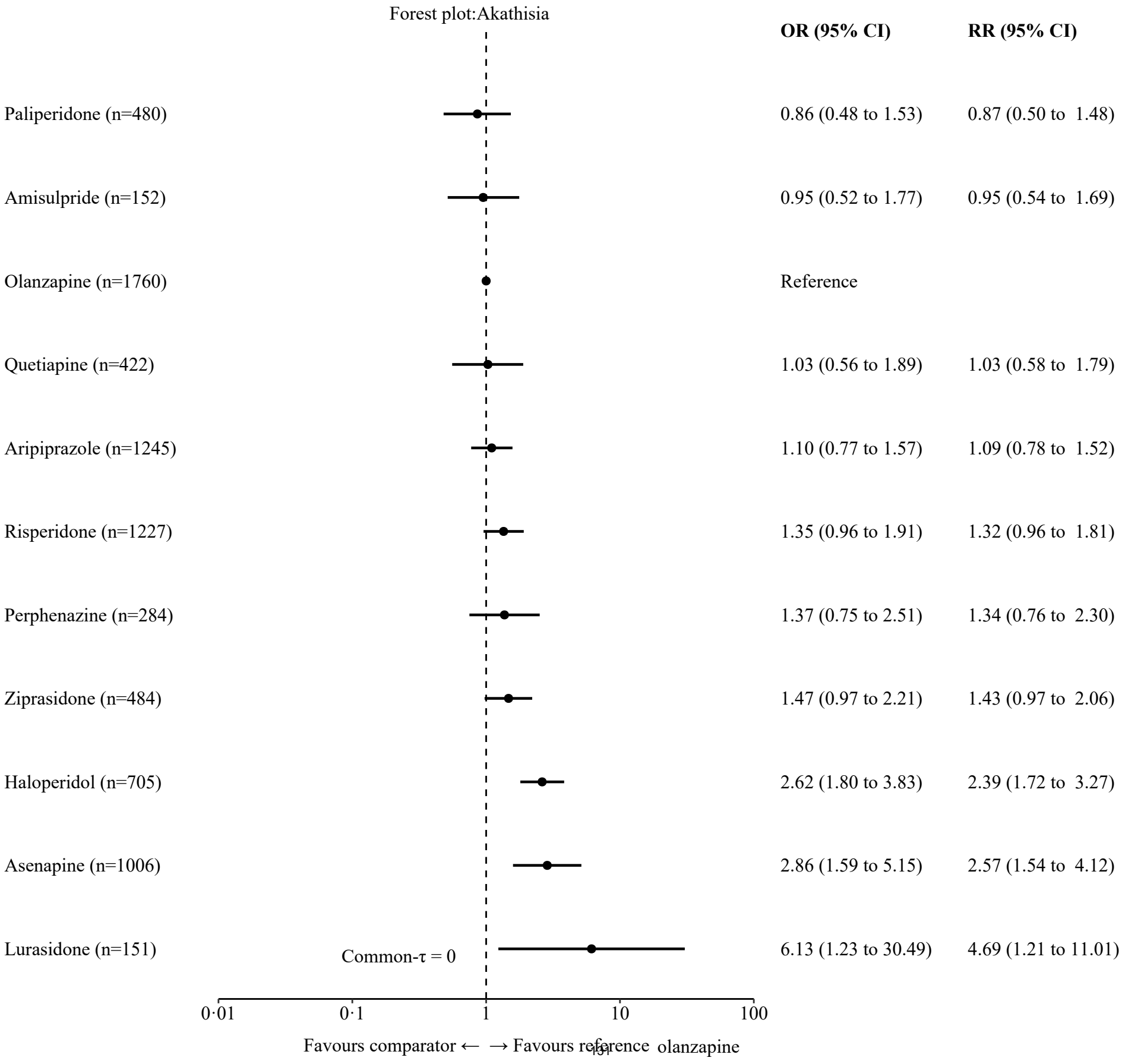
Akathisia

1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

Akathisia



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials


Forest plot:Akathisia
OR (95% CI)
RR (95% CI)
Paliperidone (n=480)
0.86 (0.48 to 1.53)
0.87 (0.50 to 1.48)
Amisulpride (n=152)
0.95 (0.52 to 1.77)
0.95 (0.54 to 1.69)
Olanzapine (n=1760)
Reference
Quetiapine (n=422)
1.03 (0.56 to 1.89)
1.03 (0.58 to 1.79)
Aripiprazole (n=1245)
1.10 (0.77 to 1.57)
1.09 (0.78 to 1.52)
Risperidone (n=1227)
1.35 (0.96 to 1.91)
1.32 (0.96 to 1.81)
Perphenazine (n=284)
1.37 (0.75 to 2.51)
1.34 (0.76 to 2.30)
Ziprasidone (n=484)
1.47 (0.97 to 2.21)
1.43 (0.97 to 2.06)
Haloperidol (n=705)
2.62 (1.80 to 3.83)
2.39 (1.72 to 3.27)
Asenapine (n=1006)
2.86 (1.59 to 5.15)
2.57 (1.54 to 4.12)
Lurasidone (n=151)
6.13 (1.23 to 30.49)
4.69 (1.21 to 11.01)
Common-τ = 0
0·01
0·1
1
10
100
Favours comparator ← → Favours reference olanzapine

League table for the outcome: Akathisia - relative risk (in the figure above both relative risks and odds ratios are shown)

Paliperidone	NA	NA	1.2 (0.5 to 2.72)	**0.55 (0.31 to 0.96)**	NA	NA	NA	NA	NA	NA
0.91 (0.44 to 1.77)	**Amisulpride**	NA	NA	0.73 (0.44 to 1.16)	NA	NA	NA	NA	NA	NA
0.85 (0.4 to 1.75)	0.93 (0.44 to 1.94)	**Quetiapine**	NA	0.81 (0.43 to 1.5)	0.77 (0.39 to 1.49)	0.63 (0.31 to 1.25)	NA	NA	**0.22 (0.05 to 0.8)**	1.07 (0.54 to 2.04)
0.79 (0.45 to 1.36)	0.88 (0.46 to 1.62)	0.93 (0.49 to 1.75)	**Aripiprazole**	NA	NA	NA	**0.49 (0.37 to 0.64)**	NA	NA	1.07 (0.68 to 1.63)
0.65 (0.4 to 1.05)	0.73 (0.44 to 1.16)	0.77 (0.43 to 1.37)	0.83 (0.55 to 1.23)	**Risperidone**	0.95 (0.5 to 1.76)	0.78 (0.39 to 1.47)	**0.48 (0.26 to 0.87)**	NA	NA	1.33 (0.93 to 1.89)
0.64 (0.31 to 1.33)	0.72 (0.33 to 1.48)	0.77 (0.39 to 1.46)	0.81 (0.43 to 1.52)	0.98 (0.55 to 1.71)	**Perphenazine**	0.81 (0.4 to 1.59)	NA	NA	NA	1.41 (0.73 to 2.63)
0.6 (0.32 to 1.14)	0.67 (0.34 to 1.28)	0.72 (0.38 to 1.31)	0.77 (0.46 to 1.25)	0.93 (0.59 to 1.44)	0.94 (0.51 to 1.68)	**Ziprasidone**	NA	NA	NA	1.39 (0.93 to 2.04)
0.37 (0.2 to 0.64)	**0.4 (0.21 to 0.74)**	**0.43 (0.23 to 0.81)**	**0.46 (0.35 to 0.59)**	**0.55 (0.37 to 0.82)**	0.56 (0.29 to 1.03)	**0.6 (0.35 to 0.97)**	**Haloperidol**	1.08 (0.29 to 2.95)	NA	**2.84 (1.64 to 4.66)**
0.34 (0.15 to 0.72)	**0.37 (0.16 to 0.81)**	**0.4 (0.17 to 0.86)**	**0.43 (0.23 to 0.78)**	**0.51 (0.27 to 0.94)**	0.52 (0.24 to 1.09)	0.55 (0.28 to 1.04)	0.93 (0.51 to 1.59)	**Asenapine**	NA	**2.65 (1.51 to 4.39)**
0.18 (0.04 to 0.81)	**0.21 (0.04 to 0.88)**	**0.22 (0.05 to 0.8)**	**0.23 (0.05 to 0.94)**	0.28 (0.05 to 1.07)	0.28 (0.05 to 1.11)	0.31 (0.07 to 1.14)	0.51 (0.11 to 1.64)	0.55 (0.11 to 1.78)	**Lurasidone**	NA
0.87 (0.5 to 1.48)	0.95 (0.54 to 1.69)	1.03 (0.58 to 1.79)	1.09 (0.78 to 1.52)	1.32 (0.96 to 1.81)	1.34 (0.76 to 2.3)	1.43 (0.97 to 2.06)	**2.39 (1.72 to 3.27)**	**2.57 (1.54 to 4.12)**	**4.69 (1.21 to 11.01)**	**Olanzapine**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. We originally calculated odds ratios but then transformed them to relative risks which can be interpreted more easily. Thus, each cell provides the relative risk and the corresponding 95% confidence interval 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% CIs excluding opposite effects. CI=confidence interval. NA=not available.

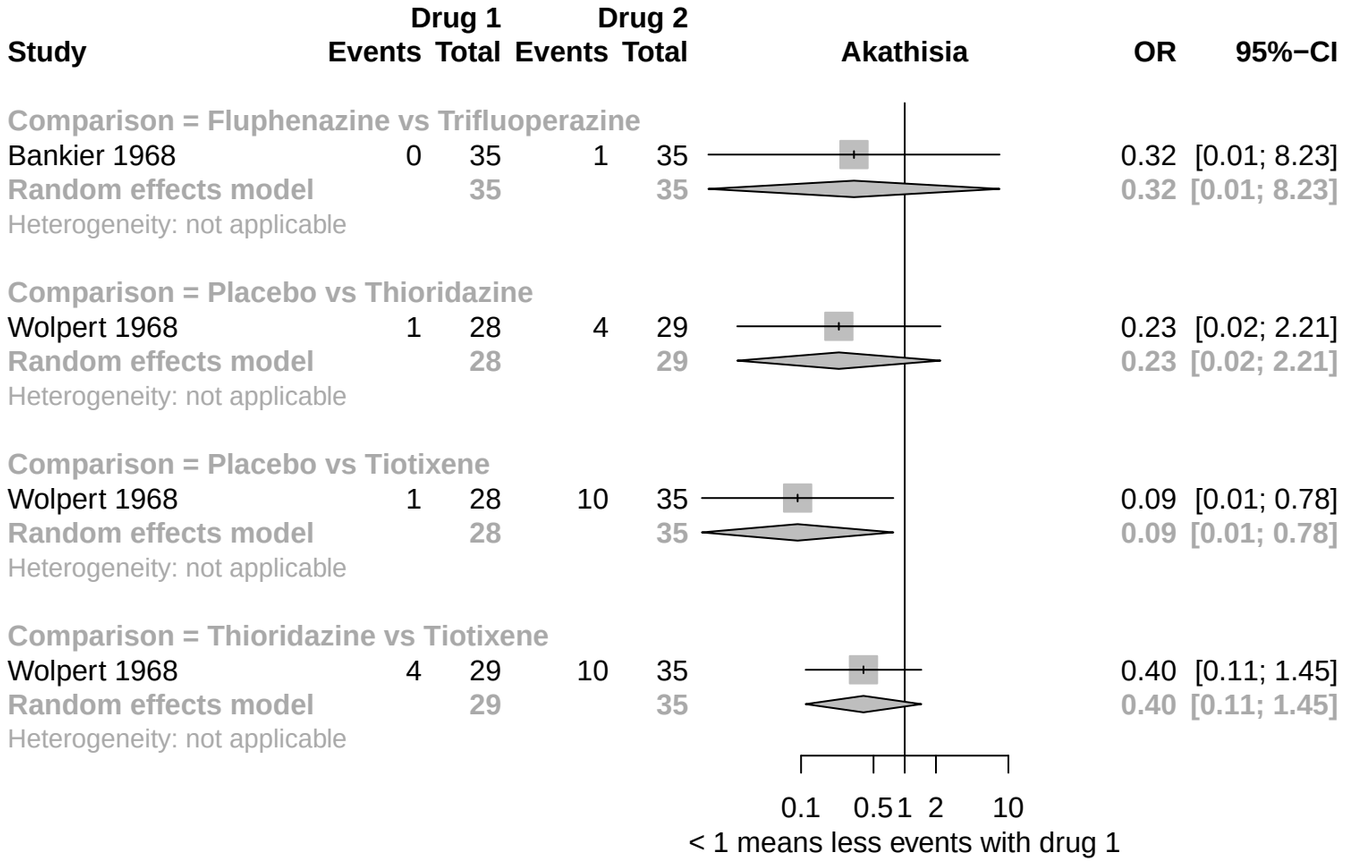
Forest plot of pairwise meta-analyses - drugs in the network. Results on the left side of the y-axis are in favour of the first mentioned drug

Study	Drug 1 Events	Drug 1 Total	Drug 2 Events	Drug 2 Total	Akathisia	OR	95%−CI
Comparison = Amisulpride vs Risperidone							
Sechter 2002	35	152	47	158		0.71	[0.42; 1.18]
Random effects model		**152**		**158**		**0.71**	**[0.42; 1.18]**
Heterogeneity: not applicable							
Comparison = Aripiprazole vs Haloperidol							
Kasper 2003	111	861	108	433		0.45	[0.33; 0.60]
Random effects model		**861**		**433**		**0.45**	**[0.33; 0.60]**
Heterogeneity: not applicable							
Comparison = Aripiprazole vs Olanzapine							
Kane 2009_28 weeks	44	285	41	281		1.07	[0.67; 1.70]
Random effects model		**285**		**281**		**1.07**	**[0.67; 1.70]**
Heterogeneity: not applicable							
Comparison = Aripiprazole vs Paliperidone							
NCT03345979	9	99	11	101		0.82	[0.32; 2.07]
Random effects model		**99**		**101**		**0.82**	**[0.32; 2.07]**
Heterogeneity: not applicable							
Comparison = Asenapine vs Haloperidol							
Kane 2010a_52w	6	93	3	43		0.92	[0.22; 3.86]
Random effects model		**93**		**43**		**0.92**	**[0.22; 3.86]**
Heterogeneity: not applicable							
Comparison = Asenapine vs Olanzapine							
Schoemaker 2010	89	913	11	312		2.96	[1.56; 5.61]
Random effects model		**913**		**312**		**2.96**	**[1.56; 5.61]**
Heterogeneity: not applicable							
Comparison = Haloperidol vs Olanzapine							
Keefe 2006	24	97	14	159		3.41	[1.66; 6.97]
Kongsakon 2006	7	132	3	144		2.63	[0.67; 10.40]
Random effects model		**229**		**303**		**3.22**	**[1.71; 6.08]**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.74							
Comparison = Haloperidol vs Risperidone							
Keefe 2006	24	97	20	158		2.27	[1.18; 4.38]
Random effects model		**97**		**158**		**2.27**	**[1.18; 4.38]**
Heterogeneity: not applicable							
Comparison = Lurasidone vs Quetiapine							
Loebel 2013_12m	19	151	2	85		5.97	[1.36; 26.31]
Random effects model		**151**		**85**		**5.97**	**[1.36; 26.31]**
Heterogeneity: not applicable							
Comparison = Olanzapine vs Perphenazine							
Lieberman 2005_18months	15	336	16	261		0.72	[0.35; 1.48]
Naukkarinen 2000	0	23	1	23		0.32	[0.01; 8.25]
Random effects model		**359**		**284**		**0.69**	**[0.34; 1.40]**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.63							
Comparison = Olanzapine vs Quetiapine							
Lieberman 2005_18months	15	336	16	337		0.94	[0.46; 1.93]
Random effects model		**336**		**337**		**0.94**	**[0.46; 1.93]**
Heterogeneity: not applicable							
Comparison = Olanzapine vs Risperidone							
Gureje 2003	6	32	5	33		1.29	[0.35; 4.75]
Keefe 2006	14	159	20	158		0.67	[0.32; 1.37]
Lieberman 2005_18months	15	336	20	341		0.75	[0.38; 1.49]
Tran 1997	16	172	22	167		0.68	[0.34; 1.34]
Random effects model		**699**		**699**		**0.74**	**[0.50; 1.08]**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.84							
Comparison = Olanzapine vs Ziprasidone							
Alvarez 2012	0	24	1	28		0.37	[0.01; 9.62]
Breier 2005	29	277	35	271		0.79	[0.47; 1.33]
Lieberman 2005_18months	15	336	14	185		0.57	[0.27; 1.21]
Random effects model		**637**		**484**		**0.70**	**[0.46; 1.07]**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.73							
Comparison = Paliperidone vs Risperidone							
NCT00210717	18	379	32	370		0.53	[0.29; 0.96]
Random effects model		**379**		**370**		**0.53**	**[0.29; 0.96]**
Heterogeneity: not applicable							
Comparison = Perphenazine vs Quetiapine							
Lieberman 2005_18months	16	261	16	337		1.31	[0.64; 2.67]
Random effects model		**261**		**337**		**1.31**	**[0.64; 2.67]**
Heterogeneity: not applicable							
Comparison = Perphenazine vs Risperidone							
Lieberman 2005_18months	16	261	20	341		1.05	[0.53; 2.07]
Random effects model		**261**		**341**		**1.05**	**[0.53; 2.07]**
Heterogeneity: not applicable							
Comparison = Perphenazine vs Ziprasidone							
Lieberman 2005_18months	16	261	14	185		0.80	[0.38; 1.68]
Random effects model		**261**		**185**		**0.80**	**[0.38; 1.68]**
Heterogeneity: not applicable							
Comparison = Quetiapine vs Risperidone							
Lieberman 2005_18months	16	337	20	341		0.80	[0.41; 1.57]
Random effects model		**337**		**341**		**0.80**	**[0.41; 1.57]**
Heterogeneity: not applicable							
Comparison = Quetiapine vs Ziprasidone							
Lieberman 2005_18months	16	337	14	185		0.61	[0.29; 1.28]
Random effects model		**337**		**185**		**0.61**	**[0.29; 1.28]**
Heterogeneity: not applicable							
Comparison = Risperidone vs Ziprasidone							
Lieberman 2005_18months	20	341	14	185		0.76	[0.37; 1.54]
Random effects model		**341**		**185**		**0.76**	**[0.37; 1.54]**
Heterogeneity: not applicable							

0.1 0.5 1 2 10

< 1 means less events with drug 1

Forest plot of pairwise meta-analyses - drugs outside the network. Results on the left side of the y-axis are in favour of the first mentioned drug

