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# **eMethods 1**.PRISMA NMA Checklist

|  |  |  |  |
| --- | --- | --- | --- |
| **Section/Topic** | **Item #** | **Checklist Item** | **Reported on Page #** |
| **TITLE** |  |  |  |
| Title | 1 | Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).* | **1** |
| **ABSTRACT** |  |  |  |
| Structured summary | 2 | Provide a structured summary including, as applicable:  **Background:** main objectives  **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.*  **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; *treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.*  **Discussion/Conclusions:** limitations; conclusions and implications of findings.  **Other:** primary source of funding; systematic review registration number with registry name. | 4 |
| **INTRODUCTION** |  |  |  |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known*, including mention of why a network meta-analysis has been conducted.* | **5** |
| Objectives | 4 | Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 6 |
| **METHODS** |  |  |  |
| Protocol and registration | 5 | Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number. | 6 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. *Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).* | **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. | 6 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 6 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 6 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 7 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 7 |
| **Geometry of the network** | **S1** | Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers. | **7** |
| 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. | 7 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.* | 7 |
| Planned methods of analysis | 14 | Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to:   * *Handling of multi-arm trials;* * *Selection of variance structure;* * *Selection of prior distributions in Bayesian analyses; and* * *Assessment of model fit.* | 7,8 |
| **Assessment of Inconsistency** | **S2** | Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found. | 7 |
| 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). | **7** |
| Additional analyses | 16 | Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following:   * Sensitivity or subgroup analyses; * Meta-regression analyses; * *Alternative formulations of the treatment network; and* * *Use of alternative prior distributions for Bayesian analyses (if applicable).* | **8** |
| **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. | 8,9 |
| **Presentation of network structure** | **S3** | Provide a network graph of the included studies to enable visualization of the geometry of the treatment network. |  |
| **Summary of network geometry** | **S4** | Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure. | **9** |
| 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. | 8,9 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment. | 9 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.* | **10-12** |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence/credible intervals. *In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons.* If additional summary measures were explored (such as treatment rankings), these should also be presented. | **10-12** |
| **Exploration for inconsistency** | **S5** | Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network. | **16** |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies for the evidence base being studied. | 9 |
| Results of additional analyses | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses*, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses,* and so forth). | **10-12** |
| **DISCUSSION** |  |  |  |
| Summary of evidence | 24 | Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers). | 13-16 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).* | 16 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 17 |
| **FUNDING** |  |  |  |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network. | **2** |

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

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

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

# **eMethods 2.** Full search strategy for PubMed.

((("Antipsychotic Agents"[Mesh] OR "Tranquilizing Agents"[Mesh] OR Antipsychotic\*[TIAB] OR “Major Tranquilizers” [TIAB] OR “Tranquillizing Agents” [TIAB] OR “Major Tranquillizing Agents” [TIAB] OR Neuroleptic\* [TIAB] OR Antipsychotic\* [TIAB] OR Amisulpride[TIAB] OR Aripiprazole[TIAB] OR Asenapine[TIAB] OR Chlorpromazine[TIAB] OR Clozapine[TIAB] OR Droperidol[TIAB] OR Fluphenazine[TIAB] OR Haloperidol[TIAB] OR Iloperidone[TIAB] OR Loxapine[TIAB] OR Lurasidone[TIAB] OR Mesoridazine[TIAB] OR Molindone[TIAB] OR Olanzapine[TIAB] OR Paliperidone[TIAB] OR Periciazine[TIAB] OR Perphenazine[TIAB] OR Pimozide[TIAB] OR Promazine[TIAB] OR Quetiapine[TIAB] OR Risperidone[TIAB] OR Sertindole[TIAB] OR Sulpiride[TIAB] OR Thioridazine[TIAB] OR Trifluoperazine[TIAB] OR Ziprasidone[TIAB] OR Zotepine[TIAB] OR Zuclopenthixol[TIAB]))) AND (("Blood Glucose"[Mesh] OR "Glycated Hemoglobin A"[Mesh] OR "Hemoglobin A"[Mesh] OR "Hemoglobins"[Mesh] OR "Glycemic Index"[Mesh] OR "Hyperglycemia"[Mesh] OR "Hypoglycemia"[Mesh] OR "Hyperlipidemias"[Mesh] OR "Cholesterol"[Mesh] OR "Lipoproteins"[Mesh] OR "Triglycerides"[Mesh] OR “Hb A1” [TIAB] OR "Glycated Hemoglobin A"[TIAB] OR “Glycosylated Hemoglobin A” [TIAB] OR “Glycohemoglobin A” [TIAB] OR “Hemoglobin A(1)” [TIAB] OR Hyperglycemia [TIAB] OR Hypoglycemia [TIAB] OR glycemia[TIAB] or glycaemia[TIAB] or glucose [TIAB] OR cholesterol [TIAB] OR cholesterolemia\* [TIAB] OR lipemia [TIAB] OR lipoproteinemia [TIAB] OR triglyceridemia [TIAB]OR HDL [TIAB] OR Lipoproteins[TIAB] OR “High-Density Lipoprotein” [TIAB] OR “High Density Lipoproteins” [TIAB] OR “alpha-Lipoproteins” [TIAB] OR “alpha Lipoproteins” [TIAB] OR “alpha-1 Lipoprotein” [TIAB] OR “Low Density Lipoprotein” [TIAB] OR “beta-Lipoprotein Cholesterol” [TIAB] OR “LDL Cholesteryl Linoleate” [TIAB] OR “VLDL” [TIAB] OR “Pre-beta-Lipoprotein Cholesterol” [TIAB] OR “Very Low Density Lipoprotein” [TIAB] OR “Prebetalipoprotein Cholesterol” OR Triglyceride\*[TIAB] OR Triacylglycerol\* [TIAB] OR fatty [TIAB] OR “insulin” [TIAB] OR “HOMA” [TIAB])) AND TRIAL

