

# THE LANCET Psychiatry

## Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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## SUPPLEMENTARY INFORMATION

### Comparative effects of 18 antipsychotics on metabolic function in schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis

Pillinger T, McCutcheon RA, Vano, L, Mizuno Y, Beck K, Arumuhan A, Hindley G, Natesan S, Efthimiou O, Cipriani A, Howes OD, 2019

#### CONTENTS

Pages 2-4	eTable 1. PRISMA NMA checklist
Pages 5-18	eAppendix 1. PROSPERO registration and protocol
Page 19	eAppendix 2. Methods to assess confidence in NMA using CINeMA
Page 20	eFigure 1. Literature search process
Pages 21-33	eTable 2. Study characteristics
Pages 34-35	eTable 3. Cochrane risk of bias assessment
Page 36	eTable 4. Baseline parameters across treatment-comparisons
Page 37	eAppendix 3. Pairwise meta-analyses
Pages 37-38	eFigures 5-7. Pairwise meta-analysis forest plots
Page 39-40	eFigures 8-10. Pairwise meta-analysis funnel plots
Pages 41-46	eTables 5-11. League tables comparing metabolic alterations associated with antipsychotic drug treatment.
Pages 47-49	eTables 12-18. P-score ranking for metabolic alterations associated with antipsychotic drug treatment.
Pages 50-61	eTables 19-25. Identifying 'hot spots' of inconsistency for the 7 network meta-analyses
Pages 62-87	eTables 26-32. CINeMA confidence ratings for the drug comparisons making up the 7 network meta-analyses.
Pages 88-92	eAppendix 4. Post hoc sensitivity analysis for antipsychotic-induced weight gain (low quality studies removed)
Page 93	eAppendix 5. Sensitivity analyses
Pages 94-97	eFigures 11-17. Forest plots (compared with placebo) for the 7 sensitivity network meta-analyses.
Pages 98-105	Supplementary References

**eTable 1.** PRISMA NMA Checklist

Section/Topic	Item #	Checklist Item	Reported on Page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review <i>incorporating a network meta-analysis (or related form of meta-analysis)</i> .	1
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: <b>Background:</b> main objectives <b>Methods:</b> data sources; study eligibility criteria, participants, and interventions; study appraisal; and <i>synthesis methods, such as network meta-analysis</i> . <b>Results:</b> number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; <i>treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.</i> <b>Discussion/Conclusions:</b> limitations; conclusions and implications of findings. <b>Other:</b> primary source of funding; systematic review registration number with registry name.	3
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known, <i>including mention of why a network meta-analysis has been conducted</i> .	4
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
<b>METHODS</b>			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. <i>Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification)</i> .	5&6
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.	Sup Info
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).	5&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	5&6

confirming data from investigators.

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
<b>Geometry of the network</b>	<b>S1</b>	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	<b>6</b>
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	<b>7</b>
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). <i>Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.</i>	<b>6&amp;7</b>
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: <ul style="list-style-type: none"> <li>• <i>Handling of multi-arm trials;</i></li> <li>• <i>Selection of variance structure;</i></li> <li>• <i>Selection of prior distributions in Bayesian analyses; and</i></li> <li>• <i>Assessment of model fit.</i></li> </ul>	<b>5-7</b>
<b>Assessment of Inconsistency</b>	<b>S2</b>	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	<b>7</b>
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).	<b>7</b>
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: <ul style="list-style-type: none"> <li>• Sensitivity or subgroup analyses;</li> <li>• Meta-regression analyses;</li> <li>• <i>Alternative formulations of the treatment network; and</i></li> <li>• <i>Use of alternative prior distributions for Bayesian analyses (if applicable).</i></li> </ul>	<b>7&amp;8</b>

## 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.	<b>8</b>
<b>Presentation of network structure</b>	<b>S3</b>	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	<b>Fig 1</b>
<b>Summary of network geometry</b>	<b>S4</b>	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	<b>8</b>
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.	<b>eTable 2</b>

Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	eTable 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. <i>Modified approaches may be needed to deal with information from larger networks.</i>	eTable 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. <i>In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons.</i> If additional summary measures were explored (such as treatment rankings), these should also be presented.	Fig 2 eTables 4-10
<b>Exploration for inconsistency</b>	<b>S5</b>	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, <i>P</i> values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	9-12
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	Figure 2 eTable 3 eTables 25-31
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, <i>alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses, and so forth</i> ).	12
<b>DISCUSSION</b>			
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).	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). <i>Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).</i>	16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16-17
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	19

## **eAppendix 1. PROSPERO Registration**

Registration number: CRD42019125322

Available online: [https://www.crd.york.ac.uk/prospero/display\\_record.php?RecordID=125322](https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=125322)

### **\*\*\*\*PROTOCOL\*\*\*\***

## **Review questions**

1. What is the magnitude of metabolic dysregulation (defined as alterations in fasting glucose, total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, and triglyceride levels) and alterations in body weight and body mass index associated with short-term ('acute') antipsychotic treatment in individuals with schizophrenia?
2. Does baseline physiology (e.g. body weight) and demographics (e.g. age) of patients predict magnitude of antipsychotic-associated metabolic dysregulation?
3. Are alterations in metabolic parameters over time associated with alterations in degree of psychopathology?

## **Searches**

We plan to search EMBASE, PsycINFO, and MEDLINE from inception using the following terms:

1

(Acepromazine or Acetophenazine or Amisulpride or Aripiprazole or Asenapine or Benperidol or Blonanserin or Bromperidol or Butaperazine or Carpipramine or Chlorproethazine or Chlorpromazine or Chlorprothixene or Clozapramine or

Clopentixol or Clopentixol or Clothiapine or Clotiapine or Clozapine or Cyamemazine or Cyamepromazine or Dixyrazine or Droperidol or Fluanisone or Flupehenazine or Flupenthixol or Flupentixol or Fluphenazine or Fluspirilen or Fluspirilene or Haloperidol or Iloperidone or Levomepromazine or Levosulpiride or Lithium or Loxapine or Loxapinsuccinate or Lurasidone or Melperone or Mepazine or Mesoridazine or Methotrimeprazine or Molindone or Moperone or Mosapramine or Olanzapine or Oxypertine or Paliperidone or Penfluridol or Perazine or Periciazine or Pericyazine or Perospirone or Perphenazine or Pimozide or Pipamperone or Pipothiazine or Pipotiazine or Prochlorperazine or Promazine or Promethazine or Prothipendyl or Quetiapine or Remoxipiride or Reserpine or Risperone or Risperdal or Risperidone or Seroquel or Sertindole or Stelazine or Sulpiride or Sultopride or Thiopropazate or Thioproperazine or Thioridazine or Tiospirone or Thiothixene or Tiapride or Tiotixene or Trifluoperazine or Trifluoperidol or trifluoperidol or Triflupromazine or trifluperazine or Veralipride or Ziprasidone or Zotepine or Zuclopentixol).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, ui, sy, tc, id, tm]

2

(Antipsychoti\$ or Anti-psychotic\$ or Neurolepic\$ or Neurolept\$).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, ui, sy, tc, id, tm]

3

schizo\$.mp.

4

psychosis.mp.

5

randomized.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, an, ui, sy, tc, id, tm]

6

'double blind'.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, an, ui, sy, tc, id, tm]

7

5 and 6

8

3 or 4

9

1 or 2

10

7 and 8 and 9



## **Types of study to be included**

Double-blind, randomised controlled trials that have been published in the English language. Clinical trials registry data relating to papers identified in the literature review will also be included.

## **Condition or domain being studied**

Metabolic alterations (glucose, total cholesterol, Low Density Lipoprotein (LDL) cholesterol, High Density Lipoprotein (HDL) cholesterol, and triglyceride levels), body weight, body mass index.

## **Participants/population**

Patients with schizophrenia and related psychoses defined according to standard operationalised diagnostic criteria (Feighner criteria, Research Diagnostic Criteria, DSM-III, DSM-III-R, DSM-IV, DSM-V, and ICD-10).

## **Intervention(s), exposure(s)**

Monotherapy with antipsychotic or placebo. We will not employ limits on antipsychotic dose, owing to the lack of clear evidence that antipsychotic treatment dose influences degree of metabolic dysregulation, although we will investigate the potential influence of antipsychotic dose on metabolic change using meta-regression (see 'Meta-regression Analyses' section).<sup>1</sup> Oral or parenteral administration will be accepted.

## **Comparator(s)/control**

Monotherapy with antipsychotic or placebo.

## **Context**

It has long been proposed that some antipsychotic drug treatments cause glucose dysregulation and lipid disturbance thereby contributing to development of the metabolic syndrome in patients with schizophrenia.<sup>2</sup> However, the relative degree to which metabolic alterations occur in acute treatment with different antipsychotics remain unclear. Furthermore, baseline predictors of metabolic dysregulation are poorly defined, and the association between metabolic change and change in psychopathology is uncertain.

## **Main outcome(s)**

For each study, we aim to collect data examining mean and standard deviation of change (i.e. from baseline to study endpoint) in the following outcomes:

1. Glucose (mmol/L)
2. Total cholesterol (mmol/L)
3. Low Density Lipoprotein (LDL) cholesterol (mmol/L)
4. High Density Lipoprotein (HDL) cholesterol (mmol/L)
5. Triglycerides (mmol/L)
6. Body weight (kg)
7. Body Mass Index (BMI, kg/m<sup>2</sup>)

All metabolic outcomes will be measured from blood tests taken under fasting conditions. Either plasma or serum samples will be accepted.

## Data extraction (selection and coding)

This systematic review and network meta-analysis will adhere to recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)<sup>3</sup> extension statement for network meta-analysis.

Extracted information will include: name of first author, year of publication, antipsychotic used in study, average dose of antipsychotic used, type of symptom scale used, patient characteristics including age, %male, %Caucasian, duration of drug intervention, mean  $\pm$  standard deviation (SD) change in symptom scores between baseline and study endpoint, mean  $\pm$  SD metabolic parameter concentrations (glucose, total/LDL/HDL cholesterol/triglycerides) and body weight/body mass index (BMI) at baseline, active drug number, placebo number.

If applicable, data may be extracted from related publications that refer to the same study. When data required for meta-analysis is unreported, corresponding authors will be contacted to request additional data.

Network meta-analysis requires reasonable homogeneity, and as such we will focus on acute treatment, which we define as 6-weeks duration.<sup>4</sup> If 6-week data are not available, the datapoint closest to 6-weeks will be given preference. Again, to maintain homogeneity in the sample, we will exclude paediatric studies (i.e. studies where participant age <18 years). We will not employ limits on antipsychotic dose, owing to the lack of clear evidence that antipsychotic dose influences degree of metabolic dysregulation, although we will investigate the potential influence of antipsychotic dose on metabolic change using meta-regression (see 'Strategy for Data Synthesis' section).<sup>1</sup> Where multiple doses of a single antipsychotic are reported, to increase statistical power, and again in the absence of clear evidence that antipsychotic dose

influences metabolic outcomes, a single weighted mean and standard deviation for each metabolic parameter pertaining to a given multi-arm study will be calculated, using formulae recommended by the Cochrane collaboration:<sup>5</sup>

Weighted mean of multiple study arms:

$$\bar{x} = \frac{\sum_{i=1}^N n_i x_i}{\sum_{i=1}^N n_i}$$

Where,

$N$  = number of observations (i.e. number of arms of the study)

$n_i$  = sample size of study arm

$x_i$  = sample mean of study arm

Weighted standard deviation for 2 study arms:

$$s = \sqrt{\frac{(n_1 - 1)sd_1^2 + (n_2 - 1)sd_2^2 + \frac{n_1 n_2}{n_1 + n_2} (x_1^2 + x_2^2 - 2x_1 x_2)}{n_1 + n_2 - 1}}$$

Where,

$n_1$  and  $n_2$  = sample sizes of study arms 1 and 2

$x_1$  and  $x_2$  = means of study arms 1 and 2

$sd_1$  and  $sd_2$  = standard deviations of study arms 1 and 2

As recommended by Cochrane,<sup>5</sup> where there are more than 2 study arms to combine standard deviations, the above formula will be applied sequentially (i.e. combining study arm 1 and 2 to create arm '1+2', then combining group '1+2' and group 3 to create group '1+2+3' and so on).

Since paliperidone represents the active metabolite of risperidone, data pertaining to these 2 antipsychotics will be merged (i.e. considered as the same intervention). Since we set out to examine mean difference between groups (see ‘Strategy for Data Synthesis’ section), data from certain studies will require conversion from conventional to SI units, which will be performed using standardised conversion factors.<sup>6</sup>

Clinical trials registry data relating to papers identified in the literature review will be included.

5 researchers (YM/LV/KB/AA/GH) will extract data, all studies will be assessed by a minimum of two researchers.

Discrepancies will be decided by TP.

## **Strategy for data synthesis**

### **Characteristics of included studies**

We will describe the study population characteristics across all eligible trials, describing the types of comparisons (i.e. which metabolic parameter is examined), and physiological/demographic variables (including age, gender (%male), ethnicity (%Caucasian), duration of drug intervention, and clinical group (i.e. first episode psychosis, established schizophrenia, treatment resistant schizophrenia, older adults).

### **Pairwise meta-analyses**

For each pairwise comparison with  $\geq 10$  studies we will synthesise data to obtain summary mean differences with accompanying 95% confidence interval using a random effects model. Analyses will be carried out in the statistical programming language R (version 3.5.1)<sup>7</sup> using ‘metafor’ (version 2.1-0). Visual inspection of the forest plots will be used to investigate the degree of statistical heterogeneity, alongside

monitoring of  $\tau$  (the estimated standard deviation of random effects) and the  $I^2$  statistic. An  $I^2$  of less than 25% was deemed to have low heterogeneity, 25-75% medium heterogeneity, and greater than 75% high heterogeneity. To help visualize the extent of heterogeneity we will also include prediction intervals in all forest-plots.

Small study effects and publication bias will be assessed for each pairwise comparison by visual inspection of the contour-enhanced funnel plot and by performing Egger's test of the intercept.<sup>8</sup>

### **Assessment of the transitivity assumption**

In an attempt to ensure transitivity in the network, we will restrict analyses to patients with schizophrenia and related psychoses (i.e. we will not examine the metabolic effects of antipsychotics in other patient groups), we will exclude studies examining paediatric patients, and we will restrict analyses to studies that only examine acute treatment (aiming for treatment duration of 6-weeks).<sup>9</sup>

Potential effect modifiers include age, gender, and ethnicity, as these parameters are known in the general population to influence metabolic change.<sup>10-12</sup> As such, we will examine if age, gender (% male) and ethnicity (% Caucasian) of participants is similarly distributed across the different treatment comparisons.

### **Network Analyses**

If the collected studies appear to be sufficiently similar with respect to the distribution of age, gender, and ethnicity, we will conduct a random effects network meta-analysis (NMA) to synthesise all evidence for each outcome. We will use a frequentist approach to NMA using 'netmeta' (version 1.0-1).<sup>13,14</sup> Network plots will be generated using the 'netgraph' function. In line with previous meta-analyses in the field<sup>15,16</sup> and to allow

intuitive clinical interpretation of results, metabolic change for each given parameter will be expressed as the mean difference (MD) with 95% confidence intervals. MD preserves original units, thus, for example, when examining difference in weight between 2 groups, a calculated MD of 2 equates to a 2kg difference. Placebo will be selected as the reference 'treatment' and forest plots created using 'ggplot2' (version 2.2.1). League tables will be created to display the relative degree of metabolic disturbance for all antipsychotics using the 'netleague' function. For each metabolic parameter, a frequentist analogue of 'Surface under the Cumulative Ranking Curve' (SUCRA) will be used to rank antipsychotics based on degree of metabolic dysregulation, using the 'netrank' function. This provides P-scores which rank antipsychotics on a continuous 0 to 1 scale: a higher P-score indicates greater degree of metabolic disturbance.

### **Assessments of heterogeneity and inconsistency**

Heterogeneity of each network will be assessed by monitoring of  $\tau$  and the  $I^2$  statistic. Consistency of each network (i.e. the agreement between direct and indirect evidence) will be evaluated using global (Q statistic) and local methods (identifying 'hot spots' of inconsistency using the 'netsplit' function).<sup>17,18</sup>

### **Sensitivity analyses**

We hypothesize that inclusion of different study populations (i.e. first episode psychosis (FEP), treatment responders, treatment resistant schizophrenia (TRS), and older adults) may contribute to heterogeneity and inconsistency. As such, the sensitivity of our findings for all 7 outcomes will be evaluated by repeating each NMA with the exclusion of studies that examine FEP, TRS, or older adults.

## **Meta-regression analyses**

In the general population it is known that body weight/BMI,<sup>19</sup> age,<sup>10</sup> gender,<sup>11</sup> and ethnicity<sup>12</sup> influence metabolic function. We will investigate if these covariates as well as treatment factors are related to change in metabolic parameters. We will perform a meta-regression of placebo-controlled data to examine the relationship between antipsychotic-associated metabolic changes and baseline body weight, BMI, baseline level of a given parameter (e.g. baseline glucose levels if examining change in glucose), age, gender (% male), ethnicity (% non-Caucasian), and olanzapine-equivalent dose (calculated using previously defined dose equivalents).<sup>20,21</sup> Since any associations between baseline parameters and antipsychotic associated metabolic change may be influenced by the type of antipsychotic a certain group may have been prescribed, we will repeat all meta-regression analyses including each different antipsychotic as a moderator. All meta-regression will be performed using 'metafor' (version 2.0.0) and representative plots generated using 'ggplot2' (version 2.2.1).

## **Measurement of strength of relationship between alterations in body weight/BMI/metabolic parameter and alterations in psychopathology**

The association between metabolic change and change in psychopathology is uncertain. As such, for placebo-controlled data, we will perform a bivariate meta-analysis, aiming to calculate the correlation coefficient between the effect size (standardised mean difference, SMD) for change in a given metabolic parameter/weight/BMI and the effect size (SMD) for change in total symptoms (assessed using the Positive and Negative Syndrome Scale<sup>17</sup> or Brief Psychiatric Rating Scale scores).<sup>18</sup> This will be performed using the bivariate meta-analysis model



proposed by Riley and colleagues.<sup>22</sup> Analysis will be performed using the package 'metamisc' (version 0.2.0).

## **Risk of bias (quality) assessment**

Risk of bias of individual studies will be assessed using the Cochrane Collaboration's Tool for Assessing Risk of Bias.<sup>23</sup> The following domains will be considered: randomization sequence generation; allocation concealment; blinding of participants/trial personnel/outcome assessment; incomplete outcome data; and selective outcome reporting.

The 'Confidence in Network Meta-Analysis' (CINeMA)<sup>24,25</sup> application will be employed to evaluate the credibility of findings from each network meta-analysis. As part of the CINeMA evaluation process, a risk of bias assessment is required for each study with each study categorised as at low, unclear, or high risk of bias. We will convert our Cochrane Risk of Bias Assessment Tool ratings into CINeMA categories as follows:

<b>Cochrane Risk of Bias Assessment Tool Rating</b>	<b>CINeMA risk of bias category</b>
All domains categorised as low risk	Low risk (1)
All domains categorised as either low risk or unclear risk	Unclear/moderate risk (2)
Any domain categorised as high risk	High risk (3)

## **Contact details for further information**

Toby Pillinger

toby.pillinger@kcl.ac.uk

## **Organisational affiliation of the review**

King's College London

University of Oxford

University of Bern

## **Review team members and their organisational affiliations**

Dr Toby Pillinger. King's College London

Dr Robert McCutcheon. King's College London

Dr Katherine Beck. King's College London

Dr Guy Hindley. King's College London

Dr Atheeshaan Arumham. King's College London

Dr Luke Vano. King's College London

Dr Yuya Mizuno. King's College London

Dr Sridhar Natesan. King's College London

Dr Orestis Efthimiou. University of Bern

Professor Andrea Cipriani. University of Oxford

Professor Oliver Howes. King's College London

## **Type and method of review**

Meta-analysis, Systematic review

## **Funding sources/sponsors**

ODH is supported by MC-A656-5QD30 from the Medical Research Council-UK, 666 from the Maudsley Charity, 094849/Z/10/Z from the Brain and Behavior Research Foundation, and Wellcome Trust. RM is supported by the Wellcome Trust (no.

200102/Z/15/Z). AC is supported by the National Institute for Health Research (NIHR) Oxford Cognitive Health Clinical Research Facility, grant RP-2017-08-ST2-006 from NIHR Research Professorship, and grant BRC-1215-20005 from the NIHR Oxford Health Biomedical Research Centre. OE is supported by project grant No. 180083 from the Swiss National Science Foundation (SNSF).

### **Conflicts of interest**

Professor Howes has received investigator-initiated research funding from and/or participated in advisory/speaker meetings organized by AstraZeneca, Autifony, BMS, Eli Lilly, Heptares, Janssen, Lundbeck, Lyden-Delta, Otsuka, Servier, Sunovion, Rand, and Roche. Drs Pillinger, McCutcheon, Vano, Mizuno, Efthimiou, and Cipriani report no conflicts of interest.

### **Subject index terms status**

Subject indexing assigned by CRD

### **Subject index terms**

Antipsychotic Agents; Humans; Network Meta-Analysis

### **Date of registration in PROSPERO**

27 February 2019

## eAppendix 2. Methods employed to assess confidence in NMA results using CINeMA

### 1. Within-study bias

Defined as per Cochrane risk of bias assessment as follows:

<b>Cochrane Risk of Bias Assessment Tool Rating</b>	<b>CINeMA risk of bias category</b>
All domains categorised as low risk	Low risk (1)
Domains categorised as either low risk or unclear risk	Unclear/moderate risk (2)
Any domain categorised as high risk	High risk (3)

### 2. Across-studies bias

Where pairwise meta-analyses are possible, grade risk of bias based on funnel plot/Egger's regression test. If <10 studies for a given pairwise comparison, downgrade confidence.

### 3. Indirectness

No indirectness assumed

### 4. Imprecision

A clinically meaningful threshold was set at a mean difference of higher or lower than 0.