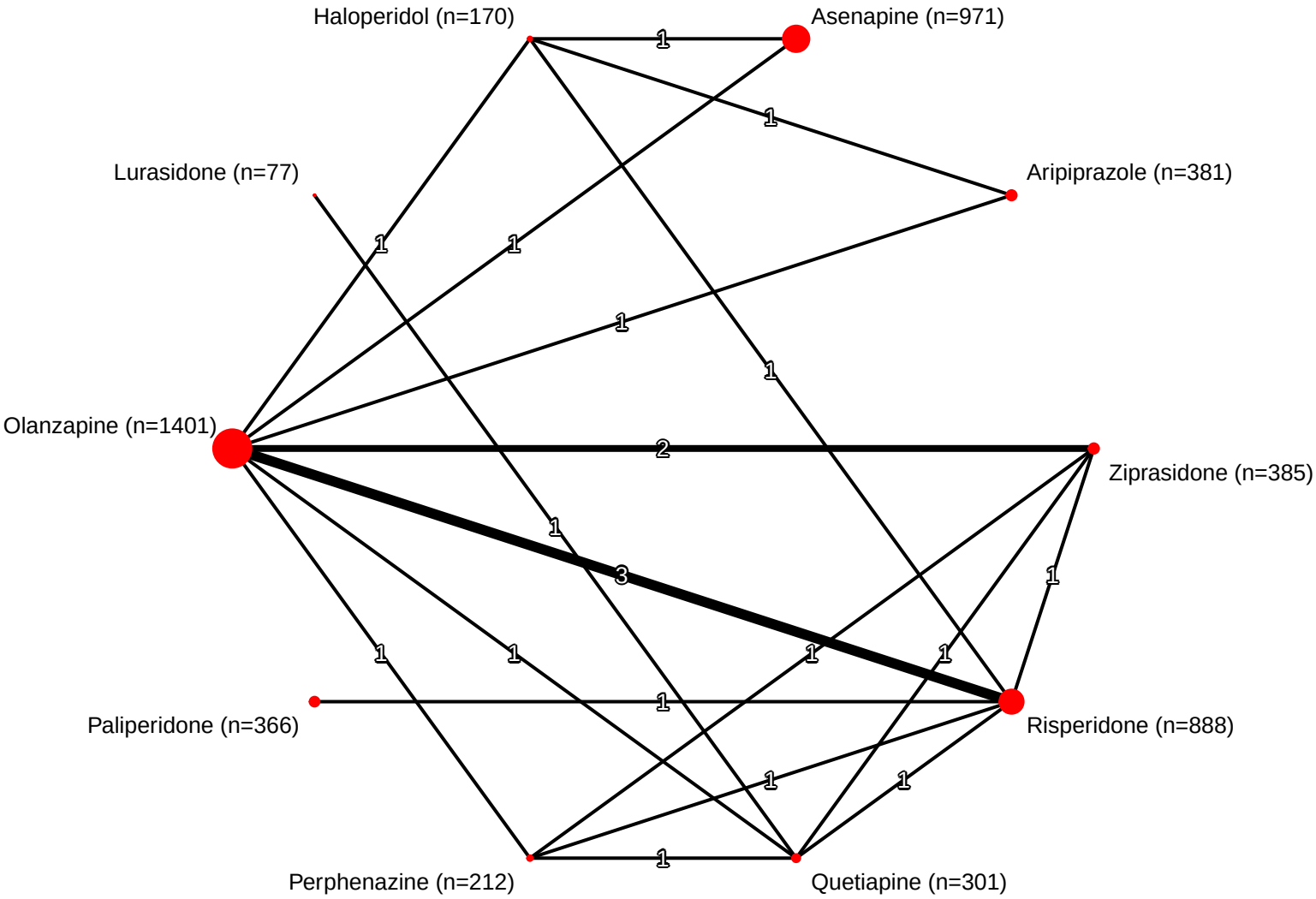


eAppendix 16

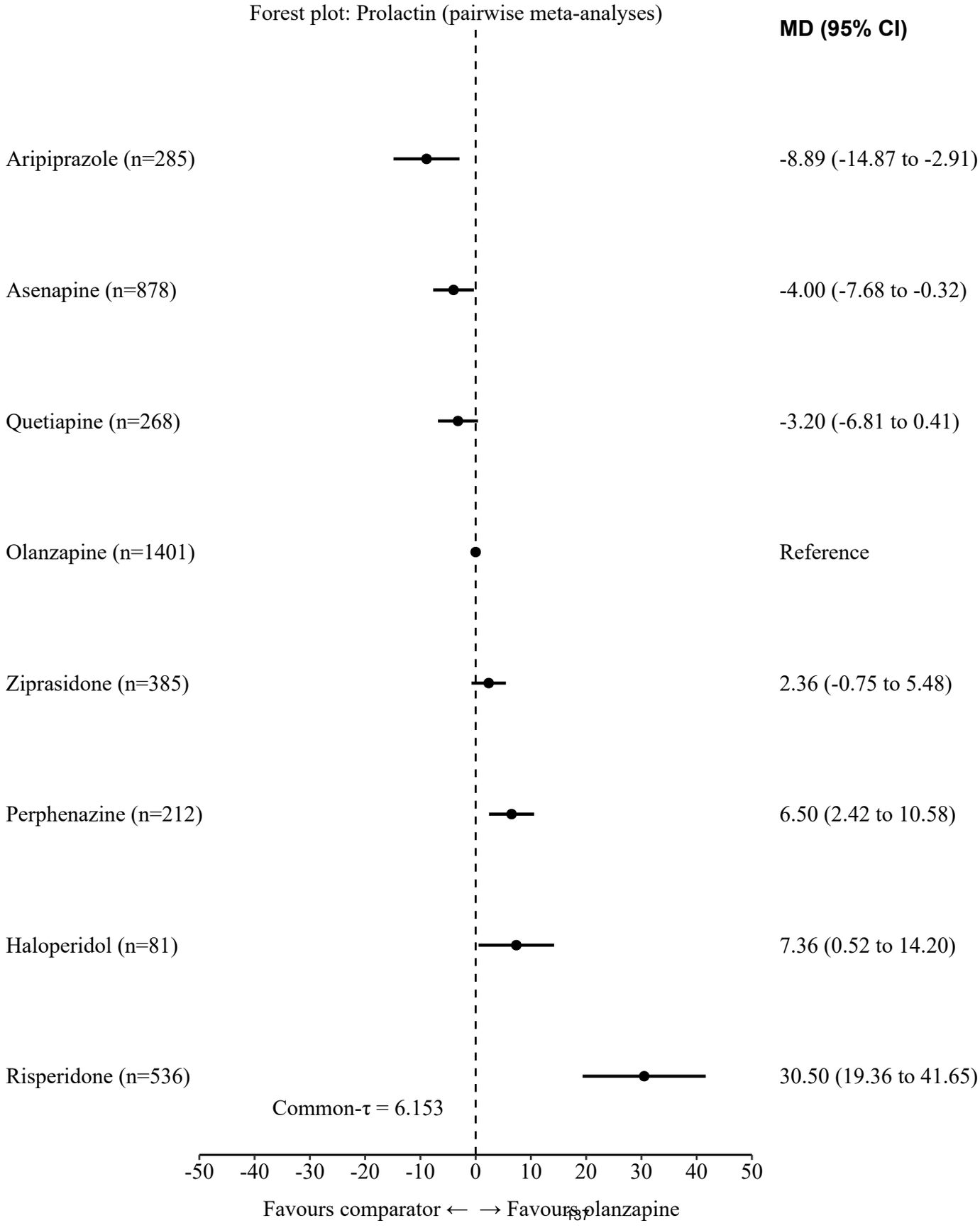
Prolactin

1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

Prolactin



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials

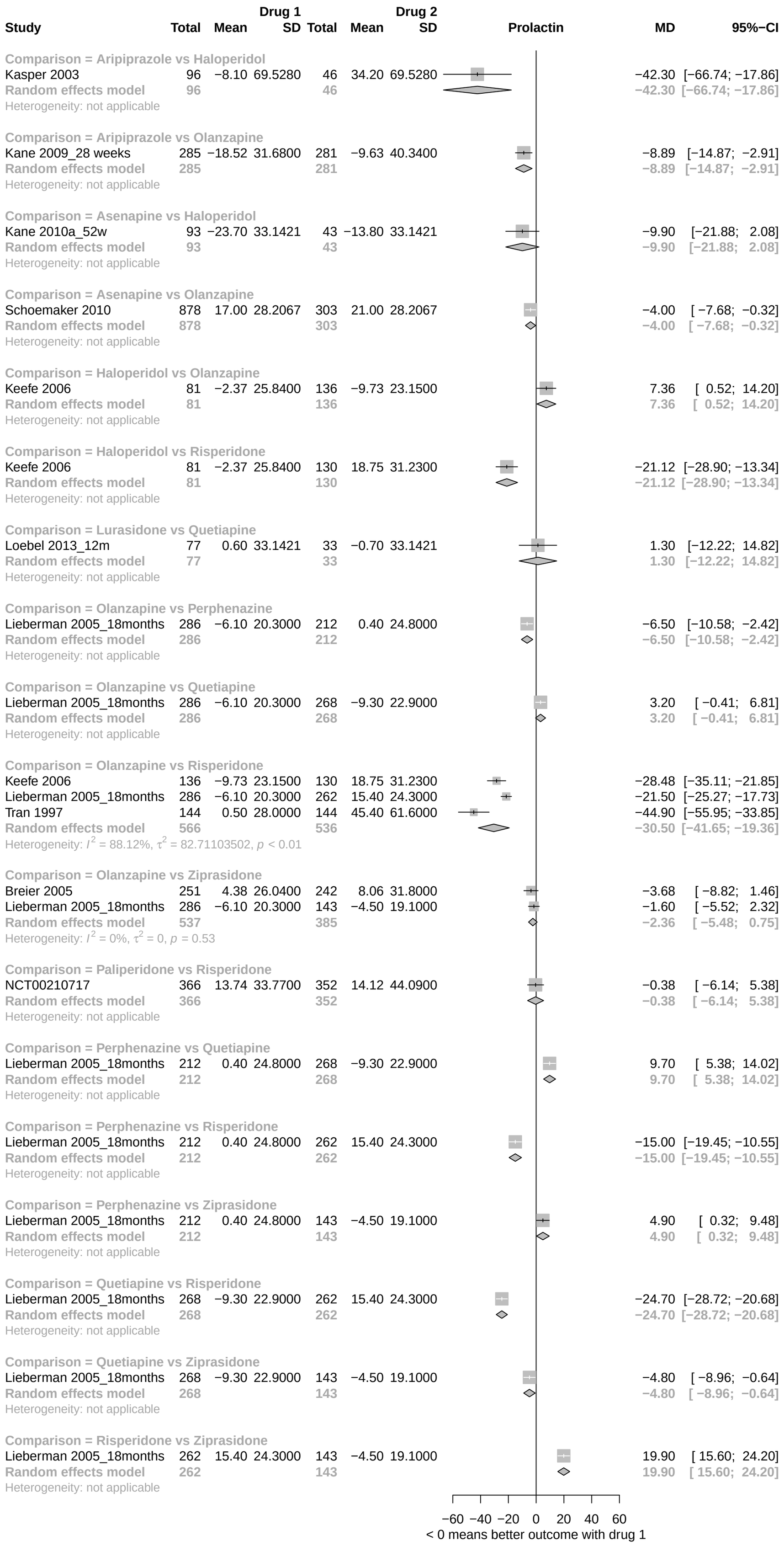

Forest plot: Prolactin (pairwise meta-analyses)
MD (95% CI)
Aripiprazole (n=285)
-8.89 (-14.87 to -2.91)
Asenapine (n=878)
-4.00 (-7.68 to -0.32)
Quetiapine (n=268)
-3.20 (-6.81 to 0.41)
Olanzapine (n=1401)
Reference
Ziprasidone (n=385)
2.36 (-0.75 to 5.48)
Perphenazine (n=212)
6.50 (2.42 to 10.58)
Haloperidol (n=81)
7.36 (0.52 to 14.20)
Risperidone (n=536)
30.50 (19.36 to 41.65)
Common-τ = 6.153
-50 -40 -30 -20 -10 0 10 20 30 40 50
Favours comparator ← → Favours olanzapine

League table for the outcome: Prolactin. It should be noted that the data were inconsistent. Readers should therefore focus on the results of pairwise meta-analysis. This table is mainly provided for completeness

Aripiprazole	NA	-8.89 (-22.35 to 4.57)	NA	NA	NA	**-42.30 (-69.55 to -15.05)**	NA	NA	NA
-10.99 (-26.83 to 4.85)	**Asenapine**	-4.00 (-16.61 to 8.61)	NA	NA	NA	-9.90 (-26.90 to 7.10)	NA	NA	NA
-13.42 (-25.66 to -1.18)	-2.44 (-13.21 to 8.33)	**Olanzapine**	3.20 (-9.39 to 15.79)	NA	-2.61 (-11.72 to 6.51)	-7.36 (-21.22 to 6.50)	-6.50 (-19.23 to 6.23)	NA	**-29.63 (-37.72 to -21.54)**
-14.05 (-30.55 to 2.45)	-3.07 (-18.43 to 12.29)	-0.63 (-11.84 to 10.57)	**Quetiapine**	-1.30 (-19.41 to 16.81)	-4.80 (-17.56 to 7.96)	NA	-9.70 (-22.51 to 3.11)	NA	**-24.70 (-37.41 to -11.99)**
-15.35 (-39.85 to 9.15)	-4.37 (-28.12 to 19.38)	-1.93 (-23.23 to 19.37)	-1.30 (-19.41 to 16.81)	**Lurasidone**	NA	NA	NA	NA	NA
-18.28 (-33.26 to -3.31)	-7.30 (-21.03 to 6.44)	-4.86 (-13.61 to 3.88)	-4.23 (-16.10 to 7.63)	-2.93 (-24.58 to 18.72)	**Ziprasidone**	NA	-4.90 (-17.80 to 8.00)	NA	**-19.90 (-32.70 to -7.10)**
-23.73 (-38.37 to -9.08)	**-12.74 (-24.86 to -0.62)**	-10.31 (-20.63 to 0.02)	-9.67 (-24.38 to 5.03)	-8.37 (-31.71 to 14.96)	-5.44 (-18.57 to 7.69)	**Haloperidol**	NA	NA	**-21.12 (-35.47 to -6.77)**
-23.75 (-40.36 to -7.14)	-12.77 (-28.24 to 2.71)	-10.33 (-21.70 to 1.04)	-9.70 (-22.51 to 3.11)	-8.40 (-30.59 to 13.79)	-5.47 (-17.48 to 6.55)	-0.03 (-14.86 to 14.81)	**Perphenazine**	NA	**-15.00 (-27.85 to -2.15)**
-42.92 (-62.45 to -23.39)	**-31.93 (-50.42 to -13.44)**	**-29.49 (-44.95 to -14.04)**	**-28.86 (-46.57 to -11.16)**	**-27.56 (-52.89 to -2.24)**	**-24.63 (-41.39 to -7.87)**	**-19.19 (-36.75 to -1.63)**	**-19.16 (-36.97 to -1.36)**	**Paliperidone**	-0.38 (-13.74 to 12.98)
-43.30 (-57.54 to -29.06)	**-32.31 (-45.08 to -19.54)**	**-29.87 (-37.64 to -22.11)**	**-29.24 (-40.85 to -17.64)**	**-27.94 (-49.46 to -6.43)**	**-25.01 (-35.12 to -14.90)**	**-19.57 (-30.96 to -8.18)**	**-19.54 (-31.31 to -7.78)**	-0.38 (-13.74 to 12.98)	**Risperidone**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why the sign (+/-) was sometimes different, but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Forest plot of pairwise meta-analyses - drugs in the network. Results on the left side of the y-axis are in favour of the first mentioned drug

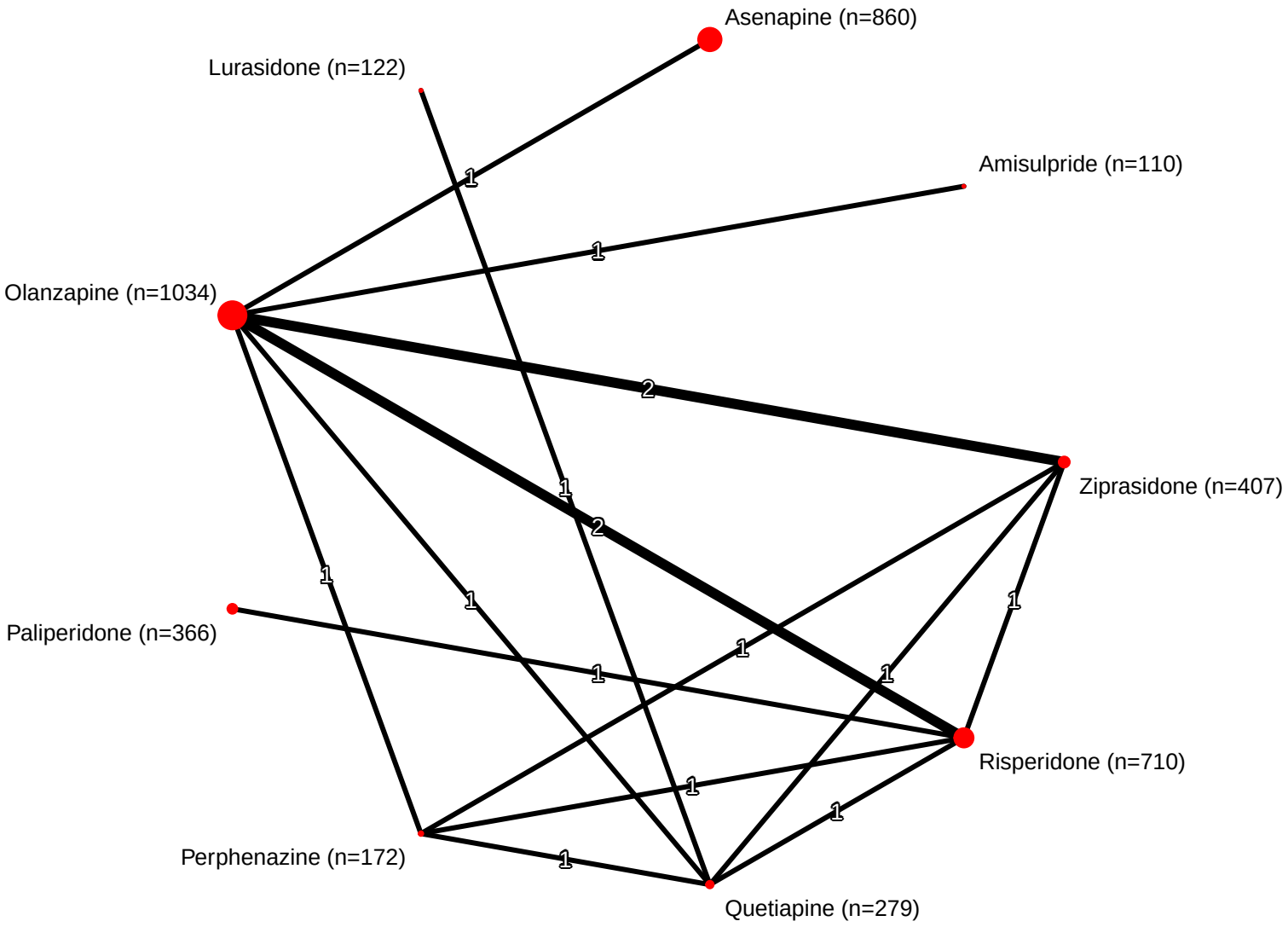


eAppendix 17

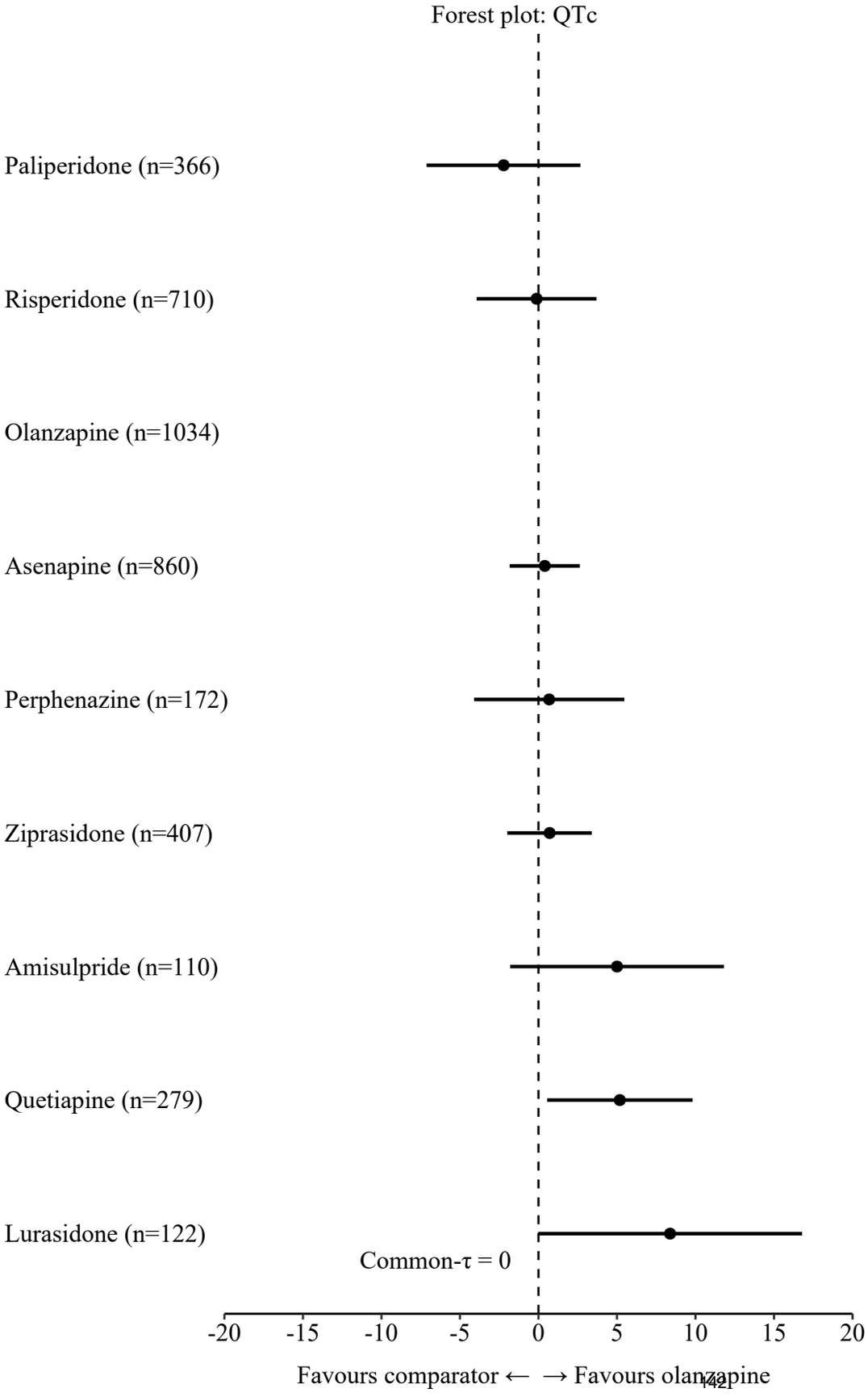
QTc prolongation

1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

QTc



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials



The lurasidone results require a comment. Unlike short-term results in which lurasidone was QTc neutral (1) it produced more QTc prolongation than risperidone here. However, the confidence interval was very large and, a single trial compared to quetiapine drove the effect because both drugs produced about the same QTc prolongation in this study,(2) but in other studies quetiapine was associated with some QTc prolongation.

References

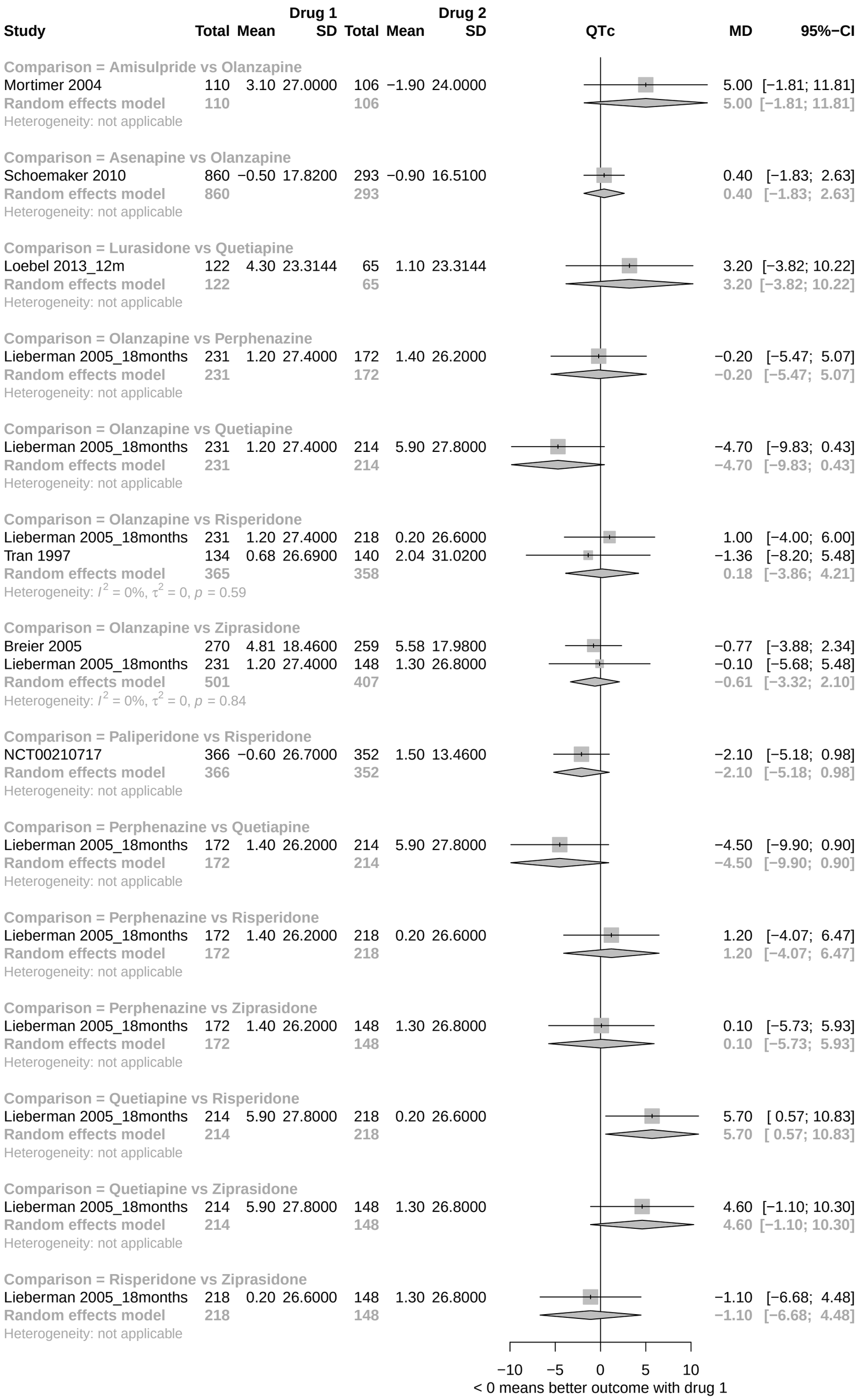
1. Huhn et al. Comparative efficacy and tolerability of 32 oral antipsychotics for the acute treatment of adults with multi-episode schizophrenia: a systematic review and network meta-analysis. Lancet 2019; 394(10202): 939-51.
2. Loebel et al. Effectiveness of lurasidone vs. quetiapine XR for relapse prevention in schizophrenia: a 12-month, double-blind, noninferiority study. Schizophr Res 2013; 147(1): 95-102

League table for the outcome: QTc

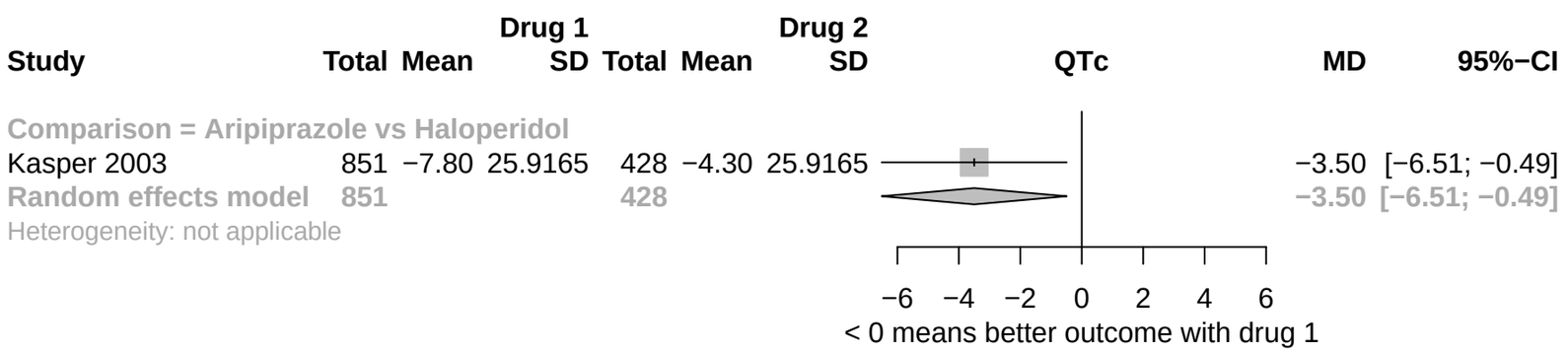
Paliperidone	-2.10 (-5.18 to 0.98)	NA	NA	NA	NA	NA	NA	NA
-2.10 (-5.18 to 0.98)	**Risperidone**	-0.18 (-4.21 to 3.86)	NA	-1.20 (-6.47 to 4.07)	-1.10 (-6.68 to 4.48)	NA	**-5.70 (-10.83 to -0.57)**	NA
-2.22 (-7.13 to 2.68)	-0.12 (-3.94 to 3.69)	**Olanzapine**	-0.40 (-2.63 to 1.83)	-0.20 (-5.47 to 5.07)	-0.61 (-3.32 to 2.10)	-5.00 (-11.81 to 1.81)	-4.70 (-9.83 to 0.43)	NA
-2.62 (-8.01 to 2.76)	-0.52 (-4.95 to 3.90)	-0.40 (-2.63 to 1.83)	**Asenapine**	NA	NA	NA	NA	NA
-2.90 (-8.82 to 3.01)	-0.80 (-5.86 to 4.25)	-0.68 (-5.46 to 4.10)	-0.28 (-5.56 to 5.00)	**Perphenazine**	0.10 (-5.73 to 5.93)	NA	-4.50 (-9.90 to 0.90)	NA
-2.93 (-8.14 to 2.28)	-0.83 (-5.04 to 3.38)	-0.71 (-3.39 to 1.98)	-0.31 (-3.80 to 3.19)	-0.03 (-5.02 to 4.97)	**Ziprasidone**	NA	-4.60 (-10.30 to 1.10)	NA
-7.22 (-15.61 to 1.16)	-5.12 (-12.93 to 2.68)	-5.00 (-11.81 to 1.81)	-4.60 (-11.76 to 2.56)	-4.32 (-12.64 to 4.00)	-4.29 (-11.61 to 3.02)	**Amisulpride**	NA	NA
-7.40 (-13.19 to -1.62)	**-5.30 (-10.21 to -0.40)**	**-5.18 (-9.81 to -0.55)**	-4.78 (-9.92 to 0.36)	-4.50 (-9.90 to 0.90)	-4.47 (-9.32 to 0.37)	-0.18 (-8.41 to 8.05)	**Quetiapine**	-3.20 (-10.22 to 3.82)
-10.60 (-19.70 to -1.51)	-8.50 (-17.07 to 0.06)	-8.38 (-16.79 to 0.03)	-7.98 (-16.68 to 0.72)	-7.70 (-16.56 to 1.16)	-7.67 (-16.20 to 0.85)	-3.38 (-14.20 to 7.44)	-3.20 (-10.22 to 3.82)	**Lurasidone**

The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. Each cell provides the standardised mean difference and the corresponding 95% confidence interval 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). Please note that in the figure above olanzapine was always the reference which explains why the sign (+/-) was sometimes different, but the results are the same. Bold print indicates 95% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Forest plot of pairwise meta-analses - drugs in the network. Results on the left side of the y-axis are in favour of the first mentioned drug



Forest plot of pairwise meta-analyses - drugs outside the network. Results on the left side of the y-axis are in favour of the first mentioned drug