# **eTable 1.** Characteristics of 98 studies included in the systematic review.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Study**  **duration**  **(weeks)** | **Type of study design** | **Population type** | **Treatment** | **Sample size** | **Males**  **(%)** | **Age**  **(years)**  **[mean±SD;(range)]** | **Dose**  **(mg/day)**  **[mean±SD; (range)]** | **Outcomes with changes from baseline** | **Network meta-analysis**  **(Y/N)** |
| Aliyazicioǧlu 2007 | 24 | open label  single arm | BD I | OLZ | 15 | 46 | 37 ± 8.2 | 5-20 | Tryglicerides;  Total cholesterol; HDL; LDL | N |
| Atmaca 2003 | 6 | open label  parallel | SCZ or PSC | CLZ | 13 | 38 | 31.3 ± 7.2 | 207.1 ± 62.4 | Weight; BMI;  Tryglicerides;  Leptin | Y |
| OLZ | 13 | 46 | 29.6 ± 8.1 | 15.7 ± 4.8 | Weight; BMI;  Tryglicerides;  Leptin |
| QTP | 14 | 43 | 30.1 ± 8.4 | 535.7 ± 110.5 | Weight; BMI;  Tryglicerides;  Leptin |
| RIS | 13 | 54 | 27.9 ± 7.8 | 6.7 ± 3.6 | Weight; BMI;  Tryglicerides;  Leptin |
| Baptista 1997 | 4 | open label  parallel | NHV | PBO | 17 | 0 | 24.7±6.5 | none | Tryglicerides;  Total cholesterol; HDL; LDL | N |
| SLP | 17 | 0 | 21.6±4.9 | 200 | Tryglicerides;  Total cholesterol; HDL; LDL |
| Baptista 2007 | 16 | open label single arm | SCZ or PSC | OLZ | 60 | 57 | NA | (10-20) | Weight; BMI;  Waist Circumference;  Glucose;  Insulin; HOMA-IR | N |
| Bobo 2010 | 8 | open label single arm | mania or BD | OLZ | 20 | 35 | 38.8±9.5  (18-60) | 15 | Weight; BMI;  Waist Circumference;  Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL | N |
| Boku 2011 | 8 | open label  single arm | MD | OLZ | 11 | 0 | 53.2 ± 24 | 5 ± 1.9 | Weight;  Glucose;  Tryglicerides;  Total cholesterol | N |
| Breier 2005 | 28 | double blind  parallel | SCZ or PSC | OLZ | 277 | 65 | 40.1±11.6  (18-75) | 15.27±4.52 | Weight;  Glucose;  Tryglicerides;  Total cholesterol; HDL | Y |
| ZPR | 271 | 63 | 38.2±12.1  (18-75) | 115.96±39.9 | Weight;  Glucose;  Tryglicerides;  Total cholesterol; HDL |
| Calabrese 2015 | 6 | double blind parallel | mania or BD | CARI | 169 | 50 | 41.2±11.3  (18-65) | 9.1  (6-12) | Weight;  Glucose | N |
| CARI | 167 | 54 | 43.1±12.2  (18-65) | 4.8  (3-6) | Weight;  Glucose |
| PBO | 161 | 55 | 41.5±11.4  (18-65) | none | Weight;  Glucose |
| Cantillon 2017 | 6 | double blind parallel | SCZ or PSC | ARI | 20 | 90 | 35±10  (18-65) | 15 | BMI;  Glucose | N |
| PBO | 38 | 71 | 36±12  (18-65) | none | BMI;  Glucose |
| Canuso 2010 | 6 | double blind  parallel | SCZ or PSC | PBO | 107 | 63 | 37.1± 11.1 | NA | Weight;  Glucose  Tryglicerides; HDL; LDL | Y |
| PP | 105 | 67 | 38.1± 10 | 5.7 ± 0.9 | Weight;  Glucose;  Tryglicerides; HDL; LDL |
| Casey 2008 | 6 | double blind parallel | SCZ or PSC | PBO | 114 | 77 | 40.8±9.4  (18-65) | none | Weight;  Tryglicerides;  Total cholesterol | Y |
| RIS | 116 | 81 | 41.1±8.6  (18-65) | 6 | Weight;  Tryglicerides;  Total cholesterol |
| Chan 2007 | 4 | double blind  parallel | SCZ or PSC | ARI | 49 | 47 | 35.2± 10.9 | 15 | Weight;  Glucose;  Total cholesterol | Y |
| RIS | 34 | 65 | 35.1 ± 8.6 | 6 | Weight;  Glucose;  Total cholesterol |
| Chen 2008 | 6 | open label  single arm | SCZ or PSC | RIS | 30 | 53 | 35.5± 11.5 | NA | BMI;  HOMA-IR | N |
| Chen 2011 | 8 | open label single arm | SCZ or PSC | QTP | 17 | 65 | 36.4±7.4  (18-60) | 435.3±78.6  (300-800) | Weight; BMI;  Glucose;  Insulin; HOMA-IR;  Tryglicerides;  Total cholesterol; HDL | N |
| Chiu 2006 | 2 | open label parallel | SCZ or PSC | OLZ | 13 | NA | 37.3±8.3  (18-60) | 10 | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| RIS | 13 | NA | 37.3±8.3  (18-60) | 2 | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Cutler 2013 | 25 | open label single arm | SCZ or PSC | ILO | 86 | 78 | 39±11.2  (18-65) | (12-24) | Weight;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol; HDL | N |
| ILO | 41 | 76 | 39.3±11.2  (18-67) | (12-24) | Weight;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol; HDL |
| ILO | 173 | 76 | 39.1±10.6  (18-64) | 21.6  (12-24) | Weight;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol; HDL |
| ILO | 46 | 74 | 39.1±8.8  (18-66) | (12-24) | Weight;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol; HDL |
| Davidson 2007 | 6 | double blind parallel | SCZ or PSC | OLZ | 126 | 76 | 36.5±10.2 | 10 | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL | Y |
| PP | 123 | 63 | 36.3±11 | 3 | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| PP | 123 | 64 | 36.2±10.9 | 9 | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| PP | 113 | 65 | 37.6±9.8 | 15 | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| PBO | 120 | 69 | 37.3±10.9 | none | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| De Hert 2011 | 60 | open label parallel | SCZ or PSC | RIS | 130 | 46 | 37  (18-62) | 4\* | Weight; BMI;  Waist Circumference;  Glucose;  Tryglicerides;  Total cholesterol; HDL | Y |
| SER | 131 | 49 | 35  (20-66) | 12\* | Weight; BMI;  Waist Circumference;  Glucose;  Tryglicerides;  Total cholesterol; HDL |
| DelBello 2017 | 6 | double blind  parallel | ASD/BD | LRS | 173 | 50.9 | 14.2 ± 2.2 | 32.5 | Weight; BMI;  Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL | N |
| PBO | 170 | 51.2 | 14.3 ± 2 | NA | Weight; BMI;  Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Durgam 2015 | 3 | double blind Parallel | MPD | CARI | 118 | 68 | 38±10.3  (18-65) | 8.8  (3-12) | Weight;  Glucose;  Tryglicerides;  Total cholesterol; HDL | Y |
| PBO | 118 | 65 | 38.7±11  (18-65) | none | Weight;  Glucose;  Tryglicerides;  Total cholesterol; HDL |
| Emsley 2004 | 52 | single blind parallel | SCZ or PSC | HAL | 23 | 65 | 50.1±8.6  (18-65) | 8.5±5.6  (10-20) | Weight;  HbA1c | Y |
| QTP | 22 | 64 | 49.2±4.5  (18-65) | 400±147.7  (400-800) | Weight;  HbA1c |
| Ercan 2012 | 8 | open label  single arm | ADHD and Conduct Disorder | ARI | 20 | 95 | 10.1 ± 2.7 | 8.55 ± 1.73 | Weight;  Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL | N |
| Faghihi 2012 | 12 | open label  single arm | SCZ or PSC or BD | OLZ | 37 | 86 | 30.83 ± 9.96 | 8.37 ± 4.21 | Weight; BMI;  Waist Circumference;  Glucose;  Insulin; HOMA-IR  Tryglicerides;  Total cholesterol; LDL; HDL; | N |
| Findling 2012 | 6 | Double blind parallel | SCZ or PSC | PBO | 73 | 58 | 15.3±1.39  (13-17) | none | Weight; BMI;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL | N |
| QTP | 74 | 60 | 15.4±1.34  (13-17) | 800 | Weight; BMI;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL |
| QTP | 73 | 59 | 15.4±1.25  (13-17) | 400 | Weight; BMI;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Findling 2013 | 26 | open label single arm | mania or BD | ZPR | 162 | NA | 13.3±2.1  (10-17) | (40-160) | Weight;  Waist Circumference;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL | N |
| Findling 2014 | 8 | double blind parallel | mania or BD | PBO | 100 | 52 | 14±2.1  (10-17) | none | Glucose;  Tryglicerides;  Total cholesterol; HDL | N |
| QTP | 92 | 49 | 13.9±2.2  (10-17) | (150-300) | Glucose;  Tryglicerides;  Total cholesterol; HDL |
| Fleischhacker 2009 | 52 | double blind parallel | SCZ or PSC | ARI | 355 | 57 | 35.9  (18-64) | 23  (15-30) | Weight | N |
| OLZ | 348 | 56 | 37.3  (18-65) | 15.4  (10-20) | Weight |
| Fountaine 2010 | 2 | double blind crossover | NHV | OLZ | 15 | 100 | 27  (18-49) | (5-10) | Insulin;  Tryglicerides | N |
| PBO | 15 | 100 | 27  (18-49) | none | Insulin;  Tryglicerides |
| Glick 2009 | 4 | double blind parallel | SCZ or PSC | ARI | 123 | 55 | 38±10.8  (18-65) | (15-30) | Weight;  Glucose;  Total cholesterol | N |
| PBO | 56 | 54 | 36.5±9  (18-65) | NA | Weight;  Glucose;  Total cholesterol |
| Grootens 2011 | 8 | double blind parallel | SCZ or PSC | OLZ | 35 | 86 | 23.1±4.4  (18-40) | (10-20) | Weight;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol | Y |
| ZPR | 39 | 79 | 24.3±4.5  (18-40) | (40-80) | Weight;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol |
| Harvey 2019 | 8 | double blind  parallel | SCZ or PSC | BNS | 129 | 58 | 41.9 ± 12.7 | 15.7 ± 6 | Weight | N |
| HAL | 132 | 59 | 42.9 ± 13.2 | 7.9 ± 3 | Weight |
| Hashimoto 2015 | 52 | open label  single arm | SCZ or PSC | QTP | 22 | 83 | 52.1 ± 14.4 | 438.6 ± 261.7 | Weight | N |
| Higuchi 2019 | 6 | double blind  parallel | SCZ or PSC | LRS | 150 | 54.7 | 42.1 ± 13 | NA | Weight; BMI;  Glucose; Hb1A;  Tryglicerides;  Total cholesterol; LDL | Y |
| PBO | 151 | 58.9 | 42.6 ± 13.4 | NA | Weight; BMI;  Glucose; Hb1A;  Tryglicerides;  Total cholesterol; LDL |
| Hoffmann 2009 | 3 | open label parallel | NHV | OLZ | 7 | 29 | 35.6±14.7  (20-66) | (5-10) | Weight;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol;HDL; LDL | N |
| OLZ | 9 | 22 | 29.1±7.8  (22-43) | (5-10) | Weight;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Hosojima 2006 | 4 | open label single arm | SCZ or PSC | OLZ | 13 | 69 | 37  (20-56) | 14.5  (7.5-20) | Weight; BMI;  Glucose;  Insulin; HOMA-IR | N |
| Hsieh 2010 | 64 | open label  single arm | SCZ or PSC | ARI | 245 | 40.;8 | 37 ± 10.9 | NA | Weight; BMI;  Glucose;  Tryglicerides;  Total cholesterol; | N |
| Huang 2020 | 12 | open label  single arm | SCZ or PSC | OLZ | 33 | 36 | 23.5 | NA | Weight; BMI;  Glucose;  Insulin; HOMA-IR;  Tryglicerides;  Total cholesterol; HDL; LDL | N |
| Hwang 2003 | 4 | open label single arm | MPD | OLZ | 80 | 76 | 74.2±5.3  (65-87) | 10.1  (2.5-20) | Weight;  Glucose;  Tryglicerides;  Total cholesterol | N |
| Ingole 2009 | 12 | open label parallel | SCZ or PSC | OLZ | 30 | 37 | 25.3±0.82  (18-60) | 10 | Weight; BMI;  Glucose | Y |
| RIS | 30 | 47 | 26.6±0.95  (18-60) | 6 | Weight; BMI;  Glucose |
| Jena 2020 | 6 | open label  parallel | SCZ or PSC | OLZ | 51 | 65 | 31.59 ± 10.3 | NA | BMI;  Glucose; HbA1c;  Insulin; HOMA-IR  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| LRS | 50 | 50 | 33.88 ± 9.25 | NA | BMI;  Glucose; HbA1c;  Insulin; HOMA-IR  Tryglicerides;  Total cholesterol; HDL; LDL |
| Jindal 2013 | 6 | double blind  parallel | SCZ or PSC | ARI | 30 | 63.3 | NA | 12.5 ± 2.55 | Glucose;  Tryglicerides;  Total cholesterol | Y |
| OLZ | 30 | 50 | NA | 11.01 ± 2.12 | Glucose;  Tryglicerides;  Total cholesterol |
| Kane 2007 | 6 | double blind parallel | SCZ or PSC | OLZ | 128 | 47 | 36.3±11.2 | 10 | Weight; BMI;  Glucose; Insulin;  Tryglicerides;  Total cholesterol; HDL | Y |
| PP | 123 | 50 | 37±10.2 | 6 | Weight; BMI;  Glucose; Insulin;  Tryglicerides;  Total cholesterol; HDL |
| PP | 129 | 53 | 36±10.6 | 12 | Weight; BMI;  Glucose; Insulin;  Tryglicerides;  Total cholesterol; HDL |
| PP | 122 | 59 | 38.5±11.4 | 9 | Weight; BMI;  Glucose; Insulin;  Tryglicerides;  Total cholesterol; HDL |
| PBO | 126 | 52 | 37.9±10.9 | none | Weight; BMI;  Glucose; Insulin;  Tryglicerides;  Total cholesterol; HDL |
| Kang 2016 | 8 | open label single arm | SCZ or PSC | PP | 75 | 55 | 30.8±11  (18-59) | 8.74±2.78  (3-12) | BMI;  Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL | N |
| Karagianis 2009 | 16 | double blind parallel | MPD | OLZ | 84 | 57 | 39±13  (18-65) | 14.33  (5-20) | Weight; BMI;  Waist Circumference;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL | N |
| OLZ | 65 | 51 | 39±12  (18-65) | 14.9  (5-20) | Weight; BMI;  Waist Circumference;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| Katzman 2011 | 52 | double blind  parallel | generalized anxiety disorder | PBO | 216 | 36.6 | 41.65 ± 12.15 | NA | Weight;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| QTP | 216 | 32.9 | 44.78 ± 10.99 | 162.8 ± 88.3 | Weight;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Kelly 2008 | 8 | double blind parallel | SCZ or PSC | OLZ | 189 | 73 | 38.9±10.5  (18-64) | 13.1±5.1  (5-20) | Weight; BMI;  HbA1c;  Tryglicerides;  Total cholesterol; HDL | Y |
| RIS | 188 | 72 | 41±11  (18-64) | 4.7±1.4  (2-6) | Weight; BMI;  HbA1c;  Tryglicerides;  Total cholesterol; HDL |
| Kim 2012 | 24 | open label  single arm | SCZ | PP | 243 | 47 | 36.4 ± 10 | NA | Weight;  Glucose;  Tryglicerides;  Total cholesterol; HDL | N |
| Kim 2018 | 12 | open label  single arm | ASD | ARI | 67 | 77.6 | 10 ± 3.1 | 5.1± 2.5 | Weight | N |
| Kinon 2006 | 24 | double blind parallel | SCZ or PSC | OLZ | 202 | NA | (18-60) | (10-20) | Weight;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol | Y |
| ZPR | 192 | NA | (18-60) | (80-160) | Weight;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol |
| Ko 2014 | 12 | open label single arm | SCZ or PSC | ZPR | 67 | 28 | 36.8±8.9  (18-55) | 101.5±47  (20-160) | Tryglicerides | N |
| Konstantinidis 2007 | 6 | open label  single arm | unipolar psychotic depression | QTP | 24 | 29.2 | 51.4 ± 14.2 | 303 ± 118 | Weight | N |
| Kryzhanovskaya 2009 | 6 | double blind parallel | SCZ or PSC | OLZ | 72 | 71 | 16.1±1.3  (13-18) | 11.1  (2.5-20) | Weight; BMI;  Glucose;  Tryglicerides;  Total cholesterol; HDL | N |
| PBO | 35 | 69 | 16.3±1.6  (13-18) | none | Weight; BMI;  Glucose;  Tryglicerides;  Total cholesterol; HDL |