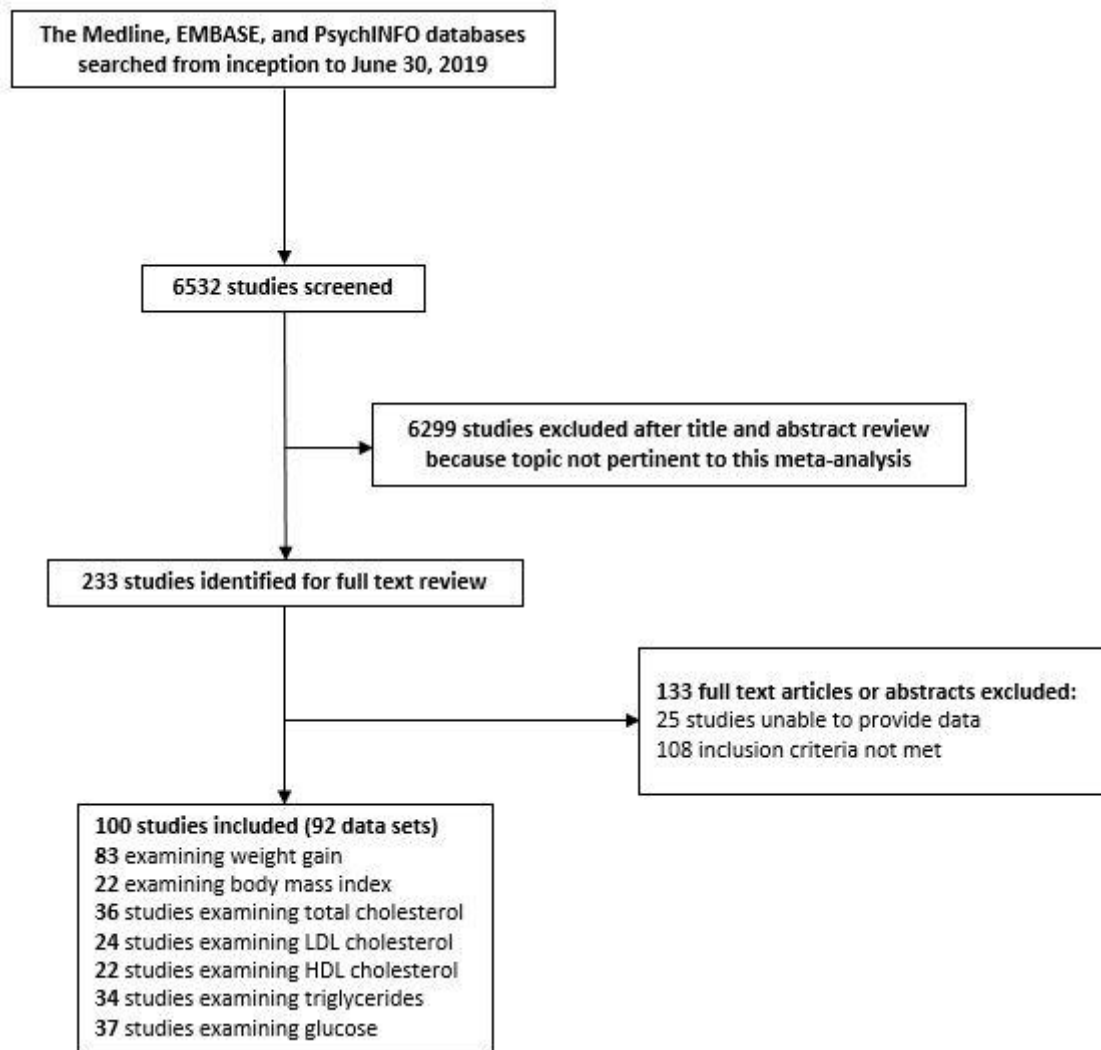
### 5. Heterogeneity

Use recommendations automatically provided by CINeMA

### 6. Incoherence

Downgrade evidence if only indirect evidence

**eFigure 1.** Search process



**eTable 2.** Studies included in meta-analysis.

Each row corresponds to a single data set, for which more than one study may correspond.

Study	Country, patient population	Physical Health Exclusion Criteria	Antipsychotic	Antipsychotic Dose (mg)	Trial Duration (weeks)	Antipsychotic (N)	Placebo (N)	Parameter
<b>Ascher-Svanum 2005<sup>26</sup></b> <b>Beasley 1996<sup>27</sup></b>	Not specifically stated, likely USA Schizophrenia Aged 18-65	'Serious unstable medical illness'	olanzapine	10	6	187	61	Weight
<b>Azorin 2006<sup>28</sup></b>	France Schizophrenia Aged 18-65	QTc over 430 (M) or 450 (F)	risperidone sertindole	6.6 16.2	12 12	61 59	N/A	Weight, BMI
<b>Baymiller 2002<sup>29</sup></b>	Not specifically stated, likely USA Schizophrenia or Schizoaffective disorder Age not stated, likely 18+	None stated	clozapine haloperidol	200-600 10-30	10 10	28 33	N/A	Weight
<b>Bhowmick 2010<sup>30</sup></b>	India Schizophrenia Aged 18-65	Pregnant, breast-feeding, neurological disease "significant disease of vital organs, adrenal or pituitary glands", receiving medication known to prolong QT or interact with study medication	amisulpride olanzapine	450 15	12 12	39 38	N/A	Weight
<b>Beasley 1996<sup>31</sup></b>	USA and Canada Schizophrenia with acute exacerbation Aged 18-65	Serious, unstable medical illness, neurological disease, use of anticholinergic medication, significantly elevated laboratory test results, active hepatitis B, or jaundice	Olanzapine	10	6	28	10	Weight
<b>Bossie, 2011<sup>32</sup></b>	USA, Europe, and Asia Schizophrenia	'Unstable systemic	paliperidone	7.32	13	252	71	Weight

	Aged 18+ Illness for at least 1yr	disease...BM I $\geq$ 40kg/m <sup>2</sup>						
<b>Breier 2005</b> <sup>33</sup>	Europe and North and South America Schizophrenia Aged 18-75	Congenital long QT syndrome, a QTc interval longer than 500, any ECG abnormality that would confound measureme nt of the QT interval, serious unstable mental illness	olanzapine ziprasidone	15.27 115.96	4 4	165 115	N/A	Weight, FG, TG, HDL, LDL, TC
<b>Buckley 2004</b> <sup>34</sup>	Not specifically stated, likely USA and South Africa Schizophrenia Aged 18+	Known sensitivity to drugs used in trial, history of idiopathic or drug- induced agranulocyt osis	quetiapine haloperidol	600 20	4 4	39 32	N/A	Weight
<b>Cantillon 2017</b> <sup>35</sup>	India, Philippines, Malaysia, Moldova and USA Schizophrenia or schizoaffectiv e disorder Age 18-65,	None stated	aripiprazole	15	4	Weight/B MI: 14 FG, TC, TG: 18	38	Weight, BMI, FG, TC, TG
<b>Canuso 2009</b> <sup>36</sup>	India, Russia, Ukraine, USA Schizophrenia Aged 18-65	None stated	paliperidone quetiapine	PAL: 10.4 QUET: 690.9	6	124,106	51	Weight
<b>Canuso 2010a</b> <sup>37</sup>	India, Russia, Ukraine, USA Schizophrenia Schizoaffectiv e disorder Aged 18-65	None stated	paliperidone	12, 6	6	98, 108	107	Weight, FG, LDL, HDL, TG
<b>Canuso 2010b</b> <sup>38</sup>	United States, Romania, India, Philippines, Malaysia, and South Korea Schizoaffectiv e disorder Aged 18-65	None stated	paliperidone	8.6	6	134	53	Weight, FG, TC, LDL, HDL, TG
<b>Canuso 2010</b> <sup>39</sup>	Not stated Schizophrenia Aged 18+	Poor general health or chronic health conditions	paliperidone	8.1	6	116	37	Weight
<b>Conley 2001</b> <sup>40</sup>	USA Schizophrenia or schizoaffectiv e disorder Aged 18-64	Neurological disease, use of disallowed concomitant therapy (e.g.	risperidone olanzapine	4.8 12.4	8 8	146 135	N/A	Weight, BMI

		mood stabilisers or antidepressants)						
<b>Conley 2005<sup>41</sup></b>	Not specifically stated, likely USA Treatment resistant schizophrenia Aged 18-65	Use of routine concomitant medications with CNS activity (e.g. antidepressants, mood stabilisers)	risperidone quetiapine	4 400	12 12	13 12	N/A	Weight
<b>Coppola 2011<sup>42</sup></b>	United states, India, Taiwan Schizophrenia Aged 18+	Any medical condition that could potentially alter the absorption, metabolism, or excretion of the study drug (e.g., Crohn's, liver, or renal disease)	paliperidone	1.5, 6	6	Weight: 58,64 FG: 55, 60	56	Weight, FG
<b>Correll 2016<sup>43</sup> (Correll 2015<sup>44</sup> NCT00905307 NCT01396421 NCT01393613)</b>	United States, Ukraine, Romania, Serbia, Latvia, Malaysia, Japan, Poland, South Korea, Canada Schizophrenia Aged 18-65	'A clinically significant medical condition'	brexpiprazole, aripiprazole  brexpiprazole	BREX: 0.25, 1, 2, 4 ARI: 15  BREX: 0.25, 1, 2, 4	6  6	41, 88, 90, 92, 50  87, 117, 359, 359	93  358	Weight, FG, TC, LDL, HDL, TG
<b>Cutler 2011<sup>45</sup></b>	United States Schizophrenia Aged 18-65	'Any significant diseases (e.g. renal and hepatic impairment, CVD, cancer)	quetiapine	400, 600, 800, 800	6	74, 61, 68, 62	66	Weight, FG, Insulin, TC, LDL, HDL, TG
<b>Chan 2007<sup>46</sup></b>	Taiwan Schizophrenia or schizoaffective disorder and were hospitalised with an acute relapse Aged 18-65	Pregnant, lactating, neurological disorder, any acute or unstable medical condition	Aripiprazole risperidone	15 6	4	38 24	N/A	Weight, FG
<b>Chan 2010<sup>47</sup></b>	Taiwan Schizophrenia neuroleptic-induced acute dystonia or parkinsonism research criteria Aged 18-65	Unstable major systemic diseases, neurological disorder that would influence the EPS assessment	Risperidone olanzapine	3.45 11.72	8	28 29	N/A	Weight
<b>Chen 2011<sup>48</sup></b>	Taiwan Schizophrenia with inadequate response to 1 FGA	None stated	Risperidone olanzapine	4.3 17.8	8	13 13	N/A	Weight



<b>Czobor 2002<sup>49</sup></b>	USA Schizophrenia or schizoaffective disorder Age not stated, likely 18+	None stated	Clozapine Olanzapine Risperidone haloperidol	401.6 19.6 7.9 18.9	14	38 38 39 36	N/A	Weight, BMI
<b>Davidson 2007<sup>50</sup></b>	North America, Canada, Eastern Europe, Asia, Israel, Mexico, South Africa Schizophrenia Aged 18+	'a medical condition that could affect absorption, metabolism or excretion of the study drug'	olanzapine, paliperidone	OLA: 10 PAL: 3, 15, 9	6	88, 70, 78, 82	47	Weight, BMI, FG, Insulin, TC, LDL, HDL, TG
<b>Del Valle 2006<sup>51</sup></b>	Not specifically stated, likely USA Schizophrenia or schizoaffective disorder Aged 18+	Abnormal laboratory findings, abnormal ECG, evidence of T1DM	Ziprasidone  olanzapine	129.9  11.3	6	TG (76) HDL (74) LDL (70) TC (76) TG (78) HDL (76) LDL (64) TC (78)	N/A	TG, HDL, LDL, TC
<b>Downing 2014<sup>52</sup></b>	Not specifically stated Schizophrenia Aged 18-65	Not specified	risperidone	4	6	96	172	Weight, BMI
<b>Durgam 2014<sup>53</sup></b>	United States, India, Russia, Ukraine, Malaysia Schizophrenia Aged 18-60	'Typical...me dical/physic al exclusions were applied'	cariprazine, risperidone	CAR: 4.5, 1.5, 3 RIS: 4	6	147, 145, 146, 140	151	Weight, FG, TC, LDL, HDL, TG
<b>Durgam 2015<sup>54</sup></b>	United States, Romania, Russia, Ukraine Schizophrenia Aged 18-60	'BMI <18 or >40'	aripiprazole, cariprazine	ARI: 10 CAR: 6, 3	6	152, 157, 155	153	Weight, FG, TC, LDL, HDL, TG
<b>Durgam 2016<sup>55</sup></b>	United States Schizophrenia Aged 18-65	Uncontrolle d medical illness BMI<18 or >40	cariprazine	3.83, 8.7	6	127, 133	129	Weight, FG, TC, LDL, HDL, TG
<b>Earley 2017<sup>56</sup> (Durgam 2014<sup>53</sup>; 2015<sup>54</sup>; 2016<sup>55</sup> and Kane 2015<sup>57</sup>)</b>	United States, India, Russia, Ukraine, Malaysia Schizophrenia Aged 18-65	Uncontrolle d medical illness BMI<18 or >40	cariprazine risperidone aripiprazole	CAR: 2.25, 5.25 10.5 RIS: 4 ARI: 10	6	539, 575, 203, 140, 152	584	Weight, FG, TC, LDL, HDL, TG
<b>Fu 2014<sup>58</sup></b>	Not specifically stated, likely USA Schizophrenia Aged not stated but likely 18+	None stated	Paliperidone Risperidone	11.9 4.7	13	104 99	N/A	Weight
<b>Gattaz 2004<sup>59</sup></b>	Germany Schizophrenia Aged 18+	None stated	Olanzapine flupenthixol	15 10	4	15 13	N/A	Weight
<b>Gopal 2010<sup>60</sup></b>	United States, Malaysia, the Republic of Korea,	Required BMI >17 'In general good health'	Paliperidone	3.43 6.86 10.29	13	47 53 12	51	Weight

	Taiwan, and Ukraine Age 18+							
<b>Grootens 2011<sup>61</sup> FEP</b>	Netherlands and Belgium Schizophrenia schizoaffective disorder, or schizophreniform disorder Aged 18-40	Epilepsy, organic mental disease, history of psychosurgery, significant medical illness, abnormal laboratory values, ECG abnormalities, use of medication prolonging QTc, pregnant, breast-feeding.	Olanzapine ziprasidone	14 104	8	30 31	N/A	Weight, FG, TG, TC
<b>Hardy 2011<sup>62</sup></b>	USA Schizophrenia or schizoaffective disorder Aged 18-65	BMI >40, DM, fasting hypertriglyceridaemia, use of medications known to affect insulin	Olanzapine risperidone	12.9 4.3	12	50 46	N/A	Weight, FG, Insulin, TG, HDL, LDL, TC
<b>Hatta 2009<sup>63</sup></b>	Japan Schizophrenia, acute schizophrenia-like psychotic disorder, or schizoaffective disorder Aged 18-64	Liver or renal dysfunction, heart or respiratory failure, DM, pregnant	Risperidone Olanzapine Quetiapine Aripiprazole	7.2 17.4 579 23.6	8	20 17 20 21	N/A	Weight, FG, TG, TC
<b>Higuchi 2019<sup>64</sup></b>	Japan, South Korea, Malaysia, Taiwan	Not specified	Lurasidone	40, 80	6	106, 116	110	Weight, BMI, FG, TC, LDL, TG
<b>Hwang 2001<sup>65</sup></b>	Taiwan Schizophrenia Aged 16-65	Hypersensitivity to study medications, neurological diseases, abnormal EEG, severe medical disease, pregnant, lactating	Zotepine Haloperidol	150 9	6	25 28	N/A	Weight
<b>Hwang 2003<sup>66</sup></b>	Taiwan Schizophrenia Aged 18-65	Hypersensitivity to study medications, neurological diseases, severe medical diseases	Amisulpride Risperidone	630 6.88	6	22 25	N/A	Weight
<b>Ishigooka 2018<sup>67</sup></b>	Japan Schizophrenia Aged 18-65	Patients with concurrent diabetes or	brexpiprazole	1, 2, 4	6	72, 81, 68	70	FG, TC, LDL, HDL, TG

		history of diabetes were also excluded.						
<b>Jeste 2003<sup>68</sup></b>	USA, Israel, Poland, Norway, Netherlands, Austria Schizophrenia or schizoaffective disorder Aged 60+	Major neurological disorder, any acute, unstable, significant, or untreated medical illness, any disease that could impair absorption, excretion, or metabolism of trial medication, history of NMS, QTc >500	risperidone olanzapine	2 10	8	63 71	N/A	Weight, BMI
<b>Kahn 2007<sup>69</sup></b>	Bulgaria, Greece, India, Indonesia, the Philippines, Russia, Romania, South Africa Schizophrenia Aged 18-65	Not specified	quetiapine	400, 400, 600, 800	6	96, 83, 92, 90	85	Weight, FG, Insulin, TC, LDL, HDL, TG
<b>Kane 2007<sup>70</sup></b>	Europe and India Schizophrenia Aged 18+	Not specified	olanzapine, paliperidone	OLA: 10 PAL: 9, 6, 12	6	90, 86, 80, 101	58	Weight, BMI, FG, Insulin, TC, LDL, HDL
<b>Kane 2008<sup>71</sup></b>	Worldwide (not specifically stated) Schizophrenia or schizoaffective disorder Aged 18-65	Recent significant physical illness, a clinically significant abnormal laboratory finding, axis 1 disorder	iloperidone haloperidol	11.8 13.2	6	1231 403	N/A	Weight, FG, TG, TC
<b>Kane 2010<sup>72</sup></b>	United States, Russia, Romania, Canada Schizophrenia Aged 18+	'A clinically significant medical condition or abnormal laboratory or physical examination findings'	asenapine, haloperidol	ASN: 10, 20 HAL: 8	6	68, 70, 65	69	Weight
<b>Kane 2011<sup>73</sup></b>	USA and Canada Schizophrenia and had failed 1 adequate antipsychotic treatment in the previous 6 months Aged 18-55	QTc >500, significant somatic of medical disorder requiring frequent changes in medication, previous psychosurgery, Neurological abnormalities, clinically	sertindole risperidone	18.1 9	12	116 60	n/a	Weight, FG, TG, TC

		significant laboratory finding						
<b>Kane 2014<sup>74</sup> NCT01663532</b>	United States, Croatia, Latvia Schizophrenia Aged 18-65	Not specified	aripiprazole	14.3	12	108	85	Weight, FG, TC, LDL, HDL, TG
<b>Kelly 2008<sup>75</sup></b>	Not specified Adults	Not specified	Olanzapine Risperidone	5-20 2-6	8	135 146	N/A	BMI, TC, LDL, TG
<b>Kinon 2011<sup>76</sup></b>	Site not specified Schizophrenia Aged 18-65	Not specified	olanzapine	15	4	62	122	Weight
<b>Kinoshita 2016<sup>77</sup></b>	Japan, Korea, Taiwan Schizophrenia Aged 20-65	BMI <16.0 or >35.0	asenapine	10, 20	6	114, 109	80	Weight, FG, FI,
<b>Kramer 2010<sup>78</sup></b>	USA, Russia, Bulgaria, Poland, Ukraine, and India Schizophrenia Aged 18-65	medical conditions that could potentially alter the absorption, metabolism, or excretion of the study medication; relevant history of significant or unstable medical illness (other than schizophrenia)	paliperidone	7.43, 3.71	9.14	51, 47	27	Weight, BMI
<b>Krakowski 2009<sup>79</sup></b>	USA Schizophrenia and schizoaffective disorder Age not stated, likely 18+	Substantial medical illness	Clozapine Olanzapine haloperidol	200-800 10-30 10-30	12	34 31 28	N/A	Weight, FG, TG, TC
<b>Landbloom 2017<sup>80</sup> NCT01617187</b>	United States, Bulgaria, Romania, Russia, Croatia Schizophrenia Aged 18+	Patients with uncontrolled, unstable, clinically significant medical conditions... body mass index <18 or >40.0 kg/m <sup>2</sup>	asenapine, olanzapine	ASN: 5, 10 OLA: 15	6	52, 67, 35	60	FG, insulin, TC, TG
<b>Lauriello 2008<sup>81</sup></b>	United States, Russia, Croatia Schizophrenia Aged 18-75	Unstable medical conditions	olanzapine	15, 21.43, 14.4	8	72, 67, 72	56	Weight, FG, TC, LDL, HDL, TG
<b>Lasser 2004<sup>82</sup></b>	Not specifically stated, likely USA Schizophrenia or schizoaffective disorder Aged 18+	None stated	Olanzapine (smokers) Risperidone (smokers) Olanzapine (non-smoker) Risperidone (non-smoker)	Not stated	8	109 102 90 74	N/A	Weight, BMI

<b>Lawson 2009<sup>83</sup></b>	USA Schizophrenia or schizoaffective disorder Aged 18+	None stated	ziprasidone	105	6	637	260	Weight, TG, TC
<b>Li 2014<sup>84</sup></b>	China Schizophrenia Aged 18-65	Pregnant, lactating, neurological disorder, severe head trauma, unstable medical condition, clinically significant abnormal vital signs or laboratory values	Risperidone aripiprazole	4.1 23	6	139 115	N/A	Weight
<b>Lin 2013<sup>85</sup></b>	Taiwan Schizophrenia , on clozapine for at least 6 months Aged 20-65	Significant medical illness, ECG or clinically significant lab abnormalities	Zotepine clozapine	397.1 377.1	12	28 24	N/A	Weight, TG, FG
<b>Lieberman 2003<sup>86</sup></b>	North America and Western Europe schizophrenia , schizophreniform disorder or schizoaffective disorder Aged 16-40	Pregnant, breast feeding, serious unstable medical illness	olanzapine haloperidol	12.5 11	12	89 71	N/A	Weight, BMI, TC, FG
<b>Lieberman 2016<sup>87</sup></b>	United States Schizophrenia Aged 18-55	Diagnosis of various medical conditions	risperidone	4	4	63	61	Weight, FG, insulin, TC, TG
<b>Lindenmayer 2003<sup>88</sup></b>	USA Schizophrenia and schizoaffective disorder Age not stated, likely 18+	Substantial medical illness	Clozapine haloperidol olanzapine risperidone	443.7 20 20.1 8.5	8	28 25 26 22	N/A	FG, TC
<b>Lindenmayer 2008<sup>89</sup> 50771L/0041</b>	United States and Canada Schizophrenia Aged 18-65	'any clinically relevant other diseases (such as renal or hepatic impairment, significant coronary artery disease)'	quetiapine	QUET: 300, 600, 800, 300, 600	6	35, 40, 41, 41, 34	29	Weight, FG, TC, LDL, HDL, TG
<b>Litman 2014<sup>90</sup></b>	United States Schizophrenia Aged 18-65	Not specified	olanzapine	15	4	18	33	Weight

<b>Litman 2016</b> <sup>91</sup>	United States Schizophrenia Aged 18-65	Participants were 'medically stable'	risperidone	4	4	26	40	Weight
<b>Loebel 2013</b> <sup>92</sup>	United States, Russia, India, Ukraine, Romania, Colombia Schizophrenia Aged 18-75	Not specified	lurasidone, quetiapine	LUR: 160, 80 QUET: 600	6	93, 89, 97	74	Weight, BMI, FG, Insulin, TC, LDL, HDL, TG
<b>Loebel 2016</b> <sup>93</sup>	United States Schizophrenia Aged 18-75	Not specified	lurasidone	20, 80, 160	6	74, 45, 36	70	Weight, FG, TC, LDL, TG Symptoms
<b>Marder 2007</b> <sup>94</sup>	United States Schizophrenia Aged 18+	medical conditions affecting absorption, metabolism, or excretion of the study drug	paliperidone olanzapine	PAL: 6, 12 OLA: 10	6	51, 54, 50	37	Weight, FG, Insulin, TC, LDL, HDL, TG
<b>Martin 2002</b> <sup>95</sup>	Belgium, Switzerland, Denmark, France, Great Britain, Czech Republic, Tunisia, Hungary, Morocco, and Portugal Schizophrenia or schizophreno form disorder Aged 18-65	Pregnant or lactating	olanzapine amisulpride	12 489	8	146 150	N/A	Weight, BMI
<b>Meltzer 2008</b> <sup>96</sup> NCT00077714 NCT00083668 NCT00078039	'23 different countries on 5 continents' Schizophrenia Aged 18+	Not specified	paliperidone olanzapine	PAL: 3,6,9,12,15 OLA: 10	6	70, 131, 164, 155, 82, 228	142	Weight
<b>Meltzer 2011</b> <sup>97</sup>	United States, Colombia, Lithuania, Colombia, Asia, the Philippines Schizophrenia Aged 18-65	Not specified	lurasidone, olanzapine	LUR: 40, 120 OLA: 15	6	77, 66, 84	71	Weight, BMI, FG, Insulin, HOMA-IR, TC, LDL, HDL, TG
<b>Meulien 2010</b> <sup>98</sup>	Eastern Europe, Asia, India, South Africa, Canada Schizophrenia Aged 18-65	'evidence of other clinically relevant conditions (e.g. renal or hepatic impairment, significant coronary artery disease)'	quetiapine	QUE: 591.48, 530.92	6	555, 215	225	Weight, FG, Insulin, TC, LDL, HDL, TG
<b>Nasrallah 2010</b> <sup>99</sup>	Schizophrenia Age not specified (mean 41) United States, South Africa, Bulgaria,	BMI <15, abnormal screening bloods	paliperidone	1.71, 3.43, 6.86	13	70, 70, 75	48	Weight, BMI