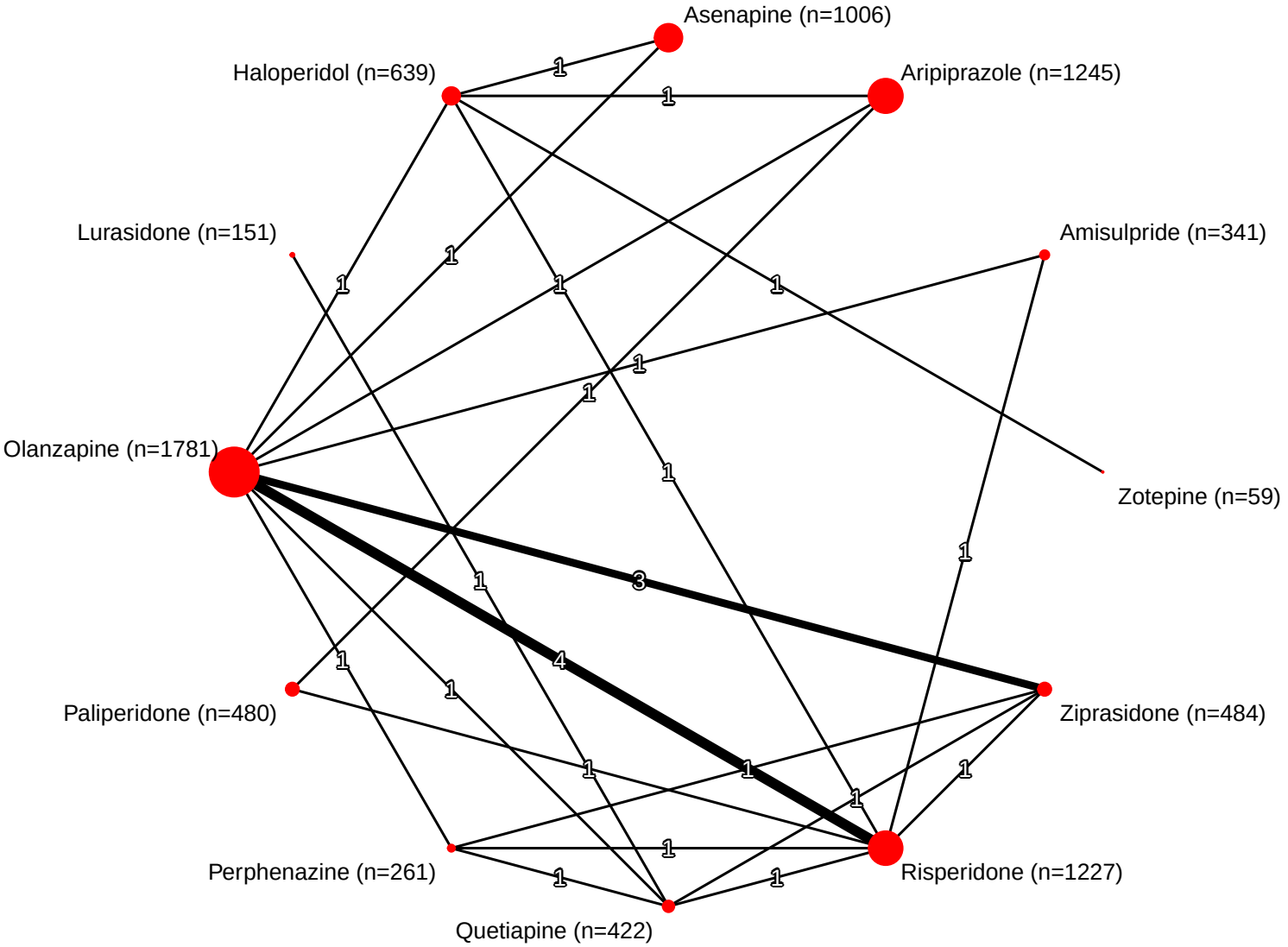


eAppendix 18

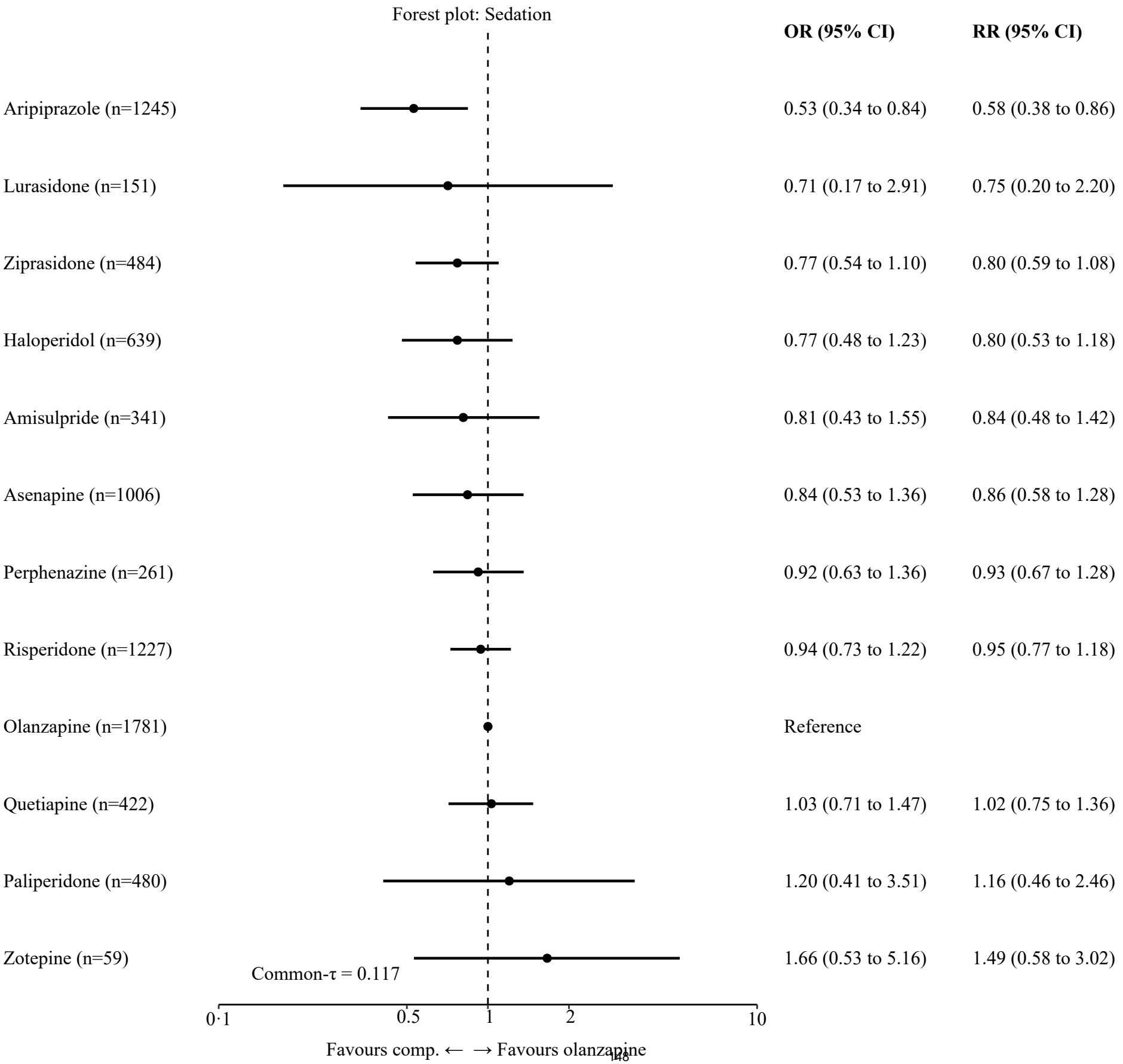
Sedation

1. Network plot
2. Forest plot
3. Network meta-analysis league table
4. Pairwise meta-analyses

Sedation



Network plot: numbers in parentheses = number of participants, numbers on the lines = number of randomised-controlled trials


Forest plot: Sedation
OR (95% CI)
RR (95% CI)
Aripiprazole (n=1245)
0.53 (0.34 to 0.84)
0.58 (0.38 to 0.86)
Lurasidone (n=151)
0.71 (0.17 to 2.91)
0.75 (0.20 to 2.20)
Ziprasidone (n=484)
0.77 (0.54 to 1.10)
0.80 (0.59 to 1.08)
Haloperidol (n=639)
0.77 (0.48 to 1.23)
0.80 (0.53 to 1.18)
Amisulpride (n=341)
0.81 (0.43 to 1.55)
0.84 (0.48 to 1.42)
Asenapine (n=1006)
0.84 (0.53 to 1.36)
0.86 (0.58 to 1.28)
Perphenazine (n=261)
0.92 (0.63 to 1.36)
0.93 (0.67 to 1.28)
Risperidone (n=1227)
0.94 (0.73 to 1.22)
0.95 (0.77 to 1.18)
Olanzapine (n=1781)
Reference
Quetiapine (n=422)
1.03 (0.71 to 1.47)
1.02 (0.75 to 1.36)
Paliperidone (n=480)
1.20 (0.41 to 3.51)
1.16 (0.46 to 2.46)
Zotepine (n=59)
1.66 (0.53 to 5.16)
1.49 (0.58 to 3.02)
Common-τ = 0.117
0·1
0.5
1
2
10
Favours comp. ← → Favours olanzapine

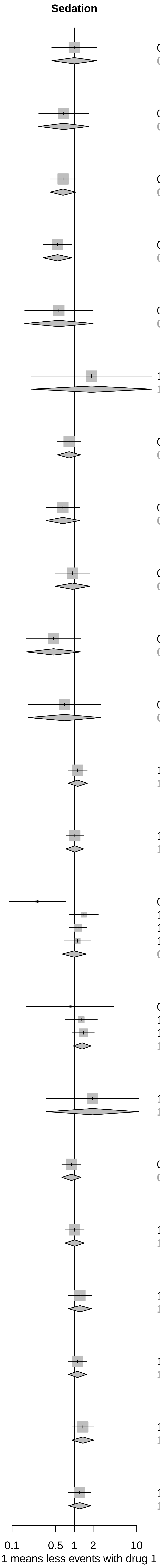
League table for the outcome: Sedation - relative risk (in the figure above both relative risks and odds ratios are shown)

Aripiprazole	NA	NA	0.69 (0.43 to 1.09)	NA	NA	NA	NA	NA	0.62 (0.19 to 1.69)	NA	**0.59 (0.34 to 0.97)**
0.77 (0.19 to 2.54)	**Lurasidone**	NA	NA	NA	NA	NA	NA	0.73 (0.21 to 2.09)	NA	NA	NA
0.72 (0.43 to 1.19)	0.94 (0.25 to 2.78)	**Ziprasidone**	NA	NA	NA	0.84 (0.54 to 1.26)	0.84 (0.55 to 1.25)	0.77 (0.51 to 1.14)	NA	NA	0.79 (0.57 to 1.07)
0.72 (0.48 to 1.07)	0.93 (0.24 to 2.87)	1 (0.6 to 1.62)	**Haloperidol**	NA	0.57 (0.07 to 3.13)	NA	0.94 (0.51 to 1.63)	NA	NA	0.53 (0.22 to 1.21)	0.7 (0.38 to 1.21)
0.68 (0.33 to 1.36)	0.89 (0.21 to 2.84)	0.95 (0.5 to 1.72)	0.96 (0.47 to 1.81)	**Amisulpride**	NA	NA	0.72 (0.3 to 1.56)	NA	NA	NA	0.99 (0.47 to 1.91)
0.67 (0.37 to 1.17)	0.86 (0.22 to 2.66)	0.92 (0.54 to 1.51)	0.92 (0.51 to 1.58)	0.97 (0.47 to 1.84)	**Asenapine**	NA	NA	NA	NA	NA	0.85 (0.56 to 1.27)
0.62 (0.36 to 1.03)	0.8 (0.22 to 2.38)	0.85 (0.57 to 1.25)	0.85 (0.5 to 1.4)	0.9 (0.46 to 1.62)	0.93 (0.54 to 1.52)	**Perphenazine**	1.01 (0.7 to 1.42)	0.92 (0.64 to 1.29)	NA	NA	0.9 (0.62 to 1.27)
0.61 (0.38 to 0.95)	0.79 (0.21 to 2.32)	0.84 (0.6 to 1.16)	0.84 (0.54 to 1.28)	0.89 (0.49 to 1.5)	0.91 (0.56 to 1.42)	0.98 (0.7 to 1.36)	**Risperidone**	0.91 (0.64 to 1.26)	0.56 (0.11 to 2.08)	NA	0.93 (0.74 to 1.17)
0.57 (0.33 to 0.93)	0.73 (0.21 to 2.09)	0.78 (0.54 to 1.12)	0.78 (0.47 to 1.27)	0.82 (0.43 to 1.48)	0.85 (0.5 to 1.37)	0.92 (0.64 to 1.29)	0.93 (0.67 to 1.26)	**Quetiapine**	NA	NA	0.98 (0.7 to 1.35)
0.49 (0.19 to 1.2)	0.64 (0.12 to 2.33)	0.69 (0.25 to 1.65)	0.69 (0.25 to 1.63)	0.73 (0.24 to 1.86)	0.75 (0.26 to 1.82)	0.81 (0.29 to 1.87)	0.82 (0.32 to 1.83)	0.88 (0.33 to 1.99)	**Paliperidone**	NA	NA
0.39 (0.13 to 0.99)	0.5 (0.09 to 1.85)	0.53 (0.18 to 1.34)	0.53 (0.22 to 1.21)	0.56 (0.17 to 1.5)	0.58 (0.19 to 1.46)	0.63 (0.22 to 1.52)	0.64 (0.23 to 1.49)	0.69 (0.24 to 1.61)	0.78 (0.2 to 2.08)	**Zotepine**	NA
0.58 (0.38 to 0.86)	0.75 (0.2 to 2.2)	0.8 (0.59 to 1.08)	0.8 (0.53 to 1.18)	0.84 (0.48 to 1.42)	0.86 (0.58 to 1.28)	0.93 (0.67 to 1.28)	0.95 (0.77 to 1.18)	1.02 (0.75 to 1.36)	1.16 (0.46 to 2.46)	1.49 (0.58 to 3.02)	**Olanzapine**

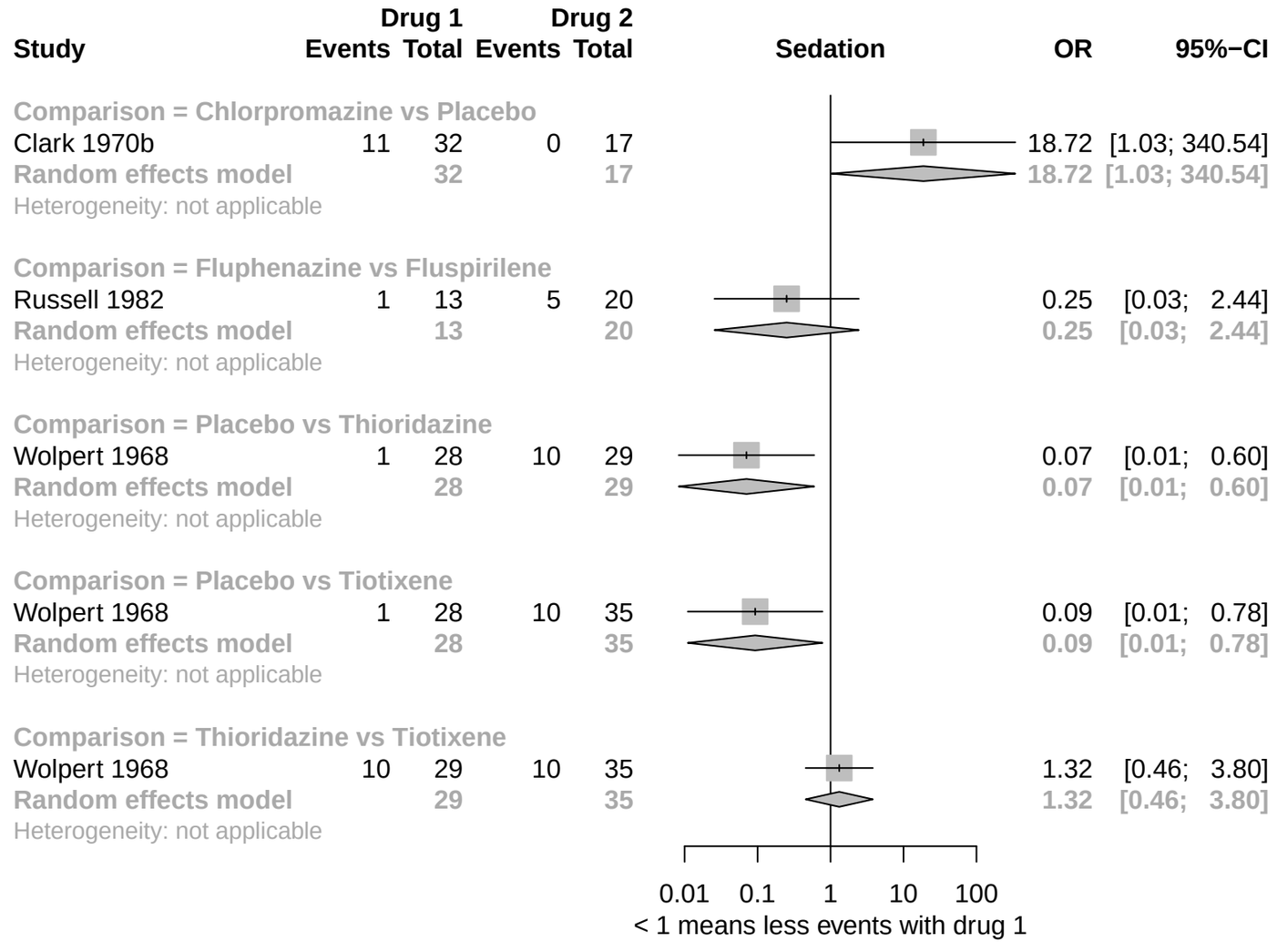
The left lower field presents the results of the network meta-analysis, the right upper field results of pairwise meta-analyses. Treatments are in order of their point estimate compared to olanzapine. We originally calculated odds ratios but then transformed them to relative risks which can be interpreted more easily. Thus, each cell provides the relative risk and the corresponding 95% confidence interval 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% CIs excluding opposite effects. CI=confidence interval. NA=not available.

Forest plot of pairwise meta-analyses - drugs in the network. Results on the left side of the y-axis are in favour of the first mentioned drug

Study	Drug 1 Events	Drug 1 Total	Drug 2 Events	Drug 2 Total	OR	95%−CI
Comparison = Amisulpride vs Olanzapine						
Mortimer 2004	12	189	12	188	0.99	[0.43; 2.27]
Random effects model		**189**		**188**	**0.99**	**[0.43; 2.27]**
Heterogeneity: not applicable						
Comparison = Amisulpride vs Risperidone						
Sechter 2002	8	152	12	158	0.68	[0.27; 1.70]
Random effects model		**152**		**158**	**0.68**	**[0.27; 1.70]**
Heterogeneity: not applicable						
Comparison = Aripiprazole vs Haloperidol						
Kasper 2003	43	861	32	433	0.66	[0.41; 1.06]
Random effects model		**861**		**433**	**0.66**	**[0.41; 1.06]**
Heterogeneity: not applicable						
Comparison = Aripiprazole vs Olanzapine						
Kane 2009_28 weeks	24	285	41	281	0.54	[0.32; 0.92]
Random effects model		**285**		**281**	**0.54**	**[0.32; 0.92]**
Heterogeneity: not applicable						
Comparison = Aripiprazole vs Paliperidone						
NCT03345979	4	99	7	101	0.57	[0.16; 2.00]
Random effects model		**99**		**101**	**0.57**	**[0.16; 2.00]**
Heterogeneity: not applicable						
Comparison = Asenapine vs Haloperidol						
Kane 2010a_52w	4	93	1	43	1.89	[0.20; 17.41]
Random effects model		**93**		**43**	**1.89**	**[0.20; 17.41]**
Heterogeneity: not applicable						
Comparison = Asenapine vs Olanzapine						
Schoemaker 2010	81	913	33	312	0.82	[0.54; 1.26]
Random effects model		**913**		**312**	**0.82**	**[0.54; 1.26]**
Heterogeneity: not applicable						
Comparison = Haloperidol vs Olanzapine						
Keefe 2006	18	97	41	159	0.66	[0.35; 1.22]
Random effects model		**97**		**159**	**0.66**	**[0.35; 1.22]**
Heterogeneity: not applicable						
Comparison = Haloperidol vs Risperidone						
Keefe 2006	18	97	31	158	0.93	[0.49; 1.78]
Random effects model		**97**		**158**	**0.93**	**[0.49; 1.78]**
Heterogeneity: not applicable						
Comparison = Haloperidol vs Zotepine						
Laborde 2000	7	66	12	59	0.46	[0.17; 1.27]
Random effects model		**66**		**59**	**0.46**	**[0.17; 1.27]**
Heterogeneity: not applicable						
Comparison = Lurasidone vs Quetiapine						
Loebel 2013_12m	5	151	4	85	0.69	[0.18; 2.66]
Random effects model		**151**		**85**	**0.69**	**[0.18; 2.66]**
Heterogeneity: not applicable						
Comparison = Olanzapine vs Perphenazine						
Lieberman 2005_18months	104	336	74	261	1.13	[0.79; 1.62]
Random effects model		**336**		**261**	**1.13**	**[0.79; 1.62]**
Heterogeneity: not applicable						
Comparison = Olanzapine vs Quetiapine						
Lieberman 2005_18months	104	336	103	337	1.02	[0.73; 1.41]
Random effects model		**336**		**337**	**1.02**	**[0.73; 1.41]**
Heterogeneity: not applicable						
Comparison = Olanzapine vs Risperidone						
Gureje 2003	9	32	20	33	0.25	[0.09; 0.72]
Keefe 2006	41	159	31	158	1.42	[0.84; 2.42]
Lieberman 2005_18months	104	336	96	341	1.14	[0.82; 1.59]
Tran 1997	45	172	40	167	1.12	[0.69; 1.84]
Random effects model		**699**		**699**	**0.99**	**[0.63; 1.56]**
Heterogeneity: I^2 = 65.09%, τ^2 = 0.12836303, p = 0.04						
Comparison = Olanzapine vs Ziprasidone						
Alvarez 2012	3	24	4	28	0.86	[0.17; 4.28]
Breier 2005	27	277	21	271	1.29	[0.71; 2.33]
Lieberman 2005_18months	104	336	45	185	1.39	[0.93; 2.10]
Random effects model		**637**		**484**	**1.33**	**[0.96; 1.85]**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.84						
Comparison = Paliperidone vs Risperidone						
NCT00210717	4	379	2	370	1.96	[0.36; 10.78]
Random effects model		**379**		**370**	**1.96**	**[0.36; 10.78]**
Heterogeneity: not applicable						
Comparison = Perphenazine vs Quetiapine						
Lieberman 2005_18months	74	261	103	337	0.90	[0.63; 1.28]
Random effects model		**261**		**337**	**0.90**	**[0.63; 1.28]**
Heterogeneity: not applicable						
Comparison = Perphenazine vs Risperidone						
Lieberman 2005_18months	74	261	96	341	1.01	[0.71; 1.44]
Random effects model		**261**		**341**	**1.01**	**[0.71; 1.44]**
Heterogeneity: not applicable						
Comparison = Perphenazine vs Ziprasidone						
Lieberman 2005_18months	74	261	45	185	1.23	[0.80; 1.89]
Random effects model		**261**		**185**	**1.23**	**[0.80; 1.89]**
Heterogeneity: not applicable						
Comparison = Quetiapine vs Risperidone						
Lieberman 2005_18months	103	337	96	341	1.12	[0.81; 1.56]
Random effects model		**337**		**341**	**1.12**	**[0.81; 1.56]**
Heterogeneity: not applicable						
Comparison = Quetiapine vs Ziprasidone						
Lieberman 2005_18months	103	337	45	185	1.37	[0.91; 2.06]
Random effects model		**337**		**185**	**1.37**	**[0.91; 2.06]**
Heterogeneity: not applicable						
Comparison = Risperidone vs Ziprasidone						
Lieberman 2005_18months	96	341	45	185	1.22	[0.81; 1.84]
Random effects model		**341**		**185**	**1.22**	**[0.81; 1.84]**
Heterogeneity: not applicable						



Forest plot of pairwise meta-analyses - drugs in the network. Results on the left side of the y-axis are in favour of the first mentioned drug



eAppendix 19

Heterogeneity and inconsistency of all outcomes

Heterogeneity and inconsistency in the network meta-analyses

Summary of results:

We compared the estimator of between-study-heterogeneity common-τ with empirical distributions for common-τ provided by Rhodes et al. [1] (for continuous outcomes measured as standardized mean difference) and Turner et al. [2] (for dichotomous outcomes). 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. Inconsistency was examined locally with the SIDE test (a proportion of SIDE test p<0.1 of more 10% was judged as considerable inconsistency) and overall with the design-by-treatment test (p<0.1 considered important).

In the following tables we summarize heterogeneity and inconsisteny. They were usually not very pronounced. However, in sparse networks heterogeneity and inconsistency cannot be addressed well. Therefore, we judged incoherence in CINeMA at some concerns in many comparisons which often led to downgrading the confidence in the evidence.

Summary of heterogeneity

Outcome	Common-τ	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
Continuous	**Value**	**From Rhodes et al. [1]**	**Median (IQR)**		
Overall symptoms (SMD)	0	Mental health outcome	0.19 (IQR 0.09, 0.42)	Below 25%-quantile	low
Positive symptoms (SMD)	0	Mental health outcome	0.19 (IQR 0.09, 0.42)	Below 25%-quantile	low
Negative symptoms (SMD)	0	Mental health outcome	0.19 (IQR 0.09, 0.42)	Below 25%-quantile	low
Depressive symptoms (SMD)	0.045	Mental health outcome	0.19 (IQR 0.09, 0.42)	Below 25%-quantile	low
Social functioning (SMD)	0	Mental health outcome	0.19 (IQR 0.09, 0.42)	Below 25%-quantile	low
Quality of life (SMD)	0.134	Mental health outcome	0.19 (IQR 0.09, 0.42)	Between 25%- and 50%-quantile	low-moderate
Weight gain (MD [kg])	1.045	Outcome estimated as mean difference (MD). No comparator available	-	-	-
Weight gain (SMD)‡	0.136	Biological marker	0.16 (IQR 0.06, 0.44)	Between 25%- and 50%-quantile	low-moderate
Prolactin (MD [ng/ml])	6.153	Outcome estimated as mean difference (MD). No comparator available	-	-	-
Prolactin (SMD)‡	0	Biological marker	0.16 (IQR 0.06, 0.44)	Below 25%-quantile	low
QTc (MD [ms])	0	Outcome estimated as mean difference (MD). No comparator available	-	-	-
QTc (SMD)‡	0	Biological marker	0.16 (IQR 0.06, 0.44)	Below 25%-quantile	low

Dichotomous	Value	From Turner et al.[153]	Median (IQR)		
All cause discontinuation (OR)	0	Withdrawal/drop-outs	0.20 (IQR 0.11, 0.36)	Below 25%-quantile	low
Use of antiparkinson medication (OR)	0.054	Adverse event	0.35 (IQR 0.21, 0.60)	Below 25%-quantile	low
Akathisia (OR)	0	Adverse event	0.35 (IQR 0.21, 0.60)	Below 25%-quantile	low
Sedation (OR)	0.117	Adverse event	0.35 (IQR 0.21, 0.60)	Below 25%-quantile	low

** Intervention comparison type always pharmacological vs pharmacological*

‡ Because no predictive distributions are available for mean differences (MD) in QTc, Body weight and Prolactin (i.e. differences in the original units) we additionally conducted network meta-analyses with standardized mean difference (SMD) for these outcomes and compared the common-tau of this analysis with the available predictive distribution for biological markers.

References

1. Rhodes KM, Turner RM, Higgins JPT. Predictive distributions were developed for the extent of heterogeneity in meta-analyses of continuous outcome data. *J Clin Epidemiol* 2015; **68:** 52–60. https://doi.org/10.1016/j.jclinepi.2014.08.012.

2. Turner RM, Jackson D, Wei Y, Thompson SG, Higgins JPT. Predictive distributions for between-study heterogeneity and simple methods for their application in Bayesian meta-analysis. *Stat Med* 2015; **34:** 984–98. https://doi.org/10.1002/sim.6381.