| Kusumi 2012 | 12 | open label parallel | SCZ or PSC | OLZ | 61 | 38 | 44.3±14 | 15.2 | Glucose; HbA1c;  Tryglicerides;  Total cholesterol; HDL | N |
| OLZ | 57 | 61 | 43.8±12.9 | 15.7 | Glucose; HbA1c;  Tryglicerides;  Total cholesterol; HDL |
| Li 2016 | 8 | double-blind  parallel | BD | PBO | 140 | 47.9 | 32.8 ± 11 | NA | Glucose; Hb1A;  Insulin | Y |
| QTP | 139 | 48.2 | 33.4 ± 11.9 | NA | Glucose; Hb1A;  Insulin |
| Lieberman 2003 | 52 | double blind parallel | SCZ or PSC | CPZ | 80 | 52 | 28.7±6.9  (15-42) | 400\* | Glucose | N |
| CLZ | 80 | 52 | 28.7±6.9  (15-42) | 300\* | Glucose |
| Lindenmayer 2003 | 14 | double blind parallel | SCZ or PSC | CLZ | 28 | 89 | NA | 477.2±157.2 | Glucose;  Total cholesterol | Y |
| HAL | 25 | 80 | NA | 25.8±5.1 | Glucose;  Total cholesterol |
| OLZ | 26 | 85 | NA | 31.4±6 | Glucose;  Total cholesterol |
| RIS | 22 | 82 | NA | 11.6±3.7 | Glucose;  Total cholesterol |
| Lindenmayer 2007 | 12 | Double  Blind  parallel | SCCZ | HAL | 19 | 100 | 39.77 ± 9.49 | 17.11 | Weight;  Glucose;  Tryglicerides;  Total cholesterol | Y |
| OLZ | 16 | 87.5 | 39.02±10.48 | 18.44 |
| Loebel 2013 | 6 | double blind parallel | SCZ or PSC | LRS | 125 | 77 | 36.2±10.9  (18-75) | 80 | Weight; BMI;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL | Y |
| SCZ or PSC | LRS | 121 | 68 | 37.9±11.3  (18-75) | 160 | Weight; BMI;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| SCZ or PSC | PBO | 121 | 64 | 37.4±10.8  (18-75) | none | Weight; BMI;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| SCZ or PSC | QTP | 119 | 65 | 37.4±10.4  (18-75) | 600 | Weight; BMI;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| Marder 2007 | 6 | double-blind  parallel | SCZ | PBO | 105 | 78 | 42.3 ± 10.7 | NA | Weight;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| PP | 111 | 68 | 42.1 ± 10.2 | 6 | Weight;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL |
| OLZ | 105 | 80 | 40.5 ± 11 | 10 | Weight;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Marni 2019 | 8 | open label  parallel | SCZ | ARI | 25 | 100 | 33.52 ± 4.72 | 17.6 | BMI;  Glucose | Y |
| RIS | 25 | 100 | 33.12 ± 4.97 | 5.04 | BMI;  Glucose |
| McQuade 2004 | 26 | double blind parallel | SCZ or PSC | ARI | 156 | 73 | 38.6 | 25.1  (15-30) | Weight;  Glucose | N |
| SCZ or PSC | OLZ | 161 | 71 | 38.2 | 16.5  (10-20) | Weight;  Glucose |
| Murashita 2005 | 24 | open label single arm | SCZ or PSC | OLZ | 7 | 57 | 46.3±15.7  (25-69) | 10.7±1.9  (10-15) | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL | N |
| Muzina 2008 | 100 | double blind parallel | mania or BD | ARI | 14 | 36 | 37.6±12.5 | 23.6±8 | Glucose;  Tryglicerides;  Total cholesterol; HDL | Y |
| PBO | 14 | 29 | 38.8±11.8 | none | Glucose;  Tryglicerides;  Total cholesterol; HDL |
| Nasrallah 2013 | 6 | double blind parallel | SCZ or PSC | LRS | 124 | 67 | (18-75) | 40 | Weight; BMI;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol; HDL | Y |
| SCZ or PSC | LRS | 124 | 74 | (18-75) | 120 | Weight;BMI;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol;HDL |
| SCZ or PSC | LRS | 121 | 64 | (18-75) | 80 | Weight; BMI;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol; HDL |
| SCZ or PSC | PBO | 127 | 73 | (18-75) | none | Weight; BMI;  Glucose; HbA1c;  Tryglicerides;  Total cholesterol; HDL |
| Nasrallah 2017 | 48 | open label parallel | SCZ or PSC | CARI | 148 | 67 | 38±11.2  (18-60) | NA | Weight;  Glucose | N |
| CARI | 361 | 69 | 37.9±10.8  (18-60) | (4.5-6) | Weight;  Glucose |
| CARI | 170 | 72 | 40.2±10.6  (18-60) | (1.5-3) | Weight;  Glucose |
| CARI | 679 | 69 | 38.5±10.9  (18-60) | NA | Weight;  Glucose |
| Newcomer 2009 | 24 | open label parallel | SCZ or PSC | OLZ | 146 | 66 | 40.5±10.4  (18-65) | 15.2±2.7  (10-20) | Weight;  Glucose; HbA1c;  C-peptide;  Tryglicerides;  Total cholesterol; HDL | Y |
| QTP | 115 | 66 | 39.4±11.1  (18-65) | 607±128.3  (338-785) | Weight;  Glucose; HbA1c;  C-peptide;  Tryglicerides;  Total cholesterol; HDL |
| RIS | 134 | 65 | 38.3±11.1  (18-65) | 5.2±1  (3-8) | Weight;  Glucose; HbA1c;  C-peptide;  Tryglicerides;  Total cholesterol; HDL |
| Newcomer 2018 | 6 | double blind  parallel | SCZ or PSC | BXP | 732 | 62 | 39±10.9 | (2-4) | Glucose;  Tryglicerides;  Total cholesterol; HDL;LDL | Y |
| PBO | 368 | 62 | 39.5±10.8 | NA | glucose;  Tryglicerides;  Total cholesterol; HDL;LDL |
| Ogasa 2013 | 6 | double blind parallel | SCZ or PSC | LRS | 50 | 72 | 39.8±9.5  (18-64) | 40 | Weight;  Glucose;  Tryglicerides;  Total cholesterol | Y |
| LRS | 49 | 74 | 41±9  (18-64) | 120 | Weight;  Glucose;  Tryglicerides;  Total cholesterol |
| PBO | 50 | 84 | 38.1±9.7  (18-64) | none | Weight;  Glucose;  Tryglicerides;  Total cholesterol |
| Ou 2013 | 6 | open label parallel | SCZ or PSC | OLZ | 130 | 57 | 27.6±8.04  (18-45) | 19±2.3  (5-20) | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| SCZ or PSC | ZPR | 130 | 53 | 26.8±7.75  (18-45) | 138.2±28.6  (40-160) | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Park 2013 | 12 | open label parallel | SCZ or PSC | OLZ | 10 | 50 | 31.5±1.25  (18-65) | 11.6  (8.2-15.5) | Weight; BMI;  Waist-Hip ratio;  Glucose;  Insulin;  C-peptide;  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| SCZ or PSC | ZPR | 10 | 50 | 34.5±0.25  (18-65) | 109  (65-140) | Weight; BMI;  Waist-Hip ratio;  Glucose;  Insulin;  C-peptide;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Perez 2007 | 12 | open label parallel | SCZ or PSC | HAL | 40 | 63 | 28.6±8.2  (15-50) | 4.2±1.7  (3-9) | Weight; BMI;  Glucose;  Insulin;  HOMA-IR;  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| OLZ | 41 | 61 | 28.5±6.5  (15-50) | 12.7±4.6  (5-20) | Weight; BMI;  Glucose;  Insulin; HOMA-IR;  Tryglicerides;  Total cholesterol; HDL; LDL |
| RIS | 47 | 60 | 26.9±8.2  (15-50) | 3.6±1.5  (3-6) | Weight; BMI;  Glucose;  Insulin; HOMA-IR;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Perez 2014 | 12 | open label parallel | SCZ or PSC | ARI | 78 | NA | (15-60) | (5-20) | Weight; BMI;  Glucose;  Insulin; HOMA-IR;  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| QTP | 62 | NA | (15-60) | (100-600) | Weight; BMI;  Glucose;  Insulin; HOMA-IR;  Tryglicerides;  Total cholesterol; HDL; LDL |
| ZPR | 62 | NA | (15-60) | (40-160) | Weight; BMI;  Glucose;  Insulin; HOMA-IR;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Robinson 2015 | 12 | double blind parallel | SCZ or PSC | ARI | 102 | 71 | 22.4±5.8  (15-40) | 14.8±6  (5-30) | Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| RIS | 96 | 71 | 21.8±5.4  (15-40) | 3.2±1.5  (1-6) | Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Sacchetti 2009 | 18 | double blind parallel | SCZ or PSC | CLZ | 73 | 67 | 38.3±11.2 | 365±83  (250-600) | Weight;  Glucose | Y |
| ZPR | 73 | 71 | 41.6±10.2 | 137±26  (80-160) | Weight;  Glucose |
| Sachs 2015 | 3 | double blind parallel | mania or BD | CARI | 158 | 67 | 35.8±11.4  (18-65) | (3-12) | Weight | N |
| PBO | 154 | 62 | 36.7±11.8  (18-65) | NA | Weight |
| Saddichha 2008 | 6 | double blind parallel | SCZ or PSC | None | 51 | 59 | 26±5.57 | NA | Weight;  Waist Circumference;  Glucose;  Tryglicerides;  HDL | Y |
| HAL | 31 | 52 | NA | 13.4±3.6 | Weight;  Waist Circumference;  Glucose;  Tryglicerides;  HDL |
| OLZ | 35 | 51 | NA | 16.5±4.6 | Weight;  Waist Circumference;  Glucose;  Tryglicerides;  HDL |
| RIS | 33 | 55 | NA | 4.4±1.2 | Weight;  Waist Circumference;  Glucose;  Tryglicerides;  HDL |
| Safa 2008 | 12 | double blind parallel | MPD | OLZ | 32 | NA | (16-45) | (5-20) | Glucose;  Tryglicerides;  Total cholesterol | Y |
| RIS | 31 | NA | (16-45) | (1-12) | Glucose;  Tryglicerides;  Total cholesterol |
| Safavi 2016 | 8 | double-blind  parallel | disruptive behaviour disorder and ADHD | RIS | 20 | 80 | 4.37 ± 0.98 | 1.05 ± 0 | Weight | N |
| ARI | 20 | 85 | 4.32 ± 1.07 | 4.69 ± 1.25 | Weight |
| Sanz 2013 | 52 | open label parallel | SCZ or PSC | CLZ | 15 | 80 | 24.5±5.2 | 226.66±97.95  (100-400) | Weight;  Glucose;  Tryglicerides;  Total cholesterol | Y |
| RIS | 15 | 60 | 24.4±5.3 | 5.22±0.97  (4-6) | Weight;  Glucose;  Tryglicerides;  Total cholesterol |
| Savitz 2015 | 96 | open label single arm | SCZ or PSC | PP | 400 | 62 | 15.4±1.6  (12-17) | 6  (1.5-12) | Weight;  Glucose;  Tryglicerides;  Total cholesterol | N |
| Scahill 2016 | 24 | single blind parallel | ASD | RIS | 124 | 85 | 6.9±2.35  (4-13) | NA | Weight;  Waist Circumference;  Glucose; HbA1c;  HOMA-IR;  Tryglicerides;  Total cholesterol; HDL; LDL | N |
| Schoemaker 2010 | 52 | double blind parallel | SCZ or PSC | ASN | 908 | 52 | 36.8±11.8  (16-71) | 13.5±5.1  (10-20) | Weight | N |
| OLZ | 311 | 59 | 36.2±12.4  (18-81) | 13.6±4.5  (10-20) | Weight |
| Shaw 2001 | 8 | open label single arm | SCZ or PSC | QTP | 15 | 53 | 15±1.2  (13-17) | 467  (300-800) | Weight; BMI;  Total cholesterol | N |
| Sikich 2008 | 8 | double blind parallel | SCZ or PSC | MOL | 40 | 58 | (8-19) | 59.9±33.5  (10-140) | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL | N |
| OLZ | 35 | 71 | (8-19) | 11.4±5  (2.5-20) | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| RIS | 41 | 66 | (8-19) | 2.8±1.4  (0.5-6) | Weight; BMI;  Glucose;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| Simpson 2004 | 6 | double blind parallel | SCZ or PSC | OLZ | 133 | 69 | 37.6±9.7  (18-59) | 13±3.1  (5-10) | Weight;  Glucose;  Insulin;  C-peptide;  Tryglicerides;  Total cholesterol | Y |
| ZPR | 136 | 62 | 37.7±9.7  (19-59) | 139±24.7  (80-160) | Glucose;  Insulin;  C-peptide;  Tryglicerides;  Total cholesterol |
| Singh 2016 | 24 | open label  parallel | PSC | OLZ | 31 | 77 | 29.42 ± 9.55 | NA | Weight; BMI;  Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| ILO | 31 | 68 | 30.81 ± 11.62 | NA | Weight; BMI;  Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Stahl 2013 | 28 | open label extension | SCZ or PSC | LRS | 246 | 77 | 36.3±10.9 | 86.3  (40-120) | Weight; BMI;  Waist Circumference;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL | N |
| Suresh 2016 | 48 | double blind parallel | SCZ or PSC | OLZ | 36 | 69 | 41.5±9.6  (18-64) | 14.4±4.6  (5-20) | Weight;  Glucose;  Total cholesterol | Y |
| SCZ or PSC | RIS | 35 | 31 | 39.8±9.5  (18-64) | 5.8±1.2  (2-8) | Weight;  Glucose;  Total cholesterol |
| Takahashi 2009 | 12 | open label single arm | SCZ or PSC | ARI | 42 | 60 | 24.4±7.3  (14-40) | 17.8±9.5 | Weight;  Glucose;  Tryglicerides;  Total cholesterol; LDL | N |
| Thase 2007 | 8 | double blind parallel | anxiety or MD | OLZ | 199 | 38 | 44.3±10.8  (18-65) | NA | Weight;  Glucose;  Tryglicerides;  Total cholesterol | N |
| OLZ | 200 | 34 | 44.3±10.2  (18-65) | NA | Weight;  Glucose;  Tryglicerides;  Total cholesterol |
| Tohen 2003 | 8 | double-blind  parallel | BD I | PBO | 377 | 37.4 | 41.7 ± 12.4 | NA | Weight;  Glucose;  Total cholesterol | Y |
| OLZ | 370 | 37.6 | 42.2 ± 12.5 | NA | Weight;  Glucose;  Total cholesterol |
| Üçok 2015 | 52 | open label  single arm | SCZ | PP | 80 | 70 | 27.5 | 6.4 ± 2 | Weight; BMI;  Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL | N |
| Wampers 2012 | 12 | open label parallel | SCZ or PSC | OLZ | 59 | 68 | 34.8±11.1 | 17.4±6.4 | Weight; BMI;  Waist Circumference;  Glucose;  Insulin; HOMA-IR;  Tryglicerides;  Total cholesterol; HDL; LDL | N |
| RIS | 54 | 63 | 31.8±10.5 | 4.4±1.5 | Weight; BMI;  Waist Circumference;  Glucose;  Insulin; HOMA-IR;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Wang 2014 | 8 | double blind parallel | mania or BD | OLZ | 34 | 35 | 28.7±8.7  (18-60) | 14.4  (5-20) | Weight;  Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| PBO | 34 | 47 | 29.6±8.1  (18-60) | none | Weight;  Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Young 2014 | 52 | Single blind parallel | mania or BD | PBO | 294 | 38 | 39.5±0.7  (18-65) | none | Weight;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL | Y |
| QTP | 149 | 36 | 41.6±0.9  (18-65) | 600 | Weight;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| QTP | 141 | 49 | 39.9±1  (18-65) | 300 | Weight;  Glucose; HbA1c;  Insulin;  Tryglicerides;  Total cholesterol; HDL |
| Zhang 2012 | 52 | open label parallel | SCZ or PSC | ARI | 71 | 63 | 25.7±6.9  (18-65) | 14.5±8.2 | Weight; BMI;  Waist Circumference;  Glucose | N |
| PP | 63 | 56 | 27.1±7.4  (18-65) | 6.4±5.3 | Weight; BMI;  Waist Circumference;  Glucose |
| ZPR | 69 | 64 | 26.3±7.2  (18-65) | 65.3±28.4 | Weight; BMI;  Waist Circumference;  Glucose |
| Zhang 2014 | 8 | Single blind parallel | SCZ or PSC | ARI | 50 | 62 | 41.7±13.7  (17-60) | 16.4±3.2 | Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL | Y |
| OLZ | 50 | 68 | 41.2±13.3  (17-60) | 18.1±3 | Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL |
| QTP | 50 | 66 | 40.2±12  (17-60) | 598±147 | Glucose;  Tryglicerides;  Total cholesterol; HDL; LDL |
| Zhao 2012 | 8 | open label  single arm | SCZ | ZPR | 27 | 51.9 | 30 ± 10.56 | 120.3± 40.34 | Weight;  Waist Circumference;  Tryglicerides;  Total cholesterol; HDL; LDL | N |