	Romania, Russia, Bulgaria							
<b>Nasrallah 2013<sup>100</sup></b>	United States, Russia, India, Ukraine, Romania, Malaysia, and France Schizophrenia Aged 18-75	acute or unstable medical condition	lurasidone	80, 120, 40	6	86, 85, 84	73	Weight, BMI
<b>Nasrallah 2016<sup>101</sup></b>	'8 countries' Schizophrenia Aged 18-70	(BMI) of 18.5 to 40 kg/m <sup>2</sup>	aripiprazole	15,75, 31.5	12	207,208	207	Weight, FG, TC, LDL, HDL, TG
<b>Nasser 2016<sup>102</sup></b>	Sites not specified Schizophrenia Aged 18-55	Not specified	risperidone	4.2, 2.1	8.14	85, 90	84	Weight
<b>Newcomer 2008<sup>103,104</sup></b>	International study with countries not specified, likely USA Schizophrenia or schizoaffective disorder must have received olanzapine monotherapy at a dose of 10 to 20 mg/day for 1 to 24 months immediately prior to screening Aged 18-65	Pregnant, breast feeding, BMI <27, DM, significant neurological disease, clinically significant vital sign, electrocardiogram (ECG), or laboratory test abnormalities	olanzapine aripiprazole	15.9 16	16	63 56	n/a	Weight, FG, Insulin, TG, HDL, LDL, TC
<b>Ogasa 2013<sup>105</sup></b>	United States Schizophrenia Aged 18-64	excluded if they had an acute or unstable medical condition	lurasidone	120, 40	6	20, 16	15	Weight
<b>Patil 2007<sup>106</sup></b>	Russia Schizophrenia Aged 18-65	Not specified	Olanzapine	15	4	27	26	Weight
<b>Patel 2009<sup>107</sup></b>	USA and Canada schizophrenia, schizophreniform, or schizoaffective disorder Aged 16-40	Pregnant, breast feeding, history of mental retardation	olanzapine quetiapine risperidone	2.5-20 100-800 0.5-4	12	133 134 144	N/A	Weight, BMI, FG, HDL
<b>Potkin 2003<sup>108</sup></b>	United States Schizophrenia and schizoaffective disorder Aged 18-65	'Any acute or unstable medical condition'	aripiprazole risperidone	ARI: 20, 30 RIS: 6	4	61, 67, 62	52	Weight
<b>Porkin 2006<sup>109</sup></b>	United States, India, Romania Schizophrenia Aged 18-64	Evidence of a clinically significant or unstable disease	risperidone quetiapine	RIS: 5 QUET: 700	2	139, 132	60	Weight

<b>Potkin 2011</b> <sup>110</sup>	USA Schizophrenia or schizoaffective disorder Aged 18-70	Pregnant, breast feeding, clinically significant medical illness, abnormal laboratory or ECG parameters	lurasidone ziprasidone	120 160	3	104 106	N/A	Weight, TG, TC
<b>Potkin 2015</b> <sup>111</sup>	United States Schizophrenia Aged 18-64	Clinically significant cardiovascular disease	lurasidone haloperidol	LUR: 20, 40, 80 HAL: 10	6	27, 28, 31, 29	36	Weight
<b>Riedel 2005</b> <sup>112</sup>	Not stated, likely Germany Schizophrenia Age not stated, likely 18+	Pregnant, lactating, significant medical history, laboratory, ECG, or EEG abnormalities	quetiapine risperidone	589.7 4.9	12	13 12	N/A	Weight
<b>Riedel 2007</b> <sup>113</sup>	Not stated, likely Germany Schizophrenia Aged 18-65	Significant medical history, ECG or EEG abnormalities, abnormal laboratory tests, pregnant, lactating	quetiapine olanzapine	586.86 15.82	8	16 17	N/A	Weight
<b>Robinson 2015</b> <sup>114</sup>	USA and Canada schizophrenia , schizophreniform, schizoaffective disorder, or psychotic disorder Not Otherwise Specified Aged 15-40	Serious neurological or endocrine disorder or medical condition/treatment known to affect the brain; medical conditions requiring treatment with a medication with psychotropic effects, DM, metabolic syndrome	aripiprazole risperidone	14.8 3.2	12	102 96	N/A	Weight
<b>Saddichha 2007</b> <sup>115</sup>	India Schizophrenia Likely 18+	History of severe psychical illness, history of hypertension or DM or family history of either	olanzapine risperidone haloperidol		6	29 22 15	N/A	Weight, BMI
<b>Schmidt 2012</b> <sup>116</sup>	Bulgaria, Estonia, Korea, Lithuania, Malaysia, Romania,	BMI<40, significant or unstable disease, NMS,	olanzapine	15	6	71	49	Weight, BMI



	Russia, South Africa, Taiwan, and Ukraine	Schizophrenia	Aged 18-65						
<b>Shen 2014<sup>117</sup></b>	United States, India	Not specified	Schizophrenia	olanzapine	15	6	71	71	Weight, FG, TC, LDL, HDL, TG
<b>Sliwa 2011<sup>118</sup></b>	Study sites not specified	Not specified	Schizophrenia	Paliperidone	3.43, 6, 7.71	13	24, 31, 29	22	Weight
<b>Tollefson 1997<sup>119</sup></b>	USA and Europe	Not stated	schizophrenia, schizophreniform disorder, or schizoaffective disorder	olanzapine haloperidol	13.2 11.8	6	888 309	N/A	Weight
<b>Tzimos 2008<sup>120</sup></b>	Study sites not specified	Not specified	Schizophrenia	paliperidone	7.5	6	64	26	Weight
<b>Vanelle 2006<sup>121</sup></b>	France, Italy, Tunisia	Pregnant, lactating, severe somatic disease, Parkinson's disease, a history of seizures, prostatic hypertrophy, paralytic ileus, phaeochromocytoma, < 55 bpm, known hyperkalemia, congenital prolongation of the QT interval and known risk for narrow-angle glaucoma.	Schizophrenia and major or minor depressive episode	olanzapine amisulpride	11.4 471	8	36 35	N/A	Weight, FG, TG, HDL, TC
<b>Wang 2006<sup>122</sup></b>	USA	Unstable metabolic, hematologic, cardiovascular, hepatic or renal function were excluded from the study	Schizophrenia spectrum disorder and stable on conventional antipsychotic medication for at least 2 years	risperidone olanzapine	5.3 13.8	7	14 13	N/A	Weight
<b>Wetzel 1998<sup>123</sup></b>	Germany	Axis I disorder, Parkinson's disease,	Schizophrenia, paranoid type,	amisulpride flupenthixol	956 22.6	6	51 37	N/A	Weight

	or undifferentiated type Aged 18-65	epilepsy, narrow-angle glaucoma, prostate hypertrophy, urinary retention, severe hypotonia or arteriosclerosis, severe liver or kidney dysfunction, other serious somatic comorbid disorders, significant laboratory, ECG or EEG abnormality, pregnancy or lactation					
<b>Zhong 2006<sup>124</sup></b>	USA Schizophrenia Aged 18-6	Pregnant, lactating, psychotic disorder due to general medical condition, mental retardation	quetiapine risperidone	8	154 168	N/A	BMI

**eTable 3.** Cochrane risk of bias assessment (low, high, unclear risk of bias)

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data addressed	Selective reporting
Ascher-Svanum 2005 <sup>26</sup> Beasley 1996 <sup>31</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	High Risk
Azorin 2006 <sup>28</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk
Baymiller 2002 <sup>29</sup>	High risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk
Bhowmick 2010 <sup>30</sup>	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk
Beasley 1996 <sup>31</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Unclear risk
<b>Bossie, 2011<sup>32</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Breier 2005 <sup>33</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Buckley 2004 <sup>34</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Unclear risk
Cantillon 2017 <sup>35</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
<b>Canuso 2009<sup>36</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Canuso 2010a <sup>37</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
<b>Canuso 2010b<sup>38</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Canuso 2010 <sup>39</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Conley 2001 <sup>40</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Conley 2005 <sup>41</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Coppola 2011 <sup>42</sup>	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Correll 2016 <sup>43</sup> (Correll 2015 <sup>44</sup> NCT00905307 NCT01396421 NCT01393613)	Low risk	Unclear risk	Low risk	Low risk	Low risk	High risk
Cutler 2011 <sup>45</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Chan 2007 <sup>46</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Chan 2010 <sup>47</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk
Chen 2011 <sup>48</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Unclear risk
Czobor 2002 <sup>49</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Unclear risk
Lawson 2009 <sup>83</sup> Containing: Daniel 1999 <sup>125</sup> Keck 1998 <sup>126</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Unclear risk
Davidson 2007 <sup>50</sup>	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Del Valle 2006 <sup>51</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Downing 2014 <sup>52</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	High risk
Durgam 2014 <sup>53*</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Durgam 2015 <sup>54*</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Durgam 2016 <sup>55*</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Earley 2017 <sup>56</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Fu 2014 <sup>58</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Unclear risk
Gattaz 2004 <sup>59</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Gopal 2010 <sup>60</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Grootens 2011 <sup>61</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Hardy 2011 <sup>62</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Hatta 2009 <sup>63</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
<b>Higuchi 2019<sup>64</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Hwang 2001 <sup>65</sup>	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Hwang 2003 <sup>66</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
<b>Ishigooka 2018<sup>67</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Jeste 2003 <sup>68</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Kahn 2007 <sup>69</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Kane 2007 <sup>70</sup>	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk
Kane 2008 <sup>71</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Kane 2010 <sup>72</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	High risk
Kane 2011 <sup>73</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
<b>Kane 2014<sup>74</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Kelly 2008 <sup>75</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Kane 2015 <sup>57</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Kinon 2011 <sup>76</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
<b>Kinoshita 2016<sup>77</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Kramer 2010 <sup>78</sup>	Low risk	Low risk	Low risk	Low risk	Low risk	High risk
Krakowski 2009 <sup>79</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Landbloom 2017 <sup>80</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Lauriello 2008 <sup>81</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk

Lasser 2004 <sup>82</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk
Lawson 2009 <sup>83</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	High risk
Li 2014 <sup>84</sup>	Unclear risk	Low risk	Low risk	Low risk	Unclear risk	High risk
Lin 2003 <sup>85</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk
Lieberman 2003 <sup>86</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
<b>Lieberman 2016<sup>87</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Lindenmayer 2003 <sup>88</sup>	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk
Lindenmayer 2008 <sup>89</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
<b>Litman 2014<sup>90</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
<b>Litman 2016<sup>91</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
<b>Loebel 2013<sup>92</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
<b>Loebel 2016<sup>93</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
<b>Marder 2007<sup>94</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Martin 2002 <sup>95</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Unclear risk
Meltzer 2008 <sup>96</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
<b>Meltzer 2011<sup>97</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Meulien 2010 <sup>98</sup>	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Nasrallah 2010 <sup>99</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Nasrallah 2013 <sup>100</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	High risk
Nasrallah 2016 <sup>101</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	High risk
Nasser 2016 <sup>102</sup>	Low risk	Low risk	Low risk	Low risk	Low risk	High risk
Newcomer 2008 <sup>103,104</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Ogasa 2013 <sup>105</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	High risk
Patil 2007 <sup>106</sup>	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Patel 2009 <sup>107</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk
Potkin 2003 <sup>108</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	High risk
Porkin 2006 <sup>109</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	High risk
<b>Potkin 2011<sup>110</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Potkin 2015 <sup>111</sup>	Low risk	Low risk	Low risk	Low risk	Low risk	High risk
Riedel 2005 <sup>112</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Riedel 2007 <sup>113</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Robinson 2015 <sup>114</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Saddichha 2007 <sup>115</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
<b>Schmidt 2012<sup>116</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
<b>Shen 2014<sup>117</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Sliwa 2011 <sup>118</sup>	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk
Pandina 2010 <sup>127</sup>						
Tollefson 1997 <sup>119</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Tzimos 2008 <sup>120</sup>	Low risk	Unclear risk	Low risk	Low risk	Low risk	High risk
<b>Vanelle 2006<sup>121</sup></b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>	<b>Low risk</b>
Wang 2006 <sup>122</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Wetzel 1998 <sup>123</sup>	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Unclear risk
Zhong 2006 <sup>124</sup>	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Unclear risk

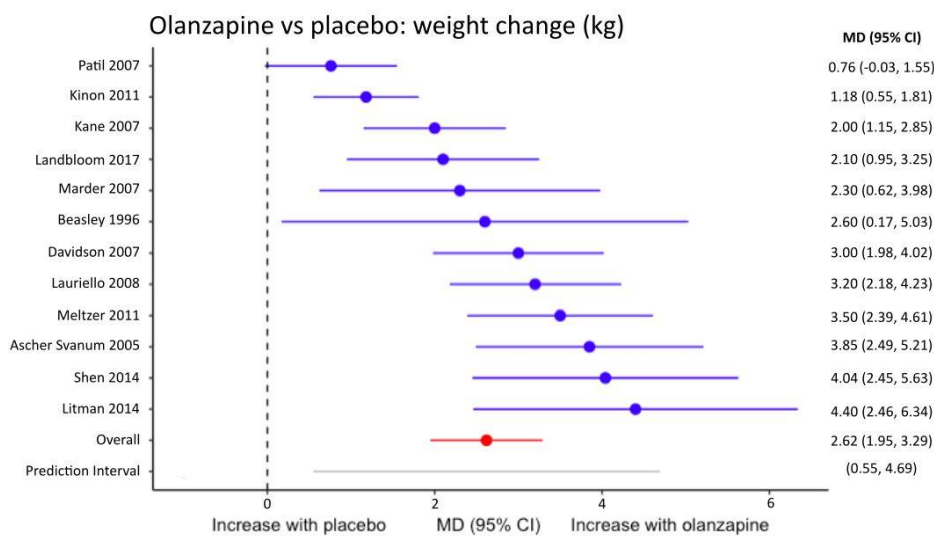
**eTable 4. Baseline parameters across treatment-comparisons**

Treatment Comparison	Mean Age (number of studies)	Mean % male (number of studies)	Mean % non-Caucasian (number of studies)	Mean Baseline body weight (number of studies)
amisulpride:flupenthixol	34.00 (1)	56.00 (1)	.	71.10 (1)
amisulpride:olanzapine	34.60 (3)	59.12 (2)	.	73.00 (2)
amisulpride:risp_pali	35.20 (2)	50.00 (1)	.	64.50 (1)
aripiprazole:brexpiprazole	39.42 (1)	63.96 (1)	35.40 (1)	.
aripiprazole:cariprazine	38.02 (1)	70.23 (1)	55.14 (1)	76.64 (1)
aripiprazole:olanzapine	39.27 (3)	52.77 (3)	30.00 (2)	81.47 (2)
aripiprazole:placebo	38.91 (4)	72.77 (4)	57.51 (4)	81.47 (2)
aripiprazole:risp_pali	34.56 (6)	60.46 (6)	51.79 (4)	71.73 (4)
asenapine:placebo	41.41 (1)	48.07 (1)	.	63.25 (1)
brexpiprazole:placebo	41.85 (2)	55.73 (2)	35.40 (1)	.
cariprazine:placebo	38.03 (1)	70.23 (1)	55.14 (1)	76.64 (1)
cariprazine:risp_pali	38.03 (1)	70.23 (1)	55.14 (1)	76.64 (1)
clozapine:haloperidol	36.22 (3)	78.02 (3)	54.23 (2)	84.75 (2)
clozapine:olanzapine	37.46 (2)	83.78 (2)	82.06 (1)	87.60 (1)
clozapine:risp_pali	40.95 (1)	84.75 (1)	.	.
flupenthixol:olanzapine	32.40 (1)	48.00 (2)	.	.
fluphenazine:quetiapine	44.73 (1)	79.00 (1)	52.67 (1)	88.53 (1)
fluphenazine:risp_pali	44.73 (1)	79.00 (1)	52.67 (1)	88.53 (1)
haloperidol:lurasidone	41.23 (1)	73.83 (1)	52.25 (1)	89.04 (1)
haloperidol:olanzapine	32.89 (3)	83.02 (3)	64.54 (2)	81.60 (2)
haloperidol:placebo	38.67 (1)	72.67 (1)	38.33 (1)	77.25 (1)
haloperidol:quetiapine	39.80 (1)	64.45 (1)	.	.
haloperidol:risp_pali	40.96 (1)	84.75 (1)	.	.
haloperidol:ziprasidone	38.67 (1)	72.67 (1)	38.33 (1)	77.25 (1)
haloperidol:zotepine	34.3 (1)	54.00 (1)	.	61.5 (1)
lurasidone:olanzapine	37.63 (1)	78.00 (1)	64.00 (1)	.
lurasidone:placebo	39.56 (6)	69.01 (6)	57.46 (6)	72.44 (3)
lurasidone:ziprasidone	42.90 (1)	70.45 (1)	75.5 (1)	.
olanzapine:placebo	38.47 (7)	74.98 (7)	41.76 (7)	80.39 (5)
olanzapine:quetiapine	33.61 (3)	60.83 (3)	27.33 (2)	.
olanzapine:risp_pali	38.94 (10)	60.97 (10)	57.37 (8)	81.13 (3)
olanzapine:ziprasidone	34.98 (3)	64.25 (1)	56.35 (1)	80.91 (2)
placebo:quetiapine	39.69 (4)	65.64 (4)	53.60 (4)	78.59 (2)
placebo:risp_pali	38.04 (16)	65.37 (16)	50.81 (13)	78.81 (13)
placebo:sertindole	36.23 (1)	.	.	.
placebo:ziprasidone	38.02 (2)	74.83 (2)	31.33 (1)	75.43 (1)
quetiapine:risp_pali	36.84 (6)	66.44 (6)	44.90 (5)	87.55 (2)
risp_pali:sertindole	36.47 (3)	67.22 (3)	29.58 (2)	73.49 (3)
ziprasidone:haloperidol	38.67 (1)	72.67 (1)	38.33 (1)	77.25 (1)

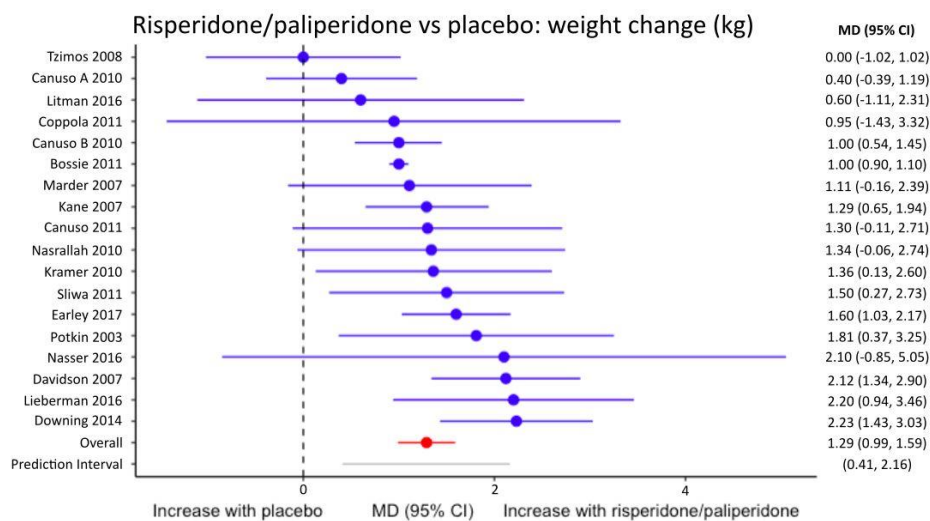
### eAppendix 3. Pairwise meta-analyses

There were 3 pairwise comparisons for antipsychotic-induced weight gain with  $\geq 10$  studies allowing meta-analysis: olanzapine vs. placebo, risperidone/paliperidone vs. placebo, and olanzapine vs. risperidone/paliperidone (forest plots recording in eFigures 2-4). Olanzapine was associated increased weight gain compared with placebo (MD: +2.62kg 95%CI: 1.95-3.29,  $p < 0.0001$ ), risperidone/paliperidone with increased weight gain compared with placebo (MD: +1.29kg 95%CI: 0.99-1.59,  $p < 0.0001$ ), and olanzapine with increased weight gain compared with risperidone/paliperidone (MD: +1.29kg 95% CI: 0.99-1.59,  $p < 0.0001$ ).

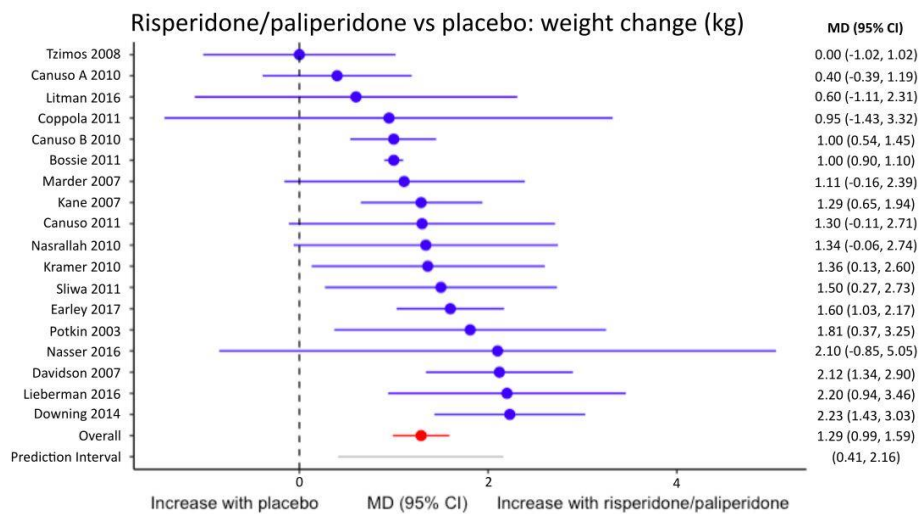
**eFigure 5. Pairwise meta-analysis forest plot: placebo vs olanzapine**



**eFigure 6. Pairwise meta-analysis forest plot: placebo vs risperidone/paliperidone**



**eFigure 7. Pairwise meta-analysis forest plot: risperidone/paliperidone versus olanzapine**



Heterogeneity was medium to large ( $I^2$  values: 59.85-76.51%), with  $\tau$  ranging from 0.42-1.00kg (see below). Visual inspection of funnel plots (eFigures 8-10) suggested symmetry for comparisons except for olanzapine vs risperidone/paliperidone (where an absence in studies reporting increases in weight with risperidone/paliperidone compared with olanzapine was noted). By contrast, Egger's regression tests only demonstrated significance for the comparison of olanzapine vs placebo ( $p=0.01$ ).