Summary of inconsistency tests

	N studies in NMA	N participants in NMA	N interventions in NMA	N designs in NMA	N comparisons in NMA	Number of comparison which could Be Splitted	Number of Inconsistent Comparisons	Proportion of Inconsistent Comparisons	P value of design by treatment test
Overall symptoms	23	9814	14	19	26	23	0	0	0,977
Positive symptoms	14	6155	10	12	12	7	0	0	0,97
Negative symptoms	14	6155	10	12	12	7	0	0	0,995
Depression	11	6686	11	11	19	15	0	0	0,313
Dropout Total	26	8882	17	21	27	20	0	0	0,999
Weight gain	16	7542	12	14	20	16	2	**0,125**	**0,00016**
Antiparkinson medication	14	7794	11	13	19	16	1	0,0625	0,321
Akathisia	16	7916	11	14	20	18	0	0	0,941
Prolactin increase	10	5152	10	10	18	15	3	0,2	0,001
QTc prolongation	7	4060	9	7	14	9	0	0	0,849
Sedation	16	8096	12	14	22	19	0	0	0,986
Social functioning	5	1390	5	5	5	3	0	0	0,99
Quality of life	8	2949	9	7	14	9	0	0	**0,092**

N = number, NMA = network meta-analysis

Results from SIDE-tests

comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	Diff	95%-CI	z	p-value
Amisulpride:Aripiprazole	0	0	-0.10	[-0.29; 0.10]	.	.	-0.10	[-0.29; 0.10]	.	.	.	.
Amisulpride:Asenapine	0	0	-0.27	[-0.47; -0.07]	.	.	-0.27	[-0.47; -0.07]	.	.	.	.
Amisulpride:Clozapine	0	0	-0.05	[-0.47; 0.38]	.	.	-0.05	[-0.47; 0.38]	.	.	.	.
Amisulpride:Haloperidol	0	0	-0.21	[-0.40; -0.01]	.	.	-0.21	[-0.40; -0.01]	.	.	.	.
Amisulpride:Iloperidone	0	0	-0.26	[-0.49; -0.04]	.	.	-0.26	[-0.49; -0.04]	.	.	.	.
Amisulpride:Lurasidone	0	0	0.23	[-0.12; 0.58]	.	.	0.23	[-0.12; 0.58]	.	.	.	.
Amisulpride:Olanzapine	1	0.59	0.06	[-0.10; 0.22]	0.02	[-0.18; 0.22]	0.12	[-0.13; 0.36]	-0.10	[-0.42; 0.22]	-0.6160	0.5379
Amisulpride:Paliperidone	0	0	-0.22	[-0.43; -0.01]	.	.	-0.22	[-0.43; -0.01]	.	.	.	.
Amisulpride:Perphenazine	0	0	-0.03	[-0.24; 0.17]	.	.	-0.03	[-0.24; 0.17]	.	.	.	.
Amisulpride:Quetiapine	0	0	-0.19	[-0.38; 0.01]	.	.	-0.19	[-0.38; 0.01]	.	.	.	.
Amisulpride:Risperidone	1	0.51	-0.06	[-0.22; 0.10]	-0.01	[-0.23; 0.21]	-0.11	[-0.34; 0.12]	0.10	[-0.22; 0.42]	0.6160	0.5379
Amisulpride:Ziprasidone	0	0	-0.31	[-0.50; -0.12]	.	.	-0.31	[-0.50; -0.12]	.	.	.	.
Amisulpride:Zotepine	0	0	-0.10	[-0.51; 0.30]	.	.	-0.10	[-0.51; 0.30]	.	.	.	.
Aripiprazole:Asenapine	0	0	-0.17	[-0.34; 0.00]	.	.	-0.17	[-0.34; 0.00]	.	.	.	.
Aripiprazole:Clozapine	0	0	0.05	[-0.36; 0.46]	.	.	0.05	[-0.36; 0.46]	.	.	.	.
Aripiprazole:Haloperidol	1	0.78	-0.11	[-0.21; -0.01]	-0.12	[-0.23; 0.00]	-0.08	[-0.30; 0.14]	-0.04	[-0.29; 0.21]	-0.2843	0.7762
Aripiprazole:Iloperidone	0	0	-0.16	[-0.32; -0.01]	.	.	-0.16	[-0.32; -0.01]	.	.	.	.
Aripiprazole:Lurasidone	0	0	0.33	[-0.01; 0.67]	.	.	0.33	[-0.01; 0.67]	.	.	.	.
Aripiprazole:Olanzapine	1	0.55	0.16	[0.04; 0.28]	0.17	[0.00; 0.33]	0.15	[-0.03; 0.33]	0.02	[-0.22; 0.27]	0.1764	0.8600
Aripiprazole:Paliperidone	1	0.23	-0.12	[-0.31; 0.07]	-0.09	[-0.48; 0.31]	-0.13	[-0.35; 0.09]	0.04	[-0.41; 0.50]	0.1903	0.8491
Aripiprazole:Perphenazine	0	0	0.07	[-0.12; 0.25]	.	.	0.07	[-0.12; 0.25]	.	.	.	.
Aripiprazole:Quetiapine	0	0	-0.09	[-0.27; 0.08]	.	.	-0.09	[-0.27; 0.08]	.	.	.	.
Aripiprazole:Risperidone	0	0	0.04	[-0.11; 0.18]	.	.	0.04	[-0.11; 0.18]	.	.	.	.
Aripiprazole:Ziprasidone	0	0	-0.22	[-0.38; -0.05]	.	.	-0.22	[-0.38; -0.05]	.	.	.	.
Aripiprazole:Zotepine	0	0	-0.00	[-0.37; 0.37]	.	.	-0.00	[-0.37; 0.37]	.	.	.	.
Asenapine:Clozapine	1	0.79	0.22	[-0.18; 0.62]	0.37	[-0.07; 0.82]	-0.35	[-1.22; 0.51]	0.73	[-0.24; 1.70]	1.4656	0.1428
Asenapine:Haloperidol	1	0.14	0.06	[-0.11; 0.23]	0.20	[-0.23; 0.64]	0.04	[-0.14; 0.22]	0.17	[-0.31; 0.64]	0.6947	0.4872
Asenapine:Iloperidone	0	0	0.01	[-0.19; 0.21]	.	.	0.01	[-0.19; 0.21]	.	.	.	.
Asenapine:Lurasidone	0	0	0.50	[0.16; 0.84]	.	.	0.50	[0.16; 0.84]	.	.	.	.
Asenapine:Olanzapine	1	0.86	0.33	[0.21; 0.45]	0.29	[0.16; 0.42]	0.57	[0.25; 0.89]	-0.28	[-0.63; 0.06]	-1.5947	0.1108
Asenapine:Paliperidone	0	0	0.05	[-0.15; 0.25]	.	.	0.05	[-0.15; 0.25]	.	.	.	.
Asenapine:Perphenazine	0	0	0.24	[0.05; 0.42]	.	.	0.24	[0.05; 0.42]	.	.	.	.
Asenapine:Quetiapine	0	0	0.08	[-0.10; 0.26]	.	.	0.08	[-0.10; 0.26]	.	.	.	.
Asenapine:Risperidone	0	0	0.21	[0.06; 0.36]	.	.	0.21	[0.06; 0.36]	.	.	.	.
Asenapine:Ziprasidone	1	0.14	-0.05	[-0.21; 0.12]	0.26	[-0.18; 0.70]	-0.09	[-0.27; 0.08]	0.35	[-0.12; 0.82]	1.4658	0.1427
Asenapine:Zotepine	0	0	0.17	[-0.22; 0.56]	.	.	0.17	[-0.22; 0.56]	.	.	.	.
Clozapine:Haloperidol	0	0	-0.16	[-0.57; 0.25]	.	.	-0.16	[-0.57; 0.25]	.	.	.	.
Clozapine:Iloperidone	0	0	-0.21	[-0.64; 0.22]	.	.	-0.21	[-0.64; 0.22]	.	.	.	.
Clozapine:Lurasidone	0	0	0.28	[-0.23; 0.78]	.	.	0.28	[-0.23; 0.78]	.	.	.	.
Clozapine:Olanzapine	0	0	0.11	[-0.29; 0.51]	.	.	0.11	[-0.29; 0.51]	.	.	.	.
Clozapine:Paliperidone	0	0	-0.17	[-0.60; 0.26]	.	.	-0.17	[-0.60; 0.26]	.	.	.	.
Clozapine:Perphenazine	0	0	0.02	[-0.40; 0.43]	.	.	0.02	[-0.40; 0.43]	.	.	.	.
Clozapine:Quetiapine	0	0	-0.14	[-0.55; 0.27]	.	.	-0.14	[-0.55; 0.27]	.	.	.	.
Clozapine:Risperidone	0	0	-0.01	[-0.42; 0.39]	.	.	-0.01	[-0.42; 0.39]	.	.	.	.
Clozapine:Ziprasidone	1	0.79	-0.27	[-0.66; 0.13]	-0.11	[-0.56; 0.33]	-0.84	[-1.71; 0.02]	0.73	[-0.25; 1.71]	1.4656	0.1428

Clozapine:Zotepine	0	0	-0.05	[-0.60;	0.49]	.		.	-0.05	[-0.60;	0.49]	.		.	.	.
Haloperidol:Iloperidone	3	1.00	-0.05	[-0.17;	0.06]	-0.05	[-0.17;	0.06]	.		.	.		.	.	.
Haloperidol:Lurasidone	0	0	0.44	[0.10;	0.78]	.		.	0.44	[0.10;	0.78]	.		.	.	.
Haloperidol:Olanzapine	2	0.48	0.27	[0.14;	0.39]	0.29	[0.11;	0.47]	0.25	[0.08;	0.42]	0.04	[-0.21;	0.29]	0.3031	0.7618
Haloperidol:Paliperidone	0	0	-0.01	[-0.20;	0.18]	.		.	-0.01	[-0.20;	0.18]	.		.	.	.
Haloperidol:Perphenazine	0	0	0.18	[-0.01;	0.36]	.		.	0.18	[-0.01;	0.36]	.		.	.	.
Haloperidol:Quetiapine	0	0	0.02	[-0.16;	0.19]	.		.	0.02	[-0.16;	0.19]	.		.	.	.
Haloperidol:Risperidone	1	0.31	0.15	[0.00;	0.29]	0.12	[-0.14;	0.38]	0.16	[-0.01;	0.34]	-0.04	[-0.35;	0.27]	-0.2696	0.7875
Haloperidol:Ziprasidone	0	0	-0.11	[-0.27;	0.06]	.		.	-0.11	[-0.27;	0.06]	.		.	.	.
Haloperidol:Zotepine	1	1.00	0.11	[-0.25;	0.46]	0.11	[-0.25;	0.46]	.		.	.		.	.	.
Iloperidone:Lurasidone	0	0	0.49	[0.13;	0.85]	.		.	0.49	[0.13;	0.85]	.		.	.	.
Iloperidone:Olanzapine	0	0	0.32	[0.15;	0.49]	.		.	0.32	[0.15;	0.49]	.		.	.	.
Iloperidone:Paliperidone	0	0	0.04	[-0.18;	0.27]	.		.	0.04	[-0.18;	0.27]	.		.	.	.
Iloperidone:Perphenazine	0	0	0.23	[0.01;	0.45]	.		.	0.23	[0.01;	0.45]	.		.	.	.
Iloperidone:Quetiapine	0	0	0.07	[-0.14;	0.28]	.		.	0.07	[-0.14;	0.28]	.		.	.	.
Iloperidone:Risperidone	0	0	0.20	[0.02;	0.39]	.		.	0.20	[0.02;	0.39]	.		.	.	.
Iloperidone:Ziprasidone	0	0	-0.05	[-0.25;	0.15]	.		.	-0.05	[-0.25;	0.15]	.		.	.	.
Iloperidone:Zotepine	0	0	0.16	[-0.21;	0.53]	.		.	0.16	[-0.21;	0.53]	.		.	.	.
Lurasidone:Olanzapine	0	0	-0.17	[-0.49;	0.15]	.		.	-0.17	[-0.49;	0.15]	.		.	.	.
Lurasidone:Paliperidone	0	0	-0.45	[-0.80;	-0.10]	.		.	-0.45	[-0.80;	-0.10]	.		.	.	.
Lurasidone:Perphenazine	0	0	-0.26	[-0.59;	0.07]	.		.	-0.26	[-0.59;	0.07]	.		.	.	.
Lurasidone:Quetiapine	1	1.00	-0.42	[-0.71;	-0.13]	-0.42	[-0.71;	-0.13]	.		.	.		.	.	.
Lurasidone:Risperidone	0	0	-0.29	[-0.61;	0.03]	.		.	-0.29	[-0.61;	0.03]	.		.	.	.
Lurasidone:Ziprasidone	0	0	-0.54	[-0.87;	-0.22]	.		.	-0.54	[-0.87;	-0.22]	.		.	.	.
Lurasidone:Zotepine	0	0	-0.33	[-0.82;	0.16]	.		.	-0.33	[-0.82;	0.16]	.		.	.	.
Paliperidone:Olanzapine	0	0	0.28	[0.11;	0.44]	.		.	0.28	[0.11;	0.44]	.		.	.	.
Perphenazine:Olanzapine	2	0.82	0.09	[-0.05;	0.24]	0.09	[-0.07;	0.24]	0.12	[-0.22;	0.46]	-0.03	[-0.40;	0.34]	-0.1595	0.8733
Quetiapine:Olanzapine	2	0.81	0.25	[0.12;	0.38]	0.24	[0.10;	0.39]	0.28	[-0.01;	0.58]	-0.04	[-0.37;	0.29]	-0.2308	0.8175
Risperidone:Olanzapine	4	0.78	0.12	[0.03;	0.21]	0.14	[0.04;	0.25]	0.04	[-0.17;	0.24]	0.11	[-0.12;	0.33]	0.9315	0.3516
Ziprasidone:Olanzapine	3	0.88	0.37	[0.26;	0.49]	0.39	[0.27;	0.51]	0.25	[-0.08;	0.59]	0.14	[-0.22;	0.49]	0.7507	0.4529
Zotepine:Olanzapine	0	0	0.16	[-0.22;	0.54]	.		.	0.16	[-0.22;	0.54]	.		.	.	.
Paliperidone:Perphenazine	0	0	0.19	[-0.02;	0.39]	.		.	0.19	[-0.02;	0.39]	.		.	.	.
Paliperidone:Quetiapine	0	0	0.03	[-0.17;	0.22]	.		.	0.03	[-0.17;	0.22]	.		.	.	.
Paliperidone:Risperidone	1	0.89	0.16	[0.02;	0.30]	0.16	[0.01;	0.32]	0.12	[-0.31;	0.55]	0.04	[-0.41;	0.50]	0.1903	0.8491
Paliperidone:Ziprasidone	0	0	-0.10	[-0.29;	0.10]	.		.	-0.10	[-0.29;	0.10]	.		.	.	.
Paliperidone:Zotepine	0	0	0.12	[-0.29;	0.52]	.		.	0.12	[-0.29;	0.52]	.		.	.	.
Perphenazine:Quetiapine	1	0.95	-0.16	[-0.32;	0.00]	-0.16	[-0.32;	0.00]	-0.11	[-0.82;	0.60]	-0.05	[-0.77;	0.68]	-0.1325	0.8946
Perphenazine:Risperidone	1	0.83	-0.03	[-0.17;	0.12]	0.00	[-0.16;	0.16]	-0.15	[-0.51;	0.20]	0.15	[-0.24;	0.54]	0.7616	0.4463
Perphenazine:Ziprasidone	1	0.74	-0.28	[-0.44;	-0.12]	-0.30	[-0.49;	-0.11]	-0.22	[-0.54;	0.10]	-0.08	[-0.45;	0.29]	-0.4257	0.6703
Perphenazine:Zotepine	0	0	-0.07	[-0.47;	0.33]	.		.	-0.07	[-0.47;	0.33]	.		.	.	.
Quetiapine:Risperidone	1	0.80	0.13	[-0.01;	0.27]	0.16	[0.01;	0.31]	0.02	[-0.28;	0.32]	0.14	[-0.20;	0.48]	0.8197	0.4124
Quetiapine:Ziprasidone	1	0.71	-0.12	[-0.28;	0.03]	-0.14	[-0.32;	0.04]	-0.08	[-0.36;	0.20]	-0.06	[-0.40;	0.27]	-0.3783	0.7052
Quetiapine:Zotepine	0	0	0.09	[-0.31;	0.49]	.		.	0.09	[-0.31;	0.49]	.		.	.	.
Risperidone:Ziprasidone	1	0.55	-0.25	[-0.39;	-0.12]	-0.30	[-0.48;	-0.12]	-0.20	[-0.40;	0.00]	-0.10	[-0.37;	0.16]	-0.7631	0.4454
Risperidone:Zotepine	0	0	-0.04	[-0.42;	0.34]	.		.	-0.04	[-0.42;	0.34]	.		.	.	.
Ziprasidone:Zotepine	0	0	0.21	[-0.18;	0.61]	.		.	0.21	[-0.18;	0.61]	.		.	.	.

Legend:
 comparison - Treatment comparison
 k   - Number of studies providing direct evidence

```
prop       - Direct evidence proportion
nma        - Estimated treatment effect (SMD) in network meta-analysis
direct     - Estimated treatment effect (SMD) derived from direct evidence
indir.     - Estimated treatment effect (SMD) derived from indirect evidence
Diff       - Difference between direct and indirect treatment estimates
z          - z-value of test for disagreement (direct versus indirect)
p-value    - p-value of test for disagreement (direct versus indirect)
```

Results from SIDE-tests positive symptoms

Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	Diff	95%-CI	z	p-value
Amisulpride:Aripiprazole	0	0	-0.13	[-0.34; 0.08]	.	.	-0.13	[-0.34; 0.08]	.	.	.	.
Amisulpride:Asenapine	0	0	-0.23	[-0.44; -0.01]	.	.	-0.23	[-0.44; -0.01]	.	.	.	.
Amisulpride:Chlorpromazine	0	0	-0.46	[-0.90; -0.03]	.	.	-0.46	[-0.90; -0.03]	.	.	.	.
Amisulpride:Haloperidol	0	0	-0.11	[-0.32; 0.09]	.	.	-0.11	[-0.32; 0.09]	.	.	.	.
Amisulpride:Olanzapine	1	0.67	0.05	[-0.12; 0.21]	0.00	[-0.20; 0.20]	0.14	[-0.15; 0.43]	-0.14	[-0.49; 0.21]	-0.7811	0.4348
Amisulpride:Paliperidone	0	0	-0.27	[-0.50; -0.04]	.	.	-0.27	[-0.50; -0.04]	.	.	.	.
Amisulpride:Risperidone	1	0.50	-0.03	[-0.21; 0.15]	0.04	[-0.21; 0.29]	-0.10	[-0.35; 0.15]	0.14	[-0.21; 0.49]	0.7811	0.4348
Amisulpride:Ziprasidone	0	0	-0.33	[-0.56; -0.09]	.	.	-0.33	[-0.56; -0.09]	.	.	.	.
Amisulpride:Zotepine	0	0	-0.14	[-0.55; 0.27]	.	.	-0.14	[-0.55; 0.27]	.	.	.	.
Aripiprazole:Asenapine	0	0	-0.09	[-0.28; 0.09]	.	.	-0.09	[-0.28; 0.09]	.	.	.	.
Aripiprazole:Chlorpromazine	0	0	-0.33	[-0.77; 0.10]	.	.	-0.33	[-0.77; 0.10]	.	.	.	.
Aripiprazole:Haloperidol	1	0.81	0.02	[-0.08; 0.12]	0.03	[-0.09; 0.15]	-0.02	[-0.26; 0.21]	0.05	[-0.21; 0.32]	0.3870	0.6988
Aripiprazole:Olanzapine	1	0.61	0.18	[0.05; 0.31]	0.16	[-0.01; 0.32]	0.21	[0.00; 0.42]	-0.05	[-0.32; 0.21]	-0.3870	0.6988
Aripiprazole:Paliperidone	0	0	-0.14	[-0.37; 0.09]	.	.	-0.14	[-0.37; 0.09]	.	.	.	.
Aripiprazole:Risperidone	0	0	0.10	[-0.07; 0.28]	.	.	0.10	[-0.07; 0.28]	.	.	.	.
Aripiprazole:Ziprasidone	0	0	-0.20	[-0.41; 0.01]	.	.	-0.20	[-0.41; 0.01]	.	.	.	.
Aripiprazole:Zotepine	0	0	-0.01	[-0.38; 0.36]	.	.	-0.01	[-0.38; 0.36]	.	.	.	.
Asenapine:Chlorpromazine	0	0	-0.24	[-0.68; 0.20]	.	.	-0.24	[-0.68; 0.20]	.	.	.	.
Asenapine:Haloperidol	0	0	0.11	[-0.07; 0.30]	.	.	0.11	[-0.07; 0.30]	.	.	.	.
Asenapine:Olanzapine	1	1.00	0.27	[0.14; 0.41]	0.27	[0.14; 0.41]	.	.	.	.	.	.
Asenapine:Paliperidone	0	0	-0.04	[-0.28; 0.20]	.	.	-0.04	[-0.28; 0.20]	.	.	.	.
Asenapine:Risperidone	0	0	0.20	[0.01; 0.38]	.	.	0.20	[0.01; 0.38]	.	.	.	.
Asenapine:Ziprasidone	0	0	-0.10	[-0.31; 0.11]	.	.	-0.10	[-0.31; 0.11]	.	.	.	.
Asenapine:Zotepine	0	0	0.09	[-0.31; 0.49]	.	.	0.09	[-0.31; 0.49]	.	.	.	.
Chlorpromazine:Haloperidol	0	0	0.35	[-0.08; 0.78]	.	.	0.35	[-0.08; 0.78]	.	.	.	.
Chlorpromazine:Olanzapine	0	0	0.51	[0.09; 0.93]	.	.	0.51	[0.09; 0.93]	.	.	.	.
Chlorpromazine:Paliperidone	0	0	0.19	[-0.23; 0.62]	.	.	0.19	[-0.23; 0.62]	.	.	.	.
Chlorpromazine:Risperidone	1	1.00	0.44	[0.04; 0.83]	0.44	[0.04; 0.83]	.	.	.	.	.	.
Chlorpromazine:Ziprasidone	0	0	0.14	[-0.31; 0.59]	.	.	0.14	[-0.31; 0.59]	.	.	.	.
Chlorpromazine:Zotepine	0	0	0.32	[-0.23; 0.88]	.	.	0.32	[-0.23; 0.88]	.	.	.	.
Haloperidol:Olanzapine	2	0.55	0.16	[0.03; 0.29]	0.19	[0.01; 0.37]	0.12	[-0.07; 0.31]	0.07	[-0.19; 0.33]	0.5243	0.6001
Haloperidol:Paliperidone	0	0	-0.16	[-0.39; 0.07]	.	.	-0.16	[-0.39; 0.07]	.	.	.	.
Haloperidol:Risperidone	1	0.43	0.08	[-0.09; 0.25]	0.09	[-0.17; 0.35]	0.08	[-0.15; 0.30]	0.02	[-0.33; 0.36]	0.1013	0.9193
Haloperidol:Ziprasidone	0	0	-0.22	[-0.43; -0.01]	.	.	-0.22	[-0.43; -0.01]	.	.	.	.
Haloperidol:Zotepine	1	1.00	-0.03	[-0.38; 0.33]	-0.03	[-0.38; 0.33]	.	.	.	.	.	.
Paliperidone:Olanzapine	0	0	0.32	[0.12; 0.52]	.	.	0.32	[0.12; 0.52]	.	.	.	.
Risperidone:Olanzapine	3	0.78	0.08	[-0.06; 0.21]	0.11	[-0.04; 0.26]	-0.04	[-0.32; 0.24]	0.15	[-0.17; 0.47]	0.9159	0.3597
Ziprasidone:Olanzapine	2	1.00	0.37	[0.21; 0.54]	0.37	[0.21; 0.54]	.	.	.	.	.	.
Zotepine:Olanzapine	0	0	0.19	[-0.19; 0.56]	.	.	0.19	[-0.19; 0.56]	.	.	.	.
Paliperidone:Risperidone	1	1.00	0.24	[0.09; 0.39]	0.24	[0.09; 0.39]	.	.	.	.	.	.
Paliperidone:Ziprasidone	0	0	-0.06	[-0.32; 0.20]	.	.	-0.06	[-0.32; 0.20]	.	.	.	.
Paliperidone:Zotepine	0	0	0.13	[-0.29; 0.55]	.	.	0.13	[-0.29; 0.55]	.	.	.	.
Risperidone:Ziprasidone	0	0	-0.30	[-0.51; -0.09]	.	.	-0.30	[-0.51; -0.09]	.	.	.	.
Risperidone:Zotepine	0	0	-0.11	[-0.50; 0.28]	.	.	-0.11	[-0.50; 0.28]	.	.	.	.

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        Ziprasidone:Zotepine 0    0  0.19 [-0.22;  0.60]      .             .   0.19 [-0.22;  0.60]     .             .       .       .