ARI= aripiprazole; ASD= autism spectrum disorder; ASN= asenapine; BD= bipolar disorder; BNS= blonanserin; BRX= brexpiprazole; CARI= cariprazine; CLZ= clozapine; CPZ= chlorpromazine; HAL= haloperidol; ILO= iloperidone; LRS= lurasidone; MD= major depression;; MPD= mixed psychiatric disorders; NHV= normal healthy volunteers; OLZ= olanzapine; PP= paliperidone; PBO= placebo; QTP= quetiapine; RIS=risperidone; SCZ or PSC= schizophrenia or psychosis; SER= sertindole; SLP= sulpiride; ZPR=ziprasidone

# eTable2. Characteristics of 52 studies excluded from the network metanalysis.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Reason for exclusion** | **Treatment**  **(dose)** | **Sample size** | **Changes in glycometabolic profile of patients treated with antipsychotic drugs or placebo**  **(as mean differences between end of study and baseline)** | | | | | | | |
| **Tryglicerides**  **mg/dL**  **(SD)** | **Total Cholesterol mg/dL**  **(SD)** | **HDL mg/dL**  **(SD)** | **LDL mg/dL**  **(SD)** | **Insulin µU/mL**  **(SD)** | **Glucose mg/dL**  **(SD)** | **HOMA**  **mmol mU/L**  **(SD)** | **Hb1Ac**  **%**  **(SD)** |
| Aliyazicioǧlu 2007 | Single Arm | Olanzapine (NA) | 15 | NA | NA | NA | NA | NA | NA | NA | NA |
| Baptista 1997 | Healthy  Volunteers | Placebo | 17 | NA | NA | NA | NA | NA | NA | NA | NA |
| Sulpiride  (200 mg/day) | 17 | NA | NA | NA | NA | NA | NA | NA | NA |
| Baptista 2007 | Single Arm | Olanzapine  (10-20 mg/day) | 60 | NA | NA | NA | NA | 4.8 | 0 | 1.1 | NA |
| Bobo 2010 | Single Arm | Olanzapine  (15 mg/day) | 20 | -12.9  (24.9) | 0.0  (34.6) | -5.3  (6.2) | 7.9  (28.2) | NA | 8.5  (31.9) | NA | NA |
| Boku 2011 | Single Arm | Olanzapine  (5±1.9 mg/day) | 11 | NA | NA | NA | NA | NA | 0 | NA | NA |
| Calabrese 2015 | No Available Data | Cariprazine  (3-6 mg/day) | 167 | 14.3  (75.4) | 0.9  (39.1) | -1.8  (12.5) | 0.1  (32.1) | NA | 8.1  (26.5) | NA | NA |
| Cariprazine  (6-12 mg/day) | 169 | -6.2  (69.9) | -1.2  (36.1) | -1.6  (10.2) | 1.4  (31.6) | NA | 6.4  (21.0) | NA | NA |
| Placebo | 161 | -7.3  (82.5) | -2.2  (31.9) | -2.6  (11.2) | 1.9  (26.5) | NA | 3.6  (23.5) | NA | NA |
| Cantillon 2017 | No Available Data | Aripiprazole  (15 mg/day) | 20 | 0.0 | 0.0 | NA | NA | NA | 0.0 | NA | NA |
| Placebo | 38 | 0.0 | 0.0 | NA | NA | NA | 0.0 | NA | NA |
| Chen 2008 | Single Arm | Risperidone (NA) | 30 | NA | NA | NA | NA | NA | NA | NA | NA |
| Chen 2011 | Single Arm | Quetiapine (300-800 mg/day) | 17 | 4.9 | 9.5 | -0.2 | NA | 3.7 mU/L | -1 | 0.9 | NA |
| Cutler 2013 | Single Arm | Iloperidone  overall  (24 or 12 mg/day) | 173 | 0.6  (71.1) | -12.6  (27.7) | -0.06  (10.4) | -13.3  (25.3) | NA | 3.4  (20.4) | NA | -0.1  (0.4) |
| DelBello 2017 | Paediatric Patients | Lurasidone  (32.5 mg/day) | 173 | -13.0 to -2.0 (-7) | -10.0 to -1.0 (-7) | -2.0 to 1.0 (-1) | NA | NA | -1.0 to 1.0 | NA | -0.1 to 0.0 |
| Placebo | 170 | -2 to 9 (3) | -5.0 to 0.0 (-3) | -3 to 0 (-2) | NA | NA | -2.0 to 1.0 | NA | -0.1 to 0.0 |
| Ercan 2012 | Single Arm | Aripiprazole  (8.55±1.73 mg/day) | 20 | NA | NA | NA | NA | NA | NA | NA | NA |
| Evers 2016 | Healthy Volunteers | Olanzapine (100mgd/day) | 15 | NA | NA | NA | NA | NA | NA | NA | NA |
| Olanzapine  (100 mg/day) and topiramate | 15 | NA | NA | NA | NA | NA | NA | NA | NA |
| Faghihi 2012 | Single Arm | Olanzapine  (8.37 ±4.21 mg/day) | 37 | NA | NA | NA | NA | NA | NA | NA | NA |
| Findling 2012 | No Available Data | Quetiapine  (400 mg/day) | 73 | 9.6  (64.7) | 7.8  (28.8) | -2.8  (9.2) | 8.6  (22.7) | 4.2  (19.2) | 0.0  (12) | NA | 0.0  (0.2) |
| Quetiapine  (800 mg/day) | 74 | 15.5  (47. 9) | 7.4  (24.6) | -0.9  (9.9) | 4.8  (21.7) | 1.2  (17.2) | -1.4  (9) | NA | 0.0  (0.2) |
| Placebo | 73 | -8.1  (59.3) | -8.0  (25.7) | -2.4  (8.9) | -3.8  (20.5) | -1  (19) | -1.7  (10.8) | NA | 0.0  (0.2) |
| Findling 2013 | Single Arm | Ziprasidone (40-160 mg/day) | 162 | -4.6  (48.6) | -10.3  (22.7) | -0.5  (9.4) | -8.9  (19.5) | -1.7  (8.1)  (µIU/dL) | -1.6  (17.1) | NA | NA |
| Findling 2014 | Paediatric Patients | Placebo | 100 | -10.62  (71.68) | -4.25  (21.62) | -0.77  (9.27) | -0.77  (19.69) | NA | 2.16  (11.53) | NA | NA |
| Quetiapine (100-300 mg/day) | 92 | 20.35  (54.87) | 1.16  (21.24) | -1.16  (8.11) | -1.54  (18.92) | NA | 1.08  (17.84) | NA | NA |
| Fleischhacker 2009 | No Available Data | Aripiprazole (15-30 mg/day) | 355 | -25.2 | -17.0 | 5.4 | -17.0 | NA | NA | NA | NA |
| Olanzapine (10-20 mg/day) | 348 | 10.5 | 5.8 | 4.8 | 2.2 | NA | NA | NA | NA |
| Fountaine 2010 | Healthy  Volunteers | Olanzapine  (5-10 mg) | 15 | 83  (29.44) | 117.7  (47.44) | NA | NA | 6  (3) | 8.5  (4.04) | NA | NA |
| Placebo | 15 | 85  (36.49) | 78.7  (27.01) | NA | NA | 7.3  (3.83) | 7.4  (2.49) | NA | NA |
| Glick 2009 | No Available Data | Aripiprazole  (15 or 20 or 30 mg/day) | 123 | NA | -12.4 | NA | NA | NA | 0.7 | NA | NA |
| Placebo | 56 | NA | -14.6 | NA | NA | NA | -3.3 | NA | NA |
| Olanzapine  (10-20 mg/day) | 161 | 79.4 | 16.3 | -3.3 | 2.2 | NA | NA | NA | NA |
| Harvey 2019 | No Available Data | Blonanserin  (15.7 ±6 mg/day) | 129 | NA | NA | NA | NA | NA | NA | NA | NA |
| Haloperidol  (7.9 ± 3 mg/day) | 132 | NA | NA | NA | NA | NA | NA | NA | NA |
| Hashimoto 2015 | Single Arm | Quetiapine  (438.6 ± 261.7mg/day) | 22 | NA | NA | NA | NA | NA | NA | NA | NA |
| Hoffman 2009 | Study On Different Drug Formulations | Olanzapine orally disintegrating tablets  (5-10 mg/day) | 7 | 16.8 | 22.8 | -0.7 | 20 | 4.6 | 3.8 | NA | NA |
| Olanzapine standard oral tablets  (5-10 mg/day) | 9 | 38.6 | 18.3 | 6.1 | 4.5 | 1.6 | -2.2 | NA | NA |
| Hosojima 2006 | Single Arm | Olanzapine (7.5-20 mg/day) | 13 | NA | NA | NA | NA | -0.7 | -3.7 | -0.2 | NA |
| Hsieh 2010 | Single Arm | Aripiprazole  (NA) | 245 | NA | NA | NA | NA | NA | NA | NA | NA |
| Huang 2020 | Single Arm | Olanzapine  (NA) | 33 | NA | NA | NA | NA | NA | NA | NA | NA |
| Hwang 2003 | Single Arm | Olanzapine (2.5-20 mg/day) | 80 | 38.4 | 1.6 | NA | NA | NA | 5.8 | NA | NA |
| Kang 2016 | Single Arm | Paliperidone  (3-12 mg/day) | 75 | 41.8 | 21.9 | 7.9 | 17.2 | NA | 3.5 | NA | NA |
| Karagianis 2009 | Study On Different Drug Formulations | Olanzapine orally disintegrating tablets  (5-20 mg/day) | 84 | 0.0  (0.0) | 0.0  (0.0) | 0.0  (0.0) | 0.0  (0.0) | 2.4  (17.7) | 0.0  (0.0) | -18.5 (58.91) | 0.0  (0.2) |
| Olanzapine standard tablets  (5-20 mg/day) | 65 | 0.0  (88.5) | 0.0  (0.0) | 0.0  (0.0) | 0.0  (0.0) | -0.1  (5.5) | 0.0  (0.0) | -9.8 (62.61) | 0.0  (0.3) |
| Kim 2012 | Single Arm | Paliperidone  (NA) | 243 | NA | NA | NA | NA | NA | -5.5 | NA | NA |
| Kim 2018 | Single Arm | Aripiprazole  (5.1 ±2.5 mg/day) | 67 | NA | NA | NA | NA | NA | NA | NA | NA |
| Ko 2014 | Single Arm | Ziprasidone (20-160 mg/day) | 67 | -20.6 | NA | NA | NA | NA | NA | NA | NA |
| Konstantinidis 2007 | Single Arm | Quetiapine  (303 ±118 mg/day) | 24 | NA | NA | NA | NA | NA | NA | NA | NA |
| Kryzhanovskaya 2009 | Paediatric Patients | Olanzapine (11.1 md/day) | 72 | 41.6  (75.3) | 10,8  (21,3) | -3.1  (8.1) | 5.8  (20.1) | NA | 2.9  (10.5) | NA | NA |
| Placebo | 35 | 4.4  (51.4) | 2.3  (20.1) | 0.8  (11.6) | 0.8  (19.2) | NA | -1.6  (9.7) | NA | NA |
| Kusumi 2012 | Study On Different Drug Formulations | Olanzapine oral standard tablets  (mean 15.7 mg/day) | 57 | 25.6  (68.5) | 10.0  (26.1) | -1.6  (10.6) | NA | NA | 0.3  (12.1) | NA | 0.3  (1.1) |
| Olanzapine orally disintegrating tablets  (mean 15.2 mg/day) | 61 | 33.2  (80.2) | 13.0  (36.4) | -0.03  (10.3) | NA | NA | 6.9  (16.1) | NA | 0.1  (0.2) |
| Lieberman 2003 | No Available Data | Chlorpromazine  (600-400 mg/day) | 80 | NA | NA | NA | NA | NA | 0.0 | NA | NA |
| Clozapine  (400-300 mg/day) | 80 | NA | NA | NA | NA | NA | 0.0 | NA | NA |
| McQuade 2004 | No Available Data | Aripiprazole (15-30 mg/day) | 156 | 6.5 | -1.1 | 3.6 | -3.8 | NA | NA | NA | NA |
| Murashita 2005 | Single Arm | Olanzapine (10-15 mg/day) | 7 | 19.1 | 13.8 | -5 | 23.4 | -0.2 | -1.4 | NA | NA |
| Nasrallah 2017 | Study On Drug Doses | Cariprazine (1.5-9 mg/day)  (Overall) | 679 | 1.2  (87.2) | -5.3  (31.1) | -0.8  (11.3) | -3.5  (26.4) | NA | 4.5  (23.2) | NA | NA |
| Sachs 2015 | No Available Data | Cariprazine  (3-12 mg/day) | 158 | 14.5  (101.3) | 2.7  (30.1) | -0.2  (9.4) | 1.3  (25.5) | NA | 6.2  (15.9) | NA | NA |
| Placebo | 154 | 8.9  (79.0) | 11.2  (28.6) | 0.8  (10.0) | 8.3  (24.8) | NA | 1.1  (17.4) | NA | NA |
| Safavi 2016 | Paediatric Patients | Risperidone  (1.05 ± 0.51 mg/day) | 20 | NA | NA | NA | NA | NA | NA | NA | NA |
| Savitz 2015 | Single Arm | Paliperidone (1.5-12 mg/day) | 400 | -0.2  (59.3) | -1.8  (26.8) | NA | -2.1  (23.3) | NA | 0.5  (15.3) | -0.1 | NA |
| Scahill 2016 | Single Arm | Risperidone (Maximum dose 3.5 mg/day) | 124 | 4.7  (31.3) | -2.3  (26.6) | -0.8  (8.4) | 0.5  (15.8) | 2.9  (5.6) | 3.5  (12.8) | 0.6  (1.3) | 0.0  (0.2) |
| Schoemaker  2010 | No Available Data | Asenapine  (5-10 mg bid) | 908 | -9.8  (92.2) | -6.0  (35.9) | NA | NA | NA | 2.4  (21.7) | NA | NA |
| Olanzapine  (10-20 mg/day) | 311 | 30.4  (202.6) | 3.2  (38.36) | NA | NA | NA | 3.5  (25.14) | NA | NA |
| Shaw 2001 | Single Arm | Quetiapine (300-800 mg/day) | 15 | NA | 5 | NA | NA | NA | NA | NA | NA |
| Sikich 2008 | Paediatric Patients | Molindone (59.9±33.5 mg/day) | 40 | -5.8  (44.7) | 0  (16) | 0.31  (10.6) | 0.48  (14.5) | 1.2  (7.1) | 0.9  (12) | 0.5  (1.9) | NA |
| Olanzapine (11.4±5 mg/day) | 35 | 21.6  (65.3) | 19.9  (23.9) | 1.1  (8.3) | 14.7  (18.7) | 5.7  (38.1) | 0.6  (15.7) | 1.2  (1.9) | NA |
| Risperidone (2.8±1.4 mg/day) | 41 | 7.1  (33.3) | -10.2  (26.7) | -0.4  (9.4) | -9.6  (22.2) | -2.4  (19.4) | 1.2  (7.3) | 0  (1.7) | NA |
| Stahl 2013 | Switch Study | Lurasidone  (40-120 mg/day) | 246 | -22.7  (94.2) | -6.7  (32.9) | -0.1  (9.8) | -0.5  (29.5) | -2.0  mU/L  (27.9) | 1.5  (33.9) | NA | -0.08  (0.4) |
| Takahashi 2009 | Single Arm | Aripiprazole (mean dose 17.8 mg/day) | 42 | 7 | -8.5 | NA | -3.7 | NA | 5.1 | NA | NA |
| Thase 2007 | Study On  Combination Therapy | Olanzapine  (6-18 mg/day)/  Fluoxetine  (50 mg/day) combination | 200 | 39.8  (122.1) | 15.1  (32.0) | NA | NA | NA | 14.1  (49.4) | NA | NA |
| Olanzapine  (6-18 mg/day) | 199 | 51.3  (184.1) | 2.7  (34.0) | NA | NA | NA | 8.3  (29.5) | NA | NA |
| Üçok 2015 | Single Arm | Paliperidone  (6.4 ± 2 mg/day) | 80 | NA | NA | NA | NA | NA | NA | NA | NA |
| Wampers 2012 | No Available Data | Risperidone (4.4±1.5 mg/day) | 54 | NA | NA | NA | NA | NA | NA | NA | NA |
| Olanzapine (17.4±6.4 mg/day) | 59 | NA | NA | NA | NA | NA | NA | NA | NA |
| Zhang 2012 | No Available Data | Aripiprazole (5 mg/day) | 71 | In lipid metabolism. *aripiprazole* group reduced triglycerides significantly and had no changes in other indices.  *Paliperidone* group reduced HDL and increased triglycerides despite no changes in glucose metabolism.  *Ziprasidone* group also had no significant changes in glucose metabolism. but reduced cholesterol. LDL and  increased HDL. | | | | | | | |
| Paliperidone (6 mg/day) | 63 |
| Ziprasidone (20 mg/day) | 69 |
| Zhao 2012 | Single Arm | Ziprasidone  (120.3± 40.34 mg/day) | 27 | 52.08 (13.63) | 25,46 (4.93) | 11,33 (-1.58) | NA | NA | NA | NA | NA |