**Pairwise meta-analysis: Assessment of heterogeneity**

**Tau**

Placebo vs olanzapine: 1.00kg

Placebo vs risperidone/paliperidone: 0.42kg

Risperidone/paliperidone vs olanzapine: 0.54kg

**$I^2$  statistic**

Placebo vs olanzapine: 76.51%

Placebo vs risperidone/paliperidone: 59.85%

Risperidone/paliperidone vs olanzapine: 64.41%

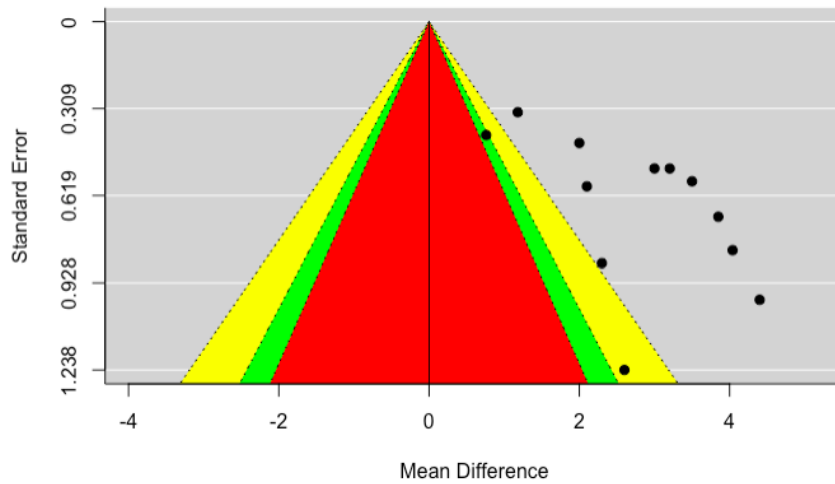
**Pairwise meta-analysis: Egger's Regression test**

Placebo vs olanzapine:  $z = 2.50$ ,  $p = 0.01$

Placebo vs risperidone/paliperidone:  $z = 0.49$ ,  $p = 0.63$

Risperidone/paliperidone vs olanzapine:  $-1.55$ ,  $p = 0.12$

**eFigure 8. Pairwise meta-analysis contour-enhanced funnel plot: placebo vs olanzapine**



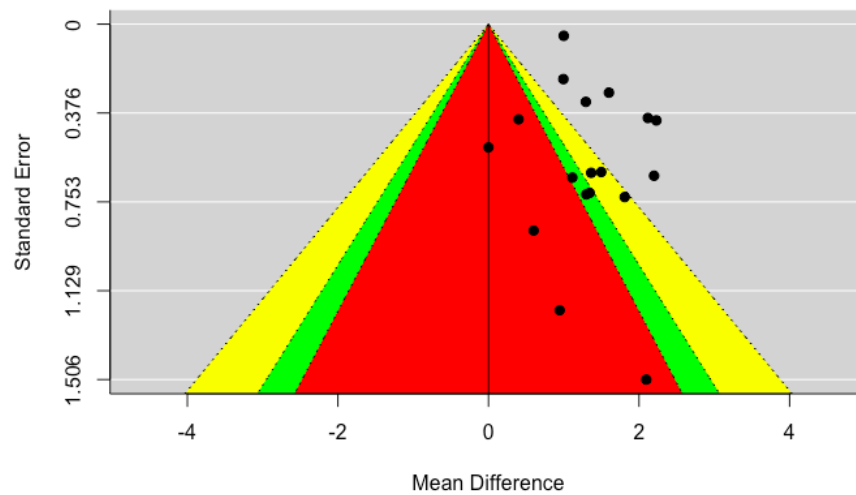
**Key:** Red:  $0.10 < p \leq 1.00$

Green:  $0.05 < p \leq 0.10$

Yellow:  $0.01 < p \leq 0.05$

Grey:  $0.00 < p \leq 0.01$

**eFigure 9. Pairwise meta-analysis contour-enhanced funnel plot: placebo vs risperidone/paliperidone**



**Key:**

Red:  $0.10 < p \leq 1.00$

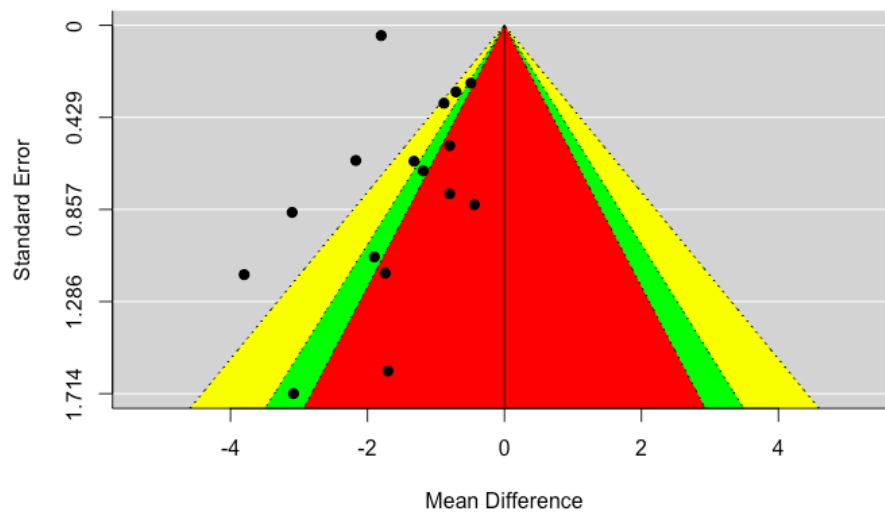
Green:  $0.05 < p \leq 0.10$

Yellow:  $0.01 < p \leq 0.05$

Grey:  $0.00 < p \leq 0.01$



**eFigure 10. Pairwise meta-analysis contour-enhanced funnel plot: risperidone/paliperidone versus olanzapine**



**Key:**

Red:  $0.10 < p \leq 1.00$

Green:  $0.05 < p \leq 0.10$

Yellow:  $0.01 < p \leq 0.05$

Grey:  $0.00 < p \leq 0.01$



**eTable 6.** League table for changes in body mass index (BMI, kg/m<sup>2</sup>) associated with antipsychotic drug treatment. For interpretation, a number larger than zero favours the column-defining treatment of a cell, i.e. this treatment leads to an increase in BMI. Values depicted are mean differences with associated 95% confidence intervals.

<b>Aripiprazole</b>									
-1.24 (-2.21 to -0.28)	<b>Clozapine</b>								
0.03 (-0.70 to 0.77)	1.28 (0.50 to 2.06)	<b>Haloperidol</b>							
-0.46 (-1.08 to 0.15)	0.78 (0.01 to 1.55)	-0.50 (-0.95 to -0.05)	<b>Lurasidone</b>						
-1.29 (-1.91 to -0.67)	-0.05 (-0.80 to 0.70)	-1.33 (-1.73 to -0.93)	-0.83 (-1.05 to -0.61)	<b>Olanzapine</b>					
-0.22 (-0.81 to 0.37)	1.02 (0.27 to 1.78)	-0.25 (-0.68 to 0.17)	0.24 (0.08 to 0.41)	1.07 (0.90 to 1.25)	<b>Placebo</b>				
-0.92 (-1.57 to -0.27)	0.33 (-0.46 to 1.12)	-0.95 (-1.44 to -0.47)	-0.45 (-0.72 to -0.19)	0.38 (0.09 to 0.66)	-0.70 (-0.96 to -0.44)	<b>Quetiapine</b>			
-0.78 (-1.39 to -0.17)	0.46 (-0.29 to 1.21)	-0.82 (-1.23 to -0.41)	-0.32 (-0.52 to -0.12)	0.51 (0.37 to 0.65)	-0.56 (-0.70 to -0.42)	0.13 (-0.13 to 0.40)	<b>Risp &amp; Pali</b>		
-0.98 (-1.78 to -0.19)	0.26 (-0.64 to 1.16)	-1.02 (-1.67 to -0.37)	-0.52 (-1.06 to 0.02)	0.31 (-0.21 to 0.83)	-0.76 (-1.29 to -0.24)	-0.07 (-0.63 to 0.50)	-0.20 (-0.70 to 0.30)	<b>Sertindole</b>	



**eTable 8.** League table for changes in Low Density Lipoprotein (LDL) cholesterol associated with antipsychotic drug treatment (mmol/L). For interpretation, a number larger than zero favours the column-defining treatment of a cell, i.e. this treatment leads to an increase in LDL cholesterol. Values depicted are mean differences with associated 95% confidence intervals.

<b>Aripiprazole</b>										
-0.04 (-0.13 to 0.05)	<b>Brexpiprazole</b>									
0.13 (0.03 to 0.22)	0.16 (0.06 to 0.26)	<b>Cariprazine</b>								
0.05 (-0.06 to 0.16)	0.09 (-0.02 to 0.20)	-0.08 (-0.19 to 0.04)	<b>Lurasidone</b>							
-0.20 (-0.29 to -0.11)	-0.16 (-0.25 to -0.08)	-0.33 (-0.42 to -0.23)	-0.25 (-0.35 to -0.15)	<b>Olanzapine</b>						
0.00 (-0.07 to 0.07)	0.04 (-0.03 to 0.10)	-0.13 (-0.21 to -0.05)	-0.05 (-0.14 to 0.04)	0.20 (0.14 to 0.26)	<b>Placebo</b>					
-0.17 (-0.30 to -0.04)	-0.13 (-0.26 to -0.01)	-0.30 (-0.43 to -0.16)	-0.22 (-0.36 to -0.08)	0.03 (-0.10 to 0.15)	-0.17 (-0.28 to -0.06)	<b>Quetiapine</b>				
-0.01 (-0.10 to 0.08)	0.03 (-0.06 to 0.11)	-0.14 (-0.23 to -0.04)	-0.06 (-0.16 to 0.04)	0.19 (0.14 to 0.24)	-0.01 (-0.07 to 0.05)	0.16 (0.04 to 0.29)	<b>Risp / Pali</b>			
0.12 (-0.04 to 0.28)	0.16 (0.00 to 0.32)	-0.00 (-0.17 to 0.16)	0.07 (-0.10 to 0.24)	0.32 (0.18 to 0.46)	0.12 (-0.03 to 0.27)	0.29 (0.10 to 0.48)	0.13 (-0.02 to 0.28)	<b>Ziprasidone</b>		

**eFigure 9.** League table for changes in High Density Lipoprotein (HDL) cholesterol associated with antipsychotic drug treatment (mmol/L). For interpretation, a number larger than zero favours the column-defining treatment of a cell, i.e. this treatment leads to an increase in HDL cholesterol. Values depicted are mean differences with associated 95% confidence intervals.

<b>Amisulpride</b>										
-0.14 (-0.37 to 0.10)	<b>Aripiprazole</b>									
-0.15 (-0.39 to 0.09)	-0.01 (-0.07 to 0.05)	<b>Brexpiprazole</b>								
-0.12 (-0.36 to 0.13)	0.02 (-0.04 to 0.08)	0.03 (-0.04 to 0.11)	<b>Cariprazine</b>							
-0.12 (-0.36 to 0.12)	0.02 (-0.06 to 0.10)	0.03 (-0.06 to 0.12)	-0.00 (-0.09 to 0.09)	<b>Lurasidone</b>						
-0.09 (-0.32 to 0.14)	0.05 (0.00 to 0.10)	0.06 (0.00 to 0.12)	0.03 (-0.04 to 0.09)	0.03 (-0.04 to 0.10)	<b>Olanzapine</b>					
-0.10 (-0.33 to 0.14)	0.04 (0.00 to 0.08)	0.05 (0.00 to 0.10)	0.02 (-0.04 to 0.08)	0.02 (-0.05 to 0.09)	-0.01 (-0.04 to 0.03)	<b>Placebo</b>				
-0.10 (-0.34 to 0.13)	0.03 (-0.03 to 0.09)	0.04 (-0.02 to 0.11)	0.01 (-0.06 to 0.08)	0.01 (-0.07 to 0.10)	-0.01 (-0.07 to 0.04)	-0.01 (-0.05 to 0.03)	<b>Quetiapine</b>			
-0.11 (-0.35 to 0.12)	0.03 (-0.02 to 0.07)	0.04 (-0.02 to 0.10)	0.01 (-0.05 to 0.07)	0.01 (-0.07 to 0.08)	-0.02 (-0.06 to 0.02)	-0.01 (-0.05 to 0.02)	-0.01 (-0.06 to 0.05)	<b>Risp / Pali</b>		
-0.14 (-0.39 to 0.10)	-0.01 (-0.09 to 0.07)	0.00 (-0.08 to 0.09)	-0.03 (-0.12 to 0.06)	-0.03 (-0.12 to 0.07)	-0.05 (-0.12 to 0.01)	-0.05 (-0.12 to 0.03)	-0.04 (-0.12 to 0.04)	-0.03 (-0.11 to 0.04)	<b>Ziprasidone</b>	





**eTable 12. P-score ranking: weight**

	P-score (random)
clozapine	0.9242
olanzapine	0.8921
zotepine	0.8773
sertindole	0.8249
iloperidone	0.6960
quetiapine	0.6831
risp/pali	0.5929
asenapine	0.5507
brexpiprazole	0.4552
flupenthixol	0.4118
fluphenazine	0.3968
amisulpride	0.3819
cariprazine	0.3819
lurasidone	0.3240
aripiprazole	0.2727
placebo	0.1462
ziprasidone	0.0977
haloperidol	0.0907

**eTable 13. P-score ranking: BMI**

	P-score (random)
olanzapine	0.9279
clozapine	0.8509
sertindole	0.7174
quetiapine	0.6829
risp/pali	0.5603
lurasidone	0.3708
placebo	0.2065
aripiprazole	0.1080
haloperidol	0.0752

**eTable 14. P-score ranking: total cholesterol**

	P-score (random)
clozapine	0.9738
olanzapine	0.9066
quetiapine	0.8242
amisulpride	0.6451
haloperidol	0.5906
risp/pali	0.5509
brexpiprazole	0.5165
aripiprazole	0.5063
placebo	0.3517
lurasidone	0.2723
sertindole	0.2560
ziprasidone	0.2519
iloperidone	0.1899
cariprazine	0.1641



**eTable 15. P-score ranking: LDL cholesterol**

	P-score (random)
olanzapine	0.9587
quetiapine	0.9121
brexpiprazole	0.6653
risp/pali	0.5388
aripiprazole	0.4836
placebo	0.4766
lurasidone	0.2735
ziprasidone	0.1173
cariprazine	0.0740

**eTable 16. P-score ranking: HDL cholesterol (reversed for clinical interpretation)**

	P-score (random)
amisulpride	0.8316
olanzapine	0.7642
placebo	0.7024
quetiapine	0.5900
risp/pali	0.5124
cariprazine	0.4678
lurasidone	0.4490
aripiprazole	0.2592
ziprasidone	0.2413
brexpiprazole	0.1821

**eTable 17. P-score ranking: triglycerides**

	P-score (random)
clozapine	0.9685
zotepine	0.9375
olanzapine	0.8309
quetiapine	0.7148
haloperidol	0.6317
iloperidone	0.6290
amisulpride	0.4189
risp/pali	0.3912
aripiprazole	0.3324
ziprasidone	0.3313
sertindole	0.2950
cariprazine	0.2811
lurasidone	0.2597
placebo	0.2523
brexpiprazole	0.2257

**eTable 18: P-score ranking: glucose**

	P-score (random)
clozapine	0.9680
zotepine	0.9375
iloperidone	0.7339
cariprazine	0.6961
olanzapine	0.6668
haloperidol	0.5907
aripiprazole	0.5477
quetiapine	0.4745
risp/pali	0.4557
ziprasidone	0.4198
brexpiprazole	0.4000

sertindole	0.3556
placebo	0.3068
asenapine	0.2234
amisulpride	0.1351
lurasidone	0.0883

**eTable 19. 'Hot spots' of inconsistency: weight**

Random effects model

- 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)

Treatment Comparison	k	prop	NMA	Direct	Indir	Diff	z	p-value
amisulpride:aripiprazole	0	0	0.3192	.	0.3192	.	.	.
amisulpride:asenapine	0	0	-0.5025	.	-0.5025	.	.	.
amisulpride:brexpiprazole	0	0	-0.2128	.	-0.2128	.	.	.
amisulpride:cariprazine	0	0	0.0032	.	0.0032	.	.	.
amisulpride:clozapine	0	0	-2.3510	.	-2.3510	.	.	.
amisulpride:flupenthixol	1	0.60	-0.0891	-1.2000	1.5633	-2.7633	-1.77	0.0771
amisulpride:fluphenazine	0	0	0.4994	.	0.4994	.	.	.
amisulpride:haloperidol	0	0	0.8967	.	0.8967	.	.	.
amisulpride:iloperidone	0	0	-1.1033	.	-1.1033	.	.	.
amisulpride:lurasidone	0	0	0.1800	.	0.1800	.	.	.
amisulpride:olanzapine	2	0.76	-2.0634	-1.6085	-3.5338	1.9252	1.91	0.0566
amisulpride:placebo	0	0	0.6626	.	0.6626	.	.	.
amisulpride:quetiapine	0	0	-0.9006	.	-0.9006	.	.	.
amisulpride:risp_pali	1	0.18	-0.6208	-1.5000	-0.4321	-1.0679	-0.90	0.3686
amisulpride:sertindole	0	0	-1.7093	.	-1.7093	.	.	.
amisulpride:ziprasidone	0	0	0.9425	.	0.9425	.	.	.
amisulpride:zotepine	0	0	-2.1398	.	-2.1398	.	.	.
aripiprazole:asenapine	0	0	-0.8218	.	-0.8218	.	.	.
aripiprazole:brexpiprazole	1	0.42	-0.5320	-0.6379	-0.4560	-0.1819	-0.20	0.8447
aripiprazole:cariprazine	1	0.68	-0.3160	-0.3723	-0.1952	-0.1771	-0.16	0.8761
aripiprazole:clozapine	0	0	-2.6702	.	-2.6702	.	.	.
aripiprazole:flupenthixol	0	0	-0.4084	.	-0.4084	.	.	.
aripiprazole:fluphenazine	0	0	0.1801	.	0.1801	.	.	.
aripiprazole:haloperidol	0	0	0.5774	.	0.5774	.	.	.
aripiprazole:iloperidone	0	0	-1.4226	.	-1.4226	.	.	.
aripiprazole:lurasidone	0	0	-0.1393	.	-0.1393	.	.	.
aripiprazole:olanzapine	2	0.14	-2.3826	-2.6374	-2.3414	-0.2960	-0.36	0.7181
aripiprazole:placebo	5	0.57	0.3434	0.3123	0.3851	-0.0728	-0.14	0.8877
aripiprazole:quetiapine	1	0.09	-1.2199	-1.7000	-1.1720	-0.5280	-0.45	0.6509
aripiprazole:risp_pali	6	0.57	-0.9400	-0.7095	-1.2456	0.5360	1.03	0.3039
aripiprazole:sertindole	0	0	-2.0285	.	-2.0285	.	.	.
aripiprazole:ziprasidone	0	0	0.6232	.	0.6232	.	.	.
aripiprazole:zotepine	0	0	-2.4590	.	-2.4590	.	.	.
asenapine:brexpiprazole	0	0	0.2897	.	0.2897	.	.	.
asenapine:cariprazine	0	0	0.5058	.	0.5058	.	.	.
asenapine:clozapine	0	0	-1.8484	.	-1.8484	.	.	.
asenapine:flupenthixol	0	0	0.4134	.	0.4134	.	.	.
asenapine:fluphenazine	0	0	1.0019	.	1.0019	.	.	.
asenapine:haloperidol	1	0.42	1.3992	0.3509	2.1635	-1.8126	-2.13	0.0332
asenapine:iloperidone	0	0	-0.6008	.	-0.6008	.	.	.
asenapine:lurasidone	0	0	0.6825	.	0.6825	.	.	.
asenapine:olanzapine	1	0.24	-1.5608	-1.1000	-1.7025	0.6025	0.68	0.4980
asenapine:placebo	3	0.85	1.1652	1.2392	0.7587	0.4804	0.49	0.6256
asenapine:quetiapine	0	0	-0.3981	.	-0.3981	.	.	.
asenapine:risp_pali	0	0	-0.1182	.	-0.1182	.	.	.
asenapine:sertindole	0	0	-1.2067	.	-1.2067	.	.	.
asenapine:ziprasidone	0	0	1.4450	.	1.4450	.	.	.
asenapine:zotepine	0	0	-1.6372	.	-1.6372	.	.	.
brexpiprazole:cariprazine	0	0	0.2160	.	0.2160	.	.	.
brexpiprazole:clozapine	0	0	-2.1382	.	-2.1382	.	.	.
brexpiprazole:flupenthixol	0	0	0.1237	.	0.1237	.	.	.
brexpiprazole:fluphenazine	0	0	0.7122	.	0.7122	.	.	.
brexpiprazole:haloperidol	0	0	1.1094	.	1.1094	.	.	.

brexpiprazole:iloperidone	0	0	-0.8906	.	-0.8906	.	.	.
brexpiprazole:lurasidone	0	0	0.3928	.	0.3928	.	.	.
brexpiprazole:olanzapine	0	0	-1.8506	.	-1.8506	.	.	.
brexpiprazole:placebo	2	0.89	0.8754	0.8321	1.2214	-0.3893	-0.29	0.7694
brexpiprazole:quetiapine	0	0	-0.6878	.	-0.6878	.	.	.
brexpiprazole:risp_pali	0	0	-0.4080	.	-0.4080	.	.	.
brexpiprazole:sertindole	0	0	-1.4965	.	-1.4965	.	.	.
brexpiprazole:ziprasidone	0	0	1.1553	.	1.1553	.	.	.
brexpiprazole:zotepine	0	0	-1.9270	.	-1.9270	.	.	.
cariprazine:clozapine	0	0	-2.3542	.	-2.3542	.	.	.
cariprazine:flupenthixol	0	0	-0.0924	.	-0.0924	.	.	.
cariprazine:fluphenazine	0	0	0.4961	.	0.4961	.	.	.
cariprazine:haloperidol	0	0	0.8934	.	0.8934	.	.	.
cariprazine:iloperidone	0	0	-1.1066	.	-1.1066	.	.	.
cariprazine:lurasidone	0	0	0.1767	.	0.1767	.	.	.
cariprazine:olanzapine	0	0	-2.0666	.	-2.0666	.	.	.
cariprazine:placebo	1	0.71	0.6594	0.7723	0.3836	0.3887	0.34	0.7307
cariprazine:quetiapine	0	0	-0.9039	.	-0.9039	.	.	.
cariprazine:risp_pali	1	0.63	-0.6240	-0.8277	-0.2827	-0.5450	-0.51	0.6086
cariprazine:sertindole	0	0	-1.7125	.	-1.7125	.	.	.
cariprazine:ziprasidone	0	0	0.9393	.	0.9393	.	.	.
cariprazine:zotepine	0	0	-2.1430	.	-2.1430	.	.	.
clozapine:flupenthixol	0	0	2.2618	.	2.2618	.	.	.
clozapine:fluphenazine	0	0	2.8503	.	2.8503	.	.	.
clozapine:haloperidol	3	0.81	3.2476	3.9795	0.0352	3.9443	2.62	0.0088
clozapine:iloperidone	0	0	1.2476	.	1.2476	.	.	.
clozapine:lurasidone	0	0	2.5309	.	2.5309	.	.	.
clozapine:olanzapine	2	0.42	0.2876	-1.2115	1.3815	-2.5930	-2.06	0.0399
clozapine:placebo	0	0	3.0136	.	3.0136	.	.	.
clozapine:quetiapine	0	0	1.4503	.	1.4503	.	.	.
clozapine:risp_pali	1	0.35	1.7302	1.9000	1.6398	0.2602	0.20	0.8436
clozapine:sertindole	0	0	0.6417	.	0.6417	.	.	.
clozapine:ziprasidone	0	0	3.2935	.	3.2935	.	.	.
clozapine:zotepine	1	0.55	0.2112	-0.6500	1.2570	-1.9070	-1.12	0.2638
flupenthixol:fluphenazine	0	0	0.5885	.	0.5885	.	.	.
flupenthixol:haloperidol	0	0	0.9858	.	0.9858	.	.	.
flupenthixol:iloperidone	0	0	-1.0142	.	-1.0142	.	.	.
flupenthixol:lurasidone	0	0	0.2691	.	0.2691	.	.	.
flupenthixol:olanzapine	1	0.48	-1.9742	-3.4000	-0.6367	-2.7633	-1.77	0.0771
flupenthixol:placebo	0	0	0.7518	.	0.7518	.	.	.
flupenthixol:quetiapine	0	0	-0.8115	.	-0.8115	.	.	.
flupenthixol:risp_pali	0	0	-0.5316	.	-0.5316	.	.	.
flupenthixol:sertindole	0	0	-1.6201	.	-1.6201	.	.	.
flupenthixol:ziprasidone	0	0	1.0316	.	1.0316	.	.	.
flupenthixol:zotepine	0	0	-2.0506	.	-2.0506	.	.	.
fluphenazine:haloperidol	0	0	0.3973	.	0.3973	.	.	.
fluphenazine:iloperidone	0	0	-1.6027	.	-1.6027	.	.	.
fluphenazine:lurasidone	0	0	-0.3194	.	-0.3194	.	.	.
fluphenazine:olanzapine	0	0	-2.5627	.	-2.5627	.	.	.
fluphenazine:placebo	0	0	0.1633	.	0.1633	.	.	.
fluphenazine:quetiapine	1	1.00	-1.4000	-1.4000	.	.	.	.
fluphenazine:risp_pali	0	0	-1.1201	.	-1.1201	.	.	.
fluphenazine:sertindole	0	0	-2.2087	.	-2.2087	.	.	.
fluphenazine:ziprasidone	0	0	0.4431	.	0.4431	.	.	.
fluphenazine:zotepine	0	0	-2.6391	.	-2.6391	.	.	.
haloperidol:iloperidone	1	1.00	-2.0000	-2.0000	.	.	.	.
haloperidol:lurasidone	1	0.20	-0.7167	-0.1616	-0.8539	0.6923	0.75	0.4555
haloperidol:olanzapine	5	0.52	-2.9600	-3.3484	-2.5365	-0.8119	-1.37	0.1721
haloperidol:placebo	2	0.30	-0.2340	0.0000	-0.3349	0.3349	0.51	0.6105
haloperidol:quetiapine	1	0.08	-1.7973	-1.9100	-1.7875	-0.1225	-0.09	0.9274
haloperidol:risp_pali	2	0.25	-1.5174	-1.9161	-1.3875	-0.5286	-0.74	0.4593
haloperidol:sertindole	0	0	-2.6059	.	-2.6059	.	.	.
haloperidol:ziprasidone	0	0	0.0458	.	0.0458	.	.	.
haloperidol:zotepine	1	0.59	-3.0364	-2.2500	-4.1570	1.9070	1.12	0.2638
iloperidone:lurasidone	0	0	1.2833	.	1.2833	.	.	.
iloperidone:olanzapine	0	0	-0.9600	.	-0.9600	.	.	.
iloperidone:placebo	0	0	1.7660	.	1.7660	.	.	.