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (SMD) in network meta-analysis
 direct     - Estimated treatment effect (SMD) derived from direct evidence
 indir.     - Estimated treatment effect (SMD) derived from indirect evidence
 Diff       - Difference between direct and indirect treatment estimates
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
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Results from SIDE-tests Depression

Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	Diff	95%-CI	z	p-value
Amisulpride:Aripiprazole	0	0	0.07	[-0.18; 0.33]	.	.	0.07	[-0.18; 0.33]	.	.	.	.
Amisulpride:Asenapine	0	0	-0.04	[-0.28; 0.19]	.	.	-0.04	[-0.28; 0.19]	.	.	.	.
Amisulpride:Haloperidol	0	0	-0.05	[-0.30; 0.21]	.	.	-0.05	[-0.30; 0.21]	.	.	.	.
Amisulpride:Lurasidone	0	0	0.41	[0.03; 0.79]	.	.	0.41	[0.03; 0.79]	.	.	.	.
Amisulpride:Olanzapine	1	0.64	0.12	[-0.06; 0.29]	0.02	[-0.20; 0.24]	0.28	[-0.01; 0.58]	-0.26	[-0.63; 0.10]	-1.4020	0.1609
Amisulpride:Paliperidone	0	0	-0.14	[-0.39; 0.12]	.	.	-0.14	[-0.39; 0.12]	.	.	.	.
Amisulpride:Perphenazine	0	0	0.08	[-0.16; 0.31]	.	.	0.08	[-0.16; 0.31]	.	.	.	.
Amisulpride:Quetiapine	0	0	0.10	[-0.13; 0.34]	.	.	0.10	[-0.13; 0.34]	.	.	.	.
Amisulpride:Risperidone	1	0.47	0.02	[-0.16; 0.20]	0.16	[-0.11; 0.42]	-0.11	[-0.36; 0.15]	0.26	[-0.10; 0.63]	1.4020	0.1609
Amisulpride:Ziprasidone	0	0	-0.02	[-0.24; 0.20]	.	.	-0.02	[-0.24; 0.20]	.	.	.	.
Aripiprazole:Asenapine	0	0	-0.12	[-0.36; 0.13]	.	.	-0.12	[-0.36; 0.13]	.	.	.	.
Aripiprazole:Haloperidol	1	0.85	-0.12	[-0.25; 0.02]	-0.12	[-0.27; 0.02]	-0.09	[-0.45; 0.26]	-0.03	[-0.41; 0.35]	-0.1437	0.8857
Aripiprazole:Lurasidone	0	0	0.34	[-0.05; 0.73]	.	.	0.34	[-0.05; 0.73]	.	.	.	.
Aripiprazole:Olanzapine	1	0.58	0.04	[-0.14; 0.23]	0.06	[-0.19; 0.30]	0.03	[-0.26; 0.32]	0.03	[-0.35; 0.41]	0.1437	0.8857
Aripiprazole:Paliperidone	0	0	-0.21	[-0.48; 0.06]	.	.	-0.21	[-0.48; 0.06]	.	.	.	.
Aripiprazole:Perphenazine	0	0	0.01	[-0.24; 0.26]	.	.	0.01	[-0.24; 0.26]	.	.	.	.
Aripiprazole:Quetiapine	0	0	0.03	[-0.22; 0.28]	.	.	0.03	[-0.22; 0.28]	.	.	.	.
Aripiprazole:Risperidone	0	0	-0.05	[-0.26; 0.15]	.	.	-0.05	[-0.26; 0.15]	.	.	.	.
Aripiprazole:Ziprasidone	0	0	-0.10	[-0.33; 0.13]	.	.	-0.10	[-0.33; 0.13]	.	.	.	.
Asenapine:Haloperidol	0	0	-0.00	[-0.25; 0.25]	.	.	-0.00	[-0.25; 0.25]	.	.	.	.
Asenapine:Lurasidone	0	0	0.45	[0.07; 0.84]	.	.	0.45	[0.07; 0.84]	.	.	.	.
Asenapine:Olanzapine	1	1.00	0.16	[0.00; 0.32]	0.16	[0.00; 0.32]	.	.	.	.	.	.
Asenapine:Paliperidone	0	0	-0.09	[-0.36; 0.17]	.	.	-0.09	[-0.36; 0.17]	.	.	.	.
Asenapine:Perphenazine	0	0	0.12	[-0.11; 0.36]	.	.	0.12	[-0.11; 0.36]	.	.	.	.
Asenapine:Quetiapine	0	0	0.15	[-0.08; 0.38]	.	.	0.15	[-0.08; 0.38]	.	.	.	.
Asenapine:Risperidone	0	0	0.06	[-0.13; 0.26]	.	.	0.06	[-0.13; 0.26]	.	.	.	.
Asenapine:Ziprasidone	0	0	0.02	[-0.19; 0.23]	.	.	0.02	[-0.19; 0.23]	.	.	.	.
Haloperidol:Lurasidone	0	0	0.46	[0.06; 0.85]	.	.	0.46	[0.06; 0.85]	.	.	.	.
Haloperidol:Olanzapine	1	0.48	0.16	[-0.03; 0.35]	0.14	[-0.13; 0.42]	0.18	[-0.08; 0.44]	-0.04	[-0.41; 0.34]	-0.1861	0.8523
Haloperidol:Paliperidone	0	0	-0.09	[-0.36; 0.18]	.	.	-0.09	[-0.36; 0.18]	.	.	.	.
Haloperidol:Perphenazine	0	0	0.12	[-0.13; 0.37]	.	.	0.12	[-0.13; 0.37]	.	.	.	.
Haloperidol:Quetiapine	0	0	0.15	[-0.10; 0.40]	.	.	0.15	[-0.10; 0.40]	.	.	.	.
Haloperidol:Risperidone	1	0.55	0.06	[-0.14; 0.27]	0.06	[-0.21; 0.33]	0.07	[-0.23; 0.37]	-0.01	[-0.42; 0.40]	-0.0465	0.9629
Haloperidol:Ziprasidone	0	0	0.02	[-0.21; 0.25]	.	.	0.02	[-0.21; 0.25]	.	.	.	.
Lurasidone:Olanzapine	0	0	-0.29	[-0.64; 0.05]	.	.	-0.29	[-0.64; 0.05]	.	.	.	.
Lurasidone:Paliperidone	0	0	-0.55	[-0.94; -0.16]	.	.	-0.55	[-0.94; -0.16]	.	.	.	.
Lurasidone:Perphenazine	0	0	-0.33	[-0.69; 0.03]	.	.	-0.33	[-0.69; 0.03]	.	.	.	.
Lurasidone:Quetiapine	1	1.00	-0.31	[-0.61; 0.00]	-0.31	[-0.61; 0.00]	.	.	.	.	.	.
Lurasidone:Risperidone	0	0	-0.39	[-0.74; -0.04]	.	.	-0.39	[-0.74; -0.04]	.	.	.	.
Lurasidone:Ziprasidone	0	0	-0.43	[-0.79; -0.08]	.	.	-0.43	[-0.79; -0.08]	.	.	.	.
Paliperidone:Olanzapine	0	0	0.25	[0.05; 0.46]	.	.	0.25	[0.05; 0.46]	.	.	.	.
Perphenazine:Olanzapine	1	0.79	0.04	[-0.13; 0.21]	-0.00	[-0.19; 0.19]	0.18	[-0.19; 0.56]	-0.18	[-0.60; 0.24]	-0.8478	0.3966
Quetiapine:Olanzapine	1	0.79	0.01	[-0.16; 0.18]	-0.03	[-0.22; 0.17]	0.16	[-0.22; 0.53]	-0.18	[-0.60; 0.24]	-0.8478	0.3965

Risperidone:Olanzapine	3	0.82	0.10	[-0.02;	0.21]	0.12	[0.00;	0.25]	-0.02	[-0.29;	0.25]	0.14	[-0.16;	0.44]	0.9253	0.3548
Ziprasidone:Olanzapine	2	0.94	0.14	[0.00;	0.28]	0.13	[-0.02;	0.27]	0.34	[-0.25;	0.93]	-0.21	[-0.82;	0.39]	-0.6932	0.4882
Paliperidone:Perphenazine	0	0	0.22	[-0.03;	0.46]	.		.	0.22	[-0.03;	0.46]	.		.	.	.
Paliperidone:Quetiapine	0	0	0.24	[-0.01;	0.49]	.		.	0.24	[-0.01;	0.49]	.		.	.	.
Paliperidone:Risperidone	1	1.00	0.16	[-0.02;	0.33]	0.16	[-0.02;	0.33]	.		.	.		.	.	.
Paliperidone:Ziprasidone	0	0	0.11	[-0.12;	0.35]	.		.	0.11	[-0.12;	0.35]	.		.	.	.
Perphenazine:Quetiapine	1	1.00	0.03	[-0.17;	0.22]	0.03	[-0.17;	0.22]	.		.	.		.	.	.
Perphenazine:Risperidone	1	0.84	-0.06	[-0.24;	0.12]	-0.03	[-0.22;	0.16]	-0.20	[-0.64;	0.24]	0.17	[-0.31;	0.65]	0.6934	0.4881
Perphenazine:Ziprasidone	1	0.77	-0.10	[-0.30;	0.09]	-0.09	[-0.31;	0.13]	-0.16	[-0.56;	0.25]	0.07	[-0.39;	0.53]	0.3091	0.7572
Quetiapine:Risperidone	1	0.84	-0.09	[-0.26;	0.09]	-0.06	[-0.25;	0.13]	-0.23	[-0.66;	0.21]	0.17	[-0.31;	0.64]	0.6936	0.4879
Quetiapine:Ziprasidone	1	0.77	-0.13	[-0.32;	0.06]	-0.11	[-0.33;	0.11]	-0.18	[-0.59;	0.22]	0.07	[-0.39;	0.53]	0.3093	0.7571
Risperidone:Ziprasidone	1	0.55	-0.04	[-0.21;	0.12]	-0.05	[-0.27;	0.16]	-0.03	[-0.27;	0.21]	-0.02	[-0.35;	0.30]	-0.1471	0.8831

Legend:
- comparison - Treatment comparison
- k - Number of studies providing direct evidence
- prop - Direct evidence proportion
- nma - Estimated treatment effect (SMD) in network meta-analysis
- direct - Estimated treatment effect (SMD) derived from direct evidence
- indir. - Estimated treatment effect (SMD) derived from indirect evidence
- Diff - Difference between direct and indirect treatment estimates
- z - z-value of test for disagreement (direct versus indirect)
- p-value - p-value of test for disagreement (direct versus indirect)

Results from SIDE-tests negative symptoms

Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	Diff	95%-CI	z	p-value
Amisulpride:Aripiprazole	0	0	-0.11	[-0.32; 0.10]	.	.	-0.11	[-0.32; 0.10]	.	.	.	.
Amisulpride:Asenapine	0	0	-0.19	[-0.41; 0.02]	.	.	-0.19	[-0.41; 0.02]	.	.	.	.
Amisulpride:Chlorpromazine	0	0	-2.33	[-2.86; -1.80]	.	.	-2.33	[-2.86; -1.80]	.	.	.	.
Amisulpride:Haloperidol	0	0	-0.25	[-0.45; -0.04]	.	.	-0.25	[-0.45; -0.04]	.	.	.	.
Amisulpride:Olanzapine	1	0.67	0.02	[-0.14; 0.19]	0.04	[-0.16; 0.25]	-0.02	[-0.31; 0.27]	0.06	[-0.29; 0.42]	0.3423	0.7321
Amisulpride:Paliperidone	0	0	-0.16	[-0.40; 0.07]	.	.	-0.16	[-0.40; 0.07]	.	.	.	.
Amisulpride:Risperidone	1	0.50	-0.18	[-0.36; 0.00]	-0.21	[-0.46; 0.04]	-0.15	[-0.40; 0.10]	-0.06	[-0.42; 0.29]	-0.3423	0.7321
Amisulpride:Ziprasidone	0	0	-0.31	[-0.54; -0.07]	.	.	-0.31	[-0.54; -0.07]	.	.	.	.
Amisulpride:Zotepine	0	0	-0.17	[-0.58; 0.24]	.	.	-0.17	[-0.58; 0.24]	.	.	.	.
Aripiprazole:Asenapine	0	0	-0.08	[-0.27; 0.10]	.	.	-0.08	[-0.27; 0.10]	.	.	.	.
Aripiprazole:Chlorpromazine	0	0	-2.22	[-2.75; -1.70]	.	.	-2.22	[-2.75; -1.70]	.	.	.	.
Aripiprazole:Haloperidol	1	0.81	-0.14	[-0.24; -0.03]	-0.15	[-0.27; -0.04]	-0.09	[-0.33; 0.15]	-0.06	[-0.33; 0.20]	-0.4738	0.6356
Aripiprazole:Olanzapine	1	0.61	0.13	[0.00; 0.26]	0.16	[-0.01; 0.32]	0.09	[-0.11; 0.30]	0.06	[-0.20; 0.33]	0.4738	0.6356
Aripiprazole:Paliperidone	0	0	-0.06	[-0.29; 0.17]	.	.	-0.06	[-0.29; 0.17]	.	.	.	.
Aripiprazole:Risperidone	0	0	-0.07	[-0.25; 0.10]	.	.	-0.07	[-0.25; 0.10]	.	.	.	.
Aripiprazole:Ziprasidone	0	0	-0.20	[-0.41; 0.01]	.	.	-0.20	[-0.41; 0.01]	.	.	.	.
Aripiprazole:Zotepine	0	0	-0.06	[-0.43; 0.31]	.	.	-0.06	[-0.43; 0.31]	.	.	.	.
Asenapine:Chlorpromazine	0	0	-2.14	[-2.67; -1.61]	.	.	-2.14	[-2.67; -1.61]	.	.	.	.
Asenapine:Haloperidol	0	0	-0.05	[-0.24; 0.13]	.	.	-0.05	[-0.24; 0.13]	.	.	.	.
Asenapine:Olanzapine	1	1.00	0.22	[0.08; 0.35]	0.22	[0.08; 0.35]	.	.	.	.	.	.
Asenapine:Paliperidone	0	0	0.03	[-0.21; 0.27]	.	.	0.03	[-0.21; 0.27]	.	.	.	.
Asenapine:Risperidone	0	0	0.01	[-0.18; 0.20]	.	.	0.01	[-0.18; 0.20]	.	.	.	.
Asenapine:Ziprasidone	0	0	-0.11	[-0.33; 0.10]	.	.	-0.11	[-0.33; 0.10]	.	.	.	.
Asenapine:Zotepine	0	0	0.02	[-0.38; 0.42]	.	.	0.02	[-0.38; 0.42]	.	.	.	.
Chlorpromazine:Haloperidol	0	0	2.08	[1.56; 2.61]	.	.	2.08	[1.56; 2.61]	.	.	.	.
Chlorpromazine:Olanzapine	0	0	2.35	[1.84; 2.87]	.	.	2.35	[1.84; 2.87]	.	.	.	.
Chlorpromazine:Paliperidone	0	0	2.17	[1.65; 2.68]	.	.	2.17	[1.65; 2.68]	.	.	.	.
Chlorpromazine:Risperidone	1	1.00	2.15	[1.65; 2.65]	2.15	[1.65; 2.65]	.	.	.	.	.	.
Chlorpromazine:Ziprasidone	0	0	2.02	[1.48; 2.56]	.	.	2.02	[1.48; 2.56]	.	.	.	.
Chlorpromazine:Zotepine	0	0	2.16	[1.53; 2.79]	.	.	2.16	[1.53; 2.79]	.	.	.	.
Haloperidol:Olanzapine	2	0.54	0.27	[0.14; 0.40]	0.24	[0.07; 0.42]	0.30	[0.11; 0.50]	-0.06	[-0.32; 0.20]	-0.4642	0.6425
Haloperidol:Paliperidone	0	0	0.08	[-0.15; 0.31]	.	.	0.08	[-0.15; 0.31]	.	.	.	.
Haloperidol:Risperidone	1	0.44	0.07	[-0.10; 0.24]	0.02	[-0.24; 0.28]	0.10	[-0.13; 0.33]	-0.08	[-0.43; 0.26]	-0.4672	0.6404
Haloperidol:Ziprasidone	0	0	-0.06	[-0.27; 0.15]	.	.	-0.06	[-0.27; 0.15]	.	.	.	.
Haloperidol:Zotepine	1	1.00	0.08	[-0.28; 0.43]	0.08	[-0.28; 0.43]	.	.	.	.	.	.
Paliperidone:Olanzapine	0	0	0.19	[-0.01; 0.39]	.	.	0.19	[-0.01; 0.39]	.	.	.	.
Risperidone:Olanzapine	3	0.78	0.21	[0.07; 0.34]	0.18	[0.03; 0.33]	0.29	[0.01; 0.57]	-0.11	[-0.42; 0.21]	-0.6503	0.5155
Ziprasidone:Olanzapine	2	1.00	0.33	[0.17; 0.50]	0.33	[0.17; 0.50]	.	.	.	.	.	.
Zotepine:Olanzapine	0	0	0.19	[-0.18; 0.57]	.	.	0.19	[-0.18; 0.57]	.	.	.	.
Paliperidone:Risperidone	1	1.00	-0.02	[-0.17; 0.13]	-0.02	[-0.17; 0.13]	.	.	.	.	.	.
Paliperidone:Ziprasidone	0	0	-0.14	[-0.40; 0.12]	.	.	-0.14	[-0.40; 0.12]	.	.	.	.
Paliperidone:Zotepine	0	0	-0.01	[-0.43; 0.42]	.	.	-0.01	[-0.43; 0.42]	.	.	.	.

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     Risperidone:Ziprasidone 0    0 -0.13 [-0.34;  0.08]      .             .  -0.13 [-0.34;  0.08]     .             .       .       .
        Risperidone:Zotepine 0    0  0.01 [-0.38;  0.40]      .             .   0.01 [-0.38;  0.40]     .             .       .       .
        Ziprasidone:Zotepine 0    0  0.14 [-0.28;  0.55]      .             .   0.14 [-0.28;  0.55]     .             .       .       .

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (SMD) in network meta-analysis
 direct     - Estimated treatment effect (SMD) derived from direct evidence
 indir.     - Estimated treatment effect (SMD) derived from indirect evidence
 Diff       - Difference between direct and indirect treatment estimates
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

Results from SIDE-tests quality of life

Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	Diff	95%-CI	z	p-value
Amisulpride:Asenapine	0	0	-0.04	[-0.48; 0.41]	.	.	-0.04	[-0.48; 0.41]	.	.	.	.
Amisulpride:Haloperidol	0	0	-0.16	[-0.66; 0.34]	.	.	-0.16	[-0.66; 0.34]	.	.	.	.
Amisulpride:Olanzapine	1	1.00	-0.00	[-0.34; 0.34]	0.00	[-0.34; 0.34]	.	.	.	.	.	.
Amisulpride:Perphenazine	0	0	-0.15	[-0.64; 0.34]	.	.	-0.15	[-0.64; 0.34]	.	.	.	.
Amisulpride:Quetiapine	0	0	-0.33	[-0.83; 0.16]	.	.	-0.33	[-0.83; 0.16]	.	.	.	.
Amisulpride:Risperidone	0	0	-0.18	[-0.59; 0.23]	.	.	-0.18	[-0.59; 0.23]	.	.	.	.
Amisulpride:Ziprasidone	0	0	-0.07	[-0.50; 0.36]	.	.	-0.07	[-0.50; 0.36]	.	.	.	.
Amisulpride:Zotepine	0	0	0.11	[-0.55; 0.77]	.	.	0.11	[-0.55; 0.77]	.	.	.	.
Asenapine:Haloperidol	0	0	-0.12	[-0.59; 0.34]	.	.	-0.12	[-0.59; 0.34]	.	.	.	.
Asenapine:Olanzapine	1	1.00	0.04	[-0.26; 0.33]	0.04	[-0.26; 0.33]	.	.	.	.	.	.
Asenapine:Perphenazine	0	0	-0.11	[-0.57; 0.35]	.	.	-0.11	[-0.57; 0.35]	.	.	.	.
Asenapine:Quetiapine	0	0	-0.30	[-0.76; 0.17]	.	.	-0.30	[-0.76; 0.17]	.	.	.	.
Asenapine:Risperidone	0	0	-0.14	[-0.52; 0.24]	.	.	-0.14	[-0.52; 0.24]	.	.	.	.
Asenapine:Ziprasidone	0	0	-0.03	[-0.43; 0.36]	.	.	-0.03	[-0.43; 0.36]	.	.	.	.
Asenapine:Zotepine	0	0	0.15	[-0.50; 0.79]	.	.	0.15	[-0.50; 0.79]	.	.	.	.
Haloperidol:Olanzapine	1	1.00	0.16	[-0.20; 0.52]	0.16	[-0.20; 0.52]	.	.	.	.	.	.
Haloperidol:Perphenazine	0	0	0.01	[-0.50; 0.52]	.	.	0.01	[-0.50; 0.52]	.	.	.	.
Haloperidol:Quetiapine	0	0	-0.17	[-0.69; 0.34]	.	.	-0.17	[-0.69; 0.34]	.	.	.	.
Haloperidol:Risperidone	0	0	-0.02	[-0.45; 0.42]	.	.	-0.02	[-0.45; 0.42]	.	.	.	.
Haloperidol:Ziprasidone	0	0	0.09	[-0.36; 0.54]	.	.	0.09	[-0.36; 0.54]	.	.	.	.
Haloperidol:Zotepine	1	1.00	0.27	[-0.17; 0.71]	0.27	[-0.17; 0.71]	.	.	.	.	.	.
Perphenazine:Olanzapine	1	0.82	0.15	[-0.21; 0.51]	0.01	[-0.38; 0.40]	0.79	[-0.06; 1.64]	-0.78	[-1.71; 0.16]	-1.6327	0.1025
Quetiapine:Olanzapine	1	0.83	0.33	[-0.03; 0.69]	0.20	[-0.20; 0.59]	0.99	[0.12; 1.86]	-0.80	[-1.75; 0.16]	-1.6312	0.1028
Risperidone:Olanzapine	3	0.96	0.18	[-0.06; 0.41]	0.16	[-0.08; 0.40]	0.61	[-0.53; 1.76]	-0.46	[-1.62; 0.71]	-0.7672	0.4430
Ziprasidone:Olanzapine	2	0.97	0.07	[-0.19; 0.33]	0.04	[-0.23; 0.31]	0.93	[-0.48; 2.33]	-0.89	[-2.31; 0.54]	-1.2179	0.2233
Zotepine:Olanzapine	0	0	-0.11	[-0.68; 0.46]	.	.	-0.11	[-0.68; 0.46]	.	.	.	.
Perphenazine:Quetiapine	1	1.00	-0.19	[-0.60; 0.23]	-0.19	[-0.61; 0.23]	.	.	.	.	.	.
Perphenazine:Risperidone	1	0.84	-0.03	[-0.40; 0.34]	0.07	[-0.33; 0.48]	-0.55	[-1.46; 0.37]	0.62	[-0.38; 1.62]	1.2170	0.2236
Perphenazine:Ziprasidone	1	0.72	0.08	[-0.32; 0.48]	0.18	[-0.30; 0.65]	-0.17	[-0.92; 0.58]	0.35	[-0.54; 1.23]	0.7674	0.4428
Perphenazine:Zotepine	0	0	0.26	[-0.42; 0.93]	.	.	0.26	[-0.42; 0.93]	.	.	.	.
Quetiapine:Risperidone	1	0.84	0.16	[-0.22; 0.53]	0.26	[-0.15; 0.67]	-0.38	[-1.31; 0.55]	0.64	[-0.38; 1.66]	1.2260	0.2202
Quetiapine:Ziprasidone	1	0.72	0.26	[-0.14; 0.67]	0.36	[-0.11; 0.84]	0.01	[-0.75; 0.77]	0.35	[-0.55; 1.25]	0.7665	0.4434
Quetiapine:Zotepine	0	0	0.44	[-0.23; 1.12]	.	.	0.44	[-0.23; 1.12]	.	.	.	.
Risperidone:Ziprasidone	1	0.48	0.11	[-0.22; 0.43]	0.10	[-0.36; 0.57]	0.11	[-0.34; 0.56]	-0.01	[-0.65; 0.64]	-0.0239	0.9810
Risperidone:Zotepine	0	0	0.29	[-0.33; 0.91]	.	.	0.29	[-0.33; 0.91]	.	.	.	.
Ziprasidone:Zotepine	0	0	0.18	[-0.45; 0.81]	.	.	0.18	[-0.45; 0.81]	.	.	.	.

Legend:
- comparison - Treatment comparison
- k - Number of studies providing direct evidence
- prop - Direct evidence proportion
- nma - Estimated treatment effect (SMD) in network meta-analysis

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direct     - Estimated treatment effect (SMD) derived from direct evidence
indir.     - Estimated treatment effect (SMD) derived from indirect evidence
Diff       - Difference between direct and indirect treatment estimates
z          - z-value of test for disagreement (direct versus indirect)
p-value    - p-value of test for disagreement (direct versus indirect)
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Results from SIDE-tests social functioning

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Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

               comparison k prop   nma          95%-CI direct        95%-CI indir.          95%-CI  Diff        95%-CI       z p-value
   Amisulpride:Olanzapine 1 0.87  0.00 [-0.19;  0.20]   0.00 [-0.21; 0.21]   0.01 [-0.54;  0.56] -0.00 [-0.59; 0.59] -0.0120  0.9904
 Amisulpride:Paliperidone 0    0 -0.29 [-0.57; -0.02]      .             .  -0.29 [-0.57; -0.02]     .             .       .       .
   Amisulpride:Quetiapine 0    0  0.18 [-0.29;  0.65]      .             .   0.18 [-0.29;  0.65]     .             .       .       .
  Amisulpride:Risperidone 1 0.82 -0.20 [-0.42;  0.03]  -0.20 [-0.45; 0.06]  -0.20 [-0.73;  0.33]  0.00 [-0.59; 0.59]  0.0120  0.9904
  Paliperidone:Olanzapine 0    0  0.30 [-0.02;  0.61]      .             .   0.30 [-0.02;  0.61]     .             .       .       .
    Quetiapine:Olanzapine 1 1.00 -0.17 [-0.60;  0.25]  -0.17 [-0.60; 0.25]      .             .     .             .       .       .
   Risperidone:Olanzapine 1 0.31  0.20 [-0.07;  0.47]   0.20 [-0.29; 0.69]   0.20 [-0.13;  0.53]  0.00 [-0.59; 0.59]  0.0120  0.9904
  Paliperidone:Quetiapine 0    0  0.47 [-0.06;  1.00]      .             .   0.47 [-0.06;  1.00]     .             .       .       .
 Paliperidone:Risperidone 1 1.00  0.09 [-0.06;  0.25]   0.09 [-0.06; 0.25]      .             .     .             .       .       .
   Quetiapine:Risperidone 0    0 -0.37 [-0.88;  0.13]      .             .  -0.37 [-0.88;  0.13]     .             .       .       .