# **eFigure 1.** Quality assessment by using the Cochrane risk-of-bias tool for randomized trials (Rob).

# **eTable 3.** Quality assessment by using the Risk of Bias In Non randomized Studies of Interventions (ROBINS-I) assessment tool

**eTABLE 3: Overall bias**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Modified Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I) assessment tool | | | | | | | | |
| Author | **Risk of bias pre-intervention and at-intervention domains** | | | **Risk of bias post-intervention domains** | | | | **Overall**  **Assessment**  **of bias** |
| **Bias due to Confounding** | **Bias in selection of participants into the study** | **Bias in classification of interventions** | **Bias due to deviations from intended intervention** | **Bias due to missing data** | **Bias in measurement of outcomes** | **Bias in selection of the reported result** |
| Aliyazicioglu 2007 | Low | Low | Low | No information | Low | Moderate | Low | No information |
| Baptista 2007 | Low | Low | Serious | Low | Low | Moderate | Low | Serious |
| Boku 2011 | Critical | Low | Low | Low | Critical | Moderate | Low | Critical |
| Bobo 2010 | Moderate | Low | Low | Low | Serious | Moderate | Serious | Serious |
| Chen 2008 | No information | Critical | Low | No information | No information | Moderate | No information | No information |
| Chen 2011 | Critical | Low | Low | Critical | Critical | Moderate | Serious | Critical |
| Cutler 2013 | Serious | Moderate | Moderate | Critical | Serious | Moderate | Low | Critical |
| Ercan 2012 | Low | Low | Low | Low | Low | Moderate | Low | Moderate |
| Faghihi 2012 | Low | Serious | Low | Low | No information | Moderate | Low | No information |
| Findling 2013 | Serious | moderate | Low | Low | Low | Moderate | Low | Serious |
| Hashimoto 2015 | Low | Low | Low | Low | Serious | Moderate | Low | Serious |
| Hosojima 2006 | Serious | Low | Low | Low | Low | Moderate | Low | Serious |
| Hsieh 2010 | Low | Low | Low | Low | Moderate | Moderate | Low | Moderate |
| Huang 2020 | Low | Low | Low | Low | Low | Moderate | Low | Moderate |
| Hwang 2003 | Serious | Low | Low | Critical | Critical | Moderate | Moderate | Critical |
| Kang 2016 | Low | Low | Low | Low | Serious | Moderate | Low | Serious |
| Kim 2012 | Low | Low | Low | Low | Serious | Moderate | Low | Serious |
| Kim 2018 | Low | Low | Low | Low | Low | Moderate | Low | Moderate |
| Ko 2014 | Serious | Low | Low | Low | Moderate | Moderate | Low | Serious |
| Konstantinidis 2006 | Low | Low | Low | Low | Moderate | Moderate | Low | Moderate |
| Murashita 2005 | Critical | Low | Low | Low | Low | Moderate | Low | Critcal |
| Nasrallah 2017 | Critical | Critical | No information | No information | No information | Moderate | Low | No information |
| Savitz 2015 | Serious | Low | Low | Critical | Serious | Moderate | Low | Critical |
| Stahl 2013 | Low | Critical | Moderate | Low | Serious | Moderate | Low | Critical |
| Shaw 2001 | Serious | Low | Low | Low | Low | Moderate | Low | Serious |
| Takahashi 2009 | Serious | Low | No information | No information | No information | Moderate | No information | No information |
| Ucok 2015 | Low | Low | Low | Low | Moderate | Moderate | Low | Moderate |
| Zhao 2012 | Low | No information | Low | No information | No information | Moderate | Low | No information |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I) assessment tool | | | | | | | | |
| Author | **Risk of bias pre-intervention and at-intervention domains** | | | **Risk of bias post-intervention domains** | | | | **Overall**  **Assessment**  **of bias** |
| **Bias due to Confounding** | **Bias in selection of participants into the study** | **Bias in classification of interventions** | **Bias due to deviations from intended intervention** | **Bias due to missing data** | **Bias in measurement of outcomes** | **Bias in selection of the reported result** |
| Marni 2019 | Low | Low | Low | No information | Low | Low | Low | No information |
| Wampers 2012 | Serious | Serious | Low | Low | Moderate | Serious | Low | Serious |

*19th Nov 2020*

# **eTable 4.** Comparison of active principles and no-treatment or placebo on **glucose change**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ARIPI**  **PRAZOLE** | . | -5.91  [-16.79; 4.97] | -0.97  [ -9.37; 7.43] | . | -7.55  [-13.33; -1.77] | . | . | . | . | -9.06  [-19.79; 1.67] | . | . | -1.30  [-22.71; 20.11] |
| -1.36  [-11.54; 8.81] | **ILOPERI**  **DONE** | . | . | . | . | . | . | . | . | -8.02  [-16.90; 0.86] | . | . | . |
| -5.11  [-10.84; 0.62] | -3.75  [-13.38; 5.89] | **ZIPRASI**  **DONE** | 1.63  [ -8.92; 12.18] | . | . | . | -6.00  [-16.49; 4.49] | . | . | -3.93  [ -8.19; 0.33] | . | . | . |
| -5.32  [-10.83; 0.19] | -3.96  [-13.68; 5.77] | -0.21  [ -5.28; 4.86] | **QUETIA**  **PINE** | 3.51  [ -5.99; 13.00] | -1.20  [-10.11; 7.71] | . | . | . | . | -4.11  [-11.18; 2.95] | . | . | 0.46  [ -4.10; 5.02] |
| -5.39  [-11.92; 1.14] | -4.02  [-14.11; 6.06] | -0.28  [ -6.21; 5.65] | -0.07  [ -5.22; 5.08] | **LURASI**  **DONE** | . | . | . | . | . | 0.00  [ -8.52; 8.52] | . | . | -1.23  [ -6.26; 3.81] |
| -5.89  [-10.51; -1.27] | -4.52  [-14.08; 5.04] | -0.78  [ -5.59; 4.04] | -0.57  [ -5.20; 4.07] | -0.50  [ -6.13; 5.13] | **RISPERI**  **DONE** | . | -0.24  [ -8.41; 7.92] | . | -2.88  [-12.23; 6.47] | -5.29  [ -9.44; -1.13] | -3.77  [ -9.69; 2.14] | . | 4.24  [ -5.10; 13.58] |
| -6.19  [-16.44; 4.07] | -4.82  [-17.67; 8.02] | -1.08  [-11.00; 8.84] | -0.87  [-10.32; 8.59] | -0.80  [-10.52; 8.92] | -0.30  [-10.01; 9.41] | **BREXPI**  **PRAZOLE** | . | . | . | . | . | . | 0.28  [ -8.43; 8.99] |
| -7.14  [-14.67; 0.40] | -5.78  [-16.77; 5.22] | -2.03  [ -8.74; 4.68] | -1.82  [ -9.09; 5.45] | -1.75  [ -9.64; 6.14] | -1.25  [ -7.65; 5.14] | -0.95  [-12.13; 10.23] | **CLOZAPINE** | . | . | -8.30  [-22.30; 5.70] | -4.50  [-16.31; 7.31] | . | . |
| -7.66  [-14.35; -0.96] | -6.29  [-16.40; 3.82] | -2.55  [ -8.58; 3.48] | -2.34  [ -7.99; 3.32] | -2.27  [ -8.43; 3.89] | -1.77  [ -7.55; 4.01] | -1.47  [-11.36; 8.42] | -0.52  [ -8.49; 7.46] | **PALIPERI**  **DONE** | . | -1.65  [ -7.35; 4.06] | . | . | 1.08  [ -4.06; 6.22] |
| -8.77  [-19.19; 1.66] | -7.40  [-20.77; 5.97] | -3.66  [-14.17; 6.86] | -3.45  [-13.88; 6.99] | -3.38  [-14.29; 7.53] | -2.88  [-12.23; 6.47] | -2.58  [-16.06; 10.90] | -1.63  [-12.95; 9.70] | -1.11  [-12.10; 9.88] | **SERT**  **INDOLE** | . | . | . | . |
| -9.38  [-14.36; -4.41] | -8.02  [-16.90; 0.86] | -4.27  [ -8.03; -0.52] | -4.06  [ -8.03; -0.10] | -4.00  [ -8.78; 0.79] | -3.50  [ -7.05; 0.06] | -3.20  [-12.48; 6.09] | -2.24  [ -8.74; 4.25] | -1.73  [ -6.56; 3.11] | -0.62  [-10.62; 9.38] | **OLANZA**  **PINE** | -0.81  [ -6.58; 4.97] | . | 2.43  [ -1.62; 6.49] |
| -10.74  [-17.26; -4.22] | -9.38  [-19.59; 0.83] | -5.63  [-11.70; 0.44] | -5.42  [-11.46; 0.62] | -5.35  [-12.04; 1.33] | -4.86  [-10.03; 0.32] | -4.55  [-14.90; 5.79] | -3.60  [-10.95; 3.75] | -3.09  [ -9.88; 3.71] | -1.98  [-12.66; 8.71] | -1.36  [ -6.40; 3.68] | **HALOPE**  **RIDOL** | . | 6.84  [ -2.83; 16.51] |
| -13.81  [-25.16; -2.46] | -12.44  [-26.18; 1.29] | -8.70  [-19.74; 2.35] | -8.49  [-19.12; 2.14] | -8.42  [-19.29; 2.45] | -7.92  [-18.78; 2.94] | -7.62  [-20.87; 5.63] | -6.67  [-18.86; 5.52] | -6.15  [-17.17; 4.87] | -5.04  [-19.37; 9.29] | -4.42  [-14.91; 6.06] | -3.07  [-14.49; 8.36] | **CARIPRA**  **ZINE** | 7.90  [ -2.08; 17.88] |
| -5.91  [-11.32; -0.50] | -4.54  [-13.99; 4.90] | -0.80  [ -5.54; 3.94] | -0.59  [ -4.25; 3.08] | -0.52  [ -4.83; 3.79] | -0.02  [ -4.30; 4.26] | 0.28  [ -8.43; 8.99] | 1.23  [ -5.78; 8.24] | 1.75  [ -2.94; 6.44] | 2.86  [ -7.42; 13.14] | 3.48  [ 0.26; 6.69] | 4.83  [ -0.74; 10.40] | 7.90  [ -2.08; 17.88] | **NONE** |

Data are reported as Mean Differences (MDs) and 95% confidence intervals (CIs). Mixed SMDs are shown in the triangle below the diagonal and direct SMDs are shown in the triangle above the diagonal. Significant results are highlighted.