iloperidone:quetiapine	0	0	0.2027	.	0.2027	.	.	.
iloperidone:risp_pali	0	0	0.4826	.	0.4826	.	.	.
iloperidone:sertindole	0	0	-0.6059	.	-0.6059	.	.	.
iloperidone:ziprasidone	0	0	2.0458	.	2.0458	.	.	.
iloperidone:zotepine	0	0	-1.0364	.	-1.0364	.	.	.
lurasidone:olanzapine	1	0.14	-2.2433	-3.1000	-2.1048	-0.9952	-1.19	0.2350
lurasidone:placebo	7	0.84	0.4827	0.6081	-0.1653	0.7734	1.14	0.2535
lurasidone:quetiapine	1	0.22	-1.0806	-0.4854	-1.2487	0.7632	0.96	0.3366
lurasidone:risp_pali	0	0	-0.8007	.	-0.8007	.	.	.
lurasidone:sertindole	0	0	-1.8892	.	-1.8892	.	.	.
lurasidone:ziprasidone	1	0.24	0.7625	0.3000	0.9108	-0.6108	-0.54	0.5863
lurasidone:zotepine	0	0	-2.3197	.	-2.3197	.	.	.
olanzapine:placebo	12	0.51	2.7260	2.5045	2.9582	-0.4537	-1.29	0.1981
olanzapine:quetiapine	3	0.25	1.1627	0.3738	1.4233	-1.0495	-1.67	0.0942
olanzapine:risp_pali	16	0.63	1.4426	1.3350	1.6231	-0.2881	-0.79	0.4283
olanzapine:sertindole	0	0	0.3541	.	0.3541	.	.	.
olanzapine:ziprasidone	2	0.40	3.0059	5.1485	1.5890	3.5595	3.86	0.0001
olanzapine:zotepine	0	0	-0.0764	.	-0.0764	.	.	.
placebo:quetiapine	5	0.56	-1.5633	-1.3576	-1.8250	0.4673	0.96	0.3376
placebo:risp_pali	18	0.66	-1.2834	-1.3015	-1.2480	-0.0535	-0.16	0.8700
placebo:sertindole	0	0	-2.3719	.	-2.3719	.	.	.
placebo:ziprasidone	1	0.45	0.2798	-1.3600	1.6002	-2.9602	-3.31	0.0009
placebo:zotepine	0	0	-2.8024	.	-2.8024	.	.	.
quetiapine:risp_pali	4	0.39	0.2799	0.5469	0.1088	0.4381	0.84	0.4029
quetiapine:sertindole	0	0	-0.8087	.	-0.8087	.	.	.
quetiapine:ziprasidone	0	0	1.8431	.	1.8431	.	.	.
quetiapine:zotepine	0	0	-1.2391	.	-1.2391	.	.	.
risp_pali:sertindole	2	1.00	-1.0885	-1.0885	.	.	.	.
risp_pali:ziprasidone	0	0	1.5633	.	1.5633	.	.	.
risp_pali:zotepine	0	0	-1.5190	.	-1.5190	.	.	.
sertindole:ziprasidone	0	0	2.6518	.	2.6518	.	.	.
sertindole:zotepine	0	0	-0.4305	.	-0.4305	.	.	.
ziprasidone:zotepine	0	0	-3.0822	.	-3.0822	.	.	.

**eTable 20. 'Hot spots' of inconsistency: BMI**

Random effects model

- 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)

Comparison	k	Prop	NMA	Direct	Indir	Diff	z	p-value
aripiprazole:clozapine	0	0	-1.2441	.	-1.2441	.	.	.
aripiprazole:haloperidol	0	0	0.0346	.	0.0346	.	.	.
aripiprazole:lurasidone	0	0	-0.4625	.	-0.4625	.	.	.
aripiprazole:olanzapine	0	0	-1.2936	.	-1.2936	.	.	.
aripiprazole:placebo	1	1.00	-0.2200	-0.2200	.	.	.	.
aripiprazole:quetiapine	0	0	-0.9173	.	-0.9173	.	.	.
aripiprazole:risp_pali	0	0	-0.7832	.	-0.7832	.	.	.
aripiprazole:sertindole	0	0	-0.9832	.	-0.9832	.	.	.
clozapine:haloperidol	1	0.73	1.2787	1.3000	1.2226	0.0774	0.09	0.9311
clozapine:lurasidone	0	0	0.7816	.	0.7816	.	.	.
clozapine:olanzapine	1	0.51	-0.0495	-0.4000	0.3151	-0.7151	-0.93	0.3498
clozapine:placebo	0	0	1.0241	.	1.0241	.	.	.
clozapine:quetiapine	0	0	0.3269	.	0.3269	.	.	.
clozapine:risp_pali	1	0.79	0.4609	0.6000	-0.0770	0.6770	0.72	0.4732
clozapine:sertindole	0	0	0.2609	.	0.2609	.	.	.
haloperidol:lurasidone	0	0	-0.4971	.	-0.4971	.	.	.
haloperidol:olanzapine	3	0.83	-1.3282	-1.4003	-0.9655	-0.4348	-0.79	0.4319
haloperidol:placebo	0	0	-0.2546	.	-0.2546	.	.	.
haloperidol:quetiapine	0	0	-0.9519	.	-0.9519	.	.	.
haloperidol:risp_pali	2	0.48	-0.8178	-0.6461	-0.9765	0.3303	0.79	0.4321
haloperidol:sertindole	0	0	-1.0178	.	-1.0178	.	.	.
lurasidone:olanzapine	1	0.31	-0.8311	-1.0538	-0.7290	-0.3248	-1.33	0.1839
lurasidone:placebo	4	0.91	0.2425	0.2734	-0.0647	0.3380	1.15	0.2509
lurasidone:quetiapine	1	0.64	-0.4547	-0.5000	-0.3753	-0.1247	-0.44	0.6598
lurasidone:risp_pali	0	0	-0.3207	.	-0.3207	.	.	.
lurasidone:sertindole	0	0	-0.5207	.	-0.5207	.	.	.
olanzapine:placebo	3	0.56	1.0736	1.0178	1.1449	-0.1270	-0.70	0.4853
olanzapine:quetiapine	0	0	0.3764	.	0.3764	.	.	.
olanzapine:risp_pali	9	0.87	0.5104	0.4778	0.7355	-0.2578	-1.17	0.2422
olanzapine:sertindole	0	0	0.3104	.	0.3104	.	.	.
placebo:quetiapine	1	0.49	-0.6973	-0.7000	-0.6946	-0.0054	-0.02	0.9836
placebo:risp_pali	7	0.83	-0.5632	-0.5451	-0.6523	0.1071	0.56	0.5752
placebo:sertindole	0	0	-0.7632	.	-0.7632	.	.	.
quetiapine:risp_pali	1	0.46	0.1341	0.0900	0.1718	-0.0818	-0.31	0.7600
quetiapine:sertindole	0	0	-0.0659	.	-0.0659	.	.	.
risp_pali:sertindole	1	1.00	-0.2000	-0.2000	.	.	.	.

**eTable 21. ‘Hot spots’ of inconsistency: total cholesterol**

Random effects model

- 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)

Comparison	k	prop	NMA	direct	indir	Diff	z	p-value
amisulpride:aripiprazole	0	0	0.1646	.	0.1646	.	.	.
amisulpride:brexpiprazole	0	0	0.1589	.	0.1589	.	.	.
amisulpride:cariprazine	0	0	0.3002	.	0.3002	.	.	.
amisulpride:clozapine	0	0	-0.3498	.	-0.3498	.	.	.
amisulpride:haloperidol	0	0	0.1129	.	0.1129	.	.	.
amisulpride:iloperidone	0	0	0.3123	.	0.3123	.	.	.
amisulpride:lurasidone	0	0	0.2456	.	0.2456	.	.	.
amisulpride:olanzapine	1	1.00	-0.1900	-0.1900	.	.	.	.
amisulpride:placebo	0	0	0.2126	.	0.2126	.	.	.
amisulpride:quetiapine	0	0	-0.0928	.	-0.0928	.	.	.
amisulpride:risp_pali	0	0	0.1514	.	0.1514	.	.	.
amisulpride:sertindole	0	0	0.2783	.	0.2783	.	.	.
amisulpride:ziprasidone	0	0	0.2543	.	0.2543	.	.	.
aripiprazole:brexpiprazole	1	0.27	-0.0057	-0.0723	0.0183	-0.0907	-0.55	0.5835
aripiprazole:cariprazine	1	0.61	0.1356	0.0558	0.2613	-0.2055	-1.17	0.2430
aripiprazole:clozapine	0	0	-0.5144	.	-0.5144	.	.	.
aripiprazole:haloperidol	0	0	-0.0518	.	-0.0518	.	.	.
aripiprazole:iloperidone	0	0	0.1477	.	0.1477	.	.	.
aripiprazole:lurasidone	0	0	0.0809	.	0.0809	.	.	.
aripiprazole:olanzapine	2	0.38	-0.3546	-0.1651	-0.4698	0.3047	2.50	0.0126
aripiprazole:placebo	4	0.69	0.0480	0.0006	0.1534	-0.1528	-1.35	0.1755
aripiprazole:quetiapine	1	0.08	-0.2575	-0.2124	-0.2612	0.0489	0.17	0.8681
aripiprazole:risp_pali	3	0.29	-0.0132	-0.1947	0.0610	-0.2556	-1.89	0.0586
aripiprazole:sertindole	0	0	0.1137	.	0.1137	.	.	.
aripiprazole:ziprasidone	0	0	0.0897	.	0.0897	.	.	.
brexpiprazole:cariprazine	0	0	0.1414	.	0.1414	.	.	.
brexpiprazole:clozapine	0	0	-0.5087	.	-0.5087	.	.	.
brexpiprazole:haloperidol	0	0	-0.0460	.	-0.0460	.	.	.
brexpiprazole:iloperidone	0	0	0.1534	.	0.1534	.	.	.
brexpiprazole:lurasidone	0	0	0.0867	.	0.0867	.	.	.
brexpiprazole:olanzapine	0	0	-0.3489	.	-0.3489	.	.	.
brexpiprazole:placebo	3	0.92	0.0538	0.0420	0.1890	-0.1470	-0.69	0.4875
brexpiprazole:quetiapine	0	0	-0.2517	.	-0.2517	.	.	.
brexpiprazole:risp_pali	0	0	-0.0075	.	-0.0075	.	.	.
brexpiprazole:sertindole	0	0	0.1195	.	0.1195	.	.	.
brexpiprazole:ziprasidone	0	0	0.0954	.	0.0954	.	.	.
cariprazine:clozapine	0	0	-0.6501	.	-0.6501	.	.	.
cariprazine:haloperidol	0	0	-0.1874	.	-0.1874	.	.	.
cariprazine:iloperidone	0	0	0.0120	.	0.0120	.	.	.
cariprazine:lurasidone	0	0	-0.0547	.	-0.0547	.	.	.
cariprazine:olanzapine	0	0	-0.4902	.	-0.4902	.	.	.
cariprazine:placebo	1	0.76	-0.0876	-0.1154	-0.0011	-0.1143	-0.61	0.5388
cariprazine:quetiapine	0	0	-0.3931	.	-0.3931	.	.	.
cariprazine:risp_pali	1	0.55	-0.1488	-0.1828	-0.1071	-0.0757	-0.45	0.6558
cariprazine:sertindole	0	0	-0.0219	.	-0.0219	.	.	.
cariprazine:ziprasidone	0	0	-0.0459	.	-0.0459	.	.	.
clozapine:haloperidol	2	0.94	0.4627	0.4910	0.0128	0.4782	0.79	0.4278
clozapine:iloperidone	0	0	0.6621	.	0.6621	.	.	.
clozapine:lurasidone	0	0	0.5954	.	0.5954	.	.	.
clozapine:olanzapine	2	0.79	0.1598	0.1800	0.0849	0.0950	0.26	0.7919
clozapine:placebo	0	0	0.5625	.	0.5625	.	.	.

clozapine:quetiapine	0	0	0.2570	.	0.2570	.	.	.
clozapine:risp_pali	1	0.41	0.5013	0.2720	0.6583	-0.3864	-1.26	0.2091
clozapine:sertindole	0	0	0.6282	.	0.6282	.	.	.
clozapine:ziprasidone	0	0	0.6041	.	0.6041	.	.	.
haloperidol:iloperidone	1	1.00	0.1994	0.1994	.	.	.	.
haloperidol:lurasidone	0	0	0.1327	.	0.1327	.	.	.
haloperidol:olanzapine	3	0.89	-0.3029	-0.2584	-0.6713	0.4130	1.30	0.1938
haloperidol:placebo	0	0	0.0998	.	0.0998	.	.	.
haloperidol:quetiapine	0	0	-0.2057	.	-0.2057	.	.	.
haloperidol:risp_pali	1	0.26	0.0386	-0.2357	0.1356	-0.3713	-1.55	0.1207
haloperidol:sertindole	0	0	0.1655	.	0.1655	.	.	.
haloperidol:ziprasidone	0	0	0.1415	.	0.1415	.	.	.
iloperidone:lurasidone	0	0	-0.0667	.	-0.0667	.	.	.
iloperidone:olanzapine	0	0	-0.5023	.	-0.5023	.	.	.
iloperidone:placebo	0	0	-0.0996	.	-0.0996	.	.	.
iloperidone:quetiapine	0	0	-0.4051	.	-0.4051	.	.	.
iloperidone:risp_pali	0	0	-0.1609	.	-0.1609	.	.	.
iloperidone:sertindole	0	0	-0.0339	.	-0.0339	.	.	.
iloperidone:ziprasidone	0	0	-0.0580	.	-0.0580	.	.	.
lurasidone:olanzapine	1	0.28	-0.4356	-0.4558	-0.4275	-0.0284	-0.18	0.8539
lurasidone:placebo	3	0.75	-0.0329	-0.0093	-0.1031	0.0938	0.66	0.5121
lurasidone:quetiapine	0	0	-0.3384	.	-0.3384	.	.	.
lurasidone:risp_pali	0	0	-0.0941	.	-0.0941	.	.	.
lurasidone:sertindole	0	0	0.0328	.	0.0328	.	.	.
lurasidone:ziprasidone	1	0.37	0.0088	-0.0518	0.0447	-0.0965	-0.59	0.5522
olanzapine:placebo	5	0.46	0.4026	0.4246	0.3836	0.0410	0.45	0.6557
olanzapine:quetiapine	1	0.06	0.0972	-0.0026	0.1038	-0.1064	-0.34	0.7303
olanzapine:risp_pali	6	0.70	0.3414	0.3788	0.2539	0.1250	1.27	0.2050
olanzapine:sertindole	0	0	0.4683	.	0.4683	.	.	.
olanzapine:ziprasidone	3	0.54	0.4443	0.4997	0.3798	0.1199	0.89	0.3742
placebo:quetiapine	4	0.93	-0.3055	-0.3054	-0.3069	0.0015	0.01	0.9951
placebo:risp_pali	6	0.71	-0.0612	-0.0521	-0.0831	0.0309	0.31	0.7552
placebo:sertindole	0	0	0.0657	.	0.0657	.	.	.
placebo:ziprasidone	1	0.37	0.0417	0.0057	0.0632	-0.0575	-0.41	0.6820
quetiapine:risp_pali	1	0.04	0.2443	0.1735	0.2475	-0.0740	-0.20	0.8398
quetiapine:sertindole	0	0	0.3712	.	0.3712	.	.	.
quetiapine:ziprasidone	0	0	0.3472	.	0.3472	.	.	.
risp_pali:sertindole	1	1.00	0.1269	0.1269	.	.	.	.
risp_pali:ziprasidone	0	0	0.1029	.	0.1029	.	.	.
sertindole:ziprasidone	0	0	-0.0240	.	-0.0240	.	.	.



**eTable 22. ‘Hot spots’ of inconsistency: LDL cholesterol**

Random effects model

- 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)

Comparison	k	prop	NMA	direct	indir	Diff	z	p-value
aripiprazole:brexpiprazole	1	0.21	-0.0369	-0.0324	-0.0382	0.0058	0.05	0.9598
aripiprazole:cariprazine	1	0.50	0.1259	0.1062	0.1460	-0.0397	-0.41	0.6835
aripiprazole:lurasidone	0	0	0.0508	.	0.0508	.	.	.
aripiprazole:olanzapine	2	0.32	-0.1996	-0.1461	-0.2251	0.0790	0.83	0.4084
aripiprazole:placebo	3	0.76	0.0003	-0.0058	0.0191	-0.0249	-0.29	0.7745
aripiprazole:quetiapine	0	0	-0.1713	.	-0.1713	.	.	.
aripiprazole:risp_pali	1	0.22	-0.0096	-0.0492	0.0018	-0.0510	-0.47	0.6366
aripiprazole:ziprasidone	0	0	0.1210	.	0.1210	.	.	.
brexpiprazole:cariprazine	0	0	0.1629	.	0.1629	.	.	.
brexpiprazole:lurasidone	0	0	0.0878	.	0.0878	.	.	.
brexpiprazole:olanzapine	1	0.26	-0.1626	-0.0790	-0.1926	0.1136	1.18	0.2381
brexpiprazole:placebo	2	0.79	0.0372	0.0213	0.0954	-0.0740	-0.91	0.3642
brexpiprazole:quetiapine	0	0	-0.1344	.	-0.1344	.	.	.
brexpiprazole:risp_pali	0	0	0.0274	.	0.0274	.	.	.
brexpiprazole:ziprasidone	0	0	0.1579	.	0.1579	.	.	.
cariprazine:lurasidone	0	0	-0.0751	.	-0.0751	.	.	.
cariprazine:olanzapine	0	0	-0.3255	.	-0.3255	.	.	.
cariprazine:placebo	1	0.78	-0.1257	-0.1269	-0.1211	-0.0059	-0.06	0.9526
cariprazine:quetiapine	0	0	-0.2973	.	-0.2973	.	.	.
cariprazine:risp_pali	1	0.39	-0.1355	-0.1554	-0.1229	-0.0325	-0.34	0.7352
cariprazine:ziprasidone	0	0	-0.0050	.	-0.0050	.	.	.
lurasidone:olanzapine	1	0.34	-0.2504	-0.2347	-0.2586	0.0239	0.22	0.8258
lurasidone:placebo	3	0.86	-0.0506	-0.0561	-0.0180	-0.0381	-0.30	0.7679
lurasidone:quetiapine	0	0	-0.2222	.	-0.2222	.	.	.
lurasidone:risp_pali	0	0	-0.0604	.	-0.0604	.	.	.
lurasidone:ziprasidone	0	0	0.0701	.	0.0701	.	.	.
olanzapine:placebo	6	0.47	0.1998	0.2249	0.1780	0.0469	0.73	0.4648
olanzapine:quetiapine	0	0	0.0282	.	0.0282	.	.	.
olanzapine:risp_pali	5	0.85	0.1900	0.2003	0.1335	0.0668	0.97	0.3312
olanzapine:ziprasidone	2	1.00	0.3205	0.3205	.	.	.	.
placebo:quetiapine	3	1.00	-0.1716	-0.1716	.	.	.	.
placebo:risp_pali	6	0.69	-0.0098	-0.0329	0.0411	-0.0740	-1.11	0.2681
placebo:ziprasidone	0	0	0.1207	.	0.1207	.	.	.
quetiapine:risp_pali	0	0	0.1618	.	0.1618	.	.	.
quetiapine:ziprasidone	0	0	0.2923	.	0.2923	.	.	.
risp_pali:ziprasidone	0	0	0.1305	.	0.1305	.	.	.