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (SMD) in network meta-analysis
 direct     - Estimated treatment effect (SMD) derived from direct evidence
 indir.     - Estimated treatment effect (SMD) derived from indirect evidence
 Diff       - Difference between direct and indirect treatment estimates
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

Results from SIDE-tests dropout due to any reason

Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	RoR	95%-CI	z	p-value
Amisulpride:Aripiprazole	0	0	0.93	[0.63; 1.38]	.	.	0.93	[0.63; 1.38]	.	.	.	.
Amisulpride:Asenapine	0	0	0.54	[0.36; 0.81]	.	.	0.54	[0.36; 0.81]	.	.	.	.
Amisulpride:Fluphenazine	0	0	0.17	[0.05; 0.58]	.	.	0.17	[0.05; 0.58]	.	.	.	.
Amisulpride:Fluspirilene	0	0	0.47	[0.05; 4.66]	.	.	0.47	[0.05; 4.66]	.	.	.	.
Amisulpride:Haloperidol	0	0	0.56	[0.37; 0.83]	.	.	0.56	[0.37; 0.83]	.	.	.	.
Amisulpride:Lurasidone	0	0	0.78	[0.39; 1.57]	.	.	0.78	[0.39; 1.57]	.	.	.	.
Amisulpride:Olanzapine	1	0.58	1.15	[0.83; 1.59]	1.20	[0.78; 1.83]	1.09	[0.66; 1.79]	1.10	[0.57; 2.13]	0.2932	0.7694
Amisulpride:Paliperidone	0	0	0.52	[0.35; 0.79]	.	.	0.52	[0.35; 0.79]	.	.	.	.
Amisulpride:Perphenazine	0	0	0.73	[0.47; 1.14]	.	.	0.73	[0.47; 1.14]	.	.	.	.
Amisulpride:Pimozide	0	0	0.21	[0.04; 1.11]	.	.	0.21	[0.04; 1.11]	.	.	.	.
Amisulpride:Placebo	0	0	0.11	[0.03; 0.46]	.	.	0.11	[0.03; 0.46]	.	.	.	.
Amisulpride:Quetiapine	0	0	0.46	[0.30; 0.72]	.	.	0.46	[0.30; 0.72]	.	.	.	.
Amisulpride:Risperidone	1	0.52	0.75	[0.54; 1.04]	0.71	[0.45; 1.12]	0.78	[0.49; 1.26]	0.91	[0.47; 1.75]	-0.2932	0.7694
Amisulpride:Tiotixene	0	0	0.49	[0.22; 1.09]	.	.	0.49	[0.22; 1.09]	.	.	.	.
Amisulpride:Ziprasidone	0	0	0.55	[0.37; 0.83]	.	.	0.55	[0.37; 0.83]	.	.	.	.
Amisulpride:Zotepine	0	0	0.58	[0.26; 1.33]	.	.	0.58	[0.26; 1.33]	.	.	.	.
Aripiprazole:Asenapine	0	0	0.58	[0.41; 0.81]	.	.	0.58	[0.41; 0.81]	.	.	.	.
Aripiprazole:Fluphenazine	0	0	0.19	[0.06; 0.59]	.	.	0.19	[0.06; 0.59]	.	.	.	.
Aripiprazole:Fluspirilene	0	0	0.51	[0.05; 4.87]	.	.	0.51	[0.05; 4.87]	.	.	.	.
Aripiprazole:Haloperidol	1	0.75	0.60	[0.48; 0.74]	0.56	[0.44; 0.72]	0.70	[0.46; 1.08]	0.80	[0.49; 1.32]	-0.8602	0.3897
Aripiprazole:Lurasidone	0	0	0.83	[0.43; 1.63]	.	.	0.83	[0.43; 1.63]	.	.	.	.
Aripiprazole:Olanzapine	1	0.53	1.23	[0.97; 1.57]	1.35	[0.97; 1.88]	1.11	[0.78; 1.58]	1.21	[0.75; 1.97]	0.7914	0.4287
Aripiprazole:Paliperidone	1	0.37	0.56	[0.40; 0.79]	0.57	[0.33; 1.00]	0.56	[0.36; 0.85]	1.02	[0.51; 2.07]	0.0612	0.9512
Aripiprazole:Perphenazine	0	0	0.79	[0.53; 1.16]	.	.	0.79	[0.53; 1.16]	.	.	.	.
Aripiprazole:Pimozide	0	0	0.22	[0.04; 1.15]	.	.	0.22	[0.04; 1.15]	.	.	.	.
Aripiprazole:Placebo	0	0	0.12	[0.03; 0.48]	.	.	0.12	[0.03; 0.48]	.	.	.	.
Aripiprazole:Quetiapine	0	0	0.50	[0.33; 0.74]	.	.	0.50	[0.33; 0.74]	.	.	.	.
Aripiprazole:Risperidone	0	0	0.80	[0.60; 1.06]	.	.	0.80	[0.60; 1.06]	.	.	.	.
Aripiprazole:Tiotixene	0	0	0.52	[0.25; 1.08]	.	.	0.52	[0.25; 1.08]	.	.	.	.
Aripiprazole:Ziprasidone	0	0	0.59	[0.42; 0.84]	.	.	0.59	[0.42; 0.84]	.	.	.	.
Aripiprazole:Zotepine	0	0	0.62	[0.29; 1.33]	.	.	0.62	[0.29; 1.33]	.	.	.	.
Asenapine:Fluphenazine	0	0	0.32	[0.10; 1.06]	.	.	0.32	[0.10; 1.06]	.	.	.	.
Asenapine:Fluspirilene	0	0	0.88	[0.09; 8.56]	.	.	0.88	[0.09; 8.56]	.	.	.	.
Asenapine:Haloperidol	1	0.19	1.03	[0.74; 1.44]	1.24	[0.58; 2.65]	0.99	[0.68; 1.43]	1.26	[0.54; 2.92]	0.5387	0.5901
Asenapine:Lurasidone	0	0	1.44	[0.73; 2.85]	.	.	1.44	[0.73; 2.85]	.	.	.	.
Asenapine:Olanzapine	1	0.90	2.13	[1.67; 2.74]	2.09	[1.61; 2.71]	2.63	[1.18; 5.85]	0.79	[0.34; 1.84]	-0.5387	0.5901
Asenapine:Paliperidone	0	0	0.97	[0.66; 1.44]	.	.	0.97	[0.66; 1.44]	.	.	.	.
Asenapine:Perphenazine	0	0	1.36	[0.91; 2.04]	.	.	1.36	[0.91; 2.04]	.	.	.	.
Asenapine:Pimozide	0	0	0.39	[0.07; 2.03]	.	.	0.39	[0.07; 2.03]	.	.	.	.
Asenapine:Placebo	0	0	0.21	[0.05; 0.85]	.	.	0.21	[0.05; 0.85]	.	.	.	.
Asenapine:Quetiapine	0	0	0.86	[0.57; 1.29]	.	.	0.86	[0.57; 1.29]	.	.	.	.
Asenapine:Risperidone	0	0	1.39	[1.01; 1.89]	.	.	1.39	[1.01; 1.89]	.	.	.	.

Asenapine:Tiotixene	0	0	0.91	[0.42;	1.95]	.		.	0.91	[0.42;	1.95]	.		.	.	.			
Asenapine:Ziprasidone	0	0	1.03	[0.72;	1.47]	.		.	1.03	[0.72;	1.47]	.		.	.	.			
Asenapine:Zotepine	0	0	1.08	[0.49;	2.39]	.		.	1.08	[0.49;	2.39]	.		.	.	.			
Fluphenazine:Fluspirilene	1	1.00	2.70	[0.38;	18.96]	2.70	[0.38;	18.96]	.			.		.	.	.			
Fluphenazine:Haloperidol	1	1.00	3.18	[1.02;	9.86]	3.18	[1.02;	9.86]	.			.		.	.	.			
Fluphenazine:Lurasidone	0	0	4.45	[1.19;	16.60]	.		.	4.45	[1.19;	16.60]	.		.	.	.			
Fluphenazine:Olanzapine	0	0	6.57	[2.06;	20.93]	.		.	6.57	[2.06;	20.93]	.		.	.	.			
Fluphenazine:Paliperidone	0	0	2.99	[0.91;	9.81]	.		.	2.99	[0.91;	9.81]	.		.	.	.			
Fluphenazine:Perphenazine	0	0	4.19	[1.26;	13.91]	.		.	4.19	[1.26;	13.91]	.		.	.	.			
Fluphenazine:Pimozide	1	1.00	1.19	[0.37;	3.82]	1.19	[0.37;	3.82]	.			.		.	.	.			
Fluphenazine:Placebo	0	0	0.64	[0.11;	3.78]	.		.	0.64	[0.11;	3.78]	.		.	.	.			
Fluphenazine:Quetiapine	0	0	2.64	[0.79;	8.78]	.		.	2.64	[0.79;	8.78]	.		.	.	.			
Fluphenazine:Risperidone	0	0	4.26	[1.33;	13.71]	.		.	4.26	[1.33;	13.71]	.		.	.	.			
Fluphenazine:Tiotixene	0	0	2.80	[0.74;	10.53]	.		.	2.80	[0.74;	10.53]	.		.	.	.			
Fluphenazine:Ziprasidone	0	0	3.17	[0.97;	10.36]	.		.	3.17	[0.97;	10.36]	.		.	.	.			
Fluphenazine:Zotepine	0	0	3.33	[0.87;	12.75]	.		.	3.33	[0.87;	12.75]	.		.	.	.			
Fluspirilene:Haloperidol	0	0	1.18	[0.12;	11.21]	.		.	1.18	[0.12;	11.21]	.		.	.	.			
Fluspirilene:Lurasidone	0	0	1.65	[0.16;	17.31]	.		.	1.65	[0.16;	17.31]	.		.	.	.			
Fluspirilene:Olanzapine	0	0	2.43	[0.25;	23.50]	.		.	2.43	[0.25;	23.50]	.		.	.	.			
Fluspirilene:Paliperidone	0	0	1.11	[0.11;	10.86]	.		.	1.11	[0.11;	10.86]	.		.	.	.			
Fluspirilene:Perphenazine	0	0	1.55	[0.16;	15.31]	.		.	1.55	[0.16;	15.31]	.		.	.	.			
Fluspirilene:Pimozide	0	0	0.44	[0.05;	4.28]	.		.	0.44	[0.05;	4.28]	.		.	.	.			
Fluspirilene:Placebo	0	0	0.24	[0.02;	3.32]	.		.	0.24	[0.02;	3.32]	.		.	.	.			
Fluspirilene:Quetiapine	0	0	0.98	[0.10;	9.65]	.		.	0.98	[0.10;	9.65]	.		.	.	.			
Fluspirilene:Risperidone	0	0	1.58	[0.16;	15.32]	.		.	1.58	[0.16;	15.32]	.		.	.	.			
Fluspirilene:Tiotixene	0	0	1.04	[0.10;	10.94]	.		.	1.04	[0.10;	10.94]	.		.	.	.			
Fluspirilene:Ziprasidone	0	0	1.17	[0.12;	11.48]	.		.	1.17	[0.12;	11.48]	.		.	.	.			
Fluspirilene:Zotepine	0	0	1.23	[0.12;	13.15]	.		.	1.23	[0.12;	13.15]	.		.	.	.			
Haloperidol:Lurasidone	0	0	1.40	[0.71;	2.75]	.		.	1.40	[0.71;	2.75]	.		.	.	.			
Haloperidol:Olanzapine	4	0.46	2.07	[1.61;	2.65]	1.91	[1.33;	2.76]	2.21	[1.58;	3.10]	0.87	[0.53;	1.43]	-0.5637	0.5730			
Haloperidol:Paliperidone	0	0	0.94	[0.66;	1.35]	.		.	0.94	[0.66;	1.35]	.		.	.	.			
Haloperidol:Perphenazine	0	0	1.32	[0.89;	1.96]	.		.	1.32	[0.89;	1.96]	.		.	.	.			
Haloperidol:Pimozide	0	0	0.38	[0.07;	1.90]	.		.	0.38	[0.07;	1.90]	.		.	.	.			
Haloperidol:Placebo	0	0	0.20	[0.05;	0.79]	.		.	0.20	[0.05;	0.79]	.		.	.	.			
Haloperidol:Quetiapine	0	0	0.83	[0.56;	1.24]	.		.	0.83	[0.56;	1.24]	.		.	.	.			
Haloperidol:Risperidone	2	0.30	1.34	[1.01;	1.79]	1.28	[0.76;	2.18]	1.37	[0.97;	1.92]	0.94	[0.50;	1.76]	-0.1930	0.8470			
Haloperidol:Tiotixene	2	1.00	0.88	[0.44;	1.76]	0.88	[0.44;	1.76]	.			.		.	.	.			
Haloperidol:Ziprasidone	0	0	1.00	[0.70;	1.42]	.		.	1.00	[0.70;	1.42]	.		.	.	.			
Haloperidol:Zotepine	1	1.00	1.05	[0.51;	2.16]	1.05	[0.51;	2.16]	.			.		.	.	.			
Lurasidone:Olanzapine	0	0	1.48	[0.79;	2.78]	.		.	1.48	[0.79;	2.78]	.		.	.	.			
Lurasidone:Paliperidone	0	0	0.67	[0.34;	1.34]	.		.	0.67	[0.34;	1.34]	.		.	.	.			
Lurasidone:Perphenazine	0	0	0.94	[0.48;	1.84]	.		.	0.94	[0.48;	1.84]	.		.	.	.			
Lurasidone:Pimozide	0	0	0.27	[0.05;	1.56]	.		.	0.27	[0.05;	1.56]	.		.	.	.			
Lurasidone:Placebo	0	0	0.14	[0.03;	0.66]	.		.	0.14	[0.03;	0.66]	.		.	.	.			
Lurasidone:Quetiapine	1	1.00	0.59	[0.35;	1.02]	0.59	[0.35;	1.02]	.			.		.	.	.			
Lurasidone:Risperidone	0	0	0.96	[0.51;	1.82]	.		.	0.96	[0.51;	1.82]	.		.	.	.			
Lurasidone:Tiotixene	0	0	0.63	[0.24;	1.65]	.		.	0.63	[0.24;	1.65]	.		.	.	.			
Lurasidone:Ziprasidone	0	0	0.71	[0.37;	1.38]	.		.	0.71	[0.37;	1.38]	.		.	.	.			
Lurasidone:Zotepine	0	0	0.75	[0.28;	2.01]	.		.	0.75	[0.28;	2.01]	.		.	.	.			
Paliperidone:Olanzapine	0	0	2.20	[1.61;	2.99]	.		.	2.20	[1.61;	2.99]	.		.	.	.			

Perphenazine:Olanzapine	2	0.86	1.57 [1.14; 2.15]	1.58 [1.12; 2.22]	1.51 [0.64; 3.54]	1.05 [0.42; 2.63]	0.0973	0.9225
Pimozide:Olanzapine	0	0	5.51 [1.07; 28.48]	.	5.51 [1.07; 28.48]	.	.	.
Placebo:Olanzapine	0	0	10.21 [2.56; 40.70]	.	10.21 [2.56; 40.70]	.	.	.
Quetiapine:Olanzapine	1	0.84	2.49 [1.79; 3.46]	2.56 [1.79; 3.67]	2.11 [0.92; 4.86]	1.21 [0.49; 3.00]	0.4183	0.6757
Risperidone:Olanzapine	5	0.77	1.54 [1.27; 1.87]	1.53 [1.23; 1.91]	1.58 [1.06; 2.37]	0.96 [0.61; 1.53]	-0.1539	0.8777
Tiotixene:Olanzapine	0	0	2.35 [1.13; 4.89]	.	2.35 [1.13; 4.89]	.	.	.
Ziprasidone:Olanzapine	3	0.97	2.07 [1.61; 2.67]	2.10 [1.62; 2.71]	1.55 [0.40; 6.03]	1.35 [0.34; 5.38]	0.4269	0.6694
Zotepine:Olanzapine	0	0	1.97 [0.92; 4.23]	.	1.97 [0.92; 4.23]	.	.	.
Paliperidone:Perphenazine	0	0	1.40 [0.93; 2.12]	.	1.40 [0.93; 2.12]	.	.	.
Paliperidone:Pimozide	0	0	0.40 [0.08; 2.10]	.	0.40 [0.08; 2.10]	.	.	.
Paliperidone:Placebo	0	0	0.22 [0.05; 0.88]	.	0.22 [0.05; 0.88]	.	.	.
Paliperidone:Quetiapine	0	0	0.88 [0.58; 1.34]	.	0.88 [0.58; 1.34]	.	.	.
Paliperidone:Risperidone	1	0.83	1.42 [1.09; 1.85]	1.43 [1.07; 1.91]	1.40 [0.74; 2.66]	1.02 [0.51; 2.07]	0.0612	0.9512
Paliperidone:Tiotixene	0	0	0.93 [0.43; 2.03]	.	0.93 [0.43; 2.03]	.	.	.
Paliperidone:Ziprasidone	0	0	1.06 [0.72; 1.55]	.	1.06 [0.72; 1.55]	.	.	.
Paliperidone:Zotepine	0	0	1.11 [0.50; 2.49]	.	1.11 [0.50; 2.49]	.	.	.
Perphenazine:Pimozide	0	0	0.28 [0.05; 1.51]	.	0.28 [0.05; 1.51]	.	.	.
Perphenazine:Placebo	0	0	0.15 [0.04; 0.63]	.	0.15 [0.04; 0.63]	.	.	.
Perphenazine:Quetiapine	1	0.97	0.63 [0.43; 0.93]	0.65 [0.44; 0.97]	0.17 [0.02; 1.81]	3.82 [0.35; 41.91]	1.0979	0.2722
Perphenazine:Risperidone	1	0.80	1.02 [0.73; 1.42]	1.05 [0.72; 1.52]	0.90 [0.43; 1.88]	1.17 [0.51; 2.67]	0.3659	0.7145
Perphenazine:Tiotixene	0	0	0.67 [0.30; 1.48]	.	0.67 [0.30; 1.48]	.	.	.
Perphenazine:Ziprasidone	1	0.68	0.76 [0.52; 1.10]	0.78 [0.50; 1.23]	0.71 [0.37; 1.37]	1.10 [0.50; 2.44]	0.2355	0.8138
Perphenazine:Zotepine	0	0	0.79 [0.35; 1.81]	.	0.79 [0.35; 1.81]	.	.	.
Pimozide:Placebo	0	0	0.54 [0.06; 4.49]	.	0.54 [0.06; 4.49]	.	.	.
Pimozide:Quetiapine	0	0	2.21 [0.42; 11.80]	.	2.21 [0.42; 11.80]	.	.	.
Pimozide:Risperidone	0	0	3.57 [0.69; 18.60]	.	3.57 [0.69; 18.60]	.	.	.
Pimozide:Tiotixene	0	0	2.34 [0.40; 13.69]	.	2.34 [0.40; 13.69]	.	.	.
Pimozide:Ziprasidone	0	0	2.66 [0.50; 13.99]	.	2.66 [0.50; 13.99]	.	.	.
Pimozide:Zotepine	0	0	2.79 [0.47; 16.51]	.	2.79 [0.47; 16.51]	.	.	.
Placebo:Quetiapine	0	0	4.10 [0.99; 16.96]	.	4.10 [0.99; 16.96]	.	.	.
Placebo:Risperidone	0	0	6.62 [1.65; 26.61]	.	6.62 [1.65; 26.61]	.	.	.
Placebo:Tiotixene	1	1.00	4.34 [1.35; 14.03]	4.34 [1.35; 14.03]	.	.	.	.
Placebo:Ziprasidone	0	0	4.92 [1.21; 20.06]	.	4.92 [1.21; 20.06]	.	.	.
Placebo:Zotepine	0	0	5.17 [1.11; 24.14]	.	5.17 [1.11; 24.14]	.	.	.
Quetiapine:Risperidone	1	0.84	1.61 [1.15; 2.27]	1.61 [1.11; 2.32]	1.66 [0.71; 3.89]	0.97 [0.38; 2.44]	-0.0743	0.9408
Quetiapine:Tiotixene	0	0	1.06 [0.48; 2.36]	.	1.06 [0.48; 2.36]	.	.	.
Quetiapine:Ziprasidone	1	0.71	1.20 [0.82; 1.76]	1.19 [0.76; 1.88]	1.22 [0.60; 2.45]	0.98 [0.43; 2.26]	-0.0449	0.9642
Quetiapine:Zotepine	0	0	1.26 [0.55; 2.88]	.	1.26 [0.55; 2.88]	.	.	.
Risperidone:Tiotixene	0	0	0.66 [0.31; 1.39]	.	0.66 [0.31; 1.39]	.	.	.
Risperidone:Ziprasidone	1	0.47	0.74 [0.55; 1.00]	0.74 [0.48; 1.14]	0.74 [0.49; 1.12]	1.00 [0.55; 1.81]	-0.0003	0.9998
Risperidone:Zotepine	0	0	0.78 [0.36; 1.70]	.	0.78 [0.36; 1.70]	.	.	.
Tiotixene:Ziprasidone	0	0	1.13 [0.52; 2.46]	.	1.13 [0.52; 2.46]	.	.	.
Tiotixene:Zotepine	0	0	1.19 [0.44; 3.23]	.	1.19 [0.44; 3.23]	.	.	.
Ziprasidone:Zotepine	0	0	1.05 [0.47; 2.34]	.	1.05 [0.47; 2.34]	.	.	.

Legend:
- comparison - Treatment comparison
- k - Number of studies providing direct evidence
- prop - Direct evidence proportion
- nma - Estimated treatment effect (OR) in network meta-analysis

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direct     - Estimated treatment effect (OR) derived from direct evidence
indir.     - Estimated treatment effect (OR) derived from indirect evidence
RoR        - Ratio of Ratios (direct versus indirect)
z          - z-value of test for disagreement (direct versus indirect)
p-value    - p-value of test for disagreement (direct versus indirect)
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Results from SIDE-tests weight

Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	Diff	95%-CI	z	p-value
Amisulpride:Aripiprazole	0	0	0.54	[-1.86; 2.95]	.	.	0.54	[-1.86; 2.95]	.	.	.	.
Amisulpride:Asenapine	0	0	0.77	[-2.05; 3.59]	.	.	0.77	[-2.05; 3.59]	.	.	.	.
Amisulpride:Haloperidol	0	0	1.12	[-1.08; 3.32]	.	.	1.12	[-1.08; 3.32]	.	.	.	.
Amisulpride:Lurasidone	0	0	0.70	[-3.00; 4.39]	.	.	0.70	[-3.00; 4.39]	.	.	.	.
Amisulpride:Olanzapine	1	0.56	-2.53	[-4.25; -0.81]	-2.30	[-4.60; 0.00]	-2.82	[-5.41; -0.24]	0.52	[-2.94; 3.98]	0.2968	0.7667
Amisulpride:Paliperidone	0	0	0.37	[-2.44; 3.18]	.	.	0.37	[-2.44; 3.18]	.	.	.	.
Amisulpride:Perphenazine	0	0	1.17	[-1.21; 3.54]	.	.	1.17	[-1.21; 3.54]	.	.	.	.
Amisulpride:Quetiapine	0	0	0.20	[-2.34; 2.73]	.	.	0.20	[-2.34; 2.73]	.	.	.	.
Amisulpride:Risperidone	1	0.57	-0.57	[-2.29; 1.14]	-0.80	[-3.07; 1.47]	-0.28	[-2.89; 2.33]	-0.52	[-3.98; 2.94]	-0.2968	0.7667
Amisulpride:Ziprasidone	0	0	1.73	[-0.43; 3.88]	.	.	1.73	[-0.43; 3.88]	.	.	.	.
Amisulpride:Zotepine	0	0	-1.88	[-5.46; 1.70]	.	.	-1.88	[-5.46; 1.70]	.	.	.	.
Aripiprazole:Asenapine	0	0	0.23	[-2.60; 3.06]	.	.	0.23	[-2.60; 3.06]	.	.	.	.
Aripiprazole:Haloperidol	1	0.63	0.58	[-1.13; 2.29]	0.66	[-1.50; 2.82]	0.44	[-2.36; 3.25]	0.22	[-3.32; 3.75]	0.1194	0.9049
Aripiprazole:Lurasidone	0	0	0.15	[-3.60; 3.91]	.	.	0.15	[-3.60; 3.91]	.	.	.	.
Aripiprazole:Olanzapine	1	0.60	-3.07	[-4.81; -1.34]	-3.16	[-5.40; -0.92]	-2.94	[-5.68; -0.21]	-0.22	[-3.75; 3.32]	-0.1194	0.9049
Aripiprazole:Paliperidone	0	0	-0.18	[-3.17; 2.82]	.	.	-0.18	[-3.17; 2.82]	.	.	.	.
Aripiprazole:Perphenazine	0	0	0.62	[-1.82; 3.07]	.	.	0.62	[-1.82; 3.07]	.	.	.	.
Aripiprazole:Quetiapine	0	0	-0.35	[-2.96; 2.27]	.	.	-0.35	[-2.96; 2.27]	.	.	.	.
Aripiprazole:Risperidone	0	0	-1.12	[-3.11; 0.88]	.	.	-1.12	[-3.11; 0.88]	.	.	.	.
Aripiprazole:Ziprasidone	0	0	1.18	[-1.03; 3.40]	.	.	1.18	[-1.03; 3.40]	.	.	.	.
Aripiprazole:Zotepine	0	0	-2.42	[-5.72; 0.88]	.	.	-2.42	[-5.72; 0.88]	.	.	.	.
Asenapine:Haloperidol	0	0	0.35	[-2.33; 3.04]	.	.	0.35	[-2.33; 3.04]	.	.	.	.
Asenapine:Lurasidone	0	0	-0.07	[-4.10; 3.95]	.	.	-0.07	[-4.10; 3.95]	.	.	.	.
Asenapine:Olanzapine	1	1.00	-3.30	[-5.54; -1.06]	-3.30	[-5.54; -1.06]	.	.	.	.	.	.
Asenapine:Paliperidone	0	0	-0.40	[-3.76; 2.96]	.	.	-0.40	[-3.76; 2.96]	.	.	.	.
Asenapine:Perphenazine	0	0	0.40	[-2.44; 3.24]	.	.	0.40	[-2.44; 3.24]	.	.	.	.
Asenapine:Quetiapine	0	0	-0.57	[-3.57; 2.42]	.	.	-0.57	[-3.57; 2.42]	.	.	.	.
Asenapine:Risperidone	0	0	-1.34	[-3.86; 1.17]	.	.	-1.34	[-3.86; 1.17]	.	.	.	.
Asenapine:Ziprasidone	0	0	0.96	[-1.68; 3.60]	.	.	0.96	[-1.68; 3.60]	.	.	.	.
Asenapine:Zotepine	0	0	-2.65	[-6.54; 1.25]	.	.	-2.65	[-6.54; 1.25]	.	.	.	.
Haloperidol:Lurasidone	0	0	-0.43	[-4.05; 3.20]	.	.	-0.43	[-4.05; 3.20]	.	.	.	.
Haloperidol:Olanzapine	2	0.67	-3.65	[-5.14; -2.17]	-3.34	[-5.15; -1.53]	-4.30	[-6.88; -1.71]	0.96	[-2.20; 4.12]	0.5961	0.5511
Haloperidol:Paliperidone	0	0	-0.76	[-3.56; 2.04]	.	.	-0.76	[-3.56; 2.04]	.	.	.	.
Haloperidol:Perphenazine	0	0	0.05	[-2.21; 2.30]	.	.	0.05	[-2.21; 2.30]	.	.	.	.
Haloperidol:Quetiapine	0	0	-0.93	[-3.36; 1.51]	.	.	-0.93	[-3.36; 1.51]	.	.	.	.
Haloperidol:Risperidone	1	0.47	-1.70	[-3.39; 0.00]	-3.15	[-5.63; -0.67]	-0.42	[-2.74; 1.91]	-2.73	[-6.13; 0.66]	-1.5771	0.1148
Haloperidol:Ziprasidone	0	0	0.60	[-1.41; 2.62]	.	.	0.60	[-1.41; 2.62]	.	.	.	.
Haloperidol:Zotepine	1	1.00	-3.00	[-5.82; -0.18]	-3.00	[-5.82; -0.18]	.	.	.	.	.	.
Lurasidone:Olanzapine	0	0	-3.23	[-6.57; 0.12]	.	.	-3.23	[-6.57; 0.12]	.	.	.	.
Lurasidone:Paliperidone	0	0	-0.33	[-4.39; 3.73]	.	.	-0.33	[-4.39; 3.73]	.	.	.	.
Lurasidone:Perphenazine	0	0	0.47	[-3.05; 3.99]	.	.	0.47	[-3.05; 3.99]	.	.	.	.
Lurasidone:Quetiapine	1	1.00	-0.50	[-3.19; 2.19]	-0.50	[-3.19; 2.19]	.	.	.	.	.	.