# **eTable 5.** Comparison of active principles and no-treatment or placebo on **HbA1c change**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **HALOPERIDOL** | . | . | . | -1.20 [-2.34; -0.06] | . | . |
| -0.99 [-2.14; 0.15] | **ZIPRASIDONE** | . | -0.20 [-0.32; -0.09] | . | . | . |
| -1.18 [-2.32; -0.04] | -0.19 [-0.33; -0.04] | **RISPERIDONE** | 0.00 [-0.09; 0.10] | -0.05 [-0.16; 0.06] | . | . |
| -1.20 [-2.34; -0.06] | -0.20 [-0.32; -0.09] | -0.02 [-0.11; 0.07] | **OLANZAPINE** | -0.07 [-0.17; 0.03] | -0.00 [-0.05; 0.05] | . |
| -1.20 [-2.34; -0.06] | -0.21 [-0.33; -0.08] | -0.02 [-0.11; 0.07] | -0.00 [-0.06; 0.06] | **QUETIAPINE** | -0.03 [-0.11; 0.06] | -0.01 [-0.05; 0.04] |
| -1.22 [-2.36; -0.08] | -0.22 [-0.35; -0.10] | -0.04 [-0.13; 0.05] | -0.02 [-0.07; 0.03] | -0.02 [-0.07; 0.03] | **LURASIDONE** | 0.04 [-0.01; 0.09] |
| -1.20 [-2.33; -0.06] | -0.20 [-0.33; -0.07] | -0.02 [-0.11; 0.08] | 0.00 [-0.06; 0.06] | 0.00 [-0.04; 0.05] | 0.02 [-0.02; 0.07] | **NONE** |

Data are reported as Mean Differences (MDs) and 95% confidence intervals (CIs). Mixed SMDs are shown in the triangle below the diagonal and direct SMDs are shown in the triangle above the diagonal. Significant results are highlighted.

# **eTable 6.** Comparison of active principles and no-treatment or placebo on **Insulin change**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ZIPRASIDONE** | 2.10 [-1.31; 5.51] | . | . | -0.30 [-3.45; 2.85] | . | . | -3.52 [-5.77; -1.26] | . |
| -0.23 [-3.15; 2.68] | **ARIPIPRAZOLE** | 3.18 [-1.37; 7.73] | . | -2.40 [-5.72; 0.92] | . | . | . | . |
| -0.67 [-3.93; 2.59] | -0.43 [-3.75; 2.88] | **RISPERIDONE** | . | . | . | -1.11 [-4.50; 2.28] | 0.25 [-3.06; 3.57] | . |
| -1.61 [-4.95; 1.73] | -1.38 [-5.30; 2.55] | -0.94 [-4.95; 3.07] | **PALIPERIDONE** | . | . | . | -0.35 [-3.49; 2.80] | 0.39 [-3.04; 3.82] |
| -1.80 [-4.23; 0.63] | -1.57 [-4.50; 1.36] | -1.14 [-4.57; 2.29] | -0.19 [-3.40; 3.01] | **QUETIAPINE** | 0.36 [-3.92; 4.64] | . | . | 1.05 [-0.63; 2.73] |
| -2.03 [-4.91; 0.85] | -1.80 [-5.36; 1.77] | -1.36 [-4.99; 2.26] | -0.42 [-3.99; 3.15] | -0.23 [-3.04; 2.58] | **LURASIDONE** | . | -0.03 [-2.68; 2.62] | 0.34 [-4.80; 5.48] |
| -2.25 [-6.24; 1.75] | -2.01 [-6.25; 2.23] | -1.58 [-4.85; 1.69] | -0.64 [-5.23; 3.96] | -0.44 [-4.60; 3.72] | -0.22 [-4.47; 4.04] | **HALOPERIDOL** | 0.76 [-3.20; 4.72] | . |
| -2.33 [-4.29; -0.37] | -2.10 [-5.08; 0.89] | -1.66 [-4.54; 1.21] | -0.72 [-3.64; 2.20] | -0.53 [-2.88; 1.83] | -0.30 [-2.63; 2.03] | -0.08 [-3.70; 3.53] | **OLANZAPINE** | 1.21 [-2.33; 4.76] |
| -0.84 [-3.46; 1.78] | -0.61 [-3.78; 2.56] | -0.18 [-3.70; 3.35] | 0.77 [-2.28; 3.82] | 0.96 [-0.63; 2.55] | 1.19 [-1.71; 4.09] | 1.40 [-2.82; 5.62] | 1.49 [-0.91; 3.89] | **NONE** |

Data are reported as Mean Differences (MDs) and 95% confidence intervals (CIs). Mixed SMDs are shown in the triangle below the diagonal and direct SMDs are shown in the triangle above the diagonal. Significant results are highlighted

# **eTable 7.** Comparison of active principles and no-treatment or placebo on **HOMAR-IR change**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **ARIPIPRAZOLE** | -0.50 [-0.96; -0.04] | -0.60 [-1.13; -0.07] | . | . | . | . |
| -0.50 [-0.96; -0.04] | **QUETIAPINE** | -0.10 [-0.54; 0.34] | . | . | . | . |
| -0.60 [-1.13; -0.07] | -0.10 [-0.54; 0.34] | **ZIPRASIDONE** | . | . | . | -0.20 [-0.51; 0.11] |
| -0.73 [-1.61; 0.15] | -0.23 [-1.06; 0.60] | -0.13 [-0.83; 0.57] | **RISPERIDONE** | . | -0.27 [-0.73; 0.19] | -0.07 [-0.70; 0.56] |
| -0.79 [-1.41; -0.17] | -0.29 [-0.83; 0.25] | -0.19 [-0.50; 0.12] | -0.06 [-0.69; 0.57] | **LURASIDONE** | . | -0.01 [-0.06; 0.04] |
| -1.00 [-1.90; -0.10] | -0.50 [-1.35; 0.35] | -0.40 [-1.13; 0.33] | -0.27 [-0.73; 0.19] | -0.21 [-0.87; 0.45] | **HALOPERIDOL** | 0.20 [-0.46; 0.86] |
| -0.80 [-1.42; -0.18] | -0.30 [-0.84; 0.24] | -0.20 [-0.51; 0.11] | -0.07 [-0.70; 0.56] | -0.01 [-0.06; 0.04] | 0.20 [-0.46; 0.86] | **OLANZAPINE** |

Data are reported as Mean Differences (MDs) and 95% confidence intervals (CIs). Mixed SMDs are shown in the triangle below the diagonal and direct SMDs are shown in the triangle above the diagonal. Significant results are highlighted

# **eTable 8.** Comparison of active principles and no-treatment or placebo on **Triglycerides change**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **BREXPI**  **PRAZOLE** | . | . | . | . | . | . | . | . | . | . | . | . | -0.71  [ -29.68; 28.26] |
| -4.11  [-47.92; 39.70] | **CARIPRA**  **ZINE** | . | . | . | . | . | . | . | . | . | . | . | 3.40  [ -29.46; 36.26] |
| -6.96  [-40.84; 26.93] | -2.85  [-40.11; 34.42] | **ZIPRASI**  **DONE** | . | 4.20  [ -26.81; 35.21] | . | . | . | . | -6.60  [ -36.50; 23.30] | . | . | -35.77  [ -51.66; -19.89] | . |
| -8.55  [-41.41; 24.30] | -4.44  [-40.78; 31.89] | -1.60  [-22.76; 19.57] | **PALIPERI**  **DONE** | . | . | . | . | . | . | . | . | -27.59  [ -47.12; -8.06] | 6.14  [ -10.59; 22.87] |
| -9.83  [-44.38; 24.72] | -5.72  [-43.59; 32.15] | -2.87  [-22.57; 16.82] | -1.28  [-23.86; 21.31] | **ARIPI**  **PRAZOLE** | . | -8.41  [ -38.93; 22.11] | . | . | -21.96  [ -48.06; 4.14] | . | . | -24.00  [ -51.77; 3.76] | 84.00  [ 4.88; 163.12] |
| -10.41  [-46.08; 25.25] | -6.30  [-45.19; 32.59] | -3.46  [-26.99; 20.07] | -1.86  [-26.22; 22.50] | -0.58  [-25.20; 24.04] | **HALOPERI**  **DOL** | -13.24  [ -38.08; 11.60] | . | . | . | . | . | -27.65  [ -50.26; -5.05] | -0.40  [ -34.16; 33.36] |
| -13.40  [-45.58; 18.78] | -9.29  [-45.01; 26.43] | -6.44  [-23.87; 10.98] | -4.85  [-23.74; 14.05] | -3.57  [-21.29; 14.15] | -2.99  [-22.98; 17.01] | **RISPERI**  **DONE** | . | -6.19  [ -37.27; 24.89] | -6.97  [ -28.08; 14.13] | . | -19.19  [ -42.30; 3.92] | -34.52  [ -48.26; -20.78] | 28.15  [ 3.52; 52.79] |
| -14.47  [-47.30; 18.35] | -10.36  [-46.67; 25.95] | -7.51  [-28.74; 13.71] | -5.92  [-26.87; 15.04] | -4.64  [-27.12; 17.84] | -4.06  [-28.50; 20.39] | -1.07  [-19.93; 17.79] | **LURASI**  **DONE** | . | -13.44  [ -47.75; 20.86] | . | . | -8.62  [ -36.39; 19.15] | 6.85  [ -11.45; 25.15] |
| -19.59  [-64.33; 25.15] | -15.48  [-62.83; 31.87] | -12.63  [-48.27; 23.00] | -11.04  [-47.41; 25.34] | -9.76  [-45.54; 26.02] | -9.18  [-46.14; 27.78] | -6.19  [-37.27; 24.89] | -5.12  [-41.48; 31.24] | **SERT**  **INDOLE** | . | . | . | . | . |
| -20.21  [-52.17; 11.74] | -16.10  [-51.62; 19.42] | -13.25  [-30.65; 4.14] | -11.66  [-30.70; 7.39] | -10.38  [-28.49; 7.73] | -9.80  [-31.83; 12.24] | -6.81  [-21.16; 7.55] | -5.74  [-23.96; 12.48] | -0.62  [-34.86; 33.62] | **QUETIA**  **PINE** | . | -24.64  [ -52.66; 3.38] | -15.23  [ -35.88; 5.42] | 15.25  [ -3.43; 33.93] |
| -30.64  [-72.99; 11.72] | -26.53  [-71.63; 18.58] | -23.68  [-55.42; 8.06] | -22.08  [-54.99; 10.83] | -20.80  [-53.89; 12.28] | -20.22  [-54.67; 14.23] | -17.23  [-48.05; 13.59] | -16.16  [-49.23; 16.90] | -11.04  [-54.82; 32.73] | -10.42  [-41.83; 20.99] | **ILOPERI**  **DONE** | . | -9.57  [ -38.08; 18.94] | . |
| -35.49  [-72.45; 1.47] | -31.38  [-71.46; 8.71] | -28.53  [-53.52; -3.54] | -26.93  [-53.10; -0.76] | -25.66  [-51.30; -0.02] | -25.07  [-52.70; 2.55] | -22.09  [-42.92; -1.25] | -21.02  [-47.07; 5.04] | -15.90  [-53.32; 21.52] | -15.28  [-37.47; 6.92] | -4.85  [-40.54; 30.83] | **CLOZA**  **PINE** | 5.05  [ -23.38; 33.48] | . |
| -40.21  [-71.53; -8.88] | -36.10  [-71.05; -1.14] | -33.25  [-47.20; -19.30] | -31.65  [-48.09; -15.21] | -30.37  [-47.17; -13.58] | -29.79  [-49.13; -10.45] | -26.80  [-38.52; -15.09] | -25.73  [-42.49; -8.98] | -20.61  [-53.83; 12.60] | -19.99  [-33.18; -6.81] | -9.57  [-38.08; 18.94] | -4.72  [-26.18; 16.75] | **OLANZA**  **PINE** | 43.63  [ 26.53; 60.73] |
| -0.71  [-29.68; 28.26] | 3.40  [-29.46; 36.26] | 6.25  [-11.32; 23.81] | 7.84  [ -7.65; 23.34] | 9.12  [ -9.70; 27.94] | 9.70  [-11.09; 30.50] | 12.69  [ -1.31; 26.69] | 13.76  [ -1.67; 29.19] | 18.88  [-15.21; 52.97] | 19.50  [ 6.02; 32.98] | 29.93  [ -0.97; 60.82] | 34.78  [ 11.83; 57.73] | 39.50  [ 27.58; 51.41] | **NONE** |