**eTable 23. ‘Hot spots’ of inconsistency: HDL cholesterol**

Random effects model

- 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)

comparison	k	prop	NMA	direct	indir	Diff	z	p-value
amisulpride:aripiprazole	0	0	-0.1359	.	-0.1359	.	.	.
amisulpride:brexpiprazole	0	0	-0.1479	.	-0.1479	.	.	.
amisulpride:cariprazine	0	0	-0.1163	.	-0.1163	.	.	.
amisulpride:lurasidone	0	0	-0.1186	.	-0.1186	.	.	.
amisulpride:olanzapine	1	1.00	-0.0900	-0.0900	.	.	.	.
amisulpride:placebo	0	0	-0.0969	.	-0.0969	.	.	.
amisulpride:quetiapine	0	0	-0.1044	.	-0.1044	.	.	.
amisulpride:risp_pali	0	0	-0.1109	.	-0.1109	.	.	.
amisulpride:ziprasidone	0	0	-0.1442	.	-0.1442	.	.	.
aripiprazole:brexpiprazole	1	0.44	-0.0119	0.0022	-0.0233	0.0255	0.43	0.6668
aripiprazole:cariprazine	1	0.66	0.0196	0.0164	0.0257	-0.0092	-0.14	0.8908
aripiprazole:lurasidone	0	0	0.0173	.	0.0173	.	.	.
aripiprazole:olanzapine	1	0.13	0.0459	0.1968	0.0232	0.1736	2.27	0.0234
aripiprazole:placebo	4	0.87	0.0390	0.0231	0.1451	-0.1220	-2.03	0.0422
aripiprazole:quetiapine	0	0	0.0315	.	0.0315	.	.	.
aripiprazole:risp_pali	1	0.30	0.0250	0.0181	0.0279	-0.0098	-0.18	0.8550
aripiprazole:ziprasidone	0	0	-0.0083	.	-0.0083	.	.	.
brexpiprazole:cariprazine	0	0	0.0315	.	0.0315	.	.	.
brexpiprazole:lurasidone	0	0	0.0293	.	0.0293	.	.	.
brexpiprazole:olanzapine	0	0	0.0579	.	0.0579	.	.	.
brexpiprazole:placebo	2	0.88	0.0509	0.0533	0.0339	0.0194	0.25	0.8026
brexpiprazole:quetiapine	0	0	0.0435	.	0.0435	.	.	.
brexpiprazole:risp_pali	0	0	0.0369	.	0.0369	.	.	.
brexpiprazole:ziprasidone	0	0	0.0036	.	0.0036	.	.	.
cariprazine:lurasidone	0	0	-0.0023	.	-0.0023	.	.	.
cariprazine:olanzapine	0	0	0.0263	.	0.0263	.	.	.
cariprazine:placebo	1	0.75	0.0194	0.0198	0.0181	0.0018	0.03	0.9792
cariprazine:quetiapine	0	0	0.0119	.	0.0119	.	.	.
cariprazine:risp_pali	1	0.63	0.0054	0.0017	0.0118	-0.0101	-0.16	0.8747
cariprazine:ziprasidone	0	0	-0.0279	.	-0.0279	.	.	.
lurasidone:olanzapine	1	0.72	0.0286	0.0371	0.0064	0.0307	0.37	0.7115
lurasidone:placebo	1	0.75	0.0217	0.0137	0.0452	-0.0314	-0.37	0.7115
lurasidone:quetiapine	0	0	0.0142	.	0.0142	.	.	.
lurasidone:risp_pali	0	0	0.0077	.	0.0077	.	.	.
lurasidone:ziprasidone	0	0	-0.0256	.	-0.0256	.	.	.
olanzapine:placebo	6	0.83	-0.0069	-0.0025	-0.0280	0.0254	0.53	0.5985
olanzapine:quetiapine	0	0	-0.0144	.	-0.0144	.	.	.
olanzapine:risp_pali	4	0.70	-0.0209	-0.0219	-0.0186	-0.0033	-0.08	0.9372
olanzapine:ziprasidone	2	1.00	-0.0542	-0.0542	.	.	.	.
placebo:quetiapine	4	1.00	-0.0075	-0.0075	.	.	.	.
placebo:risp_pali	6	0.87	-0.0140	-0.0099	-0.0408	0.0309	0.64	0.5236
placebo:ziprasidone	0	0	-0.0473	.	-0.0473	.	.	.
quetiapine:risp_pali	0	0	-0.0065	.	-0.0065	.	.	.
quetiapine:ziprasidone	0	0	-0.0398	.	-0.0398	.	.	.
risp_pali:ziprasidone	0	0	-0.0333	.	-0.0333	.	.	.

**eTable 24. ‘Hot spots’ of inconsistency: triglycerides**

Random effects model

- 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)

Comparison	k	prop	NMA	direct	indir	Diff	z	p-value
amisulpride:aripiprazole	0	0	0.0722	.	0.0722	.	.	.
amisulpride:brexpiprazole	0	0	0.1054	.	0.1054	.	.	.
amisulpride:cariprazine	0	0	0.0887	.	0.0887	.	.	.
amisulpride:clozapine	0	0	-0.8898	.	-0.8898	.	.	.
amisulpride:haloperidol	0	0	-0.1722	.	-0.1722	.	.	.
amisulpride:iloperidone	0	0	-0.1770	.	-0.1770	.	.	.
amisulpride:lurasidone	0	0	0.0970	.	0.0970	.	.	.
amisulpride:olanzapine	1	1.00	-0.3700	-0.3700	.	.	.	.
amisulpride:placebo	0	0	0.0938	.	0.0938	.	.	.
amisulpride:quetiapine	0	0	-0.2289	.	-0.2289	.	.	.
amisulpride:risp_pali	0	0	0.0548	.	0.0548	.	.	.
amisulpride:sertindole	0	0	0.0910	.	0.0910	.	.	.
amisulpride:ziprasidone	0	0	0.0702	.	0.0702	.	.	.
amisulpride:zotepine	0	0	-0.8284	.	-0.8284	.	.	.
aripiprazole:brexpiprazole	1	0.25	0.0332	-0.0099	0.0477	-0.0575	-0.39	0.6933
aripiprazole:cariprazine	1	0.68	0.0165	-0.0843	0.2278	-0.3121	-1.96	0.0495
aripiprazole:clozapine	0	0	-0.9620	.	-0.9620	.	.	.
aripiprazole:haloperidol	0	0	-0.2444	.	-0.2444	.	.	.
aripiprazole:iloperidone	0	0	-0.2491	.	-0.2491	.	.	.
aripiprazole:lurasidone	0	0	0.0249	.	0.0249	.	.	.
aripiprazole:olanzapine	2	0.35	-0.4422	-0.2232	-0.5621	0.3389	2.85	0.0044
aripiprazole:placebo	4	0.71	0.0217	-0.0256	0.1373	-0.1628	-1.55	0.1203
aripiprazole:quetiapine	1	0.11	-0.3010	-0.0825	-0.3292	0.2467	1.07	0.2865
aripiprazole:risp_pali	2	0.31	-0.0173	-0.1936	0.0612	-0.2549	-2.06	0.0396
aripiprazole:sertindole	0	0	0.0189	.	0.0189	.	.	.
aripiprazole:ziprasidone	0	0	-0.0020	.	-0.0020	.	.	.
aripiprazole:zotepine	0	0	-0.9006	.	-0.9006	.	.	.
brexpiprazole:cariprazine	0	0	-0.0167	.	-0.0167	.	.	.
brexpiprazole:clozapine	0	0	-0.9952	.	-0.9952	.	.	.
brexpiprazole:haloperidol	0	0	-0.2777	.	-0.2777	.	.	.
brexpiprazole:iloperidone	0	0	-0.2824	.	-0.2824	.	.	.
brexpiprazole:lurasidone	0	0	-0.0084	.	-0.0084	.	.	.
brexpiprazole:olanzapine	0	0	-0.4754	.	-0.4754	.	.	.
brexpiprazole:placebo	3	0.92	-0.0116	-0.0143	0.0193	-0.0335	-0.19	0.8481
brexpiprazole:quetiapine	0	0	-0.3343	.	-0.3343	.	.	.
brexpiprazole:risp_pali	0	0	-0.0506	.	-0.0506	.	.	.
brexpiprazole:sertindole	0	0	-0.0144	.	-0.0144	.	.	.
brexpiprazole:ziprasidone	0	0	-0.0352	.	-0.0352	.	.	.
brexpiprazole:zotepine	0	0	-0.9338	.	-0.9338	.	.	.
cariprazine:clozapine	0	0	-0.9785	.	-0.9785	.	.	.
cariprazine:haloperidol	0	0	-0.2609	.	-0.2609	.	.	.
cariprazine:iloperidone	0	0	-0.2657	.	-0.2657	.	.	.
cariprazine:lurasidone	0	0	0.0084	.	0.0084	.	.	.
cariprazine:olanzapine	0	0	-0.4587	.	-0.4587	.	.	.
cariprazine:placebo	1	0.77	0.0052	-0.0412	0.1643	-0.2055	-1.23	0.2176
cariprazine:quetiapine	0	0	-0.3175	.	-0.3175	.	.	.
cariprazine:risp_pali	1	0.48	-0.0338	-0.0830	0.0122	-0.0951	-0.63	0.5296
cariprazine:sertindole	0	0	0.0024	.	0.0024	.	.	.
cariprazine:ziprasidone	0	0	-0.0185	.	-0.0185	.	.	.
cariprazine:zotepine	0	0	-0.9171	.	-0.9171	.	.	.
clozapine:haloperidol	1	1.00	0.7175	0.7176	.	.	.	.

clozapine:iloperidone	0	0	0.7128	.	0.7128	.	.	.
clozapine:lurasidone	0	0	0.9868	.	0.9868	.	.	.
clozapine:olanzapine	1	1.00	0.5198	0.5198	.	.	.	.
clozapine:placebo	0	0	0.9836	.	0.9836	.	.	.
clozapine:quetiapine	0	0	0.6609	.	0.6609	.	.	.
clozapine:risp_pali	0	0	0.9446	.	0.9446	.	.	.
clozapine:sertindole	0	0	0.9808	.	0.9808	.	.	.
clozapine:ziprasidone	0	0	0.9600	.	0.9600	.	.	.
clozapine:zotepine	1	1.00	0.0614	0.0614	.	.	.	.
haloperidol:iloperidone	1	1.00	-0.0047	-0.0047	.	.	.	.
haloperidol:lurasidone	0	0	0.2693	.	0.2693	.	.	.
haloperidol:olanzapine	1	1.00	-0.1977	-0.1978	.	.	.	.
haloperidol:placebo	0	0	0.2661	.	0.2661	.	.	.
haloperidol:quetiapine	0	0	-0.0566	.	-0.0566	.	.	.
haloperidol:risp_pali	0	0	0.2271	.	0.2271	.	.	.
haloperidol:sertindole	0	0	0.2633	.	0.2633	.	.	.
haloperidol:ziprasidone	0	0	0.2424	.	0.2424	.	.	.
haloperidol:zotepine	0	0	-0.6562	.	-0.6562	.	.	.
iloperidone:lurasidone	0	0	0.2740	.	0.2740	.	.	.
iloperidone:olanzapine	0	0	-0.1930	.	-0.1930	.	.	.
iloperidone:placebo	0	0	0.2708	.	0.2708	.	.	.
iloperidone:quetiapine	0	0	-0.0519	.	-0.0519	.	.	.
iloperidone:risp_pali	0	0	0.2318	.	0.2318	.	.	.
iloperidone:sertindole	0	0	0.2680	.	0.2680	.	.	.
iloperidone:ziprasidone	0	0	0.2472	.	0.2472	.	.	.
iloperidone:zotepine	0	0	-0.6514	.	-0.6514	.	.	.
lurasidone:olanzapine	1	0.20	-0.4670	-0.6416	-0.4233	-0.2183	-1.11	0.2685
lurasidone:placebo	3	0.91	-0.0032	0.0247	-0.2812	0.3060	1.30	0.1946
lurasidone:quetiapine	0	0	-0.3259	.	-0.3259	.	.	.
lurasidone:risp_pali	0	0	-0.0422	.	-0.0422	.	.	.
lurasidone:sertindole	0	0	-0.0060	.	-0.0060	.	.	.
lurasidone:ziprasidone	1	0.09	-0.0268	-0.2825	-0.0006	-0.2819	-0.87	0.3839
lurasidone:zotepine	0	0	-0.9255	.	-0.9255	.	.	.
olanzapine:placebo	5	0.49	0.4638	0.4505	0.4766	-0.0261	-0.29	0.7742
olanzapine:quetiapine	1	0.06	0.1411	0.1435	0.1410	0.0025	0.01	0.9932
olanzapine:risp_pali	5	0.71	0.4248	0.4479	0.3686	0.0793	0.81	0.4194
olanzapine:sertindole	0	0	0.4610	.	0.4610	.	.	.
olanzapine:ziprasidone	3	0.38	0.4402	0.5823	0.3512	0.2311	1.51	0.1305
olanzapine:zotepine	0	0	-0.4584	.	-0.4584	.	.	.
placebo:quetiapine	4	0.91	-0.3227	-0.3504	-0.0339	-0.3165	-1.53	0.1250
placebo:risp_pali	6	0.73	-0.0390	-0.0414	-0.0324	-0.0090	-0.09	0.9250
placebo:sertindole	0	0	-0.0028	.	-0.0028	.	.	.
placebo:ziprasidone	1	0.66	-0.0236	-0.0757	0.0795	-0.1552	-1.06	0.2904
placebo:zotepine	0	0	-0.9223	.	-0.9223	.	.	.
quetiapine:risp_pali	1	0.10	0.2837	-0.1853	0.3345	-0.5198	-2.18	0.0294
quetiapine:sertindole	0	0	0.3199	.	0.3199	.	.	.
quetiapine:ziprasidone	0	0	0.2991	.	0.2991	.	.	.
quetiapine:zotepine	0	0	-0.5996	.	-0.5996	.	.	.
risp_pali:sertindole	1	1.00	0.0362	0.0362	.	.	.	.
risp_pali:ziprasidone	0	0	0.0153	.	0.0153	.	.	.
risp_pali:zotepine	0	0	-0.8833	.	-0.8833	.	.	.
sertindole:ziprasidone	0	0	-0.0208	.	-0.0208	.	.	.
sertindole:zotepine	0	0	-0.9194	.	-0.9194	.	.	.
ziprasidone:zotepine	0	0	-0.8986	.	-0.8986	.	.	.

**eTable 25. ‘Hot spots’ of inconsistency: glucose**

Random effects model

- 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)

Comparison	k	prop	NMA	direct	indir	Diff	z	p-value
amisulpride:aripiprazole	0	0	-0.5888	.	-0.5888	.	.	.
amisulpride:asenapine	0	0	-0.3140	.	-0.3140	.	.	.
amisulpride:brexpiprazole	0	0	-0.4958	.	-0.4958	.	.	.
amisulpride:cariprazine	0	0	-0.7169	.	-0.7169	.	.	.
amisulpride:clozapine	0	0	-1.5091	.	-1.5091	.	.	.
amisulpride:haloperidol	0	0	-0.6407	.	-0.6407	.	.	.
amisulpride:iloperidone	0	0	-0.8111	.	-0.8111	.	.	.
amisulpride:lurasidone	0	0	-0.1677	.	-0.1677	.	.	.
amisulpride:olanzapine	1	1.00	-0.6593	-0.6593	.	.	.	.
amisulpride:placebo	0	0	-0.4556	.	-0.4556	.	.	.
amisulpride:quetiapine	0	0	-0.5448	.	-0.5448	.	.	.
amisulpride:risp_pali	0	0	-0.5368	.	-0.5368	.	.	.
amisulpride:sertindole	0	0	-0.4258	.	-0.4258	.	.	.
amisulpride:ziprasidone	0	0	-0.5032	.	-0.5032	.	.	.
amisulpride:zotepine	0	0	-1.4425	.	-1.4425	.	.	.
aripiprazole:asenapine	0	0	0.2747	.	0.2747	.	.	.
aripiprazole:brexpiprazole	1	0.41	0.0930	0.1175	0.0758	0.0416	0.14	0.8892
aripiprazole:cariprazine	1	0.74	-0.1281	-0.2666	0.2596	-0.5263	-1.40	0.1614
aripiprazole:clozapine	0	0	-0.9203	.	-0.9203	.	.	.
aripiprazole:haloperidol	0	0	-0.0519	.	-0.0519	.	.	.
aripiprazole:iloperidone	0	0	-0.2223	.	-0.2223	.	.	.
aripiprazole:lurasidone	0	0	0.4211	.	0.4211	.	.	.
aripiprazole:olanzapine	2	0.38	-0.0706	0.0311	-0.1321	0.1631	0.74	0.4567
aripiprazole:placebo	4	0.65	0.1331	0.0299	0.3267	-0.2968	-1.55	0.1220
aripiprazole:quetiapine	1	0.19	0.0439	0.5217	-0.0711	0.5928	1.76	0.0783
aripiprazole:risp_pali	3	0.40	0.0520	0.1207	0.0062	0.1145	0.55	0.5811
aripiprazole:sertindole	0	0	0.1630	.	0.1630	.	.	.
aripiprazole:ziprasidone	0	0	0.0856	.	0.0856	.	.	.
aripiprazole:zotepine	0	0	-0.8537	.	-0.8537	.	.	.
asenapine:brexpiprazole	0	0	-0.1817	.	-0.1817	.	.	.
asenapine:cariprazine	0	0	-0.4029	.	-0.4029	.	.	.
asenapine:clozapine	0	0	-1.1951	.	-1.1951	.	.	.
asenapine:haloperidol	0	0	-0.3267	.	-0.3267	.	.	.
asenapine:iloperidone	0	0	-0.4970	.	-0.4970	.	.	.
asenapine:lurasidone	0	0	0.1464	.	0.1464	.	.	.
asenapine:olanzapine	0	0	-0.3453	.	-0.3453	.	.	.
asenapine:placebo	1	1.00	-0.1416	-0.1416	.	.	.	.
asenapine:quetiapine	0	0	-0.2308	.	-0.2308	.	.	.
asenapine:risp_pali	0	0	-0.2227	.	-0.2227	.	.	.
asenapine:sertindole	0	0	-0.1117	.	-0.1117	.	.	.
asenapine:ziprasidone	0	0	-0.1892	.	-0.1892	.	.	.
asenapine:zotepine	0	0	-1.1285	.	-1.1285	.	.	.
brexpiprazole:cariprazine	0	0	-0.2211	.	-0.2211	.	.	.
brexpiprazole:clozapine	0	0	-1.0133	.	-1.0133	.	.	.
brexpiprazole:haloperidol	0	0	-0.1449	.	-0.1449	.	.	.
brexpiprazole:iloperidone	0	0	-0.3153	.	-0.3153	.	.	.
brexpiprazole:lurasidone	0	0	0.3281	.	0.3281	.	.	.
brexpiprazole:olanzapine	0	0	-0.1636	.	-0.1636	.	.	.
brexpiprazole:placebo	3	0.90	0.0401	0.0549	-0.0989	0.1538	0.35	0.7258
brexpiprazole:quetiapine	0	0	-0.0491	.	-0.0491	.	.	.
brexpiprazole:risp_pali	0	0	-0.0410	.	-0.0410	.	.	.
brexpiprazole:sertindole	0	0	0.0700	.	0.0700	.	.	.
brexpiprazole:ziprasidone	0	0	-0.0074	.	-0.0074	.	.	.

brexpiprazole:zotepine	0	0	-0.9467	.	-0.9467	.	.	.
cariprazine:clozapine	0	0	-0.7922	.	-0.7922	.	.	.
cariprazine:haloperidol	0	0	0.0762	.	0.0762	.	.	.
cariprazine:iloperidone	0	0	-0.0942	.	-0.0942	.	.	.
cariprazine:lurasidone	0	0	0.5492	.	0.5492	.	.	.
cariprazine:olanzapine	0	0	0.0576	.	0.0576	.	.	.
cariprazine:placebo	1	0.69	0.2613	-0.0053	0.8489	-0.8542	-2.47	0.0136
cariprazine:quetiapine	0	0	0.1721	.	0.1721	.	.	.
cariprazine:risp_pali	1	0.68	0.1801	0.3166	-0.1096	0.4262	1.22	0.2224
cariprazine:sertindole	0	0	0.2911	.	0.2911	.	.	.
cariprazine:ziprasidone	0	0	0.2137	.	0.2137	.	.	.
cariprazine:zotepine	0	0	-0.7256	.	-0.7256	.	.	.
clozapine:haloperidol	2	0.92	0.8684	0.6980	2.7408	-2.0428	-1.72	0.0852
clozapine:iloperidone	0	0	0.6980	.	0.6980	.	.	.
clozapine:lurasidone	0	0	1.3414	.	1.3414	.	.	.
clozapine:olanzapine	2	0.88	0.8498	0.9226	0.3263	0.5963	0.61	0.5444
clozapine:placebo	0	0	1.0535	.	1.0535	.	.	.
clozapine:quetiapine	0	0	0.9643	.	0.9643	.	.	.
clozapine:risp_pali	1	0.64	0.9723	1.0212	0.8870	0.1342	0.20	0.8428
clozapine:sertindole	0	0	1.0833	.	1.0833	.	.	.
clozapine:ziprasidone	0	0	1.0059	.	1.0059	.	.	.
clozapine:zotepine	1	1.00	0.0666	0.0666	.	.	.	.
haloperidol:iloperidone	1	1.00	-0.1704	-0.1704	.	.	.	.
haloperidol:lurasidone	0	0	0.4730	.	0.4730	.	.	.
haloperidol:olanzapine	3	0.92	-0.0186	-0.0554	0.3791	-0.4345	-0.73	0.4659
haloperidol:placebo	0	0	0.1851	.	0.1851	.	.	.
haloperidol:quetiapine	0	0	0.0959	.	0.0959	.	.	.
haloperidol:risp_pali	1	0.31	0.1039	0.5383	-0.0906	0.6289	1.63	0.1034
haloperidol:sertindole	0	0	0.2149	.	0.2149	.	.	.
haloperidol:ziprasidone	0	0	0.1375	.	0.1375	.	.	.
haloperidol:zotepine	0	0	-0.8018	.	-0.8018	.	.	.
iloperidone:lurasidone	0	0	0.6434	.	0.6434	.	.	.
iloperidone:olanzapine	0	0	0.1518	.	0.1518	.	.	.
iloperidone:placebo	0	0	0.3555	.	0.3555	.	.	.
iloperidone:quetiapine	0	0	0.2663	.	0.2663	.	.	.
iloperidone:risp_pali	0	0	0.2743	.	0.2743	.	.	.
iloperidone:sertindole	0	0	0.3853	.	0.3853	.	.	.
iloperidone:ziprasidone	0	0	0.3079	.	0.3079	.	.	.
iloperidone:zotepine	0	0	-0.6314	.	-0.6314	.	.	.
lurasidone:olanzapine	1	0.27	-0.4917	-0.5588	-0.4664	-0.0924	-0.28	0.7833
lurasidone:placebo	3	0.90	-0.2880	-0.2602	-0.5471	0.2869	0.64	0.5237
lurasidone:quetiapine	0	0	-0.3772	.	-0.3772	.	.	.
lurasidone:risp_pali	0	0	-0.3691	.	-0.3691	.	.	.
lurasidone:sertindole	0	0	-0.2581	.	-0.2581	.	.	.
lurasidone:ziprasidone	0	0	-0.3355	.	-0.3355	.	.	.
lurasidone:zotepine	0	0	-1.2748	.	-1.2748	.	.	.
olanzapine:placebo	6	0.58	0.2037	0.1924	0.2194	-0.0270	-0.16	0.8725
olanzapine:quetiapine	1	0.18	0.1145	0.1110	0.1153	-0.0043	-0.01	0.9896
olanzapine:risp_pali	6	0.67	0.1226	0.0677	0.2350	-0.1673	-0.94	0.3447
olanzapine:sertindole	0	0	0.2336	.	0.2336	.	.	.
olanzapine:ziprasidone	2	1.00	0.1561	0.1561	.	.	.	.
olanzapine:zotepine	0	0	-0.7832	.	-0.7832	.	.	.
placebo:quetiapine	4	0.84	-0.0892	-0.1420	0.1940	-0.3360	-1.18	0.2377
placebo:risp_pali	9	0.79	-0.0811	-0.0573	-0.1713	0.1140	0.65	0.5128
placebo:sertindole	0	0	0.0299	.	0.0299	.	.	.
placebo:ziprasidone	0	0	-0.0476	.	-0.0476	.	.	.
placebo:zotepine	0	0	-0.9869	.	-0.9869	.	.	.
quetiapine:risp_pali	1	0.14	0.0081	-0.3552	0.0683	-0.4235	-1.22	0.2242
quetiapine:sertindole	0	0	0.1191	.	0.1191	.	.	.
quetiapine:ziprasidone	0	0	0.0416	.	0.0416	.	.	.
quetiapine:zotepine	0	0	-0.8977	.	-0.8977	.	.	.
risp_pali:sertindole	1	1.00	0.1110	0.1110	.	.	.	.
risp_pali:ziprasidone	0	0	0.0336	.	0.0336	.	.	.
risp_pali:zotepine	0	0	-0.9057	.	-0.9057	.	.	.
sertindole:ziprasidone	0	0	-0.0774	.	-0.0774	.	.	.
sertindole:zotepine	0	0	-1.0167	.	-1.0167	.	.	.
ziprasidone:zotepine	0	0	-0.9393	.	-0.9393	.	.	.