Lurasidone:Risperidone	0	0	-1.27	[-4.66; 2.12]	.	.	-1.27	[-4.66; 2.12]	.	.	.	.			
Lurasidone:Ziprasidone	0	0	1.03	[-2.41; 4.48]	.	.	1.03	[-2.41; 4.48]	.	.	.	.			
Lurasidone:Zotepine	0	0	-2.57	[-7.17; 2.02]	.	.	-2.57	[-7.17; 2.02]	.	.	.	.			
Paliperidone:Olanzapine	0	0	-2.90	[-5.40; -0.39]	.	.	-2.90	[-5.40; -0.39]	.	.	.	.			
Perphenazine:Olanzapine	2	0.83	-3.70	[-5.45; -1.95]	-4.10	[-6.02; -2.19]	-1.65	[-5.96; 2.66]	-2.45	[-7.17; 2.26]	-1.0201	0.3077			
Quetiapine:Olanzapine	1	0.72	-2.73	[-4.72; -0.73]	-3.76	[-6.10; -1.42]	-0.01	[-3.81; 3.79]	-3.75	[-8.22; 0.71]	-1.6490	0.0991			
Risperidone:Olanzapine	4	0.77	-1.96	[-3.11; -0.81]	-2.38	[-3.68; -1.07]	-0.54	[-2.94; 1.86]	-1.83	[-4.57; 0.90]	-1.3143	0.1888			
Ziprasidone:Olanzapine	3	0.91	-4.26	[-5.66; -2.85]	-4.75	[-6.22; -3.27]	0.63	[-4.03; 5.29]	-5.37	[-10.26; -0.48]	-2.1539	0.0312			
Zotepine:Olanzapine	0	0	-0.65	[-3.84; 2.54]	.	.	-0.65	[-3.84; 2.54]	.	.	.	.			
Paliperidone:Perphenazine	0	0	0.80	[-2.13; 3.73]	.	.	0.80	[-2.13; 3.73]	.	.	.	.			
Paliperidone:Quetiapine	0	0	-0.17	[-3.21; 2.87]	.	.	-0.17	[-3.21; 2.87]	.	.	.	.			
Paliperidone:Risperidone	1	1.00	-0.94	[-3.17; 1.29]	-0.94	[-3.17; 1.29]	.	.	.	.	.	.			
Paliperidone:Ziprasidone	0	0	1.36	[-1.42; 4.14]	.	.	1.36	[-1.42; 4.14]	.	.	.	.			
Paliperidone:Zotepine	0	0	-2.24	[-6.22; 1.73]	.	.	-2.24	[-6.22; 1.73]	.	.	.	.			
Perphenazine:Quetiapine	1	0.89	-0.97	[-3.24; 1.30]	-1.41	[-3.82; 1.00]	2.52	[-4.27; 9.31]	-3.93	[-11.14; 3.28]	-1.0691	0.2850			
Perphenazine:Risperidone	1	0.62	-1.74	[-3.64; 0.16]	-1.27	[-3.68; 1.14]	-2.52	[-5.62; 0.58]	1.25	[-2.67; 5.18]	0.6250	0.5320			
Perphenazine:Ziprasidone	1	0.66	0.56	[-1.45; 2.57]	-0.18	[-2.65; 2.29]	2.00	[-1.45; 5.44]	-2.18	[-6.42; 2.06]	-1.0058	0.3145			
Perphenazine:Zotepine	0	0	-3.05	[-6.66; 0.57]	.	.	-3.05	[-6.66; 0.57]	.	.	.	.			
Quetiapine:Risperidone	1	0.78	-0.77	[-2.84; 1.30]	0.14	[-2.20; 2.48]	-4.04	[-8.48; 0.40]	4.18	[-0.84; 9.20]	1.6328	0.1025			
Quetiapine:Ziprasidone	1	0.80	1.53	[-0.62; 3.68]	1.23	[-1.18; 3.64]	2.73	[-2.08; 7.54]	-1.50	[-6.88; 3.88]	-0.5475	0.5841			
Quetiapine:Zotepine	0	0	-2.07	[-5.80; 1.65]	.	.	-2.07	[-5.80; 1.65]	.	.	.	.			
Risperidone:Ziprasidone	1	0.48	2.30	[0.64; 3.96]	1.09	[-1.32; 3.50]	3.40	[1.11; 5.69]	-2.31	[-5.63; 1.02]	-1.3612	0.1735			
Risperidone:Zotepine	0	0	-1.30	[-4.60; 1.99]	.	.	-1.30	[-4.60; 1.99]	.	.	.	.			
Ziprasidone:Zotepine	0	0	-3.60	[-7.07; -0.14]	.	.	-3.60	[-7.07; -0.14]	.	.	.	.			

Legend:
 comparison - Treatment comparison
 k - Number of studies providing direct evidence
 prop - Direct evidence proportion
 nma - Estimated treatment effect (MD) in network meta-analysis
 direct - Estimated treatment effect (MD) derived from direct evidence
 indir. - Estimated treatment effect (MD) derived from indirect evidence
 Diff - Difference between direct and indirect treatment estimates
 z - z-value of test for disagreement (direct versus indirect)
 p-value - p-value of test for disagreement (direct versus indirect)

Results from SIDE-tests antiparkinson medication

Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	RoR	95%-CI	z	p-value
Amisulpride:Aripiprazole	0	0	1.98	[1.17; 3.35]	.	.	1.98	[1.17; 3.35]	.	.	.	.
Amisulpride:Asenapine	0	0	0.34	[0.12; 0.94]	.	.	0.34	[0.12; 0.94]	.	.	.	.
Amisulpride:Haloperidol	0	0	0.48	[0.29; 0.81]	.	.	0.48	[0.29; 0.81]	.	.	.	.
Amisulpride:Olanzapine	1	0.44	1.37	[0.89; 2.12]	1.60	[0.83; 3.09]	1.21	[0.67; 2.17]	1.33	[0.55; 3.20]	0.6316	0.5276
Amisulpride:Paliperidone	0	0	0.80	[0.48; 1.35]	.	.	0.80	[0.48; 1.35]	.	.	.	.
Amisulpride:Perphenazine	0	0	0.77	[0.41; 1.45]	.	.	0.77	[0.41; 1.45]	.	.	.	.
Amisulpride:Quetiapine	0	0	2.58	[1.19; 5.60]	.	.	2.58	[1.19; 5.60]	.	.	.	.
Amisulpride:Risperidone	1	0.65	0.81	[0.53; 1.23]	0.73	[0.44; 1.23]	0.97	[0.48; 1.98]	0.75	[0.31; 1.81]	-0.6316	0.5276
Amisulpride:Ziprasidone	0	0	0.80	[0.44; 1.44]	.	.	0.80	[0.44; 1.44]	.	.	.	.
Amisulpride:Zotepine	0	0	1.51	[0.60; 3.81]	.	.	1.51	[0.60; 3.81]	.	.	.	.
Aripiprazole:Asenapine	0	0	0.17	[0.06; 0.45]	.	.	0.17	[0.06; 0.45]	.	.	.	.
Aripiprazole:Haloperidol	1	0.82	0.25	[0.19; 0.31]	0.23	[0.17; 0.30]	0.35	[0.20; 0.61]	0.65	[0.35; 1.23]	-1.3170	0.1878
Aripiprazole:Olanzapine	1	0.54	0.69	[0.51; 0.95]	0.84	[0.55; 1.29]	0.55	[0.35; 0.88]	1.53	[0.81; 2.87]	1.3170	0.1878
Aripiprazole:Paliperidone	0	0	0.41	[0.25; 0.66]	.	.	0.41	[0.25; 0.66]	.	.	.	.
Aripiprazole:Perphenazine	0	0	0.39	[0.22; 0.70]	.	.	0.39	[0.22; 0.70]	.	.	.	.
Aripiprazole:Quetiapine	0	0	1.31	[0.63; 2.72]	.	.	1.31	[0.63; 2.72]	.	.	.	.
Aripiprazole:Risperidone	0	0	0.41	[0.28; 0.60]	.	.	0.41	[0.28; 0.60]	.	.	.	.
Aripiprazole:Ziprasidone	0	0	0.40	[0.24; 0.68]	.	.	0.40	[0.24; 0.68]	.	.	.	.
Aripiprazole:Zotepine	0	0	0.76	[0.34; 1.71]	.	.	0.76	[0.34; 1.71]	.	.	.	.
Asenapine:Haloperidol	0	0	1.45	[0.54; 3.85]	.	.	1.45	[0.54; 3.85]	.	.	.	.
Asenapine:Olanzapine	1	1.00	4.09	[1.61; 10.36]	4.09	[1.61; 10.36]	.	.	.	.	.	.
Asenapine:Paliperidone	0	0	2.39	[0.87; 6.58]	.	.	2.39	[0.87; 6.58]	.	.	.	.
Asenapine:Perphenazine	0	0	2.31	[0.81; 6.60]	.	.	2.31	[0.81; 6.60]	.	.	.	.
Asenapine:Quetiapine	0	0	7.71	[2.45; 24.25]	.	.	7.71	[2.45; 24.25]	.	.	.	.
Asenapine:Risperidone	0	0	2.41	[0.92; 6.33]	.	.	2.41	[0.92; 6.33]	.	.	.	.
Asenapine:Ziprasidone	0	0	2.37	[0.86; 6.60]	.	.	2.37	[0.86; 6.60]	.	.	.	.
Asenapine:Zotepine	0	0	4.51	[1.30; 15.62]	.	.	4.51	[1.30; 15.62]	.	.	.	.
Haloperidol:Olanzapine	2	0.59	2.82	[2.09; 3.82]	2.27	[1.53; 3.35]	3.90	[2.43; 6.26]	0.58	[0.31; 1.08]	-1.7286	0.0839
Haloperidol:Paliperidone	0	0	1.65	[1.03; 2.65]	.	.	1.65	[1.03; 2.65]	.	.	.	.
Haloperidol:Perphenazine	0	0	1.59	[0.90; 2.81]	.	.	1.59	[0.90; 2.81]	.	.	.	.
Haloperidol:Quetiapine	0	0	5.33	[2.57; 11.02]	.	.	5.33	[2.57; 11.02]	.	.	.	.
Haloperidol:Risperidone	1	0.47	1.67	[1.16; 2.39]	1.75	[1.03; 2.96]	1.60	[0.97; 2.63]	1.10	[0.53; 2.26]	0.2472	0.8047
Haloperidol:Ziprasidone	0	0	1.64	[0.98; 2.74]	.	.	1.64	[0.98; 2.74]	.	.	.	.
Haloperidol:Zotepine	1	1.00	3.12	[1.45; 6.71]	3.12	[1.45; 6.71]	.	.	.	.	.	.
Paliperidone:Olanzapine	0	0	1.71	[1.15; 2.55]	.	.	1.71	[1.15; 2.55]	.	.	.	.
Perphenazine:Olanzapine	2	0.76	1.77	[1.08; 2.90]	1.45	[0.82; 2.55]	3.31	[1.22; 8.99]	0.44	[0.14; 1.38]	-1.4134	0.1575
Quetiapine:Olanzapine	1	0.84	0.53	[0.27; 1.04]	0.42	[0.20; 0.87]	1.74	[0.33; 9.12]	0.24	[0.04; 1.47]	-1.5419	0.1231
Risperidone:Olanzapine	4	0.83	1.69	[1.31; 2.19]	1.55	[1.17; 2.06]	2.60	[1.40; 4.84]	0.60	[0.30; 1.18]	-1.4881	0.1367
Ziprasidone:Olanzapine	2	0.93	1.72	[1.13; 2.63]	1.67	[1.08; 2.60]	2.47	[0.51; 11.99]	0.68	[0.13; 3.49]	-0.4668	0.6406
Zotepine:Olanzapine	0	0	0.91	[0.40; 2.07]	.	.	0.91	[0.40; 2.07]	.	.	.	.
Paliperidone:Perphenazine	0	0	0.96	[0.54; 1.73]	.	.	0.96	[0.54; 1.73]	.	.	.	.
Paliperidone:Quetiapine	0	0	3.22	[1.54; 6.75]	.	.	3.22	[1.54; 6.75]	.	.	.	.
Paliperidone:Risperidone	1	1.00	1.01	[0.74; 1.37]	1.01	[0.74; 1.37]	.	.	.	.	.	.

Paliperidone:Ziprasidone	0	0	0.99	[0.57;	1.73]	.	.	0.99	[0.57;	1.73]	.	.	.	.	.
Paliperidone:Zotepine	0	0	1.89	[0.77;	4.65]	.	.	1.89	[0.77;	4.65]	.	.	.	.	.
Perphenazine:Quetiapine	1	0.99	3.34	[1.61;	6.93]	3.28	[1.58; 6.82]	25.57	[0.01;	48311.01]	0.13	[0.00;	251.05]	-0.5311	0.5953
Perphenazine:Risperidone	1	0.80	1.05	[0.64;	1.72]	1.07	[0.61; 1.86]	0.96	[0.32;	2.93]	1.11	[0.32;	3.84]	0.1635	0.8702
Perphenazine:Ziprasidone	1	0.72	1.03	[0.58;	1.84]	1.35	[0.68; 2.69]	0.52	[0.17;	1.54]	2.61	[0.72;	9.51]	1.4567	0.1452
Perphenazine:Zotepine	0	0	1.96	[0.75;	5.08]	.	.	1.96	[0.75;	5.08]	.	.	.	.	.
Quetiapine:Risperidone	1	0.89	0.31	[0.16;	0.61]	0.33	[0.16; 0.66]	0.22	[0.03;	1.76]	1.46	[0.16;	12.96]	0.3381	0.7353
Quetiapine:Ziprasidone	1	0.81	0.31	[0.15;	0.64]	0.41	[0.18; 0.93]	0.09	[0.02;	0.48]	4.67	[0.71;	30.75]	1.6047	0.1086
Quetiapine:Zotepine	0	0	0.59	[0.20;	1.68]	.	.	0.59	[0.20;	1.68]	.	.	.	.	.
Risperidone:Ziprasidone	1	0.48	0.98	[0.62;	1.56]	1.26	[0.65; 2.46]	0.78	[0.41;	1.48]	1.62	[0.65;	4.08]	1.0291	0.3034
Risperidone:Zotepine	0	0	1.87	[0.80;	4.36]	.	.	1.87	[0.80;	4.36]	.	.	.	.	.
Ziprasidone:Zotepine	0	0	1.90	[0.75;	4.78]	.	.	1.90	[0.75;	4.78]	.	.	.	.	.

Legend:
- comparison - Treatment comparison
- k - Number of studies providing direct evidence
- prop - Direct evidence proportion
- nma - Estimated treatment effect (OR) in network meta-analysis
- direct - Estimated treatment effect (OR) derived from direct evidence
- indir. - Estimated treatment effect (OR) derived from indirect evidence
- RoR - Ratio of Ratios (direct versus indirect)
- z - z-value of test for disagreement (direct versus indirect)
- p-value - p-value of test for disagreement (direct versus indirect)

Results from SIDE-tests akathisia

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Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:
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comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	RoR	95%-CI	z	p-value
Amisulpride:Aripiprazole	0	0	0.87	[0.44; 1.69]	.	.	0.87	[0.44; 1.69]	.	.	.	.
Amisulpride:Asenapine	0	0	0.33	[0.14; 0.78]	.	.	0.33	[0.14; 0.78]	.	.	.	.
Amisulpride:Haloperidol	0	0	0.36	[0.19; 0.71]	.	.	0.36	[0.19; 0.71]	.	.	.	.
Amisulpride:Lurasidone	0	0	0.16	[0.03; 0.84]	.	.	0.16	[0.03; 0.84]	.	.	.	.
Amisulpride:Olanzapine	0	0	0.95	[0.52; 1.77]	.	.	0.95	[0.52; 1.77]	.	.	.	.
Amisulpride:Paliperidone	0	0	1.11	[0.54; 2.30]	.	.	1.11	[0.54; 2.30]	.	.	.	.
Amisulpride:Perphenazine	0	0	0.70	[0.31; 1.54]	.	.	0.70	[0.31; 1.54]	.	.	.	.
Amisulpride:Quetiapine	0	0	0.93	[0.42; 2.07]	.	.	0.93	[0.42; 2.07]	.	.	.	.
Amisulpride:Risperidone	1	1.00	0.71	[0.42; 1.18]	0.71	[0.42; 1.18]	.	.	.	.	.	.
Amisulpride:Ziprasidone	0	0	0.65	[0.32; 1.31]	.	.	0.65	[0.32; 1.31]	.	.	.	.
Aripiprazole:Asenapine	0	0	0.39	[0.20; 0.75]	.	.	0.39	[0.20; 0.75]	.	.	.	.
Aripiprazole:Haloperidol	1	0.84	0.42	[0.32; 0.55]	0.45	[0.33; 0.60]	0.31	[0.16; 0.61]	1.43	[0.69; 2.98]	0.9633	0.3354
Aripiprazole:Lurasidone	0	0	0.18	[0.04; 0.92]	.	.	0.18	[0.04; 0.92]	.	.	.	.
Aripiprazole:Olanzapine	1	0.59	1.10	[0.77; 1.57]	1.07	[0.67; 1.70]	1.15	[0.66; 2.01]	0.93	[0.45; 1.91]	-0.2075	0.8356
Aripiprazole:Paliperidone	1	0.40	1.29	[0.71; 2.31]	0.82	[0.32; 2.07]	1.74	[0.81; 3.71]	0.47	[0.14; 1.56]	-1.2326	0.2177
Aripiprazole:Perphenazine	0	0	0.80	[0.41; 1.59]	.	.	0.80	[0.41; 1.59]	.	.	.	.
Aripiprazole:Quetiapine	0	0	1.07	[0.54; 2.13]	.	.	1.07	[0.54; 2.13]	.	.	.	.
Aripiprazole:Risperidone	0	0	0.82	[0.53; 1.26]	.	.	0.82	[0.53; 1.26]	.	.	.	.
Aripiprazole:Ziprasidone	0	0	0.75	[0.44; 1.28]	.	.	0.75	[0.44; 1.28]	.	.	.	.
Asenapine:Haloperidol	1	0.21	1.09	[0.56; 2.11]	0.92	[0.22; 3.86]	1.14	[0.54; 2.41]	0.81	[0.16; 4.07]	-0.2602	0.7947
Asenapine:Lurasidone	0	0	0.47	[0.08; 2.57]	.	.	0.47	[0.08; 2.57]	.	.	.	.
Asenapine:Olanzapine	1	0.84	2.86	[1.59; 5.15]	2.96	[1.56; 5.61]	2.38	[0.54; 10.55]	1.24	[0.25; 6.26]	0.2602	0.7947
Asenapine:Paliperidone	0	0	3.33	[1.48; 7.52]	.	.	3.33	[1.48; 7.52]	.	.	.	.
Asenapine:Perphenazine	0	0	2.08	[0.90; 4.82]	.	.	2.08	[0.90; 4.82]	.	.	.	.
Asenapine:Quetiapine	0	0	2.78	[1.20; 6.48]	.	.	2.78	[1.20; 6.48]	.	.	.	.
Asenapine:Risperidone	0	0	2.11	[1.08; 4.15]	.	.	2.11	[1.08; 4.15]	.	.	.	.
Asenapine:Ziprasidone	0	0	1.95	[0.95; 3.98]	.	.	1.95	[0.95; 3.98]	.	.	.	.
Haloperidol:Lurasidone	0	0	0.43	[0.08; 2.20]	.	.	0.43	[0.08; 2.20]	.	.	.	.
Haloperidol:Olanzapine	2	0.35	2.62	[1.80; 3.83]	3.22	[1.71; 6.08]	2.35	[1.47; 3.75]	1.37	[0.62; 3.02]	0.7863	0.4317
Haloperidol:Paliperidone	0	0	3.06	[1.67; 5.62]	.	.	3.06	[1.67; 5.62]	.	.	.	.
Haloperidol:Perphenazine	0	0	1.91	[0.96; 3.81]	.	.	1.91	[0.96; 3.81]	.	.	.	.
Haloperidol:Quetiapine	0	0	2.56	[1.28; 5.12]	.	.	2.56	[1.28; 5.12]	.	.	.	.
Haloperidol:Risperidone	1	0.44	1.94	[1.26; 3.01]	2.27	[1.18; 4.38]	1.72	[0.96; 3.08]	1.32	[0.55; 3.18]	0.6186	0.5362
Haloperidol:Ziprasidone	0	0	1.79	[1.04; 3.08]	.	.	1.79	[1.04; 3.08]	.	.	.	.
Lurasidone:Olanzapine	0	0	6.13	[1.23; 30.49]	.	.	6.13	[1.23; 30.49]	.	.	.	.
Lurasidone:Paliperidone	0	0	7.15	[1.33; 38.34]	.	.	7.15	[1.33; 38.34]	.	.	.	.
Lurasidone:Perphenazine	0	0	4.47	[0.86; 23.11]	.	.	4.47	[0.86; 23.11]	.	.	.	.
Lurasidone:Quetiapine	1	1.00	5.97	[1.36; 26.31]	5.97	[1.36; 26.31]	.	.	.	.	.	.
Lurasidone:Risperidone	0	0	4.54	[0.91; 22.62]	.	.	4.54	[0.91; 22.62]	.	.	.	.
Lurasidone:Ziprasidone	0	0	4.18	[0.83; 21.14]	.	.	4.18	[0.83; 21.14]	.	.	.	.
Paliperidone:Olanzapine	0	0	0.86	[0.48; 1.53]	.	.	0.86	[0.48; 1.53]	.	.	.	.
Perphenazine:Olanzapine	2	0.73	1.37	[0.75; 2.51]	1.45	[0.72; 2.94]	1.18	[0.37; 3.78]	1.23	[0.32; 4.83]	0.3011	0.7633
Quetiapine:Olanzapine	1	0.72	1.03	[0.56; 1.89]	1.07	[0.52; 2.19]	0.93	[0.30; 2.94]	1.14	[0.29; 4.45]	0.1947	0.8456

Risperidone:Olanzapine	4	0.81	1.35	[0.96;	1.91]	1.36	[0.93;	2.00]	1.32	[0.60;	2.91]	1.03	[0.43;	2.49]	0.0666	0.9469
Ziprasidone:Olanzapine	3	0.93	1.47	[0.97;	2.21]	1.43	[0.93;	2.18]	2.08	[0.47;	9.33]	0.68	[0.14;	3.25]	-0.4785	0.6323
Paliperidone:Perphenazine	0	0	0.62	[0.29;	1.37]	.		.	0.62	[0.29;	1.37]	.		.	.	.
Paliperidone:Quetiapine	0	0	0.84	[0.38;	1.84]	.		.	0.84	[0.38;	1.84]	.		.	.	.
Paliperidone:Risperidone	1	0.75	0.63	[0.38;	1.06]	0.53	[0.29;	0.96]	1.12	[0.40;	3.17]	0.47	[0.14;	1.56]	-1.2326	0.2177
Paliperidone:Ziprasidone	0	0	0.58	[0.30;	1.15]	.		.	0.58	[0.30;	1.15]	.		.	.	.
Perphenazine:Quetiapine	1	0.99	1.34	[0.66;	2.71]	1.31	[0.64;	2.67]	7.15	[0.01;	4920.29]	0.18	[0.00;	130.91]	-0.5063	0.6127
Perphenazine:Risperidone	1	0.82	1.02	[0.55;	1.88]	1.05	[0.53;	2.07]	0.88	[0.21;	3.71]	1.19	[0.24;	5.81]	0.2130	0.8313
Perphenazine:Ziprasidone	1	0.76	0.94	[0.49;	1.79]	0.80	[0.38;	1.68]	1.56	[0.41;	5.90]	0.51	[0.11;	2.34]	-0.8648	0.3871
Quetiapine:Risperidone	1	0.84	0.76	[0.41;	1.41]	0.80	[0.41;	1.57]	0.58	[0.13;	2.69]	1.37	[0.26;	7.25]	0.3686	0.7124
Quetiapine:Ziprasidone	1	0.78	0.70	[0.36;	1.35]	0.61	[0.29;	1.28]	1.14	[0.29;	4.54]	0.53	[0.11;	2.56]	-0.7843	0.4329
Risperidone:Ziprasidone	1	0.47	0.92	[0.57;	1.50]	0.76	[0.37;	1.54]	1.09	[0.56;	2.12]	0.70	[0.26;	1.84]	-0.7274	0.4670

Legend:

comparison	Treatment comparison
k	Number of studies providing direct evidence
prop	Direct evidence proportion
nma	Estimated treatment effect (OR) in network meta-analysis
direct	Estimated treatment effect (OR) derived from direct evidence
indir.	Estimated treatment effect (OR) derived from indirect evidence
RoR	Ratio of Ratios (direct versus indirect)
z	z-value of test for disagreement (direct versus indirect)
p-value	p-value of test for disagreement (direct versus indirect)