Data are reported as Mean Differences (MDs) and 95% confidence intervals (CIs). Mixed SMDs are shown in the triangle below the diagonal and direct SMDs are shown in the triangle above the diagonal. Significant results are highlighted

# **eTable 9.** Comparison of active principles and no-treatment or placebo on **Total Cholesterol change**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ARIPI**  **PRAZOLE** | . | 6.50  [ -8.06; 21.06] | . | . | . | -18.20  [-28.53; -7.87] | . | . | -8.13  [-19.25; 3.00] | . | . | -6.88  [-20.78; 7.03] | -8.00  [-35.64; 19.64] |
| -2.10  [-15.54; 11.33] | **CARIPRAZINE** | . | . | . | . | . | . | . | . | . | . | . | -2.80  [-13.94; 8.34] |
| -2.97  [-10.93; 5.00] | -0.86  [-13.50; 11.77] | **ZIPRASIDONE** | . | . | . | . | . | . | -11.30  [-25.28; 2.68] | . | . | -15.88  [-20.81; -10.95] | . |
| -5.78  [-18.08; 6.51] | -3.68  [-19.41; 12.05] | -2.81  [-14.26; 8.63] | **HALOPERIDOL** | . | . | -1.72  [-14.77; 11.32] | . | . | . | . | -27.10  [-45.48; -8.72] | -12.19  [-24.24; -0.13] | . |
| -7.46  [-16.26; 1.34] | -5.36  [-17.88; 7.16] | -4.50  [-11.76; 2.77] | -1.68  [-13.57; 10.20] | **PALIPERIDONE** | . | . | . | . | . | . | . | -12.55  [-18.82; -6.27] | 2.99  [ -3.31; 9.28] |
| -7.52  [-15.93; 0.89] | -5.42  [-17.59; 6.76] | -4.55  [-11.50; 2.39] | -1.74  [-13.43; 9.95] | -0.06  [ -7.18; 7.06] | **LURASIDONE** | . | . | . | -11.72  [-23.02; -0.43] | . | . | -12.40  [-20.75; -4.05] | 3.95  [ -1.93; 9.82] |
| -7.90  [-15.01; -0.78] | -5.79  [-18.16; 6.57] | -4.93  [-11.21; 1.35] | -2.12  [-12.67; 8.44] | -0.43  [ -7.42; 6.55] | -0.38  [ -6.95; 6.20] | **RISPERIDONE** | . | . | -8.30  [-19.90; 3.30] | -5.40  [-19.36; 8.56] | -5.52  [-21.39; 10.34] | -15.44  [-20.64; -10.23] | 5.70  [ -5.81; 17.21] |
| -9.72  [-24.65; 5.21] | -7.62  [-25.32; 10.09] | -6.75  [-20.70; 7.19] | -3.94  [-20.78; 12.90] | -2.26  [-16.59; 12.08] | -2.20  [-16.40; 12.00] | -1.82  [-15.72; 12.07] | **ILOPERIDONE** | . | . | . | . | -10.05  [-23.20; 3.10] | . |
| -10.70  [-22.45; 1.04] | -8.60  [-22.95; 5.75] | -7.74  [-18.56; 3.09] | -4.92  [-19.23; 9.39] | -3.24  [-13.93; 7.44] | -3.18  [-13.46; 7.09] | -2.81  [-13.31; 7.70] | -0.98  [-17.44; 15.48] | **BREXPIPRAZOLE** | . | . | . | . | 5.80  [ -3.23; 14.83] |
| -11.81  [-19.47; -4.15] | -9.71  [-21.88; 2.47] | -8.84  [-15.45; -2.23] | -6.03  [-17.57; 5.52] | -4.35  [-11.43; 2.74] | -4.29  [-10.50; 1.92] | -3.91  [-10.02; 2.20] | -2.09  [-16.26; 12.08] | -1.11  [-11.38; 9.17] | **QUETIAPINE** | . | . | -3.66  [-13.46; 6.15] | 4.64  [ -1.49; 10.76] |
| -13.30  [-28.96; 2.37] | -11.19  [-29.84; 7.45] | -10.33  [-25.63; 4.97] | -7.52  [-25.02; 9.98] | -5.83  [-21.44; 9.77] | -5.78  [-21.20; 9.65] | -5.40  [-19.36; 8.56] | -3.58  [-23.27; 16.12] | -2.59  [-20.06; 14.88] | -1.49  [-16.72; 13.75] | **SERTINDOLE** | . | . | . |
| -19.46  [-34.15; -4.77] | -17.35  [-35.06; 0.35] | -16.49  [-30.55; -2.43] | -13.68  [-28.41; 1.06] | -12.00  [-26.41; 2.42] | -11.94  [-26.18; 2.31] | -11.56  [-24.74; 1.62] | -9.74  [-28.46; 8.98] | -8.75  [-25.21; 7.70] | -7.65  [-21.76; 6.46] | -6.16  [-25.36; 13.04] | **CLOZAPINE** | 4.50  [-14.27; 23.27] | . |
| -19.77  [-26.83; -12.71] | -17.67  [-29.52; -5.81] | -16.80  [-21.43; -12.18] | -13.99  [-24.50; -3.47] | -12.31  [-18.01; -6.61] | -12.25  [-17.61; -6.89] | -11.87  [-16.36; -7.39] | -10.05  [-23.20; 3.10] | -9.07  [-18.96; 0.83] | -7.96  [-13.22; -2.70] | -6.47  [-21.13; 8.19] | -0.31  [-13.63; 13.01] | **OLANZAPINE** | 15.36  [ 10.10; 20.63] |
| -4.90  [-12.41; 2.60] | -2.80  [-13.94; 8.34] | -1.94  [ -7.90; 4.03] | 0.88  [-10.22; 11.98] | 2.56  [ -3.15; 8.26] | 2.62  [ -2.28; 7.51] | 2.99  [ -2.37; 8.36] | 4.82  [ -8.94; 18.57] | 5.80  [ -3.23; 14.83] | 6.91  [ 2.00; 11.81] | 8.39  [ -6.56; 23.34] | 14.55  [ 0.80; 28.31] | 14.87  [ 10.83; 18.90] | NONE |

Data are reported as Mean Differences (MDs) and 95% confidence intervals (CIs). Mixed SMDs are shown in the triangle below the diagonal and direct SMDs are shown in the triangle above the diagonal. Significant results are highlighted

# 

# **eTable 10.** Comparison of active principles and no-treatment or placebo on **HDL change**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **OLANZA**  **PINE** | -0.44  [ -5.11; 4.23] | -0.85  [ -3.58; 1.88] | . | -2.50  [ -6.44; 1.45] | -0.07  [ -4.34; 4.20] | -2.17  [ -6.94; 2.60] | -1.15  [ -3.94; 1.64] | -3.09  [ -6.34; 0.15] | -9.25  [-15.52; -2.98] | . | . | -2.00  [ -4.38; 0.39] |
| -0.77  [ -4.58; 3.04] | **HALOPERI**  **DOL** | . | . | . | . | . | -2.86  [ -7.24; 1.53] | . | . | . | . | 3.10  [ -2.24; 8.44] |
| -1.05  [ -3.44; 1.34] | -0.28  [ -4.59; 4.03] | **PALIPERI**  **DONE** | . | . | . | . | . | . | . | . | . | -0.09  [ -2.46; 2.28] |
| -1.32  [ -6.71; 4.06] | -0.55  [ -6.94; 5.83] | -0.27  [ -5.79; 5.25] | **CARIPRA**  **ZINE** | . | . | . | . | . | . | . | . | 0.20  [ -4.85; 5.25] |
| -1.77  [ -4.09; 0.56] | -1.00  [ -5.20; 3.20] | -0.72  [ -3.65; 2.22] | -0.44  [ -5.94; 5.05] | **QUETIA**  **PINE** | -0.00  [ -4.86; 4.86] | . | -0.10  [ -5.32; 5.12] | -0.70  [ -6.77; 5.37] | -3.03  [ -7.54; 1.47] | . | . | 0.88  [ -1.86; 3.63] |
| -2.01  [ -4.78; 0.76] | -1.24  [ -5.77; 3.28] | -0.96  [ -4.27; 2.34] | -0.69  [ -6.40; 5.02] | -0.25  [ -3.27; 2.78] | **LURASI**  **DONE** | . | . | . | . | . | . | 2.50  [ -0.87; 5.88] |
| -2.17  [ -6.94; 2.60] | -1.40  [ -7.50; 4.70] | -1.12  [ -6.45; 4.21] | -0.85  [ -8.04; 6.34] | -0.40  [ -5.70; 4.90] | -0.16  [ -5.67; 5.35] | **ILOPERI**  **DONE** | . | . | . | . | . | . |
| -2.34  [ -4.82; 0.13] | -1.57  [ -5.47; 2.32] | -1.29  [ -4.56; 1.97] | -1.02  [ -6.78; 4.74] | -0.58  [ -3.54; 2.39] | -0.33  [ -3.85; 3.19] | -0.17  [ -5.54; 5.20] | **RISPERI**  **DONE** | . | 1.83  [ -3.89; 7.55] | -1.55  [ -6.94; 3.84] | . | 3.70  [ -2.03; 9.43] |
| -2.88  [ -5.72; -0.04] | -2.11  [ -6.79; 2.58] | -1.83  [ -5.46; 1.81] | -1.55  [ -7.56; 4.46] | -1.11  [ -4.47; 2.25] | -0.86  [ -4.72; 2.99] | -0.71  [ -6.26; 4.84] | -0.53  [ -4.17; 3.10] | **ZIPRASI**  **DONE** | -1.10  [ -7.57; 5.37] | . | . | . |
| -3.16  [ -6.46; 0.14] | -2.39  [ -7.16; 2.38] | -2.11  [ -5.97; 1.75] | -1.83  [ -7.92; 4.25] | -1.39  [ -4.78; 2.00] | -1.14  [ -5.19; 2.90] | -0.99  [ -6.78; 4.81] | -0.81  [ -4.34; 2.71] | -0.28  [ -4.24; 3.68] | **ARIPI**  **PRAZOLE** | . | . | -4.24  [-12.62; 4.14] |
| -3.89  [ -9.83; 2.04] | -3.12  [ -9.78; 3.53] | -2.84  [ -9.15; 3.46] | -2.57  [-10.46; 5.32] | -2.13  [ -8.28; 4.03] | -1.88  [ -8.32; 4.56] | -1.72  [ -9.33; 5.89] | -1.55  [ -6.94; 3.84] | -1.02  [ -7.52; 5.49] | -0.74  [ -7.18; 5.71] | **SERT**  **INDOLE** | . | . |
| -3.89  [ -8.69; 0.90] | -3.12  [ -9.02; 2.77] | -2.84  [ -7.79; 2.10] | -2.57  [ -9.27; 4.13] | -2.13  [ -7.05; 2.80] | -1.88  [ -7.04; 3.27] | -1.72  [ -8.48; 5.04] | -1.55  [ -6.76; 3.66] | -1.02  [ -6.50; 4.47] | -0.74  [ -6.31; 4.84] | -0.00  [ -7.50; 7.50] | **BREXPI**  **PRAZOLE** | 2.77  [ -1.64; 7.18] |
| -1.12  [ -3.00; 0.76] | -0.35  [ -4.27; 3.56] | -0.07  [ -2.31; 2.16] | 0.20  [ -4.85; 5.25] | 0.64  [ -1.54; 2.82] | 0.89  [ -1.78; 3.56] | 1.05  [ -4.08; 6.17] | 1.22  [ -1.56; 3.99] | 1.75  [ -1.51; 5.02] | 2.03  [ -1.37; 5.44] | 2.77  [ -3.30; 8.84] | 2.77  [ -1.64; 7.18] | **NONE** |

Data are reported as Mean Differences (MDs) and 95% confidence intervals (CIs). Mixed SMDs are shown in the triangle below the diagonal and direct SMDs are shown in the triangle above the diagonal. Significant results are highlighted