**eTable 26. CINEMA confidence rating for weight**

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
amisulpride:flupenthixol	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:olanzapine	2	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
amisulpride:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:brexiprazole	1	Major concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Very low
aripiprazole:cariprazine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:olanzapine	2	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:placebo	5	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:quetiapine	1	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
aripiprazole:risp_pali	6	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
asenapine:haloperidol	1	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
asenapine:olanzapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
asenapine:placebo	3	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
brexpiprazole:placebo	2	Major concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Very low
cariprazine:placebo	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:haloperidol	3	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
clozapine:olanzapine	2	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:risp_pali	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:zotepine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
flupenthixol:olanzapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low

fluphenazine:quetiapine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
fluphenazine:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:iloperidone	1	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
haloperidol:lurasidone	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:olanzapine	5	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
haloperidol:placebo	2	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:quetiapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
haloperidol:risp_pali	2	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
haloperidol:zotepine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:olanzapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:placebo	7	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:quetiapine	1	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
lurasidone:ziprasidone	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:placebo	12	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
olanzapine:quetiapine	3	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
olanzapine:risp_pali	16	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
olanzapine:ziprasidone	2	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
placebo:quetiapine	5	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
placebo:risp_pali	18	Some concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
placebo:ziprasidone	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
quetiapine:risp_pali	5	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
risp_pali:sertindole	2	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:aripiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low



amisulpride:asenapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:brexiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:cariprazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
amisulpride:fluphenazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:loperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:sertindole	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
amisulpride:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:zotepine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
aripiprazole:asenapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
aripiprazole:flupenthixol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:fluphenazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:loperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
aripiprazole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low

asenapine:brexpiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
asenapine:cariprazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
asenapine:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
asenapine:flupenthixol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
asenapine:fluphenazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
asenapine:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
asenapine:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
asenapine:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
asenapine:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
asenapine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
asenapine:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
asenapine:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:cariprazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
brexpiprazole:flupenthixol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:fluphenazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:haloperidol	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
brexpiprazole:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:olanzapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
brexpiprazole:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:sertindole	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low

brexpiprazole:ziprasidone	0	Major concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:zotepine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
cariprazine:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
cariprazine:flupenthixol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:fluphenazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:olanzapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
cariprazine:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:sertindole	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
cariprazine:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:zotepine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
clozapine:flupenthixol	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
clozapine:fluphenazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
clozapine:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
clozapine:lurasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
clozapine:placebo	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
clozapine:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
clozapine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
clozapine:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
flupenthixol:fluphenazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
flupenthixol:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low

flupenthixol:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
flupenthixol:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
flupenthixol:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
flupenthixol:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
flupenthixol:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
flupenthixol:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
flupenthixol:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
flupenthixol:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
fluphenazine:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
fluphenazine:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
fluphenazine:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
fluphenazine:olanzapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
fluphenazine:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
fluphenazine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
fluphenazine:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
fluphenazine:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
haloperidol:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
haloperidol:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:olanzapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:placebo	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
iloperidone:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low

iloperidone:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Very low
iloperidone:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
lurasidone:risp_pali	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
lurasidone:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
lurasidone:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
olanzapine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
olanzapine:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
placebo:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
placebo:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
quetiapine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
quetiapine:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
quetiapine:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
risp_pali:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
risp_pali:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
sertindole:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
sertindole:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
ziprasidone:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low

**eTable 27. CINEMA confidence rating for BMI**

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
aripiprazole:placebo	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:haloperidol	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:olanzapine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:olanzapine	3	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
haloperidol:risp_pali	2	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:olanzapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:placebo	4	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
lurasidone:quetiapine	1	No concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
olanzapine:placebo	3	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
olanzapine:risp_pali	9	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
placebo:quetiapine	1	No concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
placebo:risp_pali	7	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
quetiapine:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
risp_pali:sertindole	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Very low
aripiprazole:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Very low
aripiprazole:olanzapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate

aripiprazole:risp_pali	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:lurasidone	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
clozapine:placebo	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:lurasidone	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
haloperidol:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
haloperidol:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:risp_pali	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
lurasidone:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
olanzapine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
placebo:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
quetiapine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low

**eTable 28. CINEMA confidence rating for total cholesterol**

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
amisulpride:olanzapine	1	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:brexiprazole	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:cariprazine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:olanzapine	2	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
aripiprazole:placebo	4	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:quetiapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:risp_pali	3	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:placebo	3	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:placebo	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:haloperidol	2	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:olanzapine	2	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:risp_pali	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
haloperidol:lisperidone	1	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
haloperidol:olanzapine	3	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
haloperidol:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:olanzapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:placebo	3	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:ziprasidone	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:placebo	5	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
olanzapine:quetiapine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:risp_pali	6	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Low
olanzapine:ziprasidone	3	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Low
placebo:quetiapine	4	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
placebo:risp_pali	6	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
placebo:ziprasidone	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
quetiapine:risp_pali	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
risp_pali:sertindole	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:aripiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:brexiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low





clozapine:iloperidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:lurasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:placebo	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
haloperidol:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:olanzapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
iloperidone:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
iloperidone:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
placebo:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
quetiapine:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
quetiapine:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
risp_pali:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
sertindole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low

**eTable 29. CINEMA confidence rating for LDL Cholesterol**

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
aripiprazole:brexpiprazole	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:cariprazine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:olanzapine	2	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:placebo	3	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:olanzapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
brexpiprazole:placebo	2	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:placebo	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
cariprazine:risp_pali	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:olanzapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:placebo	3	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:placebo	6	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
olanzapine:risp_pali	5	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
olanzapine:ziprasidone	2	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
placebo:quetiapine	3	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
placebo:risp_pali	6	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:cariprazine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
brexpiprazole:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
brexpiprazole:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:olanzapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
cariprazine:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
cariprazine:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low

lurasidone:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
placebo:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
quetiapine:risp_pali	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
quetiapine:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
risp_pali:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low

**eTable 30. CINEMA confidence rating for HDL Cholesterol**

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
amisulpride:olanzapine	1	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:brexiprazole	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:cariprazine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:olanzapine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:placebo	4	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexiprazole:placebo	2	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
cariprazine:placebo	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:olanzapine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:placebo	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:placebo	6	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:risp_pali	4	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:ziprasidone	2	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
placebo:quetiapine	4	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low

placebo:risp_pali	6	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:aripiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:brexiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:cariprazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:placebo	0	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:risp_pali	0	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:cariprazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:olanzapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:olanzapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low

lurasidone:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
placebo:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
quetiapine:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
quetiapine:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
risp_pali:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low

**eTable 31. CINeMA confidence rating for triglycerides**

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
amisulpride:olanzapine	1	No concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:brexiprazole	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:cariprazine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:olanzapine	2	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:placebo	4	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:quetiapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:risp_pali	2	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexiprazole:placebo	3	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:placebo	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:haloperidol	1	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Moderate
clozapine:olanzapine	1	Some concerns	Suspected	No concerns	No concerns	Major concerns	Major concerns	Very low
clozapine:zotepine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low

haloperidol:iloperidone	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
haloperidol:olanzapine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
lurasidone:olanzapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:placebo	3	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:ziprasidone	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:placebo	5	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
olanzapine:quetiapine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:risp_pali	5	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
olanzapine:ziprasidone	3	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
placebo:quetiapine	4	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
placebo:risp_pali	6	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
placebo:ziprasidone	1	Major concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Very low
quetiapine:risp_pali	1	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
risp_pali:sertindole	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:aripiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:brexpiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:cariprazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
amisulpride:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:lurasidone	0	No concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low

amisulpride:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
amisulpride:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
aripiprazole:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
aripiprazole:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
brexpiprazole:cariprazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
brexpiprazole:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:olanzapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
brexpiprazole:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
brexpiprazole:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
brexpiprazole:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
cariprazine:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low



cariprazine:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:olanzapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
cariprazine:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
cariprazine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
clozapine:iloperidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
clozapine:lurasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
clozapine:placebo	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
clozapine:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
clozapine:risp_pali	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
clozapine:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
clozapine:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
haloperidol:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
haloperidol:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
haloperidol:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
haloperidol:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
haloperidol:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
haloperidol:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
haloperidol:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low

iloperidone:olanzapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
iloperidone:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
lurasidone:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
lurasidone:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
lurasidone:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
lurasidone:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
olanzapine:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
olanzapine:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
placebo:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
placebo:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
quetiapine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
quetiapine:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
quetiapine:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
risp_pali:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
risp_pali:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
sertindole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
sertindole:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low
ziprasidone:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	Major concerns	Low

**eTable 32. CINeMA confidence rating for glucose**

Comparison	Number of studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
amisulpride:olanzapine	1	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:brexiprazole	1	Major concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Very low
aripiprazole:cariprazine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:olanzapine	2	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:placebo	4	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:quetiapine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:risp_pali	3	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
asenapine:placebo	1	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:placebo	3	Major concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Very low
cariprazine:placebo	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	Major concerns	Very low
cariprazine:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:haloperidol	2	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:olanzapine	2	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:risp_pali	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:zotepine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:iloperidone	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:olanzapine	3	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:olanzapine	1	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
lurasidone:placebo	3	No concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low

olanzapine:placebo	6	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
olanzapine:quetiapine	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:risp_pali	6	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:ziprasidone	2	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
placebo:quetiapine	4	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
placebo:risp_pali	9	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
quetiapine:risp_pali	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
risp_pali:sertindole	1	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:aripiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:asenapine	0	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:brexiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:cariprazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
amisulpride:haloperidol	0	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:loperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:lurasidone	0	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
amisulpride:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:asenapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low

aripiprazole:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
aripiprazole:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:lurasidone	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
aripiprazole:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
aripiprazole:zotepine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
asenapine:brexpiprazole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
asenapine:cariprazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
asenapine:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
asenapine:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
asenapine:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
asenapine:lurasidone	0	No concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
asenapine:olanzapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
asenapine:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
asenapine:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
asenapine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
asenapine:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
asenapine:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
brexpiprazole:cariprazine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:clozapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
brexpiprazole:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low

brexpiprazole:lurasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:olanzapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:risperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
brexpiprazole:zotepine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
cariprazine:clozapine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
cariprazine:haloperidol	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:lurasidone	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
cariprazine:olanzapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
cariprazine:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:iloperidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
clozapine:lurasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:placebo	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:sertindole	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
clozapine:ziprasidone	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
haloperidol:lurasidone	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low

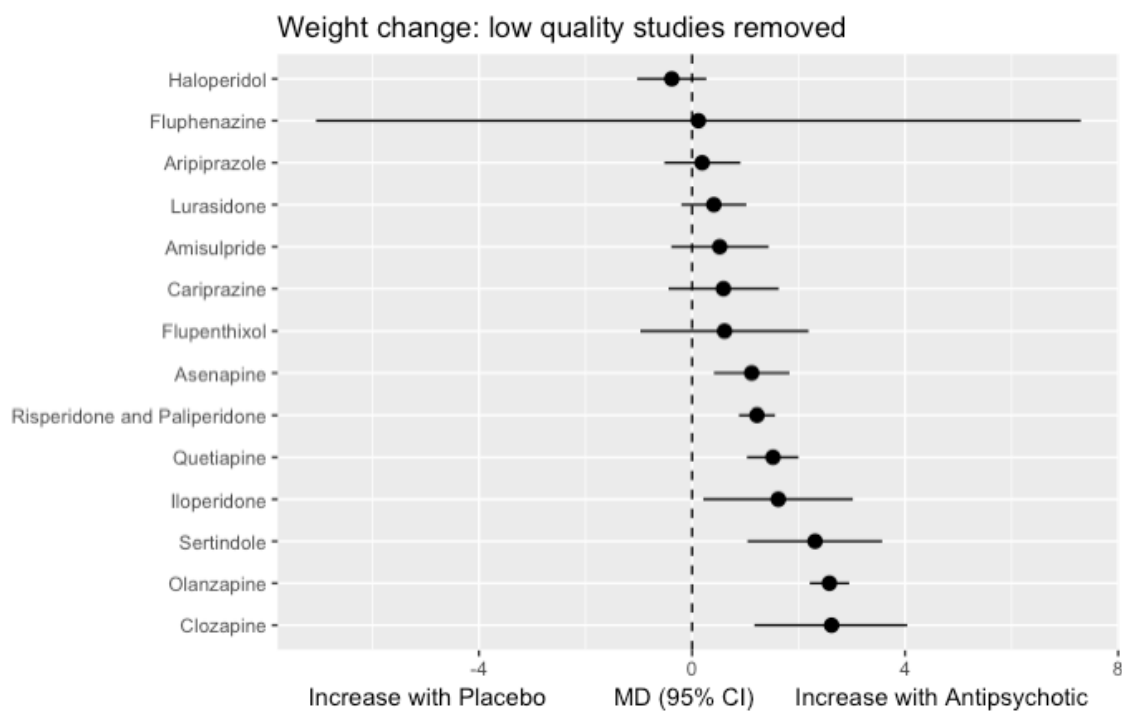
haloperidol:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
haloperidol:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:lurasidone	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
iloperidone:olanzapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:placebo	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:quetiapine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:risp_pali	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
iloperidone:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:quetiapine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
lurasidone:risp_pali	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
lurasidone:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
lurasidone:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate
olanzapine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
olanzapine:zotepine	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
placebo:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
placebo:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
placebo:zotepine	0	Some concerns	Suspected	No concerns	No concerns	No concerns	No concerns	Moderate

quetiapine:sertindole	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
quetiapine:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
quetiapine:zotepine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
risp_pali:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
risp_pali:zotepine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
sertindole:ziprasidone	0	Some concerns	Suspected	No concerns	Major concerns	No concerns	No concerns	Low
sertindole:zotepine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low
ziprasidone:zotepine	0	Some concerns	Suspected	No concerns	No concerns	Major concerns	No concerns	Low



## eAppendix 4. Post hoc sensitivity analysis for antipsychotic-induced weight gain (low quality studies removed)

In the context of increased heterogeneity and inconsistency in the NMA examining antipsychotic-induced weight change, we performed a post-hoc sensitivity analysis excluding studies at high risk of bias (identified in eTable 3). Results were broadly similar.



Tests of heterogeneity and inconsistency were as follows:  $\tau$  was 0.61kg, and  $I^2$  72%. The global Q score for inconsistency was 75.99 ( $p=0.0002$ ), and significant hot-spots of inconsistency identified in 6 of 154 treatment comparisons including disagreement between direct and indirect evidence (see below).

Random effects model

- 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)

	comparison	k	prop	nma	direct	indir.	Diff	z	p-value
	amisulpride:aripiprazole	0	0	0.3305	.	0.3305	.	.	.
	amisulpride:asenapine	0	0	-0.5931	.	-0.5931	.	.	.
	amisulpride:cariprazine	0	0	-0.0685	.	-0.0685	.	.	.
	amisulpride:clozapine	0	0	-2.1000	.	-2.1000	.	.	.
	amisulpride:flupenthixol	1	0.60	-0.0842	-1.2000	1.5740	-2.7740	-1.76	0.0777
	amisulpride:fluphenazine	0	0	0.4073	.	0.4073	.	.	.
	amisulpride:haloperidol	0	0	0.9055	.	0.9055	.	.	.
	amisulpride:iloperidone	0	0	-1.0945	.	-1.0945	.	.	.
	amisulpride:lurasidone	0	0	0.1098	.	0.1098	.	.	.
	amisulpride:olanzapine	2	0.76	-2.0562	-1.6096	-3.4801	1.8705	1.84	0.0660
	amisulpride:placebo	0	0	0.5238	.	0.5238	.	.	.
	amisulpride:quetiapine	0	0	-0.9927	.	-0.9927	.	.	.
	amisulpride:risp_pali	1	0.18	-0.6961	-1.5000	-0.5201	-0.9799	-0.82	0.4127
	amisulpride:sertindole	0	0	-1.7840	.	-1.7840	.	.	.
	amisulpride:ziprasidone	0	0	2.1581	.	2.1581	.	.	.
	amisulpride:zotepine	0	0	-2.0157	.	-2.0157	.	.	.
	aripiprazole:asenapine	0	0	-0.9236	.	-0.9236	.	.	.
	aripiprazole:cariprazine	1	0.75	-0.3990	-0.3723	-0.4804	0.1081	0.08	0.9341
	aripiprazole:clozapine	0	0	-2.4304	.	-2.4304	.	.	.
	aripiprazole:flupenthixol	0	0	-0.4147	.	-0.4147	.	.	.
	aripiprazole:fluphenazine	0	0	0.0768	.	0.0768	.	.	.
	aripiprazole:haloperidol	0	0	0.5750	.	0.5750	.	.	.
	aripiprazole:iloperidone	0	0	-1.4250	.	-1.4250	.	.	.
	aripiprazole:lurasidone	0	0	-0.2207	.	-0.2207	.	.	.
	aripiprazole:olanzapine	2	0.24	-2.3867	-2.6352	-2.3073	-0.3279	-0.37	0.7091
	aripiprazole:placebo	2	0.43	0.1934	0.1659	0.2144	-0.0486	-0.07	0.9476
	aripiprazole:quetiapine	1	0.14	-1.3232	-1.7000	-1.2618	-0.4382	-0.36	0.7164
	aripiprazole:risp_pali	4	0.64	-1.0266	-0.7352	-1.5441	0.8089	1.08	0.2804
	aripiprazole:sertindole	0	0	-2.1145	.	-2.1145	.	.	.
	aripiprazole:ziprasidone	0	0	1.8277	.	1.8277	.	.	.
	aripiprazole:zotepine	0	0	-2.3461	.	-2.3461	.	.	.
	asenapine:cariprazine	0	0	0.5246	.	0.5246	.	.	.
	asenapine:clozapine	0	0	-1.5069	.	-1.5069	.	.	.
	asenapine:flupenthixol	0	0	0.5089	.	0.5089	.	.	.
	asenapine:fluphenazine	0	0	1.0004	.	1.0004	.	.	.
	asenapine:haloperidol	1	0.44	1.4986	0.3509	2.4137	-2.0627	-2.34	0.0192

asenapine:iloperidone	0	0	-0.5014	.	-0.5014	.	.	.
asenapine:lurasidone	0	0	0.7028	.	0.7028	.	.	.
asenapine:olanzapine	1	0.24	-1.4631	-1.1000	-1.5776	0.4776	0.53	0.5961
asenapine:placebo	3	0.85	1.1169	1.2393	0.4093	0.8300	0.81	0.4161
asenapine:quetiapine	0	0	-0.3996	.	-0.3996	.	.	.
asenapine:risp_pali	0	0	-0.1030	.	-0.1030	.	.	.
asenapine:sertindole	0	0	-1.1909	.	-1.1909	.	.	.
asenapine:ziprasidone	0	0	2.7512	.	2.7512	.	.	.
asenapine:zotepine	0	0	-1.4226	.	-1.4226	.	.	.
cariprazine:clozapine	0	0	-2.0314	.	-2.0314	.	.	.
cariprazine:flupenthixol	0	0	-0.0157	.	-0.0157	.	.	.
cariprazine:fluphenazine	0	0	0.4758	.	0.4758	.	.	.
cariprazine:haloperidol	0	0	0.9740	.	0.9740	.	.	.
cariprazine:iloperidone	0	0	-1.0260	.	-1.0260	.	.	.
cariprazine:lurasidone	0	0	0.1783	.	0.1783	.	.	.
cariprazine:olanzapine	0	0	-1.9877	.	-1.9877	.	.	.
cariprazine:placebo	1	0.73	0.5923	0.7723	0.1042	0.6681	0.56	0.5752
cariprazine:quetiapine	0	0	-0.9242	.	-0.9242	.	.	.
cariprazine:risp_pali	1	0.64	-0.6276	-0.8277	-0.2662	-0.5615	-0.51	0.6117
cariprazine:sertindole	0	0	-1.7155	.	-1.7155	.	.	.
cariprazine:ziprasidone	0	0	2.2267	.	2.2267	.	.	.
cariprazine:zotepine	0	0	-1.9471	.	-1.9471	.	.	.
clozapine:flupenthixol	0	0	2.0157	.	2.0157	.	.	.
clozapine:fluphenazine	0	0	2.5072	.	2.5072	.	.	.
clozapine:haloperidol	2	0.73	3.0054	4.0952	0.0732	4.0220	2.51	0.0122
clozapine:iloperidone	0	0	1.0054	.	1.0054	.	.	.
clozapine:lurasidone	0	0	2.2097	.	2.2097	.	.	.
clozapine:olanzapine	2	0.58	0.0437	-1.2115	1.7794	-2.9909	-2.01	0.0442
clozapine:placebo	0	0	2.6238	.	2.6238	.	.	.
clozapine:quetiapine	0	0	1.1072	.	1.1072	.	.	.
clozapine:risp_pali	1	0.48	1.4038	1.9000	0.9544	0.9456	0.64	0.5226
clozapine:sertindole	0	0	0.3159	.	0.3159	.	.	.
clozapine:ziprasidone	0	0	4.2581	.	4.2581	.	.	.
clozapine:zotepine	1	0.58	0.0843	-0.6500	1.1068	-1.7568	-0.99	0.3243
flupenthixol:fluphenazine	0	0	0.4915	.	0.4915	.	.	.
flupenthixol:haloperidol	0	0	0.9897	.	0.9897	.	.	.
flupenthixol:iloperidone	0	0	-1.0103	.	-1.0103	.	.	.