Results from SIDE-tests prolactin

Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	Diff	95%-CI	z	p-value
Aripiprazole:Asenapine	0	0	-10.99	[-26.83; 4.85]	.	.	-10.99	[-26.83; 4.85]	.	.	.	.
Aripiprazole:Haloperidol	1	0.29	-23.73	[-38.37; -9.08]	-42.30	[-69.55; -15.05]	-16.18	[-33.55; 1.19]	-26.12	[-58.43; 6.20]	-1.5841	0.1132
Aripiprazole:Lurasidone	0	0	-15.35	[-39.85; 9.15]	.	.	-15.35	[-39.85; 9.15]	.	.	.	.
Aripiprazole:Olanzapine	1	0.83	-13.42	[-25.66; -1.18]	-8.89	[-22.35; 4.57]	-35.01	[-64.39; -5.63]	26.12	[-6.20; 58.43]	1.5841	0.1132
Aripiprazole:Paliperidone	0	0	-42.92	[-62.45; -23.39]	.	.	-42.92	[-62.45; -23.39]	.	.	.	.
Aripiprazole:Perphenazine	0	0	-23.75	[-40.36; -7.14]	.	.	-23.75	[-40.36; -7.14]	.	.	.	.
Aripiprazole:Quetiapine	0	0	-14.05	[-30.55; 2.45]	.	.	-14.05	[-30.55; 2.45]	.	.	.	.
Aripiprazole:Risperidone	0	0	-43.30	[-57.54; -29.06]	.	.	-43.30	[-57.54; -29.06]	.	.	.	.
Aripiprazole:Ziprasidone	0	0	-18.28	[-33.26; -3.31]	.	.	-18.28	[-33.26; -3.31]	.	.	.	.
Asenapine:Haloperidol	1	0.51	-12.74	[-24.86; -0.62]	-9.90	[-26.90; 7.10]	-15.68	[-32.97; 1.61]	5.78	[-18.46; 30.03]	0.4674	0.6402
Asenapine:Lurasidone	0	0	-4.37	[-28.12; 19.38]	.	.	-4.37	[-28.12; 19.38]	.	.	.	.
Asenapine:Olanzapine	1	0.73	-2.44	[-13.21; 8.33]	-4.00	[-16.61; 8.61]	1.78	[-18.93; 22.49]	-5.78	[-30.03; 18.46]	-0.4674	0.6402
Asenapine:Paliperidone	0	0	-31.93	[-50.42; -13.44]	.	.	-31.93	[-50.42; -13.44]	.	.	.	.
Asenapine:Perphenazine	0	0	-12.77	[-28.24; 2.71]	.	.	-12.77	[-28.24; 2.71]	.	.	.	.
Asenapine:Quetiapine	0	0	-3.07	[-18.43; 12.29]	.	.	-3.07	[-18.43; 12.29]	.	.	.	.
Asenapine:Risperidone	0	0	-32.31	[-45.08; -19.54]	.	.	-32.31	[-45.08; -19.54]	.	.	.	.
Asenapine:Ziprasidone	0	0	-7.30	[-21.03; 6.44]	.	.	-7.30	[-21.03; 6.44]	.	.	.	.
Lurasidone:Haloperidol	0	0	-8.37	[-31.71; 14.96]	.	.	-8.37	[-31.71; 14.96]	.	.	.	.
Olanzapine:Haloperidol	1	0.55	-10.31	[-20.63; 0.02]	-7.36	[-21.22; 6.50]	-13.97	[-29.44; 1.50]	6.61	[-14.16; 27.38]	0.6238	0.5327
Paliperidone:Haloperidol	0	0	19.19	[1.63; 36.75]	.	.	19.19	[1.63; 36.75]	.	.	.	.
Perphenazine:Haloperidol	0	0	0.03	[-14.81; 14.86]	.	.	0.03	[-14.81; 14.86]	.	.	.	.
Quetiapine:Haloperidol	0	0	-9.67	[-24.38; 5.03]	.	.	-9.67	[-24.38; 5.03]	.	.	.	.
Risperidone:Haloperidol	1	0.63	19.57	[8.18; 30.96]	21.12	[6.77; 35.47]	16.93	[-1.78; 35.64]	4.19	[-19.39; 27.77]	0.3482	0.7277
Ziprasidone:Haloperidol	0	0	-5.44	[-18.57; 7.69]	.	.	-5.44	[-18.57; 7.69]	.	.	.	.
Lurasidone:Olanzapine	0	0	1.93	[-19.37; 23.23]	.	.	1.93	[-19.37; 23.23]	.	.	.	.
Lurasidone:Paliperidone	0	0	-27.56	[-52.89; -2.24]	.	.	-27.56	[-52.89; -2.24]	.	.	.	.
Lurasidone:Perphenazine	0	0	-8.40	[-30.59; 13.79]	.	.	-8.40	[-30.59; 13.79]	.	.	.	.
Lurasidone:Quetiapine	1	1.00	1.30	[-16.81; 19.41]	1.30	[-16.81; 19.41]	.	.	.	.	.	.
Lurasidone:Risperidone	0	0	-27.94	[-49.46; -6.43]	.	.	-27.94	[-49.46; -6.43]	.	.	.	.
Lurasidone:Ziprasidone	0	0	-2.93	[-24.58; 18.72]	.	.	-2.93	[-24.58; 18.72]	.	.	.	.
Olanzapine:Paliperidone	0	0	-29.49	[-44.95; -14.04]	.	.	-29.49	[-44.95; -14.04]	.	.	.	.
Olanzapine:Perphenazine	1	0.80	-10.33	[-21.70; 1.04]	-6.50	[-19.23; 6.23]	-25.36	[-50.57; -0.14]	18.86	[-9.39; 47.11]	1.3083	0.1908
Olanzapine:Quetiapine	1	0.79	-0.63	[-11.84; 10.57]	3.20	[-9.39; 15.79]	-15.23	[-39.81; 9.35]	18.43	[-9.18; 46.05]	1.3083	0.1908
Olanzapine:Risperidone	3	0.92	-29.87	[-37.64; -22.11]	-29.63	[-37.72; -21.54]	-32.71	[-60.54; -4.89]	3.08	[-25.90; 32.06]	0.2082	0.8351
Olanzapine:Ziprasidone	2	0.92	-4.86	[-13.61; 3.88]	-2.61	[-11.72; 6.51]	-30.89	[-61.84; 0.06]	28.28	[-3.98; 60.54]	1.7184	0.0857
Paliperidone:Perphenazine	0	0	19.16	[1.36; 36.97]	.	.	19.16	[1.36; 36.97]	.	.	.	.
Paliperidone:Quetiapine	0	0	28.86	[11.16; 46.57]	.	.	28.86	[11.16; 46.57]	.	.	.	.
Paliperidone:Risperidone	1	1.00	-0.38	[-13.74; 12.98]	-0.38	[-13.74; 12.98]	.	.	.	.	.	.
Paliperidone:Ziprasidone	0	0	24.63	[7.87; 41.39]	.	.	24.63	[7.87; 41.39]	.	.	.	.
Perphenazine:Quetiapine	1	1.00	9.70	[-3.11; 22.51]	9.70	[-3.11; 22.51]	.	.	.	.	.	.
Perphenazine:Risperidone	1	0.84	-19.54	[-31.31; -7.78]	-15.00	[-27.85; -2.15]	-42.95	[-72.13; -13.78]	27.95	[-3.93; 59.84]	1.7184	0.0857
Perphenazine:Ziprasidone	1	0.87	5.47	[-6.55; 17.48]	4.90	[-8.00; 17.80]	9.19	[-23.85; 42.24]	-4.29	[-39.77; 31.18]	-0.2373	0.8124

```
    Quetiapine:Risperidone 1 0.83 -29.24 [-40.85; -17.64] -24.70 [-37.41; -11.99] -52.04 [-80.52; -23.56]  27.34 [ -3.84; 58.53]  1.7184  0.0857
    Quetiapine:Ziprasidone 1 0.86  -4.23 [-16.10;   7.63]  -4.80 [-17.56;   7.96]  -0.60 [-32.87;  31.67]  -4.20 [-38.90; 30.50] -0.2373  0.8124
   Risperidone:Ziprasidone 1 0.62  25.01 [ 14.90;  35.12]  19.90 [  7.10;  32.70]  33.48 [ 17.00;  49.97] -13.58 [-34.45;  7.29] -1.2757  0.2021

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (MD) in network meta-analysis
 direct     - Estimated treatment effect (MD) derived from direct evidence
 indir.     - Estimated treatment effect (MD) derived from indirect evidence
 Diff       - Difference between direct and indirect treatment estimates
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

Results from SIDE-tests QTc

Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	Diff	95%-CI	z	p-value
Amisulpride:Asenapine	0	0	4.60	[-2.56; 11.76]	.	.	4.60	[-2.56; 11.76]	.	.	.	.
Amisulpride:Lurasidone	0	0	-3.38	[-14.20; 7.44]	.	.	-3.38	[-14.20; 7.44]	.	.	.	.
Amisulpride:Olanzapine	1	1.00	5.00	[-1.81; 11.81]	5.00	[-1.81; 11.81]	.	.	.	.	.	.
Amisulpride:Paliperidone	0	0	7.22	[-1.16; 15.61]	.	.	7.22	[-1.16; 15.61]	.	.	.	.
Amisulpride:Perphenazine	0	0	4.32	[-4.00; 12.64]	.	.	4.32	[-4.00; 12.64]	.	.	.	.
Amisulpride:Quetiapine	0	0	-0.18	[-8.41; 8.05]	.	.	-0.18	[-8.41; 8.05]	.	.	.	.
Amisulpride:Risperidone	0	0	5.12	[-2.68; 12.93]	.	.	5.12	[-2.68; 12.93]	.	.	.	.
Amisulpride:Ziprasidone	0	0	4.29	[-3.02; 11.61]	.	.	4.29	[-3.02; 11.61]	.	.	.	.
Asenapine:Lurasidone	0	0	-7.98	[-16.68; 0.72]	.	.	-7.98	[-16.68; 0.72]	.	.	.	.
Asenapine:Olanzapine	1	1.00	0.40	[-1.83; 2.63]	0.40	[-1.83; 2.63]	.	.	.	.	.	.
Asenapine:Paliperidone	0	0	2.62	[-2.76; 8.01]	.	.	2.62	[-2.76; 8.01]	.	.	.	.
Asenapine:Perphenazine	0	0	-0.28	[-5.56; 5.00]	.	.	-0.28	[-5.56; 5.00]	.	.	.	.
Asenapine:Quetiapine	0	0	-4.78	[-9.92; 0.36]	.	.	-4.78	[-9.92; 0.36]	.	.	.	.
Asenapine:Risperidone	0	0	0.52	[-3.90; 4.95]	.	.	0.52	[-3.90; 4.95]	.	.	.	.
Asenapine:Ziprasidone	0	0	-0.31	[-3.80; 3.19]	.	.	-0.31	[-3.80; 3.19]	.	.	.	.
Lurasidone:Olanzapine	0	0	8.38	[-0.03; 16.79]	.	.	8.38	[-0.03; 16.79]	.	.	.	.
Lurasidone:Paliperidone	0	0	10.60	[1.51; 19.70]	.	.	10.60	[1.51; 19.70]	.	.	.	.
Lurasidone:Perphenazine	0	0	7.70	[-1.16; 16.56]	.	.	7.70	[-1.16; 16.56]	.	.	.	.
Lurasidone:Quetiapine	1	1.00	3.20	[-3.82; 10.22]	3.20	[-3.82; 10.22]	.	.	.	.	.	.
Lurasidone:Risperidone	0	0	8.50	[-0.06; 17.07]	.	.	8.50	[-0.06; 17.07]	.	.	.	.
Lurasidone:Ziprasidone	0	0	7.67	[-0.85; 16.20]	.	.	7.67	[-0.85; 16.20]	.	.	.	.
Paliperidone:Olanzapine	0	0	-2.22	[-7.13; 2.68]	.	.	-2.22	[-7.13; 2.68]	.	.	.	.
Perphenazine:Olanzapine	1	0.82	0.68	[-4.10; 5.46]	0.20	[-5.07; 5.47]	2.91	[-8.46; 14.28]	-2.71	[-15.24; 9.82]	-0.4237	0.6718
Quetiapine:Olanzapine	1	0.81	5.18	[0.55; 9.81]	4.70	[-0.43; 9.83]	7.27	[-3.44; 17.97]	-2.57	[-14.44; 9.31]	-0.4237	0.6718
Risperidone:Olanzapine	2	0.89	-0.12	[-3.94; 3.69]	-0.18	[-4.21; 3.86]	0.34	[-11.40; 12.08]	-0.52	[-12.94; 11.90]	-0.0819	0.9348
Ziprasidone:Olanzapine	2	0.98	0.71	[-1.98; 3.39]	0.61	[-2.10; 3.32]	5.98	[-14.39; 26.36]	-5.37	[-25.93; 15.18]	-0.5123	0.6084
Paliperidone:Perphenazine	0	0	-2.90	[-8.82; 3.01]	.	.	-2.90	[-8.82; 3.01]	.	.	.	.
Paliperidone:Quetiapine	0	0	-7.40	[-13.19; -1.62]	.	.	-7.40	[-13.19; -1.62]	.	.	.	.
Paliperidone:Risperidone	1	1.00	-2.10	[-5.18; 0.98]	-2.10	[-5.18; 0.98]	.	.	.	.	.	.
Paliperidone:Ziprasidone	0	0	-2.93	[-8.14; 2.28]	.	.	-2.93	[-8.14; 2.28]	.	.	.	.
Perphenazine:Quetiapine	1	1.00	-4.50	[-9.90; 0.90]	-4.50	[-9.90; 0.90]	.	.	.	.	.	.
Perphenazine:Risperidone	1	0.92	0.80	[-4.25; 5.86]	1.20	[-4.07; 6.47]	-3.60	[-21.21; 14.00]	4.80	[-13.58; 23.18]	0.5123	0.6084
Perphenazine:Ziprasidone	1	0.73	-0.03	[-5.02; 4.97]	0.10	[-5.73; 5.93]	-0.37	[-10.08; 9.33]	0.47	[-10.85; 11.79]	0.0819	0.9348
Quetiapine:Risperidone	1	0.91	5.30	[0.40; 10.21]	5.70	[0.57; 10.83]	1.15	[-15.49; 17.79]	4.55	[-12.86; 21.97]	0.5123	0.6084
Quetiapine:Ziprasidone	1	0.72	4.47	[-0.37; 9.32]	4.60	[-1.10; 10.30]	4.15	[-5.07; 13.36]	0.45	[-10.38; 11.29]	0.0819	0.9348
Risperidone:Ziprasidone	1	0.57	-0.83	[-5.04; 3.38]	-1.10	[-6.68; 4.48]	-0.47	[-6.89; 5.95]	-0.63	[-9.13; 7.88]	-0.1447	0.8850

Legend:
 comparison - Treatment comparison
 k   - Number of studies providing direct evidence
 prop   - Direct evidence proportion
 nma   - Estimated treatment effect (MD) in network meta-analysis
 direct   - Estimated treatment effect (MD) derived from direct evidence

```
indir.     - Estimated treatment effect (MD) derived from indirect evidence
Diff       - Difference between direct and indirect treatment estimates
z          - z-value of test for disagreement (direct versus indirect)
p-value    - p-value of test for disagreement (direct versus indirect)
```

Results from SIDE-tests sedation

Separate indirect from direct evidence (SIDE) using back-calculation method

Random effects model:

comparison	k	prop	nma	95%-CI	direct	95%-CI	indir.	95%-CI	RoR	95%-CI	z	p-value
Amisulpride:Aripiprazole	0	0	1.53	[0.70; 3.36]	.	.	1.53	[0.70; 3.36]	.	.	.	.
Amisulpride:Asenapine	0	0	0.96	[0.43; 2.15]	.	.	0.96	[0.43; 2.15]	.	.	.	.
Amisulpride:Haloperidol	0	0	1.06	[0.48; 2.33]	.	.	1.06	[0.48; 2.33]	.	.	.	.
Amisulpride:Lurasidone	0	0	1.14	[0.24; 5.35]	.	.	1.14	[0.24; 5.35]	.	.	.	.
Amisulpride:Olanzapine	1	0.57	0.81	[0.43; 1.55]	0.99	[0.42; 2.35]	0.62	[0.23; 1.67]	1.60	[0.43; 5.90]	0.6996	0.4841
Amisulpride:Paliperidone	0	0	0.68	[0.20; 2.36]	.	.	0.68	[0.20; 2.36]	.	.	.	.
Amisulpride:Perphenazine	0	0	0.88	[0.42; 1.84]	.	.	0.88	[0.42; 1.84]	.	.	.	.
Amisulpride:Quetiapine	0	0	0.79	[0.38; 1.64]	.	.	0.79	[0.38; 1.64]	.	.	.	.
Amisulpride:Risperidone	1	0.47	0.87	[0.45; 1.66]	0.68	[0.26; 1.75]	1.08	[0.44; 2.65]	0.63	[0.17; 2.32]	-0.6996	0.4841
Amisulpride:Ziprasidone	0	0	1.06	[0.51; 2.19]	.	.	1.06	[0.51; 2.19]	.	.	.	.
Amisulpride:Zotepine	0	0	0.49	[0.13; 1.81]	.	.	0.49	[0.13; 1.81]	.	.	.	.
Aripiprazole:Asenapine	0	0	0.63	[0.33; 1.21]	.	.	0.63	[0.33; 1.21]	.	.	.	.
Aripiprazole:Haloperidol	1	0.71	0.69	[0.44; 1.08]	0.66	[0.39; 1.11]	0.78	[0.34; 1.77]	0.84	[0.32; 2.23]	-0.3413	0.7329
Aripiprazole:Lurasidone	0	0	0.75	[0.17; 3.28]	.	.	0.75	[0.17; 3.28]	.	.	.	.
Aripiprazole:Olanzapine	1	0.63	0.53	[0.34; 0.84]	0.54	[0.30; 0.96]	0.52	[0.25; 1.11]	1.03	[0.40; 2.66]	0.0611	0.9513
Aripiprazole:Paliperidone	1	0.66	0.44	[0.16; 1.26]	0.57	[0.16; 2.04]	0.28	[0.05; 1.67]	2.04	[0.22; 18.49]	0.6325	0.5271
Aripiprazole:Perphenazine	0	0	0.58	[0.32; 1.04]	.	.	0.58	[0.32; 1.04]	.	.	.	.
Aripiprazole:Quetiapine	0	0	0.52	[0.29; 0.92]	.	.	0.52	[0.29; 0.92]	.	.	.	.
Aripiprazole:Risperidone	0	0	0.57	[0.34; 0.94]	.	.	0.57	[0.34; 0.94]	.	.	.	.
Aripiprazole:Ziprasidone	0	0	0.69	[0.39; 1.23]	.	.	0.69	[0.39; 1.23]	.	.	.	.
Aripiprazole:Zotepine	0	0	0.32	[0.10; 0.99]	.	.	0.32	[0.10; 0.99]	.	.	.	.
Asenapine:Haloperidol	1	0.09	1.10	[0.57; 2.11]	1.89	[0.20; 17.62]	1.04	[0.53; 2.07]	1.81	[0.17; 18.71]	0.4975	0.6189
Asenapine:Lurasidone	0	0	1.19	[0.27; 5.25]	.	.	1.19	[0.27; 5.25]	.	.	.	.
Asenapine:Olanzapine	1	0.96	0.84	[0.53; 1.36]	0.82	[0.51; 1.34]	1.49	[0.15; 14.64]	0.55	[0.05; 5.72]	-0.4975	0.6189
Asenapine:Paliperidone	0	0	0.71	[0.22; 2.28]	.	.	0.71	[0.22; 2.28]	.	.	.	.
Asenapine:Perphenazine	0	0	0.92	[0.50; 1.69]	.	.	0.92	[0.50; 1.69]	.	.	.	.
Asenapine:Quetiapine	0	0	0.82	[0.45; 1.49]	.	.	0.82	[0.45; 1.49]	.	.	.	.
Asenapine:Risperidone	0	0	0.90	[0.52; 1.54]	.	.	0.90	[0.52; 1.54]	.	.	.	.
Asenapine:Ziprasidone	0	0	1.10	[0.61; 1.99]	.	.	1.10	[0.61; 1.99]	.	.	.	.
Asenapine:Zotepine	0	0	0.51	[0.15; 1.73]	.	.	0.51	[0.15; 1.73]	.	.	.	.
Haloperidol:Lurasidone	0	0	1.08	[0.25; 4.75]	.	.	1.08	[0.25; 4.75]	.	.	.	.
Haloperidol:Olanzapine	1	0.51	0.77	[0.48; 1.23]	0.66	[0.34; 1.27]	0.91	[0.46; 1.78]	0.72	[0.28; 1.86]	-0.6715	0.5019
Haloperidol:Paliperidone	0	0	0.64	[0.21; 1.93]	.	.	0.64	[0.21; 1.93]	.	.	.	.
Haloperidol:Perphenazine	0	0	0.83	[0.46; 1.52]	.	.	0.83	[0.46; 1.52]	.	.	.	.
Haloperidol:Quetiapine	0	0	0.75	[0.42; 1.34]	.	.	0.75	[0.42; 1.34]	.	.	.	.
Haloperidol:Risperidone	1	0.54	0.82	[0.50; 1.35]	0.93	[0.47; 1.85]	0.70	[0.34; 1.47]	1.33	[0.49; 3.63]	0.5537	0.5798
Haloperidol:Ziprasidone	0	0	1.00	[0.56; 1.79]	.	.	1.00	[0.56; 1.79]	.	.	.	.
Haloperidol:Zotepine	1	1.00	0.46	[0.17; 1.31]	0.46	[0.17; 1.31]	.	.	.	.	.	.
Lurasidone:Olanzapine	0	0	0.71	[0.17; 2.91]	.	.	0.71	[0.17; 2.91]	.	.	.	.
Lurasidone:Paliperidone	0	0	0.59	[0.10; 3.47]	.	.	0.59	[0.10; 3.47]	.	.	.	.
Lurasidone:Perphenazine	0	0	0.77	[0.19; 3.21]	.	.	0.77	[0.19; 3.21]	.	.	.	.
Lurasidone:Quetiapine	1	1.00	0.69	[0.18; 2.71]	0.69	[0.18; 2.71]	.	.	.	.	.	.

Lurasidone:Risperidone	0	0	0.76	[0.18; 3.10]	.		.	0.76	[0.18;	3.10]	.		.	.	.
Lurasidone:Ziprasidone	0	0	0.93	[0.22; 3.86]	.		.	0.93	[0.22;	3.86]	.		.	.	.
Lurasidone:Zotepine	0	0	0.43	[0.07; 2.61]	.		.	0.43	[0.07;	2.61]	.		.	.	.
Paliperidone:Olanzapine	0	0	1.20	[0.41; 3.51]	.		.	1.20	[0.41;	3.51]	.		.	.	.
Perphenazine:Olanzapine	1	0.84	0.92	[0.63; 1.36]	0.88	[0.58;	1.35]	1.16	[0.44;	3.06]	0.76	[0.26;	2.19]	-0.5040	0.6142
Quetiapine:Olanzapine	1	0.82	1.03	[0.71; 1.47]	0.98	[0.66;	1.46]	1.25	[0.53;	2.95]	0.78	[0.30;	2.02]	-0.5040	0.6142
Risperidone:Olanzapine	4	0.90	0.94	[0.73; 1.22]	0.92	[0.70;	1.21]	1.12	[0.49;	2.57]	0.82	[0.34;	1.98]	-0.4313	0.6663
Ziprasidone:Olanzapine	3	0.93	0.77	[0.54; 1.10]	0.76	[0.52;	1.09]	0.99	[0.25;	3.92]	0.77	[0.18;	3.20]	-0.3642	0.7157
Zotepine:Olanzapine	0	0	1.66	[0.53; 5.16]	.		.	1.66	[0.53;	5.16]	.		.	.	.
Paliperidone:Perphenazine	0	0	1.30	[0.42; 4.02]	.		.	1.30	[0.42;	4.02]	.		.	.	.
Paliperidone:Quetiapine	0	0	1.17	[0.38; 3.59]	.		.	1.17	[0.38;	3.59]	.		.	.	.
Paliperidone:Risperidone	1	0.39	1.27	[0.43; 3.74]	1.96	[0.35;	10.95]	0.96	[0.24;	3.84]	2.04	[0.22;	18.49]	0.6325	0.5271
Paliperidone:Ziprasidone	0	0	1.56	[0.51; 4.79]	.		.	1.56	[0.51;	4.79]	.		.	.	.
Paliperidone:Zotepine	0	0	0.72	[0.16; 3.28]	.		.	0.72	[0.16;	3.28]	.		.	.	.
Perphenazine:Quetiapine	1	1.00	0.90	[0.59; 1.37]	0.90	[0.59;	1.37]	.			.		.	.	.
Perphenazine:Risperidone	1	0.86	0.98	[0.66; 1.46]	1.01	[0.66;	1.54]	0.82	[0.28;	2.37]	1.24	[0.39;	3.90]	0.3642	0.7157
Perphenazine:Ziprasidone	1	0.85	1.20	[0.76; 1.88]	1.23	[0.76;	2.00]	1.03	[0.32;	3.33]	1.19	[0.34;	4.24]	0.2724	0.7853
Perphenazine:Zotepine	0	0	0.56	[0.17; 1.84]	.		.	0.56	[0.17;	1.84]	.		.	.	.
Quetiapine:Risperidone	1	0.85	1.09	[0.75; 1.58]	1.12	[0.75;	1.68]	0.93	[0.36;	2.39]	1.21	[0.43;	3.39]	0.3642	0.7157
Quetiapine:Ziprasidone	1	0.84	1.33	[0.87; 2.05]	1.37	[0.86;	2.19]	1.16	[0.40;	3.39]	1.18	[0.37;	3.78]	0.2724	0.7853
Quetiapine:Zotepine	0	0	0.62	[0.19; 2.03]	.		.	0.62	[0.19;	2.03]	.		.	.	.
Risperidone:Ziprasidone	1	0.68	1.22	[0.83; 1.80]	1.22	[0.76;	1.95]	1.23	[0.62;	2.43]	0.99	[0.43;	2.26]	-0.0232	0.9815
Risperidone:Zotepine	0	0	0.57	[0.18; 1.79]	.		.	0.57	[0.18;	1.79]	.		.	.	.
Ziprasidone:Zotepine	0	0	0.46	[0.14; 1.52]	.		.	0.46	[0.14;	1.52]	.		.	.	.

Legend:
- comparison - Treatment comparison
- k - Number of studies providing direct evidence
- prop - Direct evidence proportion
- nma - Estimated treatment effect (OR) in network meta-analysis
- direct - Estimated treatment effect (OR) derived from direct evidence
- indir. - Estimated treatment effect (OR) derived from indirect evidence
- RoR - Ratio of Ratios (direct versus indirect)
- z - z-value of test for disagreement (direct versus indirect)
- p-value - p-value of test for disagreement (direct versus indirect)