# **eTable 11.** Comparison of active principles and no-treatment or placebo on **LDL change**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ARIPI**  **PRAZOLE** | . | 8.90  [ -3.20; 21.00] | -11.85  [-21.99; -1.71] | . | . | . | . | -7.30  [-16.48; 1.87] | . | . | -6.18  [-20.23; 7.87] | -6.00  [-33.25; 21.25] |
| -0.40  [-12.49; 11.69] | **CARIPRA**  **ZINE** | . | . | . | . | . | . | . | . | . | . | -3.50  [-13.29; 6.29] |
| -2.06  [ -9.26; 5.13] | -1.67  [-12.85; 9.51] | **ZIPRASI**  **DONE** | . | . | . | . | . | -14.60  [-26.44; -2.76] | . | . | -8.86  [-13.07; -4.65] | . |
| -4.23  [-11.04; 2.57] | -3.84  [-15.15; 7.48] | -2.17  [ -8.01; 3.67] | **RISPERI**  **DONE** | . | . | -2.70  [-14.33; 8.93] | . | -8.20  [-17.96; 1.56] | . | -6.00  [-19.35; 7.35] | -9.99  [-14.89; -5.08] | . |
| -4.36  [-12.06; 3.34] | -3.97  [-14.69; 6.76] | -2.30  [ -8.34; 3.75] | -0.13  [ -6.45; 6.19] | **LURASI**  **DONE** | . | . | . | -7.49  [-16.96; 1.98] | . | . | -9.53  [-16.51; -2.55] | 1.97  [ -3.34; 7.27] |
| -4.66  [-12.44; 3.12] | -4.26  [-15.01; 6.48] | -2.60  [ -8.65; 3.45] | -0.43  [ -6.78; 5.93] | -0.30  [ -6.11; 5.52] | **PALIPERI**  **DONE** | . | . | . | . | . | -7.14  [-12.47; -1.81] | 0.70  [ -4.01; 5.41] |
| -6.93  [-20.41; 6.54] | -6.54  [-22.76; 9.69] | -4.87  [-17.88; 8.15] | -2.70  [-14.33; 8.93] | -2.57  [-15.81; 10.66] | -2.27  [-15.53; 10.98] | **SERT**  **INDOLE** | . | . | . | . | . | . |
| -7.07  [-17.45; 3.32] | -6.67  [-19.06; 5.72] | -5.00  [-14.31; 4.31] | -2.83  [-12.30; 6.64] | -2.70  [-11.47; 6.06] | -2.41  [-11.20; 6.38] | -0.13  [-15.13; 14.87] | **BREXPI**  **PRAZOLE** | . | . | . | . | 3.17  [ -4.42; 10.76] |
| -7.98  [-14.87; -1.09] | -7.59  [-18.25; 3.07] | -5.92  [-11.58; -0.26] | -3.75  [ -9.50; 2.00] | -3.62  [ -8.93; 1.69] | -3.32  [ -8.99; 2.35] | -1.05  [-14.02; 11.93] | -0.92  [ -9.60; 7.77] | **QUETIA**  **PINE** | . | . | -4.08  [-12.16; 4.00] | 1.77  [ -3.32; 6.86] |
| -10.06  [-22.19; 2.08] | -9.66  [-24.33; 5.01] | -7.99  [-18.92; 2.93] | -5.82  [-16.97; 5.32] | -5.69  [-16.94; 5.55] | -5.40  [-16.62; 5.83] | -3.12  [-19.23; 12.98] | -2.99  [-16.29; 10.31] | -2.07  [-13.23; 9.08] | **ILOPERI**  **DONE** | . | -2.52  [-12.71; 7.67] | . |
| -11.60  [-24.94; 1.75] | -11.20  [-27.14; 4.74] | -9.53  [-22.16; 3.09] | -7.36  [-19.26; 4.53] | -7.23  [-20.10; 5.63] | -6.94  [-19.81; 5.94] | -4.66  [-21.30; 11.97] | -4.53  [-19.22; 10.16] | -3.62  [-16.30; 9.07] | -1.54  [-17.31; 14.23] | **HALOPERI**  **DOL** | 0.91  [-13.76; 15.58] | . |
| -12.58  [-19.17; -5.99] | -12.18  [-22.73; -1.63] | -10.51  [-14.46; -6.57] | -8.34  [-12.86; -3.83] | -8.21  [-12.97; -3.46] | -7.92  [-12.63; -3.21] | -5.64  [-18.12; 6.83] | -5.51  [-14.06; 3.04] | -4.59  [ -9.15; -0.04] | -2.52  [-12.71; 7.67] | -0.98  [-13.01; 11.05] | **OLANZA**  **PINE** | 10.68  [ 5.32; 16.05] |
| -3.90  [-10.99; 3.19] | -3.50  [-13.29; 6.29] | -1.83  [ -7.22; 3.56] | 0.34  [ -5.33; 6.00] | 0.47  [ -3.92; 4.85] | 0.76  [ -3.67; 5.20] | 3.04  [ -9.90; 15.97] | 3.17  [ -4.42; 10.76] | 4.09  [ -0.13; 8.30] | 6.16  [ -4.76; 17.08] | 7.70  [ -4.87; 20.27] | 8.68  [ 4.75; 12.62] | **NONE** |

Data are reported as Mean Differences (MDs) and 95% confidence intervals (CIs). Mixed SMDs are shown in the triangle below the diagonal and direct SMDs are shown in the triangle above the diagonal. Significant results are highlighted

# **eTable 12.** Associations between selected variables related to antipsychotic medications and SMD for BMI and weight.

|  |  |  |
| --- | --- | --- |
| **Variable** | **BMI** | **Weight** |
| pKa acidic | 0.12 [-0.647, 0.886] | 0.258 [-1.287, 1.804] |
| pKa basic | -0.049 [-0.598, 0.5] | -0.225 [-1.631, 1.182] |
| Polar surface area | -0.008 [-0.033, 0.016] | -0.017 [-0.074, 0.039] |
| Polarizability | -0.026 [-0.078, 0.027] | -0.102 [-0.237, 0.033] |
| D2 occupancy | 0.05 [-0.09, 0.19] | 0.17 [-0.17, 0.52] |
| H1 occupancy | 0.12 [0.02, 0.22] | 0.32 [0.11, 0.53] |
| M1 occupancy | 0.1 [-0.01, 0.2] | 0.28 [0.04, 0.53] |
| M3 occupancy | 0.46[0.14, 0.79] | 0.43 [-0.31, 1.17] |
| a1A occupancy | 0.02 [-0.08, 0.11] | 0.07 [-0.18, 0.32] |
| a2A occupancy | 0.03 [-0.1, 0.16] | 0.05 [-0.31, 0.4] |
| 5-HT1A occupancy | 0 [-0.18, 0.19] | -0.04 [-0.51, 0.44] |
| 5-HT2A occupancy | 0.06 [-0.07, 0.19] | 0.2 [-0.08, 0.48] |
| 5-HT2C occupancy | 0.07 [-0.09, 0.23] | 0.18 [-0.2, 0.56] |

Data are reported as β coefficients estimates from regression models of the SMD, for each outcome, on the selected variables related to antipsychotic medications. Significant results are in bold. For occupancy parameters, results are corresponding to 10-unit increments.

**eTable 13.** Drug-specific pharmacological and chemical parameters.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | pKa (Strongest Acidic) | pKa (Strongest Basic) | Polar Surface Area (Å^2) | Polarizability (Å^3) | **D2 Ki** | **D2 occupancy** | **H1 Ki** | **H1 occupancy** | **M1 Ki** | **M1 occupancy** | **M3 Ki** | **M3 occupancy** | **a1A Ki** | **a1A occupancy** | **a2A Ki** | **a2A occupancy** | **5-HT1A Ki** | **5\_HT1A occupancy** | **5-HT2A Ki** | **5\_HT2A occupancy** | **5-HT2C Ki** | **5\_HT2C occupancy** |
| **olanzapine** | 14,17 | 7,24 | 30,87 | 35,37 | 20,42 | 46,74 | 2,91 | 86,03 | 4,70 | 79,22 | 73,18 | 19,67 | 111,96 | 13,80 | 314,00 | 5,40 | 610,00 | 2,85 | 3,12 | 85,19 | 10,60 | 62,83 |
| **risperidone** | none | 8,76 | 61,94 | 45,27 | 2,91 | 84,70 | 16,19 | 49,97 | 8128,31 | 0,20 | 10000 | 0,16 | 5,00 | 76,31 | 58,89 | 21,47 | 371,54 | 4,15 | 0,29 | 98,23 | 26,00 | 38,25 |
| **quetiapine** | 15,12 | 7,06 | 48,30 | 42,78 | 296,92 | 42,76 | 10,58 | 95,45 | 127,27 | 63,54 | 1601,49 | 12,17 | 22,00 | 90,98 | 3630 | 5,76 | 304,48 | 42,15 | 209,18 | 51,47 | 1400,00 | 13,68 |
| **clozapine** | 15,90 | 7,35 | 30,87 | 35,77 | 130,00 | 41,39 | 2,01 | 97,86 | 3,10 | 96,73 | 25,00 | 78,60 | 1,60 | 98,26 | 142,00 | 39,26 | 140,00 | 39,60 | 6,51 | 93,38 | 15,14 | 85,84 |
| **aripiprazole** | 13,51 | 7,46 | 44,81 | 49,23 | 0,81 | 93,23 | 61,66 | 15,31 | 6776,42 | 0,16 | 4677,35 | 0,24 | 25,70 | 30,26 | 74,13 | 13,07 | 4,35 | 71,96 | 8,69 | 56,20 | 14,99 | 42,65 |
| **haloperidol** | 13,96 | 8,05 | 40,54 | 39,15 | 1,99 | 51,68 | 616,59 | 0,34 | 3090,30 | 0,07 | 10000 | 0,02 | 12,02 | 15,04 | 1148,15 | 0,18 | 1949,84 | 0,11 | 80,17 | 2,59 | 4701,08 | 0,05 |
| **Paliperi**  **done** | 13,74 | 8,76 | 82,17 | 45,95 | 1,60 | 95,82 | 20,00 | 64,70 | >10000 | 0,37 | >10000 |  | 2,50 | 93,62 | 3,90 | 90,38 | 617,00 | 5,61 | 1,10 | 97,09 |  |  |
| **ziprasidone** | 13,18 | 7,09 | 48,47 | 44,96 | 5,01 | 9,24 | 32,81 | 1,53 | 5128,61 | 0,01 | 10000 | 0,01 | 18,19 | 2,73 | 160,33 | 0,32 | 4,00 | 11,31 | 0,89 | 36,43 | 0,72 | 41,31 |
| **amisulpride** | 14,03 | 7,05 | 101,73 | 39,82 | 2,00 | 99,73 | >10000 |  | 10000 | 6,79 | 10000 | 6,79 | 10000 | 6,79 | 1122,02 | 39,37 | 10000 | 6,79 | 8317,64 | 8,05 | 10000 | 6,79 |
| **asenapine** | none | 7,29 | 12,47 | 30,90 | 1,30 | 40,23 | 1,00 | 46,67 | 8128,00 | 0,01 | 8128,00 | 0,01 | 1,20 | 42,17 | 1,20 | 42,17 | 2,50 | 25,93 | 0,07 | 92,59 | 0,18 | 82,94 |
| **lurasidone** | none | 8,50 | 56,75 | 56,26 | 1,69 | 32,45 | >10000 |  | >10000 |  | >10000 |  | 48,00 | 1,66 | 41,00 | 1,94 | 6,80 | 10,67 | 2,03 | 28,57 | 415,00 | 0,20 |
| **chlorpromazine** | none | 9,20 | 6,48 | 35,10 | 7,24 | 83,88 | 4,73 | 88,85 | 34,67 | 52,08 | 56,23 | 40,17 | 0,28 | 99,26 | 184,07 | 16,99 | 3019,95 | 1,23 | 2,81 | 93,06 | 12,30 | 75,39 |
| **cariprazine** | 15,68 | 7,91 | 38,82 | 48,07 | 0,59 | 79,86 | 23,20 | 9,16 | >10000 |  | >10000 |  | 155,00 | 1,49 |  |  | 2,60 | 47,37 | 18,80 | 11,07 | 134,00 | 1,72 |
| **iloperidone** | 16,14 | 7,91 | 64,80 | 46,51 | 3,00 | 18,96 | 12,30 | 5,40 | 4909,08 | 0,01 | 10000 | 0,01 |  |  | 162,18 | 0,43 | 93,33 | 0,75 | 0,15 | 82,39 | 42,80 | 1,61 |
| **molindone** | 15,34 | 6,65 | 45,33 | 32,00 | 15,00 | 89,41 | >10000 |  | 281838,3 | 0,04 | >10000 |  | 2612,00 | 4,62 | 1097,00 | 10,35 | 3154,44 | 3,86 | 5200,00 | 2,38 | >10000 |  |
| **sertindole** | 14,36 | 8,59 | 40,51 | 47,17 | 5,13 | 68,88 | 257,04 | 4,23 | 630,96 | 1,77 | 2697,74 | 0,42 | 1,82 | 86,18 | 645,65 | 1,73 | 316,23 | 3,46 | 0,31 | 97,34 | 2,34 | 82,91 |

**Differences between the protocol and the review**

In addition to MEDLINE search, we considered also EMBASE and PsycINFO databases to avoid missing relevant studies. To reduce methodological and clinical heterogeneity, we decided to exclude also studies having a non-randomized design, studies including pediatric patients or healthy volunteers, studies with administration schemes other than parallel arms treatment one, and studies not reporting a pre- and post-treatment value (or its change) for the reported outcomes. We evaluated the quality of observational studies using ROBINS tool as suggested by Cochrane handbook. We reported MD instead of SMD to improve clinical interpretability.

Finally, we did not perform subgroup analyses because of low number of studies in strata.

**eResults.** Supplementary References

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