flupenthixol:lurasidone	0	0	0.1940	.	0.1940	.	.	.
flupenthixol:olanzapine	1	0.49	-1.9720	-3.4000	-0.6260	-2.7740	-1.76	0.0777
flupenthixol:placebo	0	0	0.6081	.	0.6081	.	.	.
flupenthixol:quetiapine	0	0	-0.9085	.	-0.9085	.	.	.
flupenthixol:risp_pali	0	0	-0.6119	.	-0.6119	.	.	.
flupenthixol:sertindole	0	0	-1.6998	.	-1.6998	.	.	.
flupenthixol:ziprasidone	0	0	2.2424	.	2.2424	.	.	.
flupenthixol:zotepine	0	0	-1.9314	.	-1.9314	.	.	.
fluphenazine:haloperidol	0	0	0.4982	.	0.4982	.	.	.
fluphenazine:iloperidone	0	0	-1.5018	.	-1.5018	.	.	.
fluphenazine:lurasidone	0	0	-0.2975	.	-0.2975	.	.	.
fluphenazine:olanzapine	0	0	-2.4635	.	-2.4635	.	.	.
fluphenazine:placebo	0	0	0.1165	.	0.1165	.	.	.
fluphenazine:quetiapine	1	1.00	-1.4000	-1.4000	.	.	.	.
fluphenazine:risp_pali	0	0	-1.1034	.	-1.1034	.	.	.
fluphenazine:sertindole	0	0	-2.1913	.	-2.1913	.	.	.
fluphenazine:ziprasidone	0	0	1.7508	.	1.7508	.	.	.
fluphenazine:zotepine	0	0	-2.4229	.	-2.4229	.	.	.
haloperidol:iloperidone	1	1.00	-2.0000	-2.0000	.	.	.	.
haloperidol:lurasidone	0	0	-0.7957	.	-0.7957	.	.	.
haloperidol:olanzapine	5	0.59	-2.9617	-3.3612	-2.3916	-0.9696	-1.50	0.1340
haloperidol:placebo	1	0.24	-0.3816	0.0000	-0.5005	0.5005	0.64	0.5212
haloperidol:quetiapine	1	0.09	-1.8982	-1.9100	-1.8970	-0.0130	-0.01	0.9924
haloperidol:risp_pali	2	0.28	-1.6016	-1.9145	-1.4789	-0.4356	-0.59	0.5555
haloperidol:sertindole	0	0	-2.6895	.	-2.6895	.	.	.
haloperidol:ziprasidone	0	0	1.2527	.	1.2527	.	.	.
haloperidol:zotepine	1	0.62	-2.9211	-2.2500	-4.0068	1.7568	0.99	0.3243
iloperidone:lurasidone	0	0	1.2043	.	1.2043	.	.	.
iloperidone:olanzapine	0	0	-0.9617	.	-0.9617	.	.	.
iloperidone:placebo	0	0	1.6184	.	1.6184	.	.	.
iloperidone:quetiapine	0	0	0.1018	.	0.1018	.	.	.
iloperidone:risp_pali	0	0	0.3984	.	0.3984	.	.	.
iloperidone:sertindole	0	0	-0.6895	.	-0.6895	.	.	.
iloperidone:ziprasidone	0	0	3.2527	.	3.2527	.	.	.
iloperidone:zotepine	0	0	-0.9211	.	-0.9211	.	.	.
lurasidone:olanzapine	1	0.19	-2.1660	-3.1000	-1.9448	-1.1552	-1.32	0.1860
lurasidone:placebo	4	0.83	0.4141	0.7235	-1.0558	1.7793	2.17	0.0304

lurasidone:quetiapine	1	0.28	-1.1025	-0.4854	-1.3371	0.8516	1.02	0.3075
lurasidone:risp_pali	0	0	-0.8059	.	-0.8059	.	.	.
lurasidone:sertindole	0	0	-1.8938	.	-1.8938	.	.	.
lurasidone:ziprasidone	1	0.40	2.0484	0.3000	3.2180	-2.9180	-2.30	0.0216
lurasidone:zotepine	0	0	-2.1254	.	-2.1254	.	.	.
olanzapine:placebo	11	0.53	2.5801	2.4032	2.7830	-0.3798	-1.00	0.3157
olanzapine:quetiapine	3	0.25	1.0635	0.3726	1.2979	-0.9252	-1.46	0.1452
olanzapine:risp_pali	16	0.66	1.3601	1.3378	1.4037	-0.0659	-0.17	0.8644
olanzapine:sertindole	0	0	0.2722	.	0.2722	.	.	.
olanzapine:ziprasidone	2	0.68	4.2144	5.1518	2.2338	2.9180	2.30	0.0216
olanzapine:zotepine	0	0	0.0406	.	0.0406	.	.	.
placebo:quetiapine	5	0.57	-1.5165	-1.3575	-1.7279	0.3704	0.74	0.4584
placebo:risp_pali	15	0.66	-1.2200	-1.2901	-1.0821	-0.2079	-0.57	0.5668
placebo:sertindole	0	0	-2.3078	.	-2.3078	.	.	.
placebo:ziprasidone	0	0	1.6343	.	1.6343	.	.	.
placebo:zotepine	0	0	-2.5395	.	-2.5395	.	.	.
quetiapine:risp_pali	4	0.40	0.2966	0.5514	0.1261	0.4253	0.79	0.4267
quetiapine:sertindole	0	0	-0.7913	.	-0.7913	.	.	.
quetiapine:ziprasidone	0	0	3.1508	.	3.1508	.	.	.
quetiapine:zotepine	0	0	-1.0229	.	-1.0229	.	.	.
risp_pali:sertindole	2	1.00	-1.0879	-1.0879	.	.	.	.
risp_pali:ziprasidone	0	0	2.8543	.	2.8543	.	.	.
risp_pali:zotepine	0	0	-1.3195	.	-1.3195	.	.	.
sertindole:ziprasidone	0	0	3.9422	.	3.9422	.	.	.
sertindole:zotepine	0	0	-0.2316	.	-0.2316	.	.	.
ziprasidone:zotepine	0	0	-4.1738	.	-4.1738	.	.	.

## eAppendix 5. Sensitivity Analyses

The sensitivity of our findings for all 7 outcomes were evaluated by repeating analyses following exclusion of studies examining patients with first episode psychosis (4 studies), treatment resistant schizophrenia (5 studies), and older adults (2 studies). After exclusion of these trials the hierarchy did not change considerably (see eFigures 11-17). Tests of heterogeneity and inconsistency were as follows:

For change in weight,  $\tau$  was 0.61kg, and  $I^2$  72.1%. The global Q score for inconsistency was 83.97 ( $p < 0.0001$ ), and significant hot-spots of inconsistency identified in 5 of 154 treatment comparisons.

For change in BMI,  $\tau$  was 0.10kg/m<sup>2</sup>, and  $I^2$  26.1%. The global Q score for inconsistency was 12.48 ( $p = 0.13$ ), and no hot-spots of inconsistency identified in treatment comparisons.

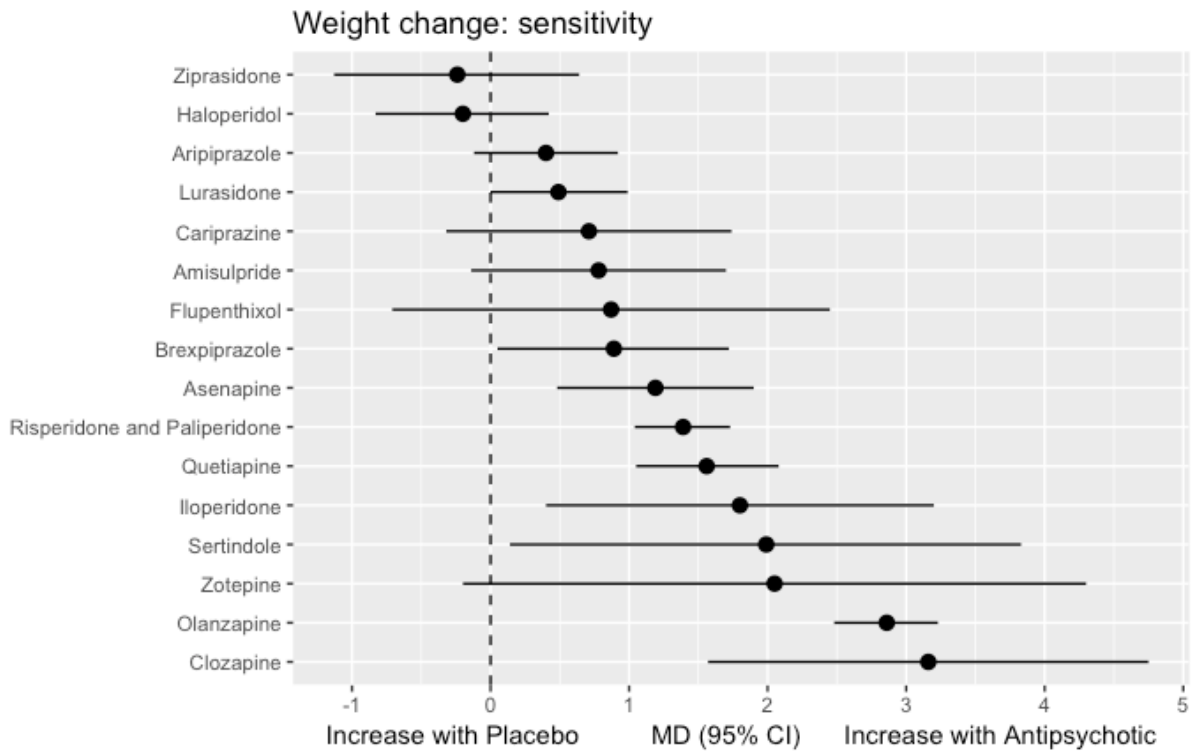
For change in total cholesterol,  $\tau$  was 0.08mmol/L, and  $I^2$  46.5%. The global Q score for inconsistency was 26.37 ( $p = 0.02$ ), and a significant hot-spot of inconsistency identified in 1 of 91 treatment comparisons.

For change in LDL cholesterol,  $\tau$  was 0.04mmol/L, and  $I^2$  19.5%. The global Q score for inconsistency was 22.67 ( $p = 0.03$ ), and no hot-spots of inconsistency identified in treatment comparisons.

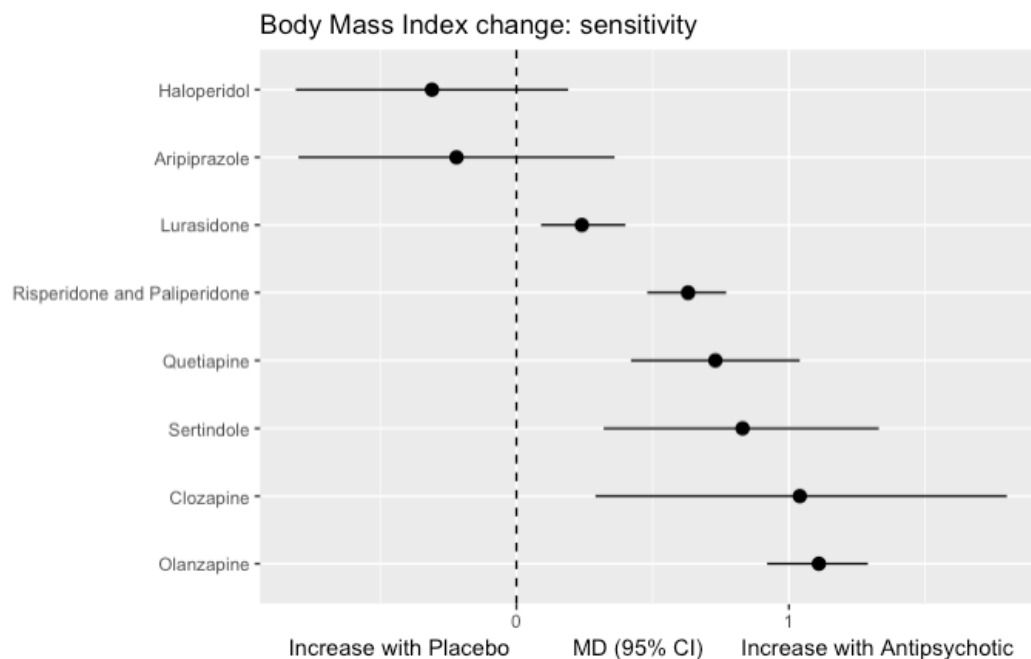
For change in HDL cholesterol,  $\tau$  was 0.03mmol/L, and  $I^2$  54.5%. The global Q score for inconsistency was 22.74 ( $p = 0.01$ ), and a significant hot-spot of inconsistency identified in 1 of 45 treatment comparisons.

For change in triglycerides,  $\tau$  was 0.07mmol/L, and  $I^2$  43.8%. The global Q score for inconsistency was 4.53 ( $p = 0.98$ ), and significant inconsistency hot-spots identified in 2 of 105 treatment comparisons.

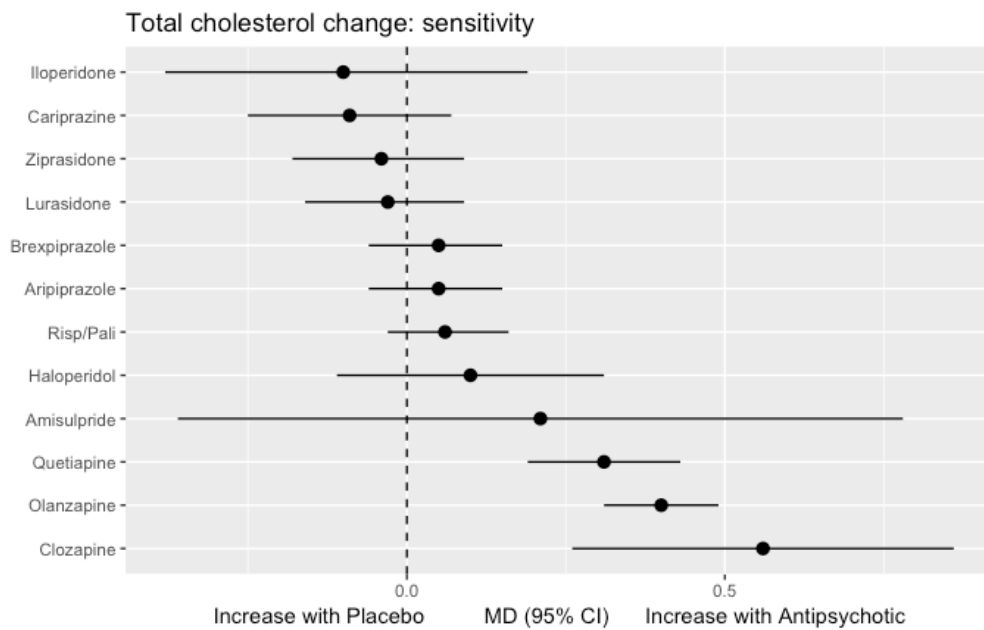
For change in glucose,  $\tau$  was 0.18mmol/L, and  $I^2$  statistic 63.1%. The global Q score for inconsistency was 31.32 ( $p < 0.01$ ), and a significant hot-spot of inconsistency identified in 1 of the 103 treatment comparisons.



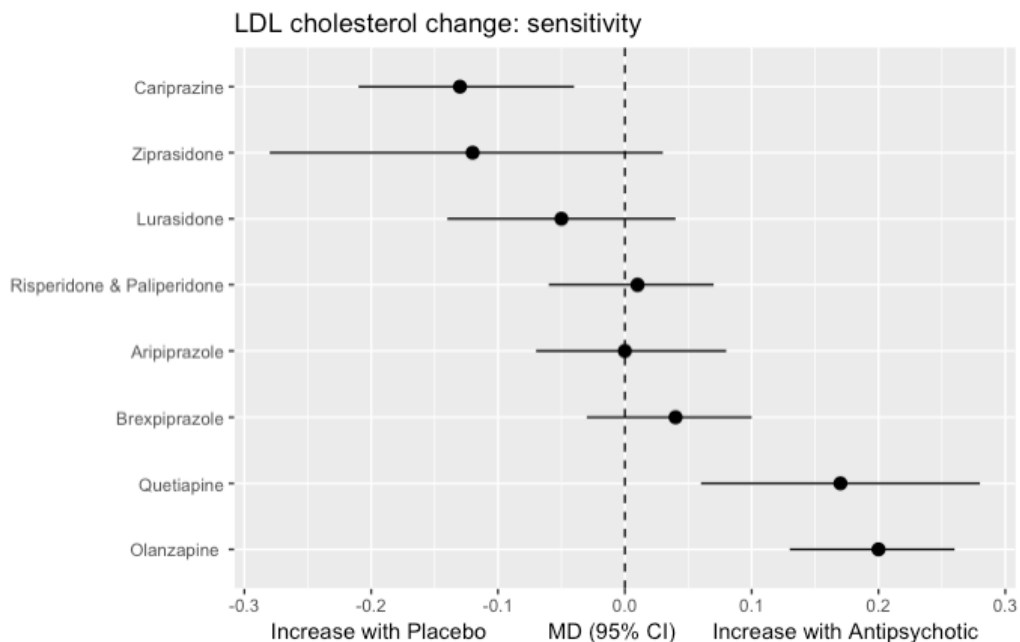
**eFigure 11. Weight change, exclusion of studies examining first episode psychosis, treatment resistant schizophrenia, and older adults.** Treatments are ranked according to mean difference (kg) compared to placebo. Mean differences are presented alongside 95% confidence intervals.



**eFigure 12. Body Mass Index (BMI) change, exclusion of studies examining first episode psychosis, treatment resistant schizophrenia, and older adults.** Treatments are ranked according to mean difference (kg/m<sup>2</sup>) compared to placebo. Mean differences are presented alongside 95% confidence intervals.

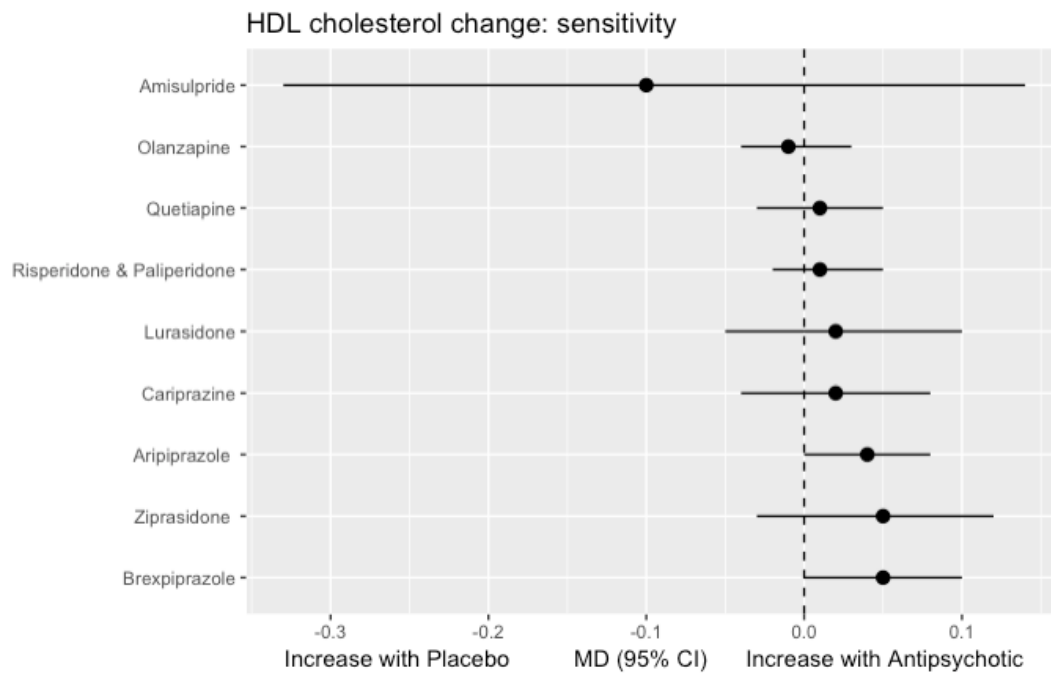


**eFigure 13. Total cholesterol change, exclusion of studies examining first episode psychosis, treatment resistant schizophrenia, and older adults.** Treatments are ranked according to mean difference (mmol/L) compared to placebo. Mean differences are presented alongside 95% confidence intervals.

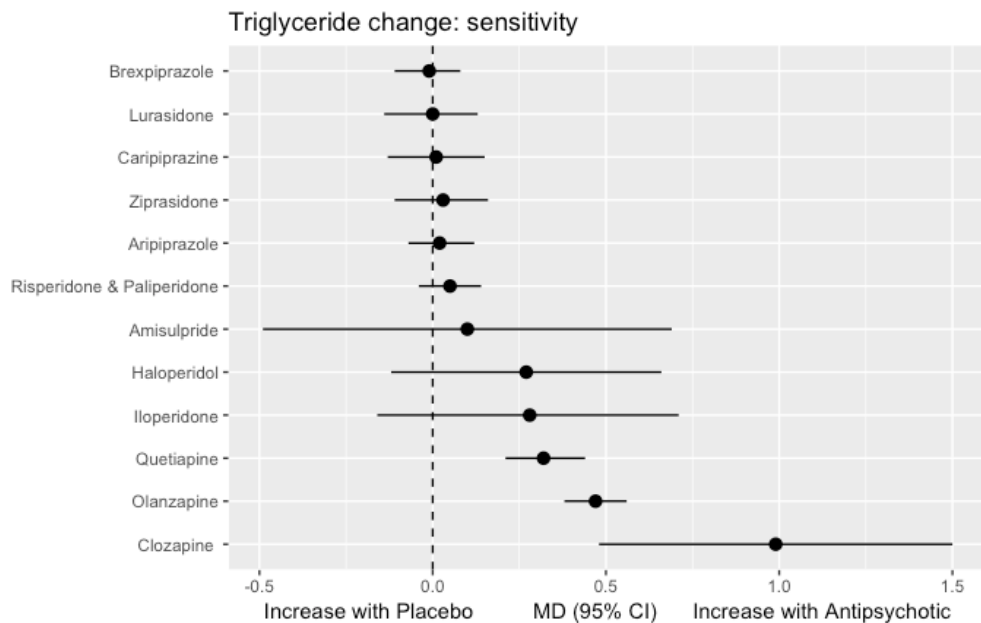


**eFigure 14. Low Density Lipoprotein (LDL) cholesterol change, exclusion of studies examining first episode psychosis, treatment resistant schizophrenia, and older adults.** Treatments are ranked according to mean difference (mmol/L) compared to placebo. Mean differences are presented alongside 95% confidence intervals.

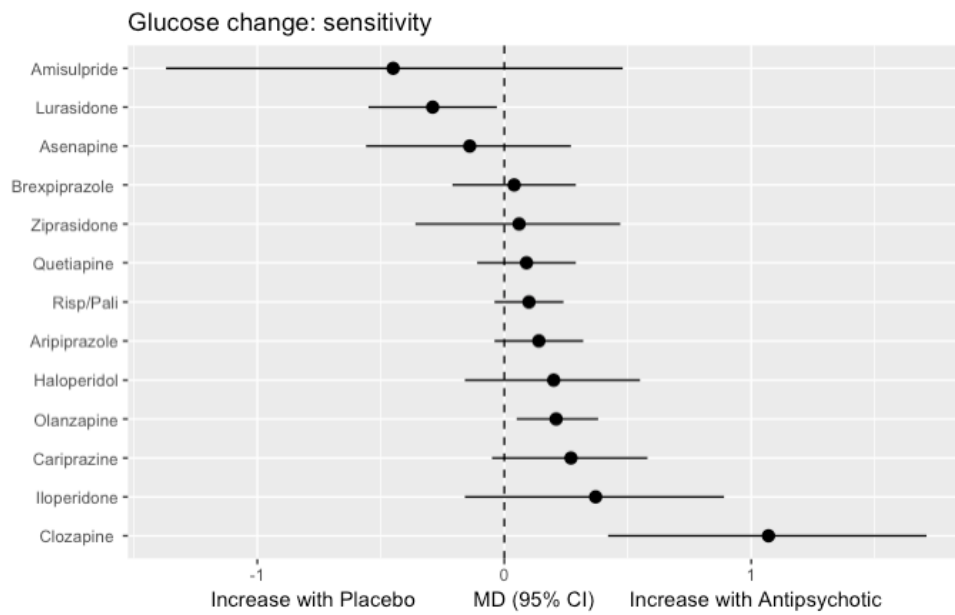




**eFigure 15. High Density Lipoprotein (HDL) cholesterol change, exclusion of studies examining first episode psychosis, treatment resistant schizophrenia, and older adults.** Treatments are ranked according to mean difference (mmol/L) compared to placebo. Mean differences are presented alongside 95% confidence intervals.



**eFigure 16. Triglyceride change, exclusion of studies examining first episode psychosis, treatment resistant schizophrenia, and older adults.** Treatments are ranked according to mean difference (mmol/L) compared to placebo. Mean differences are presented alongside 95% confidence intervals.



**eFigure 17. Glucose change, exclusion of studies examining first episode psychosis, treatment resistant schizophrenia, and older adults.** Treatments are ranked according to mean difference (mmol/L) compared to placebo. Mean differences are presented alongside 95% confidence intervals.

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